# Artificial Retina News

*Restoring Sight Through Science*

U.S. Department of Energy Office of Science • ArtificialRetina.energy.gov Fall 2006

# ENVISIONING SIGHT FOR THE BLIND

## The DOE Artificial Retina Project

*Leveraging DOE expertise to enhance the quality of life for millions*

Major advances achieved by researchers in the U.S. Department of Energy's (DOE) Artificial Retina Project are beginning to offer some hope to millions of people blinded by retinal diseases worldwide.

In a breakthrough operation performed by project leaders at the Doheny Eye Institute (University of Southern California) in 2002, doctors threaded an electrode-studded array through an incision into the eye of a man who had been blind for 50 years and tacked it onto his damaged retina. Within weeks, the 77-year-old patient could see patterns of light and dark that allowed him to detect motion and locate and differentiate simple objects. For the first time in half a century he could also envision a brighter future for himself and others whose lives have been devastated by vision loss due to retinal disease.

### In this Issue

The bold plan for the project is to build on this foundational work by using revolutionary technologies developed at the DOE national laboratories to create a vastly improved implantable retinal prosthesis. The ultimate goal is to restore unaided mobility, reading vision, and facial recognition to people with retinitis pigmentosa (RP) and age-related macular degeneration (AMD).

### A Heavy Toll

RP and AMD destroy the light-sensing cells (photoreceptors) in the retina, a multilayered membrane located at the back of the eye. Unfortunately, these cells do a poor job of repairing themselves and no effective treatments exist, so these individuals are forced to accept their condition and adapt to life in a sightless world.

Vision loss due to retinal disease affects some 6 million Americans and 25 million people worldwide. In addition to the social impact on individuals and their

*...continued on page 2*

*A retinal implant patient visits Disneyland (see article below). The vision enabled by this first device allows patients to distinguish light from dark and localize large objects. Patients have found these abilities useful for daily activities. Vastly improved devices being developed in the DOE Artificial Retina Project hold much promise for the future.*

# EYEING THE FUTURE

## One Patient's Story

Linda M., a petite brunette in her early 60s (pictured above), first realized that something was wrong with her vision when she couldn't find things she dropped. An ophthalmologist soon confirmed her suspicions and delivered a sobering diagnosis: Linda was exhibiting the early signs of retinitis pigmentosa (RP), a disease that attacks cells in the

*...continued on page 7*

## Envisioning

continued from page 1

families, blindness also takes a toll on national economies and adds to healthcare spending burdens, because patients often require significant aid over decades. With an aging population living longer, the number of those affected will continue to grow and, by some estimates, may even triple by 2025, creating a virtual pandemic of vision loss.

### An Unexpected Path to Restoring Sight

In the early 1990s, scientists led by Mark Humayun (then at Johns Hopkins University, now at Doheny) made an important discovery that led to an opportunity for intervention. They found that the remaining neural wiring in the retinas of RP and AMD patients could still receive and transmit light signals. The team began working on an implantable microelectrode array that could communicate with the remaining functional cells and stimulate visual perceptions (see sidebar, p. 3).

### Adapting DOE Technologies for New Challenges

The basic idea for the array builds on the medical microelectronics revolution that produced pacemakers and the cochlear ear implant for the deaf. The eye, however, is an especially delicate environment, requiring the use of more advanced and miniaturized technologies that also can adapt to life in a salty world. “That’s where DOE technology comes in, and it’s really the vision for this project,” says Humayun (see sidebar, p. 5). In 1999, the Doheny group began collaborating with Elias Greenbaum from DOE’s Oak Ridge National Laboratory, who was also working on approaches for restoring sight to the blind.

To speed the design and development of better models, in 2004 Doheny and DOE (including six of its national laboratories), two other universities, and Second Sight® Medical Products Inc. (a private-sector company) signed a Cooperative Research and Development Agreement (see Collaborators, p. 4). Under the agreement, the institutions will jointly share intellectual property rights and royalties from their research. This will spur progress by freeing the researchers to share details of their work with collaborators.

