How video goggles and a tiny implant could cure blindness

August 25 2017, by Theresa Johnston

Daniel Palanker uses optics and electronics to invent technology for restoring vision. Credit: Brian Smale

At 16, Lynda Johnson was ready to learn how to drive. Yes, she had a progressive eye disease, retinitis pigmentosa, which already had stolen her night vision. But throughout her childhood, the Millbrae, California, girl had kept up with her brother and sister, climbing trees, skateboarding and even riding a bike. She had studied the Department of Motor Vehicles manual and passed the written test. All she needed for her learner's permit, the DMV clerk told her, was a physician's note saying she could get behind the wheel.

When an ophthalmologist subsequently refused to give her the green light, Johnson was heartbroken. "I stormed out of his office, slamming every single door. And then I got so depressed," she recalls. " People would ask me, 'What do you want to do when you graduate?' and I'd say, 'I don't know. I'm going blind.'"

Today Johnson is a marriage and family therapist with a thriving practice in San Mateo, California, the mother of a 19-year-old son, and a counselor and support group facilitator at Palo Alto's Vista Center for the Blind and Visually Impaired. She reads and writes with the help of a laptop computer that converts text into speech, and her guide dog, a golden retriever named Mackenzie, helps her get around.

Sometimes she wonders, though: What if scientists came up with a device, similar to a cochlear implant for deaf people, that could help her to see again? At 58, Johnson still remembers the old Six Million Dollar Man television series—the one where the injured test pilot, Steve Austin,

gets new bionic limbs and a left eyeball with a 20:1 zoom lens and infrared capabilities. "Wouldn't it be weird if I could go from this point to that?" she says, laughing. "I would so do it."

Scientists and engineers still are a long way from creating a visual prosthesis that works as well as a real human eye, let alone a superhuman one. Nevertheless, two Stanford research teams are making steady progress in what was once the realm of science fiction. One of their promising new devices, a bionic vision system based on photovoltaic implants, is awaiting approval for human clinical trials in Europe. A second system, based on in vitro studies of the retina, could be ready for animal testing within four or five years. Both inventions have the same goal: to give back some measure of sight to people like Johnson, who have progressive diseases of the retina—especially retinitis pigmentosa and macular degeneration.

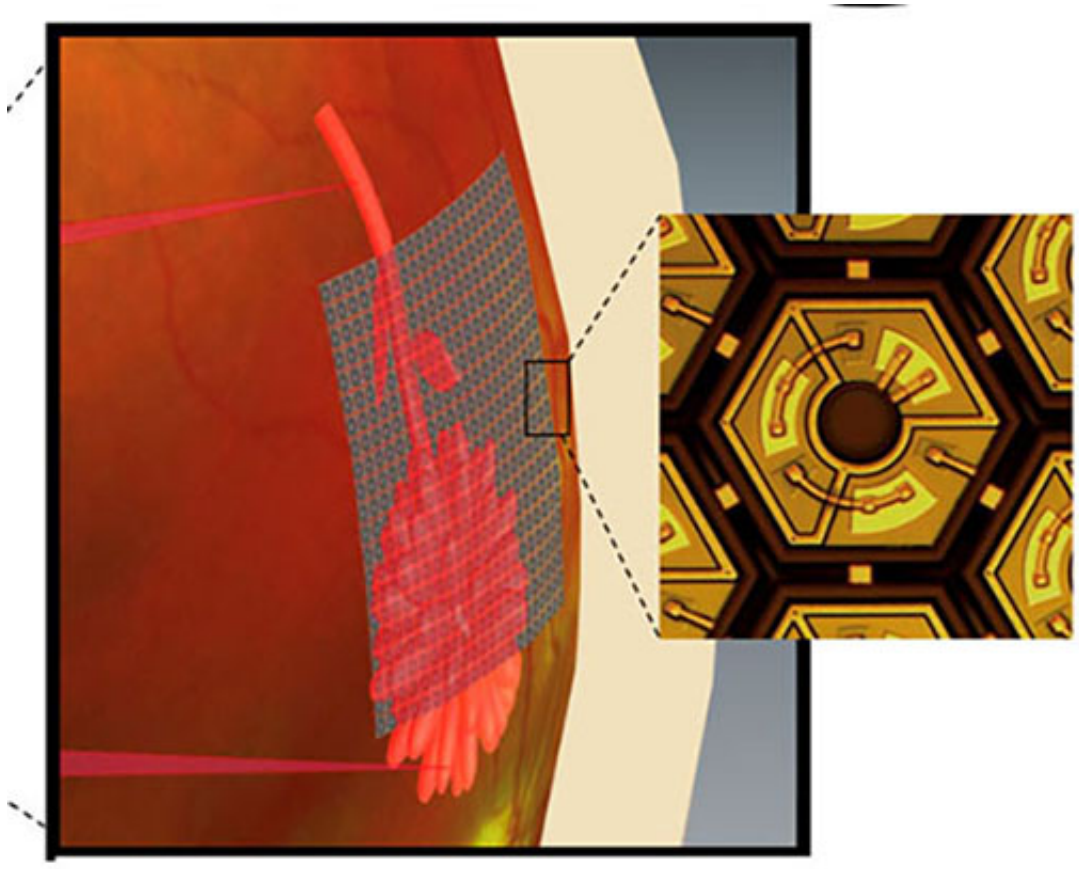
Certainly the need is there. According to the National Institutes of Health, retinitis pigmentosa is the leading cause of inherited blindness, affecting 1 in about 4,000 people in the United States. As in Johnson's case, the disease usually begins with a loss of night vision in childhood, and progresses to involve peripheral and then central vision, gradually robbing young people of the ability to read, drive, recognize faces and do routine daily tasks.

