

the Ophthalmologist™

TAKEOVER #2:
*Wills Eye
Hospital*

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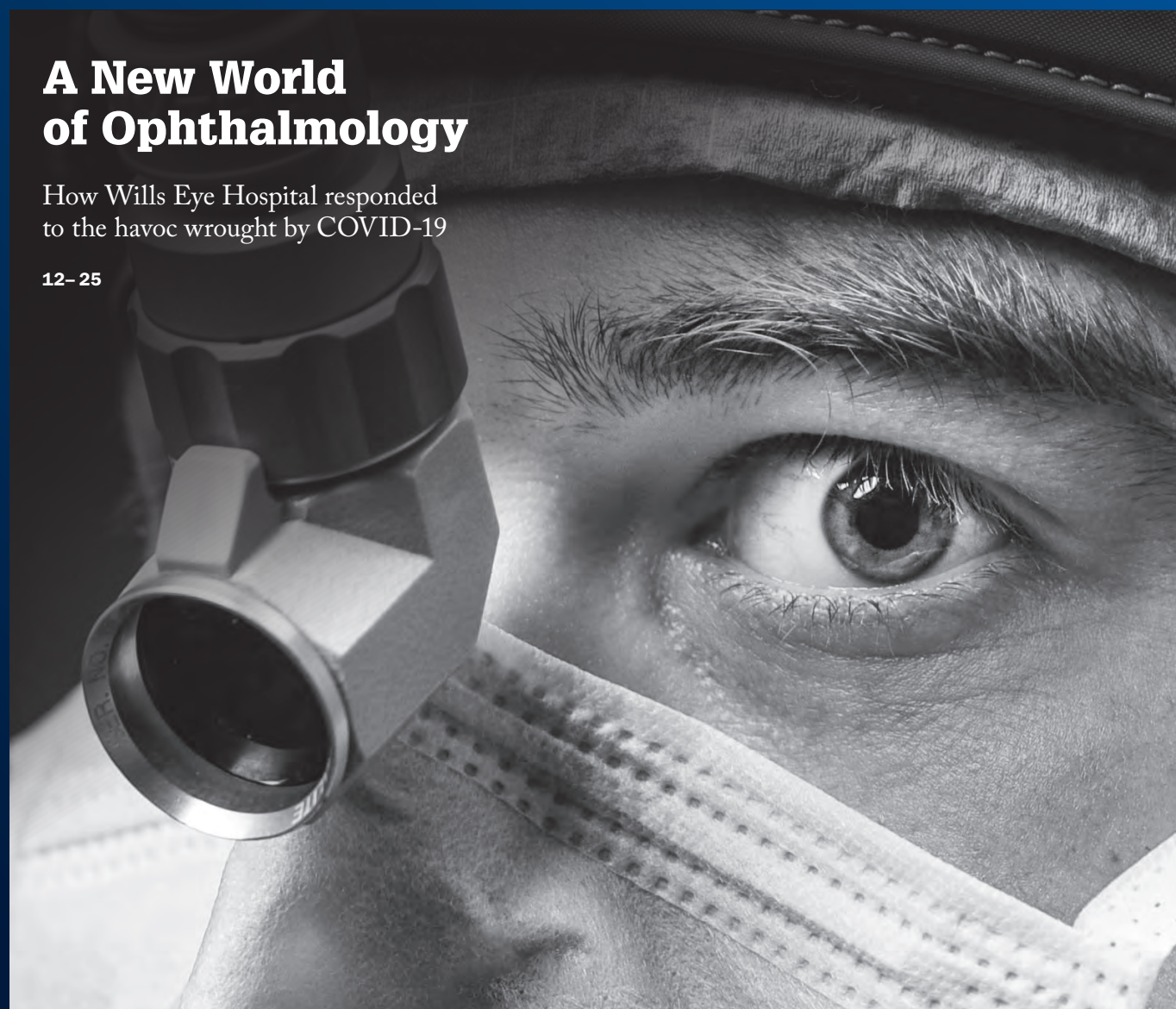
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A New World of Ophthalmology

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WORKING TO EMPOWER A NEW ERA OF PROACTIVE GLAUCOMA SURGERY

“

We might see a day in which the subjective portion of surgery is minimal and **we have more objective ways of lowering IOP.**”

— Dr. Arsham Sheybani



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Thomas Paine's words in the headline resound in new ways, as we confront the the SARS-CoV-2 pandemic. This crisis really is trying the souls of all who inhabit our planet in a manner that may seem as revolutionary as those early days of the American struggle for independence.

Paine's famous pamphlet was published in Philadelphia in 1776, and was almost certainly familiar to James Wills Sr, an industrious Londoner who had recently immigrated to Philadelphia; his only son, James, was born there in 1777. It is thought that the original idea for Wills Eye Hospital, bequeathed by the grocer's son to the City of Philadelphia when he died in 1825, came from the senior James Wills. When its cornerstone was laid in 1832, the speaker described glowingly, "this shelter from the storm [...] for those who are shut out from the light of heaven," inaugurating the storied history of one of the world's great eye centers. In 1839, the first American physician trained in ophthalmology came to Wills, establishing our educational pillar as central to our mission, and launching a program that has trained the largest number of ophthalmologists in the USA – all stamped with the Wills imprint of excellence, and aligned with our motto: "Skill with Compassion."

Almost 200 years later, Wills Eye Hospital was honored at the invitation to "take over" this issue of *The Ophthalmologist* – a publication in whose international reach and driving mission-based vigor we have found a kindred spirit! The project, hatched well before the soul-shattering COVID-19 pandemic, has pivoted over these last months, and we are proud that it can come to fruition despite the rockiness of the times. Within the following pages, we provide snapshots of our hospital and staff, indomitable through this crisis, and the important work it is our privilege to do.

You will visit our services and sample cutting-edge clinical and research projects. You will peer into our signature education and training programs. You will discover innovative telemedical initiatives – and meet some of our faculty, including Jose Pulido, who returns to Wills to direct the Henry and Corrine Bower Memorial Laboratories for Translational Medicine. We hope you will also reflect with us on how these unprecedented times have truly tried all humanity's souls, on how we have met these challenges, and on how the reverberations will continue to echo throughout our specialty in the future.

Julia A. Haller

*Ophthalmologist-in-Chief
Wills Eye Hospital, Philadelphia,
Pennsylvania, USA*



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These Are the Times
That Try Men's Souls,
by Julia A. Haller

Upfront

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An insight into how Wills Eye Hospital has dealt with the COVID-19 pandemic. Image credit: Roger Barone/Wills Eye Hospital.



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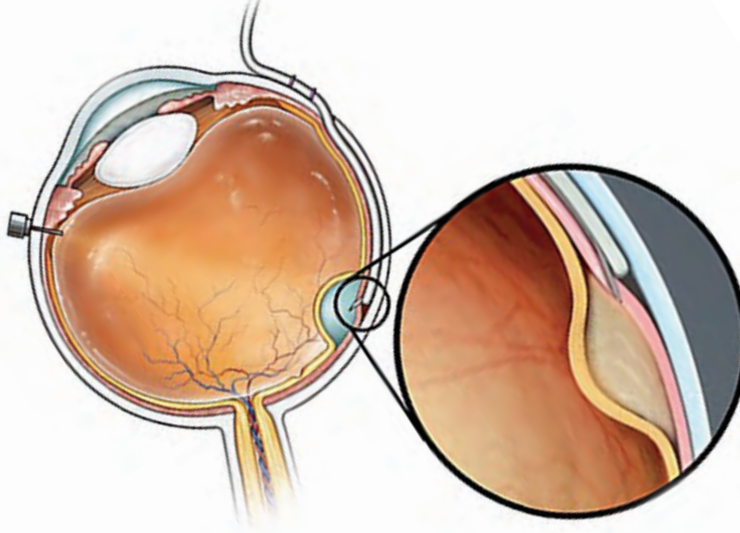
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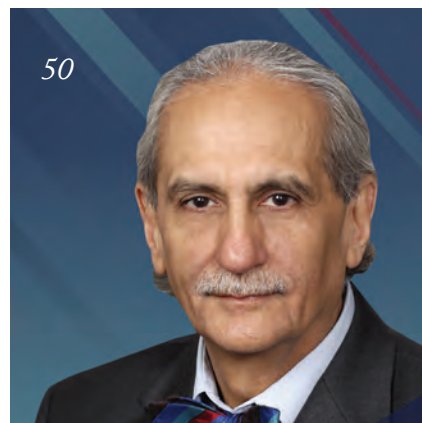
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Tara A. Uhler, Laura J. Heinmiller and John Cropsey share how the residency program at Wills instills competence, confidence – and a life-long passion for the field

Sitting Down With...

- 50 **Jose Pulido, Larry Donoso**
Endowed Chair of Translational Ophthalmology at Wills Eye Hospital and Professor Emeritus at the Mayo Clinic, Rochester, Minnesota, USA

More Than Meets the Eye

Three papers, one purpose: to save patients from melanoma-related metastasis

What's in a nevus? Choroidal nevus – a flat, benign pigmented area that appears in the back of the eye – may seem innocuous, but can lead to overlying retinal edema or atrophy with related vision loss. This seemingly innocent tumor can even have the potential to transform into malignant melanoma. And, as Carol Shields, Director of Ocular Oncology Service at Wills Eye Hospital and Thomas Jefferson University in Philadelphia, reports, choroidal nevus is present in 4.7 percent of the US adult population (1) – nearly one in 20 people.

Over the last 12 months, Shields' team has published three longitudinal studies regarding the potential of nevus to transform into melanoma, reporting on a total of 3,806 choroidal nevi examined with OCT, ultrasonography, and standard wavelength autofluorescence. Shields comments, "Using Kaplan-Meier analysis, we revealed transformation into melanoma in 5.8 percent of cases at five years and 13.9 percent of cases at 10 years. Multivariate factors predictive of transformation

included thickness more than 2 mm (by ultrasonography), subretinal fluid (by OCT), symptoms of vision loss (by Snellen acuity), orange pigment (by autofluorescence), hollow melanoma (by ultrasonography), and diameter more than 5 mm (by photography)." As she mentions, these important factors can be recalled with the mnemonic "To Find Small Ocular Melanoma Doing IMaging," or TFSOM-DIM. The mean five-year estimate of nevus growth into melanoma varied from 1.1 percent for those with no risk factors to 55 percent for those with five. Management of small choroidal melanoma typically involves plaque radiotherapy with five- and 10-year rates of tumor recurrence at 7 and 11 percent, visual acuity loss (three Snellen lines) at 39 and 49 percent, and melanoma-related metastasis at 4 and 9 percent.

There is good news on the horizon. A novel infrared dye-conjugated virus-like nanoparticle (AU-011) is currently under investigation for treatment of

small choroidal melanoma, with the goal of controlling tumors and minimizing vision loss.

Shields further asserts, "Treatment of small melanoma with plaque radiotherapy offers tumor control, but it comes with the potential for vision loss. We are currently trialing a novel nanoparticle therapy using AU-011 – we're hopeful it could have a positive impact on patient management in the future. For the time being, our best hope in the detection of small choroidal melanoma is the mnemonic, TFSOM-DIM. If we could identify all choroidal nevi at risk of transformation – and treat promptly – we could save countless lives from melanoma-related metastasis."

Reference

1. C Shields et al., "Small choroidal melanoma: detection with multimodal imaging and management with plaque radiotherapy or AU-011 nanoparticle therapy," *Curr Opin Ophthalmol*, 30, 206 (2019). PMID: 30844944.

Upfront

Research
Innovation
Trends



INFOGRAPHIC

Where There's a Wills...

America's first specialty eye hospital – in numbers

Wills Eye Hospital's Main Campus is in **Center City Philadelphia** with a ring of seven ambulatory centers in **Pennsylvania** and **New Jersey**.

The hospital has **142 FACULTY MEMBERS**, offering **EIGHT** training positions each year, and currently has **24 RESIDENTS** on staff.

Progress Through Philanthropy

The sight-saving work of Wills Eye Hospital's latest addition: the Vickie and Jack Farber Vision Research Center

The result of a US\$5 million gift, the Vickie and Jack Farber Vision Research Center was created with the singular focus of shaping the future of ophthalmology. “Wills Eye is a great institution with incredibly talented people who are committed to advancing scientific knowledge. If you put those energies together with financial support to accelerate the rate of progress, you truly make a difference in patients’ lives,” said Jack Farber (1). The Center will focus its attention on clinical, translational and community-based research, including access to care and clinical trials. Leslie G. Hyman, an ocular epidemiologist and Vice-Chair for Research at the Sidney Kimmel Medical College at Thomas Jefferson University, will lead the Center. “As one of the Data Analytic Teams selected by the AAO to have access to the IRIS Registry, the Center has recently launched an Ophthalmology Informatics Program to use big data to improve understanding of disease and treatment patterns for different eye conditions, as well as examine outcomes



of different surgical procedures among different populations,” explains Hyman.

The team is currently working on a project to estimate prevalence and associated factors of thyroid eye disease (TED), a rare disfiguring, autoimmune inflammatory disease with limited treatment options. “Studies of TED have been confined in scope and size to select geographic regions due to its relatively low frequency, raising questions about the generalizability of the findings,” says Hyman. “Results from this project will be the largest report from a national database to provide data on TED prevalence and associated factors and will provide important guidance to physicians

for counseling and management of these patients.”

This project is the first of a number of planned analyses to answer critical questions on practice patterns and treatment outcomes that can help shape clinical decisions across a wide range of conditions in ophthalmology.

Hyman is bold about the potential impact of the Center’s work: “Through collaboration and innovation, we are working together to develop preventive strategies and cures for patients in the US – and around the world.”

Reference

1. Wills Eye Hospital (2018). Available at: <https://bit.ly/2Q5bjYk>.

Wills staff treat more than
300,000 patients,
and see over
50,000
of surgical cases annually.



Wills Eye performs
MORE EYE SURGERIES
than any other
US facility and sees more
than **50 percent** of
all eye cancer cases
in the **USA**.



Wills Eye has been
consecutively ranked in
the **TOP THREE EYE
HOSPITALS** by
**US News & World
Report** for as long
as the survey
has existed.



Chance Would be a Fine Thing

Developing a nomogram to predict graft survival after penetrating keratoplasty

Corneal transplantation is the most commonly performed solid-tissue transplant procedure in the world. Corneal surgeons regularly perform various forms of corneal transplantation to treat corneal blindness, including penetrating keratoplasty (PK). Zeba A. Syed, Co-Director of the Cornea Fellowship Program at Wills Eye, comments, “Often, when we counsel patients prior to PK, they will ask us about the chances of their transplant being successful after five years.”

Typically, corneal surgeons will answer this question with a ballpark prediction based on their individual anecdotal experiences. Though numerous studies have identified risk factors for graft failure, there currently exists no mathematical tool that surgeons can use to make a personalized calculation for the chance of long-term PK success based on a patient’s known risk factors.

