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Retina Today
MAY/JUNE 2020 VOL. 15, NO. 4 | RETINATODAY.COM

eyetube

SURVIVING COVID-19

Keeping retina patients, staff, and physicians safe

RETINA SURGERY ON A COVID-POSITIVE PATIENT

IS TELEMEDICINE READY FOR PRIME TIME IN RETINA?

SPOTLIGHT ON AMD: REAL-WORLD INJECTION DATA ON WET AMD, OCT ANGIOGRAPHY AND PHOTOBIOMODULATION IN DRY AMD

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Reference: 1. Data on File. Alcon Laboratories Inc; May 2018. **2.** Data on File. Alcon Laboratories Inc; September 2017.

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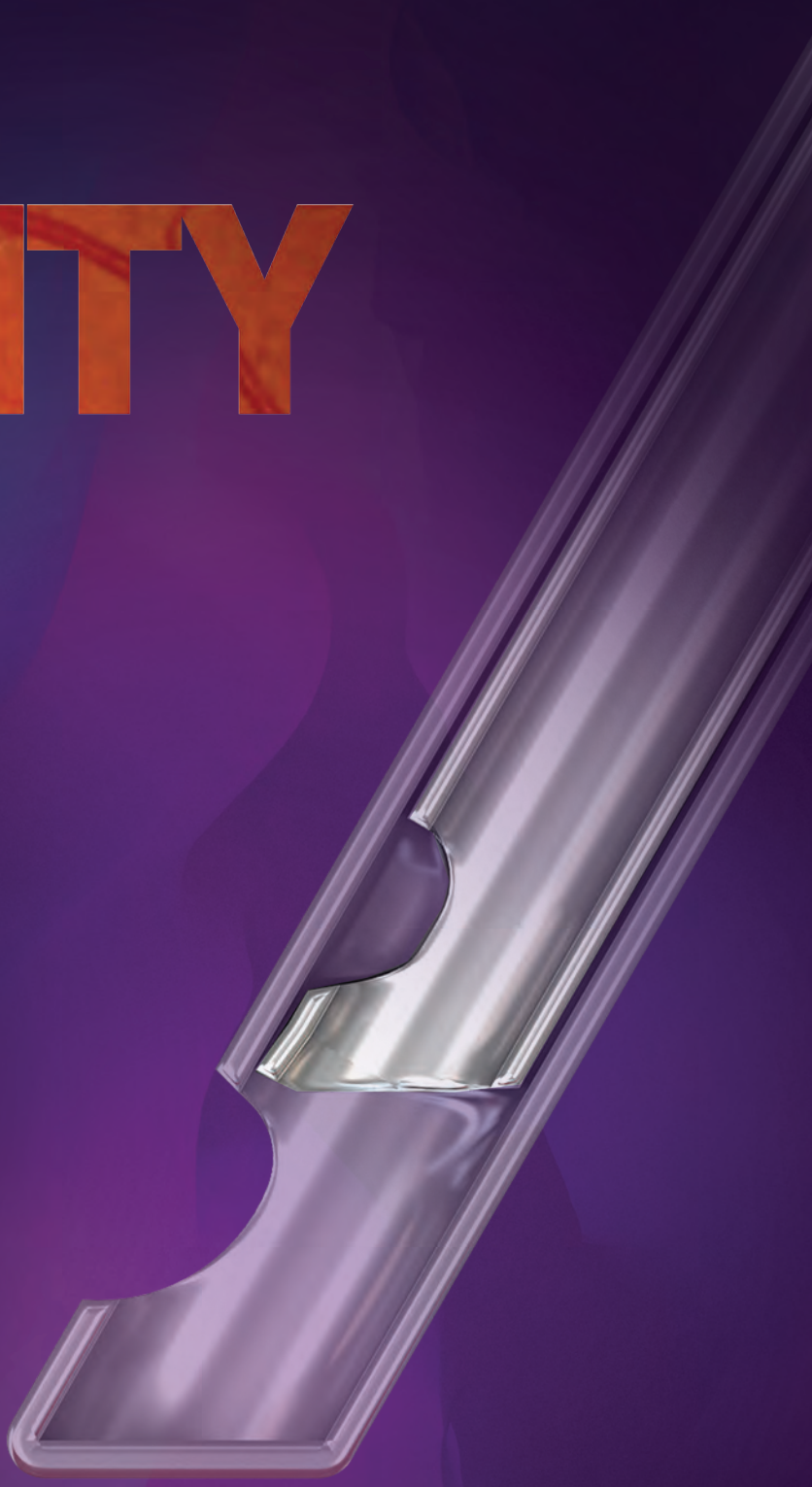

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- Enhance stability with a continuously open port and CONSTELLATION® Vision System's IOP compensation[1]
- Reduce pulsatile traction with **20 000 cuts per minute** using 25+® and 27+® gauge probes*, [2,3]
- Improve vitreous flow[4]
- Enable closer access to tissue plane with beveled tip[5]

*At similar single-blade flow rates

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References: 1. Irannejad A, Tambat S, Abulon DJK. Retropulsion and mass flow of 27-gauge vitrectomy probes: comparison of dual-blade/flat-tipped probes and single-blade/beveled probes. Poster presented at: 18th Congress of the European Society of Retina Specialists; September 20–23, 2018; Vienna, Austria. **2.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **3.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **4.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **5.** Alcon data on file. Alcon Laboratories, Inc; May 2017.

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References
1. Data on file – Results of HPLC purity tests performed on samples of compounded BBG dyes available in the U.S. **2.** Total DORC Global Sales data for ILM Blue since launch – available on file.

IMPORTANT INFORMATION ABOUT TISSUEBLUE™ (Brilliant Blue G Ophthalmic Solution) 0.025%

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WHAT IS TISSUEBLUE? TISSUEBLUE™ (Brilliant Blue G Ophthalmic Solution) 0.025% is a disclosing agent indicated to selectively stain the internal limiting membrane (ILM). The drug product will be administered by health care professionals only and should never be given to patients to handle.

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ONCOLOGY

SURGICAL PEARLS

MEDICAL RETINA

GLOBAL PERSPECTIVES

IN THE BACK

THANK YOU TO RETINA SPECIALISTS

and office staff for all you are doing amid the COVID-19 pandemic. We recognize your efforts and stand by you.

For more on Regeneron's scientific efforts to help address COVID-19, please visit our website: ***www.regeneron.com/covid19***

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THE CRISIS CONTINUES


Retina specialists wish they knew what to tell their patients when asked what will happen as the coronavirus pandemic endures. Our patients often share risk factors with patients who are most at-risk of dying from COVID-19, such as advanced age, diabetes, and systemic complications. Their fear is real and justified.

It behooves us to remember that we are physicians first and retina specialists second—that is, although our role is to treat diseases of the retina, our overall function is to care for our patients. Understanding that our patients are frequently at a unique risk in this environment requires us to rethink the very essence of our practice.

In this issue of *Retina Today*, we challenge our readers to perform a structural analysis of their practices. Rahul Reddy, MD, examines the future through a public health lens, asking which of today's adjustments are tomorrow's protocols. Low-cost additions to a practice that do not create inefficiencies (eg, wearing a mask) may be a part of our future. But how will we weigh the implementation of, say, a new practice footprint against the realities of running a practice in a building without movable walls?

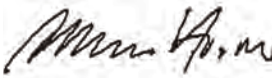
For Patrick Oellers, MD; Vamsee Neerukonda, MD; and Kevin Rosenberg, MD, the time for conceptualization of a future layout has passed: The virus is in the OR. The authors share their experience of operating on a COVID-19–positive patient. Which of their surgical protocols will remain and which will be amended remains to be seen, but the certainty is this: the OR of July 2020 will not look like it did in July 2019.

The promise of telemedicine has been discussed with enthusiasm for the past several years. To Edward S. Lu, BA; S.K. Steven Houston III, MD; Ehsan Rahimy, MD; and John B. Miller, MD (the latter three are cofounders of the new telehealth company HealTheia), the time has come to leverage the opportunities of telemedicine to ensure that patients receive the highest quality care during the pandemic. They introduce their hybrid in-person/telehealth model of teleophthalmology—what they term *HyTEC*—and discuss the execution and billing of telehealth sessions in the retina clinic.

But wait, says David A. Eichenbaum, MD: Telemedicine may be useful for some of what we do, but it cannot provide the specificity of in-person examinations. In his article, Dr. Eichenbaum explores which parts of the clinic translate well to telehealth and which elements prove challenging, and offers some examples of how creative thinking may allow us to use the tools at our disposal in such a way as to reduce patient risk and maintain high standards of care.

During a pandemic, we must rely on our colleagues elsewhere in ophthalmology—and even medicine—to learn about the changing realities we are all forced to navigate. Glaucoma specialists Cara E. Capitena Young, MD, and Malik Y. Kahook, MD, summarize two peer-reviewed studies relevant to our era. The first examines ocular findings in COVID-19–positive patients, and the second reviews the utility of telemedicine consultations from various nonophthalmic specialties.

We're not out of this yet—not by a long shot. But *Retina Today* will be with you the entire time. ■




CHIEF MEDICAL EDITOR | ASSOCIATE MEDICAL EDITOR

RT NEWS

MAY/JUNE 2020

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Even as the COVID-19 pandemic rages, news in ophthalmology doesn't stop. *Retina Today* collected these news items unrelated to the COVID-19 crisis.

ASRS TO HOLD VIRTUAL MEETING FOR 2020

In light of public health and safety concerns related to COVID-19, the board of directors of the American Society of Retina Specialists decided to conduct its 2020 Annual Meeting virtually, the organization announced in May.

The in-person meeting had been scheduled to be held in Seattle, July 24-26. In light of the fact that many potential attendees had already blocked out those dates to attend, the live streaming portion of the event will be held on the same dates, starting the evening of July 24 and ending the afternoon of July 26.

The organizers said they "plan to deliver the latest research to the global community using a virtual format that respects the contributions of the authors." They will be making more program details available and will be contacting contributors to the scientific portion of the meeting with details about their submissions.

BAUSCH + LOMB LICENSES RANIBIZUMAB BIOSIMILAR CANDIDATE

Bausch + Lomb has entered into an exclusive licensing agreement with Stada Arzneimittel and its development partner, Xbrane Biopharma, a developer of biosimilars, to develop and commercialize a biosimilar candidate to ranibizumab (Lucentis, Genentech) in the United States and Canada. The companies aim to obtain all currently approved indications for the reference biologic in both the United States and Canada. They announced the agreement jointly in a May press release.

The European generics and biosimilars companies Stada and Xbrane will be jointly responsible for finalizing development of the biosimilar, currently known as Xlucane, according to the release. Xbrane will also provide commercial supply. Bausch + Lomb will be responsible for the sales, marketing, and other commercialization efforts for the biosimilar candidate in the United States and Canada after regulatory approval.

Under the terms of the agreement, Bausch + Lomb will make an upfront payment of several million US dollars and further milestone payments subject to approval and launch of the product in the United States. Stada and Xbrane will be entitled to a share of gross profits from sales of the product and will share equally in the proceeds they receive from Bausch + Lomb.

VISION GAINS SUSTAINED AT 2 YEARS IN WET AMD WITH 12-WEEK INTERVAL

Vision gains seen at 1 year with abicipar pegol dosed every 8 weeks and every 12 weeks were maintained in year 2 in two phase 3 clinical trials in patients with neovascular age-related macular degeneration (AMD), according to an article in press in *Ophthalmology*.[1] The vision gains in year 2 were sustained with quarterly injections of abicipar, compared to monthly injections of ranibizumab, the study's authors said.

The two randomized multicenter phase 3 clinical trials, CEDAR and SEQUOIA, had identical protocols, and data from both trials were pooled for analysis. The trials compared the efficacy and safety of abicipar every 8 weeks or quarterly (after monthly loading doses) versus ranibizumab every 4 weeks in treatment-naïve patients with wet AMD. The top-line results of the trial were announced last year by the developers of abicipar, Allergan and Molecular Partners.

According to the article in press, abicipar every 8 weeks and every 12 weeks were both noninferior to ranibizumab every 4 weeks in the primary endpoint of stable vision at week 52. Intraocular inflammation was more frequent with abicipar.

The authors conclude that quarterly and every-8-weeks abicipar reduced wet AMD disease and treatment burden compared with monthly treatment with ranibizumab. ■

1. Kunimoto D, Yoon YH, Wykoff CC, et al; on behalf of the CEDAR and SEQUOIA Study Groups. Efficacy and safety of abicipar in neovascular age-related macular degeneration: 52-week results of phase 3 randomized controlled study. *Ophthalmology* [in press].

EYEWIRE.NEWS: ONGOING COVID-19 COVERAGE

Bryn Mawr Communications is prioritizing the production and distribution of news and information dedicated to COVID-19 and its impact on eye care. Eyewire has launched a special section dedicated solely to coverage of COVID-19. Sign up for email newsletters to be notified when critical updates are posted, and see updated coverage online at eyewire.news.

NO BENEFIT OF HYDROXYCHLOROQUINE SEEN IN OBSERVATIONAL STUDY

In an observational study of patients hospitalized due to COVID-19, administration of hydroxychloroquine "was not associated with either a greatly lowered or an increased risk of the composite end point of intubation or death," according to researchers at two New York hospitals.[1]

The study examined the association between hydroxychloroquine use and intubation or death in 1,446 consecutive patients hospitalized with COVID-19. Patients who were intubated, died, or discharged within 24 hours after presentation were excluded from analysis. Of the remaining 1,376 patients, 811 (58.9%) received hydroxychloroquine. Those who received the drug were more severely ill at baseline than those who did not receive it.

With a median follow-up of 22.5 days, 346 patients either died or were intubated—the composite endpoint of the study. No significant association was found between hydroxychloroquine use and intubation or death (hazard ratio, 1.04; 95% confidence interval, 0.82–1.32).

"Randomized, controlled trials of hydroxychloroquine in patients with COVID-19 are needed," the authors, from New York-Presbyterian Hospital and Columbia University's Irving Medical Center in New York, concluded. The study was funded by the US National Institutes of Health.

1. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19 [published online ahead of print May 7, 2020]. *N Engl J Med*.

CMS ADJUSTS TELEHEALTH RULES DURING COVID-19 CRISIS

Government agencies have broadened access to Medicare telehealth services during the pandemic crisis by increasing the flexibility of certain rules, so that beneficiaries can receive more services without the need to travel to a health care facility. The changes, initiated by the Centers for Medicare and Medicaid Services (CMS) and by the Department of Health and Human Services Office of Civil Rights, have included relaxing federal privacy regulations and expanding payment policies.

The aim of the changes is to keep beneficiaries healthy by increasing their access to benefits while also limiting the community spread of the virus by reducing travel to health facilities.

With the emergence of the SARS-CoV-2 virus, "there is an urgency to expand the use of technology to help people who need routine care, and keep vulnerable beneficiaries and beneficiaries with mild symptoms in their homes while maintaining access to the care they need," CMS said in announcing the changes in March.

Under the waiver, Medicare can pay for office, hospital, and other visits furnished via telehealth across the country, including in patients' places of residence. Previously, reimbursement for telehealth services was limited to its use in reaching patients in rural areas or when the patient was in a designated health facility. The changes also allow health care providers to reduce or waive cost-sharing for telehealth visits paid for by federal programs.

ANALYSIS: OPHTHALMOLOGY LOST MORE PATIENT VOLUME DUE TO COVID-19 THAN ANY OTHER SPECIALTY

Compared with figures from 2019, ophthalmology lost more patient volume during March and April of this year than any other medical specialty, according to an analysis of data from more than 2 million patient visits.

The analysis, released in May by Strata Decision Technology, found that ophthalmology lost 81% of patient volume, comparing 2-week volumes in March and April 2020 versus the same periods in 2019. The firm also noted a 97% reduction in cataract surgery volume—the largest reduction of any surgical procedure—and an 88% reduction in glaucoma procedures.

The analysis included data from 228 hospitals in 51 health care delivery systems in 40 states, with varying rates of COVID-19 cases among the hospitals. Across all service lines and in every region of the country, there was an average decrease of 54.5% in the number of unique patients who sought care in a hospital setting, the analysis found. Much of the drop in encounters is due to the cancelation of elective surgeries during the pandemic, according to Strata.

Strata released the data in conjunction with the launch of its National Patient and Procedure Volume Tracker, which will be updated weekly and is available free of charge.[1] ■

1. National Patient and Procedure Volume Tracker. Strata Decision Technology. May 11, 2020. https://www.stratadecision.com/National-Patient-and-Procedure-Volume-Tracker/. Accessed May 20, 2020.

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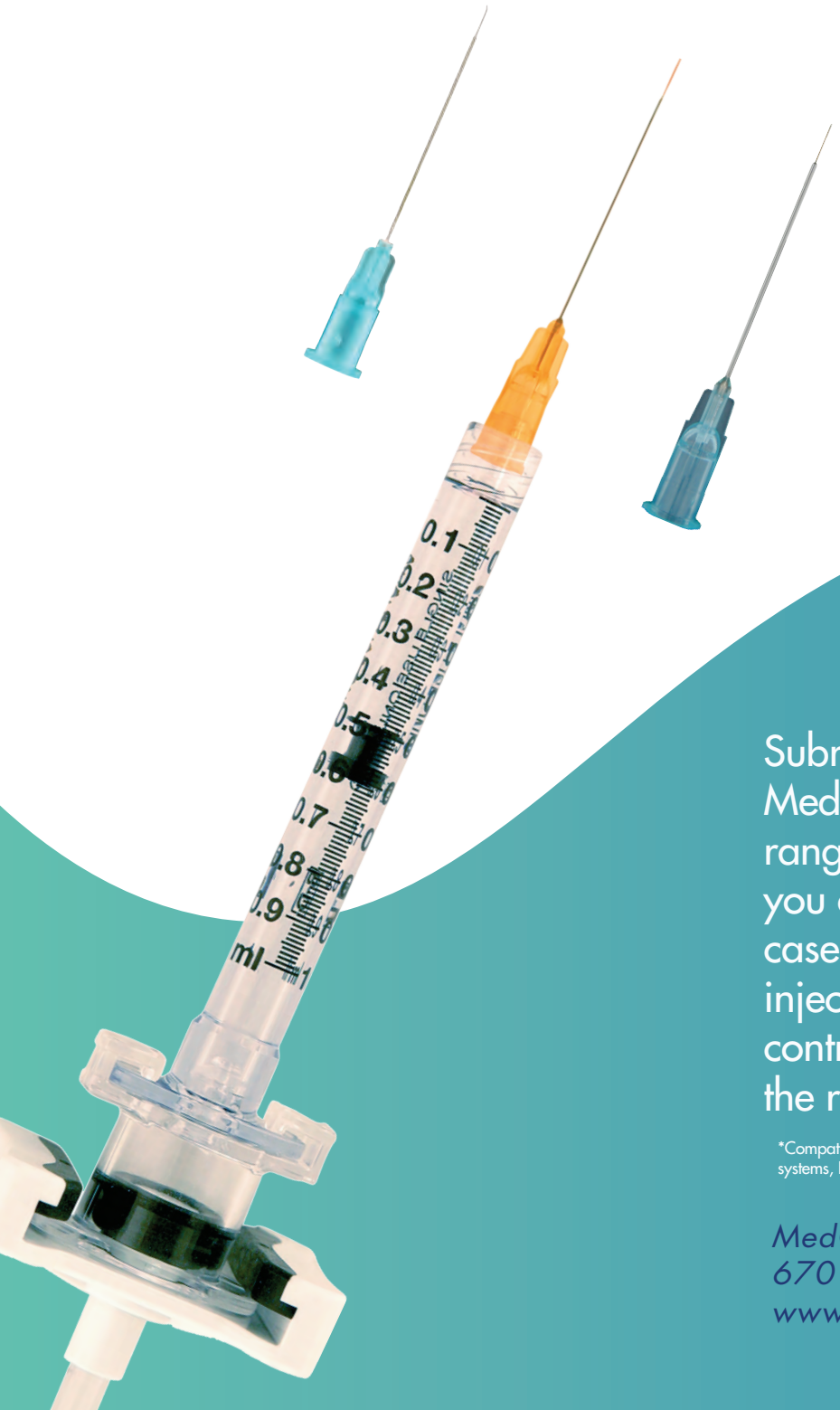

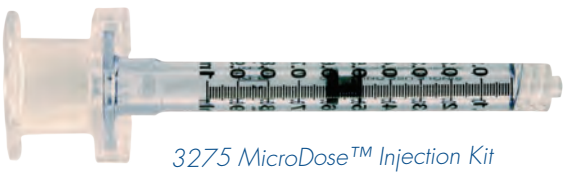

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PRESUMED TENOFOVIR TOXICITY

A patient's medication history led to retinal atrophy and other findings.

