JULY 2017 # 11

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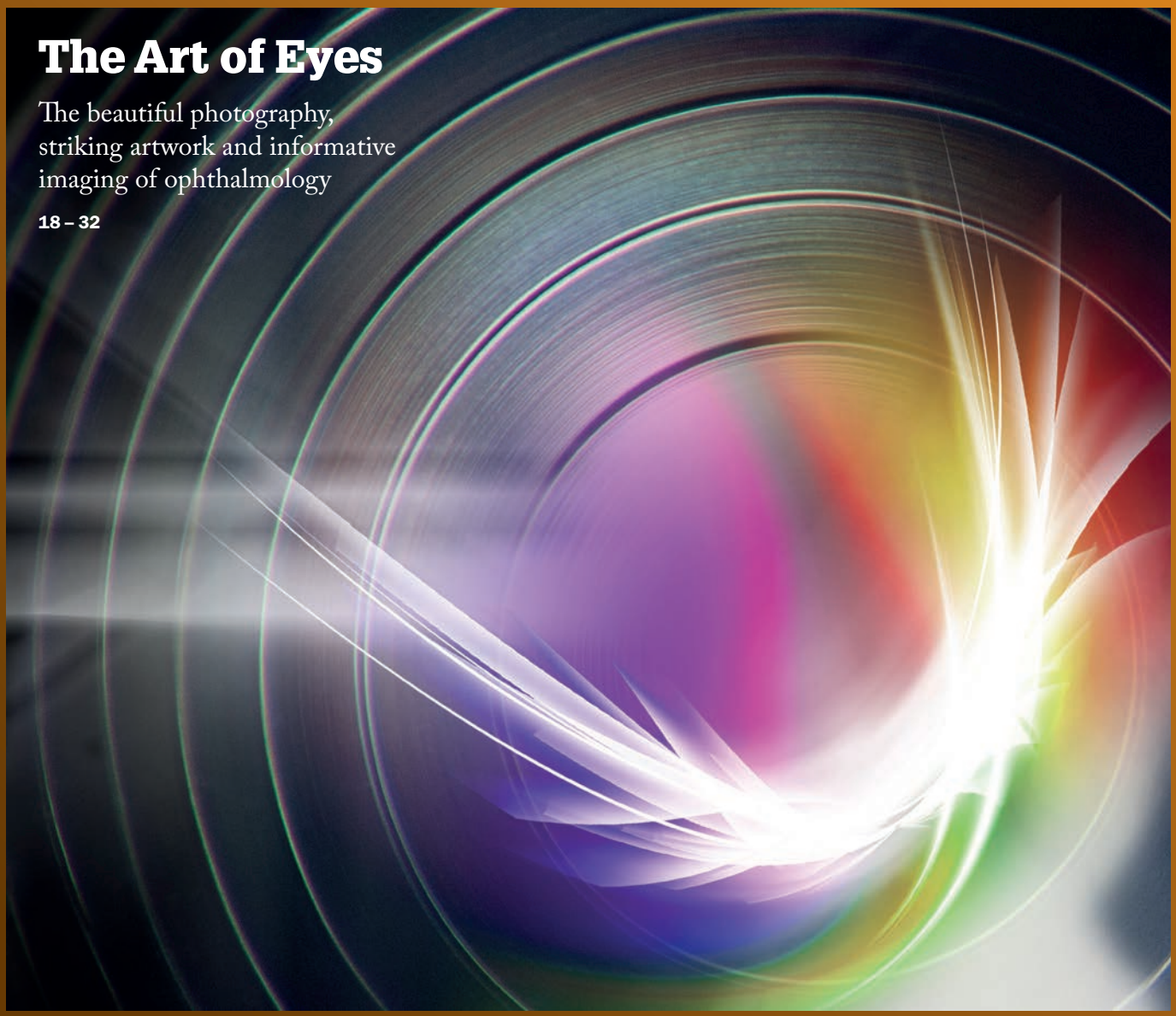

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Image of the Month

Seeing by Touch

As part of the Blindpad project, researchers from the École Polytechnique Fédérale De Lausanne (EPFL), Switzerland, have developed a touch display to help people with visual impairment find their way around unfamiliar places, interact with data, perform navigation tasks and even play games. The portable 192-"taxel" (tactile element) Bluetooth-enabled wireless haptic display can communicate with a phone or tablet. It represents graphical information as dynamic relief patterns that the user explores with their fingertips; each taxel can move up or down in under 10 milliseconds. The user can also push down raised taxels to interact with the display, meaning that they can perform tasks like zooming and panning on an image or a map. Coupled with a camera, the device can even display real-time information about a room layout. *For more info on the device visit: http://bit.ly/hapticsEM.* Image credit: Murielle Gerber, EPFL, 2017.

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A striking image of an EDOF IOL, courtesy of Karl Brasse of Vreden, Germany.

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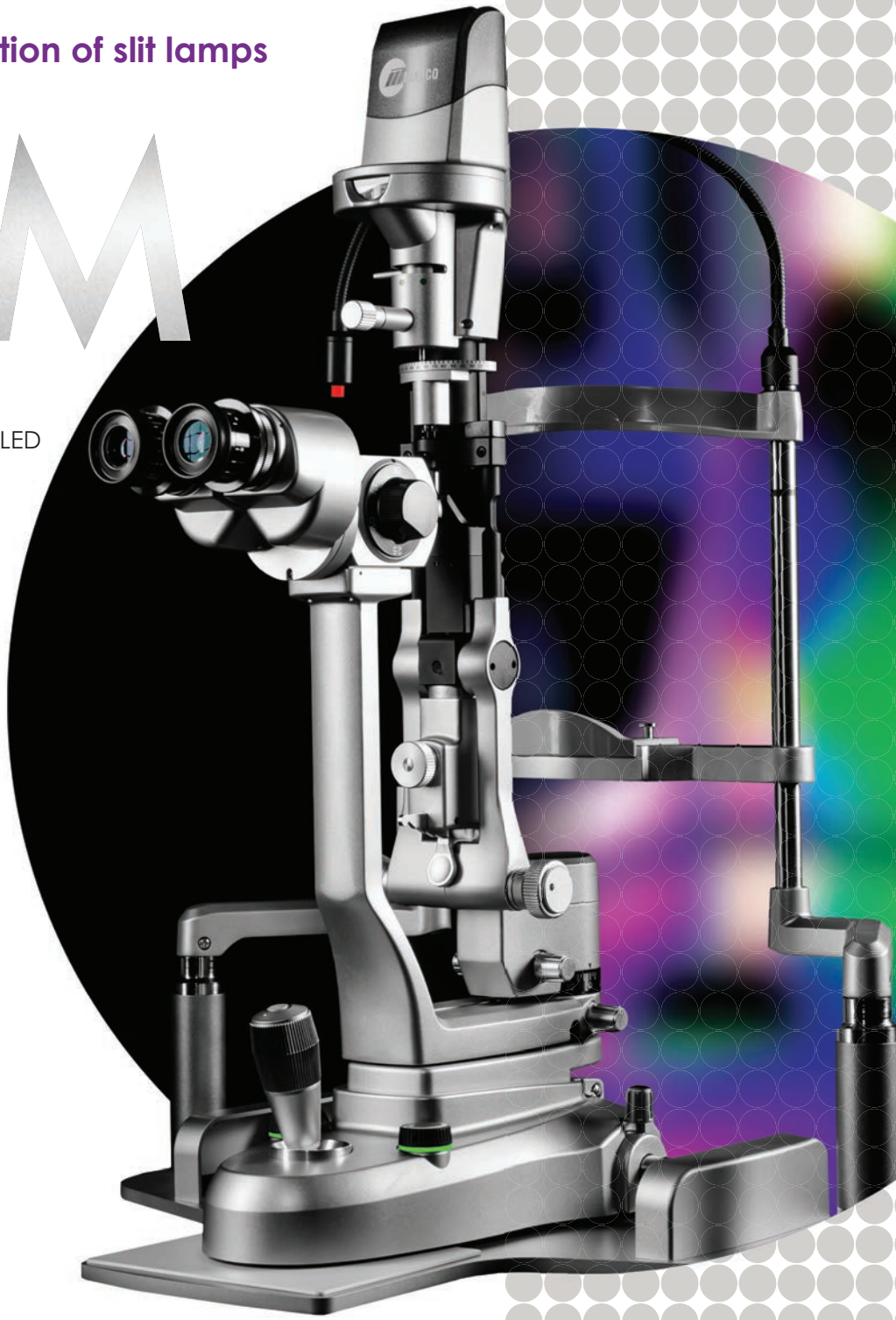

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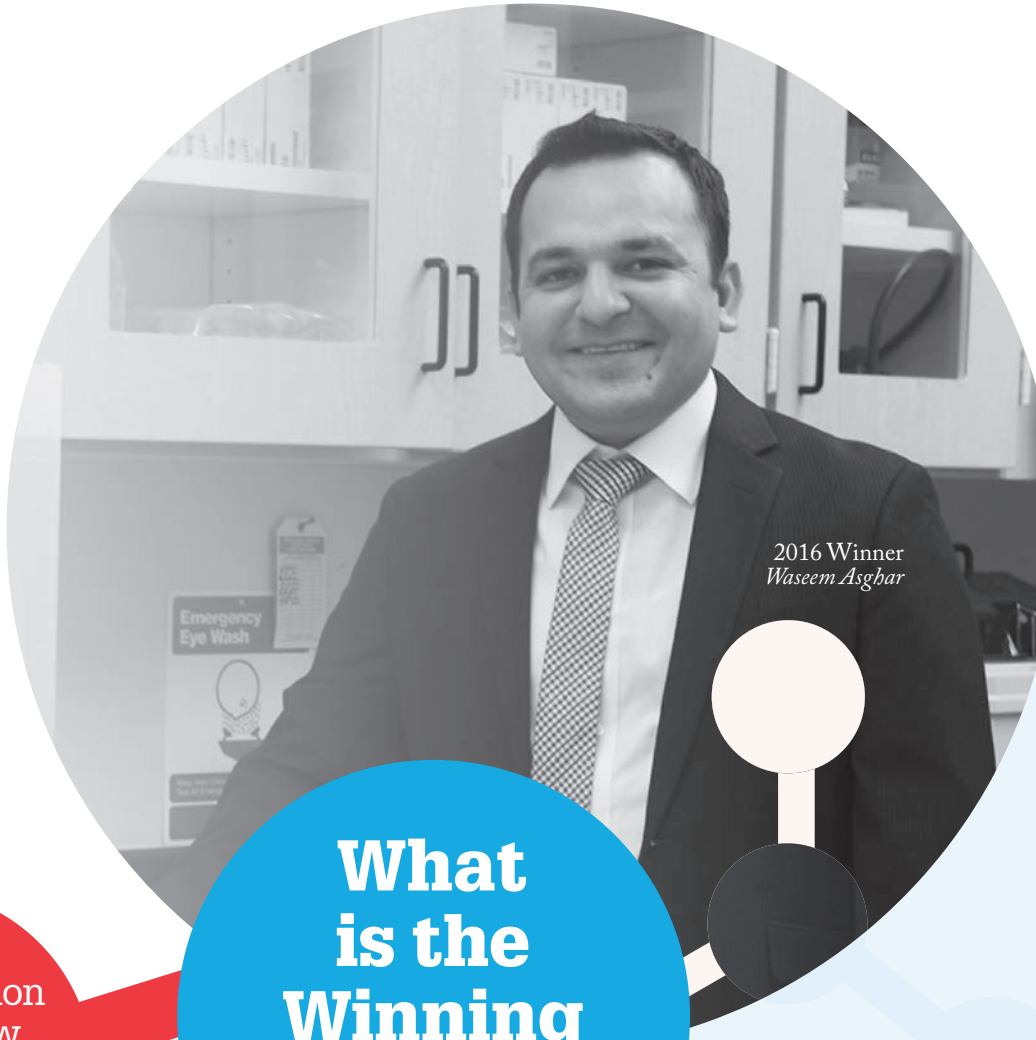

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In Practice

Profession

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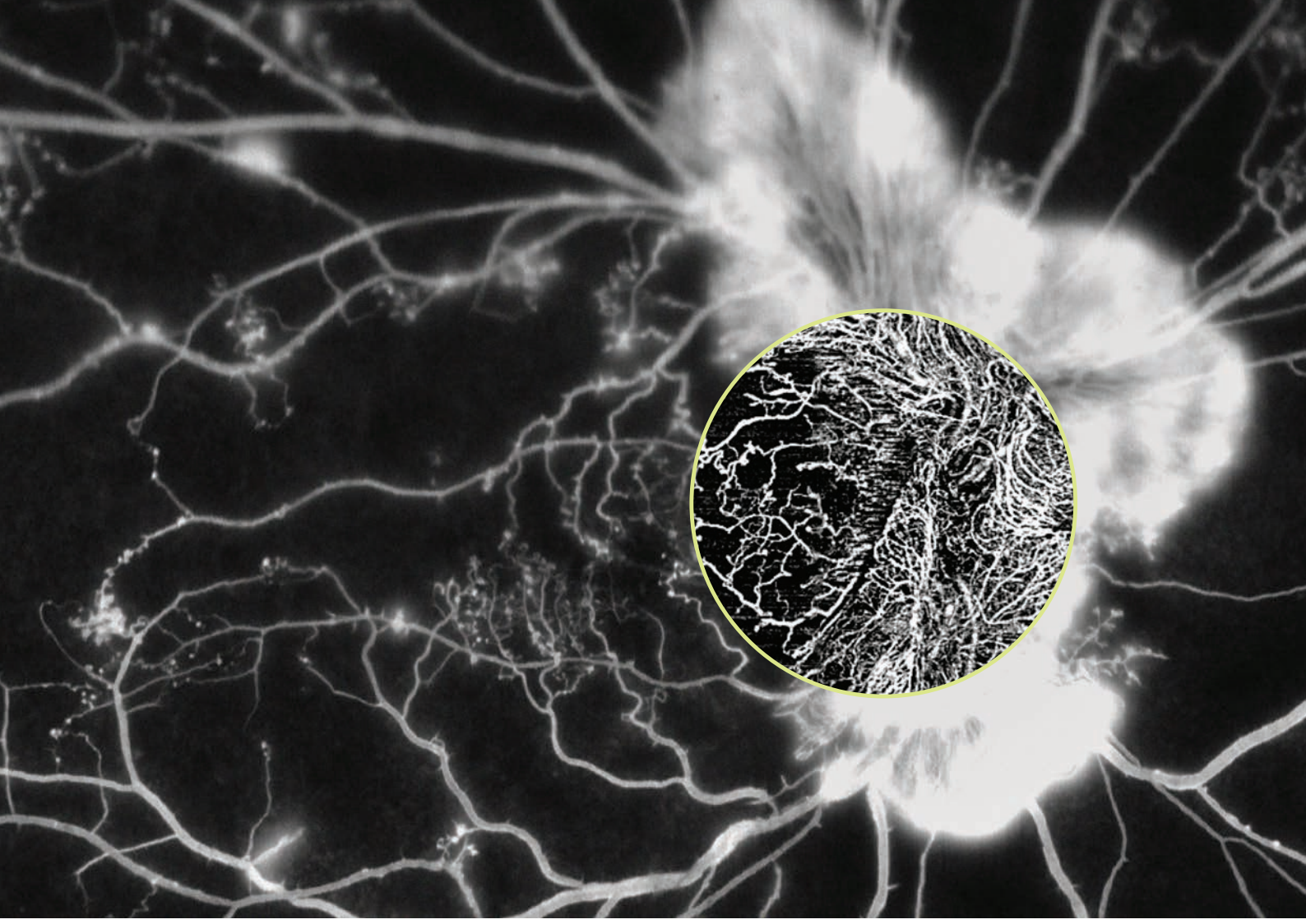

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Real World Evidence – and Rat Poison

Why practical hurdles help inferior drugs perform better in clinical trials than in real life

I've been thinking a lot about "real world evidence" recently and I've come to the conclusion that anti-VEGF drugs are essentially the warfarin of retinal disease.

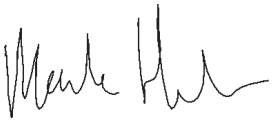
Why? Warfarin is one of the classic examples of a drug that does well in clinical trials – and far less well in real life. It's a dirty drug – it hits many proteins in the coagulation cascade, and it interacts with alcohol, many foods, and other drugs – and there are also pharmacogenomics issues. But for many years, warfarin (or its sister vitamin K antagonists) have been the centerpiece of many cardiac event prophylaxis strategies – principally, stroke prevention in patients with atrial fibrillation. Warfarin does stop those deadly fibrin clots from forming, after all!

But people on warfarin need to be assessed regularly. If test values are outside the narrow therapeutic range, the dose must be adjusted there and then. Insufficient anticoagulation risks thromboembolic stroke; too much risks hemorrhagic stroke. Quite a motivation to visit the anticoagulation clinic, right? Well, real life gets in the way. Appointments are missed. The dose adjustment doesn't happen. And people bleed, clot, suffer and often die because of it. At least the drug is orally administered...

So why did warfarin perform so well in clinical trials against newer, cleaner, single-target oral anticoagulant drugs (that lack almost all of warfarin's practical problems)? Well, all aspects are closely monitored in a clinical trial setting (such that it's far closer to the ideal standard of care), and trial patient populations are carefully selected with stringent inclusion and exclusion criteria. The real world? Not so much.

When it comes to anti-VEGF drugs, the same real-world issues exist, but the monitoring is via OCT, and dose-adjustment is essentially temporal – extending or shrinking the periods between injections. Under-dosing has obvious issues, but overdosing with anti-VEGF agents has cost implications, and may also have adverse effects on the retina (particularly photoreceptors). What might it take to beat the current generation of anti-VEGF drugs (in terms of efficacy) when they are administered monthly, in a clinical trial? The anti-PDGF approach looks like it's fading away; current approaches are all about extending dosing intervals (which is great), but will these simply aim for non-inferiority to the current crop? Given the clinical trial paradigm, I wonder if that's really the best that can be achieved.

Mark Hillen
Editor



Upfront

Reporting on the innovations in medicine and surgery, the research policies and personalities that shape the practice of ophthalmology.

We welcome suggestions on anything that's impactful on ophthalmology; please email edit@theophthalmologist.com

Traveling Without Moving

How "making light dance" can eliminate speckles from OCT scans

It is hard to underestimate the contribution OCT has made to eyecare. It has transformed our understanding of the pathology and pathophysiology of the eye – particularly, the retina, but also the cornea. OCT has made giant strides over the years – the main example being the change from time-domain to spectral-domain OCT, which heralded a huge increase in image quality, boosting utility of the technology. Another big stride forward appears to be on the horizon – and it all boils down to better speckle removal.

OCT relies on the coherent detection of backscattered light to image tissue morphology, which comes with an intrinsic drawback: speckle noise, arising from the interference of light scattered from multiple points within the tissue being examined. These scattered photons can cancel each other out, giving a false-black speckle on the image; or they can reinforce each other, generating a false-white speckle. In either scenario, these are artifacts: unhelpful and unwanted.

Many approaches have attempted to reduce speckle noise – but the tradeoff is almost always a reduction in image resolution – and they fail to eliminate speckle noise completely in any case. Enter speckle-modulating OCT (SM-OCT) (1).

