Netzhautimplantate (Chip)
Letzte Entwicklungen und
Neues an der Forschungsfront

Internationaler Vergleich

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Th. Georgi,, A. Wedrich

Universitätsaugenklinik,
Medizinische Universität Graz

- **Artificial Vision - Was ist das?**

- **Wie kann das verwirklicht werden?**

  Historischer Überblick der verschiedenen Konzepte

- **Wie weit ist man schon?**

  Technologie (Chip im Auge)

  Was erreicht man damit ?

Netzhautchip

Definition:
Hoffnung für blinde Personen.
Neuer Therapieansatz um blinden Personen wieder ein teilweises Sehen zu ermöglich.

Wie funktioniert das?
Durch die elektrische Stimulation des Netzhaut werden Lichtpunkte (Phosphene) erzeugt **Artificial Vision**

Betrifft also nur Erkrankungen die den Verlust von den Photorezeptoren der Netzhaut bewirken!!!!!

Zurzeit Erprobung bei RP- Patienten.

Technology: Implant Systeme

→

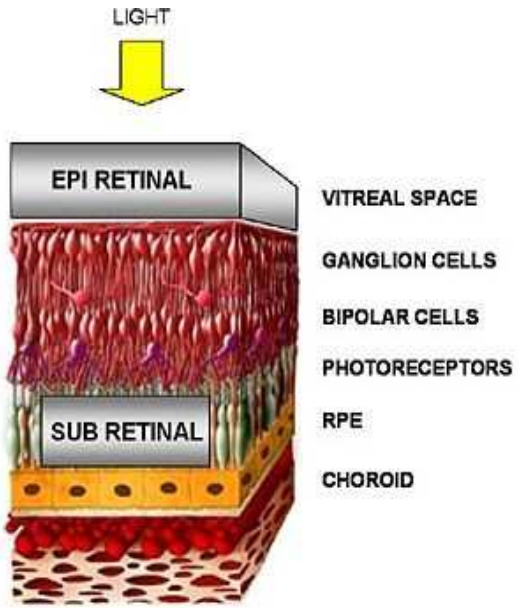
Visuelle Rehabilitation im AVC

Historischer Überblick

Proof of concept 1996

Humayun MS, de Juan E Jr, Dagnelie G *et al.* Visual perception elicited by electrical stimulation of retina in blind humans. *Arch Ophthalmol* 1996;114:40–46

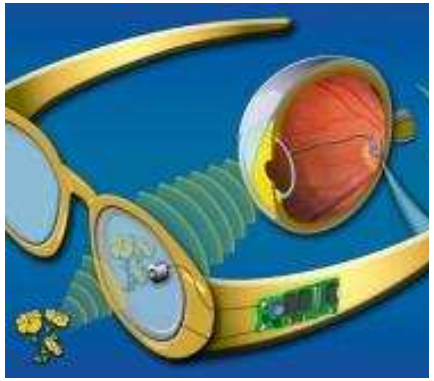
- 2 Therapie-Ansätze:

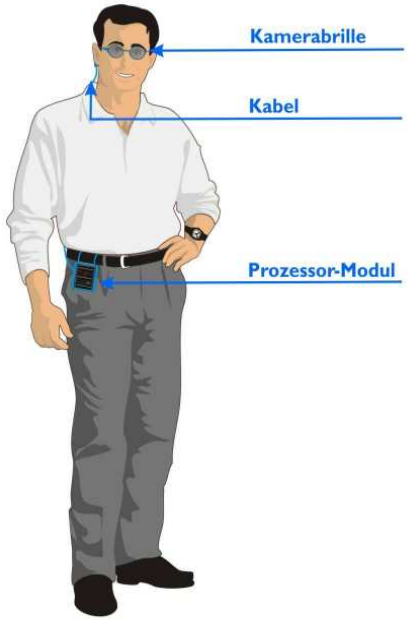


Prinzipien der Technologien:

epiretinale Implantat

Sender:
Spezialbrillen
mit integrierter
Mikrokamera

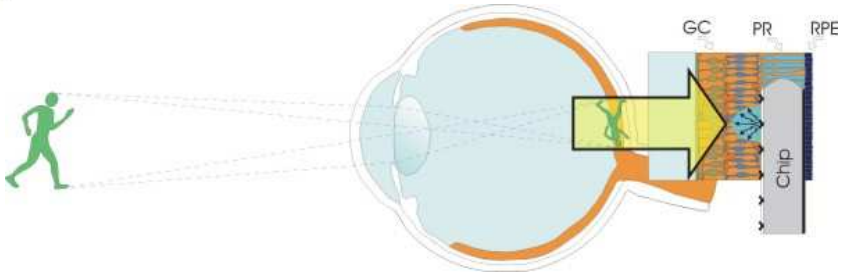




Empfänger
Retina Implant
Mit Chip

subretinale Implantat

Mikrophotodioden



Historischer Überblick

Das Projekt Artificial Vision:

