Cleveland Clinic

SPECIAL EDITION 2019

*caring for* {COMPLEX CONDITIONS}

# Ophthalmology Update

From Cole Eye Institute

# *from the* {CHAIR}

Welcome to the latest issue of *Ophthalmology Update* from Cleveland Clinic Cole Eye Institute.

We appreciate your interest in our program, and hope you find the theme of this Special Edition newsletter — complex medical and surgical treatments — to be both educational and fascinating. We asked our surgical staff to share some of their most interesting and challenging cases from the past year, and we are pleased to present them here as they help tell the story of what we do.

**Highlights include:**

- Learn how we have integrated novel technologies into the care of Argus® II retinal prosthesis recipients, including intraoperative optical coherence tomography, a 3D viewing system and computer-assisted visual rehabilitation.
- See how an ab-interno trabeculotomy restored aqueous outflow in a young man with Schwartz-Matsuo glaucoma.
- Check out how Descemet's stripping endothelial keratoplasty (DSEK) was used to treat a perforated cornea.
- Read about how a case of orbital nodular fasciitis was misdiagnosed elsewhere as sarcoma. A correct diagnosis spared the patient from having his eye removed.

**About the Cole Eye Institute**

We are also proud to share with you that we are continuing to grow in our ability to see more patients and to conduct more research, notably:

- Institute physicians and researchers continued to serve as editors-in-chief or executive editors of 14 journals.
- Clinical research continued to be a strong component of our work, with 22 clinical trials available for our patients.
- Our National Institutes of Health funding reached an all-time high, with almost every principal investigator supported by at least one R01, R21, K08 or K23 grant.
- Our philanthropic outreach efforts secured commitments of almost $100 million over the past six years.
- Community service continues to be a strong component of our mission. For example, the Cleveland Clinic & Kohl's Vision First program screens more than 5,000 children in the Cleveland Metropolitan School District each year via a specially equipped van.

In fact, 2018 was a record year in every aspect, including the highest number of patients seen and surgeries performed. Adding new practice locations this year brings our total examination lanes to over 240 on main campus and throughout the region. All of this growth has made the need more acute to expand the Cole Eye Institute's main campus facility. In 2018, we began architectural planning for a more than 100,000-square-foot addition to our building.

I am exceptionally proud of our team of ophthalmologists, optometrists, researchers, nurses, technicians and others who are committed to advancing the care of patients in everything they do. Their innovation, collaborative spirit and commitment to providing world-class care are second to none.

I hope you enjoy this special edition of *Ophthalmology Update*.

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

# Predicting Visual Acuity Response to Anti-VEGF Therapy in Macular Edema Secondary to Retinal Vein Occlusion

## IS DISORGANIZATION OF RETINAL INNER LAYERS A USEFUL PROGNOSTIC INDICATOR?

{By Amy S. Babiuch, MD, and Rishi P. Singh, MD | Center for Ophthalmic Bioinformatics}

Can we predict how a patient will respond to therapy? In previous studies, the disorganization of retinal inner layers (DRIL) demonstrated its ability to help determine visual acuity (VA) prognosis in diabetic macular edema that requires treatment.

Given this association, the research group at Cole Eye Institute studied how DRIL may affect VA outcomes in patients with retinal vein occlusion (RVO) undergoing treatment for secondary macular edema with anti-vascular endothelial growth factor (anti-VEGF) agents.

### WHAT IS DRIL?

DRIL is defined as the extent to which there is a failure in the recognition of any of the demarcations between the ganglion cell-inner plexiform layer complex, inner nuclear layer and outer plexiform layer on optical coherence tomography (OCT). This is demonstrated in Figure 1, where yellow lines course through the areas of normal demarcation and stop at those areas with poor demarcation.

### IDENTIFYING DRIL IN RVO STUDY OVERVIEW AND VISUAL ACUITY OUTCOMES

Our researchers performed a retrospective study of eyes from patients with treatment-naïve RVO and a minimum of 12 months' follow-up. The study included patients with central retinal vein occlusion (CRVO), hemiretinal vein occlusion (HRVO) and branch retinal vein occlusion (BRVO). Baseline DRIL was identified in 61.9 percent of all eyes (91/147).

DRIL burden was followed throughout the treatment course using a presence or absence approach to score DRIL across three regions (Figure 1) on the horizontal OCT line scan at baseline, six months and 12 months. At six and 12 months,

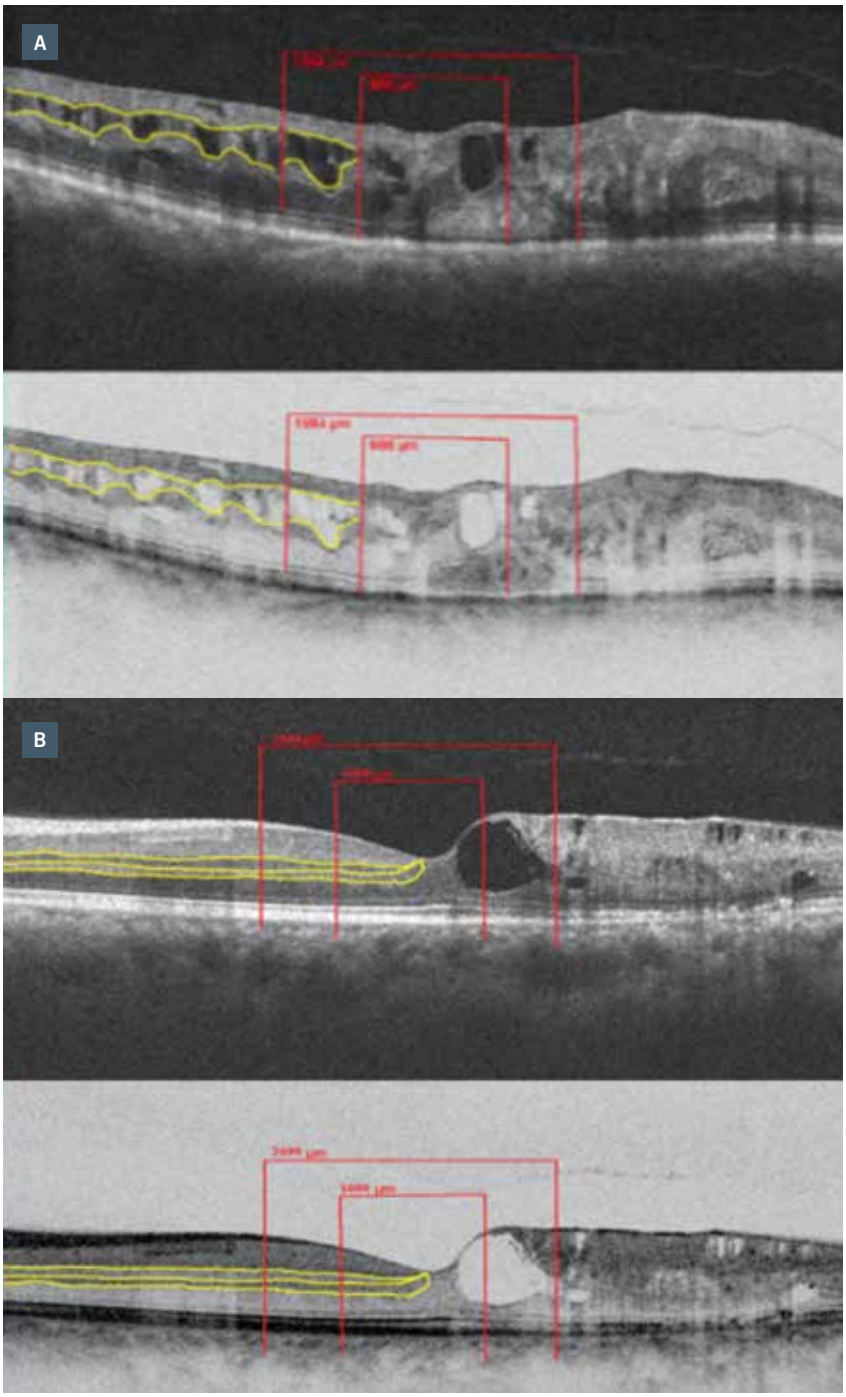



**Figure 1.** Representation of disorganization of retinal inner layers (DRIL) on spectral-domain OCT (SD-OCT) and reverse gray-scale SD-OCT. The yellow lines highlight the inner retinal layer interfaces, which disappear in the areas of DRIL. The red lines demonstrate the three regions where DRIL was scored. (A) Patient with a central retinal vein occlusion exhibiting intraretinal fluid and DRIL. (B) Patient with a branch retinal vein occlusion exhibiting intraretinal fluid and DRIL.

DRIL scores were further evaluated for stable, increasing or decreasing DRIL burden.

Based on the results of the study, our group concluded that the presence of DRIL at baseline in BRVO patients is associated with worse baseline VA. Increasing DRIL burden in CRVO and HRVO patients is associated with reduced VA gains.

### WHY DOES IT MATTER?

For patients undergoing treatment with anti-VEGF agents, it's important to identify biomarkers that might influence overall VA outcomes. In this series of RVO patients, a modest increase in DRIL detection was observed in months six through 12, and when this was compared to the number of anti-VEGF injections delivered, the average number of injections decreased by about half during those months as compared to the first six months. This decline in treatment with anti-VEGF agents may have allowed for progression of disease.

These results demonstrate how using OCT to identify novel biomarkers such as DRIL in RVO helps guide treatment with anti-VEGF therapy, and is a useful prognostic indicator for VA in RVO patients.

This work allows clinicians to better forecast how patients will progress with treatment. ●

*Dr. Babiuch presented this study on the podium at the 2018 American Society of Retina Specialists (ASRS) annual meeting, and it has been accepted by* JAMA Ophthalmology. *She and Dr. Singh are retina specialists.*

# Treating Progressive Keratoconus: Going Beyond Disease Stabilization

## COMBINED TRANSEPITHELIAL PTK, CXL YIELDS IMPROVEMENTS

{By William J. Dupps, MD, PhD}

A 24-year-old graduate student from the East Coast presented to the Cole Eye Institute for contact lens fitting. She reported having several years of increasing myopia and astigmatism with frequent spectacle and contact lens changes, and we made a diagnosis of keratoconus at that visit. She was concerned about her recent decrease in vision and reduced contact lens tolerance and was promptly referred to the Cornea and Refractive Surgery service.

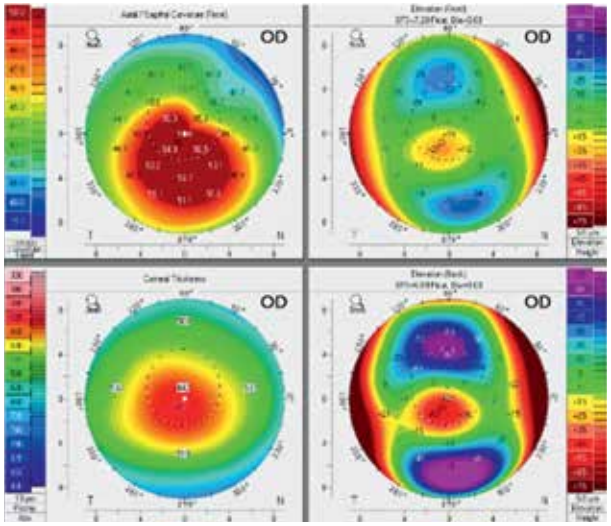



**Figure 1**

Her best spectacle-corrected visual acuity was 20/25- in each eye with manifest refractive error of -3.75 + 4.25 x 005 OD and -4.75 + 1.25 x 095 OS. Scheimpflug tomography demonstrated predominantly central cones with colocalized anterior and posterior surface elevation and thinning (right eye shown in Figure 1). Working around her busy final exam schedule, we decided to proceed with corneal cross-linking (CXL) in the right eye to address the disease progression before further loss of spectacle-corrected vision occurred.

### STABILIZING AND REGULARIZING THE CORNEA

Research conducted at the Cole Eye Institute's Ocular Biomechanics and Imaging Lab has demonstrated through patient-specific computational modeling how progressive localized weakening of the corneal stroma can occur insidiously in keratoconus with little evidence of topographic change until advanced weakening has occurred (Figure 2). If left unchecked, this weakening will lead to exponential increases in corneal steepness and asymmetry and, as a result, potentially irreversible degradation of corneal optics and retinal image quality.

CXL is a major advance for stabilization of keratoconus. But in this young patient who had already lost lines of vision from progression, we sought to customize her treatment in a way that would offer a greater chance of visual improvement while also halting disease progression.

