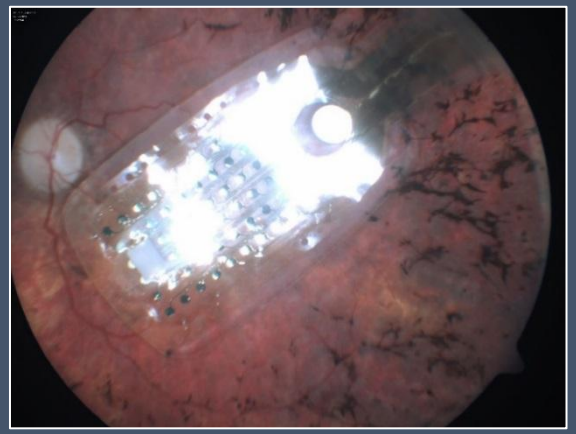
YAPAY GÖRME & RETİNAL PROTEZ (BİYONİK GÖZ)

Körlüklerin Tedavisinde Biyomateryal Dönemi ……



Prof. Dr. Emin ÖZMERT

Ankara Üniversitesi Tıp Fakültesi Göz Hastalıkları AD

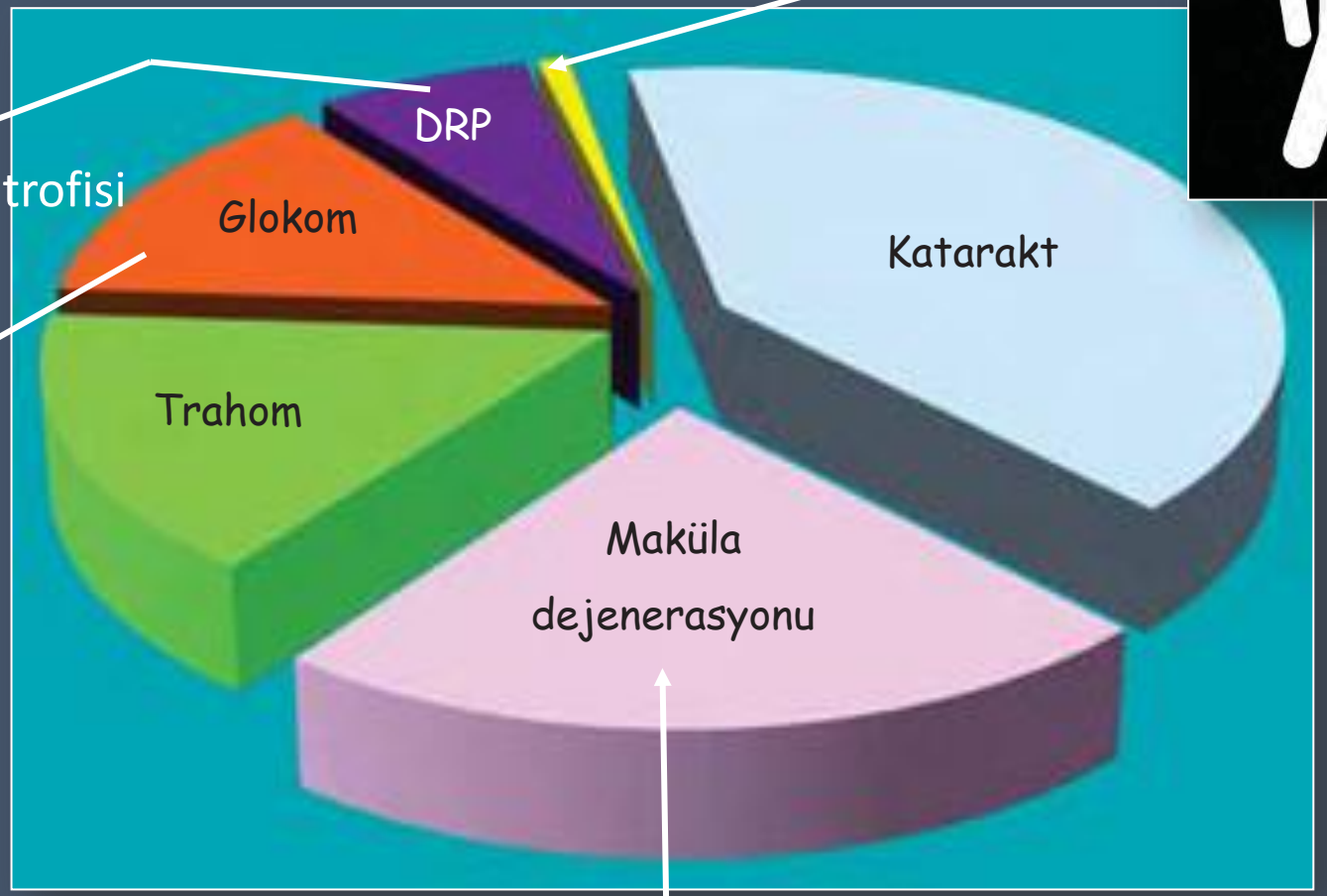
Yapay Görme & Biyonik Göz Birimi

Dünyada 45 milyon ‘görme engelli’ var

Retinitis pigmentosa: Epiretinal protez

Optik sinir atrofisi
Ameliyatlar
Kazalar

Kortikal protez

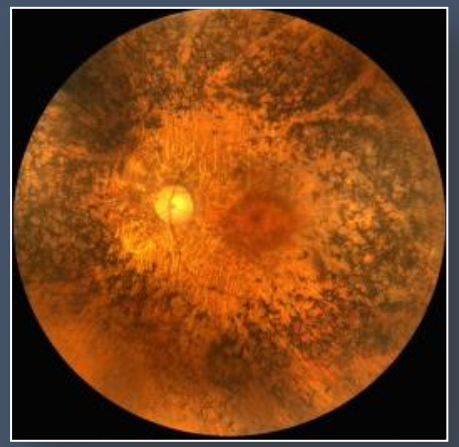


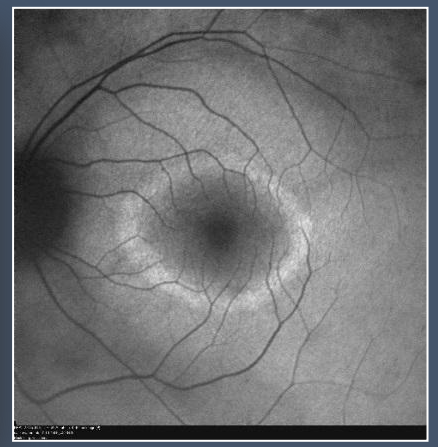
Coğrafik atrofi: Epiretinal protez

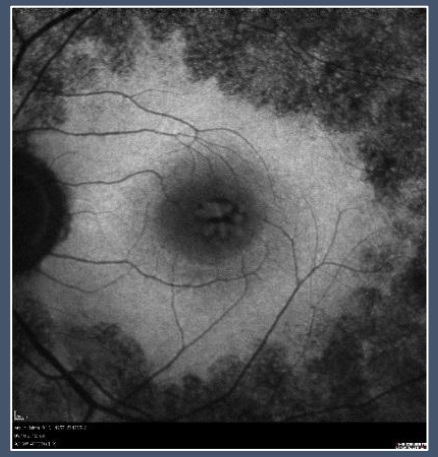
Retinitis Pigmentosa

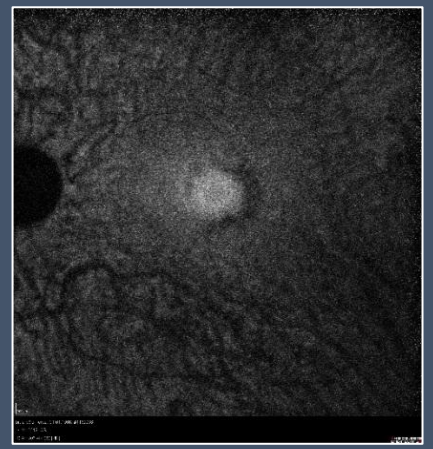
- Tüm dünyada 1,2 milyon RP hastası
- Türkiye'de prevalansı ~ 1/4000-5000

  (20.000-25.000)
- 100' den fazla genetik tipi, gençleri tutar
- İlerleyici görme alanı daralması, ciddi körlük
- Sosyo-ekonomik problemler, iş gücü kaybı









Tedavi arayışları……

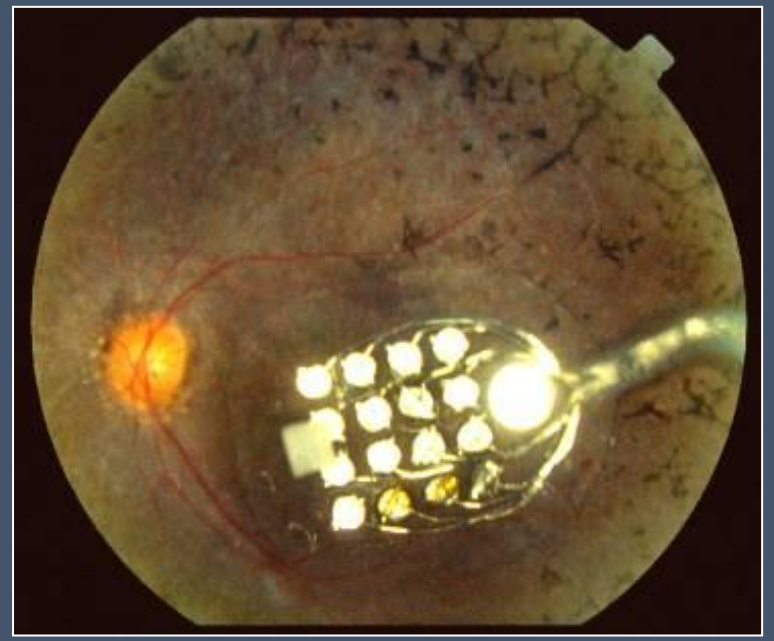
- İntravitreal büyüme faktörü
- Gen tedavisi
- Nöroretina - RPE transplantasyon
- Elektrostimülasyon
- Biyomedikal Mühendisliği ve Biyomateryallerde gelişmeler

↓

Kohlear İmplantlar

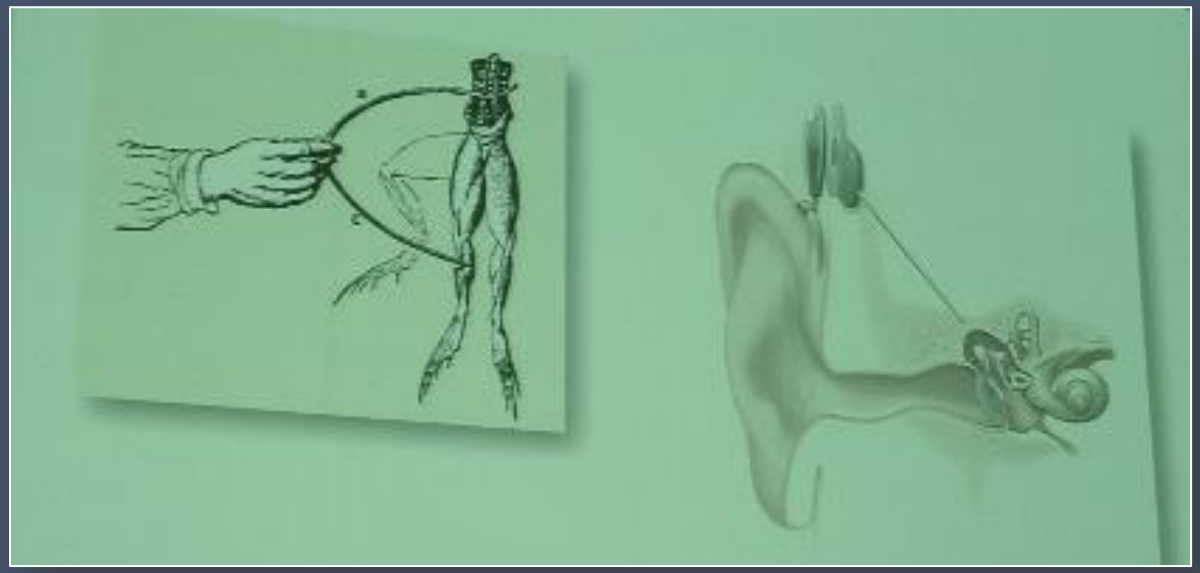
Nöro-stimülasyon

Görsel protezler= Biyonik göz



Görsel protezler fikri.....

- Charles Le Roy (1755)
- Kondansatör
- «... aşağı doğru inen alevler...»



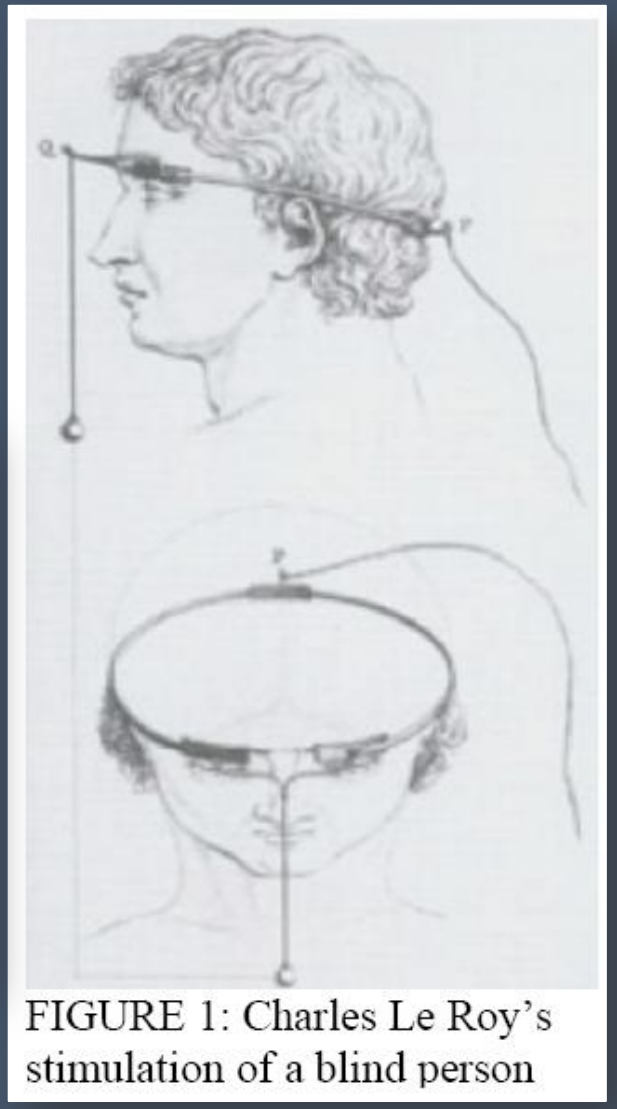
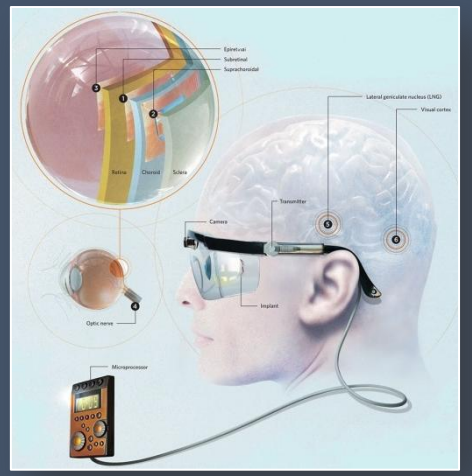


FIGURE 1: Charles Le Roy's stimulation of a blind person

Günümüzde Görsel Protez Çalışmaları……



RETİNA

- Direkt uyaranlar:
  - * Epiretinal ------ retina ganglion hücreleri
    - Argus II(Second Sight, Sylmar),
    - EPIRET III (GmbH Giessen), IRIS (Pixium Paris)
  - * Subretinal ----- bipolar hücreler
    - Alpha IMS (Retina Implant GmbH) Eksternal link var
    - Artificial Silicone Retina Chip (Optobionics USA)
    - Boston Retina Implant

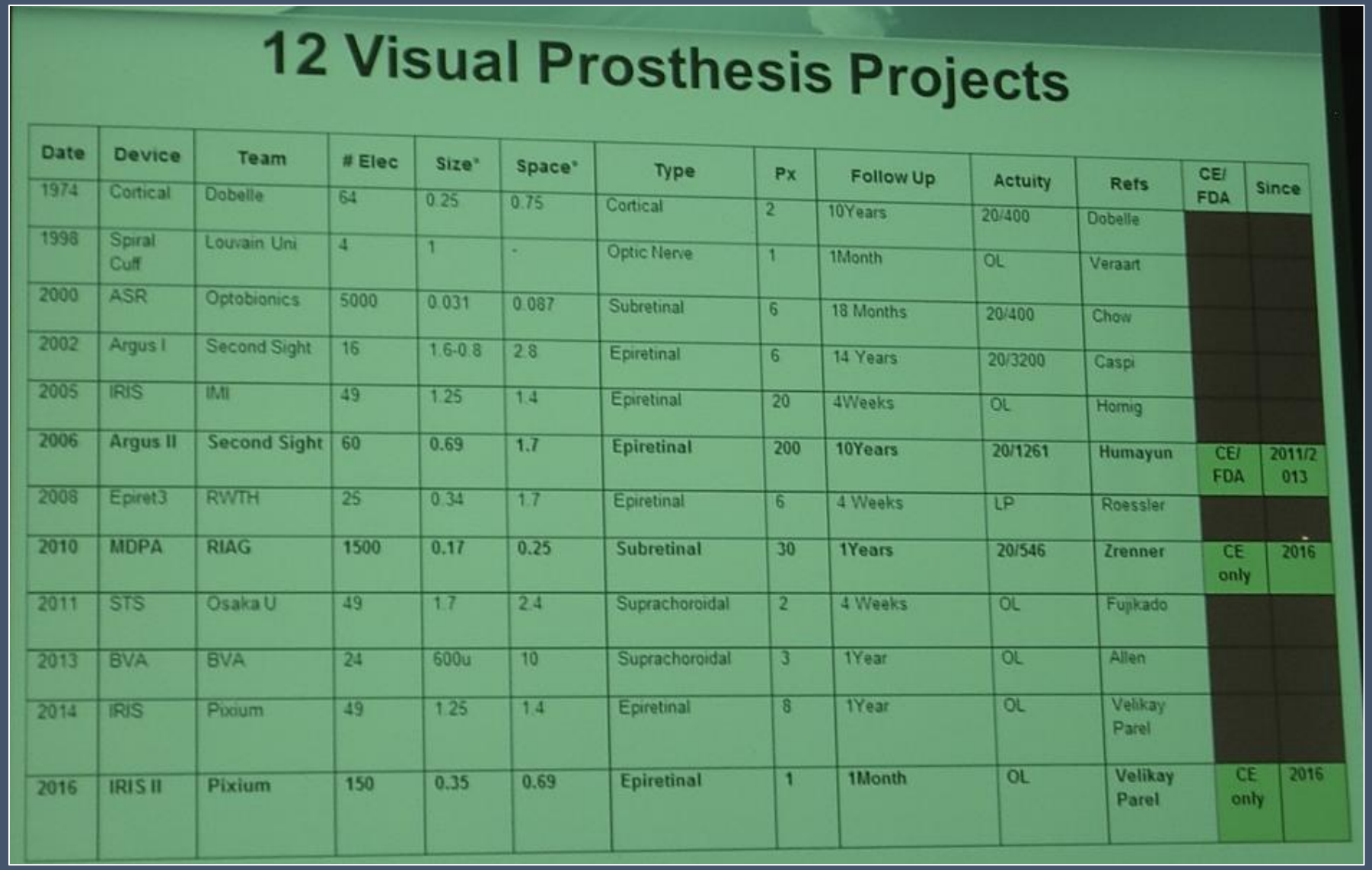
- İndirekt uyaranlar ----- suprakoroidal (bipolar hücreler)
  - Suprakoroidal Transretinal Stimülatör: NIDEK (Japonya)
  - Bionic Vision (Avustralya)

OPTİK SİNİR

LATERAL GENİKÜLAT NÜKLEUS

VİSUAL KORTEKS İMPLANTI (Second Sight – ORION 1 projesi)

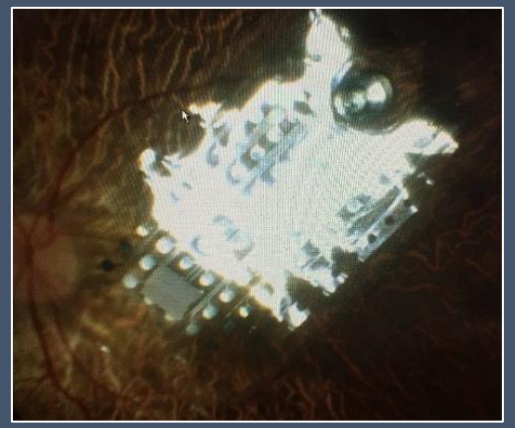
DÜNYADA YÜRÜTÜLMEKTE OLAN GÖRSEL PROTEZ ÇALIŞMALARI

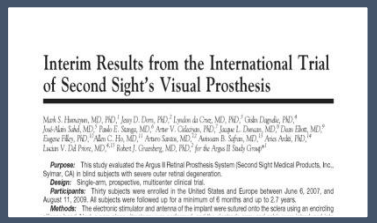


12 Visual Prosthesis Projects

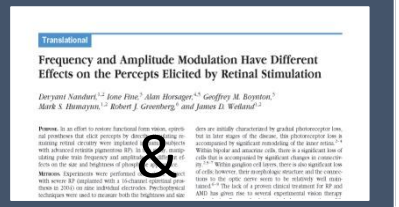
Date	Device	Team	# Elec	Size°	Space°	Type	Px	Follow Up	Actuity	Refs	CE/ FDA	Since
1974	Cortical	Dobelle	64	0.25	0.75	Cortical	2	10Years	20/400	Dobelle		
1998	Spiral Cuff	Louvain Uni	4	1	-	Optic Nerve	1	1Month	OL	Veraart		
2000	ASR	Optobionics	5000	0.031	0.087	Subretinal	6	18 Months	20/400	Chow		
2002	Argus I	Second Sight	16	1.6-0.8	2.8	Epiretinal	6	14 Years	20/3200	Caspi		
2005	IRIS	IMI	49	1.25	1.4	Epiretinal	20	4Weeks	OL	Homig		
2006	Argus II	Second Sight	60	0.69	1.7	Epiretinal	200	10Years	20/1261	Humayun	CE/ FDA	2011/2 013
2008	Epiret3	RWTH	25	0.34	1.7	Epiretinal	6	4 Weeks	LP	Roessler		
2010	MDPA	RIAG	1500	0.17	0.25	Subretinal	30	1Years	20/546	Zrenner	CE only	2016
2011	STS	Osaka U	49	1.7	2.4	Suprachoroidal	2	4 Weeks	OL	Fujikado		
2013	BVA	BVA	24	600u	10	Suprachoroidal	3	1Year	OL	Allen		
2014	IRIS	Pixium	49	1.25	1.4	Epiretinal	8	1Year	OL	Velikay Parel		
2016	IRIS II	Pixium	150	0.35	0.69	Epiretinal	1	1Month	OL	Velikay Parel	CE only	2016

Argus II Epiretinal Protez





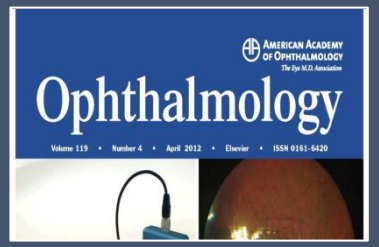
Interim Results from the International Trial of Second Sight's Visual Prosthesis



Translational

Frequency and Amplitude Modulation Have Different Effects on the Percepts Elicited by Retinal Stimulation

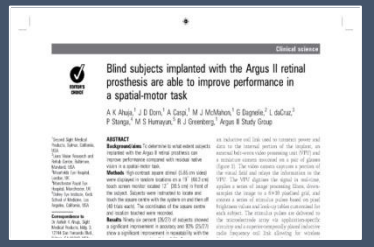
Assessment of MRI issues for the Argus II Retinal Prosthesis



Ophthalmology

CLINICAL SCIENCES

The Detection of Motion by Blind Subjects With the Epiretinal 60-Electrode (Argus II) Retinal Prosthesis



Blind subjects implanted with the Argus II retinal prosthesis are able to improve performance in a spatial-motor task

