OSLO METROPOLITAN UNIVERSITY
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Rehabilitation of the blind

With visual prostheses / Bionic eyes

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Blindness, frightening and restraining

Imagine waking up one early morning in the autumn. The darkness is enclosing the neighbourhood and the rain is pouring down as the chilly air is breaking into the room through the curtains. The sound of the few persistent yellow leaves on the birch tree outside the window dancing in the strong autumn wind overwhelms the splashing from the rain. It is so dark that not even a single beam of light is passing through the curtains. Not even from the streetlight outside the garden fence. The cell phone is lying on the bedside table, but it seems to have a flat battery because there is no light emitting from the screen when it is picked up to display the time. Beside the bed is a furry carpet to keep the feet warm as they touch the floor, but the cold is penetrating through making the foot sole sting. The fingers go quickly numb as they touch the wall to guide the way to the light switch on the other side of the bed. It makes a clicking sound, but nothing happens. Everything is still pitch black. Eternal darkness. Blindness.

The sense of sight, the ability to detect and process visible light, is in an evolutionary perspective a great advantage for organisms living in habitats where visible light is present. It functions as a long-range detection system, as opposed to the sense of touch where direct contact is required. To humans it is also a source of pleasure. We have a romanticized relationship to our sight, whether it is taking in the breath-taking view of nature, or gaze upon phenomenal art or simply enjoying cute puppies through social media. It may not be surprising that Adrienne W. Scott et al. found out that American citizens think that losing the vision is one of the worst sufferings compared to other serious conditions (Scott et al., 2016). The study was conducted as a national online survey and the subjects were asked to rate worst condition among losing the memory, speech, hearing or even a limb.

Vision impairment has an impact on the society as well as the individual that is suffering from it. According to a study conducted by Prof Rupert R A Bourne et al., published in The Lancet Global Health, it was in 2015 estimated 36 million blind people. They also estimated 217 million moderate to severe vision impaired and 188 million with mild vision impairment. Besides, the total amount of blind and vision impaired is accelerating, because of the increasing average age of the global population (Bourne et al., 2017). Blindness is also connected to diabetes (Niketeghad & Pouratian, 2019) also a globally increasing disease. Consequences of the condition are reduced quality of life and may inhibit the sufferer from taking an education. It can also have an impact on the economic situation due to treatment costs. Additionally, the family or local community may be forced to abandon work to care for the patient (Niketeghad & Pouratian, 2019). A deeper knowledge of the visual system is required to understand what vision impairment and blindness is and how the conditions can be treated.

What is blindness?

In general, blindness and serious vision impairment are consequences of the visual system lose the ability to detect and/or process the light that enters the eye. A deeper understanding of the physiology and anatomy of the visual pathway is required to be able to assess the cause. The reason we can perceive images is that visible light enters the eye via the pupil which is the black spot we can see in the middle of the colourful iris. Then, a lens makes sure to focus the light before it hits the *retina*, the first stage of the visual pathway. This is the point where the light is converted to electrical signals. The retina is a thin layer covering the inner surface of the eye consisting of light sensitive cells, called rods and cones. They respond to different wavelengths and electrical impulses spawn in the retina according to the triggered cells. The electrical impulses are sent through a complex distribution system beginning with the *optic nerve and tract*, which is the output of the eyes. The signals are further distributed through l*ateral geniculate nucleus* (LGN), a part of thalamus which is an area in the brain responsible for filtering information. From the LGN the signals finally arrive in the Primary visual cortex, an area of the cerebral cortex located in the back of the brain (Tong et al., 2020). An overview of the visual system is presented in Figure 1 (Mirochnik & Pezaris, 2019). In many cases an error in the retina is causing visual impairment. For instance, degeneration of the light sensitive cells making the retina unsusceptible to light. However, the rest of the visual pathway remains functional and can therefore perceive electrical signals generated from other sources than the eye, such as a visual prosthesis (Mirochnik & Pezaris, 2019).

