



CASEY EYE
Institute

Letter from leadership

A new lens for a new century

Friends and colleagues,

In 2020 we celebrate our department's 75th year, and a new decade harkens. With it, the prospect of needed innovation to improve the care of patients with vision threatening conditions, especially whole populations (see side bar).

Using this measure, Oregon has a visual acuity of about 20/80, based on a sampling of patients suffering from the three leading causes of legal blindness: macular degeneration, glaucoma and diabetic retinopathy. To us, leadership in ophthalmology should be about bringing that number closer to 20/20. To make progress, a critical component is to rally public awareness and education about eye health, so that people make the connection between vision and the quality of every aspect of their lives in the 21st century.

In the iconic year 2020, we will advance this theme through two ambitious projects: The Eye Love Project and the new Elks Children's Eye Clinic building.

The Eye Love Project 2020

A yearlong, statewide effort to celebrate vision, the Eye Love Project is a mobile multimedia exhibit to engage a broad community in reflections on vision health and to drive awareness of our goal to reduce preventable blindness. The exhibit will travel among major community partners throughout the year, such as the Oregon Zoo and the Oregon Museum of Science and Industry. The exhibit features a recording booth, where the public can record video messages about what their vision means to them and share memories

The three major causes of legal blindness in Oregon are age-related macular degeneration, glaucoma and diabetes. When we analyze all the patients we have seen in clinic with these three diagnoses, the average corrected visual acuity is 20/25. However, if we look at this population in total, we have to go up to

20/80

to capture 95% of all of the patients being evaluated for these three diseases. This statistical method can be used to assess our progress in addressing Oregon's overall visual health.

of special, visual moments in life. These stories will be widely shared and build on the project throughout the year to create a vision census of Oregon.

Elks Children's Eye Clinic

The Elks Children's Eye Clinic will be the nation's first freestanding eye clinic for pediatric patients, representing a world-class hub for innovative research, subspecialty patient care and leading-edge programs in gene therapy, preschool vision screening and telemedicine for retinopathy of prematurity. The 60,000-square-foot building will also house the Wold Family Macular Degeneration Center, the Paul H. Casey Ophthalmic Genetics Division, imaging technology integrated into exam spaces, a mobility maze and more. In this new space specifically designed for a new era in ophthalmology, we will have the tools, technology and talent to detect eye disease earlier, diagnose it more accurately and provide the most effective treatments possible.

As a recognized leader in pioneering vision research, OHSU Casey Eye Institute has made amazing advancements to change the future of vision health in our state and beyond. We are proud to share with you some highlights of the promising work that is transforming how we provide care to people and populations affected by eye diseases.

www.theeyeloveproject.com

OHSU Casey Eye Institute is proud to be a world-renowned academic eye center working to eliminate preventable blindness through research, education, innovation and community service.



A handwritten signature in black ink that reads "David J. Wilson".

David. J. Wilson, M.D.
Professor and Paul H. Casey
Chair, Department
of Ophthalmology
Director, Casey Eye Institute



A handwritten signature in black ink that reads "Andreas Lauer".

Andreas Lauer, M.D.
Professor and Thiele-Petti
Chair, Chairman, Department
of Ophthalmology