### Three Models Explored

To date, 6 patients have successfully been implanted with the first prototype Model 1 device, which contains 16 electrodes. In addition to providing rudimentary sight for the patients (see left figure in sidebar below), this apparatus is beginning to answer critical fundamental biological questions that will enable researchers to go much further in developing this concept. A second, more compact device awaits approval by the U.S. Food and Drug Administration (FDA) for human trials, and a third, far less invasive and higher-resolution model is under development.

### Funding and Synergies

Over the past 7 years, the DOE project has grown from a pilot funded at $500,000 (FY 1999) to a full-scale effort with support of $9.3 million (FY 2005). The DOE Office of Science funds the project.

DOE supports the design, construction, and some preclinical (nonhuman) testing of the devices. Funding is for research in the following areas:

- Neuroscience imaging studies on Model 1
- Some preclinical animal studies of Model 2
- Design and fabrication studies of Model 3

Doheny also receives other federal funding to support and extend the work on the retinal and other neural prostheses.

## *A New Kind of Vision*

The images at right approximate what patients with retinal devices see. Increasing the number of electrodes will result in more visual perceptions and higher resolution vision. Scientists worked with patients who received the Model 1 implant (a 4 x 4 array of 16 electrodes) for about one month after surgery to help them interpret what they saw. Deaf individuals with cochlear implants also need such guidance to understand sounds they are hearing for the first time.

**4 x 4**
**16 Pixels**

**16 x 16**
**256 Pixels**

**32 x 32**
**1000+ Pixels**

*(Images generated by the Artificial Retinal Implant Vision Simulator devised and developed by Wolfgang Fink at the Visual and Autonomous Exploration Systems Research Laboratory, California Institute of Technology.)*

The National Eye Institute of the National Institutes of Health supports fundamental and applied research related to the prosthesis. Commenting on the benefits of these synergies, Humayun notes that "You need to leverage all the expertise more efficiently and effectively and not reinvent the wheel."

The National Science Foundation (NSF) is providing Doheny with funding for the longer-term goals of further enhancing the retinal prosthesis and adapting the technologies to treat a wide range of other neurological disorders. For example, researchers are studying how the foundational concepts used to create the retinal prosthetic can be used to reanimate paralyzed limbs and even restore short- and long-term memory for stroke and dementia (as in Alzheimer's disease). For more information on the NSF project, see web site bmes-erc.usc.edu.

## Worldwide Projects

Other retinal prostheses projects are under way in the United States and worldwide, including Germany, Japan, Ireland, Australia, Korea, China, and Belgium. These programs pursue many different designs and surgical approaches. Some show great promise for the future, but have yet to demonstrate practicality in terms of adapting to and lasting long-term in a human eye. Thus far the projects that have progressed to clinical (human) trials are the collaborative DOE effort, a project at Optobionics (Chicago), and two efforts in Germany at Intelligent Medical Implants AG and Retinal Implant AG. [For more information on worldwide projects, see *Science* **312**, 1124-26 (2006).]

