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Details on the patient cohort and the subretinal implant Alpha IMS (Retina Implant AG, Reutlingen) in the first module of a multicentre clinical trial and video material of patient reports

Katarina Stingl,[1] Karl Ulrich Bartz-Schmidt,[1] Anna Bruckmann,[1] Florian Gekeler,[1] Udo Greppmaier,[2] Anusch Hekmat,[2] Stephanie Hipp,[1] Christoph Kernstock,[1] V. Kitiratschky,[1] Andreas Schatz,[1] Eberhart Zrenner[1,*]

[1] *Centre for Ophthalmology, University of Tübingen, Schleichstr. 12, 72076 Tübingen, Germany*
[2] *Retina Implant AG, Gerhard-Kindler-Straße 8, 72770 Reutlingen, Germany*

**Author for correspondence eberhart.zrenner@uni-tuebingen.de*

This document contains the supplementary figures and details on the patient cohort and on the stability of the implant in the first module of the multicentre clinical trial using the subretinal implant Alpha IMS (Retina Implant AG, Reutlingen) that are described in the manuscript by K Stingl et al.: *Artificial Vision with Wirelessly Powered Subretinal Electronic Implant Alpha IMS.* The electronic material also provides video documentation detailing the function of the implant and the visual experiences of the study subjects.

Introduction

In the first module of a multicenter trial *Safety and Efficacy of Subretinal Implants for Partial Restoration of Vision in Blind Patients* (www.clinicaltrials.gov, NCT01024803) nine patients blind from a hereditary retinal degeneration received a subretinal visual implant Alpha IMS (Retina Implant AG Reutlingen Germany) in one eye. Results of the efficacy testing procedures are described in the main manuscript [1]. The supplementary material provides additional information of the visual implant, patient cohort and stability of the implant.

Supplementary Figures

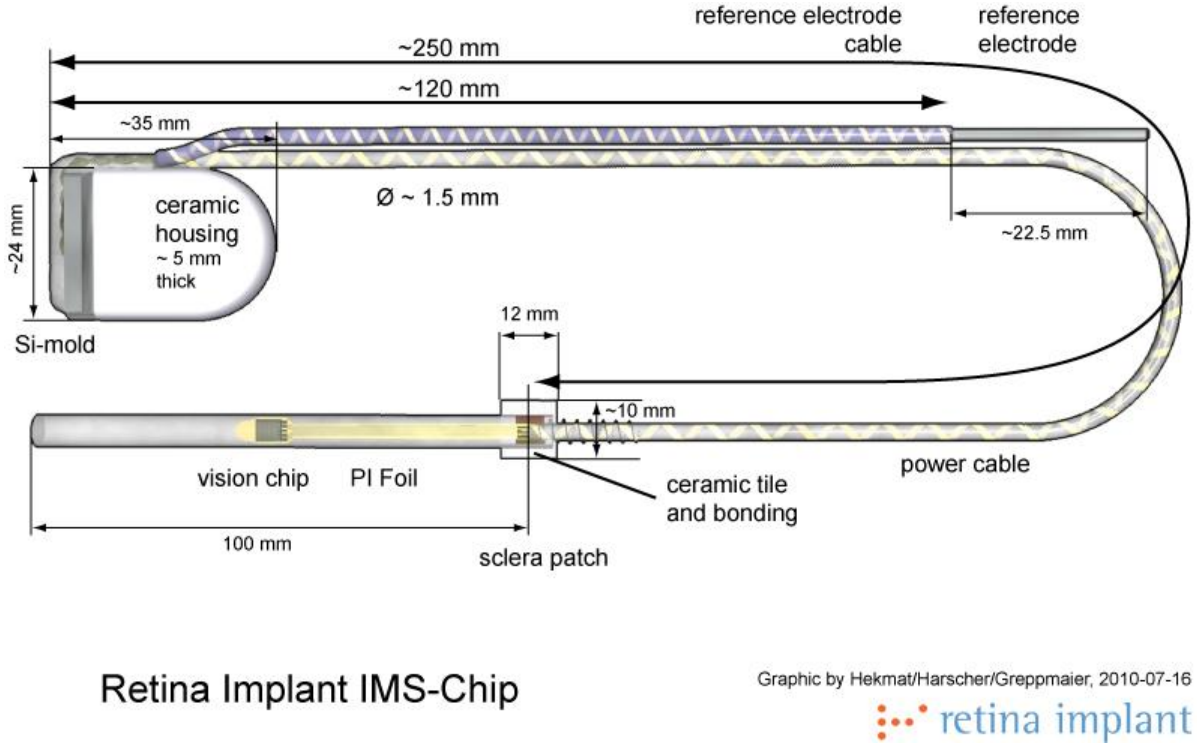

Figure S1: The Alpha IMS subretinal implant. The chip, positioned on a polyimid foil (PI) is inserted into a protective tube before surgery. The PI foil is connected to a round gold wire power cable that leads to a ceramic housing, positioned subdermally behind the ear; it contains a coil and electronics for inductive transmission of power and signals for controlling brightness and contrast. The reference electrode is positioned subdermally close to the outer orbital rim.

