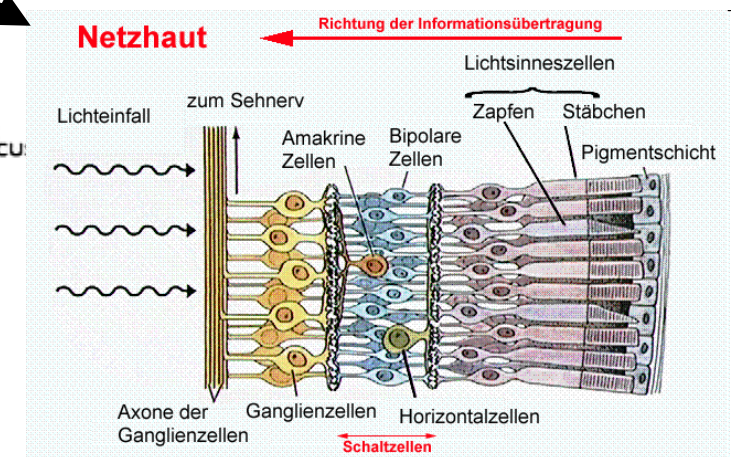
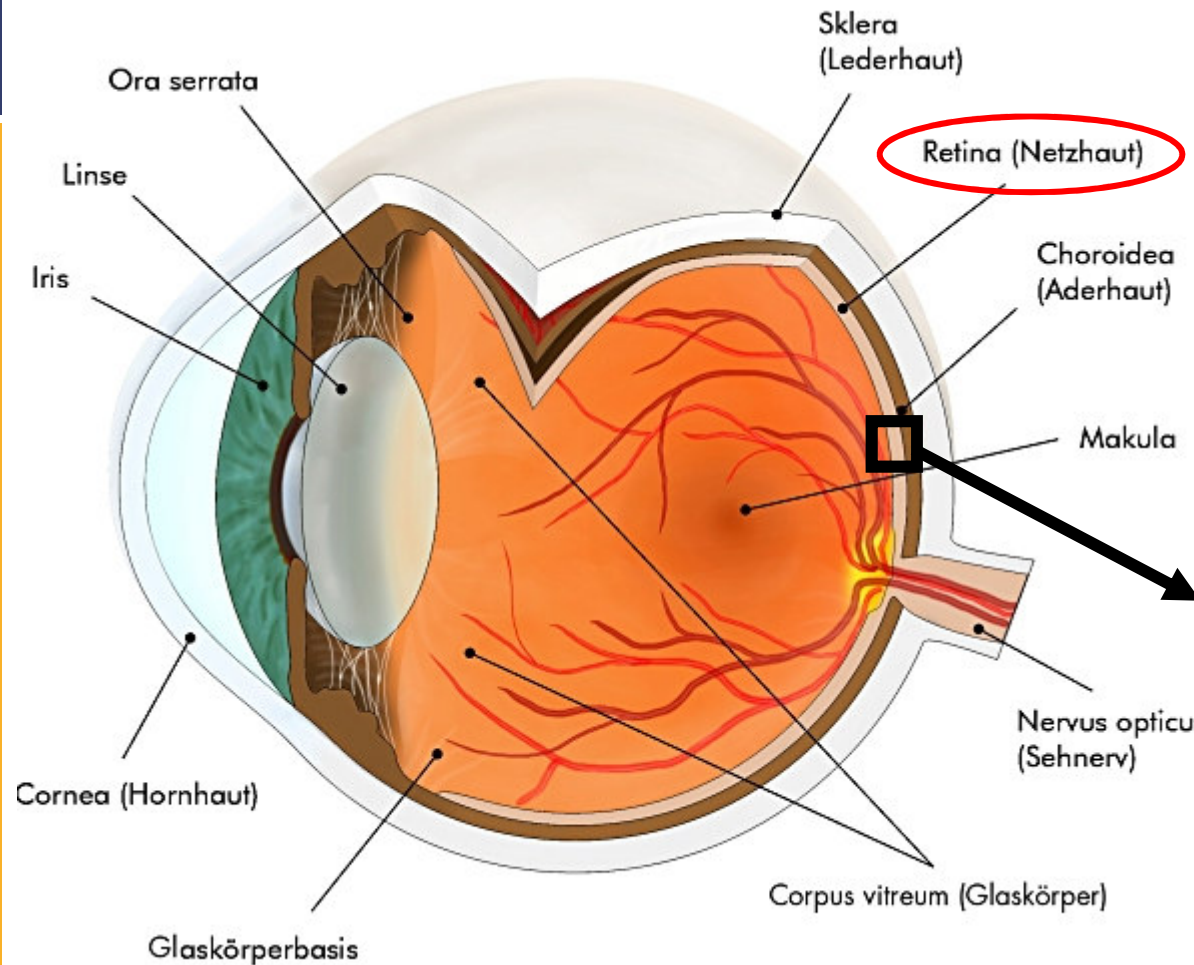




Retina Implant

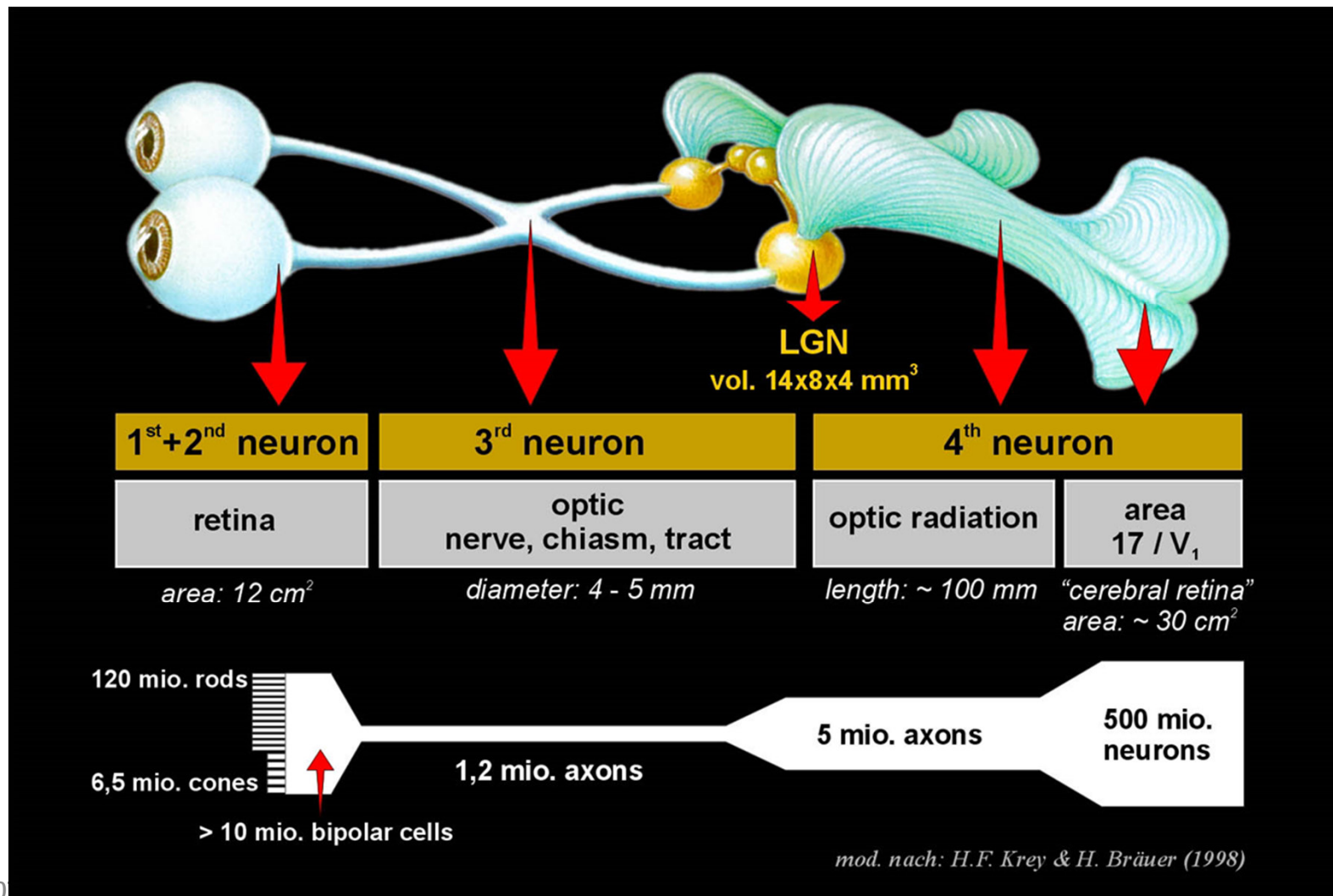
PD Dr. med. Katarina Stingl
Center for Ophthalmology

24.7.2017



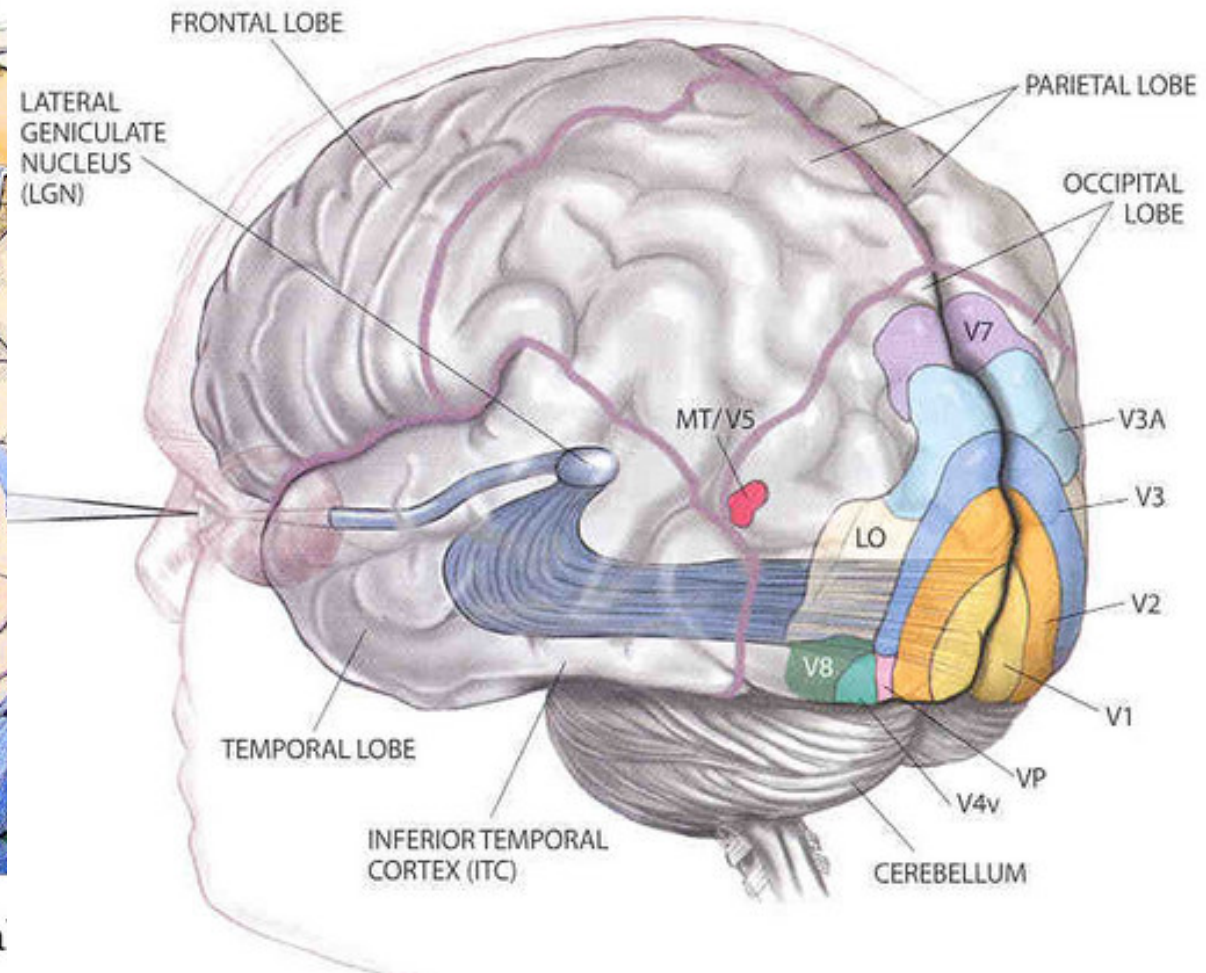
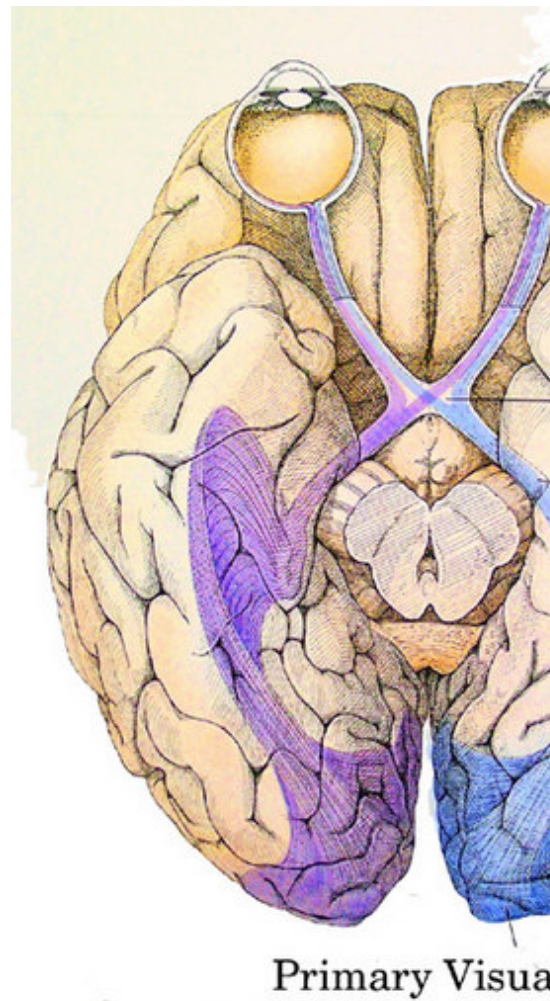


Visual Pathway





Visual cortex





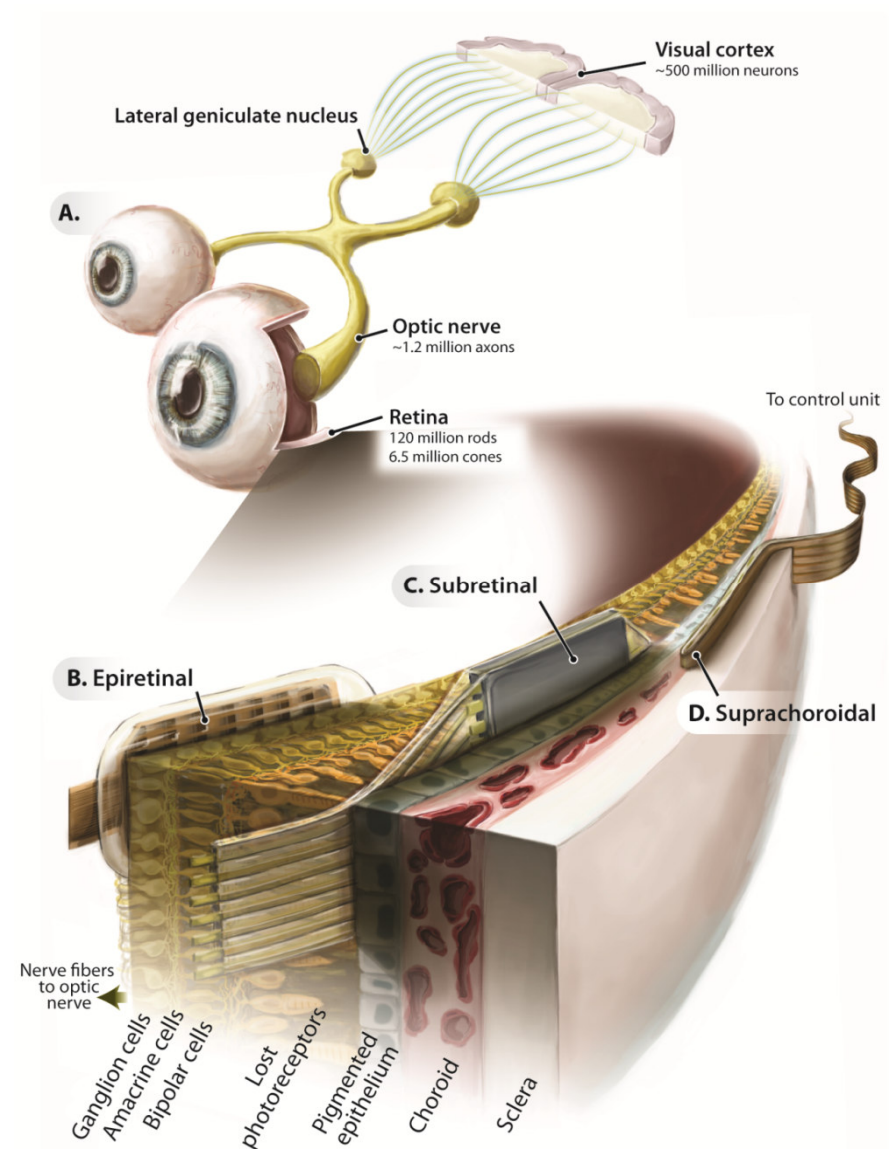
Visual cortex

- Central retina has the most important role for object processing
- Inner 5° visual field are projected onto 50% visual cortex
the most of it belongs to 2,5° visual field
- Ocular columns (Orientation, etc.) in V1
- Pattern recognition beyond 5° visual field: crowding



