Bringing Sight to the Blind

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Current positions:
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Experience:
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The Vitreous Society
The Retina Society

Dr. Mark Humayun, a professor of ophthalmology at the Keck School of Medicine and associate director of research at the Doheny Eye Institute at the Univ. of Southern California, has pioneered new ways of helping the blind to see. He is doing this is by melding high-tech materials and technology with advanced surgical methods to restore sight to those who until now had little hope of ever seeing again.

Humayun, a doctor of ophthalmology who holds a Ph.D. in biomedical engineering, is *R&D Magazine's* 2005 Innovator of the Year. The award is being presented to Humayun for his work on retinal implants and in recognition for his lifelong quest to helping the blind to see.

Humayun has spent the last 17 years working on a project that borrows from electronics technology, biocompatible materials and advanced surgical techniques to implant an intraocular retinal prosthesis, which essentially fills the role of the cells in the retina that have been ravaged by disease. The work led by Humayun is the focus of a team of researchers that includes other ophthalmologists at USC, materials and electronics researchers at five Dept. of Energy (DOE) laboratories, scientists at other universities, and Second Sight Medical Products Inc., a small California company (see sidebar).

In its current form the retinal implant is a 4 mm x 5 mm device studded with 16 electrodes in a 4 x 4 array. It is implanted in the retina where the photoreceptor rods and cones are, and it transmits electrical pulses to the intact neural paths of the patient, which in turn transmit the signals to the brain, allowing for sight. To date, Humayun has implanted Model 1 versions of the device in six blind patients, sufferers of retinitis pigmentosa (RP), restoring some limited sight to them. The first implant was done three and a half years ago and, Humayun says, it continues to operate well.

To get to that plateau of achievement, to restore hope where there was none, Humayun had to first make new discoveries about the effects of known eye diseases, like RP and age-related macular degeneration (AMD) that flew in the face of conventional wisdom. His biomedical engineering Ph.D. dissertation, which he completed after earning his M.D. in ophthalmology, outlined the device that is now used to restore vision. He continues to play an active role in the development of future generations of the device, which will be smaller and more flexible than the current experimental model. The devices that have been implanted are made by Second Sight Medical Products Inc., Sylmar, Calif.

Patents: Dr. Humayun is the sole or co-inventor of 19 patents based on his research over the past 13 years. These include patents for retinal prostheses, retinal microstimulation, intraocular drug delivery, ophthalmic surgical devices (cannulas), implantable retinal electrode arrays, and methods for training visual prosthesis.

While overcoming many technical and scientific challenges, it is what these devices do for the patient that drives Humayun. After all, he has witnessed first hand the gift of giving sight to the blind.

“The first time a patient saw something in the operating room was the happiest moment in my life,” Humayun says. “There is nothing more satisfying to me in my professional career. “You can hear it from them even to this day,” he adds, “when they come in for testing because they are laughing and giggling and really having fun with the device.”

Family inspiration

Humayun grew up in a family of physicians -- his mother and four uncles are physicians. But it was his grandmother who inspired him to become an eye surgeon and to specifically tackle the challenge of blindness.

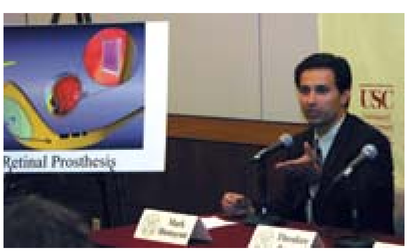
Dr. Mark Humayun uses a small external camera to transmit images to an implanted 4 mm x 5 mm retina chip with 16 electrodes, which is positioned near the ganglion cell layer of the eye. Six blind patients have been implanted with the device, one has had a device installed for more than three years. All images: USC/Doheny

Tasleem Humayun, cared for the young Mark Humayun when as a toddler his father (and mother) went to Cambridge so he could work on his master’s degree in economics at William’s College. “My grandmother went blind with diabetic retinopathy,” Humayun recalls. “She raised me and that really was the impetus for me to get into ophthalmology.”

Humayun’s grandfather and grandmother were world travelers. It was not uncommon for his grandfather, who was educated at Oxford, to travel far and wide and include the impressionable young Mark in his adventures.

