



New York
Eye and Ear
Infirmary of
Mount
Sinai

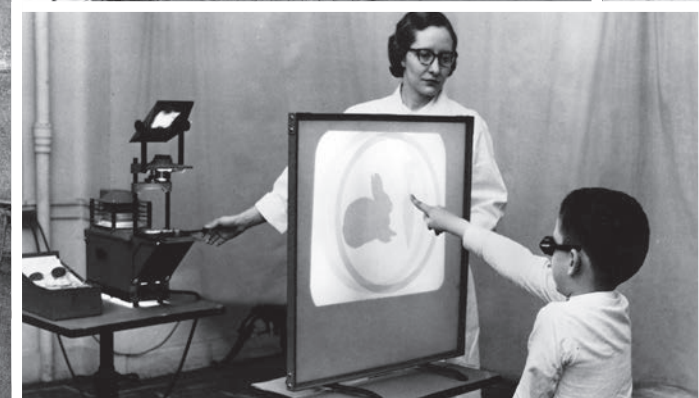
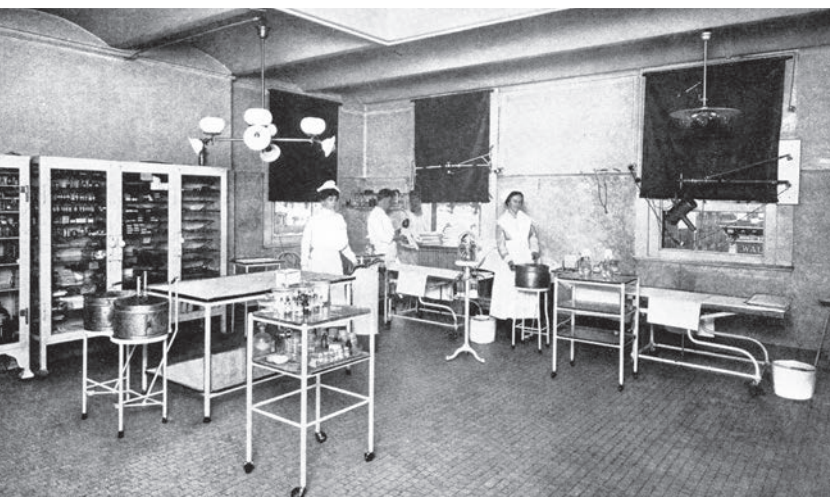
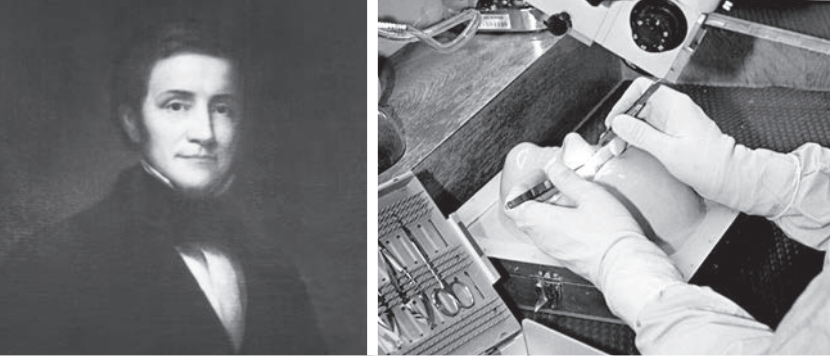
Department of Ophthalmology



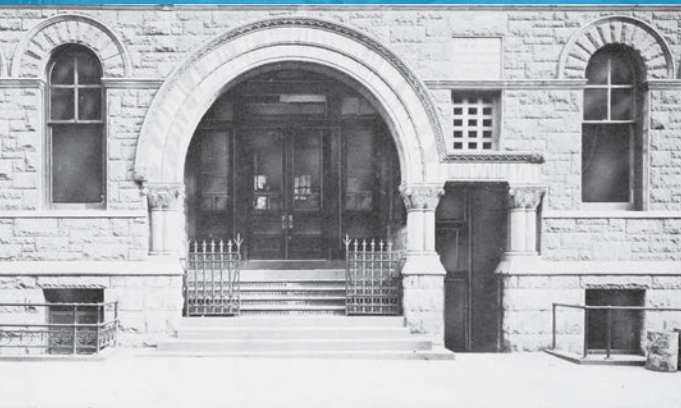
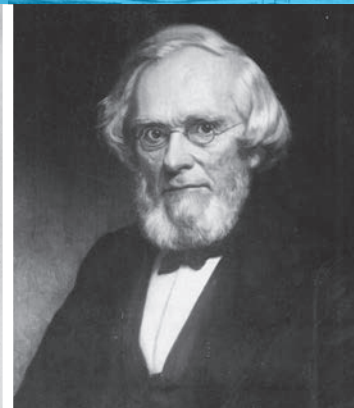
First Eye Hospital in America Turns

FALL 2020





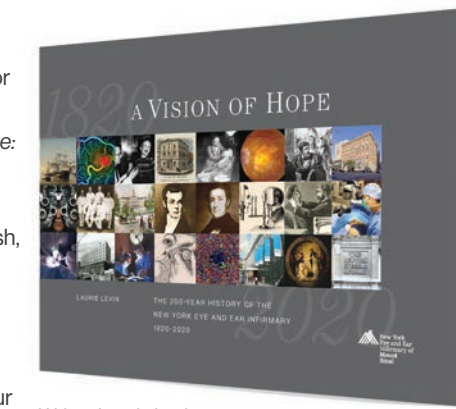
1820



A Defining Legacy of a Beacon of Hope and Help

New York Eye and Ear Infirmary's (NYEE) 200-year journey has not been an easy one. Wars, pandemics, and financial meltdowns: we have seen and endured them all. So perhaps it is fitting that an institution that has weathered the vicissitudes of history and the constant flux of the health care industry celebrated its bicentennial year in the trenches—fighting the worldwide outbreak of COVID-19 in the epicenter of the pandemic, New York City. While we were all looking forward to celebrating with friends and colleagues during numerous events, including the Bicentennial Gala Fundraiser in October, the restrictions on large gatherings due to the pandemic have caused us to postpone many of our plans until 2021. Despite the setback, NYEE faculty and staff marked our historic milestone with the publication of a history book and a dedication ceremony for a trailblazing physician.

NYEE's evolution into a leader in defining specialty surgical care for the rest of the country and the Americas has been deftly captured in the pages of the recently published history book *A Vision of Hope: The 200-Year History of the New York Eye and Ear Infirmary 1820 – 2020*. A passion project of Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System, and the late Joseph B. Walsh, MD, Professor and Chair of Ophthalmology for both NYEE and New York Medical College, the lusciously illustrated book weaves together a rich tapestry detailing the founding of the first specialty hospital in America and its growth to prominence—bringing to life people, places, and historic events that shaped our country and our institution and left a lasting impact on the fields of ophthalmology and otolaryngology.



Writer: Laurie Levin
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From the very beginning our future was tenuous, built on a dream of two young physicians, Drs. Edward Delafield and John Kearny Rodgers, freshly returned from their medical studies in Europe at the Royal London Ophthalmic Hospital (Moorfields Eye Hospital). Armed with the latest knowledge of eye diseases and guided by a deep sense of social responsibility, they believed that sight- and hearing-saving treatments could not only improve the quality of life but were often vital tools to lift patients from the grip of poverty and despair by restoring their ability to work. Therefore, New York City needed a charitable institution where people from all walks of life could receive the care they needed. And such a place would serve as a beacon of knowledge, allowing future generations of physicians to study among the best practitioners in the field, create innovative treatments, and carry forth their knowledge nationally and internationally. Despite the lack of interest from New York City authorities and the medical profession, they financed their charity personally and on August 14, 1820, the first specialty hospital in North America opened its doors in a two-room rental suite at 45 Chatham Square, now Park Row.

"Today, we and countless men, women, and children are the beneficiaries of this noble mission," said James Tsai, MD, President of NYEE and Delafield-Rodgers Professor and Chair of Ophthalmology, Icahn School of Medicine at Mount Sinai and Mount Sinai Health System. "And the Infirmary's legendary esprit de corps has fostered a deep sense of camaraderie and collegiality among physicians, nurses, and staff, creating a unique bond of purpose and

pride that has been a driving force for two centuries." It is not surprising that over the years NYEE attracted a roster of talented and driven clinicians and scientists with a deep love of humanity and commitment to patient care. And our illustrious history is highlighted by numerous firsts, scientific breakthroughs, a world-class training and educational program, and eminent alumni and faculty who have left their mark on the lives of patients at NYEE and the fields of ophthalmology and otolaryngology. While the community around the hospital has changed, NYEE remains an anchor, consistently delivering exemplary patient care—and hope—to those who need it most.

Reflecting on NYEE's history and its place in modern medicine, Dr. Rosen sees its ability not only to remain true to its founding mission but to inspire others and transmit its values and knowledge beyond its doors as one of NYEE's most enduring legacies. "Within a few years of our founding, many of NYEE's physicians began to export our

brand of expertise and helped pass it on to new institutions and departments of ophthalmology locally, nationally, and internationally, sharing the culture of caring and curing that they had learned here. New advances in anesthesia, surgical techniques, and clinical expertise to enhance patient care, and academic associations such as the American Ophthalmological Society, the New York Ophthalmological Society, and later, Association for Research in Vision and Ophthalmology and the Pan American Ophthalmology Association, were pioneered by our faculty."

While the next chapter in NYEE's history is yet to be written, the ongoing evolution of NYEE continues to enhance our ability to deliver superior patient care, outstanding clinical training, and groundbreaking research that is transforming the field of ophthalmology. "It's exciting to think about what we can do in the future with all the new technology available to us and backed by a major academic medical center," muses Paul Sidoti, MD, Chair of Ophthalmology at NYEE, and Chief of Glaucoma, Mount Sinai Health System. "We can really expand exponentially the effect that we've had in the past, touch even more lives, train even more physicians and make the experience we have here at NYEE available to many others, both physicians and patients."

The journey from a clinic in a two-bedroom rental suite to a world-renowned specialty hospital with an international reach surely surpasses our founders' wildest dreams for the Infirmary. There is no doubt that our greatest achievements are still to come, as the institution looks to the future, united by a commitment to healing and focused on making a meaningful impact on the lives of countless patients nationally and internationally.



Celebrating the Life of an Iconoclast: America's First Black Ophthalmology and ENT Specialist

On August 13, 2020, NYEE held a painting dedication ceremony to recognize a trailblazing physician who practiced at the New York Eye and Ear Infirmary, Dr. David Kearny McDonogh, America's first Black ophthalmology and otolaryngology specialist and protégé of our founder Dr. John Kearny Rodgers. "For the past 200 years, NYEE has been an incubator of the newest ideas, and it is clear that from its very beginning NYEE and its leadership were ahead of their time when it came to social and racial justice. This ceremony is a fitting tribute to both the man and the institution, working together, pushing against the forces of prejudice and fighting for justice and equity for all, regardless of their class, color, religion, or financial status," said Dr. Tsai.

Born into slavery in 1821, Dr. McDonogh fought the racial prejudices of his time to determine his own course in life. He was the first Black graduate from Lafayette College, finishing third in his class. Denied entry into New York medical schools, the aspiring physician attended classes at Columbia's College of Physicians and Surgeons unofficially, thanks to the support and mentorship of Dr. Rodgers. Unfortunately, upon his graduation in 1847, the college refused to award him a medical degree (an injustice that was rectified in 2018 by Columbia University as a result of a vigorous campaign by one of NYEE's esteemed physician faculty, Richard Koplin, MD). Nevertheless, with Dr. Rodgers's continuing support, Dr. McDonogh served on NYEE's staff as a specialist in diseases of the eye for 11 years and on New York Hospital's staff for two years, where he earned the respect of New York's medical establishment, which never failed to regard him as a full-fledged medical doctor. In league with Frederick Douglass, he became active in the abolitionist movement and a champion of workers' rights, equality, and providing health care for all. When Dr. Rodgers died in 1850, Dr. McDonogh took "Kearny" as his middle name, to honor the man who had opened doors when all others had been shut.

For Daniel Laroche, MD, the story of Dr. McDonogh has long served as a source of inspiration, a feeling he has put into action by establishing the National Medical Fellowships' Dr. David Kearny McDonogh Scholarship in Ophthalmology and ENT, whose mission is to diversify the medical profession—providing scholarships and support for underrepresented minority students interested in ophthalmology and ENT. "Dr. McDonogh is

an American hero who devoted his life to academic and medical excellence and helped to integrate colleges, and medical schools, and provide health care to all. His legacy is an important part of American history. Many of the issues he faced back in 1838 continue to be relevant today. While we have made progress by dismantling slavery and lawful segregation, we must all continue to work together to dismantle systemic racism, sexism, violence, plantation capitalism, and health care disparities," explained Dr. Laroche, Assistant Clinical Professor of Ophthalmology at the Icahn School of Medicine at Mount Sinai, and a cataract and glaucoma surgeon at NYEE. He and his wife, Marjorie, commissioned the painting, called "Tribute to David Kearny McDonogh, MD," by Leroy Campbell and donated it to NYEE.

Unfortunately, there are no known portraits of Dr. McDonogh. But this absence has allowed Mr. Campbell to capture something much more interesting than a mere likeness: his spirit. The abstract representation of Dr. McDonogh is intertwined with historical references to Impotep, the first named physician, an African from 2500 BCE; early cataract surgery being performed in the Nile Valley; abolitionism; and the progress of contemporary Black ophthalmologists in America today. Dr. Koplin, Co-Director of the Cataract Service at NYEE, also sees bigger meaning in the painting. "Perhaps it is fitting that we have no image of Dr. McDonogh. The painting of the black man being presented today is not David McDonogh, but more importantly, he might be considered an avatar, the embodiment of the young men and women of color who aspire to join our profession."

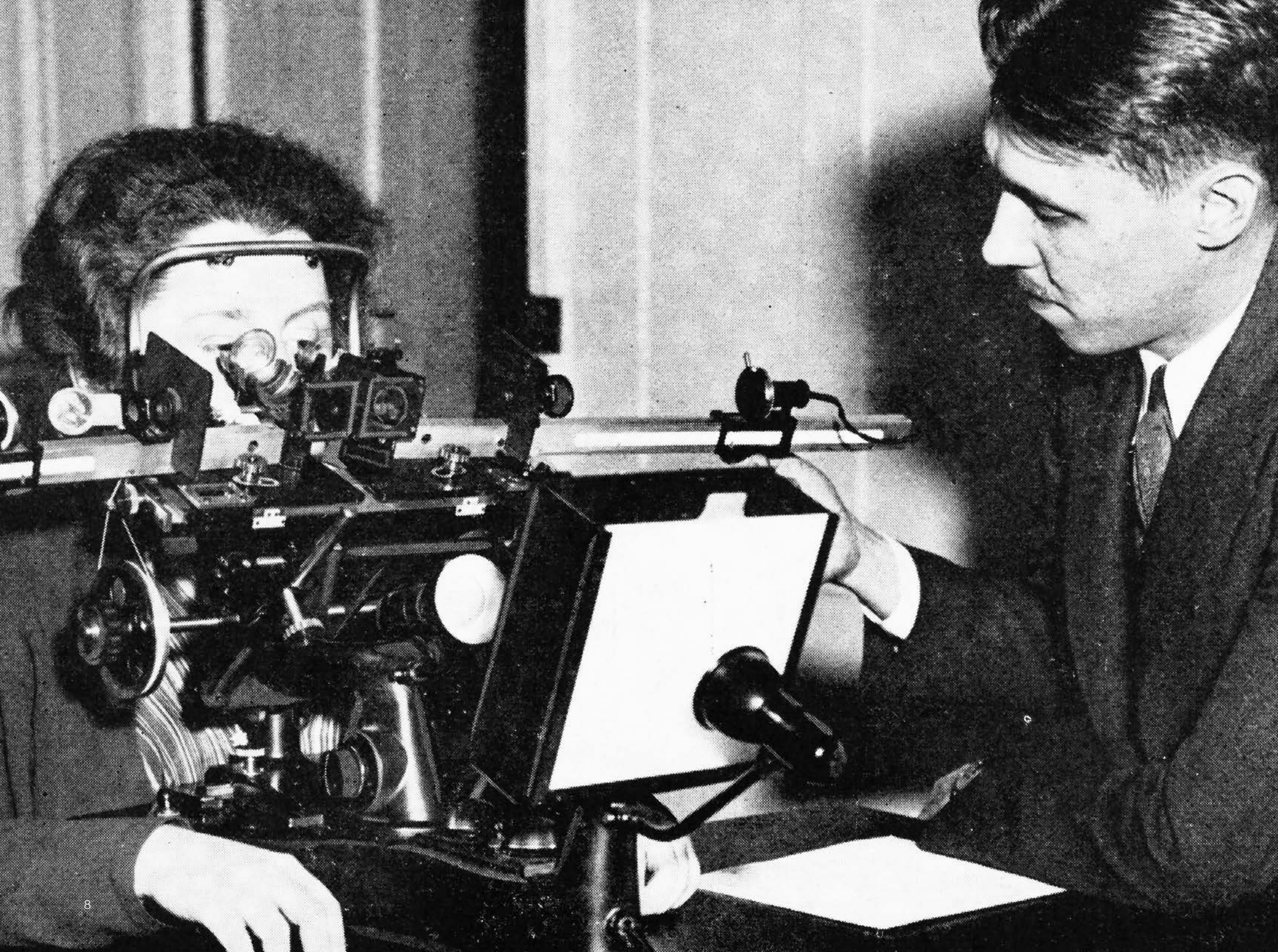
The moving tribute was concluded by the unveiling of the painting, which will remain on permanent display in NYEE's new waiting room area. As NYEE looks toward the next century of specialty care—during a watershed moment in American history that is seeing a global movement toward equity in all aspects of life, including health care—we know that the next 100 years will indeed be better. "Great things, seemingly impossible things are accomplished when we combine our efforts and support one another. Dr. McDonogh's life and legacy continue to illuminate the path forward for us all," affirmed Tameisha Frempong, MD, MPH, Vice Chair for Diversity and Inclusion, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai. Certainly NYEE's founders, Drs. Delafield and Rodgers, believed that change for the better was possible—and so does the current leadership 200 years later.



"Dr. McDonogh is an American hero who devoted his life to academic and medical excellence and helped to integrate colleges, and medical schools, and provide health care to all. His legacy is an important part of American history."

—Daniel Laroche, MD

Painting dedication ceremony at NYEE. Featured James Tsai, MD, Daniel Laroche, MD, and Tameisha Frempong, MD unveiling the portrait of Dr. McDonogh during the COVID-19 pandemic.



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Left: In 1934, NYEE acquired New York City's first eikonometer.



The safety of our community is our highest priority; some images herein were taken prior to February 2020.

Message From Department of Ophthalmology Leadership Icahn School of Medicine at Mount Sinai Mount Sinai Health System

The concurrence of the New York Eye and Ear Infirmary of Mount Sinai (NYEE) bicentennial and COVID-19 reinforces, more than we could have ever imagined, our treasured roots as a provider of world-class ophthalmic care to the local community, coupled with the dramatic changes we are making to put technology and research at the center of how we deliver our services to an expanding universe in challenging new times. That we are carrying out this transformation while remaining steadfast to our long-standing mission is a source of tremendous pride and satisfaction to all of us who are truly in awe of this remarkable institution as we begin our third century.

The pandemic that struck in March and forced NYEE to shut down most non-emergent patient services catapulted to the forefront several new modalities already under development. The most important is telemedicine. To reduce potential exposure of our staff and patients to the coronavirus, we began replacing visits to our busy walk-in clinic in downtown Manhattan with scheduled video and telephone conferences between patient and physician. The vigorous embrace of this format by all parties is now setting the stage for a paradigm shift in how we bring our services to patients. That transition will be increasingly driven by emerging technologies that allow for accurate and portable imaging of the back and front of the eye from remote locations, and by artificial intelligence (AI), which will pave the way for faster decision-making without the need for a physician to always be present.

Building on our role as an innovator in American ophthalmology for the past two centuries, NYEE is already in the forefront of exploring the vast potential of telemedicine, particularly its use in minimizing in-person examinations in hospital and urgent care settings as well as in identifying high-risk patients. To that end, we are piloting several programs aimed at improving ophthalmic care in emergency departments, through a unique program of tele-consults, as well as at primary care offices to capture patients at high risk of diabetic retinopathy while they are undergoing routine exams. In addition, a concerted effort is underway to analyze and convert physician visits to diagnostic visits, to better triage patient volume in the clinics and allow providers to focus on acute cases. This telemedicine-driven approach could provide a template for transforming ophthalmic care at hospitals and clinics and allow NYEE to extend its expertise well beyond our receiving area, in remote facilities in New York and other states that don't have ready access to an ophthalmologist.

Our reputation for excellence in clinical care and research is providing a platform to actively pursue in 2020 another technology expected to take ophthalmology in a bold new direction: the microsurgical robot. The first robotic interventional system for ocular surgery in the United States (and only the third in the world) arrived this summer from its European developer at our Jorge N. Buxton, MD, Microsurgical Education Center, a national center of excellence for ophthalmic surgical training. By increasing tenfold the precision of microsurgical procedures, the robot will open the door to future applications



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that transform the fields of retina, cornea, cataract, and glaucoma surgery. A team of experts from NYEE will begin exploring the exciting possibilities through a variety of investigational trials aimed at securing FDA approval.

Research from our labs over the past year showcased other ways we are advancing diagnosis and treatment of some of the most serious eye disorders. For example, we developed for the first time a series of AI-driven models able to identify patients at risk of adult macular degeneration (AMD), as well as those who are likely to progress to late-stage AMD in one to two years, with 86 percent accuracy. Another study uncovered more than 120 genes for primary-open angle glaucoma which could serve as valuable markers for early diagnosis, especially in individuals who are shown to have a more aggressive form of the disease.