Implants

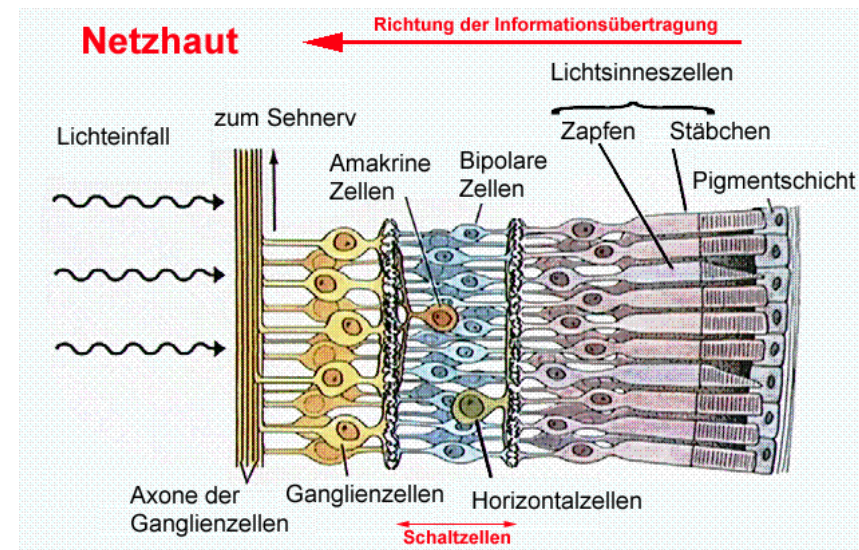
- Subretinal
- Epiretinal
- Suprachoroidal
- Optic nerve cuffs
- Cortical





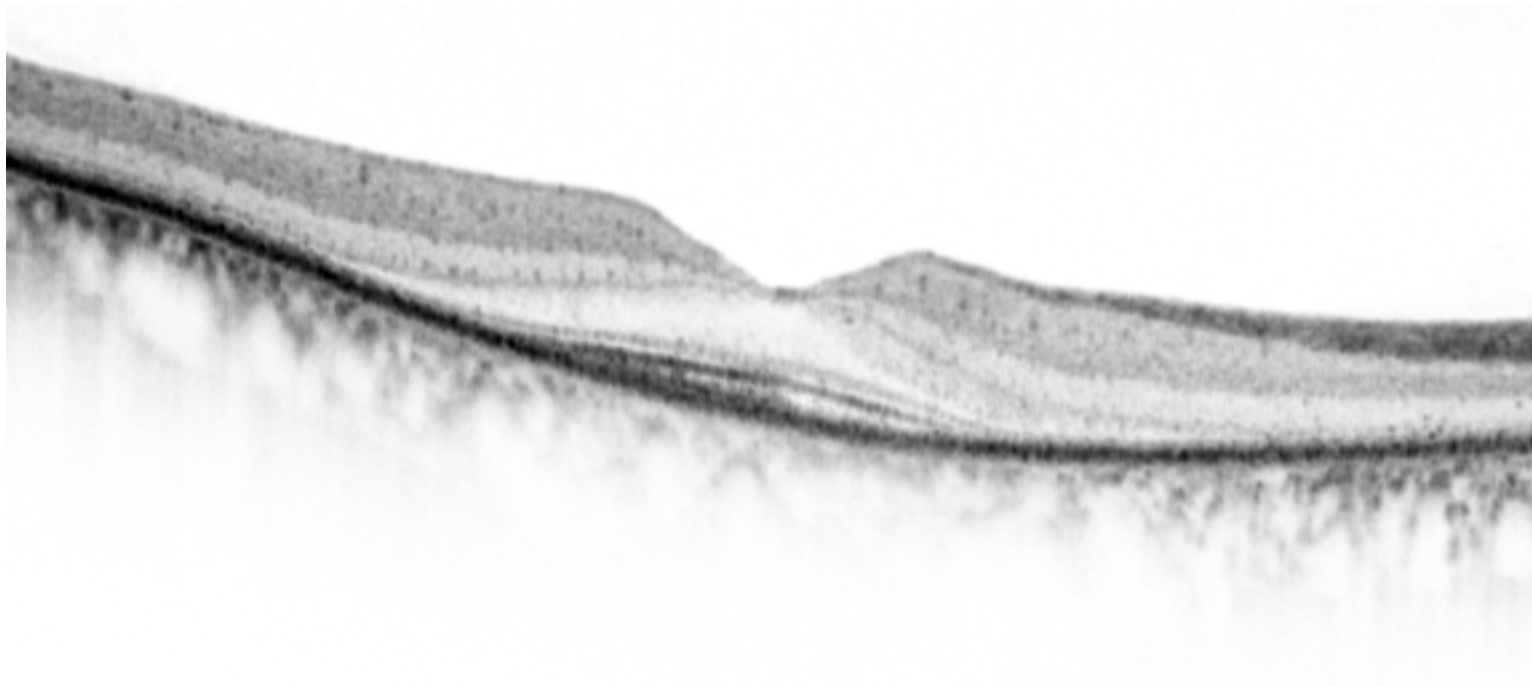
Hereditary retinal degenerations

- Degeneration of the photoreceptors
- Blindness in middle age
- No approved causal therapy



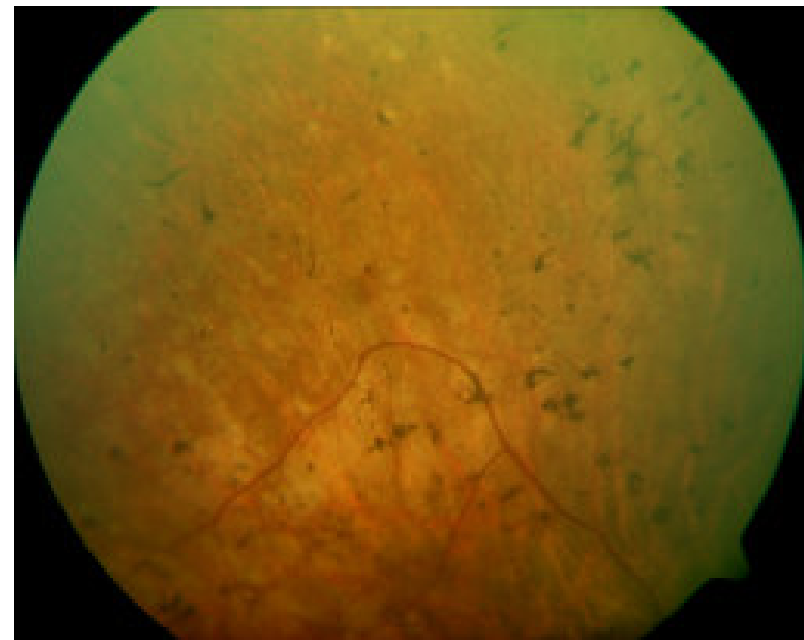
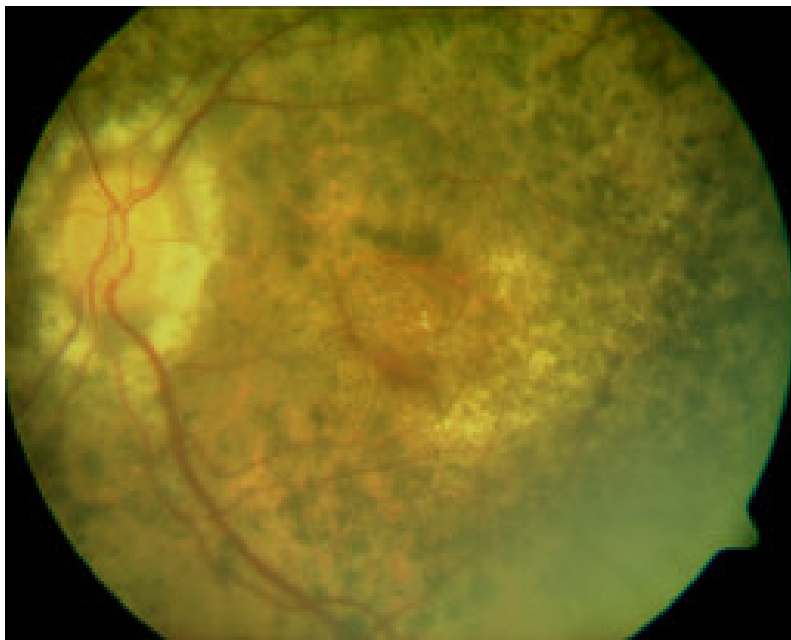


Retinitis pigmentosa





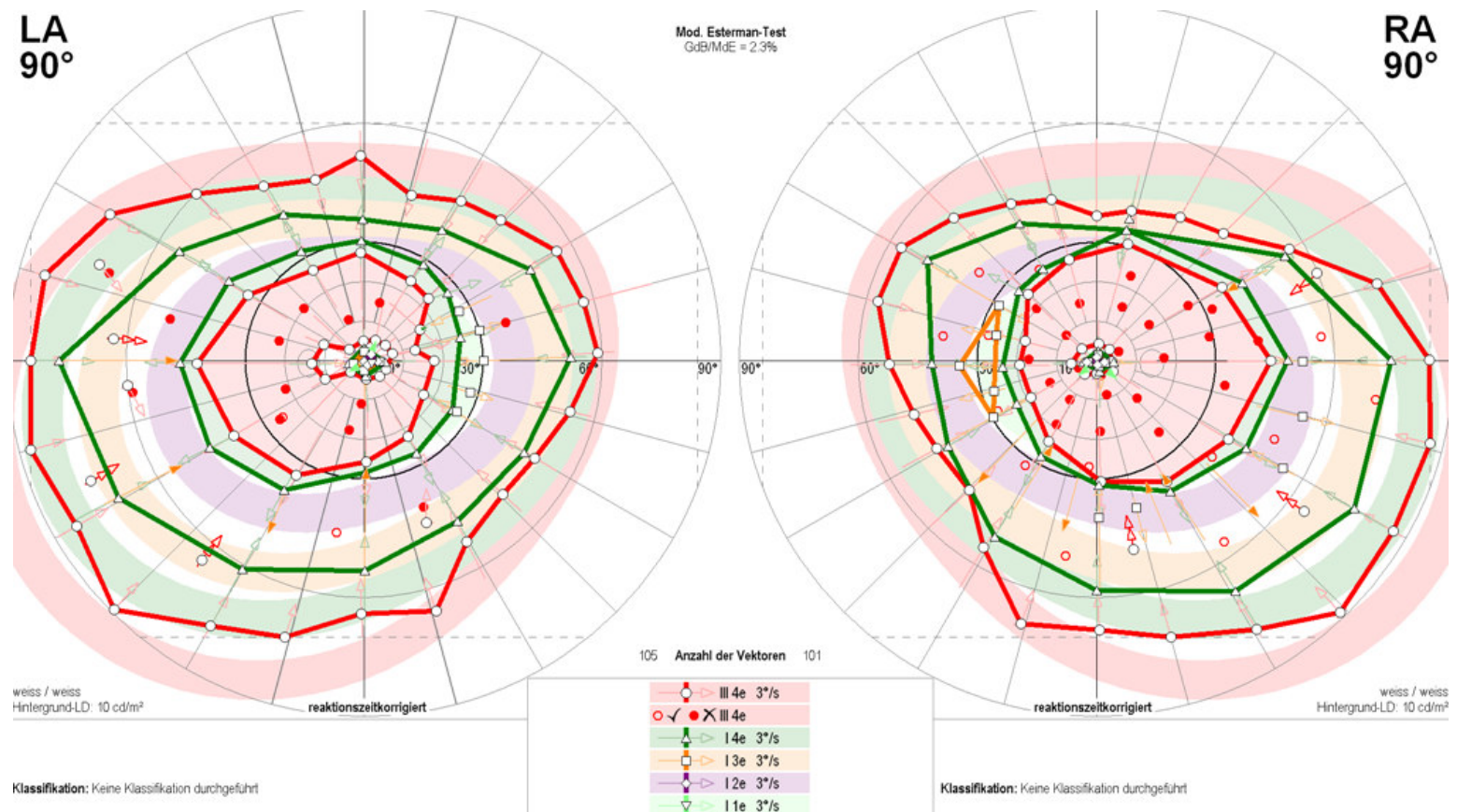
Pigments





Symptoms

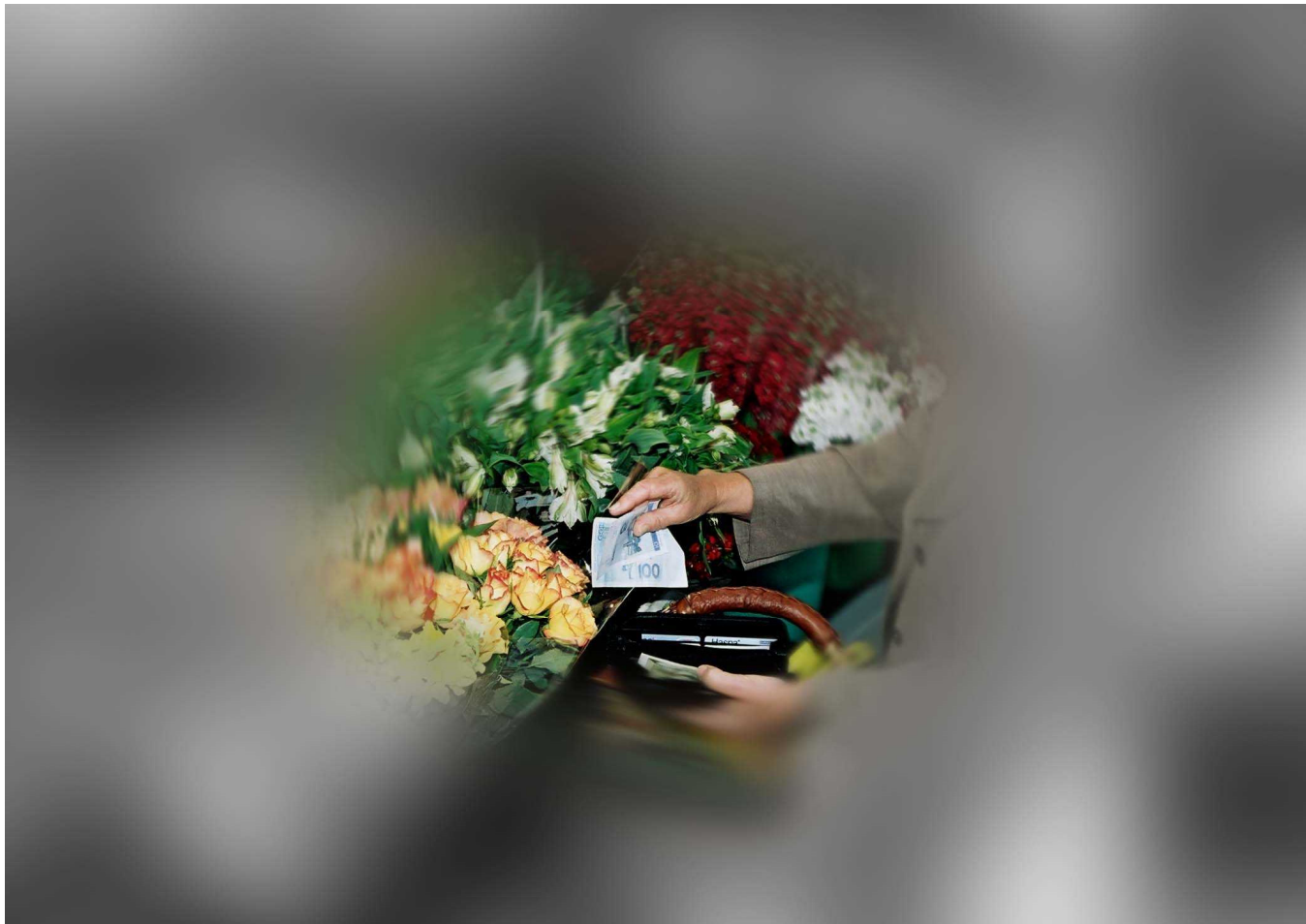
- Night blindness
- Visual field defects, tunnel vision



