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BIOENGINEERING AN ARTIFICIAL EYE - A REVIEW

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ABSTRACT:
Retinal degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) are the major significant contributors to unavoidable blindness in the world. In the past few years, the employment of artificial means to treat extreme vision impairment has come closer to reality. Recently many research groups are spending billions of dollars towards effective solutions to restore a rudimentary sense of vision to the blind. One such intervention is the bionic eye or the bioelectronic eye. The visual prosthesis delivers the image information from the outside world to the natural visual system, which enables the subject to receive a meaningful perception of the image. This paper provides an overview of the electronic hardware units, technical design aspects and different approaches in the implant placement and some technical challenges confronted when trying to enhance the functional quality of such devices.

INTRODUCTION

Blindness and visual impairment are major public health challenges. According to the WHO, it is estimated that about 253 million people live with vision impairment, including about 36 million of those who are reported to be amaurotic and 217 million with various vision impairments, worldwide [1]. Most of those suffering from moderate to severe visual impairments and are over 50 years old [1]. Though therapeutic solutions are provided by pharmacological interventions, a pharmacological treatment to the

mechanisms of blindness has not been discovered. Only less than 20% of all visual impairments cannot be prevented or cured, which is why doctors and scientists have been working on the development of a bionic eye.

Retinal diseases, like retinitis pigmentosa (RP) affecting 1/4000 people, or 0.025% of the population, often in the working age [2] and age-related macular degeneration (AMD), accounting for 5% globally [3], are the significant contributors to unavoidable blindness in the world [4,5]. Cone dystrophies, choroideremia and Stargardt disease also constitute particular fields of interest for scientists working on the bionic eye [6,7].

At present, there are a number of international research groups working towards the development of visual prostheses, covering each viable target region within the visual pathway. Nearly 20 research teams have been reported to work on retinal prostheses with varying implant locations, with groups based in the USA, Australia, Germany, Japan and France. Clinical trials of these devices have shown potential improvements in visual acuity and/or the ability to undertake activities of daily living[8]

However, there always remains the pervasive question as to how these bioelectronic approaches will actually restore functional vision after it is completely lost in a given individual. But there are promising results to go ahead with the development of sophisticated microelectronic visual prostheses as a valuable rehabilitative and therapeutic option to substitute, and restore a limited, but useful sight. Such devices have already allowed numerous deaf patients to hear sounds and acquire language abilities and the same hope exists in the field of visual neurorehabilitation. Previously our department has published extensive research on various aspects of prosthetic dentistry [9–19], this vast research experience has inspired us to research about the bionic eye. Building a bio-electronic eye requires a diverse collaboration of scientists, clinicians, engineers, rehabilitative experts and educators. So this article provides an insight into the electronic hardware units and different approaches in implant placement.

PRINCIPLES OF NATURAL VISION

In order to create a bionic eye, it is important to have a deep understanding of the processes that take place within the human eye, where light is absorbed, converted into an electrical impulse and encoded into a neural signal. The light passes the cornea and iris, and crystalline lens, help to focus light onto the photosensitive retina (figure 1). The retinal cells contain photoreceptors (PR), namely the rods and cones within which a photochemical reaction leads to transduction of light into an electrical neural signal with Retinal Ganglion Cell (RGC) stimulation . The rods, which number ~120 million in each eye are sensitive to low levels of light [20] and cones which number 6 million are responsible for colour vision and function best in bright light [21]. At the level of PRs, RGCs and interneurons, compression of the information occurs from where it is encoded for transmission via the optic nerve to the midbrain and cortical visual pathways. There are 1 million nerve axons of the RGCs that pass via the optic nerve to their respective lateral geniculate nucleus (LGN), which are located in the thalamus. The LGN is a complex layered structure in

which each part receives axons from specific ganglion cell types. Before projecting on towards the primary visual cortex, where all higher cognitive processing takes place a degree of visual processing occurs at this point [22](figure 2) Through the processing power of the retina, high spatial and temporal resolution across a broad spectrum of colour and contrast is achievable. Recognition of objects and geometric structures, appreciate distance, orientation and movement and coordination of visual interpretations with other sensory inputs and motor outputs is possible because of the neuro-cortical integration. This sequence of complex processes like capturing, assimilating, compressing and processing an enormous amount of visual information occurs in a millisecond.