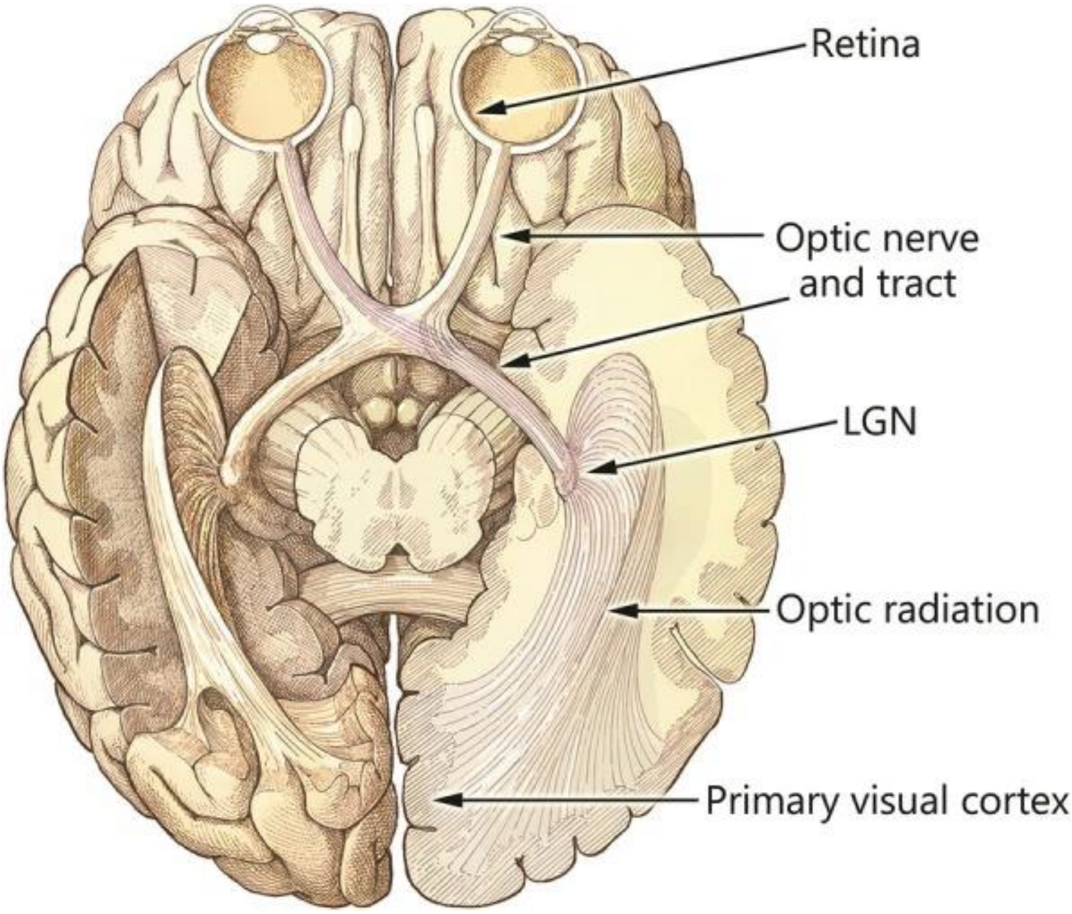


FIGURE 1 TRANSVERSAL CUT OF THE BRAIN SHOWING THE ANATOMY OF THE VISUAL PATHWAY. FROM "CONTEMPORARY APPROACHES TO VISUAL PROSTHESES", BY REBECCA M. MIROCHNIK AND JOHN S. PEZARIS, 2019, *MILITARY MEDICAL RESEARCH,* 6(1), P.19, COPYRIGHT 2019 BY CREATIVE COMMON ATTRIBUTION 4.0 (HTTPS://CREATIVECOMMONS.ORG/LICENSES/BY-NC-ND/4.0/)

What is a visual prosthesis?

Visual prostheses are electronic devices that capture light, for instance with a camera or a photosensitive array, process the information and convert the signals to electrical impulses that are transmitted to the visual pathway via an electrode array (Mirochnik & Pezaris, 2019). A prosthesis acts as a bypass to the part of the visual system that is malfunctioning. In theory can all parts of the visual pathway be a potential target, although, there are some approaches that are more common than others. Visual prostheses are therefore named and characterized from the area where the implants are inserted. The most common approaches are retinal implants, optic nerve, LGN and visual cortex (Farnum & Pelled, 2020). Retinal implants can further be divided in subcategories as there are different layers in the wall of the eye where implants can be inserted. An Epiretinal implant is placed on the surface of the retina, while a Subretinal implant is placed beneath the retina. A suprachoroidal implant is placed just beneath the white outer surface of the eye, called sclera, and the next layer called choroid. The different approaches can be seen in Figure 2.

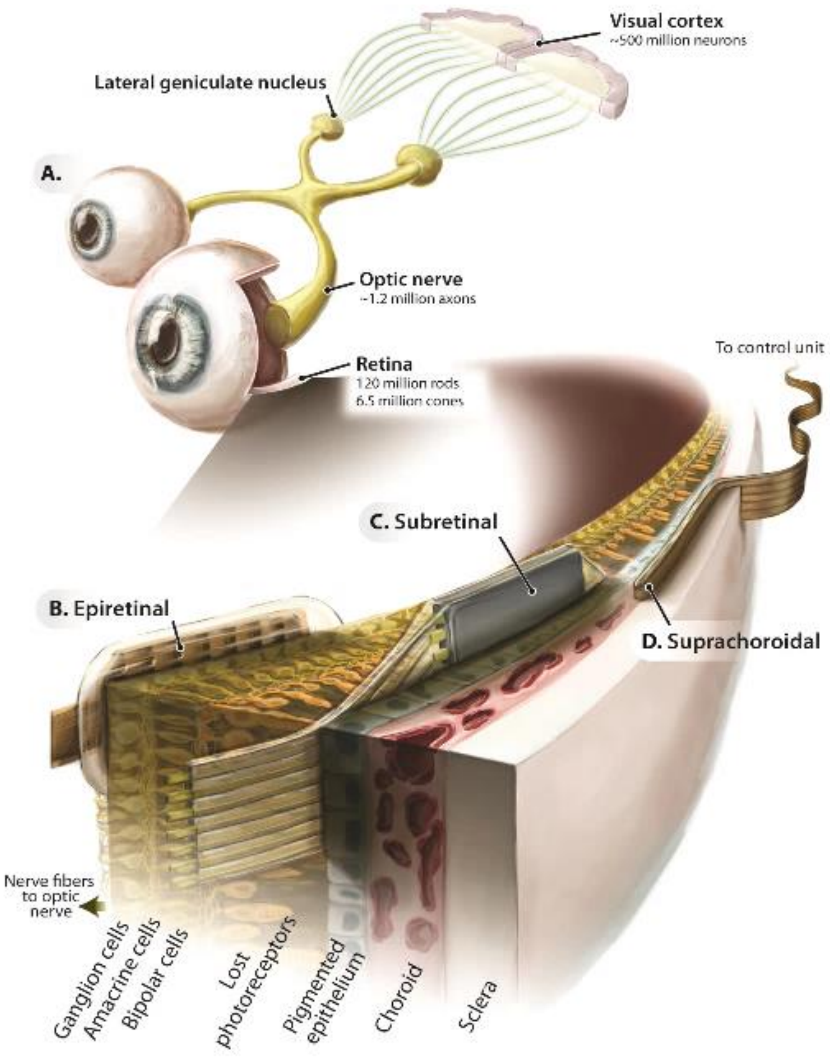
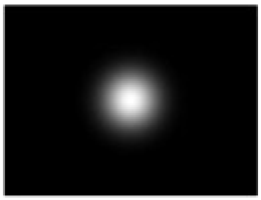


FIGURE 2 AS REPRINTED IN (THE LASKER/IRRF INITIATIVE FOR INNOVATION IN VISION SCIENCE, 2014A): OVERVIEW OF THE VISUAL PATHWAY AND POSITIONING OF RETINAL IMPLANTS. SCHEMATIC *A.* SHOWS A REPRESENTATION OF THE VISUAL PATHWAY AND HIGHLIGHTS IMPLANT POSITIONS. *B, C AND D* SHOWS THE POSITION OF EPIRETINAL, SUBRETINAL AND SUPRACHOROIDAL IMPLANTS RESPECTIVELY. FROM "CHAPTER 1 – RESTORING VISION TO THE BLIND: THE NEW AGE OF IMPLANTED VISUAL PROSTHESES", BY THE LASKER/IRRF INITIATIVE FOR INNOVATION IN VISION SCIENCE, 2014, *TRANSLATIONAL VISION SCIENCE & TECHNOLOGY*, 3(7), P.3. COPYRIGHT 2O16 BY ASSOCIATION FOR RESEARCH IN VISION & OPHTHALMOLOGY (ARVO).

How can we help?

