Next Gen Digital Sight Could Cure Blindness

The Brilliant Idea: An artificial retina that transforms a camera feed into electric pulses that stimulate the optic nerve, providing rudimentary vision for millions of people with degenerative retinal diseases.

BY JENNIFER BOGO

Barbara Campbell is going to see Waiting for Godot. A lifelong New York City resident, she loves the theater and has been attending Broadway shows for nearly 40 years, ever since she was a teenager growing up in Queens. During that time, her vision has steadily deteriorated. At first, she could distinguish the actors onstage without a problem. Then, the details began to blur, so she started using a small telescope to see their faces. Eventually, about 10 years ago, she realized that a production of Fosse had faded into a solid whitish blur, which is all she sees when she’s facing a stage or walking up a street or getting a plate of fettuccine at an Italian restaurant, as she is now.

“This looks delicious!” Barbara says, in an unmistakable New York accent, as the waiter sets her food on the table. Barbara, now 57, still thinks and talks in the language of the sighted, which is important for the clinical trial she’s about to embark on tomorrow. She needs to be able to articulate exactly what she’s seeing, if she sees anything, once she becomes the 25th person in the world to receive the Argus II artificial retina.

In a healthy human eye, 125 million photoreceptors at the back of the retina act like the world’s most sophisticated digital camera, functioning in a range of light conditions separated by 10 to 12 orders of magnitude. For example, when navigating through the woods on a moonless night, the eye’s rods can pick up a single photon, damping the “noise” of surrounding cells in order to amplify it. And when gazing down the beach on a dazzling summer day, the eye’s color-sensitive cones rapidly adapt to a flood of sunlight. Barbara has retinitis pigmentosa, a disease caused by any one of 100 different gene defects that trigger the deterioration of those photoreceptors and interrupt the complex sequence of image processing that follows.
“My sixth grade teacher first noticed it,” Barbara tells me—as a child, she had trouble filling in the bubbles next to answers on standardized tests. “I don’t think either of my parents really understood what it meant. Every few years it would get a little worse and a little worse and a little worse.” In her 30s, Barbara finally started using a white cane—but only after she’d fallen down an open manhole. You tripped over it? I asked. “No, I went into it. There was a ladder so I was able to climb out,” she says. “It was right next to a restaurant that had tables on the sidewalk. Everybody was like, Oh my God, she just went down the hole! They thought I just wasn’t paying attention.” She gets around the city perfectly well now—she took two subways and walked several blocks to meet me at the restaurant—but when she learned about the Argus II clinical trial, she enthusiastically applied.

In the morning, a surgeon at NewYork-Presbyterian Hospital will make an incision in Barbara’s left eye and lift the saran-wrap-like membrane that covers it, called the conjunctiva. He’ll then suture a small electronics package, about the size of a watch battery, to the outside wall of the eye and secure it with a piece of silicone rubber that wraps around the eye’s equator. Next, he’ll thread a thin cable through an incision in the wall; the cable connects the electronics to an array of 60 electrodes. After removing the vitreous humor that fills the inside of the eye—a material that’s essentially Jell-O, minus the sugar and food coloring—the surgeon refills the eye with fluid so that he can manipulate the array onto the retina, tacking it in place with what is perhaps the world’s tiniest pushpin. The whole procedure will take 4 to 5 hours.

Barbara seems unperturbed. In fact, she’s looking forward to it. As a rehabilitation counselor for the New York State Commission for the Blind, she understands the artificial retina won’t magically give her perfect eyesight. But what it will do is astounding nonetheless: send electric pulses that bypass the retina’s damaged rods and cones to jump-start cells that are still viable. The eye, after all, is a small, delicate organ. It’s warm and salty—a corrosive environment—and its tissue is extremely sensitive to temperature variation. Plus, the eye moves, and it moves briskly. Successfully implanting complex, wireless, biocompatible electronics in the eye is an extraordinary achievement. Bringing even rudimentary vision to someone who’s completely blind is historic.