“When I joined the Cornea Service as a



faculty member at Wills Eye Hospital two years ago, developing this mathematical model, or ‘nomogram’ – predicting PK graft survival – became my primary research goal,” Syed explains. “Working with Eric Shiuey, an outstanding medical student from the Sidney Kimmel Medical College at Thomas Jefferson University, we reviewed over 1,000 PKs performed at Wills Eye from May 2007 to September 2018. We evaluated 36 preoperative and intraoperative variables with multivariate models, and created a nomogram to predict the probability of PK graft survival at postoperative years three and five.”

The team’s multivariate analysis identified 11 variables significantly

associated with PK graft failure, a few of which included active infection at the time of PK, intraocular silicone oil, systemic autoimmune disease, and corneal neovascularization. The nomogram that was developed for PK survival based on these 11 variables exhibited an accuracy of 76 percent at 3 and 5 years after internal testing.

“We concluded that PK graft prognosis may be modeled with a relatively high accuracy based on 11 preoperative and intraoperative variables,” notes Syed. “This nomogram could play a key role in comprehensive and data-driven patient counseling prior to corneal transplantation.”

A Mother’s Son

Gene therapy injections for LHON patients

Leber’s hereditary optic neuropathy (LHON), a maternally inherited blinding disease, most often attacks young men at the prime of their life with rapid sequential bilateral loss of vision over weeks to months. Mark L. Moster’s team at Wills Eye has been involved in three

Phase III clinical trials – RESCUE, REVERSE and REFLECT – to study intravitreal gene therapy with GS010 in this blinding disease (1-3). Results of the first two trials are available and showed improvement in patients’ visual acuity, both in treated and sham-injected eyes. To further understand how contralateral eyes improved, preliminary animal studies injected GS010 in one eye and detected it in both eyes, both optic nerves, the optic chiasm, and both lateral geniculate nuclei, which is likely a biologic effect directly

related to the unilateral GS010 injection.

References

1. *Clinical Trials* (2020). Available at: <https://bit.ly/319qYLp>.
2. *Clinical Trials* (2020). Available at: <https://bit.ly/39BWSE8>.
3. *Clinical Trials* (2020). Available at: <https://bit.ly/3jKcM3M>.





IMAGE OF THE MONTH

Behind the Mask

Corneal surgery being performed at Wills Eye Hospital during the COVID-19 lockdown.

The image is part of a collection of photographs showing how Wills Eye coped during the recent crisis. Go to theophthalmologist.com to see more. Credit: Roger Barone/Wills Eye Hospital.

Would you like your photo featured in Image of the Month?
Send it to edit@theophthalmologist.com

QUOTE OF THE MONTH

"We all start out as pluripotent stem cells, and we should all retain the ability and need to adapt, evolve, and reinvent both ourselves and our profession as we develop."

Tara A. Uhler, Director of the Ophthalmology Residency Program at Wills Eye Hospital, Assistant Professor at Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia

Reclassified

Establishing an accurate classification system for conjunctival pigmentations

Accurate classification and interpretation of ocular pathology has important prognostic implications. Although some pigmented blemishes of the conjunctiva are benign and do not require close follow-up or treatment, others progress to potentially fatal conjunctival melanoma. The ideal classification system needs to be highly accurate, easy for pathologists and ophthalmologists to use and have excellent inter-observer agreement.

Tatyana Milman, Ocular Pathologist at Wills Eye, says, "We currently are re-appraising three most common classification systems for these difficult lesions and validating the most recently proposed one. We selected 83 cases of conjunctival pigmented lesions and created digital slides that were posted on an internet portal where they were assessed and scored by an international expert panel of ocular pathologists."

The experts' scores for each system have been analyzed for agreement between the experts, and graded for their accuracy in prediction of recurrence and progression to melanoma. The appraisal assessed the time required for scoring with each classification system. Milman now looks forward to the final results.

Renowned ocular pathologist Ralph C. Eagle Jr., and Tatyana Milman, who joined the Wills Eye Faculty.



The Student Becomes the Teacher

From enhanced facilities to expert faculty – what it takes to train the next generation of residents

By Douglas M. Wisner, Director, William Maul Measey Ophthalmic Surgical Training Lab at Wills Eye Hospital and Assistant Professor of Ophthalmology, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

In the months leading up to 2020, many ophthalmologists found themselves reflecting on the significance of the year ahead – and we at Wills were no exception. As we thought about our history – and our future – there seemed no better way to celebrate our legacy as the oldest and largest ophthalmology training program in the US than to reinvest in our mission: to care for patients and train ophthalmologists with skill and compassion.

After much work, the Measey Ophthalmic Surgical Training (MOST) Lab came into existence. The lab consists of nine custom adjustable workstations that can be adapted to the ergonomics of the operating surgeon and mentor. Each station has an OR-grade microscope with a camera, a monitor, and recording capability. Stations are integrated into an A/V system that allows for video sharing to a large-format monitor or individual screens, facilitating valuable collaborative learning among trainees.

We also have complete sets of surgical instrumentation, tissue models, and a diverse range of phacoemulsification and vitrectomy units. Because our program has used a virtual reality surgical training



In My View

Experts from across the world share a single strongly held opinion or key idea.

simulator (VRmagic EyeSi) in the past with good results, we added another unit and integrated it with other residency programs worldwide to provide standardized training and objective feedback. But even more valuable than our state-of-the-art equipment is our lab manager, a trained ophthalmic technician who keeps the lab organized, stocked, scheduled and, most importantly, clean!

The lab has seen almost daily usage by residents and fellows, and has played host to over 15 large-format courses this past year, many of which have benefited from our enhanced facilities. We have been excitedly updating our surgical training curriculum to maximize future use of the facility. We have started new and improved courses for upper-level residents and fellows, including MIGS, glaucoma filtering surgery, complex cataract cases, IOL fixation, DMEK/DSEK, and corneoscleral suturing. We have also integrated additional practical training earlier in residency, with first- and second-year residents now getting structured bimonthly exposure to practical, level-appropriate topics in the lab.

During the COVID-19 lockdown, we saw increased use in a safe and socially distanced fashion. We have begun trialing a remote proctoring solution whereby residents working in the lab can send video signal from the microscope

to a remote attending, allowing them to maintain and improve their surgical skills while live surgeries are on hold. Our workstations are mobile and, for larger courses, we have split them out to additional locations for appropriate social distancing. With the help of our faculty and alumni, we are now developing a new surgical resource library – including lectures, photos, surgical videos, and operative reports – to help surgeons and clinicians all over the world become better, faster, and safer at what they do. We are also working with industry to provide a location to introduce novel devices and procedures to surgeons, as well as provide hands-on CME.

When I was a resident at Wills a decade ago, I knew I was in a special place. Now that I'm on the other side of the microscope, training residents in the lab and operating room, I am even more certain. It really is amazing what a dedicated group of individuals can accomplish with vision and support. As our profession becomes more technically complex, we have a unique opportunity to help our trainees become truly proficient – and even improve our own expertise in the process. I am thankful to be a part of the next generation of excellence at our institution, and I intend to do everything I can to pay it forward.

How to Pick the Low Hanging Fruit

In an era of improved technologies, it has never been easier – or more affordable – to identify undiagnosed glaucoma patients



By Jonathan Myers, Chief of Glaucoma Service, Wills Eye Hospital

Doctors generally go to work wanting to make a difference. Fortunately, there has never been a better time for our patients with glaucoma – there are an ever-increasing number of advanced technology and treatment options. Not only do the latest OCT machines reveal incredible details of the retinal nerve fiber layer and macular ganglion cell layer, we also have the ability to measure corneal hysteresis and corneal thickness, helping further reduce a person's risk of glaucoma progression. Recent research promises quantification of apoptosis in retinal ganglion cells in vivo, while new classes of drugs and novel approaches to surgery allow more customized approaches for individual patients. These tremendous advances mean we can offer better care to our patients with glaucoma and they may even allow us to reduce the patients' risk of vision loss and burden of treatment. However, studies suggest that

a large portion of people with glaucoma – perhaps half – are undiagnosed and, as a result, untreated.

Unfortunately, it has proven challenging to identify these patients and get them the care they need; efforts to create screening have been hampered by low disease prevalence, increasing costs per identified case. And when patients fail to return for care, it reduces the impact of finding undiagnosed disease. But there is hope: recent studies suggest that there are simpler and more affordable ways to screen for the disease (1, 2). In the Philadelphia Telemedicine Glaucoma Detection and Follow-up Study (PTGDFS), screenings were done in 23 minutes, and at a cost of less than \$8 per screen and less than \$65 per vision-threatening diagnosis found. Follow-up and retention were improved by a number of small and simple steps, although retention remains a critical challenge.

So, what made the difference? The central aspects of these two studies can be summarized in just a few simple concepts. First, start with high risk populations. Both the Screening to Prevent (SToP) Glaucoma Study and the PTGDFS screened underserved populations at a high risk of ocular disease: people of color, people over the age of 65, and those who had a family history of glaucoma or diabetes. These criteria resulted in 60 percent of those screened having significant ocular diagnoses, including glaucoma and diabetic retinopathy.

Second, use low-level technology to screen. Both studies relied on visual acuity, a focused history, and non-mydratic fundus and external photography. The cameras used are hand-held, require little training, and cost about \$7,000. Remote evaluation of the photos and testing were done in a timely and efficient manner by physicians and trained non-physicians – the latter were used whenever possible to keep

costs down. Getting these underserved patients into the eye care system – and retaining them – is a difficult process as people have complex lives with many competing priorities. Elements that bolster success include involving their primary care doctors, arranging follow-ups with local eye care providers, using patient navigators, and engaging the community.

Remember: when it comes to screening, perfect is the enemy of good. An affordable, efficient screening system cannot catch every case or ensure that every patient is still being cared for a year later. However, a small investment can easily lead to hundreds of people getting care for undiagnosed glaucoma, diabetic retinopathy, and visually significant cataracts – as we found after setting up a screening program in an underserved community with the help of local primary care doctors.

If all this seems too ambitious, there is an even simpler, cheaper screening program: tell each and every glaucoma patient in your practice to have their close relatives tested annually. Monitoring these higher risk patients will inevitably lead to many saved eyes. Using the latest tools and treatment to make sure an established glaucoma patient gets great (rather than adequate) care is incredibly important – but getting an undiagnosed patient any care before they go blind is even more so. Don't underestimate the impact it can have on the patient, their family, and their community.

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2. D Zhao et al., "Optimizing glaucoma screening in high-risk population: design and 1-year findings of the Screening to Prevent (SToP) Glaucoma Study," *AJO*, 180, 18 (2017). PMID: 28549849.



A N E W

W O R L D

O F

O P T H A L M O L O G Y

HOW WILLS EYE HOSPITAL RESPONDED
TO THE HAVOC WROUGHT BY COVID-19

Images courtesy of Roger Barone/Wills Eye Hospital.

H E A R U S R O A R

By Julia A. Haller

"It was the nation that had the lion's heart... I had the luck to be called upon to give the roar." – Winston Churchill, 1954

It is a privilege to be Ophthalmologist-in-Chief at Wills Eye Hospital, and this has brought with it a generous invitation from The Ophthalmologist to tell the story of how we were affected by the pandemic. I feel tremendously lucky to give the Wills roar; the lionheart that continues to power us through this long fight beats in the courageous breasts of all Wills' faculty and staff.

We've been on a daunting journey over the last months, but it is one that has filled me with pride in our team's alert, nimble and evidence-based response to the challenges presented by the unprecedented events.

I happened to be reading the Erik Larson bestseller, "The Splendid and the Vile: A Saga of Churchill, Family and Defiance During the Blitz," just as the initial wave of SARS-CoV-2 was hurtling around the world and engulfing Boston and New York; cities not far to the north of our Wills Eye Hospital home in Philadelphia. To me, it felt as though there were uncanny parallels between the unrelenting bombardment of London in the 1940s and the incoming early reports of a virus that was hitting our cities, causing us to hunker down. Shops were shuttered, traffic was absent, and we were facing a foe that seemed as menacing to me as any squadron of approaching Nazi Messerschmitts. The COVID-19 Blitz was upon us.

WHEN THE WRITING WAS ON THE WALL

Wills was with the first hospitals in the city to halt all but urgent and emergent patient care, which necessitated closing our network of ambulatory surgical centers and funneling patients to our main Walnut Street campus. Here, we instituted stringent safety measures, closing entrances so that all entered through one access point for careful screening, hand sanitization, temperature checks, and masking. Our friendly elevator attendant even wiped down the buttons with disinfectant, ensuring not only that sanitation measures were in place at that first entry point, but also that a reassuringly warm welcome was provided to understandably anxious patients.

The writing was on the wall from that first weekend in March, when New York City hospitals were deluged with patients. The immediate response of CEO Joe Bilson, Facilities Manager Mike Wurster and their teams was to ensure that all seating was distanced and plexiglass barriers were installed at welcoming desks. In constant communication with local, state, and federal authorities, they, along with COO Michael Allen, CNO Greg Passanante and their teams, drew up new policies and procedures to allow our high standards of care to continue, while prioritizing safety of patients and staff amidst this new threat. We monitored CDC and city and state Department of Health guidelines, urgently digesting every available publication so as to adopt the strategies that were beginning to show successful transmission containment, particularly those early reports from Singapore and Hong Kong, as well as those from Boston, which showed the preservation of staff health with the use of surgical masks, distancing, and handwashing.

We maximized our PPE supplies, and right-sized our staffing through a host of strategies that preserved employment and benefits. Joe Bilson, Michael Allen, and our finance team worked through the nights to make sure that all available grant support was identified, the cumbersome data-intensive applications completed and submitted at the earliest opportunity. The outcome? During Philadelphia's surge in COVID-19 cases from March 15 through May 15, Wills surgeons were able to perform almost 700 urgent and emergent surgical procedures, they saw thousands of patients, and completed thousands of procedures, such as intravitreal injections, all while maintaining a 100 percent safety record. No case of coronavirus was contracted at Wills by any patient or staff member – a safety bar we strive to clear each and every day.

OUR FINEST HOUR

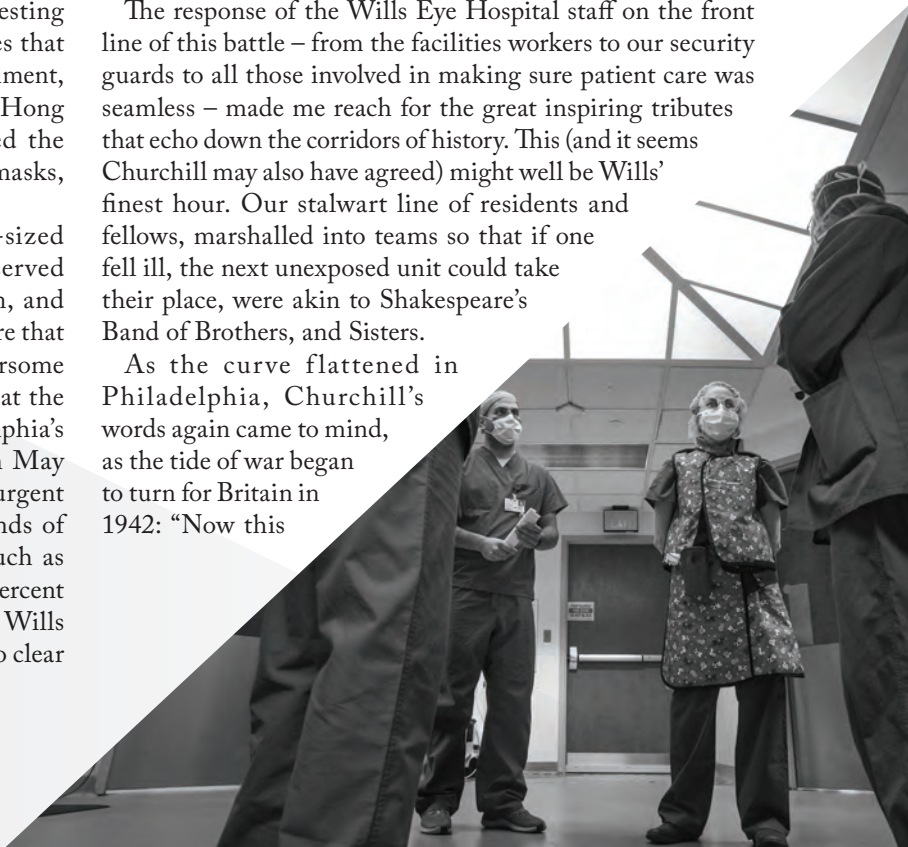
Those points only sketch the barest outline of the phenomenal work that has been done – every day our team has labored in fluctuating conditions as information changed on a daily, sometimes hourly, basis.