BY NAVNEET MEHROTRA, MBBS, DNB, FRF; MANISH NAGPAL, MBBS, MS, FRCS; AND SHAM TALATI, DO

A 46-year-old man presented with chief complaint of progressive, painless decrease in vision in both eyes for the past 1.5 months. He has been diabetic for 2 years and is HIV positive. He has been taking the retroviral drug tenofovir disoproxil orally for the past year as well as oral metformin for diabetes for the past 2 years. The patient's CD4 count was 75 and CD3 + CD4 was 278.

On examination, VA was 6/9 in each eye. The anterior segments were normal, and fundus exam showed a normal optic disc in each eye with pigmentary alterations at the macula and around the disc (Figure 1; all images acquired on Mirante, Nidek).

Spectral-domain OCT showed outer retinal atrophy in each eye (Figure 2). Autofluorescence imaging showed multiple hyperautofluorescent areas surrounding the macula and optic disc in each eye (Figure 3). Fluorescein angiography showed multiple areas of window defects in each eye (Figure 4).

DISCUSSION

We present a case of presumed tenofovir ocular toxicity. The patient had been taking tenofovir for the past year. Tenofovir is an antiretroviral drug, a nucleoside reverse

(Continued on page 14)

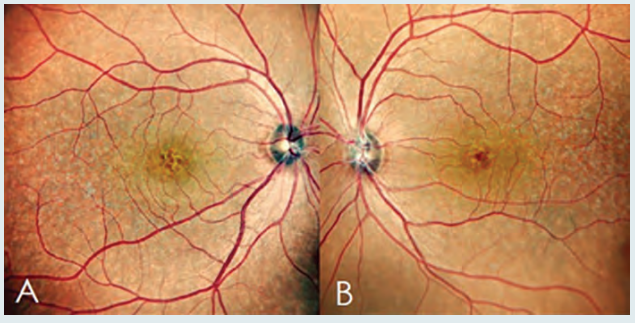

Figure 1. Central fundus photographs (right eye, A; left eye, B) show pigmentary anomalies surrounding disc and macula.

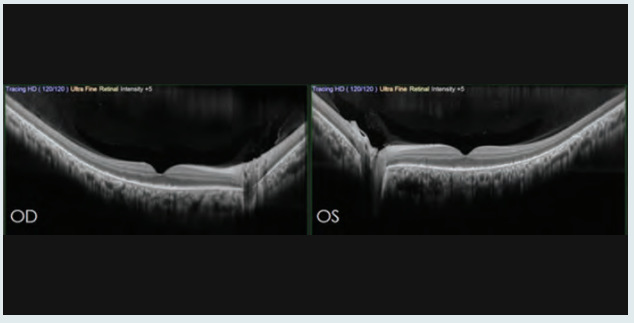

Figure 2. SD-OCT shows fairly normal foveal contour with photoreceptor disruption (outer retinal atrophy) in each eye

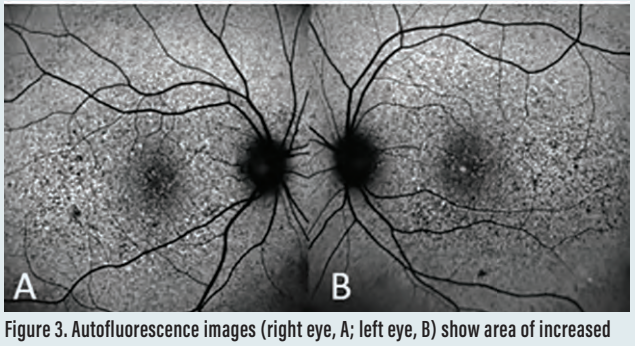

Figure 3. Autofluorescence images (right eye, A; left eye, B) show area of increased autofluorescence surrounding the macula and optic disc.

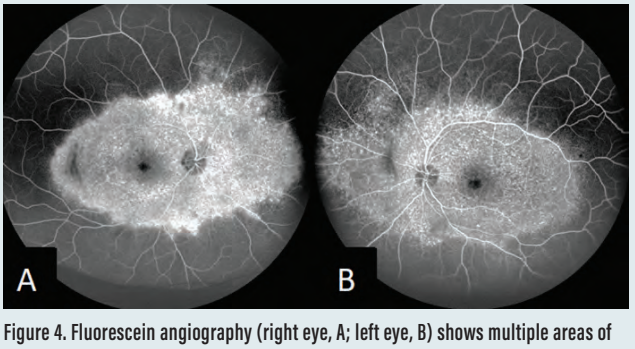

Figure 4. Fluorescein angiography (right eye, A; left eye, B) shows multiple areas of window defects.

DONUT-SHAPED SUBHYALOIDAL HEMORRHAGE

The peculiar shape led to the preservation of good vision.

BY SEBASTIAN M. WALDSTEIN, MD, PHD; JI LI, MBBS; AND ADRIAN T. FUNG, MBBS, MMED, FRANZCO

A 37-year-old man presented with sudden onset of floaters in his right eye (OD). VA was 20/16 OD. He reported no hypertension, diabetes, or trauma. When asked if he had performed the Valsalva maneuver, the patient said no.

On ocular examination, both anterior segments and the left fundus were normal. Right fundus examination revealed a donut-shaped subhyaloidal hemorrhage in the macula, a preretinal hemorrhage at the superior arcade, a flame-shaped peripapillary hemorrhage, and an inferior vitreous

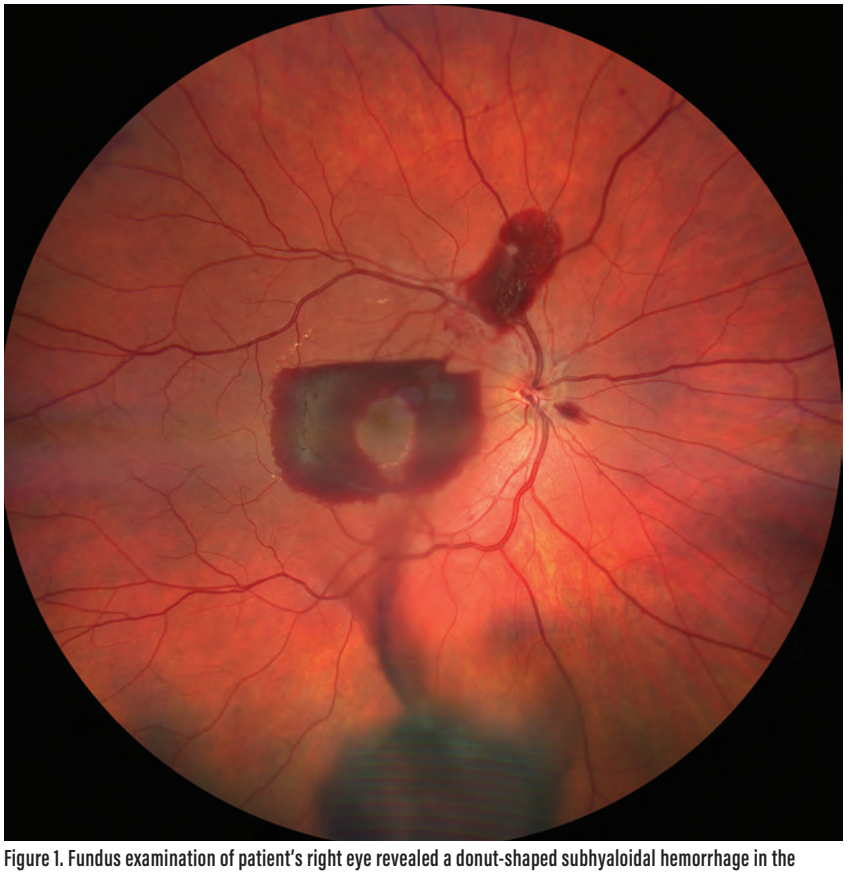

Figure 1. Fundus examination of patient's right eye revealed a donut-shaped subhyaloidal hemorrhage in the macula, a preretinal hemorrhage at the superior arcade, a flame-shaped peripapillary hemorrhage, and an inferior vitreous hemorrhage.

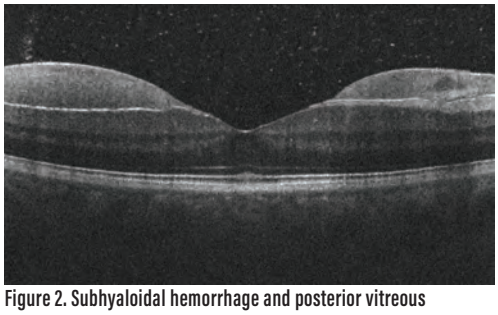

Figure 2. Subhyaloidal hemorrhage and posterior vitreous detachment were observed on OCT.

Figure 3. At 1 month, the patient's fundus examination was unremarkable.

hemorrhage (Figure 1). The diagnosis was thought to be Valsalva retinopathy, despite the patient's assertion.[1]

Interestingly, the fovea was spared by the subhyaloidal hemorrhage, allowing maintenance of good vision. This can be explained by the typical distribution of vitreomacular adhesion in people in this age group. The posterior vitreous is most adherent at the fovea, the optic disc, and around the arcades, whereas it is less adherent in the mid-macula. The relatively weaker adhesions provided a cleavage plane for the blood to spread in a donut shape, sparing the fovea. The distribution of the subhyaloidal hemorrhage, as well as a stage 1 posterior vitreous detachment,[2] were confirmed on OCT (Figure 2).

Observation was recommended. At the 1-month follow-up visit, the fundus appearance had returned to normal, with mild residual inferior vitreous hemorrhage (Figure 3) and VA of 20/16 OD. ■

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(Continued from page 12)

transcriptase inhibitor that is excreted through the kidney. Several antiretroviral drugs have been associated with retinal toxicities. Subramaniam et al reported outer retinal atrophy due to tenofovir use.[1] Our patient also showed retinal pigment epitheliopathy due to long-term use of the drug. Another nucleoside inhibitor, didanosine, has been shown to cause chorioretinal atrophic changes in the mid-periphery,[2] and ritonavir, a protease inhibitor, has been reported to cause central pigment epitheliopathy.[3] It is important to suspect early ocular toxicity with the chronic use of these antiretroviral drugs in order to prevent damage as was seen in our patient described here. ■

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OCT ANGIOGRAPHY IN NONEXUDATIVE AGE-RELATED MACULAR DEGENERATION


Will this imaging modality lead to better assessment of patients with dry eye disease?

BY LUÍSA S.M. MENDONÇA, MD; AND CAROLINE R. BAUMAL, MD

OCT angiography (OCTA) is a novel technology that produces depth-encoded segmented images of flow in the retinal and choroidal vasculature along with a coregistered structural and en face OCT. Its use has been extensively explored in exudative (wet) age-related macular degeneration (AMD) and diabetic retinopathy.

Much of the clinical utility of OCTA has been related to qualitative evaluation of macular neovascularization (MNV) in exudative AMD, as this technology is capable of providing, after proper segmentation, sharp, detailed, depth-resolved images of MNV. Because the manifestations of AMD are primarily confined to the retinal pigment epithelium (RPE)–Bruch membrane complex and choriocapillaris, swept-source OCTA (SS-OCTA) may add information in the assessment of this disease compared with spectral-domain OCTA (SD-OCTA). The longer wavelength used in SS-OCTA (1050 nm) enhances penetration through the RPE with less backscatter.[1] However, the benefit of SS-OCTA over SD-OCTA in clinical practice is not clear.

New insights into disease pathogenesis in *nonexudative* (dry) AMD are emerging from OCTA imaging. Considering the broad spectrum of clinical features that nonexudative AMD may demonstrate, we outline three areas in which OCTA may provide utility: imaging of subclinical nonexudative MNV in intermediate AMD and geographic atrophy (GA), assessment of choriocapillaris perfusion in intermediate AMD, and assessment of choriocapillaris perfusion in GA.

NONEXUDATIVE MNV IN INTERMEDIATE AMD

Before the advent of OCTA, the presence of nonexudative MNV had been demonstrated in intermediate AMD through histopathologic findings and ICG imaging.[2-5] It was hypothesized that hypercyanescent plaques on ICG angiography corresponded to MNV.[4] However, because these findings were seen before anti-VEGF therapy became available, and because ICG is an invasive test, the clinical utility of this assessment was limited.

OCTA has allowed in vivo confirmation of nonexudative MNV in eyes with intermediate AMD. Studies utilizing this technology have demonstrated a prevalence of nonexudative MNV in 14% of fellow eyes in patients with contralateral exudative AMD.[6,7] This is consistent with the prevalence of abnormal ICG findings (hypercyanescent plaque or spots) demonstrated by Hanutsaha et al in 11% of fellow eyes of patients with unilateral exudative AMD,[4] but with the advantage of using noninvasive OCTA as a screening test.[6,7]

Nonexudative MNV may be present in a low-lying fibrovascular pigment epithelial detachment imaged on structural OCT, which is referred to as the *double-layer sign*. Shi et al showed a positive predictive value of up to 76% for the double layer sign on structural OCT in identifying nonexudative MNV.[8] An OCTA imaging feature that helps to diagnose the presence of MNV within a double layer sign is the *flow overlay*, in which decorrelation signals corresponding to flow are generated for the OCTA image and superimposed onto the coregistered structural OCT. The presence of flow underneath the RPE and above Bruch membrane in a double-layer sign raises the index of suspicion for MNV and, combined with adequate segmentation, allows

AT A GLANCE

- OCTA is a useful tool for identifying and monitoring patients with nonexudative macular neovascularization.
- The use of OCTA for assessment of choriocapillaris perfusion in patients with intermediate AMD and GA is currently restricted to the research setting, with potential to yield clinical utility in the future.

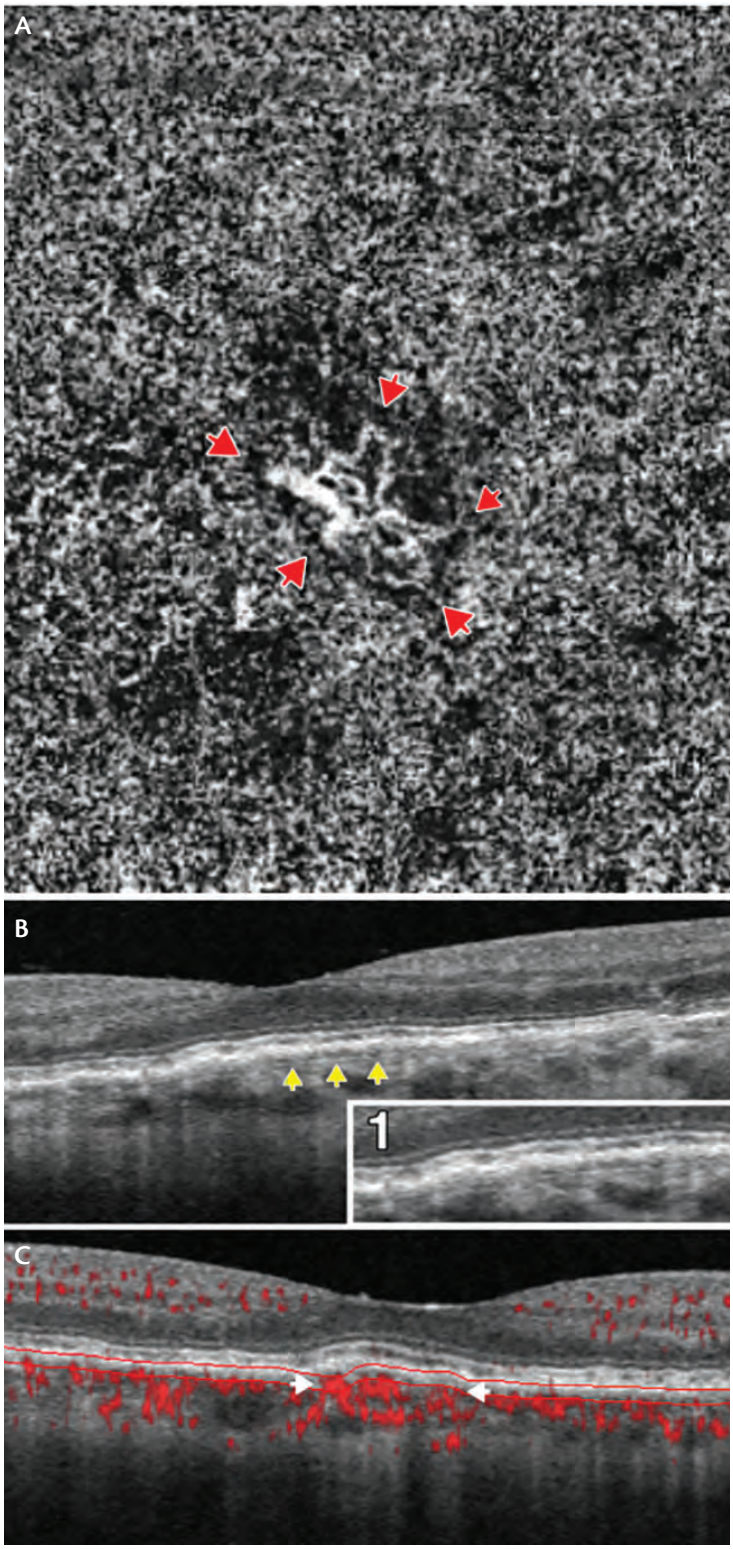

Figure 1. Nonexudative MNV in an eye with intermediate AMD. En face SD-OCTA choriocapillaris slab shows an MNV complex (A, red arrows). Corresponding structural OCT demonstrates a double-layer sign (B, yellow arrows point to Bruch membrane), seen in greater detail on image B1. Structural OCT with flow overlay demonstrating flow underneath the RPE and above Bruch membrane (C; white arrows).

the visualization of the neovascular complex on en face images (Figure 1).

Eyes with nonexudative MNV in intermediate AMD are at a higher risk of progression to exudative AMD than eyes without MNV.[6] Nevertheless, the current management for this condition remains observation. The recent PRO-CON study did not demonstrate benefit of anti-VEGF treatment, in eyes with intermediate AMD, in reducing progression to exudative AMD, and this included eyes that had nonexudative MNV on OCTA; however, this study was not specifically designed or powered to investigate the effects of anti-VEGF therapy in nonexudative MNV.[9]

Although there is no established treatment for patients with nonexudative MNV at risk for conversion to exudative AMD, OCTA is a noninvasive tool that can be used to identify and follow these patients.

