USC Roski Eye Institute

Keck Medicine of USC

2020 ANNUAL REPORT

KECK SCHOOL OF MEDICINE OF USC

DEPARTMENT OF OPHTHALMOLOGY

MESSAGE FROM THE CHAIR

The USC Roski Eye Institute's mission is to provide exceptional clinical care, train the future leaders in ophthalmology, and develop novel therapies in the fight against blindness. As our team educates tomorrow's medical leaders, we continue to be at the forefront of innovation through the integration of medicine and science.

In 2020, the USC Department of Ophthalmology ranked #1 among all ophthalmology departments in federal NIH Funding. The Department has been nationally ranked as **one of the top departments** in *U.S. News and World Report* for 27 consecutive years.

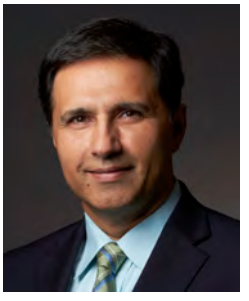
Our dedicated team of clinicians, scientists, staff, and trainees take an integrated multidisciplinary approach to provide exceptional patient care through innovative treatments and state-of-the-art diagnostic services. The USC Roski Eye Institute continues to offer treatments not widely available in the community, including the management of complex cornea, retina, glaucoma, neuro-ophthalmology, oculoplastic, and uveitis cases.

The LAC+USC Ophthalmology Residency Program is nationally ranked in the U.S. by Doximity. With the expansion of our residency, fellowship, and hands-on teaching programs, we continue to strengthen our educational mission. Notably, we are grateful to our exceptional alumni who volunteer their time at LAC+USC Medical Center to mentor the next generation of ophthalmologists.

This year, the ongoing COVID-19 crisis disrupted patient care, research and the educational curriculum. However, our residents and faculty rose to meet the challenge and are implementing the latest COVID-19 industry responses provided by the American Academy of Ophthalmology (AAO) in their work.

Eliminating blindness is far from impossible. When science, innovation, perseverance, and compassion come together, breakthroughs are made in the service of our patients. We thank you for all of your continued dedication and support of our mission and look forward to the year ahead as we strive to develop new treatments and therapies to preserve, protect and restore vision.

J. Martin Heur, MD, PhD
Professor and Interim Chair
Charles C. Manger III, M.D. Chair in Corneal Laser Surgery
USC Department of Ophthalmology
Keck Medicine of USC



Mark S. Humayun, MD, PhD
Cornelius J. Pings Chair in Biomedical Sciences
Co-Director, USC Roski Eye Institute
Director, USC Ginsburg Institute for Biomedical Therapeutics

YOUR VISION IS OUR MISSION

PRESERVE

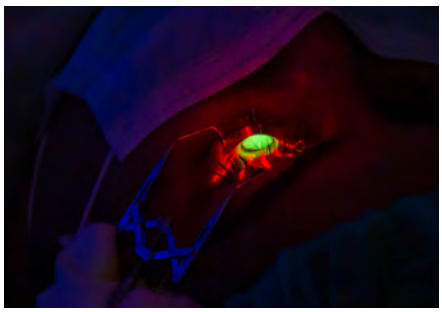
The USC Roski Eye Institute diagnoses, treats and manages the most complex eye conditions, from in utero to advanced age.

PROTECT

The USC Roski Eye Institute leads major research in the diagnosis of eye disease with advanced imaging technology to help prevent blindness.

RESTORE

The USC Roski Eye Institute integrates and applies emerging technologies to develop new methods to restore sight to the blind.



SPECIALIZED CARE for ADULTS & CHILDREN

The USC Roski Eye Institute treats the full spectrum of eye conditions - from the most common to the most complex.

- CATARACT
- CORNEA & EXTERNAL DISEASES
- GLAUCOMA
- LASER VISION CORRECTION
- LOW VISION REHABILITATION
- NEURO-OPHTHALMOLOGY AND ADULT STRABISMUS
- OCULAR ONCOLOGY
- OCULO-FACIAL PLASTIC SURGERY
- OPHTHALMIC MOLECULAR AND IMMUNOPATHOLOGY
- PEDIATRIC OPHTHALMOLOGY
- SPECIALTY CONTACT LENSES AND PROSE
- UVEITIS AND OCULAR INFLAMMATION
- RETINA, VITREOUS AND MACULAR DISEASES & SURGERY

USC DEPARTMENT OF OPHTHALMOLOGY

#1

IN NIH RESEARCH FUNDING

AMONG OPHTHALMOLOGY DEPARTMENTS

FY 2019

Top NIH Principal Investigators

#1
Arthur Toga, PhD

#23
Qifa Zhou, PhD

#50
Paul Thompson, PhD

#50
Gianluca Lazzi, PhD

#55
Mahnaz Shahidi, PhD

#90
Sarah Hamm-Alvarez, PhD

*Source: Blue Ridge Institute for Medical Research

Dry Eye Center of Excellence

Creates a Tear Biorepository for Identifying Biomarkers for Subtypes of Dry Eye

Pictured: A patient has Schirmer tear test strips inserted in her lower eyelids to collect tears

Dry eye disease remains a challenging condition for ophthalmologists to treat, due to the lack of understanding of its root causes. There has been a growing interest in identifying objective biomarkers that can be used as diagnostic tools for dry eye disease, and for objectively monitoring the progression of the disease and efficacy of treatments.

In published studies, USC Roski Eye Institute researchers, Drs. Sarah Hamm-Alvarez and Maria Edman, analyzed tears in Sjögren's Syndrome patients to identify diagnostic biomarkers for the autoimmune disease. They learned that the increased activity of the protease, Cathepsin S, was a potential biomarker for Sjögren's Syndrome. The next step was to find biomarkers for additional subtypes of dry eye disease.

This year, researchers from the USC Dry Eye Center of Excellence (whose members includes Drs. Hamm-Alvarez and Edman) received an IRB approval to create a tear biorepository for identifying biomarkers for subtypes of dry eye.

Patients seeking care for dry eye at the Dry Eye Center already receive a thorough work-up according to the recommendations of the DEWS II workshop. Together, these measurements provide an excellent view of each patient's level of aqueous deficiency, meibomian gland disease and ocular surface inflammation. With the patient's consent, the Dry Eye Center researchers will store the tears generated during clinical work-up, as well as the clinical data, in the tear biorepository.

The tear biorepository will create a solid foundation for furthering the development of Cathepsin S as a biomarker for Sjögren's Syndrome, testing its performance against other subtypes of dry eye and correlation with different clinical parameters. It will also allow researchers to characterize new alterations in tear composition in patients with different underlying conditions, varying degrees of meibomian gland disease, aqueous deficiency and other dry eye parameters. This will not only further the understanding of the different dry eye conditions but may also help identify new biomarkers and therapeutic targets.

The hope is that this will benefit a wide range of subsets of dry eye patients, paving the way for personalized medicine. Finally, the deep characterization of the dry eye disease population at the USC Roski Eye Institute will allow for better design of clinical trials for dry eye treatments performed at the clinic.