“Every summer we would spend three months with my grandparents. We would see them in different places. Sometimes it was London, sometimes China, or Egypt, Iran, or the Soviet Union. As a kid I got to see a lot of different places. ”But by the age of 18, Humayun also experienced a very different side of life; Tasleem was bearing the full effects of diabetic retinopathy, basically bleeding of the eyes. Without any type of laser surgery available at the time, she slowly went blind. “She just gave up on life,” Humayun said of his grandmother. “It was so depressing. She died shortly thereafter.

“The disease had a huge impact, and it wasn’t just because she went blind. People don’t understand that when you are old and ailing and you have all of these things going on, then you go blind, that is sort of the last straw.”



Dr. Humayun's research is sponsored by the Medical Science Division in the Dept. of Energy's Office of Science. Humayun was the Symposium Chair of the DOE's Second Intl. Symposium on Artificial Sight held this past April. Many of his artificial retinal devices are co-developed at various DOE national laboratories.

Neural paths

Arguably the first breakthrough in Humayun’s research set the course for the next 17 years. He had discovered that in the cases of certain retinal diseases -- RP and AMD -- the parts of the eye that were damaged were the “ photoreceptor” cells of the retina, the rods and cones that normally convert light into electrical impulses. But the diseases leave intact the neural paths to the brain, paths that transport the electrical signals. Thus, while the input from the photoreceptors eventually ceases, up to 70 to 90 percent of the nerve structures set up to receive those inputs remain intact.

The general thought at the time was that “once you lose the photoreceptors you lose the rest of the circuitry as well,” Humayun says. “We found that the nerve cells in the eye are left fairly intact, so the task we had was how do you take images and convert them into tiny electrical pulses. “That is exactly what the photoreceptors do, they capture light and convert it into chemical pulses and this information is sent to the brain and it allows us to see,” Humayun explains.

“What we did was take a camera image and then convert that through software code into tiny patterns of electrical stimulation that stimulate these remaining cells and allows a blind person to see."

The implant, a sliver of silicone and platinum, is but one piece of the overall system. Patients with the Model 1 device, also wear a pair of glasses equipped with a tiny video camera, radio frequency transmitter and battery. The camera captures images and sends them to a microprocessor, which converts the signal to an electrical signal. That signal is transmitted to a radio receiver behind the patient's ear and from there to the device itself, where it "lights up" electrodes and stimulates the remaining retinal neurons.

The implanted device sits a top and it attached to the retina."Retina tissue lines the inside of the eye, much like wallpaper on a wall," Humayun says. "It is very delicate, like delicate tissue paper. "The idea is to develop this whole new genre of microelectronics where the heat and the sharpness of the silicone stay away and you package them in such a way so it can survive in the eye and not damage any tissue," Humayun says.

"What actually contacts this tissue are very delicate bioelectrodes that relay the stimulation pattern to the nerve cells." Alignment of the device is critical. "Even if there is a 50 or 100 micron misalignment that can [mean you will need to] double the applied voltage and then you are dissipating more heat in the tissue," Humayun explains. "You don't want to crush the neuron either. So you have to be right in the middle. Proximity is the key."

A second key parameter is understanding how to deliver signals. "What are the nerve cells waiting to hear. What's the neural code," Humayun asks. "How best does the brain understand this? Those mechanical, electrical and software interfaces are key." The six patients with the implants, Humayun says, can now see on a limited basis. In laboratory tests, the patients experienced light and in later tests they could make out some shapes, like a one foot sized letter "L" at a distance of a few feet. They also can differentiate a plate, from a knife, from a cup."We are now taking them into the outside world and seeing what they can tell," Humayun says. "Can they tell if there is a chair right in front of them, so not to fall over it. Can they see a table."

What they cannot see is detail. They see light, but patterns in the light like the large letter "L," are very fuzzy. Differentiating the pieces of a table setting does not mean they can see the finger handle of a teacup or the scroll design in a knife.What is needed for that type of fine detail will be more sophisticated implants, better visual processing units and more sophisticated software. Humayun and his group are working on second and third generation implants and upgrades to the entire system.