Clinical Trials

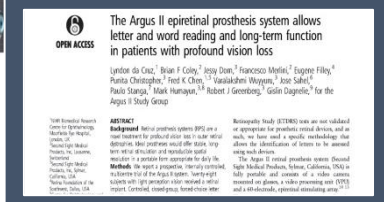
Use of the Argus II Retinal Prosthesis to Improve Visual Guidance of Fine Hand Movements

ieee spectrum

FUTURE VISION

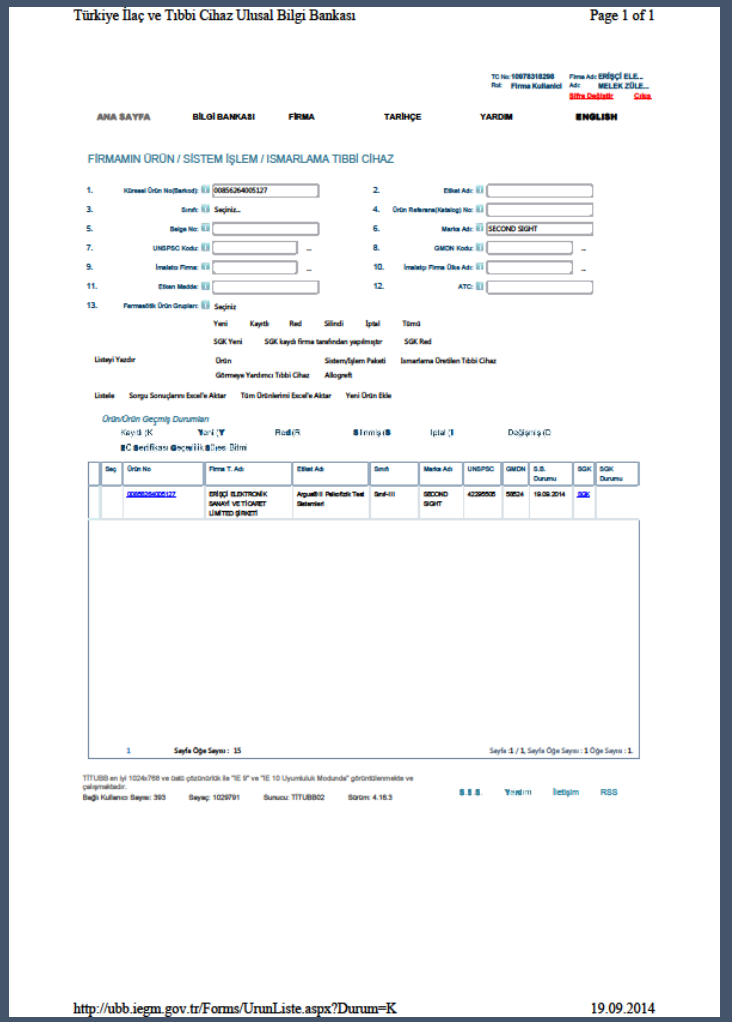
In 2012, electrodes will bring eyesight to the blind

BY ELIZA STRICKLAND



OPEN ACCESS

The Argus II epiretinal prosthesis system allows letter and word reading and long-term function in patients with profound vision loss



Türkiye İlaç ve Tıbbi Cihaz Ulusal Bilgi Bankası

Page 1 of 1

FİRMAMIN ÜRÜN / SİSTEM İŞLEM / ISMARLAMA TIBBİ CİHAZ

http://ubb.iegm.gov.tr/Forms/UrunListe.aspx?Durum=K

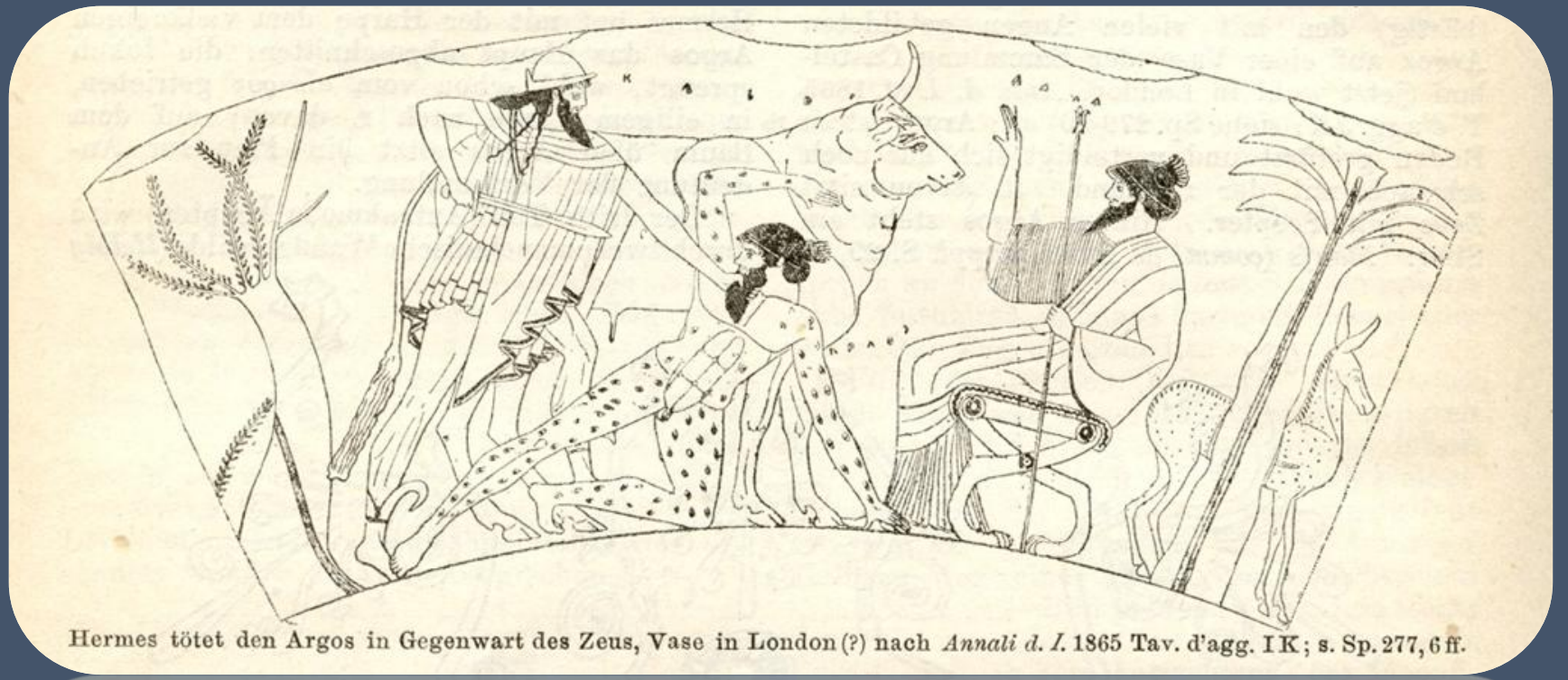
19.09.2014

CE mark - 2011

FDA - 2013

T.C. SB / SGK - UBB - 2014

Argus II Epiretinal Protez



Hermes tötet den Argos in Gegenwart des Zeus, Vase in London (?) nach *Annali d. I.* 1865 Tav. d'agg. I K; s. Sp. 277, 6 ff.

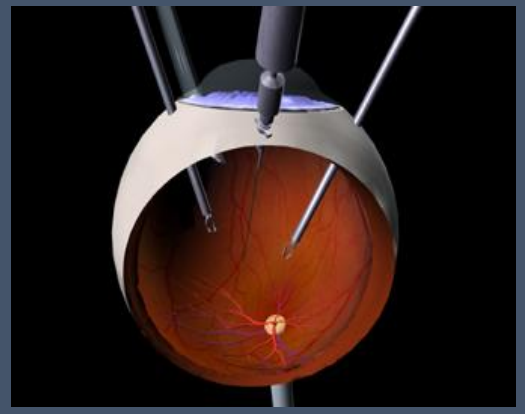
'100 gözlü dev'

Argus II Epiretinal Protezin gelişimi

Akut İnsan Çalışmaları

1990-1998 yılları arasında

- 1-2 saatlik uyarım
- 15 hasta
- Hastalar fosfen algıladı

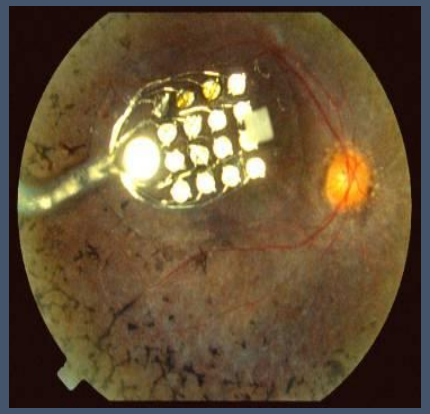


Tech in development

Argus I Fizibilite Çalışmaları

2002 Yılından itibaren (14 yıl)

- 16 elektrot
- 6 hasta
- Sistemin düzgün çalıştığının kanıtlanması

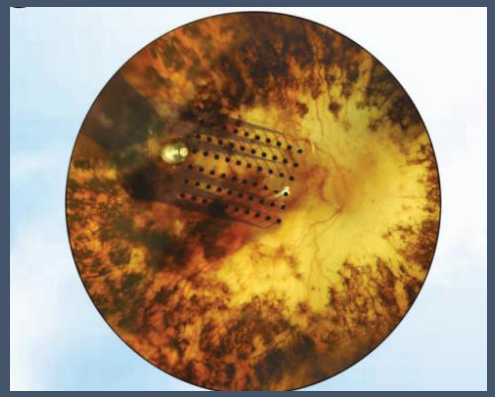


Argus I

Argus II Prospektif Deneme

2007 yılından beri (8 yıl)

- 60 elektrot
- 30 hasta
- Sistemin güvenliliği ve yeterliliği gösterilmeye çalışılmıştır.

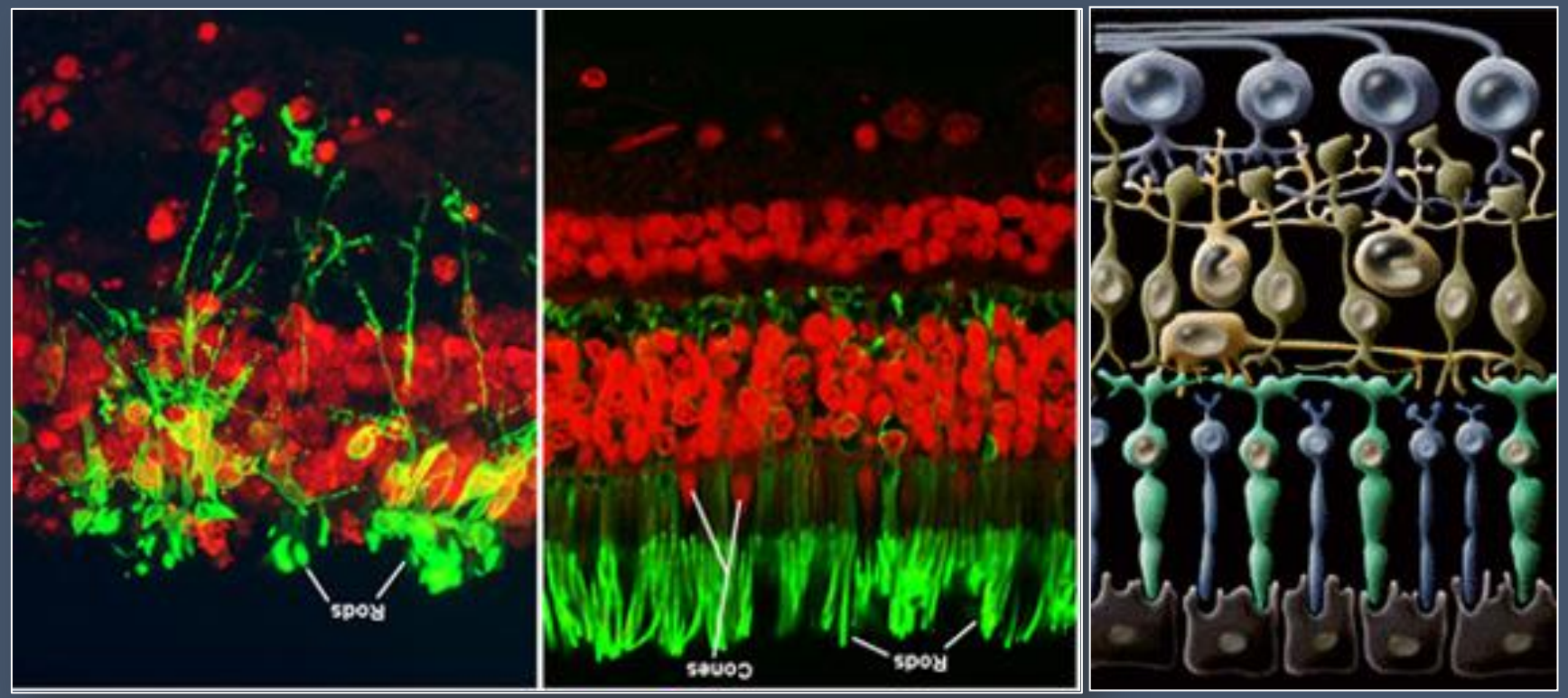


Argus II

İleri aşama dış retina dejenerasyonu

RETİNİTİS PİGMENTOSA

NORMAL



Ganglion hücrelerinin % 30’ u intakt
İç nükleer hücrelerin % 78-88’ i intakt

Humayun MS, Prince M, de Juan E,et al: Invest Ophthalmology Vis Sci 1999;40:143-148
Santos A, Humayun MS, de Juan E, et al: Arch Ophthalmol 1997;115:511-515

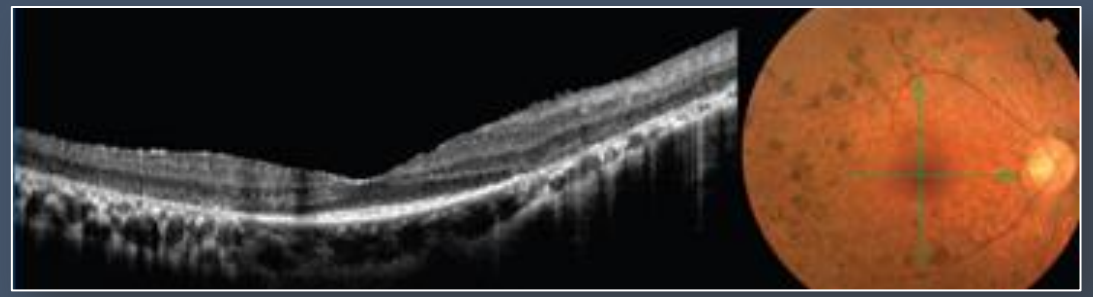
Dünyada ve Türkiye' de Biyonik Göz
Son Evre Retinitis Pigmentosa'da Argus II Retina Protezi

- Amerika ve Avrupa' da akredite olmuş 13 ülkede 250 + ameliyat
  * Dünyada onaylanmış ilk ve tek ürün, deneysel amaçlı değil !!!
  * 25-30 yıllık bir Ar-Ge
  * 12 yıllık ürün mataryeli takibi, göze mataryel zararı yok
  * 11 yıllık klinik takip sonuçları
  * Mobilite artmakta, bağımlılık azalmakta

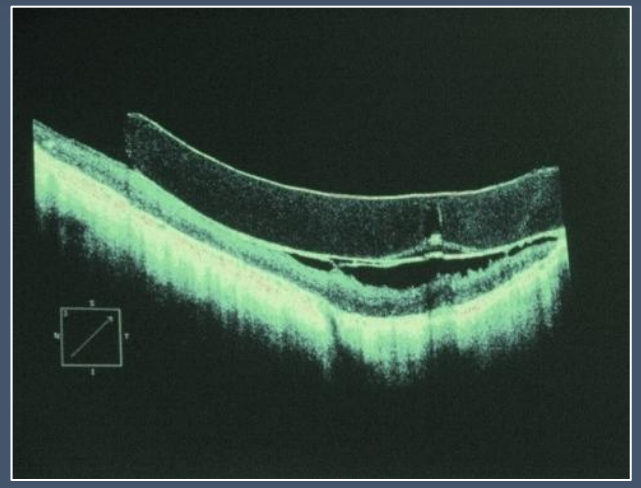
- Kliniğimiz 2013' de akredite edildi
- Rehabilitasyon ve simüle yaşam alanları, biyofizik ve elektrofizyoloji lab.
- 28 Aralık 2015, 27 Haziran 2016, 24 Mayıs 2017 : 3 adet son evre RP olgusu (+ 4 yurt dışı)
  Dünyada ilk: Endoskop destekli, 3-D dijital vitrektomi ile Argus II implantasyonu

Ho AC, Humayun MS, Dorn JD. Ophthalmology 2015; 1-8
Y Lan, Falabella P, Christopher P. Ophthalmology 2015

Argus II sistemin uygulanabileceği hastalar

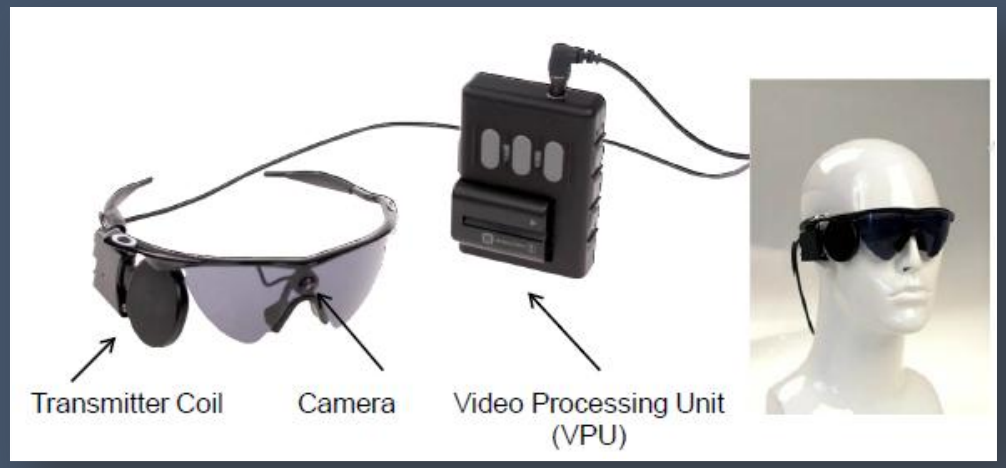


- 25 yaş ve üstü, ileri dış retina dejenerasyonu
- Sadece ışık hissi olmalı, kamera flaş testi (+) olmalı
- Daha öce, şekilleri görebilen bir görmesinin olması
- Şüpheli durumda flaş VEP ile görme yollarının durumu
- Yapılacak detaylı göz muayenesinde, göz yapılarının ve büyüklüğünün uygun olması:
    * Bulbus aksiyal uzunluğu: 20,5 – 26 mm
    * Arka stafilom olmamalı
    * İleri şaşılık ve nistagmus olmamalı
    * Konjonktiva sorunu olmamalı



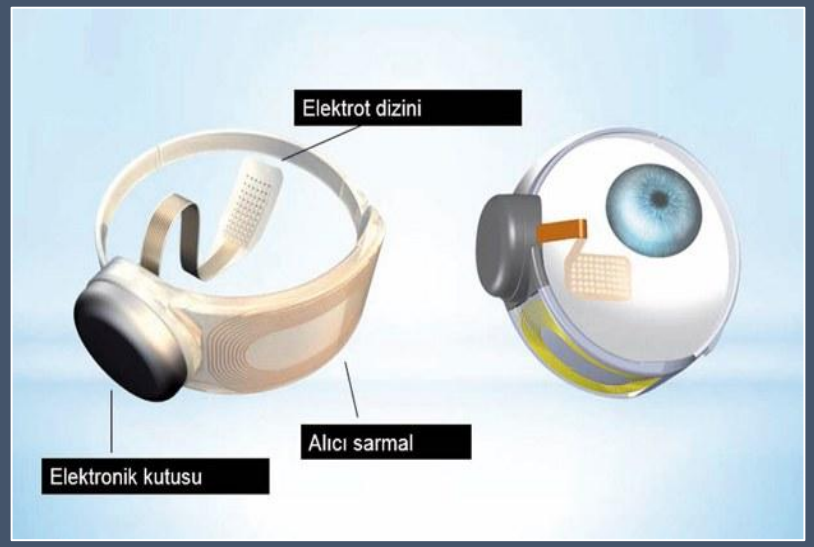
- Hastanın ve çevresinin, uzun sürecek rehabilitasyon çalışmalarını yapabilecek ve sürdürebilecek olması
- Hasta ve yakınlarının beklentilerin belirlenmesi

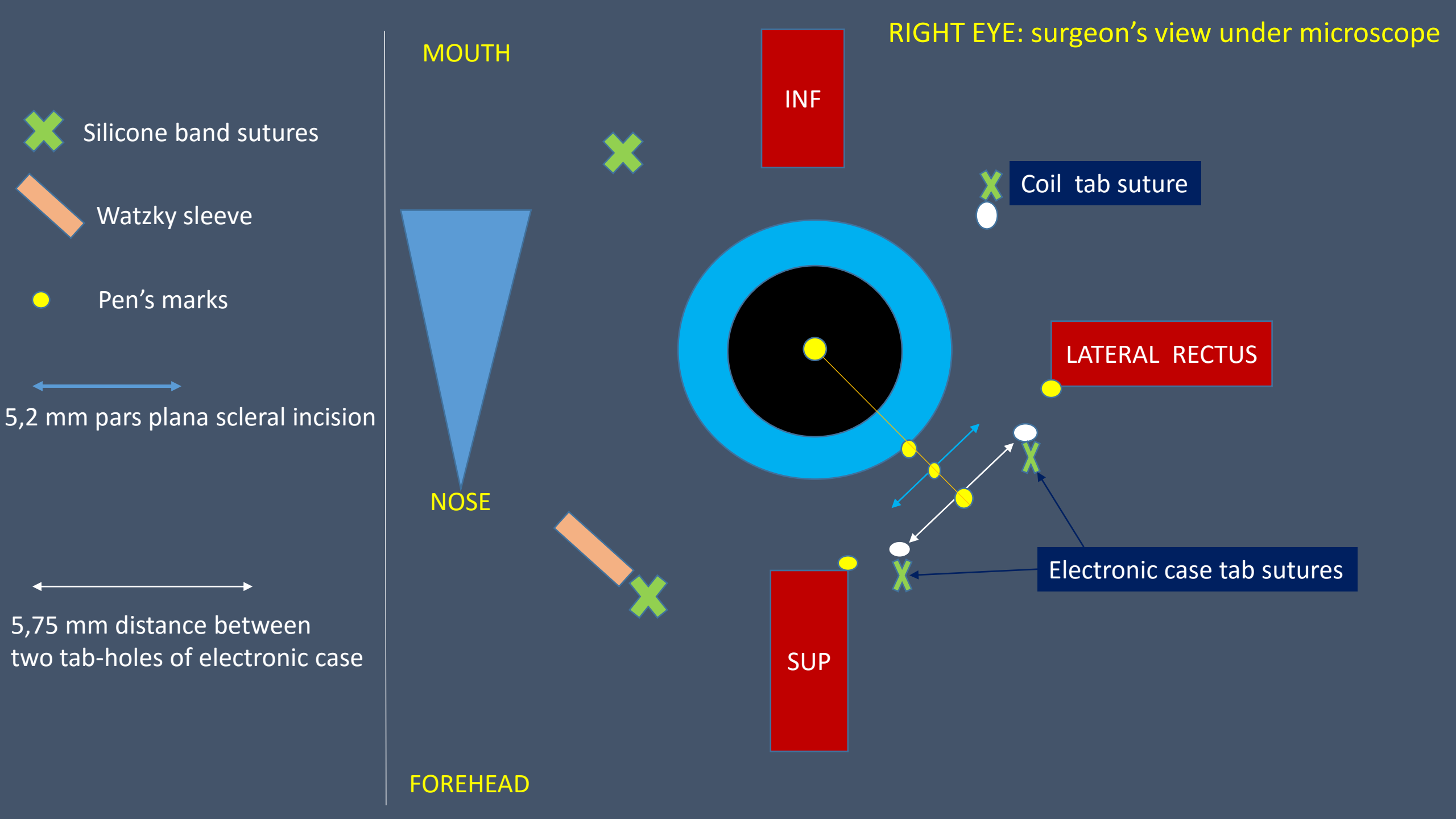
Argus II- Epiretinal İmplant (Biyonik Göz)



Inductive link: transmitter & receiver antenler
Enerji & data' yı implanta gönderir

