

## MEDICINE

# Digital Encounter

Physicians at the University Clinic Tübingen created a medical sensation: They enabled blind patients to again have basic vision. The insertion of a microchip underneath the retina led to the breakthrough.

In order to fully understand the miracle that has happened to Miika, we first need to realize in what kind of a land of shadows he is living.

“My life resembles a drive through dense fog”, says the 45-year old Finn.

His eyes perceive the world as light and dark plumes without any contours or colors. “Shadows without distinct outlines billow in front of my eyes”.

This has been the case since he was 22 years old. Miika, who only wants to be named by his first name, suffers from the hereditary disease retinitis pigmentosa. This causes him to slowly lose his eyesight.

But recently, the fog temporarily thinned out. A video documents Miika’s moment of bliss. He sits in front of a banana and an apple and says, “one object is round, the other one is elongated.”

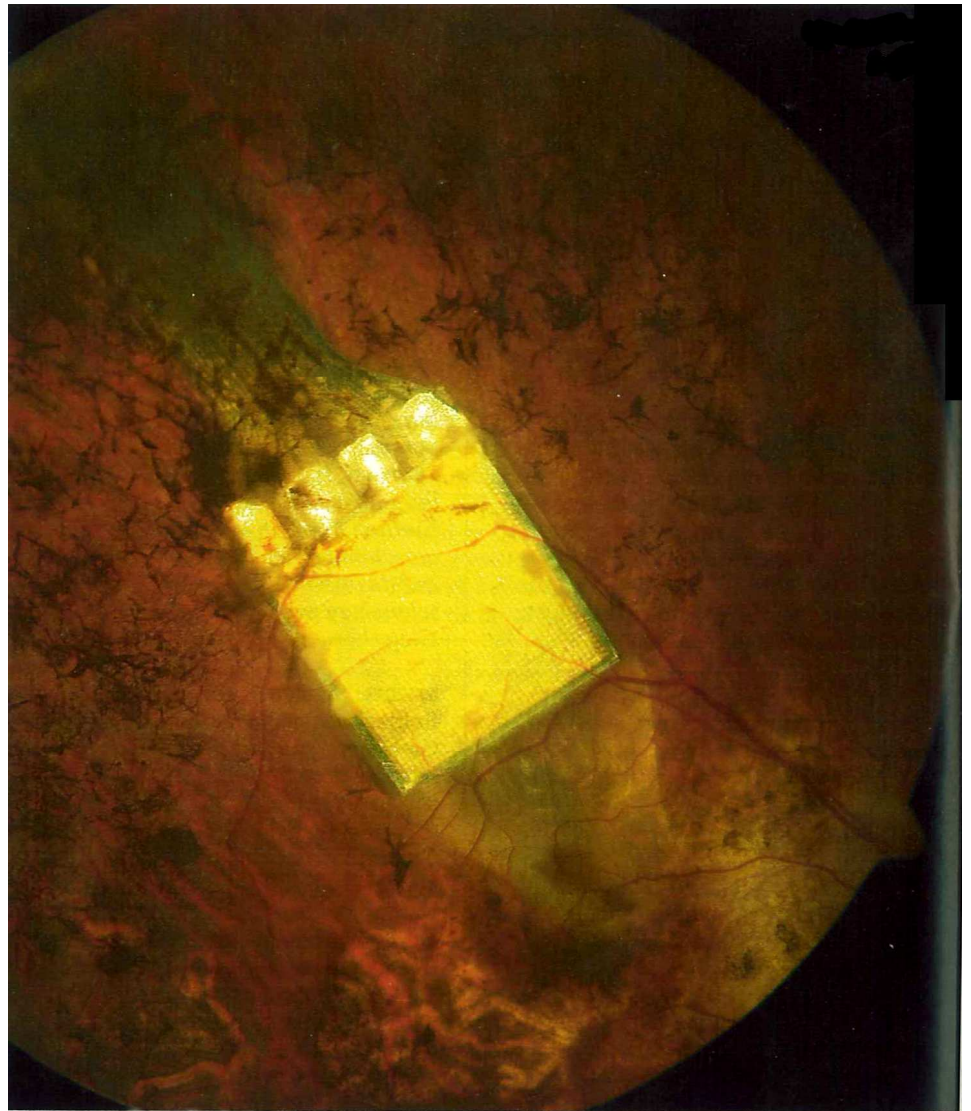
The physicians observe him mesmerized. Miika continues, “somehow the object is bent”. He hesitates. All of a sudden he is certain, “it is a banana”.

