

Press release

Chip enables blind people to gain impressions of vision

Initial results of the pilot study for the examination of the efficacy and tolerability of a sub-retinal chip implant in blind patients

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Photos:

- Chip with direct stimulation electrodes (detail)
- Complete implant with chip
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- In the operating theatre
- University Eye Hospital (exterior view)

Eberhart Zrenner MD, PhD (portrait)

Karl-Ulrich Bartz-Schmidt, MD, PhD (portrait)

Helmut Sachs, PhD (portrait)

Walter-G. Wrobel, Dr (portrait)

Reinhard Rubow (portrait)

Barbara Wilhelm, PhD (portrait)

Film:

Test "Abilities in everyday life"

Diagram:

Functional diagram of retinal implant D/E

PRESS INFORMATION

14/3/2007

Chip enables blind people to gain impressions of vision

Initial results of the pilot study for the examination of the efficacy
and tolerability of a sub-retinal chip implant
in blind patients

***Tübingen* Blind people can perceive initial impressions of vision again with the retinal chip. This is the result of a development by Retina Implant GmbH, the University Eye Hospital in Tübingen and further project partners. A tiny micro-electronic chip, which has been implanted directly under the retina of initially seven blind patients since autumn 2005, replaces the photoreceptor cells which have perished and is intended to return part of the patients' vision. The study results from the patients are now providing statements of the function of active microelectronic implants in the human eye.**

Introduction

In Germany alone, there are around 33,000 people who have become blind due to Retinitis Pigmentosa and Age-Related macular degeneration; around 4200 new people go blind every year due to these diseases. Retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are degenerative retinal diseases, in which the photoreceptors (rods and cones) in the retina are destroyed. In the case of RP, the photoreceptors degenerate from the periphery to the centre of the field of vision. In the case of AMD, the photoreceptors in the centre of the field of vision initially waste, whilst vision at the periphery is retained. Those affected are no longer capable of leading an independent life. Around eleven percent of all blind people are affected by RP; until now no treatment has been possible. This treatment method, which is currently at the research stage, is suitable for blind people whose optical nerves and associated regions of the brain are still intact, as is the case, for instance, with the inherited retinal disease RP.

In the newly-developed retinal chip, tiny light-sensitive photodiodes take over the function of the photoreceptor cells (rods and cones) which have perished by converting light into electronic signals and steering these signals to the nerve cells in the retina. The electronic chip was developed by the medical technology company Retina Implant GmbH in Reutlingen.

The sub-retinal implants and the functional tests were carried out at the University Eye Hospital in Tübingen.

A large research association, in which ophthalmologists from Tübingen and Regensburg, as well as biologists, physicists and engineers from Tübingen, Reutlingen and Stuttgart participate, has been carrying out research into sub-retinal implants in Germany since 1995. Professor Eberhart Zrenner, medical director of the Research Institute for Ophthalmic Medicine in Tübingen, is responsible for the scientific leadership of the project, and has been supported since then by the Federal Ministry for Education and Research (Bundesministerium für Bildung und Forschung, BMBF: 01 KP 0401).

The implanted retinal chip takes over the function of the photoreceptor cells which have perished. Subsequently, the retina performs 'translation' work which is important for the recognition of images. The electrical impulses are relayed via the optical nerve fibres to the visual cortex in the brain, thus enabling perception of vision there.

During the development of the chip, the research team was faced with a variety of problems which have been successfully solved in the last few years, amongst others: whether or not a foreign body can be placed permanently under the retina in the vicinity of the location of sharpest vision, how durable the chip materials are in the eye fluids, and whether or not the strength of the signals from the tiny photodiodes is sufficient to drive the chain of information into the brain. The trigger levels for the stimulation of optical nerve cells also had to be researched.

The goal of the project is, by implanting the chip, to restore a certain level of vision which is useful for daily life and allows at least some orientation, e.g. the localisation of objects. In numerous experiments (partly on animals), trigger levels for the electrical stimulation of optical nerves and the limit values for safe use were first determined. The pilot study was intended to test the safety and tolerability, as well as the functional results, within the framework of an implantation which was limited to four weeks. It served to gain knowledge with respect to numerous technical and medical data which are indispensable for further optimisation of the retinal chip.

Study results

Seven patients successfully underwent operations which healed well. All of the patients tolerated the implant, which was operatively placed under the retina by PhD Helmut Sachs or Professor Karl-Ulrich Bartz-Schmidt, well. There were no detachments of the retina, inflammations, rejection reactions, severe bleeding or the like. The power supply cable laid by PhDs Dorothea Besch and Florian Gekeler under the facial skin and the scalp also caused no problems. Swellings of the retina were able to be treated well; slight bleeding was quickly resorbed. The new operational method, executed through the choroid coat of the eye, can be considered to be safe.

