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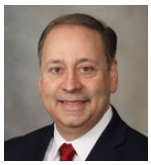
In this issue

Brittni A. Scruggs, M.D., Ph.D.



Raymond Iezzi Jr., M.D.

Alan D. Marmorstein, Ph.D.

Novel Surgical Approach for Retinal Gene Therapy Shows Promise as a Less Invasive Alternative

A Mayo Clinic study published in the September 2025 issue of *Science Advances* explores a novel approach to retinal gene therapy using fibrin hydrogels encapsulating adeno-associated virus 2-green fluorescent protein (AAV2-GFP). The findings suggest a promising, less invasive alternative for the treatment of blinding retinal diseases.

Luxturna was approved by the Food and Drug Administration in 2017 for RPE65-related inherited retinal dystrophy and was the first in vivo gene therapy (Figure 1). While subretinal injection of adeno-associated virus (AAV) is the current standard of care for retinal gene therapy and has restored functional vision to many patients, it can cause localized damage and limits gene expression to the treated area.

Figure 1. Physicians examine virtual genetics graphic.

"The traditional method for delivering gene therapy in patients with an inherited retinal disease involves surgically injecting the treatment underneath the retina," says Brittni A. Scruggs, M.D., Ph.D., the lead author of the article and a vitreoretinal surgeon at Mayo Clinic in Rochester, Minnesota. "This is a procedure with several known complications associated with this route of administration."

Dr. Scruggs and her colleagues, including Raymond Iezzi Jr., M.D., and Alan D. Marmorstein, Ph.D., in the Retinal Regenerative Medicine Laboratory at Mayo Clinic developed high-concentration fibrin gels with uniform AAV distribution and tested their epiretinal placement.

"With this newly developed, alternative approach, the therapy is placed gently on the surface of the retina within a fibrin hydrogel," says Dr. Marmorstein. "This special gel releases the gene therapy as it degrades within a few days, which offers the potential to treat larger retinal areas with less surgical trauma."

Placing the gene therapy inside a fibrin-based hydrogel directly on top of the retina — rather than underneath — allows the therapy to reach a wide area of retinal cells while using low doses (Figure 2). "In a large animal model, this epiretinal delivery method led to broad gene expression with less inflammation compared to traditional methods," says Dr. Marmorstein.

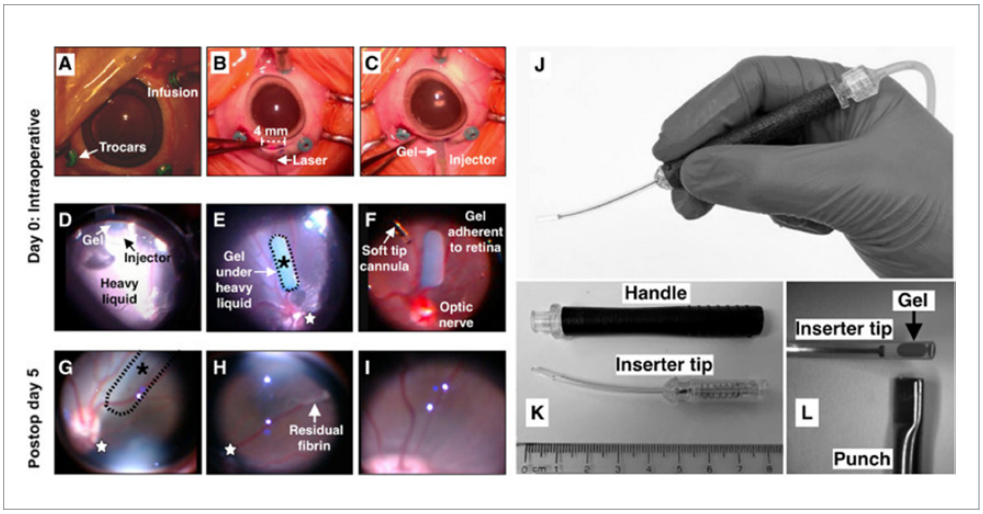


Figure 2. Surgical placement of fibrin-encapsulated AAV on the epiretinal surface.

The study's findings have shown promise for both current and future patients. "This new technique could potentially expand the range of patients who can benefit from gene therapy and make treatment safer," says Dr. Scruggs, "while also preserving — or even enhancing — the excellent results the treatments, such as Luxturna, have already achieved for eligible individuals."

