

# RT

## Retina Today

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# COVID-19 IN RETINA

PERSONAL PROTECTIVE  
EQUIPMENT 101

SUMMARIES OF THE LATEST  
LITERATURE ON COVID-19

REPORTS FROM THE GROUND: HEAR HOW RETINA DOCTORS IN  
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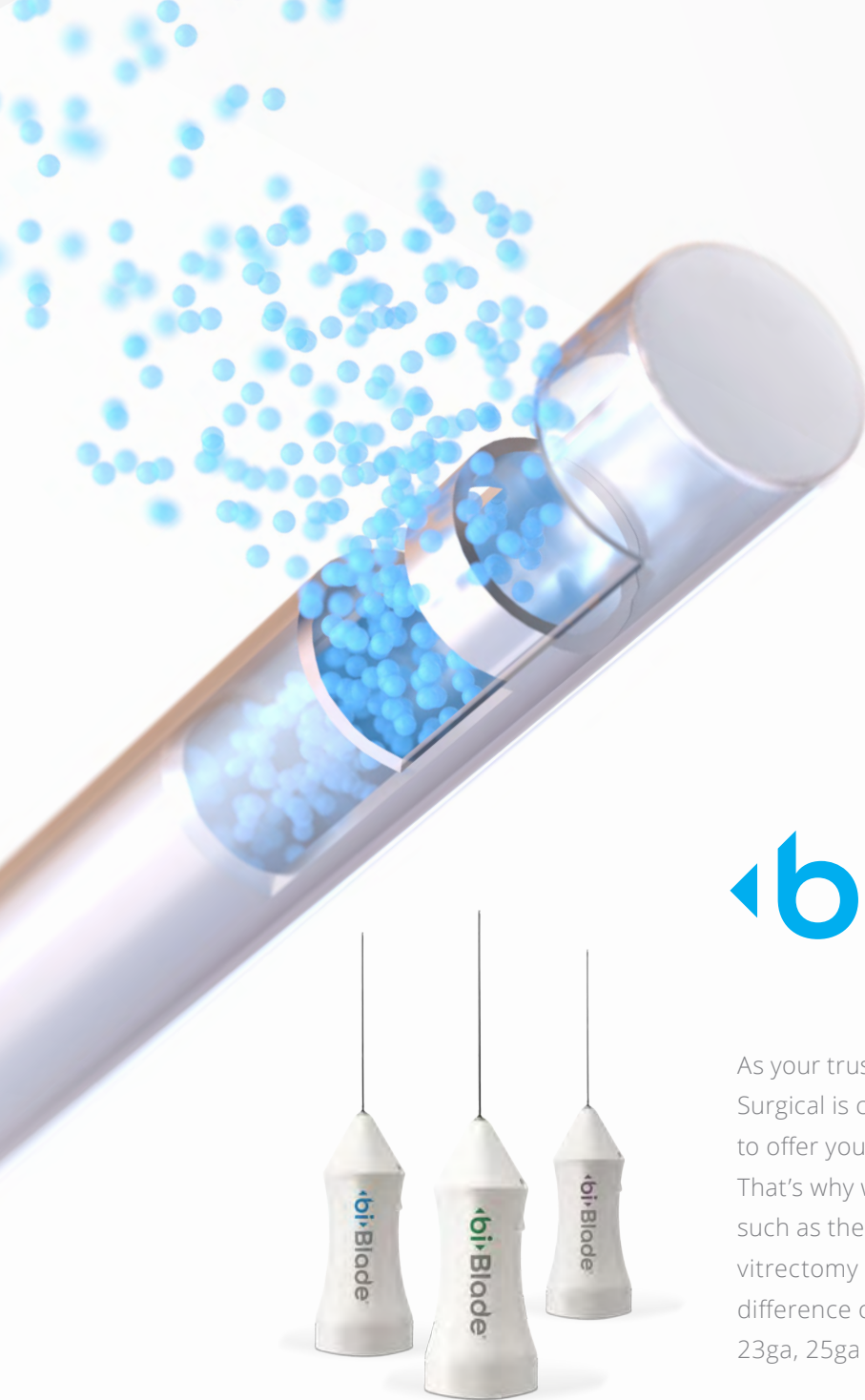
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# COVID-19 IN RETINA



No one imagined the medical landscape shifting so suddenly. Even the epidemiologists whose models and predictions forecast a dark path forward would have had a difficult time conceptualizing the on-the-ground fallout of a pandemic that tears through nations and rips at the fabric of institutions. As a profession, as a country, as a planet, we were underprepared, maladroit, and, in some cases, tragically overconfident.

Some find it easy to fold. But that is not in our nature as physicians. In war, doctors run to the front lines as soldiers retreat. In this war, we find ourselves again at the front lines. Our cover fire takes the form of N95 masks; the bullet we dodge is a tenacious strain of coronavirus.

The worldwide retina community has worked diligently for decades to foster a sense of common cause. Now, amid a maelstrom of uncertainty, it is time to cash in the dividends of our hard work. We must prop each other up, inspire each other, and push our colleagues to weather this storm. We will survive this, armed with education and collaboration.

Bryn Mawr Communications, the publisher of *Retina Today*, is an ally you can rely on during this crisis. Eyewire, a BMC entity, has built a COVID-19 resource center that tracks the latest news for ophthalmologists. *Retina Today's* ongoing coverage

of COVID-19 will examine how this new reality intersects with retina. BMC's Eyetube podcast series *New Retina Radio* and *Ophthalmology Off the Grid* are broadcasting live webinars and blasting bi-weekly episodes with reports from ophthalmologists around the world, covering everything from the response in hot zones to practice management during a disaster.

In this issue of *Retina Today*, we check in with doctors in cities where the fallout has been severe, view how personal protective equipment can be used and reused, and review the latest research on COVID-19. We did this because the members of the retina community wanted to share their knowledge—and because we knew you needed as much information as possible.

The months ahead will be difficult. When you need to hear from your peers for education, for news, or for comfort, we hope you'll turn to us. ■

CHIEF MEDICAL EDITOR

ASSOCIATE MEDICAL EDITOR

# COVID-19 IN RETINA

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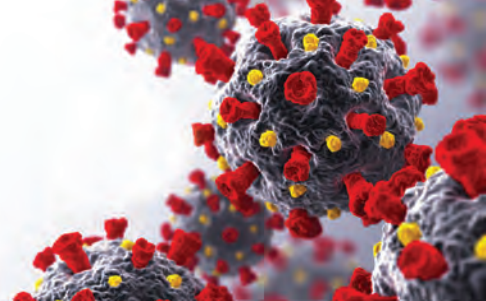
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Even as the COVID-19 pandemic rages, news in ophthalmology doesn't stop. *Retina Today* collected these news items unrelated to the COVID-19 crisis.

## SURGERY COMBINED WITH TPA INJECTION IMPROVED VISION AFTER SUBMACULAR HEMORRHAGE

In patients with fovea-involving subretinal macular hemorrhage from a range of causes, pars plana vitrectomy (PPV) combined with injection of tissue plasminogen activator (tPA) and pneumatic displacement of the hemorrhage improved visual outcomes, a retrospective study found.<sup>1</sup> Reviewing all patients (N = 37) with submacular hemorrhage who underwent PPV with subretinal tPA injection at the New York Eye and Ear Infirmary of Mount Sinai, the authors found that 61% of patients experienced some form of vision improvement, and 42% gained 3 or more lines of vision at 3 months' follow-up. Pathologies represented in the patient population included exudative macular degeneration, undifferentiated choroidal neovascularization (CNV), polypoidal choroidal vasculopathy, traumatic CNV, and proliferative diabetic retinopathy.

"This study comprises the most diverse patient cohort reported of subretinal macular hemorrhage treated with PPV and subretinal tPA, with no significant difference in outcome found between subgroups," the study authors stated.

1. Wilkins CS, Mehta N, Wu CY, Barash A, Deobhakta AA, Rosen RB. Outcomes of pars plana vitrectomy with subretinal tissue plasminogen activator injection and pneumatic displacement of fovea-involving submacular haemorrhage. *BMJ Open Ophthalmol.* 2020;5(1):e000394.

## RNA THERAPY FOR USHER SYNDROME SHOWED SIGNS OF EFFICACY IN INTERIM ANALYSIS

An investigational RNA therapy was safe and showed signs of efficacy in two of eight patients treated in a planned interim analysis of a phase 1/2 clinical trial, the therapy's developer announced in March. The clinical trial of QR-421a (ProQR Therapeutics) includes patients with Usher syndrome and with nonsyndromic retinitis pigmentosa (nsRP) due to

USH2A exon 13 mutations. The Stellar trial is a randomized, single-ascending-dose, multicenter longitudinal 24-month study comparing active versus sham procedures. In the interim analysis of a total of 14 patients in two cohorts (3-month results of cohort 2 and 9-month results of cohort 1), one treated patient in each cohort "demonstrated benefit across multiple concordant outcome measures," the company said in a press release.

In the same release, the company noted that it expects delays in this and other clinical trials due to disruptions caused by the COVID-19 pandemic. The company said it plans to resume dosing patients as soon as it is practical to do so.

## NEW LEADERSHIP POSITIONS AT TWO OPHTHALMIC COMPANIES

Two companies involved in ophthalmic drug development, Iveric bio and Clearside Biomedical, announced leadership changes in March.

Iveric bio announced the appointment of Pravin Dugel, MD, as its executive vice president and chief strategy and business officer, effective April 1. In this role, Dr. Dugel will help shape Iveric bio's business development strategy and will report to Glenn P. Sblendorio, the company's chief executive officer and president. The company is developing avacincaptad pegol (Zimura), a complement factor C5 inhibitor, for the treatment of geographic atrophy in patients with dry age-related macular degeneration (AMD).

Dr. Dugel was previously managing partner at Retinal Consultants of Arizona and the Retinal Research Institute; a clinical professor at the USC Eye Institute, Keck School of Medicine, University of Southern California; and a founding member of Spectra Eye Institute in Sun City, Arizona. He is a member of *Retina Today's* Editorial Advisory Board.

Clearside Biomedical announced that George Lasezkay, PharmD, JD, was appointed president and CEO and will continue to serve on the company's board of directors, effective March 1. He had been the company's interim CEO since



April 2019. Clearside is developing triamcinolone acetonide for suprachoroidal injectable suspension (Xipere), which was licensed by Bausch + Lomb in October of last year. The company expects to resubmit its new drug application for the drug to the US FDA in the first quarter of 2020 and believes the FDA will review the submission within 6 months of receipt.

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## ENROLLMENT COMPLETE IN ADULT DOSE GROUPS IN ACHROMATOPSIA PHASE 1/2 TRIALS

Planned enrollment has been completed in all adult dose groups in phase 1/2 clinical trials of gene therapies for patients with achromatopsia due to mutation in the ACHM *CNGB3* or ACHM *CNGA3* genes, trial sponsor Applied Genetic Technologies Corporation (AGTC) announced in March. The company reported interim 6-month data from the dose-escalation cohorts of its ongoing ACHM phase 1/2 clinical trials in January. Results in both studies demonstrated encouraging signs of biologic activity, the company said in a press release. AGTC plans to report interim data from all adult dose groups in the second half of 2020 and to use the data to inform decision-making regarding moving to phase 3 trials.

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## CASE REPORT: CHOLESTEROL-LOWERING DRUG MAY CAUSE SCLERITIS

The cholesterol-lowering drug alirocumab (Praluent, Regeneron) may cause scleritis with uveal effusion, according to a case report in *Annals of Internal Medicine*.<sup>1</sup>

Alirocumab is a human monoclonal antibody that increases the expression of low-density lipoprotein receptor and decreases levels of low-density lipoprotein cholesterol. It is used as a second-line treatment for adults whose high cholesterol levels are not controlled by diet and statin treatment.

“The case we report here is unusual, because alirocumab-induced scleritis seems to be rare but also because alirocumab does not target a molecule in the immune pathway,” the report’s authors said. “We believe that our patient’s complex autoimmune history, which includes thyroiditis and antinuclear antibodies, may have predisposed her to this reaction. We also believe that additional cases may be expected with the general increase in monoclonal antibody therapy.”

1. Breazzano MP, Chen RWS. Scleritis with uveal effusion from alirocumab [published online ahead of print March 10, 2020]. *Ann Intern Med*.

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## RETINA GROUP OF WASHINGTON NOW AFFILIATED WITH PRISM VISION GROUP

Prism Vision Group in March announced an agreement to add a new partner, the Retina Group of Washington, a provider of retinal and macular care in Washington, DC; Virginia; and Maryland. Terms of the deal were not disclosed.

Prism Vision Group is a physician-led organization that provides comprehensive support services to eye care organizations. The Retina Group of Washington includes 32 physicians practicing at 17 locations.

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## FDA APPROVED SUSTAINED-RELEASE BIMATOPROST FOR GLAUCOMA

The FDA in March approved Allergan’s new drug application for its bimatoprost implant 10 mcg (Durysta). The implant is the first intracameral biodegradable sustained-release implant indicated to reduce IOP in patients with open-angle glaucoma or ocular hypertension, according to Allergan. The FDA approval was based on results from the two 20-month (including 8-month extended follow-up) phase 3 ARTEMIS studies, in which the implant reduced IOP by approximately 30% from baseline over the 12-week primary efficacy period. ■

# 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.



**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](https://eyewire.news/covid-19)*



**Hosts: Gary Wörtz, MD;  
Blake Williamson, MD**



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



**Hosts: John Kitchens, MD;  
Allen Ho, MD**



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



**Hosts: Frank Won, OD;  
Jessilin Quint, OD, MS, MBA, FAAO**



- First-Hand Accounts From COVID-19-Positive ODs
- Taking Advantage of Telemedicine
- Handling Employee Layoffs and Furloughs

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## EYEWIRE.NEWS: ONGOING COVID-19 COVERAGE

As the eye care profession and industry, and the world at large, navigate these rapidly changing and challenging times and respond to the recent demand for credible educational resources, Bryn Mawr Communications is prioritizing the production and distribution of news and information dedicated to COVID-19 and its impact on eye care. To this end, Eyewire has launched a special section dedicated solely to coverage of COVID-19 that will be updated throughout the day. Sign up for email newsletters to be notified when critical updates are posted, and see updated coverage online at [eyewire.news](https://eyewire.news).

## RETINA VENDORS TEMPORARILY EXTEND PAYMENT TERMS

Genentech, Regeneron, Allergan, and Novartis are extending payment terms in response to the COVID-19 crisis.

George A. Williams, MD, discussed the terms of extended payment announced by Genentech and Regeneron on a recent episode of the podcast *New Retina Radio*, and details were confirmed in statements from the companies received by Eyewire. Regeneron has extended payment terms to 150 days (from 100 days), and Genentech has extended payment terms to 120 days (from 60 days).

A company statement from Allergan received by Eyewire indicated that the company will provide an additional 30-day grace period on top of its usual 120-day period for orders placed on or before March 23. A Novartis statement received by Eyewire said that it will extend terms but did not provide details.

## FDA AUTHORIZED EMERGENCY USE OF ANTI-MALARIA DRUGS FOR CORONAVIRUS TREATMENT

The FDA issued an emergency use authorization at the end of March that allows hydroxychloroquine sulfate and chloroquine phosphate products donated to the Strategic National Stockpile (SNS) to be distributed and used for hospitalized patients with COVID-19. The drugs will be distributed from the SNS to states for doctors to prescribe to adolescent and adult patients hospitalized with COVID-19, as appropriate, when a clinical trial is not available, the FDA announced. The emergency use authorization requires that known risks and drug interactions of the two treatments be made available to health care providers and patients.

Even before the FDA's action, some doctors and hospitals were investigating the use of chloroquine phosphate and hydroxychloroquine to treat patients infected with COVID-19, according to an article in *The Wall Street Journal*. Both antimalarial drugs have shown early signs of improving the symptoms of some patients diagnosed with COVID-19, based on reports

by doctors and researchers in South Korea, France, and China, the newspaper reported. The University of Minnesota recently began enrolling patients in a US clinical trial to test hydroxychloroquine against the coronavirus. Investigators there are evaluating the drug in health care workers and people who live with infected patients. Meanwhile, chloroquine is among the drugs to be studied in a multinational trial announced by the World Health Organization, and it has been used as a treatment in China and South Korea.

## CMS TO MAKE EXPEDITED ADVANCE PAYMENTS AVAILABLE TO MEDICARE PROVIDERS

CMS is expanding its accelerated and advance payment program for Medicare participating health care providers and suppliers, to ensure that they have the resources needed to combat COVID-19.

"With our nation's health care providers on the front lines in the fight against COVID-19, dollars and cents shouldn't be adding to their worries," CMS Administrator Seema Verma said in a March 28 press release. "Today's action will ensure that they have the resources they need to maintain their all-important focus on patient care during the pandemic."

