

Visual Prosthesis: an update and future directions

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Chris won first prize in the British Undergraduate Ophthalmology Society's *Innovations in Ophthalmology* essay competition.

The fascination with building a bionic human has long been the topic of science fiction. Advances in biomedical engineering have allowed neuroprosthesis to become a reality. The development of cochlear implants and prosthetic limbs are examples of how this exciting field can restore function to individuals with significant sensory and motor impairment.^{1,2} Specifically, there is growing research on the concept of restoring sight through visual prosthesis.

This article will provide an up-to-date overview of the sites available for visual pathway stimulation, highlighting the advantages, challenges and most recent advances for each. It will attempt to offer some thoughts on the possible future direction of this exciting field.

How does it work?

The theory is fairly straightforward and is based on the physiology of the human eye. Light is converted into localised electrical currents that are able to stimulate the visual pathway. The visual pathway has the potential to be stimulated at a number of distinct sites including the retinal ganglia, the optic nerve, the lateral geniculate nucleus and the visual cortex (Figure 1). Fundamentally, the site chosen must be proximal to the point of injury, in order that the neuronal messages may continue along the intact visual pathway to the visual cortex. The visual cortex develops through childhood and is responsible for making sense of the neuronal information. For this reason, the potential benefit of a visual prosthetic device is limited to those with acquired blindness. Profound blindness affects 39 million people worldwide³, and is caused by a variety of injuries and diseases that can affect anywhere along the length of the visual pathway. Retinal disease and glaucoma are the commonest causes of irreversible blindness.³

The Retina

Retinal implants are, to date, the most studied form of visual prosthesis. The complexity of neural circuitry means that there is a theoretical benefit to utilising as much of the intact visual pathway as possible.⁴

Diseases of the retina such as retinitis pigmentosa and age-related macular degeneration are generally associated with photoreceptor loss in the outer segment of the retina. The inner retinal layers, remain largely

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intact.⁴ These include the bipolar, amacrine and horizontal cells (for information processing), as well as the retinal ganglion cells that transmit the information to the lateral geniculate nucleus via the optic nerve.

Human experiments have shown that these inner layers remain responsive to localised microelectrode stimulation, even in advanced stages of retinal disease.⁵ This finding has led to an increasing amount of attention on retinal implantation. A microelectrode can be implanted either between the retinal pigment epithelium (RPE) and the sensory retina (subretinal), or attached to the inner retinal layer (epiretinal).

Subretinal Implants

The subretinal approach allows closer proximity of the implant to the bipolar cell layer, thus exploiting its inherent neural processing capacity and requiring lower levels of electrical current for neural stimulation (Figure 1-1b).^{4,6} The main limitation is the amount of physical space that can be used without damaging the retina.⁷ Surgically, there is the possibility of inserting the device through an incision on the outside scleral wall, avoiding invasion of the vitreous and its associated complications.⁶ However, although this technique has been described, it is not yet a well-established or routine surgical procedure, and requires further research.