25.07.2018



Retinitis pigmentosa

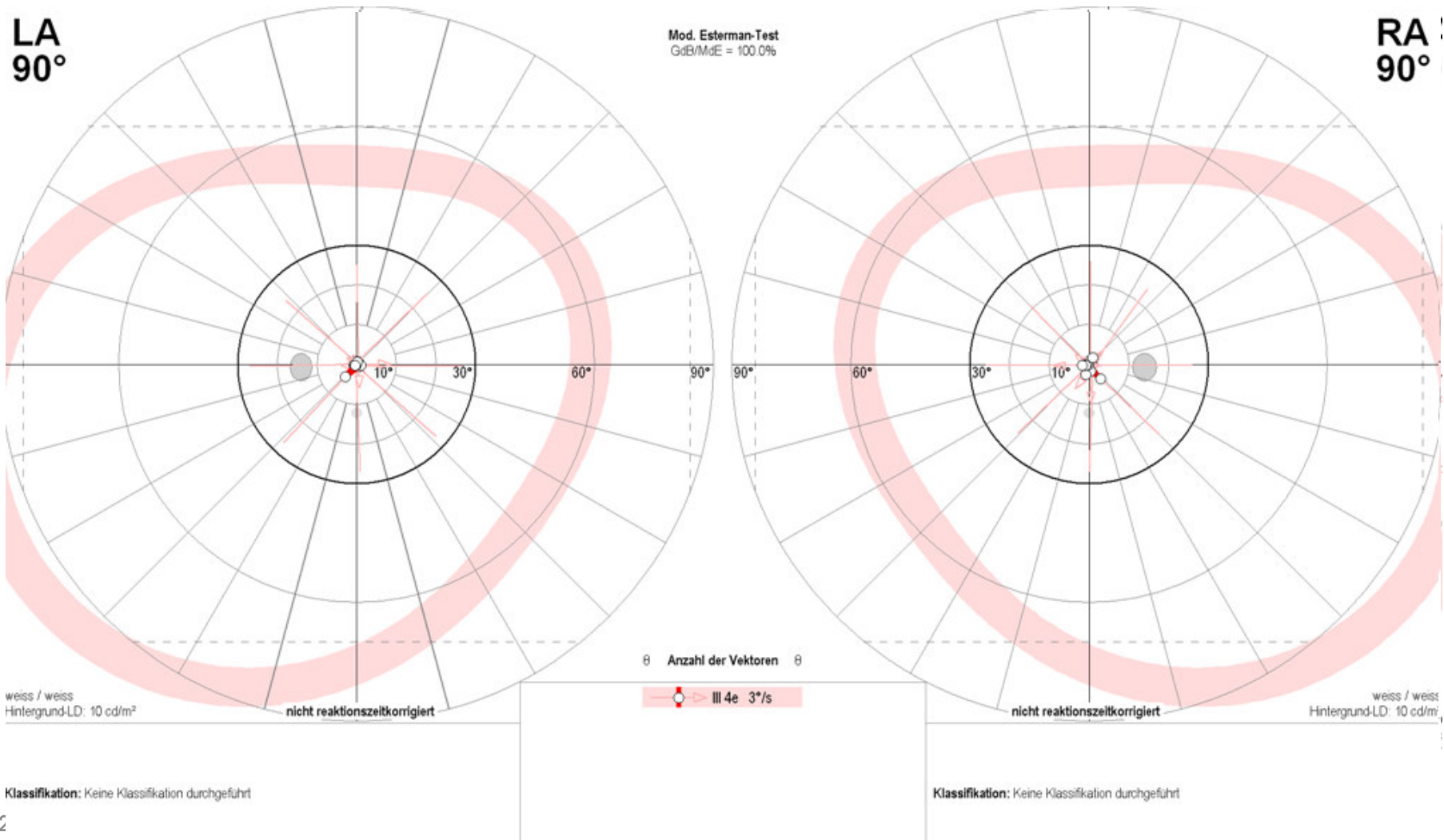


25.07.2018

Institute for Ophthalmic Research



Retinitis pigmentosa



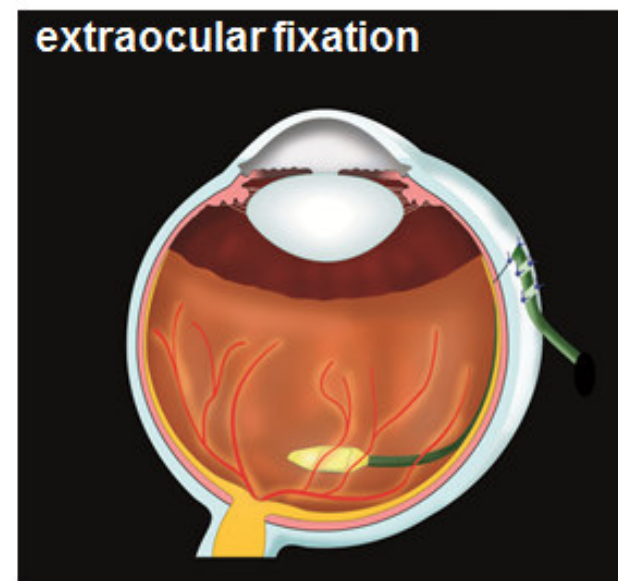
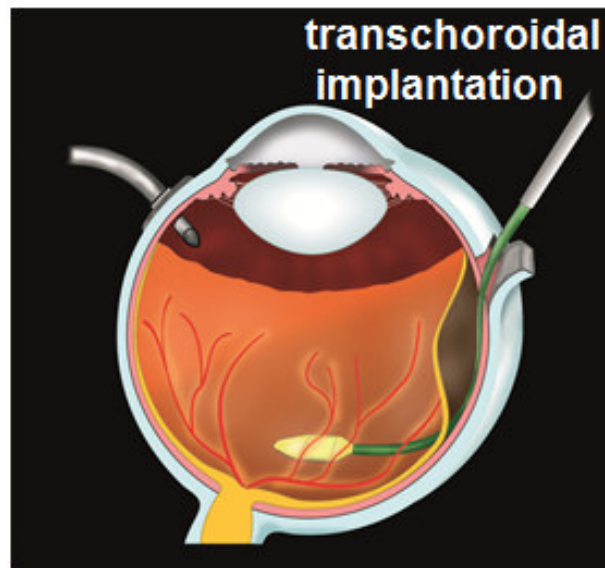
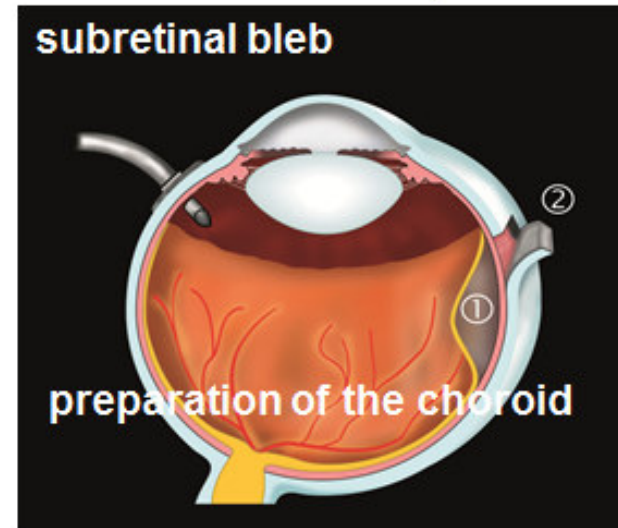
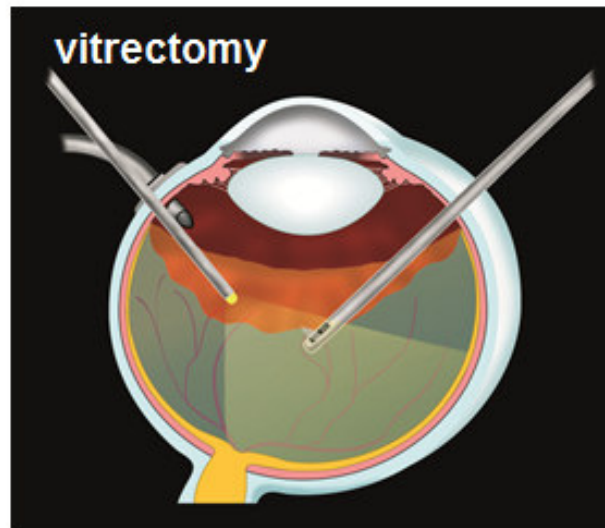


Visual implants

SUBRETINAL



Scheme of the transchoroidal implantation



Retina Implant

- Historical overview Tübingen
- Pilot trial – CE approval
- 1990–ies preclinical tests
- Biocompatibility
- Center for Ophthalmology Tübingen (Prof. E. Zrenner)
- NMI Reutlingen, IMS Stuttgart



Retina Implant

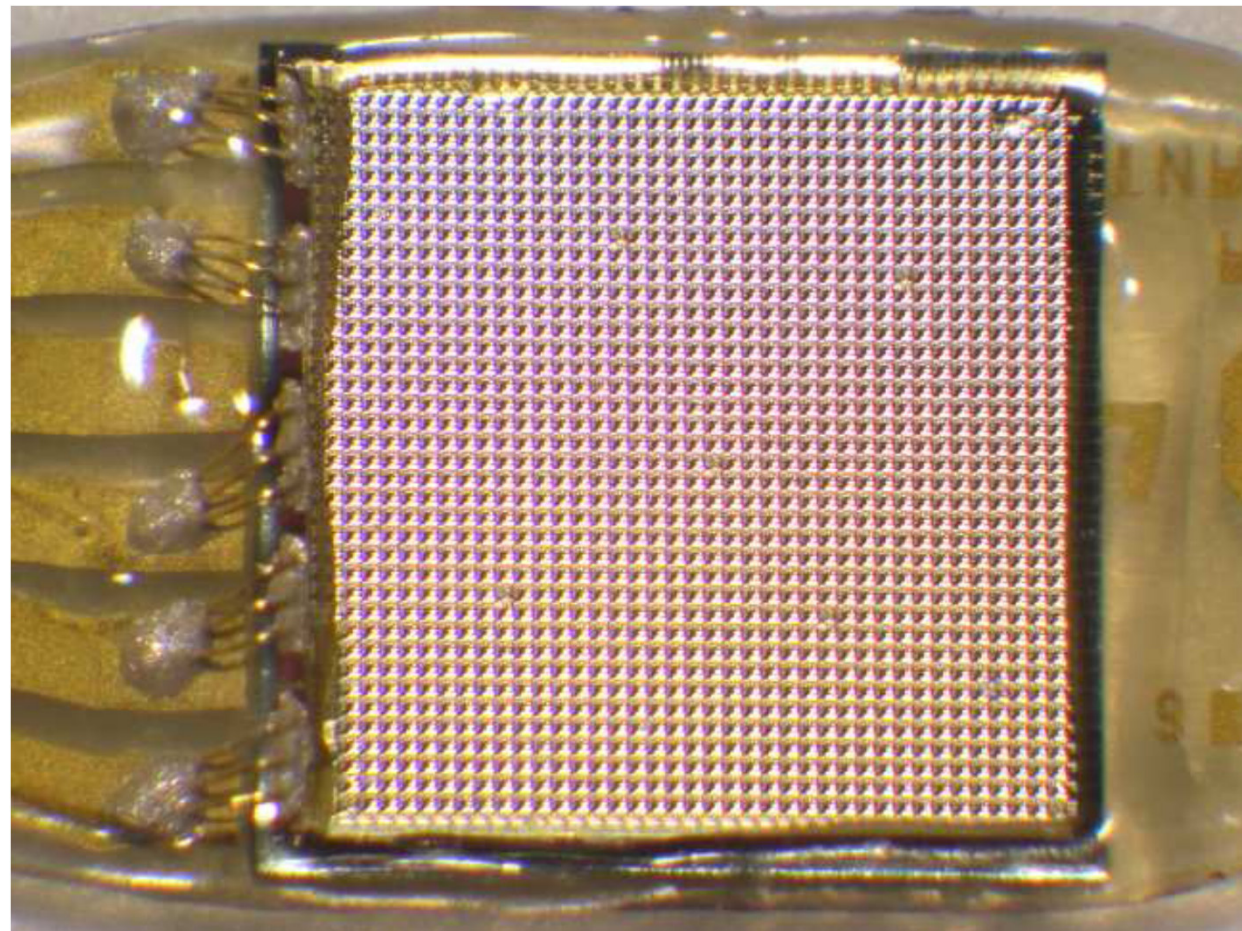
- 2005 – 2009 Pilot trial
- 11 patients received an implant in Tübingen
- 4 weeks





Microchip

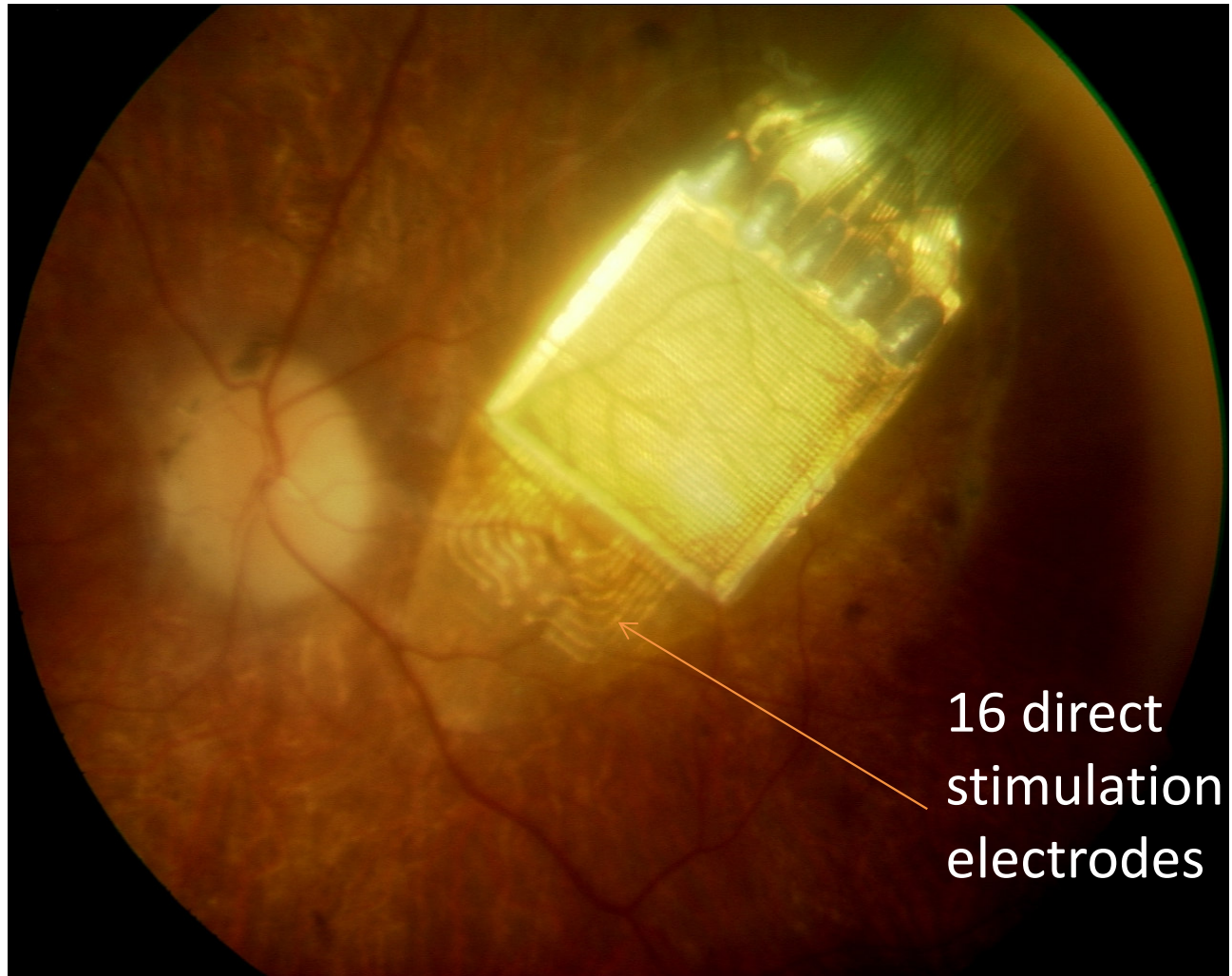
1500 Pixels



3 mm



Pilot trial





Secondary endpoints



Light perception
Grating acuity
Light localization

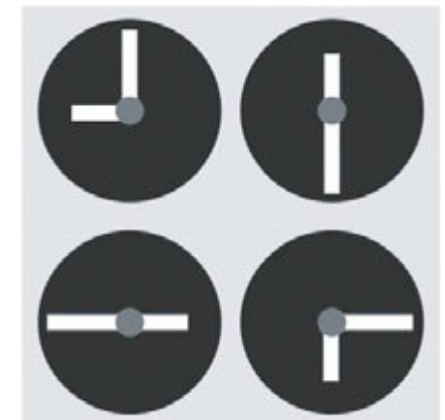


Landolt C-rings
Motion

Primary endpoints



Grey levels
Clock
Letters



Primary endpoints

- Safety
 - No retinal detachment
 - No major hemorrhages
 - No inflammations
 - No vitreoretinal tractions