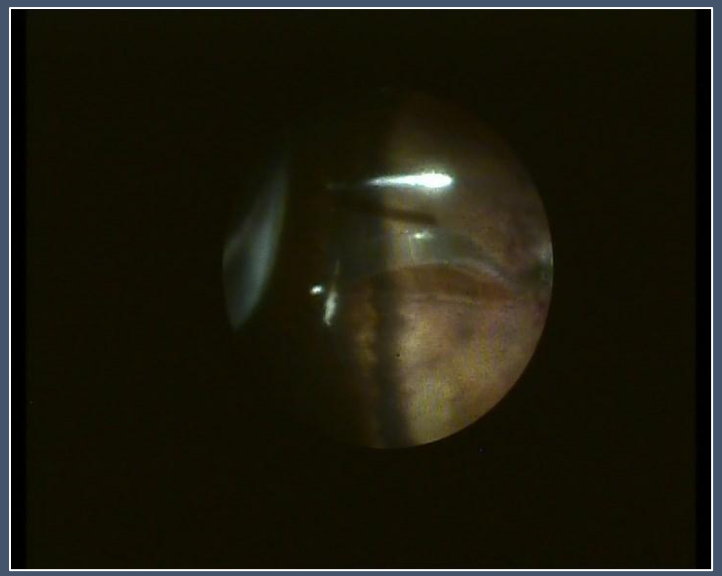
VPU: Hangi elektrot aktive edilecek ?
Stimulus amplitüdü nasıl ?
Kamera ve transmitter için enerji temini
Sinyal işleme algoritmalarını değiştirmek



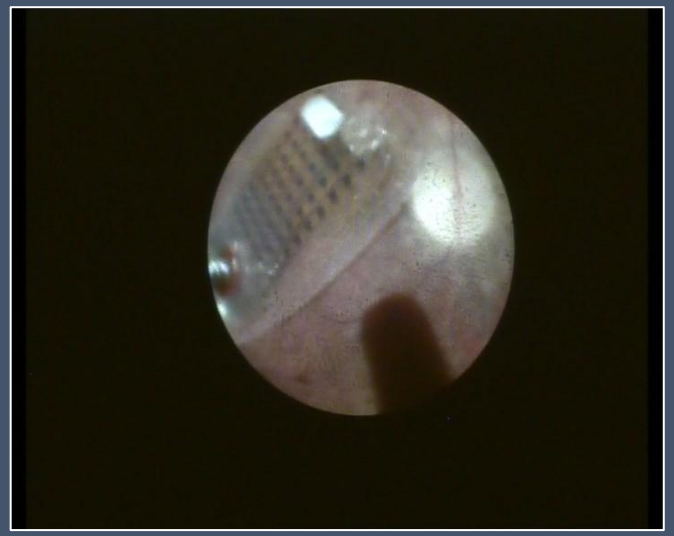

RIGHT EYE: surgeon's view under microscope
Silicone band sutures
Watzky sleeve
Pen's marks
5,2 mm pars plana scleral incision
5,75 mm distance between two tab-holes of electronic case
MOUTH
NOSE
FOREHEAD
INF
SUP
Coil tab suture
LATERAL RECTUS
Electronic case tab sutures

1- Skleraya sütüre edilen alıcı bobin, elektronik kutu, skleral bant

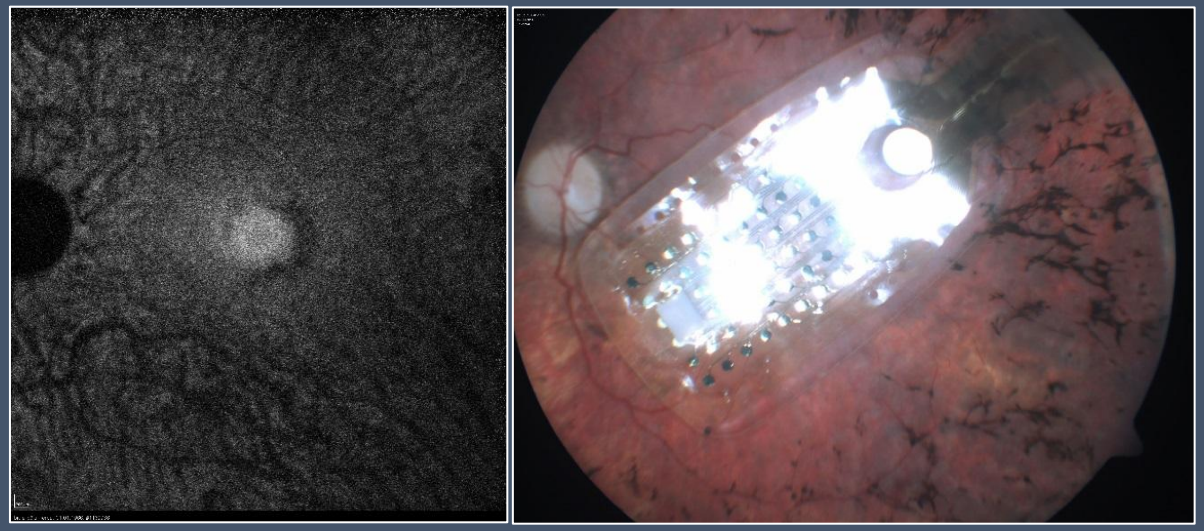
2- Mikroçipin ve elektronik kablonun
5.2 mm’ lik skleral kesiden göz içine yerleştirilmesi



3- Enerji & data iletimi için fleksibl transskleral kablo
ve dizin (elektrot array)

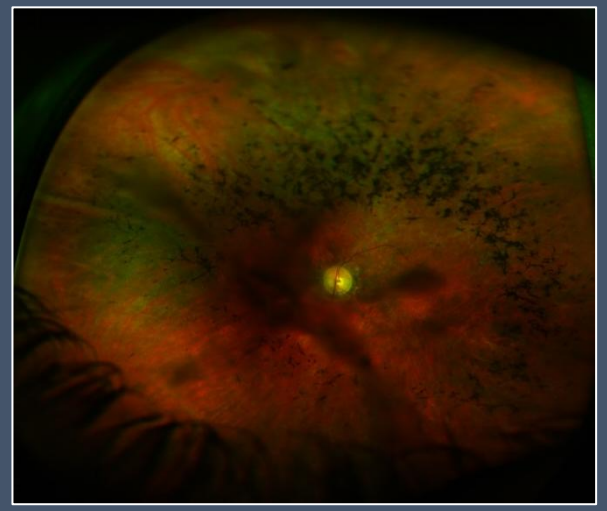


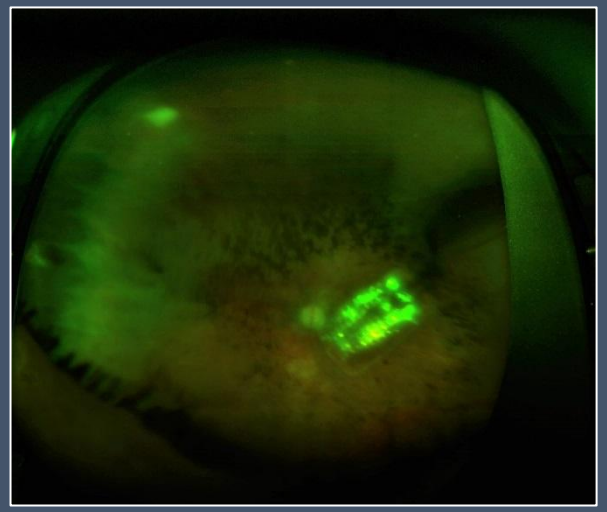
4- 60 bağımsız aktif platin elektrot (elektrot çapı: 200 µ*m*)



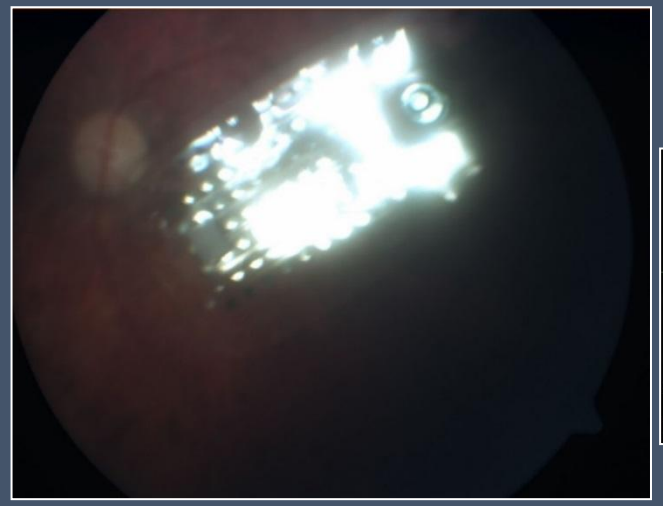
Elektrotlar silikon matrikse gömülü

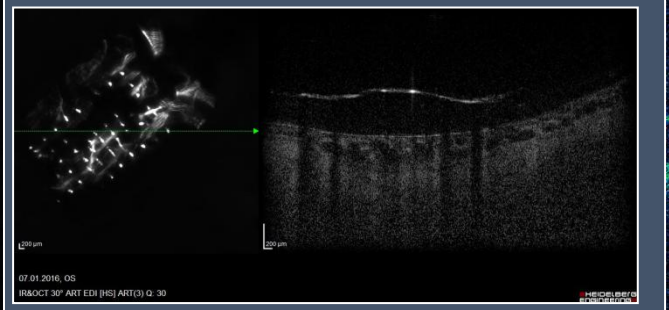
RP hastasının, ameliyat öncesi ve sonrası fundus resmi

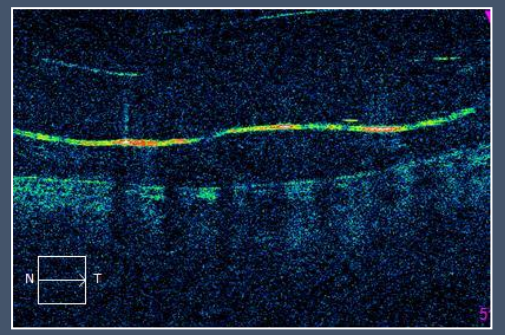




60 elektrod, çap: 200 µm
20 derecelik görme alanı

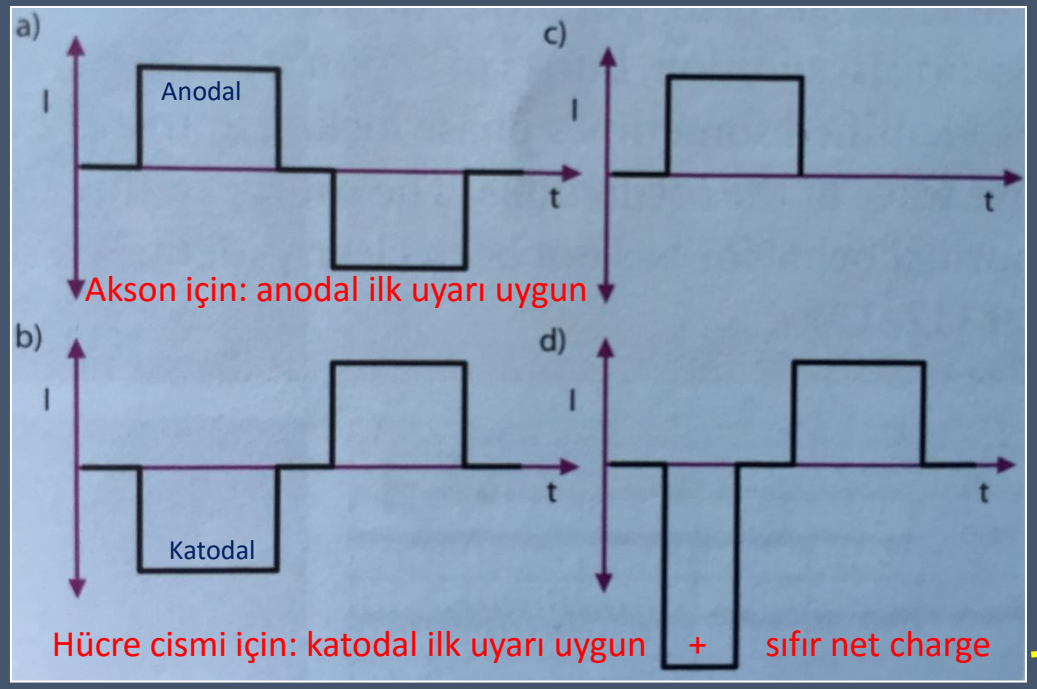






Ameliyat sonrası, ideal olarak yerleştirilmiş ve tüm elektrotları çalışan mikroçip

Elektrik stimülasyonu için kullanılan current-controlled stimülasyon pulsları



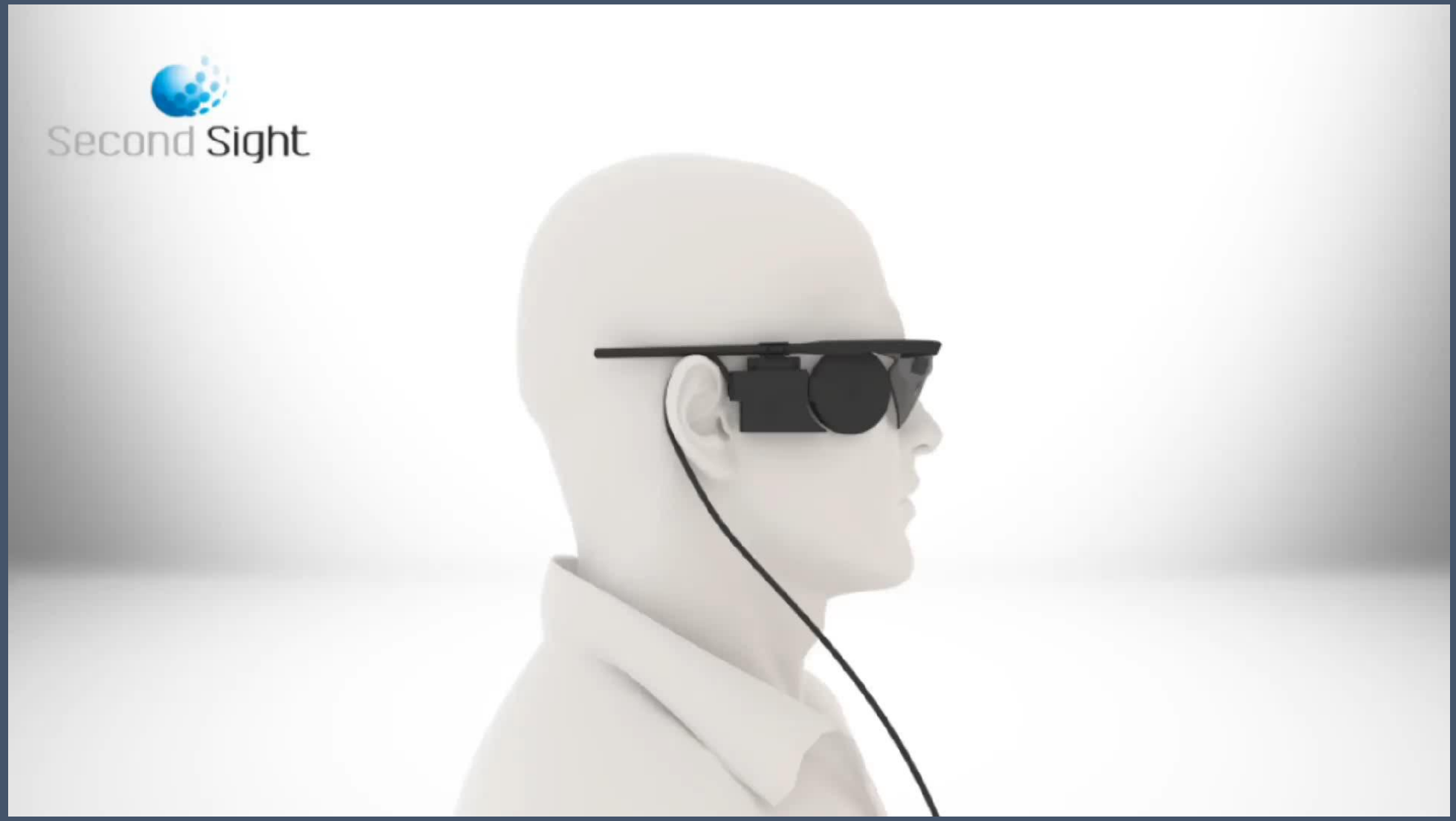
- Sadece tek pulslar, veya
  Pulslar treni uygulanabilir
- Doku hasarı olmaması için,
  sıfır net charge olmalı
- Nöral grubun toplam cevabı sıfır olmamalı
  (uyarıcı, inhibe edici cevapların toplamı
  nötralize olmamalı)

→ Ganglion hücresinin cismi uyarılmalı

- Elektrotlar ekstraselülerdir, nöronların içine girilmez
- Kullanılan elektrot çapı (200 µm) > RGC cismi (15 µm)
- Geniş bir nöral grubun / ağın uyarılması

Monopolar stimülasyon: Chip' in bir elektrodunda stimülasyon pulsu başlatılır.
Return elektrot (topraklama potansiyelinde) chip' den uzaktadır.

Bipolar stimülasyon: Return elektrot, chip' in elektrotlarından biridir.
Uyarılan retina alanı, monopolardan daha küçüktür.


Second Sight

Kliniğimizde yapay görme & biyonik göz çalışmaları

2013: Second Sight' a başvuru, merkez olabilmek için akreditasyon çalışmalarına başlama

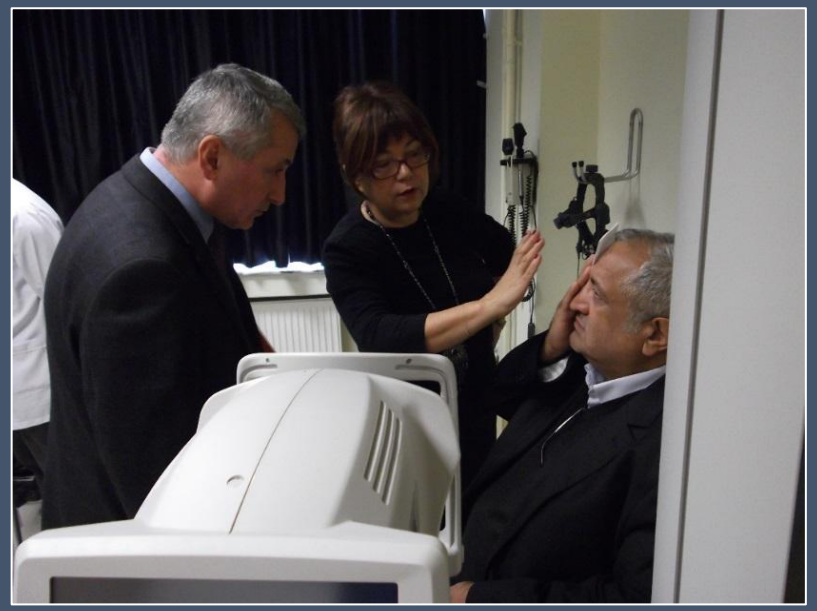
2014-2016: Hasta seçimi ve uygunluk testleri / ameliyat yöntemi ve ameliyat sonrası rehabilitasyon için alt yapı ve bilgilenme çalışmaları

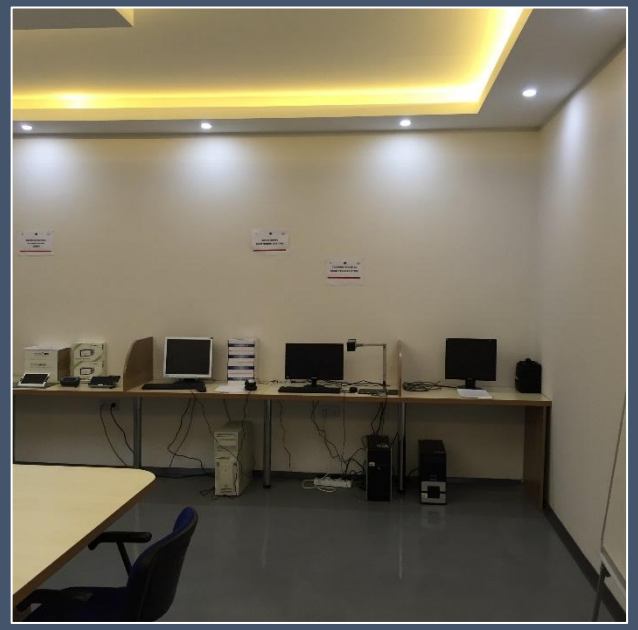
- Aachen Üniversitesi 2013
- Michigan Üniversitesi 2014
- Prof. Dr. S. Rizzo ile çalışma 2015
- Prof. Dr. Rizzo' nun Ankara - ESASO' ya daveti 2015
- Aachen Üniversitesi 2015
- 2015-2016: Kliniğimizde endoskop destekli Argus II implantasyonu
- Sunular: Frankfurt Retina Meeting 2016, Euretina-Kopenhag 2016, Floretina-Florensa 2016, Euretina-Barcelona 2017, Aachen 2017

YAPAY GÖRME & BİYONİK GÖZ BİYOFİZİK LABORATUARLARI

Ankara Üniversitesi Tıp Fakültesi - Vehbi Koç Göz Hastanesi

Yapay Görme & Biyonik Göz Laboratuarı





KLİNİĞİMİZDEKİ SİMÜLE YAŞAM ALANLARI

BÜYÜK ETİKETLER

IŞIKLI İŞ MASASI

CCTV (CLOSED CIRCUIT TV SİSTEMİ)

SINIF

MUTFAK

KONTRAST RENKLER

YEMEK MASASI

PARA ÇEKME MAKİNASI

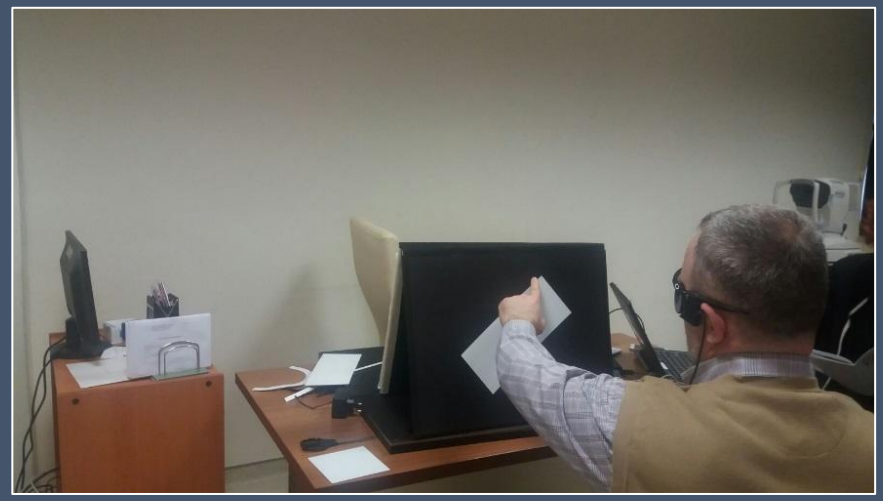
YAYA GEÇİDİ

Argus II epiretinal protez aşamaları

1- Uygun hasta seçimi
Beklentiler….

2- Ameliyat

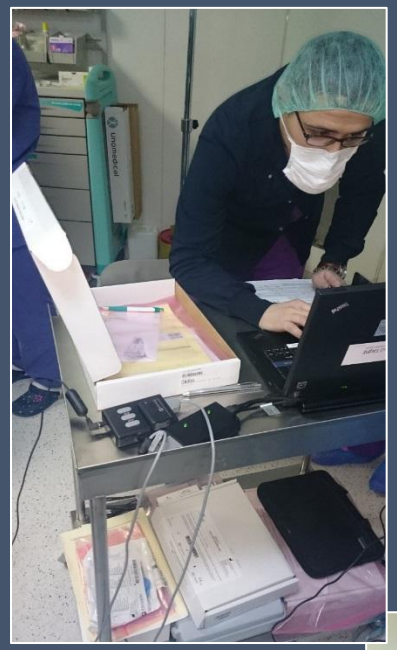
3- Fitting: elektrot aktivasyonu,
empedans, kamera ayarı



4- Rehabilitasyon

Uygun hasta seçimi, hastayı bilgilendirme ve sistemi tanıtma

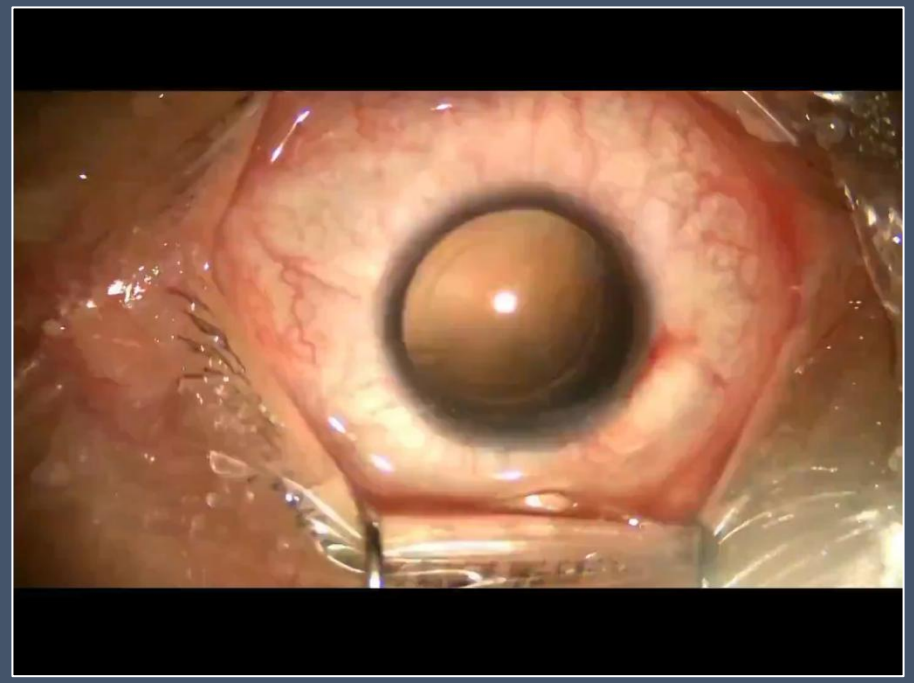
Ameliyathanede geri planda yoğun bir ekip çalışması



Dünyada ilk defa; endoskop destekli, 3-D görüntülü biyonik göz implantasyonu

Endoskop

3-D Dijital vitrektomi



3-D DİJİTAL VİTREKTOMİ…..