As we look beyond our bicentennial, the next decade will bring change unlike any we have seen in the past. NYEE is committed to not just being part of but playing a leadership role in that transformation. We will, of course, continue to serve as the hub for outstanding care to the community from our time-honored home at

Second Avenue and 14th Street. But more than ever, the focus will be on broadening the enterprise by taking our specialized brand of ophthalmic services and expertise to more patients, wherever they are. Backed by lessons learned from COVID-19, we will intensify our regional, national, and even international reach, leveraging our partnership with the Mount Sinai Health System to impact individual patient care as well as entire populations through our cutting-edge research, technology, and training of tomorrow's leaders.

For all of us who have proudly enveloped ourselves in the culture of NYEE, the changes on the horizon will do little to diminish our commitment to the ideals that led 200 years ago to the birth of America's first specialty hospital to meet the needs of New York City's population. Our link to the community remains stronger today than ever, as seen, for example, in the robust family of local physicians who regularly volunteer their time and skills to train our residents. This is indeed a time to be proud of what our founders created, but also of what thousands of dedicated people over the years have molded into one of this country's true medical gems. Part of the legacy is recognizing that our work is never done. In fact, it's only beginning.

NYEE Warmly Welcomes the Newest Addition to Its Staff: a Robot

The journey from Amsterdam to New Amsterdam on the 200th anniversary of New York Eye and Ear Infirmary of Mount Sinai (NYEE) couldn't have been more symbolic. America's first micro-interventional robot for ophthalmic surgery became the newest arrival from the Netherlands to the shores of New York this past July—a genuine cause for celebration by its new hosts.

"The significance of the moment was not lost on us," acknowledges Tsontcho (Sean) Ianchulev, MD, MPH, Professor of Ophthalmology at the Icahn School of Medicine at Mount Sinai, who was among the robot's jubilant greeters. It was Dr. Ianchulev's six-year collaboration with the creator of the device, the Dutch medical robotics company Preceyes BV, and a grant from the RICBAC Foundation to the two principal investigators, Dr. Ianchulev and Joseph Panarelli, MD, that brought this project to fruition to advance innovation and excellence in care at NYEE, not far from the site of the early Dutch colony that would eventually become New York. "Because the robotic assistant can increase the precision and resolution of surgical interventions by 20 to 30 times, it will open a new chapter for micro-interventional ophthalmic surgery in this country and globally," said Dr. Ianchulev. "This is the first ophthalmic clinical microsurgical robotic eye system in the United States, and only the third one in the world, along with the ones at Oxford (England) and Rotterdam (Netherlands)."

Before that can happen, however, much work remains. Partnering with engineers from Preceyes is a team of ophthalmic surgeons from NYEE who are collecting data necessary for the U.S. Food and Drug Administration (FDA) to approve clinical use of the device. Potentially it will have applications in the fields of retina, cornea, cataract, and glaucoma surgery. The first trial, expected to begin next year, will use the robot in retinal surgery, whose micron-level demands on hand movement push even the best surgeons to their physical limits. "The stability of even a master surgeon's hands is in range of a 100-micron tremor, which comes from just the blood pumping through your fingers," points out Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System and Vice Chair and Director of Ophthalmic Research at NYEE. "With the robot, that tremor is reduced to between one to two microns."

"This is the first ophthalmic clinical microsurgical robotic eye system in the United States, and only the third one in the world, along with the ones at Oxford (England) and Rotterdam (Netherlands)."

—Sean Ianchulev, MD



Left to right: Jun Lin, MD, Richard Rosen, MD, Sean Ianchulev, MD, Gautam Kamthan, MD and the Dutch team from Preceyes installing the microsurgical robot in the Jorge N. Buxton, MD, Microsurgical Education Center at NYEE.

That uber-precision has ophthalmologists excited about the surgical prospects. "It could enable the most complex surgical manipulations, like intraoperative cannulation of the retinal veins, gene therapy, and stem cell delivery to the sub-retinal space that could potentially treat blindness," explains Dr. Ianchulev, who is Director of the Ophthalmic Innovation and Technology Program at NYEE. "We've also started developing a module for micro-interventional glaucoma and have identified the robot's potential for corneal refractive and cataract procedures."

Microsurgical robot connected to the EyeSi virtual surgical simulator in the Buxton Microsurgical Center where ophthalmic surgeons and trainees can practice epiretinal membrane peeling.

Once the robot is cleared by the FDA, NYEE expects to initially employ the device for epiretinal membrane peeling, a delicate procedure to remove micron-thin sheets of cells that grow over the macula, distorting its surface and greatly reducing central vision in many common retinal diseases. This is the same surgical procedure for which the mechanical device won approval from European regulators last year.

The robotic assistant, emphasizes Dr. Rosen, is still in its early-stage development, with clinicians from NYEE teaming up with engineers from Preceyes to help realize its full potential. One plan is to add instrumentation that would marry the robot to intraoperative OCT. According to Dr. Rosen, this capability would "act like machine eyes so the robot could potentially navigate within a three-dimensional space." Another marriage could be with artificial intelligence (AI), allowing the machine to not just perform as an extension of the human hand, but to actually add accident avoidance features like those being added to many cars. Adds Dr. Rosen, "We're really taking the first baby steps in what we anticipate will be a total revolution in how we do increasingly complex surgical reconstruction of damaged retinas."

As part of the learning curve, NYEE has already connected the robot to the EyeSi virtual surgical simulator in the Jorge N. Buxton, MD, Microsurgical Center, where surgeons train in a safe state-of-the-art environment before transitioning new procedures to patients. The robot's team even talk of eventually including training for fellows and residents, giving the hospital's residency program an experience available nowhere else in the country.

Going forward, the robot is envisioned as the cornerstone of a new national center of microsurgical excellence in ophthalmology and the launchpad for robotic eye surgery at NYEE and in the United States. The robotic surgical program headed by Dr. Ianchulev will be one of the main pillars at the NYEE center of innovation which will lead the institution into its new century along with new initiatives in intelligent diagnostics, micro-interventions, and targeted therapeutics.



Microsurgical robot in use with an eye model in an intraoperative training scenario.

The Secret World of Ocular Melanocytes Revealed

Ophthalmologists usually associate melanocytes with the production of melanin, which gives color to the iris, ciliary body, and choroid. Little else was known about the distribution or functionality of ocular melanocytes, partly because they have been difficult to culture and study. Research from the lab of Dan-Ning Hu, MD, Research Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai, has been slowly lifting the veil, revealing that melanocytes play an important role in various physiological and pathological processes in the eye, including secretion of various growth factors, cytokines, chemokines, and proteinases involved in tissue remodeling, angiogenesis, immune reaction, and inflammation. These functions suggest that they may also play a larger role in uveitis, glaucoma, age-related macular degeneration, and myopia than was previously appreciated.

The latest work from Dr. Hu's lab involves a study of scleral melanocytes, which was recently published in *Current Eye Research* (May 2020). That study reports for the first time on the topographic distribution of scleral melanocytes within the fibrous tissue of the sclera—where they reside along with fibroblasts—and their concentration in the posterior sclera, with particular implications for myopia. "Scleral melanocytes perform various functions related to inflammatory disease in the sclera and may be involved in the development of myopia," says Dr. Hu, lead author of the study, who began investigating ocular melanocytes 30 years ago in the Tissue Culture Center he developed at New York Eye and Ear Infirmary of Mount Sinai (NYEE). "Because of their diverse functions, they could pose a new target for the prevention and treatment of disease of the sclera."

One of the study's most intriguing findings is that scleral melanocytes are largely present only in the posterior sclera. Cell density of scleral fibroblasts, by comparison, is relatively constant in different regions of the sclera. This topographic concentration may be relevant to the aberrant remodeling of the sclera in myopia, which results in excessive elongation of the axial length. This process mainly involves the posterior

pole of the eye. "Scleral weakness can be the result of degradation of the extracellular matrix in the sclera," explains Dr. Hu, adding that clinical and animal studies have found that a special kind of proteinase, matrix metalloproteinase (MMP-2), plays an important role in the development of myopia, while human uveal melanocytes have been shown in other studies to produce high levels of MMP-2. Since scleral melanocytes derive from the uveal tract and may function similarly to uveal melanocytes, NYEE researchers have hypothesized that they could be involved in the remodeling and weakness in the sclera that's characteristic of certain severe forms of myopia.

Researchers believe the similarity between uveal and scleral melanocytes could have implications for other ocular pathologies. For example, the toxic or inflammatory substances produced by microorganisms like bacteria, fungi, or viruses that attack the eye stimulate uveal melanocytes to secrete different types of cytokines and chemokines which may trigger an immune reaction. This process includes attracting various immune cells from the blood to eliminate invading pathogens, which is critical for fighting ocular infectious disease. Occasionally, however, scleral melanocytes, through their secretion of cytokines and chemokines, may trigger an intense inflammatory or autoimmune reaction referred to as scleritis.

"We still have a lot to learn about melanocytes, but this study represents a big step forward by measuring and documenting for the first time the clustering of notable numbers of melanocytes in the posterior sclera," points out Richard Rosen, MD, Vice Chair and Director of Ophthalmology Research for NYEE and a co-author of the study. "Our research, when viewed in light of other studies showing secretion of various cytokines, chemokines, and MMPs by melanocytes, suggests these cells may play a role in various disorders of the sclera that was previously unknown."

Microscopic view of scleral melanocytes and fibroblasts in different areas of the sclera (stained by hematoxylin-eosin x400).

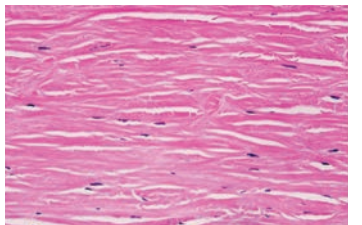


Fig. 1

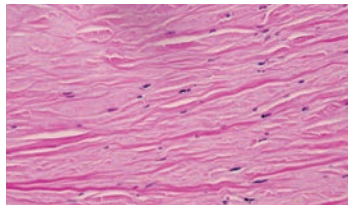


Fig. 2

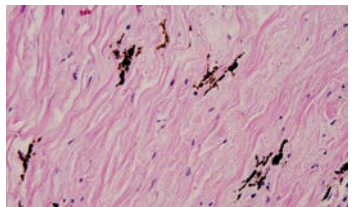


Fig. 3

Only fibroblasts can be observed in anterior area (Fig. 1) and equatorial area of the sclera (Fig. 2).

Both melanocytes and fibroblasts can be observed in the posterior area of the sclera (Fig. 3).

NYEE's Trauma Team Works Its Magic On a Patient's Eye-Shattering Injury

In a terrifying instant, a deer head mounted on the wall of a backyard workshop became a flying projectile that radically changed Matthew Dzierzanowski's world. When the deer head was dislodged by a tarp that Mr. Dzierzanowski mindlessly flung over his shoulder, his first thought was for the safety of his two-year-old daughter, who was by his side. Only then did the horror of what had occurred—the pointy tip of the deer antler had plunged directly into his left eye, piercing the cornea, sclera, iris, lens, and retina—begin to register through the unbearable pain. “An extremely scary situation got scarier by the second,” remembers Mr. Dzierzanowski, describing how he crawled on his knees the short distance back to his house in upstate New York with his daughter in tow. There, he confronted his petrified wife, Gina, who immediately summoned an ambulance.

By the time Ronald Gentile, MD, a retinal surgeon at New York Eye and Ear Infirmary of Mount Sinai (NYEE), saw the patient and his wife in his Manhattan office, they had endured a harrowing five weeks following the May 2019 accident. Mr. Dzierzanowski had been emergency airlifted to Westchester Medical Center, where a team of surgeons closed the 10 mm wound, but said he had no better than a slim chance of saving vision in the eye. He was advised to find a retinal specialist, and when his wife approached a relative at Mayo Clinic for a recommendation, Dr. Gentile's name headed the list of surgeons who could give the 49-year-old his best shot at seeing again.

Still battling intense pain and headaches and seeing nothing more than blackness from the damaged eye, Mr. Dzierzanowski, a conductor for Metro-North Railroad, recalls that first visit with Dr. Gentile as “a marriage made in heaven,” adding, “he really took charge, explaining everything in clear terms, and giving me a fighting chance, without promising anything.”

For Dr. Gentile, Co-Director of Posterior Segment Trauma for NYEE's Eye Trauma Service who has honed his skills on the toughest of the tough cases, Mr. Dzierzanowski was anything but business as usual. “In cases when the globe of the eye is damaged and the injury hits the retina, there's a high likelihood blindness or substantial loss of vision will result,” he explains. “In Matt's case, the antler perforated his eye and sliced the cornea in half. The only part of the eye that wasn't

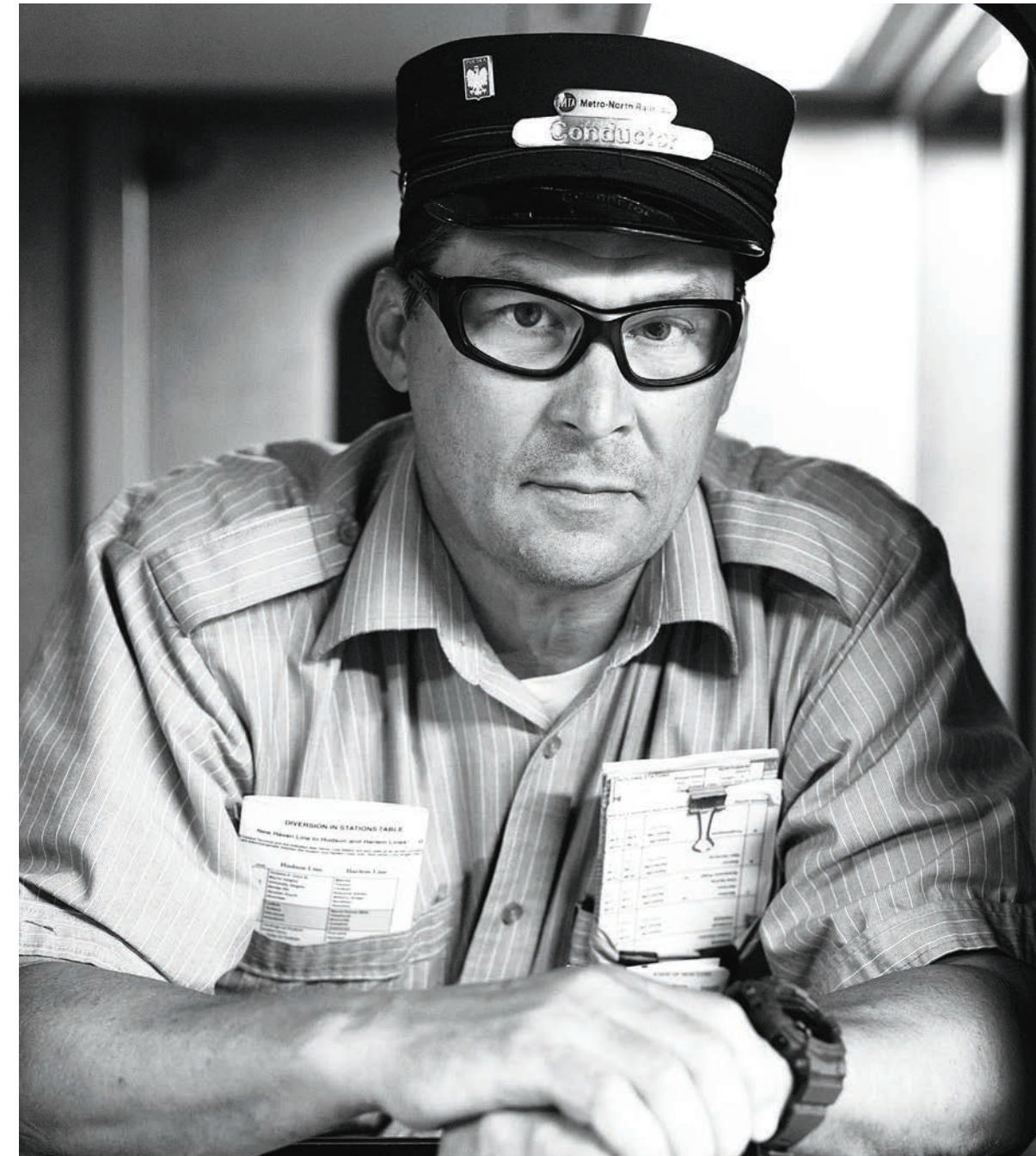
injured was the optic nerve. This was a pretty devastating injury—one of the worst I've seen. His chance of recovering useful vision from the injury was less than 2%.”

On June 13, Dr. Gentile began the intricate repair of the internal tissue of the eye. The immediate task was addressing the blood that filled the eye, a not-uncommon condition after trauma where the blood vessels rupture and the retina cannot be visualized. “Typically, I use a vitreous cutter and very fine forceps to uncover the retina and repair it, combined with laser surgery to allow the retina to seal back in place,” explained Dr. Gentile. But this case went well beyond standard repair: the tip of the falling antler had perforated the retina and eyeball, forcing retinal tissue and vitreous gel into the wound site. The delicate six-hour procedure to reattach the retina included removing not just this debris and blood but scar tissue that developed as the retina tried to heal itself, and also involved suturing a scleral buckle to the outside of the eyeball, which gently pushed it against the detached retina.

The surgery was revealing to Dr. Gentile in a crucial way. “When you start to do internal reconstruction and see that the optic nerve and the macula aren't damaged, it gives you hope that the patient has a chance,” he explains. In Mr. Dzierzanowski's case, that revelation came one hour into the procedure. The next morning, when Dr. Gentile removed the patient's bandages, his hunch proved well-founded. “As soon as they came off, I was able to see what resembled a gentleman sitting in the room,” Mr. Dzierzanowski recalls. “I could start to see shapes and colors out of the eye, and while they weren't all that clear, after months of darkness it was very exciting.”

The patient's rehabilitative journey was just beginning, though. Joining the trauma team now was John Aljian, MD, a cornea specialist and Co-Director of Anterior Segment Trauma for NYEE's Eye Trauma Service. He began removing sutures from the lacerated cornea and sclera that had been stitched up like a baseball in an earlier surgery for globe and corneal laceration repair, which had been rubbing against the eyelid causing a great deal of pain. Months of suture removal was not enough, though, to keep the cornea from decompensating, and on December 12, Mr. Dzierzanowski underwent his second major surgery, this one a corneal transplant.

continued on page 18



“When you start to do internal reconstruction and see that the optic nerve and the macula aren't damaged, it gives you hope that the patient has a chance.”

—Ronald Gentile, MD

Mr. Dzierzanowski back to work as a train conductor at Metro-North Railroad following his eye trauma.



Left Eye Trauma Overview

- Central curvilinear corneal laceration of 10 mm in length extending 2 mm past the 9 o'clock limbus
- 360-degree subconjunctival hemorrhage
- The wound was shelved superiorly with iris tissue prolapse
- Shallow anterior chamber with hyphema and inferior iridodialysis
- Intumescent lens

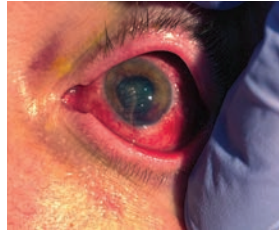


Fig. 1A: Left eye after emergency surgery at Westchester Medical Center to close the 10 mm wound.



Fig. 1B: Mr. Dzierzanowski recovering at Westchester Medical Center after surgery at NYEE to close the eye wound.

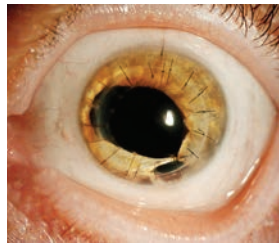


Fig. 2: Left eye after the last surgery at NYEE showing the reconstruction of the iris and pupil with a beautifully clear and successful corneal transplant.

Side by side in the operating room were Drs. Aljian and Gentile, who did their residency together at NYEE some 25 years earlier. This time the mission was to concentrate the highest level of subspecialty care possible in the same suite—a collaboration rarely seen outside a small number of major ophthalmic centers. Dr. Aljian first removed the badly scarred cornea and sewed a temporary artificial one, a keratoprosthesis, in place. This gave Dr. Gentile a clear view of the retina so he could now do additional internal repairs, including excising recurrent scar tissue on the retina, removing silicone oil that had been injected into the eye during the original retinal detachment surgery, and fixing the damaged iris. Dr. Gentile's work finished, Dr. Aljian removed the temporary cornea and replaced it with a permanent, wafer-thin live tissue donated corneal graft. Two hours later, the procedure was complete.

The outcome was better than anyone—doctors or patient—expected. "After Christmas, everything began to fall into place," says Mr. Dzierzanowski. The graft had taken, the pain subsided, and his vision gradually improved. For Dr. Aljian, a follow-up visit by Mr. Dzierzanowski in February, two months after the corneal transplant, convinced him a remarkable recovery was underway. He refracted the patient with a regular spectacle lens to 20/40 in the left eye, which improved even further to a remarkable 20/20 when a rigid, gas-permeable contact lens was placed in the eye to replace the natural lens that had been shattered and removed after the accident. Plenty of challenges remain, of course. Short-term, they include controlling the traumatic glaucoma that developed, monitoring the cornea for signs of rejection, and making sure the retina stays attached. Longer term, there is the possibility of an artificial lens implant—a procedure deemed too risky now because of the inflammation it might trigger.

Meanwhile, Mr. Dzierzanowski's life is returning to a place he thought impossible just a year earlier. He is back to his job with Metro-North, is driving again in the daytime, and has been given the green light for non-strenuous sports. "My progress in such a short time has definitely been extraordinary," he acknowledges, "but I knew early on I had the chance to do this with the help of two of the best surgeons any patient has ever had."



Left to right: John Aljian, MD, Ronald Gentile, MD, and Mr. Dzierzanowski during an office visit following his corneal transplant.

