

Bionic Eye – A Review

The path traversed and to be traversed

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Abstract

The darkness of the night is broken by the brightness of the sun and people worship sun for this. Similarly, providing even a flicker of light to a person who has lost his/her sight is one of the greatest miracles a doctor can perform. Bionic Eye- visual prosthetic devices serve this purpose and helps to restore some kind of visual perception in patients with retinal pathologies like retinitis pigmentosa and age related macular degeneration. The inception of this idea dates back to the 18th century but the recent advances in electronics, robotics and other technologies has helped in materializing the idea. The basic function of the device is to receive the images using a camera, convert it to electric signals and eventually stimulate the left-over healthier parts of the visual pathway. There are various kinds of devices based on the position of implants. Each of them have varied advantages. Understanding the existing systems would help in improvising them or in finding better systems to serve the same purpose.

Introduction

Bionic Eye is a perfect blend of physics and physiology, a boon to the blind. The word Bionic Eye is used to refer to an electronic device enabling the re-establishment of lost vision due to problems in the visual pathway i.e., it is a mixture of physics (electronics in specific) and physiology of vision in right proportions to form a miracle. As fascinating as it is, the fact that this is chosen among many other more significant topics in ophthalmology or even medicine might kindle curiosity. A research to feed that curiosity would reveal (among other things) that this year 2015 witnessed a breakthrough in this field which was the successful implantation of Bionic Eye in a patient with Age- related macular degeneration and thus giving a solution to manage the most common cause of loss of vision in developed countries.¹ This article will be focused on explaining the technical aspects of Bionic Eye in Simple terms while discussing the path traversed so far and the path to be traversed in future.

Bionic eye- lexicography

'Bionics' is a word derived from 'Bion" and 'ic' which together means life like. It can also be simply explained as a blending of the words *Bio*logy and Electronics. Literally, it is the understanding of Biology and application of its principles in engineering and technology. For example, studying the surface of lotus helped in the production of dirt and water repellant paint; understanding the echolation of bats formed the basis for Sonar, radar and ultrasonography. In medicine, Bionics includes replacing or substituting the organs and its functions by mechanical versions. The living systems are studied, devices are developed using its functioning principle and the device is itself used to serve as a proxy for the system when it is impaired. Ideal examples would be cochlear implants, artificial hearts or even the proposed nanodevice called as respirocyte which may serve as bionic red cell.² 'Bionic Eye' is also a significant member in this series.

'Bionic Eye' is a fancy word used for visual prosthetic devices. It is used to assist vision for visually challenged people. When defective vision is due to some problem with refraction, glasses or lens or Lasik is indicated. When there is pathology in the South American Journal of Medicine Special Edition 2016

cornea, corneal transplant is indicated. All these serve well because in these conditions, the basic units of vision i.e., the rods and cones remain intact. When these are affected, there comes the role of the visual prosthetic devices called "Bionic Eye".

Critical review

History of evolution of bionic eye- a timeline

The inception of concepts relating to bionic eye dates way back into the 18th century. History is not always fair in offering positions for firsts. Though Luigi Galvani is considered as the first to describe bioelectricity by discovering that when the muscles of a dead frog are struck by electricity, they twitch; about three decades before his discovery in 1780³, Benjamin Franklin had predicted an artificial vision system which is also based on the same principle where the retinal cells are stimulated rather than muscles in 1751⁴. And in 1755, Charles Leroy even performed an experiment in this aspect by discharging static electricity from a precursor capacitor of those days- a Leyden jar into a patient who was blind as a result of high fever for three months using two wires- one above the eyes around the head and the other around the leg, the patient experienced a flame like thing passing downwards in before his eyes⁵. That was the first time when a rudimentary prosthesis successfully restored a flicker of visual perception in a visually deprived individual. Since then till date, there are various waxing and waning in the development of bionic eye. The past two decades continued to show rapid progression in this field. The following timeline would help us to better understand the key aspects in the history of evolution of Bionic Eye.