As principal investigators in the Retinal Regenerative Medicine Laboratory at Mayo Clinic, Drs. Scruggs, Iezzi and Marmorstein continue to focus on the optimization of gene therapy and cell-based therapy for improved safety and efficacy in patients with retinal degeneration.

"Our next step is to test this new method head-to-head with existing techniques in models of retinal disease to see if it can further improve visual rescue," says Dr. Scruggs.

FOR MORE INFORMATION

Scruggs BA, et al. Retinal gene therapy using epiretinal AAV-containing fibrin hydrogel implants. *Science Advances*. 2025;11:eadv7922.

Facial Reanimation Clinic: Complex Conditions Require Team Approach

Elizabeth A. Bradley, M.D.

Samir Mardini, M.D.

Beth E. Robertson, M.D.

Given their complexity, facial nerve conditions are well suited for a collaborative approach to care. The facial reanimation clinic at Mayo Clinic in Rochester, Minnesota, brings a multidisciplinary team together to collaboratively assess and treat patients of all ages with a wide range of facial nerve disorders.

About 15 years ago, two Mayo Clinic physicians realized they were seeing the same patients with facial nerve conditions, and they discussed how to improve coordination and collaborative efforts. Elizabeth A. Bradley, M.D., an ophthalmic plastic surgeon at Mayo Clinic in Rochester, and Samir Mardini, M.D., a plastic surgeon and chair of Plastic and Reconstructive Surgery at Mayo Clinic in Rochester, recognized that their shared patients often also needed to have the cause of their facial nerve palsy determined prior to establishing plans for treatment. They reached out to Beth E. Robertson, M.D., their colleague and a neurologist at Mayo Clinic in Rochester, for her specialized expertise, and the first iteration of the facial reanimation clinic was born.

"Although each patient's individual needs are unique, we have found that nearly all patients benefit from the shared expertise of our team," says Dr. Bradley. The facial reanimation clinic helps patients coordinate and streamline any necessary imaging, standardized photographs, labs and appointments. Then the entire team — including physicians from plastic surgery, neurology, oculoplastic surgery, optometry, and physical medicine and rehabilitation — comes together to discuss the most effective, personalized course of treatment.

"Patients are able to have a single assessment with multiple specialties typically within one day," says Dr. Bradley. "This team approach builds trust with our patients, and they really sense that we're working together as a team to create a comprehensive, individualized treatment plan."

For example, some patients come to the clinic after losing facial function due to nerve damage from Bell's palsy, Ramsay Hunt syndrome, a parotid tumor, a skull base tumor or a stroke. Drs. Bradley, Mardini and Robertson and the team work with each patient to develop a personalized treatment plan for facial reanimation.

The facial reanimation team can employ a range of procedures to restore functionality and facial symmetry (Figure). These procedures range from nonsurgical treatments, such as Botox for overactive muscles, to more complex surgeries like nerve repair or nerve and muscle transfer. "We restore function through connecting nerves and sometimes bringing new muscles to the face to improve aesthetics and achieve a more symmetric smile," says Dr. Mardini. "It's a science, but there's also a bit of art involved."

"Oftentimes patients are referred to me primarily because of the symptoms they're encountering with their eyes. However, the patients are also experiencing equally distressing symptoms in other areas of the face," says Dr. Bradley. "Many patients have been enduring these symptoms for a long period of time, sometimes their entire lives, and have been told that there's not much that can be done. We're grateful to be able to serve a full range of patients — regarding age and diagnosis — and offer integrated medical and surgical management with a variety of treatment options."

Figure. Before and after images of a patient with restored functionality and facial symmetry.

Looking ahead, the facial reanimation team continues to collaborate on research studies to move the field forward and innovate pivotal surgical techniques together, paving the way for breakthroughs in research centered around the facial nerve, facial anatomy, regenerative medicine and craniofacial diseases.

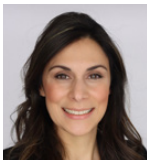
Research highlights

- Virtual surgical planning in craniofacial surgery. *Seminars in Plastic Surgery.* 2014.
- Virtual surgical planning and 3D-printed surgical guides in facial allotransplantation. *Seminars in Plastic Surgery.* 2022.
- Whole eye transplant — The journey begins. *JAMA Ophthalmology.* 2024.
- The epidemiology and treatment outcomes of facial nerve palsy using a population-based method. *Ophthalmic Plastic and Reconstructive Surgery.* 2025.