- Düşük ışık yoğunluğu, fototoksisite yokluğu
- Göz içi parlamalarda azalma
- Dijital filtreleme ile kontrastı artırma
- Artmış derinlik / genişlik hissi

Surgical Procedure Training

COMPLICATIONS & INTERVENTIONS

COMPLICATION	AWARENESS	OCCURRENCE & TREATMENT
Hypotony	*Monitor IOP.*	Hypotony occasionally appears post-implant. *Condition can generally be managed medically. If low IOP is sustained, sclerotomy may be leaking and require prompt intervention.*
Retinal Tear or Detachment	*Monitor retinal condition.*	Retinal tears or detachments occasionally appear post-implant. *Pay close attention to electrode region and sclerotomy site. If detachment occurs, surgical intervention may be required.*
Conjunctival Erosion	*Monitor integrity of conjunctiva.*	Conjunctival erosion has occurred post-implant. *Pay close attention to temporal quadrants. If suture, suture tab or electronics case erode through conjunctiva, immediate surgical intervention is recommended.*
Endophthalmitis	*Monitor intra-ocular health.*	Exogenous endophthalmitis has occurred post-implant. *Condition can generally be managed medically, with intravitreal antibiotics, after urgent sampling for microbial and fungal cultures.*
Dislodged Tack	*Monitor stability of array position.*	Tack has rarely dislodged post-implant. *If array position changes significantly, this may indicate a dislodged tack and immediate surgical intervention is recommended.*

Second Sight Clinical Update-2015

* Hypotony (6,7 %): ciliary body damage and / or detachment
* Retinal tack issues (6,7 %)
* Inadequate array – macular contact
* Retinal tear (3,3 %) / RD (6,7 %)
* Endophthalmitis – infective (10 %)

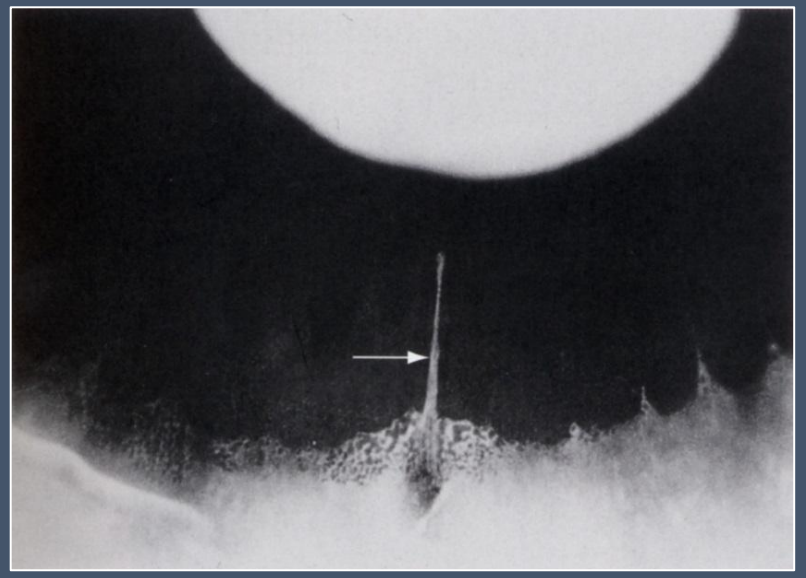
Developmental variations of the ora serrata

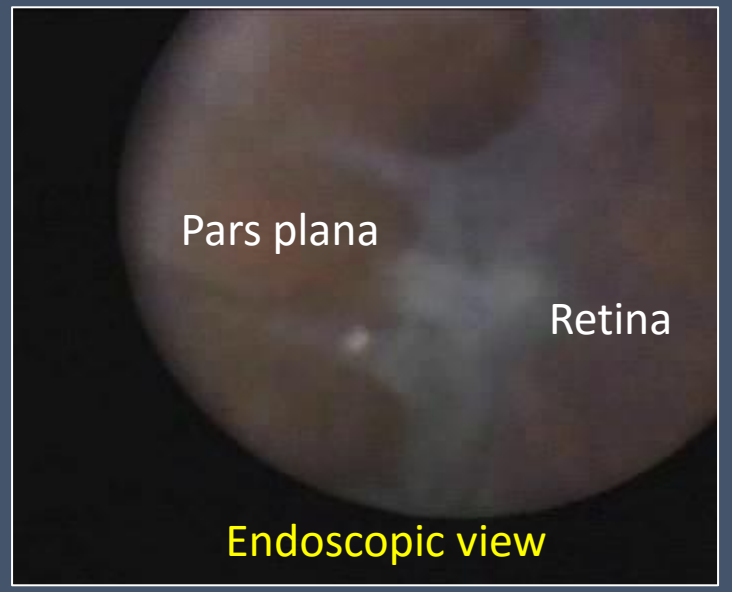
Variations in the normal pattern of the ora serrata are common (47% of 204 normal eyes)

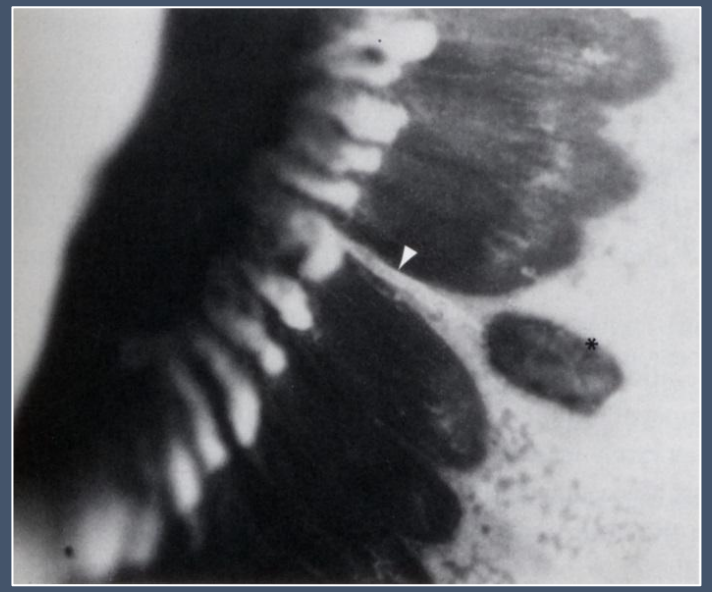
- Meridional folds (20 %)
- Meridional complexes (12 %)

} Thickened retinal tissue

- Oral bays (3%) Posterior extensions of the pars plana into the retina





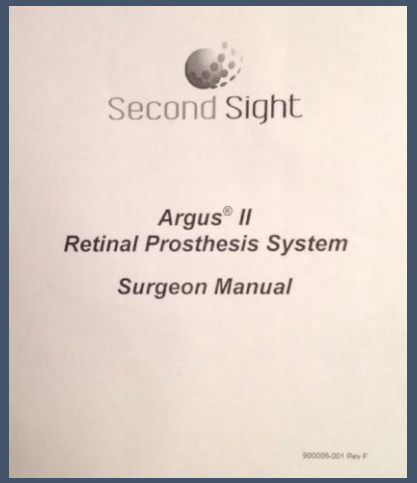


1- Michels RG, Wilkinson CP, Rice AT: Retinal Detachment. The CV Mosby Company, 1990

2- Rutnin U, Schepens CL: Fundus appearance in normal eyes. The standard peripheral fundus and developmental variations. Am J Ophthalmol 64: 840, 1967

Scleral incision issues…..

In the presence of anatomic variations, surgeon can face scleral incision-related complications, since we use the prescribed distances based on the preop. axial length measurement



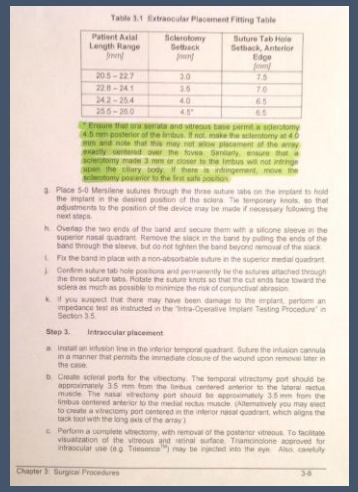


Table 3.1 Extraocular Placement Fitting Table

Patient Axial Length Range [mm]	Sclerotomy Setback [mm]	Suture Tab Hole Setback, Anterior Edge [mm]
20.5 – 22.7	3.0	7.5
22.8 – 24.1	3.5	7.0
24.2 – 25.4	4.0	6.5
25.5 – 26.0	4.5*	6.5

* Ensure that ora serrata and vitreous base permit a sclerotomy 4.5 mm posterior of the limbus. If not, make the sclerotomy at 4.0 mm and note that this may not allow placement of the array exactly centered over the fovea. Similarly, ensure that a sclerotomy made 3 mm or closer to the limbus will not infringe upon the ciliary body. If there is infringement, move the sclerotomy posterior to the first safe position.

g. Place 5-0 Mersilene sutures through the three suture tabs on the implant to hold the implant in the desired position of the sclera. Tie temporary knots, so that adjustments to the position of the device may be made if necessary following the next steps.

h. Overlap the two ends of the band and secure them with a silicone sleeve in the superior nasal quadrant. Remove the slack in the band by pulling the ends of the band through the sleeve, but do not tighten the band beyond removal of the slack.

i. Fix the band in place with a non-absorbable suture in the superior medial quadrant.

j. Confirm suture tab hole positions and permanently tie the sutures attached through the three suture tabs. Rotate the suture knots so that the cut ends face toward the sclera as much as possible to minimize the risk of conjunctival abrasion.

k. If you suspect that there may have been damage to the implant, perform an impedance test as instructed in the "Intra-Operative Implant Testing Procedure" in Section 3.5.

Step 3. Intraocular placement

a. Install an infusion line in the inferior temporal quadrant. Suture the infusion cannula in a manner that permits the immediate closure of the wound upon removal later in the case.

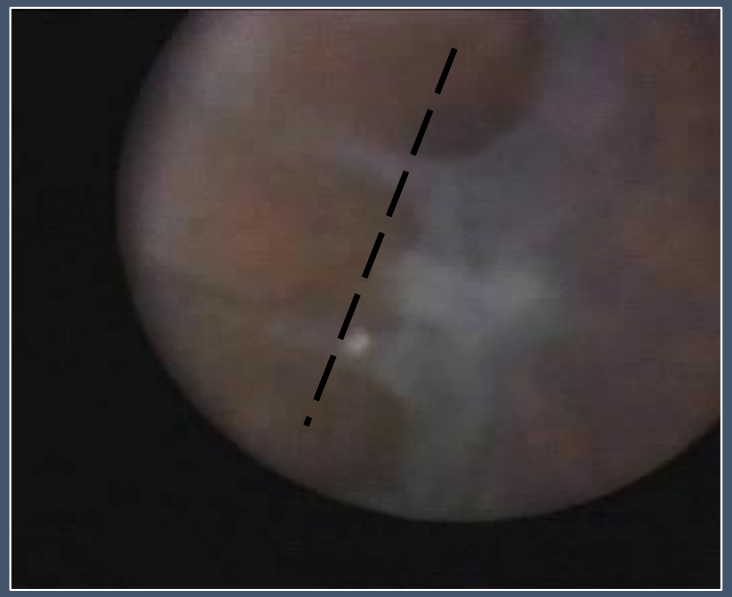
b. Create scleral ports for the vitrectomy. The temporal vitrectomy port should be approximately 3.5 mm from the limbus centered anterior to the lateral rectus muscle. The nasal vitrectomy port should be approximately 3.5 mm from the limbus centered anterior to the medial rectus muscle. (Alternatively you may elect to create a vitrectomy port centered in the inferior nasal quadrant, which aligns the tack tool with the long axis of the array.)

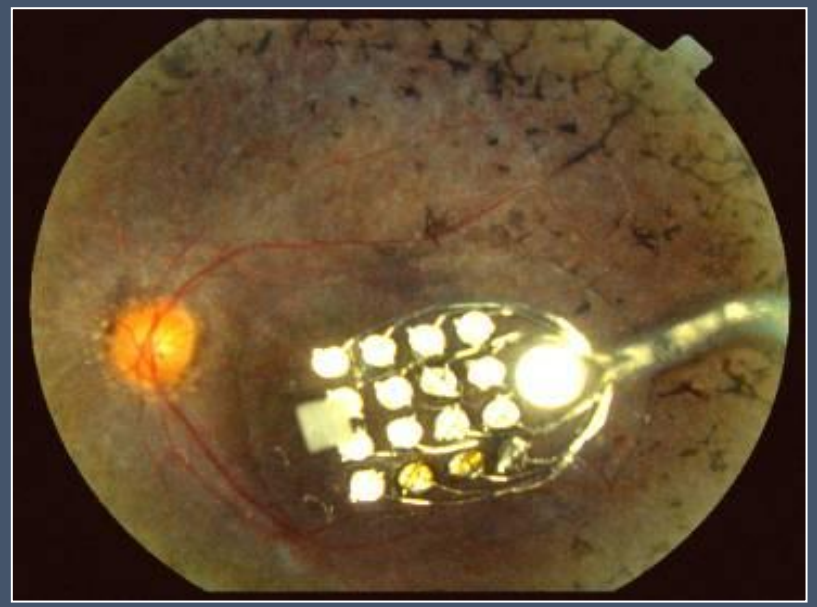
c. Perform a complete vitrectomy, with removal of the posterior vitreous. To facilitate visualization of the vitreous and retinal surface, Triamcinolone approved for intraocular use (e.g. Triesence™) may be injected into the eye. Also, carefully

Chapter 3: Surgical Procedures 3-8

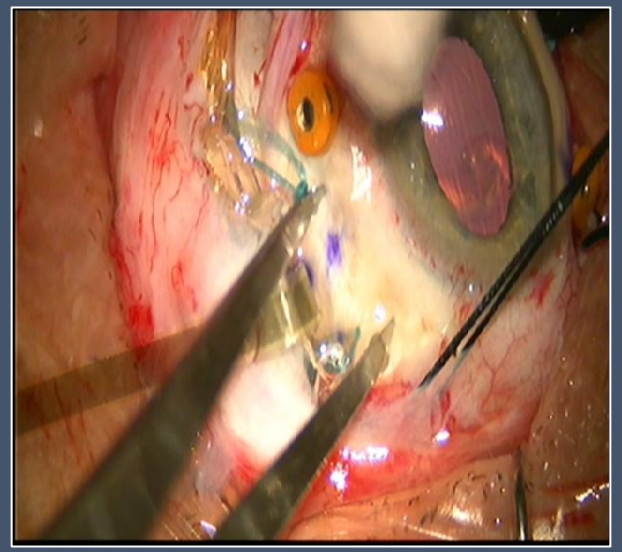
- Infringe upon the ciliary body
- Retinal damage
- Inadequate placement of the array over the fovea

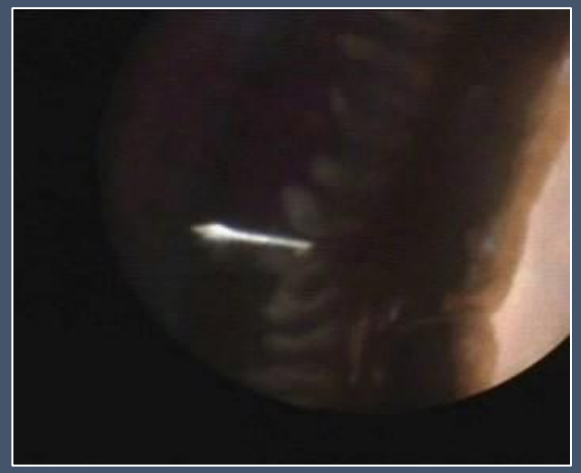
Argus II Surgeon Manual
(Second Sight Medical Products ,Inc. Sylmar, CA 91342 USA)

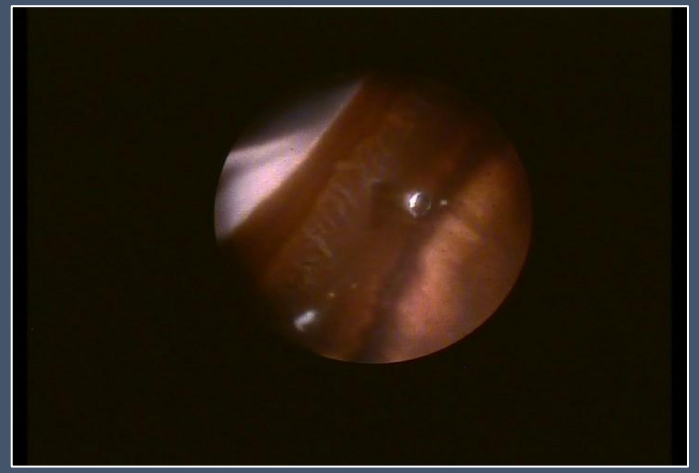


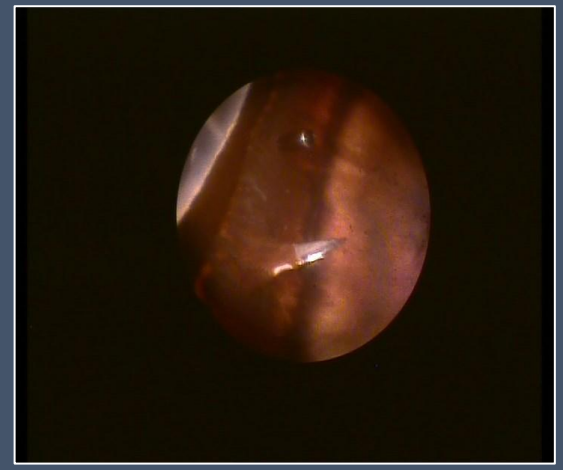


Endoscope-assisted & guided Argus II implantation





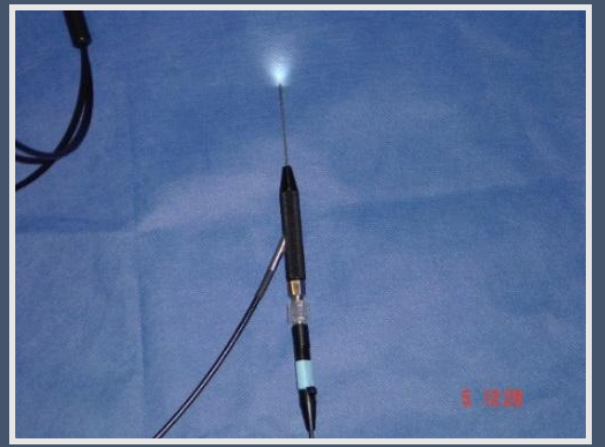




Özmert E, Demirel S: Endoscope –Assisted and Controlled Argus II Epiretinal Prosthesis Implantation in Late-Stage Retinitis Pigmentosa: a Report of 2 Cases. Case Rep Ophthalmol 2016; 7(3):315-324.

With endoscope-assisted and guided Argus II surgery …..

- We can create more suitable a 5.2 mm-pars plana sclerotomy incision for array insertion
- We can check the vitreous base / peripheral retina without scleral indentation
- If necessary, we can implement the endoscopic endolaser simultaneously
- We can assess the retinal tack compression and the contact between array-macula with the side view of angled endoscope probe

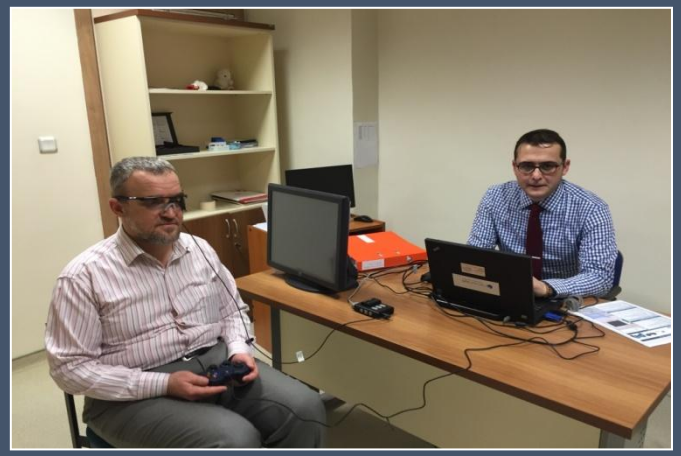


20 G / 23-G fused-fiber type endoscope

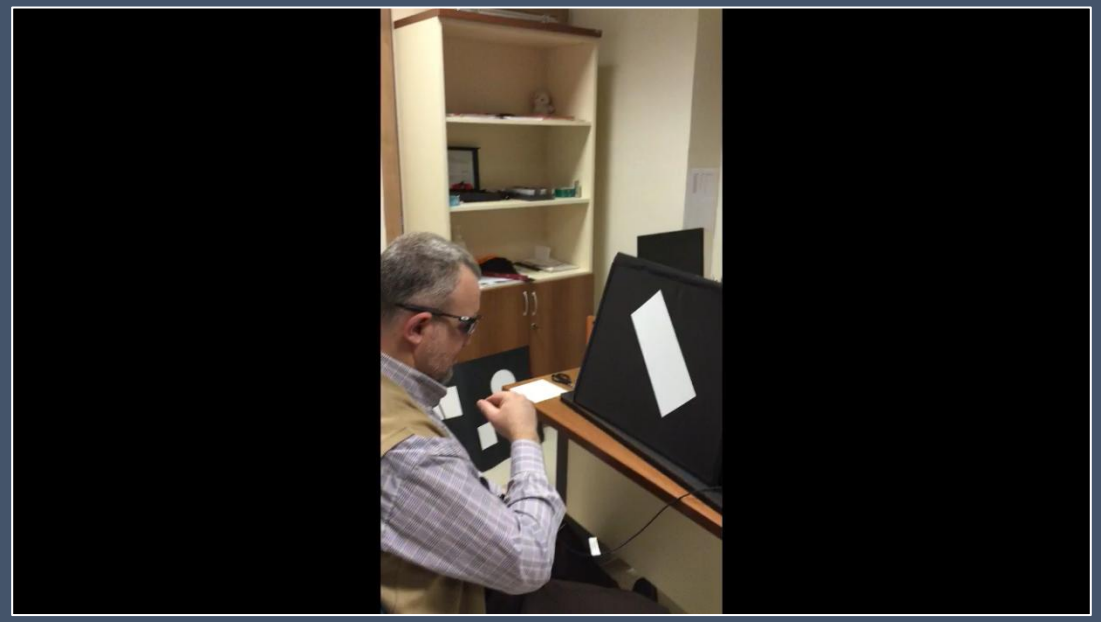
Endoscopy Assisted Argus II Epiretinal Prosthesis Implantation
DOI: 10.3207/4186093929

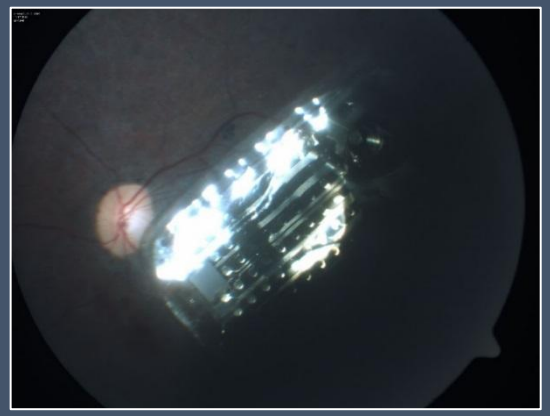
. Ameliyat sonrası 2. haftada: maküla üstü elektrotların ve sistemin aktivasyonu
. Bu işlemden 1 ay sonra, yapay görmenin öğretilmesi için uzun bir rehabilitasyon süreci gerekecektir