"We wanted to make the speckles dance, so they'd be in a slightly different pattern each time we scanned the tissue," says Orly Liba, lead author of the study. "And we found a way to do it." SM-OCT

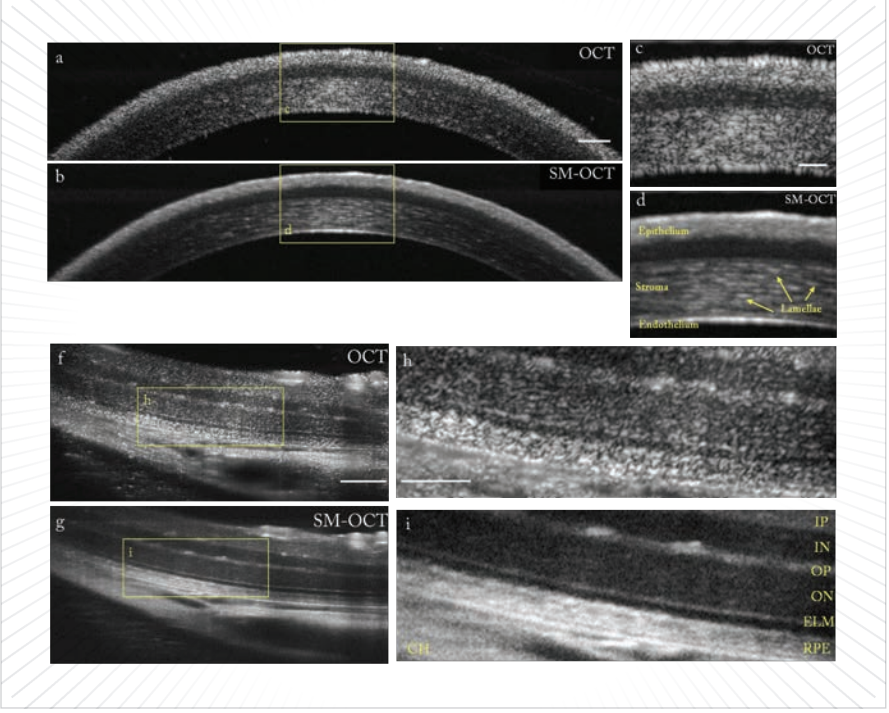


Figure 1. Mouse cornea, OCT (a, and inset, c) vs. SM-OCT (b, and inset, d), and retina OCT (f, and inset h) vs. SM-OCT (g, and inset i) (1). *Image credit: de la Zerba lab, Stanford University.*

introduces time-varying local phase shifts within the light beam that illuminates the sample, which translates into local phase shifts in the light that's scattered back from each "scatterer" within each voxel – or "resolution element." The result? Speckle patterns that change in time and that can be averaged over time to create an image with reduced speckle noise.

Crucially, because the sample remains in the same position and because the acquisition is at the same angle with the same set of illumination frequencies, an increase in the number of uncorrelated images does not result in a reduction in resolution – and averaging many images ultimately reduces speckle noise to an undetectable level (relative to other sources of noise, at least).

Adapting existing ophthalmic OCT instruments to become speckle-modulating is actually quite simple. By inserting a diffuser (essentially a plate of glass roughened by randomly etched grooves with a specific size and height) and methodically moving or rotating it between each round of repeated scans, the researchers accessed the optical equivalent of shifting the geographical relationship of the sample's components a tiny amount for each scan. Modifying the image acquisition software to average successive frames or A-lines produces speckle-free images as seen in Figure 1.

What does this all mean? The study's senior author, Adam De La Zerda, explained, "We showed that you can take effectively any OCT system out there and, with minimal changes, boost its resolution to the point where it can detect anatomical features smaller than the size of a typical cell." *MH*

Reference

1. *O Liba et al., "Speckle-modulating optical coherence tomography in living mice and humans", Nat Commun, 8, 15845 (2017). PMID: 28632205.*

Fundus-on-a-Chip

Building a better study model for retinal disease

Though organ-on-a-chip experiments are gaining in popularity in drug discovery, they have rarely been used to investigate ophthalmic disease. But Hirokazu Kaji's team from Tohoku University, Japan, believes the approach holds promise. "My group has been developing microfluidic cell culture systems for 10 years and, in collaboration with ophthalmologists, we decided to develop a model of the fundus," says Kaji.

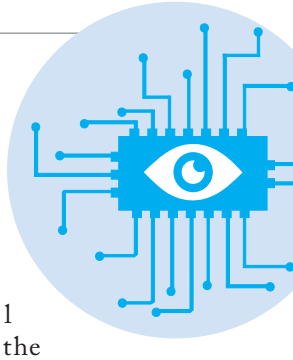
To better understand age-related macular degeneration (AMD) pathology, they built a simplified co-culture model of fundus tissue using a microfluidics platform. The model comprises human retinal pigment epithelial cells (ARPE-19s), fibronectin-coated porous membrane – to represent Bruch's membrane – and human umbilical vein endothelial cells (HUVECs), playing the role of the choroid (1).

The team first characterized monocultures of ARPE-19s and HUVECs, determining that: i) under hypoxic and hypoglycemic conditions, ARPE-19s remained stable, and VEGF secretion from the cells was significantly increased by 77.1 percent (hypoxic) and 68.1 percent (hypoglycemic) compared with control conditions; and ii) exogenously applied VEGF induced a 21.9 percent increase in HUVEC migration compared with control.

The group then co-cultured both cells under hypoxic and hypoglycemic conditions, and found that HUVECs in the lower chamber exhibited directional growth and traveled through the porous membrane towards the VEGF-secreting ARPE-19 cells in the upper chamber. Compared with control conditions, the growth area of ARPE-19 cells significantly decreased in hypoxic and hypoglycemic co-culture conditions over time ($p \leq 0.023$); growth area of HUVECs also decreased over time (non-significant).

The upshot? The authors believe the findings indicate that the "invasion" of HUVECs led to the subsequent detachment of ARPE-19 cells – a process that partially recapitulates neovascularization in wet AMD (2).

The team write that they have "taken the first step in elucidating molecular mechanisms of angiogenesis within the device" (1). Kaji comments, "The current results are very preliminary – one of the things that we have to address is the incorporation of functional microvessels into the model so that we can closely mimic choroidal neovascularization."



Ultimately, the team hope that the model will be useful in drug discovery, and for extending the anatomical and functional understanding of the blood-retina barrier. "We're also interested in the connection between retinal and neurodegenerative diseases, and we hope our model might help further research into this area," adds Kaji. *RS*

References

1. *LJ Chen et al., "Microfluidic co-cultures of retinal pigment epithelial cells and vascular endothelial cells to investigate choroidal angiogenesis", Sci Rep, 7, 3538, (2017). PMID: 28615726.*
2. *Tohoku University. "Reproducing a retinal disease on a chip", (2017). Available at: http://bit.ly/TohokuUni. Accessed June 21, 2017.*

Going for Gold

An "electric" new approach for glaucoma?

A glaucoma diagnosis typically means eyedrops – if not more invasive treatment. The negative aspects of topical medication are well known, some surgical approaches can result in bleb formation, others fail over time, and newer minimally invasive glaucoma surgery (MIGS) devices can be prohibitively expensive. No wonder that many researchers are seeking alternatives to lower IOP and help patients preserve vision.

Pedro Irazoqui (Purdue University, Indiana, USA), Simon John (The Jackson Laboratory, Maine, USA) and Gabriel Simón (Instituto Gabriel Simón, Madrid, Spain) are offering a new approach: an electromagnetic therapy device that stimulates aqueous drainage. Irazoqui tells us more about the concept and shares their aspirations.

Tell us about your device…

In essence, it looks like a normal pair of glasses, but there is a coil embedded in the frame that generates a magnetic field (Figure 1a). The magnetic field creates a current in the eye, which can electrically stimulate the structures in the limbus, such as the muscles around Schlemm's canal. Using different stimulation parameters we can modulate the flow of liquid into and out of the eye to regulate IOP. We have also incorporated a fine gold trace into a contact lens to capture and focus the magnetic current from the glasses – we use "off the shelf" hydrogel lenses (Figure 1b).

How is testing going so far?

We've performed studies in rabbits and mice, and last year we tested a "human-sized" device in four patients. We were able to demonstrate up to a 40 percent reduction in IOP in five minutes – it has a very dramatic effect. Right now, we're obtaining regulatory and ethical approvals to perform a multi-site clinical trial – we want to investigate the longevity of the effect. We're hoping to have the approvals in place within the next two months, so that we can start enrolling before the end of the summer. Our goal is to have results available by the end of 2017.

Any challenges?

Many! Figuring out how to print a tiny gold trace onto a contact lens, making the apparatus small enough to fit in a normal pair of glasses so that patients don't have to wear a bizarre contraption on their face, and working out the right stimulation parameters are just some of the challenges we've faced so far.

Where did the inspiration come from?

I'd love to tell you it was a flash of genius in the middle of the night! But the truth is that, one day, Simon John, Gabriel Simón, and I were discussing the idea of using electroceuticals for glaucoma over lunch. We had the idea, decided to try it out – and it worked much better than we anticipated!

Figure 1. a. One of Irazoqui's research students wearing an early prototype: b. A contact lens containing the gold trace that harnesses and focuses the magnetic field generated by the glasses. *Credit: Pedro Irazoqui.*

Long-term aspirations?

Eyedrops are currently the standard of care for glaucoma, but they take months to have an effect and have associated side effects – and surgical options are invasive. We're proposing a small modification to what many people do every day – wearing glasses and contact lenses. Ultimately, we hope our non-invasive device could be a first line of defense for glaucoma patients.

Consumer Reports

Four OCT-A devices go head-to-head. Was there a winner?

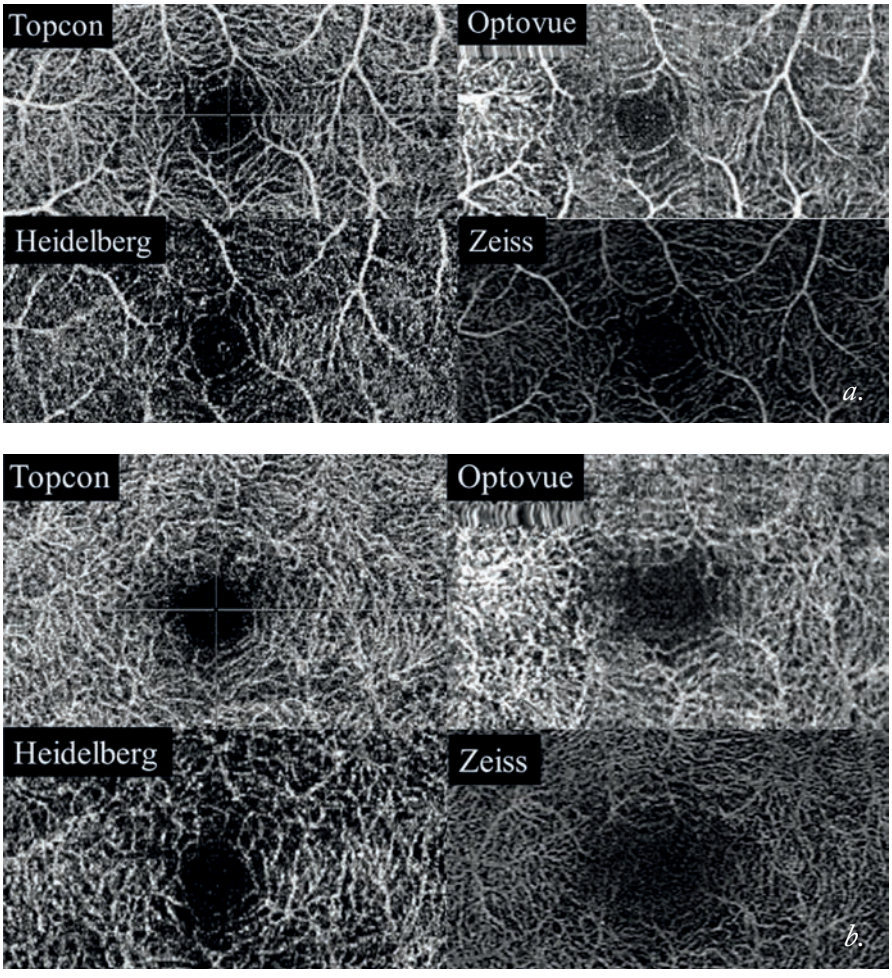


Figure 1. Representative en-face scans of, (a) the superficial capillary plexus (SCP) and (b) deep capillary plexus (DCP) using the swept source OCT Angio Topcon DRI OCT Triton (top left), the Angiovue Optovue RTVue XR Avanti, (top right), the Heidelberg Engineering Spectralis OCT2 module prototype with full spectrum decorrelation algorithm (bottom left), and the Zeiss AngioPlex Cirrus 5000 HD-OCT (bottom right). Adapted from (1).

Articles that directly compare the wares of competitors are common in consumer markets but pretty rare in the healthcare space. And yet, rather than pitting Hi-Fi components, mobile phones or cars against each other, a recent article in PLOS ONE (1) compared OCT-angiography (OCT-A) modules from Heidelberg Engineering (Spectralis OCT2), Optovue (RTVue-XR), Topcon (DRI-OCT Triton) and Zeiss (Cirrus 5000-HD-OCT).

There are a couple of caveats that should be noted up front. Heidelberg Engineering's OCT2 module was still a prototype and the area it scanned was different to the other instruments (3 mm x 3 mm vs. 4.3 mm x 1.5 mm); the Optovue instrument was an older model that lacked eye tracking; and only 19 healthy subjects (with no history or presence of eye disease, cardiovascular disease or diabetes and a VA of 20/20 or better) were employed in the study, meaning that no diseased retinae were examined.

That said, each patient was scanned by each instrument, and all images – en-face OCT-A images of the superficial (SCP) and deep capillary plexuses (DCP; Figure 1) – were evaluated and scored by a panel of three independent imaging experts. Consensus gradings were performed for each scan after an inter-grader reliability assessment. The same publically-available software package – Angiotool – was used to assess SCP vessel density. So what did they find?

There were no significant differences between the instruments in terms of Angiotool-determined overall vessel density and motion artifacts – but when it came to SCP image artifacts, the Zeiss and Topcon instruments were considered to be superior to the other devices. The foveal avascular zone (FAZ) border of the SCP slabs was "most appreciable" on the images taken with the Zeiss instrument, followed by the Optovue, and the FAZ of the DCP was most easily discerned on images from the Optovue device followed by the Heidelberg module. The numbers of discernable vessel bifurcations differed significantly between instruments (Zeiss 2 ± 0.9, Optovue 2.5 ± 1.2; Topcon 1.3 ± 0.7, Heidelberg 0.5 ± 0.6, $p<0.001$). Overall, the Zeiss module was better than the median in 90 percent of cases, the Optovue module better than the mean in 60 percent of cases, the Topcon module in 40 percent, and the Heidelberg (prototype) module in 10 percent – but these differences were not statistically significant between instruments.

OCT-A is rapidly coming of age, and the instrument manufacturers continue to develop and improve upon the technology at a ferocious pace. Since the study was performed, the Optovue instrument has gained an eye tracking function, and the Heidelberg Spectralis OCT2 module is now no longer a prototype and is commercially available in many markets. Bottom line: this technology's progress is so rapid that it's clearly a topic that will need to be revisited on a regular basis. *MH*

Reference

1. *MR Munk et al., "OCT-angiography: A qualitative and quantitative comparison of 4 OCT-A devices", PLoS ONE 12, 0177059 (2017). PMID: 28489918.*

In My View

In this opinion section, experts from across the world share a single strongly-held view or key idea.

Submissions are welcome. Articles should be short, focused, personal and passionate, and may deal with any aspect of ophthalmology. They can be up to 600 words in length and written in the first person.

Contact the editor at edit@theophthalmologist.com

On the Offensive

Why wait until there is damage to initiate treatment? To achieve the highest quality-of-life for our glaucoma patients, we should be treating proactively and breaking our eyedrop addiction

By Savak "Sev" Teymoorian, cataract and glaucoma specialist, Harvard Eye Associates, CA, USA

When it comes to the diagnosis and treatment of glaucoma, there is a culture of being reactive. The old glaucoma "playbook" has mostly been "prevent defense": when damage is seen, just enough treatment is initiated with the hopes of avoiding blindness. But we need to take a step back and evaluate what our primary goal is when we take care of patients with glaucoma. We focus on lowering IOP because this helps slow disease progression and deterioration of visual fields. The result is that patients can retain good functional vision, but more importantly achieve the true goal of maintaining the highest quality-of-life for our patients. We shouldn't lose sight of that.

Why have physicians taken a reactive approach for patients with glaucoma? It might be because until recently the treatment options were limited to eyedrops which have compliance issues, and gold-standard trabeculectomy or tube shunts which are risky procedures. Now, with micro-invasive glaucoma surgery (MIGS) growing in popularity, the paradigm is starting to shift towards more proactive care – which is a good thing. But while effective procedures, MIGS commonly isn't sufficient to cover all our pressure reduction needs. That is why there's also this growing trend for the idea of "MIGS and meds." And that brings me to my next point: why do we always resort back to handcuffing our patients – and ourselves – to medication? We know that there are multiple issues with eyedrops, whether it be patient compliance, side-effects, or treatment cost. Surely, we can do better for our patients. If we are adopting a more proactive approach to treatment with MIGS, why aren't we also being more proactive with a laser procedure such as selective laser trabeculoplasty (SLT)?

"Why do we always resort back to handcuffing our patients – and ourselves – to medication?"

Ask ophthalmologists or glaucoma specialists what first-line glaucoma procedure they'd perform on themselves or a family member, and most will choose SLT before medications. This is because they can see the benefit. It's effectively a minimally invasive light therapy that restores aqueous flow. It can be performed in the office, it's repeatable, patients tolerate it well, and it removes the issues of non-compliance, and the many other difficulties that you have with drops. I've found that patients tend to be happier after SLT because they can minimize or stop their

medications. Also, with the paradigm of care shifting towards a greater acceptance of surgical interventions, patients are becoming increasingly open to hearing about a laser procedure. And when they hear that it is more like a light therapy, I find that they're even more willing to consider it. I tell my patients in California, "It's like getting a tan to the eye!" A video of myself performing an SLT procedure plays in the waiting room to help patients appreciate what the procedure entails – and they're more likely to discuss it as an option when they come into the exam room.

So as paradigms are changing, why resort to medications when you can perform SLT? We should break our drops addiction, and consider taking a "MIGS and SLT" approach before accepting "MIGS and meds". The result is a process that can consistently lower IOP safely and allow patients to minimize or stop medication. It is time to stop being reactive and instead be offensive. This means performing proactive procedures that can offer our patients the chance to have the highest quality-of-life.

Teymoorian reports the following disclosures: Consultant for Aerie, Alcon, Allergan, Bausch & Lomb, Ellex, Glaukos; Research for Aerie, Allergan, Bausch & Lomb; and speaker for Allergan, Ellex, Glaukos.

Two in One

Phacovitrectomy may be a sensible option that makes cents

By Arsham Sheybani, Assistant Professor of Ophthalmology and Visual Sciences and Rajendra S. Apte, Paul A. Cibis Distinguished Professor of Ophthalmology & Visual Science at Washington University School of Medicine in St. Louis, MO, USA

Cataract surgery is the most commonly performed operating room procedure in elderly patients in the US, and it's estimated that over 3.5 million cataract operations are performed each year in the country (1). Many pars plana vitrectomies (PPVs) are also performed in the US each year – and by tabulating Medicare utilization data, we identified that close to 23,000 vitrectomies were performed in 2014 (2). Our point? The potential for an increase in concomitant retinal and lens-related disorders is only going to escalate in this aging population.

The overwhelming majority of phakic patients who undergo vitrectomy develop visually significant cataracts (with the risk increasing with age) whether or not gas tamponades are used (3,4) – yet this has not translated into the adoption of phacovitrectomy by vitreoretinal surgeons in the US. By comparison, glaucoma surgeons commonly perform cataract surgery combined with trabeculectomy or tube shunt surgery (5), and we suspect that the familiarity with cataract surgery by the glaucoma specialist has fueled this trend.