Macular degeneration, in contrast, is one of the leading causes of vision loss in Americans 60 and older. By 2020, the NIH estimates that as many as 3 million people in the United States may be living with various stages of the disease, which gradually destroys the densely packed light-sensitive cells, called photoreceptors, in the retina's center, or macula. "Many of these folks are going to be losing their central vision," says Chip Goehring, president of the American Macular Degeneration Foundation, "so it is absolutely vital that we have options for the restoration of sight, including biological and mechanical

approaches—stem cell therapies for photoreceptor replacement, gene therapies to restore dysfunctional retinal tissues, and prosthetic retinas that can serve an even wider population of people with vision loss."

Worldwide quest

Normal retinal tissue consists of photoreceptors: light-sensitive cells resembling rods and cones at the base of the eye, topped by interconnected layers of neurons. The signal travels from the rods and cones, through bipolar cells to ganglion cells, then via the optic nerve to several brain areas, including the visual cortex. Scientists still aren't exactly sure why the rods and cones break down in patients with retinal diseases, nor have they figured out ways to prevent, slow or reverse the process.



A camera mounted on the PRIMA “bionic” goggles captures an image, say a flower. The attached video processor and microdisplay convert that picture into pulses of near-infrared light, which are projected from the goggles into the eye. Photodiode arrays, implanted under the retina, pick up these signals and convert them into electrical pulses that stimulate the bipolar cells directly above them. The brain perceives these pulses as patterns of light. Credit: Stanford University

There is one silver lining, however: Retinitis pigmentosa and macular degeneration tend to spare some of the bipolar and ganglion cells. This means that the neurons in these patients' retinas can be stimulated artificially, with micro-electrodes, bypassing the damaged rods and cones altogether.

Daniel Palanker, PhD, a professor of ophthalmology at Stanford, has an up close view of how devastating diseases of the retina can be: His mother-in-law has age-related macular degeneration and requires high-power magnifiers to read. Trained as a physicist, Palanker directs Stanford's Hansen Experimental Physics Laboratory, and has developed and patented numerous devices over the years to diagnose and treat eye diseases. Among them are a neurostimulator for enhancement of tear secretion in patients with dry eye syndrome, a femtosecond laser for cataract surgery, and a patterned laser scanning photocoagulator that surgeons use to treat multiple retinal disorders, including diabetic retinopathy, without excessive damage to the delicate tissues around the treatment spots.

The development of a visual prosthesis may be Palanker's most challenging project yet. "It requires a combination of multiple skills," he explains, sitting outside his laboratory on the Stanford Engineering Quad, a short walk from his collaborators at the School of Medicine.

"You need a good understanding of optics, electronics, neuroscience and ophthalmic diseases."