NONEXUDATIVE MNV IN EYES WITH GA

Nonexudative MNV has also been identified in eyes with GA, often located within a low-lying pigment epithelial detachment adjacent to the edge of the atrophy.[10] It has been proposed that hypoxia secondary to choriocapillaris atrophy on the GA site leads to an increase in VEGF secretion and ultimately to development of MNV at the borders of the GA, where a remaining choriocapillaris bed supports growth of the neovascular complex.[10-12]

Utilizing OCTA for detection of nonexudative MNV in the presence of GA may be challenging, as the RPE atrophy and choriocapillaris defect on the GA site lead to hypertransmission of signal. This makes choroidal vessels from deeper layers more evident and more likely to be confounded with the MNV complex on en face visualization (Figure 2). Therefore, small nonexudative MNV may go unnoticed.[10]

ASSESSMENT OF CHOROIDAL PERFUSION IN INTERMEDIATE AMD

Histopathologic studies have demonstrated that choriocapillaris perfusion decreases with normal aging and that this reduction is more marked in eyes with AMD.[13,14] The development of OCTA, with its micron-resolved images of flow, has improved the exploration of choroidal circulation in AMD.

OCTA studies of the macula have corroborated that flow deficits in the choriocapillaris increase with normal aging[15,16] and are significantly increased in advanced stages of AMD compared with intermediate stages.[17] Flow deficits on OCTA are also increased in areas of drusen emergence and enlargement.[18] Furthermore, choriocapillaris nonperfusion is increased in areas of reticular pseudodrusen

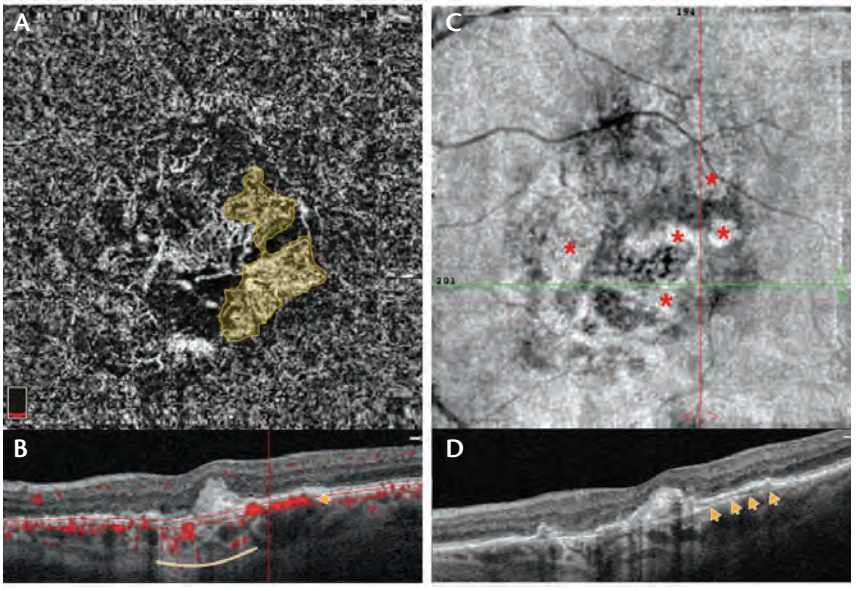

Figure 2. Nonexudative MNV in an eye with GA. En face SD-OCTA choriocapillaris slab shows an MNV complex (yellow contour) adjacent to GA (A). Note larger choroidal vessels seen in the topography of the choriocapillaris. Corresponding structural OCT demonstrates a double-layer sign with flow overlay underneath the RPE and above Bruch membrane (yellow arrow) in the topography of the nonexudative MNV and adjacent to a hyper transmission area (yellow dashed line) corresponding to GA (B). En face SD-OCT shows areas of atrophy in whitish areas (red asterisks) interleaved with dark areas, the latter corresponding to the nonexudative MNV (C). Corresponding structural B-scan demonstrating the double-layer sign without flow overlay (D; yellow arrows point to Bruch membrane).

compared with foci of sub-RPE drusen.[19] Future research will evaluate the clinical utility of these findings and whether flow impairment in the choriocapillaris in early or intermediate AMD can predict progression to advanced AMD to yield a potential biomarker of AMD progression.

It is worth noting that images of the choriocapillaris in eyes with drusen or pigmentary epithelium detachment should be interpreted carefully. Presence of shadowing due to drusen occurs in both SS-OCTA and SD-OCTA images, but it is more prominent in the latter, leading to a false-positive interpretation of hypoperfusion in the choriocapillaris (Figure 3).[20] The amount of signal loss due to shadowing as opposed to real nonperfusion is yet to be determined for both technologies.

Although these analyses are promising, they are still far from translation to a real-life clinical setting. Commercially available devices are not equipped with analytic software capable of

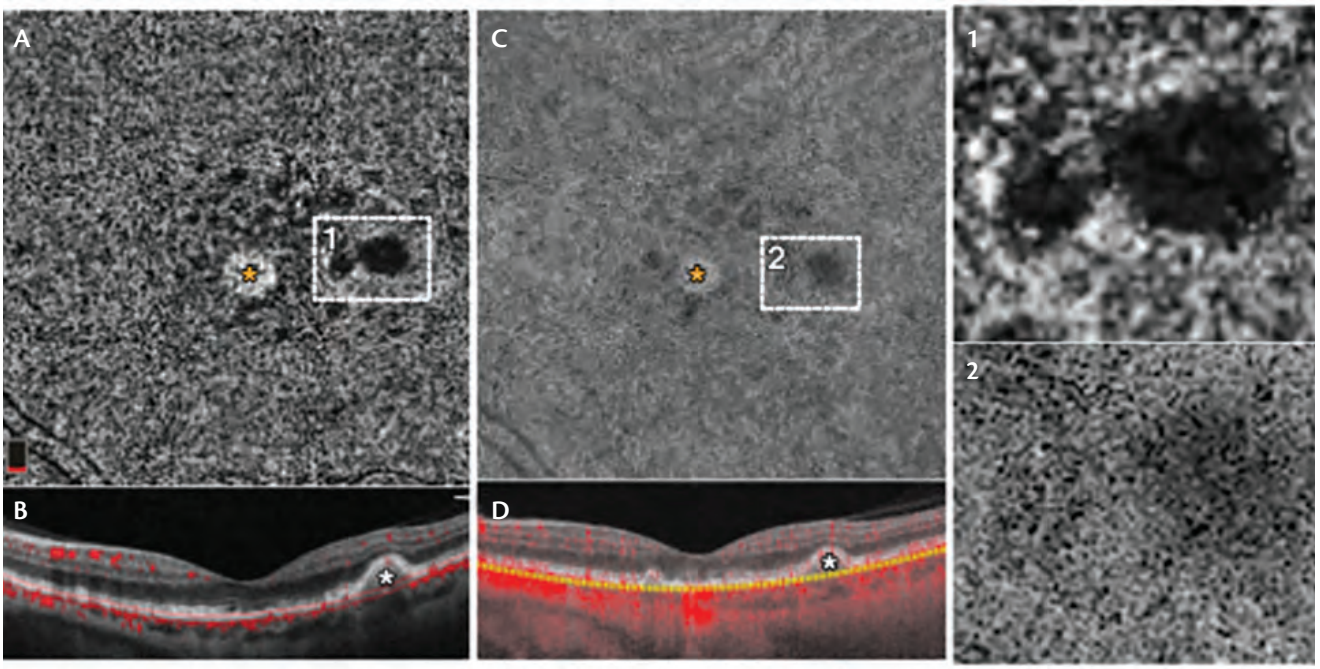

Figure 3. Choriocapillaris images of the same eye, acquired with SD-OCTA (A, B) and SS-OCTA (C, D), to compare signal loss due to drusen between these two technologies. A focus of GA can be seen in both SD-OCTA and SS-OCTA en face (A, C) images (yellow asterisks). En face SD-OCTA of the choriocapillaris slab (A) with areas of reduced signal corresponding to drusen on structural OCT (B, white asterisk). En face SS-OCTA choriocapillaris (C) with areas of reduced signal corresponding to drusen on structural OCT (D, white asterisk). Details illustrate the difference between SD-OCTA (Detail 1) and SS-OCTA (Detail 2) in the intensity of shadowing of the same drusen focus. On the SD-OCTA image (1), the signal loss underneath the drusen is more prominently impairing visualization of choriocapillaris at this site. On the SS-OCTA image (2), despite some signal loss under the drusen, the choriocapillaris can still be appreciated.

POTENTIALLY, OCTA MAY ADVANCE PATIENT CARE IN NONEXUDATIVE AMD BY IMPROVING THE UNDERSTANDING OF THE DISEASE'S PATHOGENESIS ... .

analyzing flow in the choriocapillaris, limiting these assessments to the research setting. A standard methodology of processing and analyzing images that is reproducible across research groups is needed as a first step to unify the language in the field, as the methodologies used for these assessments vary widely among imaging groups, weakening the interpretability of results.[21,22]

ASSESSMENT OF CHOROIDAL PERFUSION IN GA

GA remains a condition with no effective treatment, contributing to AMD's status as a leading cause of blindness. In parallel with clinical trials for drug development in this field, imaging research has sought biomarkers for GA progression. Choriocapillaris flow deficits have been assessed in eyes with GA, and the global hypoperfusion in this layer was correlated to the rate of GA enlargement.[23] It has also been shown that areas around GA presented higher flow deficits,[23,24] and that areas of nascent GA may be associated with focal choriocapillaris flow impairment.[25]

CONCLUSIONS

OCTA research in nonexudative AMD is an actively developing field, but it is still not entirely clear how this technology will fit into clinical practice. Potentially, OCTA may advance patient care in nonexudative AMD by improving the understanding of the disease's pathogenesis and by enhancing detection and monitoring of eyes at risk for conversion to exudative AMD. Further, as new therapies are developed, OCTA imaging features may prove to be useful endpoints for assessing treatment efficacy. ■

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REAL-WORLD INJECTION INTERVALS IN WET AMD

Aided by a large database, researchers explore treatment patterns with anti-VEGF agents.

BY MATHEW W. MACCUMBER, MD, PHD

The burden of monthly anti-VEGF injections—the gold standard treatment regimen—is considerable for patients with wet age-related macular degeneration (AMD). Anti-VEGF injections cost Medicare $2.7 billion annually, accounting for more than 12% of the Medicare Part B budget.[1] US ophthalmologists perform 2.5 million injections annually, with the busiest retina specialists performing as many as 50 per day.[1] Patients and caregivers bear the additional costs of time for appointments, lost productivity, and discomfort.

To reduce this burden of care, many physicians have adopted treat-and-extend (TAE) or as-needed (prn) treatment protocols. In the past decade, published studies have demonstrated that these variable dosing schedules can be as effective as monthly treatment while reducing treatment burden.[2-5] In the 2019 ASRS Preferences and Trends survey, 86.8% of respondents said that TAE is their preferred treatment regimen for wet AMD, and 5.5% reported that they rely on a prn regimen.[6]

IRIS REGISTRY DATA

My colleagues and I began working with Verana Health, the AAO's data curation and analytics partner, and study sponsor Novartis, to examine data on injection intervals from the AAO's IRIS Registry. The IRIS Registry is the largest specialty clinical database in medicine, with more than 300 million patient visits reported by more than 15,000 ophthalmologists and eligible clinicians as of April 2020.

The volume of data contained in the IRIS Registry and its comprehensive nature (a majority of US ophthalmic practices participate) provides an opportunity to better understand real-world treatment patterns. Verana Health uses IRIS Registry data to allow ophthalmologists to benchmark their individual clinical care patterns to a cohort of their peers. I have previously published an IRIS Registry study evaluating the effects of anti-VEGF therapy on IOP.[7] Others have used data from the IRIS Registry to assess characteristics and complications of IOL implantation after cataract surgery, factors influencing time to blindness in patients with diabetic retinopathy, and strabismus reoperation rates.[8]

STUDY DESIGN

To limit confounding factors, we reviewed data only of patients with treatment-naïve wet AMD. We assessed patients with anti-VEGF injections received from the index date (first injection) through 1 and 2 years of follow-up.[9] The follow-up periods were selected for the purpose of examining treatment patterns, such as injection interval at the end of years 1 and 2.

Patients were required to be in the IRIS Registry database for a baseline period of at least 6 months before the index date and not to have had any anti-VEGF therapy or diagnosis of other conditions that would be treated with anti-VEGF therapy (eg, retinal vein occlusion or diabetic macular edema) during that baseline period. This allowed a defined starting point and reasonable confidence that we were studying injection patterns for treatment-naïve, newly diagnosed eyes.

We looked at all injection intervals over the study period and the final injection interval (ie, time between the final

AT A GLANCE

- IRIS Registry data, curated by Verana Health, contains real-world data about treatment frequency for patients with wet AMD.
- Nearly 40% of patients treated with anti-VEGF therapy required treatment less than every 8 weeks during the first 2 years of treatment.
- During the second year of anti-VEGF therapy, patients with wet AMD were most likely to be dosed every 6 to 7 weeks or 12 weeks or longer.

and penultimate injections) at the end of years 1 and 2. The final injection interval provided us with an estimate of how long the injections had been extended by the end of each year, compared to the more frequent pattern of injections or loading doses that we would expect to see at the beginning of year 1. In the final injection interval data set, we confined our analyses to eyes that had been treated with the same drug at the beginning and end of the reference period (1 or 2 years).

Records for 56,672 eyes (54,392 patients) met the criteria for analysis. Among them, 33,601 eyes (32,354 patients) had at least 2.5 years of follow-up. The mean age of the patients was approximately 81 years, and nearly 65% were women. Approximate mean VA at baseline was 20/80. About one-quarter of the eyes had worse than 20/200 VA at baseline.

We also compared injection intervals for all anti-VEGF therapies to the intervals for eyes treated with aflibercept (Eylea, Regeneron; n = 13,467 eyes at 1.5 years and 7,654 at 2.5 years) and ranibizumab (Lucentis, Genentech; n = 9,128 eyes at 1.5 years and 5,990 at 2.5 years), which are the only commonly used drugs approved by the US FDA for the treatment of wet AMD that have a history of treatment long enough for this study.

OVERALL INJECTION INTERVAL PATTERNS

Looking at all eyes and all injections, we found that the mean number of injections per eye was approximately 5 per year among patients who received treatment within a given year (Figure 1). There was little apparent difference between years 1 and 2 among treated patients or among the two FDA-approved anti-VEGF agents studied. This represents fewer injections annually than we would have expected to occur with adherence to TAE injection protocols, and it is consistent with what has been reported by other researchers using claims databases.[10]

The data set likely includes patients who were lost to follow-up for a period of time or who saw multiple providers, and thus what appears to be a long interval may actually be a discontinuation. This may explain the large number of injections at intervals of 12 weeks or longer during year 1 (Figure 2). Obeid et al reported a similar rate of loss to follow-up or discontinuation in wet AMD patients.[11] Additionally, we know from the PrONTO study that about 20% of AMD patients can stop treatment after three injections when assessed at 1 year. The even higher percentage of injection intervals of at least 12 weeks in year 2 (Figure 2) likely reflects not only loss to follow-up and successful extension to 12 weeks, but also those patients whose disease required only a few treatments.

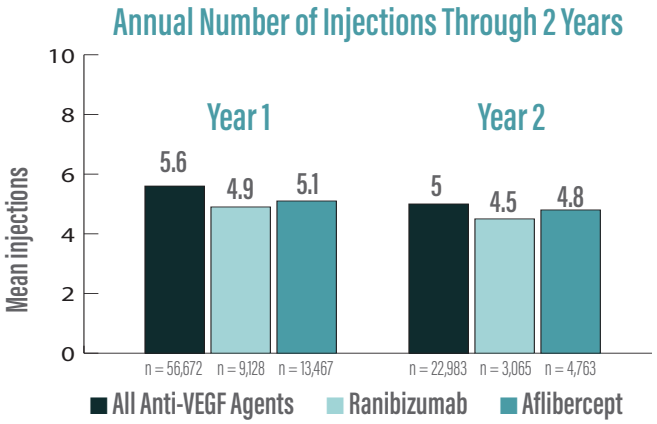

Figure 1. The average number of anti-VEGF injections through the first 2 years is illustrated here.

The most common interval (32%) for all injections in year 1 was 4 to 5 weeks. By year 2, the most common intervals for all injections were 6 to 7 weeks and 12 weeks or more (Figure 2).

DRUG-SPECIFIC RESULTS AT END-OF-YEAR

When we evaluated eyes treated with a single drug, nearly 40% needed injections more frequently than every 8 weeks by the end of the first year (Figure 3). At 2 years, the pattern was similar among eyes that continued to receive treatment, with minimal change in injection intervals.

By the end of the study periods, eyes treated with an

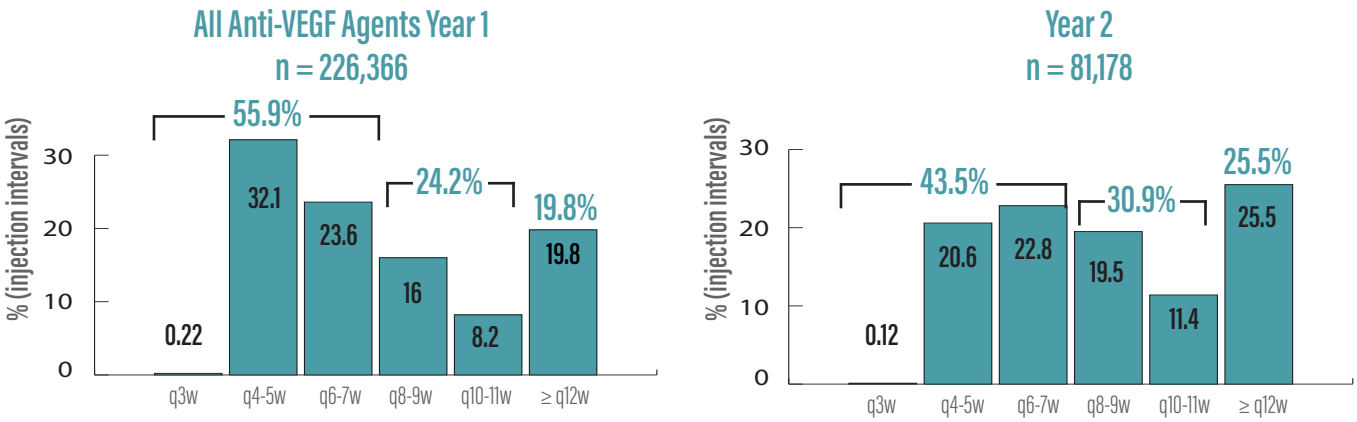

Figure 2. The most common injection interval in year 1 was 4-5 weeks. At year 2, injection intervals of 6-7 weeks and 12+ weeks were most common. The high percentage of patients who went at least 12 weeks without an injection in year 1 may be attributed to patients whose initial diagnosis was changed.