Figure 1demonstrates the anatomy of the eye and organization of the retina.

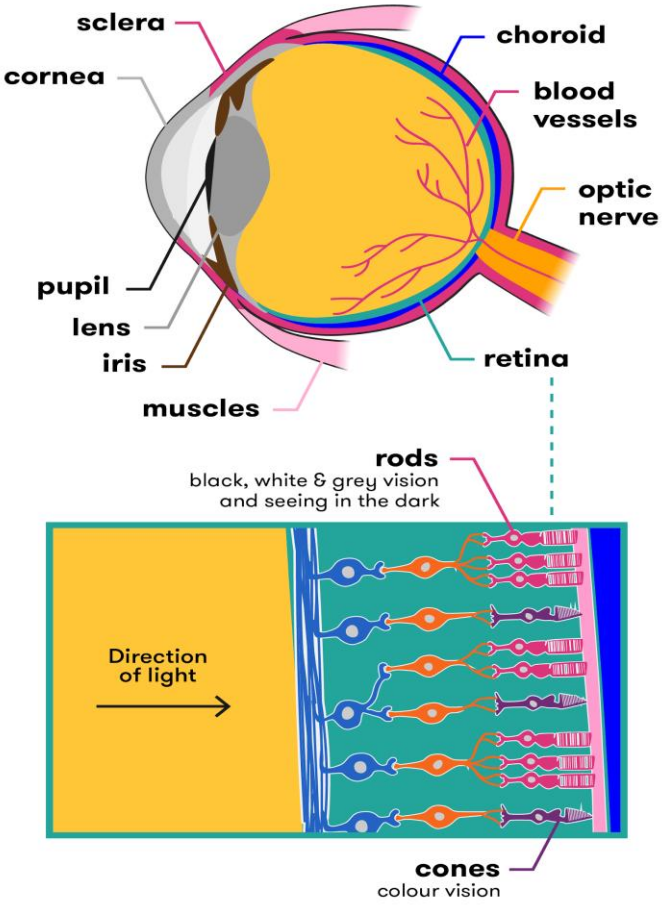
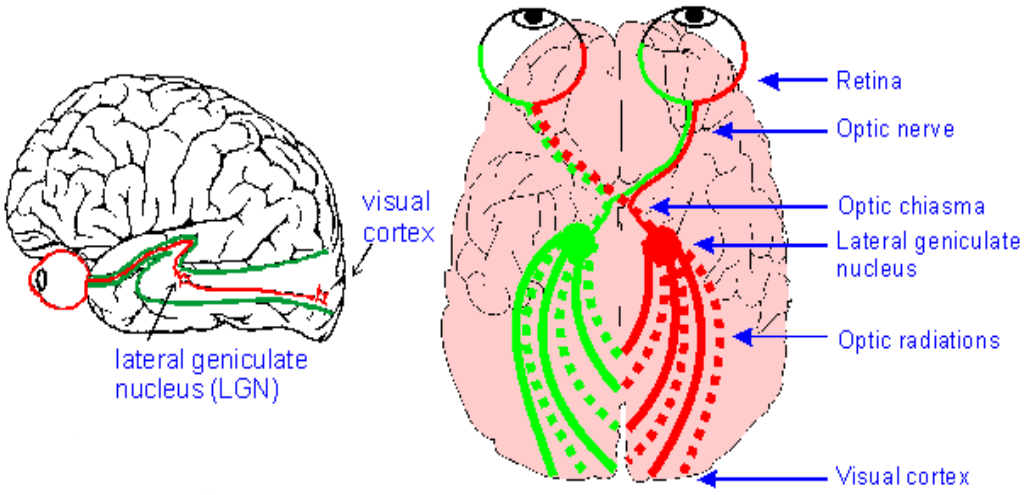


Figure 2 depicts the visual pathway from the eye to the brain. Each retina is divided into the left and the right halves. The red bar represents the right visual field and green represents the left visual field. The right visual field is projected to the left half of each retina. The reverse is true for the green bar. The right half of each retina is projected to the right half of the brain and the left half of each retina is projected to the left half of the brain.



