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# Subretinal electronic chips can restore useful visual functions in blind retinitis pigmentosa patients

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## Kurzfassung

Retinitis pigmentosa ist mit einem progressiven Verlust der retinalen Photorezeptoren verbunden und führt zur Blindheit. Wir entwickelten ein subretinales elektronisches Implantat und implantierten dieses elf Freiwilligen mit einer hereditären Entzhauterkrankung im Endstadium. Das Implantat besteht aus einem Chip mit MPDA (microphotodiode array) mit 1500 Pixeln und einer 4x4 Matrix aus Dirketstimulationselektroden. Die Direktstimulation der Netzhaut wurde mit einzelnen Elektroden oder Mustern aus der 4x4 Matrix duchgeführt und führte zum Wahrnehmen klar definierter runder Punkte. Stimulation mit Mustern konnte sicher erkannt und beschrieben werden. Fünf der elf Patienten konnte mit Hilfe des subretinalen Implantats Lichtquellen oder größere helle Objekte wahrnehmen und lokalisieren. Zwei Patienten erreichten mit dem Chip eine visuelle räumliche Auflösung bis zu 0.32 Zyklen/Grad und 0.22 Zyklen/Grad. Bei einem Patienten, bei dem das Implnatat direkt unter die Makula plaziert wurde, konnte eine Sehschärfe von 20/1000 mittels eines standardisierten Tests gemessen werden. Dieser Patient konnte auch Buchstaben und Worte erkennen. Zum ersten Mal konnten wir zeigen, dass subretinale Implnatate wertvolle visuelle Funktionen bei blinden Patienten mit erblichen Netzhautdegenerationen wiederherstellen können.

## Abstract

Retinitis pigmentosa leads to progressive loss of retinal photoreceptors causing blindness. We developed an active subretinal electronic device being implanted in 11 volunteers suffering from a hereditary retinal disease in an end-stage. The active part of the implant consists of a chip carrying a microphotodiode array (MPDA) with 1500 light sensitive pixels and of a 4 x 4 matrix of electrodes for direct retinal stimulation and assessment of the tissue-electrode interface. The direct stimulation of the retina was performed by single electrodes or patterns formed by the 4x4 matrix leading to percepts described as well defined dots. Stimulation by simple patterns could be reliable recognized and described in tested subjects. Five of the eleven patients could use the subretinal MPDA to perceive and localize light sources or large bright objects.  In two subjects spatial resolution up to 0.32 cycles/deg and 0.22 cycles/deg was achieved. In the subject, whose subretinal implant has been placed directly under the macula a visual acuity of 20/1000 could be measured by a standard test, as well as letters and words recognition. For the first time we could show that subretinal implants can restore useful visual functions in blind patients with hereditary retinal diseases.

## 1 Background

Hereditary retinal diseases such as retinitis pigmentosa lead to progressive loss of retinal photoreceptors followed by blindness mostly in a patient's middle age. Despite of many scientific approaches for treatment, these diseases remain largely incurable. One of the approaches to restore vision in these patients has been introducing visual implants, which elicit visual perceptions by electrical stimulation of retinal cells [4]

Our group has developed an active subretinal implant [2,3] which has been implanted in a pilot study since 2005 in blind volunteers with degenerative retinal disease. As for no experience with such implants in humans worldwide earlier, these chips were implanted for 4 weeks to 4 months and subsequently explanted. During the study period tests of the chip mediated visual functions as well as stimulation with direct stimulation electrodes were carried out.

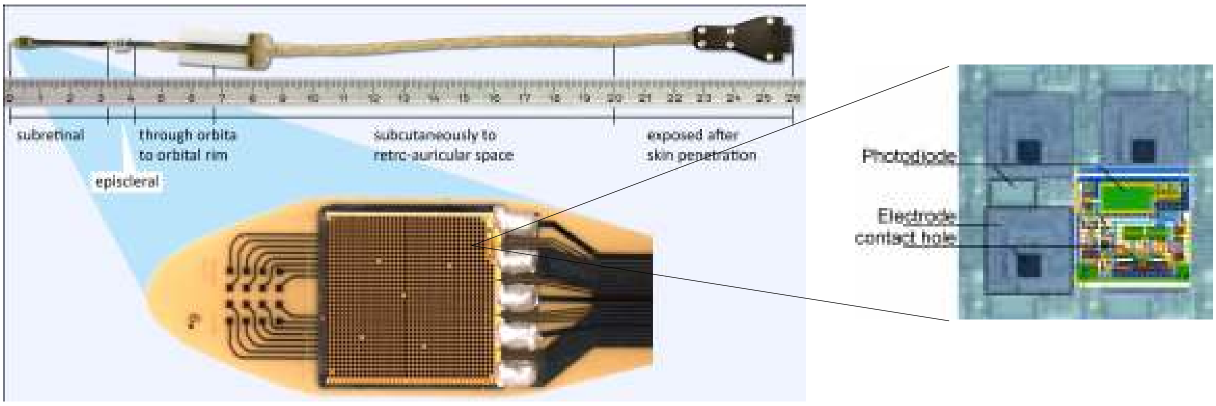


**Figure 1**: The subretinal implant with a microphotodiode array (MPDA) of 1500 pixels on a polyimide foil and the array of 4x4 electrodes. The subdermal cable unit connects the power supply and the control unit.

## 2 Methods

The active part of the implant consists of two components, a chip carrying a microphotodiode array (MPDA) with 1500 individual light sensitive pixels (see parallel abstract of Harscher, et al. in this volume) and of a second array of 4 x 4 identical electrodes in front of the MPDA for direct stimulation (DS array) and assessment of the characteristics of the tissue-electrode interface. Every MPDA pixel includes an electronic photosensor (15x30 $\mu m^2$) with a logarithmic response function, a differential amplifier, and an electronic discharge switch. Both components are positioned on a small polyimide foil (Fig. 1). The 1st generation implant employed rectangular electrodes for the DS-array covering an area of 50x50µm (subjects 1-8); whereas with 2nd generation implant this area was increased 4-fold to cover 100x100µm (subjects 9-12).