The Model 2 implant, the first commercial device, will have 60 electrodes and it will be about a fifth the size of the Model 1. Model 2 will move the receiving coil from behind the ear to somewhere near the eye. Surgery to implant this device is expected to take 90 minutes, compared to the six hours it takes to implant Model 1.

Humayun said that the FDA is currently inspecting the Model 2 device and he hopes to begin implanting these devices by the end of the year. "We will do it first at the Doheny Eye Institute, then three or four other centers are planning to use these devices," Humayun says. The Model 3 will have 1,000 electrodes. This device will use more advanced materials than the silicone/platinum used on Model 1. A special chip coating is being developed to replace the relatively bulky sealed packaging now used for the Model 1 device. The device will be built on flexible substrate materials that can conform to the shape of the inner eye, replacing the molded substrate material in Model 1.

"We are working on an on chip coating, so the package is only a few micron coating on the chip," Humayun said. "Once we get there, then we can put the entire device, including an interocular camera, in the eye."

Teamwork Has Led to the Success of the Retinal Prosthesis

Dr. Mark Humayun is quick to tell anyone that it takes a team of talented people to tackle the grand challenge of helping the blind to see. The project he leads on the retinal prosthesis is an example of that. Humayun, a professor of ophthalmology at the Keck School of Medicine and associate director of research at the Doheny Eye Institute at the Univ. of Southern California, and the 2005 *R&D Magazine* Innovator of the Year Award, says none of accolades he receives today would come if it were not for the efforts of the team he works with.

Beginning with his mentor and colleague Eugene de Juan Jr., the CEO of the Doheny Retina Institute and professor of ophthalmology at USC's Keck School of Medicine, who was a first year faculty member when Humayun was wrapping up his medical school education at Duke Univ., Durham, NC.

"He was the guy who pushed me to be involved in this project and to continue it," Humayun says. "He was the person to tell you to keep on doing this project, that it is a good idea, no matter what anyone else thinks."

There also is Jim Weiland, who did a post doc with Humayun and who has been involved in the project for more than seven years. Wentai Liu, now at Univ. of

A key concern for the 1,000-electrode Model 3 will be alignment, and bio microelectrocmechanical systems (BioMEMS) might provide a solution.“We as surgeons cannot place things within 10 micron accuracy. That is about the size of a red blood cell,” Humayun says. “We will need an inter-operative guide that tells us where certain electrodes are and are not. We are working with Sandia on a post implantation adjustment, a tiny spring adjustment on each electrode. The spring forces have to be very carefully matched, but if electrode 13 is 50 microns off, you can post process come in and move that electrode just a little bit.”

The goal for the Model 3 implant is being able to restore eyesight to the level where the user can read and recognize faces, Humayun says. It will be a device that can put those who are legally blind as well as those who are totally blind on the threshold of regaining their functional eyesight. “Everything looks like we should be able to do it, but we have to prove that we can do it,” he says.

At that point, Humayun and his team will have restored functional vision to the blind and legally blind, and they will have answered some of their critics who suggest more direct and less elaborate innovations would better benefit the patient.

“It’s one of those things where people say why not just give them a cane or a device that allows them some sort of function, but the point to make is that the sensation of seeing again is so pleasurable that even if you were able to give them a lot of functionality, but they were not able to see, it would leave them with an empty feeling.”

— Skip Derra

Skip Derra is a freelance writer in Chandler, Ariz.

California-Santa Cruz designed the first chip and the Model 2 chip. Humayun has known him since their days at Duke.

Eli Greenbaum at Oak Ridge National Laboratory, Tenn., is another key participant in the project. There are five DOE labs taking part in this project.

Oak Ridge leads the multi-laboratory effort and is testing various components developed at other DOE labs as well as developing special sensors. Argonne National Laboratory, Illinois, is investigating diamond-based electrode arrays and biocompatible components; Lawrence Livermore National Laboratory, Calif., developed the rubberized electrode arrays; Los Alamos National Laboratory, NM., developed optical methods for neural recording; and Sandia National Laboratories, Albuquerque, NM., is working on microelectromechanical (MEMS) electrode array structures.

On the commercial side of the project is Second Sight Medical Products Inc., Sylmar, Calif., which is helping develop, market and sell the implants.