Accelerated and advance Medicare payments provide emergency funding and allow providers to address cash flow issues; they are typically offered in the event of natural disasters. In the current situation, CMS is expanding the program for all Medicare providers throughout the country during the public health emergency related to COVID-19, according to the press release. Payments can be requested by hospitals, doctors, durable medical equipment suppliers, and other Medicare Part A and Part B providers and suppliers.

Earlier in March, CMS announced that it was relaxing reporting requirements for clinicians, providers, and facilities participating in Medicare quality reporting programs. Specifically, CMS is granting exceptions from reporting requirements and extensions to clinicians and providers participating in Medicare quality reporting programs with respect to upcoming measure reporting and data submission for those programs.

## BIG DATA TAPPED TO STUDY VIRUS

Adaptive Biotechnologies and Microsoft will leverage their existing partnership mapping population-wide adaptive immune responses to diseases at scale to study COVID-19, the companies jointly announced in a March press release. Finding the relevant immune response signature may advance solutions to diagnose, treat, and prevent the disease, augmenting existing research efforts that focus primarily on the biology of the virus, the companies stated. The data generated is to be made freely available to any researcher, public health official, or organization around the world via an open data access portal.

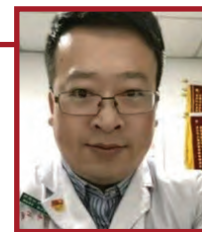
## SECOND SIGHT ANNOUNCES EMPLOYEE LAYOFFS, INTENT TO WIND DOWN OPERATIONS

Second Sight Medical Products, maker of the Argus II Retinal Prosthesis System and other visual prosthetic systems, announced in March that, in response to the impact of the global COVID-19 pandemic on the company's ability to secure financing, it intends to "pursue an orderly wind down" of operations. The company planned to lay off approximately 84 of its 108 employees, and additional layoffs are expected to be made at a later date based on the company's level of operations, according to a press release.

Second Sight also announced that Matthew Pfeffer, a member of the board and chairman of the audit committee of the board, was appointed acting CEO to guide the company through the wind down period. ■

## IN MEMORIAM

### LI WENLIANG, MD



Li Wenliang, MD, an ophthalmologist in Wuhan, China, died on February 7. Dr. Li died from COVID-19 after first raising alarm about the novel coronavirus in late December. He was 34 years old.

On December 30, 2019, Dr. Li used the Chinese social media platform Weibo to message his medical school colleagues about a cluster of illnesses resembling severe acute respiratory syndrome (SARS). Seven patients at his place of employment, Wuhan Central Hospital, had been quarantined as a result, he said. Days after his message was posted, Chinese officials forced Dr. Li to sign a document stating that he had made false comments that had "severely disturbed the social order."<sup>1</sup>

Following the incident, Dr. Li returned to work, where on January 10 he contracted the virus from a glaucoma patient who was asymptomatic for COVID-19. Dr. Li was hospitalized on January 12 and tested positive for COVID-19 on February 1. After numerous conflicting reports regarding his condition, the hospital confirmed Dr. Li's death on February 7.

In an interview with *The New York Times* after his diagnosis, Dr. Li said, "If the officials had disclosed information about the epidemic earlier, I think it would have been a lot better. There should have been more openness and transparency."<sup>2</sup>

Dr. Li is survived by his wife, who is pregnant, and their first child. On March 11, the World Health Organization declared the coronavirus outbreak a global pandemic.

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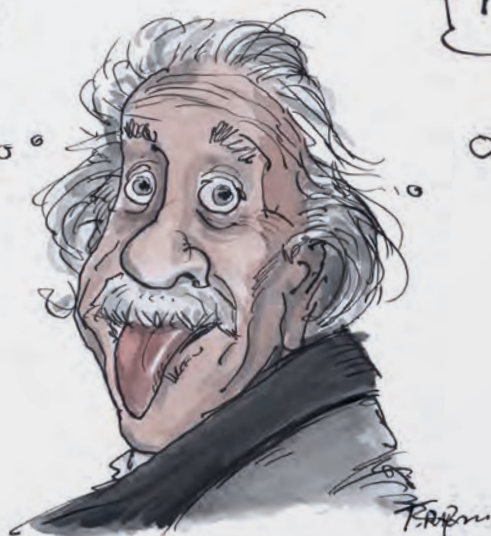
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# PRESUMED TENOFOVIR TOXICITY



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 48)*

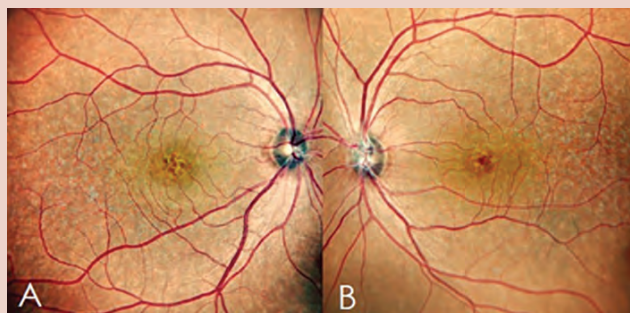


Figure 1. Central fundus photographs (right eye, A; left eye, B) show pigmentary anomalies surrounding disc and macula.

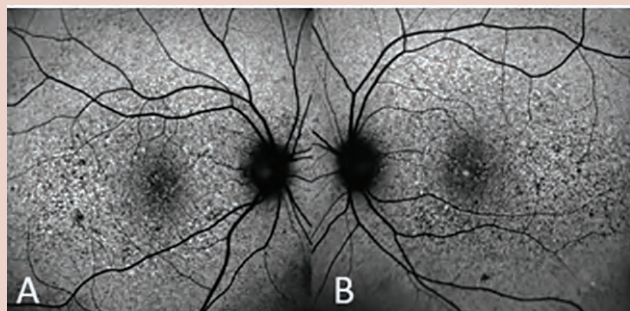


Figure 3. Autofluorescence images (right eye, A; left eye, B) show area of increased autofluorescence surrounding the macula and optic disc.



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

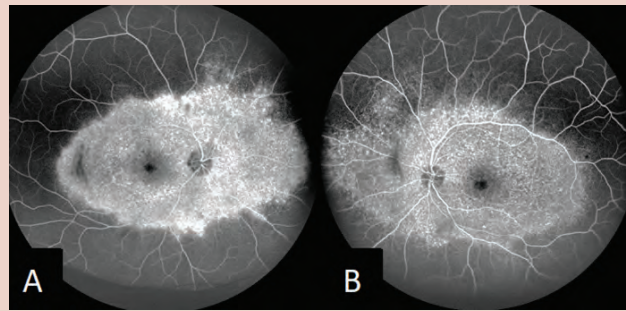
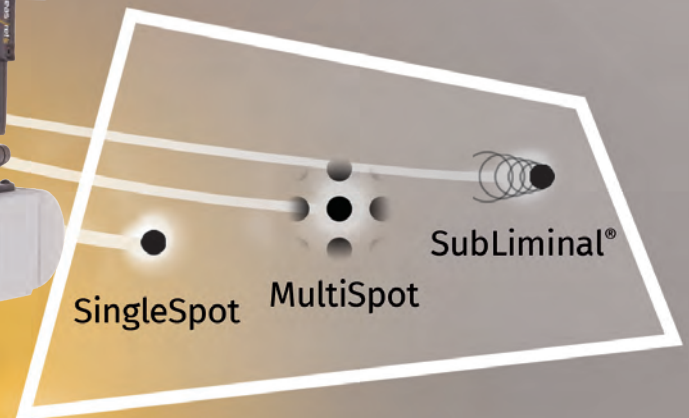


Figure 4. Fluorescein angiography (right eye, A; left eye, B) shows multiple areas of window defects.

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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

**O**CT 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.<sup>1</sup> 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.<sup>2–5</sup> It was hypothesized that hypercyanescent plaques on ICG angiography corresponded to MNV.<sup>4</sup> 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.<sup>6,7</sup> 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,<sup>4</sup> but with the advantage of using noninvasive OCTA as a screening test.<sup>6,7</sup>

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.<sup>8</sup> 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.



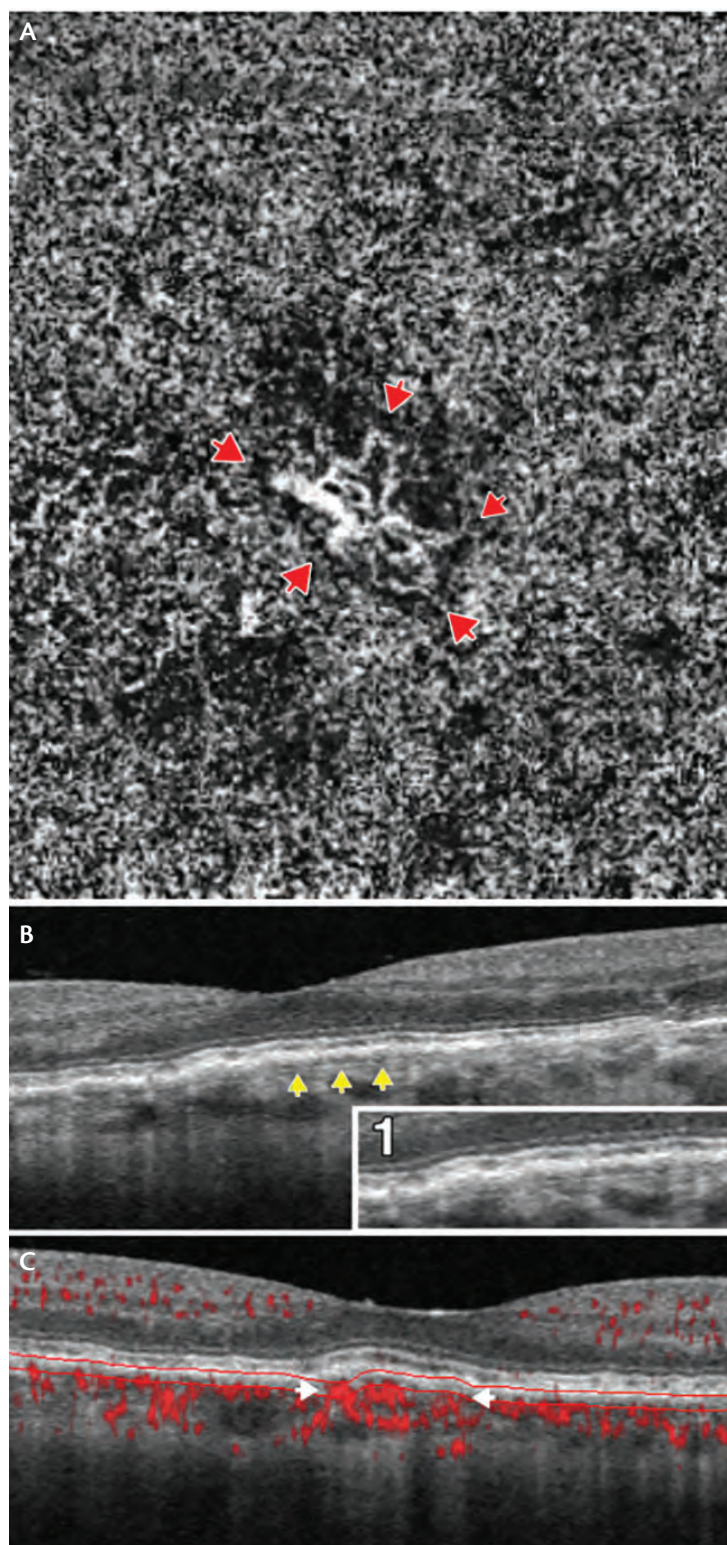


Figure 1. Nonexudative MNV in an eye with intermediate AMD. En face SD-OCT choriocapillaris slab shows an MNV complex (A, red arrows). Corresponding structural OCT demonstrates a double-layer sign (B, yellow arrows point to Bruch membrane), seen in greater detail on image B1. Structural OCT with flow 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.<sup>6</sup> 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 OCT; however, this study was not specifically designed or powered to investigate the effects of anti-VEGF therapy in nonexudative MNV.<sup>9</sup>

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.<sup>10</sup> 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.<sup>10-12</sup>

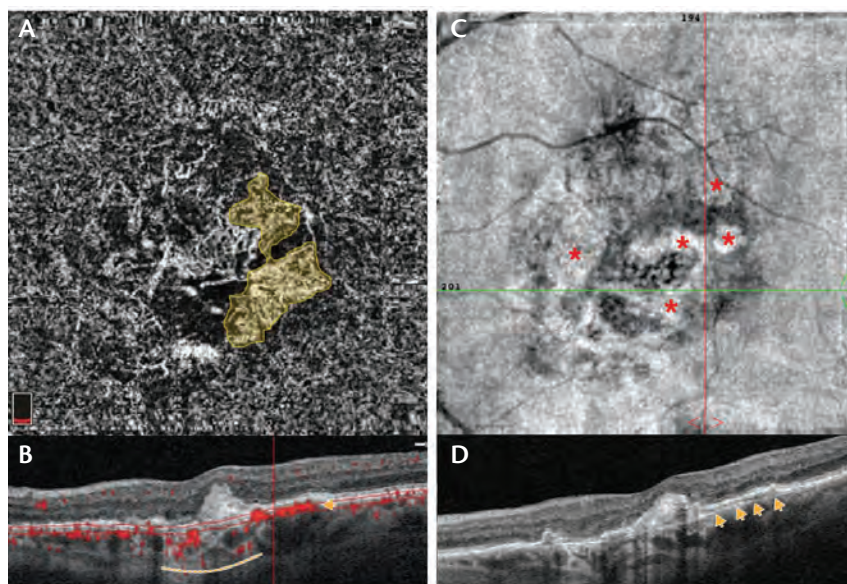
Utilizing OCTA for detection of nonexudative MNV in the presence of GA may be challenging, as the RPE atrophy and choriocapillaris defect on the GA site lead to hypertransmission of signal. This makes choroidal vessels from deeper layers more evident and more likely to be confounded with the MNV complex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

#### 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.<sup>13,14</sup> 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<sup>15,16</sup> and are significantly increased in advanced stages of AMD compared with intermediate stages.<sup>17</sup> Flow deficits on OCTA are also increased in areas of drusen emergence and enlargement.<sup>18</sup> Furthermore, choriocapillaris nonperfusion is increased in areas of reticular pseudodrusen



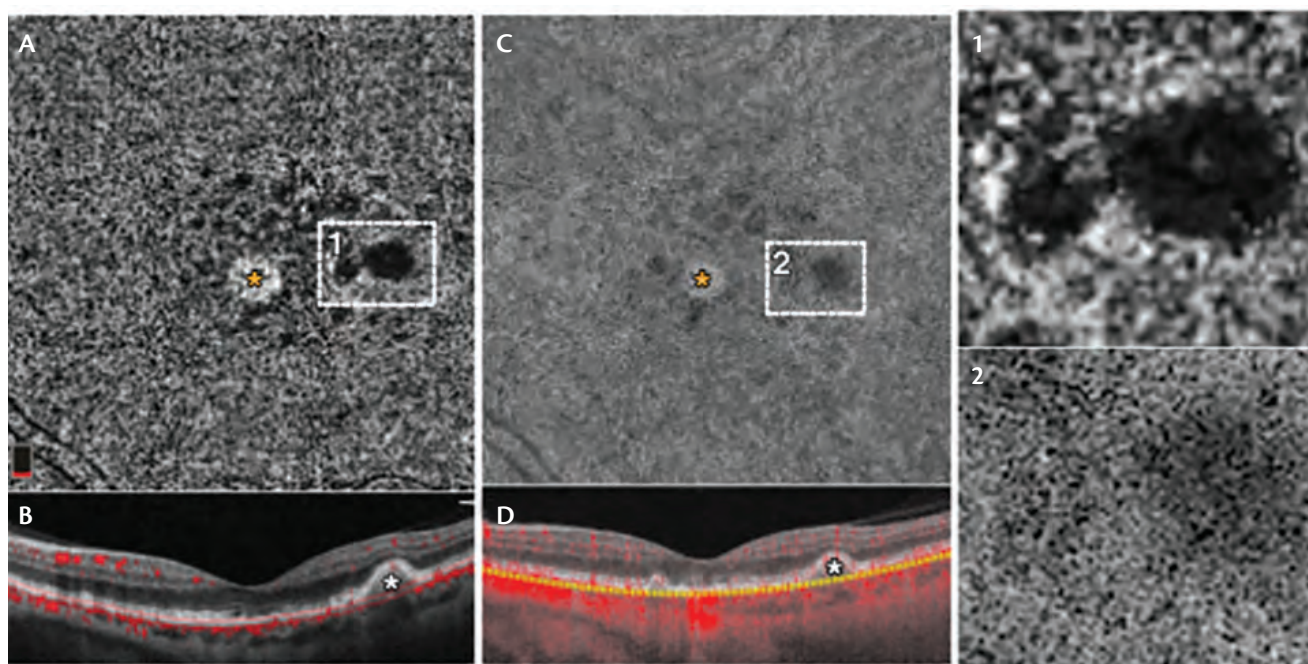


**Figure 2.** Nonexudative MNV in an eye with GA. En face SD-OCT choriocapillaris slab shows an MNV complex (yellow contour) adjacent to GA (A). Note larger choroidal vessels seen in the topography of the choriocapillaris. Corresponding structural OCT demonstrates a double-layer sign with flow overlay 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.<sup>19</sup> 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).<sup>20</sup> 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.<sup>21,22</sup>

## 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.<sup>23</sup> It has also been shown that areas around GA presented higher flow deficits,<sup>23,24</sup> and that areas of nascent GA may be associated with focal choriocapillaris flow impairment.<sup>25</sup>

## 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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# ULTRA-WIDEFIELD IMAGING FOR AGE-RELATED MACULAR DEGENERATION



This technology holds promise for the study of peripheral abnormalities.

