Cleveland Clinic

COLE EYE INSTITUTE

OPHTHALMOLOGY**UPDATE**

ISSUE 1 | 2024

MESSAGE FROM THE **CHAIR**

The final beam has been placed atop the new Jeffrey and Patricia Cole Pavilion at Cole Eye Institute. I was thrilled to commemorate the topping-out event with the Coles as well as our organization's leaders and staff, many of whom signed the beam before it was raised. An American flag and evergreen tree were lifted with the beam, symbolizing the end of structural work on our expansion project.

This building will more than double the size of our flagship location on Cleveland Clinic's main campus, adding 50 new exam rooms, a new surgical center with 12 operating rooms, a new refractive surgery suite with three operating rooms, and a leading-edge education space for our residents and fellows. Once the expansion is complete (anticipated in Q1 2025), we will begin the project's second phase, which will result in significant renovation of our existing building. This renovation will include a brand-new pediatric clinic, a comprehensive restructuring of our imaging facilities and capabilities, additional support areas for our educational programs, and new space for our ophthalmic research laboratories.

Until then, work continues as normal at the Cole Eye Institute. In this issue of *Ophthalmology Update*, our staff shares their clinical insights on these commonly encountered eye conditions:

- Thyroid eye disease
- Uveitis that erupts after intravitreal injection
- Cataracts in patients with a history of corneal refractive surgery

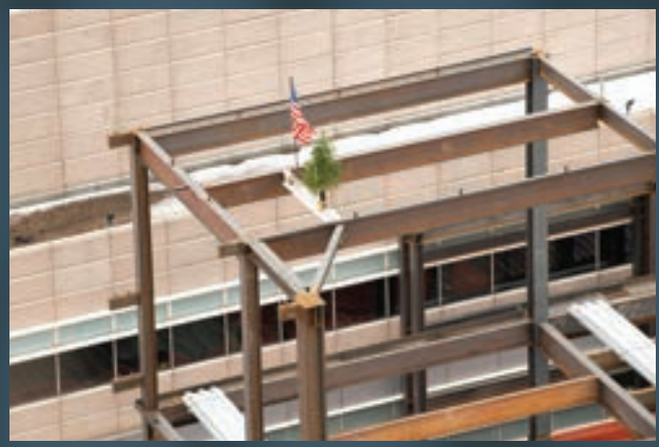
Additionally, we highlight our subspecialty care in a case study involving a rare tumor that reached from the posterior globe deep into the orbital apex. Our Director of Ophthalmic Oncology, Arun Singh, MD, worked alongside a Cleveland Clinic neurosurgeon and rhinologist to remove the tumor through the patient's nose, preserving the optic nerve and other critical structures.

These articles represent the array of conditions we see daily, from the common to the complex. Perhaps there is no better illustration of this spectrum of care than the images captured by our ophthalmic imaging specialists. I hope you enjoy the "art show" we present on pages 6-9. It is a testimony to the talent of our imaging team as well as the exceptional diagnostic and therapeutic services at the Cole Eye Institute.

As always, we welcome collaboration with you and your practice. If we can support the care of your patients, please contact us. We wish you the best in 2024!

Daniel F. Martin, MD | THE BARBARA AND A. MALACHI MIXON III INSTITUTE CHAIR IN OPHTHALMOLOGY
CHAIR, COLE EYE INSTITUTE

COLE EYE INSTITUTE TOPPING-OUT EVENT



Clockwise from top left: Cole Eye Institute Chair Daniel F. Martin, MD; Jeffrey and Patricia Cole, whose lead gift has made the expansion possible; U.S. flag and evergreen tree atop the final beam, symbolizing the end of structural work; the final beam, signed by Cleveland Clinic leaders, Cole Eye Institute caregivers and philanthropic supporters.

COLE EYE INSTITUTE BY THE NUMBERS

360,000 Outpatient visits annually

19,500 Surgeries annually

3,000 Refractive surgeries annually

125 Ophthalmologists, optometrists and research scientists

53 Residents, fellows and research graduate students

53 Clinical trials

26 Locations

INFLAMMATORY COMPLICATIONS IN RETINA CLINICAL TRIALS: WHAT ARE OPHTHALMOLOGISTS MISSING?

HOW TO SCREEN FOR AND MANAGE TREATMENT-TRIGGERED UVEITIS

Sunil Srivastava, MD

Inflammation in the eye (uveitis) is somewhat expected due to ocular surgery or infection. But when it's unexpected — such as following an anti-VEGF injection in a patient with age-related macular degeneration (AMD) — it can be troubling, says Sunil Srivastava, MD, a vitreoretinal disease and uveitis specialist at Cleveland Clinic Cole Eye Institute.

"I think it strikes fear in most ophthalmologists," he says. "It causes us to wonder what we're missing and whether the patient is at risk of permanent vision loss."

FROM 2019 TO TODAY: PREVALENCE OF INFLAMMATION AND VISION LOSS

In the past few years, inflammatory complications have been seen in several products: brolucizumab, abicipar, pegcetacoplan and faricimab, to name a few.

"We all heard rumors of inflammation in late 2019. There was even a hint of it in clinical trials," says Dr. Srivastava. "By early 2020, there were social media posts about a concerning case involving brolucizumab. That one case turned into several cases. Then ASRS [American Society of Retina Specialists] sent out a safety update, stating that they had received reports of inflammation following brolucizumab injection but that the etiology was unclear, and long-term outcomes and optimal treatment strategies were not yet defined."

At that point, there had been 14 cases of retinal vasculitis, 11 of which were occlusive. In an August 2020 press release, the drug manufacturer stated the rate of retinal vasculitis or vascular occlusion was 4.71 per 10,000 injections. The manufacturer then convened a safety review committee.

"As we reviewed the cases, looking carefully at imaging, we realized that the rate of inflammation likely was higher than initially described," says Dr. Srivastava, a member of the safety review committee.

Additionally, the committee found that patients developing inflammation had a 16% risk of mild vision loss (losing more than 15 letters) and a 10% risk of severe vision loss (losing more than 30 letters). Inflammation could happen at any time — not just in the first few months after treatment, but even 12, 14 or 18 months later.

"My take on this is that inflammation likely was present on imaging but not recognized, and retreatment occurred," says Dr. Srivastava. "Inflammation or retinal occlusive disease could erupt after multiple treatments, months later, indicating that it was a cumulative issue in some eyes."

KEY INSIGHTS

What does this mean for ophthalmologists? Dr. Srivastava offers three key insights:

1. Inflammation is difficult to assess. "A slit lamp in a retina office is sometimes no better than a penlight," he says. "Most of the time, it's not as bright as we need. Additionally, office exams are quick. It's easy to miss keratic precipitates and inflammatory cells."

Imaging may not be reviewed closely, he adds. Even in a reading center, a patient's OCT, fundus photo and fluorescein angiogram won't be reviewed at the same time.

"In a uveitis clinic, we study all those images together, looking for subtle signs of inflammation and changes over time," says Dr. Srivastava. "We also use clinical data to help us determine what's happening with the patient. The reading center doesn't have this data because the patients are masked."

"INFLAMMATION IS A KNOWN COMPLICATION OF ALL DRUG THERAPIES, ALTHOUGH IT IS NOT COMPLETELY UNDERSTOOD. IT'S EASY TO MISS SUBTLE INFLAMMATION. WE NEED TO CAREFULLY EXAMINE EYES AND IMAGE THEM LONGITUDINALLY. SEVERE VISION LOSS IS POSSIBLE ONCE INFLAMMATION STARTS, SO WE MUST ADDRESS IT AGGRESSIVELY." – SUNIL SRIVASTAVA, MD

2. Inflammation may occur more in the real world than in controlled clinical trials. "Clinical trial patients are typically healthy 'ideal' patients," says Dr. Srivastava. "More patients in the real world will be primed for inflammation. They may be sicker. They may have a history of systemic inflammatory disease or surgery, or have had previous treatments. They may be on medications that promote inflammatory disease."

3. Inflammatory complications can present months after beginning therapy. Because inflammation is threatening to a patient's vision, ophthalmologists have cause to hesitate before administering additional or new medication.

PREVALENCE IN GENE THERAPY

These points also apply to gene therapy trials, where inflammation is prevalent regardless of injection location or vector type. (Patients with retinal dystrophy and diabetic retinopathy likely already have inflammatory cells visible on clinical exam, even before receiving gene therapy.)

Ocular inflammation is seen in almost every gene therapy animal study, according to Dr. Srivastava. The degree of inflammation is related to dose. Histologic changes and cellular infiltration occur even in the absence of clinically apparent inflammation. And the effect of immunosuppressive pretreatment varies widely.