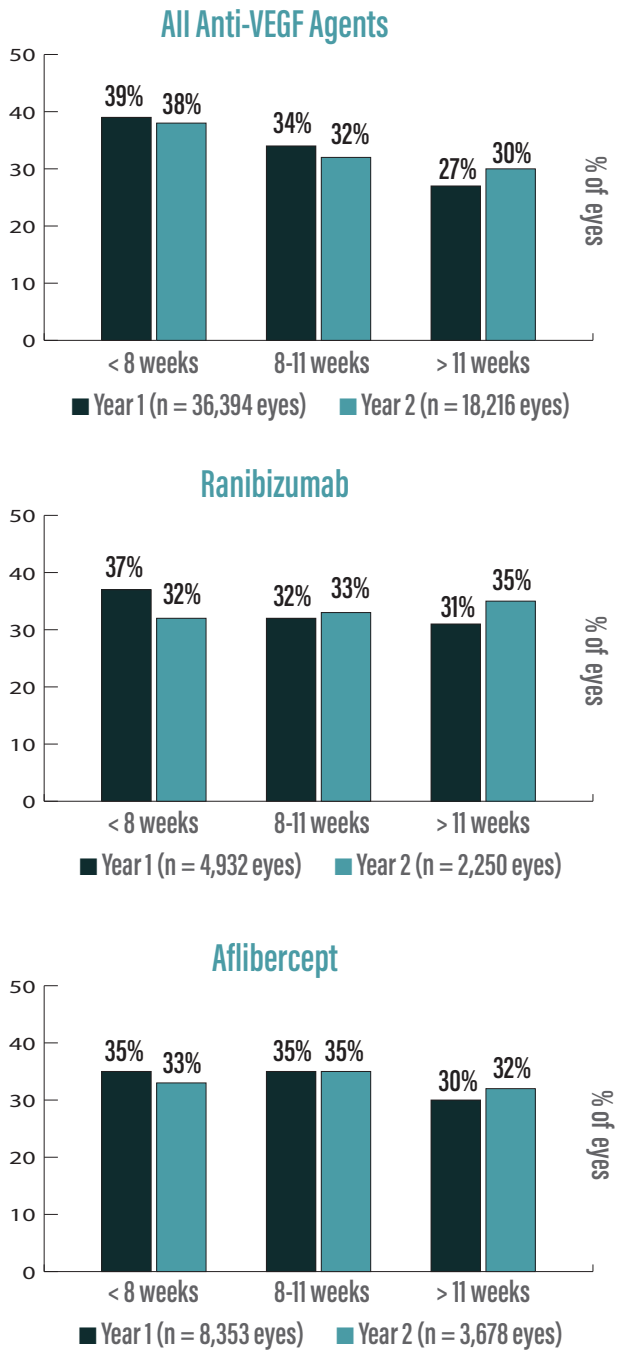

Figure 3. By the end of year 1, nearly 40% of eyes undergoing anti-VEGF therapy with any anti-VEGF agent needed injections less than every 8 weeks. Little change in injection interval was observed at the end of year 2.

FDA-approved anti-VEGF agent were more likely to require a treatment interval of at least 8 weeks compared with total eyes treated with any anti-VEGF agent (Figure 3). Note, however, that this is a descriptive study and no formal statistical analyses adjusting for differences between treatment groups were conducted.

These results confirm what we already suspected: We are getting better at extending the interval. However, injection intervals are still frequent enough to be a significant burden to patients and physicians. An extension of even a few more weeks between injections could save billions of dollars for the health care system and make effective care less burdensome.

We will continue to analyze IRIS Registry data as new drugs and devices enter the landscape. The anti-VEGF agent brolucizumab (Beovu, Novartis) has been approved for administration every 8 to 12 weeks after three monthly loading doses, and it may allow longer treatment intervals if used on a TAE regimen. We will know more in a few years; the drug was approved in 2019. Additionally, new agents that may complement anti-VEGF therapy and sustained-release devices will warrant future research to determine the extent to which they are able to reduce treatment burden.

Future studies using IRIS Registry data to evaluate clinical outcomes of AMD treatment are planned. In particular, it will be important to evaluate the impact on visual acuity or macular fluid on OCT. These outcome variables are more complex to analyze because of inconsistencies in the way they are reported by doctors in EHR systems, but correlating outcomes with injection intervals would certainly be a valuable next step.

KNOWING MORE ABOUT REAL-WORLD BEHAVIOR

Data from the IRIS Registry have provided important insights into ophthalmologists' real-world treatment patterns for wet AMD. Despite stated preferences for TAE regimens, the data show that actual injection intervals can be longer or shorter than expected. Ongoing analysis of this large trove of data can supplement what we learn from clinical trials to better understand treatment patterns and the efficacy of treatment as applied in real-world patient care. ■

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PHOTOBIOMODULATION AS A TREATMENT IN DRY AMD


Doctors and patients have found this new mode of therapy beneficial.

BY HAKAN KAYMAK, MD; AND HARTMUT SCHWAHN, PHD

The development of innovative treatments for debilitating diseases such as age-related macular degeneration (AMD) is crucial to advance patient care and to reduce burdens on patients, caregivers, and physicians. The dry, or nonexudative, form of AMD affects approximately 85% to 90% of individuals with AMD, and, until now, there have been no approved treatments for this condition aside from nutritional supplementation.

The Valeda Light Delivery System (LumiThera) was designed as a safe, multiwavelength platform for photobiomodulation (PBM). The device received the CE Mark in the European Union, where its indicated uses include treatment of ocular damage and disease using PBM, including inhibition of inflammatory mediators, edema, or drusen deposition; improvement of wound healing following ocular trauma or surgery; and increase in visual acuity and contrast sensitivity in patients with degenerative diseases such as dry AMD.

The underlying mitochondrial mechanisms of PBM therapy and recent clinical studies demonstrating positive improvements in patients[1-5] have increased interest in PBM as a treatment approach in dry AMD.

In our specialty clinic for vitreous, retina, and macula therapy, we see 20 to 40 patients with macular degeneration, particularly AMD, each day. For about a year now, we have offered PBM treatment with Valeda to patients as an alternative or supportive treatment option for dry AMD.

INTRO TO PHOTOBIOMODULATION

PBM is a light-based technology that stimulates bioenergetic output in targeted tissues. Selected wavelengths of light in the far red to near infrared spectrum (500–1,000 nm) modulate biologic function through direct and indirect cellular effects on mitochondrial respiratory chain components. The retina is one of the most energy-demanding tissues in the body. PBM activation of photoacceptors in the mitochondria improves generation of adenosine triphosphate (ATP), modulates the production of intracellular signaling molecules such as reactive-oxygen species (ROS) and nitric oxide (NO), and triggers secondary effects that produce sustained changes in cell function and viability.

These changes in cellular outcomes lead to therapeutic benefits at the clinical level. The treatment parameters of PBM are crucial, as PBM displays a biphasic dose-response output. Selection of wavelengths and the dose, timing, and delivery of PBM treatment must be appropriate to elicit these beneficial cellular effects.

Preclinical evidence supports the use of PBM as an effective treatment in retinal cell injury and multiple animal models of ocular disease and disorders.[6-8] Small pilot studies have shown promising effects for PBM in dry AMD and other ocular indications.[1-3,9-11] In recently published results, a double-masked, randomized, sham-controlled study in patients with dry AMD (LIGHTSITE I) demonstrated improvements in clinical measures (visual acuity and contrast sensitivity) and reduction in anatomic

AT A GLANCE

- The Valeda Light Delivery System is a light-based approach to treatment with a CE Mark in the European Union for multiple ocular indications, including dry AMD.
- Photobiomodulation (PBM), as performed with the Valeda, acts at the mitochondrial level by improving cellular output and reestablishing metabolic function.
- Patients with dry AMD treated with PBM have shown improvements in clinical, anatomic, and quality-of-life assessments.

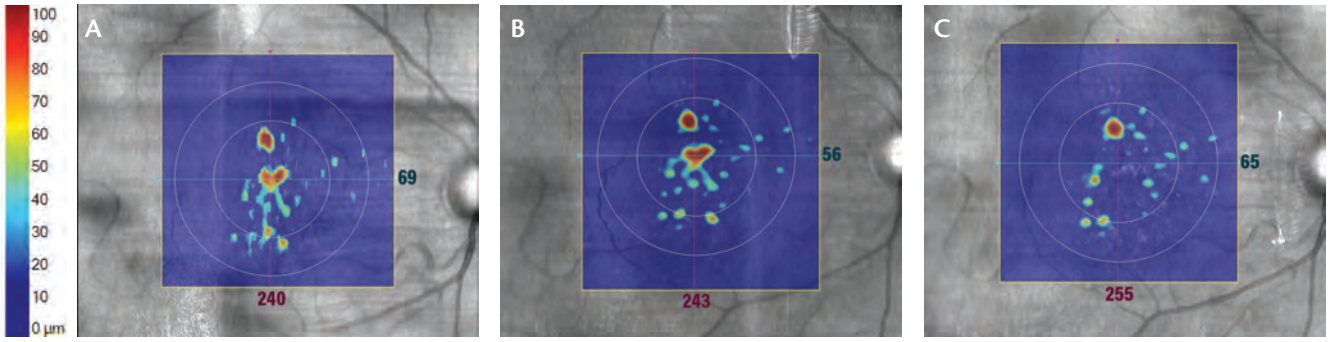

Figure 1. Color-coded analysis of retinal pigment epithelium (RPE) detachment from choroid as a measure of drusen status in OCT of the right eye at 12 months before the beginning of PBM treatment (A), at the beginning of PBM (B), and 7 months after treatment (C).

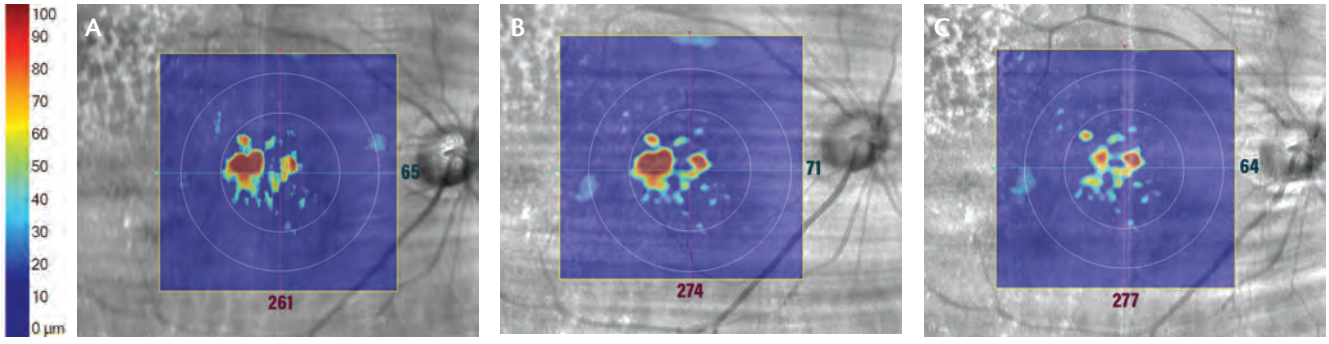

Figure 2. Color-coded analysis of RPE detachment from choroid as a measure of drusen status in OCT of the right eye at 6 months before the beginning of PBM treatment (A), at the beginning of PBM (B), and 2 months after beginning of treatment (C).

measures (drusen volume and thickness), along with improvement in quality-of-life endpoints.[3]

These findings support further study of the use of PBM as a treatment option for dry AMD patients. In our own clinic we have observed the beneficial effects of PBM treatment, as illustrated anecdotally by the following case reports.

CASE REPORT NO. 1

A 73-year-old white woman with intermediate stage dry AMD (Age Related Eye Disease Study [AREDS] category 3) for several years presented with baseline VA of 20/20 Snellen equivalent in each eye. Both eyes showed medium-sized drusen and were hyperopic and pseudophakic after cataract surgery. Drusen status was unchanged over an observation period of 12 months before the patient underwent PBM treatment.

Both eyes received a series of PBM treatments (ie, the recommended nine treatments with Valeda three times a week for three consecutive weeks). Seven months later, the patient received four additional treatments delivered twice a week over two consecutive weeks. Outcome measures included VA by objective refraction, OCT imaging, and automated microperimetry (Maia, CenterVue).

VA remained at 20/20 after treatment. After both sets of treatment, drusen had decreased notably in the right eye (Figure 1) and slightly in the left eye. On microperimetry, the functional macular integrity index improved in both eyes 7 months after initial treatment, from a baseline of "abnormal" (severe deficiency) to "suspect" (mild deficiency). Concomitantly, microperimetry average threshold improved in the right eye from "suspect" to "normal" and remained in the "normal" range in the left eye after treatment. Fixation stability improved from 85% to 96% in the right eye and from 87% to 96% in the left eye. The patient reported subjective improvements in vision quality, in particular describing brighter images, better contrast, deeper color, and increased reading speed.

CASE REPORT NO. 2

A 77-year-old white woman with intermediate stage dry AMD (AREDS category 3) for several years presented with a baseline visual acuity of 20/28 Snellen equivalent in each eye. In both eyes, large drusen and a vitreous body detachment could be identified. No retinal atrophy could be identified. The eyes were hyperopic and had undergone cataract surgery.

Both eyes received the same recommended series of PBM treatments described above. VA was assessed by objective refraction, OCT images were acquired, and peripheral dark adaptation (AdaptDX, MacuLogix) was assessed before and after the PBM treatments.

One month after the end of treatment, the retinal pigment epithelial detachment, as a measure of drusen status, decreased significantly in the right eye (Figure 2) but did not change in the

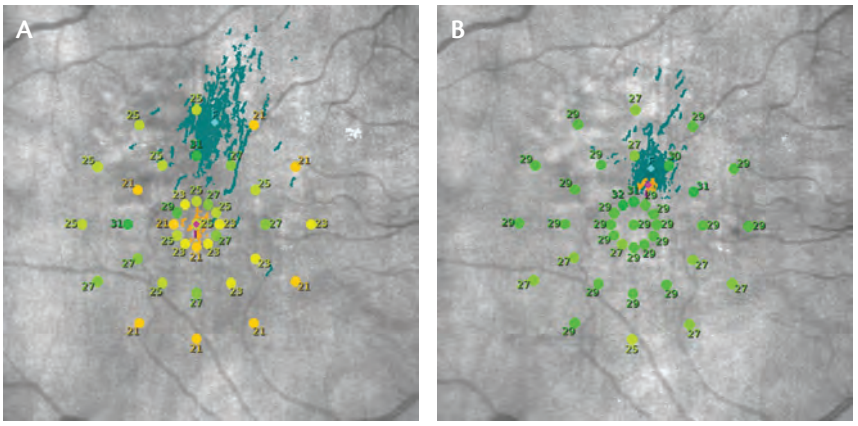

Figure 3. Color-coded results of microperimetry (response thresholds [in decibels]: green = good; yellow and orange = abnormal) and fixation position overlaid on the fundus image of the right eye, at baseline (A) and 4 months after PBM treatment (B).

left eye. Functional dark adaptation at an eccentricity of 5° did not improve, but the fixation error rate during the dark adaptation sessions improved slightly at 1 month after treatment. Although VA remained at 20/28 (0.7 logMAR), the patient reported subjective improvement in vision toward better contrast and better color after treatment.

CASE REPORT NO. 3

An 83-year-old white man with intermediate stage dry AMD (AREDS category 3) for several years presented with baseline visual acuity of 20/25 (0.8 logMAR) in both eyes with large drusen and no retinal atrophy.

The same regimen of PBM treatments with Valeda described above was administered. VA was assessed by objective refraction, OCT images were obtained, and automated microperimetry and contrast sensitivity testing (automated randomized stimuli at 6 cycles per degree) were performed before and after the PBM treatments.

Four months after the end of treatment, VA had improved from 20/25 to 20/20 in the right eye and had improved slightly in the left. On microperimetry, the functional macular integrity index improved from a baseline of "severely abnormal" to "normal," average threshold improved from "suspect" to "normal," and fixation stability improved from an "unstable" 53% to "stable" 92% in the right eye (Figure 3). Similar but less prominent results were seen in the left eye. Contrast sensitivity increased by about 15% after treatment.

WHAT'S NEXT?

The benefits of PBM have been documented in one randomized clinical trial. Now, the multicenter LIGHTSITE II[12] and LIGHTSITE III[13] clinical trials in dry AMD patients are under way in the European Union and the United States, respectively. (Valeda is investigational and not approved for use in the United States.) Additional studies are also planned or in progress to investigate the use of PBM in other ocular indications such as trauma, diabetic retinopathy and diabetic macular edema, and glaucoma.

As these additional diseases and conditions are studied, we may be able to customize light profiles and duration required for relevant treatments. Future studies will also aid in optimizing PBM treatment parameters and may expand our understanding of the mechanisms and benefit of PBM in ocular disease. ■

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EVERY MILLIMETER COUNTS FOR NEVUS TRANSFORMATION INTO MALIGNANT MELANOMA

A summary of my 2019 Wendell L. Hughes Lecture.

BY CAROL L. SHIELDS, MD

The prevalence of choroidal nevus located within two 45° screening fields centered on the foveola and optic disc was 4.7% in the 2005 to 2008 National Health and Nutrition Examination Survey (NHANES).[1] Because the NHANES evaluated only a small region in the posterior segment, however, it likely underestimated the true prevalence of choroidal nevus.

The most serious risk carried by choroidal nevus is its potential transformation into malignant melanoma. This risk is highest in the elderly population; a lifetime risk for a patient living beyond 80 years of age potentially approaches 1%.[2,3] The aging of the US population has prompted researchers to attempt to identify clinical clues to the likelihood of transformation so as to promote the earliest possible detection of melanoma. Recent studies have identified multimodal imaging factors that predict this transformation. In particular, tumor thickness (> 2 mm) has repeatedly been found to be one of the most powerful predictive factors for transformation.[4] More important, a combination of tumor thickness and other features has been found to compound the risk of transformation.[5]

In a recent retrospective analysis, my colleagues and I explored the risk of nevus transformation into melanoma per millimeter increment.[6]

TABLE. CHOROIDAL NEVUS TRANSFORMATION INTO MELANOMA BASED ON NEVUS THICKNESS

Nevus thickness	Hazard ratio for transformation into melanoma relative to flat nevus (0-1.0 mm)	*P* value
0-1.0 mm	1.0	-
1.1-2.0 mm	4.7	$P = 0.01$
2.1-3.0 mm	35.7	$P < 0.0001$
> 3.0 mm	52.0	$P < 0.0001$

METHODOLOGY

We reviewed the charts of all patients with a clinical diagnosis of choroidal nevus who were seen on the Ocular Oncology Service at Wills Eye Hospital in Philadelphia between 2007 and 2017. We analyzed each nevus per incremental increase in millimeter thickness and categorized them as flat (≤ 1.0 mm), thin (1.1–2.0 mm), thicker (2.1–3.0 mm), and thickest (> 3.0 mm).

We then followed these independent categories longitudinally with regard to the clinical outcome of growth into melanoma (Table), which we defined as enlargement in basal dimension or thickness by at least 0.5 mm in 2 years or less.

RESULTS

In all, our study included 3,806 choroidal nevi, and there was follow-up for 2,355 of these. Over the 10-year period, only 90 (3.8%) of the 2,355 nevi transformed into melanoma.

Increasing nevus thickness posed a greater risk of transformation into melanoma. Each millimeter of increased thickness posed a threat. Compared with completely flat nevi, thin nevi had a 4.7 times greater risk, thicker nevi a 35.7 times greater risk, and thickest nevi a 52.0 times greater risk of growth into melanoma. Perhaps in more relevant terms, Kaplan-Meier 10-year rate of growth was 2.2% for flat, 10.9% for thin, 40.2% for thicker nevi. The most striking increased risk occurred at transition from 2.0 mm or less to greater than 2.0 mm. This cutoff was also associated with a substantial increase in OCT evidence of subretinal fluid, overlying drusen, and overlying atrophy of the retinal pigment epithelium.