Finding a treatment to cure blindness is important because there are many affected. Visual prostheses qualify as a potential solution based on the presented theory. The purpose of the essay is therefore to investigate to what extent visual prostheses is a valuable therapeutic procedure to rehabilitate the blind. Viewing the historical perspective of visual prostheses is relevant to assess the current status and recognize the limitations that must be overcome. Comparing the past and the present provides a deeper understanding of how researchers can utilize the available technology to solve the problem.



History

To fully appreciate the modern visual prostheses and understanding the complex challenges to overcome, a glance at the historical perspective is necessary. It is truly a miracle that is being pursued.

The first evidence

One day in 1755, a French doctor named Dr. Charles Le Roy is attempting to cure the blindness of one of his patients. He had developed a metallic apparatus to mount on the head that would induce electricity into the brain (Lewis & Rosenfeld, 2016). It hard to tell what happened in the examination room where Le Roy’s experiment took place, but it could have been like this:

To remove some of the nervousness and anxiety the doctor hands over the apparatus so the blind can touch and familiarize with the device. Touching the device gives a conception that the apparatus is just a metal hoop with two plates separated at a distance that fits perfectly above the eyes. A bar with a hook at the end is hanging between the metal plates and a wire seems to be connected in the back of the hoop. This is also where, what must be, the tightening mechanism is located. The doctor takes the apparatus back and steps it over the patient’s head. The metal plates above the eyes feel cold against the skin. Suddenly, a screeching sound appears from the screws in the tightening mechanism as they turn to fit the apparatus to circumference of the head. As the machinery is booting the hoop begins to vibrate and the plates provoke a tingling feeling. A strange humming sound emerges that is so intense that it is hard to tell if it comes from the hoop passing just above the ears, or if the sound is penetrating the brain through the scalp. The effects must be caused by the currents flowing through the apparatus. Suddenly! In the visual field that had been just pitch black for so long, a flash of light appears!

Dr. Charles Le Roy was not aware of his discoveries, nor that he was the first person in approximately 1750 years to retrieve visual perception in a blind person. However, rather than performing miracles, Le Roy scientifically documented the experiment, which is why we can in hindsight designate him to be the first person to produce visual perception in a blind person with the use of electricity. His apparatus can be seen in Figure 3 (Lewis & Rosenfeld, 2016). But what was it exactly that Le Roy had achieved?

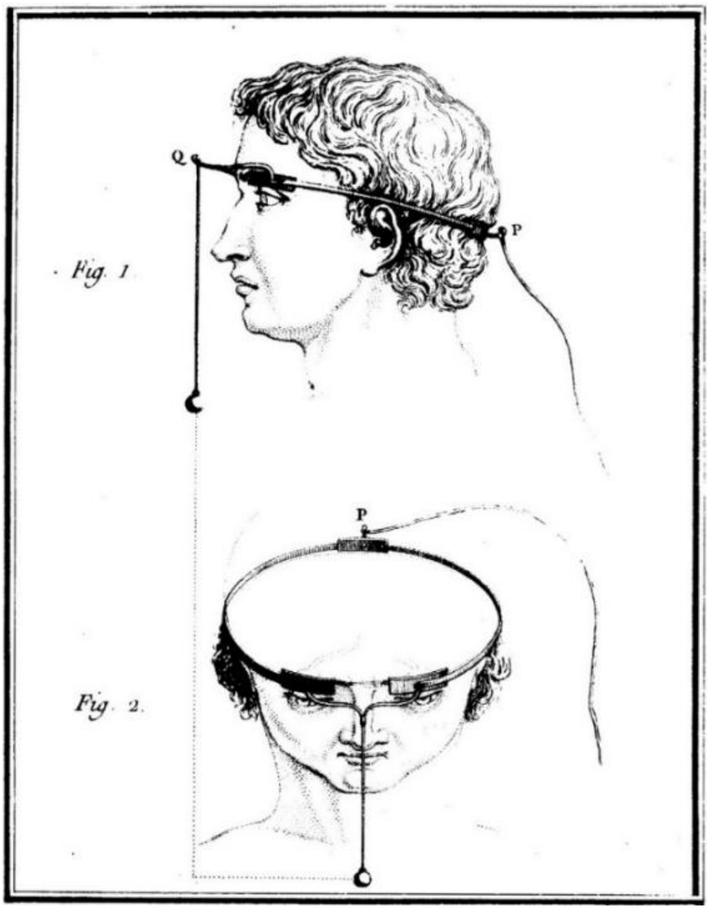


FIGURE 3 AS REPRINTED IN (LEWIS & ROSENFELD, 2016): DRAWING OF LE ROY'S APPARATUS. FROM "ELECTRICAL STIMULATION OF THE BRAIN AND THE DEVELOPMENT OF CORTICAL VISUAL PROSTHESES: AN HISTORICAL PERSPECTIVE", BY PHILIP M. LEWIS, JEFFREY V. ROSENFELD, 2016, *BRAIN RESEARCH,* 7(1), P. 210, COPYRIGHT 2016 BY CREATIVE COMMON ATTRIBUTION 4.0 (HTTPS://CREATIVECOMMONS.ORG/LICENSES/BY-NC-ND/4.0/)

The flash of light that Le Roy's apparatus produced is what we today call *phosphenes* [Greek: *phos*, light and *phanain,* to show (Cervetto et al., 2007)]. Phosphenes are, according to Spencer C. Chen and his research partners "*any visual sensation caused by means other than stimulation of the visual system by light*" (Chen et al., 2009). They gathered information about phosphene appearances reported from approved human experiments to evaluate phosphene models composed for simulations. The material of reported phosphenes indicate that the light flashes can practically come in any formation, shape and size. For instance, reported phosphenes appeared in clusters of dots, or they could be shaped as donuts, lines or even squares. Phosphenes in several different colours have been reported as well: white, orange, brown, blue, yellow etc. It might be hard to imagine what the flashes of light looks like, but phosphenes are common for normal sighted too. If you rub your eyes hard spots of lights in different colours will appear and start dancing in your visual field. These phosphenes appear due to mechanical stimulation, instead of electrical (Cervetto et al., 2007).