A longer version of this story originally appeared on our website.

Scan the QR code to read the full story:

Patient Stories

From Silhouttes to Sight:

How a Keratoprosthesis Corrected One Patient's Lifelong Struggle with Vision

Pictured: Roslymn Caldwell (right) with her ophthalmologist, Dr. Annie Nguyen

Ever since Roslymn Caldwell was born, she had eye conditions. What began as a lazy eye in childhood advanced to keratoconus in adulthood and Caldwell was blind for all of her adult life.

"My vision was blurry," she said. "It wasn't dark, but gray. I could see the silhouette of your face, but not the details."

Her condition destroyed her confidence. She needed someone to drive her, read to her, and guide her around her apartment. Caldwell underwent several cornea transplants, but her body rejected each. Ophthalmologists and optometrists throughout Southern California told her there was nothing they could do.

One day, a blind agency suggested Caldwell visit the USC Roski Eye Institute. Caldwell felt hopeless but went to a consultation with Dr. Annie Nguyen, an ophthalmologist who specializes in the cornea. Dr. Nguyen examined Caldwell's eyes and recommended a keratoprosthesis, a procedure only offered by a handful of academic medical institutions worldwide.

Dr. Nguyen performed the procedure on Caldwell by replacing diseased tissue from the eye with a full-thickness transplant graft. She added a synthetic prosthetic device to the center of the graft so Caldwell's eye would stay clear if the surrounding tissue failed. In addition, Drs. Benjamin Xu and Brian Toy performed surgeries that day to place a drainage device to control Caldwell's glaucoma.

The morning after surgery, Caldwell woke up at home with the gift of sight. She ran around the apartment she'd lived in for a year and saw her living room, kitchen, and TV for the first time. She woke her caretaker and shouted, "I can see!"

Medical transportation drove Caldwell to her next check-up with Dr. Nguyen. Driving down the 14 freeway toward Los Angeles, she saw freeway signs, hills, and the license plates of other cars for the first time in decades. When she arrived at the USC Roski Eye Institute, Dr. Nguyen asked who was with her.

"No one," Caldwell said. "I came here myself." When she read the eye chart, she could see to the 20/40 line the day after surgery. Before surgery, she only saw motion and couldn't even see the chart.

Since her surgery, Caldwell has retaken control of her life. She is in school and has rediscovered her love of reading.

"I recommend USC to anyone with an eye problem because it's such a blessing to me," Caldwell said. "Anyone who wants to see, come check them out."

Under Pressure:
How Minimally Invasive Glaucoma Surgery Saved a Promising, Young Student's Eyesight

Pictured (L to R): Interim Dean Dr. Narsing Rao, Dr. Brian Toy, and Namita Sarraf

Namita Sarraf suffered episodes of redness, pain, and light sensitivity in her left eye that seemed to recur despite treatment by her ophthalmologist. A busy graduate student trying to finish her studies in bioengineering, Namita didn't have time for this.

"When the pressure in my eye was really high, it felt like a balloon about to pop," Namita said. She was diagnosed with recurrent anterior uveitis of her left eye. Her ophthalmologist treated her with anti-inflammatory steroid eye drops, but these caused glaucoma. After a year of treatment, her condition was not improving.

At the recommendation of a family friend, she sought out the expert opinion of Dr. Narsing Rao, internationally renowned uveitis specialist and interim dean of the Keck School of Medicine of USC. Dr. Rao was concerned about the rising pressure in her left eye, which was now twice the upper limit of normal. He knew vision loss could occur as a result of glaucoma damage.

That same week, Dr. Rao referred her to see Dr. Brian Song, a glaucoma specialist at the USC Roski Eye Institute. Dr. Song initially made some changes to Namita's medications with the hope of avoiding surgery, but this only led to a minimal improvement in her pressure.

He recommended she undergo urgent surgery to lower the pressure and save her sight. He thought she was a good candidate for a newer, minimally invasive glaucoma surgery (MIGS). The advantage being a lower risk of complications and an easier recovery.

"Dr. Song was patient and informative," Namita said. "He referenced data that had been published just weeks earlier in a medical journal, indicating how he was also searching for the best way to treat his patients."

Dr. Song performed a combined canaloplasty and trabeculotomy through a small incision to open the natural drain of the eye. "The morning after surgery, the pressure in Namita's eye had dropped back to normal levels. Six months later, not only is her pressure controlled, but her uveitis has not recurred, thanks to a new, simpler treatment regimen.

"I was very happy to find that the pressure in my eye had decreased as expected, confirming that the surgery had solved the problem. I am so grateful for the care I received at USC and to be able to focus on my studies again."

A longer version of this story originally appeared on our website.

Scan the QR code to read the full story:

ACTIVE RESEARCH FUNDING - DECEMBER 2020

Pictured: Dr. Sarah Hamm-Alvarez in her lab.