TIPS FOR OPHTHALMOLOGISTS

Considering the link between injectable therapies and inflammation, ophthalmologists can take steps to protect their patients. Dr. Srivastava offers these tips:

- **Counsel patients receiving new therapies.** Advise them to watch for symptoms of inflammation, including pain, redness, light sensitivity, floaters and vision loss.
- **Perform a careful exam.** Ensure your slit lamp produces bright light. Order imaging if the slit-lamp exam is inconclusive. Use OCT to identify cells in vitreous. Use ultra-widefield photography to look for vessel changes, artery occlusion and vasculitis. If you're still in doubt, order ultra-widefield fluorescein angiography to look for leakage or occlusion.
- **Rule out infectious endophthalmitis.** If you see signs of inflammation, evaluate for infectious disease first (e.g., review the patient's symptoms and clinical exam). If you are unsure, tap and inject, and quickly start the patient on oral steroids.
- **If you suspect inflammation, do not continue anti-VEGF injections.** Aggressively treat the patient with oral steroids.
- **Refer the patient to a uveitis specialist, if needed.** If the patient cannot take oral steroids, a uveitis specialist can determine if intravenous or intravitreal steroids are needed.

"Inflammation is a known complication of all drug therapies, although it is not completely understood," concludes Dr. Srivastava. "It's easy to miss subtle inflammation. We need to carefully examine eyes and image them longitudinally. Severe vision loss is possible once inflammation starts, so we must address it aggressively." ■

the ART *of* OPHTHALMIC IMAGING

COLE EYE INSTITUTE IMAGING SPECIALISTS ARE EQUAL PARTS TECHNICIAN, ARTIST AND DIAGNOSTICIAN

Part technician, artist and diagnostician, ophthalmic imaging specialists have risen in prominence at Cleveland Clinic Cole Eye Institute. In the 1990s, the percentage of Cole Eye Institute patients requiring imaging was about 5%. Today, it's more than 50% — which explains why Cole Eye Institute accounts for the most clinical images captured at Cleveland Clinic outside of the Imaging Institute. The number of eye images is on track to total nearly 180,000 in 2023.

Ophthalmic imaging — including anterior- and posterior-segment photography, fluorescein and indocyanine green angiography, B-scan ultrasound, and ultrasound biomicroscopy — has become essential for diagnosis in modern ophthalmology. That's the reason imaging specialists will be integrated with care teams in the new Cole Eye Institute building, moved out of their designated space in the current building to be closer to patients.

HOW DO YOU BECOME AN OPHTHALMIC IMAGING SPECIALIST?

"We used to be called 'ophthalmic photographers,'" says Brandy H. Lorek, one of the 14 imaging specialists at the Cole Eye Institute and manager of the department. "Now, many of us do more than photography and have certifications in different types of imaging."

It's not a well-marked (or widely traveled) career path, she says. Few universities offer degrees in ophthalmic imaging. Most specialists fall into the career unexpectedly and learn on the job, with disciplines and techniques passed on similar to an apprenticeship.

After earning a bachelor's degree in biology, Lorek worked in an ocular oncology lab at Bascom Palmer Eye Institute. A clinician researcher there suggested she pursue mastering ophthalmic ultrasound. She began studying under another ophthalmic echographer and became certified by the International Joint Commission on Allied Health Personnel in Ophthalmology.

"There's no school or certification for most ophthalmic imaging skills," she notes. "You need to learn the practices from someone else."

WHAT MAKES GOOD OPHTHALMIC IMAGING GOOD?

Using the imaging instrument is only half the job. The other half is understanding disease processes.

"Ophthalmic imaging specialists pay extremely close attention to detail," says Lorek. "We know what to look for in certain eye diseases, and we do imaging with that knowledge. That's what separates us from someone just taking pictures. We know what ophthalmologists are trying to see, so we know what to capture to help them diagnose or rule out a disease."

The more academic knowledge you have in the field of ophthalmology, the better the images you can capture.

"I can teach someone to use a camera in one day, but that doesn't make them an imaging specialist," says Lorek. "It's easy to image the back of an eye but miss all the pathology."

Expert imaging is especially important at the Cole Eye Institute, where medical teams routinely encounter patients with severe, advanced, rare or even unique eye conditions.

"Patients travel to us from out of state for diagnoses that sometimes require a high-quality fluorescein angiogram or other specialized imaging," says Lorek. "We've seen some amazing things."

The following pages contain a collection of notable images captured by Cole Eye Institute ophthalmic imaging specialists.

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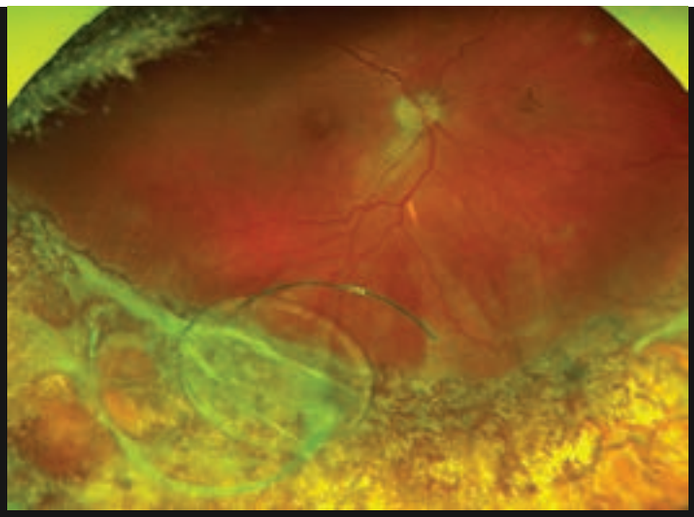
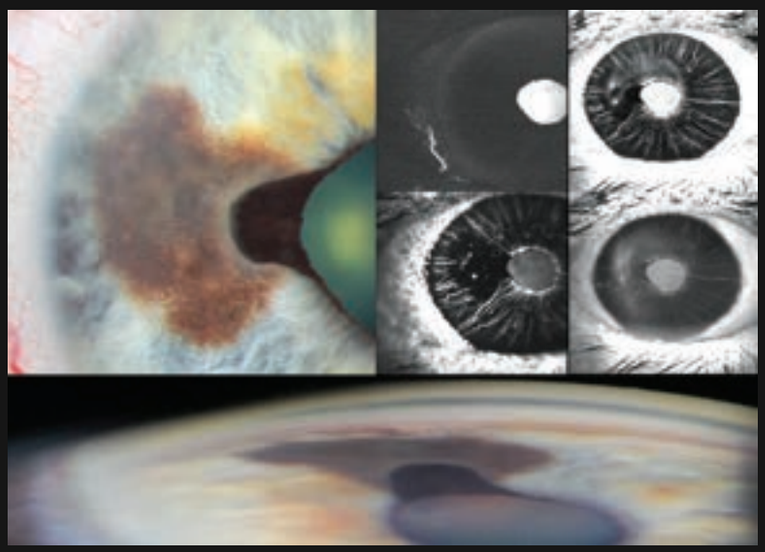
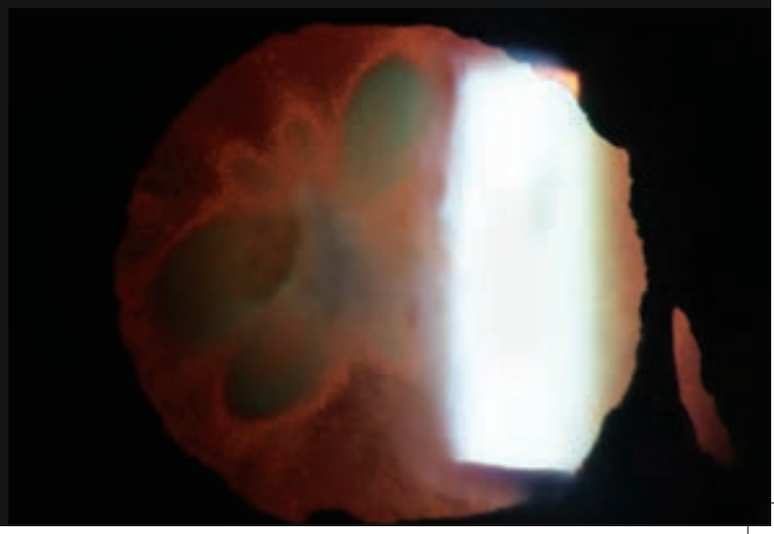


This **ultra-widefield fundus image** taken by certified ophthalmic assistant (COA) Amy Forman depicts a dislocated intraocular lens resting on the surface of the retina. This eye had a history of retinal detachment and scleral buckle surgery, as evidenced by the white matter at the bottom of the image.