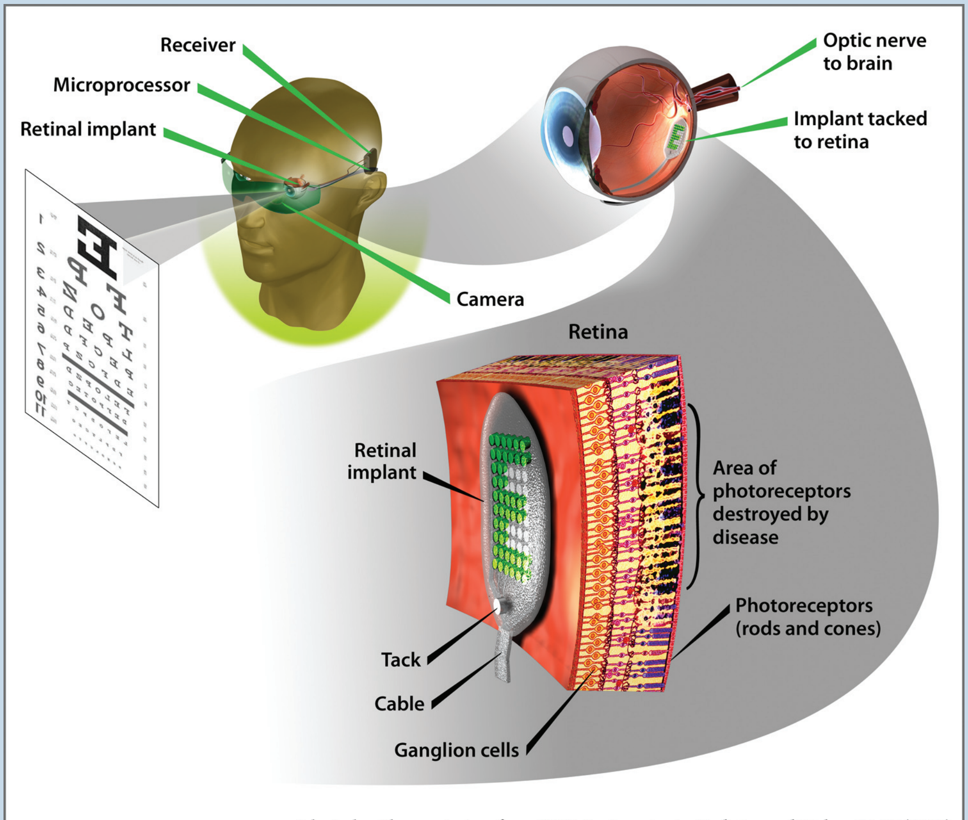
Although the DOE-Doheny team and their patients are excited by early implant successes and new hopes for the future, this is just the tip of the iceberg, says Humayun. "Revolutionary technology and new approaches will get us beyond rudimentary vision to the more functional device—it's a quantum difference," he said. "We're trying to go beyond restoring basic functions, so millions can be more integrated with society." ■

## *Engineering Sight: The Bionic Eye*

Normal vision begins when light enters and moves through the eye to strike specialized photoreceptor (light-receiving) cells in the retina called rods and cones. These cells convert light signals to electric impulses that are sent to the optic nerve and the brain. Retinal diseases like age-related macular degeneration and retinitis pigmentosa destroy the photoreceptor cells. The artificial retina device bypasses these cells to transmit signals directly to the optic nerve.

The device consists of a tiny camera and microprocessor mounted in eyeglasses, a receiver implanted behind the ear, and an electrode-studded array that is tacked to the retina. A wireless battery pack worn on the belt powers the entire device.

The camera captures an image and sends the information to the microprocessor, which converts the data to an electronic signal and transmits it to the receiver. The receiver sends the signals through a tiny cable to the electrode array, stimulating it to emit pulses. The pulses travel through the optic nerve to the brain, which perceives patterns of light and dark spots corresponding to the electrodes stimulated. Patients learn to interpret the visual patterns produced.



Adapted, with permission, from *IEEE Engineering in Medicine and Biology* **24**:15 (2005).

# DOE ARTIFICIAL RETINA PROJECT COLLABORATORS

## Includes 6 national laboratories, 3 universities, and private industry

Multidisciplinary groups across the United States are using a highly focused and coordinated approach to develop a dramatically improved retinal prosthetic device to restore sight to the blind. The Doheny Eye Institute and Oak Ridge National Laboratory lead the collaborative effort.