Macrophage-Like Cell Imaging Opens a Bold New Window on Retinal Disease

Macrophage-like cells are known to play an important role in immune surveillance in retinal disease, altering their shape, density, and distribution in response to external and internal threats like injury and infection. As reported in the June 2020 issue of *Investigative Ophthalmology & Visual Science* (IOVS), researchers at New York Eye and Ear Infirmary of Mount Sinai (NYEE) have now opened a revealing new window on how these cells respond and undergo morphological activation by imaging them in the eyes of patients for the first time using commercial spectral domain optical coherence tomography (SD-OCT).

This technology has enabled the NYEE team to visualize in the *en face* perspective how two cell types that are members of the macrophage family—microglia and hyalocytes—react to control intrusions in their environment, regulate immune reactions, and effect tissue repair. "We have been able to see how these cells move around and appear to respond to different types of retinal vascular disease, something we have never seen before in actual patients," notes Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System and co-author of the IOVS study. "This cellular level imaging has allowed us to see actual changes in the shape and spatial distribution of these macrophage-like cells as they become activated."

Indeed, NYEE researchers have imaged redistribution and altered morphology in the macrophage-like cells of patients with various retinopathies. These cells appear to aggregate toward the surface of both larger and smaller blood vessels, reducing their density in the neighboring unaffected areas. By better understanding and characterizing the patterns of change these cells undergo, clinicians may be better able to correlate them with activity of various retinal diseases, according to Dr. Rosen, who also serves as Vice Chair and Director of Ophthalmology Research at NYEE. "They could potentially be used as biomarkers of early activation or inflammation within the retina," he points out. "By seeing changes in the distribution of these cells, for example, we will be able to detect early retinal involvement

patients with diabetes before there are more macroscopic signs of retinopathy, such as microaneurysms."

Prior studies of retinal macrophages have been performed predominantly in animal models, and used only OCT B-scans or *en face* OCT reflectance imaging with relatively thick retinal layers or slabs, making it difficult to recognize these cells. "We developed an image processing approach in our lab that examines a very thin slice at the retinal surface enhanced by color-coded overlays of the macrophage-like cell layer and retinal vascular network," explains Yuen Ping Toco Chui, PhD, Director of the David E. Marrus Adaptive Optics Imaging Laboratory and Associate Professor of Ophthalmology at the Icahn School of Medicine at Mount Sinai. "This novel technique has allowed us to isolate the macrophage-like cells from background tissue, and visualize their spatial relationships to surrounding structures."

Those relationships—in the form of abnormal macrophage-like cell accumulation, movement, and clustering—could provide valuable clues into the activity of retinal pathologies such as glaucoma, diabetic retinopathy, optic neuropathy, retinal detachments, and age-related macular degeneration. In the case of hyalocytes, the immune cells residing in the vitreous gel, OCT imaging could afford scientists new insights into photocoagulation, hyperglycemia, pre-retinal membrane formation, and vascular endothelial growth factor secretion.

"We're still at a very early stage of macrophage-like cell imaging, but OCT is allowing us to visualize, with equipment that's standard in thousands of clinics and labs worldwide, things that previously could only be seen in a few research centers," says Dr. Rosen. "And that could potentially allow clinicians in their offices to one day make more informed decisions on the best ways to monitor and treat their patients."

Clinical *en face* OCT image of individual macrophage-like cells and associated retinal blood vessels in a human subject. The fovea is located to the left of all images.

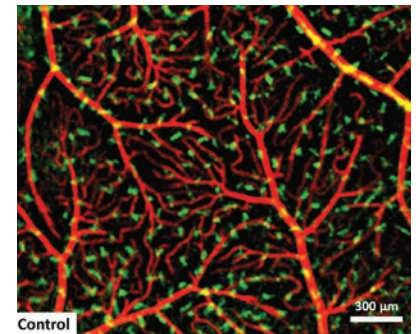


Fig. 1: Macrophage-like cells (green) superimposed upon superficial retinal vascular network (red) showing their regular distribution in a healthy control.

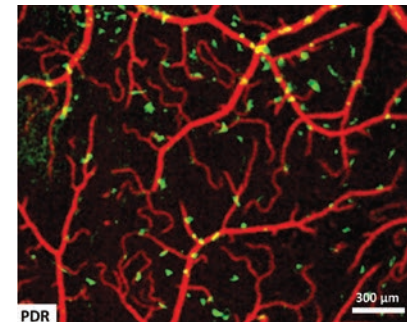


Fig. 2: Non-uniform distribution and altered morphology of the macrophage-like cells in a patient with proliferative diabetic retinopathy.

Reimagining Telemedicine For a New Era of Patient Care

As COVID-19 was shutting down most non-emergent ophthalmic care this spring, telemedicine emerged overnight as a mainstream way for patients to access our services. Scheduled video visits and telephone calls became valuable social distancing tools to reduce coronavirus exposure to physicians, staff, and patients at our high-volume walk-in clinic in downtown Manhattan, while allowing for quicker and more effective triage of patients. Telemedicine is here to stay and as Louis Pasquale, MD, Chair of Ophthalmology, The Mount Sinai Hospital and Mount Sinai Queens, observed, "Patients love the dynamics of visits that start on time, don't require any travel or parking, and give them the undivided attention of their physician."

Thanks to the overwhelming acceptance of telemedicine by patients and providers alike, New York Eye and Ear Infirmary of Mount Sinai (NYEE) is committed more than ever to bringing innovative new applications and technologies to everyday clinical practice and making it a permanent part of the patient service. Following are several ways in which our efforts are already making a difference in patient care:

Emergency Room Consults

Few emergency rooms come equipped with an on-site ophthalmologist—a disconnect that often leads to considerable waits for an on-call specialist to arrive to treat trauma or other severe eye injuries. A telemedicine-driven project underway in the ERs at several hospitals is now offering a highly promising new model. The pilot at Mount Sinai Morningside and Mount Sinai West is streamlining emergent care through a system of tele-consults between the ER doctor and an off-site ophthalmologist from NYEE.

The program is coordinated through a Mount Sinai command center, which alerts the

ophthalmologist to an emergency consult, provides information from the treating physician on the nature of the case, and then connects the ophthalmologist via video or telephone directly to the physician. The center also allows the consultant to log onto a special high-magnification camera embedded in the ER. This device lets the off-site physician view and zoom in on external portions of the patient's eye and surrounding tissue in real time from their laptop or cell phone.

"Tele-consults will make it possible for the ER doctor to get an expert opinion on a patient's condition much faster than waiting for a specialist to come to the emergency room," emphasizes David Harris, MD, Medical Director for Ophthalmology at Mount Sinai Morningside and Mount Sinai West, who is part of the team implementing the project. "They'll also help to eliminate trips to the hospital by ophthalmologists if their presence isn't really essential."

The successful implementation of the program has highlighted NYEE's ability to innovate and serves as an example of how to effectively expand access and coverage for other departments in the Health System. "As an ophthalmologist and the Director of Tele-consults for the Mount Sinai Health System, I am proud to say that the Ophthalmology Department was among the first specialties to implement tele-consults at Mount Sinai," shares Sophia Saleem, MD. "To our knowledge, this is the first synchronous tele-consult model in the United States that provides ophthalmic services for emergency room patients. As we gain more experience in this area, we look forward to optimizing the delivery of ocular care throughout the Health System and expanding our reach to patients regionally and nationally."

Propelled by future improvements in technology, Dr. Harris can envision this innovative program eventually taking hold in hospitals across the region—particularly those in remote areas that don't have access to a nearby ophthalmologist—for emergency evaluations such as a ruptured globe or angle-closure glaucoma with elevated intraocular pressure, or for less serious ones like corneal abrasions.



Sophia Saleem, MD conducting a tele-consult with a patient in the Emergency Department via InTouch Lite 4 system.



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"To our knowledge, this is the first synchronous tele-consult model in the United States that provides ophthalmic services for emergency room patients. As we gain more experience in this area, we look forward to optimizing the delivery of ocular care throughout the Health System and expanding our reach to patients regionally and nationally."

—Sophia Saleem, MD



Patient getting fundus images taken of her eyes at Mount Sinai Doctors General Medicine Associates.

Capturing Hard-to-Reach Patients

Six years before COVID-19, NYEE began to realize the enormous potential of telemedicine through a program designed to capture patients at high risk of diabetic retinopathy while they underwent routine exams at their primary care physician's office. Today, that program embraces seven sites within the Mount Sinai Health System, screening up to 1,500 patients annually. On-site fundus cameras operated by trained medical personnel provide non-mydratric images of the back of the eye, which are then transmitted through a secure platform to a specialist at NYEE for later interpretation. The patient is informed if retinal or optic nerve pathology is detected, and urged to seek follow-up care when it is.

According to Dr. Saleem, who is also the Senior Director of Tele-ophthalmology at NYEE, two of the seven participating primary care sites have added a new technology—artificial intelligence (AI)—that could revolutionize the operation and effectiveness of the existing telemedicine-based screening program. As part of the pilot underway, consenting patients get their fundus photographs read on the spot by an AI algorithm which provides immediate clinical feedback. "Instead of having to wait a week, patients are informed immediately about a potential disorder, and the primary care doctor can set up an appointment with an ophthalmologist before they ever leave the office," notes Dr. Saleem, who is leading the implementation of tele-ophthalmology across all campuses at Mount Sinai. "This is an incredible service for diabetic patients who typically would never see an eye doctor on their own."

As technology experts at NYEE see it, this enhanced program is a harbinger of the impact AI could eventually have on tele-ophthalmology. Another possible application cited by Dr. Pasquale is remote testing of residents in an apartment building within a kiosk centrally located in its lobby. Under this scenario, fundus photographs could be taken and an AI algorithm working in the background could assess the captured data to instantly determine if the individual shows signs of a disease like glaucoma or adult macular degeneration that warrants professional follow-up.

Separating Physician Visits From Diagnostic Visits

The pandemic has underscored the need for better flow and prioritization of patients in busy clinic and office settings. NYEE is demonstrating how this goal can be effectively met at its Eye Clinic, and expanding the new process to the busy Retina Center in Manhattan, by converting many physician appointments to diagnostic-only visits. After on-site imaging is performed by a resident or attending, and the patient's vision and intraocular pressure are checked, the information is relayed digitally to an ophthalmologist for later viewing. The detection of a potential problem would then trigger a virtual patient visit via telephone or video link with a physician, or an actual in-office visit.

"Our diagnostic-only program has been very well received by patients," reports Dr. Saleem. "Just as importantly, it's helping us to better regulate patient flow in our Eye Clinic and soon we will see similar benefits in the Retina Center while allowing doctors to focus on the acute pathology of patients who are most in need of immediate intervention."

Vascular Dysregulation Emerges as Central Issue in Primary Open-Angle Glaucoma

Over the years, research to better understand and treat primary open-angle glaucoma (POAG), the leading cause of vision loss in the United States, has often led to more questions than answers. A study by New York Eye and Ear Infirmary of Mount Sinai (NYEE) sheds significant new light on the disease, however, by suggesting that the blood researchers found in optic disk hemorrhages was arterial in origin and could provide a key to halting glaucoma progression. In a paper published in the April 2020 issue of the *American Journal of Ophthalmology*, the NYEE team also presents evidence that vascular dysregulation plays a central role in POAG pathogenesis, and proposes that finding a way to address the problem could yield an important new modality for treating POAG.

"I would say that disc hemorrhages are the neglected stepchild of glaucoma," says Louis Pasquale, MD, Deputy Chair for Research, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, and lead author of the study. "Many people in the field write them off as a secondary event downstream to elevated intraocular pressure. The collective evidence we and others have accumulated over the years suggests that optic disc hemorrhages are biomarkers for—and a root cause of—glaucoma in many patients. Our over-arching hypothesis is that disc hemorrhages in glaucoma develop due to impaired nitric oxide signaling."

The current retrospective study assessed densitometric profiles of disc hemorrhages from fundus photographs of 83 patients in the Ocular Hypertension Treatment Study (OHTS). OHTS was a highly impactful randomized clinical trial, designed to establish whether ocular hypotensive therapy prevented or delayed glaucoma in patients with elevated intraocular pressure (IOP). Post hoc analysis of study results found that disc hemorrhages were associated with a 3.7-fold increased risk of developing POAG, even after adjusting for the IOP level among study participants. According to Dr. Pasquale, OHTS offered a unique opportunity to gain insights on the origin of disc hemorrhages because all participants started with elevated IOP and had either mild or no optic nerve damage when disc hemorrhages were photo-documented.

Against that backdrop, the fundamental challenge for researchers became determining the source of the increased blood flow in disc hemorrhages: arterial or venous? The NYEE team, which included Massachusetts Eye and Ear and Washington University School of Medicine, found that the densitometry of blood from disc hemorrhages differed more from adjacent venules than it did from adjacent arterioles, suggesting an arterial origin. Similar findings were observed in patients with recurrent disc hemorrhages in the OHTS.

If disc hemorrhages have an arterial source, the next question confronting researchers was, why? "We believe the reason this is occurring is vascular dysregulation," offers Dr. Pasquale. "The blood flow cannot autoregulate when the patient is doing something simple, like waking up in the morning and changing from a lying-down to a standing-up position. Blood flow should remain constant during those routine movements, but in glaucoma patients it doesn't." Indeed, previous work by Dr. Pasquale showed that blood flow can increase in some instances by 100 percent when transitioning from a supine to a sitting position. And when that occurs—particularly in vessels making acute turns, as from the optic nerve onto the surface of the retina—smaller vessels fail under the intense pressure, opening up and bleeding, resulting in a glaucoma-related disc hemorrhage.

Much of the work of Dr. Pasquale, who is Director of the Mount Sinai/NYEE Eye and Vision Research Institute, has been directed at unraveling the mystery of disc hemorrhages and, more specifically, how to prevent them. One strategy he advances is reducing intraocular pressure in patients with frequent disc hemorrhages to the low teens, ideally even to 10 mm Hg. Another important approach could be to fix the impaired nitric oxide signaling that he believes leads to the dysregulation. "If retinal arterial dysregulation is contributing to these hemorrhages," he advises, "then we should be focusing glaucoma treatment on correcting that hemodynamic flaw."

To that end, NYEE researchers plan to soon launch a follow-up investigation using retinal oximetry in conjunction with Alon Harris, PhD, who recently joined the Department of Ophthalmology. Retinal oximetry allows for calculating the relative oxygen saturation of retinal blood vessels directly, as opposed to vessel densitometry, which only measures the brightness of the blood. "Ultimately, we believe that if medical science is going to find more effective ways to treat glaucoma, it needs to pay much more attention to disc hemorrhages as both a predictor and causative factor for glaucoma development," Dr. Pasquale concludes.

Years Spent in the Sun May Cause More Than Skin Damage

It's well established that basal cell carcinoma and squamous cell carcinoma are triggered in part by prolonged exposure of the skin to ultraviolet (UV) radiation. New evidence has now emerged that long hours spent outdoors by people in their younger years under an intense sun may carry other serious consequences later in life. They may have set the stage for exfoliation glaucoma (XFG), a disease characterized by more elevated intraocular pressures and faster disease progression than in the more prevalent primary open-angle glaucoma.

Researchers from the Mount Sinai/NYEE Eye and Vision Research Institute have found that a history of non-melanoma skin cancer is associated with a 40 percent higher risk of developing exfoliation glaucoma, as reported in the June 2020 issue of the *Journal of Glaucoma*. Moreover, the prospective study of more than 120,000 individuals followed for 28 years and longer reported that the risk was even greater for individuals less than 65 years of age and those living in northern latitudes, farther away from the equator.

"Our goal was to discover what biomarkers could serve as measures of ocular UV exposure, and we learned that non-melanoma skin cancers are strongly UV-related," explains Louis Pasquale, MD, Deputy Chair for Research of the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai, and lead author of the study. "That, in turn, indirectly supports our hypothesis that greater personal exposure to UV radiation from the sun may increase the risk of exfoliation glaucoma, which is the leading cause of secondary open-angle glaucoma in the world." Indeed, the NYEE team found that a history of non-melanoma skin cancer was associated with a 1.4-fold increase in the risk of XFG.

Particularly revealing were the findings with regard to age and geographic location. In citing an increased risk of XFG among younger individuals, the study supported previous reports that greater time spent outdoors during the teenage and young adult years—when blistering sunburns may occur—can actually double XFG risk. The work supports the notion that XFG is a disease with a long latency period, perhaps decades.

For that reason, Dr. Pasquale sees important public health implications from the new findings. "Teenagers and young adults often don't feel the need to wear sunglasses," he observes, "but our evidence confirms that those are critical years to be protecting your eyes from UV rays of the sun. The American Academy of Pediatrics already recommends that young people use protective glasses whenever they're outside for long periods."

Also vulnerable to the harmful effects of the sun are people living in northern latitudes, belying conventional wisdom that the closer one is to the equator, the harsher the effects of the sun. One reason is that the solar shield, which protects the earth from the damaging direct rays of the sun, is thinnest at the northern and southern poles of the earth, increasing ultraviolet intensity. Another reason is pure geophysics. The earth's 23-degree tilt to the sun when rotating on its axis creates more opportunities for sunlight to reflect off the ground and directly into the eyes. This scenario plays out more prominently in geographic locations that are located farther away from the equator.

Physicians need to be aware of this confluence of factors in treating patients with non-melanoma skin cancers, Dr. Pasquale maintains, especially those 40 to 64 years of age living in more northern regions. This group, he adds, would benefit from regular eye examinations to detect XFG in its earliest stages.

In identifying individuals at greatest risk for XFG, Dr. Pasquale believes his team has taken an important step toward better understanding a disease that's associated with considerable ocular morbidity. "We've shown how a marker of chronic ocular UV exposure contributes to disease pathogenesis," he says, "but much more research is needed in the field of XFG. Hopefully our work will provide that stimulation."

In Search of a Biological Link Between a Low-Carbohydrate Diet and Glaucoma

Your mother always said, "eat your vegetables, they're good for you." But does a high-vegetable regimen hold the key to not just lower risk for heart disease, type 2 diabetes, and weight loss, but also reduction in the risk of primary open-angle glaucoma (POAG)?

Louis Pasquale, MD, Deputy Chair for Research of the Department of Ophthalmology at the Icahn School of Medicine at Mount Sinai, explored this possibility and conducted a large-scale study to learn more. The logic behind the team's hypothesis was clear. The intra-scleral optic nerve, the main site of glaucoma-related damage, has a high mitochondrial density needed to support continuous conduction of visual information through the long unmyelinated segment to the brain. Thus, a low-carbohydrate diet, through its generation of metabolites favorable to mitochondrial function, may lower POAG risk.

The observational study, which followed more than 185,000 individuals over 25 years, reported mixed results in the journal *Eye* (July 2020). While no association was observed between adherence to a low-carbohydrate diet and POAG risk, a 20 percent lower risk of the POAG subtype with early paracentral visual loss was found when a vegetable-rich, low-carbohydrate diet was followed.

"That a diet low in carbohydrates but high in fat and protein from vegetable sources was suggestive of lower risk of early paracentral POAG is certainly an intriguing finding which needs additional research," says Dr. Pasquale. That work, in fact, is well underway at NYEE. Researchers are now using an artificial intelligence algorithm to calculate the amount of paracentral visual field loss among participants in a population-based cohort from around the country who ultimately developed POAG.

"We want to re-analyze the data to see if a stronger association emerges between a vegetable-rich, low-carbohydrate diet and POAG with early paracentral visual field loss," explains Dr. Pasquale, who is also Director of the Mount Sinai/NYEE Eye and Vision Research Institute. That review, he adds, could shed light on the mechanisms of paracentral visual field loss, and why its pattern of impairment impacts a significant subset of glaucoma patients with more central visual field loss occurring first, before affecting their peripheral vision.

Even the study's finding of no linkage between POAG and a low-carbohydrate diet may not be the last word on the matter, according to Dr. Pasquale. That's because patients in the study cohort tended to have a much higher intake of carbohydrates than people with epilepsy, for whom the low-carbohydrate diet has become established treatment when conventional medicines have failed (it's also used by individuals with other neurodegenerative disorders, including Parkinson's and Alzheimer's diseases). For these individuals, less than 1 percent of total energy intake from the diet is derived from carbohydrates, making the body much more efficient at burning fat for energy.

"Our findings don't necessarily mean that carbohydrate restriction won't work in terms of reducing POAG risk," Dr. Pasquale emphasizes. "It could simply mean that if we're going to limit carbohydrates, it needs to be done at much more stringent intake levels than what we reported in our study."



ANIMAL FOOD SERIES BY SARAH DEREMER

A New Eye Drop Regimen for Macular Holes May Spare Patients Invasive Surgery

The origin of macular holes, which require surgery for so many people over 60, has long puzzled researchers. Theories have abounded, including tangential traction, inner retinal degeneration, glial migration, and hydrodynamics. In 2011, after studying serial optical coherence tomography (OCT) images and clinical data for more than 15 years, Ronald Gentile, MD, Clinical Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai, arrived at his own theory. Based on the countervailing forces of hydration and dehydration, his idea has since spawned a novel way to treat macular holes through eye drop medications, sparing patients the risks and rigors of invasive surgery.

A Theory Is Born

When Robert Ritch, MD, Director of Glaucoma Research and Surgeon Director Emeritus at New York Eye and Ear Infirmary of Mount Sinai (NYEE), introduced a prototype imaging device known as OCT to NYEE in 1995, Dr. Gentile, an ophthalmology resident at the time, soon found an intriguing use for the device that in following years would revolutionize the diagnosis and treatment of ocular disease around the world. With the encouragement of Joseph Walsh, MD, FACS, FRCOphth, KStJ, the legendary Chair of NYEE's Ophthalmology Department for 25 years, Dr. Gentile began imaging macular holes in patients over time, enabling him to see disease progression through time lapse video created from the OCT ocular images.