Progression

At this point in the timeline, visual prostheses are merely a dream, but fortunately light is present at the end of the tunnel. Discoveries are standing in line to be uncovered during the next two centuries and it starts with Volta. in 1800 he realizes that the eyes are responsive to electric stimuli and produce phosphenes when exposed to current (Lewis & Rosenfeld, 2016). This evidence enables the possibility for eye stimulation instead the complex brain. Despite the experimental evidences, in the scientific community there is a universal scepticism as to that the brain is receptive to electrical stimulation. However, the necessary grounds are provided by the combined work of different researchers related to electric stimulation of the brain and its topography. As well as newly acquired anatomical and physiological knowledge about the visual pathway (Lewis & Rosenfeld, 2016). By the mid-19th century there is a consensus that the occipital cortex has a central role in our visual system, and the new paradigm is strengthened over the following years. But our understanding of where the visual field is represented in the cortex is limited and retinotopy requires therefore more attention (Lewis & Rosenfeld, 2016).

Retinotopy, or retinal mapping, is the discipline of making diagrams that shows the connection between the stimulated field of vision and the activated neurons in the parts of visual system of interest. It is set on the agenda in the early 20th century and in 1918 Gordon Holmes creates a correct retinal map of the occipital cortex based on his and his colleague's previous work. Their achievements initiated new studies that later gave the light responsive area in the brain the suiting name "primary visual cortex". Much of research progress of the early 1900 until 1950's can probably be dedicated to WWI. This is likely because many of the subjects in human experiments suffered from head traumas caused by gunshots or flying fragments. It was Holm's experiments supplemented with others that paved the way for the evolution of visual rehabilitation devices and the first chronical implant (Lewis & Rosenfeld, 2016).

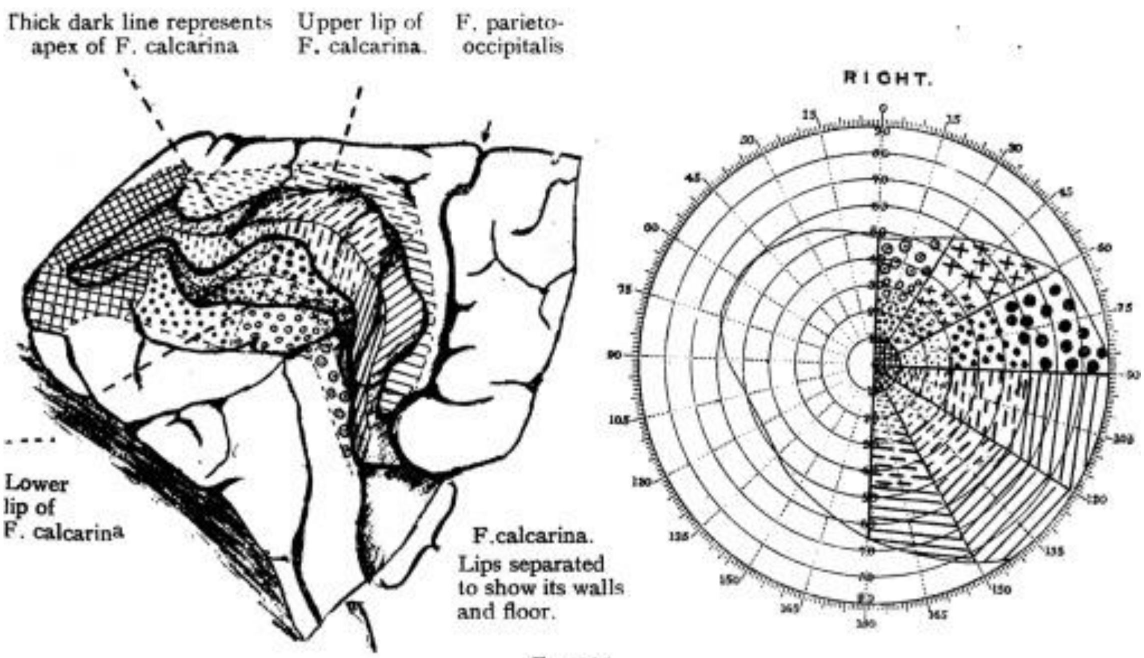


FIG. 16.

A diagram of the probable representation of the different portions of the visual fields in the calcarine cortex. On the left is a drawing of the mesial surface of the left occipital lobe with the lips of the calcarine fissure separated so that its walls and floor are visible. The markings on the various portions of the visual cortex which is thus exposed correspond with those shown on the chart of the right half of the field of vision. This diagram does not claim to be in any respect accurate; it is merely a schema.

FIGURE 4 RETINICORTICAL MAP CREATED BY GORDON HOLMES. THE DIAGRAM INDICATES WHERE ON THE VISUAL CORTEX (CALCARINE CORTEX) THE VISUAL FIELD IS REPRESENTED. FROM "ELECTRICAL STIMULATION OF THE BRAIN AND THE DEVELOPMENT OF CORTICAL VISUAL PROSTHESES: AN HISTORICAL PERSPECTIVE", BY PHILIP M. LEWIS, JEFFREY V. ROSENFELD, 2016, *BRAIN RESEARCH,* 7(1), P. 211, COPYRIGHT 2016 BY CREATIVE COMMON ATTRIBUTION 4.0 (HTTPS://CREATIVECOMMONS.ORG/LICENSES/BY-NC-ND/4.0/)

The first chronical implant

The collaboration between an osteopath and the Chief of Neurosurgery at Cedars Lebanon results in the first chronically implanted visual prosthesis. The year is 1957 when John C. Button persuades Tracey Putnam to help him in his work and they successfully implant two pairs of thin wires into a patient's visual cortex. The four electrodes are connected to an image processor that can be seen in Figure 5. The processor is simple compared to modern standard and works by utilizing a photocell to convert light into electrical impulses. The test subject, a woman that has been blind for 18 years, is able to locate a bright bulb that is being moved around in a dark room (Lewis & Rosenfeld, 2016).