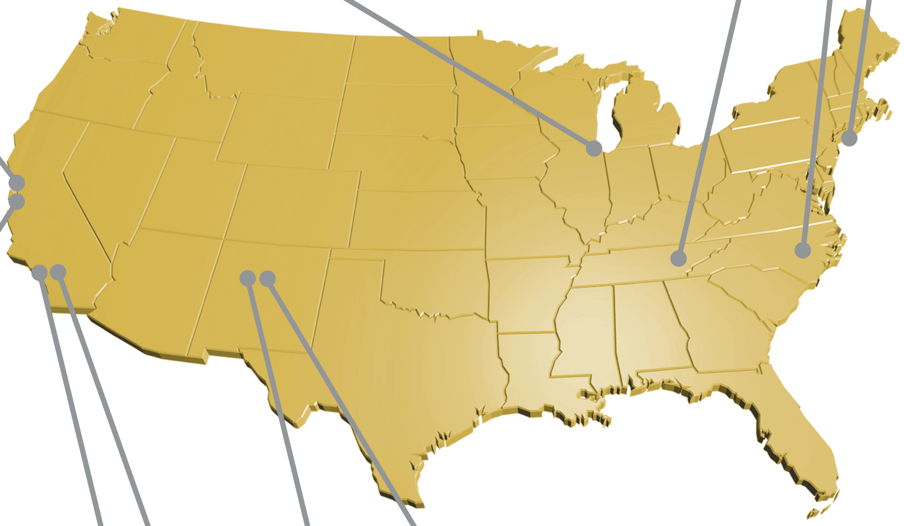
**Brookhaven National Laboratory** Upton, NY
Performs neuroscience imaging studies of the Model 1 retinal prosthesis.

**North Carolina State University** Raleigh, NC
Performs electromagnetic and thermal modeling of the device to help determine how much energy can be used to stimulate the remaining nondiseased cells.

**Oak Ridge National Laboratory** Oak Ridge, TN
Measures the effect of increasing the number of electrodes on the quality of the electrical signals used to stimulate the surviving neural cells in the retina.

**Argonne National Laboratory** Chicago
Performs packaging and hermetic-seal research to protect the prosthetic device from the salty eye environment, using their R&D 100 award-winning ultrananocrystaline diamond technology.

**Lawrence Livermore National Laboratory** Livermore, CA
Uses photolithographic technology to develop a thin, flexible implant that can conform to the curved shape of the retina.



**University of California, Santa Cruz**
Performs bidirectional telemetry for wireless communication and chip design for stimulating the electrode array.

**Doheny Eye Institute at the University of Southern California** Los Angeles
Provides medical direction and performs preclinical and clinical testing of the electrode array implants. Leads the Artificial Retina Project.

**Second Sight Medical Products Inc.** Sylmar, CA
Created the Model 1 and Model 2 devices (the latter with DOE contributions) and will integrate DOE technologies into a Model 3 design. SSMP will be responsible for integration and production of devices under FDA regulations, performance of clinical trials, and eventual commercial distribution to patients.

**Los Alamos National Laboratory** Los Alamos, NM
Performs imaging and modeling of retinal function and develops advanced optical imaging techniques. These contributions will provide a better understanding of how the prosthesis works by mapping the interaction between the brain and retina.

**Sandia National Laboratories** Albuquerque, NM
Develops microelectromechanical systems (MEMS) for electrode arrays and high-density interconnect tools, and high-voltage electronic subsystems for integration onto the electrode-array substrates.

# DESIGNING AN ARTIFICIAL RETINA: CHALLENGES AND PROGRESS

Researchers face numerous challenges in developing retinal prosthetic devices that are effective, safe, and durable enough to last for the lifetime of the individual.

The device must be biocompatible with delicate eye tissue, yet tough enough to withstand the corrosive effect of the salty environment. Moreover, it should remain stably tacked to a precise area of the retina and not overly compress or pull at the tissue, whose resilience can be compared to that of a wet Kleenex. The apparatus also needs to be powered at a high enough level to stimulate electrodes, yet not generate enough heat to damage the remaining functional retina. Additionally, image processing needs to be performed in real time so there is no delay in interpreting an object in view. Development of effective surgical approaches are critically important as well to ensure a successful implant.

Three Artificial Retina Project devices are now in testing or development. Engineering goals include enhancing the resolution (increasing the number of electrodes and thus the number of dots produced) and decreasing the size of the device and complexity of the surgical procedure.