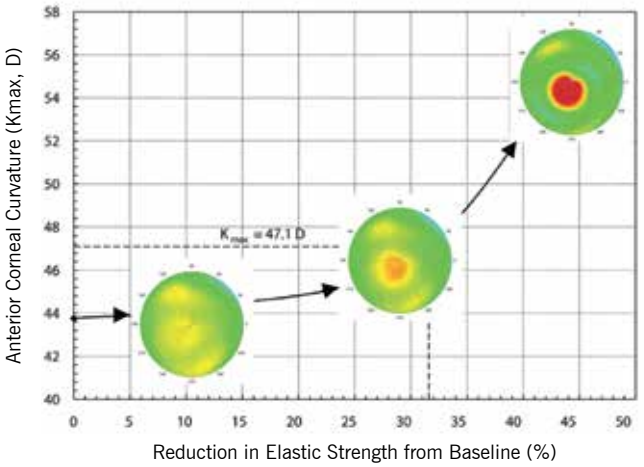



**Figure 2**

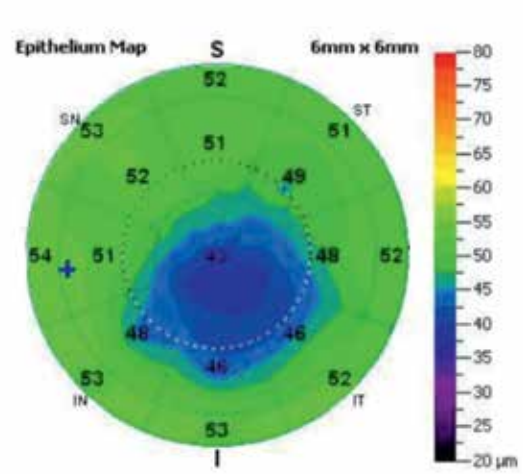



**Figure 3**

To this end, spectral-domain optical coherence tomography mapping of her corneal epithelial thickness profile was obtained. As illustrated in Figure 3, the epithelium was much thinner over the topographic cone (as thin as 39 $\mu$m) than in areas distal to the cone (up to 54 $\mu$m).

I made a surgical plan to use an excimer laser in phototherapeutic keratectomy (PTK) mode to produce a transepithelial ablation of 50 $\mu$m in depth. By leveraging the differential epithelial thickness, this approach was expected to produce a modest, selective 10 $\mu$m ablation of anterior stroma in the region of greatest stromal curvature and elevation, resulting in a targeted flattening effect. The remaining peripheral epithelium was then debrided manually to expose a 9 mm zone for the standard epithelium-off CXL protocol using riboflavin eye drops and UV light.

## OUTCOMES

Three months after combined transepithelial PTK and CXL, the patient reported that her vision was much improved. Her manifest refraction had improved from -3.75 + 4.25 x 005 to -2.50 + 0.75 x 019, and she was able to read the 20/20 line in spectacles for the first time in years. A 2.5 D reduction in corneal steepness was seen on the interval subtraction map (Figure 4). She was able to discontinue specialty contact lenses and return to toric soft lenses, and there has been no evidence of disease progression over the subsequent year.

In this case, careful consideration of corneal structure and advanced imaging informed the approach to treatment and allowed us to leverage keratorefractive surgical techniques for more optimal treatment of the patient's visual disorder. ●

*Dr. Dupps specializes in corneal diseases.*

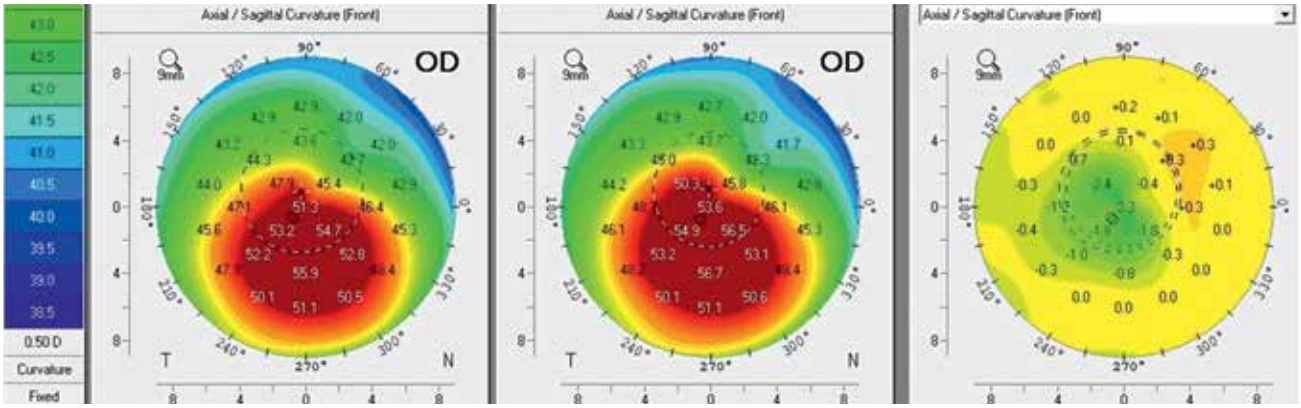
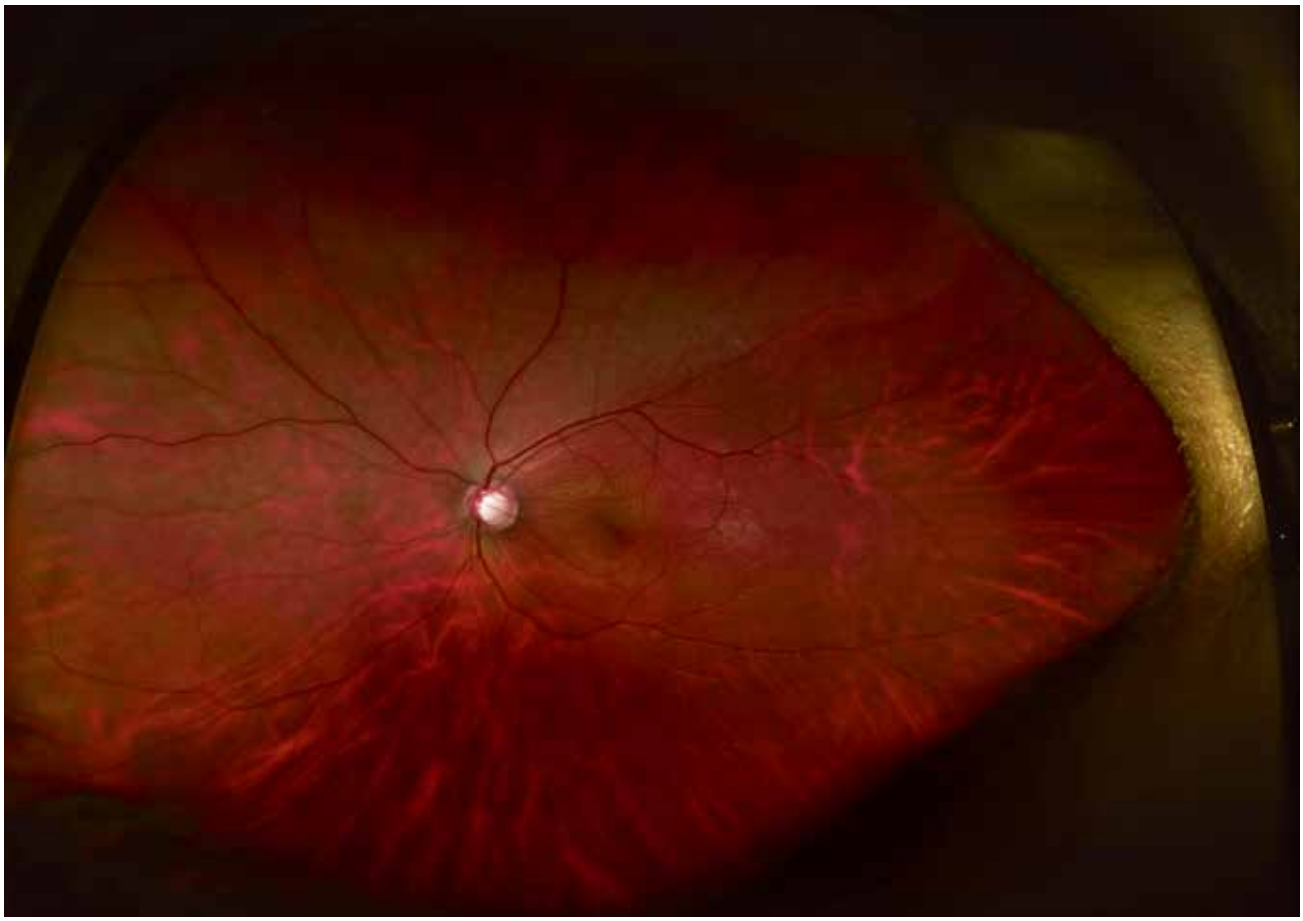



**Figure 4**

# *Ab-interno* Trabeculotomy Restores Aqueous Outflow in Young Man with Schwartz-Matsuo Glaucoma

## 20 MONTHS LATER, IOP REMAINS WELL CONTROLLED

{By Jonathan Eisengart, MD}



A large retinal detachment is seen with subretinal fluid extending right up to the optic disc.

A 29-year-old male was referred to the glaucoma service at the Cole Eye Institute for significant optic disc cupping with intraocular pressure (IOP) of around 12 mm Hg in each eye. His ocular history was significant only for prior strabismus surgery. On initial examination, his vision was 20/20 OU with a low myopic correction. IOP OD remained 12, but the left eye had increased to 40 in the six weeks since he was seen by the referring ophthalmologist. Anterior segment exam was normal OD. The left eye had a few anterior chamber cells and atrophy of the nasal iris sphincter. Gonioscopy was unremarkable OU.

Fundus exam OD revealed a large disc with no focal rim thinning and a cup-to-disc (CD) ratio of 0.8. CD ratio OS was 0.95 with severe diffuse rim thinning. The left eye also had a previously undetected large area of retinal atrophy with subretinal and intraretinal fluid encompassing most of the superonasal quadrant and extending posteriorly to the optic disc. Visual fields demonstrated an inferotemporal arcuate defect OS consistent with retinal findings, and optical coherence tomography showed a diffusely thinned retinal nerve fiber layer, OS greater than OD. The extracted optic disc tomograms OS demonstrated subretinal fluid in the superonasal peripapillary region. Further questioning revealed that three years prior, this young man's left eye had been hit with a tennis ball.

While the low-grade anterior chamber cell with fluctuation and markedly elevated IOP suggested an inflammatory glaucoma such as Posner-Schlossman syndrome, herpetic iridocyclitis or sarcoid uveitis, the retinal detachment led us to include Schwartz-Matsuo syndrome in the differential diagnosis. This patient was prescribed dorzolamide-timolol and prednisolone acetate 1%, each b.i.d. OS, and referred to the retina service for its opinion and expertise.

*While I typically address intractable glaucoma after vitreoretinal surgery with a tube implant, that surgery wasn't ideal in this situation.*

## DIAGNOSIS CONFIRMATION

Three days later, his IOP had improved to 16, and Schwartz-Matsuo syndrome was confirmed when the retina service diagnosed a chronic combined schisis/detachment with a traumatic retinal dialysis. Surgical repair would be technically challenging due to his attached hyaloid, phakic status, prior strabismus surgery complicating buckle placement and giant retinal tear. Therefore, given his well-controlled IOP, the patient was observed initially by both the glaucoma and retina services. Eventually, however, his retinal detachment progressed inferiorly toward the macula, and surgical repair was accomplished via combined pars plana vitrectomy and scleral buckle.

Although the retinal reattachment surgery was successful, his IOP quickly became uncontrolled postoperatively, reaching 29 mm Hg on four topical glaucoma medications and acetazolamide 1,000 mg daily.

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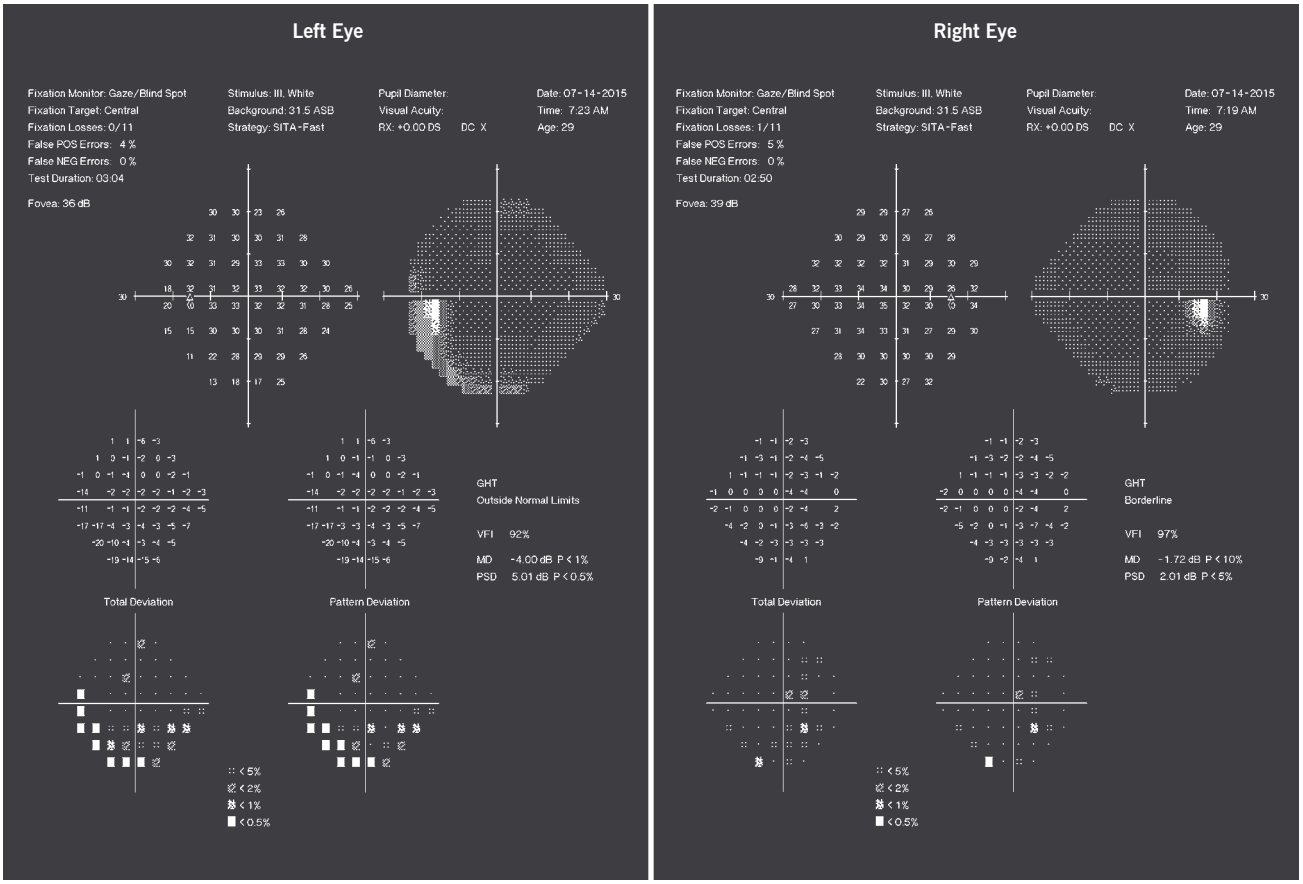
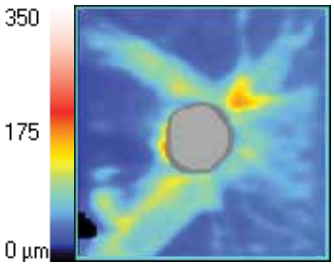



The right eye visual field is largely normal. The left field demonstrates an inferotemporal arcuate defect due to his retinal detachment.