(Continued on page 29)

LESSONS FOR FUTURE ATTENDINGS

Answers to questions about managing surgical complications and teaching trainees.

INTERVIEW BY NIMESH PATEL, MD; AND NICOLAS YANNUZZI, MD; WITH JAYANTH SRIDHAR, MD

"I've failed over and over and over again in my life, and that is why I succeed."
—Michael Jordan

With graduation rapidly approaching, I (JS) asked two senior fellows (NP and NY) for their most pressing questions as they enter their lives as attendings, in terms of avoiding complications and dealing with trainees. Here are the questions they came up with, along with my answers.

SURGERY

What do you do to try to avoid complications on certain types of cases?

When I was a fellow attending a vitreoretinal training course in Boston, Donald J. D'Amico, MD, of Cornell University, gave a talk on complications that has stuck with me. To paraphrase his words, "For any eye case, the biggest complication you can have is to operate on the wrong eye." When you are a junior attending, this seems like an impossibility, but as you get busier and are trying to hold excessive information and external distractions in your head, the chance of this devastating complication rises. So, always check the patient and check the site.

Next, understand the goals of the case, and understand that these goals differ tremendously depending on the pathology. For a rhegmatogenous retinal detachment, the objective is to seal the breaks and, if necessary, place a tamponade. For a membrane peel for a symptomatic epiretinal membrane, the goal is to relieve foveal traction. For a diabetic vitreous hemorrhage, the goals are to clear the hemorrhage and prevent future complications of diabetic retinopathy. Reiterating these goals in your head while scrubbing will help keep you clear-headed and pointed in your surgical decision-making. If you can stay focused and directed in your maneuvers, you will reduce unnecessary steps and operative time, dramatically lowering your chance of a complication.

Finally, remember the pledge, *Primum non nocere*—First, do no harm. The complications that surgeons regret the most are the avoidable ones, and those usually come from trying to do something good in a situation that is not amenable to improvement. For example, if the view deteriorates in a case due to corneal edema, peeling membranes close to the fovea without adequate visualization represents a risk-benefit ratio that is not in the patient's best interests. Take a deep breath and avoid—to borrow a phrase from the poker world—*going on tilt*. Quitting while you are still behind is sometimes the best thing you can do for your patient to preserve options for the future.

What is your stepwise approach to peeling near the macula to avoid complications?

The most important factors in safe macular peeling are good visualization and minimizing untoward movement. Good visualization comes from optimizing your viewing system (indirect vs contact lens), ensuring that there is no media opacity in the anterior chamber or vitreous cavity (eg, residual vital dye swirling around that was not cleared completely prior to peeling), obtaining good focus on the target tissue, and lighting appropriately with the fellow hand when using a light pipe.

Early career surgeons often light inadequately out of fear of coming too close to the retina, and certainly going excessively close increases the risk of iatrogenic damage from direct contact or phototoxicity. However, there is a sweet spot between two extremes, and even a couple millimeters of advancement of the light pipe can make a huge difference in ensuring safe peeling.

Patient movement can be minimized by reducing sedation of the semi-awake patient prior to peeling. I often wake the patient up prior to the peel to avoid the scary-but-all-too-possible scenario of the patient waking up mid-peel and moving his or her head.

How much surgery do you allow fellows to perform? Is it based on a certain timepoint in their training?

The first priority for any attending surgeon in the OR is getting the best possible outcome for the patient. If that can be achieved while supervising a trustworthy and capable fellow surgeon, then the fellow may operate.

Every fellow surgeon is different in his or her progression. Some fellows are ready to peel membranes within a month in the OR, and others need more time to get comfortable with visualization of the retina. Visualization is again a huge key because, if the attending can see, they will feel more comfortable and be more willing to allow the fellow to operate. If I cannot see sufficiently to ensure a safe patient outcome, then a switch of positions at the microscope is inevitable.

PATIENT INTERACTIONS

What do you do if a patient refuses to have a trainee participate in surgery?

This is the question that I asked my attendings as I left fellowship 4 years ago, and it is a situation that thankfully comes up infrequently. Most patients understand that at teaching institutions we have a dual responsibility to take the best care of our patients and to teach the next generation of surgeons for the benefit of everyone. Every once in a while, a patient specifies that he or she does not want a trainee involved in surgery. In those instances, I explain that surgery is generally a two-person operation with a capable assistant making certain maneuvers during surgery (eg, scleral depression) much easier and more effective. If a patient insists, I obey his or her wishes that I perform the critical portions of the procedure (eg, macular peeling) with the understanding that other portions of the procedure will require both the attending and fellow surgeon. I have never had a patient refuse to have a trainee at the side scope for a surgery.

When there is a surgical complication, how do you address it with the patient and family?

Rule No. 1 is to be honest and upfront. Finish the surgery and then broach the discussion with the patient after the drapes are removed. I would not recommend overwhelming patients with details with anesthesia still on board or in the immediate postoperative period, but I would state that something unplanned occured while being as reassuring as possible. (This obviously depends on the nature of the complication.)

With the patient's permission, I would recommend spending more time talking to the family member or members in the waiting room. I usually explain more details to the family and indicate that we will speak more about it the next day during the postoperative appointment.

When a patient hears that a complication has occurred, the most important thing is to translate in layman's terms what that means regarding recovery time, visual prognosis, etc. Keep open lines of communication; exchanging phone numbers and documenting this exchange is a great way to achieve this.

As painful as it may be to see your complications (more on this below), commit to seeing the patient as often as needed in the postoperative period, and be patient with questions and concerns that arise.

PSYCHOLOGY

How do you move on psychologically as a surgeon after a complication?

An attending surgeon in medical school once told me that the best surgeons are not those who have the best hands but those who handle complications with the most grace. The first thing to do is to put things into perspective: Is the complication permanently visually disabling? Striking the crystalline lens during vitrectomy is not ideal, but the patient can still have excellent visual potential in the long term after removal of a cataract and placement of an IOL. Extrafoveal iatrogenic damage during macular peeling is similarly suboptimal, but it may result in no impactful symptoms for a high-functioning patient, depending on location and degree of injury. On the other hand, direct injury to the fovea or optic nerve is a completely different story that should elicit a different reaction.

Regardless of the severity of the complication, it is normal for the surgeon to feel guilt. We all chose medicine as a field to help people and not cause harm, so it can be damaging to your self-image to experience a visually compromising complication. You need to process these emotions, swallow your ego, and accept that part of being human is making mistakes.

This process, however, comes after you fulfill your role as captain of the ship and take care of your patients. This means finishing the case even if there was a complication during it, getting a sip of water, and taking care of the other patients you have on your OR schedule. As mentioned above, support the patient and family after the surgery with open lines of communication, honesty, and optimism (when appropriate).

After this is done, I find that the most helpful way to move on psychologically is to try to understand why the complication happened so that I can prevent it from happening again. Recorded surgical video can be critical to review to see what exactly happened. Do not be afraid to use your support group of friendly fellow surgeons. Besides offering sympathy and a true understanding of what you are feeling, they can offer insights into their own experiences and help debrief in a HIPAA-compliant "Morbidity and Mortality" fashion after the fact.

Finally, stay balanced. Even on the days you have complications, do your wellness rituals. Whether that includes exercise, meditation, playing a musical instrument, or painting, remember that if you do not first take care of your psyche you will not be prepared to get back on the bike and try again the next day.

How do you, as the primary surgeon, maintain or boost confidence in a trainee experiencing complications?

As the attending, you have to acknowledge what just happened, but, as with your conversation with the

patient, immediately after the event is not the best time to dive into the nitty-gritty. Give your fellow time to process, and always emphasize that any complications that occur on your watch are ultimately your responsibility as the attending.

Every trainee is a little different in how he or she processes events. Depending on the complication, some will be ready to operate again right away, whereas others may need a couple of cases to gather their wits. Respect those differences, and do not force trainees out of their comfort zones too soon.

The best thing you can do as the attending is to have a short memory for your fellows' mistakes. (This is probably a good thing to have for life in general!) For example, if a fellow once hit the crystalline lens with the cutter with you or with another attending, never say "Be careful! Remember, you hit the lens that other time." Be positive and supportive and let the fellow understand that you are there to guide and protect him or her from complications as much as possible.

As a senior attending once told me, "The only way to avoid complications is not to operate." Complications are part and parcel of what we do as surgeons on a daily basis. Let your fellows understand that they exist, that we do everything in our power to minimize them, and that, when they do happen, we use them as learning experiences to continue to improve. ■

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INCREASING NEVUS THICKNESS POSED A GREATER RISK OF TRANSFORMATION INTO MELANOMA. EACH MILLIMETER OF INCREASED THICKNESS POSED A THREAT.

Multivariable analysis showed that, as a group, there were six important factors in the transformation of a nevus into melanoma: thickness greater than 2 mm on ultrasonography, subretinal fluid detected with spectral-domain OCT, a decrease in VA to 20/50 or worse, orange pigment on fundus autofluorescence, melanoma acoustic hollowness by ultrasonography, and a tumor diameter greater than 5 mm.

A limitation of our study was the number of patients lost to follow-up.

CONCLUSION

Ocular oncologists consider the importance of thickness of choroidal nevi when making decisions on management. Our study is the first to specifically evaluate each millimeter incremental risk of choroidal nevus for transformation into melanoma. We found that increasing nevus thickness is associated with an increased risk of transformation, but it is important to recognize that not all enlargement signals a transformation to melanoma. That said, we identified a major increase in the transformation rate for nevi that were more than 2.0 mm thick. Continuing advances in imaging technology could further elucidate the impact of submillimeter change. ■

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CONTROLLING FLARES IN CHRONIC NONINFECTIOUS UVEITIS


Two fluocinolone acetonide formulations—a newly approved one and a familiar one—offer options for long-term inflammation control.

BY STEPHEN D. ANESI, MD, FACS; AND PETER Y. CHANG, MD

We manage approximately 1,400 patients monthly, about half of whom are at risk for flares of inflammation, tissue damage, and vision loss associated with chronic noninfectious uveitis. Local, continuous, long-term control of inflammation helps minimize uveitis flares and mitigates noncompliance and poor toleration of systemic therapy.

When a patient presents with steroid-dependent recurrent or chronic uveitis, our first-line approach focuses on quieting the inflammation, typically achieved with corticosteroid administration. To achieve uveitis quiescence in the long run, however, we prefer a corticosteroid-sparing regimen that may involve oral NSAIDs, antimetabolites, calcineurin inhibitors, various biologics, and even alkylating agents. The decision of which therapeutic agent to use depends on various factors such as the location of uveitis, severity of intraocular inflammation, risk of permanent visual loss, underlying systemic disease, and patient compliance and tolerance of therapy.

Of course, not every patient is a candidate for steroid-sparing immunomodulatory treatment. A woman who wants to become pregnant may wish to avoid systemic medication and choose local inflammatory control with a steroid via a periocular or intraocular route. A patient with consistent unilateral uveitis without an underlying autoimmune disorder may also prefer a local approach. This is especially relevant during the COVID-19 pandemic, as some patients have shown concern about the use of immunomodulatory therapy in general. For elderly patients, those with comorbidities, or those with a history of poor tolerance or adherence to medications, avoidance of systemic immunosuppression via use of local corticosteroid therapy may be the most viable and safe option.

A REVIEW OF THERAPIES

Local therapies include injectable and implantable corticosteroids. The two triamcinolone acetonide injectable suspensions used to treat uveitis are Kenalog (Bristol-Myers Squibb) and Triesence (Alcon). Steroid implants approved by the US FDA to treat uveitis include the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan),

AT A GLANCE

- Fluocinolone acetonide is an effective agent for treating noninfectious uveitis.
- The fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq, EyePoint Pharmaceuticals) and the fluocinolone acetonide intravitreal implant 0.59 mg (Retisert, Bausch + Lomb) are two options for treatment. The former is implanted in the office, and the latter in the OR.
- The fluocinolone acetonide intravitreal implant 0.18mg is approved by the US FDA, is indicated for treatment of chronic noninfectious uveitis affecting the posterior segment of the eye, and may provide continuous low-dose release of drug for up to 3 years.

the fluocinolone acetonide intravitreal implant 0.59 mg (Retisert, Bausch + Lomb), and the fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq, EyePoint Pharmaceuticals).

In 2019, several European regulatory bodies approved or recommended for approval the fluocinolone acetonide intravitreal implant 0.19 mg (Iluvien, Alimera Sciences) as a treatment for posterior uveitis; the drug is not approved for this indication in the United States.

FLUOCINOLONE ACETONIDE OPTIONS

In our practice, triamcinolone and dexamethasone are used for acute flares and short-term control of uveitis. When immunomodulatory therapy fails or is not tolerated by a patient, fluocinolone acetonide intravitreal implants are an option.

SURGICAL IMPLANT

The fluocinolone acetonide intravitreal implant 0.59 mg is implanted surgically in the operating suite. It has been in use for 15 years, and has a rich data set supporting its efficacy.

FDA approval of the drug was based on a pair of double-masked multicenter trials. Researchers found that in patients receiving the fluocinolone acetonide intravitreal implant 0.59 mg, there was a statistically significant decrease in recurrence of uveitis in the 34-week period after implantation compared with the 34-week period before implantation. At 7 years' follow-up, patients who were treated with the implant performed as well as those undergoing systemic therapy during the first 5 years.[1]

The implant is not without risks. Cataract progression is certain, and cataract extraction is often performed after or even during implantation. The risk of steroid-induced glaucoma is considerable: 30% to 40% of patients eventually required incisional glaucoma surgery.[2] There is also the risk of dislodgement of the steroid-eluting pellet, or the entire strut itself, which has been seen with earlier versions of this implant[3]; however, the newer implants do not yet seem to have a known problem with this.

IN-OFFICE IMPLANT

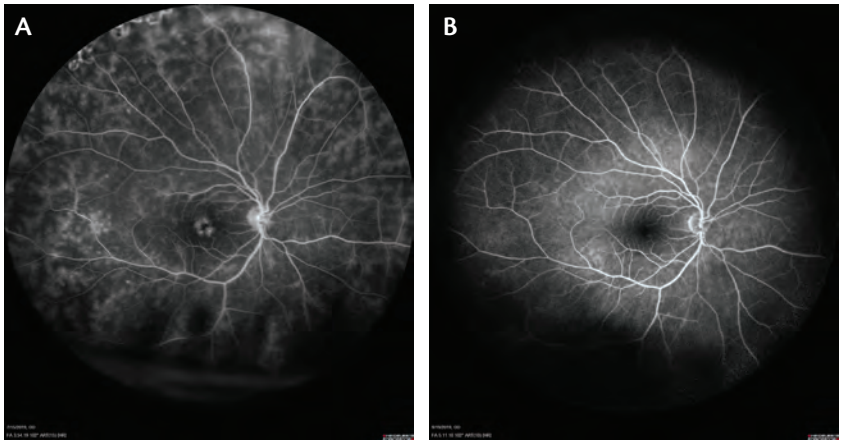
The fluocinolone acetonide intravitreal implant 0.18 mg is designed to deliver a sustained release of therapeutic agent for up to 36 months in patients with chronic noninfectious uveitis affecting the posterior segment.[4] The drug may be a suitable adjunctive therapy for patients with severe uveitis associated with systemic disease that has improved with immunosuppressive therapy and need additional inflammatory control for the eye.

The implant is supplied in a sterile single-dose preloaded applicator that is injected via the pars plana under local anesthetic in the office. Based on our experience, along with others involved in the initial clinical trials studying this implant for use in uveitis, we believe that the fluocinolone acetonide intravitreal implant 0.18 mg may effectively control inflammation for at least 30 to 36 months.[5]

(Continued on page 35)

CASE STUDY

A 29-year-old woman presented with bilateral chronic pars planitis with significant macular edema and retinal vasculitis in the right eye. Baseline fluorescein angiography showed macular leakage and diffuse abnormal punctate hyperfluorescence (A). The patient intended to become pregnant, so she did not want to start systemic immunomodulatory therapy. Treatment with the fluocinolone acetonide intravitreal implant 0.18 mg (Yutiq, EyePoint Pharmaceuticals) was initiated. Two months after the administration, resolution was observed on fluorescein angiography, and the patient reported significant improvement in visual acuity and reduction in floaters (B).



WE BELIEVE THAT THE FLUOCINOLONE ACETONIDE INTRAVITREAL IMPLANT 0.18 MG MAY EFFECTIVELY CONTROL INFLAMMATION FOR AT LEAST 30 TO 36 MONTHS.

THE MOTHER OF INVENTION: MAKING CUSTOM EQUIPMENT IN SYRIA


Developing a custom-made needle for suprachoroidal steroid injections in Syria.

BY AMEEN MARASHI, MD; AND BENJAMIN J. THOMAS, MD

Two years ago, I spoke to a vitreoretinal surgeon from Aleppo, Syria, Ameen Marashi, MD, about the day-to-day realities of practicing in the midst of the Syrian crisis. It was a profile in bravery and an extreme example of how, as physicians, we must often go to significant lengths and employ significant creativity to keep our patients safe while effectively managing disease.

I wanted to check in with Dr. Marashi to see if he had any updates from his clinic and, sure enough, Dr. Marashi had another example of using an outside-the-box framework for addressing an issue in his clinic. He and I outline it here. At a time when we are all seeking to use our creativity and compassion to care for patients in very novel circumstances, we hope it serves as another small point of inspiration.

—Benjamin J. Thomas, MD

The growing global diabetic crisis is an impartial one—no corner of the world is spared. A massive increase in the prevalence of diabetes mellitus (DM) has been predicted,[1] and countries such as India are scrambling to prepare for the largest diabetic populations in history.[2] With these changes comes a concurrent increase in the prevalence of diabetic retinopathy (DR), and a sizeable portion of these patients will eventually lose vision because of diabetic macular edema (DME).

DME is a leading cause of vision loss in the working population,[3] a problem reported in multiple populations around the world.[4] Intravitreal VEGF-blocking agents have become the most common first-line treatment for DME management,[5] but the disease is often refractory to anti-VEGF monotherapy, as has been reported in a worrisome 40% of patients in some series.[6]

At the Marashi Eye Center in Aleppo, Syria, we (A.M.) seek to deliver excellent care to diabetic patients despite an ongoing crisis. In Aleppo, just as everywhere else, DR is a commonly encountered disease, constituting about 35% of our total ophthalmic practice; however, of these diabetic cases, refractory DME makes up about 20%, adding the difficulties of finding sustainable treatments for these patients to the baseline difficulties of follow-up and reimbursement.

Intraocular steroid therapies are helpful because they can address the complex inflammatory markers induced by DR.[7] This form of treatment also tends to be longer-acting, which is a distinct advantage in regions where frequent follow-up is limited by geographic distance or restricted resources. Unfortunately, steroid therapy carries the twin risks of cataract formation and IOP elevation.[8,9] Suprachoroidal injections offer a potential solution.