## Model 1

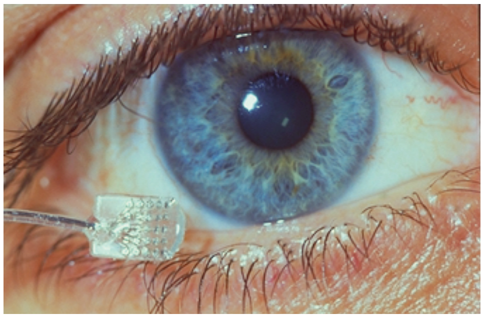
The Model 1 device [developed by Second Sight Medical Products Inc. (SSMP)] has been implanted in six patients, whose ages ranged from 56 to 77 at time of implant and all of whom have retinitis pigmentosa. The device consists of a 16-electrode array in a one-inch package that allows the implanted electronics to communicate with a camera mounted on a pair of glasses. It is powered by a battery pack worn on a belt. This implant now enables patients to detect when lights are on or off, describe an object's motion, count individual items, and locate objects in their environment. To evaluate the long-term effects of the retinal implant, five devices have been approved for home use.

## Model 2

The smaller, more compact Model 2 retinal prosthesis (developed by SSMP with DOE contributions) is currently undergoing preclinical (nonhuman) studies. This model will be much smaller, contain 60 electrodes, and eventually become the first commercial device. Subject to FDA approval, plans are to implant this device into the first patient during 2006. Surgical time has been reduced from the 6 hours required for Model 1 to 2 hours.

## Model 3

The Model 3 device, which will have more than 200 electrodes, is undergoing design and fabrication studies at the DOE national laboratories. This device will use more advanced materials than those in the two previous ones. A special coating, only a few microns thick, will replace the bulky sealed package used in previous models. Additionally, the new model will be constructed of flexible materials that will conform to the shape of the inner eye. Since Model 3 will be many times smaller than earlier ones, it will be implantable entirely inside or around the eye.



*The artificial retina consists of an electrode-studded array (shown) that is tacked to the retina inside the eye.*

The ultimate goal for the prosthetic device is to enable facial recognition and large-print reading vision, using materials that will last for a lifetime. ■

## *Why is the Department of Energy involved in retinal research?*

The challenge of developing a tiny device that can perform complicated tasks and be tough enough to survive in the eye's salty environment demands a diversity of talents and capabilities. The unique resources and expertise housed at DOE's multidisciplinary national laboratories (see pp. 4 and 6 and web site sc.doe.gov) are well suited to address the technical challenges involved, including those in materials sciences, microfabrication, microelectrode construction, photochemistry, and computer modeling. "Going to the DOE national labs is like going to a scientific supermarket," says Mark Humayun, lead investigator in the DOE Artificial Retina Project. "Their revolutionary technologies are enabling completely new approaches."

In addition to offering world-class resources, DOE has over 50 years of experience managing large multifaceted projects including the Human Genome Project, initiated by DOE's Office of Biological and Environmental Research (BER) in 1987.

The Artificial Retina Project is sponsored by the Advanced Medical Technologies Program of BER's Life and Medical Sciences Division. Past BER successes include developing the field of nuclear medicine: Nearly every nuclear medicine scan or test used today was made possible by BER-funded research, an advancement that has all but eliminated "exploratory" surgeries.