Dual Focus, One Goal: Neuro-Ophthalmology Provides Comprehensive Evaluation for an Accurate Diagnosis

As a scarce medical subspecialty, neuro-ophthalmology's dual focus on the intricate intersection of the brain and the eyes requires extensive and combined training in both neurology and ophthalmology. Ophthalmology at Mayo Clinic offers specialized care in neuro-ophthalmology, which offers patients a comprehensive evaluation and treatment with unique multidisciplinary teams.

"Many neurological diseases present with visual symptoms, which are often the earliest signs of an underlying condition. As neuro-ophthalmologists, we specialize in recognizing these manifestations and connecting them to the underlying pathophysiology," says Deena A. Tajfirouz, M.D., a neuro-ophthalmologist at Mayo Clinic in Rochester, Minnesota. "Early diagnosis of many of these conditions



Deena A. Tajfirouz, M.D.

is critical, as it can have significant implications for treatment, management and long-term outcomes. And because vision is such an important sense, neuro-ophthalmologic issues can really impact people's lives in many different ways."

Dr. Tajfirouz and her neuro-ophthalmology colleagues see a broad spectrum of neurological diseases that can range from defects of the neuromuscular junction, cranial neuropathies or inflammation of the optic nerves. Given the wide range and complexity of these conditions, Mayo Clinic offers coordinated multidisciplinary care and state-of-the-art ocular imaging and neuroimaging (Figure).

"Depending on the disease process, we commonly collaborate with a wide range of multidisciplinary teams, including neurosurgery, interventional neuroradiology, rheumatology, and various neurology subspecialties such as autoimmune, headache or behavioral neurology," says Dr. Tajfirouz. "Within ophthalmology, we work closely with retina specialists, pediatric ophthalmologists and oculoplastic surgeons."

Neuro-ophthalmic conditions treated at Mayo Clinic include:

- Multiple sclerosis.
- Neuromyelitis optica spectrum disorders.
- Myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease.
- Posterior cortical atrophy.
- Giant cell arteritis.
- Ischemic optic neuropathy.
- Idiopathic intracranial hypertension.
- Myasthenia gravis.
- Optic nerve and chiasmatic tumors.

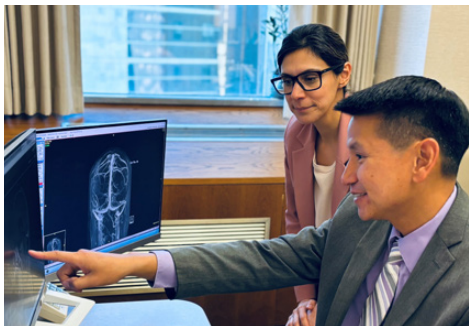


Figure. John J. Chen, M.D., Ph.D., and Deena A. Tajfirouz, M.D., discuss a neuro-ophthalmology case.

Dr. Tajfirouz has a special interest in a rare presentation of dementia called posterior cortical atrophy. "We recently saw a 45-year-old patient with unexplained vision loss who had seen multiple physicians previously where a diagnosis was not made because her eye exam and MRI results were essentially normal," says Dr. Tajfirouz.

Common symptoms of posterior cortical atrophy include trouble reading, impaired depth perception and not recognizing objects. Over time this condition often progresses, resulting in cognitive decline.

Because the first symptoms are often visual, posterior cortical atrophy can be misdiagnosed. Neuro-ophthalmologists are uniquely trained to recognize the earliest signs. "Posterior cortical atrophy only affects the parts of the brain that are for visual processing, and the signs can be very subtle," says Dr. Tajfirouz.

While there are no current treatments to cure or slow the progression of posterior cortical atrophy, accurate diagnosis can help provide access to therapies and programs so that the patient can manage the condition. "While it can be a devastating diagnosis, it's an important one not to miss because it carries serious implications for people's lives" says Dr. Tajfirouz.

About Dr. Tajfirouz

Dr. Tajfirouz completed medical school at St. Louis University's School of Medicine in St. Louis, Missouri. She completed a transitional year internship at Mercy Hospital in St. Louis, Missouri. She completed her residency in neurology and a fellowship in neuro-ophthalmology at Mayo Clinic College of Medicine and Science in Rochester, Minnesota.

Dr. Tajfirouz's research interests include:

- Neurodegenerative diseases.
- Optic neuritis.

Research highlights

- Paraneoplastic vision loss. *Handbook of Clinical Neurology.* 2024.
- Clinical characteristics and treatment of MOG-IgG-associated optic neuritis. *Current Neurology and Neuroscience Reports.* 2019.

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Cover Image
Human multicolored iris of the eye animation concept. Credit: CG Alex

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