Bascom Palmer’s ‘Moon Shot’ Project: A High-Impact Initiative to Transplant the Whole Eye

In 1961, President John F. Kennedy announced an ambitious goal: landing a man on the moon before the decade’s end. That project succeeded on July 20, 1969, when Neil Armstrong stepped onto the lunar surface, taking “one small step for man, one giant leap for mankind.”

Now, Bascom Palmer is taking on its own “moon shot” project: a whole eye transplant. It’s a high-impact ophthalmic initiative that would lead to new therapies for potentially blinding diseases like glaucoma and diabetic retinopathy. Patients with spinal cord injuries and other nerve-damaging conditions could also be helped if the Institute’s multidisciplinary research team can repair a severed optic nerve and restore vision.

“I want Bascom Palmer to be the first eye center in the world to achieve this ‘moon shot’ goal,” said David T. Tse, M.D., professor of ophthalmology and the Dr. Nasser Ibrahim Al-Rashid Chair in Ophthalmology. “A whole eye transplant is a final destination, but in the course of scientific discovery, we hope to identify and close critical knowledge gaps, overcome developmental bottlenecks, and find missing pieces of scientific puzzles. A successful eye transplant will involve groundbreaking therapies that could ultimately restore vision for millions of patients.”

A multidisciplinary approach
After decades of treating patients who have lost their eyes to injury or disease, Tse is leading a multidisciplinary initiative to perform a whole eye transplant. It involves partnerships with the University of Miami experts in surgical transplantation, neurosciences, cellular and molecular biology, bioengineering, computational science, and statistics.

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“This project can shift the paradigms of vision therapies,” said Daniel Pelaez, Ph.D., research associate professor of ophthalmology, and scientific director of the Dr. Nasser Ibrahim Al-Rashid Orbital Vision Research Center. “We have embarked on a journey that can provide many benefits to patients with different conditions. Even if we never reach our goal, this project can lead to advances in many fields of medicine.”

Pelaez said one of the hopeful aspects of the Institute’s ambitious initiative is that whole eye transplants have already been done in different species. Back in the 1960s, Nobel Prize winner Roger Sperry, Ph.D., transplanted the eyes of frogs and salamanders – two species with high regenerative ability – and found that the optic nerves reconnected with the visual centers of the brain. “We know that there is a natural biological mechanism for regeneration to occur,” said Pelaez. “It’s just a matter of understanding how this occurs in nature and being able to adapt those findings to the human system.”

To move toward that goal, Pelaez uses experimental models to study the optic nerve’s response to injury, as well as the genetic and epigenetic timing of natural repairs. “We are making progress in understanding how genes can coordinate the metabolic responses to injuries, using supercomputers to analyze these massive sets,” he said.

Addressing the challenges
Optic nerve regeneration and reconnection are far from the only daunting challenges to overcome for a successful whole eye transplant. On the surgical side, the donor eye tissues must be removed and transported to the recipient. Microsurgery and oculoplastic procedures are needed to place the eye in the right position, reconnect tiny muscles, and restore blood flow through tiny capillaries and veins.

“Our oculoplastic surgery group is on the cutting edge of clinical and basic science research,” said service director Thomas E. Johnson, M.D., professor of clinical ophthalmology. “We use our imagination, experience, and skills to find solutions to problems, no matter how difficult or complex.”

Once the donor eye tissues have been placed in the host orbit, the immune system response must be suppressed to prevent rejection, as only the retina is protected by the body’s blood-brain barrier, said Pelaez. If all those hurdles can be overcome, neuro-ophthalmologists may still need to retrain the brain to interpret the images it is receiving from the new eye.

Therefore, the whole eye transplant initiative brings together specialists from the Miami Transplant Institute, the Miami Project to Cure Paralysis, the College of Engineering’s Department of Biomedical Engineering, and other programs at the University of Miami Miller School of Medicine. “The role of teamwork and collaboration in this endeavor cannot be overemphasized,” said Pelaez.

Transplantation and survival
Despite major advances in microsurgical techniques and transplant immunology, the eye is one of only four organs that scientists worldwide have never been able to transplant. Now, the research team is developing a model workflow from donor eye procurement and preservation to recipient orbit preparation and implantation.

In a major advance for the initiative, Tse has designed a surgical technique for transplanting the globe of the eye and making the vascular connections to preserve an eye once it is removed from a donor’s blood supply. He is also working with biomedical engineers to build a pilot life support system to maintain the globe being transported from donor to recipient orbit.
recipient. Restoring the blood flow is essential for the survival of the transplanted ocular tissue, said Pelaez, who is collaborating with Robert Starke, M.D., associate professor of clinical neurosurgery, neuroradiology, and neurosciences, on this challenge. “We are also collaborating with bioengineers to develop stents smaller than a strand of hair to reconnect the vessels and restore the flow of blood,” he added.