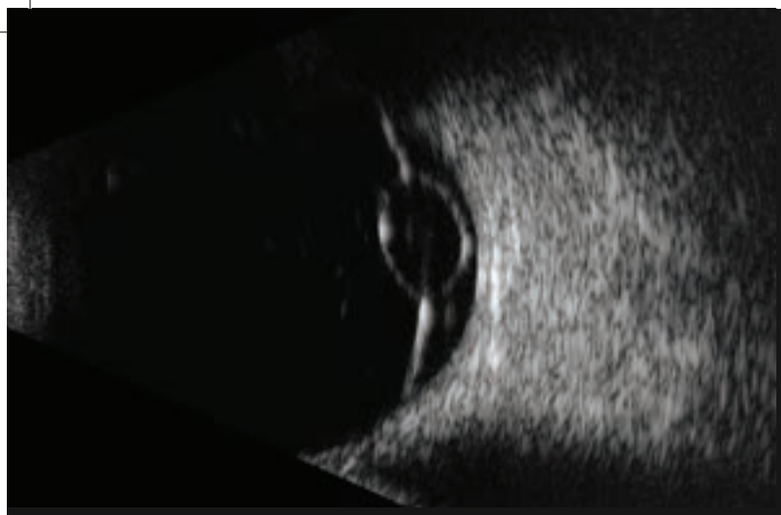


This composite image of an iris melanoma was taken by Mark Harrod, a certified retinal angiographer (CRA) who also is certified in optical coherence tomography (OCT-C). It includes modalities such as **slit-lamp and gonio imaging and anterior-segment fluorescein angiography**, highlighting the lesion's thickness and internal vascularity. This composite was among those receiving awards at the American Academy of Ophthalmology (AAO) 2019 meeting, as part of the Ophthalmic Photographers' Society annual contest.

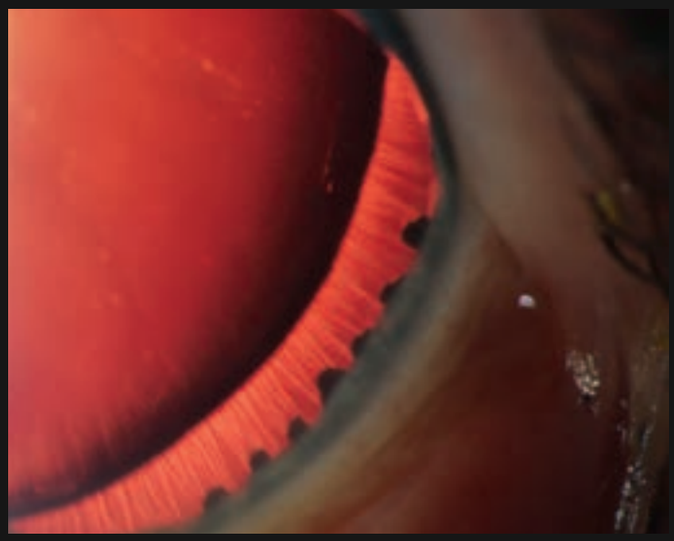
Another 2019 Ophthalmic Photographers' Society award winner, this **fluorescein angiogram** by Mark Harrod, CRA, OCT-C, depicts peripheral (sea fan) neovascularization and peripheral nonperfusion in a patient with sickle cell disease.



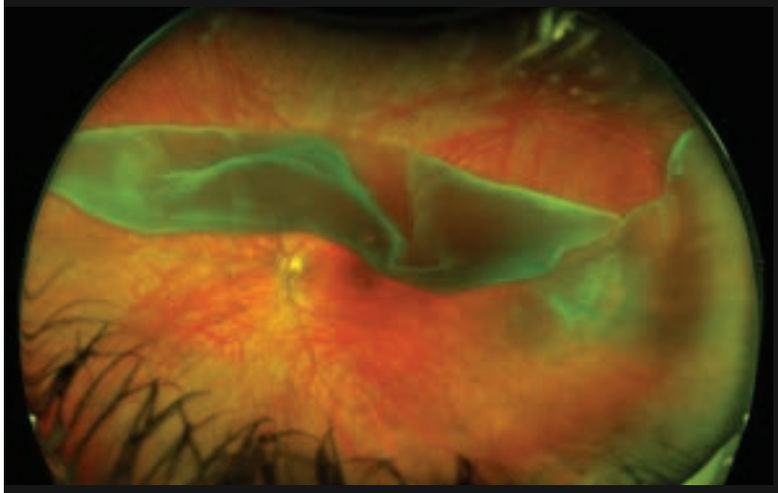
Lisa Jahn-Gregory, COA, OCT-C, captured this **retro-illuminated slit-lamp image** of a cataract in the shape of a butterfly.



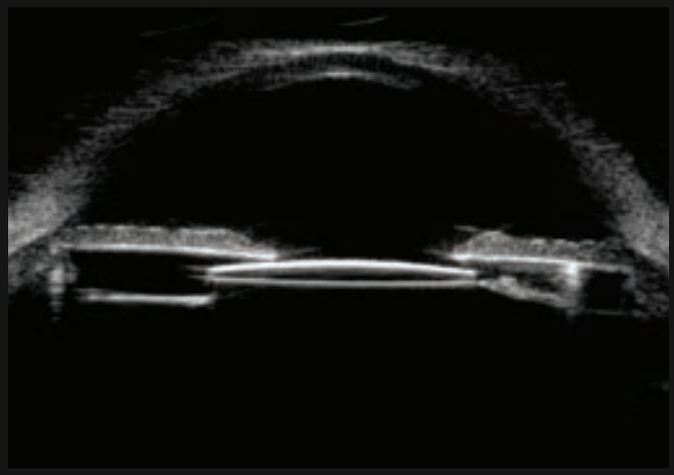
This **ultrasound image** reveals a retinal detachment with a large retinal cyst, indicative of a chronic retinal detachment. The image was captured by Beth MacQueen, a certified diagnostic ophthalmic sonographer (CDOS) and a registered ophthalmic ultrasound biometrist (ROUB).



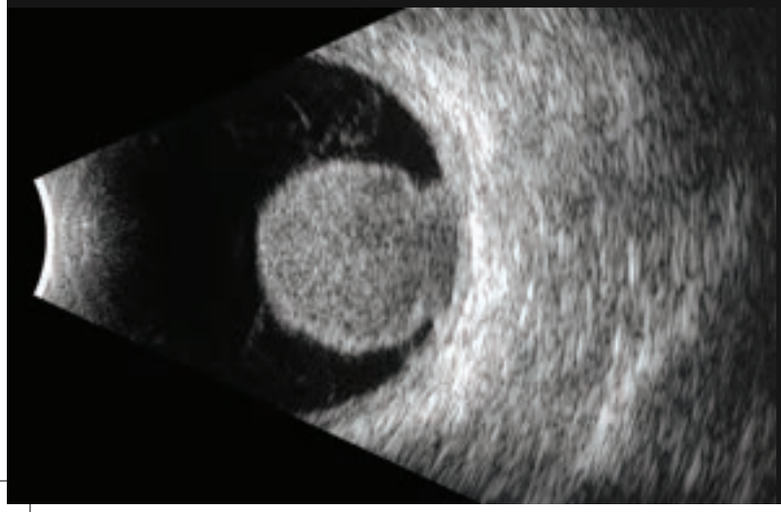
Certified ophthalmic technician (COT) Stephanie Pelton, OCT-C, took this **retro-illuminated slit-lamp image** of a patient with aniridia (absence of the iris). This image shows all the zonules that connect the ciliary processes to the periphery of the lens.



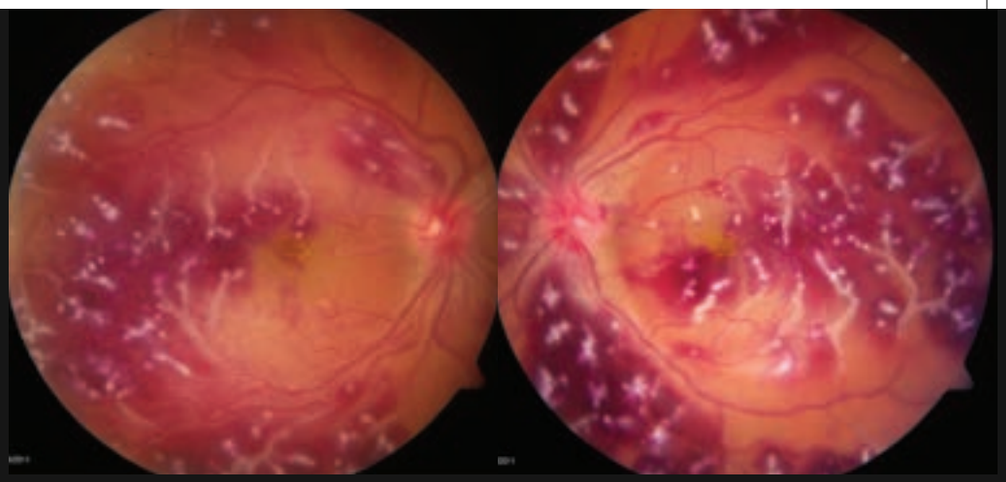
This **ultra-widefield fundus image**, captured by Lindsey VanAuker, COA, OCT-C, reveals a giant retinal tear obscuring the patient's central vision.