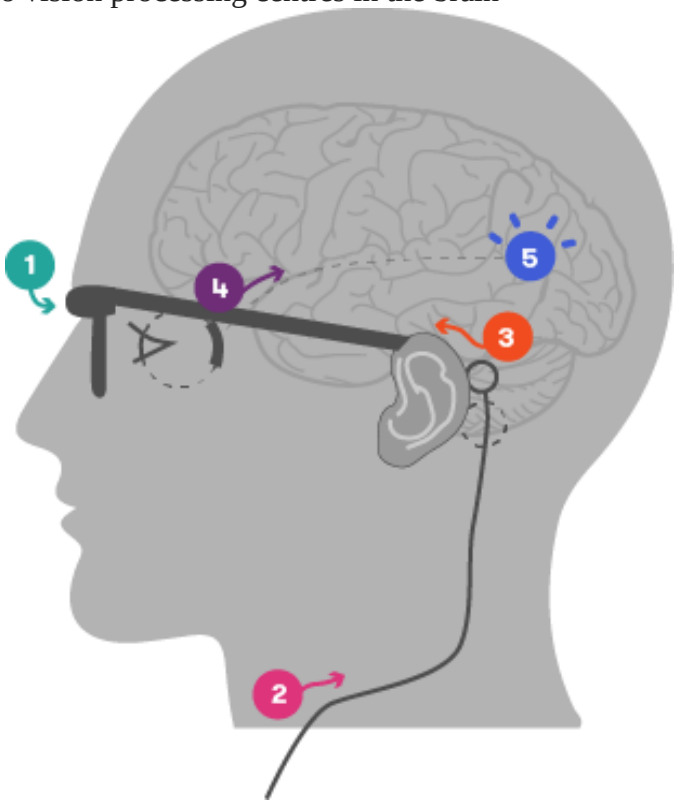
PRINCIPLES OF PROSTHETIC VISION

In conditions like retinitis pigmentosa and age related macular degeneration, a profound vision loss occurs largely due to the progressive degeneration of the light-capturing component of the outer segment of the retina, that is, the photoreceptor cells. Though the existing treatments can perhaps slow the progression of the diseases, no cure is available. Some restoration of vision in dogs and humans with RP have been reported with the recent use of molecular genetic strategies[23]. However, the retinal elements within the inner retinal layers appear to survive in large numbers and remain responsive to electrical stimulation [24].This anatomical region consists of retinal ganglion cells (RGCs) and their nerve axons, which transmit the information to the brain, along with other regulatory interneurons, like bipolar, horizontal and amacrine cells, and Müller support cells. Thus the operating premise underlying a visual neuroprosthesis is to artificially replace the function of damaged neuronal elements that make up the visual pathway. Many pivotal human experiments reported that electrical stimulation of the retinal cells of AMD and RP patients led to the generation of phosphenes [25].

Figure 3 shows the general architecture for visual prosthesis systems proposed by various groups worldwide, who are actively involved in this research domain. The bionic eye consists of an external video camera mounted on the eyeglasses that captures the images from the vision field of the patient. The data obtained is pre-processed to extract key image information and to reduce the amount of data that will be transmitted to the implant. An embedded processor on the implant side, sends the image information to a stimulation back-end, which generates analog electrical pulses. Usually, these electrical outputs are conveyed to an electrode array that interfaces to the target tissue by a flexible cable. A brief description of the aforementioned visual prosthesis electronic hardware units as well as some the associated design are elaborated in the following subsections.

Figure 3 showing the general architecture for visual prosthesis systems.
(1) Camera captures image and transmits data to an external, body-worn processing unit. (2) Data processed and sent to the implanted system via

external wire. (3) Implanted receiver passes signals onto retinal implant. (4) Implanted electrode array stimulates retina. (5) Electrical signals sent from retina via visual pathway to vision processing centres in the brain