In the US, cataract and retinal surgery are performed as separate events. Though there are advantages to that approach (as we discuss below), combining these procedures may ultimately benefit the patient and the health care system by decreasing both the operative and postoperative burden. Developed nations outside of the US have already adopted a combined approach, as vitreoretinal surgeons outside of the US perform cataract surgery. We believe that changing this practice in the US needs to begin with changing the model in US vitreoretinal training programs. Addressing fellowship training is beyond the scope of this article, instead we hope to highlight the advantages of phacovitrectomy and discuss how the two-surgeon model may work to streamline care for patients with cataracts who undergo vitreoretinal surgery.

Financially, there are potential advantages to phacovitrectomy. An analysis of phacovitrectomy vs. sequential surgery resulted in an approximate 20 percent cost savings to Medicare in favor of phacovitrectomy (6). By streamlining this surgical process, patients may also directly benefit from a reduced number of surgical and post-operative visits.

Aside from fiscal implications, there are surgical advantages to phacovitrectomy too. Phacoemulsification in a post-vitrectomy eye has a higher complication rate that could be caused by a variety of factors, including weakened zonules, unstable posterior capsules, and potential defects in the posterior capsule, which may sometimes lead to an additional surgery (7).

Another reason for considering phacovitrectomy is the higher likelihood of developing visually significant cataracts following PPV, which may occur as a result of increased oxygen tension in the lens (8). However, the development of a visually significant cataract after PPV is not universal. Performing the vitrectomy alone may reduce the number of patients that ultimately undergo cataract extraction.

Phacovitrectomy does have disadvantages for the vitreoretinal surgery in certain cases. Prolonged cataract extraction with corneal edema may make retinal viewing paradoxically more difficult in combined cases – and this becomes especially important in patients who have significant endothelial cell dysfunction.

For the cataract surgeon, surgery may also be more difficult in some situations. Dense vitreous hemorrhage may result in a poor red reflex. Hypotony due to a retinal detachment may lead to chamber instability. Intraocular lens (IOL) calculations may also be less predictable in patients who may potentially need silicone oil or scleral buckle placement. Phacovitrectomy may also result in higher postoperative refractive unpredictability in cases that require repair of extensive rhegmatogenous retinal detachments (9). Waiting until the retinal outcomes are determined may also influence consideration of accommodative or multifocal IOLs.

However, given the potential advantages of phacovitrectomy, in our academic US practice, we prefer a two-surgeon approach. When planning combined phacovitrectomy, patient counseling is paramount. Best corrected visual acuity will often depend on the underlying retinal pathology. IOL selection should also be discussed carefully; we do not recommend multifocal IOLs in patients with retinal pathology. However, with small gauge vitrectomy systems that seem to minimally affect corneal astigmatism, toric IOLs can be beneficial when the patient has good potential for visual recovery.

The cataract surgery is performed through a temporal incision while the vitrectomy is performed with the vitreoretinal surgeon operating superiorly. The scope can easily be rotated with both surgeons in position. We start with the placement of all three pars plana trocar cannulas – this is easier than when placing them through a soft globe after cataract extraction and prevents wound gape that may prolapse or decenter the IOL. The infusion is not initiated; otherwise undue posterior pressure can result. The capsulorhexis is made to approximately 5 mm in size. We do not recommend making the rhexis significantly smaller – it merely inhibits efficient cataract extraction and we have found that it does not reduce the chance for IOL prolapse out of the capsular bag. We prefer foldable acrylic aspheric IOLs given the superiority of the optics compared to three-piece acrylic spheric lenses. We have seen both styles of lens prolapse out of the bag when the posterior segment is over-pressurized. By limiting wound hydration, the cornea remains clear for the vitrectomy. We often suture the main corneal wound to ensure chamber stability during the vitrectomy and have recently found that corneal sealants work well for this purpose.

Some may argue that eyes with multiple ocular pathologies cannot tolerate the increased inflammation associated with combining surgery – but there is little evidence to support this (10). We suspect that in highly diseased eyes, minimizing the number of surgeries may decrease the chance of endothelial compromise. Phacovitrectomy may limit the exposure to pathogens that can cause endophthalmitis. We also suggest that combining surgeries decreases the systemic risk to the patient. Reducing the number of times insulin regimens are adjusted, meals are withheld, and sedation is performed may be advantageous in patients with poorly controlled diabetes. These patients also exhibit an increased incidence of cataract and retinal disease and are the very patients whom we feel benefit the greatest with this approach. There are several studies that support our line of reasoning (11). When we consider all the advantages for the patient and surgeon, we believe phacovitrectomy is a sensible option.

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Not Just for Premium Patients

Performing OCT on all patients before cataract surgery prevents visual surprises

By Steve Charles, vitreoretinal surgeon, and founder and owner of Charles Retina Institute, Memphis, Tennessee, USA

The traditional approach to office evaluation of patients being considered for cataract surgery begins with obtaining a history of significant visual symptoms followed by visual function testing and refraction, IOP measurement, slit lamp examination – hopefully including 90 D lens examination of the macula and optic nerve – and, finally, dilated pupil retinal examination with the indirect ophthalmoscope. If the visual function, visual complaints and slit lamp examination verify the need for cataract surgery; the next step is an array of tests to determine lens implant power, axis, and other parameters. In my view, OCT should also be performed in all patients.

Because of the explosive progress in development of advanced technologies to determine corneal optics and axial length, as well as multiple advanced IOL calculation algorithms, refractive surprises are becoming much less common. "Visual surprise" is a term I have coined to describe the combination of a near perfect refractive outcome with unanticipated vision less than perfect.

There are many factors that result in the visual surprise scenario. Although cataract interference with macular visualization is obviously a prime factor, indirect ophthalmoscopy has insufficient resolution to evaluate the macula (but it is essential to detect retinal detachment, retinal holes/breaks, lattice degeneration and other peripheral retinal pathologies); another factor is retinal examination that is performed by someone with inadequate training or experience.

Many macular disease processes – such as early wet age-related macular degeneration (AMD), vitreomacular traction syndrome, vitreomacular schisis, moderate diabetic macular edema, mild-to-moderate epimacular membranes, and small macular holes – are all very difficult or impossible to see using a slit lamp and a 90 D or fundus contact lens, and use of widefield imaging technology as the sole method of retinal evaluation is simply not good medical practice. Central serous chorioretinopathy (CSR) is often virtually invisible, but it is becoming more common because of widespread steroid use (nasal inhalers for sinus disease, asthma inhalers, pain management injections, topical steroids for dermatologic conditions, and oral steroids for pulmonary diseases and collagen vascular diseases are all taken by more patients than you might expect).

Fortunately, OCT technology allows us to detect and evaluate all the disease processes listed above. It is fast, easily performed by technicians, requires no dye injection, and has no unit cost other than labor. I feel strongly that OCT has become an essential part of the pre-surgical examination of all cataract patients, not just patients that will be receiving premium IOLs. OCT imaging has also become essential for the evaluation of nerve fiber loss from glaucoma and can be performed on the same device used for macular evaluation; the prevalence of both glaucoma and macular disease makes this a valid approach.

"CSR is often virtually invisible, but it is becoming more common because of widespread steroid use."

How best to use this essential tool? Pseudo-color, 3D rendering and thickness maps obscure pathology and create artifacts, and so should not be used. Instead, all black and white gray scale slices should be viewed by the ophthalmologist – easily and rapidly done using the mouse scroll wheel. The images should be viewed using the native OCT device software, and it is a bad idea for a technician or photographer to pick an image to import into the electronic medical record. Fundus auto-fluorescence is possible with several modern OCT instruments and is a highly sensitive tool when it comes to evaluating geographic atrophy in dry AMD patients, as well as retinal pigment epithelium changes from CSR.

In summary, performing OCT is essential in the evaluation of all patients before cataract surgery; it prevents visual surprises and leads to expeditious and appropriate management of macular diseases.

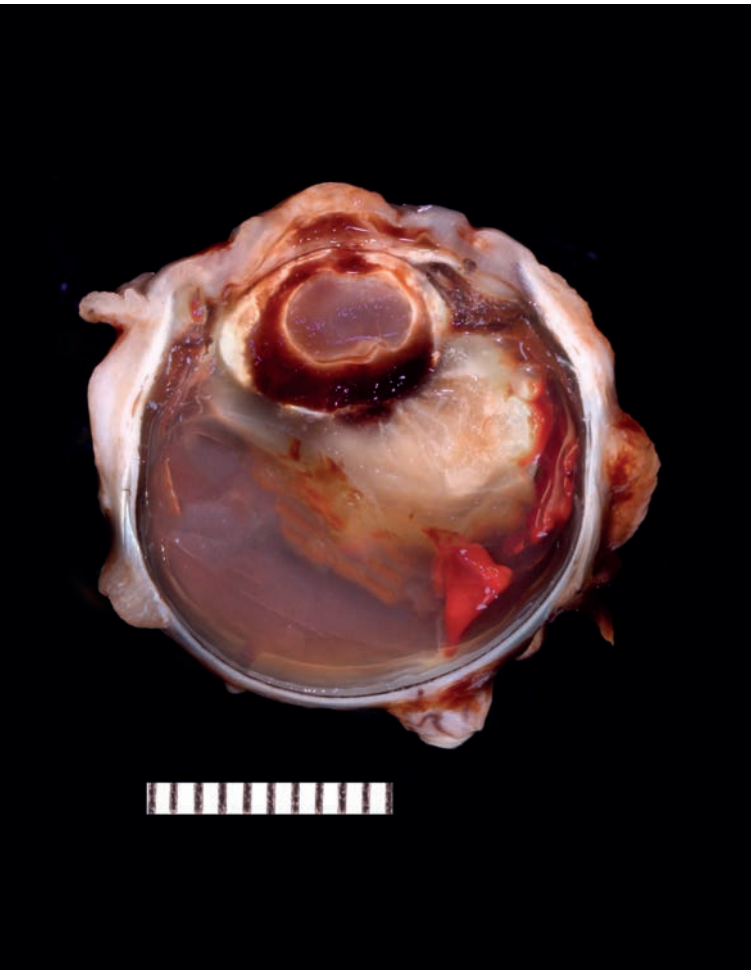
The ART *of* EYES

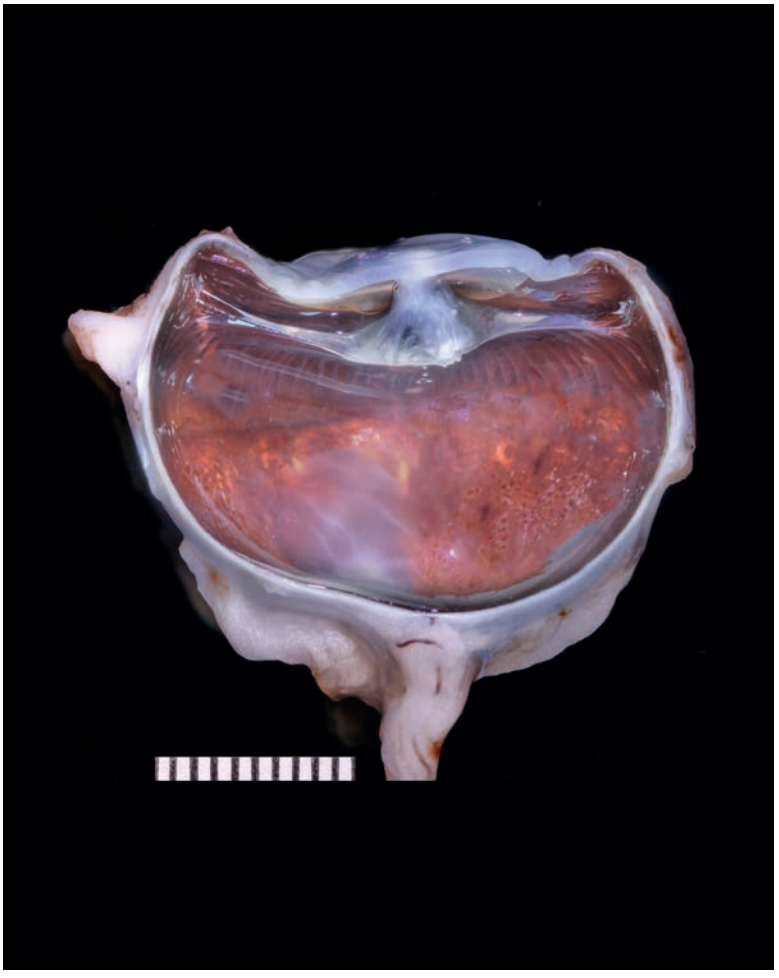
Art is everywhere. The eye allows us to perceive beauty, but beauty can also be found in the eye – and we're not just talking about beautiful irides. Let's explore some exquisite images of all things ophthalmic over the next 15 pages...

FOCUSING ON MULTIFOCALITY

Image of a extended depth of focus IOL, taken after YAG capsulotomy.

Karl Brasse, Ophthalmologist, Vreden, Germany.





RED AND RUPTURED

Canine globe with chronic intralenticular hemorrhage, evidenced grossly as red discoloration within the lens capsule. Histologically, blood vessels extended into the lens and percolated through the hemorrhage. The lens capsule was also ruptured and there was a granulomatous phakitis. The blood vessels extending from the optic nerve head remain unidentified. A diagnosis of persistent fetal vasculature (persistent hyperplastic tunica vasculosa lentis and/or persistent hyperplastic primary vitreous) was made (left image).

CHAMBER CLEAVAGE

Anterior segment abnormalities can be seen in this canine globe with anterior chamber cleavage syndrome. The small, malformed lens blends with the posterior cornea. Additionally, the iridocorneal angle structures (ciliary cleft and trabecular meshwork) were malformed with no aqueous humor outflow tracts, which was termed anterior segment dysgenesis (right image).

The Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW), USA. Further images can be found on the COPLOW Facebook page: bit.ly/COPLOW.

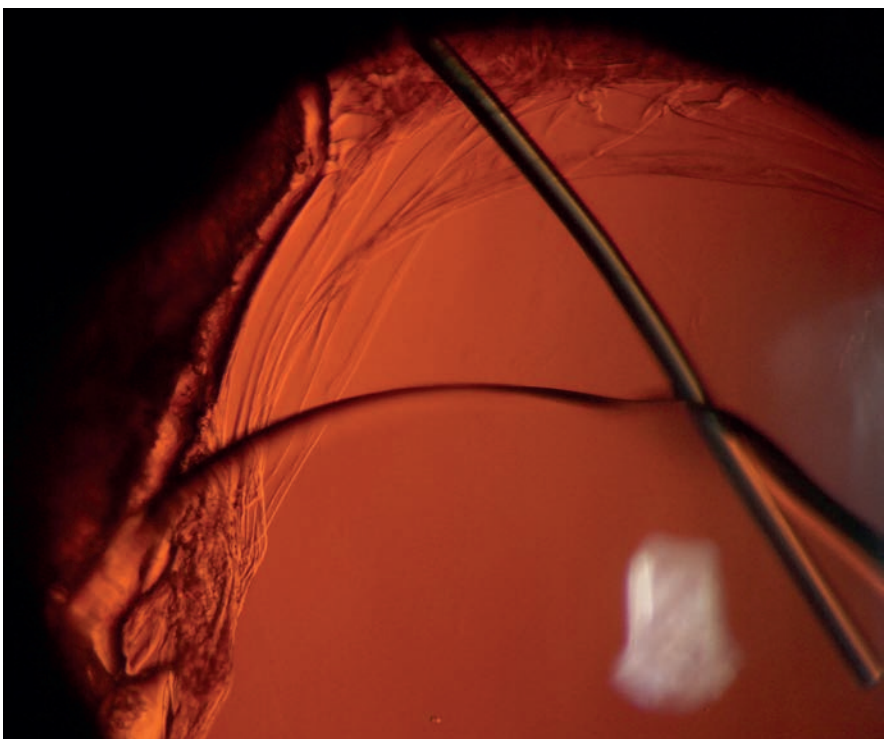
COASTAL PLAINS

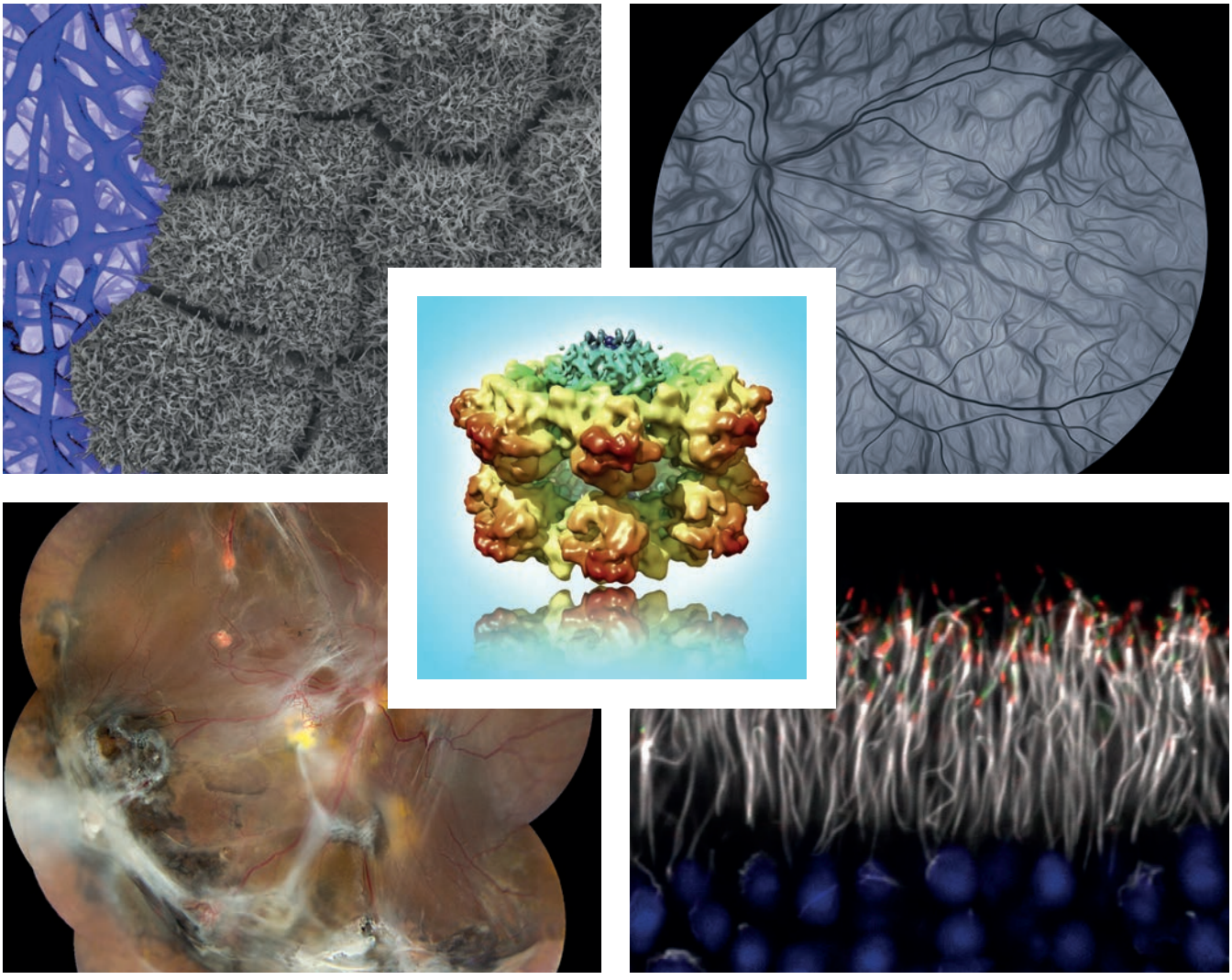
A bright beam of light and sclerotic scatter are used to expose corneal irregularities (above).

