Review Article :

BIONIC EYE – AN EYE FOR THE BLIND

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'Bionic eye' also called a Bio Electronic eye, is the electronic device that replaces functionality of a part or whole of the eye. It is still at a very early stage in its development, but if successful, it could restore vision to people who have lost sight during their lifetime. This technology can add life to their visionless eyes. The approach is to bypass damaged photoreceptors and directly stimulate the undamaged neurons. It cannot work on the congenitally blind or with damaged optic nerve, glaucoma or diabetic retinopathy. It bypasses the eye to recreate an image in the mind. It is used in patients in whom the eyes have ceased to function but the visual centres in the brain are intact.

Eye damage can occur by either damage to retinal cells or ganglion cells or damage of the optic nerve. Bionic eye restores vision loss due to damage of retinal cells. US scientists first used the monkeys to test whether stimulating an area of thalamus could produce a visual signal. The retinal prosthesis is useful for patients with compromised visual pathways posterior to retina. A microelectronic retinal implant is suitable in cases in which the patient is affected by an outer retinopathy as with retinitis pigmentosa or AMD. Retinitis pigmentosa is the leading inherited cause of blindness with 1.5 million people worldwide and an incidence of 1/3500 live births. RP results in degeneration of rods and in later stages leaves the patient with a tunnel vision. Age related macular degeneration results in defect of central vision due to damage of cones in macula. AMD is the leading cause of visual loss among adults older than 65 years, with 700 000 newly diagnosed patients annually in USA, 10 % of whom become legally blind each year. Potts and Inoue, some forty years back demonstrated the ability to evoke an electrically evoked response (EER) via ocular stimulation using a contact lens as a stimulating electrode. Knighton demonstrated that inner retinal layers could be electrically stimulated and would elicit an EER. Giles Bradley's research was a breakthrough in 1960 and was the first electrical stimulation of visual cortex by bright spots called phosphenes.

VISUAL PROSTHESIS are based on neuronal electrical stimulation at different locations along the visual pathway (i.e. cortical, optic nerve, epiretinal, sub-retinal). Analogous to the cochlear implants, these devices propose to restore useful vision by converting visual information into patterns of electrical stimulation that would excite the remaining inner retinal neurons.

A) Cortical prosthesis – Brindley ad Dobelle began work in 1960 towards functional, visual cortical prosthesis. They implanted arrays with over 50 electrodes subdurally over the occipital lobe with the hope to evoke phosphenes and patterned perceptions by electrically stimulating the occipital cortex. These implants had several disadvantages including induced pain from meningeal stimulation. Then the intracortical devices were employed. But cortical implants adverse effects outweighed their benefits.

B) Optic nerve prosthesis - Veraart et al. employed the concept of spiral nerve cuff electrode, which was surgically implanted circumferentially on the external surface of the optic nerve. It relied on the principle of retinotopic organization within the optic nerve. The open-loop stimulation allowed the collection of phosphene attributes and the ability to elicit perception of simple geometric patterns. But the surgical procedure was very complex with

possible CNS infection and interruption of blood flow to the optic nerve.

C) Epiretinal prosthesis rely on imaging devices such as a camera and then transform information to patterns of electrical stimulation to excite remaining retinal neurons. Advantages of epiretinal approach – A) it allows for the vitreous to act as a sink for heat dissipation from microelectronic device, B) A miniature number of microelectronics are incorporated into the implantable portion of the device, C) The wearable feature of electronics allows for easy upgrades without requiring subsequent surgery, and D) the electronics allows the user and the doctor for full control over every electrode and image processing parameters allowing the implant to be customized for every patient.

The disadvantages included requirement of techniques that will provide prolonged adhesions of the device to inner retina, and further distance of epiretinal device to target bipolar cells than the sub-retinal device required increased current.

ARGUS I – consists of 16-channel stimulator, similar in size to Advanced Bionics Clarion, positioned behind the ear, and attached to a cable that terminates at an electrode array on the epiretinal surface. The electrode array is a 4*4 grid of platinum disk electrodes. Overall size varies from 3*3mm. An induction coil link is used to transmit power and data to the internal portion of the implant from an external video processing unit (VPU) and a miniature camera is mounted on a pair of glasses. The video camera captures a portion of the visual field and relays the information to the VPU. The VPU digitizes the signal in real time, applies a series of image to a 4*4 pixilated grid, and creates a series of stimulus pulses based on pixel grayscale values and delivered via an inductive RF coil link and application specific circuitry to the pulse generator.