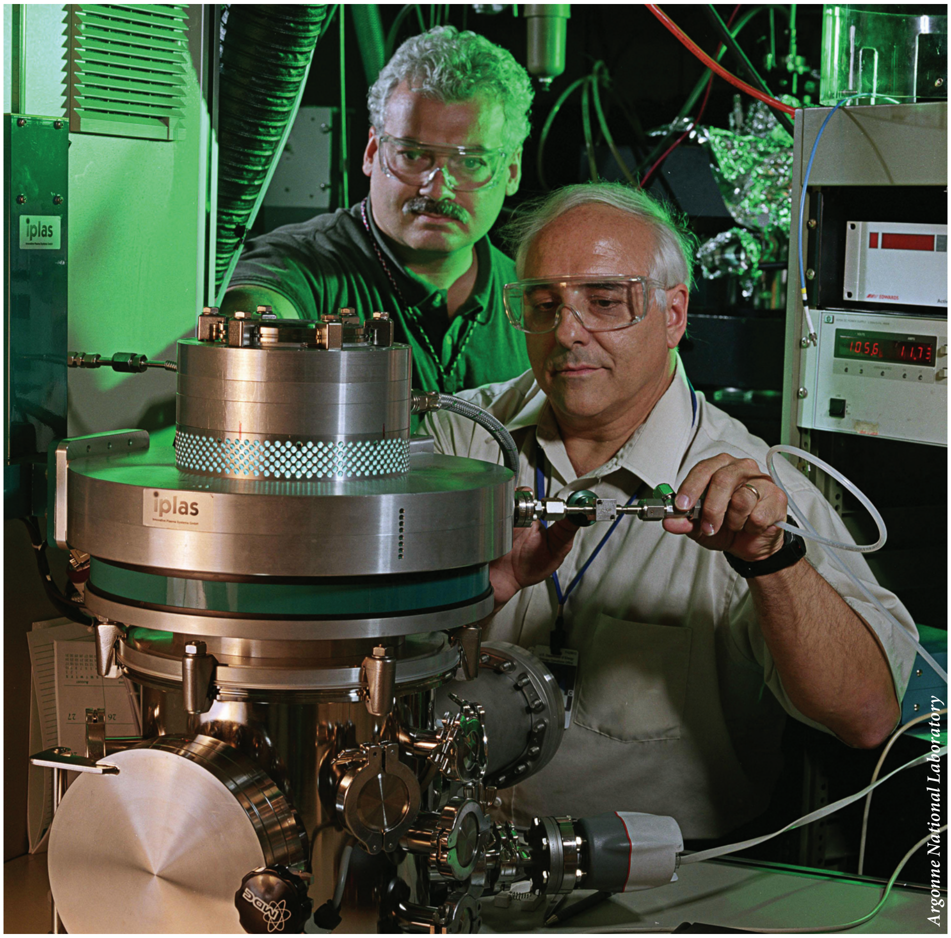
# SPOTLIGHT

# ARGONNE NATIONAL LABORATORY

## Creating Diamond Coatings for the Retinal Implant

Argonne National Laboratory (ANL) plays a critical role in the success of the electrode implants used in the Artificial Retina Project. That's where researchers Orlando Auciello and John Carlisle are using their patented ultrananocrystalline diamond (UNCD) technology to apply a revolutionary new coating to the retinal prosthetic device. The new packaging promises to provide a very thin, ultrasmooth film that will be far more compact and biocompatible than the bulky materials used to encase the earlier prototypes (Models 1 and 2).

"It's like wearing a skin instead of a space suit," says Mark Humayun (Doheny Eye Institute at the University of Southern California), leader of the Artificial Retina Project.



Argonne National Laboratory

*Researchers John Carlisle (left) and Orlando Auciello (right) are developing an ultrathin biocompatible coating for the device.*

### An Ultrathin Diamond Coating

UNCD is a form of carbon that captures many of the properties of diamond and can be deposited on a wide variety of surfaces in thin layers. The diamond grains used in the coating are only 2 to 5 nanometers in size (a nanometer is about 10,000 times narrower than a human hair). These films are as hard as single-crystal diamond, the hardest known material on earth. Unlike natural diamond, however, its properties can be adjusted and optimized for a given application.

Considered to be a platform technology, UNCD has numerous potential beneficial applications in such areas as medicine, transportation, and industrial production. It is chemically inert (nonreactive) and compatible with biological tissues, traits that make it useful in retinal prosthetic implants as well as other biodevices such as an artificial pancreas. Additionally, the material is a superb electrical insulator but also can be made to be highly conductive, and this conductivity can be tuned. This work has led to the use of UNCD for biosensors that use electrochemical reactions to detect biomolecules.

Parts of the UNCD technology received a 2003 R&D 100 award, an honor given to the most innovative developments that occur in a particular year. The technology has been licensed to Advanced Diamond Technologies (Champaign, Il.), a company founded by Carlisle and Auciello.