4. COMPONENTS OF A BIONIC EYE:

4.1. Image capture:

Presently, in the visual prosthetic systems, there are two principal means of 'image capture' that have found some success in retinal prosthetic systems. The first type consists of an external video camera usually glasses-mounted. The image and video capture is done using different types of camera, e.g. photodiode arrays [26], charge-coupled devices (CCDs) [27], and complementary metal-oxide semiconductor (CMOS) cameras [28]. This approach is not only technically simpler, but also avoids impediments in collecting high quality information about the visual scene. However, as the camera is in a fixed position, there is an increased risk of discrepancy between its orientation and that of the eye. This is likely to cause inaccuracies in the spatial location of an object being focused. To overcome this problem, it is necessary to include both the incorporation of an eye tracker to coordinate the direction of gaze with the stimulation pattern, or placement of the camera system intraocularly, for which there have been some preliminary attempts to design such a system [29]. The second image capture system that has shown promising results is the photodiode array device. This comprises a passive micro photodiode array, which was designed to intrinsically transform ambient light that falls on it into an electrical current which in turn stimulates the retinal neurons. The Artificial Silicon Retina (ASR) array consists of 5000 interconnected photodiode anodes with individual isolated cathodes, each with an iridium oxide electrode. This approach was found to be advantageous over the previous one, as it was wireless and allowed for precise coordination between the eye position and the projected visual scene. It also allowed a large number of pixels to be stimulated simultaneously [30]. Though this concept of the photovoltaic array

had faced initial failure to deliver sufficient stimulation current to obtain functional results, it has been taken up by various researchers with encouraging results. Over the past few decades, the Retina Implant AG group developed the Alpha IMS device which contains nearly 1500 independent photodiode-amplifier electrode units. The ambient light creates the stimulation pattern and an external power source amplifies the electrical signal [31]. Compared with the number of about 130 million sensing cells and 1.3 million ganglion cells in the normal human visual system, the limited number of electrodes can only elicit visual perceptions with low resolution [32]. The 'PRIMA' Photovoltaic Retinal Implant system (Pixium Vision S.A.) combines aspects of both forms of image capture, in that the visual information captured using an external camera is processed and the data is transmitted as pulsed near-infrared light patterns from a specialized visual interface in a pair of glasses directly onto a subretinal photovoltaic array [33].

4.2. Image processing:

Due to the limited number of electrodes in the implant, image resolution of the camera does not impose any particular constraints on the image processing capability of the entire system [34]. The amount of data conveying the image captured from the outside world needs to be reduced in order to comply with some system-level restrictions and constraints such as wireless transmission bandwidth and processing capabilities of the implanted module [35]. Thus aim of the image processing stage in visual prosthesis is to set the resolution of the original image corresponding to the number of stimulating electrodes and this is called Lowering Resolution with Gaussian Dot (LRG). Adjusting the contrast between the background and foreground region can optimize the visual information presentation in simulated vision. For this purpose, both color information and resolution of the image is lowered (figure 4). Applying transformations, like grayscale histogram equalization, edge detection intensity and contrast enhancement, task performance using a low resolution viewing system can be improved.

A continuous picture is formed by numerous pixels that are usually in the shape of small squares sitting by each other. In visual prostheses, each pixel corresponds to a stimulating electrode. Visual sensations in these prostheses are reported to be a matrix of separate light spots. The quality of vision restored to a patient with a visual prosthesis is highly dependent on the resolution of the image that is delivered to the visual system. This resolution is indeed defined by the number of stimulation sites on the target tissue. It is suggested that 600–1000 electrodes will be required to restore visual function to a level that would allow for reading, independent mobility, and facial recognition in retinal prostheses [36]. The processed images finally obtained are presented in the simulated vision after the process of LRG.

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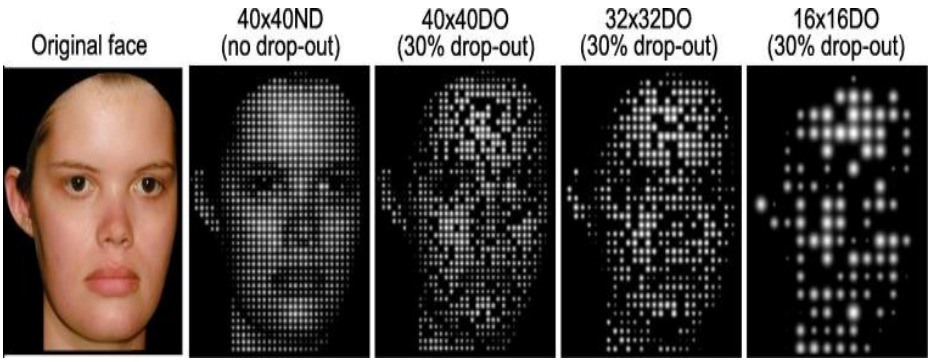

Figure 4 depicts the phosphene appearance in a bionic eye. Examples illustrate a female face high resolution color image, followed by phosphenized versions of the same face at four different resolutions[37]