FITTING

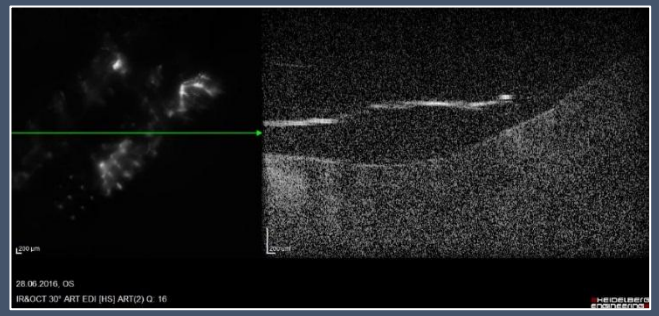


REHABİLİTASYON / 1. Hasta

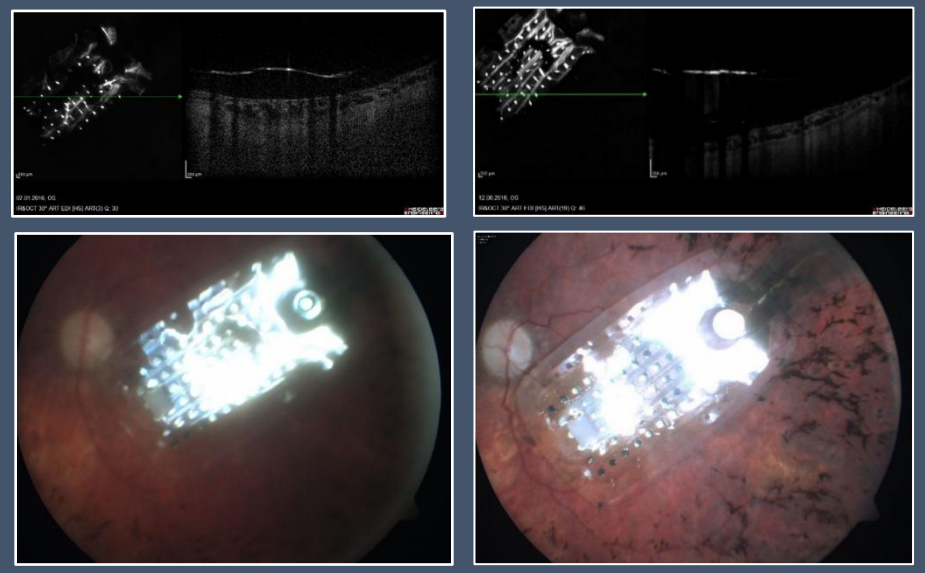




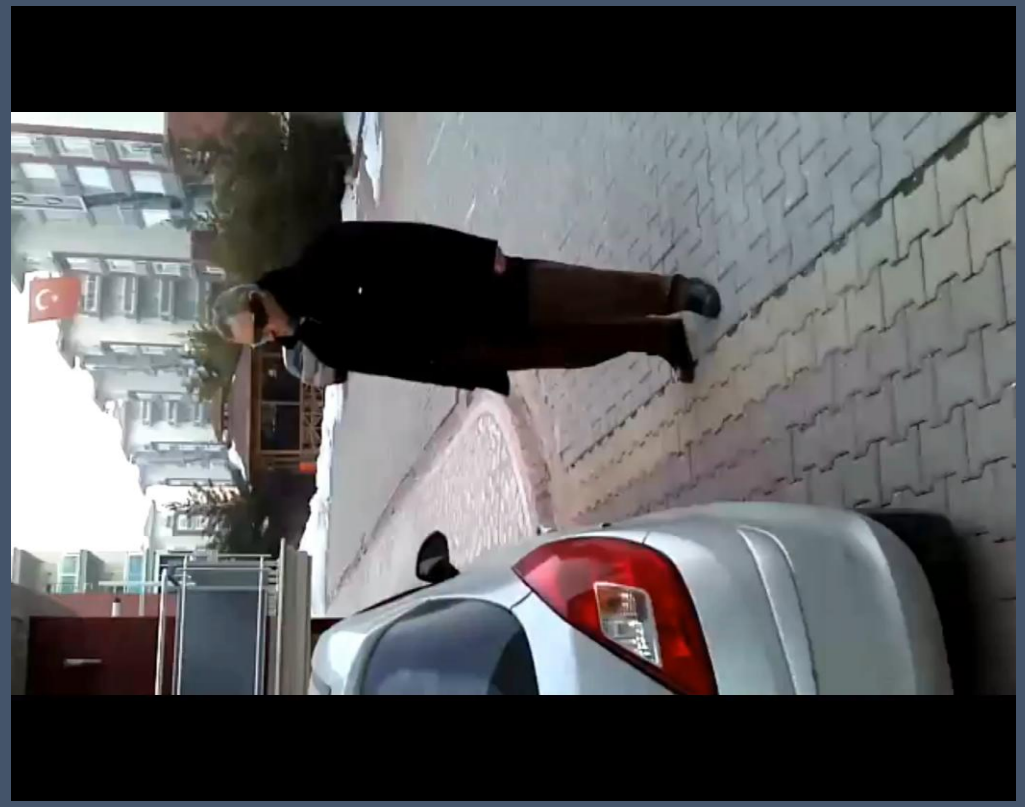
Makülada array



UA: 46 E, LE, 10 yıldır ışık hissi
(Cerrahi: 28 Aralık 2015)

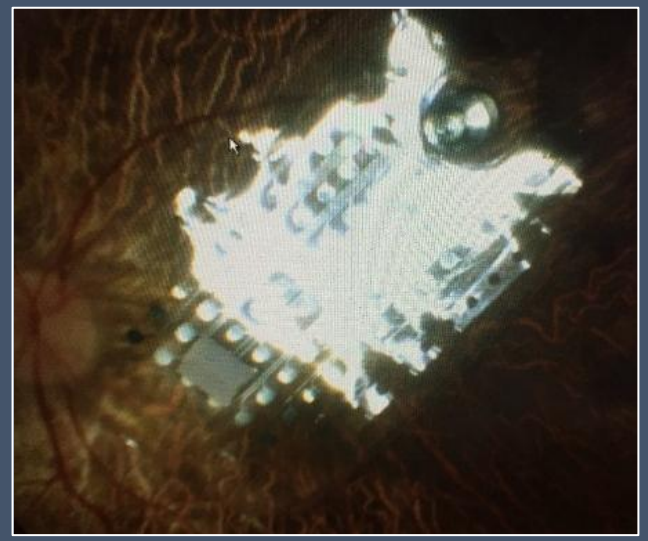


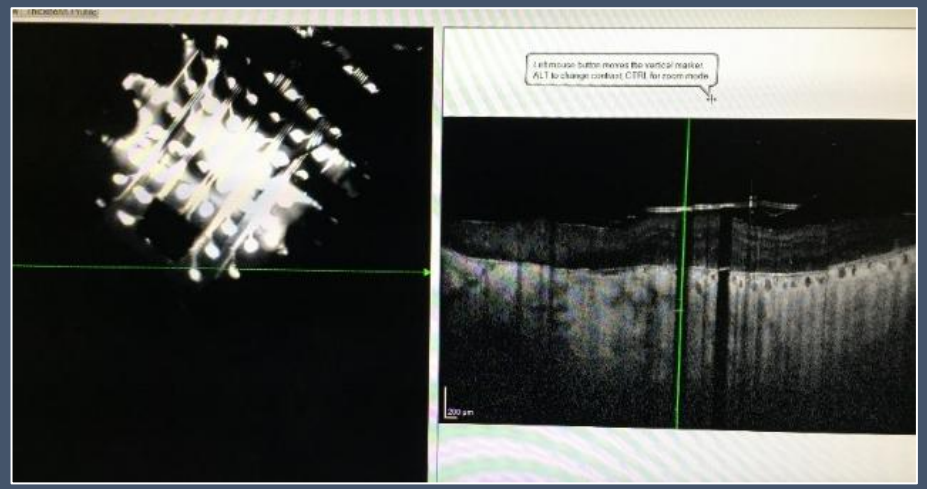
Postop. 4. gün Postop. 8. ay



Cerrahiden 16 ay sonra

TK: 52 D, LE, 15 yıldır ışık hissi
(Cerrahi: 24 Mayıs 2017)



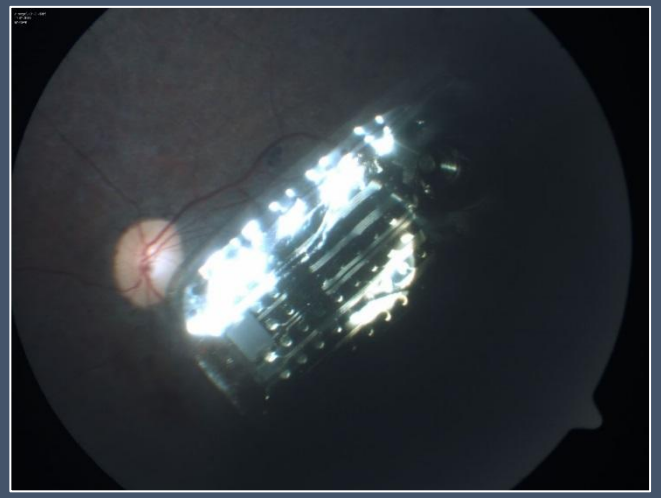


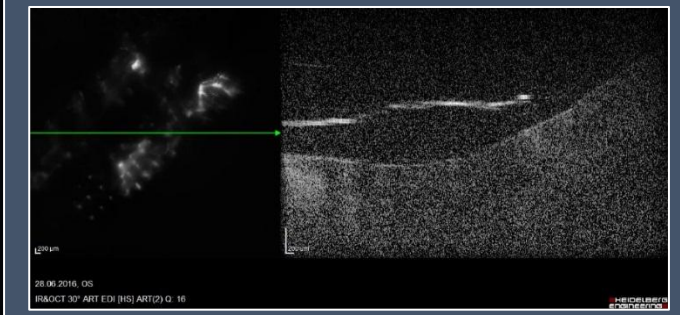
Cerrahiden 2 ay sonra

Görme rehabilitasyonu sonrası

Cerrahiden 10 ay sonra

- Hareketin yönünü ayırt etme
- Büyük harf görme, kısa kelime okuma
  (VA: 20 / 1262)
- Yön belirleme ve hareket edebilme
- Koyu ve açık renkleri ayırt edebilme
- Yaşam kalitesi artar
- Mobilite artar
- Bağımsız hareket edebilme artar
- FLORA Çalışması





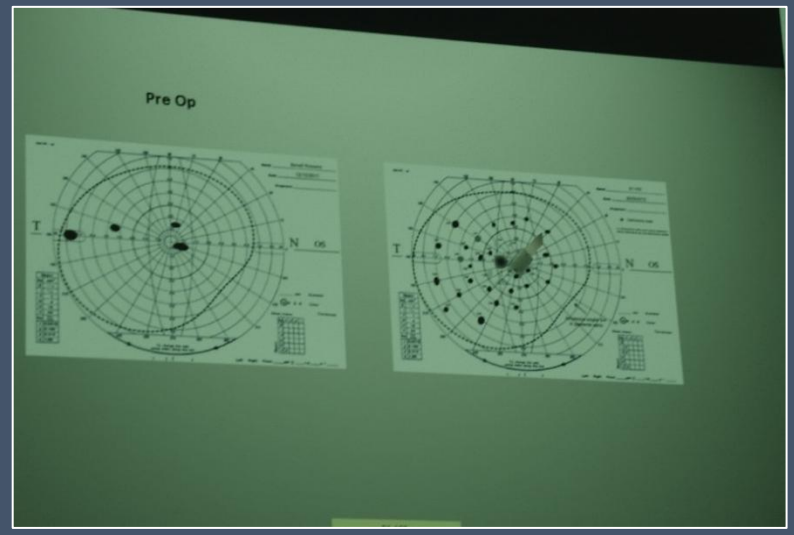
Hastanın hayat kalitesinde olan artışlar….

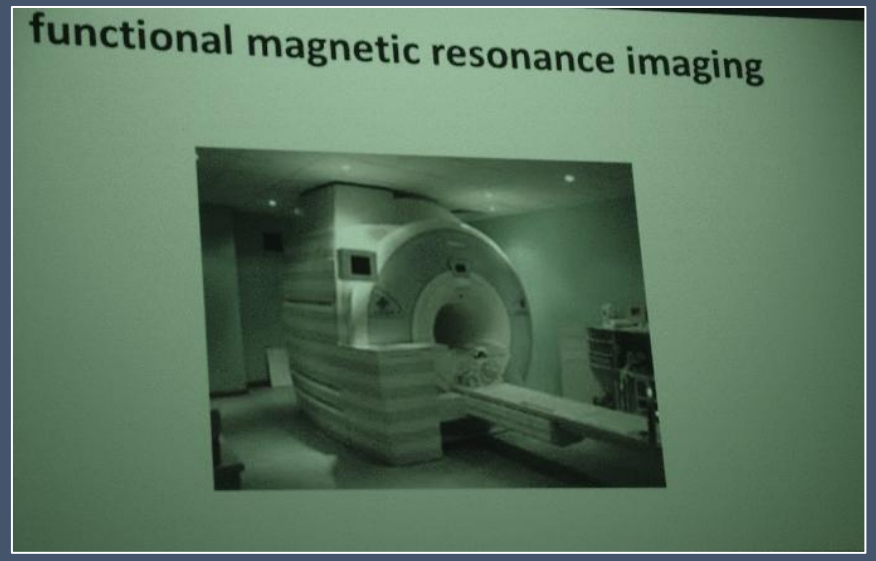
Olumlu etki % 77

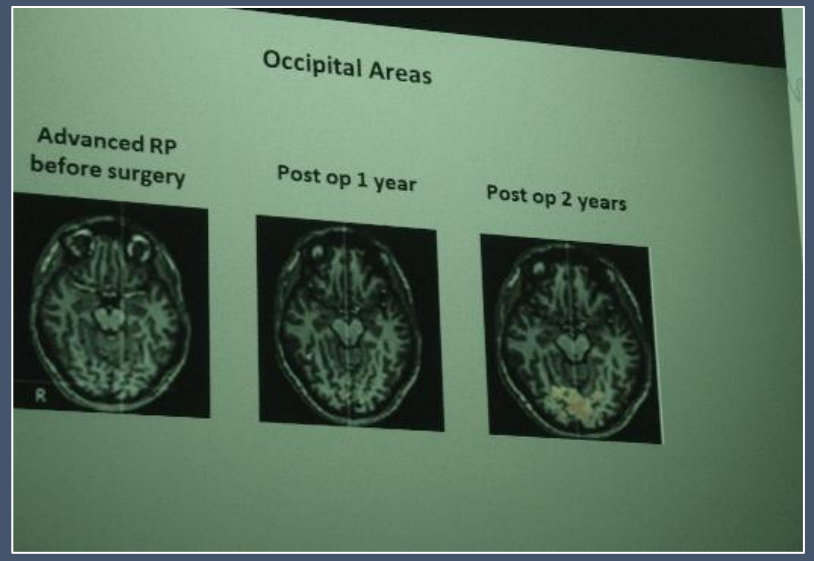
SUMMARY	Argus II System ON		Argus II System OFF	
	Number of subjects performing the task	Percent Possible	Number of subjects performing the task	Percent Possible
Locate ordinary objects at various distance (familiar environment)	24	**75.0%**	24	**20.8%**
Visually locate a place setting on a dining table	24	**83.3%**	24	**4.2%**
Sort light from dark laundry	18	**77.8%**	17	**5.9%**
Identify ordinary objects at various distances	24	**70.8%**	23	**21.7%**
Independently cross residential streets by following the lines of a crosswalk	19	**57.9%**	18	**22.2%**
Avoid obstacles while walking	25	**72.0%**	24	**29.2%**
Estimate the size of an obstacle	24	**58.3%**	22	**4.5%**
Avoid low-hanging branches, plants, head-high shelves, etc.	15	**53.3%**	15	**6.7%**
Detect curbs	23	**82.6%**	21	**19.0%**

Results from FLORA study (Functional Low-Vision Observer Rated Assessment)

AMELİYAT SONRASI GÖRME ALANI, FONKSİYONEL MRI DEĞİŞİMLERİ

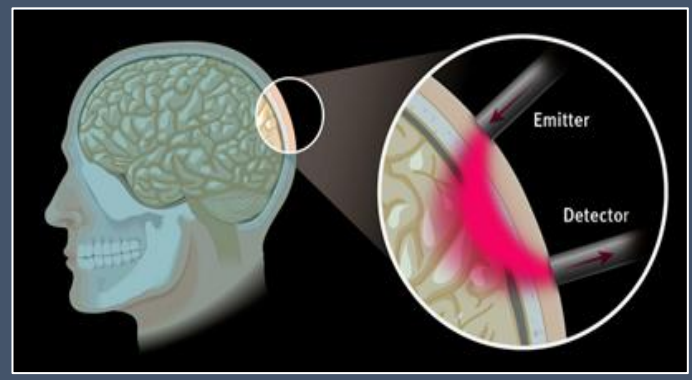


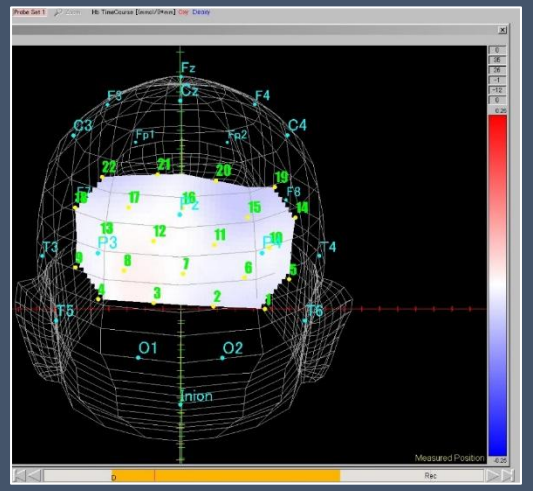


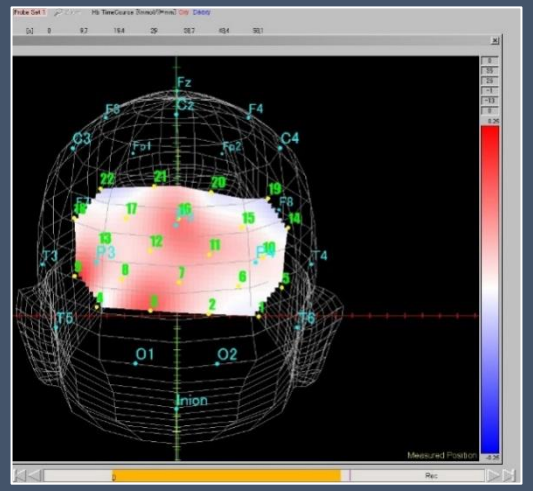


fNIRS (functional Near-Infrared Spectroscopy)

- 690 and 830nm near-infrared light is projected through the scalp and the skull into the brain by the emitters
- Near-Infrared light is transmitted to 3cm depth from the head skin (3 cm depth includes the cerebral cortex)
- The light is reflected back to the surface by drawing an arc through the tissue.
- The reflected light is collected back by the detectors
- Real time measurement is provided (calculation in 0,1 second)
- Measures relative changes in oxygenated and de-oxygenated hemoglobin







Boas DA et al: NeuroImage 23:275-88, 2004
Toronov V et al: Medical Physics ,28:521-527,2001
Wilcox T, Biondi M: Wiley Interdisip Rev Cogn Sci. 2015; 6(3):263-283

The advantages of fNIRS clearly outweigh the limitations….

	fMRI	fNIRS
Strengths	• Non-invasive • Repeatable • Widely available • Superior spatial resolution • Whole brain measurement	• Easy-to-use, non-invasive, non-ionizing • Repeatable • Portable • Relatively inexpensive • Much better temporal resolution over fMRI • Less restriction on motion • No interfere with metals in the body
Limitations	• Expensive • Physiological noise • Strict restriction on motion • Claustrophobia • Need for supine position • Noise produced by scanner • Interfere with metals in the body	• Measures information from only the cortical areas (no subcortical areas) • Lack of anatomical information • Spatial resolution is inferior to that of fMRI • Interpretation challenges related to multiple sources of vascular signals

Scarapicchia V, et al: Frontiers in Human Neuroscince . 2017; 11:1-12
Wilcox T, Biondi M: Wiley Interdisip Rev Cogn Sci. 2015; 6(3):263-283

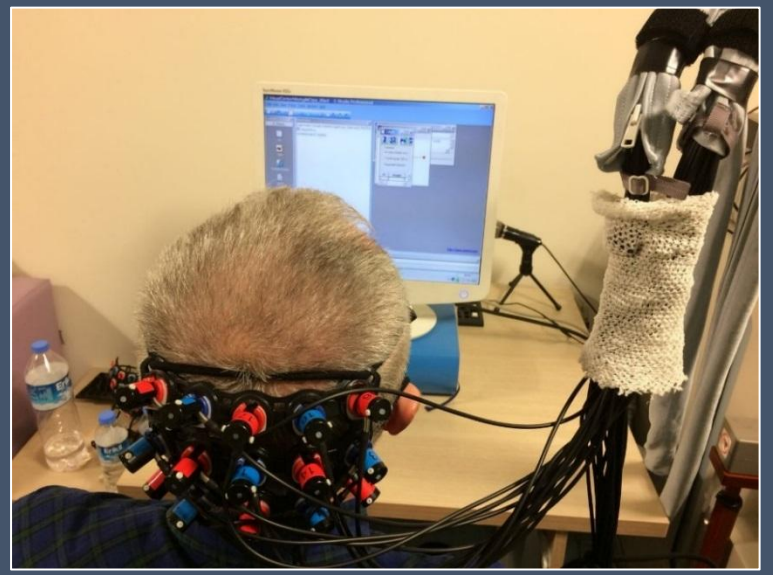
Material & Methods -1

Feasibility study of fNIRS in Argus II-implanted patients

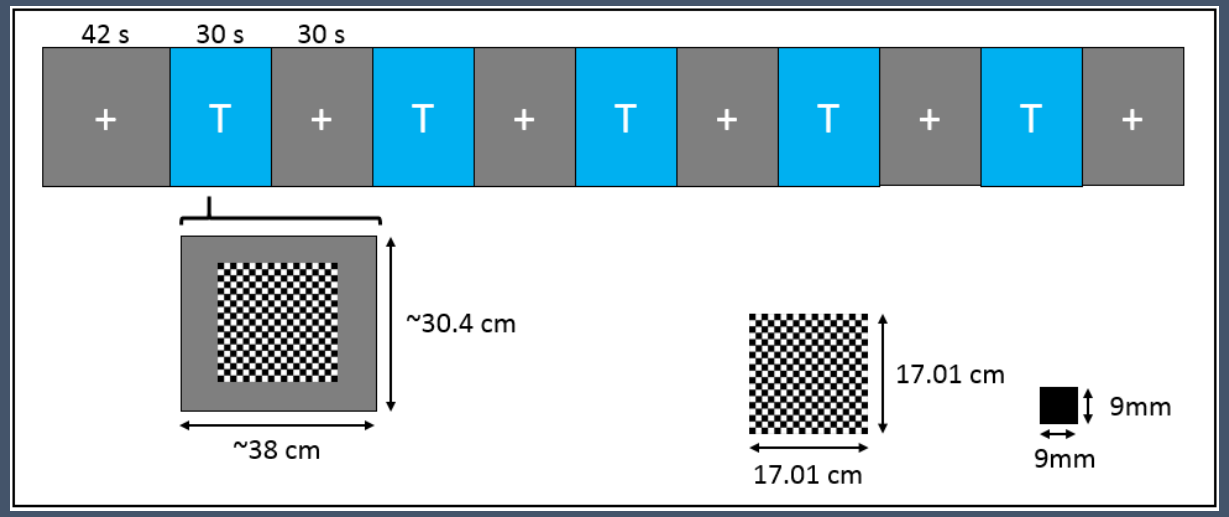
- Ankara University Brain Research Center & Department of Ophthalmology

- 3 patients were implanted with ARGUS II epiretinal prosthesis in
  Dec 2015, June 2016 and May 2017 (under the guidance and control of endoscope)