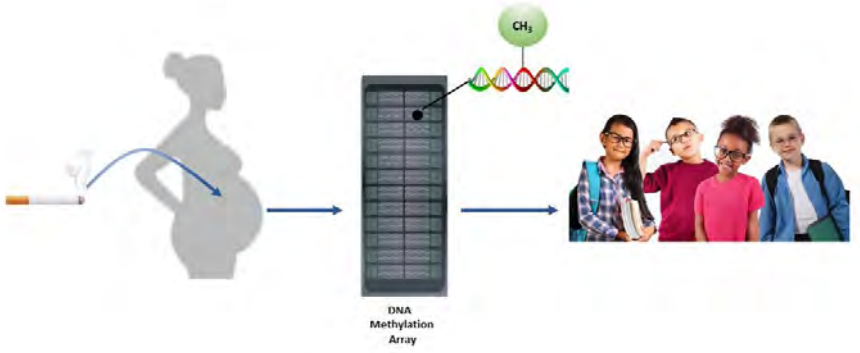
PRINCIPAL INVESTIGATOR	PROJECT	SOURCE
Jesse Berry, MD	Development of a Surrogate Liquid Biopsy from the Aqueous Humor in Retinoblastoma Eyes	NIH/NCI
Jesse Berry, MD	Prospective Longitudinal Aqueous Humor Liquid Biopsy to Predict Treatment Response and Minimal Residual Disease in Retinoblastoma	Wright Foundation
Melinda Chang, MD	Quantitative Visual Assessment in Children with Cortical/Cerebral Visual Impairment (CVI) Using a Machine-Learning Model of Eye Tracking Data	KTE
David Cobrinik, MD, PhD	Human Specific Signaling Circuitry in Cone Precursor Development	NIH/NEI
David Cobrinik, MD, PhD	Successive Responses to Oncogenic Aberrations in Retinoblastoma Genesis	NIH/NCI
David Cobrinik, MD, PhD	Transcriptomic Effects of Copy Number Alterations in Pediatric Cancers	St. Baldrick's
Charles Flowers, MD	Purchasing Breath Shields for Slit Lamp Exams to Enhance Patient and Provider Protection	CIR-SIEU
Kimberly Gokoffski, MD, PhD	Physiologic Electrical Fields Direct Optic Nerve Regeneration	USC
Kimberly Gokoffski, MD, PhD	Measurement of Vascular Tortuosity in IIH by OCTA and Optos	Fight For Sight
Kimberly Gokoffski, MD, PhD	Electric Fields Collaborate with Cdc42 to Direct Optic Nerve Regeneration	BFF
Kimberly Gokoffski, MD, PhD	In vivo Application of Electrical Fields Directs Retinal Ganglion Cell Axon Regeneration	NIH/NEI
Sarah Hamm-Alvarez, PhD	Microtubule-Based Transport in Lacrimal Gland Function	NIH/NEI
Sarah Hamm-Alvarez, PhD	Protein-polymer Nanomedicine for Sjogren's Syndrome	NIH/NEI
Sarah Hamm-Alvarez, PhD	Expansion of Tear Biomarker Studies in Parkinson's Disease Patient Cohorts	MJF
Sarah Hamm-Alvarez, PhD	RNA-Seq on Tears: Biomarker Discovery for Parkinson's Disease	USC
Sarah Hamm-Alvarez, PhD	Development of a novel tear-based biomarker assay for diagnosis of Parkinson's disease using RT-QuIC	NIH/NIA
J. Martin Heur, MD, PhD	Research to Prevent Blindness Unrestricted Grant	RPB
J. Martin Heur, MD, PhD	Enhanced Preservation of Donor Corneas	OneLegacy
Mark Humayun, MD, PhD	USC Roski Eye K12 Clinician-Vision Scientist Training Program (USC Roski Eye K12)	NIH/NEI
Mark Humayun, MD, PhD	PRPE-SF, polarized hESC-derived RPE Soluble Factors, as a Therapy for Early Stage Dry Age-related Macular Degeneration	CIRM
Mark Humayun, MD, PhD	EFRI CEE: Engineered Retinal Epigenomics	NSF
Mark Humayun, MD, PhD	EAGER: Engineered nano-scale barrier to prevent viral infections	NSF
Mark Humayun, MD, PhD	Abiotic-Biotic Interfaces for Ophthalmology Symposium	NIH/NEI
Mark Humayun, MD, PhD	Microbubble-assisted Crispr/Cas9 Delivery in Retina for Photoreceptor Therapeutics	NSF
Xuejuan Jiang, PhD	Cumulative Effects of Sickle Cell Trait on the Eye among Older African Americans	NIH/NEI

Xuejuan Jiang, PhD	Intrauterine exposure to tobacco smoke, DNA methylation, and vision disorders in preschool children	NIH/NEI
Amir Kashani, MD, PhD	Functional Imaging in Hypoxic-Ischemic Retinal Disease	NIH/NEI
Amir Kashani, MD, PhD	Imaging Cerebral and Retinal Microvasculature in Cerebral Small Vessel Disease	NIH/NINDS
Amir Kashani, MD, PhD	Motor, Visual, and Olfactory Changes in Genetic Subtypes of Alzheimer's Disease	NIH/NIA
Amir Kashani, MD, PhD	Assessment of Retinal Capillary Density, Morphology and Function in Retinal Vascular Disease Using Novel OCT Angiography Based Metrics	NIH/NEI
Gianluca Lazzi, PhD, MBA	Connectome-Derived Computational Models of Degenerated Retina for Retinal Prosthetic Design	NIH/NEI
Gianluca Lazzi, PhD, MBA	EAGER: Bioelectronic Color Vision	NSF
Gianluca Lazzi, PhD, MBA	Predictive Modeling of Bioelectric Activity on Mammalian Multilayered Neuronal Structures in the Presence of Supraphysiological Electric Fields	NIH/NIBIB
Gianluca Lazzi, PhD, MBA	CRCNS: US-Spain Research Proposal: Computational Modeling of PNS Stimulation	NIH/NIBIB
Aaron Nagiel, MD, PhD	Development and Maintenance of the Human Photoreceptor-bipolar Cell Synapse	USC
Aaron Nagiel, MD, PhD	Hippo pathway inhibition for the treatment of geographic atrophy	EDT
Aaron Nagiel, MD, PhD	Role of non-canonical Wnt signaling in the developing human photoreceptor-bipolar cell synapse	RPB
Aaron Nagiel, MD, PhD	Development and Maintenance of the Photoreceptor-Bipolar Cell Synapse in Human Retinal Organoids	CHLA
Grace Richter, MD, MPH	Defining the Relationships of Retinal Microcirculation with Glaucoma, Systemic Disease, and Ocular Anatomic Factors in African Americans	NIH/NEI
Mahnaz Shahidi, PhD	Imaging of Retinal Oxygenation and Metabolism	NIH/NEI
Mahnaz Shahidi, PhD	Center Core Grant for Vision Research	NIH/NEI
Mahnaz Shahidi, PhD	In Vivo Molecular Imaging of Vascular Disease of the Retina	NIH/NEI
Mahnaz Shahidi, PhD	Imaging of Retinal Oxygen Metabolism in Diabetic Retinopathy	NIH/NEI
Mahnaz Shahidi, PhD	Retinal vessel features as a marker of idiopathic intracranial hypertension treatment response: a secondary analysis of the idiopathic intracranial hypertension treatment trial	
Noelle Stiles, PhD	Restoring Sight to the Blind: Neural Imaging with Retinal Prostheses	NIH/NEI
John Whalen, PhD	Thermoreponsive Reversible Adhesive for Temporary Intervention of Ocular Trauma - II	DOD
Benjamin Xu, MD, PhD	Development and Validation of Quantitative Anterior Segment OCT-based Methods to Evaluate Patients with Primary Angle Closure Disease	NIH/NEI
Benjamin Xu, MD, PhD	VRC: A Stem Cell-Based Treatment Strategy for Laser-Induced Permanent Retinal Damages	NIH/NEI
Benjamin Xu, MD, PhD	Anatomical Mechanisms for Development and Progression of Primary Angle Closure Disease: A Cross-Sectional and Longitudinal Analysis	American Glaucoma Society
Benjamin Xu, MD, PhD	Quantitative OCT-based Methods for Primary Angle Closure Disease	FFS
Benjamin Xu, MD, PhD	Development of Quantitative OCT-based Methods to Detect and Evaluate Biometric Risk Factors for Primary Angle Closure Disease	USC
Brandon Wong, MD	Development of an Integrated Teleglaucoma Care Program for a Safety-Net Health System	American Glaucoma Society
Qifa Zhou, PhD	Combined OCT/US/PAT System for Intravascular Imaging	NIH/NHLBI
Qifa Zhou, PhD	Large aperture and wideband modular ultrasound arrays for the diagnosis of liver cancer	NIH/NCI
Qifa Zhou, PhD	High-resolution Elastographic Assessment of the Optic Nerve Head	NIH/NEI
Qifa Zhou, PhD	Non-invasive Ultrasound Stimulated Retinal Prosthesis	NIH/NEI
Qifa Zhou, PhD	High-resolution High-Speed Photoacoustic and Ultrasound Imaging of Small Vessel Functions in Ischemic Stroke	NIH/NINDS