After a short moment of surprise applause erupts in the small examination room on the second floor of the University Ophthalmology Clinic Tübingen. The internet entrepreneur is suddenly able to see the world with an artificial eye, with a retina made of silicon: a digital encounter.

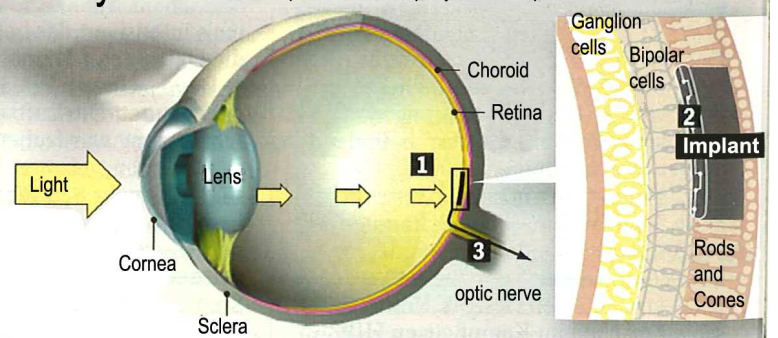
During a 4-hour surgery the physicians slid a chip under the retina. The chip was connected to a wire that came out of his body behind his ear. The ophthalmologist Eberhart Zrenner was able to control the microchip in Miika’s eye through this wire. At the push of a button the scientist made the eternal fog disappear.

The successful experiment is a medical sensation. For two decades more than a dozen research groups have been experimenting with visual prostheses that allow blind people visual orientation.

For a long time there was very little progress. But now advances are being made in this research field. US researchers from the company Second Sight recently celebrated their success. But their patients are required to wear special glasses with an integrated camera. The transfer of the images of the camera to the retinal implant is wireless. The technique developed in Tübingen does not require glasses. The chip underneath the retina processes the signals.



**Silicone in the eye** How the retinal implant of the company Retina Implant works





The German researchers have achieved a real breakthrough. Recently Zrenner proudly announced at an Ophthalmology Congress in Miami: "We were able to demonstrate that with the help of the visual prosthesis Miika exceeded the minimum requirement to not be considered legally blind anymore".

15 years ago the team of physiologists, engineers, surgeons and material scientists began looking for technical treatment options for people losing their retinal cells. Thousands of Germans lose their eyesight every year because of retinal degeneration due to old age

or as a result of a hereditary disease. Zrenner: "These people suffer immensely".

But now there is hope - hope attached to 1500 photocells. They are placed on a tiny microchip, measuring only three by three millimeters. Walter Wrobel, CEO of Retina Implant in Reutlingen, the company that plans to launch the implant, explains, "our invention resembles the chips placed in camera phones". The research project receives financial support from the German Federal Research Department as well as German entrepreneurs who joined the project with several million

Euros. The money is primarily used for the development of the chip and clinical trials. "We need to make the material resistant enough for use in the human body", says Wrobel. A plastic coating is supposed to protect the photocells against the body fluids, which contain salt. But the sensor also needs to be small enough to replace the dead cells of the retina, sensitive to light. Wrobel: "We benefit from the lessons learned while developing pacemakers and cochlear implants".

Nevertheless, procedures in the eye are acts of bold pioneers. So far eleven patients received the special chip in Tübingen. The oldest patient was 57, the youngest patient was 26 years old. For a long time the surgeons first practiced on pigs, only then did they dare to perform the surgery on humans.

At first the surgeons suctioned off the fluid from the inner part of the eye. They opened the choroid of the eye from the side after cauterization of the highly vascularized tissue with heat. Finally they slid the chip with the wire in-between the choroid and the retina until they reached the area with the highest visual acuity (see image).