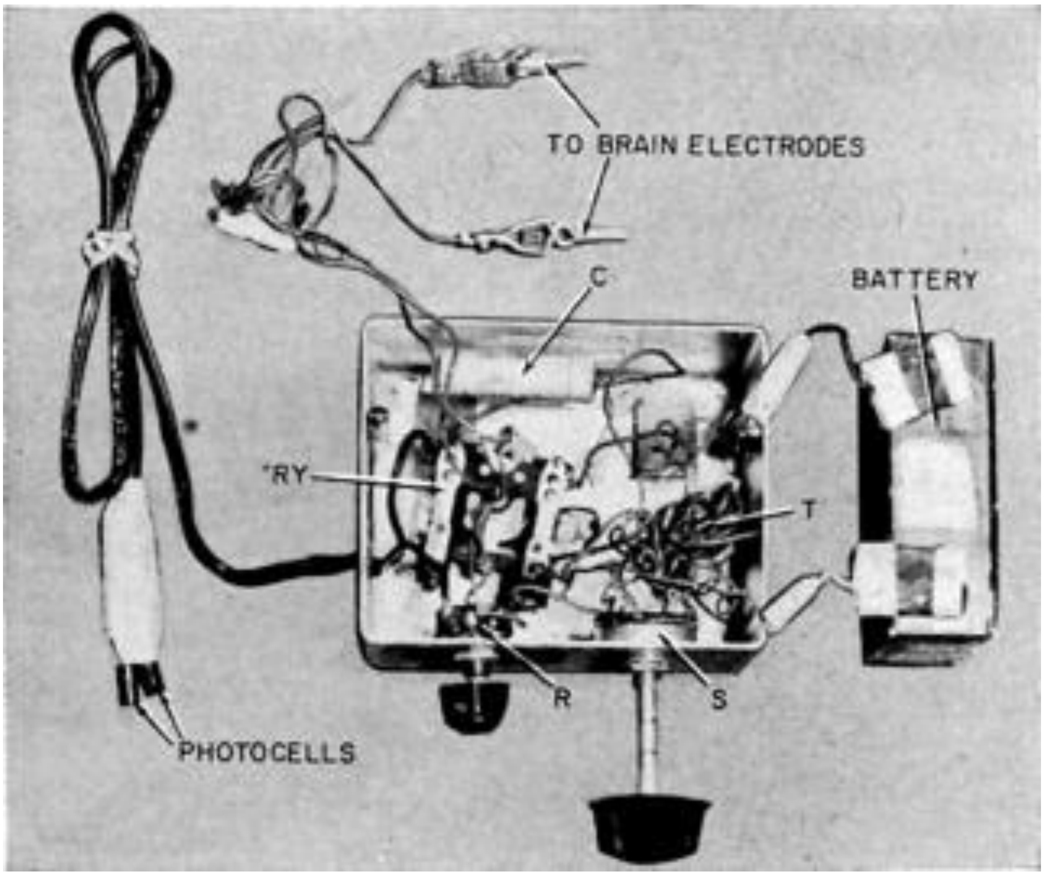


FIGURE 5 AS REPRINTED IN (LEWIS & ROSENFELD, 2016): THE IMAGE PROCESSOR OF THE FIRST CHRONICALLY IMPLANTED VISUAL PROSTHESIS MADE BY JOHN C. BUTTON AND TRACEY PUTNAM. FROM "ELECTRICAL STIMULATION OF THE BRAIN AND THE DEVELOPMENT OF CORTICAL VISUAL PROSTHESES: AN HISTORICAL PERSPECTIVE", BY PHILIP M. LEWIS, JEFFREY V. ROSENFELD, 2016, *BRAIN RESEARCH,* 7(1), P. 212, COPYRIGHT 2016 BY CREATIVE COMMON ATTRIBUTION 4.0 (HTTPS://CREATIVECOMMONS.ORG/LICENSES/BY-NC-ND/4.0/)

According to Lewis and Rosenfeld, Button and Putnam documented in their article ("Visual responses to cortical stimulation in the blind", 1962*, J. Iowa State Med. Soc.*, 52, p. 17-21), that the patient described what she saw as follows: *"somewhat as the sun might appear to a sighted person through closed eyelids" (Lewis & Rosenfeld, 2016).* How remarkable!

Until now the main work of visual prosthesis has focused on brain, but parallel in time as Button and Putnam test their cortical device a retinal prosthesis sees the light of day. Tassicker invented and inserted a retinal implant in a patient able to give simple light perception in 1956 (Farnum & Pelled, 2020).

Evolution

The next major contributors to the progress of cortical prostheses are the gentlemen Giles Brindley and his companion W.S. Lewin. They implanted a multielectrode array in a patient in 1967. Two years earlier Brindley, a physiology student at the university of Cambridge, calculated the minimum number of stimulation points necessary to read letters. He estimated that it requires ten points to read one letter, or ten modified letters, and 600 points to read a text. He also acknowledged that wired electrodes were a life-threatening risk to the patient due to possible infections. Therefore, he suggests that his implant should wirelessly transfer signals to the brain via coils. Such technology has improved over the last thirty years which provides feasibility to Brindley's solution. However, the number of stimulation points must be reduced since the technology is not capable of transmitting that much information (Lewis & Rosenfeld, 2016). The multielectrode array produce phosphenes in the central vision and the vertical periphery, but the presence of the phosphenes are some-what random. The patient is therefore only able to identify "V", "L" and "?", and Brindley must proceed on his quest to help the blind to read letters (Lewis & Rosenfeld, 2016).

Brindley, now working with Peter Donaldson and other colleagues, upgrades his device in 1972. The 2.0 version can produce 68 phosphenes which is twice as many as the previous model. The patient is able to read braille letters with the help from a processor that translates regular letters into electrical stimuli organized as braille characters (Lewis & Rosenfeld, 2016).

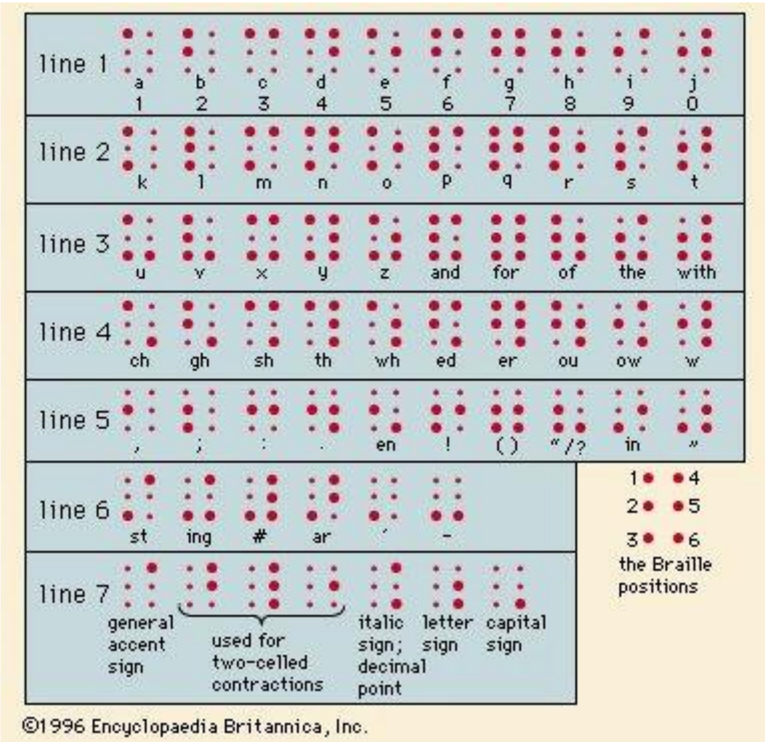


FIGURE 6 THE IMAGE SHOWS WHAT BRAILLE CHARACTERS LOOK LIKE AND HOW THEY CAN BE ARRANGED IN CELLS OF SIX DOTS. FROM *ENCYCLOPÆDIA BRITANNICA*, HTTPS://WWW.BRITANNICA.COM/TOPIC/BRAILLE-WRITING-SYSTEM, COPYRIGHT 1996 BY ENCYCLOPÆDIA BRITANNICA.