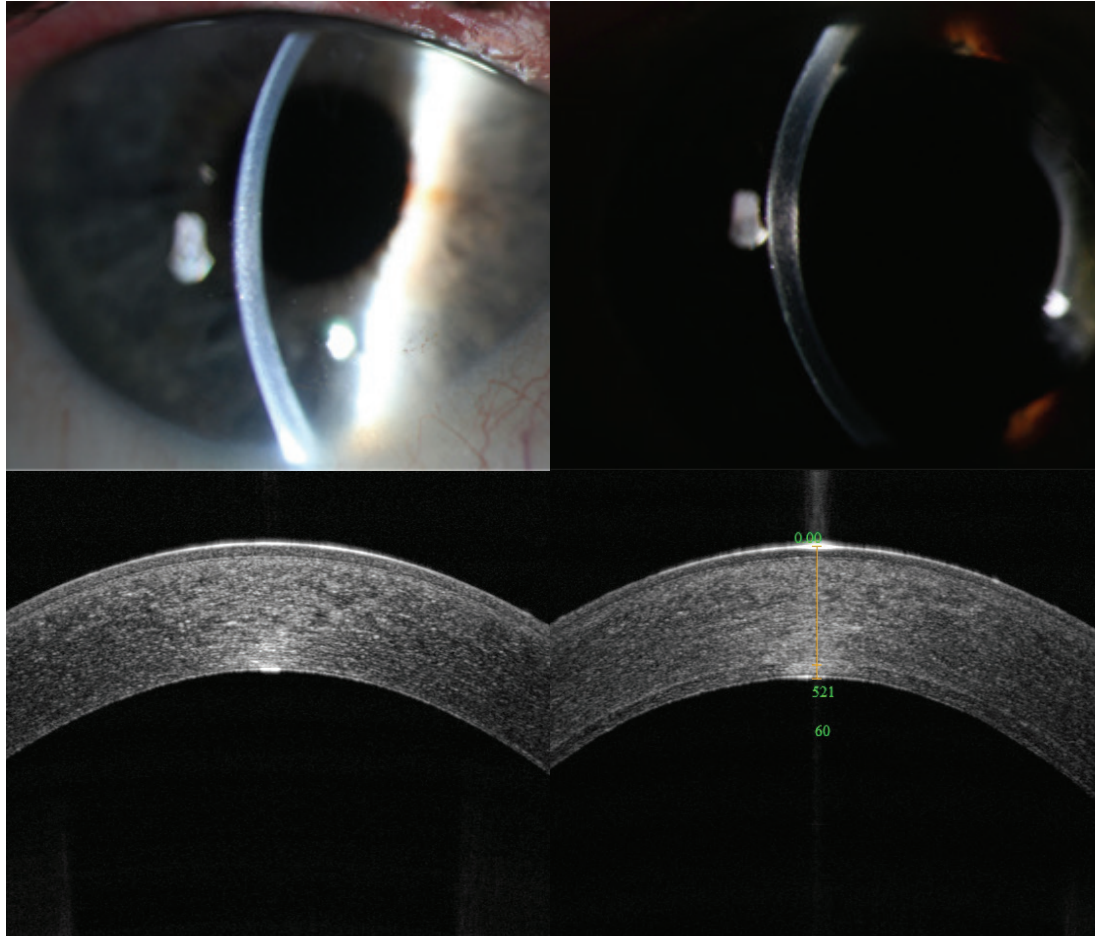


A handwritten signature in black ink that reads "Michael F. Chiang".

Michael F. Chiang, M.D.
Knowles Professor,
Department of
Ophthalmology
Associate Director,
Casey Eye Institute

Fine-tuning corneal procedures

► Slit lamp photos of DMEK (left) and UT-DSAEK (right) with corresponding OCT images (below). DMEK generates a near perfect anatomical replacement of the diseased corneal endothelium. UT-DSAEK is an easier surgery to perform, adding a thicker posterior layer.



OHSU Casey Eye Institute is setting a new standard in Level I evidence in corneal procedures and reducing subjectivity from treatment decisions. By embedding clinical research in patient care, OHSU Casey Eye Institute works to improve quality of life for patients.

“We know we will obtain better visual outcomes by pushing the bar with scientific investigation and utilizing new technologies,” said OHSU Casey Eye Institute ophthalmologist Winston Chamberlain, M.D., Ph.D.

Comparing corneal transplant methods

Posterior layer replacements of the cornea now account for more than 50% of corneal transplants in the U.S. In 2019, OHSU Casey Eye Institute (in collaboration the University of California, San Francisco and Stanford University) published the results of a comparison of visual outcomes and multiple other optical and surgical variables after Ultrathin Descemet stripping automated endothelial keratoplasty (UT-DSAEK) and Descemet membrane endothelial keratoplasty (DMEK). Patients included in the study had Fuchs' endothelial dystrophy or pseudophakic bullous keratopathy. The study set a new standard for randomized, controlled trials for this corneal surgery.

"These surgeries have been challenging for corneal surgeons to learn and have rapidly evolved over the last 10 years," said Chamberlain, who was the co-author and co-designer of the study. "It is critical to have Level 1 evidence to show we are doing the right thing for our patients."