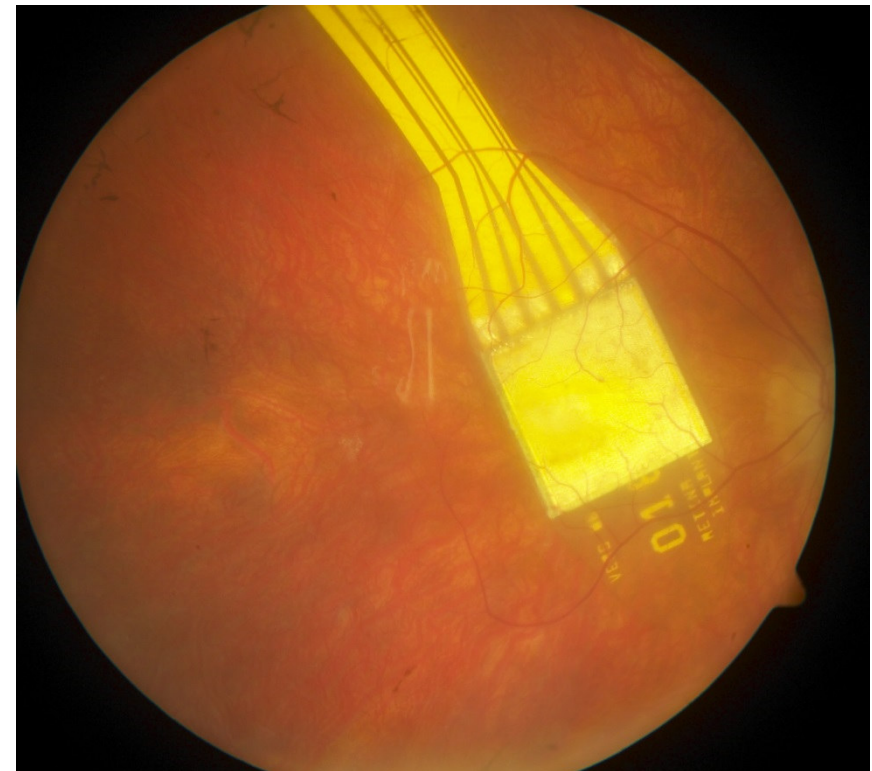
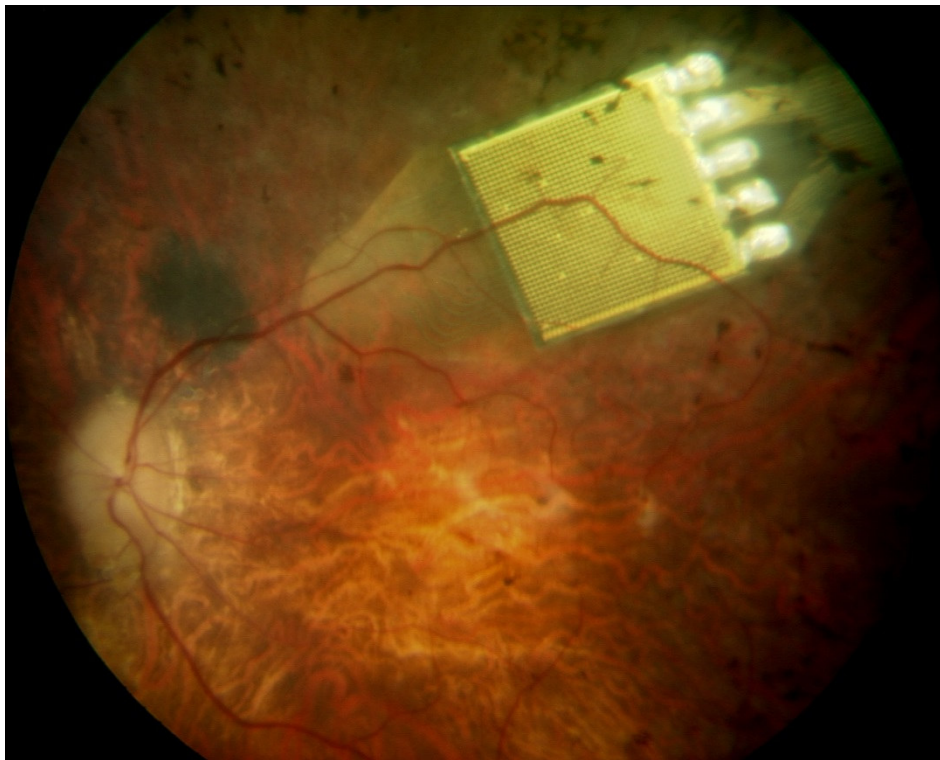
Outcome

- the best visual acuity of 21 / 1 000 (logMAR 1.69) was calculated
- 0,02 = legal blindness in Germany
- grating acuity up to 0.34 cycl./deg
- Object recognition
- Proof of concept



Outcome predictors

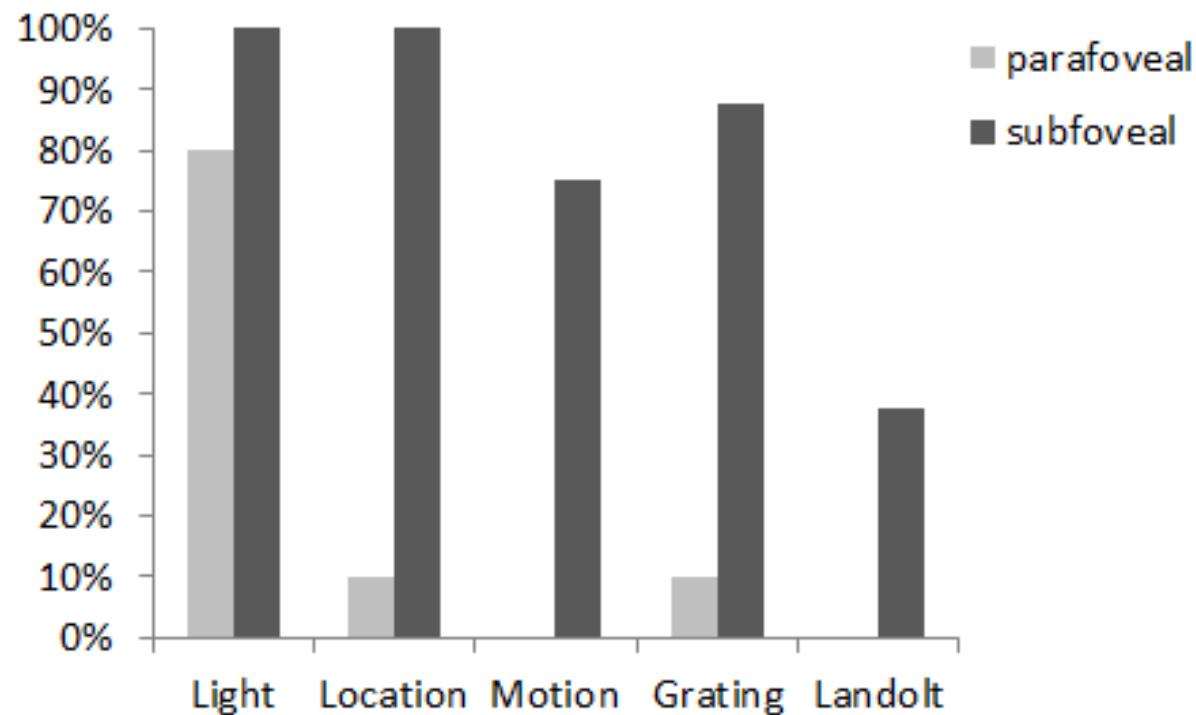
- Eccentricity of chip position





Outcome predictors

- Eccentricity of chip position: subfoveal!



Stingl K. IOVS 2013 Nov 19;54(12):7658-65.



Wireless Retina Implant Alpha IMS

- 2010–2013 multicenter clinical trial
- 29 patients
 - Tübingen, Dresden
 - Oxford, London
 - Budapest
 - Hongkong, Singapur
- Blind; hereditary retinal degenerations
- 2013 CE approval

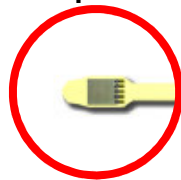


Retina Implant Alpha IMS

Power supply



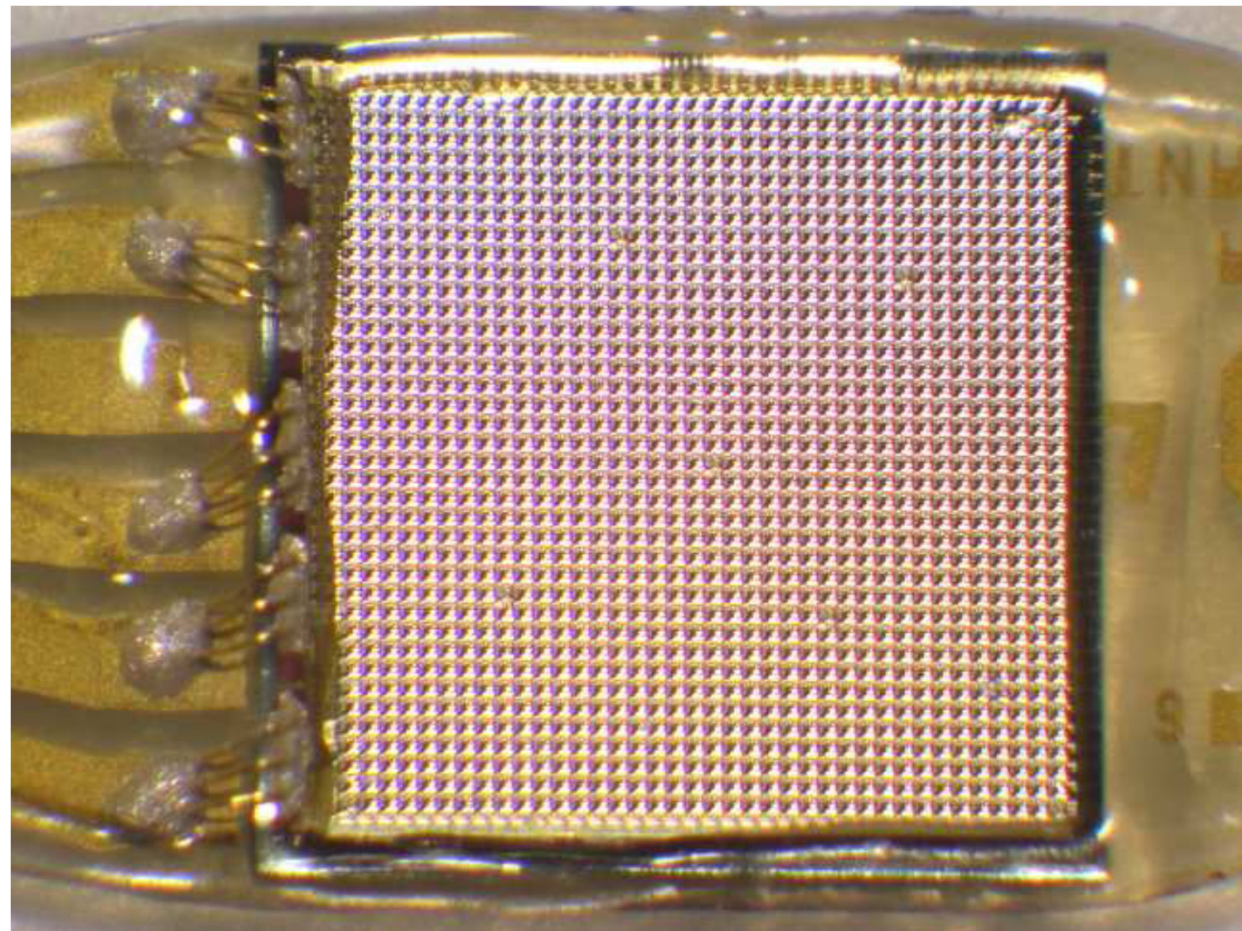
Subretinal chip





Retina Implant Alpha IMS

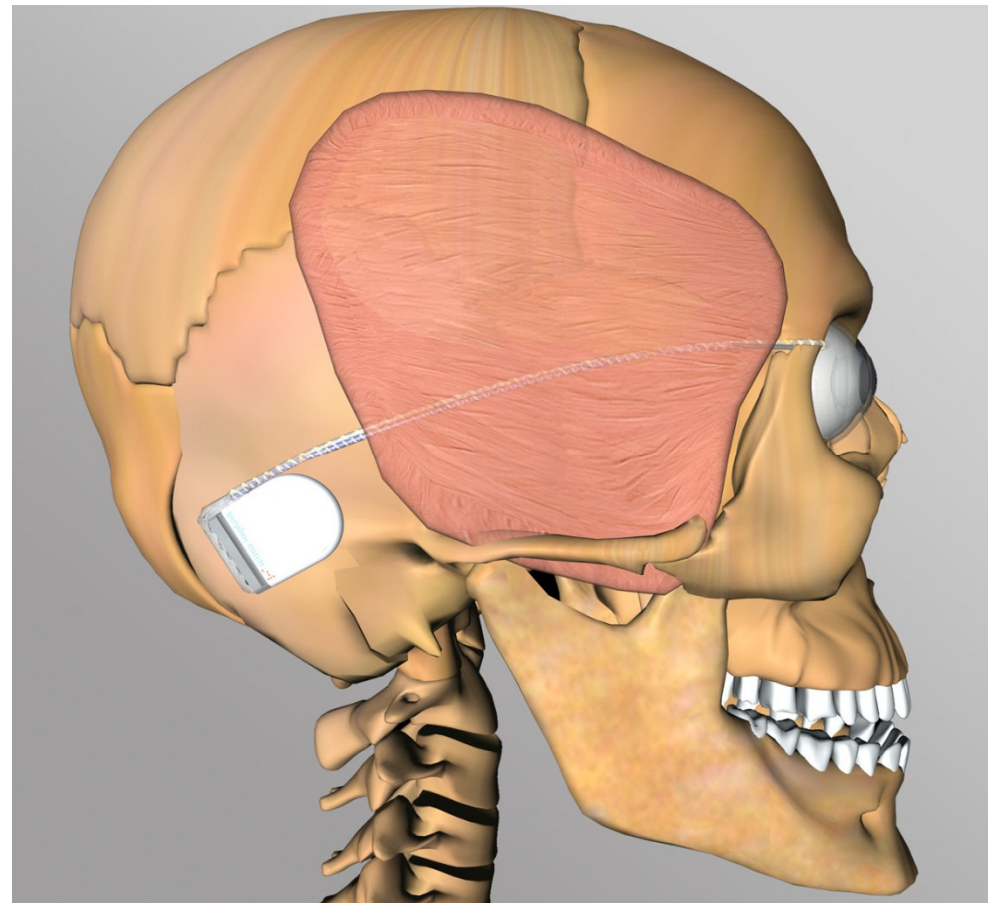
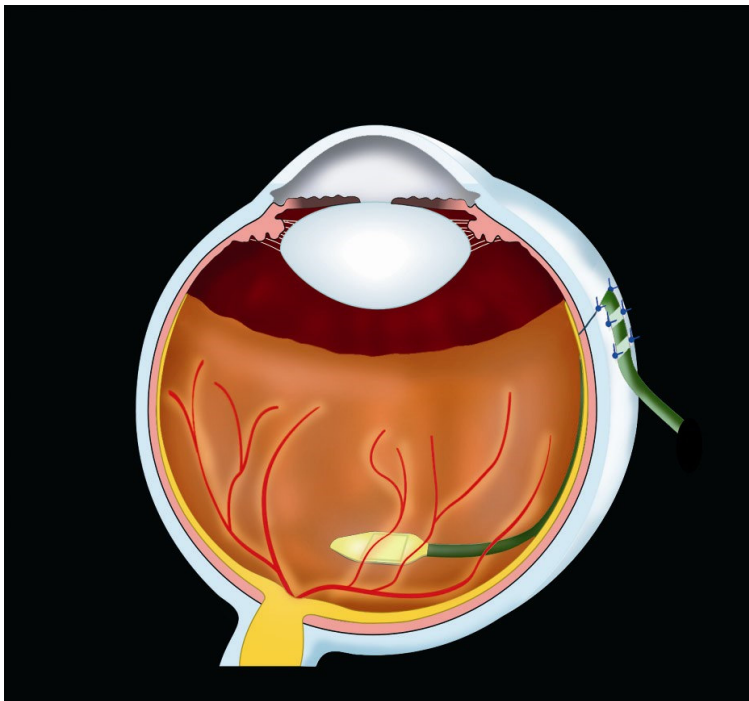
1500 Pixels