AGS (American Glaucoma Society) • BFF (BrightFocus Foundation) • CHLA (Children's Hospital Los Angeles) • CIRM (California Institute for Regenerative Medicine) • CIR-SIEU (Committee of Interns and Residents SEIU Healthcare) • DoD (Department of Defense) • EDT (Edward N. & Della L. Thome Memorial Foundation) • FFS (Fight for Sight) • KTE (Knights Templar Eye Foundation) • MJF (Michael. J. Fox Foundation) • NCI (National Cancer Institute) • NEI (National Eye Institute) • NHLBI (National Heart, Lung and Blood Institute) • NIA (National Institute on Aging) • NIBIB (National Institute of Biomedical Imaging and Bioengineering) • NINDS (National Institute of Neurological Disorders and Stroke) • NSF (National Science Foundation) • OneLegacy (OneLegacy Foundation) • RPB (Research to Prevent Blindness) • St. Baldrick's (St. Baldrick's Foundation) • USC (University of Southern California) • Wright Foundation

Research Progress

Intrauterine Exposure to Cigarette Smoke, DNA Methylation, and Vision Disorders in Preschool Children

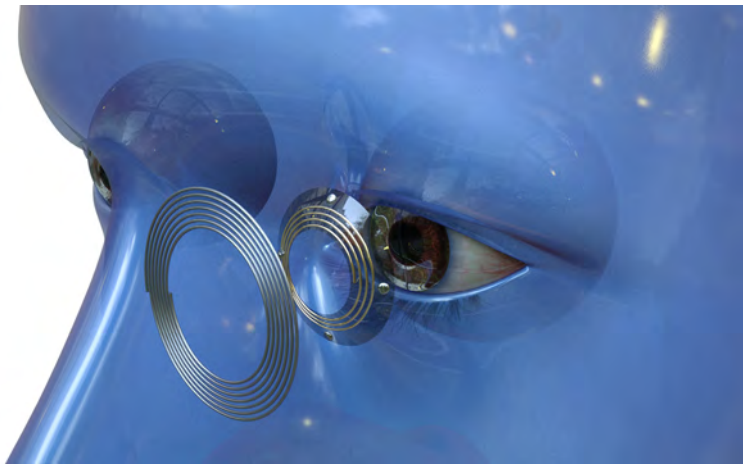


Intrauterine exposure to factors such as maternal smoking may affect the offspring's vision via epigenetic programming.

Vision disorders in early childhood, such as strabismus, amblyopia, and high hyperopia, can significantly impair the development of children's visual, motor, and cognitive functions. Maternal smoking during pregnancy has been consistently associated with several pediatric vision disorders. However, the biological mechanisms underlying these disorders and the effect of maternal smoking remain mostly unknown. Given the persistently high maternal smoking rates and emerging new sources of nicotine exposure (e.g., e-cigarettes), a better understanding of how intrauterine exposure to smoke/nicotine affects vision development is needed. Also, there have been significant advances in identifying methylation changes in newborns in response to maternal smoking during pregnancy. These led Dr. Xuejuan Jiang and her team to hypothesize that methylation changes can alter vision development in the fetus, leading to vision disorders in early childhood.

Funded by the National Eye Institute, Dr. Jiang's team is conducting a case-control study nested within the Multiethnic Pediatric Eye Disease Study to test this hypothesis. They are retrieving neonatal dried blood spots collected by the California Biobank Program from these children at birth. Using these unique resources, Dr. Jiang and her team will perform genome-wide profiling of DNA methylation in newborns' blood and measure biomarkers of intrauterine exposure to smoke/nicotine. They will then evaluate how these neonatal biomarkers may predict the risk of developing strabismus, amblyopia, and hyperopia in children. They will also conduct a genome-wide search for methylation susceptibility loci for hyperopia. Findings from their investigation will contribute novel knowledge for a better understanding of the biological mechanisms involved in the development of pediatric vision disorders, and may generate novel targets for the prevention and treatment of these diseases.

Minimally Invasive or Wearable, Adaptive, Systems for Stimulating and Controlling Neural Circuits in the Retina

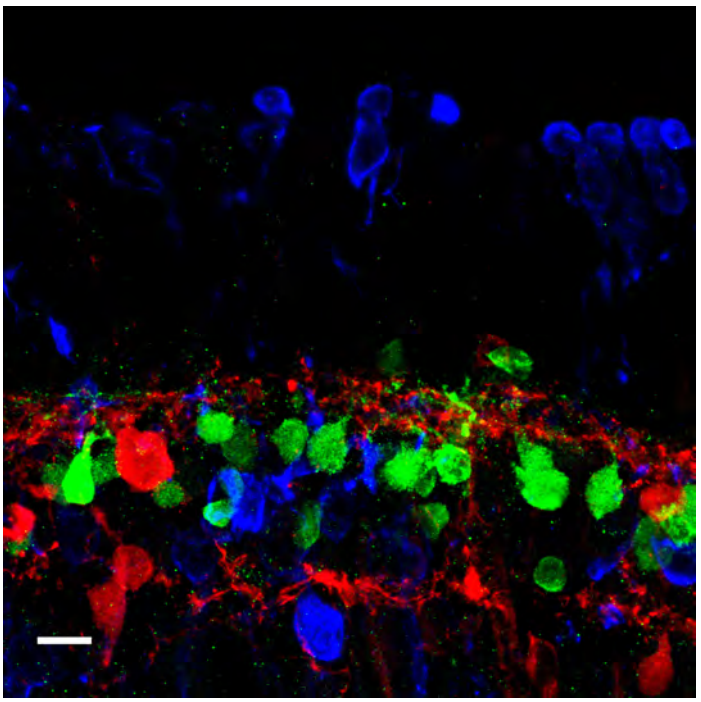


Conceptual implementation of novel contact lens for retinal stimulation. The device is an "e-lens" to provide controlled electrical stimulation of the retina.

Electrical stimulation of neural tissue is widely adopted in neuroengineering as an attempt to restore partial neural functions, usually lost due to diseases or traumatic injuries. While an increasing number of medical conditions have been treated with neurostimulators and have resulted in very encouraging, and sometimes dramatic, partial relief to lost neural functions – such as a retinal prosthesis – the limited understanding of the complex processing in the central nervous system (CNS) translates into sub-optimal bioengineered devices, which fall short of being the true biomimetic devices that researchers aspire to create. The premise in these implants is nearly identical in all cases, including retinal prosthetic: currents injected through electrodes meant to stimulate the surviving neural cells beneath them, thus bypassing the upstream diseased neural circuitry.

Research in the Department of Ophthalmology at USC has resulted in fundamental contributions in the understanding of the alterations of retinal network signaling in prevalent retinal diseases, such as Retinitis Pigmentosa (RP), Age-Related Macular Degeneration (AMD), and Primary Open Angle Glaucoma (POAG), which spearheaded research on the potential role of induced electric fields to alter or slow down the progression of these diseases. A team led by Dr. Gianluca Lazzi is working on a wirelessly-powered contact lens electrical stimulator ("e-lens"), which includes contact electrodes that do not cover or damage the cornea, and are designed to maximize electric current flow in the retina as determined through computational simulations (pictured). Highly efficient wireless powering systems have been developed and novel electrical stimulation circuits and waveforms are being investigated to stimulate specific areas of the retina.