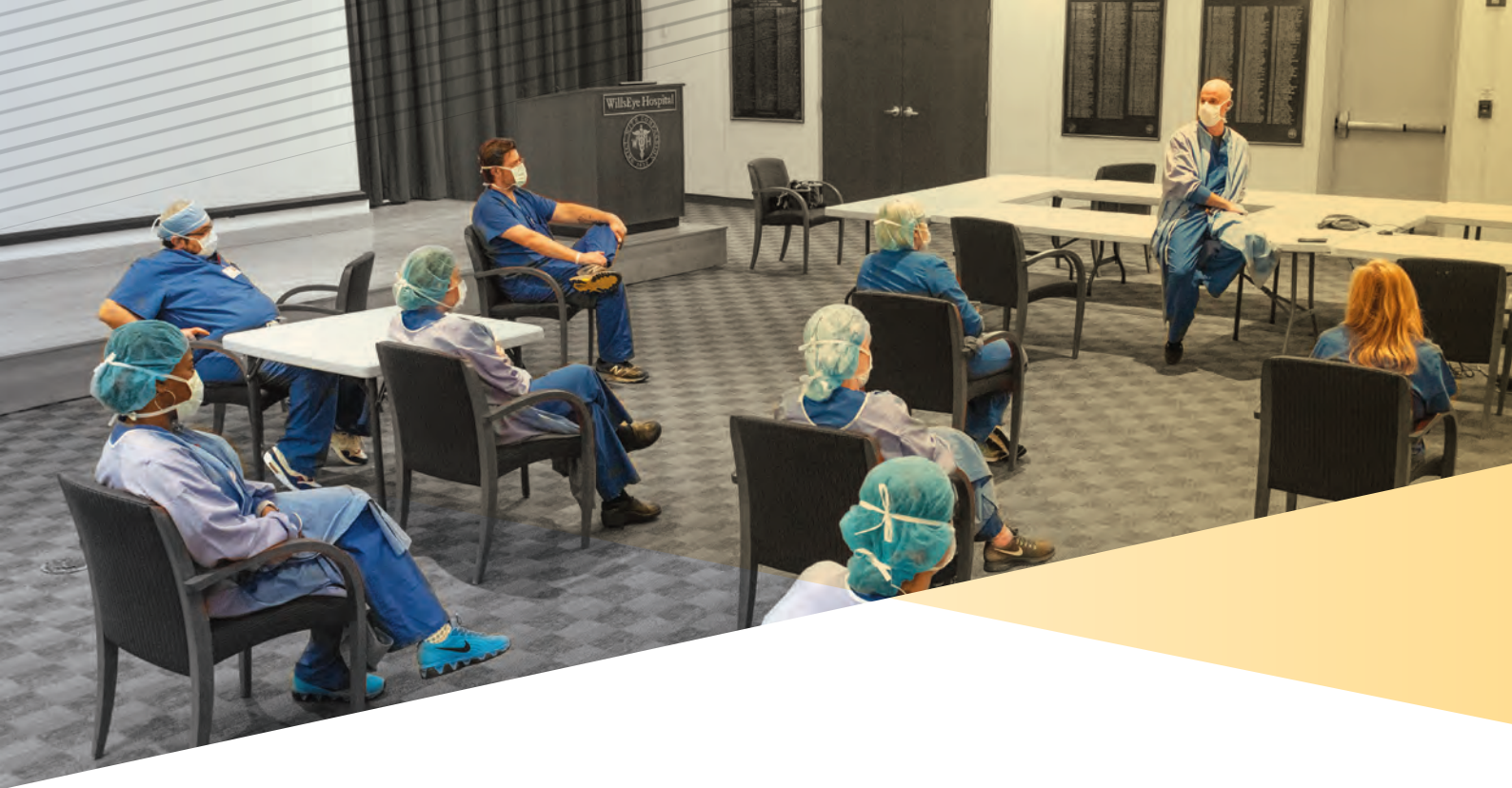
As I reflected on the oft-used term “unprecedented,” the example of the brave Londoners during the Blitz often came to mind, as did other examples from history. In “A Journal of the Plague Year” of 1665, Defoe wrote: “Yet all looked deeply concerned; and as we saw it apparently coming on, so every one looked on himself and his family as in the utmost danger. Were it possible to represent those times exactly to those that did not see them, and give the reader due ideas of the horror that everywhere presented itself, it must make just impressions upon their minds, and fill them with surprise. London might well be said to be all in tears.”

All in tears – how many times did we, stressed and worried, tear up at the thought of our endangered families, friends, and patients? But with COVID-19, we learned that even those tears could be infected! And then, as if a global pandemic were not enough, suddenly a terrible tragedy in Minneapolis ignited the smoldering fuse of outrage at ingrained social and racial inequities, and we found ourselves in a city filled with protests and marches, and escalating police presence and threats of violence. Helicopters plied the air outside my 15th floor office window.

The response of the Wills Eye Hospital staff on the front line of this battle – from the facilities workers to our security guards to all those involved in making sure patient care was seamless – made me reach for the great inspiring tributes that echo down the corridors of history. This (and it seems Churchill may also have agreed) might well be Wills' finest hour. Our stalwart line of residents and fellows, marshalled into teams so that if one fell ill, the next unexposed unit could take their place, were akin to Shakespeare's Band of Brothers, and Sisters.

As the curve flattened in Philadelphia, Churchill's words again came to mind, as the tide of war began to turn for Britain in 1942: “Now this





“All in tears – how many times did we, stressed and worried, tear up at the thought of our endangered families, friends, and patients?”

is not the end. It is not even the beginning of the end. But it is, perhaps the end of the beginning.” At Wills, we needed to gear back up to care for our huge volume of patients with renewed safety, while also dealing with the backlog of patients with medically necessary and time-sensitive problems. And we did.

BLACK CLOUDS, SILVER LININGS

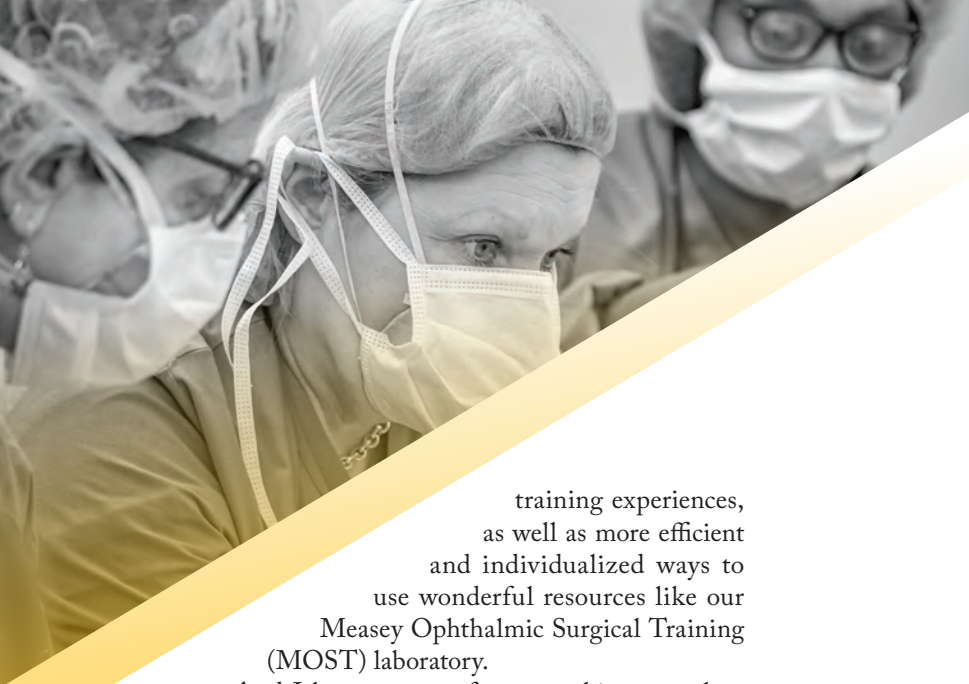
In the months since May, I have been struck so often by the grievous consequences of the many delays in care due to COVID-19 – both for patients who had no access because of closed offices and limited resources, and those whose fear of venturing out to a healthcare facility precluded evaluation. The delayed cancer diagnosis of a 90-year-old patient of mine who endured months of hand motions vision as lymphoma infiltrated both eyes and clouded her vitreous. A grandmother with Terson’s Syndrome who suffered

for five months groping her way around her daughter’s home before vitrectomies in July and August restored her vision.

The visual consequences of this pandemic will take many years to play out and understand. Wills physicians and researchers have already begun a host of analyses – already published or in press – describing the impact of the pandemic on our emergency room, trauma work, clinical case load, the types of surgery required, and the psychological stresses and concerns of the frontline workforce, amongst others.

Some of this scholarship focuses on one of the silver linings of the huge black COVID-19 cloud, and that is the rapid and significant advances that we made in delivering telemedicine to those patients who could not be seen in person. Other improvements that will stand the test of time include streamlining patient portals, optimizing wait times, and diminishing flow of people through the building, with a focus on clinic and OR operations. Other benefits may turn out to be more engaging online learning experiences, high impact residency and fellowship and CME virtual





training experiences,
as well as more efficient
and individualized ways to
use wonderful resources like our
Measey Ophthalmic Surgical Training
(MOST) laboratory.

And I know many of us are asking ourselves
whether or not we need to travel as much as we did so
routinely in the past, or if we can accomplish more by focusing
our efforts at home and using technology to connect us to our
colleagues and the world.

TOWARDS JUSTICE AND EQUALITY

Finally, this crucible of pandemic, anxiety, and uncomfortable
but necessary revelations about unequal treatment of our fellow
citizens has inspired a renewed determination that I see at
Wills, across our nation, and beyond.

A challenging year as no other in memory, where 2020, The
Year of the Eye, morphed into a modern Plague Year, further
stressed by social and political unrest, and both challenged
and uplifted by wrenching, important discussions targeting
societal inequity and the hard work needed to correct it. Martin
Luther King Jr.'s famous words continue to give hope: "The arc
of the moral universe is long, but it bends toward justice."

May the terrible cost of this worldwide disaster renew us in
our determination to stay the course, keep our patients
and staff safe, never yield in our commitment to
excellence, and work relentlessly towards a more
just world, free of healthcare disparities, with
a professional workforce representative of
the population we serve, and with
equal and perfect vision for all.
Now that would be something
to roar about!

*Julia A. Haller is
Ophthalmologist-in-
Chief, Wills
Eye Hospital.*

TELEMEDICINE: SEEING THE PATIENT THROUGH A NEW LENS

AT THE HEIGHT OF
THE PANDEMIC, MANY
PHYSICIANS RELIED ON
REMOTE SYSTEMS TO
SAFELY SCREEN AND
DELIVER PATIENT CARE.
NOW, EYE CARE
PROFESSIONALS ARE
TAKING THE OPPORTUNITY
TO PERMANENTLY
EXPAND THEIR
PORTFOLIO OF
TELEMEDICINE
SOLUTIONS.

By Joseph Anaya and Mary Fuska

Even before COVID-19, Wills Eye
Hospital had long sought to expand
its reach through telemedicine. Since
the inception of the remote diabetic
retinopathy screening program, countless
asynchronous or store-and-forward
screenings identified sight-
threatening disease and
provided timely follow-up.

We strived to further build
our service portfolio
and had hoped to
one day expand our
telemedicine practice
to include synchronous
video visits. But
there were obstacles
with clinical
utility, patient
satisfaction, and
unreimbursed costs.



Circumstances changed with COVID-19. With in-person evaluations constrained to urgent and emergent visits, we asked “How might synchronous video visits enhance our ability to care for patients in this time of need?”

In fact, synchronous video visits offered value in multiple areas. Clinically, they helped determine the urgency of an in-person visit and could, at times, appropriately enable remote management decisions. For example, many patients

evaluated in the Wills Emergency Room, received follow-up video visits that provided an interval evaluation of sufficient quality to maintain or de-escalate therapy. Concurrently, patients across the demographic spectrum were worried about coming to the office and were happy to learn about this alternative.

Though the service’s benefits became apparent, we also gained new perspectives on its costs. Down-scheduled clinics enabled physicians and personnel to dedicate time to this new way of caring for our patients. And the technology expense became necessary to continue to provide our highest-level service. Fortunately, public and private payers agreed on this necessity and expanded compensation to include these synchronous visits.

Under these changed circumstances, the case for synchronous telemedicine was clear, and we quickly initiated the rollout. The collaboration required was significant, spanning the spectrum of the hospital’s outpatient team, with clinicians, administrators, and information technology personnel working tirelessly to bring the system to life. Every subspecialty, aided by the collegial knowledge-sharing of other leading ophthalmology institutions and individuals, developed specific protocols for determining appropriateness and urgency of their telemedicine visits. And each visit provided a learning experience that informed refinement and improvement of an enhanced method of care.

The result was overwhelmingly positive. In the thousands of synchronous telemedicine visits completed, patients expressed appreciation for the care they

received, while minimizing COVID-19 exposure, travel expenses, and time lost from work or other activities. Logistical workflows were optimized, and physicians forged consensus around a multitude of valuable clinical use-cases. Residents and attendings alike expanded skills in this additional, novel approach to care. Our collective experience provides a basis for ongoing generalizable clinical research.

Now, at Philadelphia’s current stage in the pandemic, the increased availability of in-person evaluations partly relieves the imperative for synchronous telemedicine. But the future remains highly uncertain; we are continuing to build upon the capability of our telemedicine offerings, as we remain adaptable to changing circumstances. Hybrid evaluations, as pioneered at our institution by the Oncology Service, will be central to these enhanced capabilities. This hybrid model merges satellite facility diagnostics with remote synchronous video visits, and it enables an even stronger telemedicine service with expanded clinical utility.

Telemedicine — in its asynchronous, synchronous, and hybrid forms — is a tool that augments our ability to care for patients. It is here to deliver healthcare value now and beyond the COVID-19 pandemic.