### From the National Labs to the Public

A goal of the national laboratories is to provide benefits to industry and the public by moving discoveries into everyday use, a process called technology transfer. This practice leads to benefits for everyone and demonstrates the value of using tax dollars to support early-stage scientific research. In recognition of their efforts toward that end, Carlisle and Auciello received the 2006 Award for Excellence in Technology Transfer from the Federal Laboratory Consortium.

The nation's first national laboratory, ANL conducts basic and applied scientific research across a wide spectrum of disciplines, ranging from high-energy physics to climatology and biotechnology. Since 1990, Argonne has worked with more than 600 companies and numerous federal agencies and other organizations to help advance America's scientific leadership and prepare the nation for the future. Argonne is managed by the University of Chicago for the U.S. Department of Energy's Office of Science. ■

## **Eyeing** *continued from page 1*

retina and ultimately would destroy her vision, possibly within 10 years. She was only 21 at the time.

RP is a relatively rare, inherited disease that affects about one in four thousand people, and no treatments or cures are available. As in Linda's experience, symptoms often begin in early adulthood with loss of peripheral vision and grow increasingly worse. Millions more become blinded each year due to age-related macular degeneration (AMD), which strikes the same photoreceptor cells in the retina.

Linda's vision continued to deteriorate over the next 30 years, but her determination to go on with life's normal activities, with the support of her husband Roy, allowed them to enjoy a full family life and raise three daughters. Linda lost her remaining vision in her early 50s and has been completely blind for about 10 years. She views her condition with the frustration of one whose nature is strong and independent. "It's really irritating to rely on others," she says.

### Another Chance

Linda first heard about the DOE Artificial Retina Project from an ophthalmologist who thought she might be a good candidate for the study. Upon visiting the project leaders at the Doheny Eye Institute (University of Southern California), she learned that volunteers undergo a surgical procedure to implant a tiny array with 16 electrodes on the damaged retina of one eye. When activated later on, the electrodes would perform some of the light-signaling functions of the destroyed retinal cells, allowing the patient to see patterns of lights like a lit-up scoreboard (see sidebar, p. 3). For 18 months post surgery, participants would return for weekly follow-up visits.

Linda understood that the retinal prosthesis could provide only a rudimentary form of sight, but even that was intriguing. She also thought that her participation in the study would allow researchers to learn more for future generations. "OK, let's do it," she told them. One week later, the Doheny Eye Institute surgeons performed the operation. It turned out to be "a breeze," she said. "One night in the hospital, and I was on my merry way."

### Making Connections

Researchers speculate about what a patient with a retinal implant might see, but no one really knows how the brain of someone who has been blind for many years will process new visual input (see sidebar, p. 2). For this reason, researchers and patients must work together to map the new world of artificial sight.

Two weeks after the surgery, doctors activated the device. Linda admits that her reaction upon first seeing the flashing lights coming from the implanted electrodes was, "I'm going to have to connect a lot of dots before I see anything." But after several visits to the lab, she began to make some correlations between the patterns of lights and the physical world. A line of vertical lights, for example, could be a door or the edge of a table. With practice, the time needed to interpret the dot-images grew shorter. A year and a half after receiving the implant, she was given the go-ahead to try using the device at home.

### New Discoveries

Now, after almost 2 years with the implant, Linda and Roy reel off examples of how the implant has impacted their lives, including some unexpected ways. Mostly, it has helped Linda gain more control over her environment, as she negotiates more confidently around the house. "I see where the kitchen table and counters are, and I don't knock glasses over anymore," she reports.

She also needs less help in interpreting the outside world. When Linda and her husband go to church, she knows where the priest and choir sit. When someone approaches, she can turn to face them before they begin to speak. On their evening walks, she can tell whose porch lights are turned on, giving her some sense of location. Also, when riding on the freeway at night, she knows when they are passing through a tunnel or near a well-lit mall.

Linda becomes animated as she talks about attending her grandchildrens' sporting events. "Now I can follow the action after my grandchild hits the ball in a Little League game," she says with satisfaction.

She laughs as she reports that she also sees things she'd rather not. On a recent visit to Disneyland, Linda climbed into a fast ride with her grandchildren. As the speed ramped up, she automatically shut her eyes, only to discover that the external camera in the retinal prosthesis continued to provide visual input, sending signals to the brain. "Things were flashing much faster and closer than I liked," she says. "I'll know to turn it off the next time."