Wiring the Human Retina in Development and Disease: Insights from Human Retinal Organoids

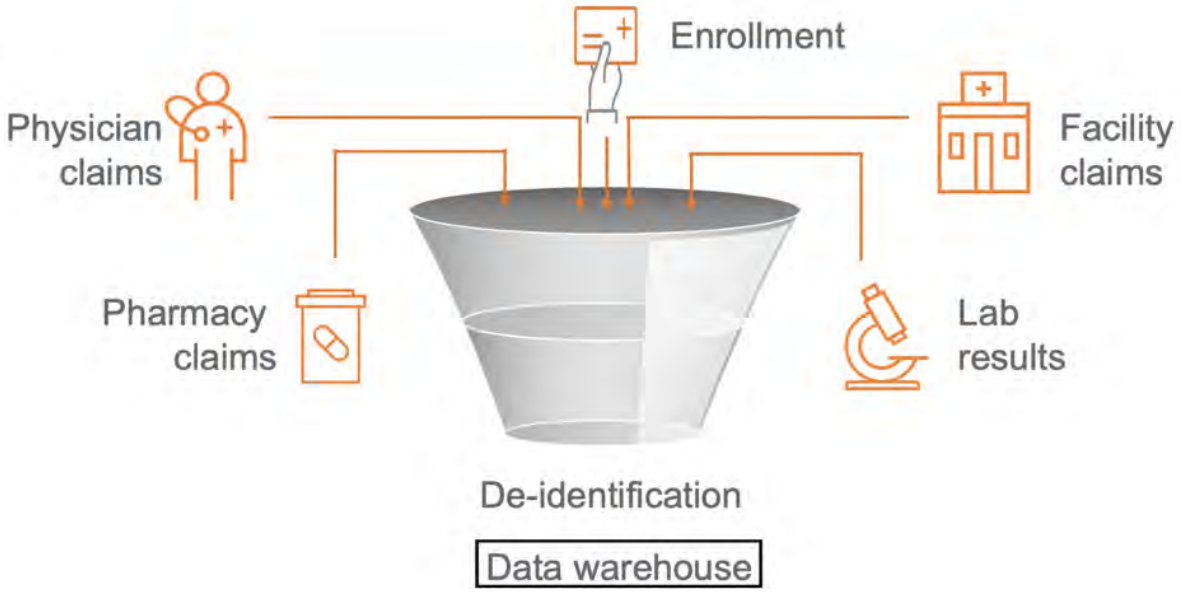


Human retinal organoid section demonstrating the laminar organization of photoreceptors (blue), horizontal cells (red), and bipolar cells (green) along the outer plexiform layer.

Inherited retinal diseases encompass a wide array of genetic disorders that can cause dysfunction and degeneration of the retina, the light-sensing tissue inside our eyes. These disorders affect approximately 1 in 2,000 individuals and can lead to severe and permanent vision loss, usually beginning in childhood. In many of these disorders, there is accumulating evidence that dysfunction occurs at the site of communication (or synapse) between photoreceptors, which convert light into electrical signals, and bipolar cells, which relay these signals to the brain via other cell types. Dr. Aaron Nagiel's laboratory aims to determine how human photoreceptors establish and maintain specific synaptic connections with bipolar cells and how this process goes awry in retinal disease.

To study this process in human tissue, Dr. Nagiel's lab utilizes retinal organoids, which are “mini-retinas” produced from human stem cells that can be made from normal blood or skin cells. These retinal organoids are being analyzed during retinal development to understand the fundamental processes that guide proper wiring of photoreceptors and bipolar cells. These studies will be bolstered by access to organoids containing live fluorescent cell types and genetically engineered cell lines that simulate inherited retinal disease. The lab's ultimate goal is to provide insights into how specific connections are made between neurons of the retina and identify ways to restore neuronal connections in disease states following the use of gene therapy or stem cell-based therapy.

Employing Big Data to Inform Health Systems Practice



Large volumes of health data are aggregated in insurance claims databases and electronic medical records. This information can be leveraged to study rare and orphan diseases for which it would be impractical to perform standard clinical trials. Furthermore, knowledge about real-world treatment patterns and costs associated with more common diseases can have important public health implications.

A research group led by Dr. Brian Toy has employed clinical informatics approaches to analyze big data to identify needs in caring for populations of patients with diabetic retinopathy, ocular inflammatory disease, angle-closure glaucoma, and idiopathic intracranial hypertension.

Employing a nationwide claims database comprising of over 65 million individuals, Dr. Toy's group identified gaps in screening for diabetic retinopathy even among insured adults with presumable access to care. This highlighted a need for innovative approaches, including telemedicine and machine learning, to improve preventive care for this sight-threatening disease. With the same database, Dr. Toy's group has characterized the epidemiology and risk factors underlying infectious ocular inflammatory diseases. Clinical informatics has the potential to improve the diagnosis and management of uveitis, thus preventing vision loss, decreasing cost and improving the quality of care for patients.

Education and Training

RESIDENCY PROGRAM

Each year, hundreds of applicants compete for seven positions. In addition to clinical rotations at the **USC Roski Eye Institute**, training is also provided at **Los Angeles County+USC Medical Center (LAC+USC)**, **Children's Hospital Los Angeles (CHLA)**, and the **VA Downtown Los Angeles Medical Center**. With a total of 21 residents, we have positioned ourselves as one of the largest programs in the Western U.S.

PROGRAM LEADERSHIP

J. Martin Heur, MD, PhD
Professor and Interim Chairman

Charles Flowers Jr., MD
Program Director

Brandon Wong, MD
Associate Program Director

Malvin Anders, MD
Chief of Ophthalmology, LAC+USC Medical Center

- Our residency program maintains its large volume of clinical encounters, consistently excellent hands-on training and high research output within the resident body. Our residents have been in the top 5% of programs nationwide for the past eight consecutive years in total ophthalmologic surgeries and procedures performed.
- Our residency continues to maintain one of the highest Accreditation Council of Graduate Medical Council (ACGME) resident survey results across all post-graduate programs at LAC+USC Medical Center.
- Our AUPO-compliant fellowship programs continue to thrive, with fellows from across the nation choosing our institute to further their subspecialty training.
- Our faculty are very involved in medical student education through lectures, workshops, hands-on teaching in the clinic and OR, and mentoring research projects. There is also a thriving ophthalmology student interest group that engages in several community outreach activities each year with faculty guidance, led by Dr. Jessica Chang, Director of Medical Student Education.