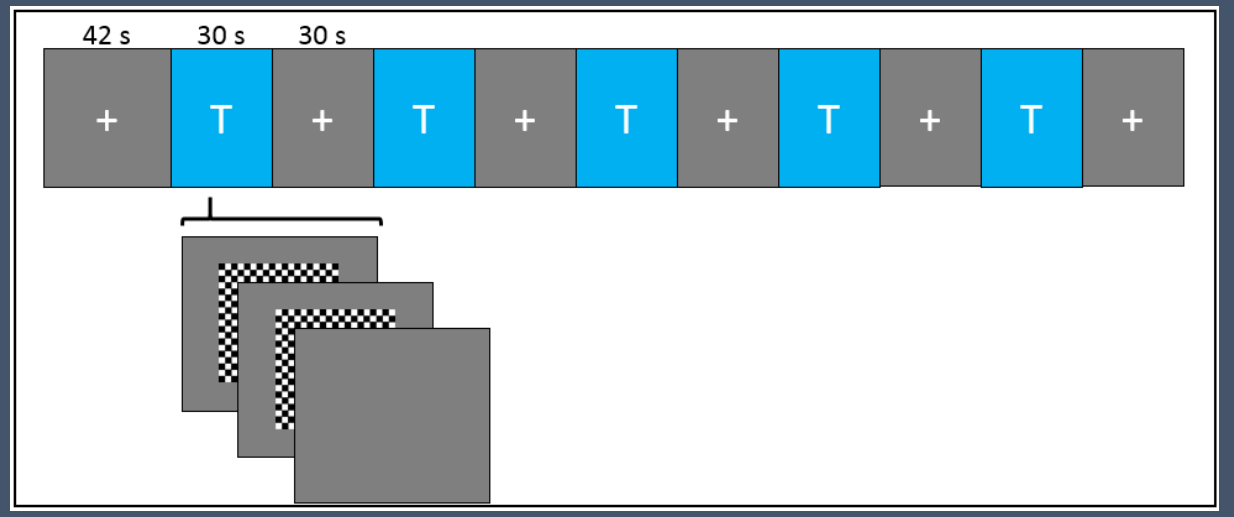
- Visual cortical activities were evaluated by fNIRS during the Argus-II system ON and OFF
  (22, 16, 5 months later after the surgeries)



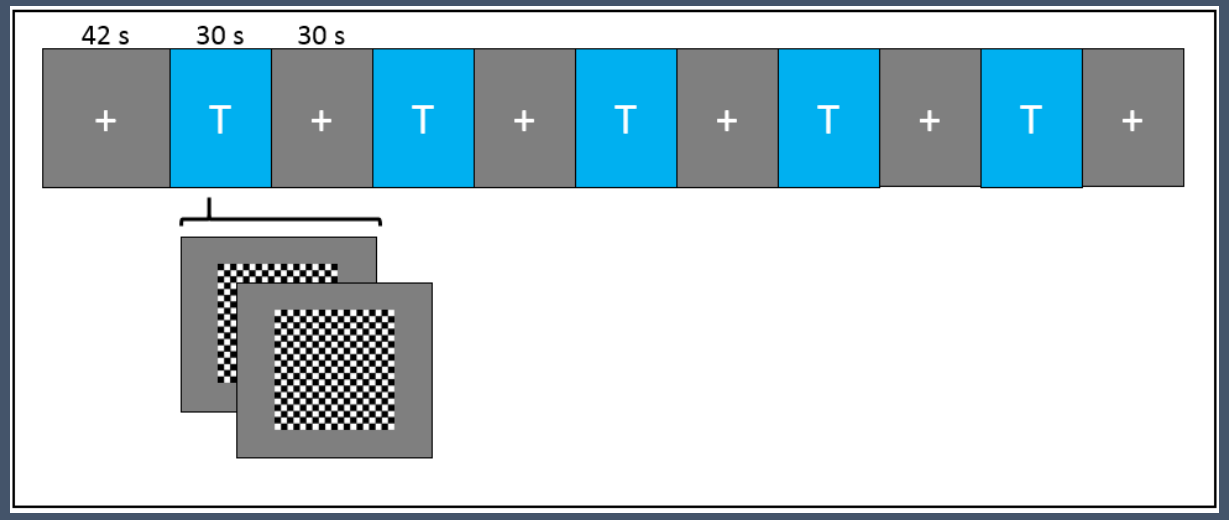
Static chequerboard



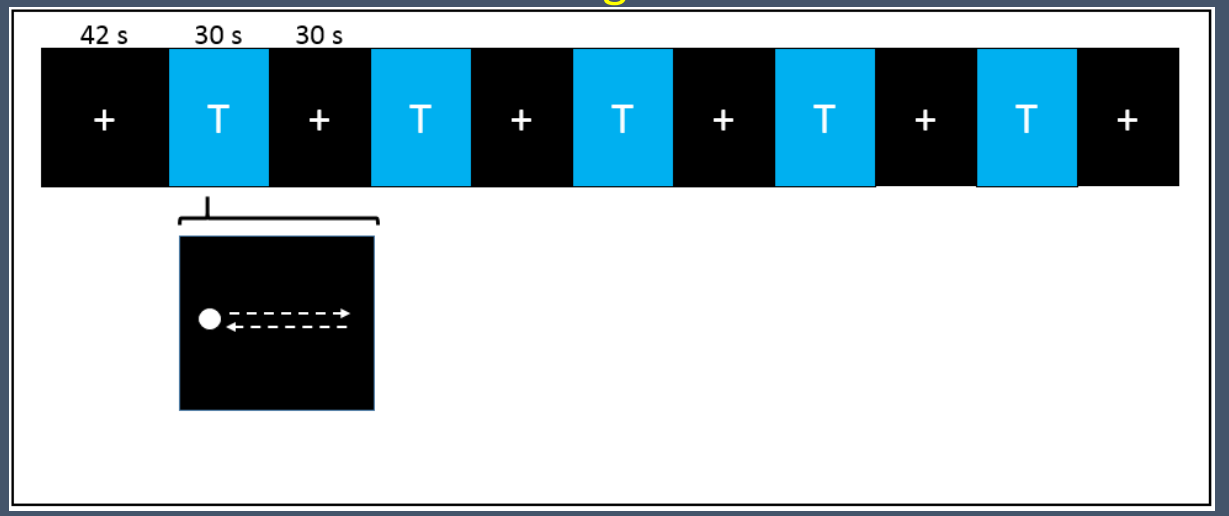
On – off chequerboard



Alternating (flicker) chequerboard



Moving ball



Moving Ball Stimulus

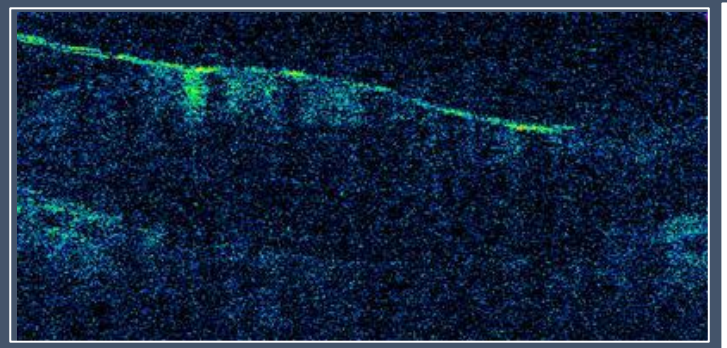
In the task blocks of the moving ball, there is a small white ball moving horizontally left-right direction for 30 seconds.

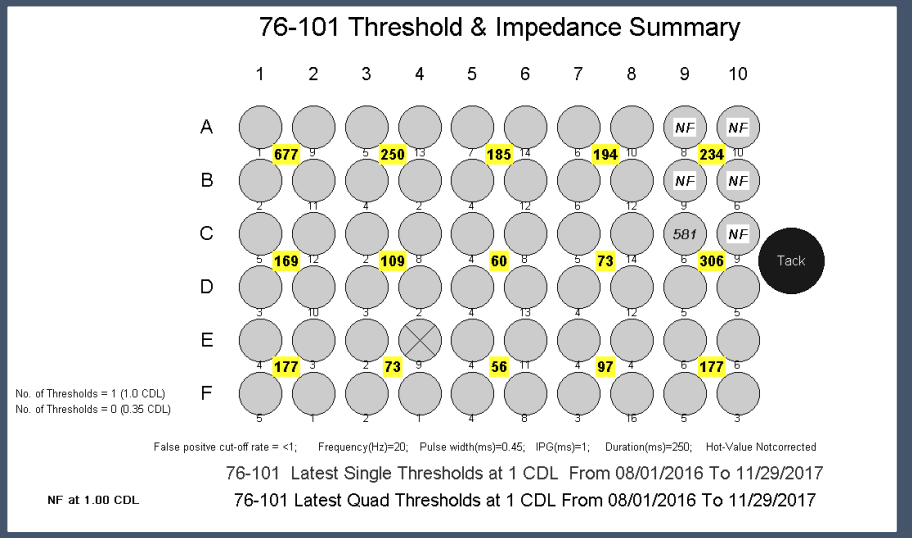
The participant was required to follow the moving ball.

The 2.2x2.2cm sized ball is seen on the screen with a 2.1° vertical and horizontal angles.

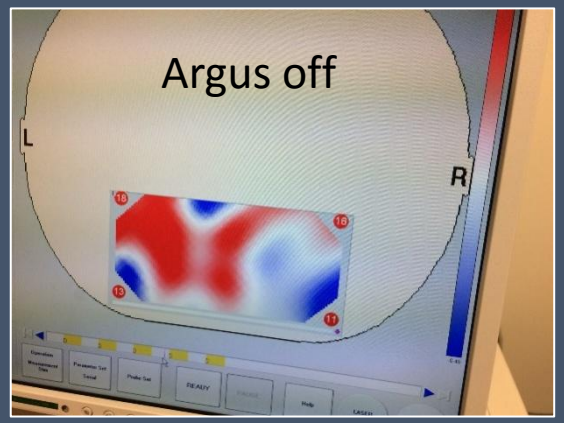
There are 5.75 left-right-left cycle within 30 seconds.