Currently there are about 20 research groups working on bionic vision systems around the world, including teams in Australia, China, Germany, Japan, Korea, the United Kingdom and the United States. Yet to date just one retinal prosthesis has been approved for the U.S. market—the ARGUS II, developed by scientists at USC and Second Sight Medical Products Inc. Used by about 200 patients worldwide, the system consists of a miniature video camera mounted on a pair of goggles, a pocket-sized video processing unit, a transmitting antenna mounted on the side of the goggles, a pea-sized receiving antenna with electronics case attached to the side of the patient's eyeball, and a 60-electrode array, tacked to the front of the retina. People who use the system say they can see broad patterns of light, such as open doorways or stripes on the floor.

A more recent system, the German-built Alpha-IMS from Retina Implant AG, has been used successfully by a handful of patients in Europe. Its implant—a tiny video camera with 1,500 light-sensitive pixels, each having an amplifier and a stimulating electrode—is placed under the retina. The device, powered via a cable that exits the eye and passes under the skin to a receiver implanted behind the ear, enables users to see the ghostly shapes of nearby objects, such as apples and bananas on a table.

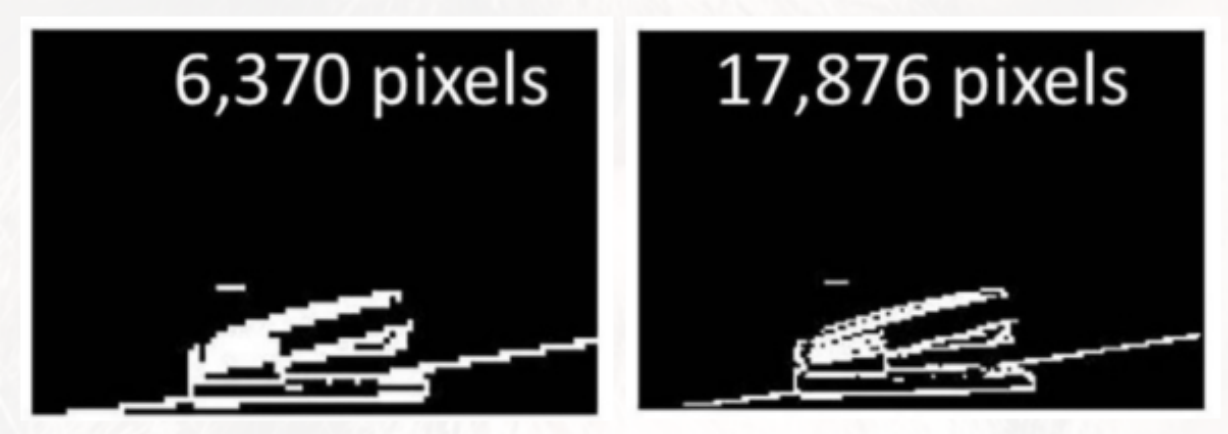
Palanker's new prosthetic device, called PRIMA, is being commercialized in partnership with Pixium Vision of France. Like the ARGUS II, it features a tiny video camera mounted atop futuristic-looking augmented reality goggles, connected to a video processor about the size of a cell phone. Yet it doesn't require the implantation of a bulky electronics case and antenna, or a cable coming out of the eye, like the German system. Instead it relies on multiple arrays of photodiodes, each about a millimeter in diameter and containing hundreds of pixels, which

work like the solar panels on a rooftop. Surgeons can lay down these tiny chips, like tiles, replacing the missing light-sensitive rods and cones in the central retina.

When PRIMA's camera captures an image of, say, a flower, the video processor transmits that picture to a microdisplay mounted inside the goggles. Powerful pulses of near-infrared light illuminate this display and are projected from the goggles into the eye, like the invisible rays of a TV remote control. The implanted photodiodes pick up these signals and convert them into tiny pulses of electrical current, which stimulate the bipolar cells directly above them. The signals propagate to the ganglion cells and then to the brain, which perceives them as patterns of light: a flower!

To test the system, Stanford researchers implanted PRIMA chips in laboratory rodents and exposed them to flashes of light, or to flickering patterns on a computer screen. By recording the resulting electrical activity in the animals' visual cortices, the scientists measured their visual acuity. "It turned out that the prosthetic acuity exactly matched the 70-micron resolution of the implant, which is half the acuity of the rats' natural vision," Palanker says. "Since the stimulation thresholds were much lower than the safety limits, we decided to develop even smaller pixels to enable better vision. More recent behavioral tests, conducted by the French collaborators in primates, have confirmed our results with rodents.