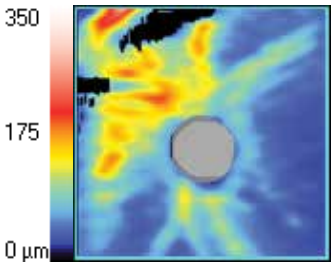
## ONH and RNFL OU Analysis: Optic Disc Cube 200 x 200 OD OS

RNFL Thickness Map

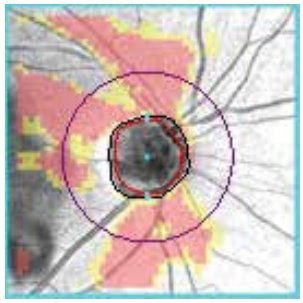



| | OD | OS |
|---|---|---|
| Average RNFL Thickness | 66 µm | 85 µm |
| RNFL Symmetry | 52% | |
| Rim Area | 0.62 mm² | 0.45 mm² |
| Disk Area | 2.30 mm² | 1.94 mm² |
| Average C/D Ratio | 0.86 | 0.89 |
| Vertical C/D Ratio | 0.89 | 0.83 |
| Cup Volume | 0.905 mm³ | 1.133 mm³ |

RNFL Thickness Map

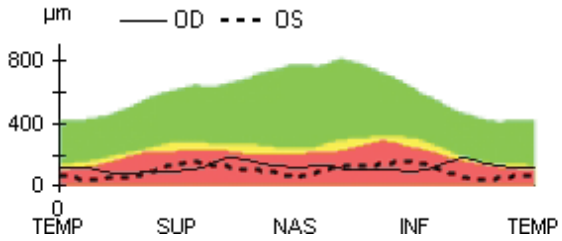



RNFL Deviation Map

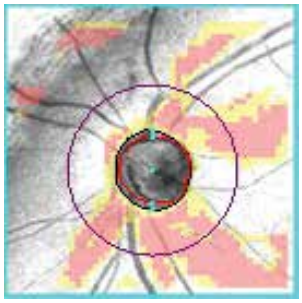


Disc Center (-0.12,-0.09) mm

Neuro-retinal Rim Thickness

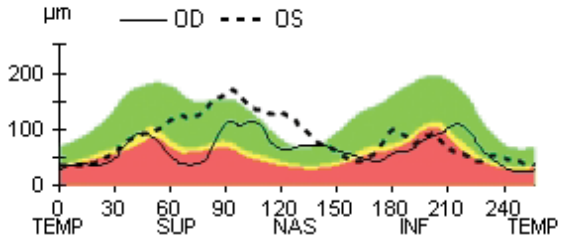



RNFL Deviation Map

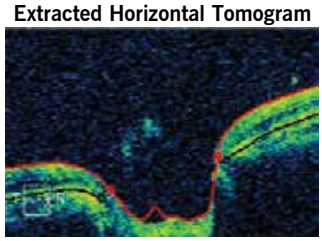


Disc Center (0.00,-0.36) mm

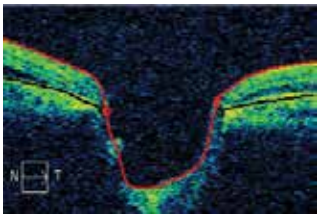
RNFL Thickness



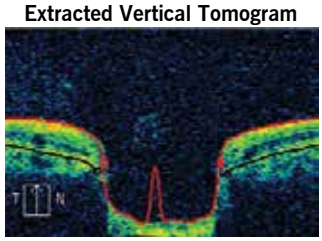

Extracted Horizontal Tomogram



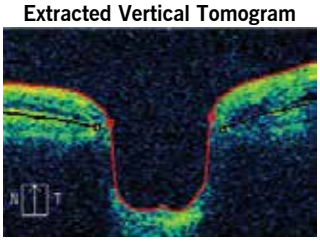
Extracted Horizontal Tomogram

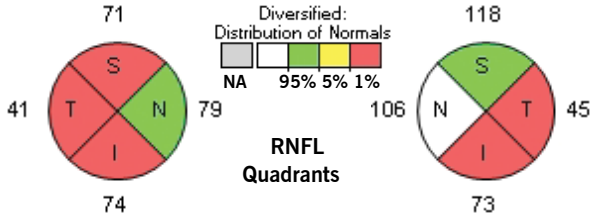


Extracted Vertical Tomogram

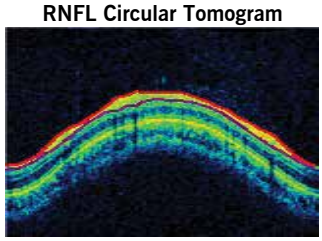


Extracted Vertical Tomogram

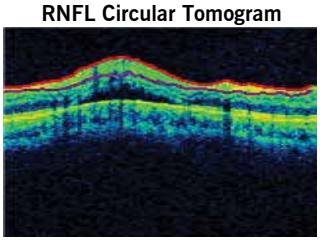


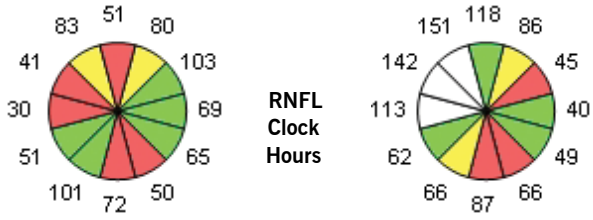



RNFL Circular Tomogram



RNFL Circular Tomogram






There is diffuse retinal nerve fiber layer thinning in the right eye. Given the patient's normal IOP and visual field, this may be physiologic. The artifactual thickening superonasally in the left eye is from intra- and subretinal fluid. Note on the "extracted tomograms" at the lower left that there is subretinal fluid superonasally. Also note the large disc area OD.

Schwartz-Matsuo syndrome is a rare type of glaucoma. In this condition, a chronically detached retina sheds photoreceptor outer segments, which in turn clog trabecular meshwork outflow, increase outflow resistance and lead to a secondary open-angle glaucoma. The cells seen in this patient's anterior chamber were not inflammatory cells, but rather actual photoreceptor segments circulating in the aqueous fluid. As would be expected, these cells are not responsive to topical corticosteroids.

While I typically address intractable glaucoma after vitreoretinal surgery with a tube implant, that surgery wasn't ideal in this situation. This patient's scleral buckle and prior strabismus surgery would complicate glaucoma drainage device implantation. Furthermore, implantation of a glaucoma drainage device at his young age would expose the patient to decades of cumulative risk for tube exposure or corneal endothelial decompensation. Therefore, we hoped to restore function of his natural outflow system rather than bypass it.

## GATT PROCEDURE

To that end, we proceeded with a 360-degree ab-interno trabeculotomy procedure, often referred to as a "GATT" (gonioscopy-assisted transluminal trabeculotomy). This sutureless, blebless procedure is performed through two clear corneal paracenteses utilizing intraoperative gonioscopy. A thin, lighted catheter is inserted through a tiny paracentesis and guided through a goniotomy incision into Schlemm's canal.

Once the catheter passes 360 degrees, the distal end of it is retrieved from Schlemm's, and the two ends of the catheter are pulled to tear through trabecular meshwork, completing a 360-degree trabeculotomy. Because this procedure augments the eye's natural aqueous outflow rather than trying to bypass it, there is essentially no risk of hypotony, and it entails none of the long-term risk associated with implanting a drainage shunt.

Surgical time for his procedure was 12 minutes. Twenty months later, the patient's IOP remains 8 mm Hg on dorzolamide-timolol fixed combination. In the end, we were able to achieve a durable repair of his retinal detachment and to achieve long-term control of his eye pressure with a quick, safe surgery that did not fundamentally alter his aqueous outflow physiology or ocular anatomy. ●

*Dr. Eisengart is a glaucoma and cataract specialist.*

# Novel Treatment for Severe Lymphangiectasia Haemorrhagica Conjunctivae

## SURGICAL DRAINAGE YIELDS EXCELLENT RESULTS

{By Jeffrey M. Goshe, MD; Gabrielle Yeaney, MD; and Arun D. Singh, MD}

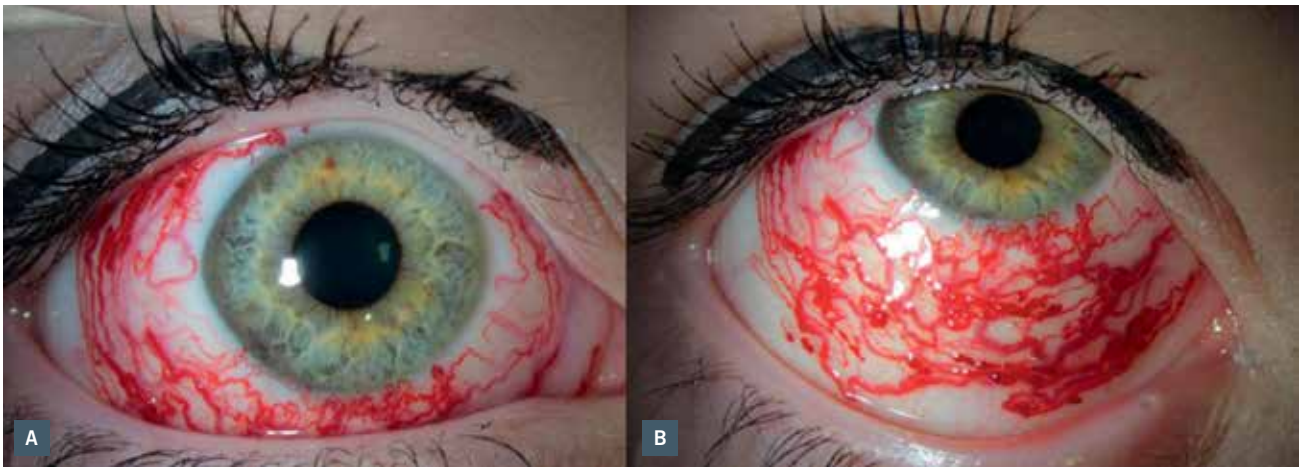



**Figure 1**. A and B Slit-lamp photographs demonstrating appearance of prominent circumferential vessels.

About one year prior to presenting to Cleveland Clinic Cole Eye Institute, a 17-year-old girl noticed a painless "red spot" affecting the inferior bulbar surface of her right eye. An outside ophthalmologist examined her and noted a small prominent conjunctival vessel inferiorly with prominent, circumferential cystic lymphatic changes. The lesion remained stable for nine months, but then suddenly and dramatically enlarged.

### UNCLEAR ETIOLOGY

When she presented to us for evaluation, we found no evidence of trauma or recent viral illness. She did not wear contact lenses. She had a remote seizure disorder, successfully managed with oral levetiracetam for five years. Her vision was 20/20 OU, her intraocular pressures were 18 and 22 mm Hg, and other eye exam measures were all within normal limits. However, slit-lamp examination demonstrated a large circumferential network of blood-filled vessels extending from the limbus in a 4-8 mm-wide zone (Figures 1A, B). The superficial vessels were freely mobile, but deeper vessels were fixed.

Magnetic resonance imaging and MRI angiography of the brain and orbits, ordered based on her seizure history, proved normal. Anterior segment fluorescein angiography revealed normal filling of surrounding conjunctival arterioles and venules. However, the angiogram did confirm no-flow sequestration of blood in lymphatic channels, confirming our suspicion of the lymphatic origin of the channels, and we diagnosed nonresolving lymphangiectasia haemorrhagica conjunctivae (LHC).

### NORMALLY SELF-LIMITING

LHC is a rare condition that occurs as a result of acute or subacute hemorrhagic engorgement of conjunctival lymphatic channels. How blood enters the channels is not well-understood. Some think it is a matter of valve malfunction that allows retrograde flow from venous vessels. It generally affects only one quadrant; circumferential cases are rare. LHC tends to be self-limiting, resolving over days to weeks, but some patients experience multiple episodes.

Because LHC lesions are usually minimally disfiguring, ophthalmologists manage them conservatively. If they progress, laser cautery can be used.