BY NATHAN ARBOLEDA, BS; JOHN B. MILLER, MD; INES LAÍNS, MD, PHD; DEEBA HUSAIN, MD; AND PATRICK OELLERS, MD

**A**ge-related macular degeneration (AMD) is the leading cause of blindness in the elderly in the developed world. AMD is a multifactorial disorder with dysregulation of complement, lipid, inflammation, and extracellular matrix pathways all implicated in its pathogenesis. The diagnosis and classification of AMD has always been focused on the macula, given the historical understanding of the disease. Thorough investigation of the periphery with photography has been limited by an inability to reliably and efficiently capture high-quality photographs of the peripheral retina as well as the absence of a standardized, systematic method of interpreting peripheral retinal changes. Although it is well established that drusen and changes in the retinal pigment epithelium occur in the peripheral fundus of patients with AMD, the clinical significance and impact of these developments on disease progression has yet to be elucidated.<sup>1-3</sup>

Advances in ultra-widefield (UWF) fundus photography have made it possible to obtain high-resolution images of both the peripheral and central retina in a rapid manner. UWF imaging has already been used for the diagnosis and grading of diabetic retinopathy, and its use for AMD research is currently being explored.<sup>4</sup>

## PERIPHERAL CHANGES MAY HAVE A ROLE TO PLAY NOT ONLY IN THE DIAGNOSIS OF AMD BUT ALSO IN DETERMINING PROGNOSIS OF DISEASE.

Investigators have demonstrated that peripheral abnormalities seen on pseudocolor and autofluorescence UWF imaging are more prevalent in patients with AMD than in healthy patients.<sup>2</sup> Systematic study and correlation of these findings with genotypic polymorphisms, disease states, or functional markers could facilitate diagnosis, prognosis, and treatment. Of note, peripheral drusen have proven associations with complement factor H genotypic variations.<sup>5</sup>

### A NOVEL GRID SYSTEM

UWF imaging for AMD opens up an entirely new field of research. UWF cameras can produce high-quality images with minimal distortion, allowing clinicians to assess perimacular

and peripheral lesions such as drusen, peripheral reticular changes, atrophy, fibrosis, choroidal neovascularization, and subretinal drusenoid deposits in eyes with AMD. The Early Treatment of Diabetic Retinopathy (ETDRS) grid has enabled the standardization and classification of macular disease. With that in mind, we have developed a novel grid that can be used to study the macular area and the peripheral retina simultaneously in AMD patients.

The novel grid system has 12 zones—three concentric circles centered on the fovea, with horizontal lines dividing nasal and temporal retina and vertical lines dividing superior and inferior retina. The concentric circles create four zones that extend radially.<sup>6</sup> The first and smallest is the macular



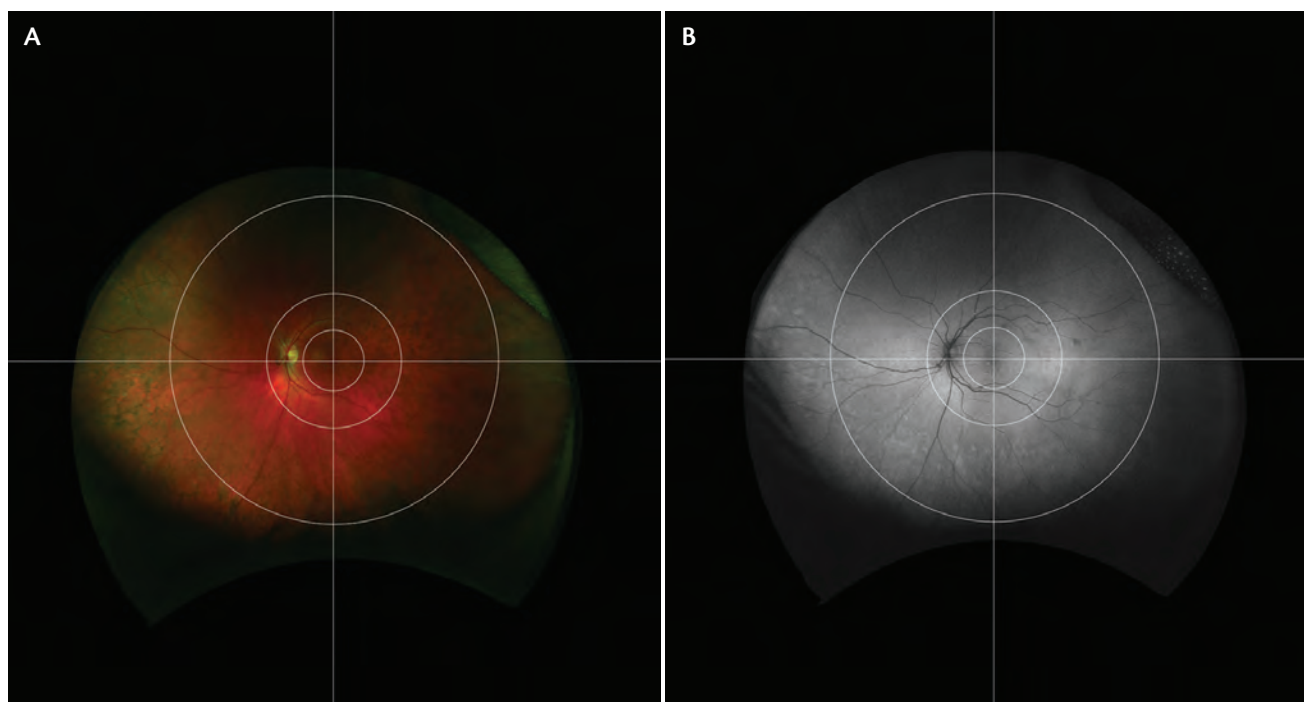


Figure. This novel UWF grid enables synchronous study of peripheral and posterior AMD lesions. Pseudocolor UWF image (A) demonstrates peripheral reticular pigmentary changes, and autofluorescence UWF image (B) shows granular increased FAF changes in a patient with AMD.

zone, which is based on the ETDRS grid as used in the landmark Age-Related Eye Disease Study. The perimacular zone extends beyond the macula and involves the optic disc. It permits a precise description of pathology that is not quite in the macula but is not far enough out to be considered peripheral. The midperiphery and far periphery are divided by a circle marked by vortex veins. This division allows a more precise description of peripheral findings.

The specific way in which images are captured using UWF technology (Optos) requires an ellipsoid mirror that can distort the peripheral retina. This distortion can make measurements of anatomic irregularities imprecise and increase the number of artifacts. Geometric distortion correction software, available in recently manufactured cameras, addresses these problems to create a reproducible, color-corrected view of the retina that can be reliably applied from patient to patient. Combining our grid with distortion-corrected UWF images offers a reproducible way to study anterior and posterior regional abnormalities in AMD.

#### **DARK ADAPTION LINKED TO ULTRA-WIDEFIELD PERIPHERAL CHANGES IN AMD**

UWF imaging in AMD research has already yielded fresh insights into the clinical significance of peripheral AMD lesions. For example, in a prospective, cross-sectional study by Láins and colleagues, the technology helped to demonstrate an association between dark adaption time and

peripheral reticular pigmentary changes in patients with AMD.<sup>7</sup>

Patients with AMD and a control group (N = 128 eyes) were included in the study. Images on UWF and fundus autofluorescence (FAF) modalities were assessed by two graders who were tasked with detecting perimacular, midperipheral, and far peripheral abnormalities. Patients were evaluated with a standard dark adaptation protocol. The study authors observed that the presence of reticular pigmentary changes on UWF fundus photography in the midperipheral and far peripheral zones were associated with more prolonged time to dark adaptation. Similarly, decreased and mottled FAF patterns in the midperipheral zone were also associated with longer dark adaptation times (Figure). Of note, reticular pigmentary changes were found exclusively in patients with AMD in this study.

Although visual acuity is widely used as a measure of retinal function, it is most useful for the detection of late-stage AMD. Time to dark adaption can identify individuals with AMD and successfully stratify them by disease severity. As detailed above, our group reported a statistically significant correlation between patients with prolonged dark adaptation and peripheral reticular pigmentary changes. The significance of this association suggests that peripheral changes may have a role to play not only in the diagnosis of AMD but also in determining prognosis of disease.

*(Continued on page 25)*

# TECHNIQUES FOR IN-OFFICE VITREORETINAL PROCEDURES



Avoiding trips to the OR when possible can improve efficiency in this busy time.

BY MARÍA H. BERROCAL, MD; CLAUDIA AMARAL, BS; AND LUIS A. ACABÁ-BERROCAL, BS

Complications of vitreoretinal surgeries are common; they include residual or recurrent vitreous hemorrhage, recurrent retinal detachment from inadequate gas fill, anterior chamber (AC) silicone oil complications, and retained perfluorocarbon liquid (PFCL).

Taking patients back to the operating room is burdensome and costly and may be difficult in periods of emergency, such as the COVID-19 pandemic. We present procedures for in-office management of several common complications that may help to expedite visual recovery and reduce the burden of a return to the OR.

## VITREOUS HEMORRHAGE AFTER VITRECTOMY

Residual or recurrent vitreous hemorrhage is the most common complication of diabetic vitrectomy.<sup>1,2</sup> Although many residual hemorrhages tend to spontaneously clear within a week, dense or recurrent hemorrhages may persist, impairing both the patient's vision and our ability to examine the retina.<sup>3,4</sup> The presence of red blood cells in the AC signals spontaneous clearing, indicating that there is communication between the vitreous cavity and the AC.<sup>4</sup> Therefore, if no red blood cells are seen in the AC, it is unlikely that spontaneous clearing will occur.

In these cases, two in-office procedures—Nd:YAG laser peripheral capsulotomy and fluid-air exchange—can be performed in order to expedite the clearing of vitreous hemorrhage and avoid the burden and costs associated with additional surgery.<sup>2,5</sup>

## Nd:YAG Peripheral Capsulotomy

Nd:YAG laser peripheral capsulotomy is a technique that can expedite the clearing of residual or recurrent vitreous hemorrhages in pseudophakic eyes only.<sup>2</sup> The technique involves first dilating the eye sufficiently so that the peripheral capsule of the lens can be visualized. The laser is then used to create an opening in the area peripheral to the IOL. Usually, two areas around the optic are treated, and the openings created should be 2 to 3 mm in diameter. The purpose is to create a free passage between the vitreous cavity and the AC to allow the hemorrhage to clear spontaneously.<sup>2,6</sup> Both the anterior and posterior capsules of the lens are opened in an area clear of the IOL (Figures 1 and 2).

In a series of 50 eyes treated with this modality, 96% achieved clearing at 6 months.<sup>7</sup> This technique is appropriate only in cases of mild to moderate hemorrhage; for denser hemorrhages, a fluid-air exchange should be performed.<sup>3</sup>

## WATCH IT NOW



A video of fluid-air exchange recorded in real time.

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## In-Office Fluid-Air Exchange

In-office fluid-air exchange is a simple technique used to expedite clearing of postvitrectomy residual or recurrent vitreous hemorrhages.<sup>3-5,8</sup> It can be performed in both phakic and pseudophakic eyes.<sup>3</sup> This procedure can also be used when there is an inadequate gas fill by removing intravitreal fluid and replacing it with a minimally expansile mixture of the gas desired. B-scan ultrasonography must be performed in eyes in which the fundus cannot be visualized in order to rule out retinal detachment<sup>3,5</sup>; the technique for both is similar.

Although several techniques for in-office fluid-air exchange have been described in the past, these procedures are not commonly performed. Some techniques are cumbersome because



Figure 1. Diagram of areas of capsulotomy outside of the optic and haptic areas.



Figure 2. Photo of an eye after capsulotomy with opening highlighted in circle.



Figure 3. Patient is reclined 180° on a chair with head tilted. The needle is inserted through inferotemporal pars plana and the syringe positioned perpendicular to the floor.

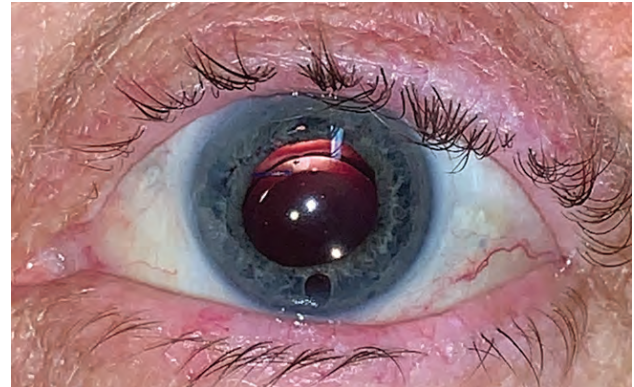


Figure 4. Inferior peripheral iridectomy in a pseudophakic eye with silicone oil.



Figure 5. Emulsified silicone oil in the AC of a pseudophakic eye 5 months after vitrectomy.

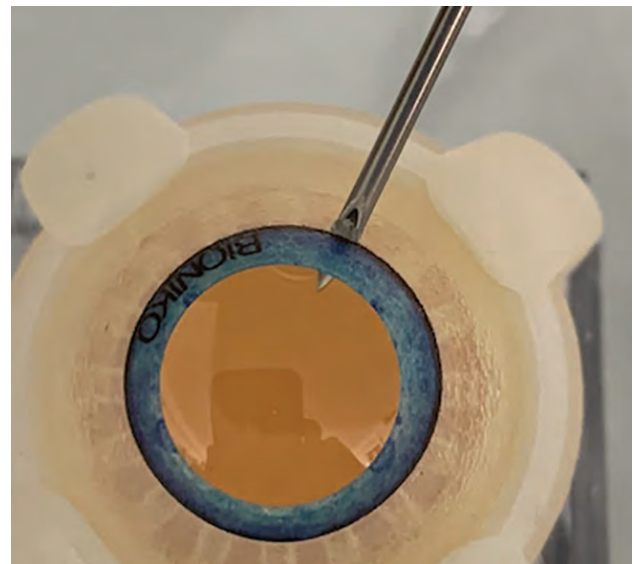


Figure 6. Technique for oil removal from the AC using a 19-gauge needle, shown in a Bioniko eye model. The hub of the needle must be simultaneously inside the silicone bubble in the AC and outside the eye at the limbus to allow oil to egress.



# IN-OFFICE FLUID-AIR EXCHANGE IS A SIMPLE TECHNIQUE USED TO EXPEDITE CLEARING OF POSTVITRECTOMY RESIDUAL OR RECURRENT VITREOUS HEMORRHAGES.

they involve the use of two syringes and are thus difficult for one person to perform. These include fluid-air exchange using air pump and gas-filled syringe as described by Lambrou et al, and two-needle pars plana injection/aspiration as described by Han et al.<sup>3,8</sup> I learned my preferred technique from Stanley Chang, MD, during my fellowship and have used it since; it is both simple and quick, as the entire procedure takes less than 2 minutes.

First, the eye is prepped in the same manner as it would for an intravitreal injection; a tetracaine drop is instilled, followed by two drops of 5% povidone-iodine. Several minutes later, a second drop of tetracaine or lidocaine gel is applied. After a 5-minute wait, a lid speculum is placed, and a drop of 5% povidone-iodine is instilled. The patient is reclined so that the head is parallel to the floor, and the head is tilted sideways so that the side of the eye being treated is also parallel to the floor.