LYON & HEALY

Retroillumination of a displaced IOL (right).

Houston Sharpe III, Ophthalmic Imaging Specialist, UNC Kittner Eye Center, Chapel Hill, NC, USA.





RPE SEM

Scanning electron micrograph of induced pluripotent stem-cell-derived RPE cells growing on a nanofiber scaffold (pseudo colored blue; top left).

Kapil Bharti, National Eye Institute/NIH.

GREYSCALE FUNDUS

Fundus photo of retina in person with ocular albinism (top right).

Kapil Bharti, National Eye Institute/NIH.

REVEALING RETINOSCHISIN

An essential adhesion protein in the retina, the loss of retinoschisin results in a form of macular degeneration in young males called X-linked retinoschisis (center).

Bernard Heymann, NIH.

ALL TOGETHER NOW

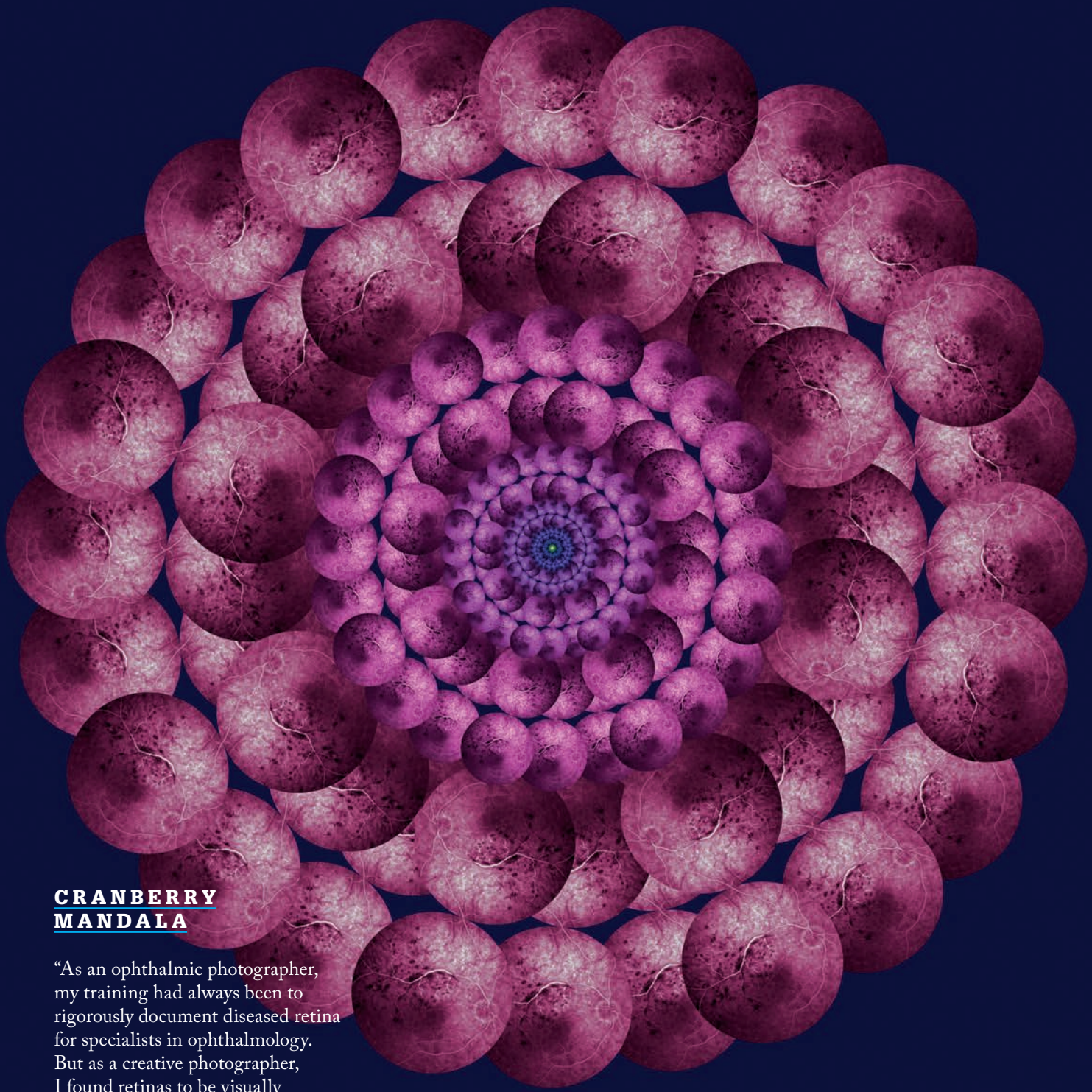
Montage photography of Von-Hippel Lindau Syndrome (bottom left).

Mike Arango, National Eye Institute/NIH.

CILIA AND CILIA

The cellular structure in photoreceptors that capture light is derived from a modified cilium. Fluorescent labeling for RPGR, a protein commonly mutated in retinitis pigmentosa, shows the photoreceptor cilia (red) within the mouse retina. Additional ciliary structures (green), the ciliary rootlet (white), and nuclei (blue) are also visualized (bottom right).

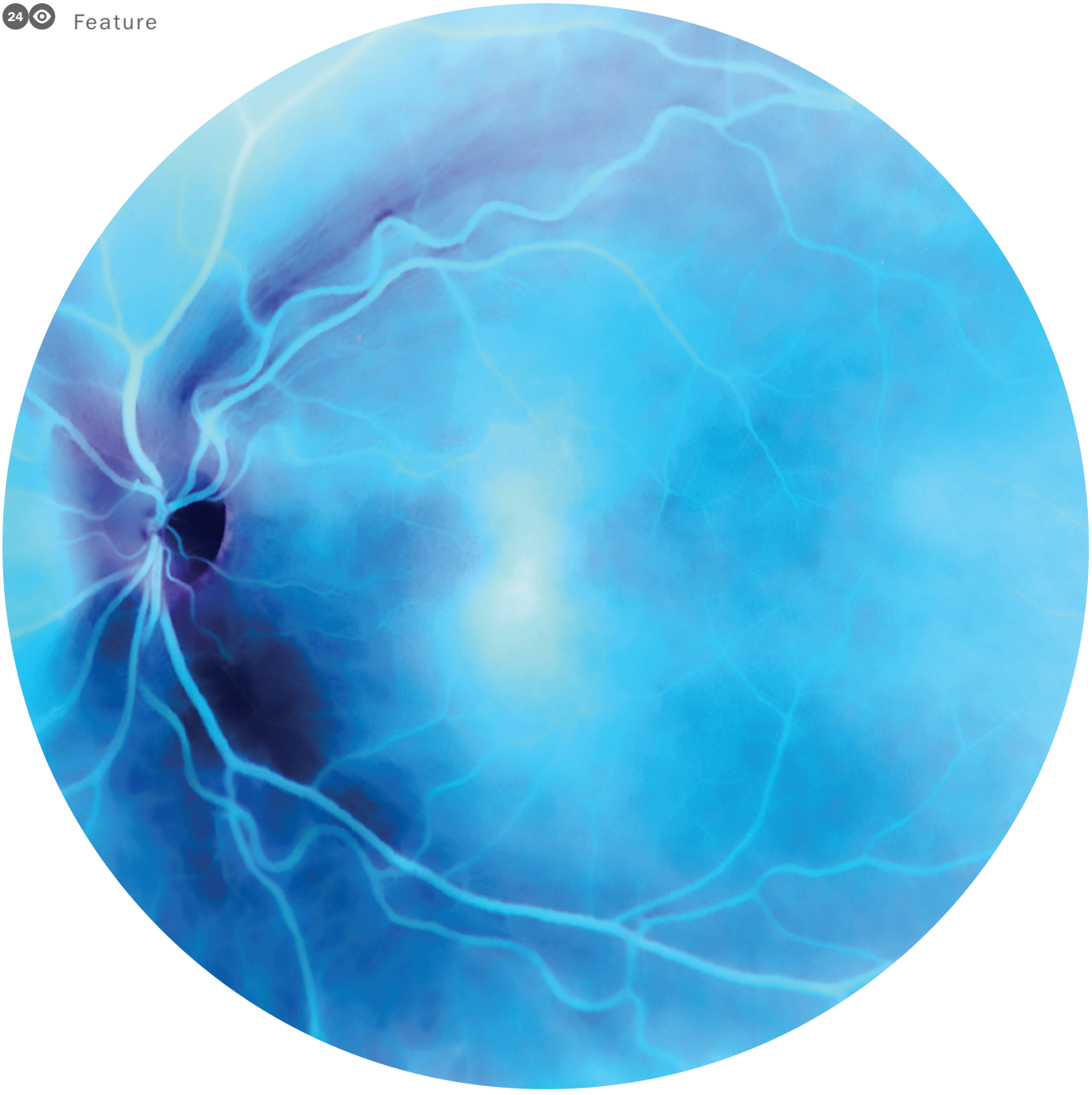
Jessica Gumerson, National Eye Institute/NIH.



CRANBERRY MANDALA

"As an ophthalmic photographer, my training had always been to rigorously document diseased retina for specialists in ophthalmology. But as a creative photographer, I found retinas to be visually fascinating. This work emerges from black and white digital images which are layered, manipulated, and colored."

Pat Saine, former ophthalmic photographer and owner of Blue Plate Books, Winchester, VA, USA.



INNER LIGHT

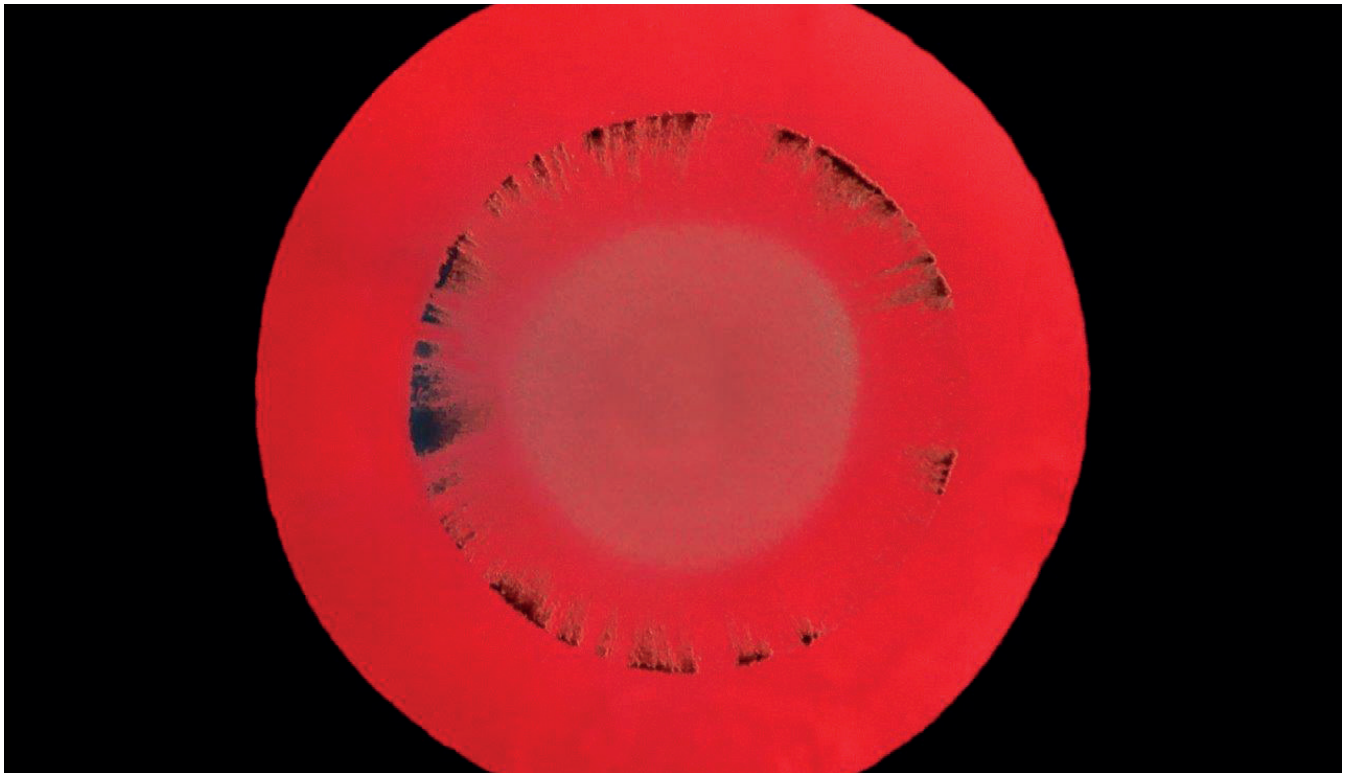
Speaking literally the retina is an internal structure that provides for light to be converted to impulses that guide the brain. The title of this photograph is a reference to our collective literal and figurative "inner light" (above).

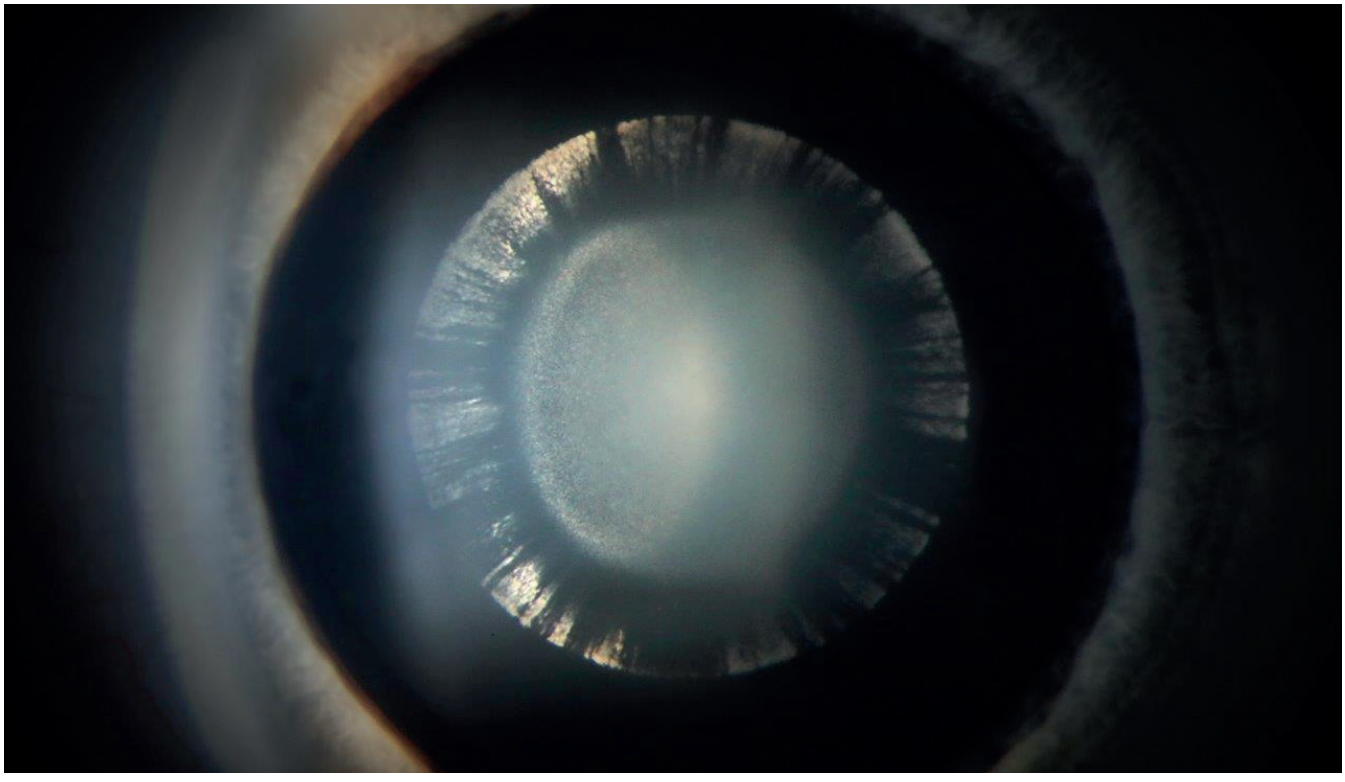
Kelly Aileen Oldstein, Certified Ophthalmic Photographer at Chester County Eye Care, and owner of Kelly Aileen Photography, Chester County, PA.

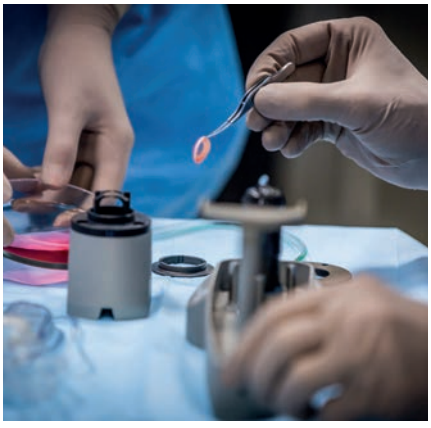
CATARACTA PULVERULENTA

These pictures (right) are from an 18-year-old female patient who suffered from photophobia and reduced vision before cataract surgery and multifocal IOL implantation were performed.

Karl Brasse, Ophthalmologist, Vreden, Germany.



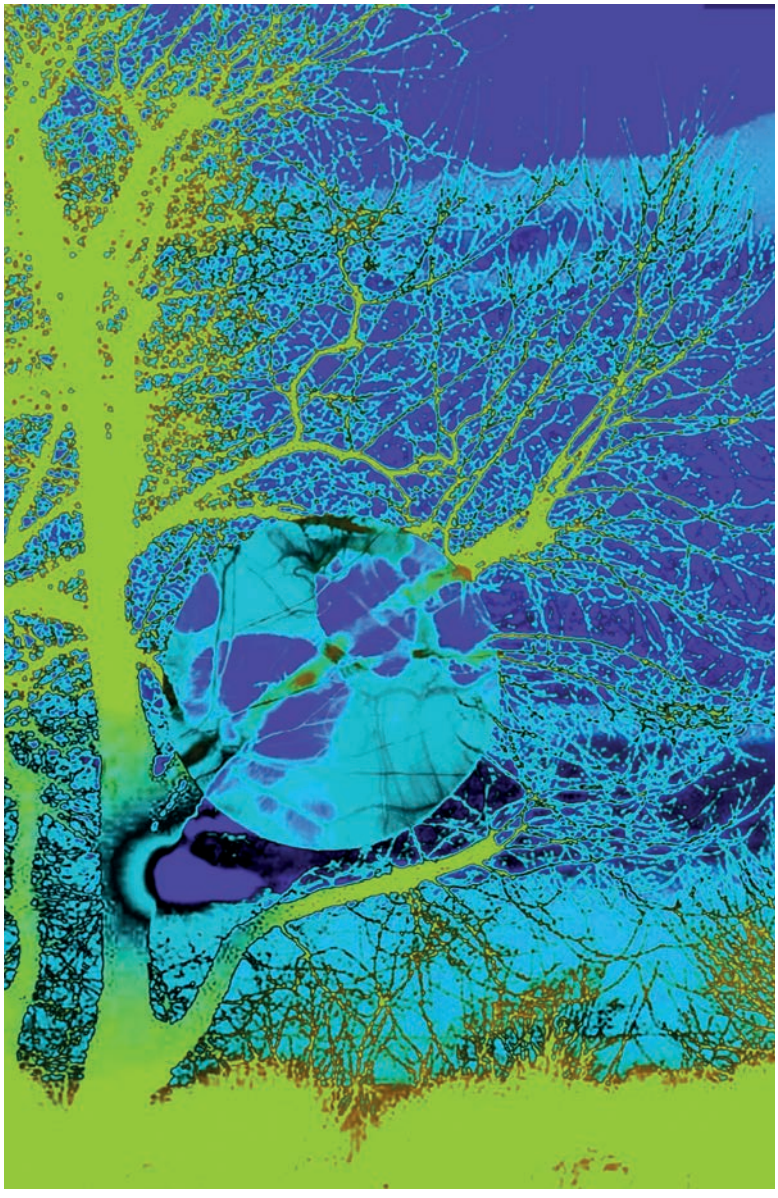




FROM RUSSIA WITH LOVE

Boris Malyugin performing corneal graft surgery at the S. Fyodorov Eye Microsurgery State Institution, Moscow, Russia. Clockwise from top left: Boris and his assistant, Ekaterina Malyutina, at the operating microscope during the procedure; transferring the corneal graft; mid-procedure instructions, and preparing the graft with a femtosecond laser.