Our case was unusual in terms of severity and chronicity. Without evidence of visible feeding vessels, we bypassed the laser cautery option and decided that surgery offered the best chance for a good cosmetic outcome, as the technique had been described previously in the *American Journal of Ophthalmology* in 2013. The patient and her family agreed.

*We were pleased at the relative ease with which blood could be drained from lymphatic channels using multiple incisions and manual drainage that also spared the surrounding conjunctiva and achieved good cosmesis.*

## CHANGING COURSE

The procedure, performed under general anesthesia, began with an 8 mm temporal conjunctival incision. It was immediately apparent upon incising the conjunctiva that sequestered blood was draining out of several of the lymphatic channels. So instead of excising the conjunctiva as planned, we decided to make multiple small incisions and apply pressure with surgical sponges to drain channels. We did cauterize larger channels, and excised a 2 mm strip for histopathology. We closed the conjunctival flap with fibrin glue, applied a 22 mm bandage contact lens and instilled topical antibiotics and steroid eye drops.

## UNEVENTFUL RECOVERY, SUCCESSFUL OUTCOME

The biopsy confirmed the LHC diagnosis. After two weeks, we removed the contact lens. Dilated lymphatic channels remain visible clinically and on optical coherence tomography, but are not evident to the normal observer (Figures 2A, B, C). The family, the patient and her ophthalmology team are all very satisfied with the results, and the patient has not experienced any recurrences after more than one year.

We were pleased at the relative ease with which blood could be drained from lymphatic channels using multiple incisions and manual drainage that also spared the surrounding conjunctiva and achieved good cosmesis. When spontaneous resolution does not occur in severe LHC, this technique could be an excellent alternative to offer patients. ●

*Dr. Goshe is in the Cole Eye Institute. Dr. Yeaney is in the Pathology and Laboratory Medicine Institute. Dr. Singh is Director of Ophthalmic Oncology.*



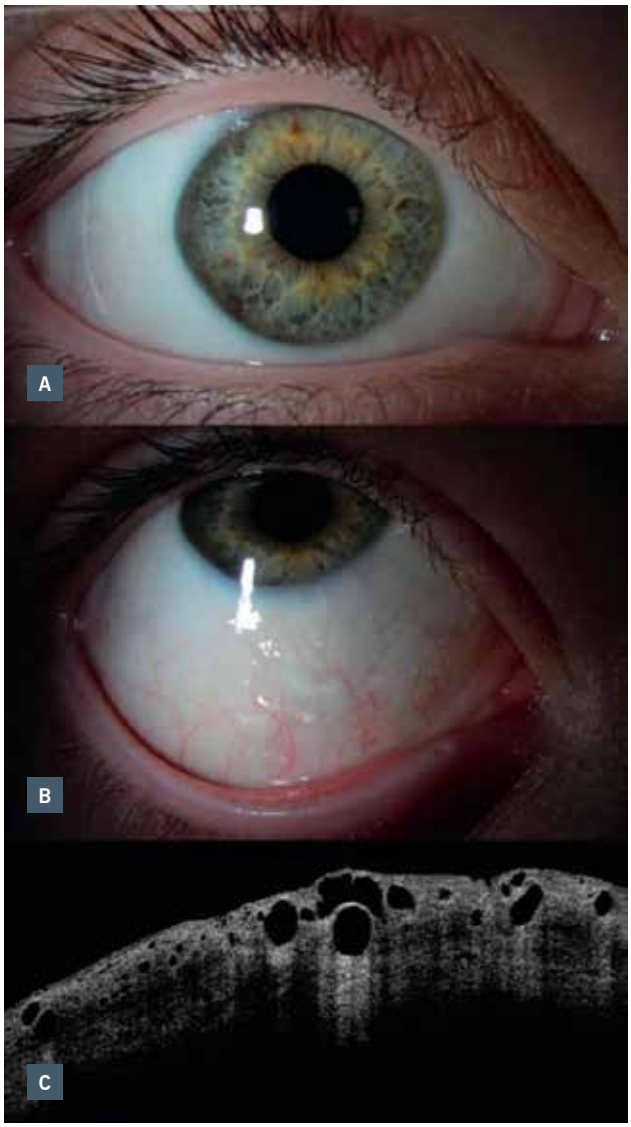



**Figure 2.** (A) and (B): Slit-lamp photographs demonstrating appearance four months after surgical drainage. Note the prominent conjunctival lymphatics visible inferiorly. (C): Anterior segment optical coherence tomography showing persistent dilated conjunctival lymphatic channels.

# Repairing Traumatic Macular Holes Using Internal Limiting Membrane Flap Technique

## TWO PATIENTS EXPERIENCE IMPROVED VISUAL ACUITY

{By Peter K. Kaiser, MD, and Rishi P. Singh, MD}

Retina specialists at the Cole Eye Institute recently reported in *Ophthalmic Surgery, Lasers and Imaging Retina* on two patients with traumatic macular holes with severe macular pathology that were treated with an inverted internal limited membrane (ILM) flap technique. Both patients experienced some degree of visual improvement.

### FIRST CASE

The first patient was a 39-year-old female who had been struck in the right eye by a baseball at a professional game three days earlier. Her vision in the eye was counting fingers only. As reported in the journal, she had a vitreous hemorrhage with subretinal and retinal pigment epithelial (RPE) hemorrhage and a choroidal rupture through the macula. On optical coherence tomography (OCT), she had a macular detachment with a possible full-thickness macular hole (FTMH). It was decided to follow the patient closely to allow the hemorrhages to resolve. Four months later, the vitreous hemorrhage had resolved, revealing two FTMHs – one involving the fovea and the second temporal to it, overlying a choroidal rupture site.

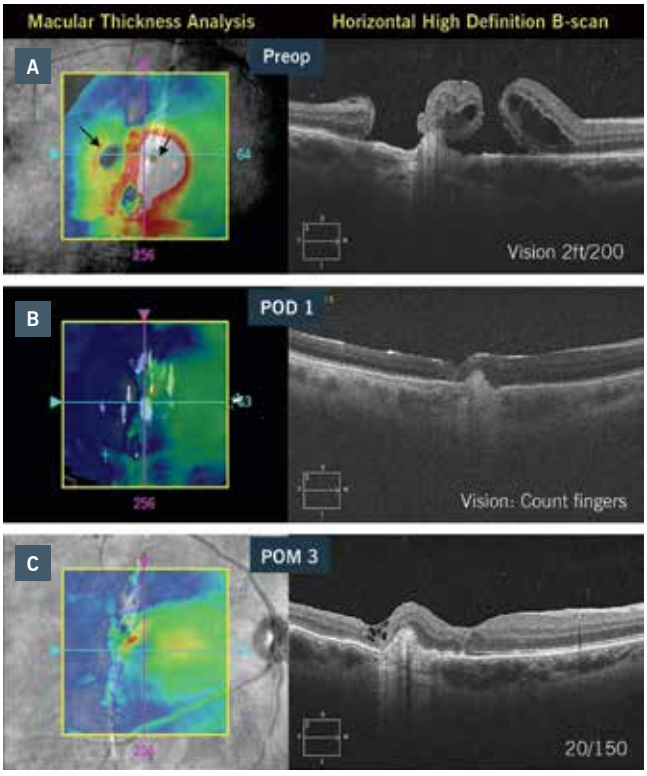



**Figure 1.** (A) Preoperative optical coherence tomography (OCT) demonstrates two macular holes overlying a choroidal rupture. (B) OCT under C3F8 on postop day one. (C) OCT three months after surgery.

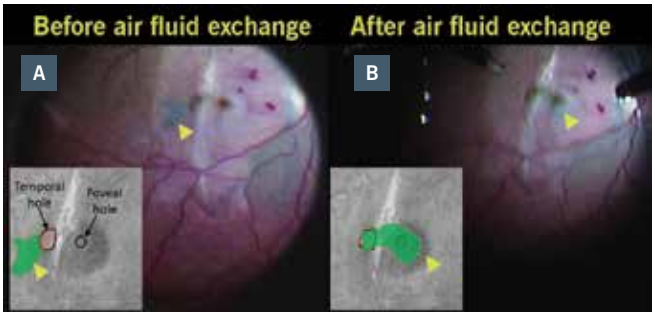



**Figure 2.** (A, B) Fundus photo and schematic drawing of the internal limiting membrane flap before and after correct placement.

Dr. Kaiser performed a pars plana vitrectomy (PPV) procedure with indocyanine green staining of the ILM, peeling of the ILM around both holes with preservation of a large temporal ILM flap that would cover both FTMH, air-fluid exchange and insufflation with C3F8 gas. The ILM flap was constructed on the temporal edge of the temporal eccentric macular hole so that during air-fluid exchange, the ocular fluidics would position the flap over both holes. Three months after surgery, both macular holes were closed and the patient had regained 20/150 vision.

## SECOND CASE

In the second case, a 22-year-old male presented one year after a motor vehicle accident in which an airbag struck his left eye. He reported a gradual decline in visual acuity since the accident. His vision in the affected eye was 20/250, with normal IOP.

Fundus exam revealed a pigmented macular scar with traumatic macular hole and vascular sheathing. OCT demonstrated dense vitreous condensation overlying an FTMH and a pigmented epithelial detachment. Over a three-month period, his vision continued to decline to 20/500.

We performed a PPV with a large temporal ILM flap with placement assisted by intraoperative OCT, and C3F8 gas tamponade. Four months after the surgery, the traumatic macular hole was closed and the patient's visual acuity had improved to 20/125.

## DISCUSSION

We have many tools available today to repair macular holes, including removal of the posterior hyaloid, epiretinal membrane or ILM, and the addition of gas or silicone oil tamponade. However, there have been no controlled trials that compare the different options for trauma patients.

This report demonstrates two cases of FTMH with severe retinal pathology. In both cases, the ILM flap technique was employed and macular hole closure with improved visual acuity was achieved.

These results point to this approach as an effective treatment option. Of course, our report is retrospective and lacks a control group that underwent PPV with ILM removal without a flap applied to the hole. Future randomized trials would be needed to better evaluate whether PPV with and without ILM flap technique is an improved approach to the treatment of patients with traumatic macular holes. ●

*Dr. Kaiser is the Chaney Family Endowed Chair for Ophthalmology Research. Dr. Singh is a retina specialist.*

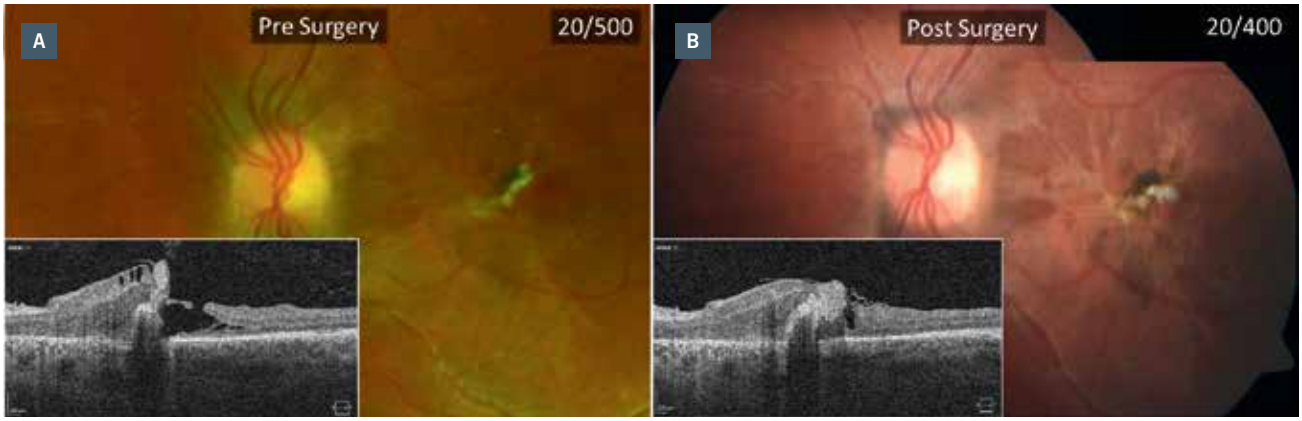



**Figure 3.** (A) Fundus photo and optical coherence tomography (OCT) displaying full-thickness macular hole and pigmented epithelial detachment pre-surgery. (B) Fundus photo and OCT showing hole closure four months after surgery.

# DSEK: An Unorthodox Approach that Benefits Patient with Perforated Cornea

## TERRIEN'S MARGINAL DEGENERATION IS UNDERLYING CAUSE

{By Craig W. See, MD}

A 55-year-old female from out of state presented to the Cleveland Clinic Cole Eye Institute for a second opinion on a chronic corneal perforation in her left eye. Three months prior, an outside ophthalmologist had performed pterygium removal. Surgery was complicated by corneal perforation, which was glued. Despite a second surgery to glue the perforation, the cornea still leaked, causing constant tearing and fluctuating vision, putting the patient at risk for infection.

At initial visit, there was a bandage contact lens in place over a large area of glue at the nasal limbus. The anterior chamber was shallow. After removing the contact lens, multiple leaks were noted at the edge of the glue. Careful examination of both eyes revealed subtle peripheral corneal thinning consistent with Terrien's marginal degeneration, which was not previously documented and likely contributed to the perforation.

I removed the glue and found very thin underlying cornea with multiple perforations and no evidence of infection. I applied cyanoacrylate glue, which revealed new leaks outside the area of gluing. I glued over the new leaks, but the cornea remained Seidel positive. There were perforations noted in three clock-hours of peripheral cornea.