Eye transplant recipients would probably need immunosuppressant medications to prevent rejection of the ocular tissues, added Pelaez. Collaborators in this aspect of the initiative include Robert Levy, Ph.D., professor of microbiology and immunology. 

Pelaez is also studying the creation of new retinal tissue in the laboratory, using the patient’s stem cells—an alternative approach to restoring lost vision. “If we can generate a new retina in a dish and integrate the new tissues into the visual system, we could avoid the issue of transplant rejection,” he said.

Optic nerve regeneration

While the initial stages of the moon shot initiative focus on the fundamentals of transplantation, the longer-term goal is to overcome perhaps the most difficult challenge: reconnecting the retina to the brain through a broken optic nerve. “We are looking at molecular and biological approaches to overcoming the scar tissue that forms a barrier at the donor-recipient optic nerve junction,” said Tse.

Sanjoy K. Bhattacharya, M.Tech., Ph. D., professor of ophthalmology, and founding director of the Miami Integrative Metabolomics Research Center, is leading a large, international, collaborative research effort for regenerating axons, the long projections of retinal ganglion cells that carry visual signals from the eye to the brain. “The axons are the most delicate part of a whole eye transplant,” said Bhattacharya. “Key questions include how much of the fibers from the donated eye can be functionally connected, how to protect their functioning with a myelin insulation sheath, and how you can coax axons to regrow in the recipient’s eye.”

Bhattacharya’s research uses high-throughput metabolomics to identify thousands of molecules involved in axon regeneration. He is also searching for clues in nerve regeneration studies published over the last 300 years using computer natural language processing and integrating those insights with today’s laboratory findings.

Now, Bhattacharya focuses on small molecules that encourage axon growth not only in young mammals but also at advanced ages of life. “If we can deliver these factors to a transplanted eye, they could do their short-term job of regenerating axons before being taken away by the vascular system without any adverse effects.”

Successful axon regeneration and reconnection will be a major step forward in restoring vision in traumatic optic neuropathies, glaucoma, and in a variety of disorders, Bhattacharya said, while cautioning that the mixture of metabolites varies in individuals. “We may need to take a portfolio approach and customize the regenerative for each patient,” he said. “Ideally, we want a long-term solution to restoring and maintaining the optic nerve connections.”

Hope for other patients

Bascom Palmer researchers are far from alone in studying potential approaches to regenerate retinal ganglion cells or regrow axons. “The whole eye transplant project could bring hope to patients with spinal cord injuries and other disorders,” said W. Dalton Dietrich, Ph.D., scientific director, Miami Project to Cure Paralysis; senior associate dean for discovery science; and professor of neurological surgery, neurology, biomedical engineering, and cell biology. “The optic nerve provides a model for repairing or regenerating the spinal cord and other parts of the central nervous system.”
“This is a great example of how Bascom Palmer’s clinicians and researchers work together on big, audacious ideas that could transform ophthalmology in the future.”

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With application support from the Institute, Kevin K. Park, Ph.D., professor of neurological surgery, The Miami Project to Cure Paralysis, was recently awarded a $1.9 million grant from the National Eye Institute to study a new long non-coding RNA (LncRNA) that regulates gene expression to protect injured retinal ganglion cells from dying. Bhattacharya and Park had earlier secured a multi-principal investigator U01 grant from the NEI and an exploratory grant from the U.S. Department of Defense to test small molecules and lipids that promote axon regeneration.

“Virtually nothing is known about this LncRNA, and this study provides an opportunity to better understand the possible molecular mechanisms underlying this process,” said Park, whose work focuses on genetic and molecular pathways that regulate retinal cells in experimental models. “Being able to protect retinal ganglion cells from dying would potentially help millions of patients with glaucoma by restoring damage to the optic nerve.”

Looking ahead
Reflecting on the value of Bascom Palmer’s moon shot initiative, Tse believes the Institute’s multifaceted approach to eye transplants will lead to medical breakthroughs, benefiting patients with incurable vision, spinal cord, and other nervous system disorders. “This is a great example of how Bascom Palmer’s clinicians and researchers work together on big, audacious ideas that could transform ophthalmology in the future.”

“Whatever we are able to do with the transplanted eye, we will need to grow or regenerate long-distance axons from the retinal ganglion cells within the retina of the donor eye.”

– Dr. Sanjoy Bhattacharya