Injecting triamcinolone into the suprachoroidal space may reduce the risk of IOP spikes because drug delivery is directed to the choroid and the retina and is restricted from the trabecular meshwork, enhancing therapeutic efficacy in the target tissue and presenting less interference with the anterior chamber.[10]

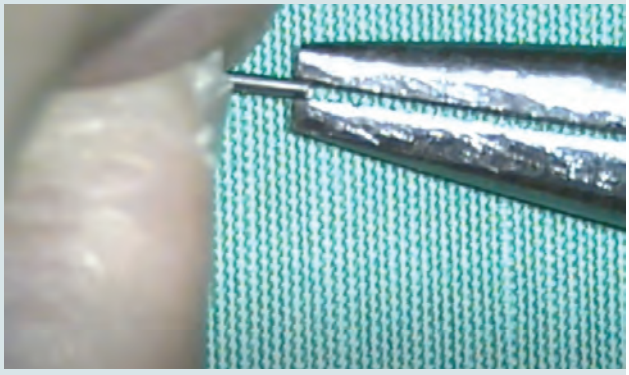
Recent studies have highlighted the safety and effectiveness of needle-based suprachoroidal drug delivery systems.[11] In this minimally invasive technique, a microneedle penetrates transconjuctivally to the appropriate depth during drug delivery. The problem for us was where to obtain the needles.

AT A GLANCE

- Diabetic macular edema (DME) is a leading cause of early-onset vision loss and blindness among working-age adults. The disease is commonly treated with steroids.
- Targeting the suprachoroidal space may represent a safe and effective option for steroid delivery in patients with DME.
- Without access to ready-made sources for appropriate needles, a vitreoretinal specialist in Syria developed his own to make intravitreal steroid injections available to his patients.

WATCH IT NOW

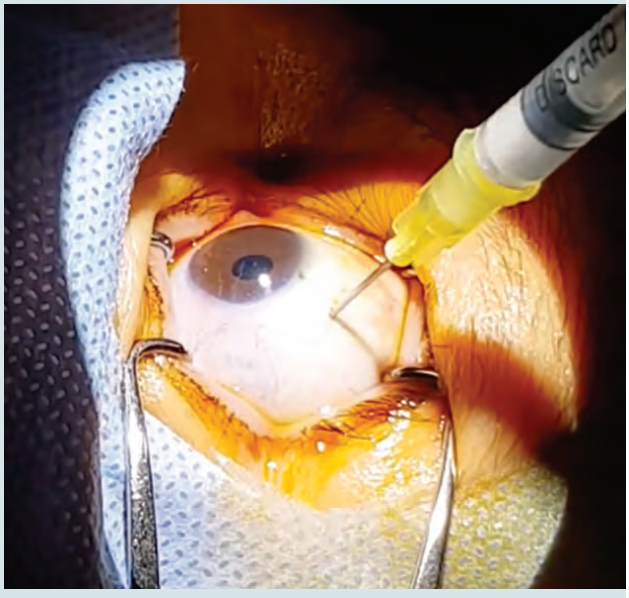
VIDEO 1: CREATING A NEEDLE FOR SUPRACHOROIDAL INJECTION



Ameen Marashi, MD, shows how to modify a 30-gauge needle so it can administer suprachoroidal injections.

BIT.LY/MARASHI0520-1

VIDEO 2: SUPRACHOROIDAL INJECTION TECHNIQUE



Ameen Marashi, MD, demonstrates his technique for suprachoroidal injection using a needle constructed in his clinic.

BIT.LY/MARASHI0520-2

NECESSITY, THE MOTHER OF INVENTION

Years of crisis and western embargo had presented extreme challenges to the practice of medicine. Because the required needle was unavailable in Syria, we set about the task of producing one (Figure 1). We identified a medical manufacturer and designed a needle to the following specifications:

The needle should be made from a 30-gauge needle with a 23-gauge sleeve stopper obtained from a 5-mL needle (Video 1). This would create a guarded sleeve over the 30-gauge needle and thus permit an injection depth of only 1,000 µm (including the shaft).

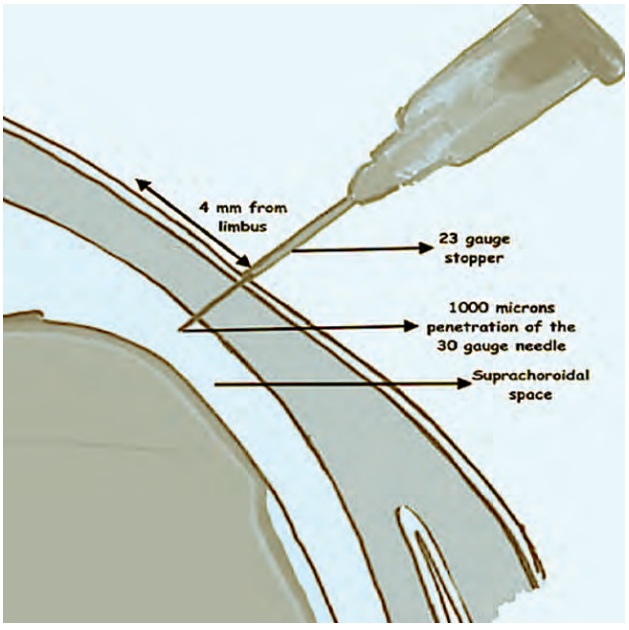


Figure 1. The position of the custom-made needle relative to the limbus, sclera, and suprachoroidal space.

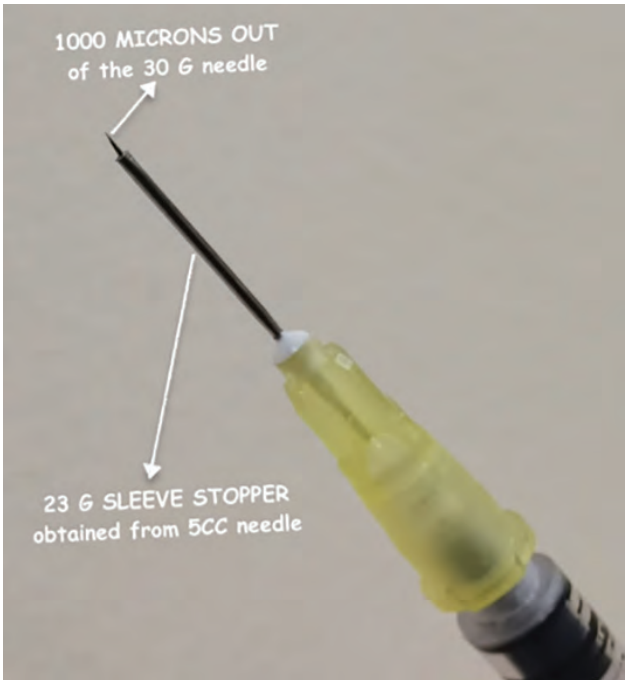


Figure 2. The design of the custom-made needle with a 23-gauge sleeve stopper that permits only 1,000 µm to exit the 30-gauge needle. Photo credit: Ameen Marashi, MD

The 23-gauge needle should be rasped to have smooth edges and to allow only 1,000 µm (± 200 µm) of the 30-gauge needle beyond the sleeve, as measured by Vernier calipers (Figure 2). The needle must be durable enough to undergo autoclaving. Once the needle had been created, I (A.M.) began administering suprachoroidal injections under sterile conditions after the skin and conjunctiva had

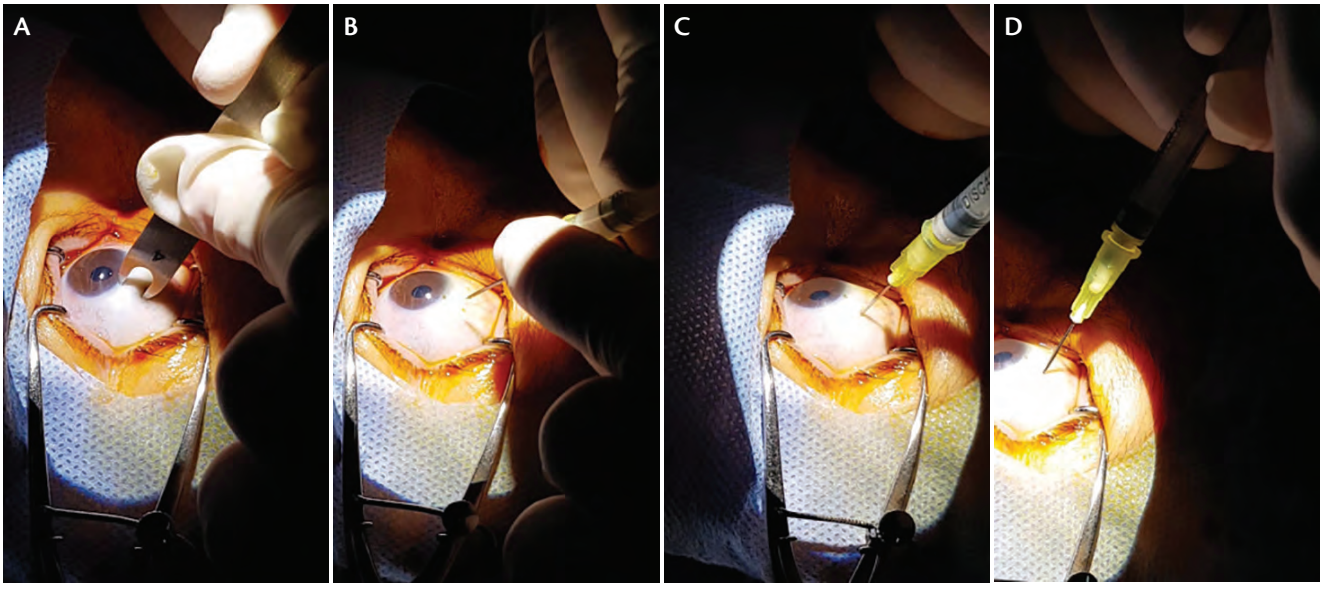


Figure 3. The injection site is located 4 mm from the limbus (A). The needle is positioned perpendicular to the sclera (B). Medication is injected with gentle pressure (C). The needle is withdrawn obliquely from the eye (D).

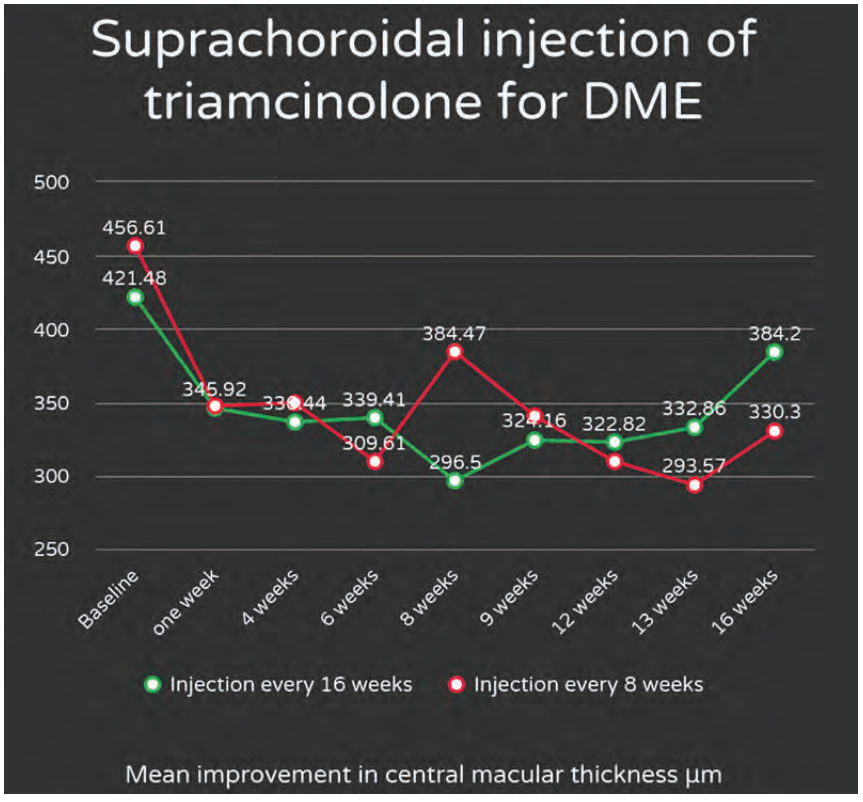


Figure 4. Mean improvement and changes in central macular thickness.

been disinfected using 10% and 4% povidone-iodine under topical anesthesia, respectively. Injections were performed after sterile draping and placement of a lid speculum to isolate the eyelashes.

Our technique is straightforward: In the superotemporal quadrant, the injection site is marked 4 mm from the corneal limbus (Video 2). Next, the needle is positioned with the bevel edge directed away from the limbus, and then the needle is inserted perpendicular to the sclera. Using gentle pressure, 0.1 mL of triamcinolone is slowly expressed into the suprachoroidal space (Figure 3). The needle is then withdrawn obliquely from the eye to prevent egress of the medication.

EFFICACY AND SAFETY

We assessed the safety and efficacy of our results in an interventional, single-center study of 50 eyes of 36 patients. Patients with DME received a suprachoroidal steroid injection using the custom-made needle every 8 or 16 weeks, based on the observed effect of treatment. We measured central macular thickness with spectral-domain OCT and evaluated BCVA, IOP, cataract progression, and treatment tolerability.

Approximately 42% of eyes required an injection within 8 weeks; the mean central macular thickness was 456 µm at baseline and decreased to 309 µm within 6 weeks, but the central macular thickness increased to 384 µm in 8 weeks and decreased again to 330 µm after the second injection (Figure 4). On average, BCVA improved from

20/125 to 20/45 at 16 weeks in these eyes. Approximately 58% of eyes required only one injection during 16 weeks; the mean central macular thickness was 421 µm at baseline and decreased to 339 µm within 6 weeks, but the central macular thickness increased to 384 µm at 16 weeks. On average, BCVA improved from 20/80 to 20/50 at 16 weeks in these eyes.

Suprachoroidal triamcinolone injections reduced central macular thickness by 147 µm on average by 8 weeks. In many of these patients, DME had previously been refractory to anti-VEGF monotherapy.

No patient experienced a suprachoroidal hemorrhage, choroidal or retinal detachment, or endophthalmitis.

More work is needed and more data must be collected, but we are pleased with the early efficacy and safety that we have observed in our first round of patients. More so, we are happy to see the treatment options in Syria expand through our efforts. The development of a custom needle available in Syria may offer an affordable, safe, and effective method to treat chronic DME in difficult settings. ■

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(Continued from page 31)

The FDA approved the fluocinolone acetonide intravitreal implant 0.18 mg based on clinical data from two randomized, sham injection-controlled, double-masked, phase 3 clinical trials with patient follow-up for 3 years. After 6 and 12 months, both clinical trials achieved the primary efficacy endpoint of preventing recurrent uveitis flares compared with sham injection.

At year 1 in both studies, eyes treated with the implant demonstrated significantly lower rates of inflammatory flares (28% and 33%) compared with those in the control group (86% and 60%). Cataract rates in phakic eyes were higher in the implanted group (56%) compared with the sham group (23%). IOP elevation and rates of pressure-lowering surgery were similar at 1 year.[4]

Three-year data from one of the phase 3 studies showed that fewer patients in the treatment arm demonstrated uveitis recurrence compared with those in the control arm (56% vs 93%).[6]

For an illustration of the efficacy of this fluocinolone acetonide option, see *Case Study*.

PIPELINE

Future treatment options for chronic noninfectious posterior uveitis look promising. Among the noteworthy formulations in the pipelines are a preservative-free triamcinolone acetonide formulation delivered via suprachoroidal injection (Xipere, Clearside Biomedical) and a platform that uses plasmid encoding for the production of anti–TNF-alpha to treat noninfectious uveitis (EYS606, Eyevensys). ■

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How COVID-19 May Change the Future of Retina Practice

When we think of what the future may hold, it behooves us to think from a public health perspective.

BY RAHUL REDDY, MD, MHS

As I thought about how the spread of COVID-19 will affect ophthalmology care around the world, I found myself drawn to framing my forecasts vis-a-vis my experiences in public health and in a large retina practice. We are health care providers to populations with comorbidities (ie, diabetes) and risk factors (ie, age) that may make a COVID-19 infection fatal.

With this in mind, and at the guidance of organizations such as the ASRS and AAO, many retina specialists have altered their practice patterns. But which changes are here to stay and which are temporary? Given what we know and don't know about the coronavirus, it stands to reason that a number of the changes we have implemented will be permanent or semipermanent. It is worth noting that some of these changes can be implemented even after the pandemic eases, as they may be useful in slowing disease transmission during annual flu seasons.

CHANGES TO THE OFFICE

The changes that are most obvious are those that have been felt in retina clinics around the world: the empty waiting rooms, the face masks, and the ubiquity of sanitizing materials.

Low-Cost/High-Impact Changes

Some low-cost solutions we have implemented, such as mask wearing and alterations to slit-lamp shields, do not disrupt workflow in the clinic and may also have a high impact on decreasing disease transmission. These help mitigate disease transmission when paired with fixed factors such as variable patient flow, room size, and ventilation systems.

Access to negative-pressure and positive-pressure rooms is limited. Mask wearing may continue in health care settings, especially in sites such as retina clinics that care for at-risk populations. We will know more about the effects of mask wearing during a pandemic as more research is published. For the near future, this may be a low-cost safeguard that reduces the risk of transmission within our clinics without causing a major disruption to workflow.

AT A GLANCE

- Modifications made to retina practices in the COVID-19 era may be here to stay even after the threat of coronavirus fades.
- Some low-cost high-impact changes could result in significant reduction in disease transmission risk without adversely affecting workflow or quality of care.
- Adjustments to treatment paradigms that focus on extending duration of treatment may be important for populations particularly vulnerable to complications due to infectious diseases.

GIVEN THE RELATIVELY LOW COST AND SMALL LIKELIHOOD THAT A DETAILED CLEANSING OF HIGH-TOUCH SURFACES IN AN EXAM ROOM WOULD DISRUPT PATIENT FLOW, IT SEEMS POSSIBLE THAT PRACTICE STAFFS WILL CONTINUE TO WIPE DOWN ROOMS WHEN EACH PATIENT LEAVES.

Some protocols of the COVID-19 era may disrupt or delay workflow despite their low (or zero) monetary costs. Questionnaires about patient history of travel and staff encounters with disease-positive patients may disrupt workflow, but a few simple questions at check-in (eg, "Have you had contact with anyone who was sick in the past week?" or "Have you been on a cruise in the past 30 days?") may gel with current practices.

Sanitation protocols for examination rooms may become more thorough. Given the relatively low cost and small likelihood that a detailed cleansing of high-touch surfaces in an exam room would disrupt patient flow, it seems possible that practice staffs will continue to wipe down rooms when each patient leaves.

Practice Layouts

Since the start of the COVID-19 pandemic, some retina practices have adjusted their patient flow structures. At Associated Retina Consultants in Phoenix, for example, family members remain in their vehicles and patients never double back to the same hallway. Patients move in one direction for their entire visit, which maximizes efficiency and reduces the likelihood of patient-to-patient transmission of an infectious disease. The feasibility of applying this convention to another practice location depends, of course, on the clinic's available site and existing structure. This layout may be advantageous during annual flu seasons, too.

We have designated an isolated exam room in our office for patients who present with an urgent need for care and have been identified as positive for COVID-19. We may keep this room for similar use in the future.

Changes to practice footprint and patient throughput patterns require more deliberate action and investment than some of the easier changes I mentioned earlier. Practices with space to spare will find it easier to implement changes than practices that function in tight quarters. Bear in mind, these adjustments to our clinics could be useful to reduce the transmission of disease in future outbreaks, be they of coronavirus, flu, or another threatening entity. Groups that purchased the building in which they practice may wish to keep this in mind. Without protocols in place, there may be profound consequences.

Physician and Staff Adjustments

Modifications in clinics are not limited to patients and architecture. Doctors and staff will see changes in routine if their practice makes serious adjustments. Some of these changes will be small, and others may require more time- and money-intensive resources.