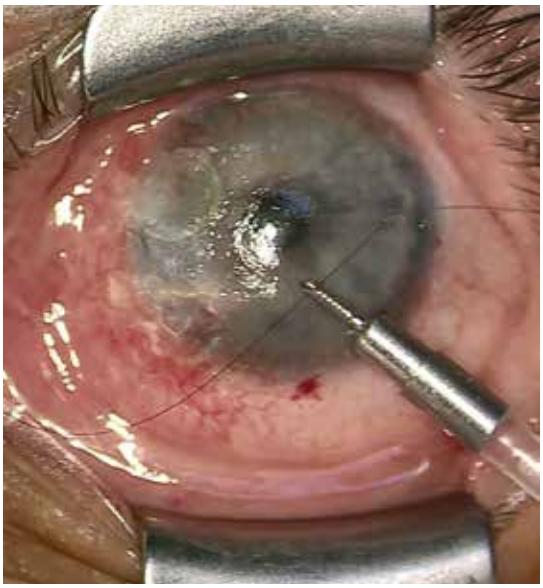


**Figure 1.** Intraoperative view prior to graft insertion. The glued patch is visible at 10 o'clock. A second area of glue at 8 o'clock has already been removed. Peripheral neovascularization is consistent with Terrien's marginal degeneration. A suture has been pre-placed, and a Lewicky AC maintainer is in place.

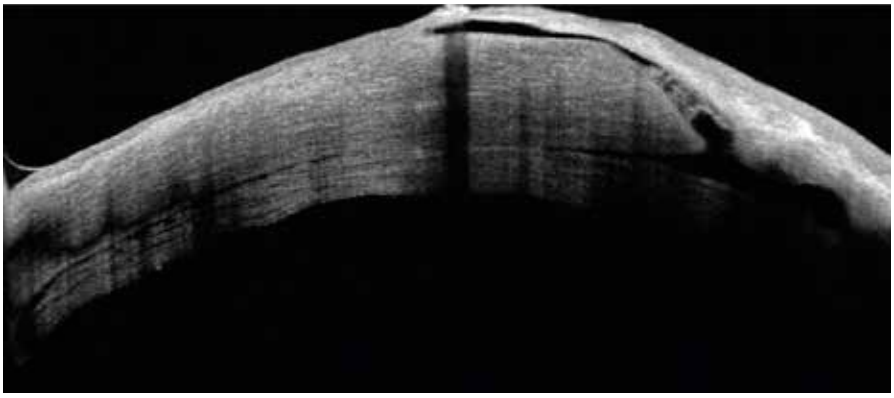


**Figure 2.** One-week postoperative optical coherence tomography (OCT) shows partially attached Descemet's stripping endothelial keratoplasty (DSEK) graft. Note the extremely thin connection between healthy cornea and the thinned peripheral cornea. A fluid tract is allowing aqueous to create a bleb at the top of the image.

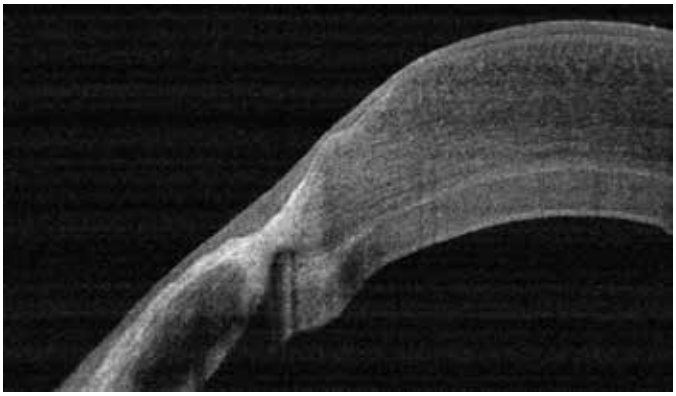


**Figure 3.** Three months after surgery, an intact cornea and clear DSEK graft can be seen.

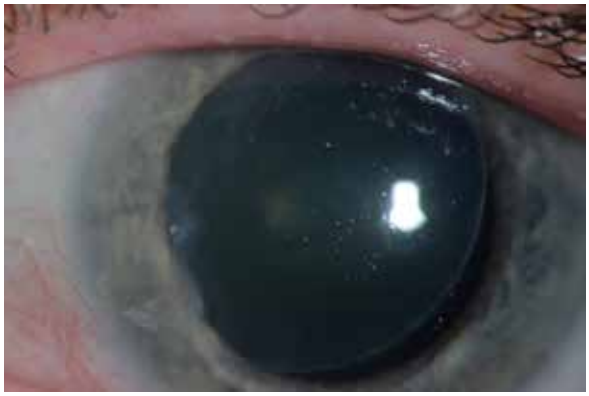


**Figure 4.** OCT image taken three months postoperatively shows attached DSEK graft that is plugging the extremely thin peripheral cornea.

## OPTIONS

It became clear that glue would not provide definitive repair. Traditional repair methods include eccentric corneal patch graft or penetrating keratoplasty. Her marginal degeneration meant her peripheral cornea was thin and could easily perforate during dissection or suturing. In addition, the perforated area was poorly defined and large (Figure 1). A traditional repair can rapidly become a more extensive surgery than anticipated in cases like this.

We discussed an unorthodox approach: an eccentric Descemet's stripping endothelial keratoplasty (DSEK). The DSEK tissue would act as a patch over the multiple perforations. Advantages of this approach include sparing corneal stroma, avoiding sutures into thin cornea and speeding visual recovery.

DSEK has been described as a treatment for central perforations and corneal hydrops, but not for multiple peripheral perforations, as in this situation.

## PROCEDURE

I performed DSEK (without stripping) the following week. The graft was oversized to allow more extensive overlap in the periphery and avoid the graft edge splitting the pupil. I considered using a semicircular graft but worried about graft adherence with her brisk leak.

One week postoperatively, her chamber was shallow and her cornea Seidel positive. Optical coherence tomography (OCT) demonstrated a partially detached graft and an extremely thin host cornea (Figure 2). An in-office air bubble was successful in attaching the graft.

Three months postoperatively, the patient's cornea is watertight and her chamber deep, and her vision corrects to 20/25. The graft remains clear (Figure 3). OCT demonstrates the DSEK graft plugging areas of perforation and thinning (Figure 4).

Corneal perforations can be challenging to manage, particularly when the surrounding cornea is abnormal. In this case, careful examination of the other eye revealed not only the cause of her perforation but informed my decision to avoid traditional repair.

Thinking outside the box can improve patient outcomes and allows us to push the field forward. ●

*Dr. See is a cornea and external disease specialist.*

# Orbital Nodular Fasciitis in an Adult Misdiagnosed as Sarcoma

## NODULE REMOVAL AVOIDS NEED FOR EXENTERATION

{By Arun D. Singh, MD}

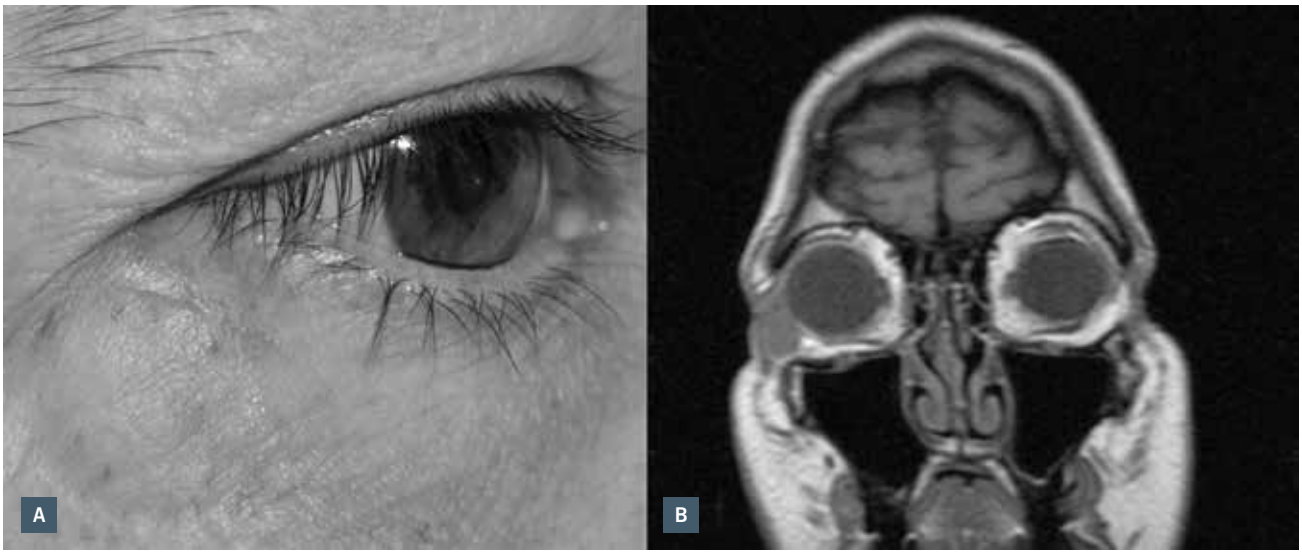



**Figure 1.** (A) External photograph showing inferotemporal orbital nodule. (B) T1 weighted coronal MRI showing well-circumscribed nodule in the inferotemporal orbit, which is isointense to muscle.

Nodular fasciitis is a reactive fibroblastic growth arising from subcutaneous or superficial fascia. Commonly presenting as a rapidly growing mass in the trunk or extremities, nodular fasciitis rarely presents in the periorbital tissues. Herein, we report the case of a 51-year-old man with nodular fasciitis of the inferolateral orbit, which was initially misdiagnosed as sarcoma.

### CASE PRESENTATION

The patient was referred to the ocular oncology clinic at the Cole Eye Institute for exenteration for a rapidly enlarging right lower orbital mass of two months' duration. His medical history was significant for non-Hodgkin's mantle cell lymphoma two years prior to presentation, for which he had received chemotherapy and subsequent bone marrow transplant.

Initial evaluation and incisional biopsy at an outside hospital led to the diagnosis of a pleomorphic undifferentiated sarcoma. A 2.2 cm x 2.5 cm round, hard mass was palpated at the inferolateral orbit that was adherent to underlying tissues and separate from the overlying skin (Figure 1A). Proptosis and abnormal extraocular movements were absent. There were no signs of optic disc compression. Orbital magnetic resonance imaging with gadolinium showed a 1.7 cm x 1.0 cm x 1.4 cm homogeneously enhancing subcutaneous mass in the right inferolateral orbit, which was hyperintense on T2 and isointense to muscle on T1, with mild diffusion restriction (Figure 1B). The mass was localized to the preseptal tissues without invasion of the globe, muscles or bone.

Given the ramifications of exenteration and the well-circumscribed appearance of the mass on imaging, a decision was made to undertake excisional biopsy, accepting the possibility of microscopic residual disease to be treated by radiation therapy and chemotherapy. The patient underwent anterior orbitotomy with excision of the mass in its capsule. Intraoperatively, the mass was noted to be free from rectus muscle or sclera, but was adherent to the inferolateral periosteum, which was removed with the capsule.

The patient did well post-excision with no evidence of recurrence.

### PATHOLOGY

Hematoxylin and eosin-stained sections showed a well-marginated proliferation of cytologically bland spindle cells arranged in short fascicles with intermixed osteoclast-like giant cells and extravasated red blood cells (Figure 2A/B). Nuclei were uniform without significant atypia. Scattered mitotic figures were noted, but there were no atypical mitotic forms. Immunohistochemical stains showed the spindle cells to be positive for smooth muscle actin (Figure 2C) and negative for STAT6 and desmin. Taken together, these findings were most consistent with nodular fasciitis.

### DISCUSSION

Nodular fasciitis is a reactive fibroproliferative growth that arises from the subcutaneous and superficial fascia. Typically found in the trunk and extremities, nodular fasciitis rarely

presents in the ocular and periorbital tissues. In all, nodular fasciitis has been reported in the orbit, the eyelid, the periorbita and the epibulbar tissues. To the authors' knowledge, 11 cases of nodular fasciitis in the orbit have been reported, with only three being in adults. The pathophysiology of nodular fasciitis is debated; previous reports have postulated that it is a reactive process to repetitive trauma. Discovery of a recurrent *USP6* gene rearrangement in nodular fasciitis, however, suggests that it may be a transient neoplastic process.

Nodular fasciitis often presents as a rapidly growing mass that can be difficult to distinguish from malignant sarcoma clinically and histologically. Histopathology typically shows hypercellularity with spindle-shaped fibroblasts in a myxoid matrix, with scattered mitotic figures but no atypia. Fine needle aspiration biopsy has been explored as a less invasive method for diagnosing nodular fasciitis, but has proved difficult. In a sample of 34 fine needle aspiration biopsies of nodular fasciitis, only four cases were interpreted as nodular fasciitis, only six cases were definitively benign and two cases were interpreted as malignant neoplasm. In this case, incisional biopsy prior to presentation was interpreted as pleomorphic undifferentiated sarcoma, for which definitive treatment (i.e., exenteration) would have been unnecessarily invasive and morbid. New molecular markers such as *USP6* gene rearrangements, reported in 92 percent of cases in one series, may be useful to differentiate nodular fasciitis from malignant entities such as fibrosarcoma and enable less invasive treatment in the future.