4.3. Wireless interface:

It is very important to reduce the implant size and provide a wireless interface to reduce the risk of infections. The most common approach is to create an inductive link between the two closely-coupled coils that wirelessly sends the power and data from the external world to implantable biomedical devices [383940]. A primary or transmitting coil is placed on the outside and a secondary or receiving coil is placed inside the body with the thin layers of living tissues between them. Both sides of the link are tuned to the same resonant frequency, referred to as the carrier frequency. The general structure of an inductive coupling system contains a power amplifier that sends power to the receiver circuits by using two loosely-coupled inductors[41]. These windings form an air cored transformer with a low coupling factor, which results in low magnetizing inductance and high leakage inductance. High frequency power converters are used to implement wireless inductive power transfer. Thus, soft-switching is of great importance in order to achieve high efficiency. A dual band telemetry link has been proposed so as to achieve the high data rate and to achieve power efficiency simultaneously. Lower frequency signals are used for power transmission and higher frequency signals for data transfer [42]. To achieve real-time moving images, a continuous power transfer is required. Due to the limitations of implanted batteries like finite lifetime and the need for surgery to replace them, the inductive link is mostly used to transfer power for retinal implant application.

Capacitive links have been proposed recently as novel alternatives which offer several advantages over the inductive links . The most specifically welcomed advantage of the capacitive coupling approach is the high-pass nature of the link [43] This helps to enhance the quality of the images telemetered to the implant where high data rates are required. Dissipation of power in the human eye is one of the most important issues in wireless telemetry. This may result in excessive temperature rise in biological tissues, which can lead to tissue damage [44]. Therefore, when designing wireless interfaces,it is important to evaluate the amount of absorbed radio frequency (RF) energy and compare it with the human safety levels expressed in terms of specific absorption rate (SAR) in associated standards.

4.4. Embedded Control Unit:

Both setup and stimulation data in a visual prosthesis is received from an external module. An embedded centralized controller in the implantable microsystem is in charge of both administering the implant operation and generating stimulation commands/data. Thus the need for the hour is to design an embedded controller that consumes a small amount of power with small physical dimensions, and utilize a limited bandwidth for data telemetry according to frequency allocation regulations. The collected data are sent to a stimulation back-end, according to which appropriate stimulation pulses are generated and delivered to the desired target tissue. The microstimulator is commanded by the embedded controller to generate electrical pulses with various amplitudes and pulse widths according to the data received from the external module. This block also controls other parameters like inter-phase interval and stimulation period. It also controls the sequence and order of stimulations for all the electrodes. Most of the research groups developing visual prosthesis systems prefer to design their own special-purpose controller than to use commercially available ones [45]. This is because a minimum possible interconnections are preferred and also operate at a fast pace that allows the system to stimulate the natural visual system for real-time, flicker-free video streaming.

4.5: Stimulation Circuitry:

According to the digital commands and data issued by the embedded controller, analog stimulation pulses are generated in a microstimulation system. A stimulation back-end generates and delivers electrical stimulation pulses to the target site. These simulations can be in the form of voltage, current, or charge pulses. Both monophasic and biphasic pulses are used for stimulation. A single pulse is generated to deliver a certain amount of electric current, charge, or voltage to the target tissue in monophasic stimulation. In this case it is important to consider provisions for discharging the stimulated area as the accumulation of charge can cause damage to the target sites. In biphasic stimulation each stimulation pulse (anodic pulse) is followed by a pulse of reverse polarity (cathodic pulse) which helps to collect charges delivered to the stimulated area by the anodic pulse. Based on patient's feedback on visual perception, timing specifications and amplitude of the stimulation pulses need to be adjusted [46]. Studies have reported that a typical pulse amplitude is within the 10–600 μA range, and the pulse widths range from 100 μs to around 2 ms. A delay of 0–1 ms is considered between the anodic and cathodic pulses, and 10 Hz to 125 Hz is the pulse repetition rate for visual prostheses [47]. In this type of stimulation a small residual charge at the stimulation sites is dissipated due to the unavoidable systematic mismatches during the design and fabrication. Other issues like leakage of charge from adjacent stimulation sites over a period of time may result in the buildup of electric charge in the tissue being stimulated. Hence, it is necessary to incorporate a charge cancellation circuitry that is envisioned to periodically discharge stimulation sites by connecting the electrodes to the common ground potential.