← 3 mm →

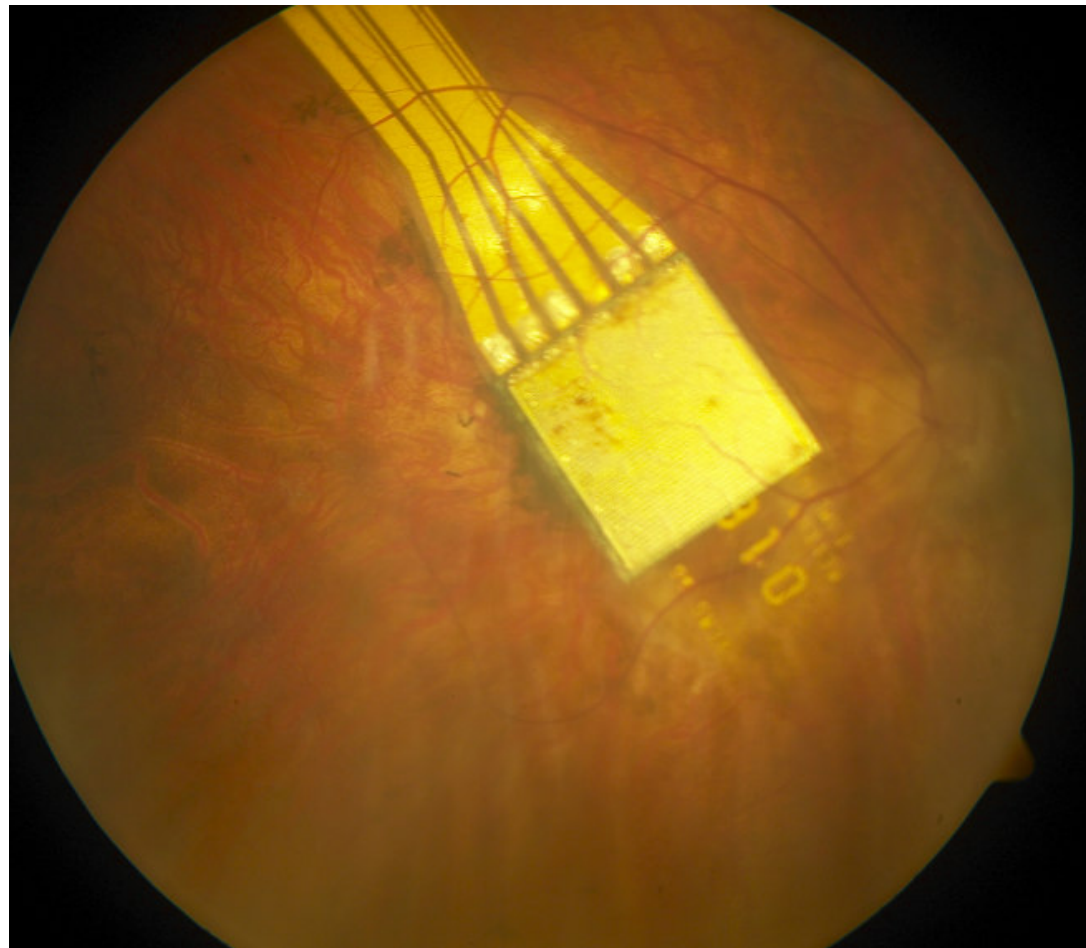


Retina Implant Alpha IMS/AMS





Retina Implant Alpha IMS

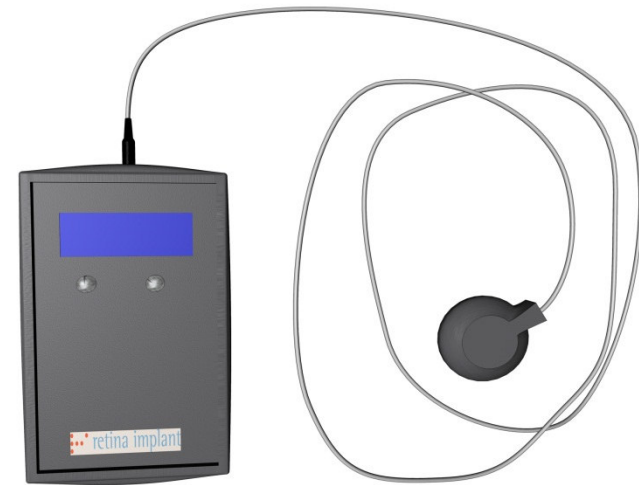




Retina Implant Alpha IMS



- externe power supply
- electromagnetic induction
- magnet





Retina Implant Alpha IMS

- Visual acuity < 0.1
- No color vision
- Visual field $10-15^\circ$
- Manual contrast/brightness adjustment
- Changes blindness into (very) low vision
- Help in orientation



Retina Implant Alpha IMS





Secondary endpoints



Light perception
Grating acuity
Light localization

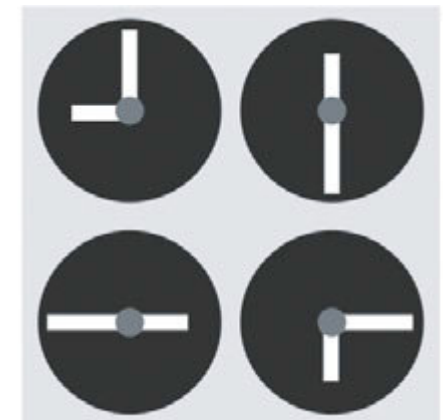


Landolt C-rings
Motion

Primary endpoints



Grey levels
Clock
Letters



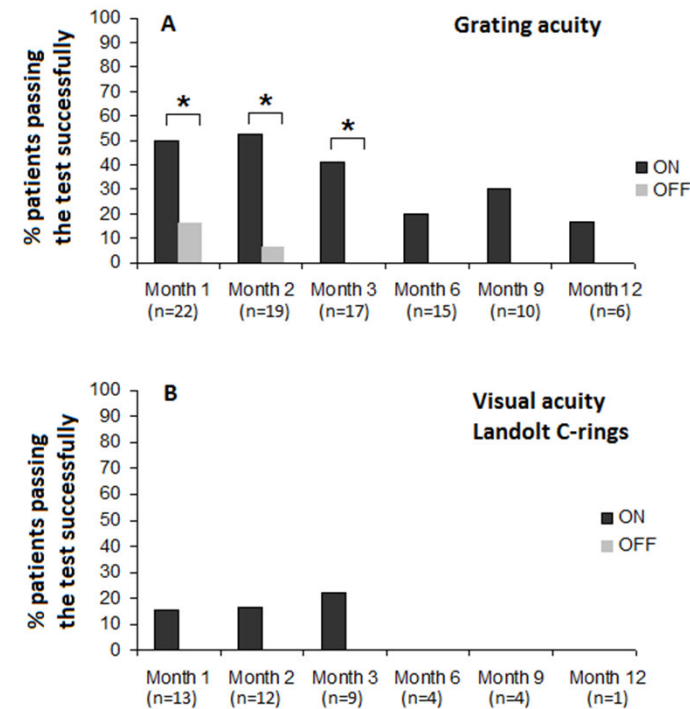
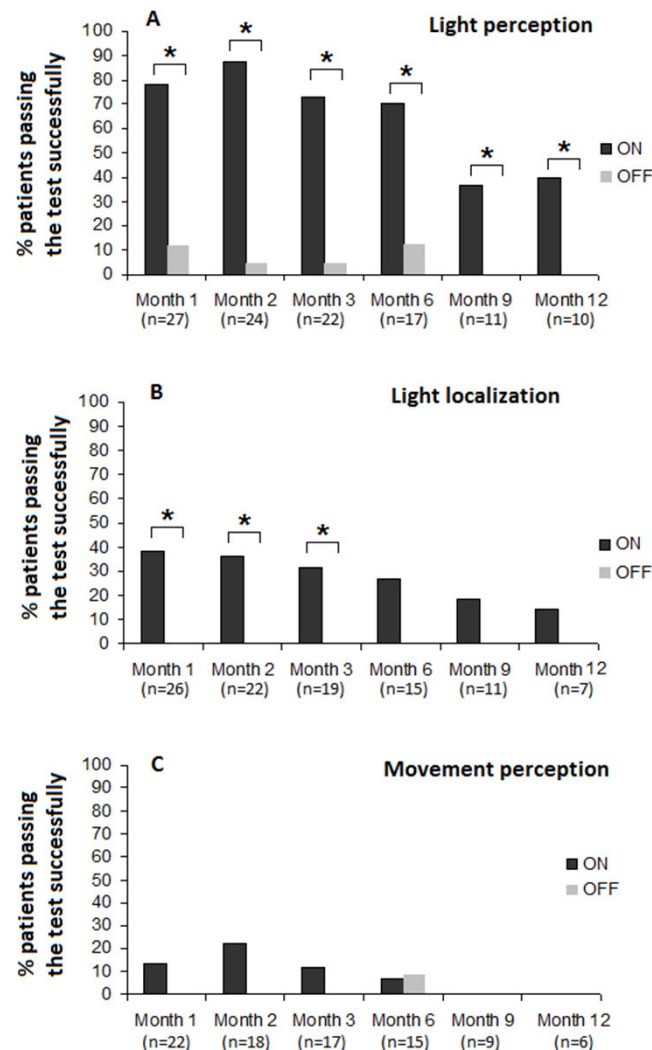


Vision in daily life





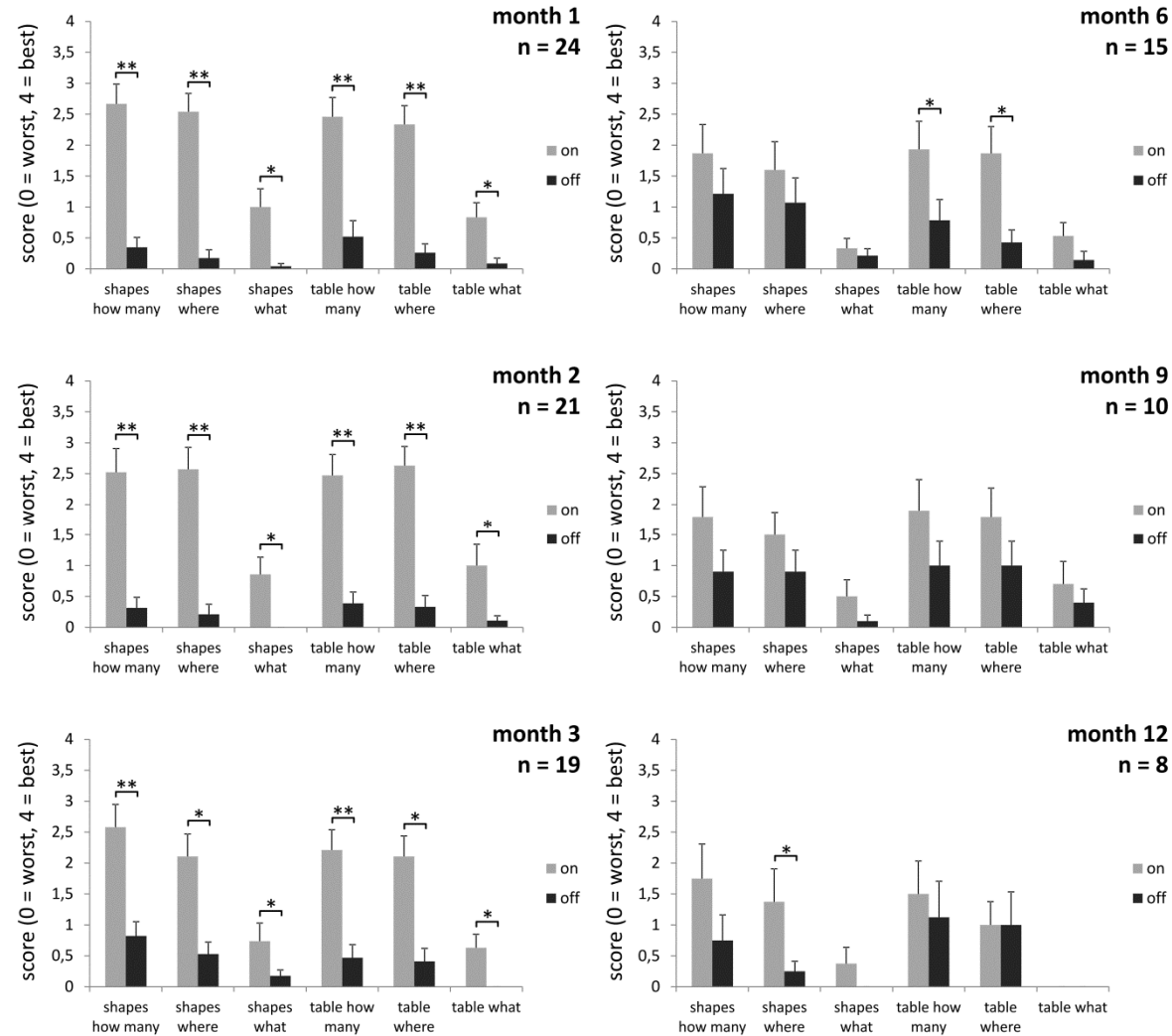
Outcome



Stingl K. et al. Vision Res. 2015 Jun;111(Pt B):149-60



Outcome



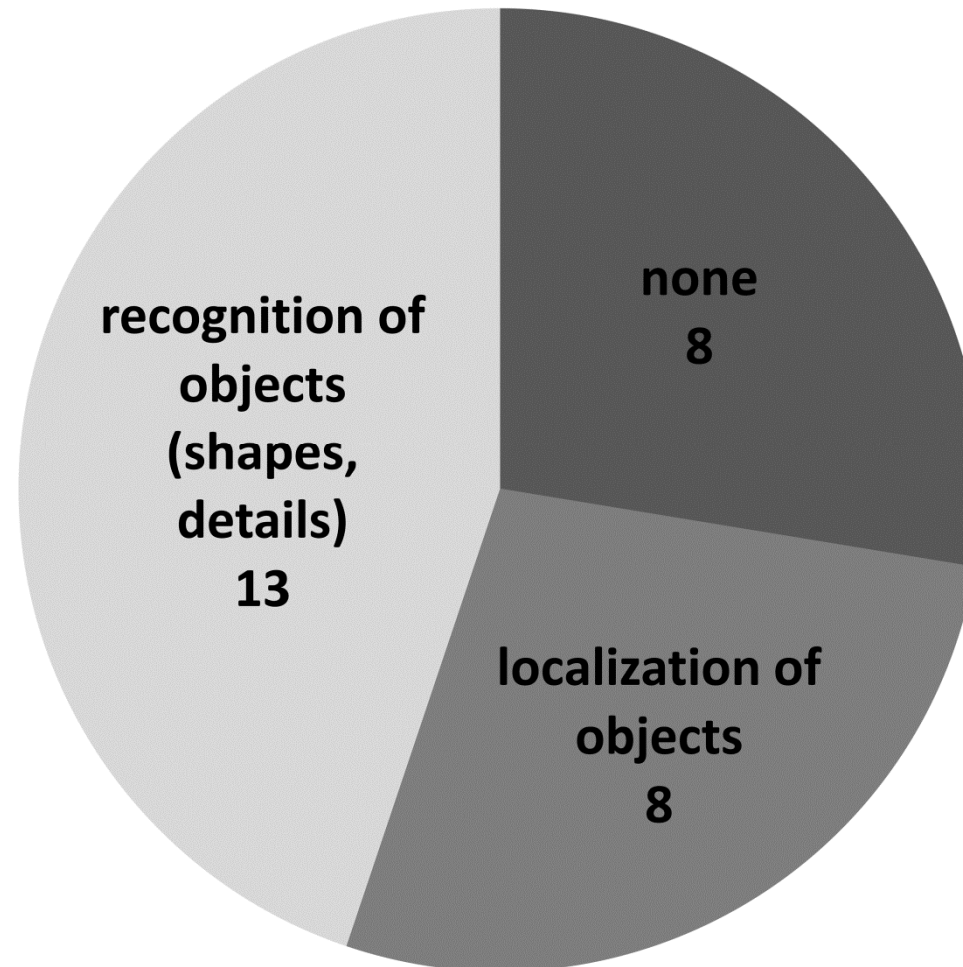
Stingl K. et al. Vision Res. 2015 Jun;111(Pt B):149-60.