Surgical excision with pathology is the definitive diagnosis and treatment for nodular fasciitis. Recurrence after complete excision is rare; in a series of 272 cases of nodular fasciitis in China, only one recurred post-excision. Recurrence rates in ocular and orbital nodular fasciitis post-excision have not been examined, in part due to the condition's rare presentation in these locations. Notably, however, there were no recurrences in the 11 previously reported cases of orbital nodular fasciitis, despite incomplete excision in two of these cases.

In conclusion, we present the case of a 51-year-old man with orbital nodular fasciitis, highlighting this rare entity and the importance of differentiating it from malignant mimics. ●

*Rachel C. Chen, MD, Jose J. Echegaray, MD, Ryan S. Berry, MD, and John Goldblum, MD, contributed to this article. Dr. Singh is Director of Ophthalmic Oncology.*

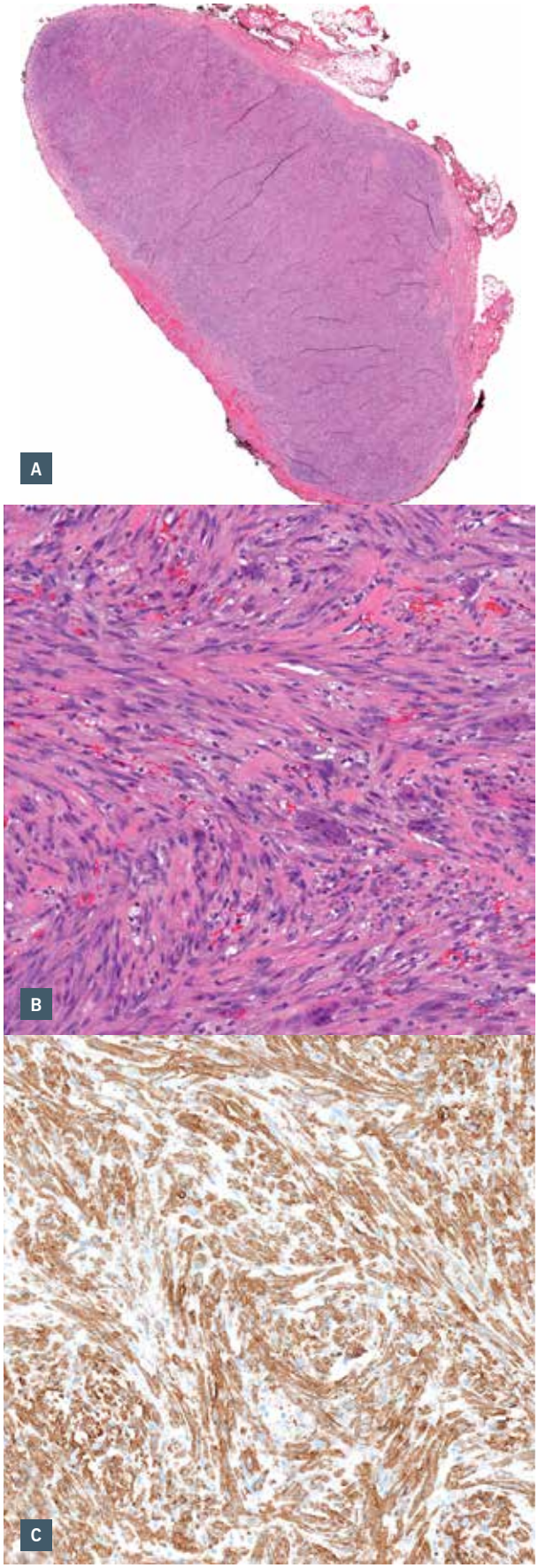



**Figure 2.** (A) Hematoxylin- and eosin-stained section of well-circumscribed nodule in its capsule. (B) Higher magnification hematoxylin- and eosin-stained section showing spindle cells arranged in short fascicles and scattered red blood cells. (C) Spindle cells stained highly positive with smooth muscle actin.

# Immunosuppressants Can Be Scary but Are an Effective Option if Used Properly

## TEEN WITH UVEITIS, GLAUCOMA, CATARACT ILLUSTRATES VALUE

{By Sunil Srivastava, MD}

- **A teenager with uveitis.**
- **A teenager with active uveitis treated with steroids.**
- **A teenager with active uveitis treated with steroids who develops glaucoma.**
- **A teenager with active uveitis treated with steroids and glaucoma treated surgically with a tube, with a cataract.**
- **A teenager with active uveitis treated with steroids, glaucoma treated with a tube, and now pseudophakic, who can only see counting fingers.**

This is the nightmare scenario for any ophthalmologist. Not only do we want to improve our patient's vision, but we want our interventions not to lead to worse outcomes. In these complicated cases, where it seems every treatment choice is followed by yet another setback, sometimes it is best to take a step back and re-evaluate the plan.

The patient is a teenage girl who presented to me after one year of declining vision. Diagnosed with idiopathic uveitis in one eye, she had been treated with topical steroid therapy without much success. In order to get control of her disease, local steroid injections were required. Unfortunately, the combination of active uveitis and steroids led to elevated intraocular pressure. She required placement of a glaucoma tube in order to control her pressure. Her vision continued to decline, and then she developed a cataract. The hope was that her vision would improve immediately after her cataract surgery.

She presented to the Cole Eye Institute one week after that surgery, performed elsewhere, with counting fingers vision and symptoms of a dark spot in her central vision, fearful about the possibility that her vision would not return.

### FINDINGS

Her examination and imaging began to give us more of the story. Widefield fluorescein angiography (FA) showed evidence of diffuse retinal vascular leakage in her right eye. Optical coherence tomography (OCT) revealed mild cystic changes, but more worrisome was outer retinal loss indicating chronic damage to her retina. Although her anterior chamber and vitreous did not reveal much cellular activity, the presence of the diffuse leakage and outer retinal loss on OCT told me her eye was severely inflamed, and had been for quite some time. It was time to have a discussion with the patient and her family about the need to adjust her immunosuppressive therapy.

Immunosuppression can be a scary topic for patients, especially for young people. Despite the excellent data on the safety and efficacy of immunosuppressive therapy for patients like ours,

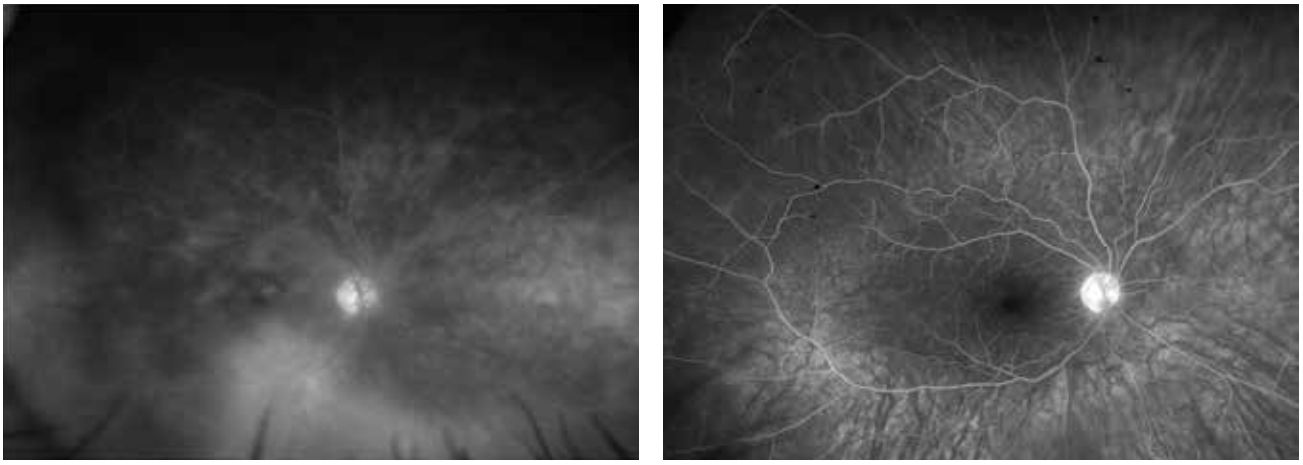


**Figure 1.** Initial fluorescein angiogram (left) with diffuse retinal vascular leakage indicates activity. Fluorescein angiogram one year later (right) shows significant improvement in leakage after immunosuppression

it does take buy-in from the patient and family in order to treat this disease effectively. At the Cole Eye Institute, we often will manage our patients in conjunction with an adult or pediatric rheumatologist, very commonly with same-day appointments.

For this case, my pediatric rheumatology colleague Andrew Zeft, MD, immediately completed a work-up and adjusted the patient's therapy to methotrexate and adalimumab. We decided to start her on oral steroids as well, to get her eye under control quickly. Since she already had a tube in place and was pseudophakic, there was a short discussion on using local therapy, but given the severity of disease at onset, I decided to start with oral medication first.

The patient returned in two weeks with some improvement — she was 20/400. Small win in the world of retina and uveitis! With time, we began to see other developments, including reduction in leakage and improvement in foveal contour. A few months later, no leakage was visible on FA, and her outer retina began to look normal. Twelve months after her initial presentation, the patient returned with 20/60 vision. She and her parents were ecstatic, as were we.

## COMPLIANCE A CHALLENGE

Just when you think things are going well, you are reminded how challenging chronic diseases can be. The hardest thing about immunosuppression is that it is chronic, and sometimes it is difficult for some patients to adhere to, even when things are going well. So it was not a big surprise when six months later, this patient presented with worsening vision.

Her macular edema had returned. The EMR showed that her medication was unchanged, but my nurse, Kim, picked up the truth — the patient does not like adalimumab injections, so she had been skipping some.

After some encouragement and discussion about whether to choose a different medication, she agreed to give it another try. Upon return one month later, her vision was back to 20/60. We have come a long way, but we know that she will need continued coordinated care for many years.

We came up with a plan, adjusted some medications and plan to check on her progress soon. We hope for the best but know it's a long road ahead. ●

*Dr. Srivastava is a uveitis and retina specialist.*

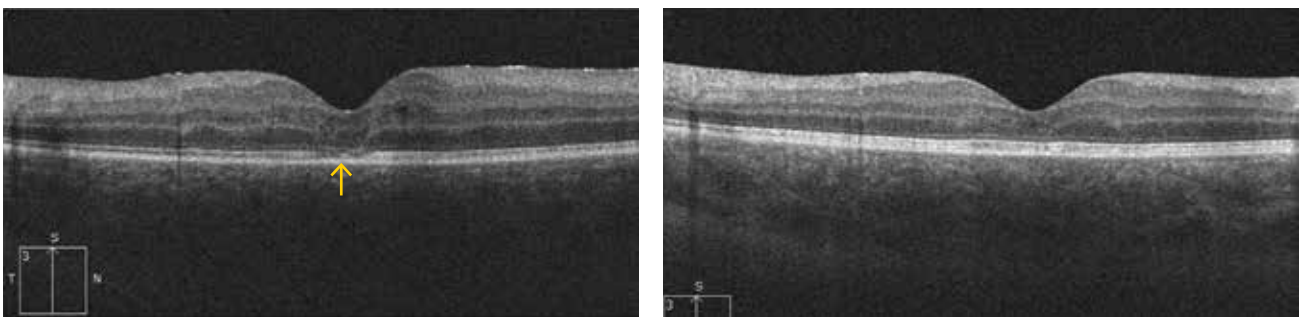


**Figure 2.** Optical coherence tomography of patient's right eye at presentation (left image) indicates loss of ellipsoid zone (yellow arrow). At right, normalization of outer retinal anatomy is seen 12 months later.

# Novel Technologies Improve Argus II Implantation and Patients' Visual Rehabilitation

## INTRA- AND POSTOPERATIVE TECHNOLOGIES MAKE A DIFFERENCE

{By Aleksandra Rachitskaya, MD; Alex Yuan, MD, PhD; and Meghan DeBenedictis, MS, MEd, LGC}

A 66-year-old male came to the Cole Eye Institute for an eligibility evaluation for the Argus® II retinal prosthesis system. He and his wife were anxious. He had been diagnosed with retinitis pigmentosa when he was 10 years old and had lost his vision completely in the past seven years. Despite being completely blind, he was hoping for a chance to enjoy some vision again.

The Cole Eye Institute has rapidly become the leader in Argus II implantation since the first retinal implant surgery at Cleveland Clinic was performed in the summer of 2015. The Argus team, led by retina surgeons Aleksandra Rachitskaya, MD, and Alex Yuan, MD, PhD, as well as Meghan DeBenedictis, MS, MEd, LGC, has implanted the highest number of prostheses in North America and has developed innovative research initiatives that advance the understanding of how the device works and how the patient experience can be improved.

The Argus II retinal prosthesis system (Second Sight Medical Products Inc., Sylmar, CA), the team explained to the potential Argus II recipient, is approved for patients with bare light perception or worse vision in both eyes due to retinitis pigmentosa. The prosthesis provides artificial vision, which can help with independence, orientation, mobility and social integration.

Following an eligibility evaluation, the patient was scheduled for surgery and postoperative rehabilitation.

### INTRAOPERATIVE OCT

To optimize the retinal prosthesis array placement, the Cole Eye Argus II team used intraoperative optical coherence tomography (i-OCT). Cole Eye Institute is one of a few centers that routinely uses i-OCT, which allows for visualization of the implant-retina interface before, during and after the implant array is secured to the macula with the use of a specially designed tack.[1] It allows for optimal placement of the Argus II array, which may translate into better visual outcomes.