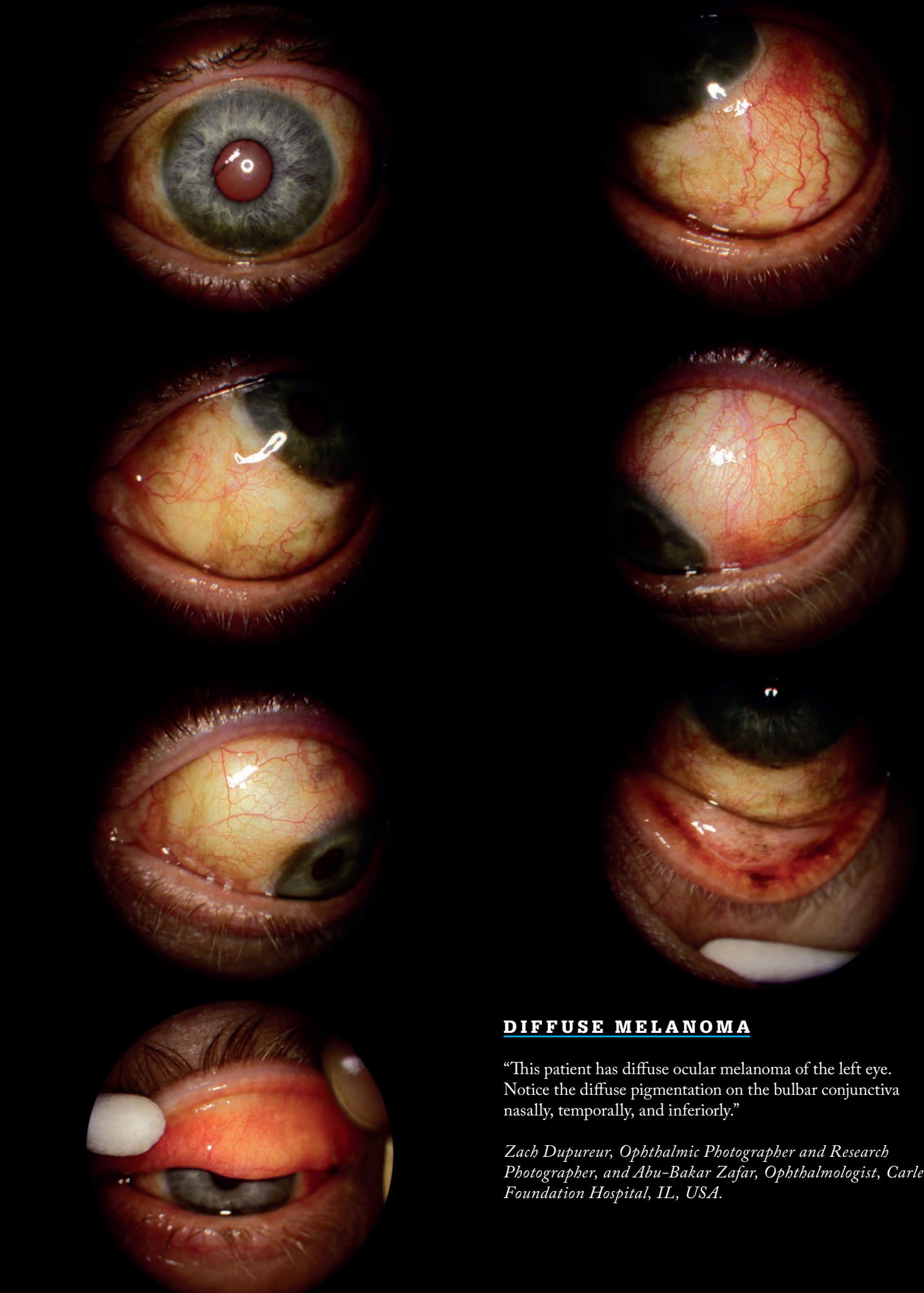
Terry Cooper, Cap d'Ail Photos, London, UK. www.facebook.com/capdailphotos/



ART AFTER EYE INJECTIONS

Artist Tracy Ellyn creates ophthalmology fine art pieces as a way of expressing and sharing her first-hand experience with wet macular degeneration. The artist uses multiple layers of her own OCT images, in combination with hand drawings, watercolor painting, photography, and other mixed media. "Finding the beauty in all things, including scotomas, tint loss and the kaleidoscopic visual effects people experience after eye injections, as well as the connection between the outer world of nature and the inner world of the eye, is the inspiration for my work," says Ellyn. Her "Ophthalmology Series" of artwork can be viewed on her website: www.tracyellyn-recentworks.com.

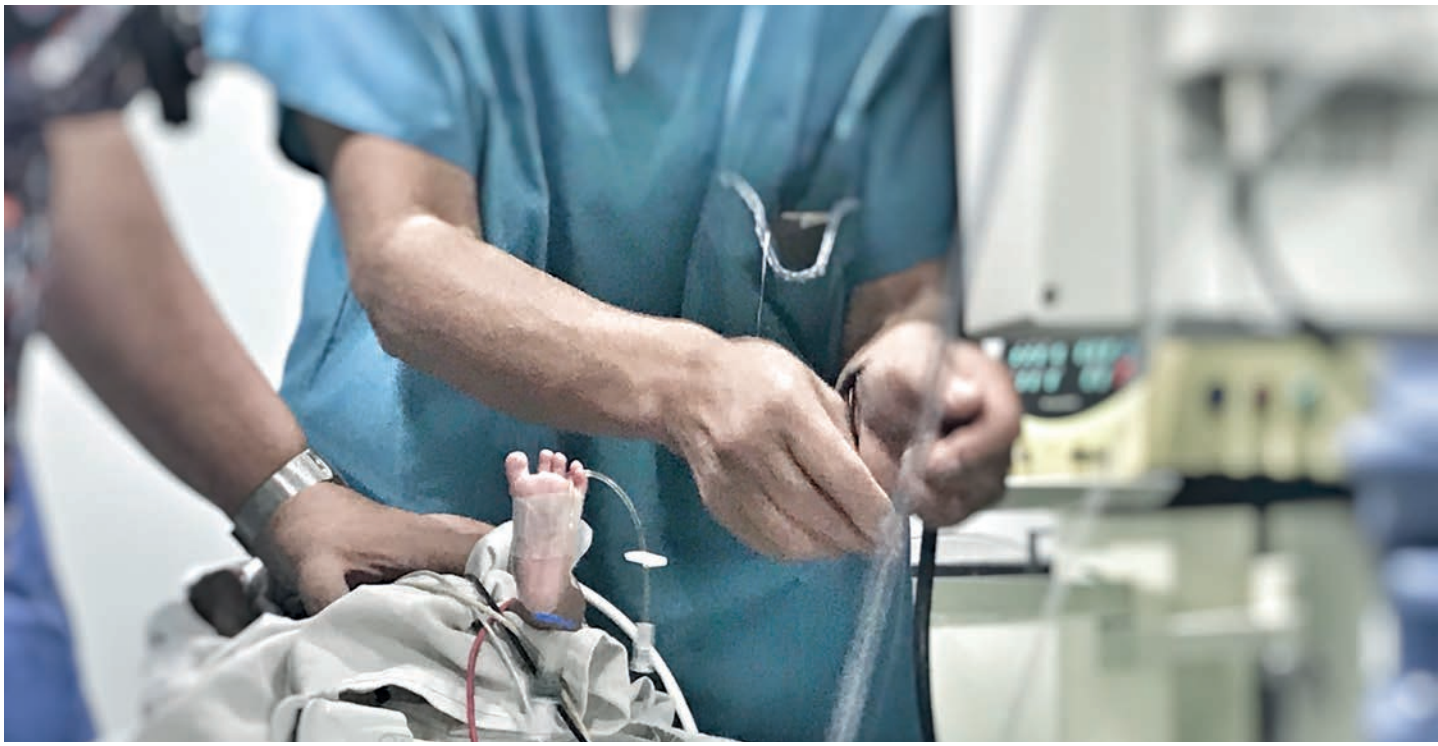
Tracy Ellyn, Artist, Tracy Ellyn Fine Arts, Miami, FL, USA.



DIFFUSE MELANOMA

"This patient has diffuse ocular melanoma of the left eye. Notice the diffuse pigmentation on the bulbar conjunctiva nasally, temporally, and inferiorly."

Zach Dupureur, Ophthalmic Photographer and Research Photographer, and Abu-Bakar Zafar, Ophthalmologist, Carle Foundation Hospital, IL, USA.



INTREPID VITRECTOMY

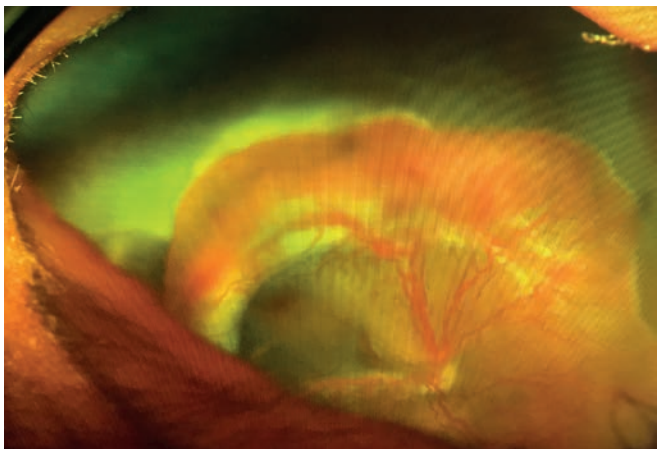
These images document the case of premature baby girl with stage 4a retinopathy of prematurity (ROP) who underwent vitrectomy – the first vitrectomy ever performed on such a young baby in Mexico using heads-up surgery technology. "The surgery was challenging, not only technically, but because of the logistics it involved; no ophthalmology hospital had a neonatal intensive care unit (NICU) and no NICU had equipment for eye surgery."

HOPE

The baby being prepared for vitrectomy (above).

HEADS UP!

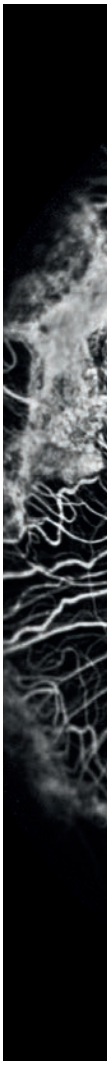
The surgeon performing the vitrectomy – and the team – all viewing the procedure in real time on the heads-up display (right).



ROP

The eye that underwent surgery (bottom right).

Maria Ana Martinez-Castellanos, Pediatric Retina Surgeon, Asociación para Evitar la Ceguera en Mexico, Mexico City, Mexico.



STEPHEN WITH A MAGNIFIER

This painting (acrylic on canvas, 2014) is part of Lucy Burscough's "Look200" series which explores color vision deficiency. The subject is Stephen Golding, a dispensing optician at the UK's Manchester Royal Eye Hospital. Standard vision color range is shown within his magnifier, while outside is a simulation of the colors seen by someone with severe deuteranopia.

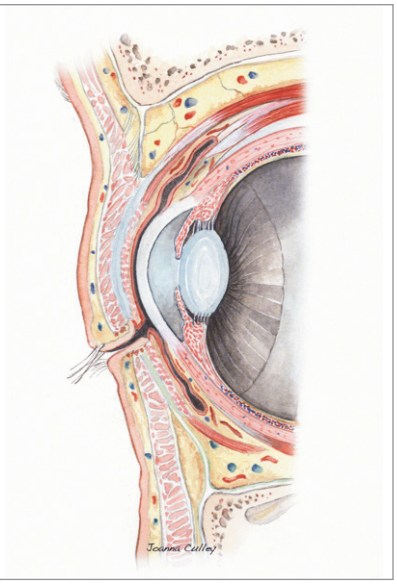
The image was developed using Kazunori Asada's Chromatic Vision Simulator app and was painted in the waiting areas of clinics at Manchester Royal Eye Hospital as part of an Arts Council England funded "arts for health" residency. The whole series and Lucy's other vision related artwork can be seen at www.LucysArt.co.uk.

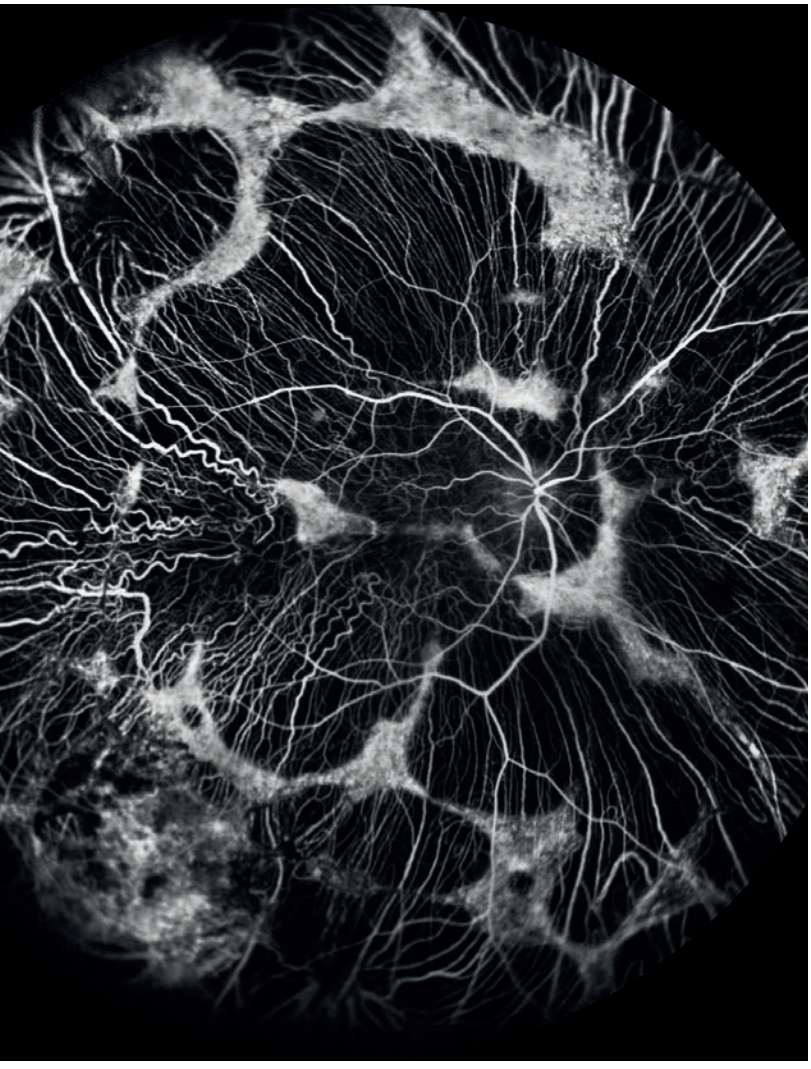
Lucy Burscough, Artist, Manchester, UK.

ANATOMY ARTISTRY

Watercolour illustration by Medical Artist Joanna Culley of www.medical-artist.com.

Joanna Culley, Medical Artist, Haslemere, Surrey, UK.

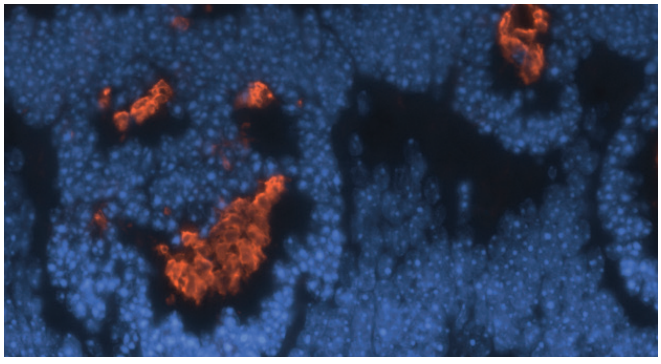


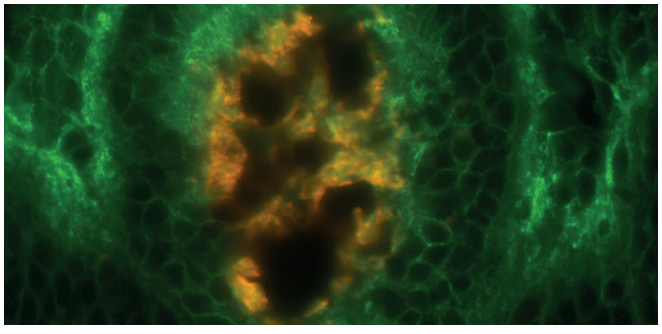


CHOROIDEREMIA

"Anticipation and timing is key in my work as both a professional sports photographer and as an ophthalmic photographer. Anticipating and capturing the dynamic flow of fluorescein through retinal blood vessels is important when performing angiography. In this case of choroideremia, both the retinal and choroidal vessels are visible along with arc-like remnants of what remains of the RPE."

Joe Territo, senior photographer, Retina Associates of Western New York, Rochester, NY, USA. His personal work can be viewed at: http://bit.ly/JoeTerrito.