A 10-cc syringe is filled with filtered air to 6 cc, the filter is removed, and a 27-gauge needle is placed on the syringe. The needle enters the eye in the inferotemporal quadrant, aimed at the center of the globe. The syringe is positioned perpendicular to the floor (Figure 3). Fluid is aspirated and will accumulate at the base of the syringe by gravity. Air is injected as the eye becomes soft, and then more fluid is aspirated.

This sequence is repeated several times until fluid no longer comes out of the eye, or alternatively until around 5 cc of fluid has accumulated in the syringe. The plunger is taken back to the starting point at 6 cc, and the

needle is removed as a sterile cotton tip applicator is pressed on the area. Finally, the vitreous is examined with the indirect ophthalmoscope and the IOP is measured.

A demonstration of a live fluid-air exchange can be found on Eyetube at [bit.ly/Berrocal0420](http://bit.ly/Berrocal0420).

## IOL OPTIC CAPTURE

Anterior dislocation of the IOL optic with iris capture can occur in pseudophakic eyes with gas tamponade or silicone oil.<sup>9,10</sup> This complication can usually be prevented by avoiding long-term dilation and stressing postoperative prone positioning. In an eye that has been prepped with tetracaine and a drop of 5% povidone-iodine, optic capture can be easily corrected at the slit lamp by inserting a 30-gauge needle through the limbus and pushing the optic posteriorly behind the iris. It is important that this complication be corrected as soon as it is noticed in order to prevent the formation of synechiae between the IOL and the iris.<sup>9,10</sup>

## SILICONE OIL COMPLICATIONS

In eyes filled with silicone oil, chronic hypotony or a closed inferior iridectomy can cause a shallowing of the anterior chamber in pseudophakic eyes or migration of silicone oil to the AC in aphakic eyes.<sup>11,12</sup> In the event of a closed inferior iridectomy, Nd:YAG laser can be used at high power (3-6 mJ) to open the closed iridectomy. Ideally, a large opening should be created to avoid reclosure (Figure 4).

In eyes with chronic hypotony with

an open inferior iridectomy and a shallow or silicone oil-filled AC, an OVD can be injected through the limbus at the slit lamp through a 27-gauge needle to reform the anterior chamber. This is done under topical anesthesia, with a lid speculum and 5% povidone-iodine prep.

## Silicone Oil in the AC

Migration of silicone oil into the AC can occur in the perioperative period in both phakic and pseudophakic eyes (Figure 5). Its removal is important, both to improve visual acuity and to prevent the formation of band keratopathy.<sup>13</sup> The best technique for removal was described by Soliman and Smiddy, and it can be performed at the slit lamp.<sup>12</sup> Topical anesthesia and 5% povidone-iodine are instilled in the eye and a lid speculum is placed. A 19-gauge needle on a syringe is utilized. The hub (the beveled opening) of the needle is placed halfway into the AC at the limbus between the 11:00 and 1:00 clock hours. The tip of the needle is inserted into the silicone bubble, and pressure is applied on the globe to express the silicone from the eye through the needle hub (Figure 6).<sup>12</sup>

## Retained PFCL

Retained PFCL is a common complication after its use with either gas or silicone oil tamponades. If the PFCL migrates to the AC, it can be removed at the slit lamp in one or several sessions.<sup>14</sup> The patient is asked to position prone to facilitate the migration of the PFCL to the AC. Under local anesthesia, with a lid speculum in place and the



patient at the slit lamp, the PFCL is aspirated with a 27- or 30-gauge needle on a 3-cc syringe. If significant PFCL is present, several sessions can be done some days apart.

## CONCLUSION

In-office techniques to manage complications of vitreoretinal surgeries are useful adjuncts to the armamentarium of every vitreoretinal surgeon. The techniques we describe here can help expedite recovery, aid visualization of the retina, prevent further AC complications, and decrease the burden and cost of a repeat visit to the OR. ■

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(Continued from page 21)

## CONCLUSION

UWF imaging is ushering in an exciting new era in AMD research. Future studies could provide important information on the clinical significance of peripheral abnormalities in AMD. ■

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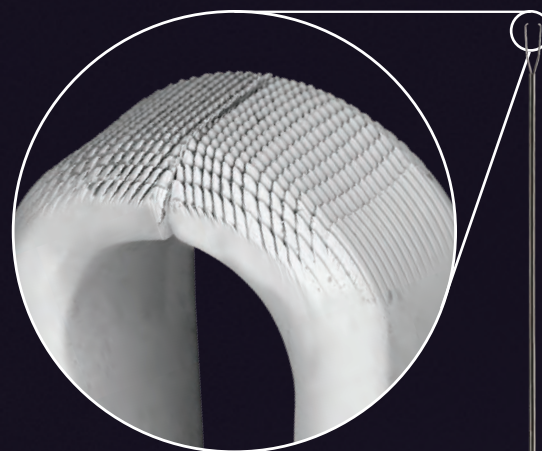
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**Reference:** 1. Data on File. Alcon Laboratories Inc; May 2018. 2. Data on File. Alcon Laboratories Inc; September 2017.



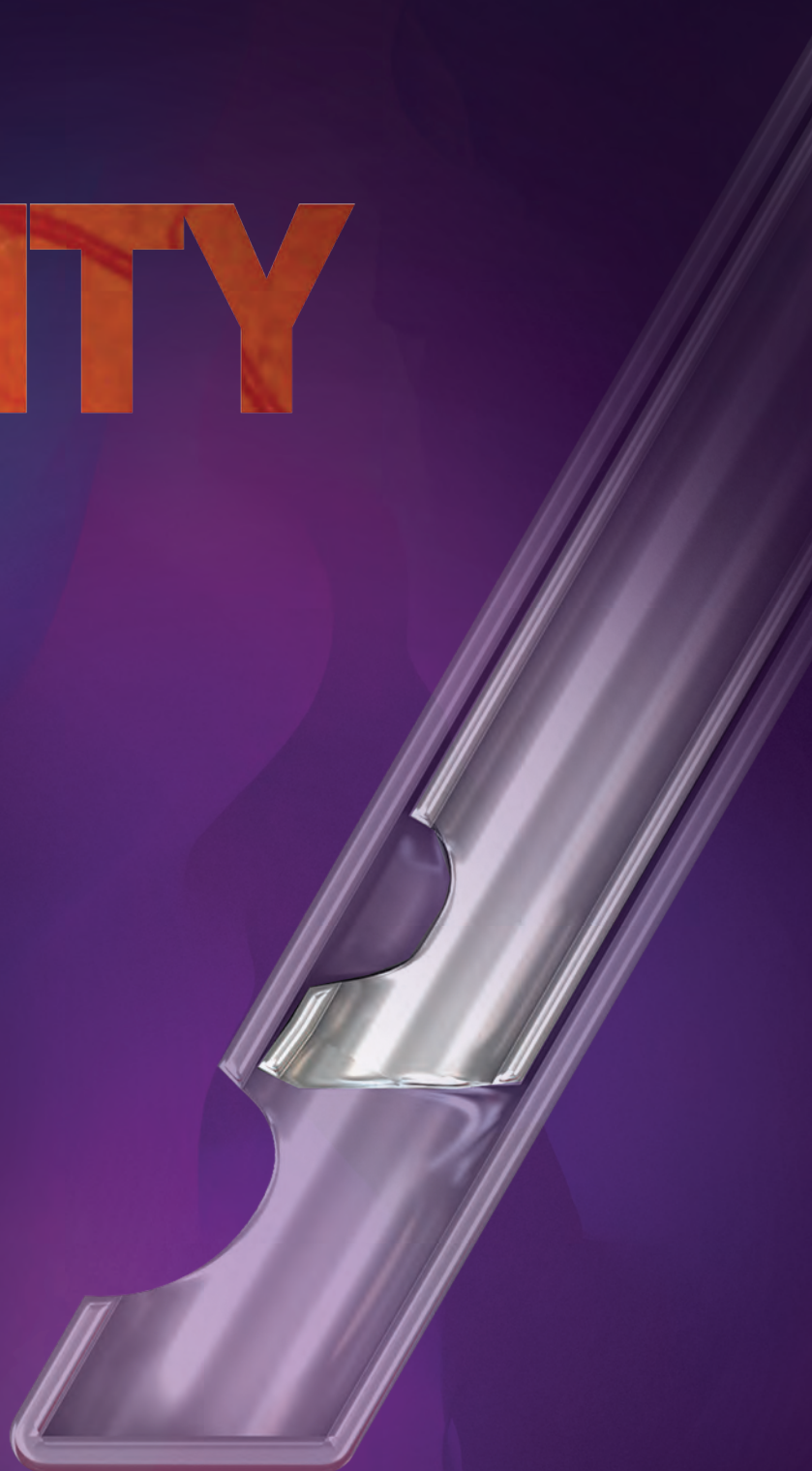
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**References:** 1. Irannejad A, Tambat S, Abulon DJK. Retropulsion and mass flow of 27-gauge vitrectomy probes: comparison of dual-blade/flat-tipped probes and single-blade/beveled probes. Poster presented at: 18th Congress of the European Society 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.

# COVID-19 Roundtable:

## How Retina Doctors From Around the United States Are Adjusting Their Clinics



A look at how retina practices have changed their protocols during the COVID-19 outbreak.

**MODERATED BY S.K. STEVEN HOUSTON III, MD; WITH YEWLIN CHEE, MD; ALLEN CHIANG, MD; JOHN B. MILLER, MD; EDWIN H. RYAN, MD; AND THANOS PAPAKOSTAS, MD**

*I asked some of my colleagues in the United States to share the early actions their practices have taken during the COVID-19 crisis. Doctors from a number of hot spots—from New York to Seattle—have shared their tactics. We also received a check-in from Minneapolis, a city with an experience different from that of outbreak zones but aware of the impending risk.*

*These interviews were conducted shortly before Retina Today went to press in early April. The physicians quoted in this piece may have altered their practices by the time you read this. Nevertheless, this roundtable serves as an important snapshot in time, and we believe you will find the tactics shared by these retina specialists helpful.*

*For the most up-to-date information as it pertains to retina specialists, visit the COVID-19 Member Update page on the ASRS website by visiting [bit.ly/ASRSCOV19](https://bit.ly/ASRSCOV19). For news as it pertains to ophthalmology during this crisis, visit [Eyewire.news](https://www.eyewire.com/news).*

—S.K. Steven Houston III, MD

### Yewlin Chee, MD

University of Washington School of Medicine  
Seattle



#### What precautions are you taking in your clinic to protect your patients?

We are using screening questions to evaluate for symptoms of fever and acute respiratory infection. Patients with symptoms who need to be seen are given a surgical mask to wear and are brought directly to a private room to minimize exposure to other patients. We have limited the number of people who enter the building by restricting clinic visits to only urgent and emergent patients, per AAO guidelines. We have a new rule regarding

patient caregivers that allows each patient to bring only one other person with them to an appointment.

We have limited imaging as much as possible to obviate patient movement after an initial workup. For example, if I use a treat-and-extend protocol for a wet AMD patient, I would consider forgoing an OCT and only administering an injection. I would then schedule the follow-up at the most recent interval where stability had previously been demonstrated.

#### What personal precautions are you taking to protect yourself as a physician?

I have relatives in Singapore who are ophthalmologists and who practiced during the SARS and COVID-19 outbreaks. When it was evident that community spread was occurring in Seattle, I found their experience to be useful in guiding our plan.



Our practice installed large slit-lamp shields that serve as an additional barrier between patient and physician. Providers wear surgical masks for exams. Personally, I also wear eye protection and change my scrubs after clinic. I wear my hair up in a bun and shower as soon as I get home.

**The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?**

The patients who remain on my schedule are chiefly those receiving anti-VEGF therapy for wet AMD, recent postoperative follow-up patients, or patients with new or worsening visual symptoms.

Many nursing homes in the Seattle area are on lockdown, and I have a handful of monocular patients with wet AMD who receive anti-VEGF injections in their seeing eye. They have missed their appointments as a result of the lockdown. In these cases, I call the nursing home and discuss the patient's case with the nursing home's medical staff to emphasize the importance of treatment and the potential consequences of missing injections. In some cases, these patients have come to the office for an expedited injection-only visit.

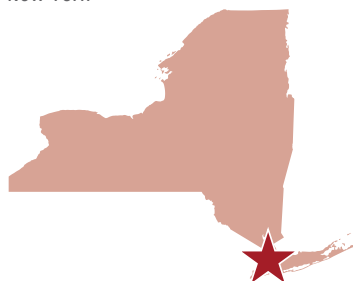
**The AAO has also advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?**

The University of Washington has a moratorium in place on nonurgent surgeries through mid-May. The cases that remain on my schedule include rhegmatogenous retinal detachments and secondary vitrectomies after open globe injuries. Macular holes (particularly if they are long standing), diabetic vitreous hemorrhage without additional macula-threatening pathology, membrane peels for epiretinal membranes or vitreomacular traction, silicone oil removal, and dislocated lens cases are nonurgent and can be rescheduled.

There are exceptions, however. Consider a scenario in which a monocular patient needs surgery that would allow him or her to perform the activities of daily living. In these situations, I think the case can be made to take the patient to the OR.

## Thanos Papakostas, MD

*Assistant Professor of Ophthalmology,  
Weill Cornell Medical College  
New York*



**What precautions are you taking in your clinic to protect your patients?**

Patients are screened before they come to the office for COVID-19 symptoms. Clinics are down-booked and appointments

are spaced to avoid crowding in waiting rooms. Patient workups and examinations occur in the same room to minimize patient movement in our practice. After a patient leaves a room, it is thoroughly cleaned, and patients are advised to wear masks.

**What personal precautions are you taking to protect yourself as a physician?**

I wear an N95 mask, goggles for eye protection, and gloves. If a patient has COVID-19 symptoms, I wear a gown, too. We installed protective shields at the slit lamps. Other measures include the usual ones, such as social distancing and frequent handwashing.

**The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?**

The cases that need to be seen are anything involving acute vision loss and acute eye pain. Regarding injections, I extend the interval in as many patients as I can; I continue to administer injections to patients on monthly therapy. Unfortunately, patients with AMD are vulnerable patients who, should they get COVID-19, have the highest chance for admission to ICU and mortality.

Before an appointment, I have a phone call with the patient in which I discuss the pros and cons of a visit, and a decision to proceed is made on a case-by-case basis. Postoperative patients are also seen in the clinic. There is a telemedicine initiative in our facility that works nicely for other ophthalmic subspecialties and medical specialties. For our field, given the nature of the exam and practice, telemedicine consultations are limited in general.

**The AAO has advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?**

Retinal detachment (macula-on and recent macula-off), endophthalmitis, intraocular foreign bodies, and open globe injuries must be addressed. Cases of epiretinal membranes, macular holes, diabetic tractional retinal detachments, vitreous hemorrhages without tears or detachment, IOL fixation, and floater removal are examples of nonurgent cases.

As we speak, our ORs are converted into ICU rooms to deal with the astronomic surge of critical COVID-19 patients in New York City.

## A Final Note

The first rule in medicine is, "Do no harm." The risk of an elderly, immunocompromised, or diabetic patient (which are the majority of the patients in every retina practice in the United States) contracting a catastrophic COVID-19 infection by coming to an eye care facility (especially in a hospital setting) is much higher than the risk of vision loss by delaying eye care for most of our patients. Please try to keep these vulnerable patients out of offices.

## S.K. Steven Houston III, MD

*Florida Retina Institute  
Orlando*



### What precautions are you taking in your clinic to protect your patients?

As a first step, we talked to all of our employees, explaining the risks of COVID-19 to our patients, staff, and physicians. We then established company-wide policies regarding basic procedures for hand

hygiene, office and equipment cleaning, and cleaning of high-touch points.

We reviewed common signs and symptoms of COVID-19 and reviewed when to discuss a situation with a supervisor. Employees with signs or symptoms of a cold, flu, or COVID-19 are asked to stay home from work and contact a supervisor for testing steps and information on when to return.

Second, we adjusted our schedules to prioritize patients that need intravitreal injections to maintain disease stability. We prioritize other urgent patients with potentially sight-threatening issues. We have rescheduled all other patients for a later time. Our staff calls all patients who were kept on the schedule to confirm their appointments. At the time of confirmation, we ask about signs, symptoms, and risks of COVID-19, and reschedule the patient if necessary.

After prioritizing patients that need to be seen, our clinical staff works with each individual physician on in-office precautions. By design, our practice does not have more than one physician in an office at the same time. As a result of having 19 offices, the same staff travels with each physician to each clinic. There is some cross-coverage during OR days, but we are attempting to limit potential spread among physician teams. Any staff member who develops fever, cough, nasal congestion, or shortness of breath will be asked to stay home and self-quarantine until the fever has subsided for 48 to 72 hours without medication and symptoms have improved.