"Of course, until the implants are done in human patients," he adds, "we won't know for sure." But when human clinical trials do start later this year in Europe, they hope to achieve resolution corresponding to 20/250 vision with 70-micron pixels. That still is worse than the standard for legal blindness, 20/200, but it may be enough for a user to read very large print, or to see the face of a newborn granddaughter.



Each implant contains scores of pixels. The more pixels there are in the eye, the sharper the resulting vision will be. For the next generation of the device, researchers are aiming for more than 12,000 pixels within just a small section of the visual field. Credit: Stanford University

In the next generation of the device, Palanker says, "We should be able to put more than 12,000 pixels within 15 degrees of the visual field," taking the system to 20/150 or even better. And while PRIMA can't reproduce color vision yet—only various shades of gray—"We are working on single-cell selectivity in retinal stimulation, which might enable color perception," he says. With more experience, surgeons also might be able to expand the visual field to about 20 degrees.

The next generation

Scientists' ultimate dream is to build a visual prosthesis so small and powerful that it can stimulate specific neurons inside the retina, rather than sundry patches of them. That's the goal of E.J. Chichilnisky, PhD, a Stanford professor of neurosurgery and of ophthalmology.

"Think of the retina as an orchestra," Chichilnisky explains. "When you try to make music, you need the violins to play one score, the oboes to play a different score and so on." Likewise, the retina's 1 million or so ganglion cells are composed of about 20 distinct types. Each plays a slightly different role in transmitting the perception of shape, color, depth, motion and other visual features to the brain.

Chichilnisky joined the Stanford faculty in 2013, after 15 years at the Salk Institute for Biological Studies. Since his days as a Stanford doctoral student in the mid-1990s, he has worked with a variety of physicists and engineers, notably Alan Litke, PhD, of the UC-Santa Cruz Institute for Particle Physics, to develop small but powerful electrode arrays capable of measuring neural activity at the cellular level.

To better understand the patterns of electrical activity in the retina, Chichilnisky and his colleagues use eye tissue taken from primates that have been euthanized for other medical studies. By placing small pieces of retinal tissue atop the microchip arrays, then exposing those samples to various patterns of light, they've been able to record and study the distinctive electrical responses of five different types of retinal ganglion cells, which together account for 75 percent of the visual signal sent to the brain. They've also developed techniques to replicate those electrical patterns, artificially stimulating the ganglion cells with high precision, comparable to the natural signals elicited by the rods and cones.

By learning how to replicate these complex signals, Chichilnisky and his team are one step closer to their ultimate goal: a high-acuity visual prosthesis that behaves like an orchestra conductor, signaling the retina's myriad neurons to fire in precisely the right ways, at precisely the right times. "I'm not saying we've got it nailed," he says, "but we certainly now have proof of concept for how to make a better device in the future."

Chichilnisky says the next challenge will be to fit his lab's formidable

computing power onto an implantable electrode array that can do its job safely inside the eye, without overheating surrounding tissues, and autonomously, "without any graduate students or postdocs running it," he says, laughing. If all goes well, a prototype of the implant could be ready for testing in lab animals in four to five years.

With offices near each other at the Hansen Experimental Physics Laboratory, Chichilnisky and Palanker frequently get together to discuss their research informally and debate the best ways to proceed toward replicating the natural function of the retina. Both men have the sense that they are pushing scientific boundaries—and that their work someday may help more than blind people. Electro-neural interfaces already are being used to assist in the control of several vital organs, including the heart, bladder and limbs. Before long, they even may be hooked up to different parts of the brain, helping people with memory loss, for example or, incredible as it sounds, even enabling telepathic communication.

As Palanker says, "We live in an era when we are starting to overcome the limitations imposed on us by our biological nature ... This is how evolution goes."

Provided by Stanford University

Citation: How video goggles and a tiny implant could cure blindness (2017, August 25) retrieved 2 May 2024 from https://medicalxpress.com/news/2017-08-video-goggles-tiny-implant.html

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