“I really have nothing to lose,” Barbara says, looking slightly above and beyond my right shoulder. She leans forward and feels for the edge of her plate. We’ve met only 20 minutes ago, but she offers me some of her pasta, which I readily accept—it is delicious. “I feel I’m very prepared for this,” she says matter-of-factly. “I understand I’m not going to be seeing with my eye, I’m going to be seeing with electronics. There’s no way it will look like whatever I saw before.”

The Argus II implant that Barbara will be receiving is the second generation of the device; the first had only 16 electrodes. Information gleaned from this clinical trial will be used to improve the 60-electrode version, which will be commercialized, first in Europe, as early as December. But even as the trial continues, a much larger effort, involving six national labs, four universities and a commercial partner, Second Sight Medical Products, is developing technologies that will enable third- and fourth-generation models using as many as 1024 electrodes—which could provide enough detail to read 24-point font and recognize faces. There are 100,000 people in the U.S. with retinitis pigmentosa and 10 million with degenerative retinal diseases. “I’m optimistic,” Barbara tells me. “Whatever happens, somebody will benefit.”

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Two weeks later, I meet Barbara in front of her apartment on New York’s Upper East Side. We’re traveling together to her first weekly appointment at Lighthouse International, a nonprofit that conducts research to benefit people with low vision. On the train, she tells me the surgery was long, but painless, and that the doctors seem pleased. As we emerge from the station, I pause, uncertain. “Bloomingdale’s should be behind us,” she says. “Pottery Barn is on the right. Lighthouse is about a third of the way up the street.”

The main goal of today’s appointment is to confirm which of the array’s electrodes are working properly. Inside the dimmed office, a Second Sight technician hands Barbara a battery-powered microprocessor about the size and heft of a first-generation iPod. It will take information from a camera mounted on sunglasses and convert it to a signal, which is beamed wirelessly to a receiver in the electronics package on Barbara’s eye. The receiver then sends a corresponding pattern of electric pulses to the electrode array.

Typically, when light passes through the transparent tissue of the retina and strikes photoreceptors, they initiate electrochemical signals that propagate forward through a layer of bipolar cells to ganglion cells. Millions of nerve fibers running from the ganglion cells dive through the eye’s “blind spot” and form the optic nerve that carries impulses to the brain. The electronic array sits like a postage stamp on the ganglion layer, stimulating the cells directly with a small amount of electricity. This produces phosphenes, the same sensation of light created by rubbing one’s eyes.

The technician touches the keyboard of a laptop—today it will be standing in for the camera, sending information to stimulate specific electrodes—and it emits a loud bloop. “Can you see that?” she asks Barbara. “Yes, it was like a flash,” Barbara responds.
Eighteen years ago, a blind patient saw a similar flash of light when Mark Humayun, an ophthalmologist and biomedical engineer at the University of Southern California’s Doheny Eye Institute, placed an electrode directly on the person’s retina during surgery. Until that moment, no one knew whether an optic nerve that had gone unstimulated for decades could still carry a signal to the brain. “The mantra was, if you don’t use it, you lose it,” Humayun says. His discovery made the eye a candidate for neural prosthetics—devices that interface with the nervous system to restore function lost to disease or injury. At the time, another neural prosthetic was just gaining traction: cochlear implants, which bypass damaged cells in the inner ear to directly stimulate the auditory nerve.

Stimulating the optic nerve, however, is much more complex. Besides involving millions of points that create a picture, synapses that communicate across each layer of the retina play an important role in honing and sharpening images—a step the electronic array skips. “You have to re-create that processing,” Humayun says. “Each electrode can’t just ping the spot.” Software in the external microprocessor converts the visual feed into signals that should convey the correct shape—a doorway, say, or a lamppost. But each subject must also train to better interpret that information. “If you’ve been blind, your brain doesn’t just sit there twiddling its thumbs,” Humayun says. “It ends up taking over functions such as hearing and maybe even touch. When you replace that lost function to the brain, those areas have to regroup, reorganize and begin to relearn.”