"I was seeing the disease in a new way, and discovered that not every macular hole was the same," Dr. Gentile recalls. "Some holes had traction on them, others didn't. Some had hydration, others didn't." Digging deeper to learn why, he came up with the "combined tractional hydration theory of macular hole." To wit, traction of the vitreous gel on the center of the macula creates just enough force to open a hole in the macula. Dehydration provides an opposing force to close it. And when the forces of dehydration are able to overcome those of hydration, the macular hole will repair itself without the need for surgical intervention.

"It's the same principle we use in surgery for macular hole," Dr. Gentile points out. "We overcome the forces of hydration and of traction by inserting a gas bubble in the eye, which coaxes the edges of the hole toward one another so that they eventually close."

Creating a Spin-Off Treatment

Dr. Gentile's unique offshoot of the tractional hydration theory was a concept called cystoid dehydration, which proposes closing a macular hole by using eye drops. The simple procedure is designed to dehydrate the retina and alleviate swelling around the hole. As the fluid departs and swelling decreases, the edges of the macular hole creep together, sometimes closing the opening.

Putting his new idea to the test in 2011, Dr. Gentile gave a patient—who was leery of surgery for his macular hole—three drops: a steroid, a non-steroidal and a carbonic



Ronald Gentile, MD, at the Tom Otterness playground sculpture.

anhydrate inhibitor. A follow-up visit two weeks later showed the macular hole had closed. Similar results were observed with other patients of Dr. Gentile. And in 2013, the retinal surgeon presented his cystoid dehydration of macular holes concept—thoroughly critiqued along the way by Dr. Walsh—before two of the most prestigious retinal organizations, the Macula Society (36th Annual Meeting) and the American Society of Retinal Specialists (31st Annual Meeting).

"People were in awe," remembers Dr. Gentile, which paved the way for presentations before other professional groups, and for growing support from nationally known retinal surgeons like Raymond Iezzi, Jr., MD, at Mayo Clinic and Dean Elliott, MD, at Harvard Medical School. After hearing Dr. Gentile speak at one of those conferences four years ago, Dimitra Skondra, MD, PhD, Director of the J. Terry Ernest Ocular Imaging Center at the University of Chicago, also became a firm believer, using the eye drop approach as an option for some of her macular hole patients with rewarding results. She has been joined by a growing number of specialists around the country, including the retinal team at NYEE.

Weighing the Results

As part of her own research, Dr. Skondra teamed up with Dr. Gentile to prepare for publication this year a retrospective case series of 18 patients at multiple centers whose macular holes successfully closed through a three-drug regimen of prednisolone, ketorolac, and brinzolamide.

Dr. Gentile cautions that treatment with eye drops is not meant for every patient with a macular hole. In fact, it works best in holes less than 200 microns in diameter since larger sizes have more scar tissue or gel tugging on the edges of the hole, diminishing the effectiveness of drops. Nonetheless, cystoid dehydration continues to gain traction in the ophthalmic world. "It takes time for an idea like this to evolve and become accepted," Dr. Gentile concedes, "but when you weigh invasive surgery against administering eye drops in cases where the patient's macular hole is small, the choice seems pretty obvious. As a physician, my goal is to look at each patient and their disease in a new way; sometimes that means reaching for an eye dropper instead of the scalpel."

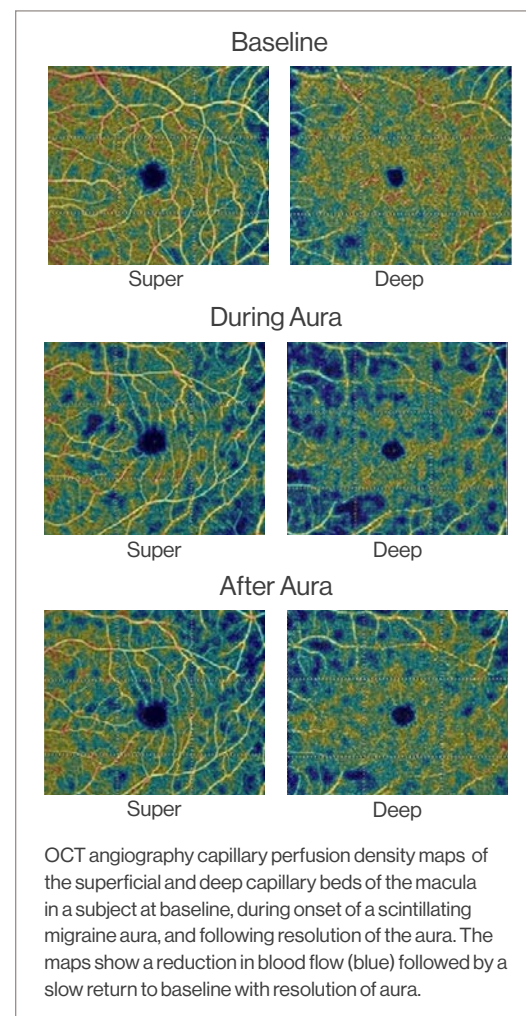
Retinal Metabolic Imaging Reveals Functional Signals Preceding Structural Alterations in Disease



Advanced imaging technologies like optical coherence tomography (OCT) angiography and quantitative retinal fluorescence are for the first time enabling researchers at New York Eye and Ear Infirmary of Mount Sinai (NYEE) to visualize metabolic signals in the retina that precede structural changes, offering paths to objective validation of both patient symptoms and early responses to retinal vascular therapies. Among these findings are vascular constriction coincident with the light shows many people report at the onset of migraine headaches, and improvements in mitochondrial energetics responsible for visual acuity gains from anti-vascular endothelial growth factor therapy prior to structural restoration in diabetic retinopathy.

Giving Clinical Meaning to Migraine's Aura

People who experience migraines have described them as fireworks, zigzag ovals, expanding fortress walls, and more, which move across their field of vision and then resolve. They are the transient patterns of light and darkness lasting about 10 minutes that people report seeing prior to the onset of headache or sometimes alone without the subsequent headache. Conventional clinical evidence has attributed these phenomena to aberrant electrical waves occurring within the brain, since previous migraine studies have demonstrated alterations in cortical blood flow and electrical activity during attacks.



NYEE researchers are now offering an intriguing new perspective. "With the advent of OCT angiography, we've been able to actually witness what's occurring in the retinal circulation during these episodes as they are experienced," says Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System. "And what we found was a measurable reduction in blood flow in the retina while these episodes were taking place. This was the first time anyone was able to capture these events as they are taking place."

Making that analysis possible was the serendipitous application of clinical resources, both people and technology. "Most often, patients present describing episodes that previously took place, seeking reassurance that they do not represent an emergent retinal tear or detachment. By the time they are seen, the symptoms have abated," clarified Dr. Rosen.

To perform imaging while a migraine sequence was actually in progress, NYEE researchers, led by Alexander Barash, MD, a recent graduate of the NYEE Retina Fellowship (and voluntary faculty member at Elmhurst Hospital and NYEE), enlisted the help of clinicians at the NYEE Bendheim Retina Center who described onset of such attacks while on the job. Investigators employed a newly approved non-invasive imaging tool, OCT angiography, to assess subtle changes in retinal capillary blood flow using quantitative perfusion software originally introduced and developed in the David E. Marrus Adaptive Optics Imaging laboratory.

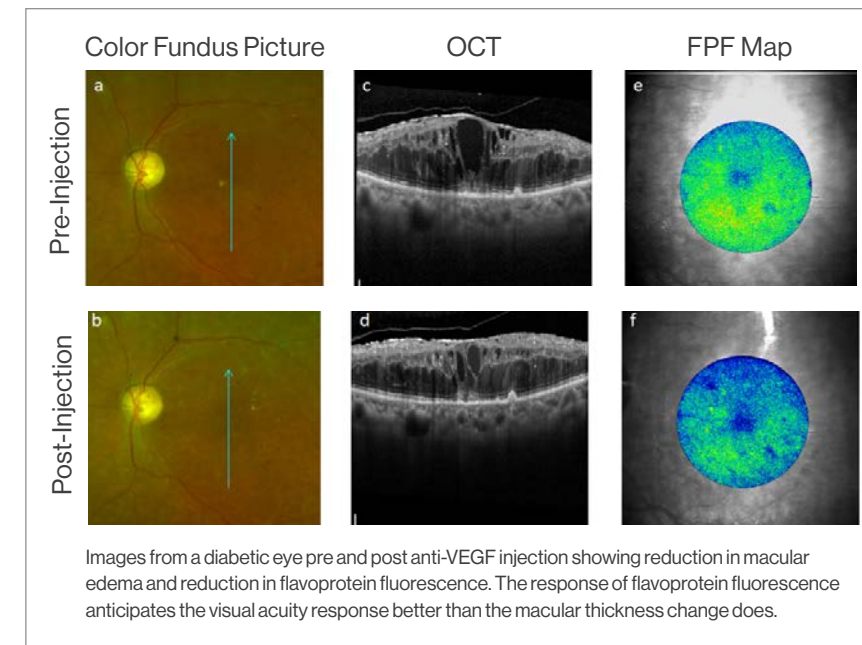
Dr. Rosen refers to these now-identifiable metabolic changes in the retina as "an important diagnostic confirmation for patients." Those with migraines or other disease states that trigger shimmering shapes or contorted configurations may finally have answers for these often strange and disturbing auras. "It may also explain previous studies which have documented progressive thinning of retinal nerve fiber layers in patients with frequent migraines and point to new directions for research in the relationship of migraine to normal tension glaucoma," he explains. "This technology can not only help to improve the patient experience, but ultimately give clinicians greater insights into the origins of a wide range of ocular and non-ocular conditions."

A Dynamic New Marker for Mitochondrial Energetics

Mitochondria are the powerhouses of cells and are responsible for maintaining the metabolic machinery of life. The ability to detect subtle changes in metabolic function and cellular energy levels has long been a goal of clinicians for monitoring disease prior to the onset of structural damage or evidence of repair. In a study reported in *Oxidative Medicine and Cellular Longevity* (August 2018), NYEE researchers reported that flavoprotein fluorescence (FPF) imaging, a newly introduced clinical tool for dynamic measurement of mitochondrial oxidative stress, can reveal evidence of response to therapy earlier than structural changes, objectively confirming coincident subjective visual acuity improvements.

"Changes in intracellular mitochondria function occur long before they're detectable as alterations in retinal tissue conformation, even by OCT imaging," explains Dr. Rosen, who is also Vice Chair and Director of Ophthalmology Research at NYEE and senior author of the study. "We've been able to confirm that flavoprotein fluorescence may be a promising clinical biomarker for gauging retinal metabolic integrity. Flavoproteins are critical components of the electron transport chain which drives the energetics of all of our cells. When they are damaged by oxidative stress from a variety of diseases, they emit abnormal levels of fluorescence, which can be monitored as an indicator of healthy function."

Jorge Andrade Romo, MD, a research associate in The Shelley and Steven Einhorn Clinical Research Center (and current PGY-2 NYEE resident), along with the NYEE retinal imaging team, in collaboration with scientists at OcuSciences, Inc., a research spinoff from the University of Michigan, studied individuals with diabetic macular edema who were noted to have significantly higher FPF values. Patients with



diabetes have increased levels of oxidative stress, which reduces mitochondrial membrane potentials, leading to elevation in their FPF levels. When these patients were treated with anti-vascular endothelium growth factor (anti-VEGF) injections to reduce their macular edema, their vision improved followed by a gradual reduction in their retina swelling. Interestingly, their FPF levels decreased in direct correlation with their vision improvement, prior to the structural restoration documented by OCT.

"FPF signal imaging may prove to be an important new bioenergetic marker which can detect early response to new treatments based upon improvement in cellular vitality as indicated by mitochondrial integrity. Additional studies have shown its value in detecting pre-structural indications of glaucoma, macular degeneration, and other slow degenerative conditions," Dr. Rosen observes. "We believe that future studies at NYEE and at other academic centers will reveal whether FPF imaging will be able to enhance our recognition of earlier disease as well as speeding our detection of drug efficacy in the treatment of chronic disease."

3D Simulator Takes Ophthalmoscopy Instruction From the Dark Age to the Digital Age

Seymour Fradin, MD, has impressive skills as a medical artist that are matched only by his reputation as one of New York City's top retinal surgeons prior to his retirement in 1994. Since then, the one-time Associate Director of Retina Service at New York Eye and Ear Infirmary (NYEE) has been anything but idle. In addition to volunteering his time as an indefatigable instructor at NYEE for the past 25 years, he has developed, with Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System and Vice Chair and Director of Ophthalmology Research at NYEE, the first digital ophthalmoscopy simulator which teaches proficiency in one of the most difficult procedures for residents to master.

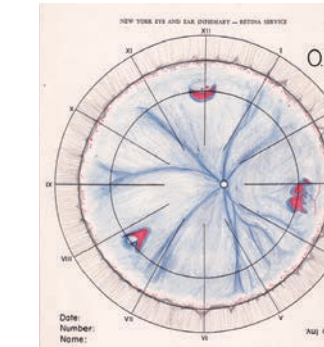
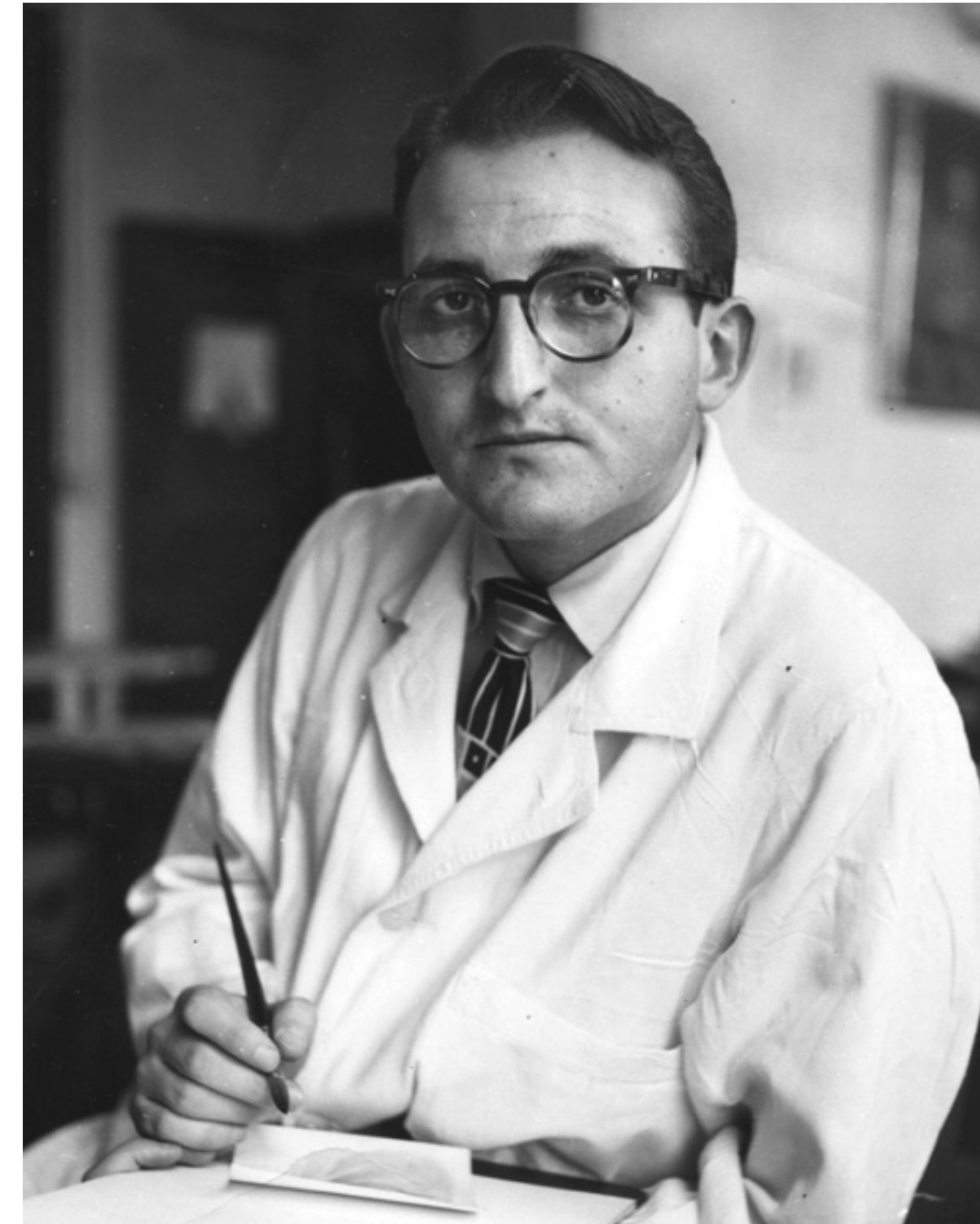
That project is expected to launch in the next few months as a highly animated, fully interactive learning tool that can be accessed by trainees from a web browser or through a downloadable app to their tablets and smaller mobile devices. "The program uses amazing graphics and animation to simulate what residents would see if they had an indirect ophthalmoscope on their head and were looking into the interior of the patient's eye," explains Dr. Fradin, who began his own three-year residency at NYEE in 1959. "It's designed to allow them to comfortably transition from computer screen to actual patient in the exam room."

To be sure, indirect ophthalmoscopy with scleral depression has always been a challenge for students to learn, instructors to teach, and patients to endure. "That's precisely why we designed this program," says Dr. Fradin. "Patients can often take a beating at the hands of someone unfamiliar with the technique. I realized this learning process was obsolete and that we needed to do something much better."

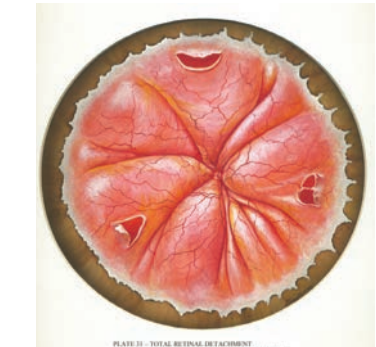
That brainstorm came naturally to a physician who has loved teaching ever since he trained at Johns Hopkins' Department of Art as Applied to Medicine, following World War II, and joined the University of California in San Francisco as a medical illustrator. Those experiences, along with the encouragement of his childhood friend Morton Rosenthal, MD, founder of the NYEE Retina Service, made him want to become a doctor. He realized that dream with a medical degree from Downstate University of New York in 1958, a residency and fellowship at NYEE, and eventually a leadership role with the hospital's newly launched Retina Service in 1963.

Seeds for the ophthalmoscopy simulator were planted by Dr. Rosen in the mid-90s when Dr. Fradin retired from active clinical practice and thought about writing a book to share his extensive expertise. With the support of the department chair, Joseph Walsh, MD, who helped re-establish NYEE's reputation as one of the nation's leading teaching hospitals, Dr. Fradin was encouraged to create a more dynamic teaching tool using newly available computer simulation techniques. Fortunately, he found a young graphic artist, Carl Lydon, who was working with

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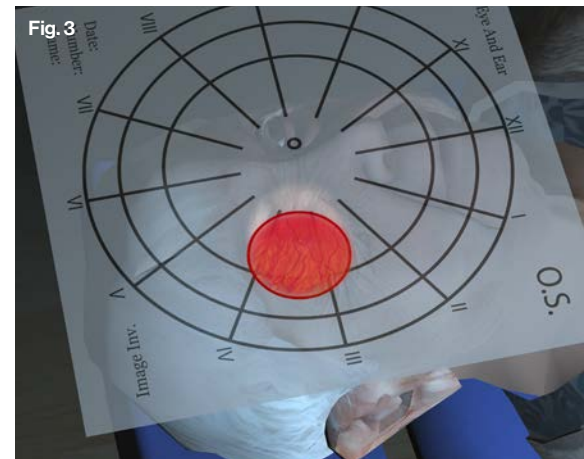
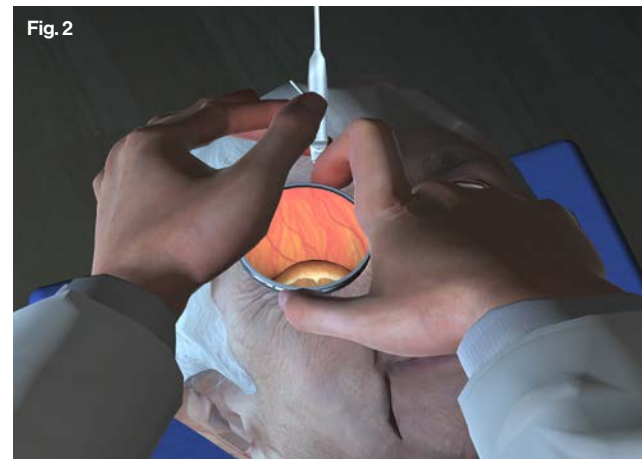
Dr. Fradin's retinal drawing of a total detached retina with three large holes and posterior rolled edges.



A painting of the total detached retina by William Stenstrom used in the simulation module.

"The program uses amazing graphics and animation to simulate what residents would see if they had an indirect ophthalmoscope on their head and were looking into the interior of the patient's eye."

—Seymour Fradin, MD



Indirect Ophthalmoscopic Exam

Fig. 1: Simulation of an indirect ophthalmoscopic exam.

Fig. 2: Simulated eye exam using a scleral depressor and showing normal ora serrata.

Fig. 3: Map of the retina showing orientation of exam placement.

the nascent media, which Dr. Fradin found at once stunning and fascinating. It took the form of animated 3D pictures on a computer screen that were leagues beyond the hand-drawn renderings of ocular disease and indirect ophthalmoscopy techniques that Dr. Fradin had perfected over the course of his lengthy career.

Dr. Fradin's fascination with this new digital format resulted in the production and release, in 1997, of a CD-ROM that NYEE used internally for resident training and shared with all of the training programs throughout the country. This first edition of the retina simulator provided a series of didactic animations laying out the history, theory, and practice of indirect ophthalmoscopy. Most notably, it featured a set of interactive retinal models which allowed users to test their newly acquired examination and documentation skills by sketching a detailed drawing of each animated fundus they examined in the program.