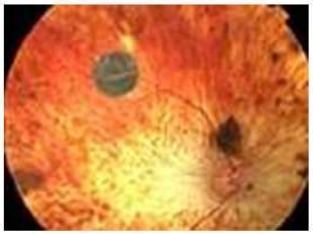
Welches Material?
Wieviel and welche Energie soll appliziert werden?
Wie soll die Bildinformation umgewandelt werden?
Wie wird implantiert?

Labor, Tests, Versuche,Labor, Test Tests, Versuche,Labor Tests, Versuche,Labor Tests, Versuche,Labor Tests, Versuche,Labor…….

2000

Subretinal Implant, ARS

Chow AY: January 2000, the FDA authorized
Optobionic Optobionics to implant their Artificial Silicon Retina™ (ASR™)



No light perception in ambient daylight

Chow AY: Artificial Silicon Retina Microchip for the treatment of vision loss from RP 2002-3 (Arch.Ophthalmol.2004 (April) 122, pp 460-469)

2009

2000

Subretinal Implant, ARS

Chow AY: January 2000, the FDA authorized
Optobionic Optobionics to implant their Artificial Silicon Retina™ (ASR™)

2002

Epiretinal implant, retinal Prosthesis

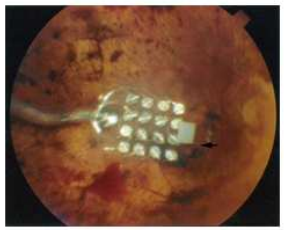
2002 FDA approval received

M. Humayun, Eu. DeJuan

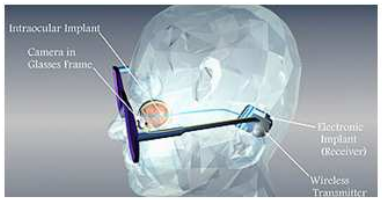
Doheny Retina Institute at the University of Southern California

Second sight

Intraocular Retinal Prosthesis Group



4X4 Retinal Prosthesis
Operation 6-8 hours



Six patients, computer generated perception

2009

2000

2002

2003

2009

Subretinal Implant, ARS

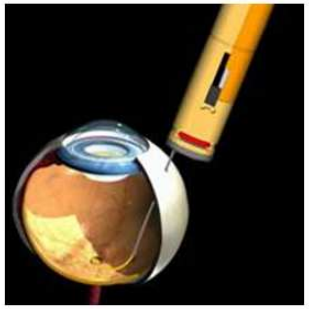
Chow AY: Optobionic January 2000, the FDA authorized Optobionics to implant their Artificial Silicon Retina™ (ASR™)

Epiretinal implant, retinal Prosthesis

European multicenter trial (2002-2003)

Treshold evaluation study (RP patients), 2002 authority approval
IMI Intelligent medical implant

- G.Richard, Dept. of Ophthalmology, University Medical Center Hamburg-Eppendorf, Hamburg
- N. Bornfeld, Th. Laube, Dept. of Ophthalmology, University Medical Center Essen, Essen
- P. Walter, G. Rössler Dept._ of Ophthalmology, University Medical Center Aachen, Aachen
- M. Velikay-Parel, Dept. of Ophthalmology, University Medical Center Vienna



Knowledge gain:
Threshold charges: 20 to 768 nC with single or multiple electrodes .
Size of electrodes 200-300 µm.
Patients with end stage RP over decades can show low thresholds.