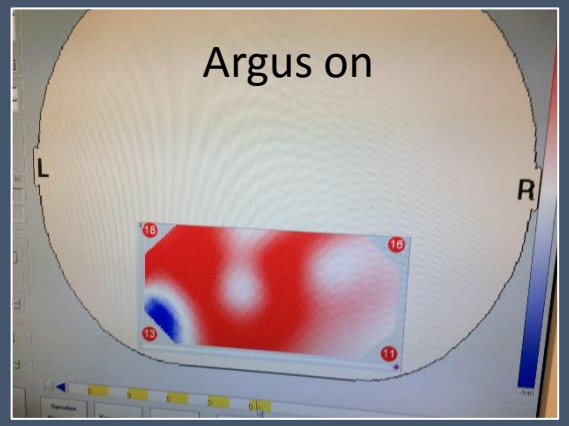
1- UA



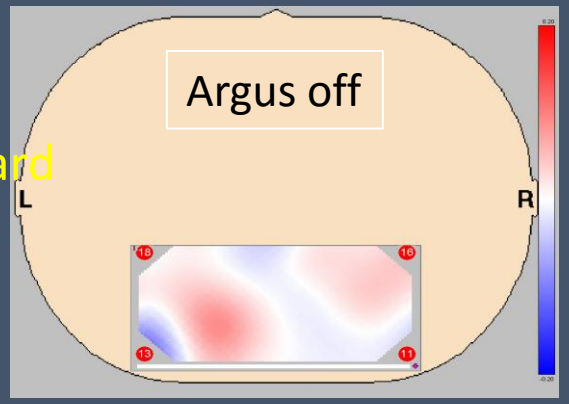


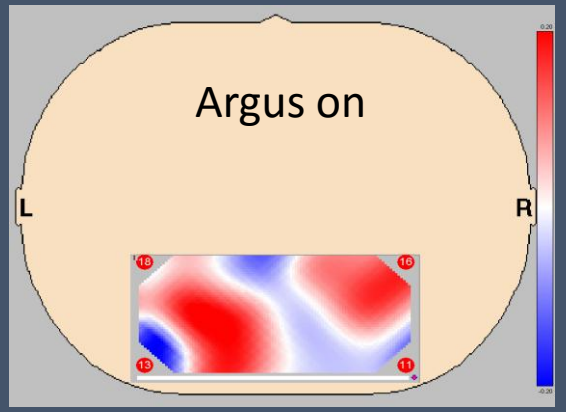
Moving ball

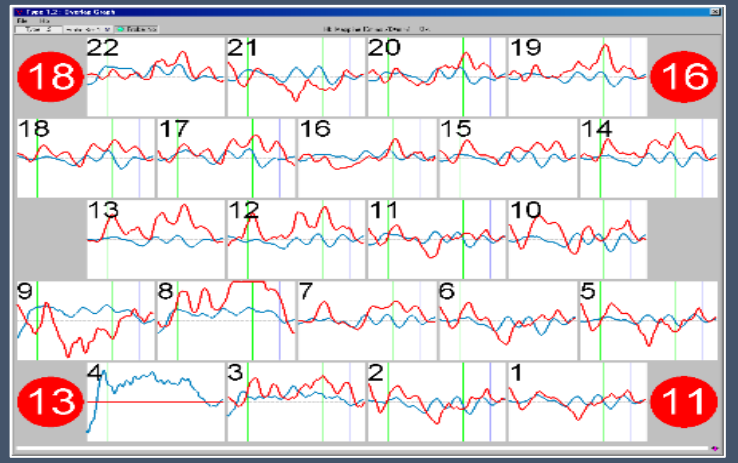




Flicker chequerboard





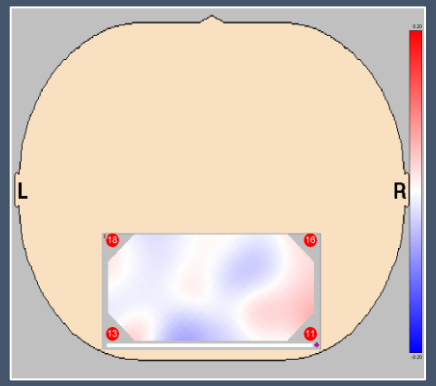


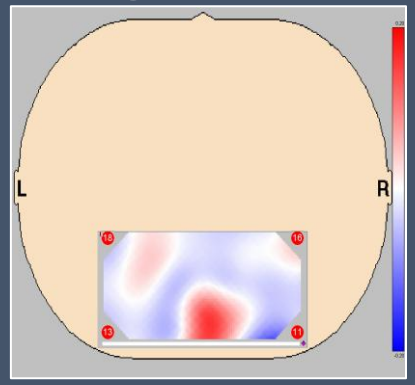
2-UY

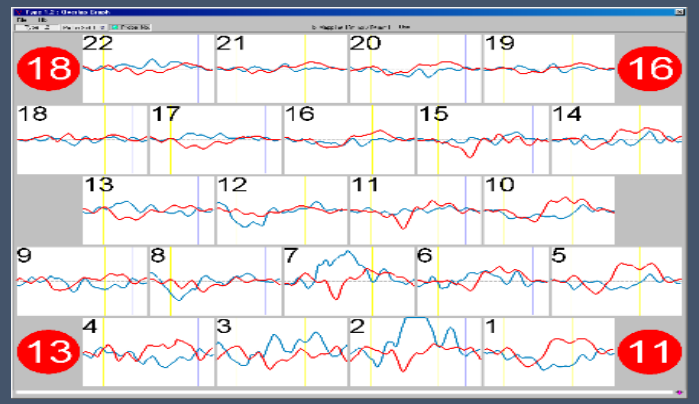
Argus off

Argus on

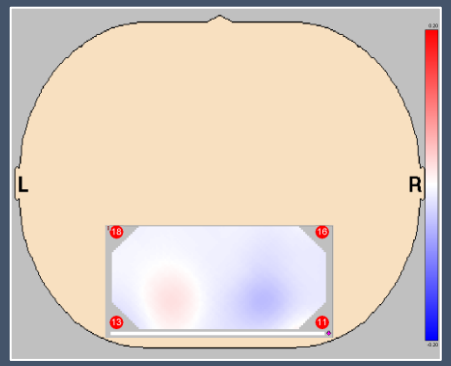
Static

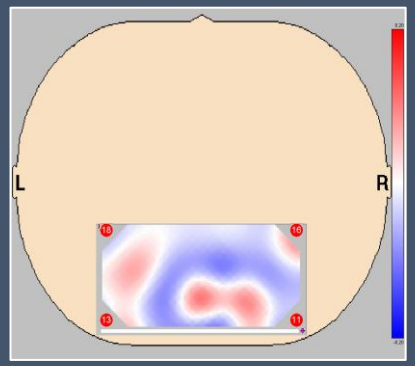


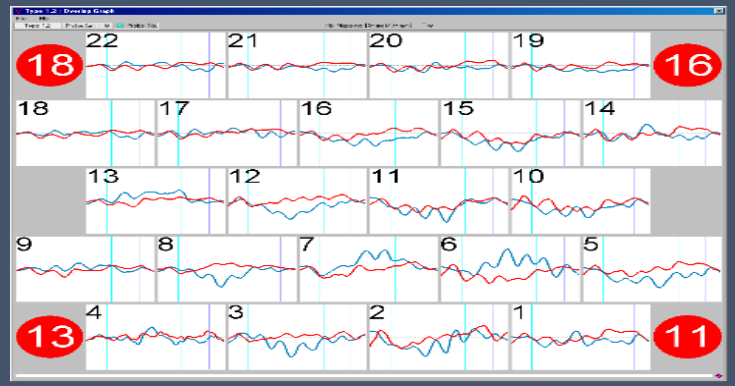


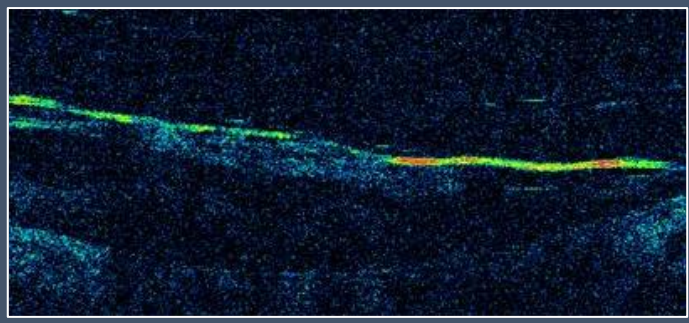


On-off

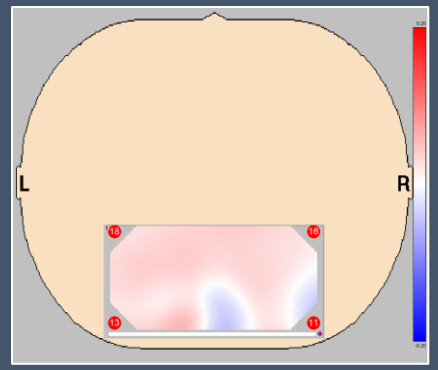


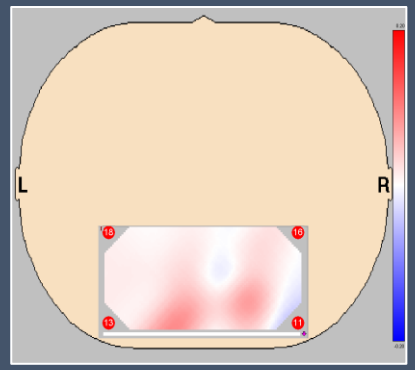


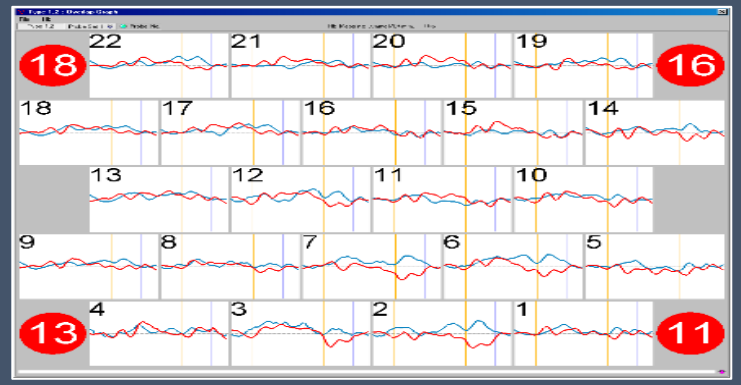


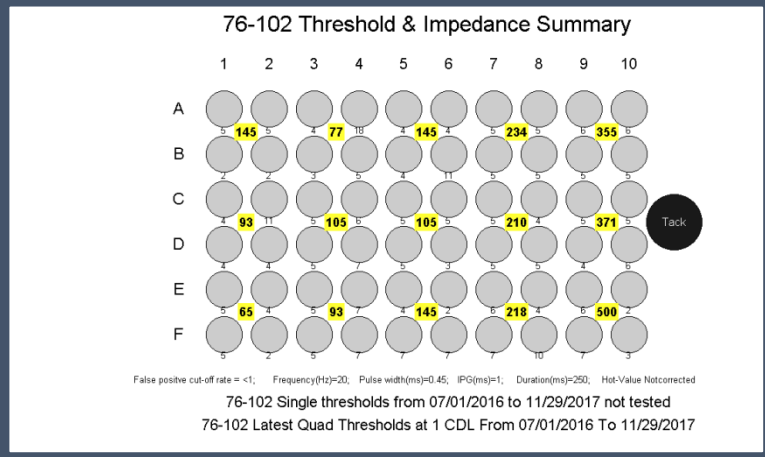


Moving ball

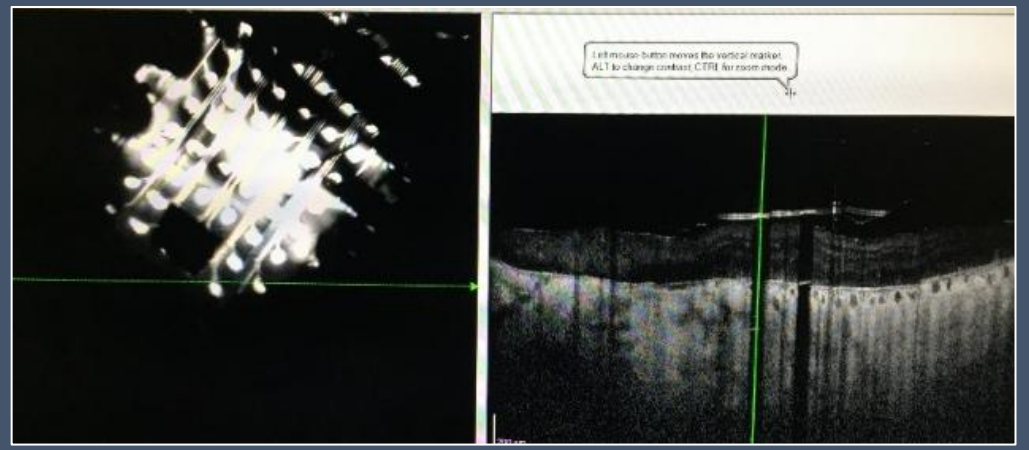


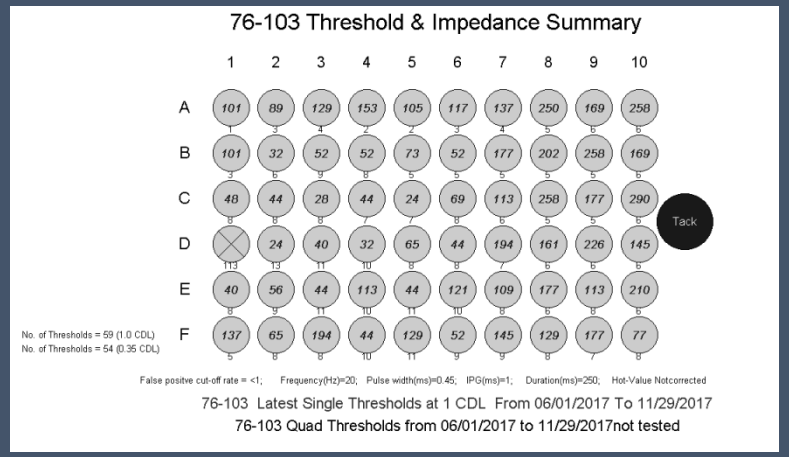




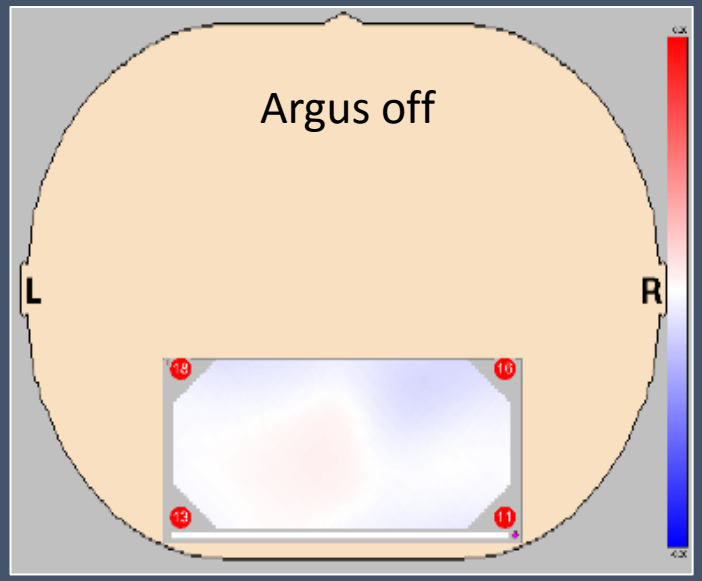


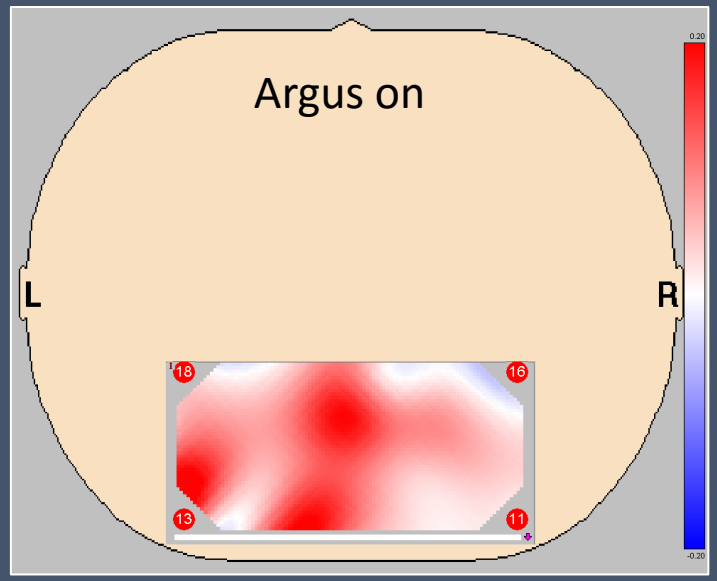
3-TK

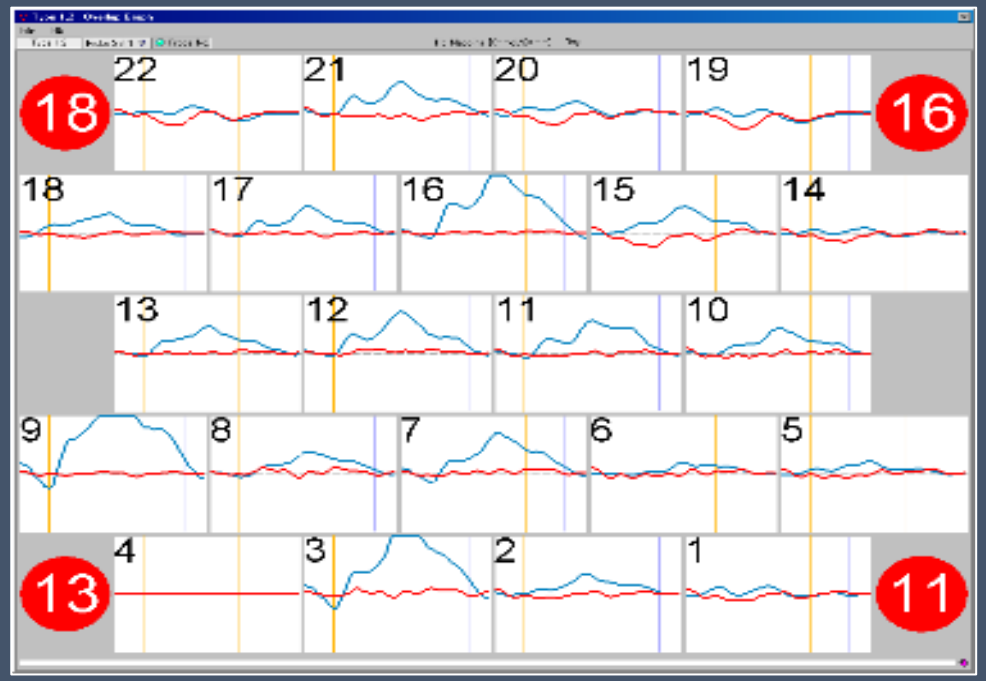




Moving ball







Artificial Vision, Almanya-Aachen, 1-3 Aralık 2017

Second Sight Inc – USA: International Surgical Mentor and Proctor (Kasım 2017)

Second Sight Global Press Release December 5, 2017

Second Sight

December 5, 2017

Second Sight Announces Market Entry into Iran with First Two Implants of Argus II Retinal Prosthesis System

- Marks Continued Global Expansion of Argus II for Individuals Blinded by Retinitis Pigmentosa -

SYLMAR, Calif.--(BUSINESS WIRE)-- Second Sight Medical Products, Inc. (NASDAQ: EYES) ("Second Sight" or "the Company"), a developer, manufacturer and marketer of implantable visual prosthetics that are intended to create an artificial form of useful vision to blind patients, today announced market entry into Iran, implanting the first two patients with the Company's Argus® II Retinal Prosthesis System ("Argus II"). The implant was facilitated by the country's exclusive distribution partner, Arshia Gostar Darman Co. Ltd.

"These first implants in Iran are part of our strategy to selectively target and partner with leading eye centers and distribution partners around the world in order to increase the availability of the Argus II to individuals with Retinitis Pigmentosa. The adoption of Argus II by a growing number of centers globally is a testament to the increasing acceptance of our technology," said Will McGuire, Chief Executive Officer of Second Sight.

The implants were performed in Shiraz, Iran during November 2017 by Professor Mohsen Farvardin and his team at the Shiraz Pars Hospital and Khalili Hospital, Shiraz Medical Science University in 44-year-old and 33-year-old patients with Retinitis Pigmentosa.

Professor Emin Özmert from the University Faculty of Medicine, Department of Ophthalmology, Ankara, Turkey acted as a supporting surgeon.

About the Argus II Retinal Prosthesis System

Second Sight's Argus II System provides electrical stimulation that bypasses the defunct retinal cells and stimulates remaining viable cells inducing visual perception in individuals with severe to profound Retinitis Pigmentosa. The Argus II works by converting images captured by a miniature video camera mounted on the patient's glasses into a series of small electrical pulses, which are transmitted wirelessly to an array of electrodes implanted on the surface of the retina. These pulses stimulate the retina's remaining cells, intending to result in the perception of patterns of light in the brain. The patient must learn to interpret these visual patterns, having the potential to regain some visual function. The Argus II was the first artificial retina to receive widespread commercial approval, and is offered at approved centers in Canada, France, Germany, Italy, Russia, Saudi Arabia, South Korea, Spain, Taiwan, Turkey, the United Kingdom, and the United States. Further information on the benefits and risks can be found in the peer reviewed paper at: http://www.sciencedirect.com/science/article/pii/S0161642016305796

About the Orion™ Visual Cortical Prosthesis System

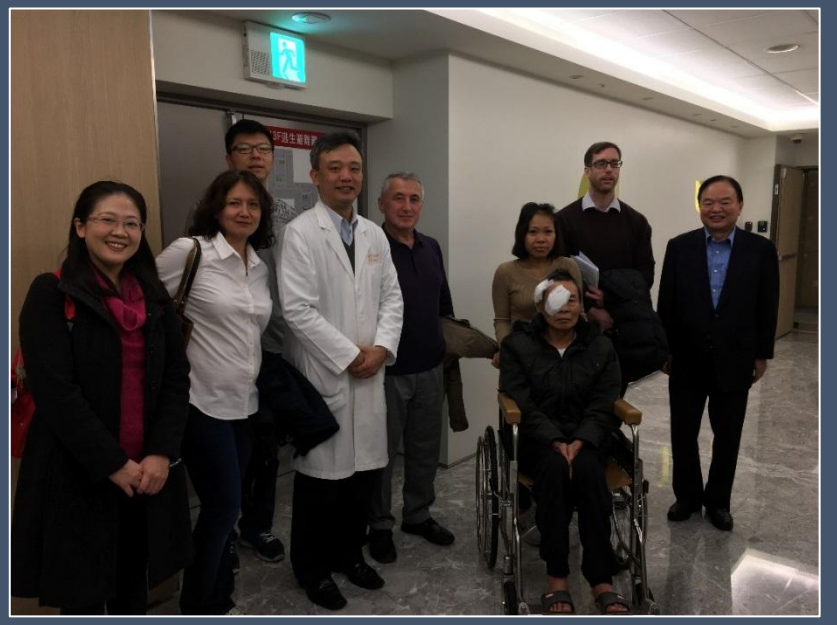
Second Sight, the manufacturer of the Argus II Retinal Prosthesis System (Argus II), has developed a new device, the Orion. A proof-of-concept clinical trial at UCLA demonstrating the viability of stimulation of the human visual cortex with a commercially available device from a different manufacturer was announced in Q4 2016. First-in-human clinical studies with the Orion are planned to begin in 2017. Like the Argus II, the idea behind Second Sight's Orion is to convert images captured by a miniature video camera mounted on the patient's glasses into a series of small electrical pulses. The Orion is designed to transmit these electrical pulses wirelessly to an array of electrodes implanted on the surface of the visual cortex, intended to result in the perception of patterns of light. By bypassing the retina and optic nerve and directly stimulating the visual cortex, a cortical prosthesis system has the potential to restore useful vision to patients completely blinded due to many reasons, including glaucoma, diabetic retinopathy, or forms of cancer and trauma - many fold more patients than for the current Argus II indications. No clinical data is yet available for the Orion.

About Second Sight

Second Sight's mission is to develop, manufacture and market innovative implantable visual prosthetics to enable blind

İran-Şiraz 3 kasım 2017

Tayvan 21 Aralık 2017

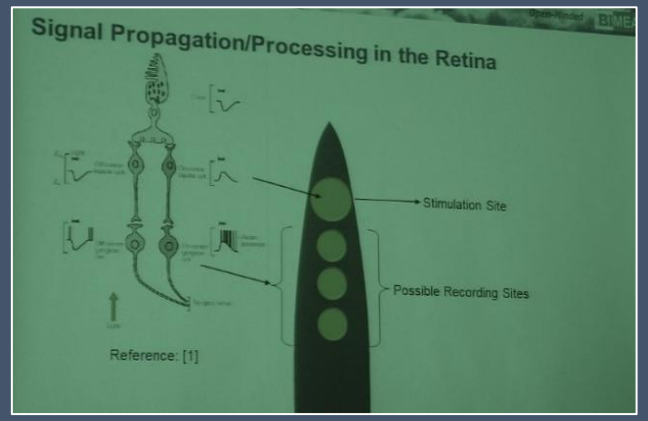


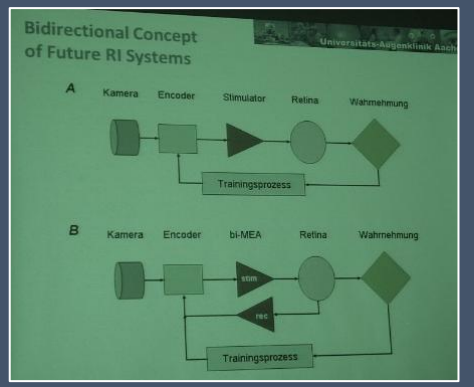
Singapur 18 Ocak 2018

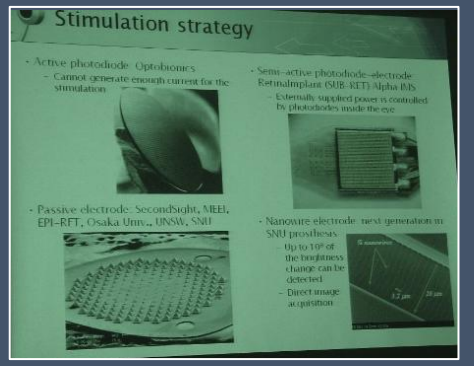
GELİŞMELER ……

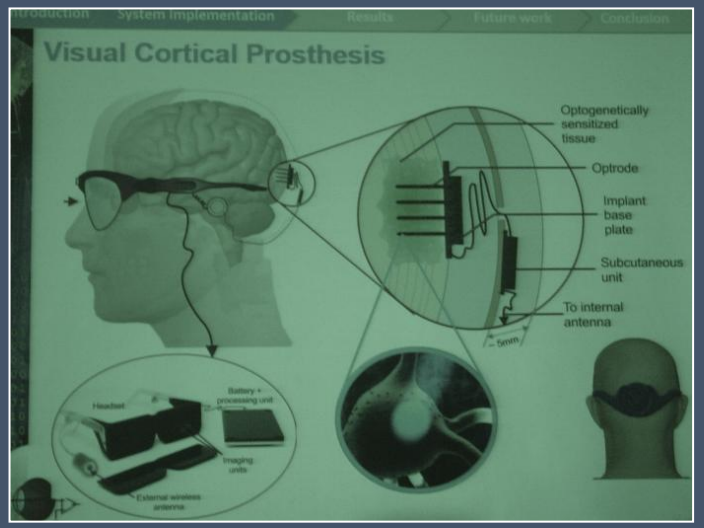
- Retina hasarını önleyen yeni stimülasyon stratejileri
- Fitting işlemini hızlandırmak için yeni algoritmalar
- Sanal elektrot oluşturma
- Punctate fosfen oluşturma
- Yüz tanıma
- Eye tracking
- Renk görme
- Derinlik bilgisi
- Gözlük, video, VPU, pil gelişmeleri, dijital kamera
- İğne, 3-D elektrotlarda gelişme, reverse telemetry
- Görme korteksi uygulamaları (ORION 1 projesi)

- İmplantasyon öncesi prognoz tayini testleri
- Argus II implantasyonundan sonra elektrofizyoloji

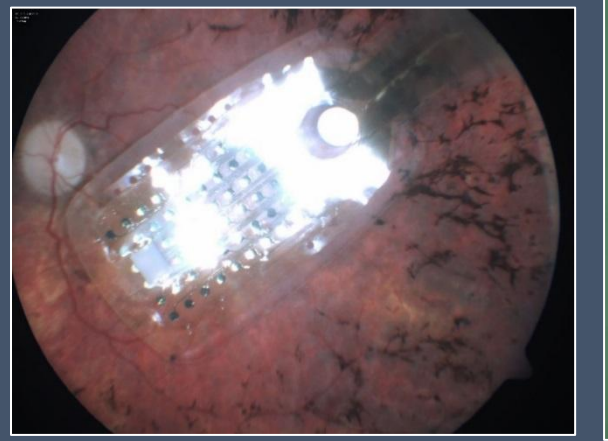


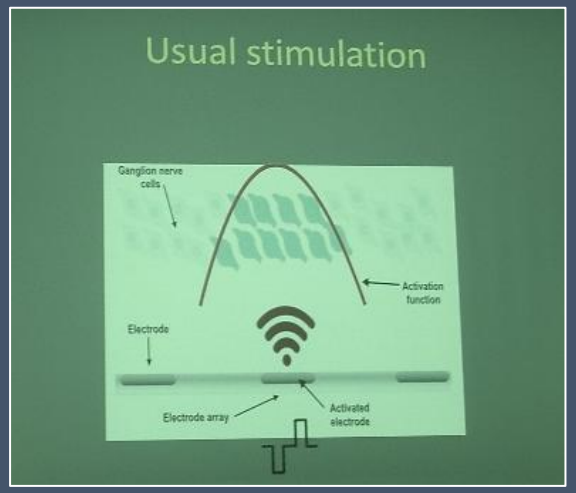


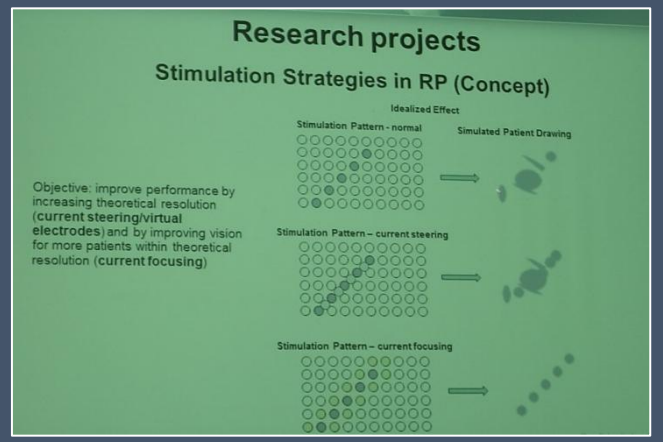


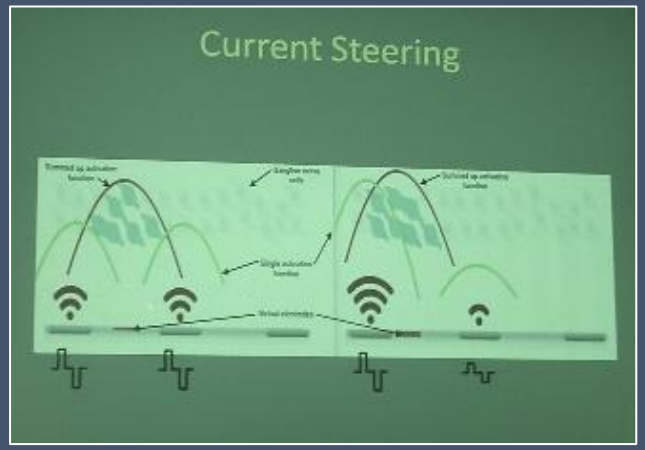


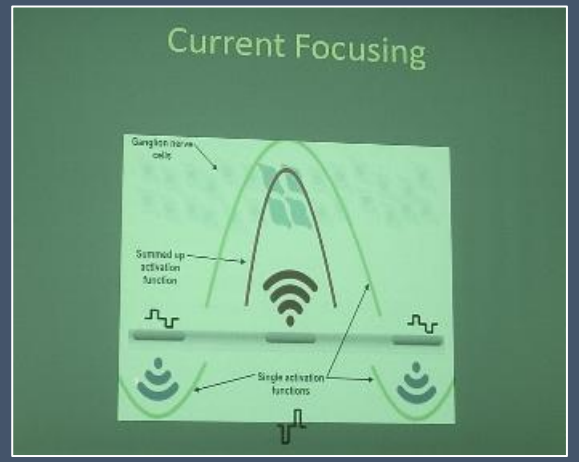
RESOLÜSYONU ARTIRMA-SANAL ELEKTROTLAR

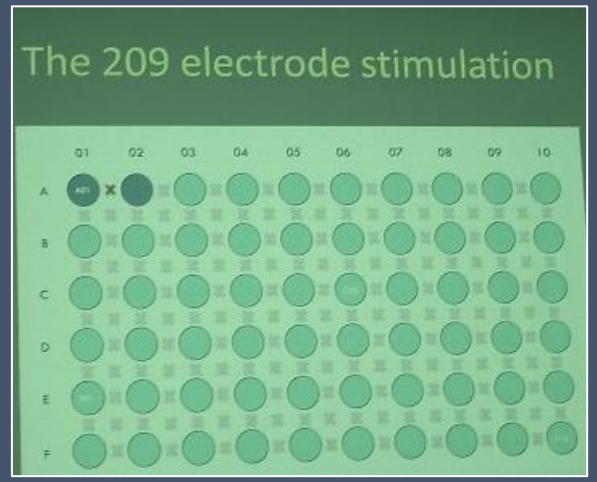








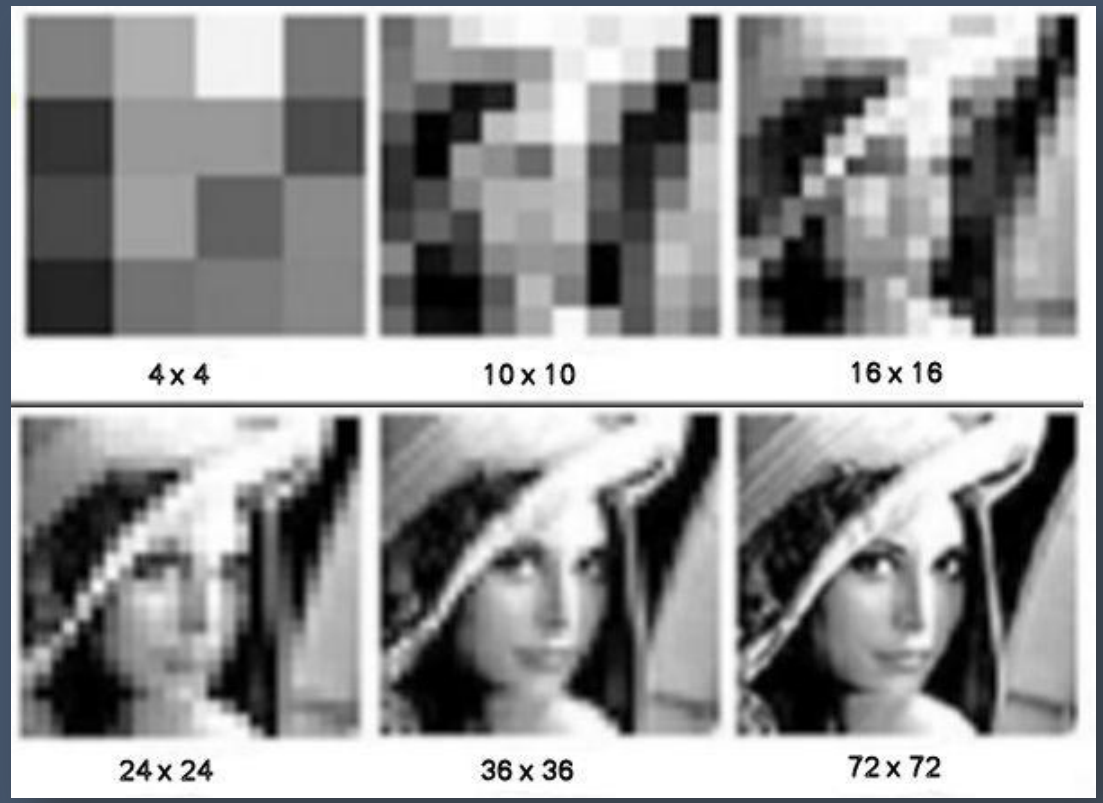




Argus II / Yazılımla sanal elektrot oluşturma

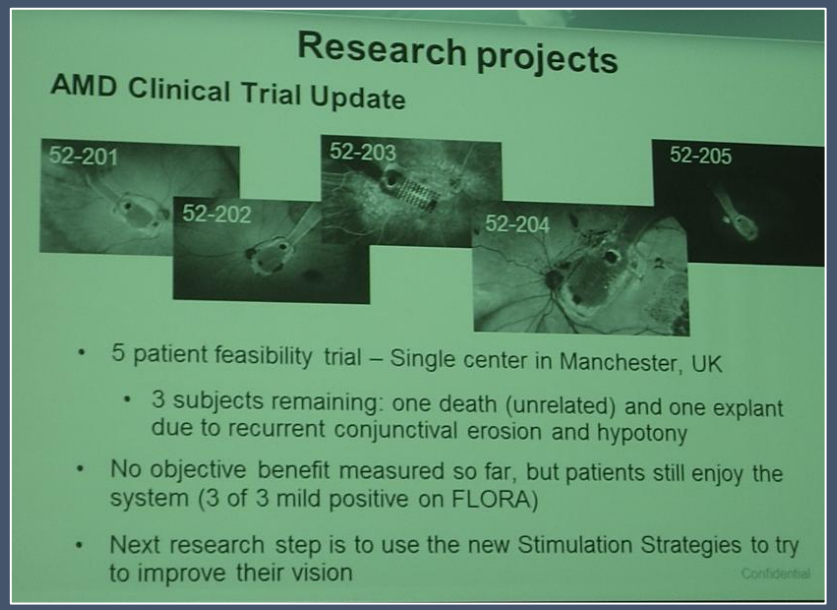
- Elektrotlar aracılığı ile kontrollü elektriksel pulslar verilir
- Buna karşılık gelen bölgede fosfen oluşur
- Birçok fosfenin bir araya gelmesi ile imaj oluşur

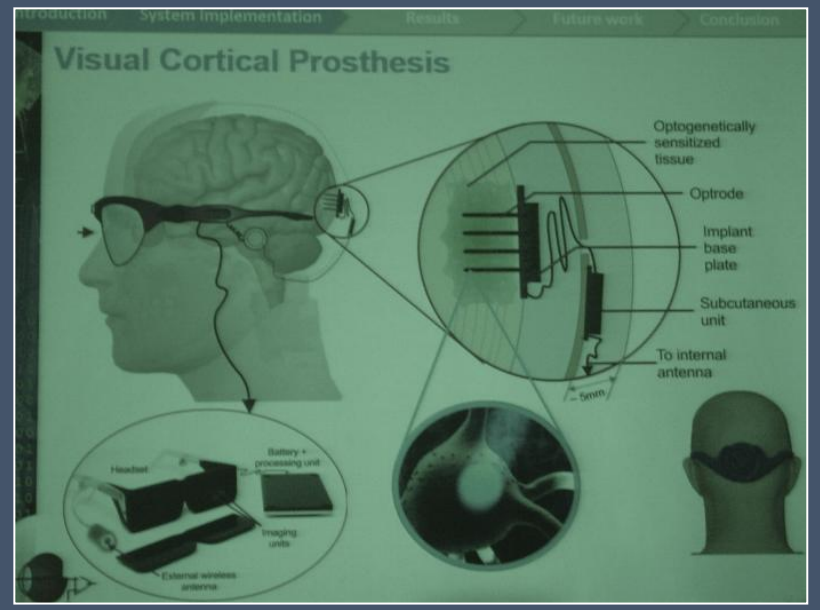
- Kabul edilebilir elektrot sayısı: ~600
- Elektrot çapı küçük olmalı, çap küçüldükçe charge dansitesinde artma, retinaya toksik elektro-kimyasal reaksiyonların oluşması