1751	•Benjamin Franklin
	•Mentioned Artificial Vision System in the report of his Kite and Key
	experiment ⁴
1755	•Charles Leroy
	•First use of an electronic device as a rudimentary prosthesis producing a
	flicker of sensation in a blind eye ⁵
1780	•Tiberius Cavallo
	•wrote an essay on theory and practice of medical electricity ⁶
1929	•Foerster observed that electrically stimulating occipital pole produced
	perception of a small spot of light called as Phosphene ⁷
1931	•Krause and Schum
	•visual cortex retains function despite long time deprivation of visual input ⁸
1956	•Graham Tassicker
	•Obtained Patent for Photosensitive selenium cell producing phospene ⁹
1960-70	•Brindley and Dobelle
	•Artificial vision by cortical stimulation was capable of producing
	consistent phosphenes ⁴
1983	•Joao Lobo Antunes
	•First implanted a Bionic Eye in a patient born blind ¹⁰
1989	•Massachusets Eye and Ear Infirmary along with MIT identified the
	feasibility of retinal prosthesis ¹¹
1990	•Early 1990s, Mark Humayun, Eugene Dejuan, Howard D Phillips, Wentai
	Liu, Robert Greenberg invents the Argus Retinal Prosthesis
	•Late 1990s, Second Sight company was formed by Greenberg with Alfred
	E. Mann
	•Suprachoroidal implant (silicone carrier with 33 platinum disc shaped
	electrodes invented in Osaka university in Japan and Nanobioelectronics
	and Systems Research Centre of Seoul National University of South korea
1995	•Eberhart Zrenner in South German university Hospital in Tubingen
	identified subretinal prosthesis which utilizes microphotodiode arrays ¹²
1996	•Electrically evoked cortical potentials were identified by stimulation of

	retina with a microfabricated electrode array ¹³
1998	•Begining of Epiretinal stimulation trials in Harvard and MIT ¹¹
2000	•Experiments were performed on isolated retina such as multi-electrode stimulation and multisite stimulation ^{14,15}
2002	•Microsystem based visual prosthesis was developed by Claude Veraart at University of Louvain ¹⁶⁻²⁰
	•Artificial Silicon Retina (ASR device) was invented. ²¹
	•Argus I with 16 electrodes were implanted and studied in 6 subjects (2002-2004) ^{22,23}
2003	•Experiments were done for thresholds required for extracellular retinal
	stimulation, pattern reconition and visual resolution with retinal prosthetic devices ²⁴
2004	•Suprachoroidal Electrode was tried for transretinal stimulation
	•Electronic retinal prosthesis was proposed for the treatment and
	rehabilitation of visually challenged
2007	•Trials of Argus-II with 60 electrodes commenced ²⁵
	•Dobelle Eye-similar to MIT device, but the stimulator sits in visual cortex ⁴
2010	•Bionic Vision Australia was formed by Kevin Rudd with 42 million
	dollars fund from the government to develop a retinal prosthetic device
	•Retinal implant with 1500 electrodes developed in Germany
2011	•Argus -II approved for commercial use in Europe
2012	•First UK implant by Oxford University and King's College Hospital
	•Photovoltaic Retinal Prosthesis with high pixel intensity was developed
2013	•Argus -II obtained FDA approval and was recorded to be the First FDA approved Bionic Eye ²⁶
2014	•Argus-II was implanted in a Retinitis Pigmentosa Patient and continued to
	be used for the same
2015	•Argus -II was successfully implanted in a patient with age-related macular
	degeneration

Basic units of bionic eye- deciphering the technical jargon

"If you can't explain it simply, you don't understand it well enough"- Albert Einstein

The basic components in Bionic Eye are image sensors, processors, transmitters, receivers, retinal implant, and cortical implants. Image sensor is a device similar to a camera and captures the images in front of the eye. Processors process the image obtained and convert them into electric impulses or signals. Transmitters transmit the signal and receivers receive it and transfer it to the electrodes implanted in the retinathe retinal implant. Cortical implants are small electrodes implanted directly into the visual cortex of the brain. The topography of the implant varies in different types of devices. It may be either:

- 1. In the Eye
 - a. Epiretinal Implants
 - b. Subretinal Implants
 - c. Suprachoroidal Implants
 - d. Intrascleral Implants
- 2. Extraocular Retinal Prosthesis
- 3. Optic Nerve Prosthesis
- 4. Into the Brain
 - a. Visual Cortical Implants
 - b. Lateral Geniculate Nucleus Prosthesis

Epiretinal implants

Epiretinal implants generally consists of a camera that captures images, a component that transforms the captured image into electric stimulation that forms the visual signal and the last component that receives these electric stimulation and then stimulates the remaining cells in the retina by lying on the inner surface of retina.²⁷ There are various epiretinal implants like Argus II epiretinal prosthesis, Learning retinal implant, EPI-RET3 implant, Epiretinal implant from Bionic Vision Australia, artificial retinal implants using liquid crystal polymers. Each of these devices will be described separately.