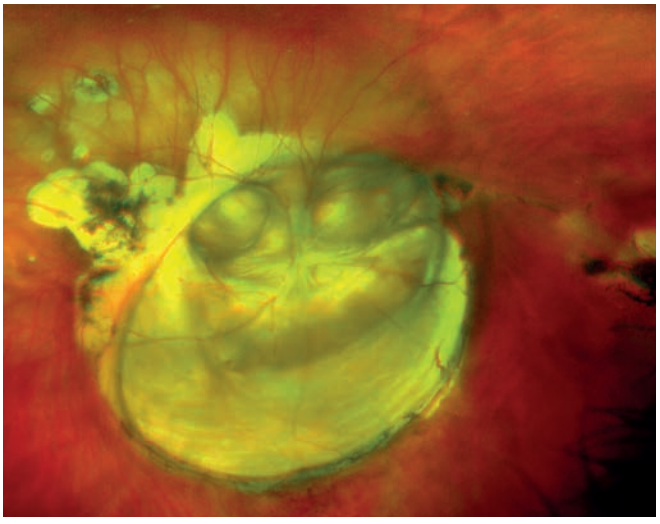


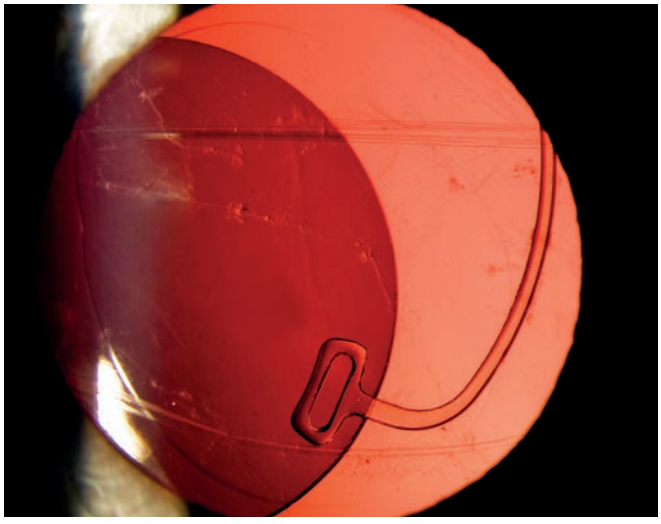


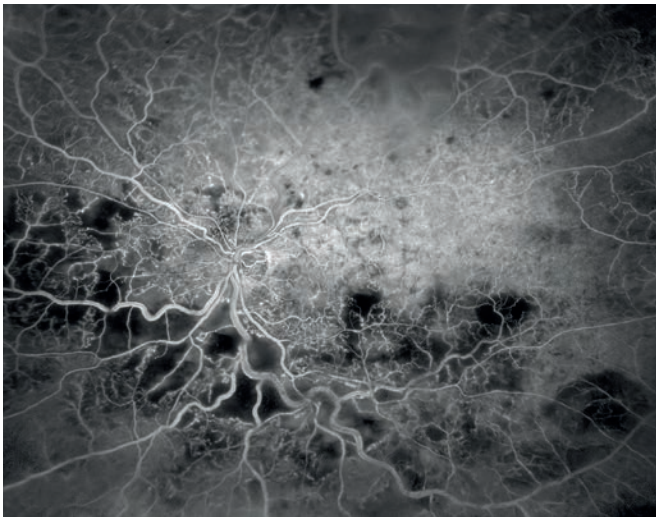
SEEING FACES

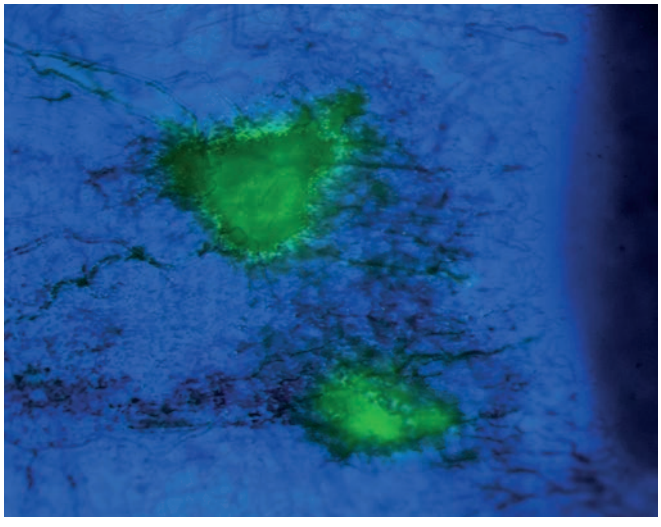
Histological retinal sections from mice that have had NRL and RDS proteins knocked out that appear to depict, respectively, a "happy" and a "monkey/ghost" face (images above). The top image shows photoreceptor outer segments labeled with anti-S-opsin antibody (red) and the bottom image shows photoreceptor inner segments labeled with anti Na^+/K^+-ATPase antibody (green) and outer segments labelled with anti-S-opsin (red).

Rafal Farjo, CEO of EyeCRO LLC and Charlesson LLC, Oklahoma City, OK, USA.









OPHTHALMIC PHOTOGRAPHY IN PRACTICE

This selection of images was contributed by Kim Baxter, Ophthalmic Photography Team Leader at Addenbrooke's Hopsital, Cambridge, UK. Baxter, who specializes in all types of ophthalmic imaging including slit-lamp photography and retinal angiography, is a member of the Institute of Medical Illustrators and has won two gold awards at their annual exhibitions, along with bronze and silver awards. Her work has been selected for the Wellcome Trust and twice by the Royal Photographic Society's *Visualising Medicine* exhibitions.

COLOBOMA CLOSE-UP

This coloboma covers the macula area, including the optic nerve, and was captured with ultra-widefield imaging (above left).

SUBLUXED IOL

This image of a subluxed IOL was taken on an anterior segment camera using retroillumination to show the position of the lens prior to surgery (above right).

SEEING CRVO

Ischemic central retinal vein occlusion taken on a wide-field camera during a fluorescein angiogram to document the level of ischemia before treatment (bottom left).

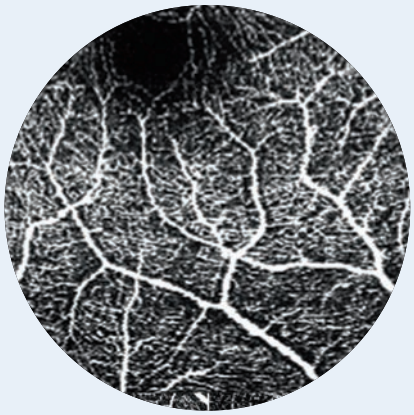
IMAGING INFECTION

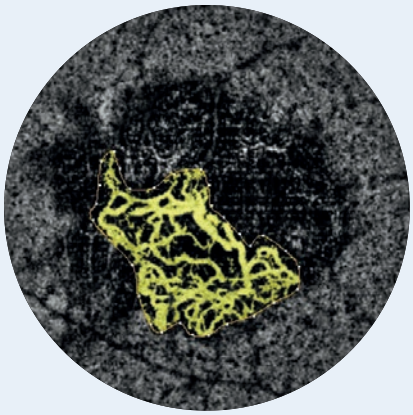
Using an anterior segment camera, topical fluorescein dye and blue filters, the areas of conjunctival infection can be seen in green (bottom right).

Kim Baxter, Ophthalmic Photography Team Leader at Addenbrooke's Hospital, Cambridge, UK.

Technology to Empower: Imaging

Imaging. It's a cornerstone of the diagnosis and management of a large swathe of ophthalmic disease, and recent advances in imaging technology have revealed more – about the eye's anatomy, how it functions, how disease manifests and develops – than was ever thought possible. Here, leading ophthalmic imaging equipment manufacturers showcase their latest offerings, and explain what these advances mean for you and how you practice ophthalmology.





UNLOCK THE POWER

ZEISS HD Ultra-widefield Fundus Imaging

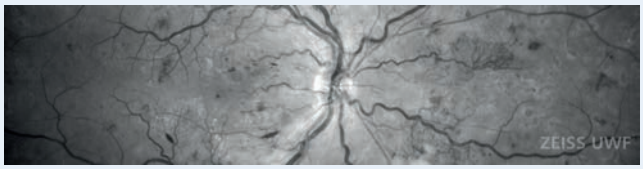
Managing patients with retinal disease can be challenging – they present to practices with a greater diversity of age and disease states (and in far greater numbers) than ever before. As always, effective initial disease detection and progression management – with the right treatment option at the right time – remains crucial for truly effective long-term vision preservation. And this is where widefield imaging comes into play.

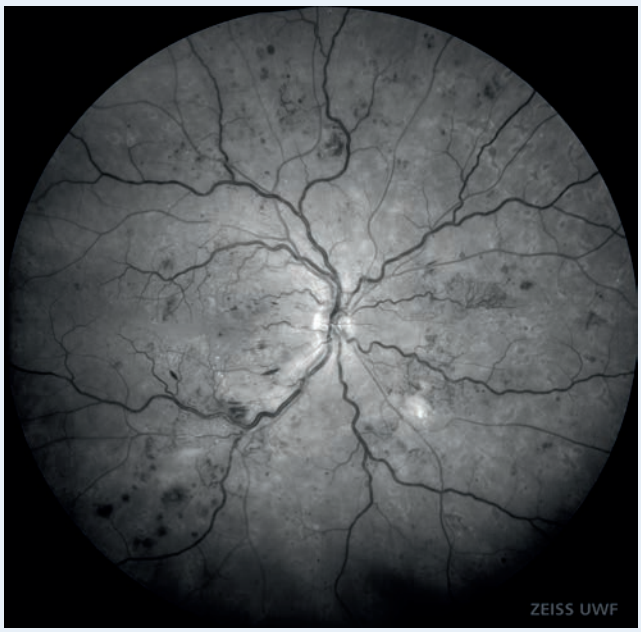
Widefield imaging has shown us the possibility of uncovering more pathology by imaging a larger area of the retina than standard fields. Widefield imaging allows for more thorough documentation and detection of peripheral retinal pathology, leading to earlier diagnosis of diseases and better management of patients. However, traditional fundus imaging systems remain the gold standard for macular disease diagnosis and optic nerve evaluation.

The launch of ZEISS HD ultra-widefield system represents the next generation of widefield fundus imaging. Leveraging ZEISS optics, the technology promises to deliver exceptional clarity from the macula to the far periphery in a true color image. True color images are generated through sequential illumination by a full spectrum red, green and blue LEDs. Unlike other scanning laser technologies, ZEISS HD-UWF images closely resemble the coloration of the fundus as seen through direct observation.

In addition to imaging the peripheral retina in high resolution, the ZEISS HD UWF system captures high quality images of the optic nerve head and the macula. This eliminates the need for clinicians to maintain more than one fundus imaging system in their practice and helps them manage a broader range of patients.

Case studies



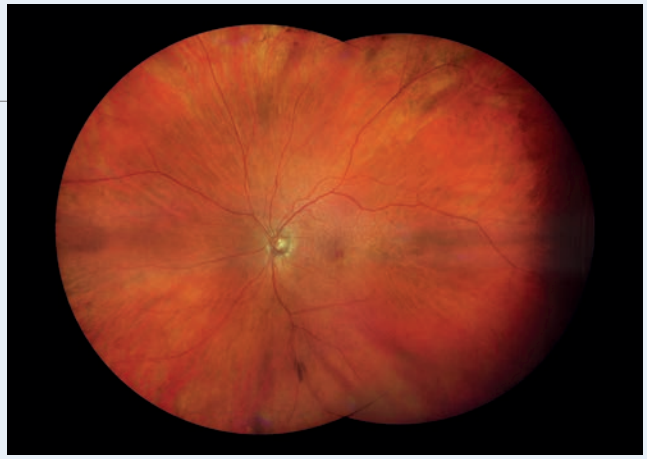


Diabetic retinopathy

Ultra-widefield (UWF) imaging is the ideal tool to detect diabetic retinopathy. Recent studies have demonstrated the importance of peripheral retinopathy, and its role in predicting disease progression. UWF imaging provides a fast, reliable method for imaging the peripheral retina.

Green channel separation images further highlight hemorrhages and microaneurysms, making it easier to visualize subtle retinopathy.

To achieve an ultra-wide field of view, many systems compromise on image resolution. The ZEISS system maintains excellent clarity and color, giving the ability to zoom into any part of the image and view the retina in great detail. In this case study, the patient has neovascularization nasal to the optic disc. The fine neovascular frond can be seen clearly on the image. Having both field of view and good resolution gives the clinician confidence when managing their diabetic patients.

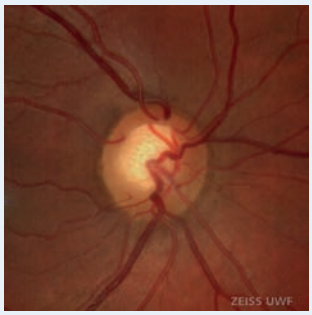


AMD

For dry age-related macular degeneration, accurate coloration is important for documenting RPE pigment changes and drusen. This patient was imaged on the ZEISS UWF system as part of his exam. Scattered drusen can be seen throughout the macular region. Reticular degeneration, which is a risk factor for AMD progression, can also be seen in the peripheral retina. Even though AMD is primarily a macular disease, UWF imaging still plays a role in documenting peripheral risk factors. The ZEISS system has the advantage of peripheral imaging, while still maintaining the image quality of a traditional fundus camera.

Glaucoma

Because of the subtle and slow-changing nature of the disease, glaucoma necessitates precise, high resolution, repeatable documentation of the optic disc, whether it be with OCT, fundus photos, or visual fields. In fundus imaging, having a high quality, true color image that allows for quantitative measurements is critical. ZEISS color and resolution enables evaluating focal changes in rim tissue or nerve pallor with confidence. The review software makes it easy to compare images over time, aiding in the detection of early glaucomatous changes.



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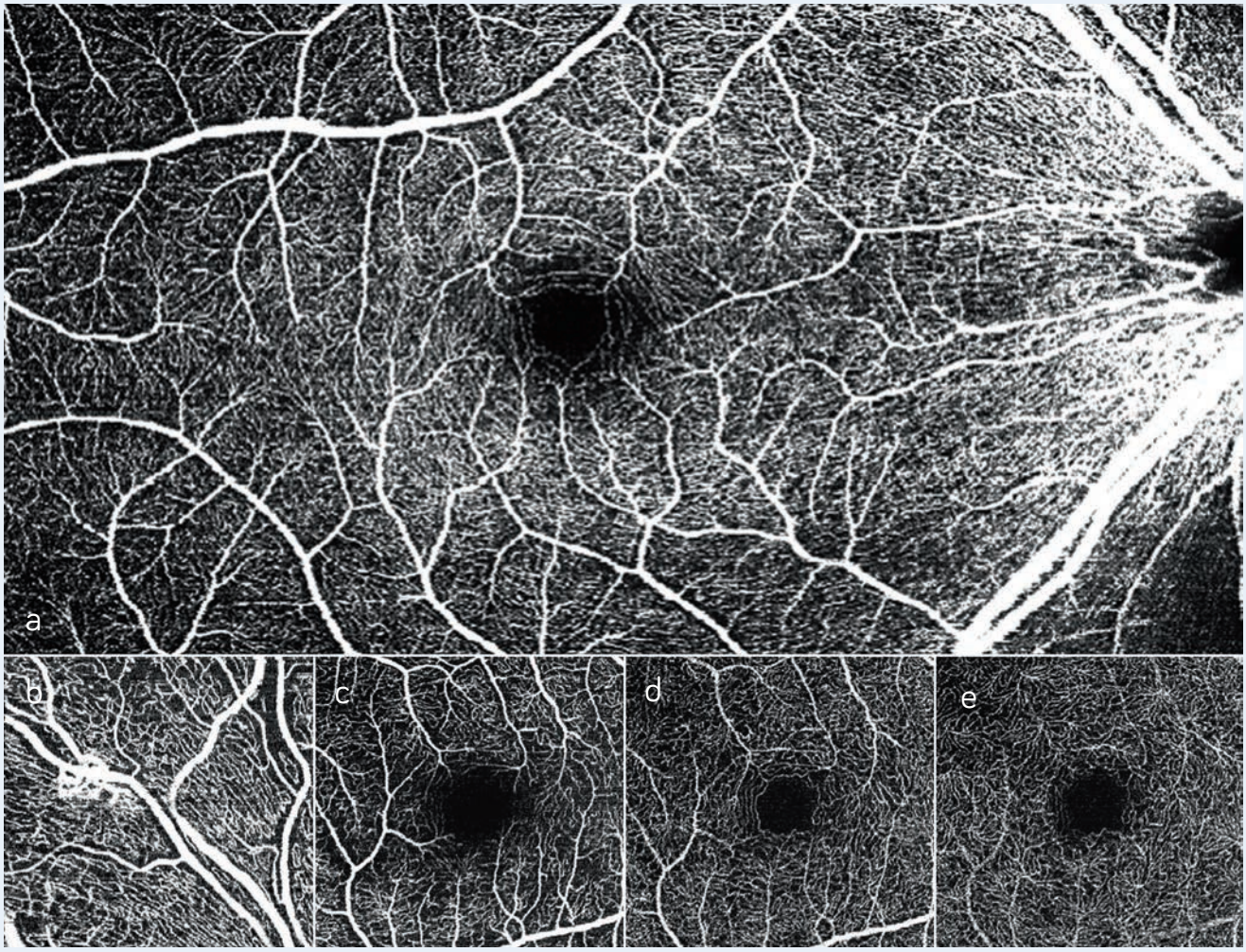
The SPECTRALIS® SD-OCT is Heidelberg Engineering's expandable diagnostic imaging platform which combines scanning laser fundus imaging with high-resolution OCT. It can be configured according to different diagnostic workflows with options including OCT, multiple scanning laser fundus imaging modalities, widefield and ultra-widefield modules, scanning laser angiography and OCT angiography (OCTA). The OCT Angiography Module* is the latest addition to the SPECTRALIS platform and offers three-dimensional insights into vascular flow, with a flexible combination of non-invasive high-resolution imaging and a high-speed widefield view (see image a).

The SPECTRALIS OCT Angiography Module delivers high-resolution OCTA images depicting fine capillary networks in great detail and a precise segmentation of all four histologically-validated retinal vascular plexuses (see images b-e) with minimal motion artifacts. The module offers the flexibility to customize the slab position on every B-scan image, allowing for visualization of pathology in any retinal layer. The dynamic image fusion of OCT and OCTA supports precise localization of flow in abnormal vessels. The SPECTRALIS also enables a unique hybrid approach to angiography with a precise, pixel-to-pixel correlation of OCTA follow-ups on existing FA and ICGA images.

In short, the SPECTRALIS OCT Angiography Module provides the dynamic tools needed to master the application and interpretation of this novel imaging modality. It combines OCTA with structural OCT and fundus imaging resulting in a powerful multimodal approach to support clinical assessment and treatment decisions.

Case study



The SPECTRALIS OCT Angiography Module provides high-resolution OCTA images with a lateral resolution of 5.7 µm per pixel for the visualization of capillary vessels. The axial resolution of 3.9 µm per pixel enables detailed retinal layer segmentation. All four vascular networks can then be examined: vasculature in the nerve fiber layer (b), in the ganglion cell layer (c), at the border of the inner plexiform layer to the inner nuclear layer (d), and at the border of the inner nuclear layer to the outer plexiform layer (e).

**The OCT Angiography Module is available for purchase only outside the United States.*

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AngioVueHD

Technical Capabilities of the Software

By Tony Ko PhD

Powered by proprietary technologies like SSADA (split spectrum amplitude-decorrelation angiography), DualTrac™ Motion Correction and Projection Artifact Removal (PAR), Optovue's newly developed high-density (HD) scan patterns provide best-in-class OCTA image quality for 6×6 mm macular and 4.5×4.5 mm optic disc scans. Known as AngioVueHD, sampling density has been increased from 304×304 A-scans to 400×400 A-scans. Overall sampling points have been increased by 73 percent, resulting in a 33 percent improvement in detail resolution compared to older OCTA scans. Now capillaries can be resolved to 15 µm allowing for visualization of very fine vasculature, which should provide greater confidence to physicians when imaging pathologies extending beyond the central 3×3 mm macular region.

Importantly, the enhanced resolution is preserved over a wider field-of-view (FOV), so a 6×6 mm scan now provides the same detailed visualization of microvasculature and pathology as the previous 3×3 mm scan. This enables physicians to eliminate capturing two scans – one 3×3 mm scan for the best image quality, and one 6×6 mm scan for wide FOV. Now both high-resolution imaging and a wide FOV exist in one scan. Optovue currently offers the widest FOV and the highest density scanning of any commercial OCTA solution.

AngioVueHD extends high-density imaging to montage mode by combining two high-density AngioVue scans to provide greater than 10×6 mm of coverage, while still visualizing fine retinal microvasculature details. AngioMontageHD automatically creates the image from scans of the macula and the optic disc, and is essential for imaging pathologies that extend into the periphery, such as diabetic retinopathy (DR) and retinal vein and artery occlusions.

Beyond better image quality, high-density imaging is of paramount importance to the accuracy of OCTA quantification. Optovue's AngioAnalytics*, the world's first OCTA quantification, leverages the improved resolution of AngioVueHD. Quantifying retinal vasculature provides an objective assessment of vascular traits more closely associated with visual functional outcomes than morphological traits alone. Current analysis tools include Flow Area in the outer retina and choroid (for assessment of choroidal neovascularization), Non-FlowArea of the superficial plexus (for assessment of ischemic regions in diabetic retinopathy) and Vessel Density analysis of the superficial plexus.

Case study

Maddalena Quaranta-El Mafoutouhi, MD, and
Adil El Maftouhi, OD, Centre Rabelais, Lyon, France.