Joseph Anaya is a Resident Physician and Mary Fuska is the Director of Telemedicine and Diagnostics at Wills Eye Hospital.

C A N C E R N E V E R S T O P S — A N D N E I T H E R D O W E

ORGANIZING OUR OCULAR ONCOLOGY SERVICE IN UNPRECEDENTED CIRCUMSTANCES

By Carol L. Shields

The Ocular Oncology Service at Wills Eye never stopped working during the COVID-19 pandemic – instead of putting the brakes on patient care, we flipped the switch and nearly overnight converted to a telehealth system. Our cancer patients needed us, so we balanced patient care with clinician and staff safety. At first it seemed daunting to decide on how to evaluate an ocular oncology patient under these novel circumstances but, in the end, we discovered new ways to implement care without requiring the doctor to be present. In fact, we have been able to deliver care with a skeleton crew of two office staff at a remote

setting, taking patients in one by one, with family waiting in the car, and turning over care every 15-20 minutes, including all imaging, teleconferencing with the doctor and family, and a personally dictated letter to the referring physicians. It might sound impossible, but with an already solid base in ophthalmic imaging, and with outstanding photographers and technicians, we set up imaging “camps” to keep patients away from the downtown Philadelphia virus “hotspot.”

If I had to select five steps that we specifically focused on during this overwhelming transition, I would include: i) safety in the clinic, ii) constructing telehealth confidence for eye cancer, iii) COVID-19 testing on patients before surgery, iv) maintaining employee and patient satisfaction, and, the most important one, v) establishing imaging centers in the suburbs of Philadelphia.

S A F E T Y I N T H E C L I N I C

Virtually overnight we realized that our exposure to patients required more than a mask and hand sanitizer. To reduce contact, we asked new patients to wait in their cars until we were ready for them to check in, leaving all family members in the car. Only the patient entered our office, with a mask and sanitizer, checked in, and had their vision and intraocular pressure checked, and images taken. Then the patient was examined by a doctor using a transparent shielded slit lamp and shielded indirect ophthalmoscopy. That was followed by a virtual review of images on the computer, short counseling, and letter dictation to a tablet. The patient only occupied one





“It is highly important to recognize the sacrifice of the office staff to maintain care during the viral pandemic.”

room during their stay, and only up to four patients were allowed in the waiting room. Following the consultation, the patient met virtually with our surgical coordinator and the surgery was scheduled. Upon departure, technicians applied sanitizer and the room was cleaned. From arrival to discharge, the new patient spent no longer than an hour in our office.

CONSTRUCTING TELEHEALTH CONFIDENCE FOR EYE CANCER

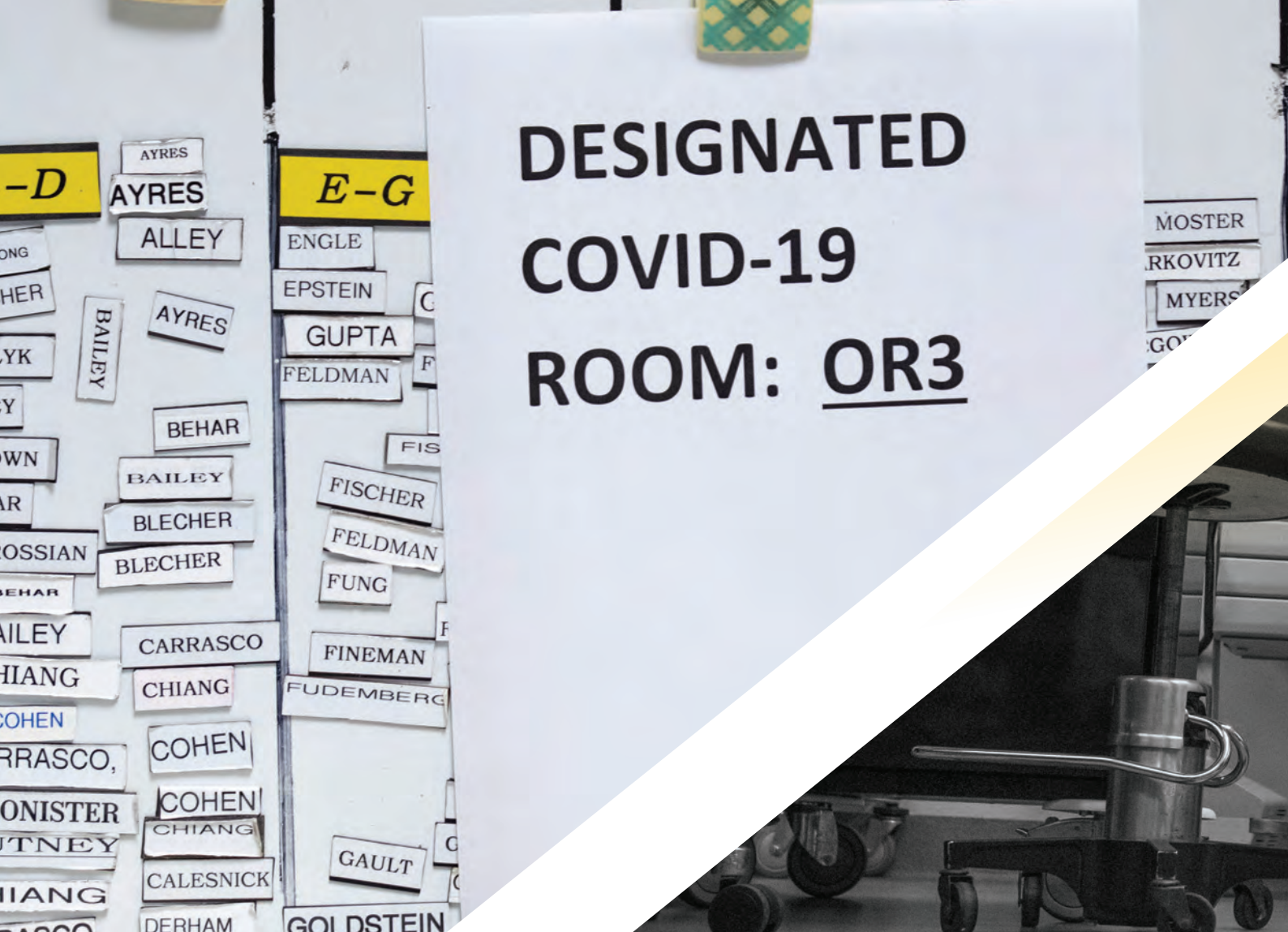
New cancer patients and emergency patients were evaluated in person, but existing patients were redirected to telehealth services. In our office, the technician would contact the patient, take the history, gather information on visual acuity, motility, and visual fields, and then pass the case to the doctor who would review any recent fundus images or diagnostic tests taken, counsel the patient, and dictate a letter. Initially some patients found this set-up unsatisfactory, but after participation, nearly 100 percent of them enjoyed the convenience, the one-on-one with the doctor, and the rapid evaluation. Satisfaction and confidence in telehealth escalated quickly during the pandemic.

COVID - 19 TESTING ON PATIENTS BEFORE SURGERY

From the start, we required COVID-19 testing on all patients before surgery, even children being examined under anesthesia. This provided some safety for operating personnel. The testing was done within two days of surgery and we luckily caught a few infected patients before it was too late.

MAINTAINING EMPLOYEE AND PATIENT SATISFACTION

It is highly important to recognize the sacrifice of the office staff to maintain care during the viral pandemic. This disruption to our normal office and operating flow could have led to anxiety and depression in those who give and receive the care. Physicians should be careful to recognize distraught or stressed persons and give them the time and help they need – often virtually. I must admit, our employees have been strong and willing to make this new arrangement work. Our patients have been completely



satisfied with their telehealth experience and very happy with our remote imaging centers (camps), sparing them the extra travel time and avoiding COVID-19 hotspots.

THE BIG ONE: ESTABLISHING IMAGING CENTERS IN THE SUBURBS OF PHILADELPHIA

Developing remote image centers was our best idea and it solved numerous problems. We realized that adequate assessment of an ocular oncology patient required high-quality imaging of the entire eye. This quality often surpasses that available in an average ophthalmology office, so we established three remote imaging centers approximately one hour from Philadelphia to the east, south and northwest, to capture images for patients who wished to avoid traveling into the city. These centers were fitted with high-quality fundus cameras (with autofluorescence), ultrasound (and UBM), and OCT. It was an investment, but we suspect

that the fear of traveling to metropolitan areas will continue even after COVID-19 is gone. Patients appreciate the shorter travel, quicker visit, and avoidance of a downtown urban setting. We staff each center with two employees: one ophthalmic photographer and one technician, both connected virtually to our “mothership” at Wills Eye Hospital. We have invested in the best imaging cameras for best patient care. For now, each center is open one day a week to provide ophthalmic care and imaging, followed by immediate virtual consultation with the ocular oncologist. We sense that this will increase as patients get comfortable accessing this type of care. This arrangement has allowed us to continue to offer the highest quality of care, while minimizing direct patient contact.

The pandemic brought fear, anxiety, and sickness, but it also brought an education on how to best help our patients in an efficient, virtual manner. Cancer and COVID-19 are a “double whammy” but, at Wills Eye Hospital Ocular Oncology Service, we worked to “tame the tiger” and managed to solve the seemingly insurmountable challenge.



“Developing remote image centers was our best idea and it solved numerous problems.”

WHAT DOES THE FUTURE HOLD?

I think imaging centers with virtual doctor consultations are here to stay. These centers impressively simplify medical care for patients, without the need to wait long hours, travel long distances, and risk exposure in crowded circumstances. In fact, the remote location is attractive because the doctor is “virtually transported” to the patient. I believe patients will seek this convenience once they experience it. However, “in-person” initial consultation remains a gold standard, especially for ocular oncology, as evaluation of specific details can best be done in person. As I see it, the

role of virtual examination will likely be used mostly by follow-up patients.

Over the past five months of the pandemic – which is by no means over – Ocular Oncology at Wills Eye Hospital has survived, and patient visits are increasing. I am confident we will get back to a “new normal,” with our usual volume of patients spread over four offices. Our staff have taken leadership roles in this transition, and together we have journeyed into this new world of ophthalmic care.

Carol L. Shields is the Director, Ocular Oncology Service, Wills Eye Hospital and Thomas Jefferson University in Philadelphia, Pennsylvania, USA.

TRIALS, INTERRUPTED

CHIEF OF THE RETINA SERVICE AT WILLS EYE HOSPITAL DISCUSSES THE IMPACT OF COVID-19 ON RETINA RESEARCH

By Carl D. Regillo

The pandemic has had a significant impact on our work as all studies for newly recruited patients were put on hold. We also halted new recruitment to minimize the number of patients coming in, so as to limit their exposure to any risk, as well as the risk to our staff. Only trials that involved administering a drug for essential care, such as established anti-VEGF therapy for wet AMD or diabetic macular edema, continued uninterrupted. We also continued administering investigational drugs to those undergoing clinical trials so as to not compromise the integrity of our studies. And that meant we had to be cautious from the very beginning of the virus spreading. It was only by creating a safe environment – providing proper sanitation, wearing masks, and allowing adequate space and time between patients – that we were able to continue delivering essential care to those who needed it most.

Inevitably, there was a small hiatus in certain studies – those considered to be non-essential – such as the dry AMD trial, where there is currently no established treatment. Instead, we found alternative ways to monitor patients who experienced a gap in their so-called treatment (so-called, because it may or may not have been working). Where possible, we transitioned to a telemedicine approach, whereby patients would be reviewed over the phone and only brought in if there were any issues. Fortunately, since the pandemic only kept us in lockdown for three months, most patients only missed one or two visits.

Once restrictions were eased, all studies went back to active status. We are now almost back to normal in terms of the way we conduct clinical trials and we are even recruiting new patients into our studies. Though we are up to speed from a clinical and research standpoint, we have protections in place to guard against COVID-19. I'm happy to say that the overall impact on our annual research output was minimal. Many projects continued, and we continued writing and publishing papers, so we are not far behind. As long as we don't get a major second wave, I don't feel as though we have lost

significant ground. And that's great news; we were initially concerned that an extended lockdown would affect patients' ability to visit the site, and compromise the integrity of our data as a result. Fortunately for us, a three-month delay has allowed us to preserve trial integrity across the board.

It seems to me that it is not the research institutions who have been most affected by the pandemic, but the companies that sponsor the trials. Delays to new patient recruitment leads to delays in a trial being completed, which impacts businesses financially. That said, given that it takes 1–1.5 years to recruit patients into a study, it could be argued that three months is not such a significant amount of time...

There are undoubtedly lessons to be learned from the past few months, especially when it comes to protecting patients from infection. I think that many of our current safeguards – from thoroughly sterilizing equipment to maintaining adequate space between patients – will remain in place long after the pandemic ends. And the humble handshake is probably gone for good. Clinical research mirrors what we do in practice, so it would make sense for a lot of these safety measures to stay the same. But of all the creative solutions put in place throughout lockdown, telemedicine is perhaps the most significant.

I have no doubt that future studies will incorporate virtual approaches to following study participants. In ophthalmology, it can be hard to do everything virtually, but with more and more resources made available, I am sure both clinical care and research trials will be quick to take advantage of both available and future technology. And why not? The benefits of this new approach – both in terms of safety and cost effectiveness – benefit everyone. The types of measures being explored now will hopefully minimize and streamline study visits, and will perhaps even become a high priority in protocol designs in years to come.

Carl D. Regillo is Chief of the Retina Service at Wills Eye Hospital.





O C U L A R T R A U M A A N D C O V I D - 1 9

**DELAYED PRESENTATION, LONGER
DISTANCES TO TREATMENT CENTERS,
LESS INSURANCE COVERAGE – OUR
PATIENTS FACE A HOST OF NEW
CHALLENGES IN A PANDEMIC**

By Connie Wu, Samir N. Patel, Thomas L. Jenkins, Anthony Obeid, Allen C. Ho and Yoshihiro Yonekawa

Nationwide stay-at-home orders during the COVID-19 pandemic have caused serious issues for patients seeking emergency care. We conducted an investigation into the patients seeking urgent ophthalmic care for severe ocular injuries (1). We reviewed health records at the Wills Eye Emergency Room – one of the few 24/7 Emergency Departments exclusively

dedicated to treating eye emergencies in the country – and found significant differences between the quarantine period and a comparable time period from the prior year.

Even though the overall number of patients presenting for emergency eye evaluations during the stay-at-home orders decreased, the number of severe ocular trauma patients remained unchanged. Compared with the previous year, patients who presented with severe ocular injuries during the pandemic were more likely to travel further to seek emergency care, more likely to have a delayed presentation after injury, and more likely to have suffered ocular trauma at home.

The significantly higher incidence of ocular injuries that happened at home is partly explained by a big spike in do-it-yourself home improvement projects. Most ocular injuries across both of our study periods occurred because of poor adherence to eye protection guidelines. To us, this highlights a need for patient education in the prevention of ocular injuries, specifically targeting the issues of health and safety, and protective eyewear. Education on eye protection for potentially hazardous at-home activities is especially important for a healthcare system already overburdened by a global pandemic.