As patients come into our offices, we are again asking about signs, symptoms, and travel history, including recent cruises. We use infrared thermometers to measure temperatures. Patients with concerning signs and symptoms, or who recently traveled to an endemic area or were on a recent cruise, are rescheduled. We ask all nonpatient visitors to wait outside unless they are required to be in the office, and we restrict children from accompanying parents or grandparents to appointments.

Patients are given the option to wait in their car, and

then we send them an SMS text message when the physician is ready. Personally, I have converted most of my rooms (approximately four to six rooms depending on the office) to procedure rooms to ensure faster throughput of patients.

### What personal precautions are you taking to protect yourself as a physician?

All of our clinical staff wear surgical masks and gloves and maintain strict hand hygiene measures, equipment cleaning, and high-touch point cleaning.

We have installed plastic shield barriers on slit lamps. However, I minimize my use of the slit lamp in favor of indirect ophthalmoscopy. Our practice approaches all patients as if they are asymptomatic COVID-19 positive. Per guidelines, I am wearing a surgical mask (preferably a N95 mask), eye protection (goggles/safety glasses), and gloves. These personal protective equipment (PPE) recommendations enhance the safety of the clinic for patients, staff, and physicians.

If a patient who visited our clinic reports symptoms and tests positive for COVID-19, the department of public health contacts the patient and finds out where he or she was during the past week. If a physician or staff member wasn't wearing appropriate PPE, then that physician or staff member will be sent home for self-quarantine for 2 weeks or until a negative test is confirmed, which can take 5 to 10 days to turn around.

### The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?

After discussions with my partners and several retina specialists around the country, our practice has decided to prioritize patients who need intravitreal injections for wet AMD, central retinal vein occlusion, proliferative diabetic retinopathy, and (in some cases) diabetic macular edema. Without injections, many of these patients risk worsening complications that may have permanent effects on vision.

Regarding specific patient visits, we are still prioritizing all injection patients, as well as emergent patients with acute posterior vitreous detachments and potential retinal tears, retinal detachments, and acute diabetic complications (eg, vitreous hemorrhage, new or progressing tractional retinal detachment). Additionally, individual patient characteristics need to be assessed on a case-by-case basis, notably in monocular patients with acute changes in their remaining functional eye.

### The AAO has advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?

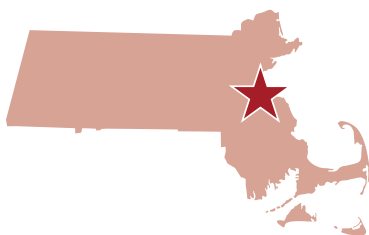
Not only has the AAO advised against performing nonurgent surgeries, but increasingly the hospitals and ASCs where we operate are limiting nonurgent surgeries to preserve anesthesia staff and equipment for potential surges

in COVID-19 cases in hospitals. As a result, we are focusing on urgent cases with sight-threatening complications that will have consequences if not treated in a timely manner. This includes all rhegmatogenous retinal detachments, endophthalmitis, retained lens fragments, and progressing tractional retinal detachments.

As discussed above, cases with extenuating circumstances, notably monocular patients, should be approached on a case-by-case basis. For full thickness macular holes that are acute, I recommend initial observation for 4 to 6 weeks and surgery if the condition is unresolved. Elective cases such as macular puckers, vitreous opacities, and dislocated IOLs are rescheduled.

### John B. Miller, MD

*Assistant Professor of Ophthalmology,  
Harvard Medical School  
Boston*



#### What precautions are you taking in your clinic to protect your patients?

We have significantly reduced appointments in all clinics since March 16. Visits have been limited to

postoperative evaluations, anti-VEGF injections, and urgent evaluations for events such as retinal detachment, PDR, and ruptured globes. All staff are required to wear surgical masks, and patients wear masks for injections (which was common practice for some physicians prior to the COVID-19 outbreak). We are also spreading out schedules to minimize the number of patients in the waiting room.

#### What personal precautions are you taking to protect yourself as a physician?

I have tried to limit my trips into the hospital by consolidating multiple clinic days into one or two half-day sessions. I wear a mask, gloves, and eye protection for all patient encounters. At this point, we have to assume that asymptomatic carriers are bypassing any screening that is occurring at the front door.

#### The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?

It's a tough call because we don't know how long it will be until we can return to clinical operations. I think it is reasonable to postpone some injection patients for a few weeks or a month, and we have done that when possible. Retinal detachments and retinal tears still have to be seen right away, as do endophthalmitis, acute retinal necrosis, and posttraumatic injuries. Fortunately, such cases normally arise

on call, and we have consolidated those urgent visits to a single physician on call.

#### The AAO has also advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?

We consider any case involving an epiretinal membrane, macular hole, dislocated IOL, or chronic retinal detachment to be nonurgent. We consider some diabetic cases nonurgent, and those are determined on a case-by-case basis.

### Allen Chiang, MD

*Mid-Atlantic Retina and Wills Eye Hospital  
Philadelphia*



#### What precautions are you taking in your clinic to protect your patients?

The majority of retina patients are elderly, and many have significant medical comorbidities,

making them the most vulnerable to COVID-19. One of our highest priorities is to reduce their risk of exposure in the office by trimming schedules down to those with active or urgent and emergent issues and implementing some changes to the office environment. We are actively reviewing charts and rescheduling patients who can be reasonably postponed to a later date. Before patients arrive, they are asked screening questions to identify those who are either symptomatic or at increased risk (eg, if the patient or someone who lives with them has traveled internationally, on a cruise, or to the New York metro area in the past 2 weeks). Those who are symptomatic or have had exposure are instructed not to come to the office but instead to contact their PCP or self-quarantine, respectively. If they screen positive on our questionnaire and are experiencing acute vision loss, they are directed to our Wills Eye Hospital location for further evaluation as either a presumed or confirmed COVID-positive individual.

In the office, we use noncontact thermometers to screen every individual before entering the office, including physicians and staff. Chairs in the waiting area and break room are spaced 6 feet apart. We have also instituted a virtual waiting room, which allows patients to wait in their cars until notified that it's their turn to be seen. Family or friends are asked not to accompany the patient into the clinic unless it's out of a medical necessity. Staff who are in and around exam lanes have been reduced.

We have sought to increase awareness by utilizing various platforms, including our website, social media, and call center patient liaisons. In addition to understanding the CDC, AAO, and state public health guidelines, we want patients to



be apprised of the steps we are taking to ensure each visit is as safe as possible. Coordinating with our referring doctors to focus on patients with problems of an urgent nature is important, too.

### What personal precautions are you taking to protect yourself as a physician?

We have installed large breath shields on the slit lamps. Rooms are disinfected after each patient is examined, with special attention paid to high-touch surfaces. Mobile phones are wiped down periodically throughout the day and social distancing is observed throughout the office. Doctors and staff who work within 6 feet of patients don PPE consisting of protective glasses, masks (surgical, or N95 if available), and gloves. These steps are taken even with asymptomatic patients because there is evidence that asymptomatic or presymptomatic infections are fueling the pandemic.

When I get home, I change my clothes in the garage; sanitize anything that I touched including the interior surfaces of my car, bags, and belongings; throw my lab coat and scrubs into the washer; and wash my hands and face before greeting my family. I have been extra focused on eating balanced meals, getting sufficient sleep, and exercising regularly in order to maintain my immune system.

### The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?

Trauma and acute-onset eye pain or vision loss certainly still need to be evaluated emergently. Examples include intraocular foreign body, retinal detachment, and infection. We have prioritized patients for whom the potential risk and severity of irreversible vision loss increase as evaluation and treatment are delayed. Examples include acute posterior vitreous detachment, wet AMD patients who historically require a frequent injection interval, postoperative follow-up after recent surgery, and acutely worsening complications of PDR. There will, however, be exceptions to any line that we draw, such as in the case of a monocular patient.

We must recognize that the circumstances of the pandemic change week to week, if not day to day, particularly in certain parts of the country. Ongoing communication is critical so that practice patterns can be modified in real time as the situation evolves.

### The AAO has advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?

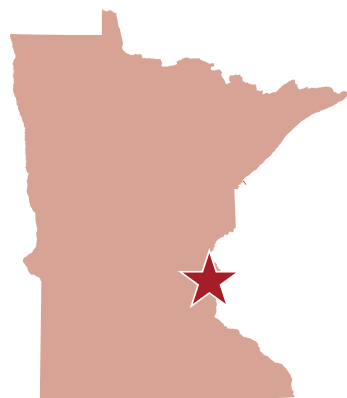
The ASCs where we operate are closed. At Wills Eye Hospital, surgery is limited to urgent cases in order to conserve and redirect resources to handling COVID-19 cases. Nonurgent refers for conditions that are not immediately sight-threatening and can be postponed for at least a few

weeks or longer without significant adverse visual or prognostic consequence. Vitreous opacities and hemorrhage, chronic nonprogressing diabetic tractional detachment, dislocated IOLs, and macular pucker are some examples. Most macular holes can be postponed for several weeks. However, as was the case with in-office care, there will be some exceptions (eg, a monocular patient who is worsening) that will require our best judgment as surgeons.

We should approach patients with empathy when communicating with them about postponing surgery. Although many will be relieved to do so, some may express that the visual problems they are enduring, while not urgent, are being trivialized or marginalized. Acknowledging their sentiments while focusing on our shared societal responsibility to flatten the curve can be both reassuring and compelling.

### Edwin H. Ryan, MD

*Vitreoretinal Surgery PA  
Minneapolis, MN*



### What precautions are you taking in your clinic to protect your patients?

Our practice is screening for risk. When we contact patients by phone to remind them of their appointments, we ask them about their travel and exposure history and if they're demonstrating symptoms such as fever or cough.

We also ask them at the time they arrive for an appointment. We have diligently wiped down surfaces after every patient visit, and we have spaced out seats in our waiting room to reduce the likelihood of transmissions (Figure).

The mostly elderly patients who visit a retina clinic are at high risk of death if they contract COVID-19, and we are taking our preparation seriously. As of the week of March 23, physicians and staff have started wearing masks; we are wearing whatever masks are available. Still, our staff and physicians operate as if we are not wearing masks—that is, we remain 6 feet away from each other. It is unclear what benefit (if any) these masks provide, but they at least provide some psychologic comfort.

### What personal precautions are you taking to protect yourself as a physician?

Our practice has made a few temporary changes to protect physicians, many of which overlap with our mission to protect patients.



Figure. Seats in the waiting room at VitreoRetinal Surgery PA in Woodbury, Minnesota, have been moved further apart.

We have minimized talking in our practice. The social aspects of patient encounters have been all but eliminated for the sake of safety. We have a policy in place that only patients may visit the examination rooms.

Avoiding slit-lamp examination is impossible, but we have reduced our use significantly. When a slit-lamp examination is required, we use protective breath shields. We have been diligent about sanitizing our hands upon entry and exit of any exam room. I cannot stress enough how important it is to sanitize your hands and work stations. From the research so far, it appears to be the best way to mitigate risk of transmission.

**The AAO has advised that retina specialists offer only urgent and emergent in-office care. Where do you draw the line between urgent and nonurgent in-office care?**

Our office considers routine exams, referrals for nevi, epiretinal membranes, and asymptomatic background diabetic retinopathy evaluations to be nonurgent. Those patients will hopefully be seen in the summer. Patients with acute vision loss or symptoms that suggest a retinal detachment are considered emergent cases and are seen.

Patients who receive anti-VEGF therapy for wet AMD are still being seen in our practice. We use a treat-and-extend regimen for many of these patients. Rather than extending them to some unknown treatment date, we decided to treat these patients. There is a certainty that they will lose vision if we do not treat them; there is a low risk that coronavirus will be transmitted if they visit the office. That's the calculus we've operated with so far, but of course it may change as the situation evolves.

**The AAO has also advised against performing nonurgent surgical procedures. Which types of surgical cases do you consider nonurgent?**

We have determined that surgery for epiretinal membranes, chronic vitreous hemorrhage, and chronic macular

hole are all nonurgent. Surgeries that have been scheduled for macular holes and dislocated IOLs can be delayed by 1 to 2 months.

Still, much of what we see in the OR is emergent. Cases involving rhegmatogenous retinal detachment, endophthalmitis, dropped nucleus, and a number of other conditions must be seen immediately, and we will not delay those surgeries.

Again, I must stress that this is an evolving situation. Delaying surgery for a macular hole by 1 or 2 months should be fine; delaying by 5 or 6 months could have negative consequences. ■

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# COVID-19 in the Literature

A digest of published pieces on novel coronavirus.

*In December 2019, Wuhan, China, experienced the beginning of an outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). That outbreak grew to an epidemic, and the epidemic then grew to a pandemic. The literature on the COVID-19 pandemic and the virus that causes it is swiftly growing as the world confronts this novel disease. Here, we present summaries of a sampling of recent publications.*

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## Clinical Course and Risk Factors for Mortality of Adult Inpatients With COVID-19 in Wuhan, China: A Retrospective Cohort Study

*Zhou F, Yu T, Du R, et al.<sup>1</sup>*

In this retrospective, multicenter cohort study, the authors examined risk factors for mortality in all adult inpatients with laboratory-confirmed COVID-19 at two hospitals in China who had been discharged ( $n = 137$ ) or had died ( $n = 54$ ) by January 31, 2020.

Older age, higher sequential organ failure assessment score, and d-dimer greater than  $1 \mu\text{g/L}$  on admission to hospital were associated with higher rates of death due to COVID-19, the authors found.<sup>1</sup>

Nearly half of the patients in the study presented with comorbidities, led by hypertension (30% of patients), diabetes (19%), and coronary heart disease (8%). Viral shedding persisted for a median of 20 days in survivors, and SARS-CoV-2 RNA was detectable until death in nonsurvivors.

These data “could help clinicians to identify patients with poor prognosis at an early stage,” the study authors wrote. The prolonged viral shedding observed in the study “provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future,” they concluded.

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## A Trial of Lopinavir-Ritonavir in Adults Hospitalized with Severe COVID-19

*Cao B, Wang Y, Wen D, et al.<sup>2</sup>*

To date, no drug has been proven to be effective for the treatment of COVID-19. Cao et al conducted a randomized,

controlled, open-label trial of treatment with the combination of lopinavir and ritonavir in hospitalized adult patients with confirmed SARS-CoV-2 infection. They found that the treatment provided no benefit compared with standard of care in hospitalized adult patients with COVID-19.

Treatment with lopinavir-ritonavir was not associated with a difference from standard care in the time to clinical improvement, mortality at 28 days, or percentages of patients with detectable viral RNA at multiple time points. A modified intention-to-treat analysis showed that lopinavir-ritonavir led to a median time to clinical improvement that was shorter by 1 day than that with standard of care.

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## Interventions to Mitigate Early Spread of SARS-CoV-2 in Singapore: A Modeling Study

*Koo JR, Cook AR, Park M, et al.<sup>3</sup>*

Since the beginning of the SARS-CoV-2 outbreak, the virus has been imported to more than 170 countries on six continents.<sup>4</sup> Researchers in Singapore investigated options for early intervention to prevent disease spread once community transmission of the virus has been detected. They determined that a combination of strategies—including isolation of infected individuals and quarantining of family members, school closure, and workplace distancing—was the most effective method and could substantially reduce the number of infections. The model made assumptions about the reproduction number (the expected number of cases directly generated by one case) and the percentage of infections that are symptomatic. “When these variables are increased, the authors said, “the effectiveness of the intervention could be substantially reduced.”



## Assessing Viral Shedding and Infectivity of Tears in Coronavirus Disease 2019 (COVID-19) Patients

Yu Jun IS, Anderson DE, Zheng Kang AE, et al.<sup>5</sup>

SARS-CoV-2 is known to be transmitted via droplets, but other routes of transmission—such as through infected ocular tissues or fluids—are unknown. It has been hypothesized that the nasolacrimal system might act as a conduit for viruses to travel from the upper respiratory tract to the eye, and, therefore, ocular tissues and fluids might be a potential source of transmission.

This study by Yu et al suggests that the risk of transmission through tears, regardless of the phase of infection, is likely to be low. These authors attempted to determine the possibility of transmission through tears by comparing viral shedding in tears with nasopharyngeal swabs (NP) throughout the course of infection in 17 patients with COVID-19. Tears were collected with Schirmer test strips at various time points from day 3 to day 20 after onset of symptoms and sent to a research laboratory for processing. NPs were assessed at a diagnostic laboratory. No patients presented with ocular symptoms, but one patient developed conjunctival injection and chemosis during the study. Of the 64 tear samples taken during the study period, all tested negative for SARS-CoV-2, including the patient who developed ocular symptoms.