Screening doctors and staff for fevers upon arrival to the clinic is a low-cost way to reduce the chance that transmission is spread from the clinic to a patient. Cross-training staff may be required for future employee training, as sending home a specialized staff member could disrupt the clinic's workflow. Questions about how to replace a doctor—especially in a small or solo practice—will be more difficult to address.

Contact tracing for doctors and staff, should they test positive for an infectious disease, may require the clinic to retrace the steps of that employee. Whom did they contact? Which rooms were they in? How many patients must be notified? In many locations, local public health authorities may be able to assist. For larger groups with multiple practice sites, it may be prudent to avoid employee travel between offices during high-risk seasons. Although such action is disruptive to the clinic, it is necessary to ensure patient and employee safety.

CHANGES TO TREATMENT PARADIGMS

We often talk about the benefit of extended-duration treatments and the promises they hold. The thought many retina specialists used to have was this: If patients can go several months without visiting our practice while maintaining visual acuity and remaining safe, then they will be more likely to comply with treatment recommendations. Being able to serve more patients as a result of this would be a windfall. Now, we have to consider whether or not we reduce patient risk for disease exposure if we extend duration between treatments, for example, for wet age-related macular degeneration (AMD).

(Continued on page 45)

Open Globe Injury in a COVID-19 Patient: Lessons Learned

Special precautions are required to safely and quickly treat patients with potential infection.

BY VAMSEE NEERUKONDA, MD; KEVIN ROSENBERG, MD; AND PATRICK OELLERS, MD

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the viral pathogen that causes the disease COVID-19, originated in Wuhan, China, and has evolved into an unprecedented public health threat.[1] It is crucial to understand the means for transmission and to adopt prevention measures to minimize its transmission.

The virus is known to spread mainly via respiratory droplets (> 5–10 µm in diameter, spread within 1 m)[2] from infected patients or indirectly from fomites. It enters via respiratory mucosa or conjunctival tissue. Debate exists regarding spread via tears and the ocular surface.[3-8] Management of patients with COVID-19 is complex, and there are many implications for ophthalmologists, including retina surgeons. We present a case of an open globe injury in which surgical repair was complicated due to COVID-19 infection.

CASE PRESENTATION

A 39-year-old woman with a history of chronic dry cough and emphysema presented to the emergency department (ED) with persistent blurry vision 4 days after blunt force injury to the left eye. The patient was evaluated at bedside in the ED. The examining physician wore personal protective equipment (PPE) that included a powered air-purifying respirator (PAPR; Sentinel XL HP, ILC Dover).

The patient's VA was light perception and IOP was 4 mm Hg in her left eye. Anterior segment examination revealed a superotemporal sectoral bullous subconjunctival hemorrhage, a shallow anterior chamber, and total hyphema with no view of the retina. Her right eye was normal.

CT imaging of the patient's orbits revealed an irregular

AT A GLANCE

- COVID-19 typically spreads via droplet transmission or fomites. Respiratory mucosa and conjunctiva are vulnerable sites of entry for viruses. Airborne transmission may be possible during intubation and extubation.
- Using PPE and following proper sanitization practices may help reduce the risk of transmission in the OR.
- Use of negative pressure ORs may help minimize airborne transmission during intubation.

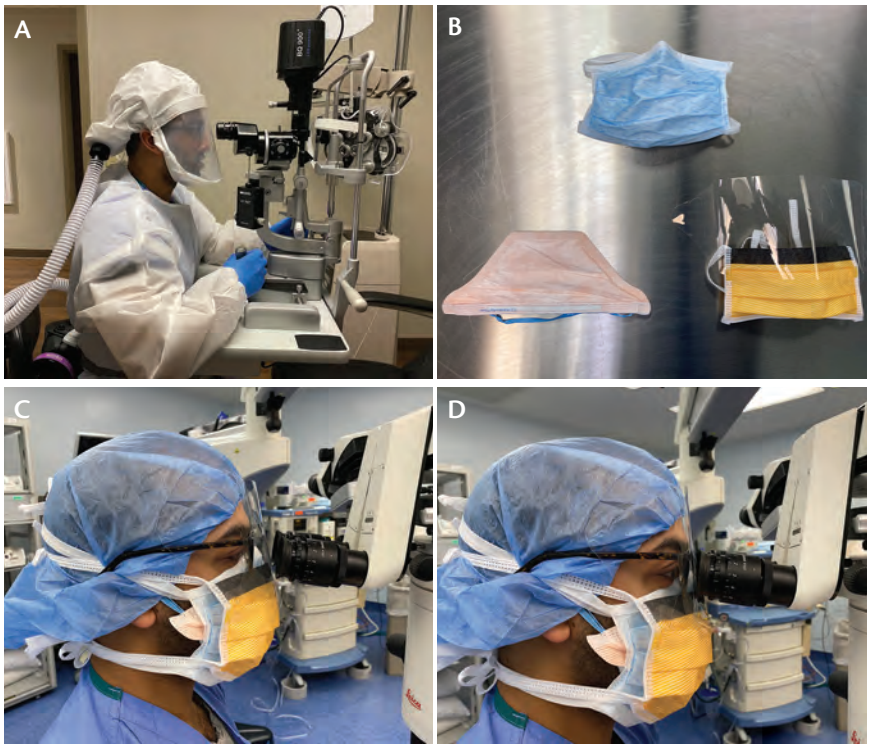

Figure. A variety of PPE was used in the OR during surgery on a patient with potential COVID-19 infection. Dr. Neerukonda is shown using a PAPR at the slit lamp (A). The three masks used during surgery were an N-95 respirator mask, a surgical face mask, and a surgical mask with a face shield (B, left to right). Wearing three pieces of PPE while aligning with microscope oculars proved to be difficult (C), and maximum visualization was achieved with adjustments (D).

contour of the superolimbal sclera, no visible crystalline lens, and no intraocular foreign body. We determined that she likely had a ruptured left globe. Prophylactic intravenous vancomycin (1 g every 12 hours) and ceftazidime (2 g every 8 hours) were administered, and a Fox shield was placed over the eye. We recommended emergent surgical exploration.

PREPARING FOR SURGERY

Due to her nonproductive cough and emphysema, the ED physicians' suspicion for COVID-19 was low, albeit still present and concerning. Notably, she was afebrile and reported no exposure to infected individuals. A nasopharyngeal swab was sent to the reference laboratory for SARS-CoV-2 polymerase chain reaction (PCR) testing. After discussion among the stakeholders on how to proceed regarding the urgent nature of the case, she was transported to the OR.

Multiple precautions were taken to minimize airborne transmission. The anesthesia team wore PAPRs, and the patient was intubated in a negative pressure OR. She was then transferred to the ophthalmology OR, which is equipped with a wall-mounted operating microscope.

For patient and physician protection, the surgeons wore three masks in sequential order: N-95 respirator (Respirator and Surgical Mask, 46727, Kimberly-Clark), a regular surgical face mask (Fog-Free Surgical Mask, Halyard), and a surgical mask with a plastic face shield (Fluidshield Fog-Free Surgical Mask, WrapAround Visor, Halyard).

SURGICAL AND POSTSURGICAL PERIODS

The ensuing surgical exploration revealed a superior 8-mm curvilinear scleral laceration with uveal prolapse 3 mm posterior to the limbus, which was successfully repaired with seven interrupted 9-0 polyglactin sutures. The patient was transported back to the negative pressure OR for extubation and was admitted overnight for observation and a continued course of intravenous antibiotics.

The next day, the COVID-19 PCR test returned positive. The ophthalmology team wore PAPRs for bedside examinations. The patient's VA was hand motion and a formed globe was observed. B-scan ultrasound revealed vitreous hemorrhage and possible retinal detachment. The patient was educated about her COVID-19 diagnosis, discharged from the hospital, and asked to self-isolate for 14 days. Subsequent postoperative follow-up was arranged in the ED due to the availability of ancillary support and PPE.

LESSONS LEARNED

COVID-19 has presented newfound obstacles to medical care. This case highlights the myriad complexities involved in caring for patients with ophthalmic surgical emergencies and concurrent potential or confirmed COVID-19 infection.

Barriers to routine care during both examination and surgery were manifold. PPE was needed. A surgical delay amid hospital protocol was resolved by a discussion among the surgical team members and hospital leadership. Concerns regarding viral transmission in the perioperative period, including airway management, had to be addressed.

Perioperative Management, Anesthesia, and Intubation

Airway management, ophthalmic evaluation, and surgery all expose physicians to sources of viral shedding. An ophthalmic exam exposes the physician to risk of transmission via respiratory droplets due to proximity to the patient as well as indirect contact via equipment. Intubation specifically introduces a novel transmission risk via the airborne route.

Aerosols that are generated may contain droplet nuclei, which are smaller than 5 µm, may remain in the air for extended periods of time, and may be transmitted beyond 1 m.[6-13] If possible, intubation should occur in a negative pressure room, which is designed to prevent air and particles from escaping. Typical ORs provide positive pressure, and air is flow-directed to flush particles out of the room.

PPE

Wearing PPE that fits appropriately is crucial for all personnel in contact with a patient who may be COVID-19–positive. We wore PAPRs for perioperative ophthalmic examination. Although a PAPR may provide the greatest protection, it is less than ideal for slit-lamp examination or indirect ophthalmoscopy.

Each mask worn by the surgeons was deemed necessary for different protective purposes.[14] The N-95 respirator created a facial seal and minimized small droplet exposure, the surgical mask protected against larger droplets or splashes, and the face shield mask protected the surgeons' conjunctiva from exposure. Wearing multiple masks, particularly the face shield mask, created a challenge for aligning with microscope oculars (Figure).

Hospital Protocols

Given the uncertainty of the patient's COVID-19 infection at the time of presentation, emergent discussions between the ophthalmology team and hospital leadership were required to ultimately facilitate a safe surgery. Our hospital's policy regarding known COVID-19 patients states that urgent surgery should be delayed if possible until the infection is cleared and that only emergency surgery should be performed with special precautions taken. Of note, all elective surgeries in the hospital have been postponed during the COVID-19 pandemic.

This case emphasized the importance of a fast-paced, comprehensive algorithm to address emergent surgery in possible or confirmed COVID-19 patients. It is imperative that ophthalmologists be involved in the development of these protocols. We should all have worst-case scenario plans on hand.

Keep Your Guard Up

Despite a low pretest probability, the patient was tested for COVID-19, and everything proceeded as if she were positive. It is crucial to have a low threshold to rule out COVID-19. At the time this patient presented, rapid COVID-19 testing was not yet available. Patients should be treated as COVID-19–positive until proven otherwise, and rapid COVID-19 testing should be employed whenever feasible.

CONCLUSION

This case highlights novel barriers to ophthalmic patient care. It raised numerous questions regarding safe and efficient management of surgical emergencies in the COVID-19 era. To safely and efficiently care for vulnerable COVID-19 patients with ocular emergencies, our profession must be prepared and proactive. ■

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Literature Review: Eye Care in the Era of COVID-19


Two studies have implications for improving the safety of patients and providers during the current pandemic.

BY CARA E. CAPITENA YOUNG, MD, AND MALIK Y. KAHOOK, MD

Characteristics of Ocular Findings of Patients With Coronavirus Disease 2019 (COVID-19) in Hubei Province, China

Wu P, Duan F, Luo C, et al[1]
Industry support: No

ABSTRACT SUMMARY

This retrospective case series evaluated 38 patients with clinically confirmed COVID-19 who were treated in the Chinese province of Hubei between February 9 and 15. The investigators collected information on ocular signs and symptoms as well as the reverse transcriptase polymerase chain reaction (RT-PCR) results of both conjunctival and nasopharyngeal swabs. They found that approximately one-third of patients (31.6%) had ocular symptoms, including conjunctivitis, conjunctival hyperemia, chemosis, epiphora, and increased ocular secretions. Overall, ocular symptoms were more common in patients who had more severe disease and more severely deranged blood counts. Although 73.7% of patients had positive nasopharyngeal RT-PCR results for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), only two patients (5.2%) had positive conjunctival swabs. Both patients with positive conjunctival swabs exhibited ocular symptoms.

DISCUSSION

What is the relationship between the ocular manifestations of the virus and severity of COVID-19?

Of the 12 patients with ocular manifestations of the virus, half were judged to be critically ill based on clinical guidelines. Furthermore, univariate analysis showed that patients with ocular symptoms were more likely to have higher white blood cell counts; neutrophil counts; and levels of procalcitonin, C-reactive protein, and lactate dehydrogenase compared to patients without ocular symptoms. These results suggest that ocular manifestations of the virus may be more common among patients with severe disease.

Can SARS-CoV-2 be transmitted through ocular secretions?

This study found SARS-CoV-2 within conjunctival secretions via RT-PCR, albeit in a minority of patients. Despite the relatively low incidence, these results suggest that the virus could be transmitted through ocular secretions. Additional research is warranted to investigate this link further.

What are the limitations of this study?

This study had a small sample size of 38 patients. None of the patients underwent a detailed ocular examination, meaning that all ocular findings were limited to external signs and symptoms and that data on potential intraocular or microscopic findings were not investigated.

Utility, Appropriateness, and Content of Electronic Consultations Across Medical Subspecialties: a Cohort Study

Ahmed S, Kelly YP, Behera TR, et al[2]
Industry support: No

ABSTRACT SUMMARY

This retrospective cohort study sought to assess the utility and appropriateness of electronic consultations (e-consults) among primary care and specialty practices within a single integrated health system comprising both academic and community medical centers. Specifically, five specialties were included: hematology, infectious disease, dermatology, rheumatology, and psychiatry. Of 6,512 eligible e-consults, 750 were randomly selected for review. Four reviewers, each of whom worked independently, assessed the appropriateness of the consultation based on four predefined criteria: point-of-care resource test, logistics only, urgency, and complexity. The utility of the e-consult was determined by avoided visits, which were defined as the lack of an in-person visit to the same specialty within 120 days.

Demographic data were similar across specialties with some minor exceptions. Most e-consults were completed within 1 day. Questions regarding therapy and diagnosis were the most commonly asked at 49.9% and 46.2% of e-consults, respectively. Although there was variation by specialty (60.5% rheumatology, 68.5% infectious disease, 70.7% dermatology, 73.3% hematology, 77.9% psychiatry), 70.2% of e-consults overall were rated as appropriate. Interrater agreement regarding the defined appropriateness criteria was moderate (K = 0.57 [95% CI, 0.36–0.79]). The most common reasons that an e-consult was deemed to be not appropriate were asking a question of inappropriately high complexity and failing the point-of-care test result, meaning a point-of-care resource that answered the question was widely available to the referring doctor.

DISCUSSION

What is the key learning point from this study?

It is important to define and assess the appropriateness and clinical utility of e-consults via clearly defined criteria. Ahmed and colleagues found high rates of utility—measured as avoided visits—and appropriateness among the specialties that they evaluated.

What applications does this study have for eye care?

Although this study does not directly investigate the clinical utility of e-consults for eye care, providers in this field have similarly busy schedules and cannot spend time on a program that includes high rates of inappropriate consultations. Of the specialties included in this study, dermatology offers the most direct comparison because both fields require a high degree of visual inspection for examination. Dermatology had a 70.7% appropriateness rating but also the lowest rate of avoided visits (61.9%). Although this represents a majority of the patients, the lower rate of avoided visits may be because of the visual nature of dermatology.

The e-consults included in this study were strictly questions and did not include photographic documentation. The inclusion of patient images might have produced different results for a visual specialty such as dermatology. E-consults would pose unique challenges for eye care providers because these e-consults do not permit slit-lamp or dilated fundoscopic examinations. Nor could testing such as IOP checks or imaging be performed. Regardless, this study illuminates the usefulness of e-consults and validates that they deserve further exploration for wider implementation in eye care.

What are the main limitations of this study?

This study was conducted within an integrated hospital system with providers who shared a common electronic health record that had been in use for several years. The results are therefore not immediately generalizable to a group just getting started with e-consults who would inevitably experience growing pains. The applicability of these findings to physicians communicating across different electronic health record systems and/or e-consult platforms is unknown.

In addition, provider satisfaction with the e-consult system was not assessed. Moreover, the study focused on urban centers with mostly white patients. Data therefore may not be generalizable to rural settings or minority populations. This study also does not provide information on concurrent use of e-consults with patient images such as those often received in ophthalmology. ■

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Curbing Our Enthusiasm for Telemedicine and Deciding on Treatments During COVID-19

COVID-19 has changed the way we think about telemedicine and treatment decisions. Is retina ready for telemedicine? How much have treatment decisions actually changed?

BY DAVID A. EICHENBAUM, MD

Some of the foreseen promises of telehealth have come to fruition in the past several years. Patients have shown that they sometimes prefer the convenience of telehealth consultations for routine matters handled by their primary care provider and selected specialists. A prescription for a round of antibiotics for a common infection, for example, might be acquired via a telehealth visit. What works in general medicine, however, may or may not translate to surgical specialties.

In some instances, telemedicine can provide convenience without sacrificing the quality of care. A patient consulting with a cardiologist to review data (test results, lifestyle, various metrics) that will inform a decision whether or not to initiate statin therapy, for example, is an effective use of telemedicine, particularly because the physician does not require a physical examination to make that decision.

Because so many decisions in retina practice are informed by imaging and physical examination, and because we do not yet have commercial access to at-home imaging platforms, I believe that retina and telemedicine are not yet fully ready for each other.

LIMITATIONS OF AT-HOME EVALUATION IN NEOVASCULAR AMD

During the COVID-19 pandemic, many retina clinics have forgone retinal imaging for patients scheduled to receive anti-VEGF therapy for neovascular age-related macular degeneration (AMD), particularly if the patient's history is long enough that a response pattern can be established. By skipping imaging and providing an injection-only visit at the most recent fluid-free interval, retina specialists spared these neovascular AMD patients from exposure to staff members and equipment surfaces, mitigating the risk of disease spread by minimizing the number of potential infection points.

These efforts should be applauded, as they provided the proper amount of care tailored to this medical

AT A GLANCE

- Although telemedicine has been shown to be effective in other areas of health care, the unique dynamics of retina care require in-office examination.
- At-home diagnostics will be foundational technology in the potential expansion of telemedicine in retina.
- Extended-duration steroid therapy may provide a convenient bridge treatment for diabetic macular edema patients who have been requiring frequent anti-VEGF injections.

THERE IS GREAT PROMISE FOR TELEMEDICINE IN RETINA, BUT UNTIL HOME DIAGNOSTICS ARE VALIDATED AND APPROVED FOR COMMERCIAL MARKETING AND AVAILABLE IN PATIENT'S HOMES, SAFE AND EFFECTIVE RETINA THERAPY WILL REQUIRE IN-OFFICE EVALUATION AND MANAGEMENT.

environment. Given that many practices already employed injection-only visits for selected patients, we have been able to use that blueprint for how these visits can be modified to fit the moment. The only risk to this approach during the pandemic is a temporary compromise of individualized extension intervals, which is a minimal risk in the COVID-19 ecosystem.

Relying largely on telehealth to determine if a patient staying at home requires an intravitreal injection requires us to rely on subjective acuity data, because that is the only data that patients may be able to provide (that is, the patient's estimate of how vision has improved, stabilized, or worsened). Given that no modern clinical trial has used patient-gathered visual acuity as a primary or secondary endpoint, and that no patient can acquire imaging data to inform a treatment decision, it would be essentially impossible to make a reliable determination of the need for treatment via telemedicine.