4.6. Microelectrode Arrays:

The microelectrode arrays (MEA) used in advanced neural and visual prosthesis microsystems have multiple electrode sites developed for chronic implantation[48]. A ribbon cable containing multiple interconnects coated by or sandwiched in between flexible biocompatible polymeric protective layers is used to connect the MEA to the electronic platforms. This protective layer which provides insulation is removed from over the electrode sites in order to allow them to electrically interface with the target tissue. For passivation, polymeric materials such as Parylene-C[49] epoxy-based negative photoresist (SU-8) [50]and polydimethylsiloxane (PDMS) [51]and high-temperature silicon oxide[52] are used. Gold [50], platinum [53] and iridium oxide [49] are usually used for electrode sites. The electrode substrates commonly employed are polyethylene terephthalate (PET) [50], liquid crystal polymer [54], silicon [55] and polyimide [56].

5. THE DEVELOPMENT OF VISUAL PROSTHESES - DIFFERENT APPROACHES:

The visual pathway extends from the retina in the eye to the visual cortex in the brain. Thus in a visual prosthesis, the image information recorded from the external world is delivered to the natural visual system at any point along this path, provided that from there on, the rest of the system is healthy and functioning (figure 5). Hence, various approaches taken to restore vision to the blind, can be categorized into:

1). Stimulation of the retina
2). Optic nerve stimulation
3). Cortical stimulation.
4). LGN stimulation

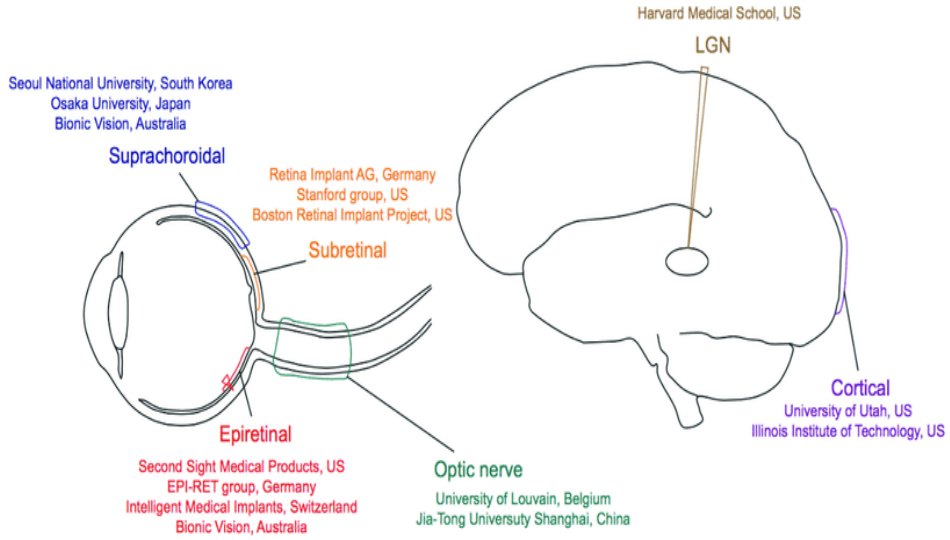

Figure 5 depicts different approaches to restore vision. Six main sites namely epiretinal, subretinal, suprachoroidal, optic nerve, lateral geniculate ganglion, and cortical are currently investigated to implant the electrodes (reprinted from Lorach et al. (2013))[57]

5.1: Retinal prosthesis:

Numerous structures of the retina that can be targeted for electrical stimulation include the outer layer of light-sensitive photoreceptor cells, inner layer of bipolar cells, and the layer of retinal ganglion cells whose axons form the optic nerve [58]. The reasons for choosing retina as a visual prosthesis target are many. Even with advanced degeneration, sufficiently many retinal neurons are still vital and are capable of generating signals to convey images [59]. Its extracranial location and architectural organisation allows easy surgical access, and an implant in a single eye can cover nearly the entire visual field [60]. However, the retina is very delicate and has varying availability across its extent, which can restrict field of view, electrode count, and subsequent visual acuity. Retinal diseases may lead to complication of known retinal maps, retinal reorganization, stimulation parameters, and evoked percepts. For the retinal implants to be successful a significant number of remaining retinal ganglion cells is required, limiting scope and applicability[59]. There are two main approaches to stimulate these retinal ganglion cells: (I) Epiretinal stimulation, in which, the prosthetic device is attached to the inner retinal surface; and (II) the sub-retinal approach, which involves implanting an electrode array between bipolar cells and the retinal pigment epithelium [61]. Suprachoroidal approaches are also in use.