“All tear samples tested negative even when NPs continued to test positive,” the authors concluded. “Furthermore, patients with symptoms of upper respiratory tract infections did not demonstrate any viral shedding in tears, suggesting the hypothesis of the lacrimal duct as a viral conduit may not be true.”

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## Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients With Coronavirus Disease 2019 — United States, February 12–March 28, 2020

CDC COVID-19 Response Team.<sup>6</sup>

People in the United States with underlying health conditions appear to be at higher risk for more severe COVID-19,

consistent with findings from other countries, according to the Centers for Disease Control and Prevention (CDC) COVID-19 Response Team. The team reached this conclusion after analyzing data from laboratory-confirmed COVID-19 cases reported to the CDC with dates of onset from February 12 through March 28.

Among the 122,653 US COVID-19 cases reported to the CDC as of March 28, 7,162 (5.8%) patients had data available pertaining to underlying health conditions or risk factors. Among these patients, these authors found, higher percentages of patients with underlying conditions were admitted to the hospital and to an intensive care unit (ICU) than were patients without reported underlying conditions. Specifically, out of 457 ICU admissions, 358 (78%) were for patients with one or more reported underlying health condition. Similarly, among 1,037 non-ICU hospitalizations, 732 (71%) were for people with such conditions. By contrast, of 5,143 COVID-19 patients who were not hospitalized, 1,388 (27%) were reported to have at least one underlying health condition.

“These results are consistent with findings from China and Italy, which suggest that patients with underlying health conditions and risk factors, including, but not limited to, diabetes mellitus, hypertension, [chronic obstructive pulmonary disease], coronary artery disease, cerebrovascular disease, chronic renal disease, and smoking, might be at higher risk for severe disease or death from COVID-19,” the study authors said. They noted that their analysis was limited by small numbers and missing data, and the findings might change as additional data become available. ■

1. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054–1062.

2. Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe covid-19 [published online ahead of print March 18, 2020]. *N Engl J Med*.

3. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study [published online ahead of print March 23, 2020]. *Lancet Infect Dis*.

4. Mapping the worldwide spread of the coronavirus. Washington Post. <https://www.washingtonpost.com/graph-ics/2020/world/mapping-spread-new-coronavirus/>. Accessed March 31, 2020.

5. Yu Jun IS, Anderson DE, Zheng Kang AE, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology*. 2020 [journal pre-proof].

6. CDC COVID-19 Response Team. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019. United States, February 12–March 28, 2020 [published online ahead of print March 31, 2020]. *MMWR Morb Mortal Wkly Rep*.

# Slit Lamp Droplet Shield



Keep yourself safe, and keep your patients safe.

BY A. JOHN KANELLOPOULOS, MD

The current state of health worldwide is in flux as we deal with the fallout from the novel coronavirus disease 2019 (COVID-19). Because the risk of infection with this respiratory illness is highest among individuals who are in close contact—within about 6 feet—with individuals known to have the disease,<sup>1</sup> it is important that we, as health care professionals, do as much as we can to protect ourselves and to protect our patients during routine examinations and surgical procedures. One way that we can protect both parties is by using a disposable slit-lamp droplet shield like the one I describe here.

## BACKGROUND

COVID-19 is rapidly spreading from person to person. As of April 7, the website corona.help reports that the global number of confirmed cases of the disease totals more than 1.3 million. There have been more than

77,000 total deaths.<sup>2</sup> On that day, the website reports that 30,988 new cases were confirmed. The main way that COVID-19 is transferred is through respiratory droplets via sneezing, coughing, and even breathing, but it can also be transferred by first touching a surface or object that has the virus on it and then touching the mouth, nose, or eyes.<sup>1</sup>

The World Health Organization (WHO) advises that all countries, communities, and individuals help to contain the spread of COVID-19 through “robust containment and control activities” that include identifying individuals who are sick and bringing them to care, alerting individuals with whom the infected person has come into contact, preparing hospitals and clinics to manage the patient surge, and training health care workers.<sup>3</sup>

“Every person has the capacity to contribute, to protect themselves, to protect others, whether in the home, the

*(Continued on page 39)*



## DR. KANELLOPOULOS DEMONSTRATES HOW TO MAKE A DISPOSABLE SLIT-LAMP SHIELD



Figure 1. A reduced-size image of the template for the disposable slit-lamp shield.



Figure 2. A cardboard replica of the template.



Figure 3. An example of the disposable slit-lamp shield.

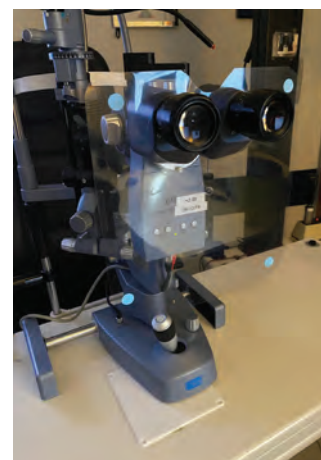


Figure 4. The disposable slit-lamp shield placed on the oculars of a slit lamp.

[BIT.LY/SHIELD0420](https://bit.ly/Shield0420)

# Personal Protective Equipment in the Era of COVID-19



A take on how a Philadelphia ophthalmologist is handling the COVID-19 crisis.

BY OMESH P. GUPTA, MD, MBA

## 1. What do you wear when seeing asymptomatic patients?

As I answer this from Philadelphia, the rates of infection from COVID-19 continue to rise. People can be infected with this virus and be asymptomatic for 2 to 14 days. The safest practice is to assume that every patient might be COVID-19 positive. Therefore, I wear an N95 mask and goggles for all patients.

## 2. Is it necessary for a doctor to wear an N95 mask when examining asymptomatic patients?

Absolutely not. N95 masks are required for suspected or positive COVID-19 patients who are undergoing procedures involving airborne and fluid hazards. A simple surgical mask should suffice for asymptomatic patients in our offices. In my case, I had commercial N95 respirator masks available to me, and I reuse my mask due to the limited supply.

## 3. How do you reuse your N95 masks?

There have been a number of recommendations, but I found two that are practical for me. I found that letting the mask air dry for 3 to 4 days before reuse may be effective. Coronavirus needs a host to survive, so if you let the mask hang dry or place it in a clean, breathable container such as a brown paper bag for 3 to 4 days, the virus will not survive. I have also hung the mask in an oven at 150°F for 30 minutes. I use a wood clip to hang the mask in a toaster oven that I bought specifically for this purpose. I do not want to find out how coronavirus tastes on the next day's toast or lasagna!

Keep in mind that the polypropylene in N95 masks may degrade when exposed to UV light or sunlight. The data are inconclusive on this topic. Make sure to wash your hands before and after you remove your mask. When placing your mask on your face, avoid touching the inside.

## 4. Do you require patients to wear a mask?

I do not require patients to wear a mask, but it is a good idea for everyone, especially high-risk patients. This includes patients who are over 65 years old, live in a nursing home or long-term care facility, have chronic lung disease or asthma, are immunocompromised, or have severe obesity. Pregnant patients may be at high risk, too.

I wear a mask to protect my patients and staff. Similar to many retina practices, retina specialists at Mid Atlantic Retina see a number of patients and travel to a variety of offices. If I test positive for COVID-19, I could potentially have placed all patients and staff with whom I've interacted at risk to be quarantined.

## 5. What is the proper precaution for patients who are COVID-19-positive?

The full personal protective equipment attire includes surgical cap, gown, goggles, N95 mask, and gloves for procedures that involve airborne and fluid hazards. The amount of coronavirus in tear fluid remains unclear, but a recent report did not detect the virus in tear samples.<sup>1</sup> That said, as long as the protective equipment is available, it seems reasonable to take all necessary precautions. ■

1. Yu Jun IS, Anderson DE, Zheng Kang AE, et al. Assessing viral shedding and infectivity of tears in coronavirus disease 2019 (COVID-19) patients. *Ophthalmology*. 2020 [Journal pre-proof].

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- Financial disclosure: None



# Resources for Retina Specialists for COVID-19 Education



Stay on top of the latest news by consulting these resources.

BY JAYANTH SRIDHAR, MD

You can zoom in and zoom out on the roles of retina specialist. From a bird's-eye view, we are part of the general community of physicians serving as pillars of the medical community. Zoom in, and we are ophthalmologists who help lead the world of eye care. Zoom in further, and we are retina specialists who primarily manage diseases of the retina and vitreous.

In the COVID-19 era, it can be difficult to know where to turn for reliable information, and information that you generally need as a physician might not be the same information you need specifically as a retina specialist. Here are a few resources you can use for updates as this public health crisis evolves.

## FOR THE PHYSICIAN

Physicians are local doctors who need information on COVID-19 from a logistical perspective. They need to know which local services are available, as these services may affect how patients visit a clinic.

Going to resources such as a local newspaper to figure out how COVID-19 is going to affect your immediate area allows you to keep up on the day-to-day happenings of your community and, more specifically, your patients' lives. Fortunately, most newspapers have taken down paywalls for COVID-19–related online articles and publish daily updates.

Ultimately, physicians are scientists who need to know the latest research. *The New England Journal of Medicine* and *The Lancet* are two of the best peer review journals publishing the most recent data about COVID-19. Both journals'

websites have a designated COVID-19 resource center with the most up-to-date information about the crisis. You can read a summary of the latest findings from these and other journals elsewhere in this issue.

The Centers for Disease Control and Prevention (CDC) is a source of information on how to handle your practice and patients during the COVID-19 crisis. The CDC website's section titled "Information for Healthcare Professionals" is particularly useful. This website is updated regularly throughout the day, making it a prime resource for everyone.

## FOR THE OPHTHALMOLOGIST

Ophthalmologists need specialized information about COVID-19's ocular implications. The AAO's online content includes recommendations for ophthalmologists, practice managers, and patients. The AAO regularly updates its recommendations as new data and research are available and suggests tactics for mitigating the spread of coronavirus. Familiarizing yourself with the recommendations of the AAO during this time may be important from a medicolegal perspective as the COVID-19 crisis evolves.

Eyewire is a news source for ophthalmologists who wish to stay informed about how COVID-19 is affecting the specialty at large. Eyewire's news website (Eyewire.news) is updated regularly with breaking news ranging from peer-reviewed literature to medical society protocols. During noncrisis moments, it is a clearinghouse for all news items in ophthalmology; during this particular period, it serves as our specialty's most robust source of COVID-19 information.

Eyetube has been hosting video webinars about COVID-19 in ophthalmology. Sessions are hosted by Zoom video conference and are archived on Eyetube.net. Audio-only sessions are distributed via the podcasts *New Retina Radio* and *Ophthalmology Off the Grid*.

### FOR THE RETINA SPECIALIST

The ASRS has been the premium source for retina-specific information as this crisis evolves. The ASRS online guide for retina surgeons explains which surgeries should be canceled and which surgeries should continue as scheduled. The ASRS website also offers coding information and tips, printouts for practice use, and suggestions for tools to use if you are seeing patients, such as slit-lamp shields.

Social media is extremely helpful as well to get a sense of the retina landscape. As a member of the Young Retina Forum Telegram group (run by Mitul Mehta, MD, and Hemang Pandya, MD; email [mcmehtha@gmail.com](mailto:mcmehtha@gmail.com) to join), it has been illuminating to see different practice patterns across the country and get real-time news on changes. Some useful Twitter accounts (this is not an all-encompassing list) to follow are @vitreouscutter (Shriji Patel, MD), @drvihau (Vi Hau, MD, PhD), @drrishisingh (Rishi Singh, MD), and @surgeonretina (Rajesh Rao, MD).



A unique way to receive retina-specific updates is through podcasts. I host *Straight From the Cutter's Mouth* ([www.retinapodcast.com](http://www.retinapodcast.com)), a discussion-based podcast which typically focuses on retina-related issues such as practice patterns, surgical approaches, and journal clubs. In a recent episode, we discussed COVID-19 with AAO CEO David W. Parke, MD. *Straight From the Cutter's Mouth* has been monitoring news sources. If there are drastic policy changes or recommendations, we will record an episode with updates for the audience.

### CONCLUSION

As new data and information become available, it is essential to stay up to date so that you can properly prepare your practice and treat your patients. Knowing where to look is the first step. Stay safe, stay healthy, and be well my friends. Together we will get through this! ■

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- Financial disclosure: Founder, Host (*Straight From the Cutter's Mouth: A Retina Podcast*, non-revenue generating)

(Continued from page 36)

community, the health care system, the workplace, or the transport system," the WHO statement reads. "Leaders at all levels and in all walks of life must step forward to bring about this commitment across society."<sup>3</sup>

### DO YOUR PART

We can do our part to help contain the spread of the virus by being diligent about sanitation in our clinics. The slit-lamp droplet shield may not be a significant medical innovation, but it is one easy way that we can protect ourselves from COVID-19 and other pathogens. Most slit lamps are equipped with a protective shield, and several after-market models are commercially available for purchase.

As an alternative or in addition to those shields, I have devised a protective disposable shield out of simple letter-sized cellophane sheets. These can be easily made in minutes and installed on slit lamps and surgical microscopes by personnel in your clinic.

Figure 1 is a sample of the template for the protective shield, which was modified from a commercially available plexiglass protective shield product. (Editor's note: The full-size template can be downloaded at [bit.ly/slitlampshield0420](http://bit.ly/slitlampshield0420).) In short, a cardboard replica of the template is made (Figure 2). The cardboard cutout can then be used to trace the template on top of a piece of cellophane. The cellophane is then cut following the pattern on Figure 1, and foam stickers are placed on the four corners to protect technicians from bumping into it (Figure 3).

Lastly, the kidney bean-shaped opening near the top of the template is placed on the slit-lamp or microscope oculars (Figure 4). The product can fit almost any slit-lamp or microscope oculars.

### CONCLUSION

A disposable protective slit-lamp shield is an easy, cheap, and effective way that we can increase safety not only for our medical staff and colleagues, but also for our patients. It is one small step in helping to contain the spread of COVID-19. ■

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# WHAT IS THE TRUE RISK OF RETINAL TEAR OR DETACHMENT WITH MODERN LENS SURGERY?



It's not as great as you might think, but here are some pointers for avoiding it.

BY STEVE CHARLES, MD, FACS, FICS

**W**hat is the true risk of a retinal tear or detachment associated with modern refractive lens exchange (RLE) surgery? An answer firmly backed by scientific evidence would be hard to come by. The reason is that level 1 evidence would be very challenging to acquire because of the many clinical and surgical variables as well as the timeline issue.<sup>1-7</sup>

The timeline is a key problem; if a retinal detachment occurs years after RLE, was the complication related to this surgical procedure? If, on the other hand, an RLE is performed on Monday and there is a retinal detachment on Tuesday, many would conclude causation—but it could be a random temporal association.

Similarly axial length is often used as a proxy for retinal detachment risk after RLE, but axial length is not the cause. Clinicians often confuse population statistics and individual risk; if a patient has -10.00 D of myopia, most ophthalmologists would agree that he or she has a significantly increased risk of retinal detachment after RLE. If, however, a careful peripheral retinal examination with indirect ophthalmoscopy of this theoretical patient detected no lattice degeneration or peripheral retinal pathology, his or her actual risk is minimal—certainly less than population statistics would predict for a patient with -10.00 D of myopia.

Although an evidence-based answer is difficult, my experience suggests that the risk of a retinal tear or detachment with modern lens surgery is lower than most cataract surgeons might think. Here is my advice for minimizing the risk in your practice.

## CAREFUL SCREENING

Evidence of lattice and retinal holes on a dilated fundus examination is a far more important predictor of retinal detachment than axial length. Careful peripheral screening

with indirect ophthalmoscopy and a dilated pupil is mandatory before RLE. Scleral depression should be used if any suspicious areas are seen.

Wide-angle imaging systems can provide additional information, but they cannot replace indirect ophthalmoscopy. These systems rarely provide high-quality superior or inferior images because the patient's eyelids and lashes obscure the view. Wide-angle imaging systems may be more useful in photophobic patients.

The Pan-American Collaborative Retina Study (PACORES) Group screened a large number of patients before LASIK and found substantial retinal pathology requiring laser retinopexy, which almost certainly reduces retinal detachment rates compared with the natural history in such patients.

If any retinal breaks are noted during the preoperative evaluation, they should be treated with laser. The standard academic view is that only symptomatic flap tears require retinopexy. Standard teaching is that round holes have no traction, but, using widefield OCT, Charteris et al<sup>8</sup> recently showed that 98% of round holes do indeed have traction. Calling round holes *atrophic* is meaningless.

The consensus view is that holes within lattice degeneration do not require laser retinopexy. Pigmentation indicates chronicity, not adherence.