USC Roski Eye Institute
Keck Medicine of USC

LAC+USC
HEALTHCARE NETWORK

Children's Hospital
LOS ANGELES
We Treat Kids Better

2020-2021 Graduating Residents

Charles DeBoer, MD, PhD
USC
Los Angeles, CA

William Gange, MD
Loyola University
Chicago, IL

Hong-Uyen Hua, MD, Co-Chief
University of Miami
Miami, FL

Nicole Koulisis, MD
University of Massachusetts
Worcester, MA

Diana Lee, MD
Georgetown
Washington, DC

Jonathan Lu, MD
UC Davis
Davis, CA

Maggie Runner, MD, Co-Chief
Emory University
Atlanta, GA

2020-2021 Graduating Fellows

Mashal Akhter, MD
Surgical Retina
Northest Ohio Medical University
Rootstown, OH

Christine Bokman, MD
Oculoplastics
UCLA
Los Angeles, CA

Andres Gonzalez, MD
Surgical Retina
University of Florida
Gainesville, FL

David Kay, MD
Glaucoma
UT Health San Antonio
San Antonio, TX

Peter Lam, MD
Cornea
LSU Shreveport
Shreveport, LA

Grand Rounds Case Study

"Up, Up, and Away!"

CHALLENGING EYE CARE

Sona Shah, MD
PGY-2 Ophthalmology Resident

Kimberly Gokoffski, MD, PhD
Assistant Professor of Clinical Ophthalmology

HISTORY

- 25-year-old male with no significant past medical history presenting with: progressively worsening headaches, nausea/vomiting, and acute altered mental status x1 day.

EXAM FINDINGS

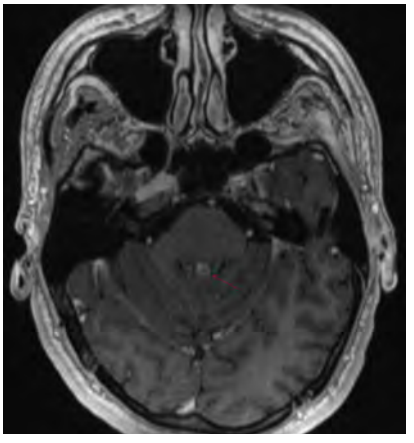
- In the ER, patient AAOx1 with tachycardia and leukocytosis.
- CT Head: Ventriculomegaly and a 2.5 cm cystic lesion in the region of the Tectal plate, likely resulting in obstructive hydrocephalus with trans-ependymal edema (cyst not clearly visible on initial imaging but can be seen below on a later study (Figure 1).
- MRI Brain (Figure 2): Obstructive hydrocephalus.

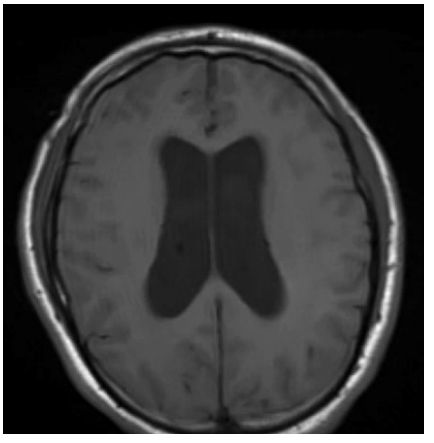
MANAGEMENT

- Admitted to the ICU for urgent shunt placement, with an opening pressure elevated at > 30mmHg.

Figure 1 (below, left): MRI Brain w/ and w/out contrast after initial presentation, illustrating cystic lesion in the 4th ventricle.

Figure 2 (below, right): MRI Brain w/ and w/out contrast on day of initial presentation, exhibiting hydrocephalus. It was evident that this was not a typical communicating hydrocephalus and that a mass effect was present, however the cysts were not clearly visible on imaging.





- Dilated fundus examination showed no evidence of intraocular cysts.
- Patient then initiated on albendazole 15mg/kg/day + praziquantel 50mg/kg/day + 0.2 – 0.4mg/kg/day of dexamethasone.
- Neurocysticercosis (NCC) antibodies returned positive.
- Patient remained inpatient and then in rehabilitation for appropriate NCC treatment.

PATIENT COURSE

- Patient returns four months after initial presentation with complaints of binocular diplopia.
- Since being in rehabilitation, patient has noted limited up-gaze and persistent dysconjugate gaze, with worsening symptoms of diplopia x2 days.

OCULAR EXAMINATION

- Pupillary exam significant for: light-near disassociation.
- External exam showed (Figure 3, 4)
  - 4 mm ptosis bilaterally
  - Abduction: full and intact bilaterally (ruling out a CNVI palsy)
  - Adduction: full and intact bilaterally w/out evidence of slowed adduction saccades

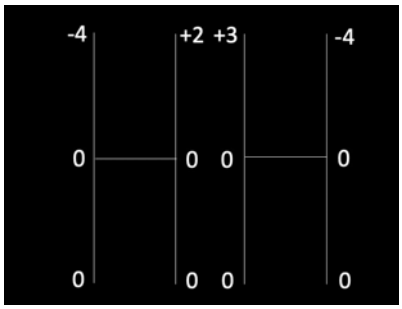


Figure 3 (above): Extraocular muscle movements.

Figure 4 (above): Versions

(ruling out internuclear ophthalmoplegia, but not ruling out a partial nuclear third nerve palsy)
- Right and left gaze: the adducting eye shoots up, indicating inferior oblique overaction (indicating bilateral CN IV palsy)
- Up-gaze: cannot move eyes beyond midline (indicating up-gaze palsy)

DIAGNOSIS AND DIFFERENTIAL

- Summary: Bilateral ptosis with upgaze palsy, convergence retraction nystagmus, alternating hypertropia and near light dissociation. Our patient displayed 30 degrees of excyclotorsion. With the Parks-Bielschowsky three-step test, there was suspicion for either a bilateral CNIV palsy versus skew deviation. Distinguishing between the two requires testing for relative cyclotorsion using a double Maddox rod: skew deviation has no relative cyclotorsion while CNIV palsy demonstrates relative excyclotorsion.

ANATOMICAL DAMAGE UNDERLYING DORSAL MIDBRAIN SYNDROME

- Components of dorsal midbrain syndrome (many of which were present in the case at hand) include:
  - Light-near dissociation: results from damage to the posterior commissure
  - Upgaze palsy: results from damage to the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF)
  - Convergence-retraction nystagmus: results from damage to the midbrain supranuclear fibers in posterior commissure

TREATMENT AND PROGNOSIS

- Management of dorsal midbrain syndrome is targeted at treating the underlying cause.
- Full resolution of symptoms is rare, and some degree of persistent symptoms is expected.
- Given treatment of NCC and control of intracranial pressure (ICP), we would offer surgical correction after approximately six months of recovery.