### Future Enhancements

Researchers at the Doheny Eye Institute say Linda's experience and that of five other patients with implants is just the beginning of what they hope to provide for people with retinal diseases. A second, improved model with 60 electrodes is now in preclinical testing and soon will be implanted in a new group of volunteers. A third, vastly improved model containing hundreds of electrodes is now in early stages of development. The ultimate goal is to restore unaided mobility, facial recognition, and the ability to read large print. "If I'm still around then," says Linda, "I'll want one of those models. I'd do it again." ■

### *Who is Eligible for a Retinal Implant?* *The devices discussed in this newsletter are experimental and not yet available to the public.*

Studies are now being conducted at the Doheny Eye Institute at the University of Southern California Medical Center. Although enrollment is not currently open, to be eligible for consideration as a candidate for future studies patients must have a confirmed history of retinitis pigmentosa. For more information call Second Sight at 818.833.5000 and ask for the Clinical Research Department.

## Humayun Named Innovator of the Year

Mark Humayun, lead investigator of the U.S. Department of Energy Artificial Retina Project, received the prestigious Innovator of the Year award for 2005 from *R&D Magazine*. The award recognized him for creating an implantable artificial retina that promises to restore sight to blind patients. Each year, this international award recognizes one individual who has demonstrated excellence and creativity in the design, development, and introduction to the marketplace of one or more technologically significant products over the past 5 years.

Humayun, a surgeon who also holds a doctorate in biomedical engineering, began working on the retinal implant 17 years ago. His inspiration, however, goes back much further, to the memory of his beloved grandmother whose decline was hastened by blindness in old age.

Humayun is a professor of ophthalmology at the Keck School of Medicine and of biomedical engineering in the Viterbi School of Engineering at the University of Southern California (USC). He is also associate director of research at the Doheny Eye Institute at USC. ■

## Related Web Sites for More Information

**DOE Artificial Retina Project**
*ArtificialRetina.energy.gov*

**Doheny Eye Institute**
*www.usc.edu/hsc/doheny/*

**Second Sight Medical Products Inc.**
*www.2-sight.com*

**Biomimetic MicroElectronic Systems**
*bmes-erc.usc.edu*

**Foundation Fighting Blindness**
*www.blindness.org*

**Prevent Blindness America**
*www.preventblindness.org*

**AMD Alliance**
*www.amdalliance.org*

**American Council of the Blind**
*www.acb.org*

**National Alliance for Eye and Vision Research**
*www.eyeresearch.org*

## Artificial Retina News

Prepared for the U. S. Department of Energy Office of Science by the Genome Management Information System (GMIS) at Oak Ridge National Laboratory, 1060 Commerce Park, MS 6480, Oak Ridge, TN 37830.

Denise K. Casey, Editor and Writer
Shirley Andrews, Graphic Designer
Marissa Mills, Web Designer

Special thanks to:

Lindy Yow, Science Project Director at Doheny Eye Institute, University of Southern California

**Sponsor Contacts**

Michael Viola, M.D.
Michael.Viola@science.doe.gov

Dean Cole, Ph.D.
Dean.Cole@science.doe.gov
Send announcements and suggestions for future issues to Dean Cole.

*ArtificialRetina.energy.gov*

Office of Science
U.S. DEPARTMENT OF ENERGY

## Free Subscriptions and Extra Copies of *Artificial Retina News* Available

To sign up for a subscription or request multiple copies of this newsletter, see website *ArtificialRetina.energy.gov* or call 865.574.0597.

**Genome Management Information System**
**Oak Ridge National Laboratory**
**1060 Commerce Park, MS 6480**
**Oak Ridge, TN 37830, U.S.A.**

***Postmaster:*** *Do Not Forward*
*Address Correction Requested.*
*Return Postage Guaranteed.*

FIRST CLASS MAIL
U.S. POSTAGE
PAID
OAK RIDGE, TN
PERMIT NO. 3