## CONCLUSION

The risk of a retinal tear or detachment after RLE is likely low; however, anterior segment surgeons can take steps to reduce that risk and ensure a safe and effective surgery for their patients (see *Do's and Don'ts in Surgery*). ■

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## DO'S AND DON'TS IN SURGERY

### **Do avoid a retrobulbar block for RLE surgery.**

This is important because of the risk of ocular perforation, especially in myopic eyes with high axial lengths.

**Do make every effort to prevent anterior chamber shallowing during RLE.** Shallowing causes the lens capsule and vitreous to move anteriorly, potentially creating vitreoretinal traction.

**Do not, under any circumstances, use a large-bore needle to aspirate illusory liquid vitreous.** Acute vitreoretinal traction can occur with this technique.

**Do carefully manage the vitreous if a capsular defect occurs during RLE.** Avoid using cellulose sponges or sweeping the vitreous. Be sure to apply triamcinolone—a particulate marking agent—to the vitreous to enhance visualization.

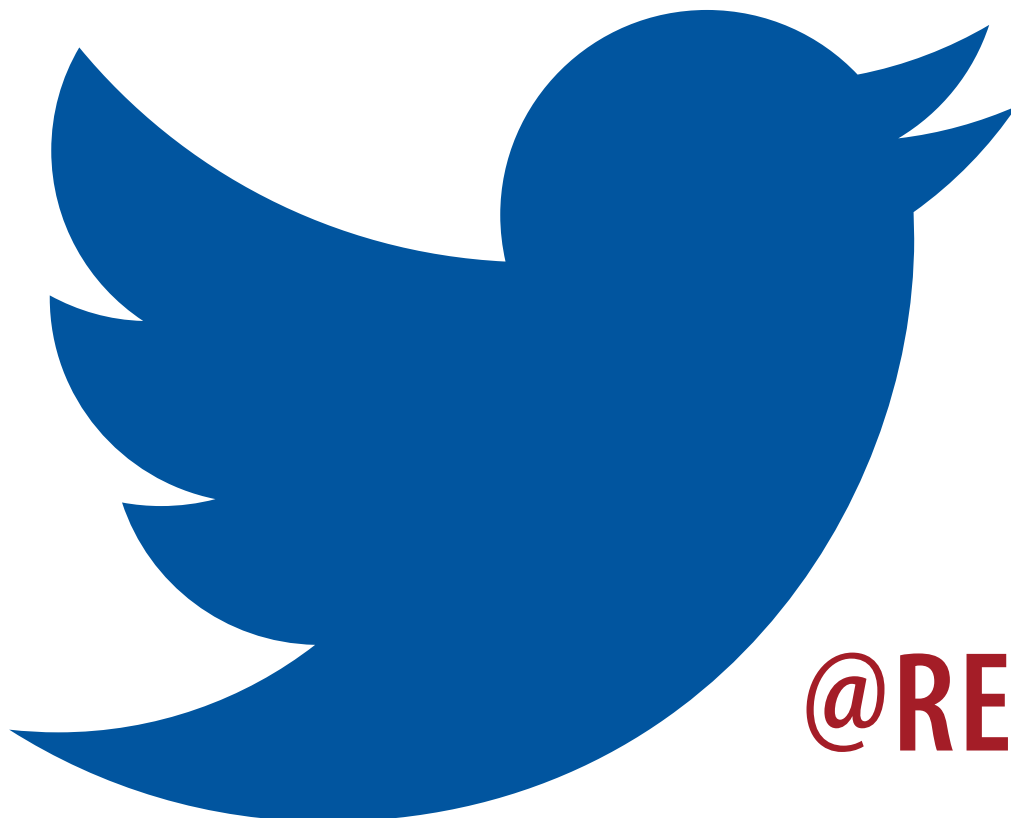
**For performing a vitrectomy, do use the highest cutting rates and very low vacuum.** The vitreous cutter should be used through the pars plana or a second sideport incision, with infusion also through a sideport. Avoid pulling the cutter back while vacuum is applied.

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# Refining the Use of OCT in Diagnosing Glaucoma



Advances in OCT technology limit the potential for misinterpretation errors to affect diagnostic accuracy in eyes with suspected or diagnosed glaucoma.

BY KI HO PARK, MD, PHD

OCT has become an indispensable tool for evaluating eyes of patients with suspected glaucoma. However, there are several sources of error that may lead to misinterpretation of images, either by the platform technology or by the operator/clinician.

One user-specific source of error is in selecting the wrong map or in failing to review a complete set of information. In my practice, in which I use the swept-source OCT (SS-OCT) DRI OCT Triton (Topcon, Figure 1), I look at both the thickness map and the SuperPixel map (deviation map from the normative database) for peripapillary and macular scans. Retina nerve fiber layer (RNFL) or ganglion cell layer defects located in the typical glaucoma-vulnerability region are important findings for any glaucoma diagnosis. Both peripapillary and macular parameters are reviewed, as they are complementary in establishing a diagnosis. In cases of suspected glaucoma in the optic nerve head, evaluation of peripapillary RNFL thickness, including the average RNFL thickness, RNFL thickness map, and deviation map, is very important. In addition to that, evaluation of the macular ganglion cell layer in order to rule out suspect cases is important, as well.

In all cases, it is important to confirm that the scan quality score is sufficient for interpreting an image. Scan quality, or signal strength, is generally understood to be the averaged intensity of the signal pixels in the OCT image. Correspondingly, image defocus may artificially depict thinning of the RNFL.<sup>1</sup> In this respect, the DRI OCT Triton, which uses laser lighting as opposed to halogen lighting, may be advantageous in clinical practice. SS-OCT employs a narrow bandwidth laser that rapidly sweeps over a broad range of wavelength, thereby producing less



Figure 1. The SS-OCT DRI OCT Triton.

light scatter and yielding high-quality images that are less prone to glare.

In the following, other common sources of OCT misinterpretation are reviewed, with a particular emphasis on how swept-source technology improves the ability to diagnose glaucoma compared to spectral-domain (SD-OCT) technology.

## OCT ARTIFACTS

Segmentation errors are a common reason for misinterpretation of OCT images. The introduction of spectral-domain technology has reduced the incidence of segmentation errors compared to time-domain; however, the former is still associated with potential to inaccurately depict RNFL thickness. Several risk factors have been identified, including decreasing RNFL thickness, decreasing scan quality, and increasing age.<sup>2</sup> In the latter study, automated segmentation was found to result in thinner RNFL measurement compared to manual refinement. Thus, it is important to review OCT images, specifically noting the boundaries of the RNFL, and make corrections as necessary. The need to do so is especially relevant in eyes with epiretinal membrane, long axial length, poor visual acuity, cataract, and

advanced glaucoma. In addition, OCT devices designed with faster scan speeds may help to overcome segmentation errors that result from poor signal strength, while use of longer wavelength light sources are less prone to errors due to media opacities.

Software features on some OCT devices that account for eye movement during scanning help to minimize misinterpretation due to motion artifacts. Subtle eye movements or blinks can lead to misalignment of the image, which may ultimately result in errors on RNFL thickness measurement. Eye tracking with registration to the iris or blood vessels on some SD-OCT platforms may help to improve reproducibility of RNFL measurements. SS-OCT accounts for this issue in a different manner. With respect to the DRI OCT Triton, the platform is equipped with the Active Eye Tracking feature for use during angiography; more importantly, though, the device is capable of 100,000 A-scans/sec—more than double that of SD-OCT—which reduces the impact of microsaccades.

Another source of OCT image misinterpretation fits more so into the category of patient-specific characteristics while also representing a known limitation in imaging technology. Media opacities, such as cataracts, have been shown to affect RNFL thickness measurement. Mwanza and colleagues reported that removal of a cataract increased signal strength by 24.1% and RNFL thickness measurement by 9.3% postoperatively, indicating that suggested glaucomatous progression on OCT may be an artifact of an advancing cataract.<sup>3</sup> In cases of early-to-moderate cataract, OCT seems to be better than photography. However, in severe cataract, image quality might not be good enough. It should be noted that because SS-OCT uses a longer wavelength light source compared to SD-OCT, it is less prone

to deflection by ocular opacities, including cataracts. Whether this is meaningful in severe cataracts is not entirely clear; however, this aspect of SS-OCT suggests a benefit relative to SD-OCT in early-to-moderate cortical and posterior subcapsular cataracts.

As noted above, there is growing recognition regarding the importance of gathering data beyond the peripapillary and/or macular area. In this respect, SS-OCT has the great advantages of faster scanning speed and wider-area scan coverage compared to SD-OCT.

## HIGHLY MYOPIC EYES

A specific category of patients, those with long axial length, bears mentioning with respect to misinterpretation errors in the context of diagnosing glaucoma. Eyes with high myopia present a unique assessment challenge for glaucoma, as elongated axial length is a risk factor for deformation of the optic nerve head and the peripapillary region. Indeed, studies show an association between lamina cribrosa defect and associated acquired optic nerve and peripapillary pits in highly myopic eyes.<sup>4</sup> This has obvious implications for the accuracy of the normative database used during a patient's assessment. High myopia is underrepresented in the population of most normative databases, and Asian ancestry may be as well. However, recent evidence suggests a dramatic increase in myopia in several Asian countries.<sup>5</sup> In turn, myopia is a significant risk factor for glaucoma: in one study, moderate to high myopia was associated with a 2.6 odds ratio for glaucoma, and in the Korea National Health and Nutrition Examination Survey, the odds ratio for glaucoma in moderate myopia was 2.2 and for severe myopia it was 4.6.<sup>6,7</sup>

Serial imaging in the same patient is helpful in overcoming this issue. Over time, images can be compared to baseline to judge glaucomatous progression, especially when combined with other parameters of the evaluation. In this sense, each patient becomes his or her own normative database, with one important caveat: RNFL thickness

decreases with age even in healthy, normal eyes. Thus, any change in RNFL thickness should be evaluated in this context. As well, it is important that serial imaging be registered to the same anatomic location. On the DRI OCT Triton, SMARTTrack capabilities ensure reproducibility of imaging over the same location during follow-up scans.

Overall, special care should be taken when performing OCT imaging in eyes with myopia, as the superotemporal and inferotemporal RNFL bundles may shift temporally, thereby giving the appearance of pseudo RNFL defects, specifically a temporal shift of the superior and inferior RNFL bundle peaks that may be misinterpreted as thinning—especially in comparison to a normative database that underrepresents myopia. Such false positives, termed red disease, occur in between 26 and 31% of myopic eyes on the SD-OCT RNFL thickness map. They typically appear in the superior and inferior region of the optic disc, and are more common in eyes with longer axial length and/or smaller disc area.<sup>8,9</sup> The false positive rate on SD-OCT ganglion cell-inner plexiform layer maps is slightly higher at about 40% and is more common in eyes with longer axial length and a larger fovea-disc area.<sup>9</sup>

In addition to false-positive results, SD-OCT technology may, in some cases, produce images that indicate a false negative. There are at least two limitations with SD-OCT in this regard. First, SD-OCT technology employs a spectrometer to detect returning wavelengths of light; by comparison, SS-OCT uses a point photodetector, which is considered a simpler reconstruction mechanism, thus allowing faster scan speeds. It is not the case that SD-OCT is necessarily inferior technology, but rather that the greater scan speed of SS-OCT has implications both for reducing the signal-to-noise ratio, as well as for depicting relevant pathology. The second potential source of false-negative findings with SD-OCT relates to the size of the scanning area: the faster scan speed with reduced degradation with SS-OCT permits a wider scan area, which may assist in detecting pathology beyond the peripapillary and/or macular areas.

## CONCLUSION

The move from time-domain to SD-OCT

technology represented an incremental improvement in imaging capabilities, with attendant implications for the ability to accurately detect glaucoma. SS-OCT is poised to make a similar impact. In addition to the specific examples noted above, the DRI OCT Triton offers the clinician access to various other imaging modalities, including angiography (OCTA).<sup>\*</sup> Ongoing research is investigating a potential role for OCTA in evaluating glaucoma. Currently, there is not a definitive role for OCTA in diagnosing glaucoma, but it may provide additional information in support of glaucoma evaluation.

What is becoming apparent, however, is that differences in how SS-OCT and SD-OCT perform segmentation and measurements have definite implications for the ability to diagnose pathology. For instance, the faster scan speed, wider scan area, and higher penetration available on SS-OCT allows for a more accurate depiction of RNFL defects, especially in myopic glaucoma. As well, SS-OCT is more sensitive for depicting RNFL defects compared to SD-OCT. Finally, the wider scan range of SS-OCT has an advantage in detecting RNFL defects that may have been missed in the conventional SD-OCT scan range. ■

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<sup>\*</sup>OCTA is not available for sale in the United States on the DRI OCT Triton.

To see the first insert in this series from Topcon, "SS-OCT: Clinical Applications for Diagnosing and Following Ocular Pathology," go to [bit.ly/ssoctretinatoday](http://bit.ly/ssoctretinatoday)



# GUARD AGAINST PVR: METHOTREXATE FOR PROLIFERATIVE VITREORETINOPATHY AFTER RETINAL DETACHMENT SURGERY



The phase 3 GUARD trial is evaluating the safety and efficacy of this innovation.

BY S.K. STEVEN HOUSTON III, MD; AND DAVID R. LALLY, MD

Vitreoretinal surgery has seen tremendous advances in the past few decades. Vitrectomy platforms now offer small-gauge instrumentation (23, 25, and 27 gauge), vitreous cutters operate at 10,000 to 20,000 cuts per minute, and a plethora of advanced surgical instruments (forceps, scissors) and surgical adjuvants (perfluoro-n-octane, gas, silicone oil) are available. Visualization has also seen significant advances in the form of widefield noncontact and contact systems as well as digitally assisted vitrectomy surgery (DAVS) platforms. Despite all of the improved safety and efficacy of modern day vitreoretinal surgery, however, one complication still eludes us: proliferative vitreoretinopathy (PVR).

PVR is a complex disease process that can occur after rhegmatogenous retinal detachment surgery in 5% to 10% of patients.<sup>1</sup> PVR is initiated as a reparative process following a retinal break and retinal detachment. It is characterized by glial cell or retinal pigment epithelium cell migration with resulting proliferation of preretinal or subretinal membranes. Contraction of these membranes after surgical repair is the most common cause for failure of primary retinal detachment surgery. Rates of PVR can increase substantially with retinal detachments secondary to trauma or giant retinal tear. Additionally, several risk factors have been identified that may increase the risk of PVR, including preoperative PVR, extent of retinal detachment, number and extent of retinal breaks, choroidal detachment, vitreous hemorrhage, and duration of retinal detachment.<sup>2,3</sup>

PVR has been shown to be associated with multiple cytokines, chemokines, and growth factors, as well as other extracellular matrix proteins. This complex pathophysiology

hints at the difficulty of developing pharmaceutical treatments for PVR.

Treatment for retinal redetachment from PVR requires surgery to achieve anatomic stabilization. Preretinal and subretinal membrane peeling, internal limiting membrane peeling, relaxing retinectomy, perfluoro-n-octane liquid, and silicone oil are all elements in our armamentarium for successful treatment of PVR.

Primary prevention of PVR would represent a major breakthrough in vitreoretinal surgery. Many pharmaceutical candidates have been investigated, including corticosteroids,

## AT A GLANCE

- PVR occurs in 5% to 10% of patients with retinal detachment. Surgical options are used to address PVR in these cases.
- The GUARD trial will assess whether postoperative administration of ADX-2191 (intravitreal methotrexate 0.8%, Aldeyra Therapeutics) has an effect on rates of redetachment due to PVR that requires surgery.
- Updates on GUARD are expected in the next 1 to 2 years.

# GUARD Trial Injection Protocol

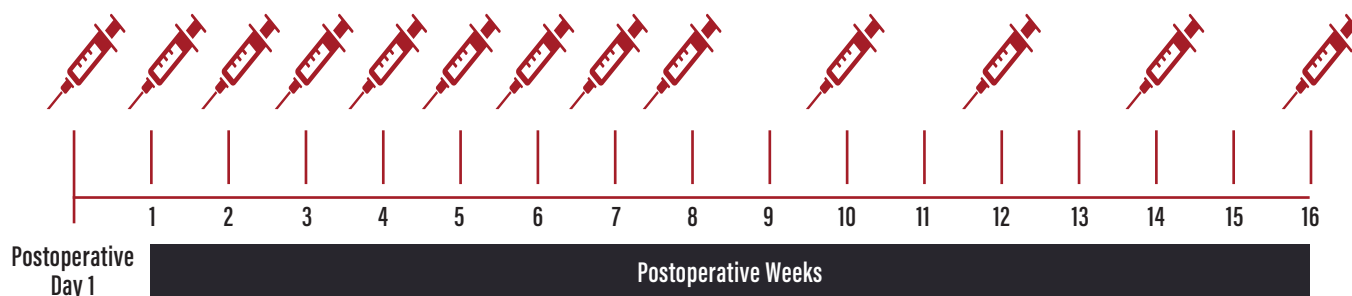


Figure 1. The injection protocol for the GUARD trial requires 13 doses of ADX-2191 over 16 weeks.

retinoic acid, 5-fluorouracil, platelet-derived growth factor, VEGF, heparin, and others, with varied responses. Despite some evidence of efficacy for some of these agents, the evidence has not been sufficient to lead to widespread adoption of any treatment.