5.1.A : Epiretinal prosthesis:

In this approach, the prosthesis is implanted on the surface of the retina at the vitreous cavity and secured with a tack. Its close proximity to the retina allows for a low stimulation threshold which accounts for a smaller size, while contact with the vitreous cavity fluids helps dissipate heat from the device[62]. However, the conventional use of a tack to anchor the electrode array may possibly cause retinal damage and long-term mechanical stability issues [63]. To avoid unintended activation of fibers originating from other parts of the retina that tends to pass under the electrodes, it is important to stimulate only the cell bodies of the retinal ganglion cell.

With an increased number of clinical trials, epiretinal approach has advanced the farthest within the field, with devices receiving governmental approval for clinical use in both the United States and Europe [64]. The drawbacks include difficulty changing phosphene color, acuity that is quite low compared to normal vision and a field of vision restricted to the typically small span of the electrode array. At present, Second Sight's Argus II is the only visual prosthesis to have received both United States Food and Drug Administration (FDA) and European Commission (CE) approval, both for use against Retinitis Pigmentosa [65]. The Argus II provides maximum visual acuity of 20/1260 over a highly-limited visual field. The IRIS 2 [51] carries a CE mark for use with outer retinal degeneration, and is being tested in an ongoing clinical trial for additional indications [66]

5.1.B: Subretinal prosthesis:

It is an attractive method in which the prosthesis is implanted on the outer retina, given that even in highly degenerated retinas, neural activity can be

evoked by prosthetic electrical stimulation. This location of the array enables such devices to take advantage of both natural eye movements and retinal circuitry, and recipients can use a subretinal prosthesis with little learning effort. Moreover, close proximity of the stimulating contacts to the retinal circuitry allows for lower stimulation thresholds than with other approaches[62]. The subretinal prosthesis can be held in place without a tack as the limited available space is taken up by the implant thickness and power. Like the epiretinal approach, the subretinal implants also include limited possible visual acuity using photodiodes with an expected maximum of Snellen 20/250 due to limitations based on current spread, the limited field of vision and the lack of color perception.

The subretinal implant device that has received governmental approval in Europe is AG's Alpha IMS and its successor the Alpha AMS. The latter consists of an array of 1600 photodiodes which converts light to current which in turn stimulates the adjacent bipolar cells. The highest visual acuity measured was Snellen 20/546, an important improvement compared to both epiretinal and suprachoroidal prostheses, as well as current non-retina devices [67]. The adverse effect in Alpha AMS and Argus II is elevated intraocular pressure (IOP), retinal detachment and conjunctival erosion [68]. PRIMA is a subretinal prosthesis currently undergoing clinical testing. This design uses an array of photodiodes that convert varying intensities of infra-red illumination to localized electrical stimulation of retinal tissue. There is a substantial promise in this hybrid approach of translating the external visual field into an infrared image, potentially modifying it along the way, delivered with sufficient brightness to power the local circuitry at each photosensitive cell. The Artificial Silicon Retina (ASR) developed by Optobionics Corporation contains approximately 5,000 micro-photodiodes, each containing its own stimulating electrode

5.1.C: Suprachoroidal prosthesis:

The suprachoroidal retinal prosthesis is implanted between the choroid and sclera. Sometimes the implants are placed in the scleral pocket for the suprachoroidal-transretinal variant, and stimulates retinal neurons. The position in the scleral pocket provides mechanical stability and the choroid blood vessels aid in dissipation of heat. This location also facilitates less challenging surgery than other visual prostheses. But, due to the increased distance from the retina, these prostheses require higher electrical resistance of the retinal pigment epithelium, which results in higher stimulation thresholds which can increase the risk of damage. [69]

5.2: Optic Nerve Stimulation:

Development of visual prosthesis with an attempt to stimulate the optic nerve was first proposed by Veraart et al [70]. This method can be employed in blind patients with surviving retinal ganglion cells and/or an intact optic nerve. However, achieving focal stimulation and unravelling the exact retinotopic distribution within it is challenging [71]. Veraart in 1998, demonstrated that at safe stimulation currents, phosphenes could be reproducibly elicited. Then the group developed a computational model in which the recipients could recognize and orient complex shapes and perform object localization, discrimination and grasping. The surgical technique in the first patient

involved an implant consisting of a four-electrode, non-penetrating silicon cuff implanted around the optic nerve, accessed via a pterional craniotomy and a trans-Sylvian approach. The second recipient received an intraorbital implant. It was noted that the impedance of the dural sheath between the electrodes and the nerve, higher stimulation currents were required.