The electrical stimulation brought much important and valuable knowledge about the behavioural response of the retina and thus about the optimal electronic setting of the chip. Several technical improvements could already be made during the course of the study. Due to the electrical stimulation, patients could perceive light in certain shapes and patterns. Visual perceptions via the chip itself made the recognition and localisation of sources of light (windows, lamps) possible, which is of great importance to self-sufficient orientation. The patients sometimes noticed light objects (e.g. crockery) against a dark background.

The pilot study (leader: Professor Zrenner, MD, co-ordination: Barbara Wilhelm, PhD) provided extremely valuable data on the strength of the stimulation currents and their optimum duration and polarity, on the temporal sequence of light stimulants, on spatial resolution, on the homogeneity and stability of the perceptions and on the tolerability and reactivity of the retina.

All patients viewed their participation in the study as a positive, exciting experience, despite the stress of the operation and the often protracted tests. At the end of the study they declared that, if they had to choose again, they would again decide to participate.

The implant

The implant used is a sample which has been manufactured for research purposes only and is not yet approved under medical product laws. Exhaustive tests on animals were carried out first in order to check whether the implantation was in principle possible and tolerable.

Technology and application of the microchip

The core of the implant is a microchip, approximately 3 mm x 3 mm in size and 70 µm thick, in which about 1500 pixel fields are arranged, including circuitry for amplification, brightness adjustment and safety switching. The size of one pixel is 70 µm x 70 µm. This produces a field of view of twelve degrees, which is already sufficient to enable mobility and the orienting recognition of objects. Each pixel cell is assigned one photodiode, an amplification circuit and a stimulation electrode. Each photocell takes the light entering the eye and converts it into the electrical energy which is required to electrically stimulate the intact nerve cells in the retina. The nerve impulses from these cells are relayed to the brain via the optical nerve and ultimately lead to impressions of vision there.

The implant is placed under the retina in the area where the light-sensitive sensory cells are located in healthy persons. This ensures that the electrical charges emitted by the implant are actually transmitted to the same nerve cells in the retina which are supplied with information from the photoreceptors in people with intact retinas. The retina's information processing network is thus used in a natural way.

A kind of tongue is located at the tip of the implant, on which an additional 16 small electrodes are mounted; these are activated individually or in groups via direct electrical stimulation in order to check how the nerve cells react. This test serves to specifically generate perception of light and to find the optimal electronic setting for the conveyance of the perception. Independent of the chip function, further important information is gained via the direct stimulation.

Retina Implant GmbH's concept promises the most success, because it solves decisive problems such as implantability, tolerability and technical realisation in a simple and convincing manner.

Materials

The components of the active implant are fixed on a highly flexible polyimide film. With the exception of the stimulation chip, the entire implant is encapsulated in silicone. The total length of the implant is approx. 100 mm, the width 3 mm and the thickness 0.1 mm. The right half of the implant is laid under the retina; the left, thicker part is sewn onto the eyeball from outside and covered over with the conjunctiva. All materials have been proven in numerous animal experiments over a longer period of time to be biotolerable.

Power supply

In order to overcome the trigger levels required to successfully stimulate the nerve cells in the retina, amplification is necessary, which is integrated in the 'active' implant. Otherwise, no impression of vision would be possible in normal daylight. The necessary power was supplied in the initial clinical tests by a small power supply (about the size of a Walkman), which can be worn on a strap around the neck. For a product capable of being marketed, the wireless supply of power via a coil under the skin is foreseen.

Study participants

Patients who are blind in at least one eye, or who can only localise light so indistinctly that it is insignificant with regard to their orientation, can take part in the study. The participants must be at least 18 years old and no older than 75 years old, and must be suffering from retinitis pigmentosa, chloroideremia or extensive cone-rod dystrophy. They must have had at least twelve years experience of vision in their lives and thereby have had at least 5 percent sharpness of vision.

A retinal implant as a potential vision implant is out of the question for a wide variety of causes of blindness, e.g. glaucoma (cataract), diseased optical nerve, disorders of the blood supply to the retina, detachment of the retina or blindness due to accidental injuries. Patients with age-related macular degeneration can also not participate in the study at present.

Operation and hospital stay

After a preliminary examination at the Department for Ophthalmic Medicine in Tübingen (medical directors: Professor Eberhart Zrenner and Professor Karl-Ulrich Bartz-Schmidt), the patients underwent an operation performed by either Helmut Sachs, PhD (Chief Consultant at the University Eye Hospital, Regensburg) or Professor Karl-Ulrich Bartz-Schmidt. They initially remained in the Tübingen Eye Hospital for at least a week for ophthalmic examinations and daily check-ups. In the three weeks which followed, the functionality and tolerability of the chip was tested in special outpatient examinations. The patients were able to stay in a hotel in Tübingen during this time and were also psychologically supported by the doctors from the University Hospital.