2000

2002

2003

2005

2009

Subretinal Implant, ARS

Chow AY: Optobionic January 2000, the FDA authorized Optobionics to implant their Artificial Silicon Retina™ (ASR™)

Chow AY: Artificial Silic
(Arch.Ophthalmol.2004

Epiretinal implant, retinal Prosthesis

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IMI Intelligent medical implant

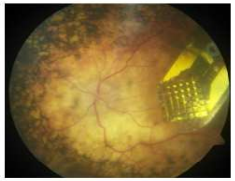
- G.Richard, Dept. of Ophthalmology, University Medical Center Hamburg-Eppendorf, Hamburg
- N. Bornfeld, Th. Laube, Dept. of Ophthalmology, University Medical Center Essen, Essen

Early Human Trial

IMI Intelligent Medical Implant

2005-2006

4 patients enrolled, Hamburg
ARVO 2006, Club Jules Gonin, Euretina,…



Knowledge gained:

- Threshold charges lower than in acute trial
- Human biocompatibility
- Simple pattern recognition,
  point to point discrimination verified
- Evaluation of stimulation strategies

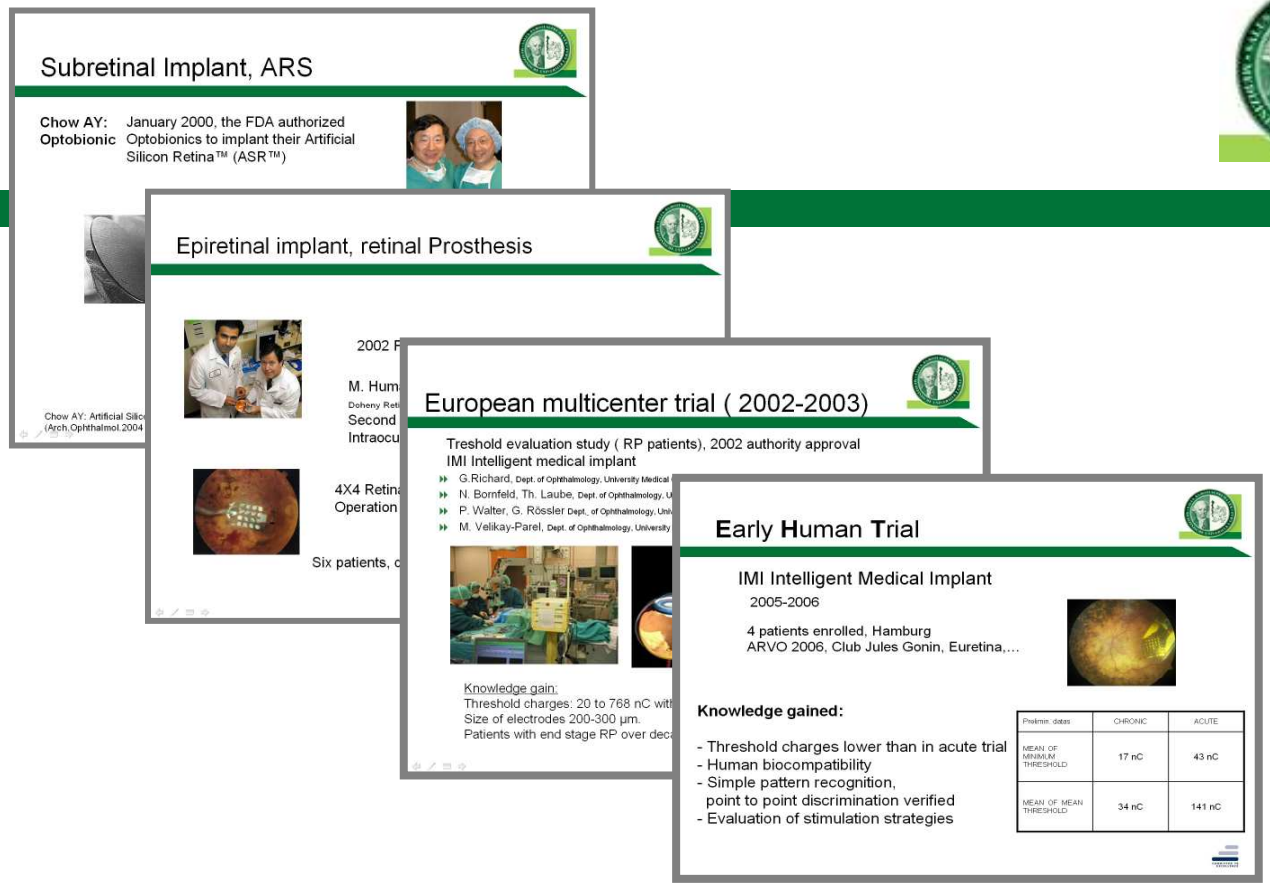
Prelimin. datas	CHRONIC	ACUTE
MEAN OF MINIMUM THRESHOLD	17 nC	43 nC
MEAN OF MEAN THRESHOLD	34 nC	141 nC

2000

2002

2003

2005



Derzeit laufende Studien:

(sub) Retinal Implant	**2005**	**Retina Implant AG**
(epi) Retinal Implant	**2006**	**IMI Intelligent Medical Implant**
(epi) Retinal Implant	**2007**	**Second Sight**
(epi) Retinal Implant	**2008**	**EpiRet GmbH**

2009

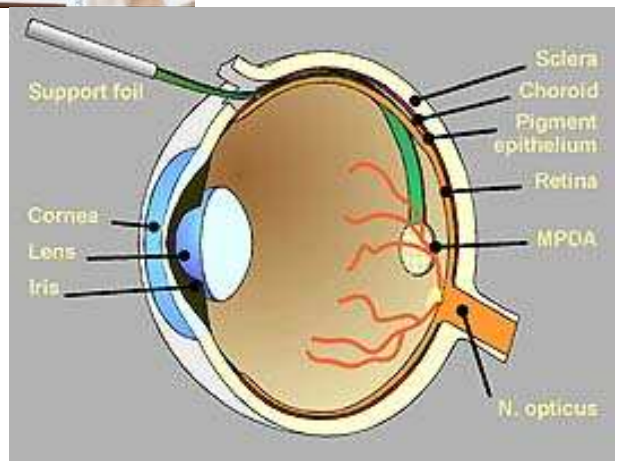
Technologie
Sehwahrnehmung

Subretinal Implant

2005

Retina Implant AG

NCT00515814

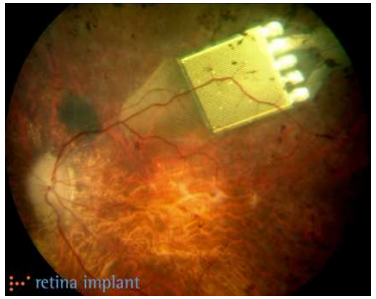


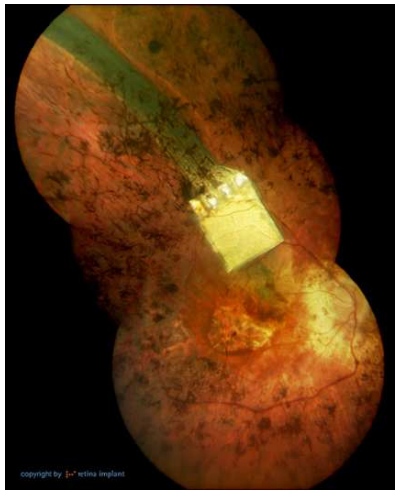
1500 mikrophotodiodes, 4x4 electrodes
external Amplification,
retro-auricular transdermal cabel ending
radio-controlled battery driven stimulation box