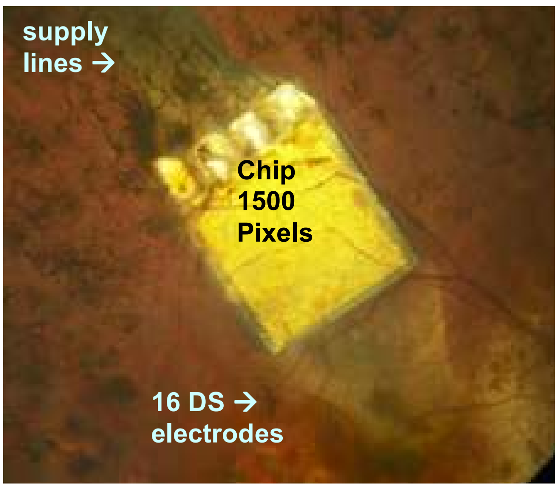


**Figure 2**: Position of the subretinal implant on the posterior eye pole

Power and control signals for the chip and voltage for the DS array are provided via a subretinal transchoroidal line. The intraorbital part of the foil leaving the eyeball near its equator is connected to a flexible silicone-embedded cable at the orbital rim. The cable leaves the skin behind the ear, ending in a plug that is connected to a small stimulation box attached to a necklace. This setup enables to assess the implant's functions, to measure electrode / tissue impedance via DS-electrodes and to adjust the MPDA's light sensitivity.

The chip has been implanted into subretinal space in 11 volunteers (10 males, 1 female) by an established surgical procedure [1], placing the chip on the posterior eye pole (Fig. 2). All patients suffered from a hereditary retinal disease (10 patients retinitis pigmentosa, 1 patient chorioderemia) in an end stage with a visual acuity of light perception or light projection recognition.

The light perception evoked by the direct stimulation of the retina by the implanted DS electrodes was done by monophasic or biphasic pulses. Threshold sensation was assessed for voltage for each electrode. Using values above the threshold patterns in the 4x4 matrix of the DS have been applied. Testing the light mediated visual percepts via the MPDA was done by a test battery that was applied in a hierarchical order from less demanding tests to the most challenging ones.

The test battery consisted of the Basic Light and Motion Test (BaLM) to assess light perception, temporal resolution, light localization and movement sensitivity, followed by testing recognition of stripe direction, object recognition; visual acuity tests with Landolt- C rings and tasks of daily living.

# 3 Results

## 3.1 Direct Stimulation

Three of the eleven subjects had no reproducible visual sensations by the direct stimulation. In two of them the fluorescein-angiography after implantation revealed virtually absent retinal perfusion. The third subject suffered from an early failure of the implanted device.

All remaining eight subjects had visual perception upon activation of one or more electrodes. With stimulation by the DS electrodes the patients described perceptions as well defined yellowish round dots. Two of the patients described the perception as lines, semicircles or circles when electrodes were activated. Five patients were able to recognize patterns such as lines or simple letters by direct stimulation [5]. When more than one electrode was activated at once, all 8 subjects had reliable and reproducible percepts.

Electrodes were activated also sequentially in a row or column to test the perception of movement in 4 persons. All of them were able to recognize correctly the direction of movement. The perception of the orientation of simple pattern resembling the letter “C” was tested in the most recent 3 subjects. Two of them reliably differentiated 4 orientations of the object.

The last subject was able to recognize surely different shapes of letters formed by the 4x4 DS-array presented in a four alternative forced choice test.

## 3.2. Vision mediated by the MPDA chip

Five of the eleven patients could use the subretinal MPDA to perceive and localize light sources or large bright objects.

The last three patients passed already at the first trial for light detection and basic temporal resolution in the BaLM test; the latest patient (P11) passed for object location and movement test and was able to recognize the direction of stripe patterns up to 0.32 cycles/deg. Another patient was able to resolve 0.22 cycles/deg.

In the object recognition tasks the three patients (each in an individual extent) were able to localize, recognize and differentiate geometric forms, various dishes (white on a black background) and flatware or fruits on a plate as well as grasp them.

The best chip-mediated spatial resolution in this study was achieved by P11, the only patient, whose implant was placed directly under the macular region [5].

In a standard visual acuity test using Landolt “C” rings he achieved a visual acuity of approximately 20/1000 with bright optotypes on a dark background (log Minimum Angle of Resolution (MAR) =1.69). He was able to differentiate correctly white letters (8.5 cm high and 1.7 cm line width) on black background and also read words built from a set of 16 different letters, such as LOVE, MOUSE, SUOMI, etc (Fig. 3) [5]. Movement of random dot patterns in 4 directions was recognized correctly at an angular speed of 1.11°/s.

# 4 Conclusions

This is the first time that direct stimulation electrodes have been implanted subretinally in human volunteers. Spatial percepts of higher complexity could be reliably elicited with an artificial vision device.

Furthemore, we could show that an electronic subretinal device containing a MPDA is able to mediate a useful vision in blind patients with degeneration of the retinal photoreceptors.


**Figure 3:** Patient P11 (end stage of retinitis pigmentosa) reads letters and combines them to words using the subretinalMPDA Implant.

Our results are proving that electronic implants can enable an artificial vision of visual acuity of 20/1000 and perception, localization as well as recognition of objects of daily living in proper contrast conditions. The best results have been achieved by placing the MPDA directly under the macula.

# 5 Acknowledgment

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