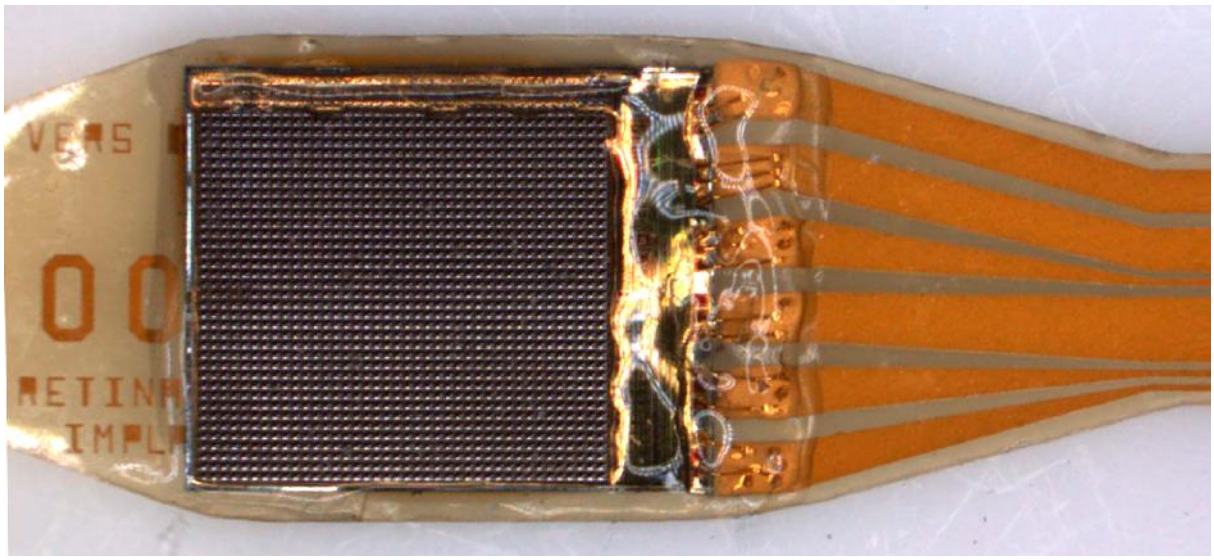

Figure S2: Magnification of the vision chip with 1500 photodiodes, amplifiers and electrodes. The bonding points connect the chip to the gold wires for power and signal transmission, positioned onto the subretinal foil that leaves the eye through a scleral flap close to the equator of the eye bulb.