During the pandemic, patients not only traveled further, but also waited longer to seek emergency eye care, which

“During the pandemic, patients not only traveled further, but also waited longer to seek emergency eye care, which highlights problems with delivery of urgent ophthalmic care, with factors dependent on both patients and the healthcare system.”

highlights problems with delivery of urgent ophthalmic care, with factors dependent on both patients and the healthcare system. Delayed presentation to the emergency room during the pandemic may be linked to the observed increase of uninsured patients, possibly the result of unprecedented levels of COVID-19-driven unemployment. Other late-presenting patients may have been worried about the safety of visiting a medical center in the midst of a viral pandemic. This latter point underscores the need for i) robust personal protective equipment supply for both the patients and eye care professionals, ii) patient education to promote safety in seeking emergency care, iii) satellite emergency clinics, and iv) telemedicine, which can more efficiently assess and triage patients with ocular trauma.

The pandemic has forced us to cope with unprecedented alterations to the healthcare landscape, and severe ocular trauma is no exception. Our Wills Eye Hospital Emergency Room investigation clearly highlights a need for targeted healthcare interventions to address both patient and provider factors that play a role in the delivery of emergency care. Our Wills Eye Hospital mission remains undeterred by the global pandemic as we aim to provide superior

24/7 emergent eye regionally and inform others nationally and globally about best practices for severe ocular trauma.

Reference

1. C Wu et al., “Ocular trauma during COVID-19 stay-at-home orders: a comparative cohort study,” *Curr Opin Ophthalmol*, [Epub ahead of print] (2020). PMID: 32740065.

Authors are specialists at Wills Eye Hospital, Mid Atlantic Retina and Thomas Jefferson University in Philadelphia.





VISUALIZE THIS

Welcome to the surgery suite of the future – the OR-Bot™ Surgery Visualization Theatre™

A recent survey of AAO members found that 51.8 percent of surgeons reported neck, lower back, upper body, or other musculoskeletal pain, with 15 percent being limited in their work as a result. Of those, 7 percent required corrective surgery. The reality is that current operating systems often are center of ergonomic issues.

Enter the OR-Bot™ Surgery Visualization Theatre from Ocutr, a new, all-digital surgery system that safeguards surgeons by minimizing the strain on their upper body with three unique visualization options:

- ORLenz™: a 4K AR/XR headset that has the widest field-of-view in the industry and the highest resolution the eye can see at 20/20 – 60 pixels per degree.
- StereoLenz™: an 8K auto-stereoscopic 3D “glasses-free” monitor that enables the surgeon to look straight ahead, instead of turning their head to see a monitor.
- MiniLenz™: a 4K VR microscope that is detached from the standard operating microscope and camera combination, alleviating constraints in the surgeon’s operating space.

Unlike existing systems, the OR-Bot does not require the surgeon to crane their neck to view the monitor, which allows surgeons to practice their art for longer, with less pain – thus

giving them the best chance to improve patient outcomes and perform surgeries longer into their careers. How? Each option delivers a live-action 4K video feed, guaranteeing the surgeon sees holographic images in the highest resolution the eye can see.

To guarantee maximum performance, Ocutr Vision Technologies partnered with Qualcomm for its newest and most powerful chipset, the XR-2 – an exclusive, energy-efficient design that facilitates both wireless and tetherless operation. The Artificial Intelligence engine within the chipset boasts seven teraOPS of computing capability – roughly 7 trillion calculations per second – for running machine learning models on the OR-Bot’s visualization systems. But it doesn’t stop there. AT&T, a global Internet of Things (IoT) leader, teamed up with Ocutr to provide the suite’s IoT and 5G solutions, making the OR-Bot the most connected surgical system on the market today.

Ocutr Vision Technologies developed the technology in response to direct feedback from surgeons. In addition to tackling the key concern of musculoskeletal pain, the OR-Bot also solves a number of space-constraint issues that surgeons face by separating the camera from the microscope, which reduces the amount of equipment between patient and physician.

With real-time access to data, and improved resolution, ergonomics, visuals, and field-of-view, the OR-Bot is more than a piece of equipment – it’s the stuff of fatigued surgeons’ dreams.

WEEKLY NEWSLETTERS

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It Takes a Village

When it comes to the skull base – an area where multiple specialties intersect, patient management and treatment is a group effort

By Jurij R. Bilyk

When most healthcare workers hear the word “ophthalmology,” they quite appropriately think about pathology that occurs in the eye rather than near the eye. A more encompassing metric is to consider the eye an extension of the brain and a critical structure making up the skull base. To exemplify the need for this critical distinction, consider the following case: a 65-year-old patient was referred to Wills Eye Hospital from Arizona with a 14-month history of progressive facial problems. His symptoms started with numbness of the right side of his forehead, developing over several months to a facial palsy and double vision. He was eventually sent to us because his right eye had progressively worsening motility. Multiple MRIs performed locally were read as normal. He was evaluated by the Neuro-Ophthalmology Service and was found to have multiple cranial nerve abnormalities and severe restriction of the movement of the right eye. A detailed past medical history was not contributory. So, what should we do now?

At Wills, we have ophthalmologic subspecialists that can manage any ocular problem. We're also extremely fortunate to be affiliated with Thomas Jefferson University Hospital (TJUH) and a group of neurosurgeons, otolaryngologists, neuroradiologists, oncologists, and radiation therapists that are second to none. Over several decades, I've had the privilege of working closely with these professionals and we have established a collaborative skull base team that has

managed complex cases from the entire country and abroad.

Anatomy of the skull base

The skull base is an anatomic confluence of the base of the brain, the orbits, and the paranasal sinuses. It's densely packed with critical structures, including the internal carotid arteries, the optic nerves, the venous sinuses, and cranial nerves that travel through the various “nooks and crannies” that connect the orbits to the intracranial vault. The skull base is also the confluence of multiple surgical specialties; successful patient management requires a complex interplay between orbital surgery, neurosurgery, and otolaryngology, which may not be available at many institutions.

Furthermore, technologic advances in neuroradiology, intraoperative image guidance, cerebral angiography, and trans-nasal endoscopic techniques have allowed for minimally invasive surgical management. Our otolaryngologists,

neurosurgeons, and orbital surgeons can access the orbital apex, pituitary fossa, and clivus through the nose. Our neurovascular team can snake a catheter into an infant's ophthalmic artery to directly treat retinoblastoma with chemotherapy, or close a carotid-cavernous fistula through the superior ophthalmic vein via a lid crease incision. And if a combined tumor resection is needed, the microvascular free flap team can safely close large defects across the orbit, face, and skull. Such cases are not easy. They require a trust and collaboration between surgeons that is built over many years and many procedures – and that's what we've achieved here at Wills and TJUH. Each surgical specialty learns from the other and, consequently, patients benefit.

It's been a long road to get to where we are – a lot of long hours, sleepless nights of worry, and days of inpatient rounding. Some cases are less successful than we initially hoped for, but patients quickly



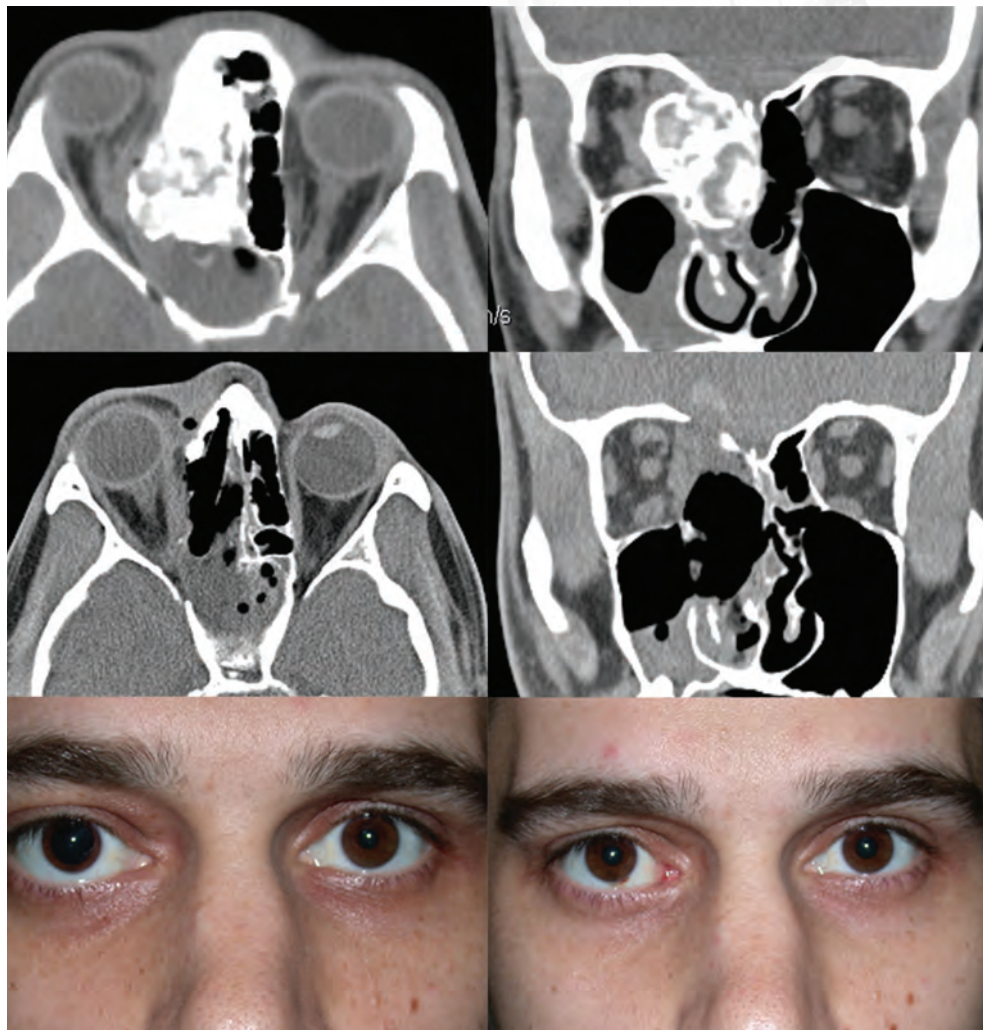


Figure 1. Top: CT scan of a 31-year old-man who presented with acute onset of diplopia and right proptosis. Imaging shows a large bony mass in the right ethmoid sinuses, orbit, and skull base. Middle: CT immediately following a combined transnasal endoscopic and transconjunctival extirpation of the tumor. The small hemorrhage in the gyrus rectus was asymptomatic. Bottom left: Preoperative appearance. Bottom right: 12 days postoperatively, the patient had improvement in proptosis, normal vision, and complete resolution of diplopia. The lesion proved to be an osteoblastoma.

realize that they are in a center with experience and dedication: our physicians try their best in every single case.

When specialists work together
So, what happened to our patient from Arizona? A skull base MRI was obtained and the patient was seen by orbital surgery and neurosurgery, all on the same day. Review of all previous MRIs by our neuroradiologists revealed that there was in fact a process along the supraorbital nerve (the sensory nerve that supplies the forehead) that had progressed over many months and had now extended into the cavernous sinus. The patient was noted to have sun damaged skin across his entire face, but denied any history of skin cancer. However, on more detailed questioning, he recalled that his dermatologist had been “freezing and burning things off my forehead for years.” A skull base biopsy was performed and confirmed our suspicions – the patient had an undiagnosed squamous cell carcinoma

from his forehead skin that had invaded his supraorbital nerve and crept back into the cavernous sinus, infiltrating multiple other nerves in the skull base. The case was discussed at the Head and Neck Tumor Board and radiation and chemotherapy were recommended.

It’s been a privilege to work with my colleagues at TJUH – their technical expertise is humbling and their

dedication is inspirational. And it’s just one of the many puzzle pieces that makes Wills a great place to be – for both patients and physicians.

Jurij R. Bilyk is Attending Surgeon on the Oculoplastic and Orbital Surgery Service at Wills Eye Hospital, and Professor of Ophthalmology at Thomas Jefferson University.

Putting Out Uveitis Fires

Accurate and timely uveitis identification can save a patient's vision – and sometimes their life

By James P. Dunn

Case after case...

A six-year-old boy with a history of acute leukemia – and seemingly doing well after bone marrow transplantation and immunosuppressive therapy – developed blurred vision and uveitis in one eye and was referred to Wills Eye Hospital with suspicion of recurrent leukemia. Because the eye is an “immunologically privileged” site, intraocular inflammation in a child with a history of leukemia is recurrent leukemia until proven otherwise. The young patient's family was understandably distraught.

A 25-year-old man came to the Wills Eye Uveitis Unit in the Retina Division for multiple recurrences of acute-onset pain, redness, and light sensitivity alternating between his eyes. At his examination, he was very surprised to be asked about low back pain, which he had suffered from for several years. He said, “My back is really stiff when I wake up, but then loosens up after an hour or two.” He was equally puzzled about the interest shown in his family history of inflammatory bowel disease, wondering what any of that had to do with his eyes.

A 32-year-old woman was referred to the Wills Eye Uveitis Unit

for a severe, but unusual case of uveitis involving the front of one eye. It hadn't responded to the typical regimen of steroid eye drops, and the iris was noted to be extremely thickened throughout, almost filling up the anterior chamber. She was promptly referred to the Uveitis Unit.

An 80-year-old accountant came to Wills from New York City because his eyes had become so red, irritated, and blurred that he could barely open them. He was no longer able to work, which he had continued into his 80s out of love for his job.

He was seen in the Ocular Pemphigoid Clinic at Wills Eye, where the severe scarring of his conjunctiva and cornea in both eyes was evaluated by a team of uveitis, cornea, and oculoplastics specialists.

Day in, day out

The above cases are examples of complex ocular infectious and inflammatory eye diseases seen in the Retina Division's Uveitis Unit at Wills Eye. As the unit's director, I see about

500 new and 4,000 follow-up patients in my practice every year.

Uveitis – intraocular inflammation – is an uncommon but potentially blinding

“One of the advantages of seeing uveitis patients at Wills Eye is the potential for collaboration with other eye specialists.”

“Proper diagnosis and prompt treatment can be not only vision-saving but, in some cases, even life-saving.”

collection of diseases that can be infectious or non-infectious, unilateral or bilateral, acute or chronic, and can affect any age group. Uveitis is described as the fifth or sixth (depending on the source) leading cause of blindness in the developed world because its complications include cataract, glaucoma, macular edema, and retinal scarring or detachment. There are many different types and causes of uveitis; some are fairly easy to treat with a course of steroid drops or steroid injections in or around the eye, whereas others require antibiotic therapy, oral steroids, or immunosuppression. Often, uveitis is part of a disease affecting other parts of the body, and the ophthalmologist may be the first physician to make the connection.

Proper diagnosis and prompt treatment can be not only vision-saving but, in some cases, even life-saving.

Working together, case after case

One of the advantages of seeing uveitis patients at Wills Eye is the potential for collaboration with other eye specialists. In some ways, a uveitis specialist is almost like a primary care physician, because so many uveitis patients suffer from diseases in other parts of their body.