### 3D VISUALIZATION SYSTEM

To facilitate communication during surgery, the surgeons used the Ngenuity(R) 3D Visualization System (Alcon, Fort Worth, TX), which allows everyone in the operating room to experience the same surgical views. Argus II implantation surgery involves several steps that greatly benefit from this technology, as described in a recent article by the Cole Eye Argus II team.[2] For example, creation of the sclerotomy for introduction of the array into the vitreous cavity and the intraocular work including array tacking was greatly enhanced using the 3D system.

## COMPUTER-ASSISTED VISUAL REHABILITATION

One of the key components of being able to use the Argus II system successfully is post-implant rehabilitation and training. However, the standard approach might not be effective for everyone. This Argus II recipient had a difficult time interpreting the visual stimulation he was experiencing. In collaboration with Jay Alberts, PhD, from the Cleveland Clinic Lerner Research Institute Department of Biomedical Engineering, the Cole Eye Argus II team investigated the role of computer-assisted rehabilitation in Argus II recipients.

The Computer Assisted Rehabilitation ENvironment (CAREN) (Motekforce Link, Amsterdam, Netherlands) consists of a 10-camera motion capture system (Vicon Inc., Oxford, UK), D-Flow control software (Motekforce Link), a 180-degree curved projection screen and a six-degrees-of-freedom motion platform and treadmill. It simulates a variety of environments while the patient is using the Argus II system in the safety of a monitored setting. The patient was able to train with the Argus II system while safely ambulating on a treadmill using virtual reality.

Following this four-week training protocol, the patient reported having more confidence in moving around, increased motivation to use the Argus II, an improved ability to scan while walking and improved balance. The Cole Eye Institute is the only Argus implantation facility to offer this unique virtual reality experience.

## NOVEL TECHNOLOGIES

This patient, like many other Cole Eye Institute patients, benefited from the Argus II implant. This was possible due not only to the Argus II system itself, but also to the novel technologies that the Argus II team at the Cole Eye Institute is continuously working on with its many collaborators.

These new technologies offer hope of improving vision provided by a retinal prosthesis. This hope is essential to patients with retinal degeneration, many of whom were previously told they were going blind and had no treatment options. ●

*Drs. Rachitskaya and Yuan are retina specialists.*
*Ms. DeBenedictis is a genetic counselor and coordinator.*

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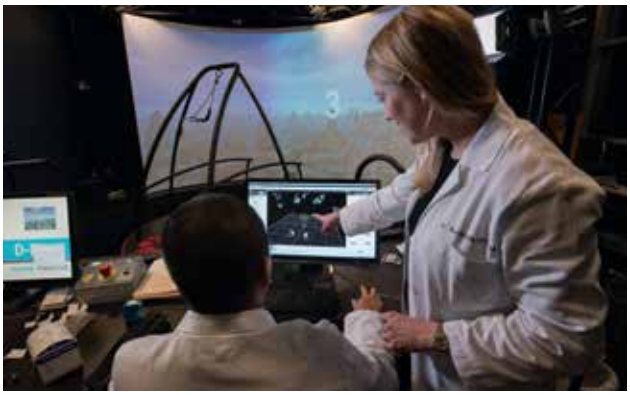


# Clinical Trials

The following studies are either currently enrolling new patients or are pending approval by the Institutional Review Board and should be enrolling shortly.

## RETINAL DISEASES

**› A Phase III, Multi-Center, Randomized, Double-Masked, Sham-Controlled Study to Compare the Efficacy and Safety of Intravitreal APL-2 Therapy with Sham Injections in Patients with Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD)**

**Objective:** To determine if intravitreally injected APL-2 reduces the progression of GA compared to sham injections in patients with GA secondary to AMD.

**Contact:** Rishi Singh, MD, 216.445.9497, or Angela Meador, 216.445.7176

**› Randomized Trial of Intravitreous Aflibercept versus Intravitreous Bevacizumab + Deferred Aflibercept for Treatment of Central-Involved Diabetic Macular Edema (CI Edema)**

**Objective:** To compare the efficacy of intravitreous aflibercept with intravitreous bevacizumab + deferred aflibercept if needed in eyes with CI Edema and moderate vision loss.

**Contact:** Aleksandra Rachitskaya, MD, 216.445.9519, or Angela Meador, 216.445.7176, or Tyler Mullen, 216.445.3840

**› A Phase III Multicenter, Randomized, Double-Masked, Active Comparator-Controlled Study to Evaluate the Efficacy and Safety of RO6867461 in Patients with Diabetic Macular Edema (RHINE)**

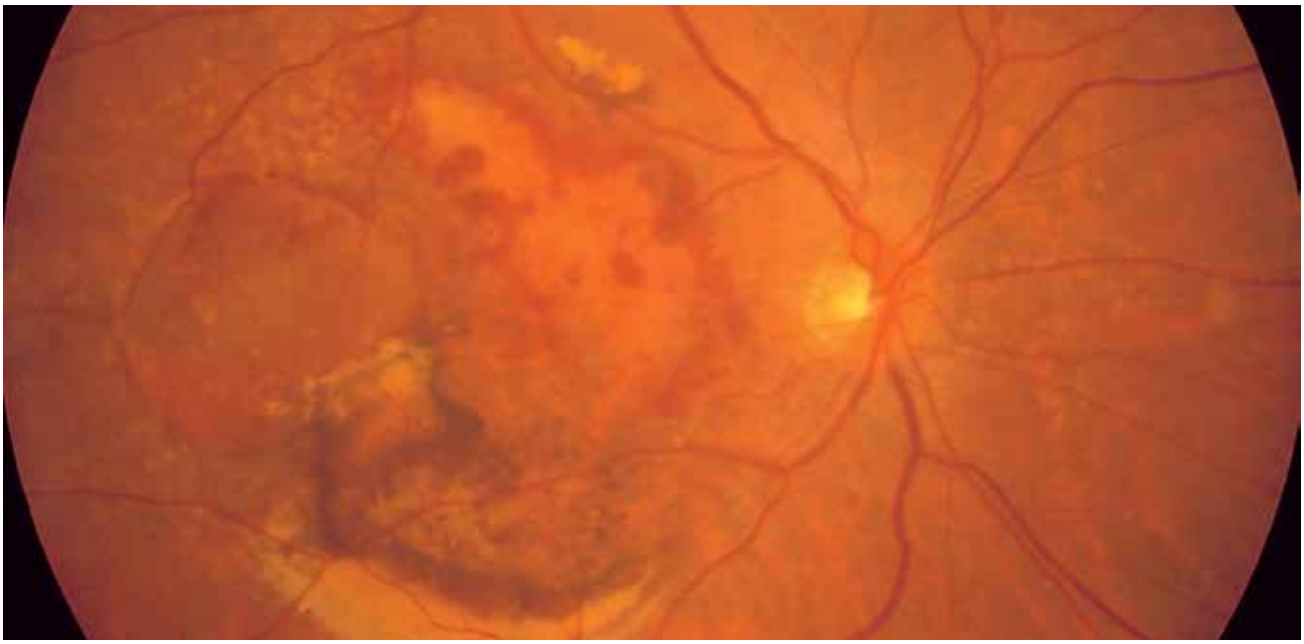
**Objective:** To evaluate the efficacy of IVT injections of the 6-mg dose of RO6867461 on BCVA outcomes.

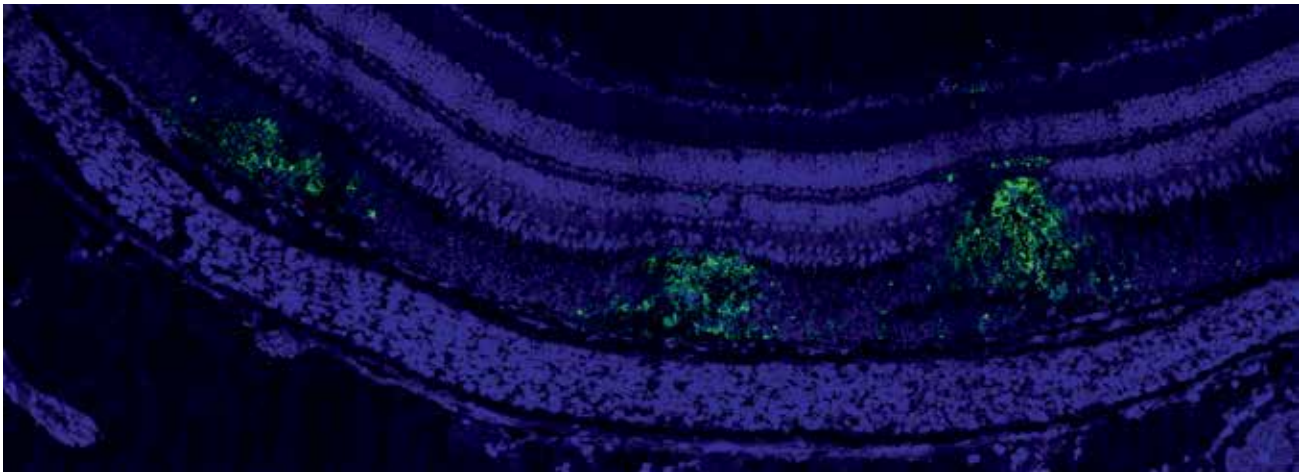
**Contact:** Sumit Sharma, MD, 216.445.4904, or Angela Meador, 216.445.7176

**› A Two-Year, Three-Arm, Randomized, Double-Masked, Multicenter, Phase III Study Assessing the Efficacy and Safety of Brolucizumab versus Aflibercept in Adult Patients with Visual Impairment due to Diabetic Macular Edema (KESTREL)**

**Objective:** To demonstrate that brolucizumab is non-inferior to aflibercept with respect to the visual outcome in diabetic macular edema.

**Contact:** Aleksandra Rachitskaya, MD, 216.445.9519, or Tyler Mullen, 216.445.3840





### › A Phase III, Multicenter, Randomized, Visual Assessor-Masked, Active-Comparator Study of the Efficacy, Safety, and Pharmacokinetics of the Port Delivery System with Ranibizumab in Patients with Neovascular Age-Related Macular Degeneration (ARCHWAY)

**Objective:** To evaluate the port delivery system implant with ranibizumab compared with monthly ranibizumab injections in participants with wet age-related macular degeneration.

**Contact:** Aleksandra Rachitskaya, MD, 216.445.9519, or Tyler Mullen, 216.445.3840, or Angela Meador, 216.445.7176

### › A Multicenter, Double-Masked, Randomized, Dose-Ranging Trial to Evaluate the Efficacy and Safety of Conbercept Intravitreal Injection in Subjects with Neovascular Age-Related Macular Degeneration

**Objective:** To evaluate the efficacy and safety of 0.5 mg and 1.0 mg conbercept IVT injected compared with the VEGF antagonist drive control, aflibercept IVT injections in subjects with neovascular age-related macular degeneration.

**Contact:** Rishi Singh, MD, 216.445.9497, or Tyler Mullen, 216.445.3840

### › A randomized, double-masked, placebo-controlled exploratory study to evaluate safety, tolerability, pharmacodynamics and pharmacokinetics of orally administered BI 1467335 for 12 weeks with a 12-week follow-up period in patients with nonproliferative diabetic retinopathy without center-involved diabetic macular edema (ROBIN study)

**Objective:** To evaluate safety and tolerability of 12 weeks' treatment of oral BI 1467335 compared to placebo in patients with moderately severe to severe non-proliferative diabetic retinopathy (NPDR) without center-involved diabetic macular edema (CI-DME) and secondarily to explore the efficacy of BI 1467335 on improvement of diabetic retinopathy.

**Contact:** Justis Ehlers, MD, 216.636.0183, or Laura Stiegel, 216.636.0183

### › A Phase IIa Trial of TLC399 (ProDex) in Subjects with Macular Edema due to Retinal Vein Occlusion (RVO): A Double-Masked, Randomized Trial to Evaluate Efficacy and Tolerability

**Objective:** Evaluate the efficacy of three different strengths of TLC399 (ProDex) administered as a single intravitreal (IVT) injection in the improvement of visual acuity in subjects with macular edema due to RVO.

**Contact:** Sumit Sharma, MD, 216.445.4904, or Angela Meador, 216.445.7176

### › Prospective Intraoperative and Perioperative Ophthalmic Imaging with Optical Coherence Tomography (PIONEER Study)

**Objective:** Assess the feasibility and utility of intraoperative OCT and perioperative OCT in optimizing the management of surgical ophthalmic diseases.

**Contact:** Justis Ehlers, MD, 216.636.0183, or Jamie Reese, RN, 216.636.0183

## CORNEA

### › Corneal Elastography and Patient-Specific Modeling

**Objective:** Develop and translate OCT-based corneal elasticity imaging and advance patient-specific computer simulations to enhance predictive models of disease risk and surgical outcomes in keratoconus and refractive disorders of the eye.

**Contact:** William Dupps, MD, 216.444.8396, or Angela Meador, 216.445.7176

## UVEITIS

### › An Observational Bilateral Evaluation of Corneal Endothelial Cell Density in Subjects Who Have Had a Fluocinolone Acetonide Implant for at Least One Year

**Objective:** Investigate the impact of the fluocinolone acetonide (FA) intravitreal implants (0.59 mg and 2.1 mg) on corneal endothelial cell density.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › Automated Analysis of Anterior Chamber Inflammation by Optical Coherence Tomography

**Objective:** A prospective, observational case series investigating the feasibility of utilizing optical coherence tomography scans of inflammation in the anterior chamber, vitreous and scleral of patients with uveitis.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › Automated Analysis of Anterior Chamber Cells Surrounding Cataract Surgery with Aqueous Fluid Analysis

**Objective:** Quantify the number of anterior chamber cells identified using OCT and compare it to clinical exam. Collect fluid obtained during cataract surgery and analyze the aqueous fluid using a hemocytometer to measure the actual number of cells in the anterior chamber.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › A Phase 2, Randomized, Placebo-Controlled Trial Evaluating the Efficacy and Safety of Filgotinib in Subjects with Active Non-Infectious Uveitis

**Objective:** Evaluate the efficacy of filgotinib versus placebo for the treatment of the signs and symptoms of non-infectious uveitis.