ARGUS I Surgical procedure requires a botulinum toxin injection two weeks prior to surgery in superior, inferior, medial and lateral rectus muscles of the test subjects since their eye movements might break the cable connection of the intraocular electrode array to the extraocular electronic case. Under general anaesthesia, the implant is placed in a recess well created in the temporal skull. Cable is placed in the shallow groove created in temporal skull and delivered through a lateral canthotomy into the periocular space. A complete pars plana vitrectomy is performed and the array introduced to the eye through a 5mm circumferential sclera incision placed 3 mm posterior to the limbus. The array is placed temporal to the fovea and a single retinal tack inserted to secure the array in place.

The clinical trial of ARGUS I device began in 2002 and enrolled 6 retinitis pigmentosa patients. Subjects were able to discriminate between different percepts, identify everyday objects and detect the direction of motion. Perceptual thresholds were within safe limits and were stable over time.

ARGUS II – uses an external camera system very similar to ARGUS I, but the implanted part of the device is completely different. It comprises of an encircling band (sclera buckle), an inductive coil, a case containing electronic components attached to the band, an integrated ribbon cable and an electrode array which spans 20º of visual field corner to corner. All components fit inside the orbit. Implantation procedure is similar to pars plana vitrectomy with encircling buckle. Device is placed under the four rectus muscles, with the implanted electronic components sutured on the superior temporal quadrant, with the anterior edge of the case 7 mm posterior from the limbus and sutures around the encircling band on the other four quadrants. The optimal placement of the array is over the macular area. External component of the system are similar

to ARGUS-I and the basis of operation is the same.

ARGUS II being evaluated in a single arm prospective multicenter clinical trial, and a total of 30 subjects were enrolled. Experiments documented improvement in object localization. Motion detection also improved, but to a lesser extent some subjects report the perception of colour, which can be reliably produced under certain conditions. 96 % of subjects performed better in localizing the object with system ON versus OFF. The best result to date is 1.8 log MAR (equivalent to Snellen 20/ 1262). Some subjects were able to read sentences. Most subjects had no SAE (serious adverse events). Based on results, and manufacturing details provided by Second Sight Medical Products Inc., the ARGUS-II received a CE mark in March 2011, making it the first retinal implant to be sold as a medical device in Europe. This was a major milestone in the field of artificial vision and will allow many more patients to be implanted and allow further

ARGUS II 60 electrode array placed in the surface of retina with tack in place Schematics of ARGUS II system and the eye post-marketing studies.

Intelligent Medical Implants (IMI, Bonn) is developing as active epiretinal prosthesis. The electronics are located in same location as ARGUS-II implant. Inductive coupling is used for power and an optical link is used for data. Not much success with this device.

49 electrode epiretinal device – Intelligent Medical Implants Epi-Ret- where the electronic module is placed right behind the iris, resembling an IOL scleral fixation. Low perceptual thresholds were reported.

Epi-ret 25 electrode device

D) Sub-retinal prosthesis : involves implanting a microphotodiode (solar cells) array between bipolar cell layer and retinal pigment epithelium accomplished surgically either via an intraocular approach through a retinotomy site or a transscleral approach. Using these solar cells alone as a powering mechanism offers an attractive solution to enhance vision of patients affected by retinitis pigmentosa and AMD. However, several limitations currently hinder this technique from realizing its goal of being a visual prosthesis.

Active sub-retinal device

In 2009, Retina Implant AG (RI) started a clinical trial on a new subretinal prosthesis. The study was first to report letter reading, providing strong support for functional vision via electrical stimulation, the short duration of implantation (1 or 3 months) limited the amount of data available from these tests.

The Boston Retina Implant Project (BRIP) has developed a 15-channel implantable stimulator with some drawbacks and was not much successful.

Recent alternative approaches –

Suprachoroidal transretinal stimulator (STS), advantages are surgically less complex, less invasive to retina, and relatively easy to remove or replace if damaged. The approach remains to be proved over longterm implantation, specifically because electrodes are further from the target neurons. Has been tested in animals.

The Microfluidic retinal prosthesis is an alternative approach that has been designed to mimic normal chemical signalling between neurons in retina and brain.

Electrotherapeutics : The optobionics artificial silicon retina (ASR) has shown efficacy in improving vision through a neurotrophic effect. ASR was implanted (subretinal and extramacular) in 10 patients in a single-centre study and then in 20 subjects in a multi-center study. Subjective improvement in vision was seen in first six patients. The ASR's presence in subretinal space was acting via an indirect effect,

possibly through release of growth factors, and improving the health of retina. Adverse events included ASR migration, fracture of device during implantation, and visually significant cataract.