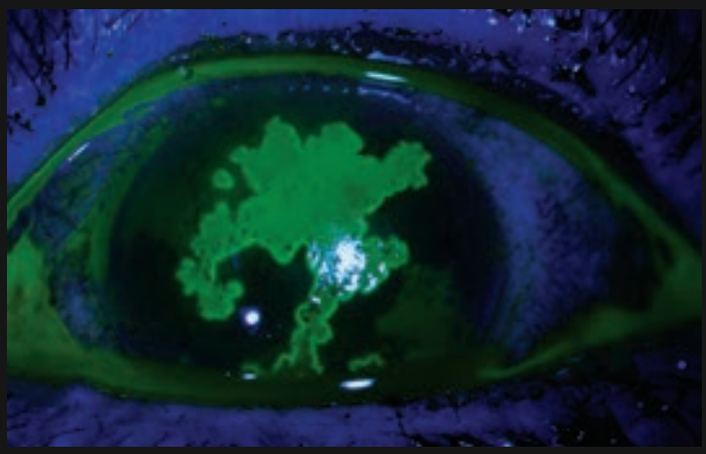
This **ultrasound biomicroscopy image** by Brandy H. Lorek, CDOS, ROUB, shows a grossly centered presbyopia-correcting intraocular lens with dislocated haptics, causing uveitis glaucoma hyphema (UGH) syndrome.



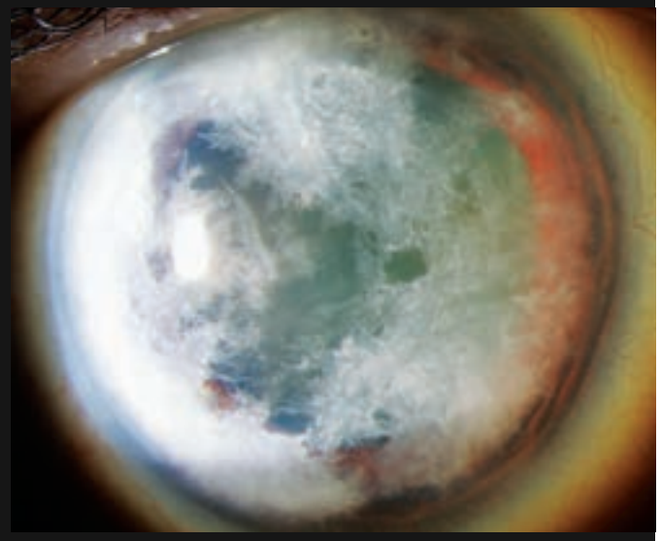
A large choroidal melanoma was captured on **ultrasound** by Brandy H. Lorek, CDOS, ROUB. The tumor's rupture of Bruch's membrane resulted in the pathognomonic collar-button shape.



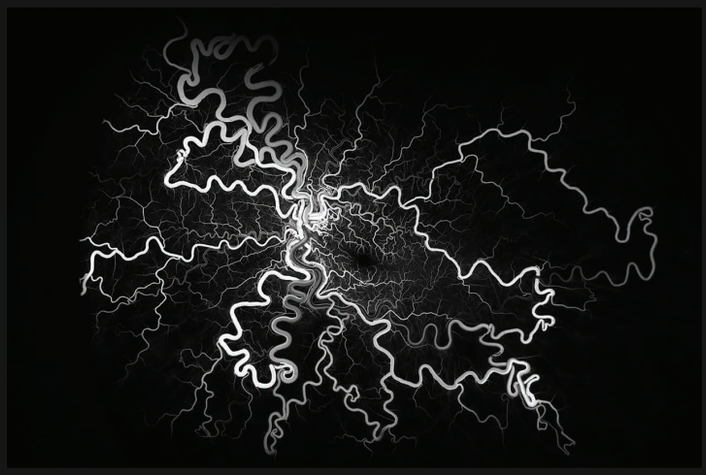
These **fundus images** illustrate severe retinopathy and vasculitis, a rare ophthalmic manifestation of dermatomyositis.



An epithelial defect secondary to herpes simplex virus is depicted in this **slit-lamp image** using fluorescein stain. This large, well-defined defect caused severe pain and vision impairment.



This **slit-lamp image with broad-beam lighting** shows diffuse infiltration of the cornea in a patient with multiple myeloma.



This early frame from a **fluorescein angiogram** was captured with an ultra-widefield fundus camera by Stephanie Burke, CRA, OCT-C. This image illustrates retinal manifestations of Wyburn-Mason syndrome, including multiple arteriovenous malformations.

This **slit-lamp photograph** captured by Stephanie Burke, CRA, OCT-C, depicts iridodialysis (disinserted iris) secondary to severe trauma. This image shows the patient looking straight at the camera.

EYE, BRAIN AND NOSE SURGEONS REMOVE ORBITAL TUMOR THROUGH PATIENT'S NOSE

NOVEL COLLABORATIVE APPROACH HELPS PATIENT AVOID ORBITAL EXENTERATION

Pablo Recinos, MD

Raj Sindwani, MD

Arun Singh, MD

A 54-year-old woman with left eye pain, proptosis and limited ocular motility was evaluated at a non-Cleveland Clinic hospital. Following imaging and a transcranial biopsy, she was diagnosed with a *GLI1*-amplified spindle cell tumor behind her left eye.

This type of tumor, while rare, previously had been reported in various head and neck sites but never in the eye. In addition to its rare presentation, the tumor was uniquely positioned, reaching from the posterior globe deep into the orbital apex.

The outside institution recommended removal of the entire left orbit. However, orbital exenteration, a disfiguring surgery for any patient, would have had additional repercussions in this case. The patient mostly relied on her left eye for vision because visual acuity in her right eye was 20/300 due to a previous retinal detachment.

To explore other treatment options, the patient presented at Cleveland Clinic, where a multidisciplinary skull base surgery team helped pioneer the endonasal removal of similar tumors. Neurosurgeon Pablo Recinos, MD, and rhinologist Raj Sindwani, MD, reviewed the case with a tumor board.

CROSSING SURGICAL BOUNDARIES

"The pathology was so rare and the location was incredibly challenging, but Dr. Sindwani and I were confident that we could access the tumor — at least the back of it," says Dr. Recinos, Section Head of Skull Base Surgery in Cleveland Clinic's Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center.

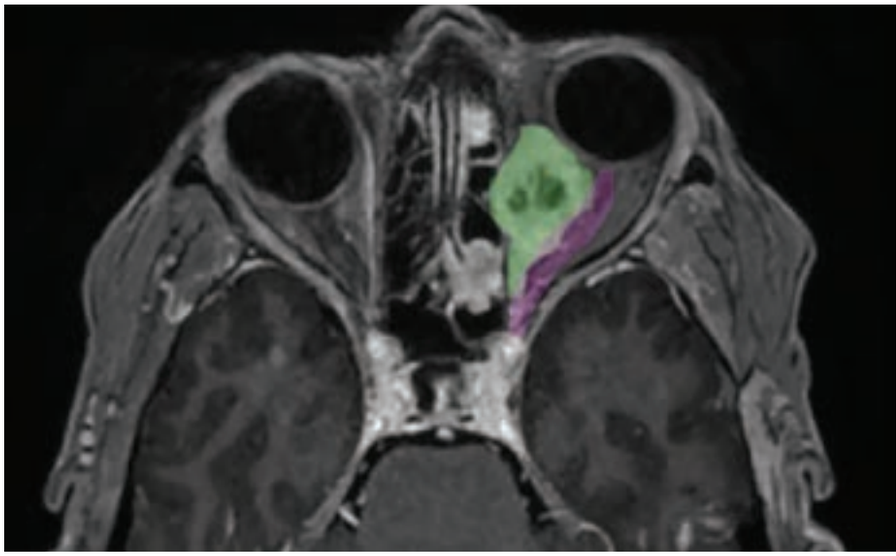
Drs. Recinos and Sindwani recently published a study of their endoscopic endonasal approach to intraconal orbital tumors.[1] A review of 20 of their patients from 2014 to 2021, the article presents the largest cohort and most experience with the surgical approach published to date.

"In this case, our one concern was how far anteriorly we could go," notes Dr. Recinos. "We didn't think we could reach far enough into the orbit to resect the front of the tumor."

As a result, the team collaborated with ophthalmologist Arun Singh, MD, Director of Ophthalmic Oncology at Cleveland Clinic Cole Eye Institute. All three surgeons working together would make it possible to resect a tumor that would be impossible for any one of them alone.

"Tumors like this are in a no-man's-land that crosses the surgical boundaries of ophthalmic, brain, and head and neck specialists," explains Dr. Sindwani. "For masses located toward the back of the eye, the endoscopic approach through the nose that Dr. Recinos and I routinely perform is very effective. For tumors extending toward the front of the eye, as in this case, it is necessary to have the expertise of all three specialists. We each bring a unique skill set and perspective to this multidisciplinary approach, in which we as a team make one or more corridors to gain access to the tumor and then safely remove it, avoiding unwanted complications."

Drs. Recinos, Sindwani and Singh recently published an article on this rare case in *Orbit*.[2]



A rare *GLI1*-amplified spindle cell tumor reached from the patient's posterior globe deep into the orbital apex. The tumor is highlighted in green. The optic nerve is highlighted in purple.

COMBINING ENDONASAL AND LID-SPLIT APPROACHES

The six-hour procedure was performed in three steps:

1. Drs. Recinos and Sindwani used a four-handed, endoscopic, endonasal approach to create a corridor through the sinuses to access the intraconal component of the tumor. By going through both nostrils, they gained access to the deep compartment of the eye and dissected the posterior portion of the tumor in the orbital apex.