Subretinal Implant

Visual field: 8° - 12°
Silicon oil
4 weeks

11 Patients, extension to 3 months in the last 3 patients,
one patient refused the explantation

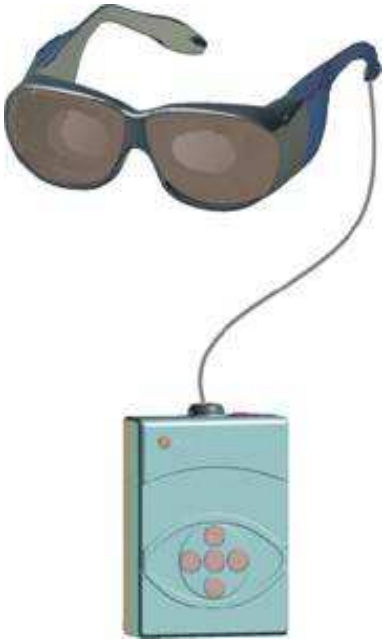




Intelligent Retinal Implant SystemTM

2006
IMI Intelligent Medical Implant
NCT00427180 Eurpean Multicenter Trial

61 Electrodes
Wireless energy transmission
Optical infrared data transmission
18° visual field



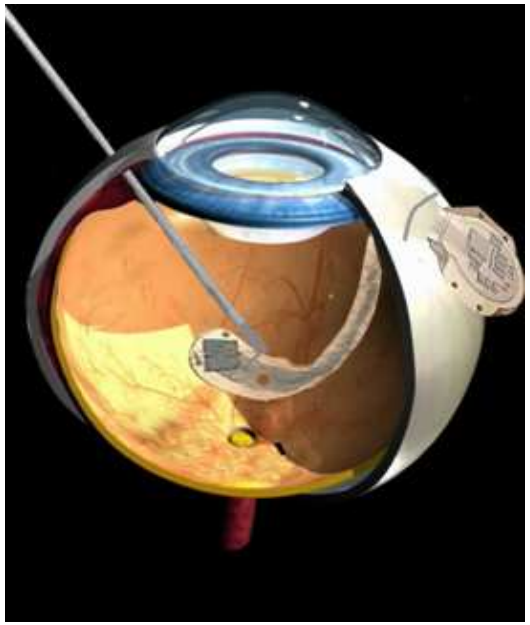
Visual Interface with integrated Camera

Pocket Processor

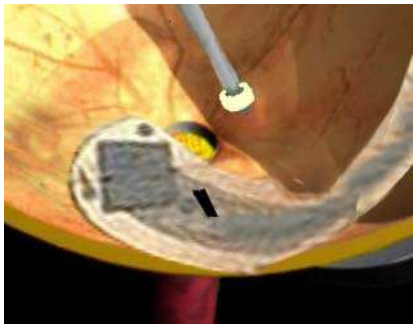
highly adaptable System

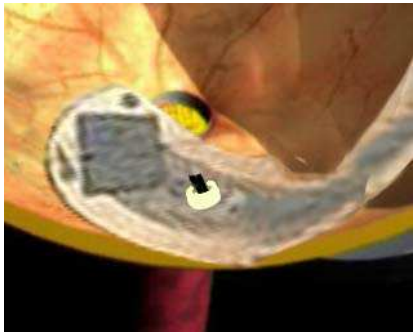
Zoom

Intelligent Retinal Implant SystemTM



2.5 hours



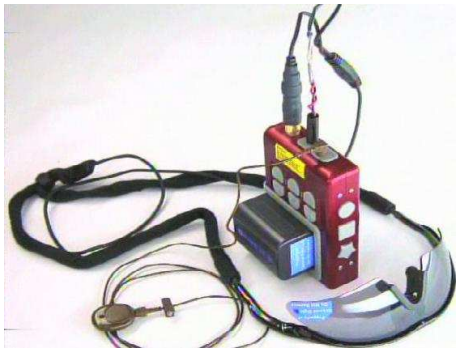


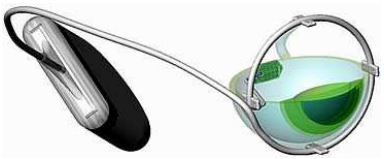
Option for atraumatic explantation

Argus™ II Retinal Stimulation System

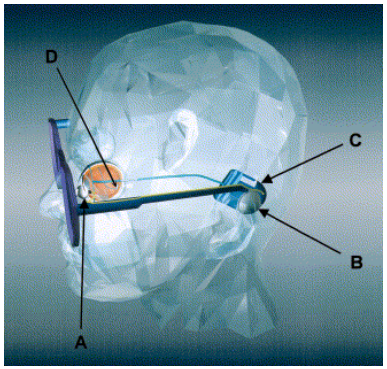
2007
Second Sight
NCT00407602

Change of implant design

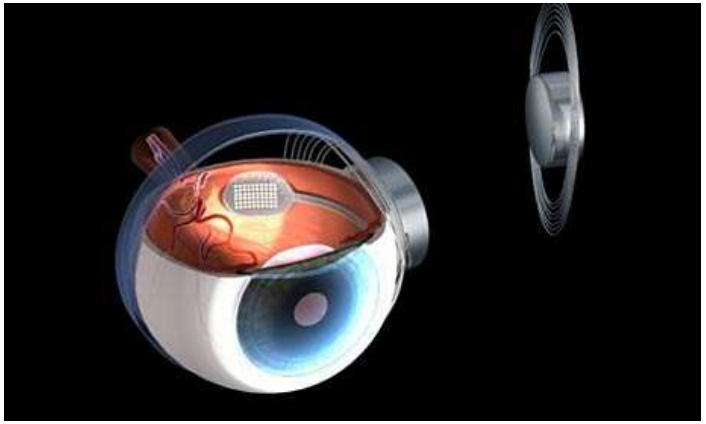




4x4



6-8 hours



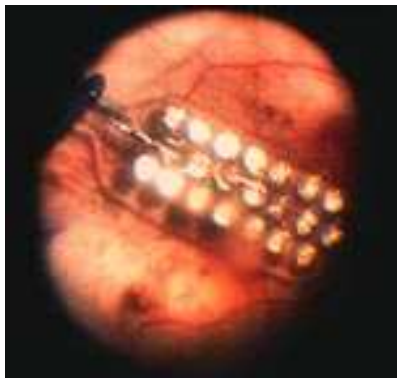
2-3 hours

Argus™ II Retinal Stimulation System

2007
Second Sight
NCT00407602

USA,
Mexico,
France, UK, Switzerland

60 electrodes

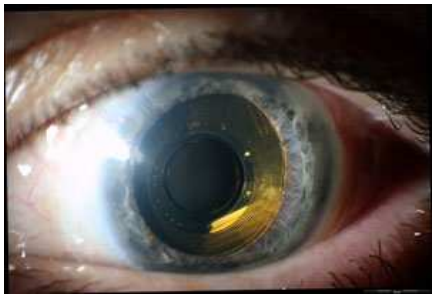


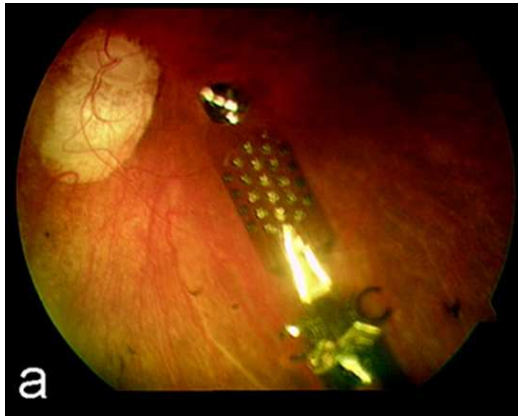