## THE GUARD TRIAL

In 2011, a phase 1b, investigator-initiated clinical trial was conducted at Mass Eye and Ear by Dean Elliott, MD, and Tomasz Strykowski, MD, to determine the safety and tolerability of administering repeated, weekly intravitreal injections of methotrexate into eyes at high risk for the development of PVR after retinal detachment repair.

The rationale for use of intravitreal methotrexate for treatment of PVR is based on its mechanism of action. Methotrexate suppresses inflammation and inhibits cellular replication, both of which are key in the pathogenesis of PVR. PVR typically manifests weeks to months after surgical repair, so the treatment is given repeatedly throughout the entire risk period rather than as a single injection at the time of surgery.

In December 2019, enrollment began in the Gain Understanding Against Retinal Detachment (GUARD) trial, a two-part multicenter, randomized, controlled, adaptive phase 3 clinical trial investigating the efficacy of ADX-2191 (intravitreal methotrexate 0.8%, Aldeyra

Therapeutics) for the prevention of recurrent retinal detachment due to PVR.<sup>4,5</sup> ADX-2191 has received orphan drug and fast track designations from the US FDA.

## Inclusion and Exclusion Criteria

The GUARD trial is recruiting patients undergoing vitrectomy for recurrent retinal detachment due to PVR with star folds in at least 3 cumulative clock hours documented on retinal imaging, or for retinal detachment associated with open globe injury.

Exclusion criteria include no light perception vision, pre-phthisis, severe nonproliferative diabetic retinopathy or proliferative diabetic retinopathy, severe dry eye or corneal disease, previous incisional glaucoma surgery, a history of intraocular inflammation, sensitivity to methotrexate, and being 17 years old or younger. In addition, a history of more than six retinal detachments in the study eye is exclusionary.

## Study Protocol

Patients are randomly assigned 1:1 intraoperatively to ADX-2191 or control. Part 1 of the study will enroll approximately 100 patients. The results of part 1 will be used to power part 2 of the study, which will enroll an additional 100 to 360 individuals.

Study participants in the treatment arm receive intravitreal ADX-2191 at the

conclusion of surgery or on postoperative day 1, and then weekly for 8 weeks, followed by every-other-week treatment through postoperative week 16. Thus, a total of 13 ADX-2191 injections are administered over 16 weeks (Figure 1). Neither the surgeon nor the patient is masked to treatment.

Significant membranes, including epiretinal, subretinal, and epipilary, are all surgically removed to the extent possible. Use of intravitreal dyes, scleral buckle, relaxing retinectomy, and perfluorocarbon liquid are allowed at the discretion of the investigator. Retinal breaks are sealed using moderate to intense white laser retinopexy burns, and then all eyes receive 1,000 or 5,000 centistoke silicone oil tamponade. Subconjunctival, peribulbar, intravenous, oral, or sustained-release intraocular steroids are prohibited.

The individual is enrolled at the end of the surgery only after successful reattachment is confirmed by the investigator. All participants receiving the investigational product are required to use lubricating drops or ointment at least four times daily postoperatively. Maintaining a well-lubricated cornea is crucial to reduce the risk of epithelial defects and other forms of keratopathy, that may occur during repeated intravitreal injections of methotrexate. Silicone oil may be removed after week 24.

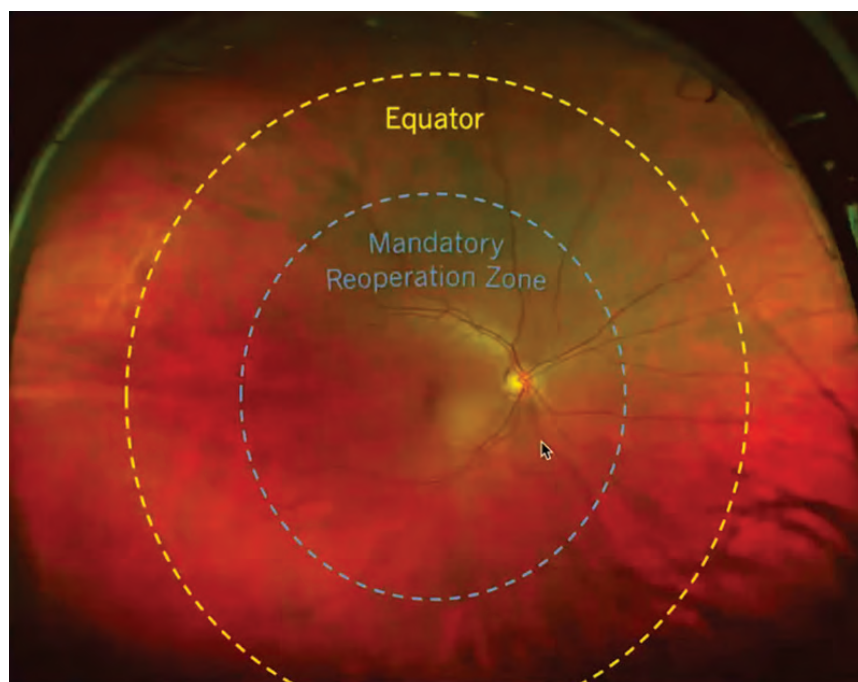


Figure 2. The primary endpoint of recurrent retinal detachment is defined as a retinal detachment that has progressed posterior to the mandatory reoperation zone, as defined by Standardized Study Figure 2, which depicts a circle centered on the fovea that is located halfway between the arcades and the equator (Source: Aldeyra Therapeutics).

## Outcome Measures

The primary outcome is the rate of retinal redetachment due to PVR requiring reoperation within 24 weeks of randomization. Retinal redetachment requiring reoperation is defined as either spectral-domain OCT demonstrating a fovea-off retinal detachment with subretinal fluid that is contiguous with a peripheral detachment, or color wide-field imaging documenting a recurrent detachment in the mandatory reoperation zone. The *mandatory reoperation zone* is defined as a redetachment that has progressed posterior to Standardized Study Figure 2 (Figure 2). The secondary endpoint is BCVA change from preoperative examination to week 24.

## Protocol Regarding Lens Status

The vitrectomy surgery is performed using a small-gauge system (23, 25, or 27 gauge). If the eye is phakic with a clear lens, the lens may be preserved. If there is a cataract, lensectomy with removal of the entire capsule may be performed at the discretion of the investigator. Cataract extraction with

implantation of a posterior chamber IOL is allowed. If the eye is pseudophakic, the IOL can be left or removed at the discretion of the investigator. If the eye is aphakic, secondary IOL implantation is not permitted.

## FINAL THOUGHTS

PVR plagues surgeons and patients as the main cause for failure of primary retinal detachment surgery. The pathophysiology of PVR is complex, with multiple targets contributing to its development and progression. Initial studies of intravitreal methotrexate for PVR have led to the initiation of the phase 3 GUARD trial. We anticipate that the results of this trial will illuminate the efficacy of this potential treatment for patients with rhegmatogenous retinal detachments secondary to advanced PVR or open-globe injuries.

Although the treatment burden of 13 injections over the course of 16 weeks is intense, proof of concept in this study would likely lead to development of slow-release implants or other sustained-release drug delivery

approaches. We look forward to updates on this exciting study over the next 1 to 2 years. ■

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# THE WINNING PITCH CHALLENGE



A resource for innovative retina specialists who need a helping hand.

AN INTERVIEW WITH JOHN POLLACK, MD

**John Pollack, MD:** David Williams, MD, MBA; Vance Thompson, MD; and I launched The Winning Pitch Challenge in 2017, after it became clear to us that there are numerous ophthalmologists who have novel ideas for important innovations that can improve patient care, but who don't have the tools they need to move their early-stage concepts further along the development process. The Winning Pitch Challenge events are designed to motivate retina specialists to act on their ideas.

We realized that physician-innovators need more than just prize money—they need mentorship from experts in the field. To that end, we developed The Winning Pitch Challenge mentorship program that pairs participants with highly qualified mentors who provide relevant business expertise and guidance that can help overcome potential barriers associated with securing intellectual property, developing a working version of the product, identifying a team, and designing early-stage studies. The Winning Pitch Challenge mentorship program has more than 50 world-class experts who volunteer their time and expertise to help advance innovation in ophthalmology. Although the prize money is attractive, participants find that the greatest value is available to all participants through the guidance, networking opportunities, and exposure to potential financial resources they receive from both the mentorship program and through feedback from judges.

**WE REALIZED THAT PHYSICIAN-INNOVATORS  
NEED MORE THAN JUST PRIZE MONEY—  
THEY NEED MENTORSHIP FROM  
EXPERTS IN THE FIELD.**

**Dr. Pollack:** The spectrum of submissions has been quite broad, ranging from therapeutic devices to pharmaceutical products to surgical accessories. Past winners have included a disposable lid speculum designed for comfort (Speculet, Jeffrey Gross, MD), a novel, hands-free scleral depressor (Gani-Hand, Gary Ganiban, MD), and assisted-reality low-vision glasses (iLoopes, Jeffrey Heier, MD).

**Dr. Pollack:** The submission process is simple and completed online at [www.WinningPitchChallenge.net](http://www.WinningPitchChallenge.net). There are three rounds of competition. The first round is a quick screening round with a relatively simple application. After that is filed, submitters receive rapid feedback on whether they advance to Round 2, which begins with pairing the applicant with a mentor who will help develop a product pitch deck, which is used to determine the finalists who will advance. In Round 3, finalists live pitch to a panel of judges with expertise in venture capital, incubators, and strategic partnerships.

*The Round 1 submission deadline is Sunday May 17, 2020.* Submitters should keep in mind that the sooner they submit, the sooner they are paired with a mentor and receive assistance with pitch deck development. I encourage everyone to submit sooner rather than later.

There is no entry fee, and the primary requirements are that submitters must be members of the American Society of Retina Specialists and be key members of the product's innovation-development team. We are most interested in very early stage ideas that will benefit most from the resources offered by The Winning Pitch Challenge.

**Dr. Pollack:** There is no cookie-cutter applicant. Sometimes, a submission is just one person with an idea and a sketch. Other applicants have already developed a simple prototype but have no business plan or team to help move the idea forward. And others have a small team and some product but lack a compelling story, business plan, and funding.

We encourage all retina specialists

with very early-stage ideas to submit them—even those who have only a great idea. We can help you, too.

We recommend that submitters take an important step toward protecting their idea by submitting at least a provisional application for patent. We are happy to provide some guidance on how accomplish that before completing the submission.

We have a panel of four or five judges. Each finalist is given 5 minutes to pitch their idea, followed by a moderated question-and-answer session with the judges that lasts 10 minutes.

The final judging criteria include the magnitude of the problem, innovativeness of solution, market strategy and potential for reimbursement, competitive analysis, business model, and intellectual property information.

Importantly, we do *not* expect anyone to have addressed any of these issues at the time of their original submission. Fleshing out these important components of a business plan is the goal of The Winning Pitch Challenge ecosystem, which includes participation in the mentorship program, receiving feedback from judges at the end of Round 2, and utilization of free resources available through the website.

After the judges vote for the winners, the finalists receive feedback from each judge, and then we present the winners with a \$25,000 first place prize, \$15,000 for second place, and \$5,000 for third place.

The Winning Pitch Challenge is generously supported by the judges, mentors, and industry. No one benefits financially from this except for the participating physician innovators. None of the event directors, judges, or mentors receive any compensation for their participation. In fact, they support this event both financially and with their time and effort. They continue to support this program because they believe it can help accelerate innovation in retina, and we are grateful to all of them for their continued support. ■

#### JOHN POLLACK, MD

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- Financial disclosure: Founder (The Winning Pitch Challenge)

## Need More Info?

**Deadline:** May 17, 2020

**Mentorship Assignments:** Mentors are paired on a first-come, first-served basis.

**Website:** [winningpitchchallenge.net](http://winningpitchchallenge.net)

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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.<sup>1</sup> 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,<sup>2</sup> and ritonavir, a protease inhibitor, has been reported to cause central pigment epitheliopathy.<sup>3</sup> 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.

1. Subramaniam S, Jeat AW, Nasaruddin RA, Hamzah JC, Omar RNR. Presumed tenofovir-induced ocular toxicity. *Medical Journal of Malaysia*. 2018;73(Suppl 2):43.

2. Haug SJ, Wong RW, Day S, et al. Didanosine retinal toxicity. *Retina*. 2016;36 (Suppl 1):S159-S167.

3. Papavasileiou E, Younis S, Zygoura V, et al. Ritonavir-associated toxicity mimicking retinitis pigmentosa in an HIV-infected patient on highly active antiretroviral therapy. *Retin Cases Brief Rep*. 2017;11(4):306-309.

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- Financial disclosure: None

To share an image, contact Manish Nagpal, MBBS, MS, FRCS, at [drmanishnagpal@yahoo.com](mailto:drmanishnagpal@yahoo.com).

Note: Images should be 400 dpi or higher and at least 10 inches wide.

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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 early April.

## RESCHEDULED

### 6TH SAN RAFFAELE OCT AND RETINA FORUM

Milan, Italy  
Hotel NHOW Milano

**Rescheduling Information:**

**New Date:** July 17-18, 2020

**To Register:** Visit [octforum2020.eu](http://octforum2020.eu)

### DUKE AVS

Duke Eye Center  
Durham, North Carolina

**Rescheduling Information:**

**New Date:** September 11-12, 2020

**To Register:** Visit [MedConfs.com](http://MedConfs.com)

### MILANO RETINA MEETING 20/20

Milan, Italy  
**Rescheduling Information:**

**New Date:** September 11-12, 2020

**To Register:** Visit [APMeetings.com](http://APMeetings.com)

### VISION EXPO EAST

Javits Center  
New York City

**Rescheduling Information:**

**New Date:** September 23-26, 2020

**New Location:** Sands Expo Center, Las Vegas

**To be held at the same time as Vision Expo West**

### VITREX (VITREO RETINAL EXPERIENCE)

Congress Center  
Venice, Italy

**Rescheduling Information:**

**New Date:** October 29-31, 2020

**To Register:** Visit [APMeetings.com](http://APMeetings.com)

## POSTPONED

### AMERICAN-EUROPEAN CONGRESS OF OPHTHALMIC SURGERY (AECOS) EUROPE

Florence, Italy  
**Rescheduling Information Forthcoming**

### BOSTON 20/20: CONTROVERSIES IN RETINA

Tufts Medical Center  
Boston, Massachusetts  
**Rescheduling Information Forthcoming**

## CANCELED

### VIT-BUCKLE SOCIETY ANNUAL MEETING

Fontainebleau Miami Beach  
Miami Beach, Florida

### ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY (ARVO) ANNUAL MEETING

Baltimore Convention Center  
Baltimore, Maryland

### AMERICAN SOCIETY OF CATARACT AND REFRACTIVE SURGEONS (ASCRS) ANNUAL MEETING

Boston Convention Center  
Boston, Massachusetts

### MOTOR CITY RETINA

Marriott Renaissance Center  
Detroit, Michigan

## NEED UP-TO-THE MINUTE UPDATES?

For the latest on meetings in retina, visit [RetinaToday.com/events.asp](http://RetinaToday.com/events.asp).

For the latest on meetings in all of eye care, visit [Eyewire.news/events](http://Eyewire.news/events).

# GO AHEAD. BE A SHOWOFF!



Have a video of an innovative technique or interesting case?

Upload it to [Eyetube.net/submit](https://eyetube.net/submit). It's easy!



Videos should be **3-7 minutes** long.

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Videos must be accompanied by an **English** narration. Narration should describe what the surgeon is doing and why. Explain subtle maneuvers, and name any instruments and/or devices that were pivotal to the case.

Files up to 2 GB are accepted. However, files larger than 1 GB may not transfer completely. Ensure you have a **good internet connection**, or contact us for an alternate upload method.



Include any relevant **financial disclosures**, either in the video or the video description.

**Avoid** background noise, music, movie clips, or animations that may distract viewers.



Companies may submit **educational or instructional videos** for consideration. Promotional material consisting of product advertisements, webinars, and/or symposia captures will not be accepted.

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SCIENCE IS JUST THE BEGINNING OF OUR INNOVATION.  
LET'S PARTNER IN DOING MORE TO GIVE PEOPLE THE

# VISION TO LIVE