The study assembled an incredibly well-matched set of patients. With randomization of treatment, Chamberlain noted there was an excellent degree of sensitivity in detecting differences.

"DMEK resulted in better vision than UT-DSAEK, with no difference in complications," he said. "Patients' visual acuity improved, and they recovered faster with single cell layer treatment."

Study participants continued to have better acuity and fewer higher-order aberrations (microscopic optical distortions) in their corneas up to two years later. Data are still coming out of this trial, and the

investigation has generated new questions about graft survival and the role of novel pharmacotherapeutics. OHSU Casey Eye Institute plans to pursue these questions in a larger-scale, multicenter clinical trial currently in the planning stage.

Modifying crosslinking for better acuity

OHSU Casey Eye Institute is seeking to improve the corneal crosslinking (CXL) modality and taking the next step toward visual rehabilitation in patients with keratoconus. CXL strengthens corneal tissue by using riboflavin eye drops as a photosensitizer and ultraviolet-A. Chamberlain, Huang, Afshan Nanji, M.D., M.P.H., and Richard Stutzman, M.D., use OCT to image subtle changes in the layers of corneas affected by keratoconus. This imaging then guides the sculpting and shaping of the cornea using an excimer laser before locking in the shape with crosslinking for improved visual acuity and long-term stability.

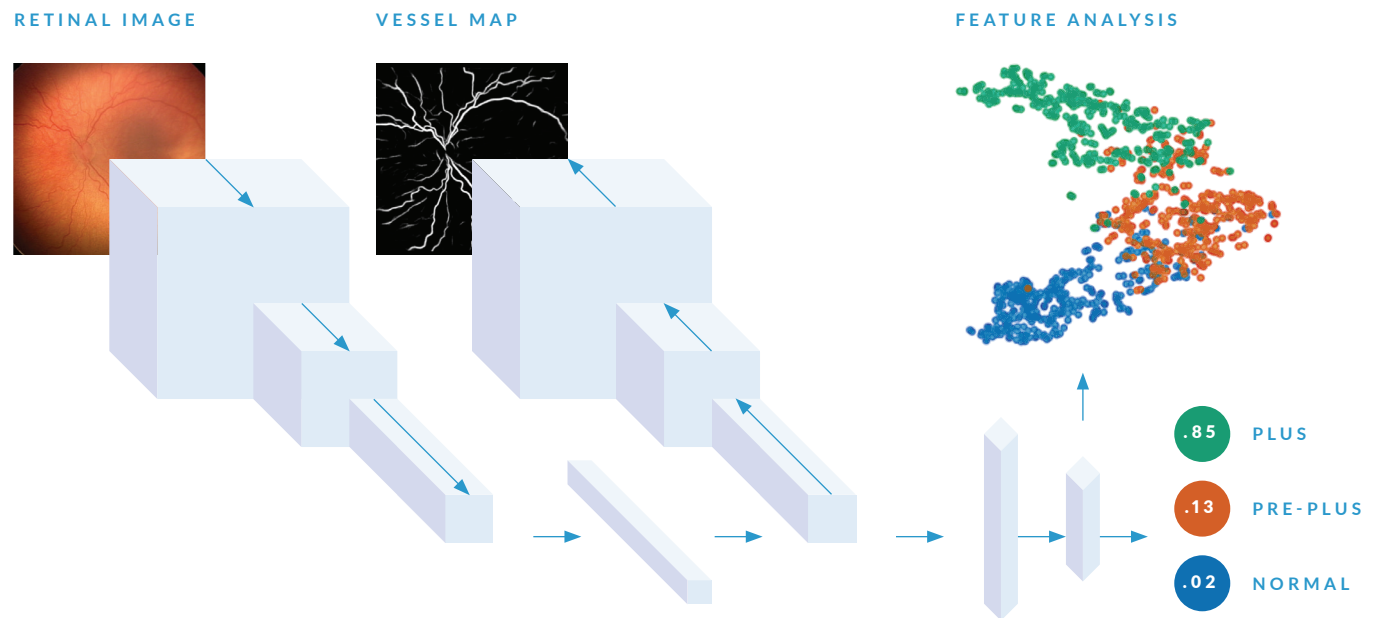
Reducing subjectivity in corneal transplant decision-making

Imaging cornea disease states is essential to staging disease and surgical intervention. Yan Li, Ph.D., of the COOL lab at OHSU Casey Eye Institute is collaborating with Chamberlain to develop a protocol to image and quantify the subtle changes in every layer of the cornea very early in corneal endothelial disease. The goal is to find thresholds of disease to guide surgical decisions for posterior layer corneal transplantation. The methods will utilize optical coherence tomography (OCT), pioneered by OHSU Casey Eye Institute's David Huang, M.D., Ph.D.