complications n=17: 4 hypotony, 5 conjunctival erosion, 3 endophthalmitis

Epiretinal Implant

2008

EpiRet GmbH





25 electrodes

6 patients
4 weeks

Wireless
Electromagnetic data transfer
Computer generated

complications : 1 steril hypyon, 1 retinal breack

Was sieht man damit ?

- Derzeit keine Resultate, Versuche noch nicht beendet.
- Derzeit nur Zwischenberichte und Medienberichte.
- Versuche dienen dazu, herauszufinden, ob die erzeugten Lichtpunkte auch zu einem sinnvollen Bild zusammengesetzt werden können.
- Wissenschaftlich bedeutet das: Wie können wir am Besten stimulieren und gleichzeitig den Patienten trainieren? Wie schnell lernt der Patient?

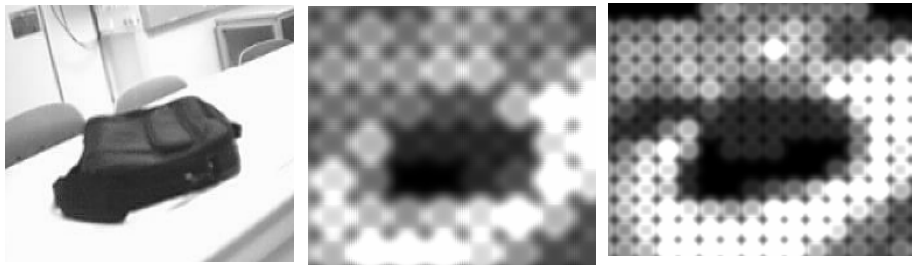
Was sieht man damit ?

- Wir sind erst bei den Anfängen !!!
- Die wenigen Lichtpunkte haben auch ein geringes Auflösungsvermögen.

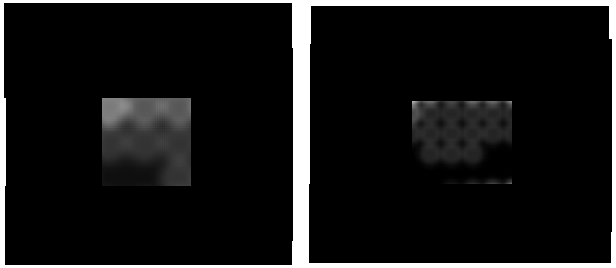
Wie kann man sich das Neue Sehen vorstellen?

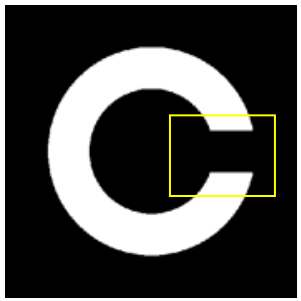
Was sieht man damit ?

Sehschärfe und Gesichtsfeld



GF of 12°
(app.11cm 17 inch screen)





Bei dieser Sehwahrnehmung ist das Gesichtsfeld gleichwichtig wie die Sehschärfe !!!!

Was sieht man damit ?

Eines der Ziele ist eine Verbesserung in der Orientierung zu erreichen.