When Drs. Fradin and Rosen decided to upgrade the simulator some 10 years ago, Dr. Rosen presented the idea to the leadership of the American Academy of Ophthalmology (AAO). The Academy saw a perfect fit with its ONE Network, a global platform for continuing ophthalmic education that could make this valuable educational tool available to a wider audience, and agreed to become a collaborative partner. Currently in mid-stage

development, the digital learning tool will be offered by the Academy free from its website, and promoted to residents and other trainees worldwide.

Known as "Techniques of Indirect Ophthalmoscopy," the program is being built with the same gaming engine as today's interactive videos. Users will be able to select randomly among 10 virtual patients they first encounter lying down in an exam chair. Each patient will display a retinal disorder digitally modeled from actual paintings provided by William Stenstrom, a noted medical artist in the field. The user will be provided with a short case history of the patient's condition, then allowed to freely explore and move around the eye using the computer mouse or touch controls on a tablet or touchscreen. Through the magic of digital animation and 3D rendering, users will even be able to visually simulate the effect of scleral depression by manipulating an icon button until the depressor is properly positioned against the eye.

Looking back on the long journey that got his ophthalmoscopy simulator to this point, Dr. Fradin muses, "We've gone from a crude process that used an actual patient as teacher to a digital patient that not only avoids the discomfort of a novice examination, but puts the trainee in a much better position to master this difficult technique." Characteristically, Dr. Fradin at 94 is already enthusiastic about the next step he has charted for his advanced learning tool: virtual reality.

Largest Residency Training Program in U.S. Is Reinventing Its Approach to Education

Despite the lower clinical volume during the height of the COVID-19 pandemic, the New York Eye and Ear Infirmary of Mount Sinai (NYEE) and The Mount Sinai Hospital ophthalmology residency program hardly skipped a beat. Instead, the largest accredited ophthalmology residency training program in the country revved up its educational engine through remote learning, a new hands-on curriculum for teaching basic skills, and thoughtful learning plans that paired each resident with a faculty member.

"We really ramped up the didactics portion of our education," emphasizes Harsha S. Reddy, MD, Ophthalmology Residency Program Director at NYEE and Site Director for Oculoplastics, Orbital and Reconstructive Surgery at NYEE and Mount Sinai Beth Israel. "We found multiple ways for our residents to continue their lifelong learning process during the pandemic that partially made up for not seeing as many patients."

One of those ways was actively pursuing an online education platform grounded in videotaped lectures, surgical cases, and other learning materials. "We even found that attendance at grand rounds rose significantly when it was available via Zoom," notes Dr. Reddy. "And the online resource also enabled some of our alumni in different states to log on and interact with our residents."

Reinforcing the digital agenda was the sharing of educational content with the residency programs of other institutions throughout New York, a development made possible by the declaration of a pandemic training emergency under the rules of the Accreditation Council for Graduate Medical Education. This online collaboration through Zoom and Webex platforms broke down traditional barriers between schools to allow for the immediate sharing of lectures and other learning resources. "This was one of the unexpected blessings of COVID-19, and it will hopefully continue into the future," says Douglas Fredrick, MD, Deputy Chair for Education of the Department of Ophthalmology and Chief of Pediatric Ophthalmology for the Mount Sinai Health System. "It's an acknowledgement that there are many excellent teachers throughout the city, as well as a good example of how we used technology to bring learning to students at a time when on-site instruction wasn't possible."

The intensified use of online learning dovetailed with another major innovation introduced into NYEE's residency training: the flipped classroom. This model, which

is gaining currency in many types of educational settings around the country, allows for more targeted and interactive learning. NYEE recently started using the format to segment resident training into online viewing of videotaped lectures, followed by application of this knowledge through interactive Q&A sessions and case reviews involving a class and instructor.

NYEE's residency training reached another milestone in July 2020 with the launch of its Joint Internship Program. Nine trainees became part of the inaugural class to start their residency enrolled in a one-year internship at Mount Sinai's Beth Israel, which includes nine months of general medicine and three months of ophthalmology training. "By the time these trainees start their residency," observes Dr. Fredrick, "they will be comfortable examining patients and treating ocular emergencies, and will have been engaged in an ophthalmology research project. Once they enter their first year of residency, they can start their microsurgery training learning through a structured curriculum that leverages the state-of-the-art Jorge N. Buxton, MD, Microsurgical Education Center for skills practice and surgical simulation."

Dr. Fredrick also sees great opportunities ahead both for the joint training program and the incoming residents who will benefit from exposure to the kinds of patients, instructors, and learning opportunities they couldn't find anywhere else in the country. He is particularly excited about the trainees' exposure to the field of research, particularly health policy research, where they will work with epidemiologists and public health experts as part of the Icahn School of Medicine Division of Public Health, learning about innovative ways to deliver health care with limited resources. "Residents will get the chance to see firsthand other professional pathways in public health administration and global health they might wish to pursue at some point in their career," notes Dr. Fredrick.

The recent revamp of NYEE's education platform is creating a fertile ground for future success of the largest training program in the United States. "We don't just want to be known as a big program," notes Dr. Reddy. "Combining the extensive resources of NYEE and The Mount Sinai Hospital was just the first step. Now we are really working to reinvent how we deliver education to help our trainees hone their clinical and surgical skills and help pursue their research interests. It's all about delivering a 360-degree training experience that is tailored to our residents using the latest tools."



Attacking Hydroxychloroquine-Related Retinal Degeneration at Its Source

Chloroquine (CQ) and hydroxychloroquine (HCQ), which have been important drugs for treating malaria since the early twentieth century, gained new popularity in the 1950s as effective agents in the battle against autoimmune disease. While they are extremely well tolerated in the short term, prolonged usage of these drugs, which most autoimmune patients require, poses an ominous risk of blindness, one that is often played down by internists. Epidemiological studies have shown that retinal degeneration occurs in up to 7.5 percent of people who use HCQ for more than five years, increasing to nearly 20 percent following 20 years of drug therapy.

New York Eye and Ear Infirmary of Mount Sinai (NYEE) has now taken a promising first step toward developing antidotes to the toxic effects of HCQ on the retina. A research team has identified the mechanism and molecular metabolic pathway responsible for the development of HCQ-related retinal degeneration and has found that certain medications which stimulate adrenaline receptors appear to reverse HCQ's toxicity to the vulnerable retinal pigment epithelial (RPE) cells, potentially preventing the devastating loss of central vision that follows. These findings were reported in *The International Journal of Ophthalmology* (April 2020).

"Our RPE cell culture studies have identified several medications which can potentially modify this disease and hopefully be useful for the prevention and treatment of HCQ-related retinal degeneration," says Dan-Ning Hu, MD, Research Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai, and co-author of the study. "The urgency of our efforts is prompted largely by the absence of any current medical therapy for HCQ toxicity—other than stopping the drug—and the widespread popularity of HCQ as a long-term solution for autoimmune diseases like lupus, rheumatoid arthritis, and mixed connective tissue disorders."

NYEE's work with RPE cells began in the 1980s when it established a variety of human ocular cell lines from donor eyes to investigate a spectrum of eye diseases at a cellular level. When Dr. Hu was recruited to NYEE in the mid-1980s to develop the Ocular Cell Culture Laboratory, the initiative expanded exponentially to include studies on glaucoma, melanoma, and proliferative retinopathy as well. In 2016, development of an in vitro model of HCQ toxicity using cultured human RPE

cells revealed many important dysregulatory features of HCQ-induced damage, culminating in cell death at higher doses of the drug.

"We were able to identify a certain threshold of exposure where RPE cells lose their ability to metabolize HCQ, resulting in drug accumulation, which leads to malfunction of these critical caretakers of the overlying photoreceptor cells, which in turn slowly disappear," explains Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System, and senior author of the study. "Ultimately, the RPE cells themselves are lost." The latest research, he adds, has identified the importance of the protein kinase A (PKA) signaling pathway and the ability of certain adrenergic agonists to help maintain its function, as a novel strategy to address HCQ-related retinal degeneration.

According to Dr. Hu, the mechanism can be traced to the fact that retinal toxicity effects of HCQ are initiated mainly by a reduction in acidity of the lysosomes. This results in inhibition of lysosomal enzyme activity, blockage of the autophagy process, increased vacuolization, and death of RPE cells which, in turn, leads to the death of photoreceptors and loss of vision. Adrenergic agonists—developed over the past 20 years and used safely for long-term management of various chronic diseases—activate the PKA pathway, increasing the acidity of lysosomes, and potentially protecting the RPE cells against HCQ toxicity.

Which adrenergic agonists will turn out to be most effective against HCQ-related retinal degeneration? "We've tested dozens of medicines belonging to many different biomedical systems and have narrowed it down to 10 that effectively protect RPE cells in vitro," Dr. Hu says. "We are currently developing an animal model to help select from several promising candidates that seem the safest and most effective for clinical trials."

Dr. Rosen sees the possibility that off-label repurposing of one of the many beta-1 or beta-2 adrenergic agonists already on the market could emerge as a readily available, safe, and effective agent for the prevention and treatment of HCQ-related retinal degeneration. Moreover, he adds, research underway at NYEE in this field—using an array of in vitro models and one of the most extensive collections of eye cells in the world—could well be applied to discovering medications for other serious eye disorders.

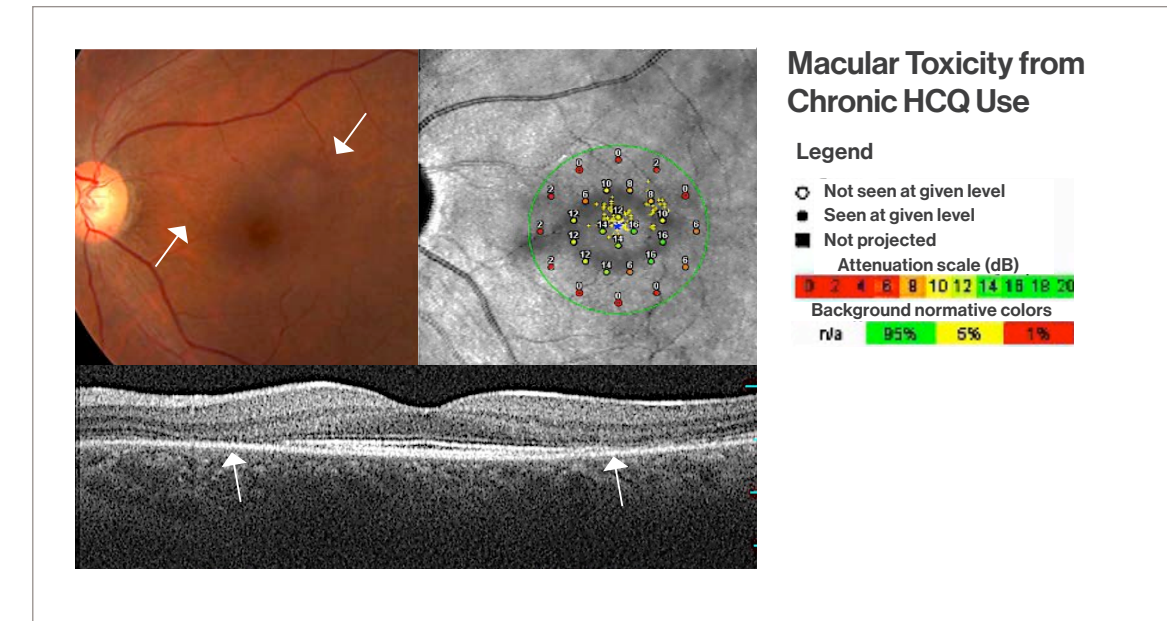


Fig. 1

Fig. 1: Fundus image of bullseye maculopathy (left), microperimetry demonstrating reduced perifoveal sensitivity (right) and OCT (bottom) demonstrating collapse of outer retinal layers corresponding to bullseye pattern, often referred to as the "flying saucer sign."

Fig. 2: (Top) Cell culture images of normal RPE cells (left), cells demonstrating hydroxychloroquine toxicity following exposure to 100 uM of drug (middle), and cells spared by addition of beta-adrenergic agonist (right). (Bottom) Higher power images of normal RPE cell culture (left), vacuolization of cells at high power following exposure to 30 uM of hydroxychloroquine (middle), and reduction of vacuoles in similarly exposed cells by addition of beta-adrenergic agonist (right).

Fig. 3: (Top) Animal model of photoreceptor loss in hydroxychloroquine toxicity. Control mouse retinas at 200x (left) and 400x magnification (right). (Bottom) Outer retinal damage due to 30 days of exposure to hydroxychloroquine at 200x (left) and 400x magnification (right).

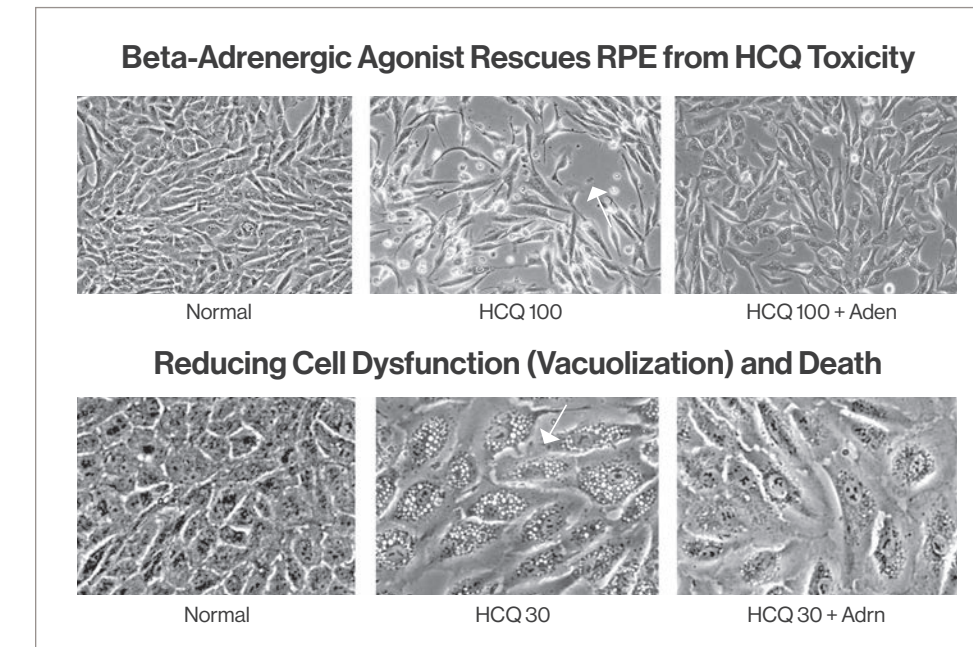


Fig. 2

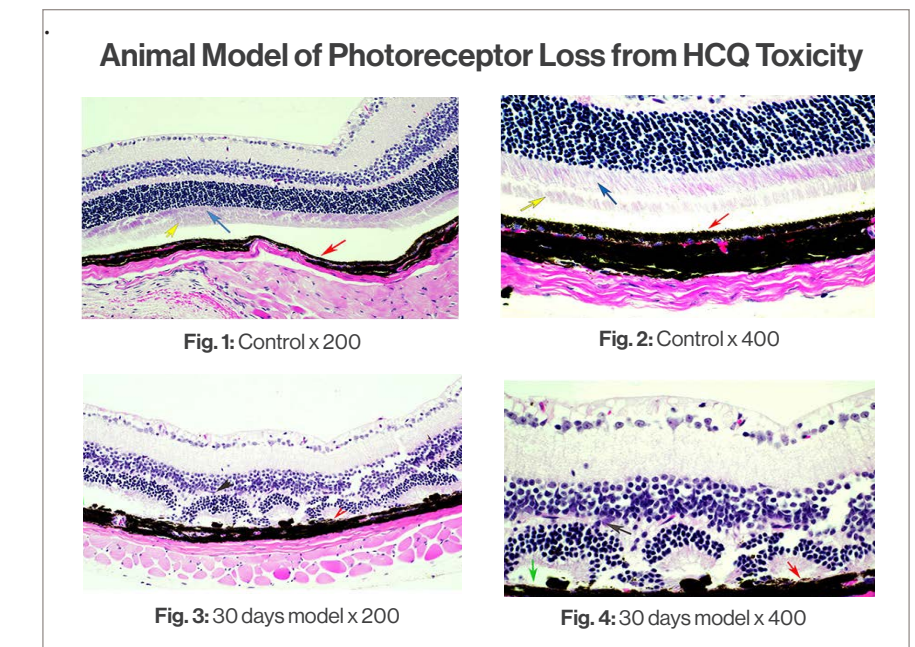


Fig. 3

First-Time Parents Brave COVID-19 Fears To Get Their Infant Emergency Treatment

When Mia Alvarez was born on March 17 with congenital cataracts in both eyes, parents and physicians alike were thrust into a perfect storm. There was the issue of timing: to prevent permanent vision impairment, the cataracts had to be removed from the newborn's eyes within a two-month window. Not a difficult task in normal times, perhaps, but this was the height of COVID-19 in New York City, when surgical practice everywhere was being upended and personal fears for health and safety, especially those of a month-old baby, were rampant. But each day was critical to Mia's development, and so her surgery was scheduled for April.

For Mia's mother, Kristal Alvarez, this meant presurgical COVID-19 testing for her daughter, her husband, and herself, and wearing protective coverings to and from New York Eye and Ear Infirmary of Mount Sinai's uptown satellite and The Mount Sinai Hospital, where the ophthalmic surgery was performed. The situation was further complicated by the endless frustrations of attempting to get approval from Medicaid, which was grappling with its own shutdown orders and working remotely, for the absolutely necessary procedure.

The stakes for Mia became even higher when Ms. Alvarez and her husband, Alex, learned their daughter would require follow-up surgery just two months after the first one to remove secondary cataracts that had formed. "The stress was incredible because we were going to the hospital every week," recalls Ms. Alvarez. "Faced with the need to social distance even from family members, my husband and I had to make plans for who would care for the baby if either of us or both of us tested positive for the virus."

The experience enabled them to form a close bond with Douglas Fredrick, MD, Chief of Pediatric Ophthalmology at Mount Sinai Health System, who performed both surgeries and helped the couple in multiple ways, including cutting through the insurance red tape. Aware from the day of



Douglas Fredrick, MD performing fixate and follow eye exam on Mia and in the operating room.

Mia's birth that she would need ocular surgery, the parents acted on the recommendation of their pediatrician at Mount Sinai and chose Dr. Fredrick, internationally known for his treatment of pediatric cataracts and complex strabismus. "We believed Dr. Fredrick could give our daughter the best chance of having good eyesight as she got older," says Ms. Alvarez. Nothing was more important to the 28-year-old mother, whose right-eye vision is 20/200 and left-eye vision is 20/400, the result of Marfan syndrome and microphthalmia, a developmental disorder that produces abnormally small eyes. She, too, was born with cataracts, but they weren't removed until she was nine.

Even by the miniaturized standards of infant surgery, Mia was a challenge for Dr. Fredrick. "We were dealing with a smaller workspace and smaller tolerances in an eye where the diameter of the cornea was just 7 millimeters, compared to 11 millimeters normally," he explains. "The reduced exposure required us to use 25-gauge surgical instruments, among the smallest made, to cut away some of the vitreous gel from the eyeball." On the positive side, because infant cataracts are usually soft and gelatinous, the surgical team was able to remove them through simple aspiration, versus the ultrasonic energy required for adult cataracts.

Once the initial surgery was complete, the Alvarezes were faced with another challenge. Both legally blind, they had to follow a strict post-op regime of administering four eye drops three times a day into both eyes of an infant who made her displeasure with the process abundantly clear. Just as demanding was the work around maintaining the tiny contact lenses that had been prescribed for Mia. Since these soft silicone lenses, with a strength of +32 diopters, enabled oxygen to pass through to the surface of the cornea, they could be worn a week at a time without the risk of infection. Still, they had to be removed,

cleaned, and reinserted into the infant's eyes weekly.

At first, Dr. Fredrick lent a helping hand during the couple's office visits. After that, the couple learned to master the delicate task themselves, drawing on the wellspring of strength and resilience that had already sustained them through each day of their young and challenged lives.



Douglas Fredrick, MD, with Mia and parents during an office visit one month following her second eye surgery.

They tag-teamed to deliver Mia's daily eye drops and Mr. Alvarez mastered the delicate task of placing and removing her tiny contact lenses. "It was a struggle," admits Mr. Alvarez, of the two-person job. "We tried using our fingers, a Q-tip, and even a tiny plunger to squeeze the contact lenses into her small eyes. Sometimes they would stick on perfectly, other times they wouldn't. Mia would get very frustrated and angry."

Their determination also helped carry them through the second surgery on June 2 to remove the membrane that had formed behind the pupil of each eye, flush against the iris. This complication, not uncommon, required Dr. Fredrick to perform a vitrectomy to excise the scar tissue without damaging the iris—again working in the tiniest and most demanding of spaces. "We had to make small incisions at the edge of the pupil to allow it to expand," says Dr. Fredrick of the intraocular surgery. "That increased the visualization we needed to

do the surgery, while allowing the pupil to retain its function and shape after the procedure."

The success of this difficult surgery can perhaps be measured best by what happened afterwards, when Mia was back home, mom and dad hovering over her crib. "There was a toy to the side of her, and she just reached out and grabbed it," remembers Ms. Alvarez. "We were incredibly excited because she had never done that before."

Their optimism has only grown since then as Mia continues to heal well, and Dr. Fredrick has given a prognosis of good functional vision in the longer term—perhaps as good as 20/40 corrected—if the eyes develop properly. "From the time she was conceived I dreamed of her having the best vision possible," says Ms. Alvarez wistfully. "To know that Mia may be able to drive one day and live her life the way she wants is just amazing to us."