"This has the potential to provide more objective guidelines for committing patients to surgery and also to predict optical outcomes after the surgery."

Winston Chamberlain, M.D., Ph.D.

Leading in artificial intelligence applications



Retinal Image → Vessel Map → Diagnosis



Leveraging AI in eye disease

OHSU Casey Eye Institute is a leading center nationwide for investigating telemedicine, AI and data analytics for ophthalmic care. Michael F. Chiang, M.D., is the Chair of the Artificial Intelligence Task Force assembled by the American Academy of Ophthalmology in 2019. OHSU Casey Eye Institute's J. Peter Campbell M.D., M.P.H., is also one of the seven members in the group. The purpose of the national taskforce is to define the state-of-the-art in AI and to develop a roadmap for the ophthalmic community to use it and teach it.

Following a decade of research into how to deliver consistent, accurate diagnoses for retinopathy of prematurity (ROP), OHSU Casey Eye Institute is another step closer to bringing an artificial intelligence (AI)-based algorithm system to patients. In collaboration with Massachusetts General Hospital, Northeastern University and University of Illinois-Chicago, OHSU Casey Eye Institute recently received a “Breakthrough Device” designation for an AI system called i-ROP DL (deep learning) as an assisted medical device for diagnosing clinically-significant ROP.

“Our motivation is that ROP is the leading cause of preventable childhood blindness in the U.S. and world,” said OHSU Casey Eye Institute ophthalmologist Michael F. Chiang, M.D., principal investigator of the i-ROP study. “ROP presents challenges for ophthalmologists because it relies on subjective diagnoses and presents logistical hurdles. Also, there is a huge imbalance in the number of premature infants needing evaluation and the number of available experts. A missed or misdiagnosed infant will go blind, so the stakes are high.”

In comparison trials, even experts are not very consistent in making ROP diagnosis. In one example, some international experts diagnosed severe treatment-requiring ROP 6 times more frequently than other experts, even when examining the same eyes. Finding ways to standardize a quantitative assessment has been a passion for Chiang. He is the current Chair of the International Classification of ROP Committee, which is developing worldwide standards for ROP diagnosis.

“Because ophthalmology is heavily image-based, it is a good field to analyze and quantify data using AI and computing systems,” Chiang said. “Through deep learning, the algorithm uses the collective knowledge of ophthalmologists and creates a mathematical model that accurately diagnoses ROP from images. The AI system we are working on had comparable or better results than our panel of experts in accurately identifying ROP.”

Chiang believes that many of the challenges in ROP are true across ophthalmology and medicine in general.

“Though OHSU Casey Eye Institute is leading to get this one product to the FDA, we are also applying machine learning and AI to create more precise, quantitative scales for other eye diseases,” he said.

Impacting the field

The Eye Love Project

OHSU Casey Eye Institute is leaning into the iconic year 2020, furthering the mission of providing world-class specialists and state-of-the-art technologies to promote eye health by embracing art, science and technology in the name of vision. The Eye Love Project seeks to ask questions that inspire participants to reflect on how sight improves their quality of life and what vision means to them on a personal level.

www.theeyeloveproject.com



Macular Degeneration and Vision Expo for the community

For 22 years, OHSU Casey Eye Institute's Macular Degeneration Center and Vision Rehabilitation Center has hosted a free, one-day program in Portland for community members with macular degeneration and other conditions that impair sight. The event attracts as many as 900 attendees each year. The expo features presentations by OHSU Casey Eye Institute faculty on the latest advances in macular degeneration research and treatment, small group sessions on adjusting to vision loss, and exhibits of community services, optical aids and assistive technology.