- Unsere Orientierung: Informationen aus der Wahrnehmung werden zu einem räumlichen Bewußtsein zusammengesetzt. Das ist der wesentliche Schritt der Orientierung.
- Diese Informationen setzt sich aus einer Kombination unserer Sinne zusammen:

  Sehen
  Hören
  Riechen
  Tasten
  Proprioception= Eigenwahrnehmung des Körpers

Was sieht man damit ?

Functional Results

Subretinal implant:

ARVO 2006+7
8 patients
4 weeks
Pattern recognition (4x4)

Arvo 2006:
Subretinal Chronic Multi–Electrode Arrays in Blind Patients: Perception of Dots and Patterns
R. Wilke, C. Kuttenkeuler, B. Wilhelm, H. Sailer, H. Sachs, V.–P. Gabel, D. Besch, K. Bartz–Schmidt, E. Zrenner, and Subretinal Implant Study Group

ARVO 2007:
Psychometric Analysis of Visual Sensations Mediated by Subretinal Microelectrode Arrays Implanted Into Blind Retinitis Pigmentosa Patients
E.Zrenner1, R.Wilke1, T.Zabel1, H.Sachs2, K.Bartz-Schmidt1, F.Gekeler1, B.Wilhelm3, U.Greppmaier4, A.Stett5, SUBRET Study Group.

ARVO 2008
3 Pat logMar 1,85
1 Pat: 8,5 cm high, 1.7 cm line width, 62 cm distance

ARVO 2008 :
Blind Retinitis Pigmentosa Patients Can Read Letters and Recognize the Direction of Fine Stripe Patterns With Subretinal Electronic Implants
E. Zrenner1, R. Wilke1, K. Bartz-Schmidt1, H. Benav1, D. Besch1, F. Gekeler1, J. Koch1, K. Porubská1, H. Sachs2, B. Wilhelm3.

Functional Results

Argus™ II Retinal Stimulation System

ARVO 2009

July 2009 32 Patients
FDA 2009 another 20 Patients

Paul Chinn / The Chronicle

The Argus II Retinal Prosthesis Enables Blind Subjects to Localize Objects
M.J. McMahon1, J.D. Dorn1, A.K. Ahuja1, A. Caspi1, E. Filley2, G. Dagnelie3, R.J. Greenberg1
12 subjects: 8 subjects responded significantly more accurate and more clustered with the system on than with it off ($p<0.05$).

The Argus II Retinal Prosthesis Enables Blind Subjects to Identify the Direction of Motion*A.K. Ahuja1, J.D. Dorn1, A. Caspi1, E. Filley2, G. Dagnelie3, R.J. Greenberg1, M.J. McMahon1*
Four subjects did not have significantly different error distributions with the system on vs. off.

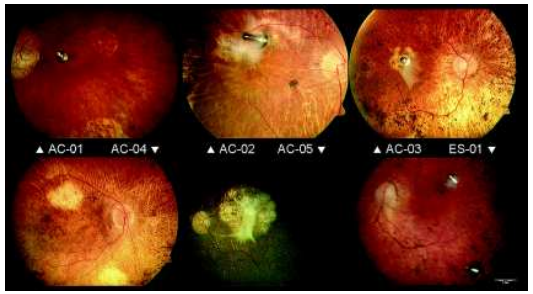
Spatial Summation of Phosphenes With Electrode Pair Retinal Stimulation*D. Nanduri1A, M.J. McMahon2, J.D. Dorn2, M.S. Humayun1A,1B, R.J. Greenberg2, J.D. Weiland1A*

Second Sight received a $26 million 10-year grant from the NIH (October 2009)!!!

Functional Goals

EpiRet GmbH

25 electrodes
6 Patients
4 weeks, all light perception



- Primary Outcome Measures:
- Visual Acuity / Light-perception / Object-orientation
  shown via FrACT / BaLM / grating test
- Secondary Outcome Measures:
- Activities of Daily Living shown via Tasks of Daily Living test / Orientation & Mobility test

Invest Ophthalmol Vis Sci. 2009 Jun;50(6):3003-8

Implantation and Explantation of a Wireless Epiretinal Retina Implant Device: Observations during the EPIRET3 Prospective Clinical Trial

Gernot Roessler,[1] Thomas Laube,[2] Claudia Brockmann,[2] Thomas Kirschkamp,[1] Babac Mazinani,[1] Michael Goertz,[3] Christian Koch,[4] Ingo Krisch,[3] Bernd Sellhaus,[5] Hoc Khiem Trieu,[3] Joachim Weis,[5] Norbert Bornfeld,[2] Harald Röthgen,[6] Arthur Messner,[6] Wilfried Mokwa,[4] and Peter Walter[1]

Purpose. Visual sensations in patients with blindness and retinal degenerations may be restored by electrical stimulation of retinal neurons with implantable microelectrode arrays. A prospective trial was initiated to evaluate the safety and efficacy of a wireless intraocular retinal implant (EPIRET3) in six volunteers with blindness and RP.