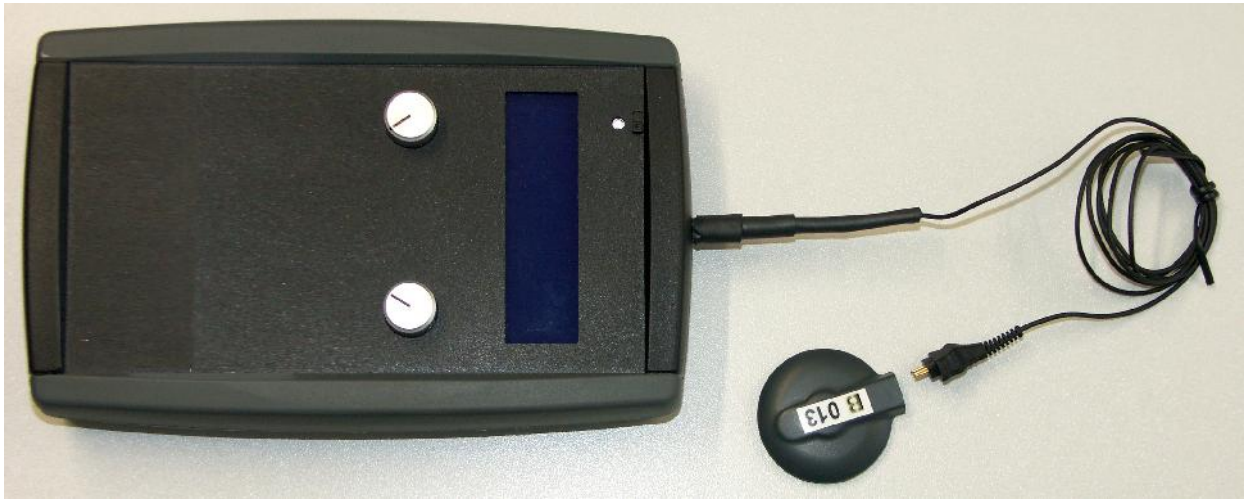

Figure S3: Handheld unit for power supply and adjustment. The user can adjust the contrast sensitivity and gain using the two knobs. The handheld unit is connected to the implant by an electromagnetic coil that is magnetically held in position over the retroauricular secondary coil.

Patient characteristics

The following characteristics were tested in all the patients prior to enrolment in the study: retinal thickness via optical coherence tomography (OCT), retinal perfusion (via fluorescein angiography), and excitability of the inner retina (via transcorneal electrical stimulation). All patients were pseudophakic.

Patients S2 and S9 were myopic earlier in life (ca. -9 dioptres and -12 dioptres, respectively). Patients S4 and S5 had undergone so called "Cuba surgery" in Cuba 15 and 11 years previously, respectively, for the treatment of retinitis pigmentosa. This technique involves suprachoroidal surgical placement of retro-orbital fat tissue in combination with electro-stimulation and ozone therapy in an attempt to stimulate neuronal regeneration [2]. Similarly, subject S6 underwent a series of ENCAD treatments with hydrolysate of yeast RNA, another non-evidence-based therapeutic approach [3] 10 to 20 years ago, and subject S1 had received a retrobulbar implantation of placental cells more than 30 years ago.
All patients underwent cataract surgery on the study eye at least 6 weeks prior to the implantation of the subretinal device described in this report.

Patients with severe general health conditions were excluded from the study because of the relatively long period of general anaesthesia associated with the implantation and of the ensuing additional health risks in certain conditions, such as cardiovascular problems.

Subject S3 suffered from increased cholesterol levels and impaired glucose tolerance; both conditions were treated with medications. In the past, subject S3 had also had an inguinal hernia. Subject S4 had experienced a deep vein thrombosis 6 years prior to the study. Subject S5 reported a gynaecological myomectomy in the anamnesis. Subject S6 is a smoker and had a single gout episode some years ago that was treated with allopurinol. Subject

S9 suffered from occasional migraines and leg oedemas (not cardiac) and underwent laparoscopic sterilisation 8 years before taking part in the study. Subjects S1, S2, S7 and S8 reported no general diseases or relevant medical history.

Subject	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**
Age	52	48	62	45	46	45	44	35	45
Diagnosis	RP	RP	RP	RP	RP	RP	RP	RP	CRD
Gender	Female	Female	Male	Male	Female	Male	Male	Male	Female
Visual function prior to implantation	LP	No LP	LP	LP	LP	LP	LP	LP	LP
Last reading before blindness	28 years	15 years	20 years	15 years	24 years	24 years	4 years	8 years	13 years

Table S1: Patient characteristics. (RP = Retinitis Pigmentosa; LP = Light Perception; CRD = Cone-Rod Dystrophy).

Stability of the implant system

Previously, a problem resulted from the mechanical stress on the intraorbital cable caused by eye movements. This issue led to an intraorbital cable break in three subjects (S2, S3, S4), resulting in functional failure of the implant after three to nine months. The problem was solved by the surgical placement of a parabulbar cable loop or by encircling the eye with the cable. This intervention prevented further cable breaks in the remaining patients by reducing changes in the cable's curvature during eye movements.

A second problem was caused by the quality of the chip's hermetic seal. Corrosion of the IMS chip periphery was observed in three implants after approximately 250 days in situ. As a result, the chip gradually lost function and the patients opted for explantation (S1, S6, S7).

Eight from nine study patients had light perception via the subretinal implant. For further results and complete study description see the corresponding main publication.

Video material

Video S1: Animated illustration of the subretinal visual implant. Light falling onto the retina is absorbed point by point by the implant's subretinal micro-photodiodes. After amplification, a graded electrical signal is transmitted into the second retinal layer, i.e., the bipolar cells. This "electronic image" is then naturally processed by the remaining components of the visual pathway.

Video S2: Subject accompanied by the mobility trainer in a restaurant.

Video S3: How a subject perceived his wife's face.

Video S4: How a subject described his visual experiences during an evening in a foreign city.

Video S5: Videotape of a subject observing a wild goose in nature.

References

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