5.3: Cortical stimulation:

The optic nerve is considered a potential target for visual replacement if it is intact and functioning. The nerve has an extracranial segment which makes it easy to access with minimally invasive surgery, and would support a full field view despite a high level of retinal cell disease [72]. However, only low resolution and low brightness can be achieved through these implant prostheses. The visual potentials through the nerve stimulation has been proved to have the same wave shape as normal visual potentials. These prostheses take 2 different forms: cuff electrodes and penetrating electrodes.

5.4: LGN stimulation:

The lateral geniculate nucleus (LGN) is one of the primary processing centers for visual information. The information from the retinal ganglion cells is directly sent to the LGN and projects to the primary visual cortex. It has been demonstrated that LGN microstimulation in monkeys produces predictable visual percepts[60]. Thus LGN holds promise as a target for electrical stimulation for artificial visual percepts. One possible disadvantage of this approach is the limited number of electrodes that can be inserted in the LGN which results in limited visual resolution. Also the neurons in the LGN are in close proximity to each other to be stimulated individually, which would be important in trying to reproduce natural vision. Furthermore, most of the projections to the LGN are from the primary visual cortex making it difficult to create complex visual percepts.

CHALLENGES ALONG THE WAY

With all the advances going around the world, realization of a visual prosthesis requires continued and extensive collaborative effort among basic scientists, engineers and clinicians. Despite great technical progress, certain drawbacks and problems must be solved before a visual neuroprosthesis can be considered a viable clinical therapy [73]. The limitations of electrode geometry must be taken into consideration as it is intimately related to the amount of current that can be delivered at safe levels to the target tissues. When the electrodes are placed closed to each other, the theoretical resolution is affected. Moreover as these prosthesis are to be implanted and used for very long-periods of time, the effect of prolonged and focal electrical stimulation delivered to delicate neuronal tissue remains unknown. Another issue to be addressed is how the captured image is co-registered with the natural movement of the eye. Perceptual mismatch can occur as a result of inappropriate compensatory eye movements, causing the patient wearing the implant to mis-localize objects in the external world. This potential confound is particularly true of designs that use an external mounted camera. Thus sophisticated eye-tracking mechanisms have been proposed and designed to generate appropriate shifts in the image. However these results await further research and development [74].

Recently, developments in the field of visual stimulations report that following training, implanted patients may learn to carry out appropriate compensatory head and camera movements to generate more stable percepts[75]. Establishing diagnostic techniques that allow for correlations between objective measures of visual function and eventual implant success would be highly desirable. In retinal implants, the use of high resolution optical coherence tomography (OCT) provides detailed characterisation and analysis of retinal laminar anatomy. This provides insight into detailed anatomical findings indicating that there is extensive retinal reorganization of cellular components and interconnections in patients with longstanding retinal pathologies such as RP. Thus a degenerating retina may respond very differently to electrical stimulation over time.

CONCLUSION

Blindness has a devastatingly negative impact on the quality of life of an individual. The restoration of vision in the blind is a very complex problem which requires extraordinarily diverse, lengthy and intimate collaborations among basic scientists, clinicians, engineers, rehabilitative experts and educators. Despite the technical challenges, it is very important to understand how the brain adapts to the loss of vision itself and what it means to "see" again. The issues of neuroplasticity also need to be addressed. Therefore, it is essential to emphasize on the mechanisms that underlie brain plasticity following the loss of vision in the future research. Such insight helps in developing and refining strategies to merge the visual sensations that are generated by the prosthesis. The ultimate goal of a visual prosthesis is to restore functional vision to blind, while certainly valiant, still there are formidable challenges before it will ever become a tractable reality. With the recent developments and clinical trials, there are grounds to be cautiously optimistic and there is every reason to believe we are on the path to achieve this goal.

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