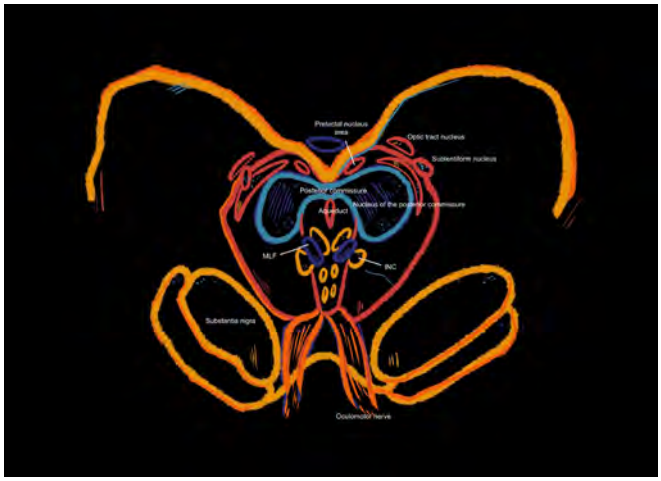
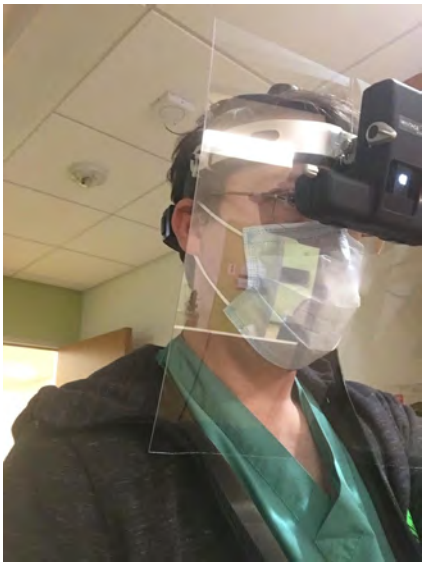


Figure 5 (above): This illustration demonstrates the geographic relationship of the posterior commissure to its surrounding structures. MLF = medial longitudinal fasciculus. INC = Interstitial nucleus of Cajal.

REFERENCES

- Miller, N. R., Subramanian, P. S., & Patel, V. R. *Walsh and Hoyt's clinical neuro-ophthalmology: The essentials*. Philadelphia, PA: Lippincott Williams & Wilkins. 2016.
- Sawhney, I. M. S., Singh, G., Lekhra, O. P., Mathuriya, S. N., Parihar, P. S., & Prabhakar, S. Uncommon presentations of neurocysticercosis. *Journal of the Neurological Sciences*, 154(1), 94-100. 1998.
- Hoehn ME, Calderwood J, Armstrong GT, Gajjar A. Children with dorsal midbrain syndrome as a result of pineal tumors. *Journal of American Association for Pediatric Ophthalmology and Strabismus*, 21(1):34-8. 2017.
- Mesraoua, B., Deleu, D., D'souza, A., Imam, Y. Z. B., & Melikyan, G. Neurocysticercosis presenting as a vertical one-and-a-half syndrome with associated contralesional horizontal gaze paresis. *Journal of the Neurological Sciences*, 323(1-2), 250-253. 2012.
- Baloh, R. W., Furman, J. M., & Yee, R. D. Dorsal midbrain syndrome: clinical and oculographic findings. *Neurology*, 35(1), 54-54. 1985.
- Keane, J. R. Neuro-ophthalmologic signs and symptoms of cysticercosis. *Archives of Ophthalmology*, 100(9), 1445-1448. 1982.

As COVID-19 Disrupts Education, Ophthalmology Residents Adapt



When Dr. Charles DeBoer, a third-year resident in the USC Department of Ophthalmology, learned that barrier shields meant to protect patients and physicians from COVID-19 droplet transfer were nationally backordered, he spent his own time and personal resources to build PPE customized for ophthalmic exams.

"I saw a barrier shield design in the paper, 'Stepping up infection control measures in ophthalmology during the novel coronavirus outbreak: an experience from Hong Kong (2020)' and thought the way they implemented infection control made sense," said Dr. DeBoer. "So I copied it for our clinics and we refined the design." In collaboration with co-resident Dr. Diana Lee and two attending physicians, Dr. DeBoer created barrier shields out of polycarbonate sheets for slit lamps, the microscopes used to look into patients' eyes.

Dr. DeBoer's barrier shields now enable physicians to examine a patient closely while still reducing the risk of infection for them both at LAC+USC Medical Center (LAC+USC) and Keck Medical Center (KMC) ophthalmology clinics. This is only one example of how residents are adapting within the drastically disrupted learning environment due to the ongoing COVID-19 pandemic.

In addition, residents are continuously implementing the latest COVID-19 industry responses provided by the American Academy of Ophthalmology (AAO). They are strengthening their history taking skills to learn more about their patients' health histories, and have increased in-depth provider-to-provider discussions with their fellow residents, fellows, and faculty. Furthermore, residents are learning how to use new technology to provide telehealth services to meet patient needs.

"Telehealth allows us to perform a quick external exam of a patient's eye," said Dr. Hong-Uyen Hua, a third year and co-chief resident. "While it does not allow for a full assessment, it can help patients avoid in-office visits for non-urgent issues."

Dr. Hua elaborated that patients often call with eye problems that can be resolved over the phone. Several patients who tested positive for COVID-19 have called with concern that they

are developing an eye infection, as well. "In this situation, we ensure that the patient has no vision-threatening issues. We educate and counsel them on supportive care, emphasize the importance of social distancing, and make sure they practice good hygiene. As a result, we minimize exposure for everyone."

Several residents expressed their belief that COVID-19 will permanently affect the ophthalmology landscape and that it has opened the door for telemedicine to play a more frequent role in the field.

Away from clinic, residents are reading journal articles to stay updated on their respective fields and studying for their annual Ophthalmic Knowledge Assessment Program (OKAP) exams.

In addition, the residency program's education curriculum has quickly shifted to online learning. All faculty lectures and Grand Rounds continue to be conducted via Zoom.

Despite the disruption that COVID-19 has caused to the residents' training, they share great pride in their colleagues' resilience. "Too often likened to war, this pandemic has heroic troops battling this microscopic, insidious enemy every day," said Dr. Hua. "When we chose medicine as a career, no healthcare worker imagined we would have to risk our own lives to save others. I am in awe of all of my colleagues on the frontline. I feel re-affirmed in my decision to choose medicine as a career and vocation during this unprecedented pandemic."

LAC+USC Ophthalmology
Alumni Spotlight: Dr. Charles Manger III

Dr. Charles Manger III graduated from the LAC+USC Medical Center Ophthalmology Program in 1980. He subsequently founded the Saddleback Eye Center in Laguna Hills, CA, where he has performed ~89,000 LASIK surgeries since 1996. In 2007, Dr. Manger made a generous donation to the USC Roski Eye Institute to establish the Charles C. Manger III Endowed Chair in Corneal Laser Surgery, a chair currently held by the USC Department of Ophthalmology's interim department chair, Dr. J. Martin Heur.

To reflect on his ophthalmology career, Dr. Manger recently donated his time to share how the residency program prepared him for a successful career and impart wisdom on the next generation of ophthalmologists.

Can you tell us about your experience as a resident at the Keck School of Medicine?
When I started training, Dr. Steve Ryan and Dr. Ron Smith had just arrived at USC to establish a full-time academic program. As a first-year resident, I remember the Tuesday Morning Resident Teaching Rounds were something to fear. Dr. Ryan would lead the rounds and he was a very serious, focused man. I'd spend two to three hours preparing myself for the next morning's rounds, because he'd call on the residents at random to ask questions about the case. But what impacted me the most was the independence the program gave me to evaluate and treat a significant number of patients at the Los Angeles County/USC Hospital. Senior residents and staff were available to assist if I had a question, but the program gave us autonomy.