In the cases listed above, the six-year-old boy with possible recurrent leukemia was seen with the ocular oncologists at Wills. His exam showed a viral infection in the eye (secondary to his immunosuppression after the bone marrow transplant), rather than recurrence of the leukemia, and he was successfully treated with antiviral therapy without having to undergo a painful bone marrow biopsy to evaluate for leukemia.

The 25-year-old man with recurrent episodes of uveitis was successfully treated with steroid eye drops, but also tested positive for a gene called HLA-B27. The gene is strongly associated with both recurrent uveitis and a type of arthritis called ankylosing spondylitis, which explained his low back pain. In collaboration with the rheumatologists at Thomas Jefferson University Hospital in Philadelphia, he was placed on a biologic immunosuppressant – adalimumab – that effectively controlled both his uveitis and his ankylosing spondylitis.

The 32-year-old woman with the uveitis and iris mass was referred to Wills Eye Ocular Oncology because her exam suggested a “masquerade syndrome,” one of a variety of diseases in which inflammation that looks like uveitis is actually caused by something else. In her case, a biopsy confirmed a rare type of lymphoma, and she was successfully treated in collaboration with Jefferson Oncology with combination chemotherapy known as R-CHOP – one of

Passing on the knowledge

The Wills Eye Uveitis Unit is actively involved in teaching medical students, residents, and our Wills Retina fellows. Many medical students have become interested in ophthalmology as a career after spending time on the Uveitis Unit and seeing how important those interactions with other ocular and medical specialists are in the management of ocular inflammatory disease. The residents and fellows participate in surgery on uveitic cataracts, which tend to be much more complicated than age-related cataracts due to comorbidities such as scarring of the iris and edema of the retina. Although the surgical technique is, of course, critical to the visual outcomes, so is the pre- and postoperative medical management of the uveitis.

the very few cases in the world successfully treated in this way.

Finally, the 80-year-old accountant was diagnosed with a rare autoimmune eye disease, usually found in older patients, called ocular cicatricial pemphigoid. The Pemphigoid Clinic provided him a multidisciplinary team to evaluate and treat his corneal and conjunctival scarring and the abnormal eyelashes that were turned in and irritating his eyes. He was successfully treated with rituximab, a new therapy for pemphigoid, and was able to return to the accounting work he loved.

James P. Dunn is the Director of the Uveitis Unit at Wills Eye Hospital.

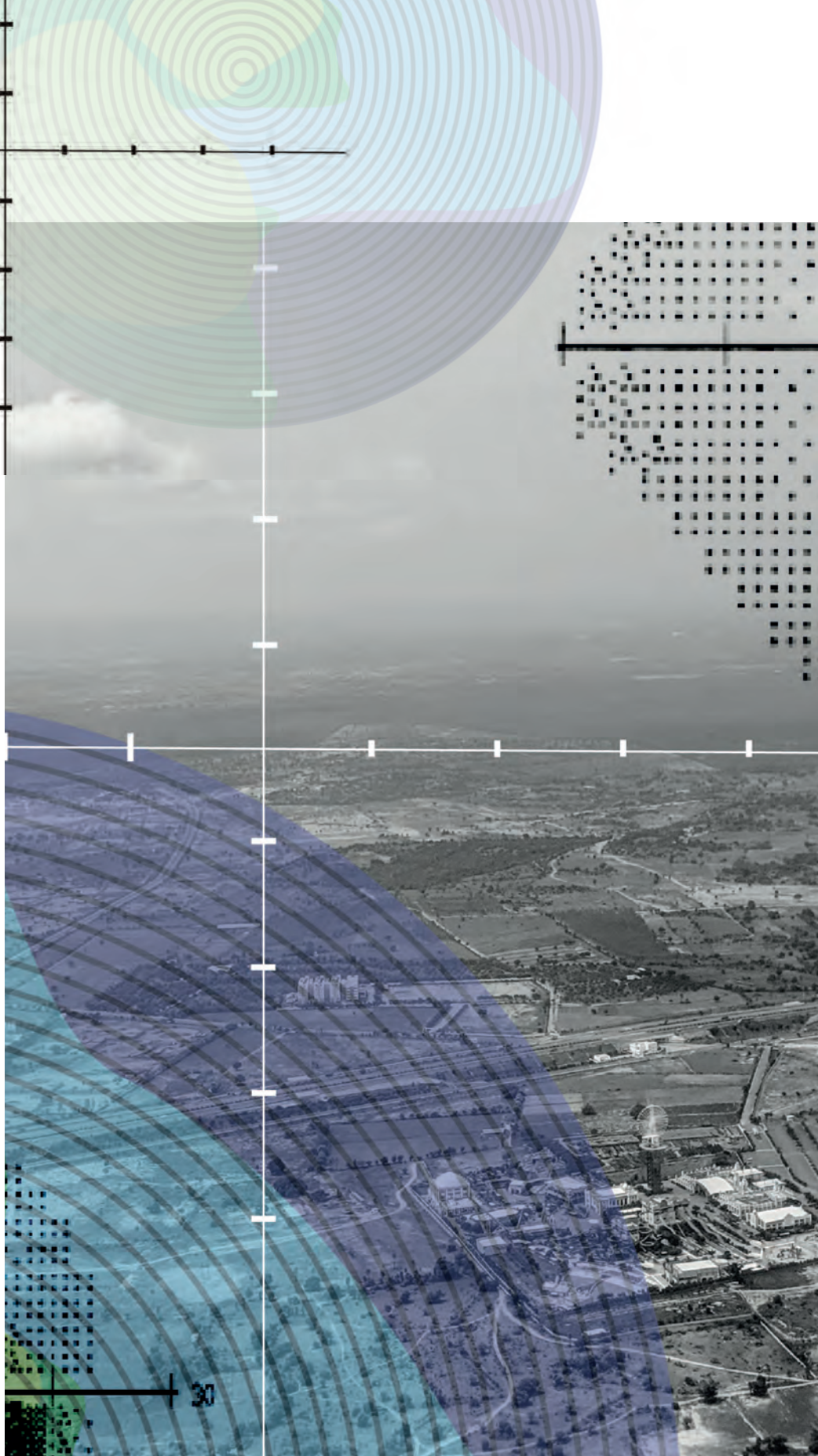
In the Field

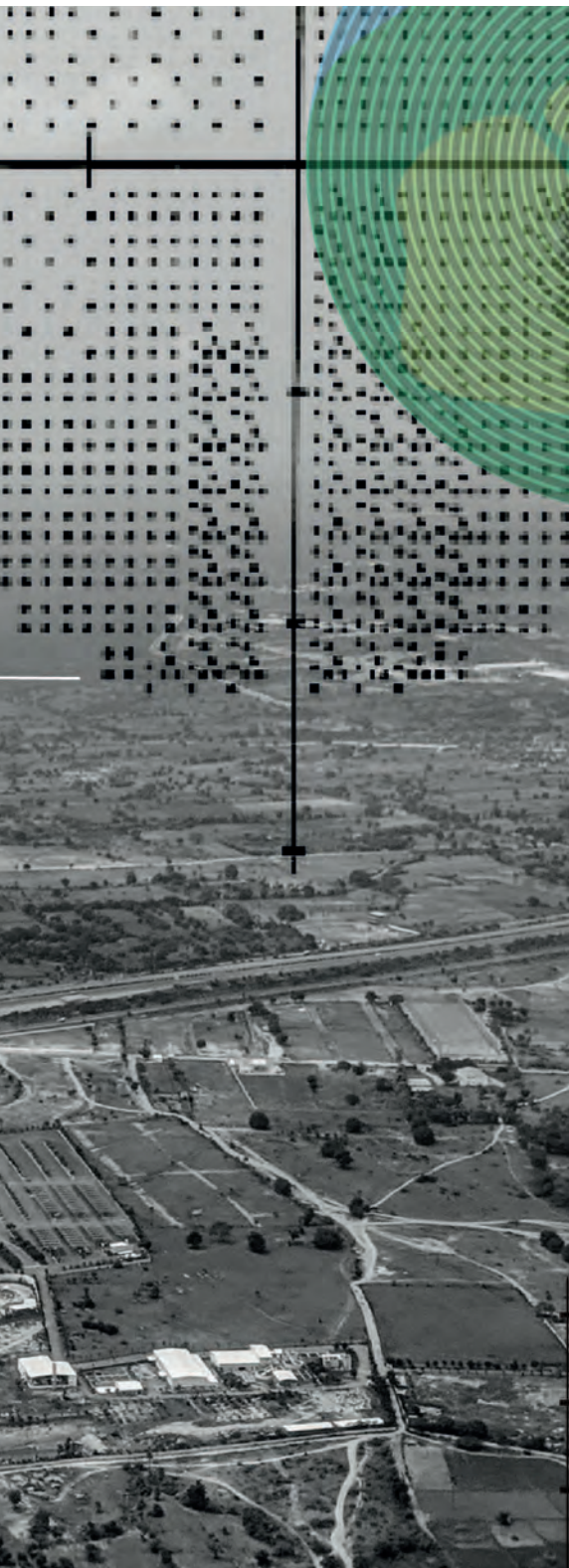
How does a novel portable head-mounted perimeter compare with the gold standard in visual field testing?

*By Reza Razeghinejad and
Aakriti G. Shukla*

Visual field testing is integral to the diagnosis and monitoring of patients with glaucoma and neuro-ophthalmic diseases. Perimetry has predominantly relied on automated devices that are large and cumbersome – and clearly not practical outside of the testing room. They also require the patient to maintain constant fixation for several minutes, which can be difficult or stressful for patients with learning difficulties, for the elderly, or for those who are simply nervous during the visual field test. Patients with musculoskeletal problems and those who have to maintain a horizontal position may have unreliable, artifact-laden results

“Perimetry has predominantly relied on automated devices that are large and cumbersome – and clearly not practical outside of the testing room.”





Pandemic perimetry

In the last few months, another important consideration for perimetry has come to our attention. Glaucoma services, like all other ophthalmic subspecialties, have been heavily affected by the COVID-19 pandemic. It is possible for the perimeter bowl to become contaminated in a traditional visual field-testing setting. Alcohol spray can be used to clean the interior of the perimeter bowl, but

given the significant surface area of the bowl, this may be a time-consuming process. Head-mounted perimeters can be sanitized using alcohol and do not require the use of the bowl normally used for testing. Portable visual field tests have great potential in the delivery of good-quality vision care for glaucoma patients in situations where access to standard perimeters is difficult – in rural or remote locations, in developing countries, and under special circumstances, when patients are required to socially distance.

or may be unable to assume the correct position for the test.

Over the years, several devices have been introduced to make visual field testing easier for patients. And though these new modalities have brought much-needed portability, the lack of fixation, monitoring methods, and hardware standardization have limited their widespread use (1, 2). More recently, a new generation of head-mounted perimetry innovations have been developed and brought to market; their aim: to close the gap in visual field testing.

From theory to practice

At the Wills Eye Hospital Glaucoma Service, we recently conducted a study comparing a novel perimeter, the VisuALL Field Analyzer (from Olleyes Inc., Summit, New Jersey, USA). This head-mounted device (HMD) has eye tracking capabilities and its results have been found to be well-correlated with the well-known, widely-used Humphrey Field Analyzer (3, 4).

First, let us share some general information on the VisuALL perimeter: it is an FDA Class 1 device, and does not require the patient to use an eye patch or maintain a particular head position during

the test. Its ergonomic design and minimal weight (0.3 kg) allow the patient to have unprecedented freedom of movement. Patients can wear their own glasses, eliminating the need for trial lenses. The device is composed of the HMD, a laptop, smartphone or tablet, and a Bluetooth-connected response button (see Figure 1). The HMD display is divided into two halves, one for each eye. Two tracking systems allow for an accuracy better than one degree.

So how does it work? The machine checks gaze position before presenting the stimulus, stops the test, and adjusts the location of stimulus properly if fixation is less than 15 degrees off center. If that is the case, the device presents a signal requesting that the patient returns to the central fixation target. The point pattern is similar to the -2 pattern in Humphrey Field Analyzer: a 6-degree grid pattern that straddles the horizontal and vertical midlines. VisuALL is technician independent as a demonstration video at the beginning of the test educates the patient on the simple testing process. The patient can take control over pausing and resuming the test. Once the test is finished, the results are saved into cloud storage.



Testing the test

Our study included 25 healthy subjects and 26 mild or moderate glaucoma patients. The diagnostic performance was assessed by means of receiver operating characteristic (ROC) curves, which provide a sensitivity/specificity trade-off (the value of the area under the ROC curve of 1 represents 100 percent accuracy). Bland-Altman plots were used to assess the discriminative ability of the device between healthy and glaucomatous eyes.

We found that the VisuALL testing time was approximately three minutes longer than on the Humphrey Field Analyzer for both healthy and glaucoma patients. The VisuALL uses full threshold strategy, which takes more time than SITA-standard. Retinal sensitivity measured by the VisuALL was similar to that of the Humphrey, and both were affected by the age of the individuals. The mean sensitivity of the whole visual field and all quadrants correlated significantly in both the healthy and glaucoma groups. The mean sensitivity of the VisuALL had a greater ROC than that of the Humphrey,

“Our work showed that the VisuALL perimeter successfully distinguished healthy subjects from glaucoma patients.”

although the difference was not statistically significant. The Bland-Altman plots also showed a good agreement between the mean sensitivity of the VisuALL and the HFA in both healthy and glaucoma patients.

The data from this pilot study are very encouraging: the VisuALL Field Analyzer was at least as good as, if not better than the Humphrey. The portability of the device allows it to be used in home-based settings, where many more tests could be done over time, potentially leading to earlier detection of glaucoma progression (5). We conducted another study to assess device performance in home-based perimetry – the results of which are being analyzed. Established glaucoma patients received the device by mail and checked their visual fields several times over one week. The results of the tests will be compared with the Humphrey data available in the patients' charts.

Adding pressure

Home tonometry is complementary to portable visual field testing. Our group continues to study home tonometry, which has demonstrated significant promise in providing accurate intraocular pressure measurement outside of office hours (6). Additionally, previous work has shown that mean IOP, maximum IOP, and IOP fluctuation can lead to significant changes in the visual field (7). What's more, disc hemorrhages lead to visual field loss that is more apparent in the central visual field, which may be more important for our patients' day-to-day activities, such as reading or driving (8). Linking home visual field testing with home tonometry allows for the close correlation of these two important data points outside of the glaucoma specialist's office.

Our work showed that the VisuALL perimeter successfully distinguished healthy subjects from glaucoma patients, and its results correlated well with the Humphrey Field Analyzer. We are already

working on additional studies on patient preferences, repeat test performance, and clinical utility, as well as creating a normal visual field database.

Reza Razeghinejad and Aakriti G. Shukla are glaucoma specialists, practicing at the Glaucoma Service of Wills Eye Hospital.