Innovative AI Prediction Models Provide Early Alert System for Eye Disorders

Ophthalmologists have long fretted over the number of people who are unaware they have disorders like macular degeneration or diabetic retinopathy until sudden vision loss or a retinal hemorrhage forces them to seek emergent care. Researchers at New York Eye and Ear Infirmary of Mount Sinai (NYEE) have now set the stage for dramatic change, as revealed in two recently published clinical studies.

The first study, in the April issue of *Translational Vision Science & Technology*, describes a family of artificial intelligence (AI)-driven models developed by the NYEE team that, for the first time, can identify not only patients at risk for age-related macular degeneration (AMD), but also those who are likely to progress to late-stage AMD within one to two years and should be seeking ophthalmic care. The second study, in *Diabetes Care*, reports on the development and validation of an automated diabetic retinopathy screening tool which could help pave the way for detection of potentially blinding ocular disease in diabetic patients during routine visits to their primary care doctor.



R. Theodore Smith, MD, PhD in the Retinal Imaging Lab of NYEE.

Predicting AMD

The unique models for detecting adult macular degeneration use an ensemble of deep learning screening methods and AMD-specific algorithms to classify patients into early, intermediate, or advanced AMD categories, and then a machine learning technique to predict progression to late-stage AMD. The accuracy of this innovative system for predicting disease progression within one to two years was 86 percent, higher than any other tool currently available. When measured on its ability to further predict who would progress to dry or wet forms of the disease—a considerably more demanding parameter—the accuracy of the NYEE models was around 67 percent.

“This technology could be particularly useful in identifying someone who has slipped across the boundary to intermediate or higher-risk AMD and is thus more statistically likely to progress,” says R. Theodore Smith, MD, PhD, Director of Biomolecular Retinal Imaging at NYEE and corresponding author of the study. “By alerting patients and their physicians to the potential dangers ahead, we believe this approach could play a very important public health role.”

Early detection of AMD—the leading cause of vision loss in people over 50—has never been more important. The Age-Related Eye Disease Study (AREDS), the largest study of its type to date, showed that specific antioxidants and vitamin supplements could reduce the risk of progression from intermediate- to late-stage AMD, allowing for additional preventive strategies. Those treatments might include photobiomodulation and sub-threshold nanosecond laser.

To train and validate their AI-based models for AMD screening and prediction, Dr. Smith and his team started with nearly 117,000 color fundus photographs from 4,139 participants in AREDS. A deep-learning image classifier was used to distinguish no-AMD or early-stage AMD from intermediate-stage AMD with near-perfect accuracy. The deep-learning classifier relied on six algorithms that provided probabilities of where an image would reside on one of 12 more detailed AREDS scales. These outputs were then combined with socio-demographic clinical data and AMD-specific imaging data through a logistic model tree—a sophisticated machine learning technique—to identify individuals at risk of progressing from intermediate- to late-stage AMD within one to two years. For those found to be in danger, the technology further predicted the type (dry or wet) of progression.

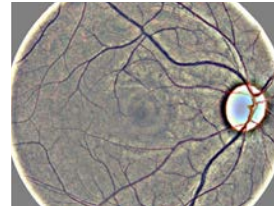
"We were able to train these convolutional neural networks on hundreds of thousands of photographs to be able to recognize features that determined if they fell into the broad categories of early, intermediate, or advanced AMD," explains Dr. Smith, who is also Professor of Ophthalmology, and Neuroscience, at the Icahn School of Medicine at Mount Sinai. "And that's the beauty of AI: it can define patterns and make inferences from gigantic data sets that humans could never wrap their minds around."

Screening for Diabetic Retinopathy (DR)

AI deep learning software is also the linchpin of the automated screening tool for diabetic retinopathy developed in the NYEE labs. In the *Diabetes Care* paper (October 2020), researchers described the five-point scale they created for grading the severity of the disease (no DR, mild, moderate, severe, and proliferative) based on the presence and extent of microaneurysms, exudates, hemorrhages, and other abnormalities found in the fundus photographs they examined in their study. When measured prospectively in Mount Sinai clinics against the gold standard—human expert screening—the AI deep learning system achieved remarkable results for referral level DR (moderate or worse): a sensitivity of 82.6 percent, adequate for FDA approval of a screening system, and a specificity of 93.7 percent.

In the wake of this success, plans are afoot to further test the five-point diabetic retinopathy algorithm with a much larger audience on the road to FDA approval. Dr. Smith, senior author of the *Diabetes Care* study, envisions the automated system eventually residing in primary care settings in the community to screen and classify patients on the spot for diabetic retinopathy. "Physicians would be able to inform patients if they are at risk for a problem before they even leave the office and, if so, encourage them to get specialized care," he points out. "It could represent a major step for public health by alerting patients to problems that too often today lead to advanced disease and even blindness."

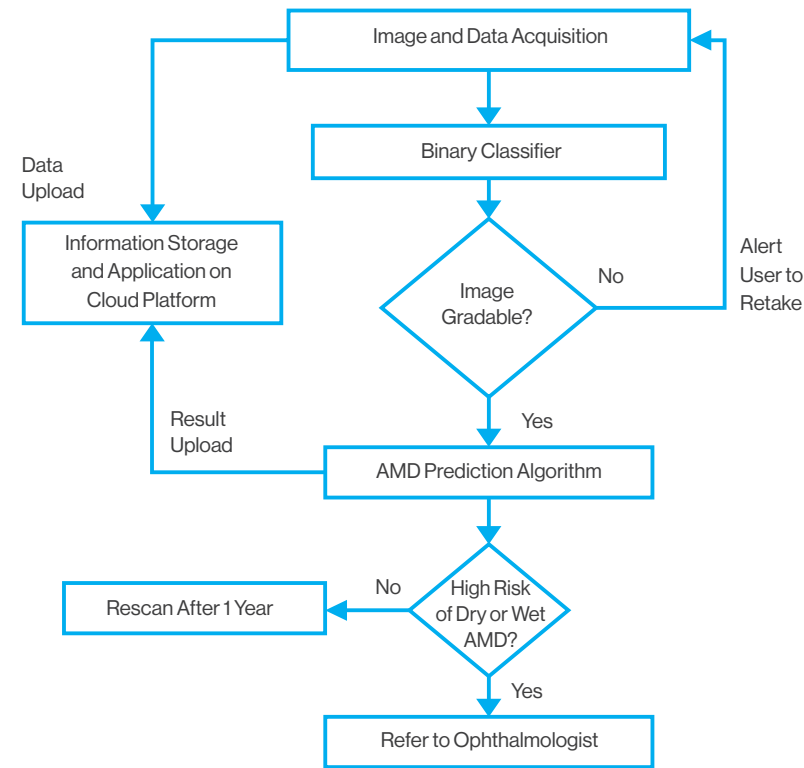
To that end, NYEE hopes to team up with the new Institute for Health Equity Research at Mount Sinai to further investigate both the AMD and diabetic retinopathy screening tools. Announced in May 2020 by the Icahn School of Medicine, the Institute is designed to examine the causes and magnitude of health care disparities impacting nonwhite, low-income, immigrant, and other underserved communities. Introducing the screening algorithm to community health care clinics staffed by the Institute could, Dr. Smith stressed, be the perfect way to develop strategies aimed at detecting as early as possible common ophthalmic diseases that prey disproportionately on disadvantaged populations.



Screening for Diabetic Retinopathy: Ensemble Framework of Deep Learning-Based Diabetic Retinopathy (DR) Screening System

The preprocessed and the original RGB images are input to ensembles of three and two deep learning (DL) models, respectively, differing in type of architecture and input image size. Each model then produces a set of 5 probabilities of belonging to each of the 5 DR classes: None, Early, Intermediate, Severe, and Proliferative DR. The 25 total probabilities are then concatenated (grouped) as input to a logistic model tree (LMT), which is a machine learning decision tree. The LMT has been trained to decide the DR class based on the totality of the DL inputs, and is the final classifier.

High-Level Flow Chart for the Overall Screening and Prediction of Late AMD



	Subject 1	Subject 2	Subject 3
A			
B			
C			
D			

Left: Fundus photos of 3 subjects at baseline (Row A) and the corresponding heat maps (Row B) of early AMD signs detected by our classifier. Blue color, strong signs of AMD. Green color, weaker signs of AMD. Row C, followup fundus photos showing transformation to late AMD in each case. Row D, followup heat maps showing much larger areas and worse signs signifying late AMD.

Translational Imaging Techniques Could Change How We Treat Retinal Disease

A collection of advanced new retinal imaging techniques in which New York Eye and Ear Infirmary of Mount Sinai (NYEE) is playing prominent development roles promises to grow our understanding of disease processes and interventions in ways never before possible, especially in the case of age-related macular degeneration (AMD). A newly published paper in *Asia-Pacific Journal of Ophthalmology* (May-June 2020) describes several of those imaging modalities that have the potential to significantly impact mainstream clinical practice.

"We know that the highest level of patient care occurs when we use every available form of imaging," says R. Theodore Smith, MD, PhD, Director of Biomolecular Retinal Imaging at NYEE, and lead author of the paper whose research is providing the building blocks for these technologies. "Each mode of imaging yields a different set of information, which helps to create a picture that's greater than the sum of its parts. The result is an understanding of the disease that improves our ability to effectively diagnose and treat patients."

Quantitative autofluorescence (qAF) imaging is one of those translational technologies, developed and introduced by Dr. Smith and several colleagues in 2011 while he was a Professor of Ophthalmology at Columbia University, and now being enhanced by his lab at NYEE as a predictor of AMD progression. qAF builds on fundus autofluorescence (FAF), an established qualitative tool for judging the health of the retina through the retinal pigment epithelium (RPE). Because this layer is flush with molecules that have fluorescence properties, the appearance of dark patches on a patient's autofluorescence images could indicate RPE cell deterioration, with the potential to progress over time to advanced AMD.

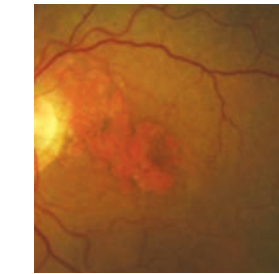
Quantitative autofluorescence imaging takes FAF to a bold new level by measuring lipofuscin-related FAF from the retinal pigment epithelium. A decline in lipofuscin suggests a decrease in RPE health and increasing severity of non-neovascular AMD. According to Dr. Smith, qAF provides a new understanding of the pathogenesis of AMD by putting FAF values on a quantitative scale that can measure the level of disease in the RPE throughout the macula, making it a marker for AMD progression. This novel imaging tool also has the ability to highlight various AMD subtypes like the soft drusen pathway, which is identifiable through its much darker images.

"If you look at macular degeneration through fundus photography or optical coherence tomography (OCT), you might be misled in terms of the severity of the disease," asserts Dr. Smith. "But when you examine it through the lens of quantitative autofluorescence you get a dramatic picture of how extensively the disease has progressed in this particular cell layer."

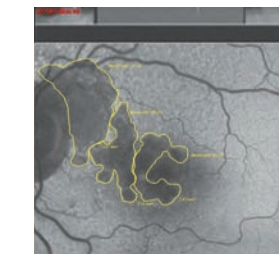
While qAF has already been deployed in some research labs globally, widespread clinical use awaits further investigation.

Hyperspectral autofluorescence (AF) imaging is another established technology which Dr. Smith is re-engineering to give it the ability to detect the precursors of AMD even before OCT and other imaging modalities. Like the retinal pigment epithelium, soft drusen—the lipid-rich signature of early AMD—emit a very specific fluorescence which can be measured through hyperspectral AF imaging. This unique modality combines spectral (or wavelength) components with spatial data of light emanating from the image. Because the human eye cannot visualize this constellation of data, researchers are working to understand it by decomposing it into different spectral components with the help of advanced image analytics being created by Dr. Smith.

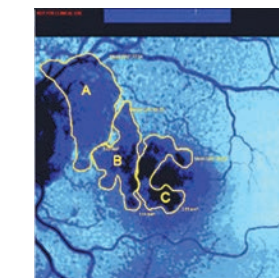
Quantitative Autofluorescence (qAF) in Advanced Dry AMD (multilobular geographic atrophy (GA))



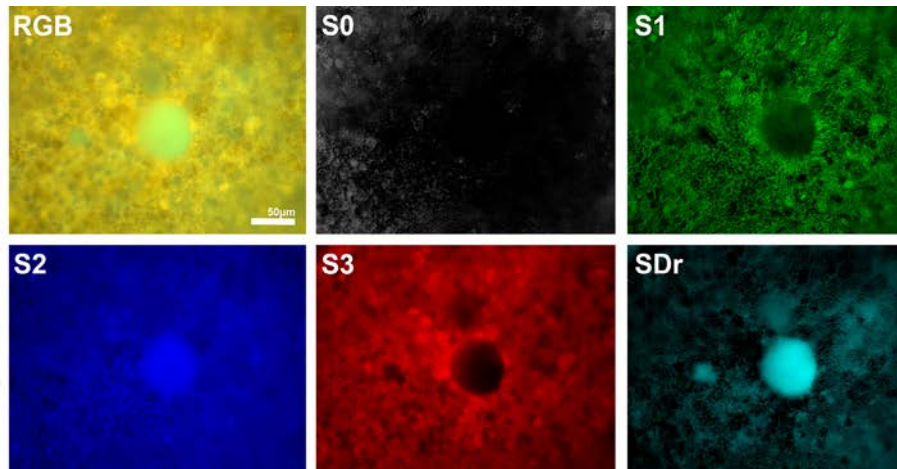
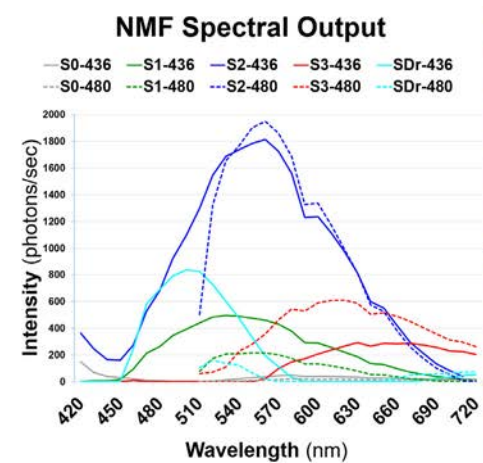
The left eye on color fundus photography.



The qAF image in gray scale. Three lobules of GA are outlined in yellow. The qAF values were obtained by calibrating the standard AF values to the internal fluorescent reference above.



The color-coded qAF map with a reference bar showing qAF intensities. Areas damaged by AMD are identified by low qAF, coded dark blue and black (qAF imaging courtesy of Wei MD).



Hyperspectral AF Imaging in AMD Tissue With Drusen

Left: After mathematical “unmixing” of the autofluorescence from the AMD tissue, 3 distinct spectra are found in the RPE, labeled S1, S2 and S3, presented graphically in green, blue and red, and a distinct new spectrum SDR (azure) is found for drusen emission around 510 nm.

Right: The original unmixed full color AF of the sample with drusen is marked RGB. Note the yellowish AF from the RPE cells, and greenish AF from the drusen. After unmixing, the color-coded tissue localizations of the individual fluorophore sources of the spectra S1, S2, S3 and SDR are shown.

These mathematical tools separate complex data into major bands that represent emissions from lipofuscin granules within the RPE and, more importantly, from a thin layer just beneath the RPE known as the basal linear deposit—a precursor of drusen which is perhaps the earliest warning sign of AMD. According to Dr. Smith, hyperspectral AF imaging has the ability to “tell when macular degeneration is starting to develop extremely early in the AMD cycle—in fact, as soon as the basal linear deposit gets laid down.”

Essential to the use of hyperspectral autofluorescence imaging in a clinical setting will be a compatible hyperspectral camera. This piece of the technology is being developed by NYEE in collaboration with Liang Gao, PhD, Assistant Professor of Bioengineering at UCLA, and Christine Curcio, PhD, Professor of Ophthalmology at the University of Alabama School of Medicine and a worldwide authority on AMD pathology. The sophisticated camera will have dual functionality as a hyperspectral camera and as computational adaptive optics OCT for high-resolution structural imaging.

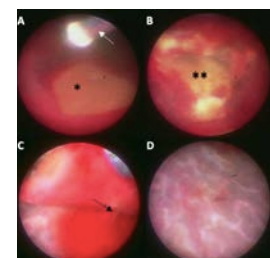
The **ophthalmic endoscope** could open the door worldwide to a radically different approach to vitreoretinal

surgery. By offering unprecedented access to the subretinal space, the ophthalmic endoscope—developed in Japan—could represent a major advance for intraocular observation during vitrectomy. For example, in a patient with a large subretinal hemorrhage caused by a leaky blood vessel from the exudative form of macular degeneration, the endoscope could afford an extremely direct way to access the subretinal space and remove the hemorrhage from underneath the retina. This compares to the current approach which steers clear of the subretinal area and instead fills the eye with an expanding gas that acts like a bubble to push the hemorrhage away from the macula.

The ophthalmic endoscope with its high resolution of 20 microns per pixel could also serve as a powerful research tool. “By putting this camera under the retina, you can look directly at the choroid and at the choroidal neovascularization and be able to see the abnormal structures that develop into different forms of macular degeneration,” says Dr. Smith, who serves as technical advisor to the developers of the imaging device. “These images are quite remarkable and hard to obtain through any other technique. We believe they will play a valuable role in understanding the pathogenesis of ocular disease.”

Ophthalmic Endoscopic Subretinal View of Large Subretinal Hemorrhage Due to AMD

(Modified from Retina. 2019 May; 39(5):896-905. with permission)



A. The RPE is a pale orange tissue (asterisk) surrounded by remaining subretinal hemorrhage from choroidal neovascularization (CNV). The vitreous cutter is above (arrow). This entire field is 2.5 mm in diameter, captured by the 10,000 fibers of the endoscope.

B. The CNV is seen directly as a mosaic-brown mass lesion (double asterisks).

C. Beneath the CNV, a feeder vessel originates from the choroid as a thin white cord-like tissue (arrow).

D. After removal of the CNV, tortuous white choroidal vessels are revealed, suggesting ischemia.

Surgical Management of Submacular Hemorrhage Offers New Hope to Patients

Submacular hemorrhage presents ophthalmologists with one of their greatest challenges for restoring visual function. The high risk of dramatic visual loss in patients following an acute event has spurred the search for better interventions than the current standard of care: anti-vascular endothelial growth factor, injections and conservative monitoring.

A study in the New York Eye and Ear Infirmary of Mount Sinai (NYEE) Department of Ophthalmology (*BMJ Open Ophthalmology*, March 2020) offers support for early surgical intervention in submacular hemorrhages from all causes. Researchers found significant benefits using pars plana vitrectomy and injection of subretinal tissue plasminogen activator (tPA), along with pneumatic displacement of the submacular blood. In their retrospective review of 36 patients, 22 (61%) experienced visual improvement, with 42% gaining three or more lines at the three-month follow-up. Moreover, these results were observed regardless of the underlying pathology, be it exudative macular degeneration (43% of patients), undifferentiated choroidal neovascularization (19%), polypoidal choroidal vasculopathy (19%), traumatic choroidal rupture (11%), or proliferative diabetic retinopathy (3%).

“For the first time we were able to show the effectiveness of this treatment in a highly diverse patient population,” states Carl Wilkins, MD, lead author of the study and former chief resident at The Mount Sinai Hospital and current NYEE retina fellow. “Our analysis showed substantial visual recovery in each subgroup regardless of the underlying cause.”

The regimen of pars plana vitrectomy and tPA with pneumatic displacement has been used for years at NYEE as well as other major academic centers around the country. But as Richard Rosen, MD, Chief of Retina Service at Mount Sinai Health System, and senior author of the study, points out, not all retinal specialists are convinced that this invasive management of submacular hemorrhage is superior to the more conservative approach, anti-VEGF therapy. Specifically, surgical

management utilizes vitrectomy with subretinal injection of tPA to liquefy the trapped blood clot, followed by reconstitution of the vitreous cavity with an air bubble and a small percentage of expansile gas that displaces the clot inferiorly, out of the central visual space of the retina, preventing damage to the photoreceptors.

Potential complications which may affect visual restoration from the hour-long procedure include the presence of deeper blood trapped beneath the retinal pigment epithelium (RPE), which may only become apparent during the surgery, and the risk of recurrence of bleeding following successful surgery.

Findings from the NYEE study, according to Dr. Rosen, who is also Vice Chair and Director of Ophthalmology Research at NYEE, could help raise the confidence level for retinal specialists who have little or no experience with this approach. “I would encourage any ophthalmologist who has a patient presenting with new-onset submacular hemorrhage and substantial vision loss to give this approach strong consideration, regardless of the underlying pathology,” he noted. “And it’s most important for physicians to understand that the best results occur when treatment is initiated within two weeks of the event.”

Robotics could eventually provide an additional layer of precision and standardization for surgeons employing the vitrectomy/tPA technique. A state-of-the-art robotic assistance system, expected to begin clinical trials this year at NYEE, could offer an unprecedented level of instrument stabilization for the vitreoretinal surgeon. “Trans-retinal injection of tPA is an extremely delicate aspect of the procedure, and robotic stabilization could ensure the most accurate delivery of medication beneath the retina without injuring the underlying retinal pigment epithelium,” says Dr. Wilkins, who will work alongside Dr. Rosen to introduce the system. NYEE is teaming up with Preceyes BV, the Dutch engineering company that manufactures the device, to secure approval from the Food and Drug Administration for the tremor suppression system, the first commercial system of its type in the United States for complex ocular surgery.



Fig. 1: Color fundus of subretinal hemorrhage following double RPE rip. Patient vision on presentation of finger counting.

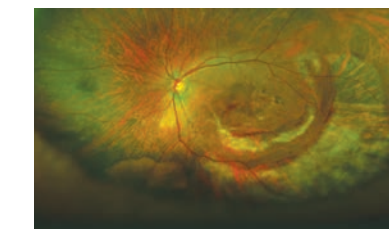


Fig. 2: Color fundus image 2 months post-surgery with vision improvement to 20/200.