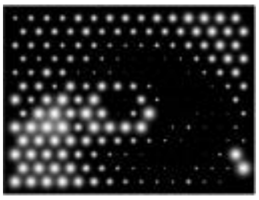
In Utah, USA, is a research team with outstanding expertise making rapid progress to their cortical device. The prosthesis is a part of a dedicated research program that initiates in 1968 at the University of Utah (Lewis & Rosenfeld, 2016) under the Institute of Biomedical Engineering. The head of the institute is none other than the "Father of Artificial Organs", Willem J. Kolff (J. Willard Marriott Library, n.d). and the director of the dedicated research program is William Dobelle. In 2003 they become nominated for the Nobel prize of physiology or medicine (Deseret News, 2004). Dobelle's electrode design is different than Brindley's. For instance, Dobelle has chosen a wired solution that can be externally disconnected which makes it accessible and upgradeable. Despite the differences, the patient's phosphene observations seem to correlate between the two devices. In the 1970's, after several upgrades is applied to Dobelle's device the patient is able to read braille characters. And the patient reads faster with the device than with his fingers (Lewis & Rosenfeld, 2016).

Brindley is persistent and getting closer to his goal. However, further improvements of his device are necessary before the patient can read handwritten characters. He is determinedly continuing his work, but unfortunately in 1982 he discontinues his work after the next prototype must be removed within the first year of trial due to infections (Lewis & Rosenfeld, 2016). William Dobelle on the other hand continues to upgrade his device with more and more advanced hardware and software. One of his devices remained functional and free of infections for over twenty years (Lewis & Rosenfeld, 2016). This very implant belongs to Jeremiah Teehan from USA who, in the year of 2000, is awarded the Guinness World Record for having the first successful artificial eye. With his implant he was able to orient around a room and find a black hat that hang on a white wall. Jeremiah then managed to locate a manakin and put the hat on the manakins head (Guinnes World Records, n.d). A comparison of Brindley's and Dobelle's last upgraded version can be seen in Figure 7.

FIGURE 7 COMPOSITION OF TWO IMAGES AS REPRINTED IN (LEWIS & ROSENFELD, 2016): COMPARISON BETWEEN THE LAST UPGRADED VERSION OF BRINDLEY'S IMPLANT AND THE FIRST ARTIFICIAL EYE, THE DOBELLE IMPLANT. FROM "ELECTRICAL STIMULATION OF THE BRAIN AND THE DEVELOPMENT OF CORTICAL VISUAL PROSTHESES: AN HISTORICAL PERSPECTIVE", BY PHILIP M. LEWIS, JEFFREY V. ROSENFELD, 2016, *BRAIN RESEARCH,* 7(1), P. 215-216, COPYRIGHT 2016 BY CREATIVE COMMON ATTRIBUTION 4.0 (HTTPS://CREATIVECOMMONS.ORG/LICENSES/BY-NC-ND/4.0/)

Behind the functional achievements of Brindley's and Dobelle's cortical prostheses lies great feats of engineering. The electrodes became ever smaller and increased in number, and eventually they evolved into compact arrays enabling more precise neuron targeting and denser electrode placement. In addition, improvements in wireless technology increased the number of stimulation points, and consequentially a better resolution is achievable (Nowik et al., 2020). These technological accomplishments were transferable to retinal implants as well, and the leading technology for visual prostheses is about to change.

Most of the attention has been in favor of cortical approaches, and It seems as history has forgotten about retinal implants. However, retinal implants are about to make their entry from the 1990's as the most common visual prosthesis. Almost forty years after Tassicker inserted the first retinal implant in 1956 Humayun et al. successfully produce visual perception to a human. Their experiment initiates a rapid progression to retinal implants. One of the contributing factors to the success is the implant's strategic position early in the visual pathway (Farnum & Pelled, 2020). Retinal approaches benefit from utilizing the biological image processing feature built into the visual system, which gives them a functional advantage due to the simplification of the technology. Another contributing factor is that the risks associated with retinal implants are lower because of safer and relatively uncomplicated surgical procedures (Niketeghad & Pouratian, 2019). The minimized risks lower the ethical bar for approvals of clinical trials, patient recruitment and approval to enter market. This is partly why retinal prostheses advance to be the favorable approach for future development of visual prostheses.



Current status

Despite that cortical procedures have been the major contributor to the progression of visual prostheses there are not yet any commercialized devices. However, there are prominent prototypes being tested in clinical trials that hopefully will be available in the future (Mirochnik & Pezaris, 2019). Fortunately, there is one retinal prosthesis that has made it into the market, but what is it like to see with a visual prosthesis?

Take it from someone who can tell from their own experience. Jerry became completely blind in his 30's and received an Argus II retinal implant at the age of 66 (Maldonado et al., 2015). In an interview with 60 minutes Australia he explains that when the device was turned on for the first time, he suddenly saw bright flashes of light. They were so bright, he said, that his head shook backwards, which is noticeable from the video of him recorded during the system launch (60 Minutes Australia, 2020). When asked what Larry can see of the reporter, as they are sitting around the table eating cakes, Larry explains that there are flashes around her forming a silhouette. Later in the reportage the creator of the Argus II, Dr. Robert Greenberg, explains that Argus II users can see flashes of light in levels of grayscale, which facilitates more visual information over just black and white. He usually compares it to as looking at a very blurry black and white tv (60 Minutes Australia, 2020). There is 350 people worldwide assisted by an Argus II (Second Sight, n.d.), and it is one of four visual prostheses that has received approval to enter the EU market (Edwards et al., 2018). However, Argus II is the only visual prosthesis available today, and is therefore highlighted in next section.