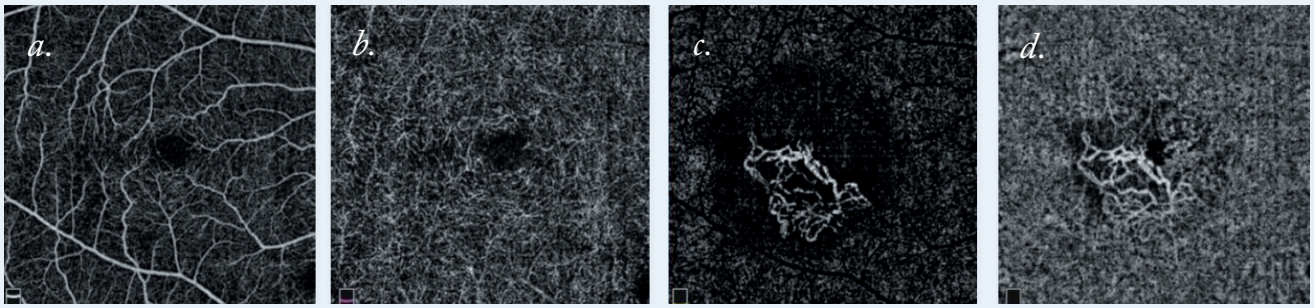

Image 1 (Top). 6×6 mm AngioVue HD imaging of the retina of a wet AMD patient with type 1 occult CNV.
a. Superficial Plexus, b. Deep Plexus, c. Outer Retina, d. Choriocapillaris

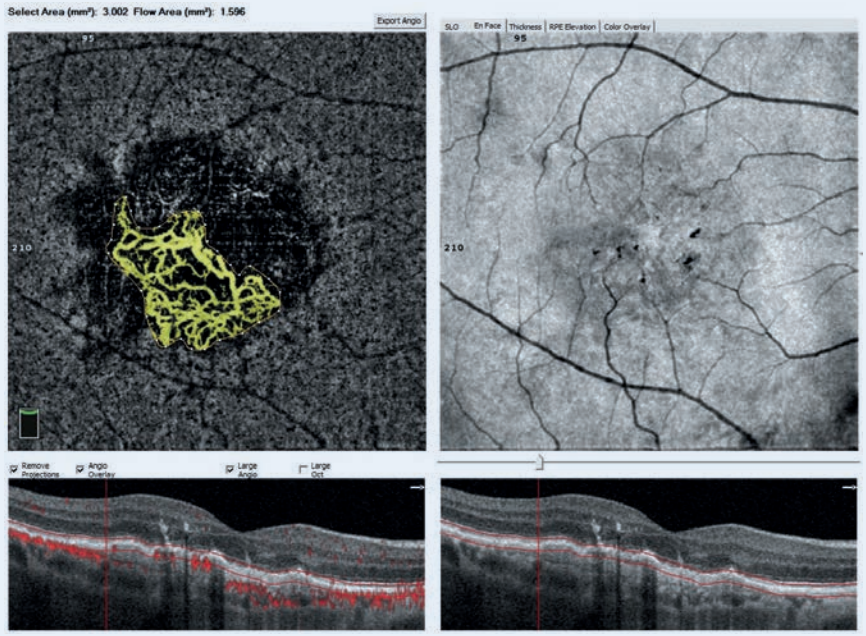

Image 2. Quantification of the Type 1 (occult) CNV lesion with the AngioAnalytics Flow Area tool.

Here we present 6×6 mm AngioVue HD imaging of the retina of a wet AMD patient with type 1 (occult) CNV (Image 1), where the flow area was quantified using Optovue's AngioAnalytics* software (Image 2). The patient was followed-up for three months and underwent an induction phase of three intravitreal anti-VEGF injections. Their vision recovered from 6/10 to 10/10 on the day of the third injection – which is when these AngioVueHD 6×6 mm scans were performed. Furthermore, the new AngioVueHD software from Optovue now allows you to monitor CNV with a larger scan size of 6×6 mm, with similar details and vessel area quantification as 3x3 mm scans, but with the added benefit of a wider field of view.

**AngioAnalytics is not FDA cleared for sale in the U.S.*

OPTOVUE

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If you are based in the US or Canada, visit www.theophthalmologist.com to sign up for the print edition of The Ophthalmologist North America.

In Practice

Surgical Procedures
Diagnosis
New Drugs

Seeing Your Way to a Well-Rounded Trabeculotomy

In cases of pediatric congenital glaucoma, consider 360° trabeculotomy

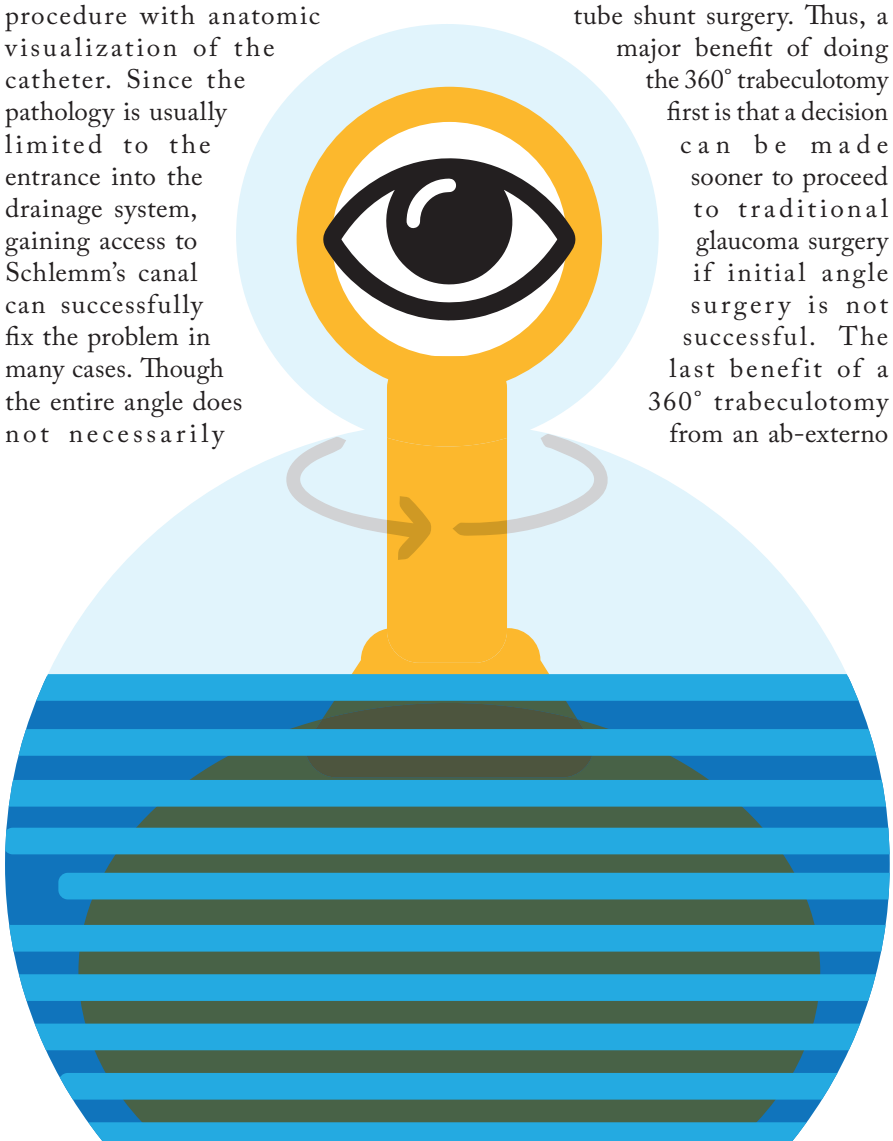
By Joseph Panarelli

Treating children with congenital glaucoma is often a considerable challenge. Early detection and timely intervention are essential to achieving successful outcomes. These children can present with severely elevated IOP, and if untreated, the natural course is rapid progression to blindness from optic nerve damage. Another significant contributor to vision loss is dense amblyopia from anisometropia or corneal opacification. Surgical options had typically been limited to goniotomy and trabeculotomy with either a Harms trabeculotome or suture, but the 360° trabeculotomy with an illuminated microcatheter, performed via an ab-interno or ab-externo approach, is gaining increased popularity. The main advantage of this approach is that it allows the surgeon to treat the entire angle in a single procedure with anatomic visualization of the catheter. Since the pathology is usually limited to the entrance into the drainage system, gaining access to Schlemm's canal can successfully fix the problem in many cases. Though the entire angle does not necessarily have to be treated each time to have a successful outcome, a full 360° treatment likely enhances the chances of success. I have had numerous cases where we started with a nasal goniotomy and then moved on to a temporal trabeculotomy, and in some cases went back a third time into the angle to try a more extensive goniotomy.

Another advantage of the 360° trabeculotomy is that the procedure leaves no question as to whether additional angle surgery is needed. If the IOP becomes elevated again, then the presumption is that these children have pathology in the downstream collector channels and need traditional glaucoma surgery, either a trabeculectomy or tube shunt surgery. Thus, a major benefit of doing the 360° trabeculotomy first is that a decision can be made sooner to proceed to traditional glaucoma surgery if initial angle surgery is not successful. The last benefit of a 360° trabeculotomy from an ab-externo

At a Glance

- *To save pediatric patients the stress of multiple interventions, the ideal surgical approach should adequately lower IOP in a single procedure when successful – and guide subsequent therapeutic strategy when unsuccessful*
- *Procedures such as goniotomy treat only a portion of the angle; reliance on such techniques may require repeated angle procedures to achieve the desired IOP lowering effect. To perform a goniotomy, good visualization of the angle structures is necessary and this can be an issue when children present with significant corneal clouding*
- *The 360° trabeculotomy, by contrast, treats the entire angle at once. If this procedure is not effective in controlling the IOP, traditional glaucoma surgery (filtering surgery or glaucoma drainage device surgery) is needed*
- *Illuminated devices (visible through the sclera as they are pushed around Schlemm's canal) help the surgeon guide the catheter during the 360° trabeculotomy procedure, irrespective of corneal opacity.*



"Congenital glaucoma is rare, and thus mastering various angle-based surgeries is difficult."

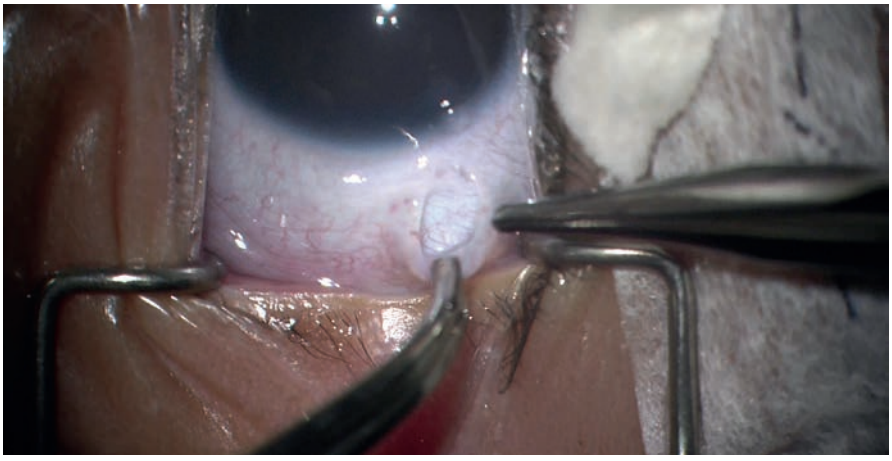


Figure 1. The first step in the 360° trabeculotomy is to create a temporal conjunctival peritomy and gain access to the sclera.

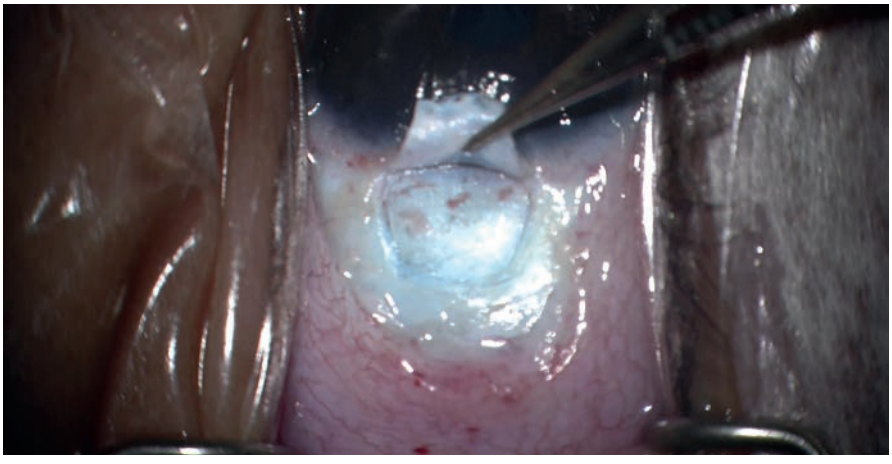


Figure 2. Dissecting a scleral flap to access Schlemm's canal. Reaching Schlemm's requires very delicate dissection to "un-roof" the canal.

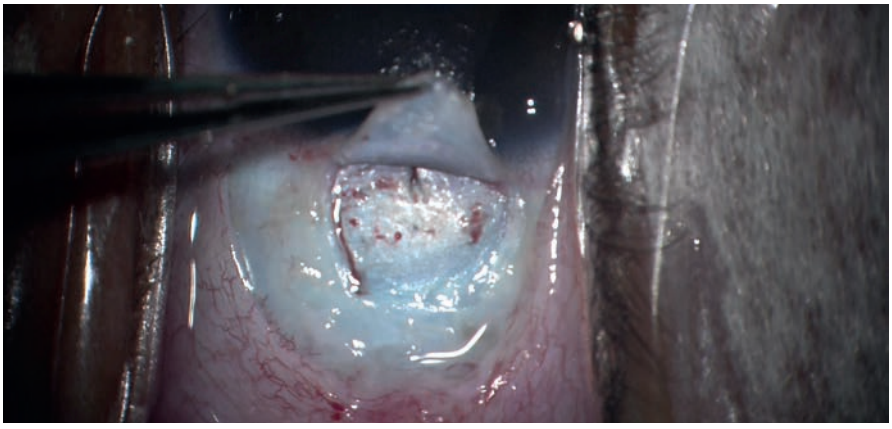


Figure 3. Scratch down incision to gain access to the canal. An egress of fluid or blood is a sign that it has been opened.

approach is that it can be performed regardless of how well the angle can be viewed. Elevated IOP in children with congenital glaucoma often leads to significant corneal edema and haze, which obscures the surgeon's direct view of the angle when attempting to perform a goniotomy or even the gonioscopy-assisted transluminal trabeculotomy (GATT) procedure.

Congenital glaucoma is rare, and thus mastering various angle-based surgeries is difficult. Due to the many advantages of an ab-externo 360° trabeculotomy, it makes sense to learn this procedure and be prepared to use it as the first intervention for congenital glaucoma cases.

Breaking into Schlemm's Canal

I start with a temporal conjunctival peritomy (spare the superior conjunctiva), which gives me access to the sclera (Figure 1). The next step is to make a scleral flap of your choice (Figure 2); I prefer a 3.5 × 3.0 mm trapezoidal flap as I do for my trabeculectomy. Maintaining depth here is key (90 percent depth if possible). I then make a scratch-down incision with a #75 blade to "un-roof" Schlemm's canal (Figure 3). Picking the right spot is a challenge as the limbal anatomy in these children is often distorted due to the large size of the eye. There are landmarks that can help

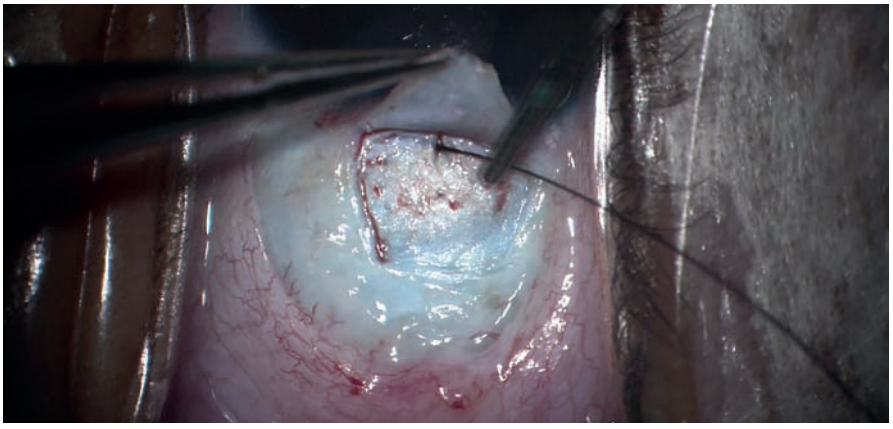


Figure 4. Confirming correct positioning. Confirm that the canal has been broached by inserting a nylon suture; it is essential to avoid entering the anterior chamber or the suprachoroidal space and creating a false passageway!

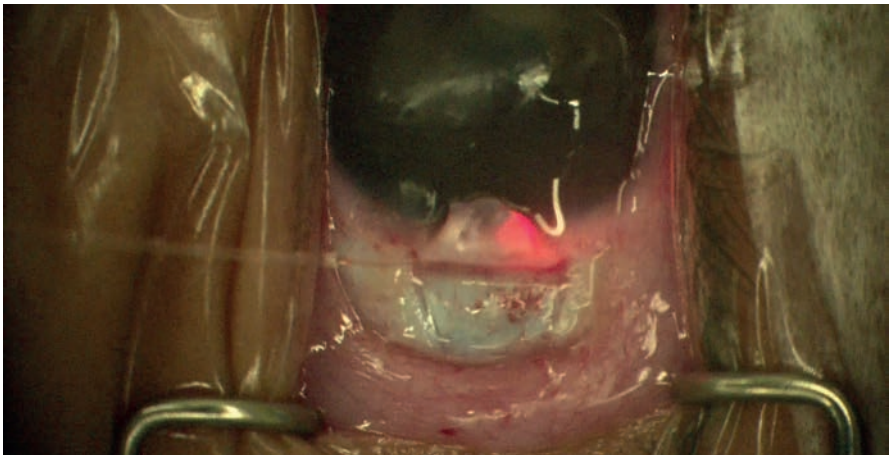


Figure 5. Passing a catheter through the canal. Use of a catheter with an illuminated tip allows the surgeon to follow the catheter progress as it is pushed through the canal.

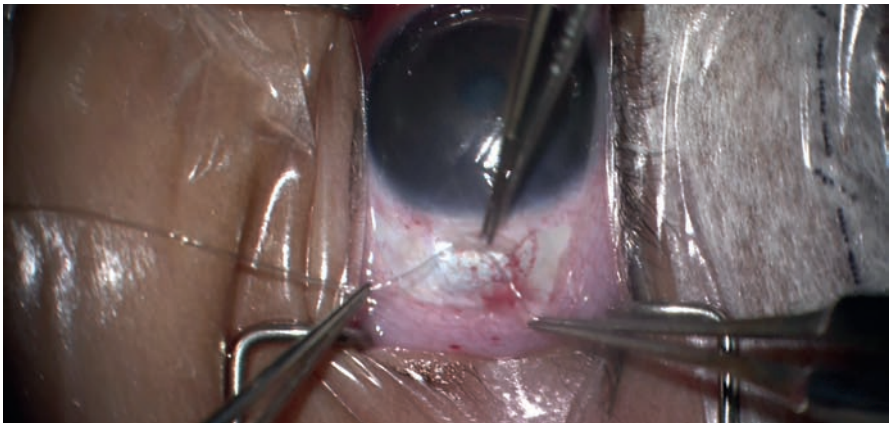


Figure 6. Breaking open the canal. When the catheter has been pushed all the way through the canal, it is simple to break open the canal wall by pulling together both ends of the catheter.