25.07.2018



Primary endpoints – Alltag

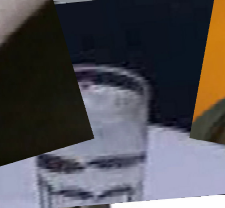
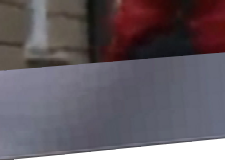
Visual experiences in daily life



Stingl K. et al. Vision Res. 2015 Jun;111(Pt B):149-60.



Retina Implant Alpha IM

People		8
Houses		
Streets		9
Cars		
Nature		
Reading		
Own body		
Near / At home		

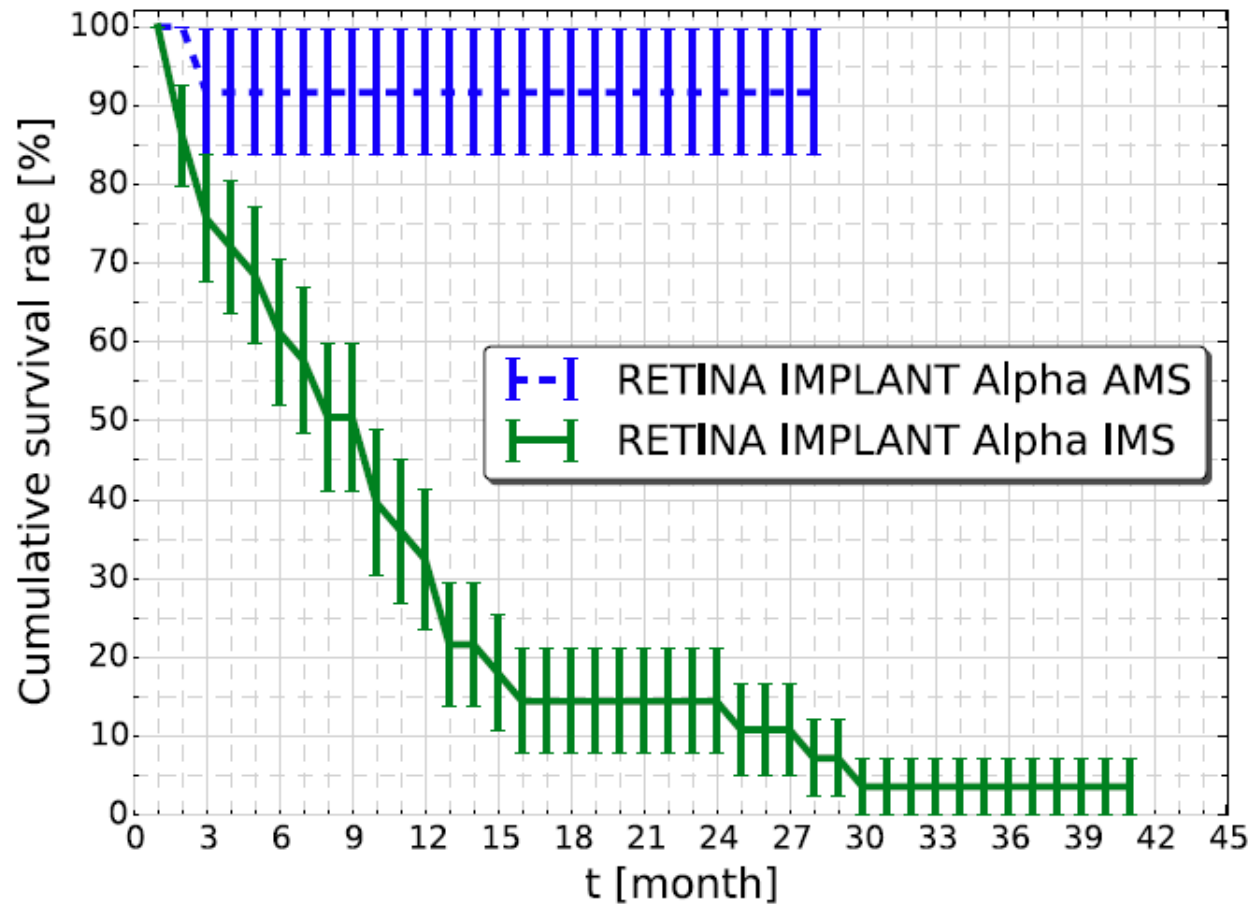








Retina Implant Alpha IMS

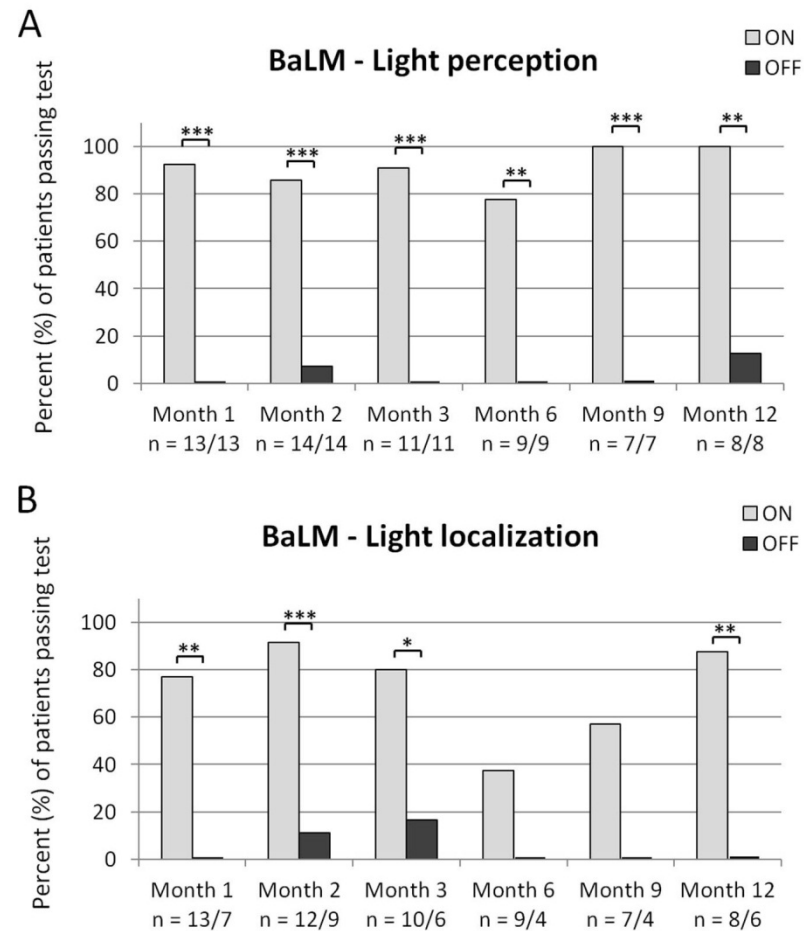


Retina Implant Alpha AMS

- 2014–2017 clinical trial
- 10 patients
Tübingen, Dresden, Kiel
- 6 patients Oxford
- Blind; hereditary retinal degenerations
- 2016 CE approval
- Approved therapy in Germany