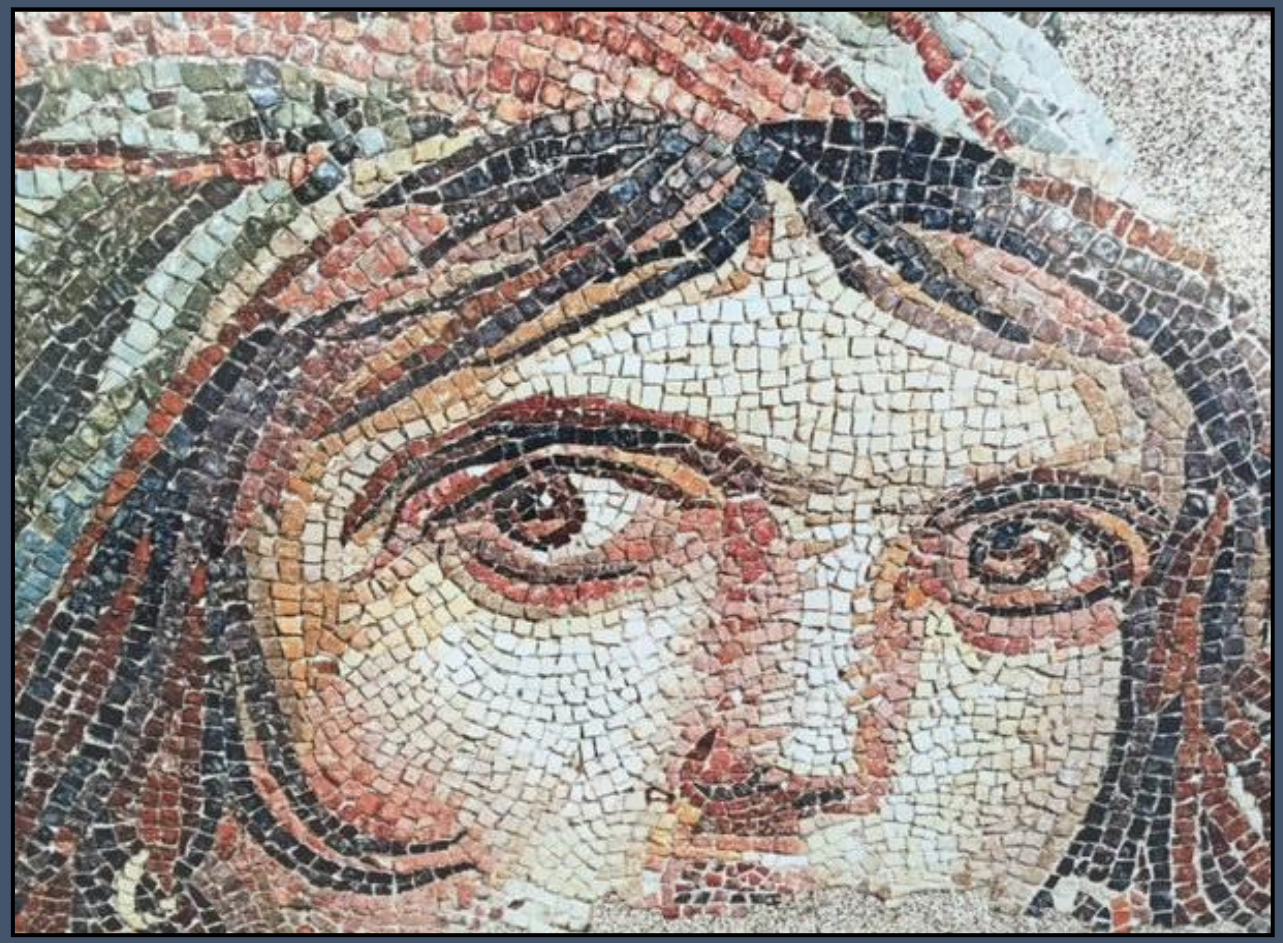


Retinitis Pigmentosa Dışı Endikasyonlar:

- Yaşa bağlı maküla dejenerasyonunun kuru ve ileri tipi: Coğrafik atrofi (5 hsta)
- Tüm nedenlere bağlı tam körlüklerde: Beyin görme merkezinin uyarımı
- ORION 1 projesi, 2017’ de FDA şartlı onay (Pilot çalışma: 1+ 5 hasta)





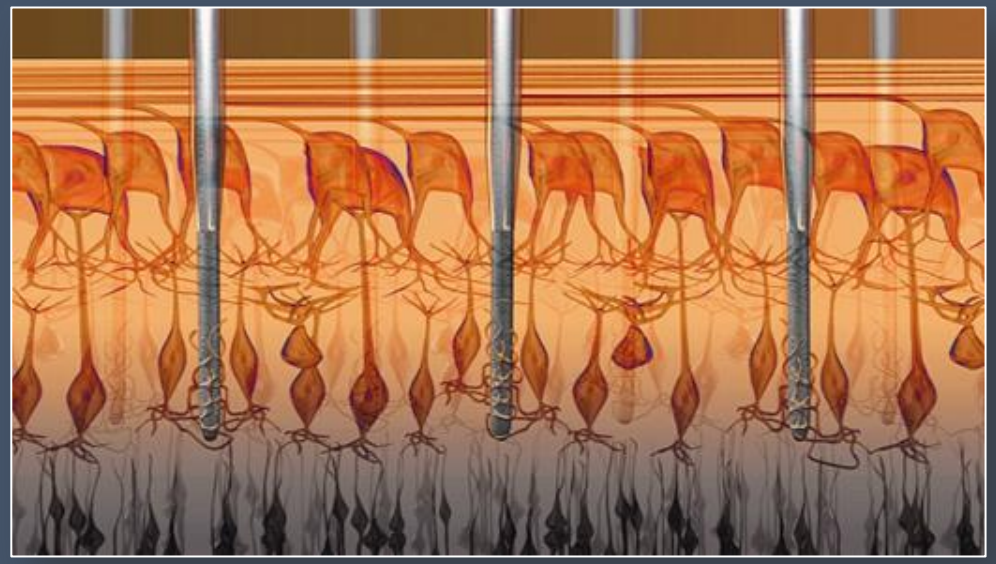


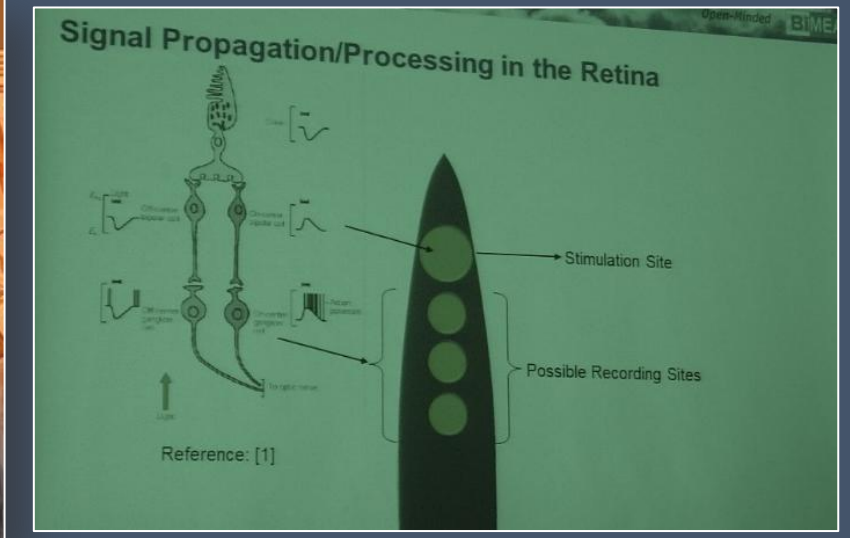
Sabrınız ve dikkatiniz için teşekkürler……

ELEKTROD TEKNOLOJİSİNDE GELİŞMELER……
Revers telemetri çalışmaları

Gömülmüş implant elektrodlarından direk ölçüm

Revers telemetri ---- daha sıhhatli eERG kayıtları





Ameliyat öncesi, cerrahinin prognozunu değerlendirme

- Daha önceden şekil görme olmalıdır
- Işık hissi, kamera flaş testi ile karar verilir
- Şüpheli durumda flaş VEP ile görme yollarının durumu

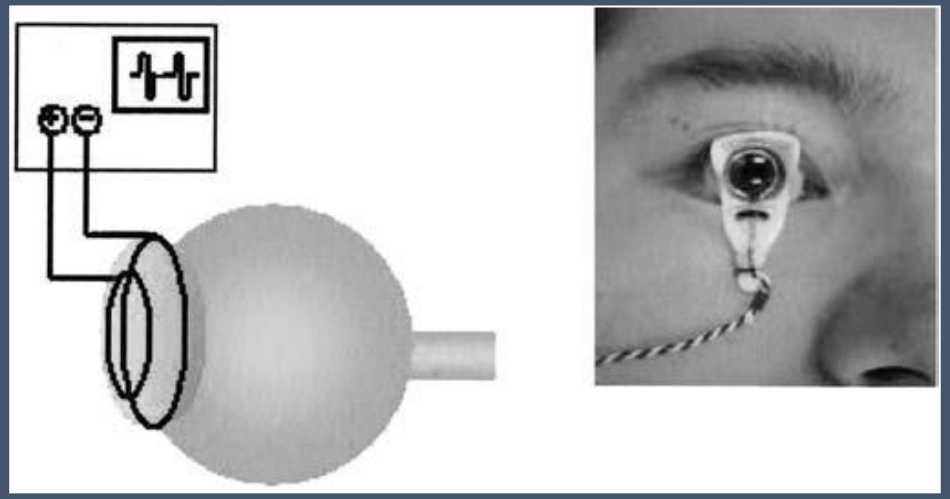
- Retina ışık yerine elektrikle uyarılır
- Hasta fiksasyon yapamaz: P-VEP, P-ERG ve mf –ERG için fiksasyon gerektirecek kadar görme lazım
- Retinada yaygın dejenerasyon var: flaş ERG ile kayıt alınamaz

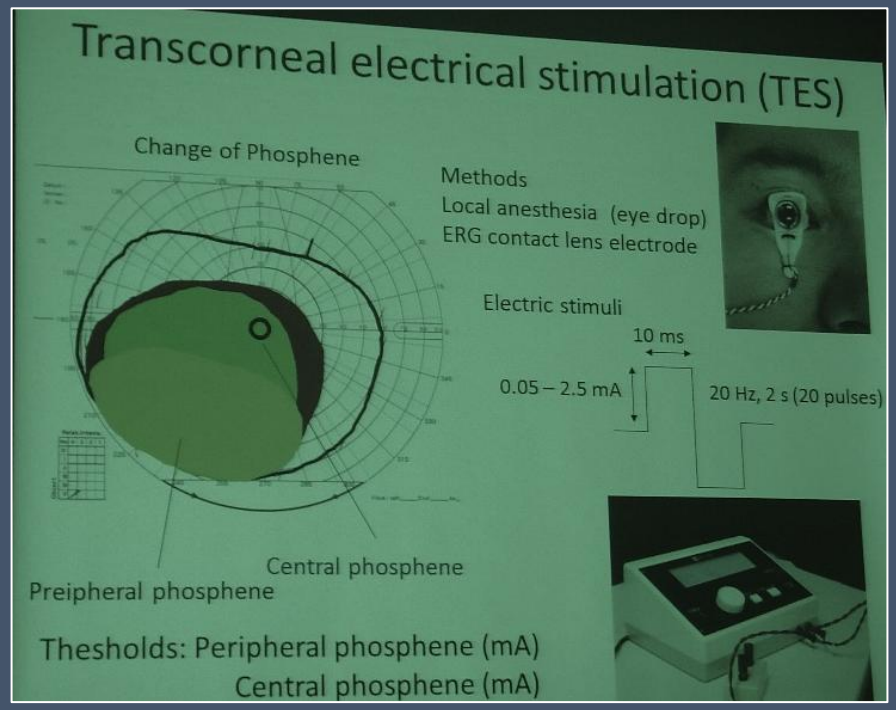
RP / İmplantasyon öncesi retinanın durumunu değerlendirme

- Fonksiyonel: iç retinanın durumunu değerlendirme

TES: Transkorneal Elektrik Stimülasyonu: ganglion, aksonların uyarımı

ERG bipolar kontakt lens elektrodu





Fosfen algılarsa, prognoz iyi ?

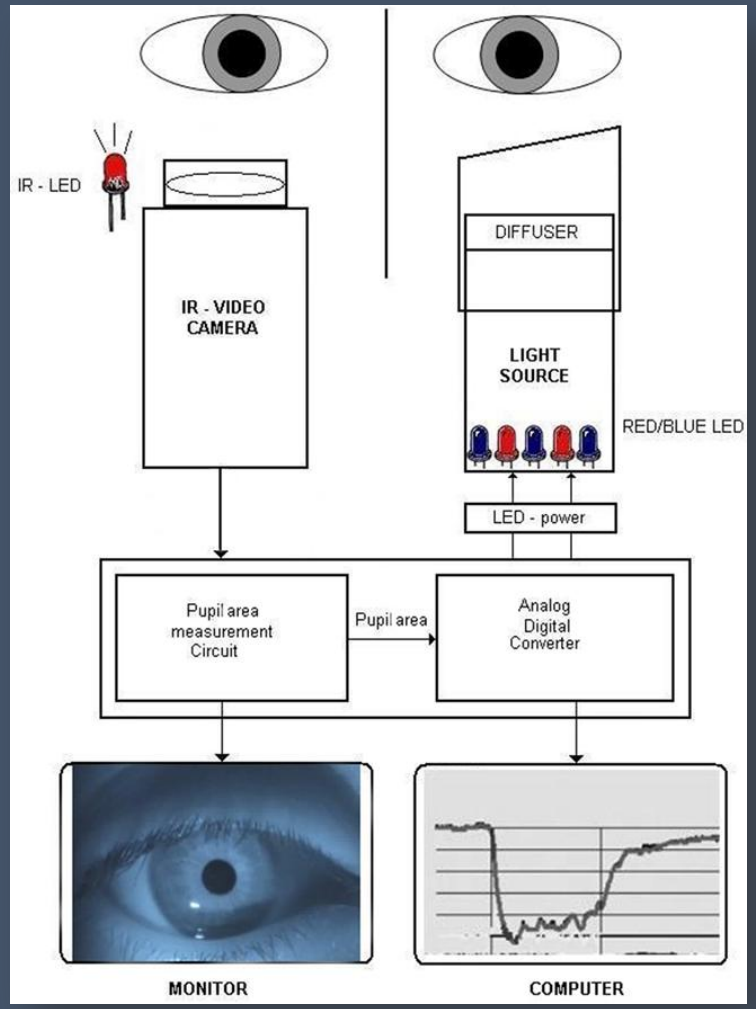
Fosfen (+) olan gözlerde OCT retinal kalınlık daha fazla

Pupillometri – Argus II

Kromatik pupillometri ile:

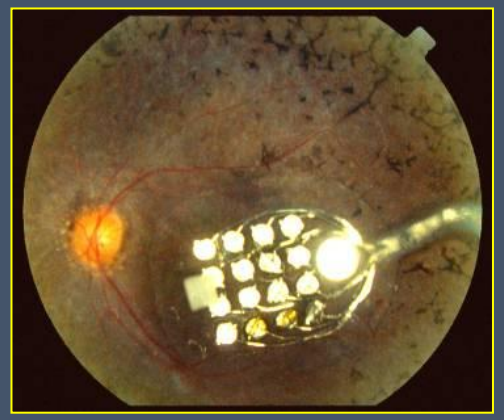
İntrinsik fotosensitif retina ganglion hücrelerinin (ipRGC) fonksiyonu ile, aydınlatma sonrası pupil cevabının (PIPR) ilişkisini değerlendiren çalışmalar var

PIPR amplitüdü ve görsel fonksiyon testleri arasında ilişki saptanmamış

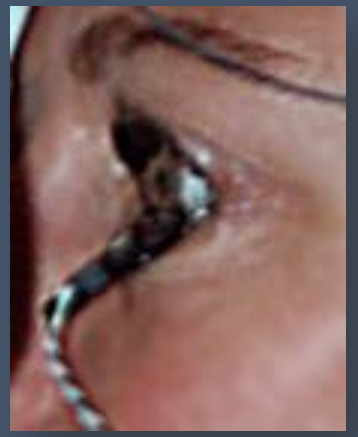


eERG ve eVEP

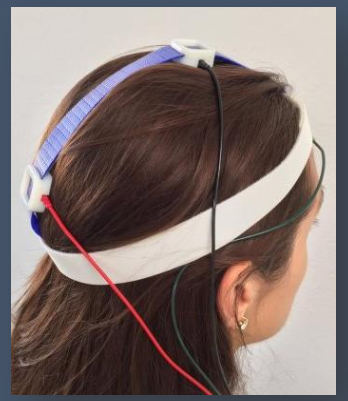
Elektrik uyaranı



Korneal kayıt
(eERG)



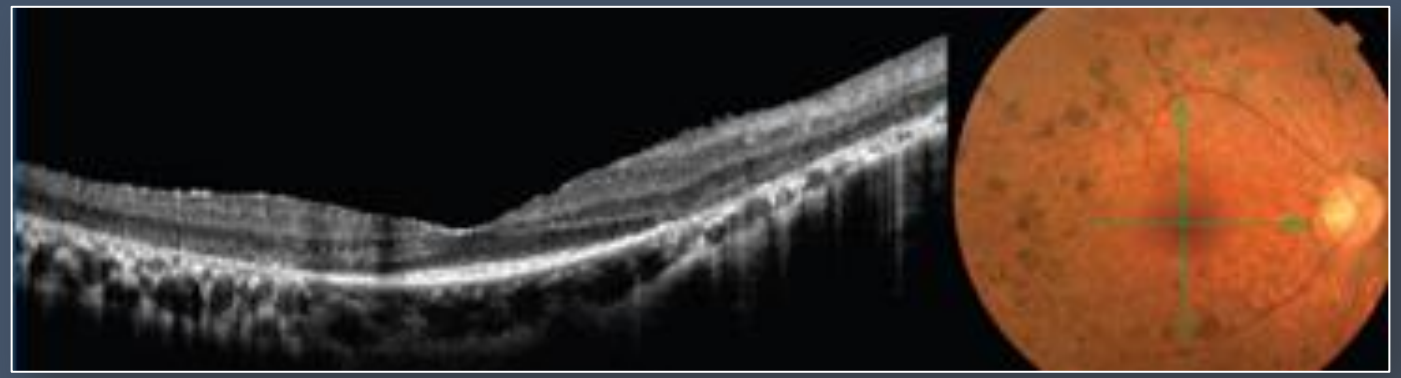
Kafa derisinden kortikal cevap kaydı
(eVEP)

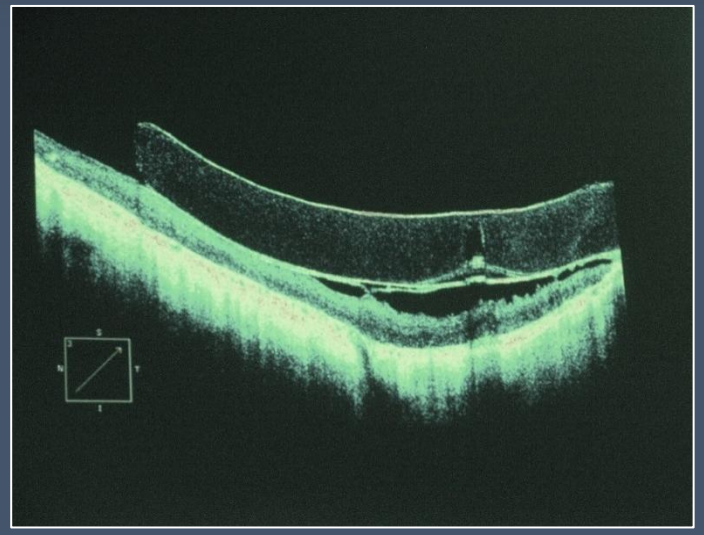


- Fizyoloji ve psikofiziği ilişkilendirmek
- Retinal aktivasyonun tahmini aralığını belirlemek
- Uyarı parametrelerini optimize etmek

RP / İmplantasyon öncesi retinanın durumunu değerlendirme

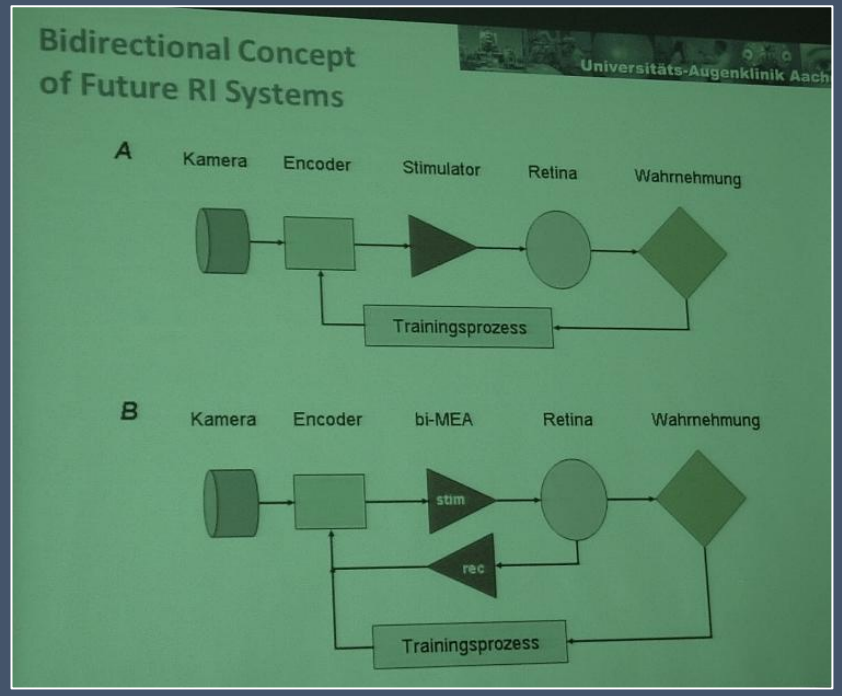
- Yapısal (SD – OCT):

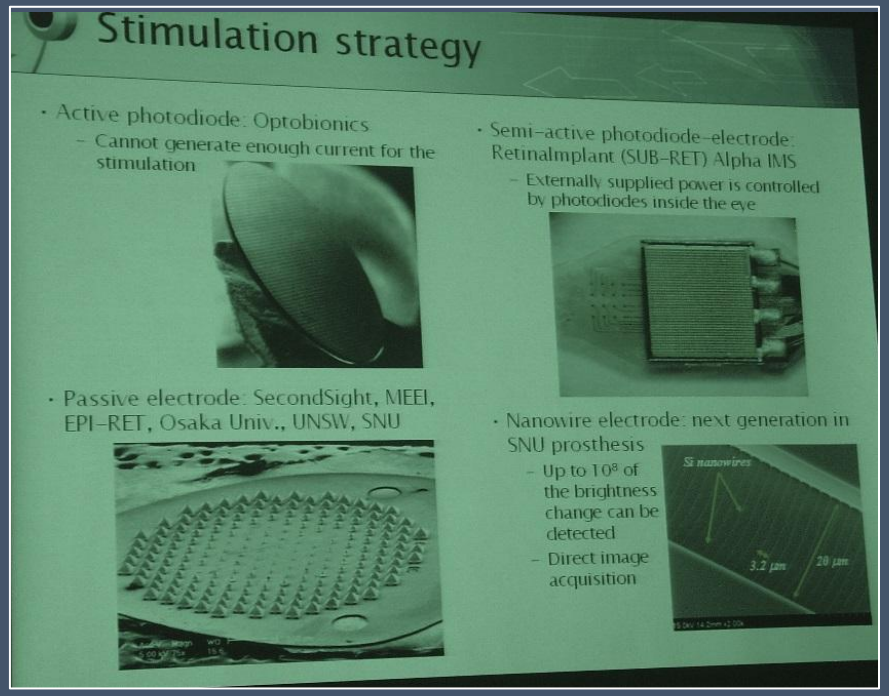




Arka stafilom varlığı
Retina içi tabakalar

Stimülasyon Stratejileri…….





KORTİKAL İMPLANTLAR