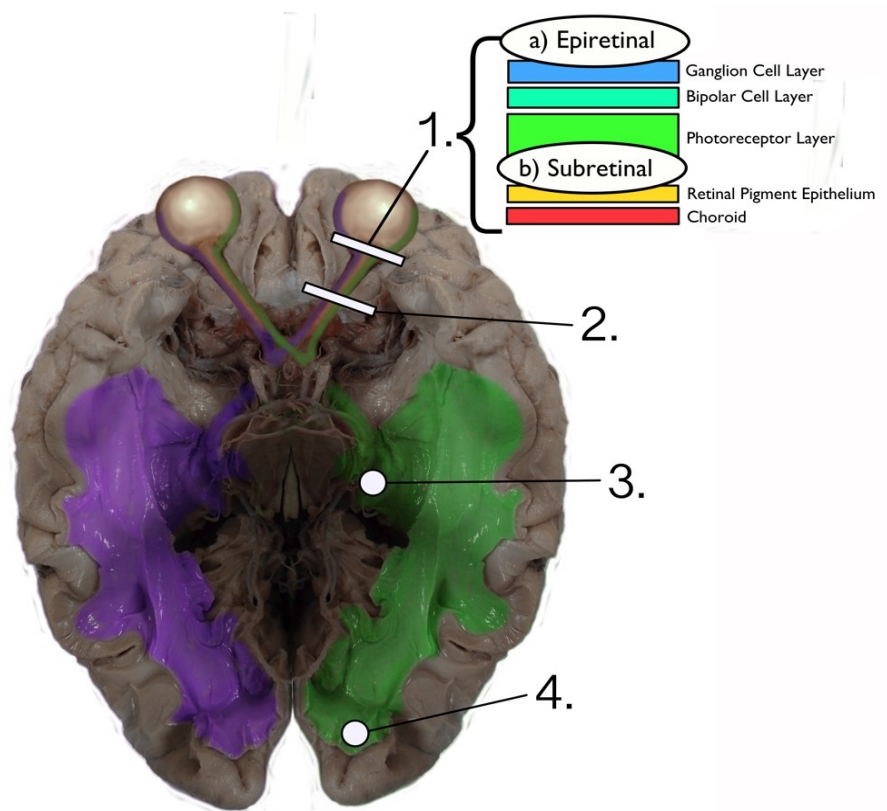


Figure 1 | Sites for artificial stimulation of the visual pathway. 1) The retina; 2) The optic nerve; 3) The lateral geniculate nucleus; 4) The visual cortex. RPE – Retinal pigment epithelium. *Cadaveric images used were taken with permission, under the auspices of the HTA Licence held by Brighton and Sussex Medical School.*

The Boston Retinal Implant Project (BRIP) favours this approach and uses an external video camera and microprocessor to capture and process images and wirelessly transmit them to the subretinal implant. This device is currently undergoing animal studies.⁶

Retina Implant AG is a German group that has designed a device capable of incorporating both image capture and neuron stimulation in a single subretinal implant.⁸ Although this is a more elegant solution than the BRIP, and allows visual input to be under the conscious and unconscious control of the extraocular muscles, it comes with a caveat; the bulk of technology is inaccessible. This creates difficulty in making in-vivo alterations to image processing algorithms, as well as the replacement or repair of malfunctioning equipment.⁶ The latest version of this prosthesis has been successfully implanted in nine humans, with the majority demonstrating restoration of light perception (8/9), light localization (7/9), motion detection (5/9), and a degree of visual acuity (up to Snellen visual acuity of 20/546).⁸

Epiretinal Implants

An advantage of the epiretinal prosthesis is the well-established vitreoretinal approach to surgical implantation (Figure 1-1a). In addition, the size of the vitreous cavity permits the implantation of larger devices, when compared to the subretinal space. Furthermore, the vitreous contents may help to dissipate additional heat generated, and prevent host tissue damage.⁹

There is a selection of research groups that have demonstrated interest in the epiretinal implant. Second Sight's Argus II implant is arguably the most advanced retinal prosthesis and the only product that has received commercial approval within the United States and Europe.^{9,10} The implant consists of 60 independently controllable electrodes and is fixed in place on the retinal surface temporal to the fovea. An external camera and processing unit are used to capture and translate images. These signals, as well as the power required are transmitted via trans-scleral wires to the implant.

The group's most recent report in the British Journal of Ophthalmology demonstrates the functional improvement in 21 subjects with light perception only or worse prior to implantation.¹¹ These subjects were asked to identify each letter of the alphabet (22.6 cm in size) on a screen at a distance of 30cm. There was a significant difference between the ability to accurately and reproducibly identify letters with the system turned on, and with it turned off. A subset of six patients were able to consistently identify letters as small as 2.3cm at a distance of 30cm, with four subjects able to read two-, three- and four-letter words. The time taken to recognise letters varied between subjects and ranged from seconds to minutes. An additional report shows that 54% of subjects (15/28) with bare light perception or worse fitted with the Argus II were able to perform a motion detection task that they could not do with their native vision.¹² The factors associated with differentiation between higher- and lower-performing individuals fitted with the Argus II is not clear and will require further research.

The Optic Nerve

Stimulating the optic nerve (Figure 1-2) is also a possibility in patients with functioning retinal ganglion cells. One group has described the use of a self-sizing cuff electrode encapsulating the optic nerve and connected to a head-worn video camera.¹³ It allowed the recipient, who was completely blind from retinitis pigmentosa, to be trained to localise, discriminate and grasp objects. A second group in Japan has described an optic nerve implant in a blind patient that allowed localised perception of light by stimulating individual electrodes.¹⁴ The precise relationship between the site of ganglion cell bodies within the retina and the position that their axons take within the optic nerve is yet to be mapped in sufficient detail.⁹ This relationship may hold the key to viable optic nerve prosthesis.