Building momentum with new facility

The new Elks Children's Eye Clinic facility, a 60,000-square-foot building adjacent to OHSU Casey Eye Institute, will provide more space for crucial programs, including the Elks Children's Eye Clinic pediatric service, the Paul H. Casey Ophthalmic Genetics Division and the Wold Family Macular Degeneration Center. With this new facility, OHSU Casey Eye Institute will expand clinical trial capacity for gene therapy to accommodate the expected tripling of patient volumes, grow research and clinical trials for age-related macular degeneration, and serve as a statewide hub for pediatric eye care programs, including telemedicine for retinopathy of prematurity, pediatric vision screening and treatment of inherited eye disease. The facility will open in the fall of 2020.

Expanded annual conference to mark 75th anniversary

The year 2020 marks the 75th anniversary of the ophthalmology department at OHSU. In honor of this milestone, OHSU Casey Eye Institute is hosting a two-day Oregon Ophthalmological Alumni Association Meeting in June that has attracted some of the top ophthalmologists in the country to speak to faculty and alumni. OHSU Casey Eye Institute has grown exponentially in the last 75 years, so it is exciting to celebrate the achievements and future innovations.

www.ohsu.edu/ooaameeting



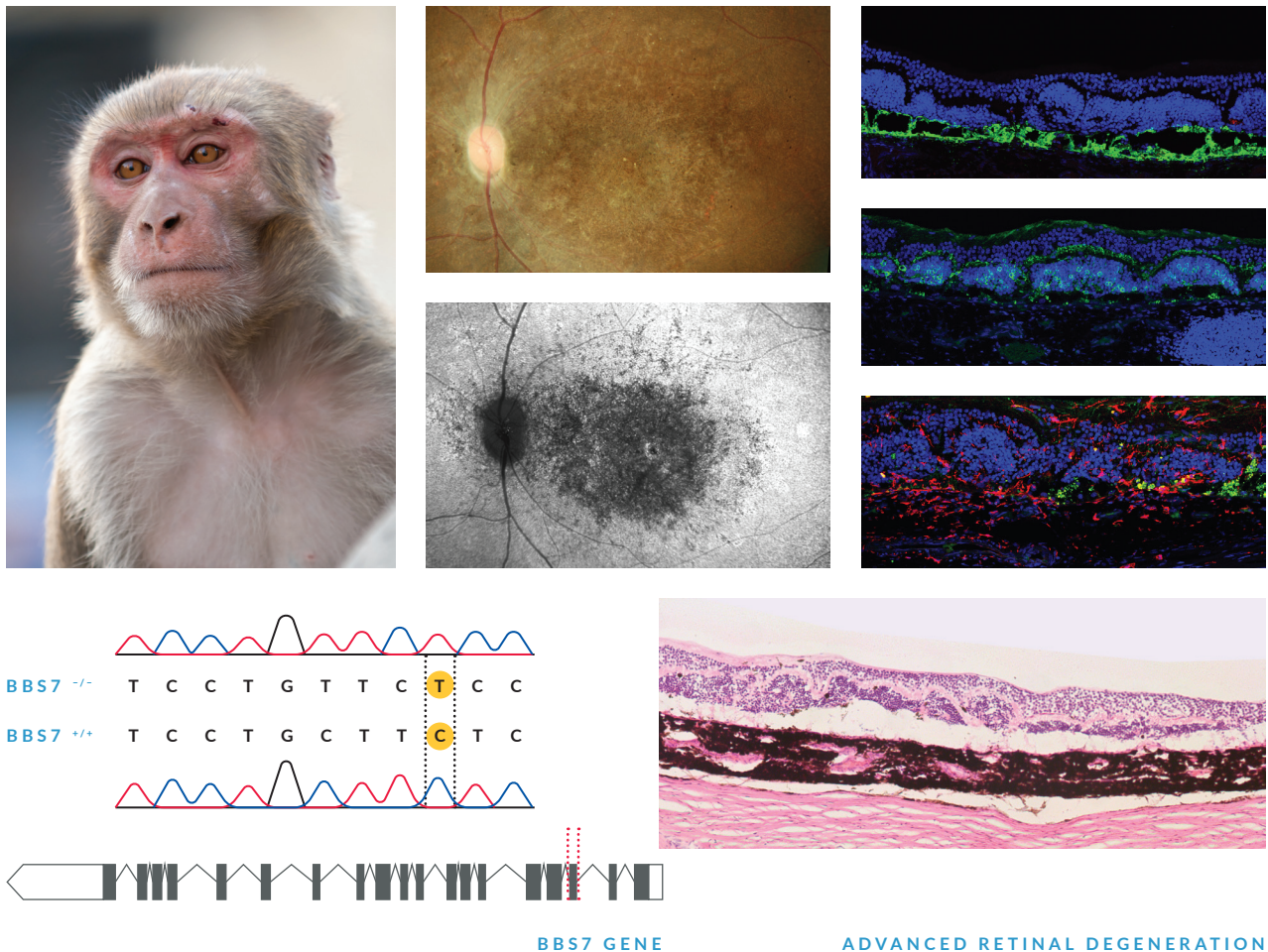
Innovative curriculum deepens engaged learning for residents