Argus II epiretinal implant, a product of the Second Sight Medical Products Inc, is actually a well-developed version of the product of the original inventors of active epiretinal prosthesis Mark Humayun, Eugene Dejuan, Howard D. Phillips, Wentai Liu, and Robert Greenberg in 1990s. Later, the Second Sight Company was formed by Robert Greenberg along with Alfred E. Mann. It consisted of an intraocular epiretinal multielectrode array with 6 platinum electrodes. The array is placed temporal to the fovea and positioned using a single spring-tensioned retinal tack inserted into it. The extraocular component was an external spectacle mounted camera which served as a visual processing unit. This information along with the power was transmitted to magnetic coils implanted in the skull using inductive link telemetry system. The electric signal then reaches the epiretinal multielectrode array via the trans-scleral cables. The power required was supplied by a battery pack that was externally worn. This First generation implant called Argus I with 16 electrodes was implanted into six subjects in the Clinical Trial conducted by Dr. Humayun in 2002 at the Doheny Retina Institute. The subjects had Retinitis Pigmentosa with the vision reduced to bare light perception. On testing them, improvements were observed in object detection, object counting, object discrimination and direction of movement with the implant turned on compared to off.^{22,23} Sight restoration was identified to be a learning process based on the fact that the subject's performance in tasks improved with increased usage.²² The next generation prosthesis Argus II was approved for clinical study in 2007. The trial was conducted in 11 centres worldwide. The Argus II implant consisted of 60 independently controllable electrodes making it better than its predecessor. It received commercial approval in Europe in March 2011. In February 2013, it became the first of its kind to be approved by the US Food and Drug Administration - First Bionic Eye approved by FDA.²⁶ It was thereafter used in restoring vision to those affected by retinitis pigmentosa. On 21st July 2015, the Bionic eye- Argus II epiretinal implant was implanted into a patient with dry age related macular degeneration by the surgeons of Manchester. This formed a breakthrough because ARMD was the most common cause of loss of sight in the developed world.¹

The Learning Retina Implant System is a product developed by Intelligent Medical Implants AG. It consists of an extraocular and intraocular portion. A retinal encoder placed on the frame of a pair of glasses formed the extraocular portion. The intraocular portion is a retina stimulator that rests on the inner surface of retina and positioned using retinal tacks.^{27,28} The processing capability of the Retinal Encoder is comparable to that of the functions of the retinal ganglion cell by its receptive field properties and filtering operations. It improves the visual processing capabilities of the retina by means of 100 to 1000 individually tunable spatiotemporal filters. This implant can be used in assisting the patient with the adjustment of the stimulation parameters individually.²⁷ Its trials were started in 2003 where 19 out of the 20 patients with Retinitis Pigmentosa who underwent electrical stimulation for 45 minutes described sensation of phoshenes.²⁹ That result helped in starting the chronic studies that commenced in 2005. Results showed identification of simple patterns and location of light sources. A Second chronic study was done to identify the use of full

unit with its wearable camera and a pocket sized processing unit. A multicentric clinical trial was registered in Europe and its current status is unknown.

The Aachen University Clinic and the Fraunhofer Institute for Microelectronic circuits in Germany form the EpiRET GmbH group. They have developed a device similar to the Argus epiretinal prosthesis. It also has an extraocular and intraocular part. The image is captured by a metal-oxide semiconductor camera in the frame of the glasses. This is transferred wirelessly to a receiver which is placed in the anterior vitreous similar to an intraocular lens. This eventually stimulates the epiretinal implant through a micro-cable that connects it to the array of 25 electrodes apposed to the ganglion cells. The greatest advantage of the EPI-RET3 implant is that it has all the ocular devices within the eyeball- no wire passing by means of a sclerostomy. It underwent human trials in six patients for 4 weeks in 2007. It was tolerable with mild inflammatory changes and remained stable in its position until removal.³⁰ A second generation of the same is being developed with more electrodes and better signal processing capabilities.³⁰

Boston Retinal Implant Project developed an epiretinal prosthesis which underwent acute clinical trials. Since they could not get consistent results, they have abandoned the epiretinal implant and are now developing a subretinal implant instead.^{31,32} It is discussed under subretinal implants.