Retina Implant Alpha AMS



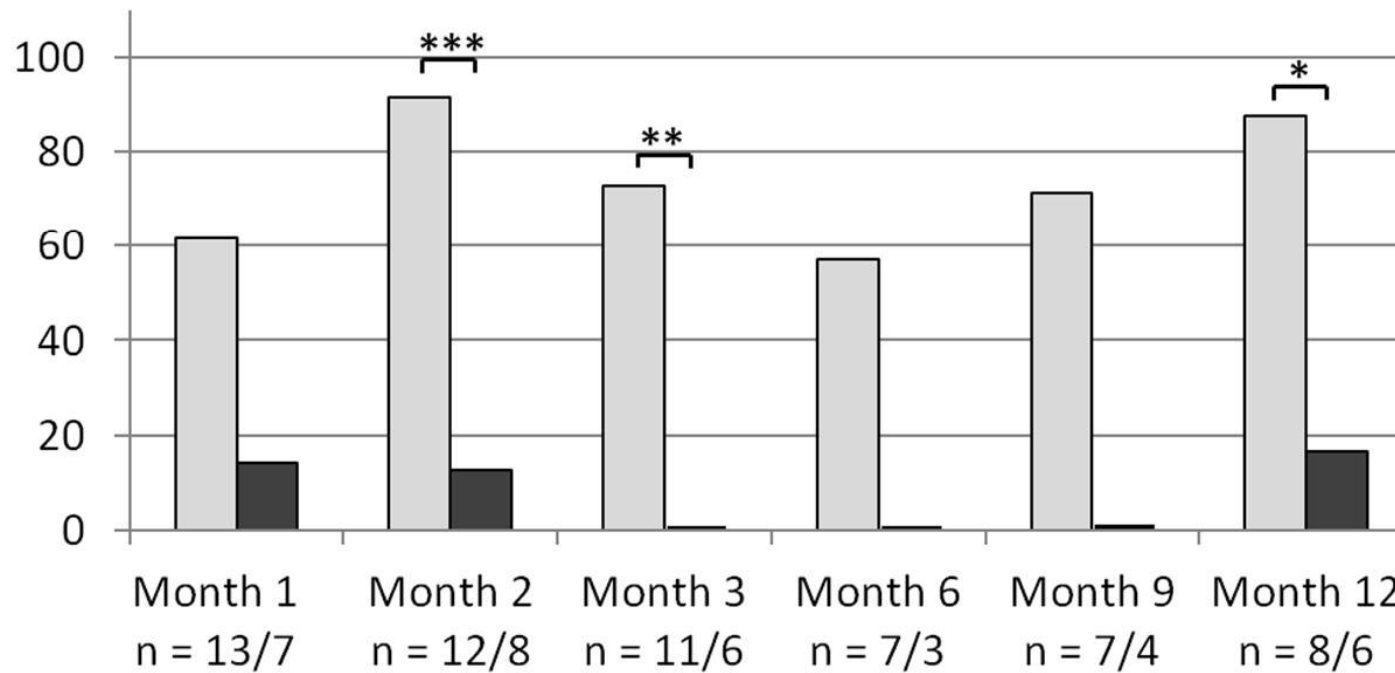


Retina Implant Alpha AMS

A

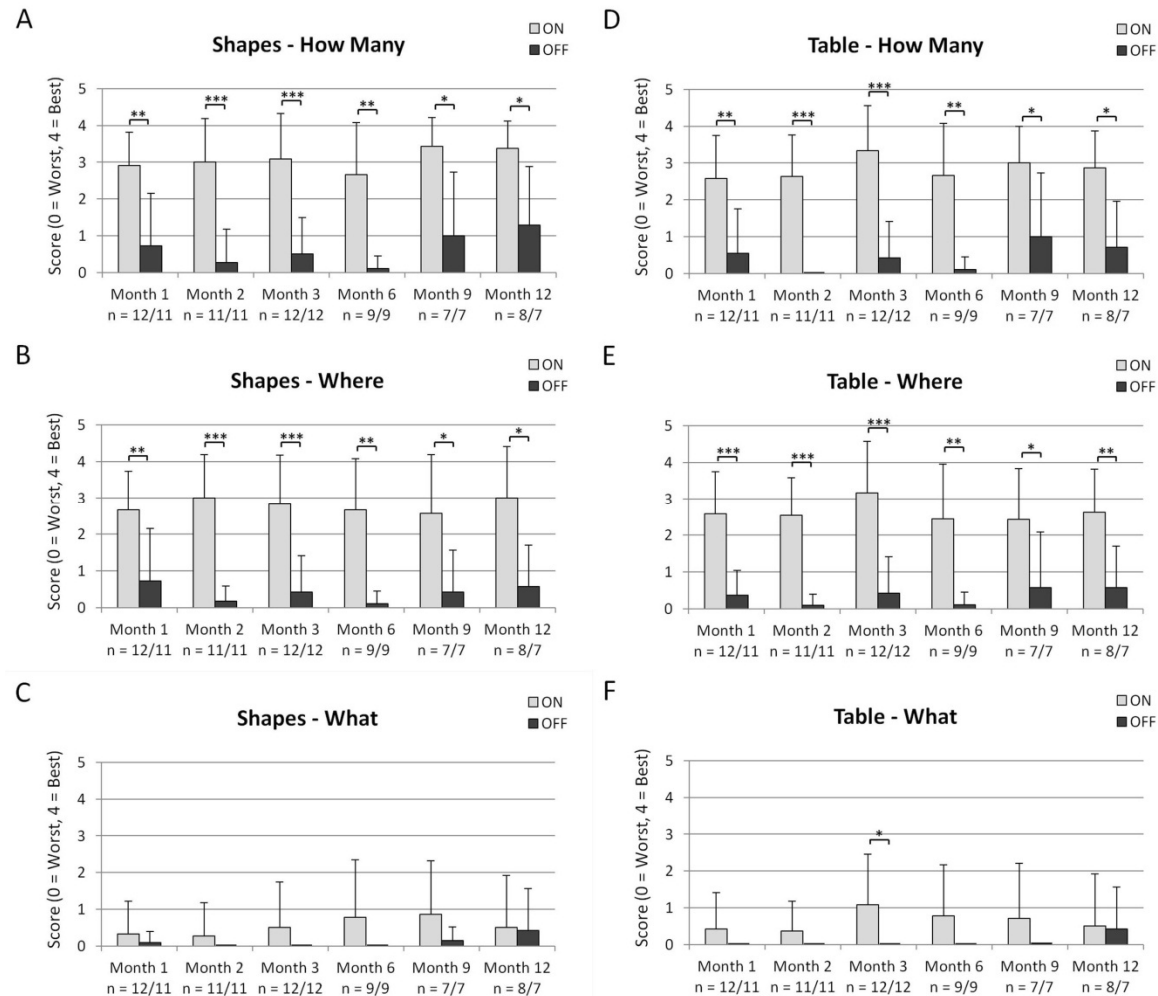
Percent (%) of patients passing test

Basic Grating Acuity

□ ON
■ OFF



Retina Implant Alpha AMS



Post marketing surveillance

- Retina Implant Alpha AMS
- CE approval
- Reimbursed by insurances in Germany



Visual implants

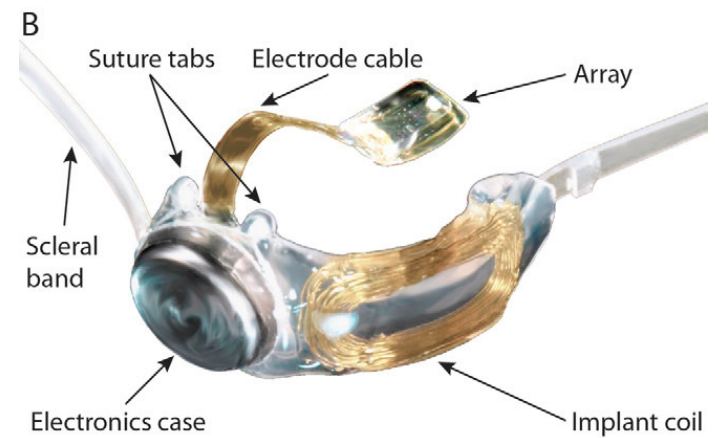
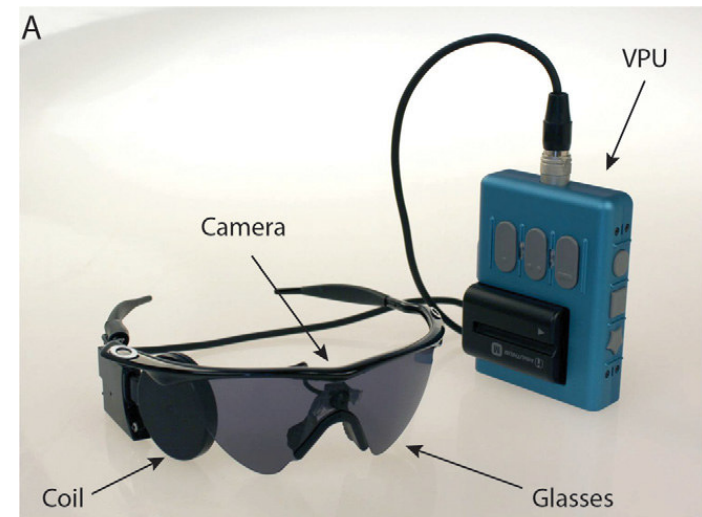
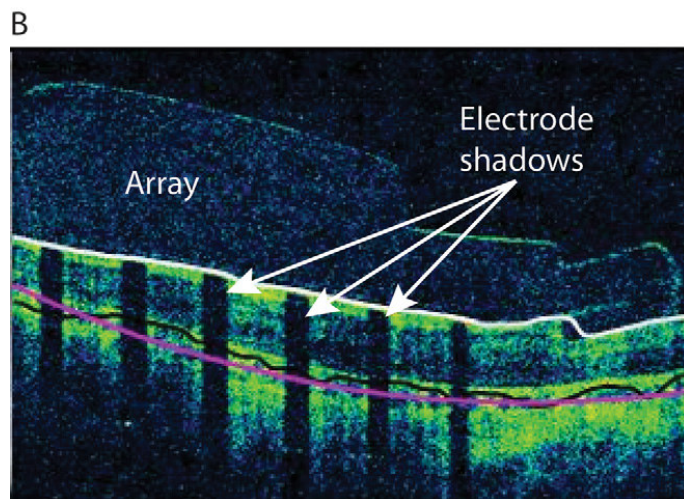
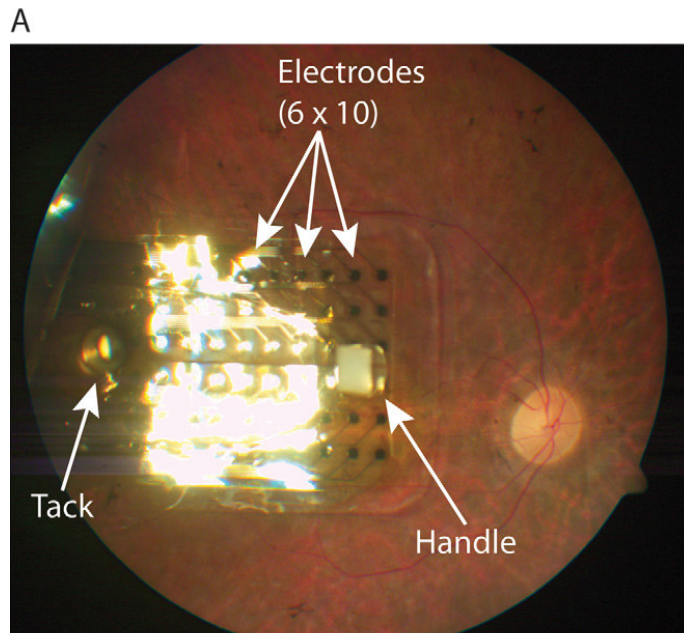
EPIRETINAL

Epiretinal implant

- Argus II
- Second Sight (California)
- CE approval
- FDA approval
- > 5 years durability



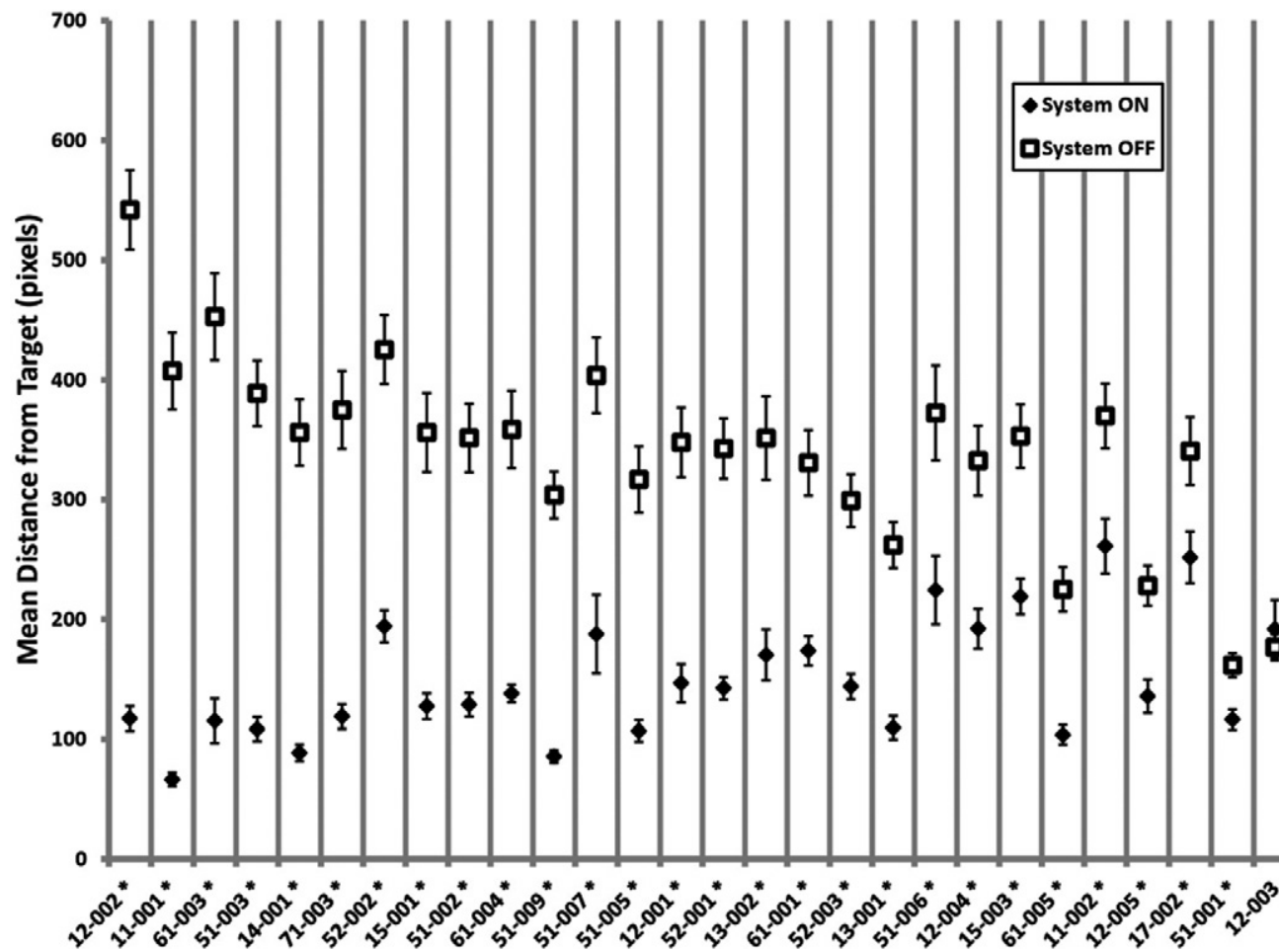
Argus II





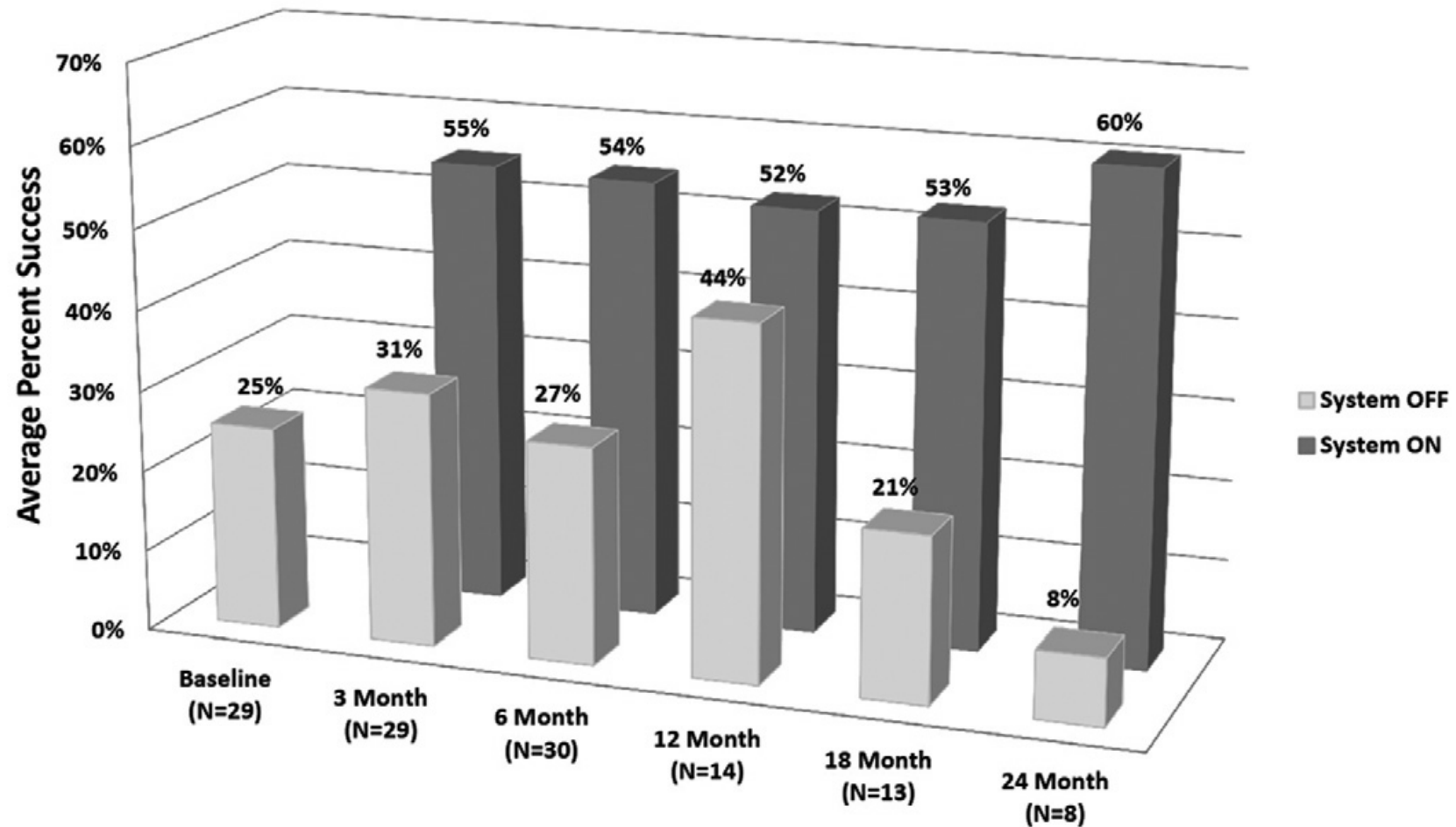
Humayun M et al. *Ophthalmology*. 2012 Apr;119(4):779-88.

Argus II: square location task





Argus II: find the door task

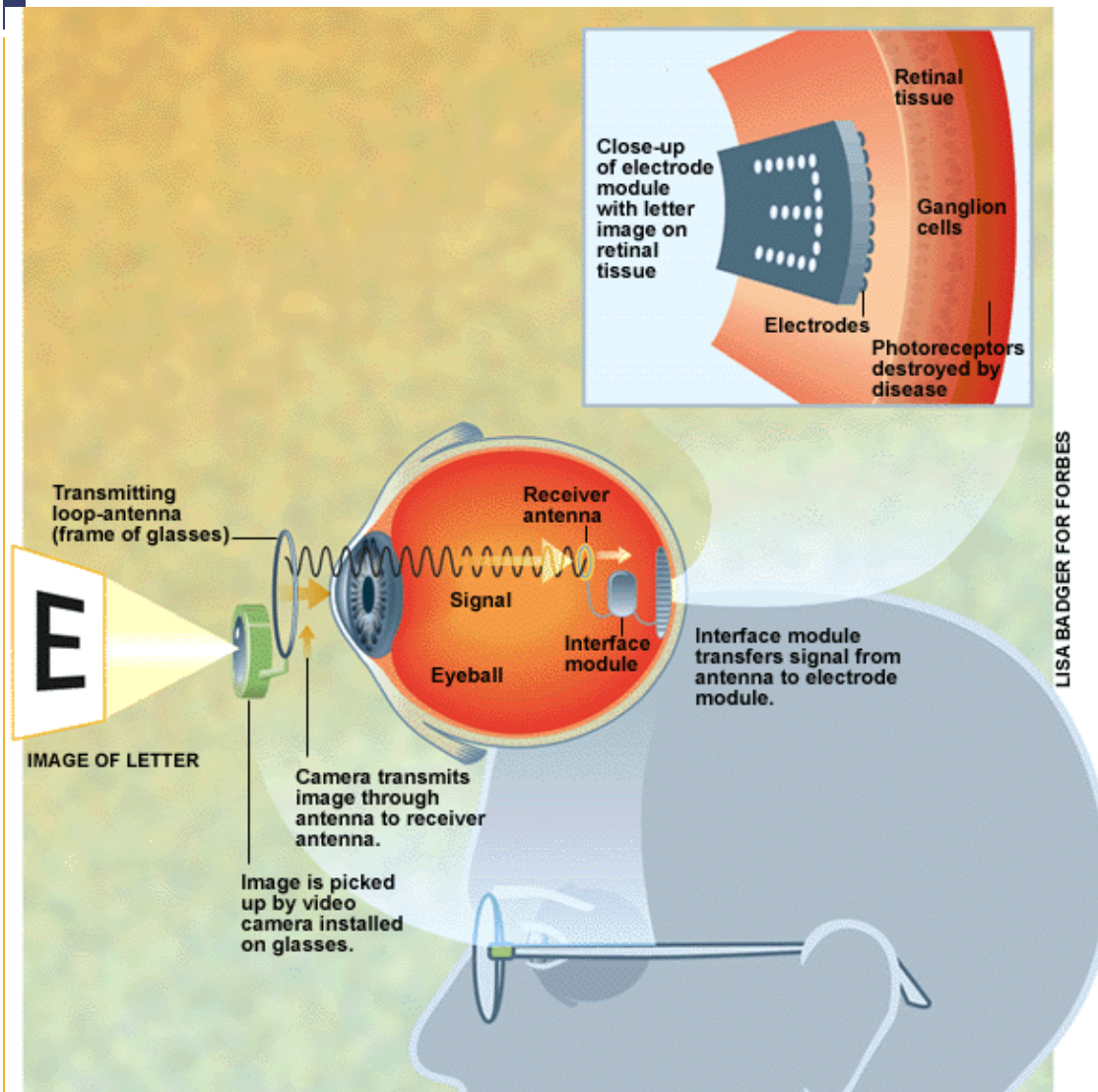


Humayun M et al. Ophthalmology. 2012 Apr;119(4):779-88.



Epiretinal

- Reading letter
- following a white line



Humayun, DeJuan et al.
Rizzo and Wyatt et al.
Eckmiller et al.
Richard et al.
Abrams et al.