In the coming year, OHSU Casey Eye Institute is switching to an adult-learner focused curriculum that emphasizes case-based learning with faculty experts, as compared to the traditional didactic structure. "I am very excited to be part of an active learning environment, where residents can more deeply engage in the learning process," said Sarah Glass, M.D., class of 2021. "The focus on continual educational improvement is what truly sets Casey apart and makes me excited to train here."



Accelerating scientific research in retinal disease

The discovery of naturally occurring retinal degeneration due to a BBS7 gene mutation in three rhesus macaques offers the first opportunity to study an inherited photoreceptor degeneration in a nonhuman primate model. The macaques are part of a colony at the Oregon National Primate Research Center at OHSU.



▲ This graphic illustrates the appearance of an affected retina in fundus autofluorescence imaging; retinal sections stained by H&E and by immunohistochemistry; the position of the mutation within exon 3 of the BBS7 gene (red dotted lines); and the base pair change (from C to T) as detected in a Sanger sequence chromatogram.

The retinas of rhesus macaques are nearly identical to human retinas, so this animal model of Bardet-Biedl Syndrome (BBS), a form of retinitis pigmentosa, will provide new insight into disease progression and interventions.

“This discovery highlights the important role nonhuman primate models can play in developing therapies for retinal diseases,” said Martha Neuringer, Ph.D., a neuroscientist and research associate professor of ophthalmology. “We have been involved in testing several gene therapies that have gone on to clinical trials — achromatopsia and retinoschisis, as examples — but we were testing the surgical technique or the delivery of a vector or the side effects of a treatment, not curing the disease itself. Now, we can track the progression of the disease in the animals and test potentially curative retinal gene or cell replacement therapies.”

Though having the animal model may lead to a cure for BBS in the future, the possibilities expand beyond one form of disease.

“The expectation and hope of this discovery are that having nonhuman primate models will accelerate the development of therapies for retinitis pigmentosa and other retinal degenerative diseases,” Neuringer said.

Neuringer and her colleagues received grants from the National Eye Institute and Research to Prevent Blindness to breed more animals with the naturally occurring BBS7 mutation. The Oregon National Primate Research Center — one of only seven in the nation — has several

strengths to support this effort, including the Assisted Reproductive Technology Core Laboratory, the Primate Genetics Division and a full spectrum of retinal imaging instruments and surgical suites.

“Our facilities and procedures are up to human standards,” Neuringer said.

“We work with an incredible team of vitreoretinal surgeons from OHSU Casey Eye Institute, and we have a full range of noninvasive retinal imaging instruments to measure disease progression and effects of treatments.”

OHSU Casey Eye Institute’s Primate Genetics Division genome project locates mutations

Betsy Ferguson, Ph.D., of the Oregon National Primate Research Center at OHSU leads an effort to genetically sequence 2,000 rhesus macaques, funded by the National Institutes of Health. Ferguson and Samuel Peterson, Ph.D., examined the genomes of the animals that the Neuringer lab discovered, and they quickly found that they had a mutation of the BBS7 gene, one of at least 21 genes associated with BBS. Using this information, they quickly located a third monkey with the mutation, and identified over 50 carriers of the gene mutation within the rhesus macaque colony at OHSU. They have also identified a pedigree of primates with neuronal ceroid lipofuscinosis, a storage disease that is associated with progressive retinal degeneration. This pedigree will also enable pioneering work on gene therapy in this type of disease.



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