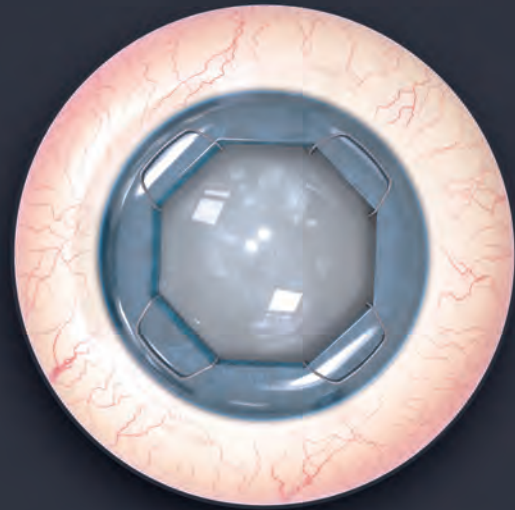
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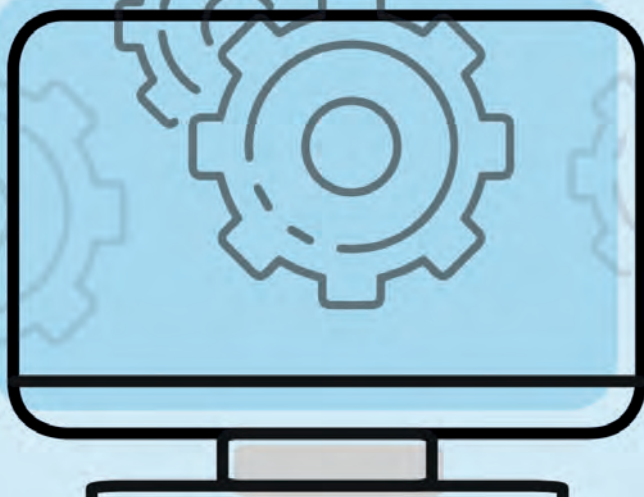


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A Brave New World

Since its inception in 1832, Wills Eye Hospital has been a leader in translational clinical research. Allen Ho and Carl Regillo share the cutting-edge work transforming the lives of patients worldwide

A Brave New World

Cutting-edge translational retina research for patients in Philadelphia and around the world

By Allen C. Ho

We live in an age where science and technology are advancing fast – but not nearly fast enough for those afflicted by blinding eye conditions. Since its inception in 1832, Wills Eye Hospital has been a leader in patient care, medical education, and translational clinical research (1). But this is no time to rest on our past achievements when there are still so many needs left unfulfilled in our clinics and surgical suites and when translational scientific advances offer potential opportunity for great benefit. These patient needs drive our team – and the whole institution – forward.

As Director of Retina Research at Wills Eye, I lead our innovative collaborations between brilliant Wills Eye Retina specialists, dedicated Wills Retina Research teammates, and industry and global study group partners – all focused on elevating the standards of care for patients in our exam rooms and around the world. Further, our highly sought-after retina fellowship programs continually bring in the best and brightest minds in our field to train with us and challenge the status quo.

Wills Eye Retina is among the most active translational retina clinical trial units in the world. Our patients have access to the latest clinical research because our doctors conceive, design, and lead studies both alone and with partners who share in our mission to elevate standards of care.

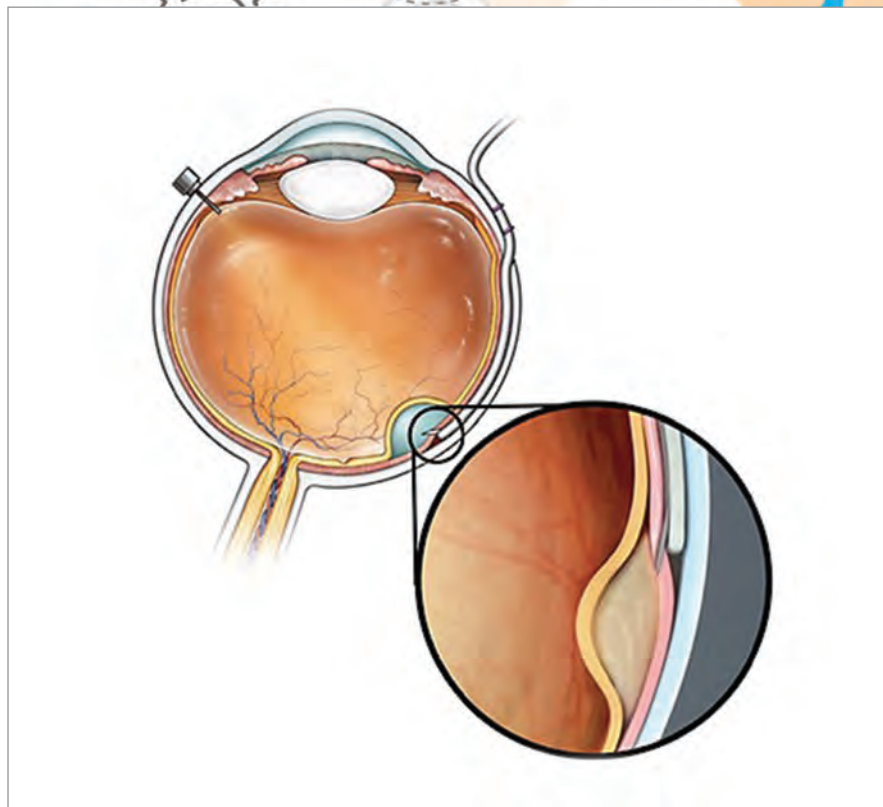


Figure 1. Access to the subretinal space can be achieved using a catheter in the suprachoroidal space. The Orbit Subretinal Delivery System (Orbit SDS; Gyroscope Therapeutics), pictured here, is designed to avoid the need for vitrectomy and perforation of the retina by using a suprachoroidal approach. When the suprachoroidal catheter is in the desired position, the surgeon advances a microneedle to access the subretinal space. Image courtesy of Gyroscope Therapeutics.

Inspired by patients' courage We have refined an implantable subretinal microelectrode chip and technology from a biomedical laboratory (designed by my retina colleague Mark Humayun), evolved the surgery procedure in animal surgery labs, and implanted the device, a commercially approved Argus II bionic eye, so that patients blinded by severe retinal degeneration can see again (2).

When you can't see, it's not just your vision that is cut off. My patient Fran utilizes her Argus II daily to navigate her world and connect with others. She no longer has to say "hello" to an empty elevator; she can see if another person is there. Although the Argus II was recently discontinued due to business conditions,

we're moving forward on other translational research fronts to attack blindness. The courage of our patients inspires us.

Rigorous, disciplined, driven by science Stem cells are in vogue – and the lay press often presents them as a cure for almost everything. Dozens of essentially unregulated "stem cell clinics" around the country have surfaced, offering "treatments" with sometimes blinding consequences as highlighted with caution by my partner and Wills retina surgeon Ajay Kuryan (3). In contrast, our independent, safety-monitored (and FDA-approved) clinical trial programs for potential cell therapies are among the most advanced in the world. We



Allen C. Ho

have next-generation cell lines for safety and efficacy, delivered using new surgical techniques and tools developed by Wills Eye study leaders and surgeon investigators (4). I am immensely proud of our research team's commitment as we pursue translational solutions to vision loss from advanced AMD. Scientific rigor is what our patients deserve.

The time is now

A patient-centered ecosystem of gene therapy clinical trials is growing around the world, and Wills Eye Hospital and our retina surgeons are leading and at the cutting edge. Philadelphia's own Spark Therapeutics claimed the first approved in-human gene therapy for the Leber congenital amaurosis biallelic RPE65 mutation, led by local colleagues Jean Bennett and Albert Maguire and presented to the FDA by

Wills Eye Ophthalmologist in Chief Julia Haller (5). At Wills, we partner with industry to explore gene therapy programs for sight-limiting conditions from the common to the obscure. The preclinical and translational science is impressive and we deliver it to our patients in a portfolio of gene therapy clinical trials.

For patients with rare, blinding retinal degenerations, we investigate injectable mRNA silencing strategies and disease disabled viral vectors gene therapies, aiming to attack some of the 250 known genetic mutations responsible for these conditions. In more common diseases such as AMD and diabetic retinopathy, our programs aim to turn the eye itself into an ocular biofactory, using gene therapy by intravitreal or suprachoroidal injection or subretinal surgery to deliver DNA sequences that encode therapeutic

proteins. Patients now receive these injections on a monthly basis in our offices and the burden of treatment is high (6). We don't give our patients unrealistic expectations – but we do instill hope, and the preliminary data for these therapies look promising.

We are focused, collaborative, dedicated, and driven by science to deliver the best vision to patients in our hospital and around the world, now and in the future. In my view, there is no better environment in which to pursue these goals than Wills Eye Hospital. We welcome you to come and see us in action.

Allen C. Ho is Attending Surgeon and Director of Retina Research at Wills Eye Hospital, Professor of Ophthalmology at Thomas Jefferson University, and President of The Retina Society.

History Still in the Making

By Carl D. Regillo

From early on, Wills Eye has taken part in every major clinical trial in retina, going back to some of the largest and most influential studies, such as the Early Treatment in Diabetic Retinopathy Study (ETDRS, 7), the Diabetic Retinopathy Study (DRS) Landmark Trial (8), and ophthalmitis/vitrectomy studies.

Over the past 25 years, we have participated in many industry-supportive trials, which provide a very productive, collaborative environment. Although Wills Eye's participation is not unique, we have been at the forefront of these trials, involved in every major development in ophthalmology – including treatments that are now used every day, everywhere on the planet. We've also helped bring new surgical technologies and innovations to market. Of course, like any major research center, we've also tested many innovations that have failed! Not everything that is tested comes to fruition. It is the nature of cutting-edge research.

These days, we are still involved in the most important trials in retina. Every year, the Wills Eye Retina Service produces over 40 major, peer-reviewed publications. The magnitude and impact of our research has attracted some of the finest fellow candidates and retina specialists from around the world – and we now even have a dedicated retina research fellowship.

In with the new
Recently, Allen Ho and I, with other colleagues, researched sustained delivery of drugs to the eye for retinal conditions – a project I feel very passionate about. Our successful Phase III program,

undertaken with Genentech, involved testing a surgically inserted reservoir that delivers a concentrated version of ranibizumab. In the past month, Genentech announced that the study had met its primary endpoint. This is the first sustained-release platform to deliver a drug to the retina and it is likely to be commercially available within the next year or so. We were closely involved in FDA studies from the very beginning.

More recently, our research has focused on stem cells in the form of suspensions. The suspensions can be injected under the retinas of patients with advanced dry AMD, who have already lost visual acuity to a severe degree. We hope to give them some of their sight back. And that's not all; soon,

we'll be involved in Phase II of another exciting stem cell technology coming out of Southern California – a patch of stem cell-derived retinal pigment epithelial cells on a platform that is inserted under the center of the retina in eyes with advanced dry AMD.

Addressing unmet needs

We have made a lot of progress on treating common retinal conditions over the past two decades, but there is room for improvement. We can work toward better outcomes, more efficient and less burdensome therapeutic approaches, and more durable treatments. Unfortunately, there are still many conditions with no treatments at all, such as the very common dry AMD or the much less





common inherited retinal diseases (IRD) – both being blinding conditions for which gene therapies are our big hope. In the future, as well as traditional gene therapy, we hope to see gene editing and enhancements that will allow us to treat some of these devastating hereditary conditions. We have brought in Jose Pulido, a world-renowned retina specialist from Mayo Clinic, to lead IRD diagnostics and therapeutics (see “Sitting Down With...” on page 50).

We see patients’ needs and we see the progress being made with bench research – now, we must bring the two together.

Our mission is to excel in all aspects of clinical care; to offer our patients new and emerging therapies; to provide the best fellowships and training for

the future leaders of our field. Only by staying at the cutting edge can we continue to drive the field forward.

Carl D. Regillo is Chief of the Retina Service at Wills Eye Hospital.

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The background of the page is a stylized illustration. It features a teal roller coaster track winding upwards against a light blue sky with white clouds. At the top of the track, a roller coaster car is visible, with a large eye on its front. The track itself is composed of a grid of teal lines. In the center of the page, there is a large heart shape with a pink border and yellow dots. Inside this heart is a smaller heart with a pink border and yellow dots, which in turn contains a large, detailed eye with a blue iris and orange eyelids. A white paperclip is positioned to the right of the large heart. In the top right corner, there is a blue circle containing the word 'Profession' in white, followed by three lines of text: 'Your career', 'Your business', and 'Your life'.

Profession

*Your career
Your business
Your life*

46–49

Helping Ophthalmology
Residents Fall in Love

Tara A. Uhler, Laura J. Heinmiller
and John Cropsey share how the
residency program at Wills instills
competence, confidence – and a life-
long passion for the field

Helping Ophthalmology Residents Fall in Love

How the residency program at Wills Eye instills competence, confidence – and a life-long passion for the field and their careers

By Tara A. Uhler

Whatever students and residents might think on the road to becoming an ophthalmologist, medical school and residency do not last long. As Director of the Ophthalmology Residency Program at Wills Eye, I have the privilege of working with people in just a snapshot of their time across the whole medical educational spectrum – from undergraduate medical education (UME), through graduate medical education (GME), to continuing medical education (CME). For residents, training is just the beginning of the next step of their journey.

After internship, there are only three years in which we have to provide both a solid foundation, and a springboard for life-long learning and skill acquisition. And that is both a challenge and an opportunity. A former resident likened residency to a trip to a theme park: there are so many rides and not enough time to ride them all as often as you'd like – a good analogy. The ability to meet that challenge and opportunity is the shared mission of any training program. To succeed, we need all parties engaged at every level – and we are incredibly fortunate to have that at Wills Eye, and in ophthalmology in general. We

have eager trainees ready to soak up every minute of this time, and to take advantage of each experience; we also have a wide range of educators.

Applicants and advisors often ask what type of residents we want to train. More specifically, they ask what we hope our graduates will do. My answer: we want to equip residents to pursue whatever career they wish, and to do so with competence and confidence.

Ophthalmology trainees are life-long learners – and they need to be; our field changes quickly, and people change throughout training and their careers. What individuals want to achieve and specialize in, what technology and techniques are available, and how



“A former resident likened residency to a trip to a theme park: there are so many rides and not enough time to ride them all as often as you'd like.”

We Are Family

By Laura J. Heinmiller

I feel very fortunate to have completed my residency at Wills Eye Hospital, having graduated with the 2013 class. From watching the giants in our field shape the standards of care, to seeing the most diverse and unexpected cases in our emergency room, I graduated with a quiet confidence that I, too, could manage the toughest, most challenging patients with grace and expertise. There is no doubt that the education and experience you receive prepares you for your future – whatever path that may be. My co-residents have embarked on many different journeys from academia to private practice, to working with industry and creating their own hybrid models. The Wills education doesn't stop when you move on: I know I can always call on my mentors for a second opinion or advice, even halfway across the country.

However, the best part of Wills goes well beyond medical education. For me, it is the personal relationships and valuing the role of the family. It is a place where the fact that I was pregnant while interviewing and again as a chief resident was celebrated. I wasn't made to feel ashamed for wishing to grow my family. I remember interviewing at another program and asking about residents having children, to which one of the current residents replied, "We don't really do that here," which was a real eye-opener. Seeing Julia Haller, Kammi Gunton, Carol Shields and many other strong female role models thrive both as clinicians and mothers inspired me to follow my dream of having a large family, with five amazing kids. They epitomize my belief that you can in fact "have it all and do it well."