2. Dr. Singh used a lid-split approach, entering through the eyelid, to release the anterior portion of the tumor from the ocular muscles, globe and optic nerve.

3. Dr. Singh pushed the freed anterior aspect of the tumor into the patient's sinuses, where Drs. Recinos and Sindwani retrieved the entire mass and delivered it through the patient's nose.

"Normally, we use the corridor between the medial and inferior rectus muscles of the eye to gain access to orbital tumors," says Dr. Recinos. "In this case, the tumor sat superior to the medial rectus, a much more challenging position. So, we developed a corridor above the medial rectus muscle and were aided by an anterior dissection by Dr. Singh through an eyelid approach."

Drs. Recinos and Sindwani called on their experience resecting skull base tumors in the intracranial space through the nose — as well as the use of angled endoscopes and other surgical instruments designed for ear, nose and throat procedures — to successfully remove the tumor from the back of the eye while preserving the optic nerve and other critical structures.

"I have collaborated with neurosurgeons on several cases, when we needed open-skull access to remove orbital hemangiomas, for example," says Dr. Singh. "However, it is rare for me to work alongside a rhinologist. In this case, removing the tumor required skills from three specialties. We each approached a different part of the anatomy with comfort and confidence."

Two weeks after surgery, the patient had 20/80 vision in her left eye. Following a 30-fraction course of radiation therapy, she showed no residual disease at six months. Her vision continues to improve.

AN OPTION FOR MORE 'INOPERABLE' TUMORS

The number of tumors that require this cross-specialty coordination is quite small, say the surgeons. The tumor in this case was abnormally large compared to the orbit and touched different anatomic compartments. More commonly, orbital tumors can be removed endonasally without involvement from an ophthalmic surgeon.

"Today, patients often are told that their orbital tumor is inoperable or that radiation therapy is their only treatment option," says Dr. Sindwani. "With our approach, many of these tumors can be removed. In fact, many more tumors in the medial and posterior orbit and orbital apex can be removed exclusively through the nose without any cuts or even bruises." ■

References

1. Sindwani R, Sreenath SB, Recinos PF. Endoscopic endonasal approach to intraconal orbital tumors: Outcomes and lessons learned. *Laryngoscope.* 2023 May 30.

2. Godse NR, Alsulaimani S, Singh AD, et al. Unique case of a GLI1 amplified biphasic mesenchymal tumor of the orbit. *Orbit.* 2023 Jun 21:1-5.

HOW TO OPTIMIZE OUTCOMES FOR PATIENTS HAVING CATARACT SURGERY AFTER REFRACTIVE SURGERY

CORNEAL IMAGING AND INTERPRETATION PLAY A MAJOR ROLE

J. Bradley Randleman, MD

Twenty years ago, few patients presented for cataract surgery after refractive surgery. "Now, we typically have two or three of these patients per week on our surgery schedule," says J. Bradley Randleman, MD, a cornea and refractive surgery specialist at Cleveland Clinic Cole Eye Institute.

Refractive outcomes of cataract surgery in this patient population are worse than in patients without prior corneal refractive surgery. Still, the population tends to have high expectations regarding uncorrected visual acuity.

"Someone who had refractive surgery years ago to stop wearing corrective lenses does not want to go back to wearing them," says Dr. Randleman.

Complicating these high expectations, many cataract surgeons do not perform refractive procedures and may not be aware of recent developments in corneal imaging and interpretation, notes Dr. Randleman.

"Corneal imaging and interpretation play a major role in the outcomes of cataract surgery in post-refractive patients," he says.

These factors prompted Dr. Randleman to head up a review article in *Survey of Ophthalmology* summarizing evidence-based strategies and guidelines for maximizing surgical success in these patients.[1]

"We felt like there was a great opportunity to provide a collection of practical information," he says. "Our goal was to offer a guide for busy cataract surgeons who are wanting to better understand corneal imaging and its use in patients with prior refractive surgery."

CORNEAL IMAGING IS CRITICAL

Comprehensive corneal imaging before cataract surgery is critical in patients who have had refractive surgery. This imaging helps determine a patient's refractive surgery ablation pattern (myopic or hyperopic), degree of corneal irregularity, higher-order aberration (HOA) profile and suitability for additional postoperative refractive surgery, if needed — all steps that the review authors recommend when evaluating patients.

Determining the refractive surgery ablation pattern guides the selection of intraocular lens (IOL) power formula. Corneal topography is often sufficient to reveal corneal curvature patterns, although more subtle ablations may not be as obvious. The authors caution that using only axial curvature maps may result in missing focal extremes and misreading myopic and hyperopic ablation patterns. They recommend using tangential curvature topographic maps to improve accuracy.

Epithelial thickness mapping is also helpful, although it's unnecessary in some patients. The Gullstrand ratio is another way to determine ablation pattern if corneal topography is unclear.

Corneal imaging also can detect irregular astigmatism and refractive surgery complications such as central islands, corneal haze, decentered ablations and postoperative corneal ectasia, all of which may jeopardize optical quality after cataract surgery.

BEST WAY TO PREDICT IOL POWER CALCULATIONS

Accurately predicting IOL power calculations for patients with prior refractive surgery is the biggest challenge. There are multiple formulas available, many included in the widely used American Society of Cataract and Refractive Surgery (ASCRS) online IOL calculator.

"PREOPERATIVE EVALUATION OF PATIENTS WHO HAVE HAD REFRACTIVE SURGERY IS MORE COMPLEX THAN IN PATIENTS WHO HAVEN'T HAD REFRACTIVE SURGERY. WE MUST CONTINUE TO RECOGNIZE AND ADDRESS THE DIFFERENCES IN THESE TWO PATIENT POPULATIONS." – J. BRADLEY RANDLEMAN, MD

"The ASCRS calculator is a great tool that gives you multiple outcomes from different formulas," says Dr. Randleman. "However, it does require accurate manual data entry."

Another study coauthored by Dr. Randleman found that using the Barrett True-K formula built into most biometers is comparable to using multiple formulas in the ASCRS calculator for post-myopic and post-hyperopic eyes.[2]

"It's as accurate as the ASCRS calculator, if not a little better," says Dr. Randleman. "We used to look at a lot of different formulas to find the outlier, but that's no longer necessary."

SELECTING IOL BASED ON SPHERICAL ABERRATION

HOAs aren't often an issue for the average patient with no history of refractive surgery, but they can be big issues for patients who have had refractive surgery. Refractive surgery often changes spherical aberration profiles, which can affect contrast sensitivity.

The *Survey of Ophthalmology* article includes a table that details how to select IOLs based on spherical aberration profiles. For example, aspheric IOLs are best for positive spherical aberration profiles (commonly found after myopic correction). Spheric IOLs are best for negative spherical aberration profiles (commonly found after hyperopic correction).

CORRECTING ASTIGMATISM AND PRESBYOPIA

The article also discusses managing astigmatism in cataract surgery patients to optimize their satisfaction and quality of vision. Toric IOL implantation and astigmatic keratotomy have been effective in some patients.

Considering the significance of the advent of presbyopia-correcting lenses in cataract surgery, these options also are discussed, including pseudophakic monovision, light-adjustable IOL, trifocal IOL, extended depth-of-focus IOL and small-aperture IOL.

Dr. Randleman says determining candidacy for presbyopia-correcting lenses in patients with prior refractive surgery is especially important because, as noted previously, most patients are particularly motivated to reduce their reliance on glasses or contacts. The need for accuracy also is increased in these patients.

"You've got to be better with your calculations and your final target, as these patients are more likely to need a follow-up treatment," he says.

REFRACTIVE LASER CORRECTION FOLLOWING CATARACT SURGERY

Patients often ask if they can have another refractive surgery if needed after cataract surgery.

"The only way to answer that question is to do a screening and evaluation prior to cataract surgery," says Dr. Randleman. "It's much better to answer the question ahead of time rather than after cataract surgery, when you may find that the patient is not a candidate for repeat corneal refractive surgery."

TWO PATIENT POPULATIONS IN CATARACT SURGERY

As advancements in diagnostics, IOL options and IOL power formulas continue, there's much more to learn about their impact on patients with a history of refractive surgery.

"Preoperative evaluation of patients who have had refractive surgery is more complex than in patients who haven't had refractive surgery," concludes Dr. Randleman. "We must continue to recognize and address the differences in these two patient populations." ■

References

1. Ferguson TJ, Randleman JB. Cataract surgery following refractive surgery: Principles to achieve optical success and patient satisfaction. *Surv Ophthalmol*. 2023 Aug 26:S0039-6257(23)00113-3.

2. Ferguson TJ, Downes RA, Randleman JB. IOL power calculations after LASIK or PRK: Barrett True-K biometer-only calculation strategy yields equivalent outcomes as a multiple formula approach. *J Cataract Refract Surg.* 2022 Jul 1;48(7):784-789.