Bionic Vision Australia^{33,34} is working on two specific devices; one of which is a High acuity device consisting of an epiretinal microchip and implant with 1024 electrodes aimed to provide functional central vision and to assist with face recognition and large print.

The Seoul National University College of Medicine in South Korea has developed a liquid crystal polymer based long term implantable retinal stimulation microelectrode array and it was demonstrated that they were safe, compatible and mechanically stable to be a part of a chronic retinal implant system.³⁵

The advantage of an epiretinal implant is that the surgical technique to access the vitreous cavity and hence the inner surface of retina is a well-known procedure.³⁶

Subretinal implants

Subretinal prostheses involve implantation of the implant in the space between the retina and the Retinal Pigment Epithelium. Surgically, subretinal space can be accessed either externally through scleral incision or internally through the vitreous cavity and retina. Artificial Silicon Retina, Retina Implant AG and Boston Retinal Implant, Photovoltaic Retinal Prosthesis.

The Artificial Silicon Retina was the earliest retinal prosthesis which was developed by Alan Chow and Vincent Chow in Optobionics Corporation.²¹ It was an optobionic device, the energy required by retinal prosthetic devices was derived from incident light, and was composed of approximately 5000 independently functioning electrode tipped microphotodiodes. The Artificial Silicon Retina produced electric charges which altered the membrane potential of contacting retinal neurons and formed images in a way that the retina functions normally. It was found to be safe in animal models and was implanted in six patients with Retinitis Pigmentosa following the FDA approval for clinical trial in 1999.³⁷ The Artificial Silicon Retina was well tolerated by all six patients. Visual function improvements occurred in all patients and also included some unexpected vision improvements in retinal areas distant from the implant. This suggested some kind of neurotrophic effect on the retina. They hypothesized that chronic low level electrical stimulation induces an up regulation of protective neurotrophic survival factors that improves the function of remaining photoreceptors. But it was demonstrated that the energy from an optobionic equipment would be insufficient to activate the remaining retina.³⁸ After Phase II trials, an involuntary petition to liquidate under Chapter 7 was filed in 2007 and

approved against Optobionics Corporation³⁶ halting the further research using Artificial Silicon Retina.

Retina Implant AG was the temporary culmination of the upgradation of an optobionic implant consisting of microphotodiode array with 7000 microelectrodes in a checker-board pattern configuration which was founded in 2003 in Tübingen, Germany.¹² When used in animal models, they discovered that the energy generated from the microphotodiode array was insufficient and additional source of power would be needed.³⁹⁻⁴¹ A compound visual prosthesis device consisting of subretinal, extraocular and subdermal components was developed.⁴² The subretinal part consists of an array of titaniumnitride electrodes and a microphotodiode array with 1550 photodiodes and electrodes. The extraocular portion is a foil strip carrying 22 golden connection lanes to the external connection and the reference electrode. The subdermal portion consists of a silicone cable that leads subperiosteally to the retro-auricular space where it penetrates the skin transmitter and ends in a plug. When implanted for 4 weeks in 12 subjects with Retinitis Pigmentosa without complications, it showed better object localization and differentiation of individual letters in some subjects.⁴²⁻⁴⁵ A multicentre clinical trial has been registered at http://clinicaltrials.gov/ct2/results?term=NCT01024803 and the results are not yet published. The device is now undergoing further upgradation.

Boston Retinal Implant Project's subretinal prosthesis consists of a small hermetically encased, wireless device. This array is implanted in the subretinal space using a specially designed surgical technique by an external scleral incision. It affixes the bulk of the prosthesis to the scleral surface. The implanted device includes a hermetic titanium case containing a 15-channel stimulator chip and power supply components. Feedthroughs from the case connect to secondary power and data receiving coils.^{46,47} The device is undergoing animal studies.

Photovoltaic Retinal Prosthesis was developed in Stanford University. It consists of a subretinal photodiode array and an infrared image projection system mounted on video goggles. The light from image is captured by the video camera which is processed by a pocket device and displayed on pulse near Infrared video goggles, infrared image is projected into the retina and stimulates photodiodes which ultimately stimulates the retina.^{48,49}

The Subretinal implants have the advantage of better stimulation of the retinal ganglion cells than their epiretinal counterparts but they are constrained by limited space and difficulty in accessibility to the space. Large implants cannot be used subretinally.³⁶

Suprachoroidal implants

One of the devices of Bionic Vision Australia is a wide view device with a microchip containing 98 stimulating electrodes placed in the suprachoroidal space aimed to provide increased mobility to the blind patients. Suprachoroidal transretinal stimulation device is a silicon carrier with 33 platinum disc shaped electrodes. The advantage is that it could provide a wider visual field and a simpler surgical technique.^{33,34}

Intrascleral implants

Osaka University in japan is now trying the development of an intrascleral prosthetic device which could ensure safer surgery while still accessible enough to stimulate the retina.