What was your most memorable experience of residency?
It was January 1, 1980. I was on call and asleep when an intern woke me to say a patient had arrived with retina symptoms and insisted that I see him. I examined the patient's eye and found he had a retinal detachment. After making some calls, I arranged for the staff at the Eye Institute to fix his detachment the next morning. The patient became a neurologist and lives in Orange County and we have kept in touch since. My residency experience was so vital because it empowered me to make decisions regarding patient care.

Before you started residency, you went to Annapolis and served on a nuclear missile submarine. Did those experiences shape your approach to healthcare?
The common thread through those experiences is I learned you must find a purpose and then make a commitment. These places taught me that you must be willing to work every waking hour of most days to fulfill your goals. Eight hours a day and free weekends are not a given in these endeavors.

With those kinds of demands, what keeps you going?
When patients first meet with me, they have fear of the LASIK procedure. But my staff and I talk to them and let them know this is something I've been doing for 24 years. I tell them I'm going to do the surgery technically correct and it's going to improve their vision. A few hours after the procedure, they can't believe the difference. LASIK makes a truly positive change in their quality of life.

What advice would you give to our residents and alumni?
Consistent communication with patients and staff is key to an organized office environment. It is essential not to be absorbed with patient care to the exclusion of those relationships. In my practice, we have 15-minute staff rounds with the doctors and staff every workday. We talk about the day before, the correct way to handle given situations, how we may handle those situations better in the future, upcoming procedures, etc. The practice comes from the Navy, where rounds are held every morning when in port. Although the Navy was not the right career for me, it provided me with routines I apply to my practice to this day.

What advice would you give to our residents who want to go into private practice?
If the business and entrepreneurship aspects of medicine are important to you, you must work hard and communicate continually with your staff, so you are consistent with procedures and instructions. You must stay involved from a distance and manage all aspects of your office operations, while also managing the clinical and surgical work on your patient.

What inspired you to make such a transformational gift to our department?
Before I was born, my grandfather, Charles Manger was a Professor of Neurology at the USC Medical School [1911-1918]. I wanted to recognize both my grandfather's work and that USC allowed me to pursue my dream of a career in medicine at 28 years old. My wife Carol and my daughter Laurie have degrees from USC. In appreciation of the opportunities that USC provided for our family, we wanted to help other people seeking a medical career.

At the chair installation for Dr. J. Martin Heur, Dr. Manger gave a guest lecture and was accompanied by his family. As a father, Dr. Manger has always stressed to his children the importance of getting a good education and pursuing the work that they love. His daughter Laurie Manger has a B.A. and Masters in Strategic Public Relations from USC, and today works as the Director of Marketing and Public Relations at the Saddleback Eye Center. His older son Charles Manger IV has degrees from Claremont McKenna and George Washington University, and has worked as a software engineer for more than 10 years. His younger son Joey Manger has a B.A. from Chapman University, and is a commercial airline pilot.

When Dr. Manger is not leading a busy practice, he enjoys gardening at both his office and home. He has a special interest in palms and cycads. In addition, he spends 30-60 minutes every day on physical training and stretching exercises.

TRAINING the NEXT GENERATION at LAC+USC

Residents at LAC+USC Medical Center engage in a rich learning environment seeing everything from trauma to complex neurological conditions involving the eye to common eye ailments, including diabetic retinopathy, cataracts, and glaucoma. They simultaneously manage the complex inpatient and emergency consult service for ophthalmology as well as run the busiest outpatient clinic in the hospital. Between 250-350 patients are seen in the ophthalmology clinic daily with 8-10 surgeries also being performed daily. Our residents come out of their three year residency with supreme experience and extraordinary skills prepared for any job or fellowship they desire.

ALUMNI BY THE NUMBERS

56 **VOLUNTARY FACULTY**

15 **DEPARTMENT CHAIRS**

279 **RESIDENTS TRAINED**

306 **FELLOWS TRAINED**

Notable Accolades & Achievements

Jesse Berry, MD
National Research Mentoring Network Scholar, National Institutes of Health

Cheryl Craft, PhD
ARVO Foundation 2020 Distinguished Honoree

J. Martin Heur, MD, PhD
Charles Manger III, MD, Chair in Corneal Laser Surgery Installation

Mark Humayun, MD, PhD
Institute of Electrical and Electronics Engineers (IEEE) Medal for Innovations in Healthcare Technology
Lecturer, Seventeenth Annual Carl M. Franklin Lecture on Science and Society
Retina Research Foundation's Gertrude D. Pyron Award

Gianluca Lazzi, PhD, MBA
Fellow of the National Academy of Inventors
President-Elect of the IEEE Antennas and Propagation Society (APS), 2021

Andrew Moshfeghi, MD, MBA
Candidate for Membership in Club Jules Gonin Society

Narsing Rao, MD
International Gold Award of Chinese Ophthalmological Society 2020
Featured in Living Legend Series, Indian Journal of Ophthalmology

Grace Richter, MD, MPH
Paul Harris Fellow Award, Rotary International

Paul Thompson, PhD
Authored multiple papers in the last decade ranked in the top 1% by citation for his field and year of publication

Arthur Toga, PhD
Authored multiple papers in the last decade ranked in the top 1% by citation for his field and year of publication

Sandy Zhang-Nunes, MD
Top Doctor, Los Angeles Magazine

Qifa Zhou, PhD
National Academy of Inventors Senior Member

Hossein Ameri, MD, PhD;
Charles Flowers, MD;
Linda Lam MD, MBA;
Karen Morgan, MD;
and Narsing Rao, MD
Top Doctors 2020, Pasadena Magazine

Annual Report Cover Image: This volumetric rendering shows the visual system fiber bundles, orbit, optic tract, and vascular system of the brain. Also visible, with reduced opacity, are the inferior fronto-occipital fiber bundles. Image credits: Jim Stanis and Arthur Toga. Data provided by data Yonggang Shi and Ryan Cabeen. Laboratory of Neuro Imaging, USC Stevens Neuroimaging and Informatics Institute.

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HOSPITAL IN THE NATION

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The USC Roski Eye Institute and LAC+USC Medical Center see patients at the following locations:

Keck School of Medicine of USC
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USC Roski Eye Institute
1450 San Pablo Street, 4th Floor
Los Angeles, CA 90033
(323) 442-6335

USC Roski Eye Institute - USC Village
835 W. Jefferson Boulevard,
Suite 1720
Los Angeles, CA 90089
(833) USC-EYES

USC Roski Eye Institute - Arcadia
65 N. First Avenue, Suite 101
Arcadia, CA 91006
(626) 446-2122

Children's Hospital Los Angeles
The Vision Center
4650 Sunset Boulevard
Los Angeles, CA 90027
(323) 660-2450

USC Roski Eye Institute - Pasadena
625 S. Fair Oaks Avenue, Suite 400
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