The people I met during my time at Wills remain some of my dearest friends today. These are deep, true friendships based upon a mutual effort and grind we put in to achieve our education and pursue our goals. Continuously working to cover for each other, juggling call schedules and clinic coverage, and always ending our days together in the clinic that was finishing last, ensuring no one left before all the work was completed. I suffered an unthinkable tragedy during my chief year at Wills, when my older brother suddenly passed away. I was immediately enveloped in support and allowed any and all flexibility to grieve.

I never once felt alone.

The friendships started at Wills are so strong because they come from respect and sacrifice. In fact, they are so meaningful that I named a child after my dear co-resident Mila and am honored to be godmother to her child. It goes without saying that the education you receive at Wills is second to none, but the true magic lies in the sense of family, support and encouragement that is woven throughout the hospital.

Laura J. Heinmiller practices pediatric ophthalmology at Park Nicollet Eye Care, Saint Louis Park, Minnesota, USA.

A Safe Bet

How the Wills Eye training program prepared me to set up an ophthalmic clinic in Sub-Saharan Africa

By John Cropsey

"I'll bet you a thousand bucks, you'll never move to Africa!" Those were the words of Bill Benson, retina specialist at Wills Eye, after asking me what I wanted to do with my life when I arrived for my first day on the Retina Service. My dream was to open an eye hospital in Sub-Saharan Africa that would be a center for training local eye care specialists. Wills had decided to roll the dice and take a chance on this crazy dreamer, and Benson felt the need to call my bluff, as he thought I had clearly hoodwinked the selection committee with a bit of snake oil.

Over a decade later, here I am, working full-time in Africa, and not a day goes by that I don't think of Benson and countless others who poured their lives into me at Wills Eye. The sky was the limit at Wills. If you were motivated, you could learn everything you wanted and needed from some of the best in the field, and have a total blast doing it.

I knew I would be seeing a lot of cancer in Africa, given my experience growing up at a mission hospital in Togo in West Africa. That's why, any time I had a chance, I'd try to catch a surgery with Jerry and Carol Shields, but it was a bit like the story of Zaccheus, trying to catch a glimpse through the crowds. There was always a massive entourage of fellows and visiting doctors gathered round, and I was just a lowly resident.

Miraculously, they would call me out of the crowd, have me scrub in with them and really let me get into the action. Today, our little eye clinic at Kibuye Hope Hospital in Burundi treats many patients with advanced cancer and provides the only retinoblastoma treatment center in the region with a population of 15 million. To this day, I write to Carol and Jerry Shields regularly for advice on tough cases.

On the other end of the spectrum, there is the bread and butter of eye care the world over, cataracts. Robert Bailey and Mark Blecher, the Directors of the Cataract Service, courageously allowed me to learn and then perform the first manual small incision cataract surgery (MSICS) at Wills. MSICS is the key to eliminating unnecessary blindness from cataracts in the world.

Then there is the bane of glaucoma, a huge problem that I face daily. Last week alone I operated on four young people, ranging in age from seven months to 27 years old, all presenting with cup-to-disc ratios of 0.99, with pressures in the 50s and 60s. I was most thankful for the many trabs and tubes I got to do under the supervision of George Spaeth and Marlene Moster, to name just a couple of great glaucoma specialists at Wills.

What really gets my heart rate going is when I have to venture into the territory of other specialties – like ENT

or neurosurgery – that don't exist here. When I'm doing an optic nerve sheath fenestration or trying to get a CSF leak to stop, that's when I'm thankful for spending time with unflappable, stone-cold surgeons like Jurij Bilyk.

Thanks to my training at Wills, Kibuye also offers the only corneal transplantation and vitreoretinal surgical services in the country – thanks to Sadeer Hannush and Joseph Bilson, respectively. My co-residents provided all the memories, and Tara Uhler and Julia Haller gave us this wonderful place to learn and thrive. Of course, I have to mention Brad Feldman for pioneering the Wills Eye Center for Academic Global Ophthalmology and its fellowship program.

And if you're curious to know: yes, Bill Benson was good for the thousand bucks!

John Cropsey is Professeur d'Ophthalmologie, Université Espoir d'Afrique, Chef de Service, Ophthalmologie, Hôpital Espoir de Kibuye in Burundi, Clinical Instructor at the University of Michigan Department of Ophthalmology and Visual Science, Adjunct Clinical Instructor at Wills Eye Hospital's Center for Academic Global Ophthalmology, and Adjunct Clinical Instructor at the Rwanda International Institute of Ophthalmology in Kigali, Rwanda.





“We all start out as pluripotent stem cells, and we should all retain the ability and need to adapt, evolve, and reinvent both ourselves and our profession as we develop.”

healthcare is delivered will continually evolve throughout our lives.

Of course, our training program cannot be everything to everyone, but we can provide the clinical and surgical foundation to support any career in eye care. We can provide the environment, opportunity, and introductions to support further future development and differentiation throughout the educational spectrum, across generations, and around the globe.

It is important to mention that we can only accomplish the above because of the incredible network of global, national and local organizations, and individuals that support us. The ophthalmology community is one huge collaboration of educators, mentors, innovators, patients, staff, donors, and volunteers at institutions and organizations supporting eye

training and eye health worldwide. Their individual and collective efforts allow us to provide all trainees with a solid foundation to pursue any career, including ones not yet imagined.

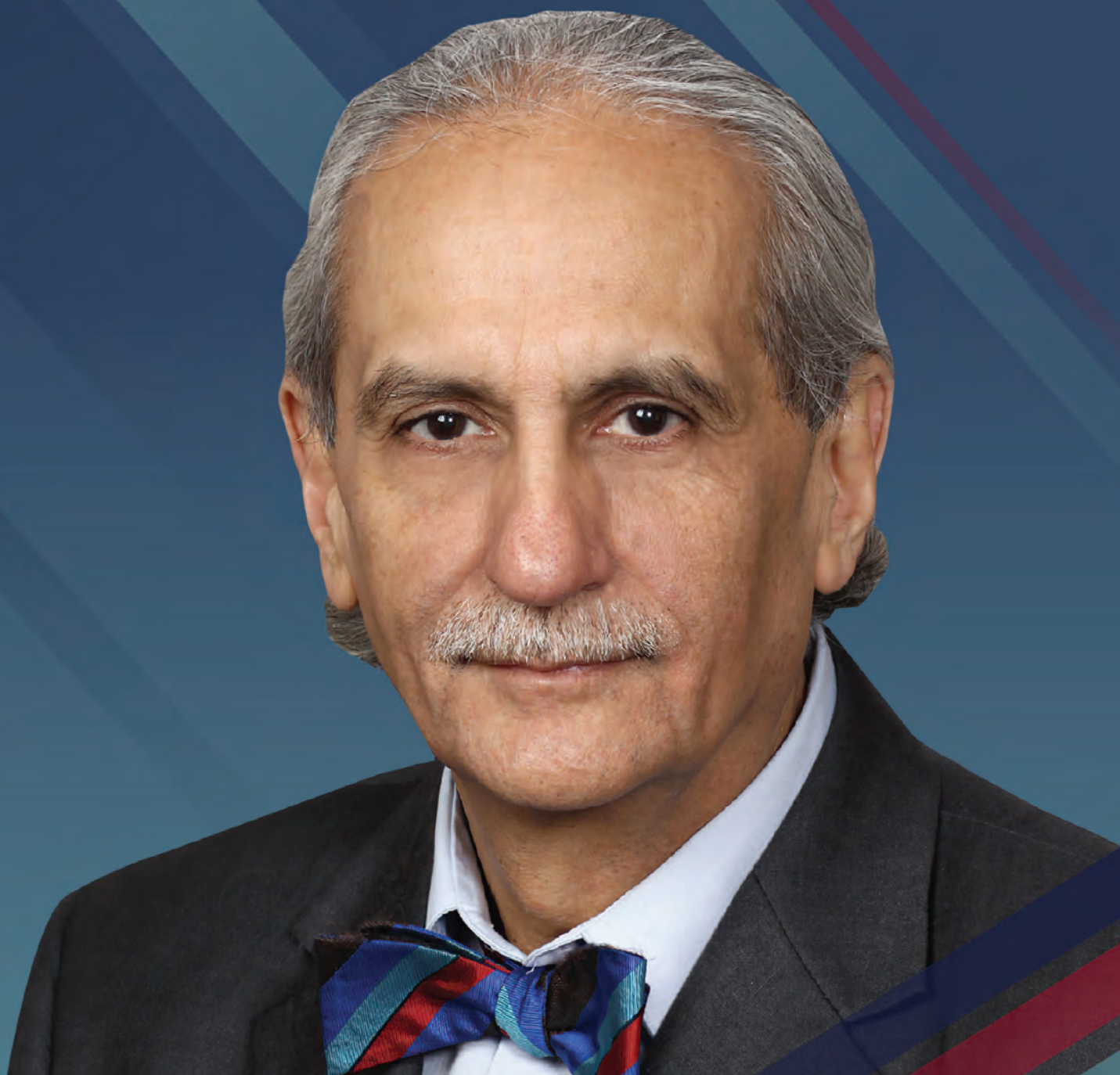
We all start out as pluripotent stem cells, and we should all retain the ability and need to adapt, evolve, and reinvent both ourselves and our profession as we develop. We hope our graduates use the foundation and opportunity they receive at the Wills Eye ophthalmology residency to fall in love with the field and their careers, over and over again.

Tara A. Uhler is Director of the Ophthalmology Residency Program at Wills Eye Hospital. She is also an Assistant Professor at Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, USA.



Rage Against the Dying of the Light

Sitting Down With... Jose Pulido, Larry A. Donoso Endowed Chair and Director of the Henry and Corrine Bower Memorial Laboratories for Translational Medicine, the Vickie and Jack Farber Vision Research Center at Wills Eye



Who were your mentors?

I was very lucky that, when I did my residency at the University of Illinois, an incredible group of people were based there who really shaped my career: Morton Goldberg, Gholam Peyman, Lee Jampol, Joel Sugar, and Gerald Fishman. They supported my aspirations and I have to credit them all.

What one piece of your research have you found the most rewarding?

I was a first-year resident during the AIDS crisis. People were dying from the disease, but they were first going blind from cytomegalovirus (CMV) retinitis. Many would tell me that they were more concerned about blindness than death – it was terrible. At that time, there was a new drug that had yet to be approved by the FDA, called BWB759U. It was being considered for systematic use in CMV retinitis cases, as well as CMV pneumonitis and gastrointestinal problems. It occurred to me that, if I could inject BWB759U directly into the eye, I might be able to help these people. With the approval of Morton Goldberg – then Chairman of the University of Illinois Hospital – and the help of Gholam Peyman and my future wife, Colleen Howe, we did some ERG studies on rabbits and showed that the drug would create very little toxicity. A patient who was rapidly losing vision wanted to receive the drug on a compassionate plea basis – and we managed to save his vision! That drug was subsequently named ganciclovir and went on to save the vision of countless others.

How rapidly did other clinicians follow suit and administer the drug to AIDS patients?

Pretty quickly. After we published the toxicity study, a doctor in Minnesota injected it into somebody else's eye and published on that, and it then became the way to do things. That's not to say there was no pushback. People said, "It can

be given systemically, so why inject it intravitreally?" The problem with systemic administration is that you struggle to achieve the levels of efficacy needed to rapidly diminish disease spread in the eye.

How quickly did you start to see an effect?

Patients noticed that their vision loss was halted almost immediately. It was transformative because it made me realize that this is what I want to do. This is how I want to spend my time – trying to improve peoples' lives.

Was that one of your proudest moments?

I've had a few others that are just as important, but I think this was the start of wanting to pursue academic translational medicine. In terms of key milestones, I would say that some of my most important work has been when I have caused a shift in how people think about – or take care of – a disease. My children choosing to go into medicine is another source of pride for me.

Have you seen a direct improvement in vitreoretinal lymphoma diagnosis and treatment?

Now that the disease can be detected earlier, we can use targeted drugs to combat it. Early diagnosis leads to early, local treatment instead of systemic treatments (and central nervous system involvement). Making the diagnosis earlier is very important for the patient's wellbeing and quality of life.

What are your predictions for the use of gene therapy in ophthalmology?

I think that we are always uncovering new frontiers – anyone who says there are no boundaries left is wrong! The more we cut down the brush, the more we see that there is still a lot to be explored. The important thing is to know the history; as George Santayana wrote, "Those who cannot remember the past are condemned to repeat it." The key is not to let prior history

"We are always uncovering new frontiers – anyone who says there are no boundaries left is wrong!"

taint how you move forward.

When I got into vitreoretinal lymphoma, people thought that it led to death within a year and not much could be done about it. Likewise, with CMV retinitis, people accepted that blindness was inevitable. To this day, I still remember a patient telling me that it was God's will. I hate that. I recall the Dylan Thomas line, "Rage, rage against the dying of the light." That's our duty.

You took up an endowed chair position at Wills Eye earlier in the year. What have been the highlights of working at Wills so far?

It has been great! We've already had a paper accepted with Carol Shields, Tatyana Milman, and a group in Austria on minimal residual disease in uveal melanoma. Tatyana Milman and I are discussing a new classification way to treat inflammatory eye diseases. It's yet another awakening for me.

What do you like to do outside work?

I exercise, I go walking with my wife, I listen to classical music, and I learn new things. My family is extremely important and I want to thank them for their support along the way.

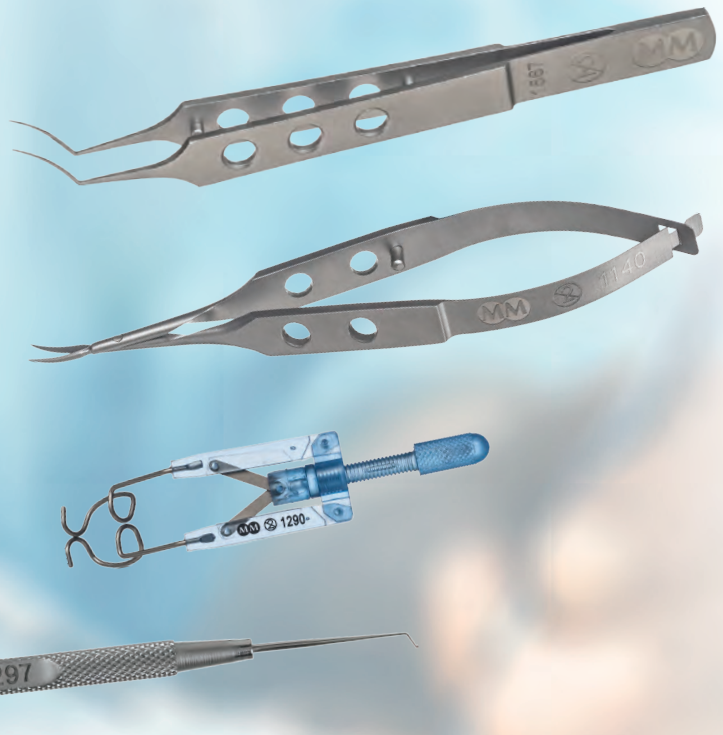
To read an extended version of this interview, go to top.txp.to/rage-against-the-dying-of-the-light



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