**Contact:** Sumit Sharma, MD, 216.636.2286, or Emily Fisher, 216.445.1649

### › International Collaborative Study of Susac Syndrome

**Objective:** To prospectively, retrospectively and efficiently collect scientifically sound clinical information on at least 50 current, 50 past and 50 future patients with Susac syndrome (SS) from around the world so that we can learn more about the immunopathogenesis, clinical features, clinical spectrum, clinical assessment, natural history, treatment, clinical course and long-term outcome of SS.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › Swept Source Optical Coherence Tomography (OCT) Imaging in Ophthalmic Diseases (SWORD)

**Objective:** To evaluate the use of swept source OCT in patients evaluated for ophthalmic disease.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › Imaging Quantification of Inflammation (IQI)

**Objective:** Perform observational study utilizing real-time quantification of ocular inflammation to determine minimal important change.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › Vitreous and Blood Sampling of Patients with Uveitis and Birdshot Choroidopathy

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

## NEUROLOGIC

### › A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered by Single or Multi-Dose Intravitreal Injection(s) to Subjects with Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

**Objective:** To assess the safety and tolerability of QPI-1007 intravitreal injections in subjects with recent onset of NAION.

**Contact:** Gregory Kosmorsky, DO, 216.444.2855, or Tyler Mullen, 216.445.3840

## GENETICS

### › Molecular Genetics of Eye Diseases

**Objective:** Study the molecular ophthalmic disorders through the compilation of a collection of DNA, plasma and eye tissue samples from patients and from families with a broad range of eye diseases and malformations.

**Contact:** Elias Traboulsi, MD, 216.444.4363, or Meghan J. DeBenedictis, 216.445.7671

### › Genetics in Uveitis

**Objective:** Identify changes in genes that may lead to uveitis.

**Contact:** Sunil Srivastava, MD, 216.636.2286, or Kim Baynes, BSN, RN, COA, 216.444.2566

### › An Observational, Multicenter Study of the Prevalence of Cerebrotendinous Xanthomatosis (CTX) in Patient Population Diagnosed with Early-Onset Idiopathic Bilateral Cataracts

**Objective:** Assess other manifestations of CTX within patients presenting with idiopathic bilateral cataracts.

**Contact:** Marina Eisenberg, MD, 216.444.4363, or Angela Meador, 216.445.7176

# News Briefs


## Vision First Bus Program Reaches Children in Cleveland Elementary Schools

The Cleveland Clinic & Kohl's Vision First program screens more than 5,000 children each year who attend the Cleveland Metropolitan School District, reaching more than 75,000 children over the past 15 years.

The program provides free eye examinations for every 4- to 6-year-old child enrolled in the Cleveland schools, as well as at some school-based health centers in the area, primarily in a customized van with two examination spaces that visits all elementary schools in the district each year.

Staffed by an ophthalmic technician, the Vision First van is equipped to provide screenings for a variety of eye diseases and conditions. For children who fail this initial screening, an optometrist is available to perform complete ocular examinations, write prescriptions for corrective lenses and provide referrals to local pediatric ophthalmologists as needed.

The Vision First program also performs pediatric screenings in community settings, including at the recent opening of Cleveland Clinic's Children's, at which about 75 children were screened.

It is estimated that only 14 percent of all children under the age of 6 undergo an eye examination, which is why this outreach program is so important. Several cities have replicated it, including Philadelphia and Baltimore.

Almost 15 percent of students who receive an exam are in need of additional attention to correct their vision. For eight years, the Cleveland Browns Foundation partnered with Vision First to provide eyeglasses to all the students who needed them. Kohl's Department Stores took on that role starting in 2013.

Vision First was launched in 2002 as a collaborative effort of the Cole Eye Institute, the Cleveland Metropolitan School District, the Federation for Community Planning and the Cleveland Initiative for Education and through seed funding from the Cleveland Foundation, the Board of County Commissioners, the Mt. Sinai Foundation, Forest City Foundation and Ohio Savings Bank. ●

## Rishi Singh, MD, Delivers ASRS President's Award Lecture

Cleveland Clinic Cole Eye Institute's Rishi P. Singh, MD, gave the prestigious American Society of Retina Specialists (ASRS) President's Award Lecture at the society's annual meeting in Vancouver, British Columbia, in July.

The award is given in recognition of an outstanding paper published during the past year and other accomplishments that signal potential for future impactful contributions to the field. Dr. Singh spoke on the topic of "Advancing Insights into Diabetic Eye Disease," summarizing his 12-plus peer-reviewed research papers published on the topic in 2017.

Dr. Singh's clinical interests include both medical and surgical treatments of retinal diseases and disorders. He has extensive experience in the management of age-related macular degeneration, diabetic retinopathy and surgical retinal conditions, such as retinal detachments.

"Dr. Singh is a multitalented, multifaceted ophthalmologist who we are indeed fortunate to have on staff," says Daniel F. Martin, MD, Chair, Cole Eye Institute, and Barbara and A. Malachi Mixon III Institute Chair in Ophthalmology. "His interests and talents represent the best of academic medicine – from performing vital clinical research to serving as journal editor, from leading our electronic medical record effort to being a prolific author, and most important, being a compassionate clinician. I, along with our entire staff, congratulate Dr. Singh on his latest well-deserved honor, the ASRS President's Award."

*continued next page* ›

# News Briefs (continued)

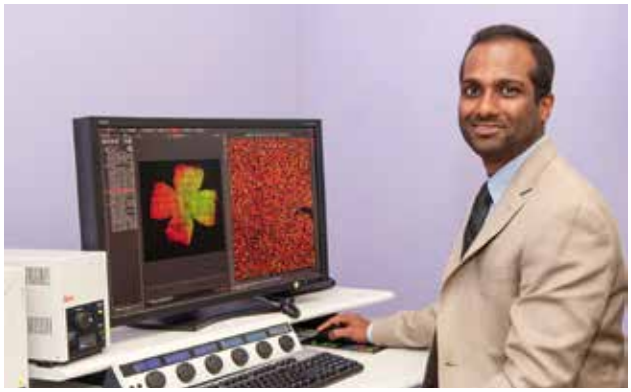
Dr. Singh's primary research interest is clinical investigation that harnesses data from the electronic record to help elucidate mechanisms of disease and better inform treatment decisions.

As Medical Director of the Clinical Systems Office, Dr. Singh oversaw successful implementation of the electronic medical record for the Cole Eye Institute. He is now focused on big data analyses, machine learning, lean process improvement and decision support modules for clinical practice.

Dr. Singh has authored more than 110 peer-reviewed publications, books and book chapters, and he serves as principal investigator for numerous national clinical trials advancing the treatment of retinal disease. He is President of the Retina World Congress and is on the ASRS board. He also is associate editor of *Ophthalmic Surgery, Lasers and Imaging Retina Journal (OSLI-Retina)* and is one of the editors of the *American Journal of Ophthalmic Clinical Trials.*


He maintains a strong relationship with drug development and commercial entities by serving on scientific advisory boards.

Dr. Singh, a member of Cleveland Clinic's Board of Governors, completed medical school at Boston University followed by residency in ophthalmology at Massachusetts Eye and Ear Infirmary, Harvard University. He completed a fellowship in vitreoretinal surgery and diseases at Cleveland Clinic. ●



Onkar Sawant, PhD, is studying the link between hypothyroidism during pregnancy and ROP.

## Grant Helps Fund Research into Hypothyroidism, ROP Link

Cleveland Clinic has been awarded a $64,773 grant from the Knights Templar Eye Foundation in support of a new study, "Effect of Maternal and Congenital Thyroid Anomalies on Fetal Retinal Programming."

Using a mouse model, Onkar Sawant, PhD, researcher at Cleveland Clinic's Cole Eye Institute, and his team (under the leadership of Sujata Rao, PhD) will use the grant to investigate whether hypothyroidism during pregnancy is linked to long-term vision complications in children, including retinopathy of prematurity (ROP).

"It is known that normal thyroid hormone levels in pregnant women are essential for fetal development," Dr. Sawant said. "However, the effects of thyroid complications during pregnancy on fetal eye development have not been thoroughly studied. This study will explore the long-term effects of thyroid anomalies on a child's eyesight later in life." ●

Members of the Knights Templar present their donation to (from left) Sujata Rao, PhD, Bela Anand-Apte, MD, PhD, Onkar Sawant, PhD, and Cole Eye Institute Chairman Daniel Martin, MD.

## RESOURCES FOR PHYSICIANS

### Stay Connected with Cleveland Clinic's Cole Eye Institute

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OPHTHALMOLOGY UPDATE

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The Cole Eye Institute is one of the few dedicated, comprehensive eye institutes in the world. Our internationally recognized staff diagnoses and treats the entire spectrum of eye conditions, managing nearly 220,000 clinical visits and performing more than 10,000 surgeries annually. The Cole Eye Institute is one of 26 clinical and special expertise institutes at Cleveland Clinic, a nonprofit academic medical center ranked as the No. 2 hospital in the country by *U.S. News & World Report*, where more than 3,500 staff physicians and researchers in 140 specialties collaborate to give every patient the best outcome and experience.
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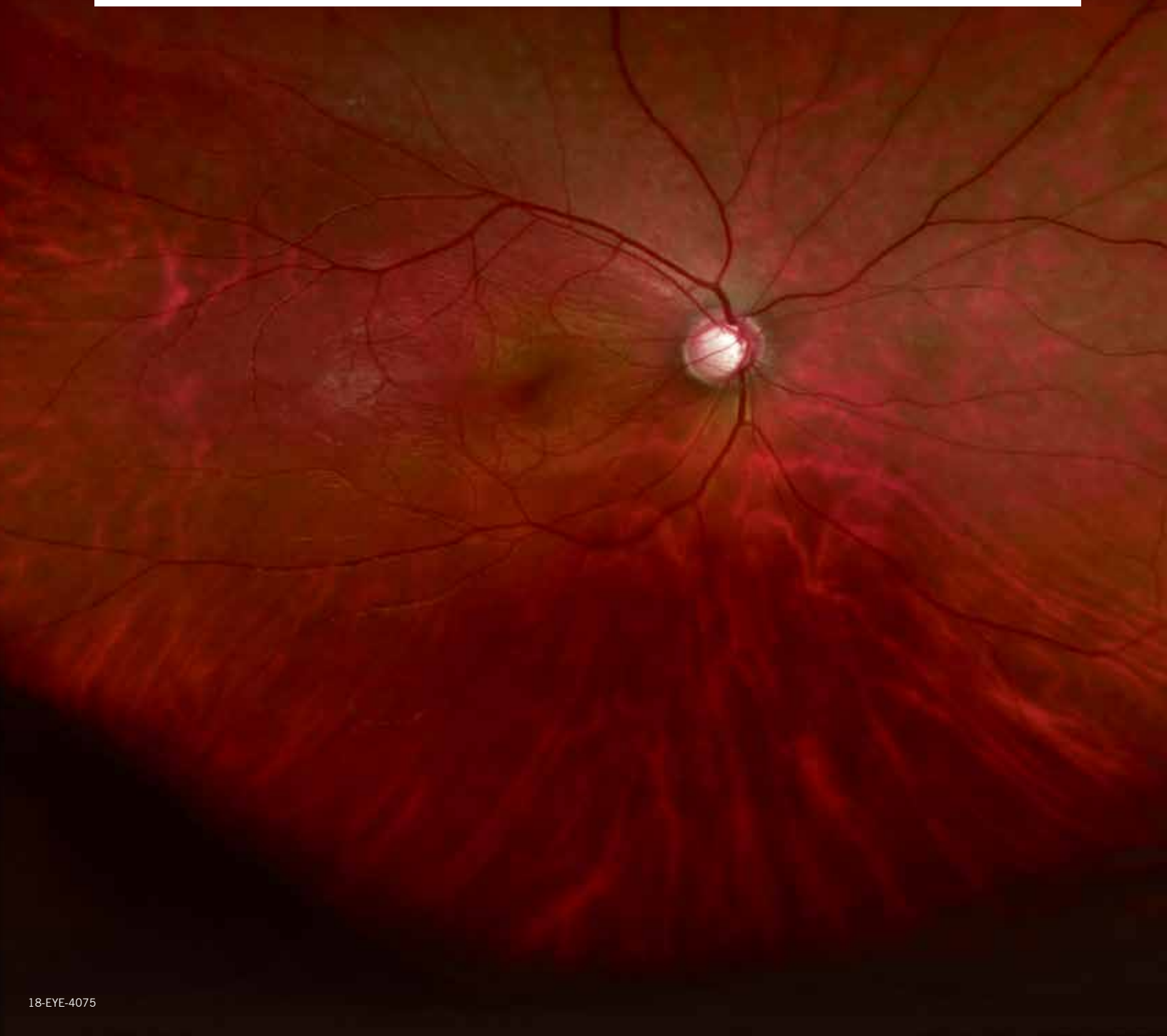

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