(Illustration by Dogo)

1. A camera mounted on a pair of glasses  
2. The microprocessor converts the
captures video and sends this information through a cable to an external microprocessor.

3. The transmitter wirelessly beams the data and power to a receiver in an electronics package on the eye. A tiny cable carries the stimulation signals through the wall of the eye to the electrode array.

4. Electrodes implanted on the ganglion cell layer of the retina fire. Electric impulses then travel through the optic nerve to the brain for interpretation.

Four months after Barbara's surgery, we're back at Lighthouse International for an appointment in which she will try to identify letters of the alphabet. Barbara uses the camera now; it's embedded discreetly in a pair of sunglasses. Her face is lit by the glow of an LCD screen in the darkened room, and I can see a white, 10-inch "L" reflected in the lenses. Barbara scans her head methodically, left and right, up and down, because the visual feed is coming from her glasses, not her eyes. "This could be an 'L,'" she says tentatively.

"That is an 'L!' Wow, very nice," responds Aries Arditi, a principal investigator and senior fellow in vision science at Lighthouse. Barbara laughs: "Beginner's luck."

After a few more letters, Arditi has her take a timed test. It's a control, with the device turned off. Barbara rattles off 10 letters at random as they appear on the screen, sometimes a beat before that, and gets them all wrong. Now, the real test: “Take as much time as you want,” Arditi says. Barbara spends a few minutes studying each letter. Her answers gradually get more confident, and she misses only three out of 10. “I only got three wrong?” Barbara asks. “Whoa! I'm impressed!”

The following week she gets them all correct. “Barbara's big advantage is Barbara,” Arditi tells me later. “She is really very good at exploiting what very minimal information she does have. The fact that she can recognize letters is astounding. She's not going to be reading the newspaper anytime soon, but any bit of visual information you get is helpful.”

As a sighted person, I still don’t understand exactly what Barbara sees through the artificial retina, so on my next trip to California I drop by Caltech to visit theoretical physicist Wolfgang Fink (now at the University of Arizona). He seats me in front of a 15-inch MacBook Pro in a windowless basement lab. The image displayed by the laptop’s camera is me, sort of. It is a 4 x 4 array of fat, square pixels in a mosaic of black, gray and white; I’m the black blocks on the left-hand side.

“Current retinal implants have orders of magnitude less [pixels] than what a camera delivers,” he says. “Therefore, one of the first tasks of image processing is to sample the hi-res image to make the low-res image out of it.”

Fink changes the view from 16 pixels to 64, roughly the equivalent of Barbara’s implant. Now, when I pass my hand in front of the camera, gray blocks shimmer diagonally across the array. "The levels of brightness the camera takes in are translated to levels of visual stimulation—strong phosphenes versus weaker ones," Fink says. Then he loads a 32 x 32--pixel array, or 1024 electrodes, the goal. The image sharpens to graphics akin to an old Atari game. I can pick out the plaid of my shirt, my
Now Fink begins to manipulate the image with an Artificial Vision Support System (AVS2): He turns on a contrast enhancement filter, which makes the dark and light pixels starker; when he activates edge detection I can see the outline of my hand, and adding image blur causes it to become more avatar-like. Each layer of processing improves the utility of the otherwise limited arrays. “We’d like to make sure we can give the blind subject as many image-processing filters in real time as possible to choose from to make their visual experience better,” Fink says.

He cautions me that what I’m seeing, however, is still through the filter of my own healthy retina, so it’s an ideal image. Fink leads me to a National Science Foundation–funded project: a rover about the size of a large Tonka truck with a camera gimbaled at the front center. Loaded with the AVS2, the rover, called Cyclops, can navigate around a room using only the number of pixels a researcher gives it, providing a much better approximation of what the blind might see. (Two of Barbara’s electrodes, for example, turned out to be disabled.) Plus, researchers can use it 24/7, allowing them to home in on optimal image processing for different environments, sparing test subjects exhausting groundwork.
area,” says Satinderpall Pannu, a mechanical engineer in Livermore’s Center for Micro- and Nanotechnologies. “So you increase the density by a factor of four, and that’s a challenge.” He’s referring—through a face mask, since we’re both dressed in sterile garments from head to toe—to the 1024 electrodes that an interdisciplinary Department of Energy team hopes to eventually squeeze onto the device. “One of the interesting scientific questions is: If you increase the density, how do the electric fields overlap with each other?” Pannu says.