Artificial Silicon Retina (ASR)

Optogenetics : Pioneered by Deisseroth, this technique modifies individual neurons to include light-sensitive ion channels, namely channel rhodopsin 2 (ChR2). When light is shone on to the cell, ChR2 opens resulting in depolarization of the cell. Adeno-virus vectors can be used to get the ChR2 DNA into the cell. Bi et al. First demonstrated that light evoked neural responses were present in a mouse model of retinal degeneration when the mouse retinal ganglion cells contained ChR2. By incorporating a second light-sensitive channel (Halo-rhodopsin) into the dendrites of retinal ganglion cells and ChR2 in the soma, and enabling a center-surround response dependent on the wavelength of light, the optogenetic approach has some significant advantages over the bioelectronic approaches. By making each cell light sensitive, vision can potentially be restored to near normal acuity. However, many potential challenges must be overcome before this approach can be clinically viable, the main issue being sensitivity. These modified cells require bright, blue light (460 nm) to be activated, roughly four orders of magnitude above cone light sensitivity threshold in normal people. It is unclear how such intense light would interact with diseased retina.

CONCLUSION :

Both the epiretinal and subretinal implants have demonstrated the ability to convey form vision through electrical stimulation of retina in end-stage outer retinal degenerations. The surgical procedure for subretinal implant is more complex. The advantage of the RF (inductively coupled) ARGUS implant obviates the need for clear media and also can overcome image blur caused by nystagmus. The ARGUS II is the largest study of a retinal prosthesis to date and there is cumulatively more than 60 subject years of implant experience with this device. Moreover, ARGUS II trial is the only FDA approved study and more recently the only retinal implant to get a CE mark to be sold as a medical device in Europe. In ARGUS series improved visual acuity with increased number and density of electrodes is seen. The subjects who have received either ARGUS or Retinal Implant AG device can read large letters using their implants. These implant recipients benefit by being able to do their daily activities to a certain extent. If optogenetic therapies can be made more sensitive then that may result in near normal vision. The artificial vision for the blind through bionic eye is indeed a complex, longterm, expensive and interdisciplinary undertaking, but still we hope for a better future for the blind people where these prosthesis could restore near normal vision.

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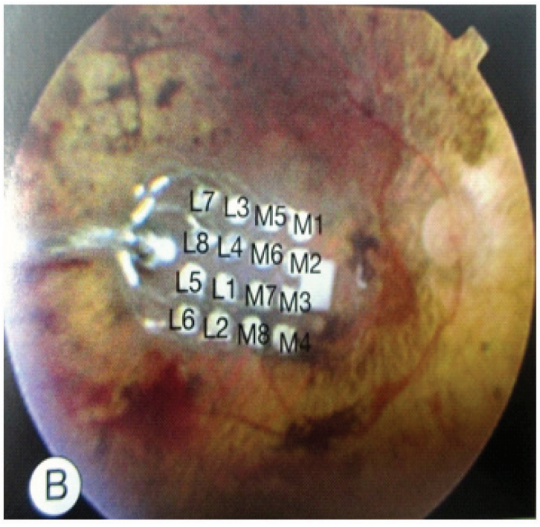
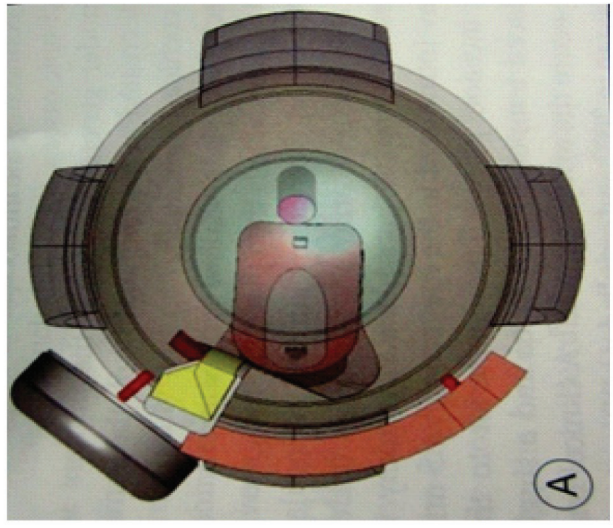
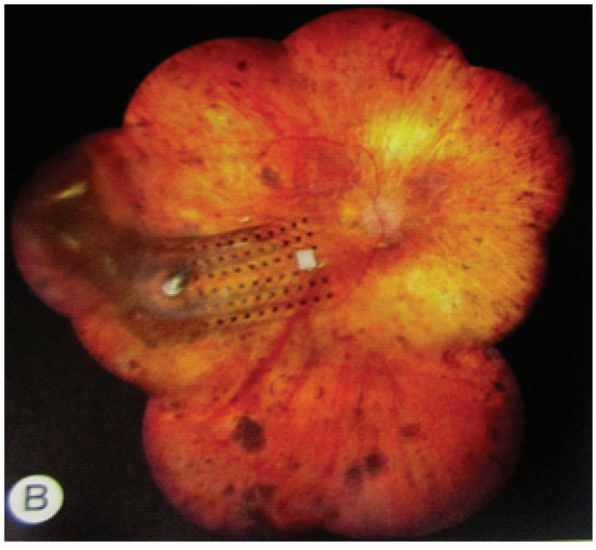