After the examinations were completed, the chips were removed again. One patient retained the chip at his own risk and has carried the implant in his eye for 16 months without any complaints.

The current research status and the postoperative course after explantation suggest that a second implant in the same eye is possible. A later-generation implant could in any case be implanted without reservations in the other eye which was not operated on.

Retina Implant GmbH

Retina Implant GmbH was founded in 2003. The company emerged from the BMBF-sponsored SUBRET consortium, in which the University Eye Hospitals in Tübingen and Regensburg, as well as well-known research institutes (NMI Reutlingen, IMS Stuttgart, IPE Stuttgart) have been researching into the basic principles of a retinal implant and developing a clinically useable sample since 1996. Retina Implant GmbH now occupies a technologically leading position in the development of an active sub-retinal chip. The chairman of the supervisory council of Retina Implant GmbH is the leader of the Research Institute for Ophthalmic Medicine in the Department of Ophthalmic Medicine in Tübingen, Professor Eberhart Zrenner; his deputy is Professor Hugo Hämmerle, PhD; executive managers are Walter-G. Wrobel, Dr. (chairman of the board of directors) and Reinhard Rubow (executive manager).

Studies of the ophthalmic medicine market forecast growth rates up to an annual turnover of one billion US dollars. In new markets, the supplier who first presents a fully-functional solution has the best chance of remaining market leader for decades.

The Mediplan GmbH investment company has invested 7.5 million Euros in Retina Implant GmbH and has committed itself to investing a further 7.5 million Euros after the granting of CE approval (prerequisite for the permission to sell medical products in Europe). Mediplan, which invests on behalf of a German Business Angel, thus has a 25 % stake in the company.

Ethical aspects of the clinical pilot study

The pilot study was medically and ethically examined on 14/9/2005 by the Ethics Commission of the Faculty of Medicine at the University of Tübingen and positively evaluated as a research project.

Particular thanks must go to the patients who volunteered to take part in this study. They are pioneers and did not take part for personal profit, as they had no lasting benefit from a time-limited implantation. Their motivation was much more the advancement of research. The statement from all seven patients, that none of them would have wanted to miss the positive experiences gained in the pilot study, was also very pleasing.

Competition situation and goals

If we can succeed in restoring part – albeit a very small part - of the patients' vision, this already represents a significant improvement in their quality of life. The ability to see after implantation should fulfil the following requirements for an ambient brightness from 10 to 100,000 Lux: orientation in the room, field of vision from eight to twelve degrees; ability to count fingers or even recognise faces without optical aids, with magnifying optical aids even letters.

Comparison with other methods and technologies show that, up to now, there has been no product which can restore the vision of blind patients with degenerative retinal diseases. Retina Implant GmbH's concept is that which promises the most success, because it solves decisive problems such as implantability, tolerability and technical realisation in a simple and convincing manner.

Participating facilities

Department for Ophthalmic Medicine at the University Hospital, Tübingen

Research Institute for Ophthalmic Medicine
Pathophysiology of Vision and Neuro-ophthalmology
Medical director: Professor Eberhart Zrenner
Leader of the clinical study, medical support of patients

University Eye Hospital
Medical director: Professor Karl-Ulrich Bartz-Schmidt
Operations and post-operative support

Retina Implant GmbH, Reutlingen

Chairman of the Board of Directors: Walter-G. Wrobel, Dr
Gerhard-Kindler-Str. 8
72770 Reutlingen
Sponsor of the study and manufacturer of the implant

University Hospital Regensburg

Clinic and Polyclinic for Ophthalmic Medicine
Chief Consultant: Helmut Sachs, PhD
Development of the sub-retinal operation method, operations

STZ Steinbeis Transfer Centre

Autonomous nerve system and safety studies
Barbara Wilhelm, PhD
Co-ordinator of the clinical study for the Tübingen Eye Hospital

NMI Natural Science and Medical Institute at the University of Tübingen

Professor Hugo Hämmerle, PhD
Development of the biophysical principles of retinal stimulation

Institute for Microelectronics Stuttgart

Development of the chip

Contact information for press enquiries

Retina Implant GmbH
Marketing and PR
Gerhard-Kindler-Strasse 8
72770 Reutlingen
Phone: 071 21/ 3640 3110, Fax: 07121/ 36403 115
info@retina-implant.de
www.retina-implant.de

Contact information for press enquiries regarding the medical area

University Hospital Tübingen
Press and Public Relations
Phone: 07071/2980 112, 2983 659
oeffentlichkeitsarbeit@med.uni-tuebingen.de
www.medizin.uni-tuebingen.de

Contact for patient enquiries

A service telephone for enquiries regarding the method of treatment is available from 15/3/2007 under the number **Phone: 071 21 / 7012 180.**