Extraocular retinal prosthesis

A research done at the University of New South Wales, Australia demonstrated the stimulation of retina with a prototype extra ocular retinal prosthesis placed over sclera.⁵⁰ This might lead to the development of a low resolution visual prosthesis. The advantage of this type of prosthesis is that it requires a minimally invasive surgery compared to other types of visual prosthesis. The research was only an animal experiment, this has a long way to go to be successfully available for implantation.

Optic nerve prosthesis

Microsystem based visual prosthesis was developed at the university of Louvain by Claude Veraart.¹⁶ The basic functioning of this implant is as follows: The light rays are received by an externally worn camera that sends signals to a spiral cuff of electrode wound around the optic nerve and connected to a stimulator implanted in the skull. The signals received are translated into electric signals that stimulates the optic nerve directly. Similar stimulation of the optic nerve can be achieved by inserting multiple penetrating electrodes through the optic nerve and optic disc. This has to undergo refining to be used as an alternative for retinal prosthesis.

Cortical implant

Research to provide vision for patients whose optic nerve is not intact or has not developed at all is aimed at cortical visual prosthesis. This is done in various institutes like Illinos Institute of Technology, University of Utah, the Ecole Polytechnique de Montreal in Canada, Miguel Hernandez University in Spain etc. The Utah Electrode Array developed by University of Utah has obtained FDA approval for short term implantation in human subjects.⁵¹ Though these are the recent works, Dobelle's Eye⁴ developed by Brindley and Dobelle in 1960s and 1970s were the first of its kind. But it was unsuccessful because the milliampere range current needed to evoke phosphenes by cortical stimulation resulted in poor spatial resolution, discomfort and epileptic activity.⁵² This shortcoming was overcome by Schmidt's intracortical electrodes which produced average thresholds of below 25 micro-ampere with better two point resolution.⁵³

Lateral geniculate nucleus prostheses

Lateral Geniculate Nucleus is a significant part of the visual pathway. Since the location of the nucleus is adjacent to areas that are targeted for deep brain stimulation therapy for movement disorders, it makes it an ideal location for a visual prostheses implantation as the surgical techniques need only slight modifications.⁵⁴⁻⁵⁶ But this is at a very premature stage of development in which animal studies are performed.⁵⁷⁻⁵⁹

Conclusion

The Bionic Eye seems to be a promising solution for the individuals who were thought to have total irreparable sight loss a while ago. But for the visually challenged individuals of the medium and low income group and especially of the developing nations, it seems like a far outreach by an unfair play of fortune.⁶⁰ Even the ultrasonic devices which are now used quite commonly by visually challenged individuals was a distant dream during its days of inception. Bionic Eye is in its initial stages of implementation in the field of ophthalmology, hence it needs to be at a price that can help in further development of the product enough to make it at an affordable price and greater quality. The extensive research on the topic bionic eye has hiked my astonishment and wonder of Human body and Science. I also felt guilty that I had to know these only now while this field has been progressing rapidly with its origin somewhere in the 18th Century itself. I'm sad for the fact that I was not able to mention about the research in India anywhere in this field. I hope events like this kindles the minds of young researchers in India and in future the timeline bears the name of India also. While researching on this topic, I found an app developed by Bionic Vision Australia for educational purposes. It helps us to know what phosphene

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vision is and what the bionic eye actually sees. This is an example of such an image of a paper weight:

Only the outline can be deciphered, that too when the object lies in a contrast background. Though this makes up for no vision, this has to be significantly improved. David Hubel and his companion Torsten N. Weisel had long back deduced that: the higher the neuron is located in the Brain's Visual Pathway- the more complex the stimulus it responds to. So, while researchers work on improving the resolution by increasing the number of electrodes and even electrically stimulating the visual cortex, why can't they think about sensitizing higher neurons to respond to even in a smaller number of electrical signals? Why always physical stimulation, why not think a little bit of chemistry?

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