Retinal Implant AG was in 2013 granted permission to enter the market with the Alpha IMS implant. Its successor Alpha AMS gained approval in 2016. These devices are using subretinal implants of photovoltaic arrays which converts the light entering the eye into electrical impulses. The advantage with this technology is that the electrodes is smaller and the arrays contains 1500 (Bloch et al., 2019) and 1600 stimulation points respectively (Edwards et al., 2018). The technology is not dependent on an external camera either. However, further development of the devices was terminated in 2019 after the shareholders decided to dissolve the company. This decision was partly justified by not delivering in up to expectations, despite that the majority of the patient benefitted from the implants (Retina Implant AG, n.d.).

The third technology granted CE approval was the Intelligent Retinal Implant System (IRIS) II made by a French company named Pixium (Edwards et al., 2018). This system uses an epiretinal implant consisting of a 150-microelectrode array and a camera mounted on a pair of glasses, similarly to the Argus II. The video recordings are then adjusted to fit the low resolution of the implant. The system has implemented a machine learning algorithm which can optimize the function of the device over time. The device was approved to enter the EU market in 2016, but due to shorter lifespan of the device than expected the clinical trials have been delayed (Bloch et al., 2019).

Argus II

Second Sight has made a visual prosthesis based on the epiretinal principle. The implant consists of a 60-channel microelectrode array mounted directly at the surface of the retina, a customized circuitry for generating the electrical impulses, and an internal coil for wireless communication with the external components. The external components comprise of a camera, image processor unit and an external coil. The camera is mounted on a pair of glasses and is acting as the input to the image processor, which converts and compress the information to match the resolution of the microelectrode array. Electrical power to drive the internal components and the signals are transferred from the external coil to the internal coil. The best recorded visual acuity performance of the Argus II was 20/1262, which is the same as being nearly blind. This result does not sound significant, but it did improve the performance of the majority of the blind patients in different tests (Luo & da Cruz, 2016).

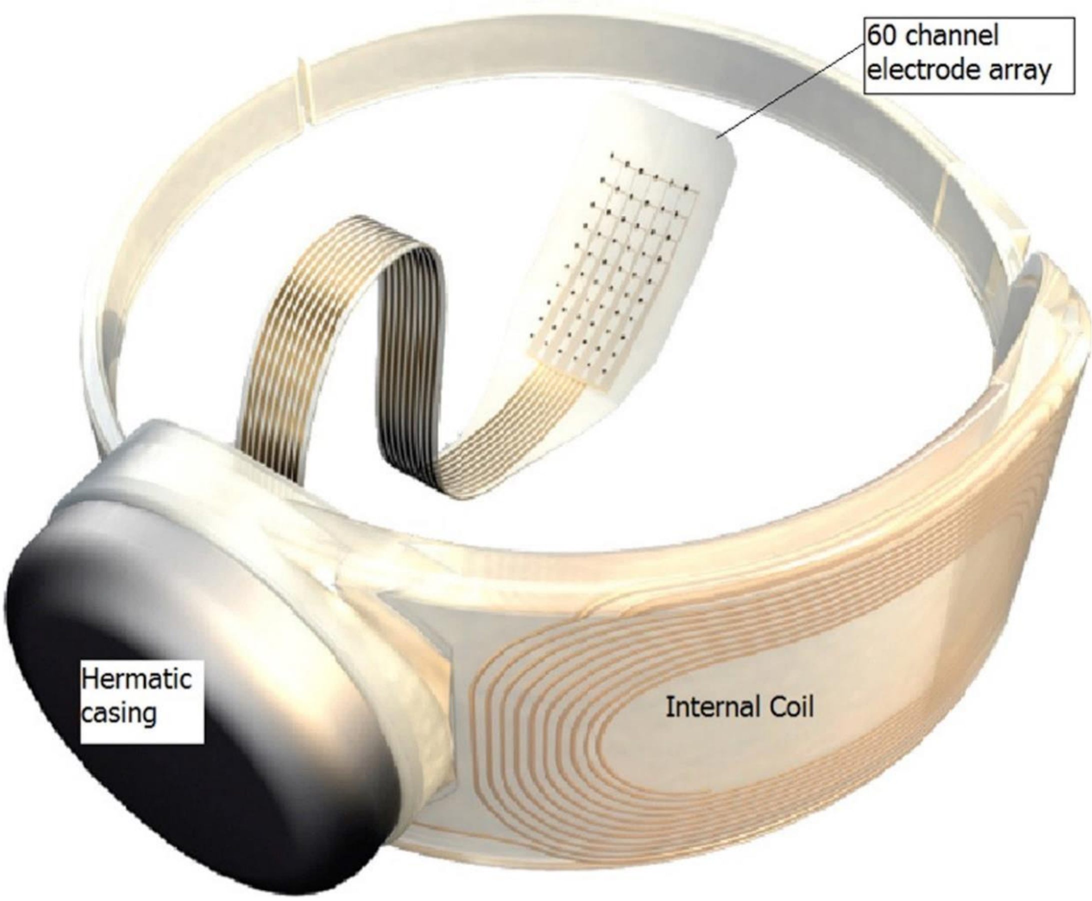


FIGURE 8 AS REPRINTED FROM (LUO & DA CRUZ, 2016): THE INTERNAL COMPONENTS OF THE ARGUS II. FROM "THE ARGUS® II RETINAL PROSTHESIS SYSTEM", BY YVONNE HSU-LIN, LYNDON DA CRUZ, 2016, *PROGRESS IN RETINAL AND EYE RESEARCH,* 50(1), P.92, COPYRIGHT 2015 BY ELSEVIER LTD.

What does it mean that a patient regained vision equal to 20/1260, and how can a person's vision be assessed? This is a concern that needs further attention.

Assessment

There are several therapeutic procedures to cure visual impairment, for instance getting a pair of glasses, take medicines, gene therapy or acquiring a visual prosthesis. The assessment of the vision with regards to grading and how the functional tests are performed is a common denominator for all therapeutic procedures. However, there is no existing standard and it is up to the researcher to find the best applicable test. In addition, the tests are often well suited in experiments but does not necessarily represent the real world very well. It is therefore challenging to assess and compare daily life functionality of different visual prostheses (Bloch et al., 2019).

A commonly used test to assess visual acuity is the Snellen eye chart. This is the basis of the rating used by the World Health Organisation. The classification of WHO is presented in table 1 (WHO, 2020):

TABLE 1 WHO'S CLASSIFICATION OF VISION IMPAIRMENT WHICH IS BASED ON THE INTERNATIONAL CLASSIFICATION OF DISEASES 11 (2018) THE NUMBERS ARE LISTED IN METERS.