"The human body tolerates the implant well," reports Zrenner. "We did not observe any serious problems such as inflammations in any of the patients."

The real challenge, however, starts three or four days after the surgery. The eye and the brain need to learn again how to see. Patient Miika remembers the moment very well when Zrenner switched on the optical chip. "All of a sudden I saw once again sharply defined objects in front of me," reports the Finn. But they did not make any sense. "They were bouncing up and down in front of my eye."

This did not surprise Zrenner, "the eye first needs to synchronize itself with the brain to take a look at an object."

But within a few hours the objects, such as forks and knives, began to assume familiar shapes. Miika was even able to notice typos in his name: letters with a size of about five to eight centimeters.

Finally Zrenner led his patient into the large auditorium of the University Clinic. There, several physicians were waiting for him. "I clearly saw their outlines," remembers Miika. "I was able to tell who was taller and who was shorter". Miika carefully went towards them - without the white cane he usually needs.

Wrobel constructed special glasses for seeing people. They simulate how previously blind people see with the help of the optical chip. The image is tiny,



Implanting the Retinal Chip at the University Eye Hospital Tübingen

1 Light falls on the light sensitive implant that has been inserted directly underneath the retina of the blind person. The implant works in a similar way as the chip of a digital camera.

2 The photocells of the implant transform the light into electric impulses. These stimulate the nerve cells of the retina per the optical signals received.

3 The impulses of the nerve cells are conducted to the brain via the optical nerve.



Patient Miika



coarse and grey - but for a blind person this is a new and exciting world.

“We deliberately decided to implant the chip underneath the retina”, says Zrenner. This procedure allows the use of a large part of the natural image processing capabilities of the inner retina nerve cells. They are usually still intact, even in blind people.

Other research groups, however, need an external camera to capture the images. The US company Second Sight, located in Sylmar, north of Los Angeles, is the world leader in this technique. The current implant of the company is called Argus II. Its approval in the US and Europe as a medical device with a cost of about 100'000 dollars is already scheduled for next year.

In contrast to the Tübingen project, the American visual device contains only 60 electrodes, resulting in an image resolution of about eight by eight pixels. The chip of the device is not located underneath the retina either; it is on the retina. The electrodes of the implant stimulate the nerve cells that are there. The company has been conducting a clinical trial with 32 patients from the US, Mexico and Europe since the end of 2006. The advantage of the US system: Argus II can remain in the eyes of the patients for years. The blind people are therefore able to test the implant in their everyday life, not just in the hospital.

“Many patients report that they can orient themselves better, that they find doors and windows and are able to discern movement” says Brian Mech of Second Sight. Also, preliminary data shows that a majority of the subjects are able to read large letters.

However, experts caution to not have unrealistic expectations. “It takes a majority of the patients months to correctly interpret contrasts, even strong contrasts”, points out the ophthalmologist Jacques Duncan of the University of California in San Francisco (UCSF), where Second Sight patients are treated. “My patients enjoy being part of the clinical trial; however, the implant has not changed their everyday life significantly.”

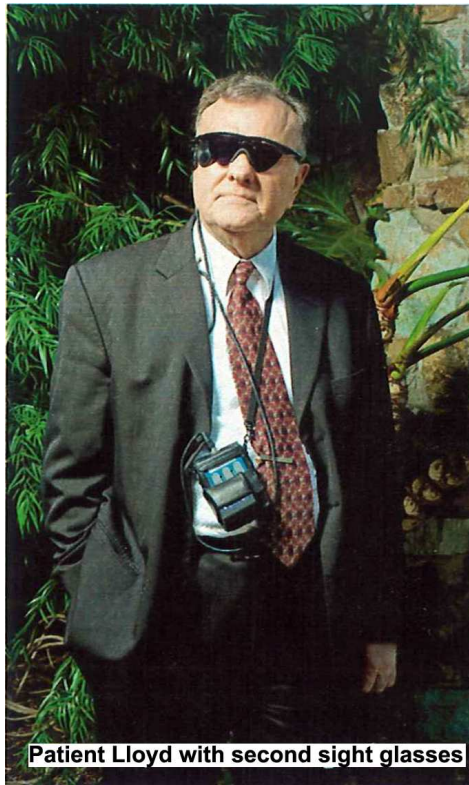
“The enthusiasm of the people is very mixed,” admits Mech. “But we do not have a single patient who has not liked it at all.” Many patients even leave their device on all day long.