MANAGING THYROID EYE DISEASE: INSIGHTS FOR GENERAL OPHTHALMOLOGISTS

INTERVENTIONS ABOUND FOR ACTIVE AND STABLE PHASES OF TED

Catherine Hwang, MD

Thyroid eye disease (TED) has many names: Graves' ophthalmopathy or orbitopathy, dysthyroid ophthalmopathy, malignant or endocrine exophthalmos, and thyroid-associated or -related orbitopathy. Patients have varied clinical presentations, and there's no way to identify which patients will have more severe TED.

"It's an autoimmune disorder with a loose association between the thyroid and periorbital region," explains Catherine Hwang, MD, an oculofacial plastic surgeon at Cleveland Clinic Cole Eye Institute. "The pathogenesis is not completely understood, which is why TED is one of the most difficult diseases I treat."

There are two types of TED:

› **Type I, with more fat involvement.** Patients tend to be younger and have less risk of optic neuropathy but can have eyelid retraction and proptosis.

› **Type II, with more extraocular muscle involvement.** Patients are typically older and have a history of smoking. These patients tend to have optic neuropathy. Type II TED is more challenging to treat.

"I try to educate my patients that the active phase of TED can be around 18-36 months," says Dr. Hwang. "During this time, they could have some improvement but usually won't completely return to baseline. After the active phase, patients enter a stable phase, when corrective surgery becomes an option."

INTERVENTIONS FOR ACTIVE TED

Active TED "can feel like an eternity to patients," says Dr. Hwang. "It's important to support patients as they ride the emotional roller coaster of the disease."

Medical interventions used early in the disease may help curb severity. The main goals during the active stage are to:

1. Establish a euthyroid state by working with the patient's endocrinologist. If medications aren't effective, Dr. Hwang recommends thyroidectomy rather than radioactive iodine.

2. Help patients stop smoking. "Most of my patients with severe TED are smokers," says Dr. Hwang. "We always try to help our patients with smoking cessation as we know it can help prevent worsening of TED."

> **"I TRY TO EDUCATE MY PATIENTS THAT THE ACTIVE PHASE OF TED CAN BE AROUND 18-36 MONTHS.** DURING THIS TIME, THEY COULD HAVE SOME IMPROVEMENT BUT USUALLY WON'T COMPLETELY RETURN TO BASELINE."
>
> – CATHERINE HWANG, MD

3. Treat dry eye and exposure symptoms, the primary complaint in many patients with TED. In addition to conservative treatment with artificial tears and plugs, a small lateral tarsorrhaphy can reduce retraction of the upper eyelid and symptoms of exposure keratopathy. Hyaluronic acid fillers also can be used in the levator plane, transconjunctivally, to help with lid retraction. Fillers act like a gold weight and stretch the levator muscle. Botulinum toxin also can be used.

4. Follow patients regularly. "If the disease is more severe, I see the patient more often; if it's less severe, I see them less often," says Dr. Hwang. "At each visit I take measurements, but I also consider how the patient feels: the same, better or worse. If they feel worse or have worsening symptoms, we consider immunosuppression."

5. Consider immunosuppression. Intravenous methylprednisolone (500 mg per week for six weeks, then 250 mg per week for six weeks) is the first-line treatment to reduce inflammation and help patients feel better. It doesn't address fibrosis, however, and is not recommended for patients with hepatic, renal, cardiovascular or psychiatric disease, or uncontrolled diabetes. Other immunotherapies are being studied, including IL-6 receptor antibodies and insulin-like growth factor receptor antibodies such as teprotumumab.

6. Consider orbital radiotherapy, which may have some effect on inflammation, motility and proptosis. It is administered in 10 treatments over two weeks (total 20 Gy) and produces minimal side effects (e.g., corneal dryness, cataracts).

7. Consider orbital decompression in cases of optic neuropathy. Optic neuropathy affects approximately 5% of patients with TED, including some without significant proptosis. Patients who smoke or have diabetes are at highest risk. Intravenous methylprednisolone is often the first-line treatment. If inflammation does not decrease, medial decompression surgery may help create more space for the optic nerve.

SURGICAL TREATMENT FOR STABLE TED

Although patients can be eager to return to their normal eye function and appearance, surgery should not be considered (unless for optic neuropathy) until TED stabilizes.

"Performing decompression, eyelid surgery or eye muscle surgery too soon could be detrimental," says Dr. Hwang. "During the active phase of TED, things are continually changing and sometimes improve on their own. In addition, early surgery could trigger a reactivation of the disease."

Remember Rundle's curve, she advises (Figure 1). Lid retraction resolves in 57% of patients. Extraocular muscle involvement remains stable in 50%, worsens in 25% and improves in 25%. Following a period of maximum severity, proptosis tends to abate and stabilize.

"When it's time to consider surgery, I try to help patients set realistic expectations," says Dr. Hwang. "Patients likely won't return to how they looked before TED, but we strive to improve their quality of life and help them feel better. I stress that surgery is for the health of their eyes, but of course we also think of cosmesis with every surgery."

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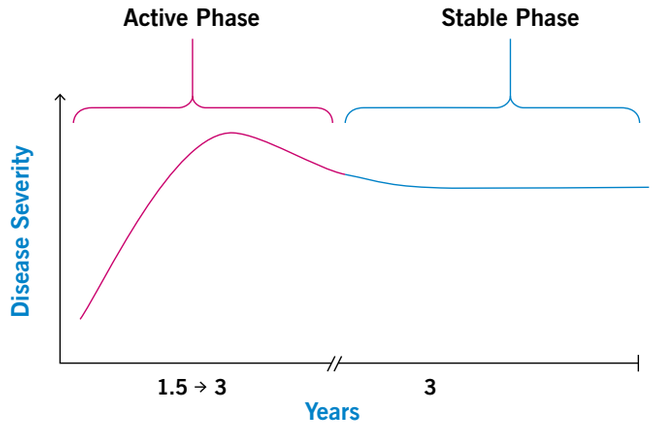


Figure 1. The Rundle's curve concept illustrates how severity of TED increases during the early phase of the disease and stabilizes during the later phase.

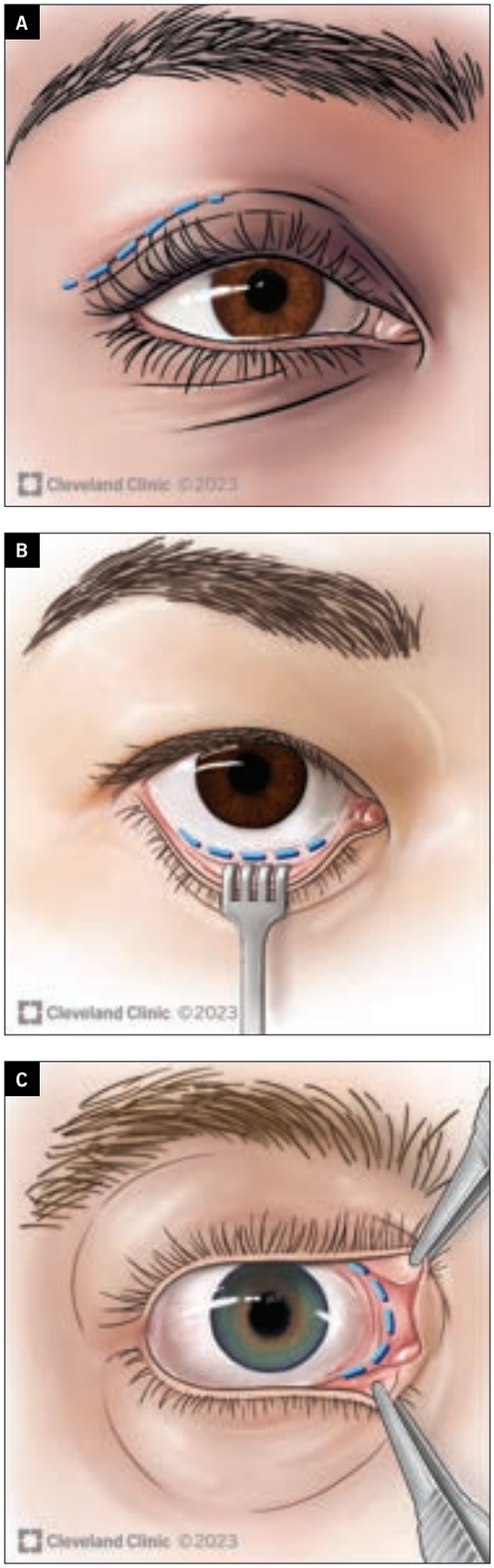


Figure 2. Three approaches to decompression surgery for TED: lateral eyelid crease (A), transconjunctival (B) and transcaruncular (C).

Surgical treatment often requires multiple steps.

Step 1: Decompression. Decompression surgery involves removing bone or intraconal fat in patients with proptosis, pressure pain, congestion, exposure or optic neuropathy.

Decompression procedures are customized for each patient according to the severity of proptosis; the size of the lacrimal gland, lateral sphenoid and medial rectus; and other factors. Dr. Hwang usually obtains an orbital imaging study, such as a CT scan, to evaluate the patient's anatomy. Then, to access the desired locations for decompression, she recommends one or more surgical approaches: lateral eyelid crease, transconjunctival or transcaruncular (Figure 2).