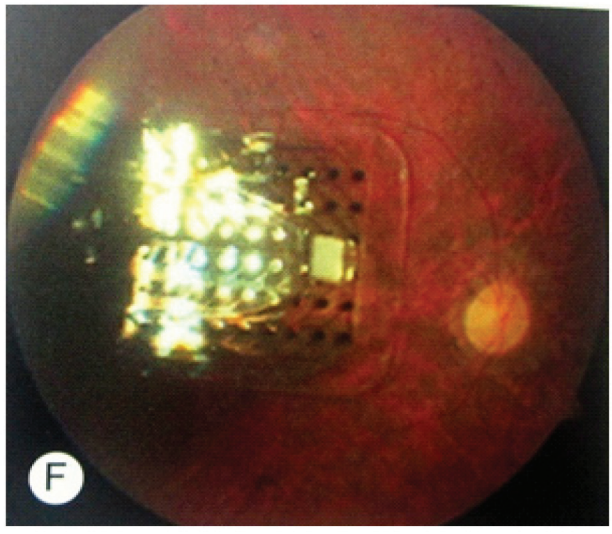
ARGUS I



Schematics of ARGUS II system and the eye



Post-Marketing Studies.



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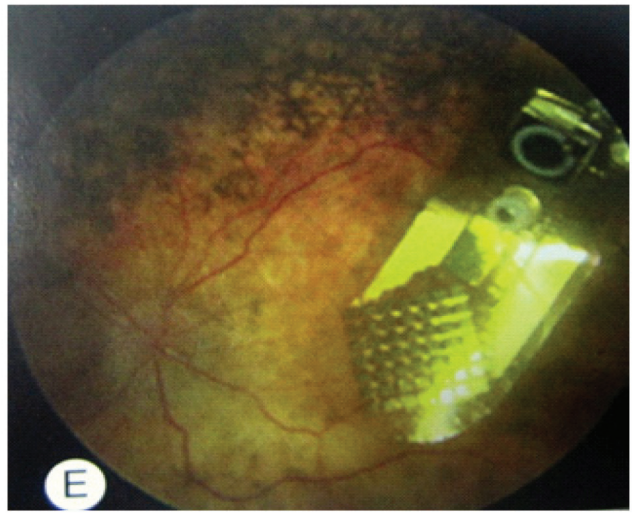

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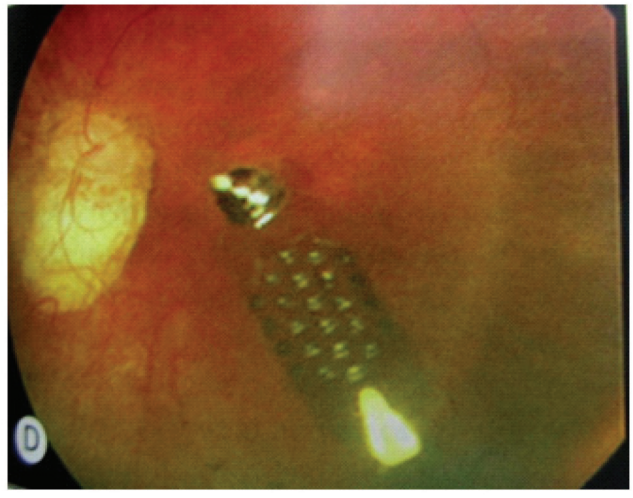

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