Seeding the Future of Ophthalmology

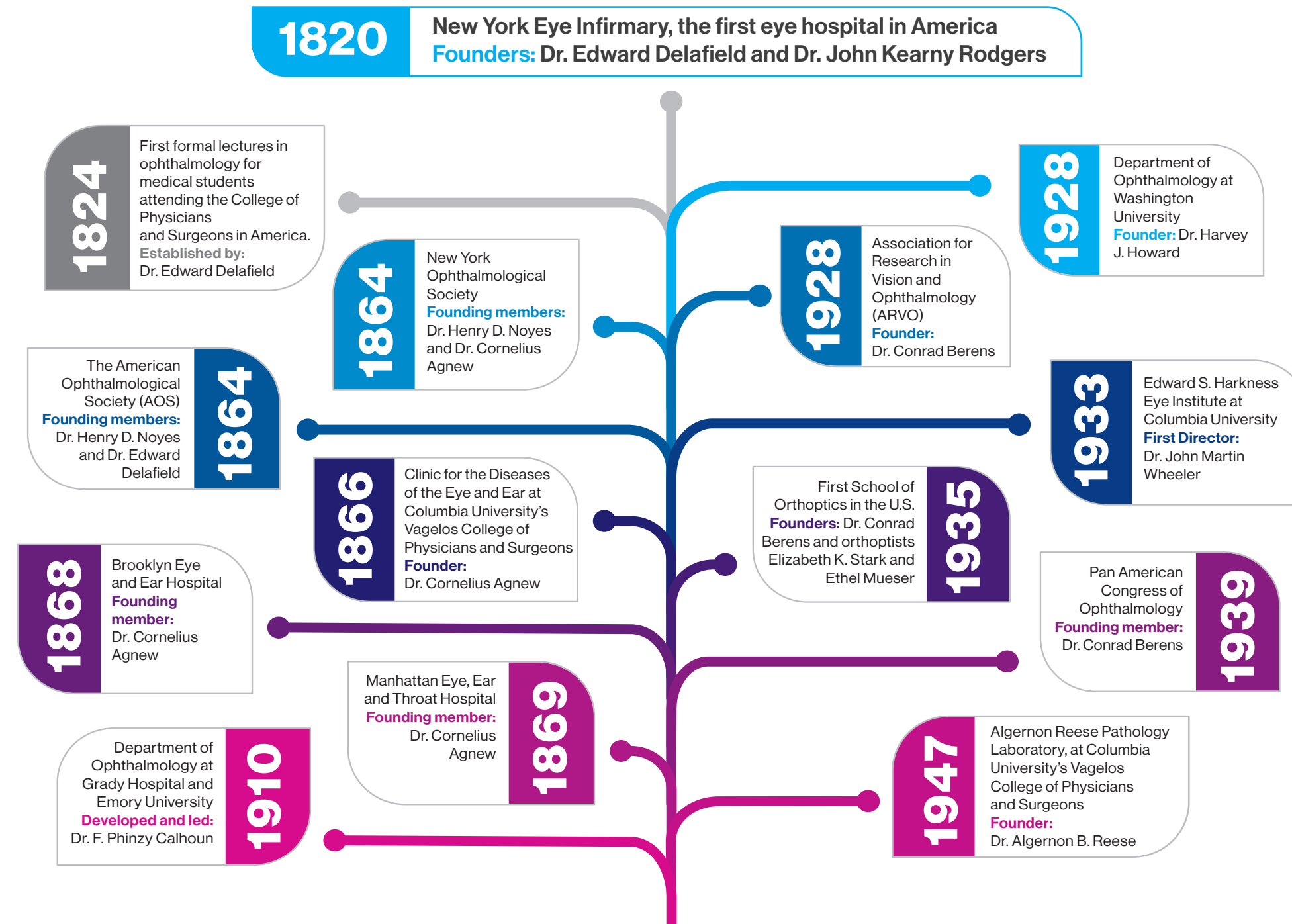
The distinction of being the first specialty hospital in America has given NYEE a coveted place in the history and development of Ophthalmology. From the seeds we have planted over the past 200 years have sprouted many of the clinical standards of care and surgical innovations that define our specialty today. The spirit of our founders and their ironclad commitment to patient care, education, and research have inspired future generations of NYEE faculty and alumni to establish new hospitals, clinics, and organizations with global import.

And our numerous innovations and clinical and research breakthroughs have led to new medical and surgical treatments and diagnostic modalities that revolutionized the field and helped millions of patients worldwide. We are proud of our lasting legacy and the pioneering spirit of our founders, faculty, trainees, and scientists.



In 1824, NYEE creates its original seal depicting the Great Physician restoring the sight of Bartimaeus. The American Ophthalmological Society adopts the Infirmary's seal as its own upon its founding forty years later within the institution.

NYEE Contributions to Organizational Ophthalmology in America

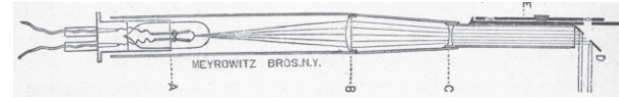




1862 Dr. Henry D. Noyes, Executive Director of NYEE, takes the first photographic image of the retina in a live subject, a rabbit.



1871 Dr. Cornelius Agnew invents a new incision for draining the lacrimal sac made through the conjunctiva between the caruncle and the inner commissure of the eyelids.



1885 Dr. William Dennett, a NYEE attending, invented first Ophthalmoscope with illuminating light bulb.



1958 Dr. Louis J. Girard co-designs the first small, thin contact lens.



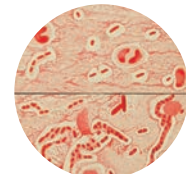
1958 Dr. Aran Safir, during his NYEE residency, invents an early electronic retinoscope and files for a patent.



1959 Dr. Bruno S. Priestley, an NYEE physician, establishes the Department of Pleoptics – the first of its kind in the U.S. and the largest of its kind in the Western Hemisphere.



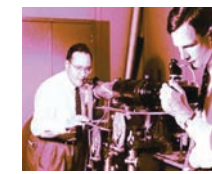
1886 Dr. Agnew details a groundbreaking operation for divergent strabismus, in an article entitled "A Method of Operating for Divergent Squint," published in the *Transactions of the American Ophthalmological Society*.



1886 Haemophilus aegyptius or Koch-Weeks bacillus is discovered by Drs. Robert Koch and John E. Weeks, head of the NYEE staff, as a cause of acute conjunctivitis.



1888 Dr. Edward G. Loring enhances the Helmholtz Ophthalmoscope with design features to improve ergonomics for the clinician.



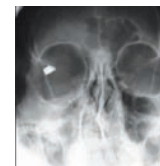
1961 Early studies of laser photocoagulation in rabbit retina were conducted at Bell Labs by Morton L. Rosenthal, MD and Seymour Fradin, MD, along with Charles Townes, MD and Arthur Leonard Schawlow. This would eventually become the mainstay treatment for diabetic retinopathy.



1966 A seminal article, "The Technique of Binocular Indirect Ophthalmoscopy," is published by Morton L. Rosenthal, MD and Seymour Fradin, MD. Illustrated by Dr. Fradin, the methodology described for a retinal exam is still used today.



1967 NYEE attending Dr. Norman B. Jaffe was among the first three surgeons in the U.S. to implant an intraocular lens following cataract extraction.



1904 The first x-ray localization of a foreign body in a patient's eye is performed by Drs. John E. Weeks and George Dixon. Subsequently, Dr. Dixon develops the Weeks and Dixon method of ocular foreign body localization.



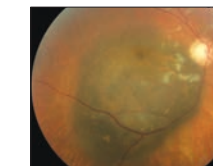
1934 Dr. John Martin Wheeler pioneers the specialty of ophthalmic plastic and reconstructive surgery with the new techniques for the repair of eyelid abnormalities, including lower eyelid entropion, which is still in use today. He also introduces the first oculoplastic courses at the American Academy of Ophthalmology.



1935 NYEE establishes the first School of Orthoptics in the U.S. under the direction of Dr. Conrad Berens and orthoptists Elizabeth K. Stark and Ethel Mueser.



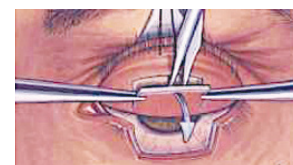
1971 NYEE's Retina Diagnostic Center, for retinal photography and fluorescein angiography, is established under the leadership of Thomas O. Muldoon, MD, class of 1966.



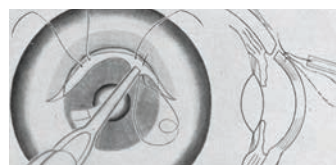
1974 NYEE physicians David Krohn, MD, Donald Morris, MD, and Ron Jacobs, MD, pioneer the use of hematoporphyrin derivatives for diagnosis and photodynamic therapy of choroidal melanoma.



1979 The first digital A-scan ultrasound system for intraocular lens measurements is created at NYEE's Bioengineering and Computer Science Division, established by Richard Koplin, MD and Martin Gersten, an engineer.



1939 NYEE's Chief of Ophthalmic Plastic and Reconstructive Surgery, Dr. Wendell Hughes, develops the "Hughes Procedure" for reconstructing lower eyelid defects following the removal of large tumors.



1944 Absorbable sutures for cataract surgery are introduced by NYEE physicians Drs. Wendell Hughes, Hunter Romaine, and Loren Guy.



1949 NYEE-trained Dr. Louis J. Girard conducts the first clinical investigation of corneal contact lenses.



1982 A team of clinician-scientists at NYEE—Virginia Lubkin, MD, Martin Gersten, Richard Koplin, MD, and Dennis Gormley, MD—invented corneal topography and built the first corneal mapper, leading the way to precision corneal vision correction.



1983 Robert Ritch, MD, joined NYEE, expanding glaucoma research and creating the Ocular Imaging Center for the study of optic nerve structure and blood flow. The Center becomes a world-class glaucoma imaging resource with the advent of high-resolution ultrasound biomicroscopy (1994) for investigating the anterior segment anomalies such as plateau iris, and employs (1995) one of the first OCT systems outside MIT, where it was developed.



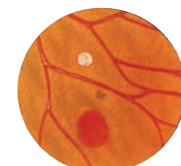
1984 The New York Eye Trauma Center, the first of its kind in New York City, opens at NYEE under the leadership of Richard Koplin, MD.



1951 Dr. Conrad Berens and Dr. Jerry Hart Jacobson conduct pioneering clinical studies of electroretinography at NYEE. Dr. Jacobson became a leading contributor to the development and standardization of clinical electroretinography.



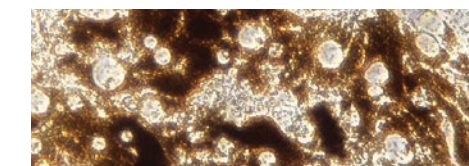
1954 Dr. Louis J. Girard is the first ophthalmologist to perform and document corneal transplantation.



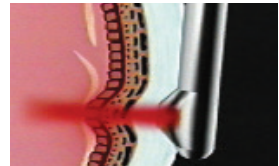
1957 New York City's first Retina Service is formally established by Morton L. Rosenthal, MD. Dr. Rosenthal introduced at NYEE techniques of indirect ophthalmoscopy and fundus drawing for visualizing the retinal periphery, ushering in a new era in modern retinal surgery.



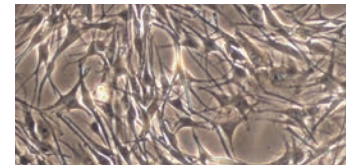
1987 Aran Safir, MD and Leonard Flom, MD invented iris recognition biometrics for unique identification.



1990 First photo of cultured, purified human iris pigment epithelial (IPE) cells was taken at NYEE's Ocular Cell Cultural Lab, thanks to Dan Ning Hu, MD, Robert Ritch, MD, and Steven A. McCormick, PhD, who were the first to develop the methodology for isolation and culture of human IPE.



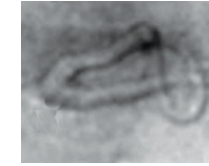
1992 Richard B. Rosen, MD, Thomas O. Muldoon, MD, and David Buzawa, MEng (in partnership with Iris Medical) developed the first commercial trans-scleral laser retinopexy probe for treatment of retinal tears and detachments.



1992 Dan Ning Hu, MD, Robert Ritch, MD, and Steven A. McCormick, PhD, developed the methodology for isolation and culture of human uveal melanocytes (UM). The first photo of UM was taken 12 days after the seeding of a UM isolated from the choroid of a donor eye. Exfoliation material is identified for the first time in cells extracted from glaucoma patients diagnosed with exfoliation syndrome.



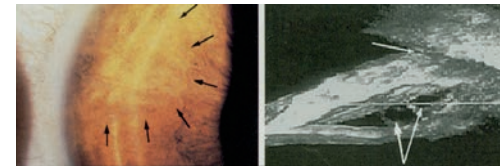
2013 Ronald Gentile, MD, class of 1995, developed the cystoid dehydration of macular holes theory, which resulted in a new approach to treating macular holes non-surgically, using eye drops. He presented his new treatment, which consists of three drops (a steroid, a non-steroidal and a carbonic anhydrase inhibitor), at the Macula Society (36th Annual Meeting) and the American Society of Retinal Specialists (31st Annual Meeting).



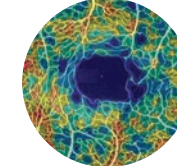
2014 Dynamic histopathology, introduced by Richard B. Rosen, MD and Yuen Ping Toco Chui, PhD, under the auspices of NYEE's David E. Marrus Adaptive Optics Laboratory, using adaptive optics serial imaging allowed physicians for the first time to study retinal capillary microvascular remodeling longitudinally in patients at extended time intervals.



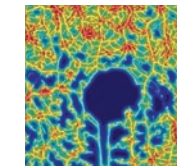
1992 The New York Eye and Ear Infirmary Ophthalmology Associates, P.C., a self-sustaining organization for resident education and patient care, is formed to leverage the expertise of NYEE's large voluntary teaching staff of community ophthalmologists.



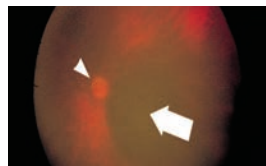
1996 3-D ultrasound biomicroscopy (UBM) imaging is developed, on the commercial Humphrey device, by Ray lezzi, MD, Richard B. Rosen, MD, Celso Tello, MD, and Robert Ritch, MD, for volumetric visualization of anterior segment eye trauma and tumors.



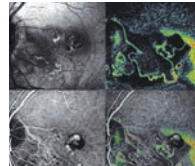
2015 Richard B. Rosen, MD and Yuen Ping Toco Chui, PhD, introduced quantitative analysis of capillary density using adaptive optics scanning light ophthalmoscopy with fluorescein angiography. This provided unprecedented clinical measurements of microvasculature in the retina.



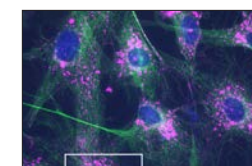
2016 With the introduction of OCT angiography, the clinical utility of *en face* OCT becomes widely recognized. By providing rapidly accessible noninvasive capillary imaging, OCT angiography opened the way for monitoring changes in patients with glaucoma, diabetic retinopathy, and macular degeneration at a resolution previously available only with adaptive optics. Richard B. Rosen, MD and Yuen Ping Toco Chui, PhD, introduced a full spectrum of quantitative tools for precision assessment and follow-up of clinical microvascular disease, based upon their adaptive optics work.



1996 Paul T. Finger, MD, Ray lezzi, MD, Richard B. Rosen, MD, and Eliot L. Berson, MD introduce self-illuminating branchytherapy plaques, enabling improved precision in the placement of radioactive plaques implanted for treatment of sub-macular choroidal melanomas.



2002 20 years ahead of their time, Richard B. Rosen, MD, Patricia Garcia, MD, Mark Hathaway, PhD, and Rishard Weitz, BEng (working with Adrian Podoleanu, PhD and George Dobre, PhD) turned the *en face* OCT/Confocal Scanning Laser Ophthalmoscope (SLO) into a high-resolution clinical tool by combining it with indocyanine green angiography (ICG) to create a simultaneous multi-channel OCT/SLO/ICG angiography device. This project was done in collaboration with the University of Kent, which created the first *en face* OCT.



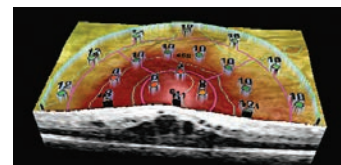
2017 Mount Sinai/New York Eye and Ear (NYEE) Eye and Vision Research Institute is established. As the first of its kind in the New York City metropolitan region, the Institute brings together eye and vision researchers from NYEE, The Mount Sinai Hospital, and Icahn School of Medicine at Mount Sinai.



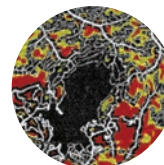
2018 Bo Chen, PhD demonstrated how the gene transfer of β -catenin and three transcription factors, in a living mouse, can successfully reprogram retinal glial cells into rod photoreceptors. Congenitally blind mice were now able to see light for the first time in their lives following treatment.



2005 NYEE holds the "Eye on the Future" colloquium, the first of its kind to bring together specialists focusing on the future of organ, tissue and eye transplantation and donation.



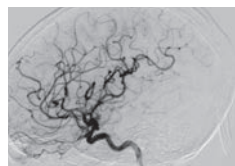
2007 Taking OCT to the next dimension, Richard B. Rosen, MD, Patricia Garcia, MD, Gennady Landa, MD, and Rishard Weitz, BEng (with a Toronto-based Ophthalmic Technologies Inc. team) integrated SLO microperimetry and OCT/SLO 3-D topography. For the first time, clinicians had one instrument, an *en face* OCT, that combined 3-D structural imaging with visual functional testing.



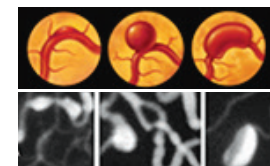
2018 Building upon earlier work in adaptive optics, Richard B. Rosen, MD, Yuen Ping Toco Chui, PhD, and their collaborators in the Medical College of Wisconsin added the first normative data mapping to OCT angiography, to enable instantaneous quantification of abnormalities of blood flow to the retina.



2019 NYEE and The Mount Sinai Hospital merge their ophthalmology residency programs to form the largest ophthalmology residency program in the nation.



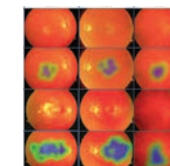
2008 Richard B. Rosen, MD and Mark Kupersmith, MD, in collaboration with Continuum Health Partners' Department of Neurosurgery, develop the "Eye Attack Protocol" for treatment of central retinal artery occlusion.



2012 The study of retinal microvascular disease took a leap forward with the introduction of adaptive optics. Richard B. Rosen, MD and Yuen Ping Toco Chui, PhD (in collaboration with Alfredo Dubra, PhD and Joseph Carroll, PhD, at the Medical College of Wisconsin) merged fluorescein imaging with adaptive optics scanning light ophthalmoscopy to reveal changes in retinal vasculature and the internal fluid dynamics of retinal capillary microaneurysms.



2020 Tsoncho A. Ianchulev, MD, at NYEE, in collaboration with the Dutch developer of Preceyes Surgery System, introduces the first robotic interventional system for ocular surgery in the U.S., ushering in a new era of unlimited potential in precision surgery. The first micro intervention robotic eye surgical system was installed at NYEE in August 2020.



2020 R. Theodore Smith, MD, PhD and his team developed a family of artificial intelligence (AI)-driven models that, for the first time, can identify not only patients at risk for age-related macular degeneration (AMD), but also those who are likely to progress to late-stage AMD within one to two years and should be seeking ophthalmic care.