Methods. The implant is a remotely controlled, fully intraocular wireless device consisting of a receiver and a stimulator module. The stimulator is placed on the retinal surface. Data and energy are transmitted via an inductive link from outside the eye to the implant. Surgery included removal of the lens, vitrectomy, and implantation of the EPIRET3 device through a corneal incision. The clinical outcome after implantation and explantation of the device was determined. The implant was removed after 4 weeks, according to the study protocol.

Results. Implantation was successful in all six patients. While the anterior part was fixed with transscleral sutures, the stimulating foil was placed onto the posterior pole and fixed with retinal tacks. The implant was well tolerated, causing temporary moderate postoperative inflammation, whereas the position of the implant remained stable until surgical removal. In all cases explantation of the device was performed successfully. Adverse events were a sterile hypopyon effectively treated with steroids and antibiotics in one case and a retinal break in a second case during explantation requiring silicone oil surgery.

Conclusions. The EPIRET3 system can be successfully implanted and explanted in patients with blindness and RP. The surgical steps are feasible, and the postoperative follow-up disclosed an acceptable range of adverse events. (*Invest Ophthalmol Vis Sci.* 2009;50:3003–3008) DOI:10.1167/iovs.08-2752

Although major progress has been achieved in the treatment of retinal disorders, the hereditary dystrophies of retinal photoreceptors are still untreatable and eventually lead to blindness. It is estimated that in the Western countries approximately 5% to 7% of newly diagnosed blindness is attributable to retinitis pigmentosa (RP), a heterogeneous group of receptor dystrophies caused by mutations in key enzymes of the visual cycle or major cell-signaling pathways.[1-3]

It has been proposed that electrical stimulation of remaining neurons in the visual system may restore vision in patients with blindness.[4] Research groups worldwide are investigating the use of implantable devices for the electrical stimulation of the retina, the optic nerve, or the brain.[5-7] Several groups have demonstrated that, in subjects with blindness and RP, phosphenes can be elicited by stimulation of the retina.[8-10]

One of the major problems with the devices currently under investigation is the sufficient transfer of data and energy from an external device to the implanted stimulator. This transfer is usually achieved by a cable connecting an external power supply with the implant inside the eye. Other major concerns are (1) the positioning of the stimulating electrodes as close as possible to retinal neurons, (2) the safety limits of the electrical current applied to the tissue, (3) the avoidance of adverse electrochemical processes at the interface between the electrode material and neural tissue, and (4) the transfer of enough information into the visual system to provide useful visual perception.

The EPIRET3 retinal prosthesis is designed and fabricated as a remotely controlled wireless device implanted completely within the eye. No cable connections crossing the eye's wall

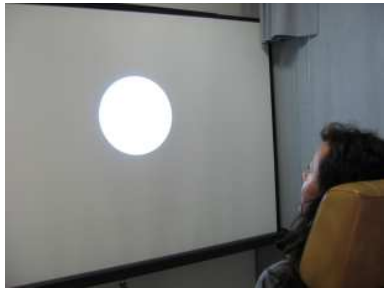
COMMITTED TO EXCELLENCE

Functional Goals

IMI Intelligent Medical Implant

Standardised evaluations with the camera mode:

- Light perception test accomplished
- Light localisation test accomplished
- Motion direction test accomplished



Video ⇨

VF 16°

ARTIFICIAL
VISION CENTER

COMMITTED TO
EXCELLENCE

Schlußfolgerung

- Eine sinnvolle Wahrnehmung ist erzielbar. Wir wissen, daß das Gehirn lernt die Reize umzusetzen.
- Die erzielten Ergebnisse entsprechen der Erwartung.
- Biologische Verträglichkeit ist bestätigt

- Die Versuche sind aufwendig.
- Die selbe Technologie – unterschiedlicher Fortschritte
- Nicht alle Patienten profitieren von dem Systemen.
- Erfahrungen helfen die Systeme entsprechend zu adaptieren.(Technologieverbesserungen)