Dean Lloyd is one of his model patients. The 68-year old attorney has a law firm in Palo Alto, California. He suffers from retinitis pigmentosa. He is only able to work as an attorney because his secretary is reading the files to him.

Lloyd wears a suit, a pattern tie and cowboy boots. He has large sunglasses on his nose. A tiny video camera is embedded in the bridge of the glasses. It provides the images that allow him a rudimentary visual experience.

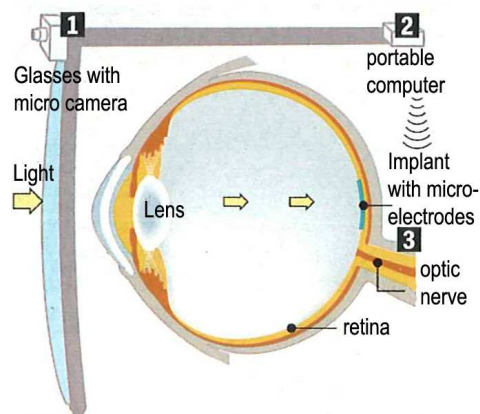
It took the surgeons of UCSF over three hours to attach the electrodes to Lloyd’s right retina. The implant receives data from a minicomputer that the lawyer wears on his belt. The minicomputer transforms the video signals from the sunglass camera into electric impulses (see image).

Lloyd sees his ophthalmologist Duncan regularly. The patient learns to point to white



## Glasses for the blind

How the implant of second sight works



1 A micro camera on the bridge of special glasses records images of the surrounding area.

2 A portable computer transforms the video images into electric impulses and transfers them wirelessly to an implant on the retina of the blind person.

3 The stimulation of the optic nerve and the conduction of the electric impulses to the brain work the same way as with the German implant.

dots on a computer screen, to make the difference between a triangle and a square and to recognize lines on the monitor.

“At first the implant was rather useless,” remembers Lloyd. “I expected to see images; but it isn’t like that.” Instead he sees flashes of light, “like stars illuminating the night sky”.

Lloyd perceives the eyes of other people because the tear fluid reflects light, “like when you shine the light on a cat in the dark”. He sees shapes, borders and boundaries as flashing lines. He needs to constantly turn his head back and forth if he wants to scan his surroundings since the video camera is only able to film the area right in front of him. “I turn my head back and forth like a chicken,” he laughs.

Lloyd likes to talk about the success of science, about the visual cortex and the amazing adaptability of the brain. All along he is doodling small circles on a piece of paper. “I remember the images of the past,” he explains. “They help me to correctly interpret the signals of the electrodes.”

For example, when he walks on a sidewalk. The light gray of the sidewalk sets it apart from the darker shade of grass and the black asphalt. That’s how Lloyd finds his way. He is able to sort socks into white, grey and black pairs. In the meantime he is even able to recognize a few colors. Blue appears as a “glistening sky blue”, green is lighter than normal, red shines in the color of rubies. “This is only possible with a lot of experience,” Lloyd says proudly, “but now it clearly makes life more enjoyable.”

Miika, the patient from Tübingen, had better visual acuity than fellow sufferer Lloyd - but only for a short amount of time. His chip was removed again a few weeks after the surgery. This was one of the requirements of the ethics commission of the Tübingen University. At the beginning of the experiments there had not been sufficient data available regarding the long-term tolerance of these implants.

It was a sad moment for Miika. “I would love to be able to orient myself to some degree, to be able to go outside without the help from other people, and without the fear of overlooking something in my path.”

Next year Zrenner plans to provide two dozen patients with new, wireless, visual chips. They will permanently remain in the eyes of the patients. Miika: “I longingly wait for that.”

PHILIP BETHGE, GERALD TRAUFFETTER