"Pediatric glaucoma is not the easiest condition to treat, but providing care to children with glaucoma is always rewarding."

you locate Schlemm's canal, as well as distinct patterns in the orientation of the scleral fibers to help guide the surgeon, but often a certain feel is required. I'll admit it's not very scientific but you will know you've found the correct spot once you see an egress of fluid or blood. During this procedure, you should take great care to avoid penetrating the anterior chamber (AC) as this can lead to collapse of the canal and increases the difficulty of threading Schlemm's canal. The key to un-roofing Schlemm's canal is to go slowly. You can always continue deeper with your dissection but you cannot go back once you have entered the AC.

Are you where you think you are?

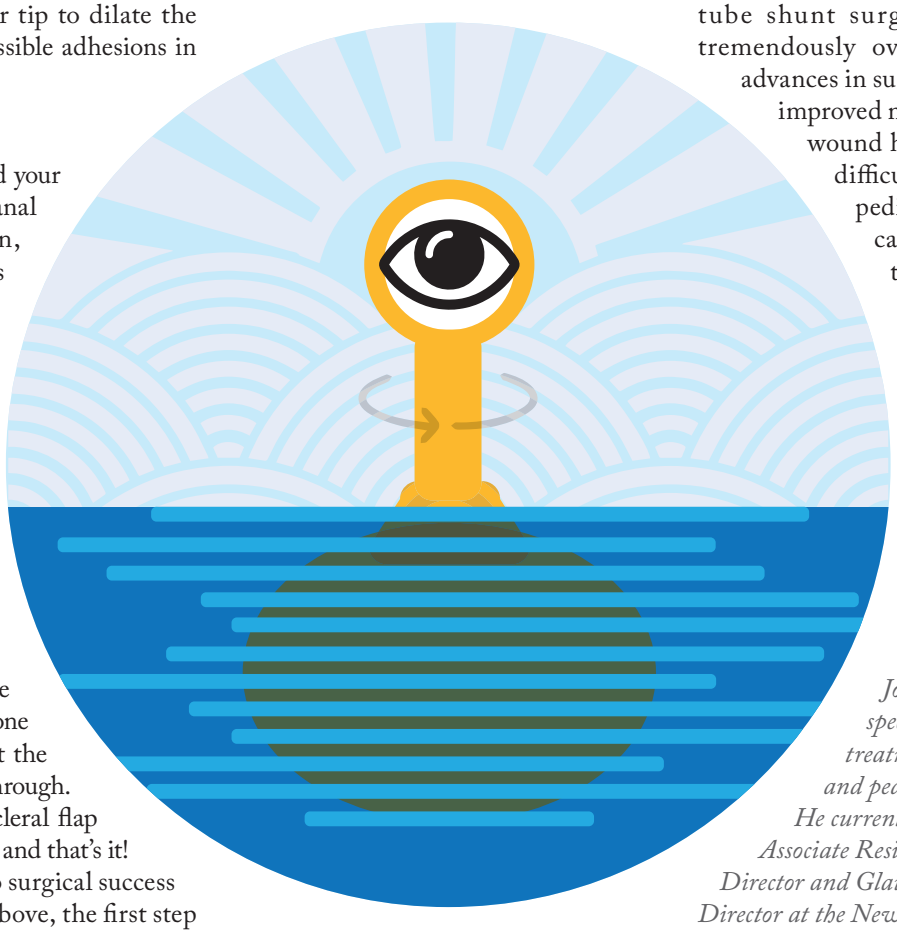
At this stage, I insert a 6-0 nylon suture into the canal to ensure that I'm not in a false channel (Figure 4). If the nylon suture passes through freely, you can be reasonably sure you're in the right spot. In the past, you would have to pass a suture blindly around the entire canal and it would be difficult to tell if one veered off into a collector channel or into the suprachoroidal space. The illuminated microcatheter allows the

surgeon to see the exact location of the probe tip as it is being advanced (Figure 5). Many surgeons would agree that the canal "likes the catheter" and it can be advanced smoothly. If the catheter encounters resistance, cohesive viscoelastic can be injected through the catheter tip to dilate the canal and release possible adhesions in the area.

Tying up loose ends

Once you have passed your device around the canal and back out again, you grab both ends and pull (Figure 6). The angle is now open and a cleft is created, exposing the inner wall of Schlemm's canal. If possible, leave a strip of tissue in place where you made the scratch-down incision to allow for easier closure of this site. This can be achieved by releasing one end of the catheter at the very end as you pull through. We then close the scleral flap and the conjunctiva – and that's it!

Though the keys to surgical success have been outlined above, the first step in treating these children is to make the correct diagnosis. An examination under anesthesia (EUA) is almost always required, since a thorough examination in the office is often not possible. A complete examination includes: IOP check (Tonopen and/or Perkins Tonometer readings) at the time of anesthesia induction, slit-lamp examination of the anterior segment, measurement of corneal diameter and central corneal thickness, gonioscopic evaluation of the angle, axial length measurement, optic nerve examination, and dilated funduscopic examination. Once examination is complete and the diagnosis of glaucoma is made, the surgeon must decide whether or not surgical intervention is appropriate.



In most cases of childhood glaucoma, surgery is required. I always have a thorough discussion in the office prior to the EUA about the risks, benefits, and alternatives, to the potential surgical procedure as that is the best time for the parents to ask questions and gain a better understanding of what we hope to achieve. After the EUA, I review my findings with the family and emphasize my recommendation to proceed with same day surgery to prevent additional trips to the operating room. As discussed, the 360° trabeculotomy via an ab-externo approach is my first option. If the IOP is not controlled after this procedure, I proceed to either tube shunt surgery or trabeculectomy. Though both trabeculectomy and tube shunt surgery have evolved tremendously over the years with advances in surgical technique and improved methods to modulate wound healing, they remain difficult to perform in the pediatric population and carry significant long-term risk.

Pediatric glaucoma is not the easiest condition to treat, but providing care to children with glaucoma is always rewarding. These children can go on to live a life with their full visual potential.

Joseph Panarelli specializes in the treatment of adult and pediatric glaucoma. He currently serves as the Associate Residency Program Director and Glaucoma Fellowship Director at the New York Eye and Ear Infirmary of Mount Sinai. He received his undergraduate and medical education from Georgetown University and began his postdoctoral education at the Lenox Hill Hospital with a general medicine internship. He then completed his ophthalmology residency at the New York Eye and Ear Infirmary and his glaucoma fellowship at the Bascom Palmer Eye Institute in Miami, FL.

To view the video online, visit top.txp.to/issues/0717/501

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From Inauspicious Beginnings...

Nobody is born a great cataract surgeon. You may struggle at first – but that's normal

By William E. Flanary II

I lost points on instrument velocity and eye centration. Although my capsulorhexis was improving, I still occasionally shot my instruments wildly across the eye or torqued everything out of view. A computer simulated female voice would repeat, "Do not operate without the red reflex," sometimes so frequently, she would fail to finish the first scolding before starting in with the second. "Do not operate without the—Do not operate without the red reflex." Eventually, I expected her to get tired of providing constant reminders and go completely off script:

"Excuse me, Doctor. Please take your instruments out of the bionic eye. This is embarrassing. Have you considered a non-surgical specialty? It's not too late!"

For most residents, the EyeSi simulator provides the most realistic cataract surgery experience. It's a point of emphasis during residency interviews. Every tour includes a quick glimpse of the beloved simulator. During my first year of residency, I spent hours creating a little flap with my fake cystitome, followed by a fake capsulorrhexis with my fake Utrata forceps. I would play games on the simulator designed to improve the dexterity of my left hand, maneuvering two virtual chopsticks into a tiny dumbbell and holding it there until it turned green. I would either be rewarded or punished with a grade based on my performance, all with the goal of preparing me for the real deal. In hindsight, the simulator training actually led to much more irrational thinking and anxiety than surgical skill proficiency. I remember thinking, "If I can't corral these little spheres into a tiny circle in the middle of this virtual eye, how will I ever be able to divide and conquer a nucleus?" In my mind, as a first year resident with no ophthalmic surgical experience, this was a completely reasonable concern.

Why do we do this training? Some studies have shown a decrease in phaco times, fewer intraoperative complications, and a shorter learning curve in residents who trained with a simulator (1). Ultimately, it's our best opportunity to prepare for a surgery that medical education is unable to. No amount of skin suturing or bowel retracting as a medical student can prepare you for microsurgery inside an eyeball.

Because of the difficulty with providing pre-residency training, there is so much self-doubt surrounding our first handful of cataract surgeries. Is it normal to look this way? Is it normal for this to be so difficult? Shouldn't my tremor at least help with nucleus disassembly? Throughout residency, we are inundated with videos of beautiful surgeries on social media. We see YouTube videos of famous surgeons doing extraordinary things inside an eye.

"Watch as Ike Ahmed retrieves a dislocated lens and reforms a zonular apparatus using 15-0 suture."

"Amazing! David Chang chops a brunescent lens into 50 pieces while blindfolded with one hand tied behind his back."

In the months leading up to my first cataract surgery, I feasted on open access surgical videos, aspiring to be the next Ike Ahmed. However, after my first few cases, all I wanted to know was that my hands were just as shaky as my peers – and that my case times were just as long, and my rhexis just as oddly shaped. I kept telling myself, there's no way Amar Agarwal ever took 40 minutes to do a routine case. It's hard to reconcile what we see in high definition videos of surgeons doing their 8,000th case with that of a second-year resident trying desperately to insert a cannula into a paracentesis wound. We need to let novice ophthalmic surgeons know that it's normal to struggle. Nobody is born a cataract surgeon.

To that end, I am excited to share my first cataract surgery with a minute-by-minute commentary on my thought process, hopes, and fears during the case. At the time of writing, I am three months away from finishing residency. My surgeries look a lot different now than they did in the beginning. By sharing my first surgery, I hope to reassure those residents heading to the operating room for the first time that it's ok to be shaky; it's okay to be slow. Will I be the next Ike Ahmed? Who knows? But I'm willing to bet he looked like me right out of the gate.

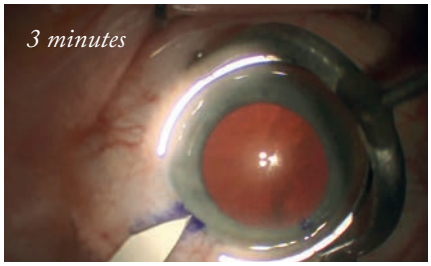
CASE #1

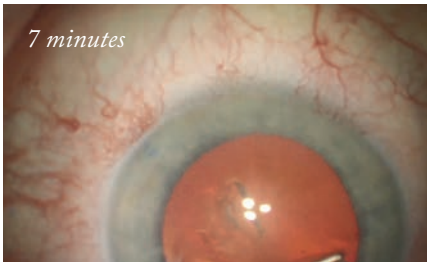
Disclaimer: The residents at my program receive tremendous instruction from our comprehensive faculty. In these videos, whenever you see an instrument come onto the screen that is moving fluidly and with purpose, please assume that it is my intrepid attending – making my life easier and his blood pressure lower.

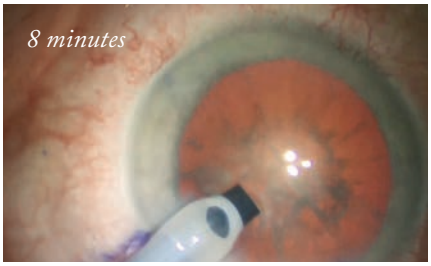
20 s: After collecting my thoughts, I ask for the paracentesis blade in my best impression of a confident surgeon. I grab the blade with

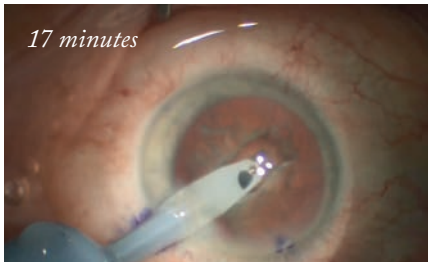
At a Glance

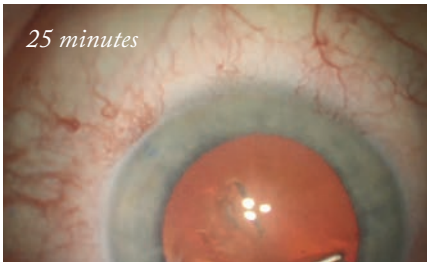
- *You might admire – and even aspire to have – the skills of ophthalmology's rock stars, but where do you start?*
- *No amount of skin suturing or bowel retracting as a medical student can prepare you for microsurgery inside an eyeball – simulator use and plain old study are cited as the keys to success*
- *But simulated surgery and actual surgery are two very different beasts – and the transition from one to the other can be terrifying*
- *Here, I "live-blog" the terror I felt in my first cataract case!*

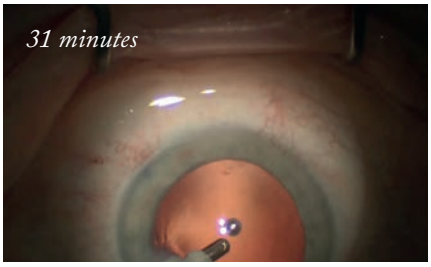












my dominant right hand and the fixation ring in my left, followed by a quick switch that I hope my attending didn't notice.

25 s: I make my paracentesis. It goes according to plan. I mentally congratulate myself for successfully completing three percent of a routine cataract surgery. I am then instructed to fill the anterior chamber with viscoelastic. However, it takes me several seconds to register this request as I remain transfixed by the tremendous paracentesis I have just created.

1 minute: The 2.8 mm keratome is handed to me. I am nervous about making the incision. The concept of a three-tiered incision within 800 µm of cornea seems daunting. I tunnel forward, thankful to be securely embedded in the cornea where my tremor was less noticeable. I stop at the end of my tunnel for about five seconds before deciding to enter the eye. Like a child learning to swim, my attending coaxes me a little to get me to jump in.

3 minutes: The capsulorhexis goes surprisingly well. I take my time with it, creating a flap while maintaining a healthy fear of the pupil edge. At some point, I realize I haven't taken a breath in a while, so I use the transition from cystitome to Utrata forceps to reoxygenate my blood. Four minutes and an entire syringe of viscoelastic later, I've finished a (mostly) circular capsulorrhexis.

7 minutes: I call this video "The Art of Helping a Resident Insert a Phaco Handpiece Through a 2.8 mm Incision"

8 minutes: Making a groove for the first time is terrifying. Beginning residents haven't developed the keen sense of lens depth that comes with experience. Every pass seems impossibly close to breaking through the posterior capsule. After a quick 32 passes through the nucleus resulting in what I would call the grand canyon of grooves, the nucleus is ready for disassembly. I should point out that for our first 5–10 cases our attending performs the nucleus rotation during phacoemulsification. We have to learn how to use our dominant hand before we earn the privilege of operating with both hands.

17 minutes: I remove the final nuclear fragment then take my second breath of the case. I have successfully divided and conquered a cataract. Streamers and confetti rain down from above.

20 minutes: Irrigation/aspiration goes according to plan. I exhibit all the telltale signs of a brand new surgeon: staying too light on the pedal, afraid of extending the instrument tip beyond the iris into the equator of the capsular bag, and going slowwwwwww.

What every Ike Ahmed YouTube video appears like to a newbie surgeon.

25 minutes: The lens is inserted and rotated into position. After hydration, my first clear corneal incision seals without difficulty.

31 minutes: As I pull off the drapes, I take my third – and perhaps deepest – breath of the case. One down, a career to go.

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To view the videos online, please visit top.txp.to/issues/0717/701/

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The Impatient Innovator

Sitting Down With... Sean Ianchulev, Professor of Ophthalmology at New York Eye and Ear Infirmary of Mount Sinai; Founder and CEO, Eyenovia; and Founder and Chairman of the Board, Iantech Medical.

You're a true innovator – where does that stem from?

I come from an academic background, but I'm very impatient and find the academic approach to product development too slow, which is partly why I work closely with industry. Such collaborative approaches are increasingly necessary, because product development is now so complex. If you want to get even a simple device into patients today, you need to partner with people from many disciplines: engineering, medicinal chemistry, quality, manufacturing, and venture capital. It's no longer as easy as coming up with a Sinskey hook and trying it on patients! For example, even something as safe and non-invasive as intraoperative aberrometry took more than 10 years and millions of dollars of development to get to patients. On the pharmaceutical side even more so – when I was at Genentech and led the clinical development of Lucentis, it needed more than a decade and hundreds of millions of dollars to get it into the clinic. Product development and commercialization are non-trivial parts of the science and innovation process, which is like launching a mission in space – thoughtful, well-planned and disciplined development are required, and this costs real money.

Which of your innovations do you consider to be the most disruptive?

Intraoperative aberrometry is a good example. When I came up with the idea, I tried it on my patients using a simple auto-refractor during cataract surgery in 2003. It was so powerful and predictive that even 20 patients were enough to get a signal. Getting clinical information early in the process was critical – we published the original series in JCRS. Little did I realize this would break down a 50 year-old paradigm of pre-operative biometry, which had changed only incrementally since the 70s – from the time of Fyodorov's IOL fundamental models. There have been many permutations and improvements in preoperative formulae since then, but intra-operative aberrometry was based on a categorically different paradigm – in-theater measurement of aphakic autorefraction. And now aberrometry has been used to improve care for more than half a million patients, and counting – the method is almost ubiquitous. Similarly, when I joined Eugene de Juan and Transcend Medical to develop the CyPass Micro-Stent nine years ago, people couldn't see the point – they were happy with their trabeculectomies and tubes. But today, microstents have revolutionized glaucoma treatment, and MIGS is the fastest growing category in ophthalmology. You simply don't know where innovation will take you, and building market models is often so treacherous – it is necessary, but often gives investors a false sense of security as they are trained in excel spreadsheets and data analytics. From my experience, all the technologies I have been involved in exceeded estimates by a factor of at least 10. On the venture side, I have seen the flip side of the coin as well – when beautiful and intricate forecasting models come to naught. So, I trust my clinical gut and try to ask one simple question – how can I make patients' and physicians' lives better? What is the clinical utility? And then disruption and adoption seem to follow.

What's the biggest challenge in ophthalmology today?

First, we need more bright, entrepreneurial ophthalmologists to get involved and step out of the clinical practice treadmill. Ophthalmology has genericized itself both technologically and practice-wise; it is all about volume and less about differentiation and eminence. There are so many ideas out there – I get approached every week by a colleague or resident who have had a light bulb go off. But an idea is just the beginning – it needs to be matured into a solution, the solution developed into a product and ultimately into a business which can scale and touch many patients, and that takes a village, or as the Transcend team say, it takes a tribe! I think we need to get more efficient and smarter about how we practice medicine. My team published a study in Ophthalmology 18 months ago, where we analyzed a database of 20,000 office-based cataract surgeries, and found it to be pretty safe – not a single case of endophthalmitis. This gave some people heartburn, but it has tremendous implications: avoiding the OR frees up OR space for other procedures, and aligns cataract surgery with refractive surgery in terms of how it's done. It reduces resource use and improves efficiency – leaving the OR rooms for the more major procedures which need it.

What advice would you give to aspiring innovators?

Follow your passion and trust yourself. Doctors are not always the greatest businessmen, but being able to wear a clinician's hat when judging new technologies – to really understand their clinical utility – is tremendously helpful. But you can't know from the outset which ideas will result in paradigm shifts; you have to persevere – and for that you need passion.

An extended version of this interview is available online at: top.txp.to/issues/0617/802

Sean Ianchulev reports the following relevant disclosures: Founder and Chairman of Iantech, Inc; Founder and CEO of Eyenovia, Inc; Advisor to Alcon-Novartis; and a partner of PME Ventures.

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