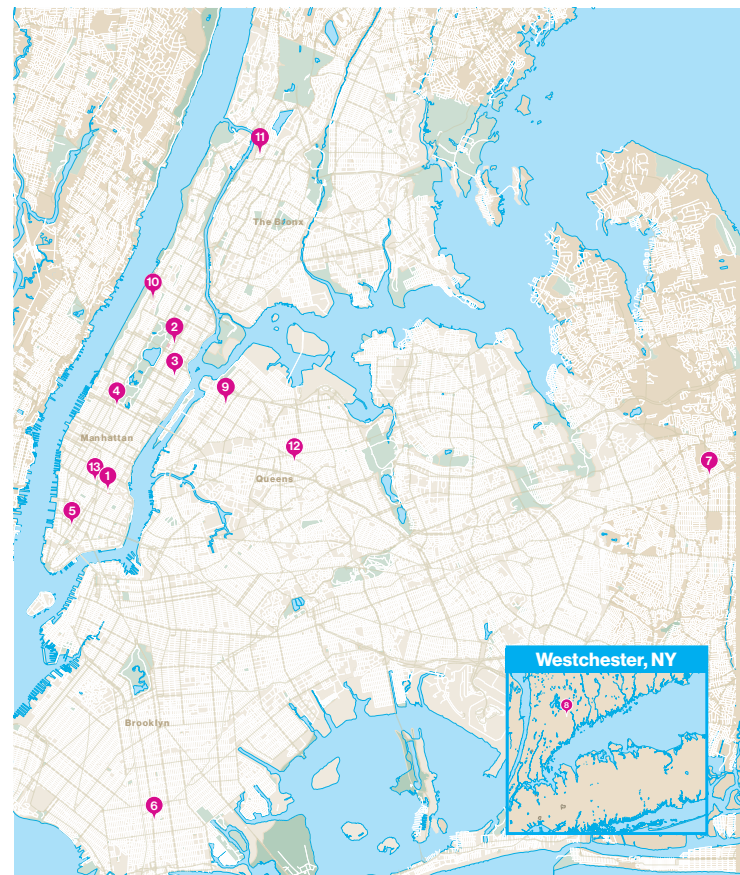
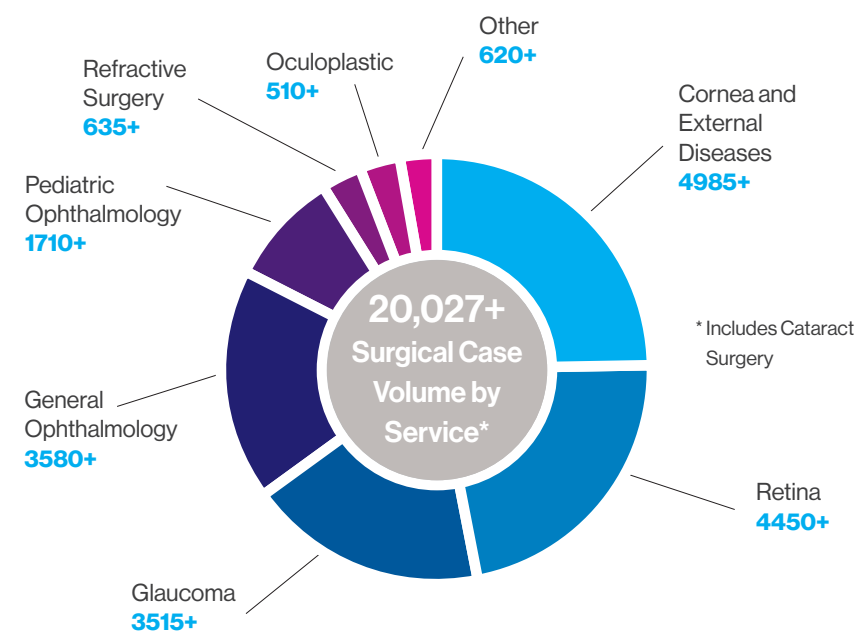
Department of Ophthalmology at a Glance:

New York Eye and Ear Infirmary of Mount Sinai (NYEE) and The Mount Sinai Hospital (MSH) / Icahn School of Medicine at Mount Sinai

NYEE No. 11

BEST HOSPITALS
U.S. News & World Report
NATIONAL OPHTHALMOLOGY 2020-21

(Highest-ranked in NYC) in Ophthalmology by 2020-2021
U.S. News & World Report "Best Hospitals" in America



- Main Campus**
1 New York Eye and Ear Infirmary of Mount Sinai
310 East 14th Street
New York, NY 10003
- Satellite Locations**
- 2 NYEE-East 102nd Street
17 East 102nd Street
New York, NY 10029
 - 3 NYEE-East 85th Street
234 East 85th Street
New York, NY 10028
 - 4 NYEE-Columbus Circle
200 West 57th Street
New York, NY 10019
 - 5 NYEE-Tribeca
77 Worth Street
New York, NY 10013
 - 6 NYEE-Midwood
1630 East 15th Street
Brooklyn, NY 11229
 - 7 NYEE-Mineola
200 Old Country Road
Mineola, NY 11501
 - 8 NYEE-Westchester
90 South Ridge Street
Rye Brook, NY 10573
- Affiliated Clinical Site**
- 9 Mount Sinai Queens
25-10 30th Avenue
Long Island City, NY 11102
 - 10 Mount Sinai Morningside
440 West 114th Street
New York, NY 10025
- Affiliated Teaching Institutions**
- 11 James J. Peters VA Medical Center
130 West Kingsbridge Road
Bronx, NY 10468
 - 12 NYC Health+Hospitals/Elmhurst
79-01 Broadway
Queens, NY 11373
 - 13 Mount Sinai-Union Square
10 Union Square East
New York, NY 10003

2019 STATISTICS*

* Combined 2019 numbers for NYEE and MSH

33 Residency Positions	7 Fellowship Positions	One of the largest ophthalmology graduate medical education programs in the country	33 Funded Clinical Trials	152,272 Outpatient Visits
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Faculty News

Accolades



Alon Harris, MS, PhD, FARVO, an internationally recognized leader in clinical ophthalmic research, received a Silver Plate Award from the 4th International Congress of the Italian Association for the Study of Glaucoma (A.I.S.G.). Dr. Harris accepted the award for his longstanding clinical research programs investigating ocular blood flow and metabolism in glaucoma optic neuropathy.

Dr. Harris joined Mount Sinai in 2019 as Vice Chair of International Research and Academic Affairs for the Department of Ophthalmology in Icahn School of Medicine at Mount Sinai and Director of Ophthalmic Vascular Diagnostic Research Program at The Mount Sinai Hospital.

New Recruits



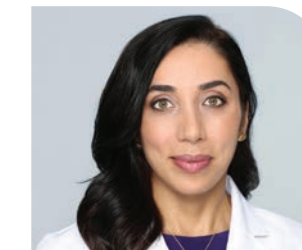
Mary-Abigail Craven, MD

Fellowship trained in both neuro-ophthalmology and in orbital and ophthalmic plastic surgery, Dr. Craven joins the faculty as Director of Neuro-Ophthalmology Consultative Service for Mount Sinai West and Assistant Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai. After earning her medical degree at The Ohio State University College of Medicine, she completed her residency in ophthalmology and a dual fellowship in neuro-ophthalmology and oculoplastics and orbital surgery at The Ohio State University Wexner Medical Center.



Shreya Jayasimha, OD

As an Instructor in the Department of Ophthalmology, Dr. Jayasimha is focused on co-managing and treating various ocular diseases, pediatric and binocular issues, fitting contact lenses, and providing vision services for low vision patients. She earned her doctorate of optometry from New England College of Optometry followed by a residency, with a concentration in ocular disease, at the Bascom Palmer Eye Institute.



Yogita Kashyap, MD

Dr. Kashyap joins the faculty as an Assistant Clinical Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai, specializing in oculoplastic, orbital, and reconstructive surgery. Dr. Kashyap graduated from SUNY Downstate College of Medicine with a degree in medicine. She then completed a residency in ophthalmology and a fellowship in ophthalmic plastic and reconstructive surgery at New York Eye and Ear Infirmary.



Varun K. Pawar, MD

A uveitis specialist, Dr. Pawar joins the faculty as an Assistant Clinical Professor of Ophthalmology at Icahn School of Medicine at Mount Sinai. He received his medical degree from University of Cincinnati College of Medicine and then completed his residency in ophthalmology at Saint Louis University, followed by a fellowship in uveitis at Francis I Proctor Foundation at UCSF.

The Harold W. McGraw, Jr. Family Foundation Professorship in Neuroregeneration

New York Eye and Ear Infirmary of Mount Sinai (NYEE) has received a generous donation from The Harold W. McGraw, Jr. Family Foundation to establish an endowed professorship in the Department of Ophthalmology to support neuroregeneration research. Considered one of the most prestigious honors in academic medicine, the above named professorship will enable NYEE to continue to advance its ongoing mission of groundbreaking research, education, and clinical care. The \$2 million gift represents a significant investment in current and future scientific discoveries in the revolutionary field of neuroregeneration at NYEE, ensuring that innovative research in this area will be led in perpetuity by internationally renowned investigators. NYEE proudly acknowledges the impact its donors have in enabling the institution to achieve its overarching mission, and is immensely grateful for the support of its partners in advancing sight saving therapies to improve quality of life.

Current Residents and Fellows

NYEE Residents

PGY-4

Michael Chua, MD
Karen Hu, MD
Mary Labowsky, MD
Kelly Lee, MD
David MacPherson, MD
Duaa Sharfi, MD
Daniel Wang, MD

PGY-3

Julia Fallon, MD
Roxanne Lee, MD
Sarah McCord, MD
Shravan Savant, MD
Young Seol, MD
Tommaso Vagaggini, MD
Bella Wolf, MD

PGY-2

Jorge Andrade Romo, MD
Laura Barna, MD
Nitin Chopra, MD
Jeanette Du, MD
Mona Fayad, MD
Giselle Lynch, MD
Michael Schatz, MD

NYEE Fellows

Levon Djenderedjian, MD
(Glaucoma)
Joel Pakett, MD (Cornea)
Alexander Pinhas, MD (Retina)
Thomas Quehl, MD (Pediatric)
Vincent Sun, MD (Retina)
Matthew Wieder, MD (Retina)
Carl Wilkins, MD (Retina)

MSH Residents

PGY-4

Cesar Alfaro, MD
Kirolos Ibrahim, MD
Ekta Patel, MD
Ethan Sobol, MD

PGY-3

Rupak Bhuyan, MD
Karina Esquenazi, MD
Susel Oropesa, MD
Kevin Wu, MD

PGY-2

Jeffrey Brown, MD
Jonathan Levenson, MD
Heather McGowan, PhD, MD
Nancy Worley, MD

Department of Ophthalmology Faculty and Administration

Icahn School of Medicine at Mount Sinai Departmental Leadership

James C. Tsai, MD, MBA

President, NYEE
Chair, Department of Ophthalmology, MSHS

Louis R. Pasquale, MD, FARVO

Chair, Department of Ophthalmology, MSH and MSQ
Deputy Chair for Research, ISMMS
Director, Mount Sinai/NYEE Eye and Vision Research Institute, MSHS

Paul A. Sidoti, MD

Chair, Department of Ophthalmology, NYEE
Chief, Glaucoma, MSHS

Douglas Fredrick, MD

Deputy Chair for Education, MSHS
Chief, Pediatric Ophthalmology and Strabismus, MSHS

Richard B. Rosen, MD

Deputy Chair for Clinical Affairs, ISMMS
Vice Chair and Director of Ophthalmic Research, NYEE
Chief, Retina Service, MSHS

Salvatore Loiacono, Jr., MPA

Deputy Chair for Finance and Administration, MSHS
Vice President for Ophthalmology Services, NYEE

Christopher T. Spina, MS

Senior Vice President and Chief Operating Officer, NYEE

Tamiesha Frempong, MD, MPH

Vice Chair for Diversity and Inclusion, Department of Ophthalmology, ISMMS

Anita Gupta, MD

Vice Chair for Professional Development, MSHS
Director, Cornea and External Diseases, NYEE

Alon Harris, MS, PhD, FARVO

Vice Chair of International Research and Academic Affairs, Department of Ophthalmology, ISMMS
Director, Ophthalmic Vascular Diagnostic Research Program, MSH

Mark Kupersmith, MD

Vice Chair, Translational Ophthalmology Research, MSHS
Chief, Neuro-Ophthalmology, MSHS

Sandra K. Masur, PhD

Vice Chair for Academic Development and Mentoring, MSHS

Paul S. Lee, MD

President, NYEE/MSH Department of Ophthalmology Alumni Associate Residency Program Director, MSH

Residency and Fellowship Programs

Harsha S. Reddy, MD

Director, Ophthalmology Residency Program, NYEE

Tamiesha Frempong, MD, MPH

Director, Pediatric Ophthalmology Fellowship Program, NYEE

Richard B. Rosen, MD

Director, Vitreo-Retinal Fellowship Program, NYEE

Kateki Vinod, MD

Director, Glaucoma Fellowship Program, NYEE

Angie E. Wen, MD

Director, Cornea and External Diseases Fellowship Program, NYEE

Medical Directors

Avnish Deobhakta, MD

Medical Director, East 85th Street

Valerie Elmalem, MD

Interim Medical Director, Mineola

Robin N. Ginsburg, MD

Medical Director, East 102nd Street

Gennady Landa, MD

Medical Director, Tribeca

Kira Manusiis, MD

Medical Director, Midwood

Paul A. Sidoti, MD

Medical Director, East 14th Street

Erin Walsh, MD

Interim Director, Comprehensive Ophthalmology Clinic, NYEE

Angie E. Wen, MD

Medical Director, Columbus Circle

Clinical Divisions at Mount Sinai Health System Faculty Practices

Cornea, External Diseases, and Refractive Surgery

Sumayya Ahmad, MD
Priti Batta, MD
Anita Gupta, MD
David Harris, MD
Kira Manusiis, MD
Neha Shaik, MD
Angie E. Wen, MD

Eye Trauma

John Aljian, MD
Ronald C. Gentile, MD
Harsha S. Reddy, MD

Glaucoma

Paul Sidoti, MD
Chief, Glaucoma, MSHS

Nisha Chadha, MD

Donna Gagliuso, MD
Tsontcho Ianchulev, MD
Louis R. Pasquale, MD, FARVO
Nathan Radcliffe, MD
Tania Tai, MD
James C. Tsai, MD, MBA
Kateki Vinod, MD
Sze Wong, MD

Neuro-Ophthalmology

Mark Kupersmith, MD
Chief, Neuro-Ophthalmology, MSHS

Mary-Abigail Craven, MD

Valerie Elmalem, MD
Joel Mindel, MD

Ocular Oncology

Paul Finger, MD

Ophthalmic Pathology

Jodi Sassoon, MD
Chair, Pathology, NYEE

Nada Farhat, MD

Alan Friedman, MD
Codrin Iacob, MD

Oculoplastic, Orbital and Reconstructive Surgery

Robert Della Rocca, MD
Chief, Oculoplastic, Orbital and Reconstructive Surgery, MSHS

Mary-Abigail Craven, MD

Monica Dweck, MD
Valerie Elmalem, MD
Yogita Kashyap, MD
Harsha S. Reddy, MD

Pediatric Ophthalmology and Strabismus

Douglas Fredrick, MD
Chief, Pediatric Ophthalmology and Strabismus, MSHS

Tamiesha Frempong, MD, MPH

Edward Raab, MD
Steven Rosenberg, MD
Erin Walsh, MD

Primary Care Ophthalmology/Optomety

Bessie Abraham, OD
Karen Hendler-Goldberg, MD
Vanessa Hernandez, OD
Shreya Jayasimha, OD
Varun K. Pawar, MD
Elena Schmidt, OD

Retina

Richard B. Rosen, MD
Chief, Retina Service, MSHS

Avnish Deobhakta, MD

Robin Ginsburg, MD
Meenakashi Gupta, MD
Gennady Landa, MD
Gareth Lema, MD, PhD
R. Theodore Smith, MD, PhD

Uveitis and Ocular Immunology

Varun K. Pawar, MD
Sophia Saleem, MD

Basic Science/Translational Research Faculty

Yuen Ping Toco Chui, PhD
Bo Chen, PhD
R. Theodore Smith, MD, PhD
Jose Mario Wolosin, PhD

Voluntary Faculty Leadership

John Aljian, MD
Co-Director, Trauma Service (Anterior Segment), NYEE

Ronald C. Gentile, MD
Co-Director, Trauma Service (Posterior Segment), NYEE

Douglas F. Buxton, MD
President, Jorge N. Buxton, MD Microsurgical Education Foundation

Richard Koplin, MD
Co-Director, Cataract Service, NYEE

Steven E. Rosenberg, MD
Co-Director, Pediatric Ophthalmology and Strabismus Service, NYEE

Jeanne L. Rosenthal, MD
Associate Director, Retina Service, NYEE

Affiliated Leadership

Paul Lee, MD
Chief of Ophthalmology, James J. Peters VA Medical Center

Robert Fischer, MD
Director of Ophthalmology, Elmhurst Hospital

Michelle Rhee, MD
Associate Director of Ophthalmology, Elmhurst Hospital

ISMMS - Icahn School of Medicine at Mount Sinai

NYEE - New York Eye and Ear Infirmary of Mount Sinai

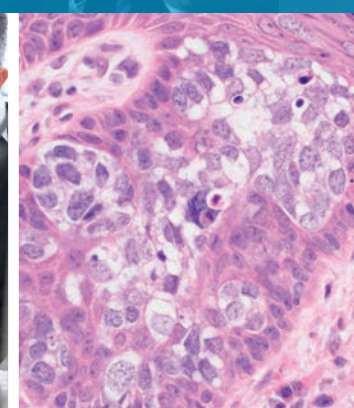
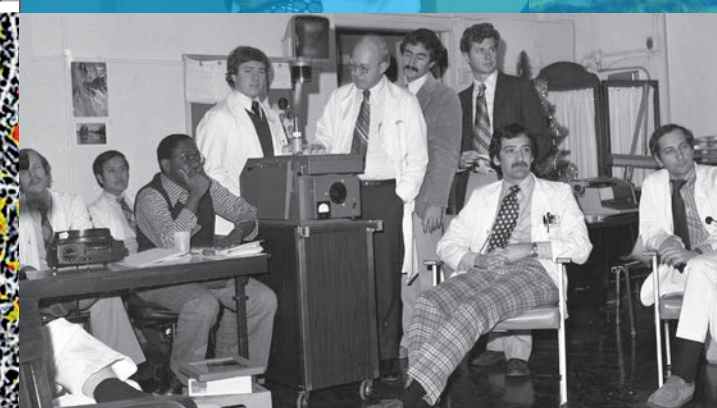
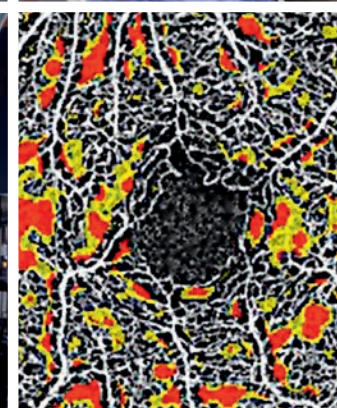
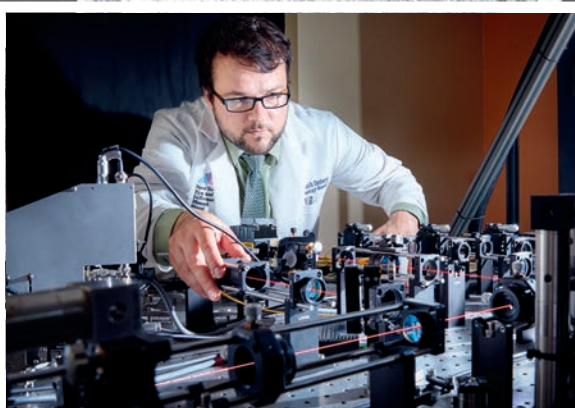
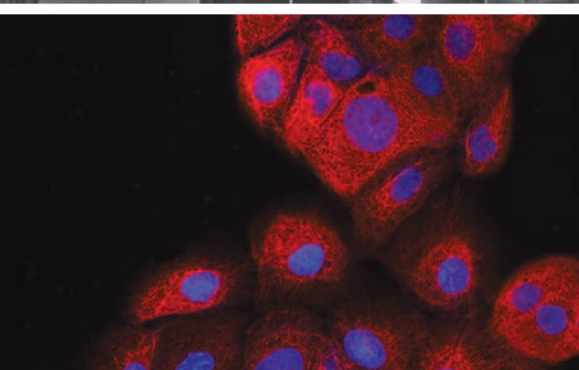
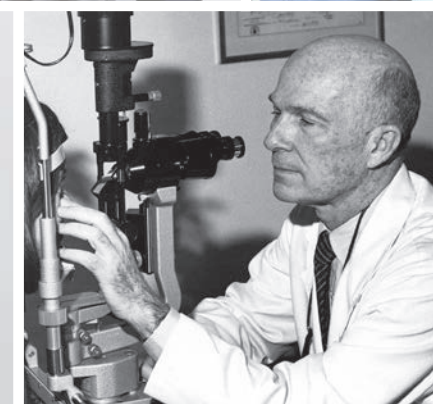
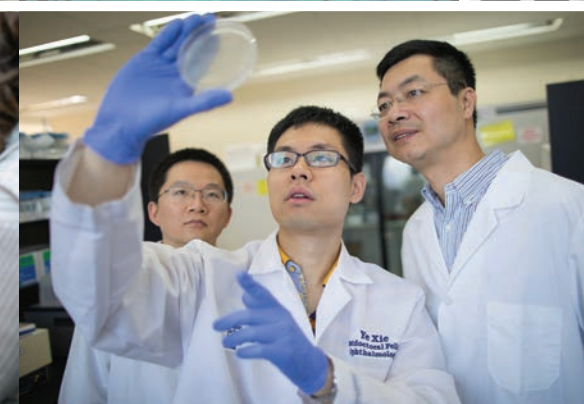
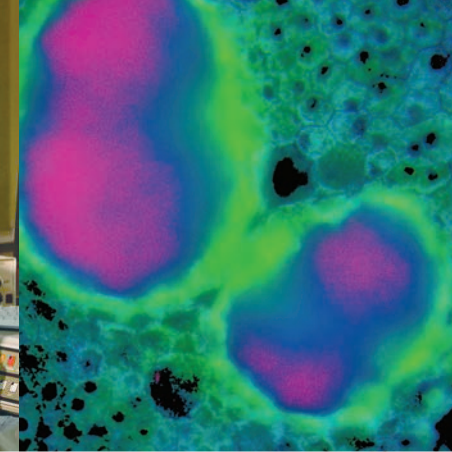
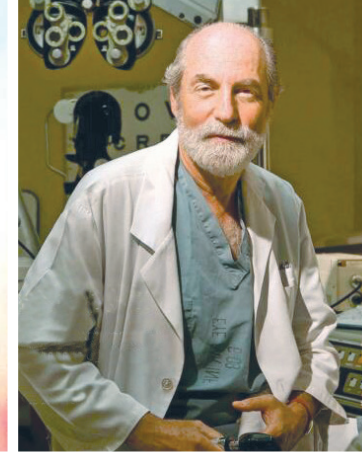
MSBI - Mount Sinai Beth Israel

MSHS - Mount Sinai Health System

MSH - The Mount Sinai Hospital

MSQ - Mount Sinai Queens





> NEW DATES

NYEE Celebrates Its 200th Anniversary

Due to the worldwide pandemic, our bicentennial events have been postponed to 2021.

Join faculty, alumni, and friends of NYEE in a celebration of our 200-year legacy of leadership, innovation, and excellence in patient care.

Bicentennial Gala

The Plaza Hotel
768 5th Avenue
New York, NY

October 14, 2021

Transformational Ophthalmology 2021: Envisioning Our Third Century

New York Academy of Medicine
1216 5th Avenue
New York, NY

October 15, 2021

For more information and tickets go to:
www.nyee.edu/200years

Celebrating
200
YEARS
1820 - 2020



New York
Eye and Ear
Infirmary of
Mount
Sinai