A researcher at Oak Ridge National Laboratory is currently mapping those electric fields in order to arrive at an effective design. Scientists elsewhere are developing more advanced radio-frequency electronics and a biocompatible film that could coat the device, reducing its size. “We all had a unique piece of the puzzle needed to develop these implants,” Pannu says. “This was a great vehicle to push all these different technologies along.”

For its part, the team at Lawrence Livermore applies microfabrication techniques common to the semiconductor industry, such as photolithography, to manufacture the array. Pannu shows me a 4-inch-diameter silicon wafer with 10 of the thin-film devices, shaped like elegant hockey sticks, layered onto the surface. The same process is used to manufacture inertial sensors, accelerometers and gyroscopes, which now appear in products from automobiles and Wii controllers to critical components in aircraft.

“We have somewhere between 100 and 125 million photoreceptors in our eye,” Pannu says. “And so if I was losing vision, I’d want to have roughly that same resolution after I put my device in. So the real question is, how do we go from a thousand electrodes to a million or 100 million?” Though that feat could easily be decades away, the researchers have already begun to think about how to put an integrated circuit directly onto the retina.

The engineering being perfected with the Argus device could also improve other neural implants. For example, microfabrication could make cochlear implants, pacemakers and deep-brain stimulators for treating Parkinson’s disease smaller and less invasive. The tiny, lightweight camera could be used in applications ranging from security to endoscopy. And the implant’s hermetic packaging could protect environmental sensors, especially ones used in underwater locations such as the Gulf of Mexico.

At Christmastime, Barbara is able to string the lights on her tree unassisted—and know for herself that they are evenly spaced. A month later, she’s become very good at identifying the bus stop and can see the light at the entrance to her apartment building from up the block. By spring, she can distinguish the white line representing the crosswalk as she approaches the street, a milestone she calls “huge.” And a year after she received her artificial retina, she wears it to Disneyland, where the lights fly by her in Space Mountain.

The 30 subjects in the clinical trial appreciate the Argus II for varied reasons, according to Second Sight’s vice president of business development, Brian Mech. “Barbara talks about bumping into a lot fewer things when she wears it outside,” he says. “For other people, it’s being able to see their grandchildren, even if they can’t recognize them—being able to see the moon or fireworks. They feel more connected to their environment. They value things they can do with the device, but they value a reduction in isolation even more.”

A handful of other teams, in Germany, Australia and elsewhere in America, have begun to develop retinal implants as well, though currently none of the devices is in a U.S. clinical trial. In recent
years, scientists have grown new retinal cells from stem cells and shown progress in developing an
effective gene therapy. Each approach brings its own challenges. But someday all of them could
offer a valid treatment for retinitis pigmentosa as well as for age-related macular degeneration,
which gradually destroys photoreceptors in the center of the retina and is the leading cause of
blindness in adults over age 55.

The Argus II represents a concrete step in that direction. I meet Barbara one autumn evening for a
screening of The Wizard of Oz in Central Park. As we take our seats on the bleachers she pulls her
glasses out of a black padded case and plugs the cord into the microprocessor, which she slings
over her arm. Speakers surround us, but when the movie starts, she turns her head to the left,
toward the screen. “How tall would you say that is?” she asks. About 40 feet, I say. “That’s what I
thought!” To her, the structure looks like a giant block of white pixels that dim and brighten
depending on whether Dorothy is skipping through the Haunted Forest or toward the Emerald City.
“Oh, this looks so awesome!” she says.

http://www.popularmechanics.com/science/health/breakthroughs/next-gen-digital-sight-could-
cure-blindness