The Lateral Geniculate Nucleus

The lateral geniculate nucleus (LGN) remains largely intact in individuals with acquired disease or injury of

the retina or optic nerve. This makes it a potential site for stimulation in those groups of patients with ocular trauma, retinal disease or optic neuropathy (including that caused by glaucoma, ischaemia and optic neuritis). This 10mm target is deeply sited and so might offer a stable site for electrode implantation and allows access to the entire visual field.⁷ It is surgically accessible, being anatomically adjacent to the regions targeted in deep brain stimulation for movement disorders.

However, as the LGN lies posterior to the optic chiasm and the decussation of nasal retinal ganglion cells, accessing the entire visual field would require bilateral implantation. In addition, the LGN does not receive fibres from the medial root of the optic tract. The medial root carries about 10% of nerve fibres and has been associated with the visual grasp reflex, automatic scanning of images, visual association pathways and arousal function.¹⁵ It is not fully understood how much these unconscious visual pathways contribute to everyday visual function.

The Visual Cortex

Direct stimulation of the visual cortex is the oldest described method of artificially inducing the perception of light. Its biggest advantage is the potential to restore sight in individuals with acquired disease or injury almost anywhere along the visual pathway, including those previously described as well as cerebrovascular disease affecting the optic radiation. It is a relatively large anatomical area that might permit restoration of high-resolution images. However, surgical approaches will need to overcome the challenge of targeting areas of the cortex embedded within the calcarine fissure.⁷ Surface electrodes have been shown to degrade over time, and cause meningeal irritation.^{7,9}

Future directions

Based on current research, and anatomical knowledge, the future of visual prosthetic design will need to consider a variety of factors.

High-resolution images

As discussed, the most advanced progress to date has centred around retinal prosthetic devices. Clinical trials have shown that these implants are able to improve visual function, and their efficacy seems to improve with a higher concentration of electrodes.¹¹ Achievable levels of visual acuity are still some way off being comparable to those of a normal human eye. The high-resolution central field of vision is a product of the highly concentrated photoreceptor and retinal ganglion cells around the fovea. The ganglion cells in this area are packed 5-7 cells deep¹⁵ and for this reason, visual acuity may be limited in retinal prostheses. As the cell axons enter the optic nerve and travel toward the LGN, they become more evenly distributed. This results in a larger cross-sectional area of the pathway being dedicated to central, as opposed to peripheral vision.⁷ In order to achieve the best possible improvements in visual acuity, post-retinal neuron stimulation may soon become the favoured option.

Automatic gaze direction and motor control

Every second, the physiological eye makes multiple automatic movements from one point of regard to another.⁷ Most current prosthetic systems utilise an extraocular camera for visual input, relying on head movement for gaze direction. An intraocular camera, under the intrinsic control of the extraocular muscles may be an important step forward in improving the function of these prostheses. This is currently under-explored but has shown some promise.¹⁶

Colour

Current visual prostheses rely on the detection of light intensity by microelectrodes sited throughout the visual field. This produces a degree of spatial resolution but is unable to account for variations in hue. Indeed the perception of colour may be more important than first thought.¹⁵

Our current understanding of physiological colour processing is still too limited to make visual prostheses in colour a reality. It would seem that in

order to detect colour in a retinal prosthesis, this would require differential stimulation of the bipolar cells associated with each of the trichromatic cone cells. Currently, this seems unfeasible. At the LGN and visual cortex, some research has been carried out on the anatomical basis for colour opponency, but there are still significant gaps.¹⁷ The neural computations required to elicit colour vision are complex. It is unlikely that visual prosthetics will be able to accommodate these computations in the near future.

Conclusion

Forty years after 'The Six-million Dollar Man' first aired on television, the bionic eye is emerging as a reality. There are a number of anatomical considerations in its design, with each site along the visual pathway offering advantages and challenges to artificial stimulation. Retinal implants have already shown some promising results, and we will likely see great strides in progress as technological, surgical and rehabilitative techniques all improve. That said, this article highlights that there is still much work to be done if the visual prosthesis is ever going to provide a physiologically comparable degree of visual function. ■

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