Eligibility for extension of treatment interval in a neovascular AMD treat-and-extend regimen is determined by the presence of exudative activity on OCT or hemorrhage on exam. Here, too, we cannot get any information via telehealth to make a determination on whether a patient's treatment interval can be extended.

Consider a patient who reports a red eye after an injection. A telehealth appointment—even one in which high-definition video is used to examine the patient—would not provide the information needed to determine if the patient's condition is due to an abrasion, uveitis, high IOP, endophthalmitis, or something unrelated to an injection or surgical procedure. Similarly, we lack in-home tonometry or OCT to gather data in these situations.

There is great promise for telemedicine in retina, but until home diagnostics are validated and approved for commercial marketing and available in patient's homes, safe and effective retina therapy will require in-office evaluation and management.

DECIDING ON DIABETES TREATMENT

The homogeneous nature of neovascular AMD allows us to make some generalized statements regarding treatment during the COVID-19 era. When we consider patients with diabetic eye disease, however, there are important differences in the manifestations of disease that may influence treatment decisions in this climate.

Take, for example, a patient receiving treatment for severe nonproliferative diabetic retinopathy (DR). If this patient forgoes treatment for 8 weeks, he or she will probably be fine. The same could be said for deferring a patient with potentially sight-altering diabetic macular edema (DME) for 4 to 8 weeks.

For patients with proliferative DR (PDR), treatment interruptions pose a risk for a significant and long-lasting vision-threatening complications such as a vitreous hemorrhage. Binocular patients may be able to tolerate a PDR event in one eye, but monocular patients with PDR are at the highest risk for a substantial alteration in independence and livelihood if treatment is interrupted, as even transient vision loss secondary to a hemorrhage would result in de facto blindness until the hemorrhage clears or the patient undergoes vitrectomy.

Patients with DME whose disease is managed with anti-VEGF therapy present an interesting scenario during the era of social distancing. These patients, particularly if they are receiving frequent treatment (ie, every 4 or 6 weeks), could potentially benefit from a single dose of the dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan). This could obviate the need for injections for 3 to 4 months. Initial intravitreal steroid use appropriately mandates an IOP check at approximately 6 to 8 weeks after the injection, but that short office visit would require contact with the physician only if IOP measurements are high.

Retina specialists with concerns about an increased risk for cataract development in phakic patients after steroid exposure may find solace in data from the MEAD trial,

which reported that "longer exposure to repeat [dexamethasone intravitreal implant 0.7 mg] was associated with an increase in cataract development or progression in phakic eyes."[1] A single Ozurdex dose, in the MEAD population, did not significantly increase the risk of cataract development in this trial. In other words, if a physician uses a single dexamethasone intravitreal implant 0.7 mg as bridge therapy during the COVID-19 era in a patient with DME, the risk for that patient of developing a cataract is not high.

Considering one-time sustained-release steroid therapy in pseudophakic patients who normally undergo anti-VEGF therapy is an easier decision. Because the risk of cataract development is off the table, the chief factor to consider is glaucoma risk.

THE FUTURE

Telemedicine may become more applicable to retina practice in the near future. Availability of home-based imaging platforms could make remote treatment decisions easier and more reliable. Publicly-based ophthalmic imaging platforms (akin to automated blood pressure cuffs found in pharmacies) that rely on artificial intelligence software to interpret images could alert retina specialists to new or worsening pathology, and those images could allow doctors to begin analyzing patient data before the patient presents to the office. Until then, our field is wise to continue to use the reliable, validated, clinic-based imaging platforms we have at our disposal.

In the same way that we have to use the technologies familiar to us while we weather the storm, we must consider the potential short-term advantages of all of the treatment options we have at our disposal. ■

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Some patients require monthly therapy and others do not. Those who are enrolled in prn regimens may be shifted to more targeted treat-and-extend (TAE) protocols. TAE regimens have been shown in wet AMD populations to significantly reduce treatment burden without adversely affecting visual acuity compared with monthly protocols[1] and have been shown to produce significantly better visual acuity results compared with prn regimens.[2] Given forecasted trends in population, perhaps TAE regimens will be sought sooner in some patients with wet AMD.

Some clinicians may be more inclined to leave small volumes of fluid as detected on imaging in wet AMD patients if it means that patients will have to attend fewer clinical sessions during heightened periods of infectious disease transmission. Patient treatment patterns will always remain a function of individual patient needs, but variables such as fluid volume may play a larger role going forward.

In patients with diabetic macular edema, use of long-acting intravitreal implants is often considered. Patients who do not fit the treatment profile for these therapies should be excluded from initial consideration, but some clinicians who have not considered steroid treatment in appropriate patients as a first-line therapy may be inclined to do so in a post-COVID world. Given the fact that diabetes is included among the underlying conditions that may exacerbate COVID-19 infections, clinicians should consider how they can best mitigate the risk of infection while still providing optimal ophthalmic care.

WHAT COMES NEXT?

It remains to be seen how the coronavirus will permanently affect retina practice. Perhaps the changes we have undergone will be fleeting and, in years to come, will seem like quirks from a bygone chapter of medical history. But I suspect that many of the changes we have already implemented will remain in some form, and that the framework we use to understand the interaction of infectious disease and retina care will become more symbiotic than siloed. ■

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Telehealth Implementation in Retina Practices During COVID-19

Retina specialists can use this time to gather information about the feasibility of teleophthalmology consultations.

BY EDWARD S. LU, BA; S.K. STEVEN HOUSTON III, MD; EHSAN RAHIMY, MD; AND JOHN B. MILLER, MD

The COVID-19 pandemic has magnified the issues facing access to specialty care in retina and ophthalmology. With social distancing measures in place, retina specialists must remotely meet the needs of complex patients while accurately diagnosing them and treating their diseases. Although it has not yet been widely adopted in routine practice, teleophthalmology has the potential to increase access to care, decrease costs, and improve outcomes for patients when in-person visits are not feasible.[1]

NASA demonstrated one of the first applications of teleophthalmology in 1987, when astronauts' retinal vessels were monitored in real time during space flights with the use of a portable video fundoscope.[2] Telemedicine has been applied at the domestic and global levels to detect retinopathy of prematurity and diabetic retinopathy, with a focus on rural and underserved urban areas as well as developing nations with limited resources for systematic screening and monitoring.[3,4] It has also been used in monitoring glaucoma.[5]

Given the aging population in the United States, an expansion of telemedicine applications for monitoring and treating eye disease may help to improve compliance and reduce the burden of vision loss on the country's health care system. The COVID-19 crisis, because it demands innovative solutions for clinical care delivery, has accelerated the need for and implementation of long-standing principles of teleophthalmology.

A hybrid telemedicine/in-person approach may have the greatest impact during the COVID-19 crisis and after it subsides. In order to have a robust conversation about the potential of teleophthalmology, clinicians and leaders must first understand

AT A GLANCE

- Changes to CMS regulations and improved telehealth conferencing platforms have arrived to meet the COVID-19 pandemic.
- Hybrid Tele-EyeCare (HyTEC), model for teleophthalmology, combines in-office advanced imaging with virtual patient-physician consultation.
- Barriers to implementation include assurances that reimbursements will continue into the future as well as patient comfort with this new medium and new technologies.

the potential telemedicine platforms, the related billing and reimbursement concerns, and the ways telemedicine may continue to prove fruitful to patients and providers in the future.

TELEMEDICINE PLATFORMS

During the COVID-19 crisis, telemedicine has allowed retina specialists in various practice environments to remotely perform follow-up visits and consultations, allowing patients to avoid busy offices and exposure to the coronavirus.

Improvements in videoconferencing platforms allow them to be used for high-quality virtual interactions between patients and providers. The general population's increased exposure during the past decade to video-based communication with friends and family via platforms such as Facetime and Google Duo has made patients more accepting of video consultations. Zoom for Healthcare offers improved privacy (ie, multilayer security with AES-256 encryption), integration with Epic electronic health record (EHR) applications, and the ability to use enhanced collaboration features such as screen-sharing and annotations (Figure).[6] Privacy in a health care setting remains paramount. One should note that *Zoombombing*, wherein unwanted third parties gain access to Zoom meetings, has occurred on the free version of Zoom.

Application- and browser-based telehealth platforms each have advantages and drawbacks. Application-based platforms such as EyecareLive are easy to use and allow patients to check in ahead of time. However, patients need to download and install the application, which may be challenging for some. With browser-based platforms such as doxy.me, patients are provided with a URL for connection, which may be easier.

A HYBRID APPROACH

COVID-19 has changed all of our lives since mid-March, but some of the most important changes to health care occurred in early March.

On March 6, CMS announced an expansion of telemedicine coverage and reimbursement, along with several key regulatory changes. These changes extended telemedicine coverage to all Medicare beneficiaries. Previously, the use of telemedicine was restricted to rural and underserved populations. CMS now considers telehealth visits the same as in-person visits, and reimbursements for telehealth video visits are the same as for in-office visits. This change has allowed our field to leverage improved video technology against expanded coverage options to minimize exposure to office-based settings.

Traditional clinical workflows included overbooked schedules, long wait times, packed waiting rooms, and patient interaction with multiple staff members. COVID-19 requirements have allowed us to reassess retina clinics. This new reality emphasizes precautions for patients, staff, and physicians that include symptom screening, temperature checking at the door, "virtual waiting rooms" in patients' vehicles or outside, lighter schedules (to accommodate social distancing), and increased sanitizing measures (ie, performing hand hygiene, wearing masks, etc.).

As patients start seeking medical care, after weeks of stay-at-home orders and mandatory rescheduling of nonemergent patients are lifted, we anticipate a surge in patient volume during the next few months. We need not only to make patients safe, but also to make them *feel* safe. As precautionary measures and social distancing become a way of life, we must think about new paradigms and protocols that allow us to deliver care while enhancing safety and efficiency.

To accommodate patients in our practice, we have developed a novel hybrid telemedicine approach we call Hybrid Tele-EyeCare (HyTEC). HyTEC combines efficient, in-office advanced imaging with virtual consultation to facilitate diagnosis and decision-making for complex retinal diseases. Within a week of the CMS announcement regarding the changes in telehealth requirements, we piloted this hybrid approach at the Florida Retina Institute, a large retina-only private practice, under the leadership of S.K. Steven Houston III, MD (CEO and co-founder of HealTheia), with his partners Matt Cunningham, MD: Benjamin Thomas, MD; Elias Mavrofrides, MD; Jaya Kumar, MD; and Abdallah Jeroudi, MD, all implementing these visits into their clinics.

In this practice model, Dr. Houston runs two parallel clinics. One is an in-office clinic, for patients who need injections or other routine procedures and

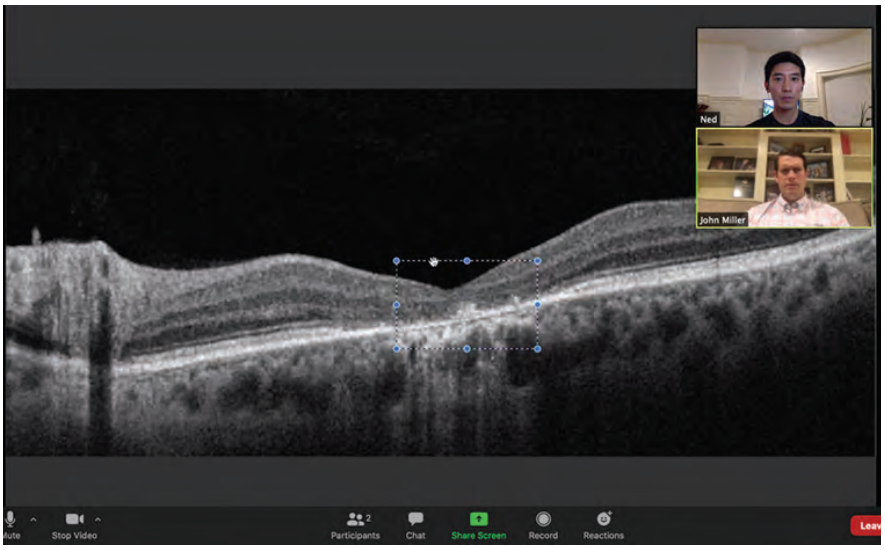

Figure. In a Zoom for Healthcare video call with a retina patient (in this example, the author Edward S. Lu, BA), the screen sharing feature allows display of an OCT image.

PARADOXICALLY, VIRTUAL ENCOUNTERS MAY FORCE MORE FACE-TO-FACE INTERACTION AND SMALL TALK COMPARED WITH IN-PERSON VISITS IN A BUSY CLINIC. TYPING INTO EHR SOFTWARE, DICTATING TO SCRIBES, AND INTERACTING IN A DARK ROOM WILL NOT BE PRESENT DURING TELEMEDICINE CONSULTS.

for new patients or returning patients with new symptoms.

The approximately 20% to 30% of patients who require chronic disease monitoring (ie, patients with diabetic retinopathy, dry age-related macular degeneration, etc.), are seen via the HyTEC model. While Dr. Houston sees patients at the in-office clinic, one or two technicians are imaging patients at a separate office. Between in-office patients or on a separate day, Dr. Houston connects virtually with the patients who underwent imaging at the remote office.

This hybrid approach makes his in-office clinic lighter and more efficient—patient time spent in the clinic is down to 30 minutes, for example—while still allowing him to consult with the same number of patients, generating revenues similar to an all-in-office consultation model.

The HyTEC approach to telemedicine has been successfully deployed in a multispecialty hospital-affiliated private practice (Palo Alto Medical Foundation) with Dr. Ehsan Rahimy and a large academic center with Dr. John Miller (Mass Eye and Ear). At these multispecialty group practices, the hybrid approach has also worked for ophthalmologists outside of retina. Each site has offered different advantages and obstacles to implementation. Regardless of the practice setting, key steps include:

- a reliable and secure video communication platform
- remote access to retinal imaging, ideally with merged or at least simultaneously accessible databases
- pre-visit education of administrative and clinic staff, physicians, and patients about the new virtual visit workflows
- flexibility to meet patient needs and adequately deliver care in a safe manner
- appropriate patient selection

Hybrid telemedicine platforms such as HyTEC may be viable options for retina practices, given the test-heavy nature of our clinical evaluations. We expect that the hybrid approach will extend further into ophthalmology (eg, comprehensive, cornea, glaucoma) and optometry with time.

BILLING AND REIMBURSEMENT

With the cancellation of elective procedures, retina practices must adapt to patient needs while remaining financially solvent. The loosening of CMS billing restrictions on telehealth services provided an opportunity for retina providers to remotely deliver individualized care.

Under the emergency waiver, CMS temporarily expanded Medicare telehealth coverage to allow patients across the country to receive telehealth services in their homes. Previously, Medicare covered only patients in designated rural areas who left their homes to receive telehealth care at medical facilities. The loosening of billing restrictions encourages providers to explore the use of allowed Medicare telemedicine services, which include outpatient visits for new or established patients (codes 99201-99215), brief (5-10 minutes) virtual check-ins for established patients (G2012, G2010), and e-visits for established patients through an online patient portal (99421, 99422, 99423, G2061, G2062, G2063).[7]

HyTEC visits allow the physician to bill for E/M or eye code visits based on medical decision-making while also billing imaging (OCT, 92134; and fundus photography, 92250) based on local coverage determinations and Medicare administrative contractor regulations.

Although CMS's expansion of telehealth coverage is encouraging, maintained reimbursement for virtual visits is necessary, at least in the short to medium term, so that practitioners can continue investing resources into building their telemedicine capacity. Continuing to reimburse virtual visits at parity with office visits will promote telehealth innovation and buy-in.

THE FUTURE OF TELEMEDICINE

When practices again begin to operate at full capacity, telemedicine may help to alleviate a post-outbreak surge in clinic visits. Off-hour and weekend virtual visits can accommodate patients who are concerned about coming into the office with relaxed social distancing measures.

Paradoxically, virtual encounters may force more face-to-face interaction and small talk compared with in-person visits in a busy clinic. Typing into EHR software, dictating to scribes, and interacting in a dark room will not be present during telemedicine consults.

The long-term buy-in to teleophthalmology by patients and

providers in the aftermath of COVID-19 remains to be seen. Changing patient management processes, reimbursement concerns, and disruption of traditional practice structures will present barriers to telemedicine implementation. However, among the early adopters coauthoring this article, our experience shows that many patients embrace this change and value its enhanced safety and efficiency.

This quote from one of our patients captures this sentiment: "I've been following up with a retina specialist for years. This was the best and most efficient visit I have ever had. Why have you not been doing this before? Can I continue to have all my visits with HyTEC?" ■

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CONVENTION UPDATES

Many ophthalmology meetings set to be held this spring have been rescheduled, postponed, or canceled. This list is accurate as of *Retina Today's* press date in mid-May.

STREAMING LIVE

AMERICAN SOCIETY OF RETINA SPECIALISTS ANNUAL MEETING

Dates for Live Streams: July 24-26, 2020
For More Info: Visit asrs.org/annual-meeting

RESCHEDULED

DUKE AVS

Duke Eye Center
Durham, North Carolina
New Date: September 11-12, 2020
To Register: Visit MedConfs.com

AMERICAN-EUROPEAN CONGRESS OF OPHTHALMIC SURGERY (AECOS) EUROPE

Florence, Italy
New Date: June 3-6, 2021
To Register: Visit aecosurgery.org

MILANO RETINA MEETING 20/20

Milan, Italy
New Date: September 11-12, 2020
To Register: Visit APMeetings.com

VITREEX (VITREO RETINAL EXPERIENCE)

Congress Center
Venice, Italy
New Date: October 29-31, 2020
To Register: Visit APMeetings.com

POSTPONED

BOSTON 20/20: CONTROVERSIES IN RETINA

Tufts Medical Center
Boston, Massachusetts
Rescheduling Information Forthcoming

CANCELED

MOTOR CITY RETINA

Marriott Renaissance Center
Detroit, Michigan

PROCEEDING AS PLANNED

AAO ANNUAL MEETING: RETINA SUBSPECIALTY DAY

Sands Expo Center
Las Vegas, Nevada
November 13-14, 2020
To Register: www.aao.org/annual-meeting/education/retina

AAO ANNUAL MEETING

Sands Expo Center
Las Vegas, Nevada
November 14-17, 2020
To Register: www.aao.org/annual-meeting

NEED UP-TO-THE MINUTE UPDATES?

For the latest on meetings in retina, visit RetinaToday.com/events.asp.
For the latest on meetings in all of eye care, visit Eyewire.news/events.

COVID-19 UPDATES

Bryn Mawr Communications, industry members, and eye care professionals are coming together to create programs that connect the vision community in these unprecedented times.

bmc vision

Hear from your eye care peers as they navigate the uncertain waters of the COVID-19 crisis through special audio- and visual-based editions of our podcast programs.

Listen in your podcast feed, or watch the episode at: eyewire.news/covid-19

COVID-19 COVERAGE

Hosts: Gary Wörtz, MD; Blake Williamson, MD


- *The Impact on Training Programs*
- *Eye Care Industry's Response*
- *A New Normal: Predictions for the Aftermath*

NEW RETINA RADIO

COVID-19 COVERAGE

Hosts: John Kitchens, MD; Allen Ho, MD


- *Which Procedures Are Essential?*
- *COVID-19: The Global View*
- *Opportunities for Telehealth*

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COVID-19 COVERAGE

Hosts: Jessilin Quint, OD, MS, MBA, FAAO; Rachael Wruble, OD, FAAO


- *First-Hand Accounts From COVID-19–Positive ODs*
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