Lateral eyelid crease decompression is best for patients with large lacrimal glands and prominent brow fat. The goal of surgery is to remove the thicker bone in the lacrimal area as well as the sphenoid diploe, creating more room for the orbital contents.

The lateral transconjunctival approach is best to avoid a lateral eyelid crease incision and gain access to the thick lateral bone, especially useful in Asian patients. It's also useful for patients with less proptosis or those with more congestion than proptosis.

The transcaruncular approach often provides the most proptosis reduction. According to Dr. Hwang, the procedure is best for patients with significant proptosis. The surgeon can access the medial wall and open it into the sinuses. Caution is taken in patients with larger medial rectus muscles. These muscles can fall into the sinus and cause worsening diplopia, but patients are counseled to be prepared for this risk.

Orbital decompression progresses in a graded fashion (Table), beginning with orbital fat and adding the lateral bone and medial wall if needed for more reduction. Rarely is the orbital floor used for decompression as surgery there can cause setting-sun eye phenomenon and infraorbital nerve damage.

Balanced lateral and medial decompression is useful in patients with severe proptosis. However, patients may have worsening postoperative diplopia.

Area	Reduction in proptosis
1. Orbital fat	2-3 mm
2. Lateral bone	3-6 mm
3. Medial wall	4-7 mm
4. Orbital floor	5-9 mm

Table. Stages of orbital decompression

Step 2: Eye muscle surgery. Some patients require eye muscle surgery, primarily to correct diplopia in primary vision and downward gaze. Eye muscle or strabismus surgery is performed after decompression surgery as decompression surgery could affect diplopia.

Step 3: Eyelid repositioning. Upper eyelid retraction surgery can be performed either posteriorly or with a full-thickness blepharotomy. Posterior release may provide a longer tarsal platform show, while full-thickness blepharotomy may better adjust lid crease height. The approach depends on the surgeon as well as the amount of retraction.

In the lower eyelid, release of the retractors can be performed alone or with a hard palate or other graft, with or without a midface lift depending on the patient's anatomy.

Eyelid retraction surgery can help significantly with dryness and exposure keratopathy. Lateral permanent tarsorrhaphy also may help and be used alone or in combination with eyelid retraction surgery.

Step 4: Cosmetic procedures. Procedures can include upper and lower blepharoplasty, fillers and botulinum toxin treatments.

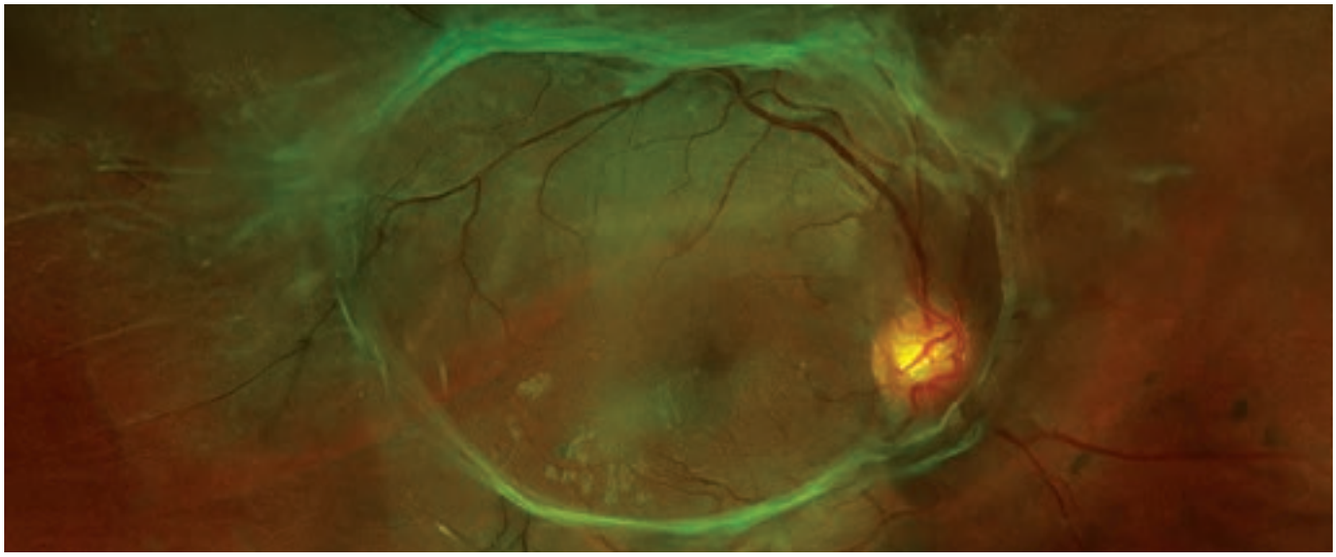
"These four surgical steps are only guidelines," says Dr. Hwang. "Some steps can be combined or skipped depending on patient needs. The goal is to offset the disfiguring effects of TED, empowering patients to feel more confident about resuming their normal activities." ■

"WHEN IT'S TIME TO CONSIDER SURGERY, I TRY TO HELP PATIENTS SET REALISTIC EXPECTATIONS. ... WE STRIVE TO IMPROVE THEIR QUALITY OF LIFE AND HELP THEM FEEL BETTER. I STRESS THAT SURGERY IS FOR THE HEALTH OF THEIR EYES, BUT OF COURSE WE ALSO THINK OF COSMESIS."

– CATHERINE HWANG, MD

CLINICAL TRIALS

THE FOLLOWING STUDIES ARE EITHER CURRENTLY ENROLLING NEW PATIENTS OR ARE PENDING APPROVAL BY THE INSTITUTIONAL REVIEW BOARD AND SHOULD BE ENROLLING SOON.



RETINAL DISEASES

- **ALLUVIUM:** A Phase 2, Multicenter, Randomized, Double-Masked, Active-Comparator Controlled Study to Investigate the Efficacy, Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of RO7200220 Administered Intravitreally in Patients With Diabetic Macular Edema

  Contacts: Sumit Sharma, MD (216.445.4904)
  Nicole Shepherd (216.445.8499)

- **DEXTENZA:** Intracanalicular Dexamethasone Insert for Management of Postoperative Pain and Inflammation in Patients Undergoing Vitreoretinal Surgery

  Contacts: Katherine Talcott, MD (440.988.4040)
  Theresa Kovacs (216.445.3762)

- **DRCR Protocol AF:** A Randomized Clinical Trial Evaluating Fenofibrate for Prevention of Diabetic Retinopathy Worsening

  Contacts: Aleksandra Rachitskaya, MD (216.445.9519)
  Teresa Randle (216.444.3735)

- **HONU:** A Multicenter, Prospective, Observational Study of the Progression of Intermediate Age-Related Macular Degeneration (GE43220)

  Contacts: Sumit Sharma, MD (216.445.4904)
  Nicole Shepherd (216.445.8499)

- **JANSSEN:** Global Patient Registry of Inherited Retinal Diseases

  Contacts: Elias Traboulsi, MD (216.445.8514)
  Angela Meador (216.445.7176)

- **PREGONDA:** A Multicenter, Nonrandomized, Open-Label, Multiple Ascending Dose Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of RO7497372 Following Intravitreal Administration in Participants With Diabetic Macular Edema

  Contacts: Sumit Sharma, MD (216.445.4904)
  Nicole Shepherd (216.445.8499)

- **TELESCOPE:** A Prospective, Multicenter Clinical Study of the Implantable Miniature Telescope, Model SING, in Patients With Central Vision Impairment Associated With End-Stage Age-Related Macular Degeneration

  Contacts: Aleksandra Rachitskaya, MD (216.445.9519)
  Angela Meador (216.445.7176)

UVEITIS

› **ACELYRIN:** A Phase 2b Pivotal Study to Evaluate the Efficacy and Safety of Izokibep in Subjects With Noninfectious Intermediate, Posterior or Panuveitis

Contacts: Sumit Sharma, MD (216.445.4904)
Bolisa Savic (216.978.1264)

› **OPTIMTX:** Optimizing Methotrexate Use for Management of Chronic Pediatric Noninfectious Uveitis

Contacts: Sunil Srivastava, MD (216.636.2286)
Bolisa Savic (216.978.1264)

› **SANDCAT:** A Phase 3, Multicenter, Randomized, Double-Masked, Sham-Controlled Study to Investigate the Efficacy, Safety, Pharmacokinetics and Pharmacodynamics of RO7200220 Administered Intravitreally in Patients With Uveitic Macular Edema

Contacts: Sumit Sharma, MD (216.445.4904)
Stacie Dempsey (216.445.1649)

GENE THERAPY

› **ASCENT:** A Randomized, Partially Masked, Controlled, Phase 3 Clinical Study to Evaluate the Efficacy and Safety of RGX-314 Gene Therapy in Participants With nAMD

Contacts: Katherine Talcott, MD (440.988.4040)
Dusica Vasic (216.445.3840)

› **ATMOSPHERE:** A Randomized, Partially Masked, Controlled, Phase 2b/3 Study to Evaluate the Efficacy and Safety of RGX-314 Gene Therapy in Participants With nAMD