Subretinal vs. Epiretinal

- Higher resolution
 - No decoder needed
 - Natural retinotopy
 - on/off bipolar cells
 - overlapping receptive fields of the ganglion cells
 - amakrine cells: motion, space-time function
 - Natural eye movements can be used
- Shorter surgery
 - No clear optic media needed



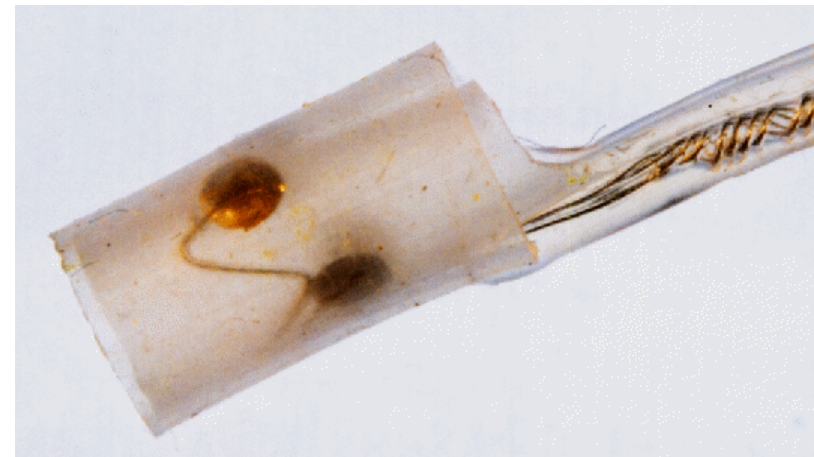
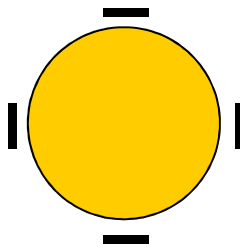
Visual implants

OPTIC NERVE CUFFS

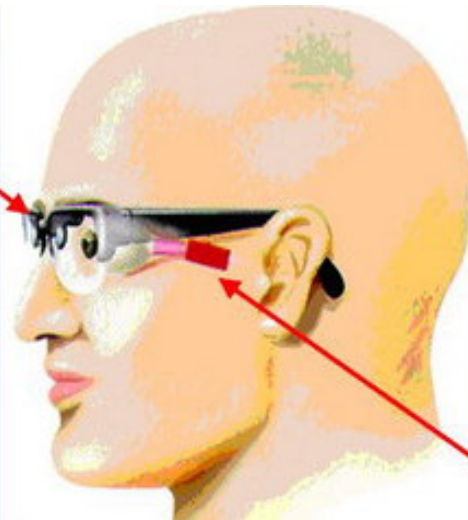


Optic nerve cuffs

4 electrodes



Main image camera



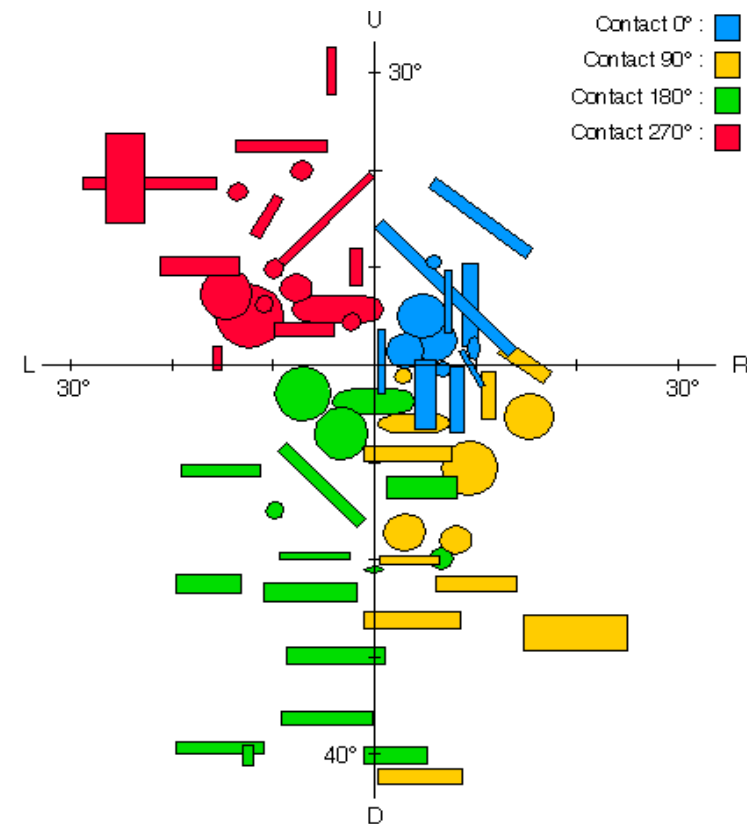
Electrode array

C. Veraart et al., Belgium



Optic nerve cuffs

- irregular phosphenes
- visual evoked potentials (VEP)



Brelén ME, Vince V, Gérard B, Veraart C, Delbeke J. Measurement of evoked potentials after electrical stimulation of the human optic nerve. Invest Ophthalmol Vis Sci. 2010 Oct;51(10):5351-5.



Visual implants

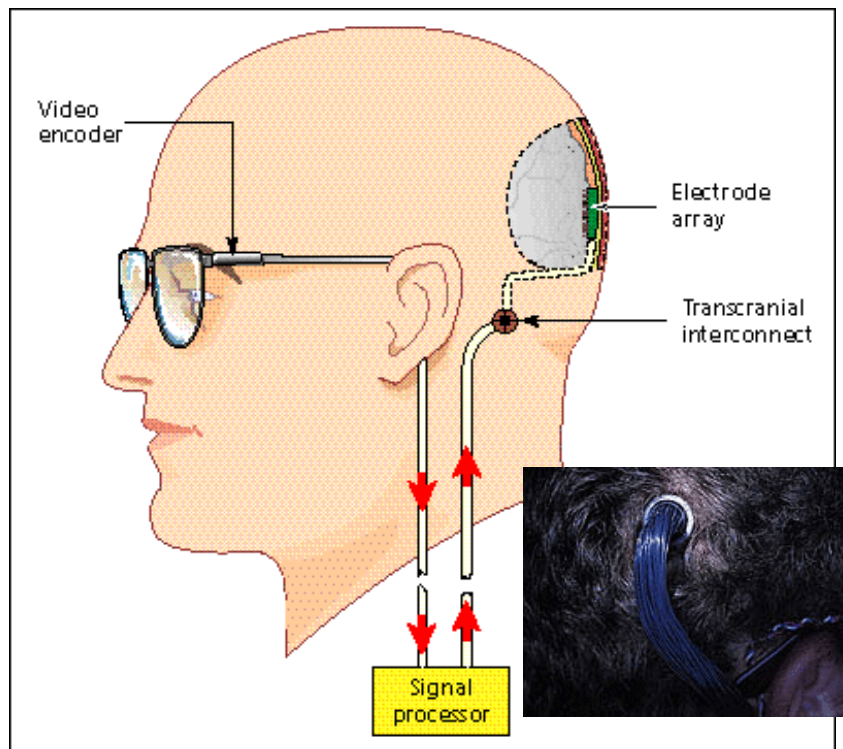
CORTICAL



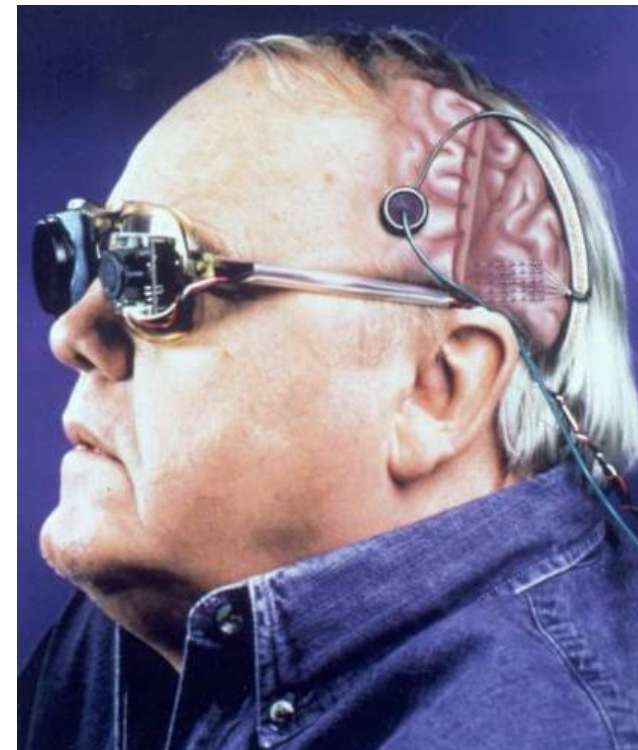
Cortical implants

G.S. Brindley 1972, MacNichols, 1972; T. Hambrecht 1996:

Epidural electrodes in few patients
different responses



W.H. Dobelle, 1974, 2000
20 electrodes



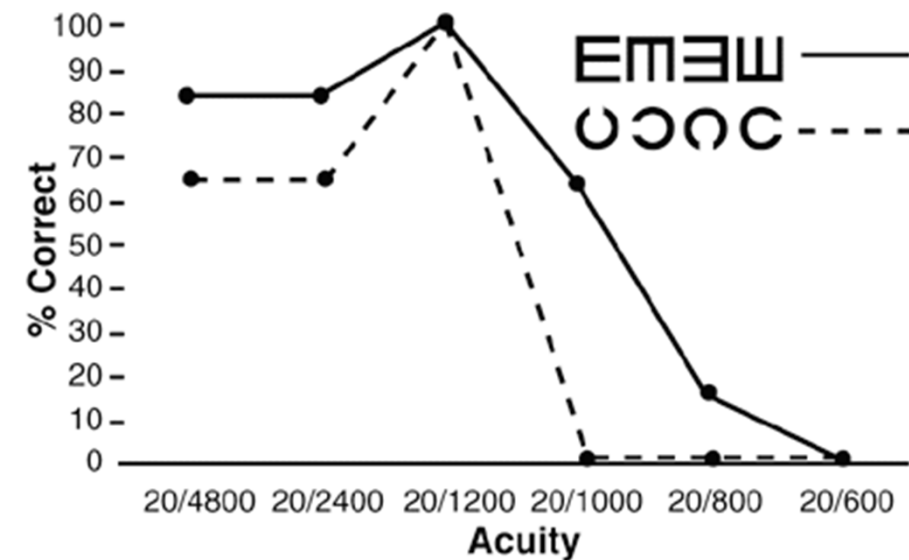
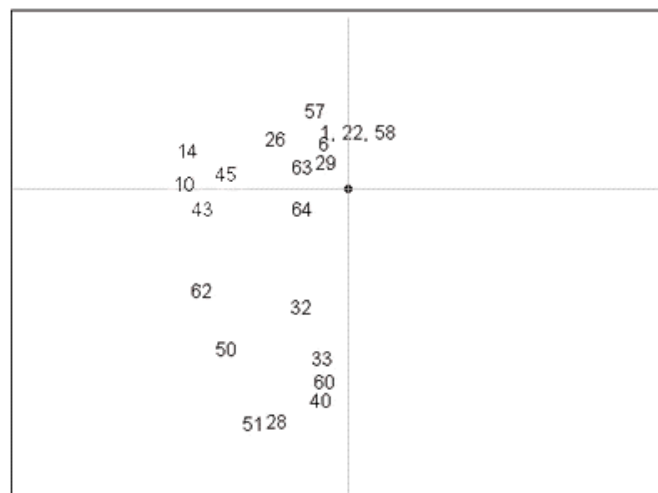
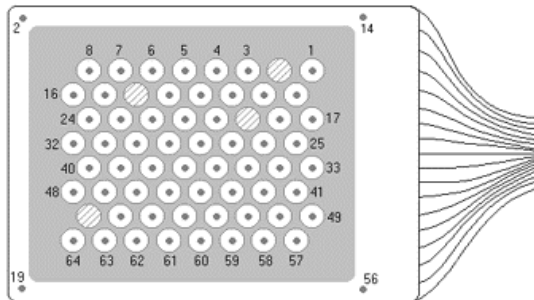
Artist's view

From Dobelle-Institute, Portugal



Cortical implants

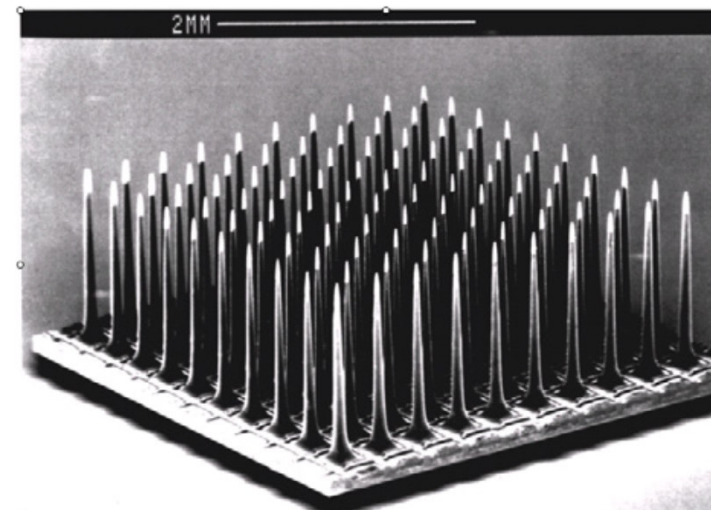
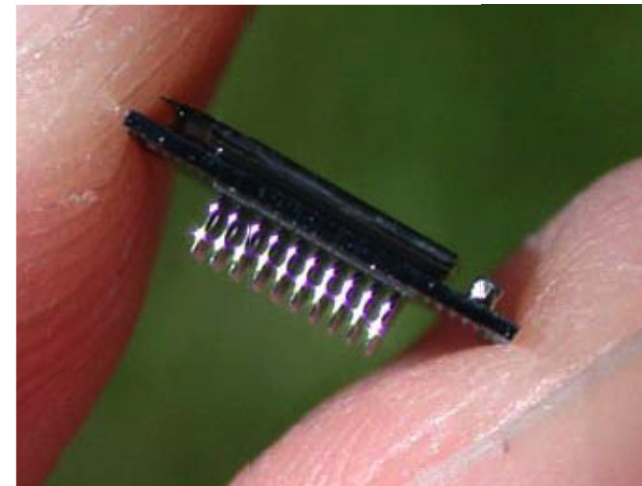
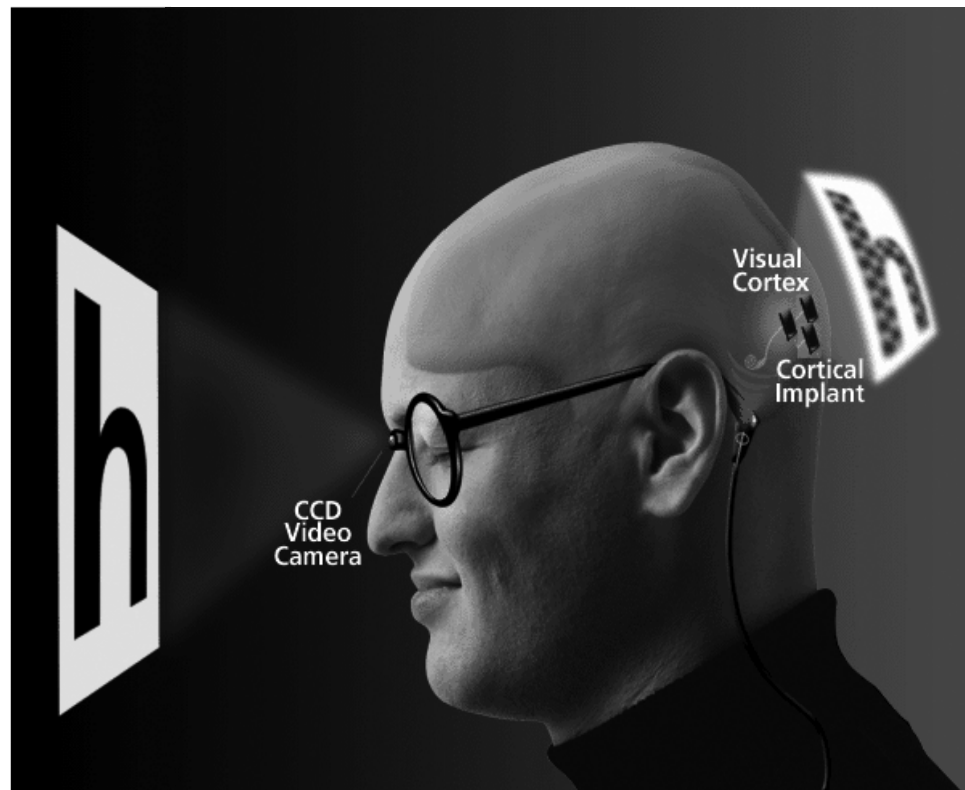
With 20 functioning electrodes Dobelle's patient has only a very limited vision. Some improvement in navigation and mobility was observed.



From Dobelle-Institute, Portugal



Cortical





Vielen Dank für Ihre Aufmerksamkeit