Contacts: Alex Yuan, MD, PhD (216.444.0079)
Dusica Vasic (216.445.3840)

› **DAWN:** A Phase 1/2, Open-Label, Dose-Escalation Study to Evaluate the Safety and Efficacy of AGTC-501 (rAAV2tYF-GRK1-RPGR) and a Phase 2, Randomized, Controlled, Masked, Multicenter Study Comparing Two Doses of AGTC-501 in Male Participants With X-Linked Retinitis Pigmentosa

Contacts: Aleksandra Rachitskaya, MD (216.445.9519)
Angela Meador (216.445.7176)

› **ORACLE:** A Long-Term Follow-Up Study to Evaluate the Safety and Durability of GT005 in Participants With Geographic Atrophy Secondary to Age-Related Macular Degeneration Treated in a Gyroscope-Sponsored Antecedent Study

Contacts: Alex Yuan, MD, PhD (216.444.0079)
Theresa Kovacs (216.445.3762)

› **PARASOL:** A Phase 2b, Randomized, Double-Masked, Multicenter, Dose-Ranging, Sham-Controlled Clinical Trial to Evaluate Intravitreal JNJ-81201887 (AAVCAGsCD59) Compared to Sham Procedure for the Treatment of Geographic Atrophy Secondary to Age-Related Macular Degeneration

Contacts: Katherine Talcott, MD (440.988.4040)
Nicole Shepherd (216.445.8499)

GLAUCOMA

› **COAST:** Clarifying the Optimal Application of SLT Therapy

Contacts: Ang Li, MD (216.445.0346)
Dusica Vasic (216.445.3840)

› **PILOCARPINE:** In-Office Pilocarpine Challenge as Predictor of Goniotomy Outcome — Pilot Project

Contacts: Ang Li, MD (216.445.0346)
Nicole Shepherd (216.445.8499)

ONCOLOGY

› **AURA:** A Phase 3, Randomized, Masked, Controlled Trial to Evaluate Efficacy and Safety of Belzupacap Sarotalocan (AU-011) Treatment Compared to Sham Control in Subjects With Primary Indeterminate Lesions or Small Choroidal Melanoma

Contacts: Arun Singh, MD (216.445.9479)
Angela Meador (216.445.7176)

ANTERIOR SEGMENT

› **BEYEONICS:** An Image Performance Study to Validate the Ability of the Beyeonics One iOCT to Visualize the Anterior and Posterior Segment of the Eye

Contacts: Katherine Talcott, MD (440.988.4040)
Teresa Randle (216.444.3735)

› **ReGenTree (SEER-2):** A Phase 3, Multicenter, Randomized, Parallel, Double-Masked, Placebo-Controlled Clinical Study to Assess the Safety and Efficacy of 0.1% RGN-259 Ophthalmic Solution for the Treatment of Neurotrophic Keratopathy

Contacts: Rony Sayegh (216.215.4001)
Theresa Kovacs (216.445.3762)

NEW STAFF

THE COLE EYE INSTITUTE WELCOMED THESE NEW STAFF MEMBERS IN 2023.

Kevin Keppel, MD, is a comprehensive ophthalmologist with clinical interests in cataracts and comprehensive eye care. He completed a residency at the Cole Eye Institute after earning his medical degree from University of Pittsburgh School of Medicine.

Thomas Krainz, OD, specializes in eye care for older adults as well as specialty and routine contact lens fitting. After graduating from The Ohio State University College of Optometry, Dr. Krainz completed a residency in ocular disease at the Louis Stokes Cleveland Department of Veterans Affairs Medical Center.

Ananth Sastry, MD, is a vitreoretinal surgeon with a specialty interest in uveitis. He earned his medical degree from the University of Miami Miller School of Medicine before completing a residency at the USC Roski Eye Institute. Dr. Sastry then completed a fellowship in vitreoretinal surgery at the Duke Eye Center.

Robert Stern, MD, returned to Cleveland Clinic after 36 years in private ophthalmology practice in Westlake, Ohio. He completed his residency at Cleveland Clinic following his graduation from University at Buffalo (SUNY) Jacobs School of Medicine and Biomedical Sciences. Dr. Stern provides comprehensive eye care.

Mansi Talati, MD, is a cornea and comprehensive disease specialist. She earned her medical degree from Saint Louis University School of Medicine and later completed a residency at Drexel University College of Medicine, followed by a fellowship in cornea and external disease at The Ohio State University Wexner Medical Center.

News BRIEFS

NEW APPOINTMENT

Brian Perkins, PhD, has been appointed Vice Chair, Department of Ophthalmic Research, at Cleveland Clinic Cole Eye Institute. Dr. Perkins joined the institute in 2012. His research explores the genetic and cellular basis of photoreceptor degeneration and regeneration.

Brian Perkins, PhD

NATIONAL EYE INSTITUTE GRANT

Dr. Perkins recently received a four-year, $2.1 million National Eye Institute grant to study the role of inflammation in retinal regeneration. “Our lab’s work with zebrafish could be valuable in helping develop ways to induce retinal regeneration in humans,” he says.

ROSCOE KENNEDY, MD, LECTURESHIP

Tamara R. Fountain, MD, Past President of the American Academy of Ophthalmology, was the featured speaker at the 2023 Roscoe Kennedy, MD, Lectureship, hosted in October at the Cole Eye Institute. The lectureship was established in 1987 to attract world-renowned physicians and scientists to Cleveland Clinic to present educational programs for staff, fellows, residents and alumni. It is named in honor of Dr. Kennedy, past Chair of Cleveland Clinic’s Department of Ophthalmology, who helped foster the department’s commitment to research and education.

2023 ACGME GIENAPP AWARD

Elias I. Traboulsi, MD, MEd, was honored with the 2023 ACGME John C. Gienapp Award for outstanding contributions to the enhancement of residency education and ACGME accreditation activities. Dr. Traboulsi is the Stanley Stone Professor of Pediatric Ophthalmology and Vice Chair for Education at the Cole Eye Institute.

LIFETIME ACHIEVEMENT AWARD

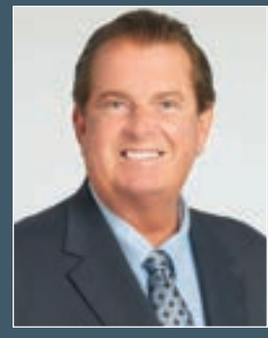
Daniel F. Martin, MD, Chair of the Cole Eye Institute, was honored with the Lifetime Achievement Award for Excellence in Clinical Trials at the 2023 Clinical Trials at the Summit conference.

ISRS LANS DISTINGUISHED AWARD

J. Bradley Randleman, MD, of the Cole Eye Institute, received the 2023 Lans Distinguished Award from the International Society of Refractive Surgery (ISRS). He was recognized for his innovative contributions to the field of refractive surgery, especially in the correction of astigmatism.

ISRS PRESIDENTIAL RECOGNITION AWARD

Steven E. Wilson, MD, of the Cole Eye Institute, was honored with the 2023 Presidential Recognition Award from ISRS. He was lauded for his decades of contributions to enhancing the safety and efficacy of refractive surgery as well as training dozens of refractive surgery fellows.



Steven E. Wilson, MD

MILITARY HEALTH SYSTEM OUTSTANDING RESEARCH

Dr. Wilson also received the Individual Award for Outstanding Research at the 2023 Military Health System Research Symposium. The U.S. Department of Defense recognized Dr. Wilson for his innovative work on the use of topical losartan to treat corneal fibrosis. His research is anticipated to revolutionize the treatment of U.S. service members with eye trauma.

OPHTHALMOLOGY WALK OF FAME

For his career contributions to corneal and refractive surgery, **Dr. Wilson** has been honored with a star on the Ophthalmology Walk of Fame outside the Sorocaba Eye Hospital in São Paulo, Brazil, home to one of the largest eye banks in the world.

Alex Yuan, MD, PhD

AAO SECRETARIAT AWARDS

The American Academy of Ophthalmology (AAO) honored **Drs. Randleman and Traboulsi** with 2023 Secretariat Awards for their special contributions to the academy and ophthalmology.

TEACHER OF THE YEAR

Alex Yuan, MD, PhD, was selected as 2023 Teacher of the Year by residents at the Cole Eye Institute.

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Cleveland Clinic is a globally integrated multispecialty healthcare system combining hospital and outpatient care with research and education for better patient outcomes and experience. Cleveland Clinic has more than 76,000 caregivers worldwide, including more than 5,600 physicians and scientists. The health system consists of 22 hospitals and 275 outpatient locations, including a main campus in Cleveland; 14 regional hospitals in Northeast Ohio; five hospitals in Southeast Florida; a center for brain health in Las Vegas, Nevada; executive health and sports health services at two locations in Toronto, Canada; a hospital and outpatient center in London, United Kingdom; and a hospital and cancer center in Abu Dhabi, United Arab Emirates. Cleveland Clinic is currently ranked as one of the nation's top hospitals by *U.S. News & World Report*.
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OPHTHALMOLOGY UPDATE

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