Rating: Distance vision impairment	**Classification**
Visual acuity < 6/12	Mild
Visual acuity < 6/18	Moderate
Visual acuity < 6/60	Severe
Visual acuity < 3/60	Blindness
Rating: Near vision impairment	**Classification**
Near vision acuity < N6 or M.08 with existing correction	Vision impaired

The Snellen eye chart is the recognizable letter chart that is hanging on the wall in every examination room. The numerator in the table is the distance from where the patient can read the letters clearly, the denominator is the distance where normal sighted can see the same. For instance, 6/12 means that the patient must stand 6 meters away from the chart to be able to recognize the same letters as a normal sighted at 12 meters (Levenson & Kozarsky, 1990). The Snellen chart itself is not necessarily used in the psychophysical tests, because there is an equation for converting performance into a Snellen equivalent.

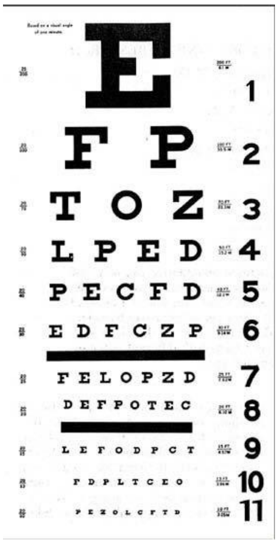


FIGURE 9 SNELLEN CHART USED TO ASSESS VISUAL ACUITY. FROM ENCYCLOPÆDIA BRITANNICA, [HTTPS://WWW.BRITANNICA.COM/SCIENCE/SNELLEN-CHART](https://www.britannica.com/science/Snellen-chart). ACCESSED 11/29/20.

According to The Lasker/IRRF Initiative for Innovation in Vision science, WHO have used a different rating system than the one in table 1. The difference is just that the numbers are listed in feet, but since this version seems to be frequently used in clinical trials of visual prostheses it is listed in table 2 (The Lasker/IRRF Initiative for Innovation in Vision Science, 2014b),

TABLE 2 RATING OF VISUAL IMPAIRMENT IN FEET, (THE LASKER/IRRF INITIATIVE FOR INNOVATION IN VISION SCIENCE, 2014B).

Rating	Description
20/30 - 20/60	Near normal vision or mild vision loss
20/70 – 20/160	Moderate visual impairment, or moderate low vision
20/200 – 20/400	Severe visual impairment. Or severe low vision
20/500 – 20/1000	Profound visual impairment, or profound low vision
Below 20/1000	Near-total visual impairment, or near total blindness
No light perception	Total visual impairment, or total blindness

Edward Bloch et al. clarifies in their review that a problem with the Snellen scale is that it is not quantifiable below a certain point. The state-of-the-art visual prostheses retrieve vision below this point, and it might therefore not be the most appropriate way of assessing them (Bloch et al., 2019). The Snellen equivalent is still frequently used, maybe in lack of other options for characterization. A more suitable assessment method could be to evaluate how well patients perform in tests with the bionic eye turned ON versus OFF. Perhaps that could have prevented the shutdown of the AMS implant. Another issue with the tests is that they are designed for experiments. Such as the object recognition tests in the clinical trials of the Alpha AMS and the Argus II, where the test subjects tried to identify geometrical shapes with high contrast to the background. However, according to Cheng Qiu, the results of these tests were evaluated on the wrong basis since pre-trained objects were used. He refers to the fact that in the literature this is called pattern or object discrimination (Qiu et al., 2018). Either way, the tests are only to a small extent transferable to everyday life, but on the other hand, such tests can be very expensive to organize (Bloch et al., 2019).

A self-proclaimed taskforce called the International Harmonization of Outcomes and Vision Endpoints in Vision Restoration Trials (Hover) has taken the initiative to resolve the assessment problem. The HOVER Taskforce consists of over eighty experts in fields of ophthalmology that have participated in a consensus document containing guidelines regarding psychophysical tests and visual measurement. They have also obliged to keep a website up to date that lists all applied methods and related results in visual restoration trials. There is a whole section in the consensus dedicated to visual perception produced by electrical impulses, such as visual prostheses (Ayton et al., 2020).

Although there are issues with regards to assessment, it is important to verify that the resolution is limited. It will not be substantially improved before the next generation of implants. There are currently a few studies of novel extremely compact retinal implants, but they are yet only tested on animals (Li et al., 2017). One implant is an optically controlled subretinal array with 1512 stimulation points tested in rabbit retinas (Bosse et al., 2018). Because of their current status it is reason to believe they are most likely not going to be commercialized anytime soon. In the meantime, it is a high demand for other strategies to enhance the visual performance of existing devices.

Performance boost of existing prostheses

Different approaches to how the functionality of current visual prostheses can be enhanced is being explored. Some researchers focus on filtering out unnecessary information by implementing image processing techniques and optimization algorithms into the image processors. Others think that extended training and movement/usage strategies can improve the users understanding of the surrounding world. Additionally, the amount of visual information available for the user might be expandable if the total amount of phosphenes can be increased and/or their shape can be changed controllably by how the electrode array is stimulated.

One advantage of the first two methods is that the solutions can be tested in simulation systems, such as augmented reality or virtual reality. The experimental setup does therefore not pose any risk to the test subject. In addition. the participants can be normal sighted humans. This is more ethically approvable, and the pool of potential test subjects increase significantly, which simplifies the recruitment process. Both image processing techniques and the lateral head movement approach in the next paragraphs was tested in simulations. Compared to prototyping these methods are easier to readapt. However, the results are only predictive, and the solutions must eventually be tested in a functional visual prosthetic system to be verified.

Object recognition does often have a central role in visual tasks encountered in daily life, and several sophisticated attention models have been proposed. An attention model is an image processing algorithm that emphasize information considered important to the user (Li et al., 2017). In many cases the essential information is in the foreground. Therefore, removing background clutter to emphasize the object in front is a proposal by Jae-Hyun Jung and his three colleagues. They use "active confocal de-cluttering" of the images in their developed multi-camera system consisting of video camera and light-field camera. Confocal means having the same focus, and the light-field camera is used to detect the plane at which the object of interest is. The video camera is then set to focus on the same object. De-cluttering is the process of removing the background from the image. This is done by applying image processing techniques, such as high-pass filtering or other image blurring. The active part is referring to the user interface where system parameters can be adjusted according to the current situation. The attention model showed promising functionality during system tests as can be seen in Figure 10 (Jung et al., 2015).

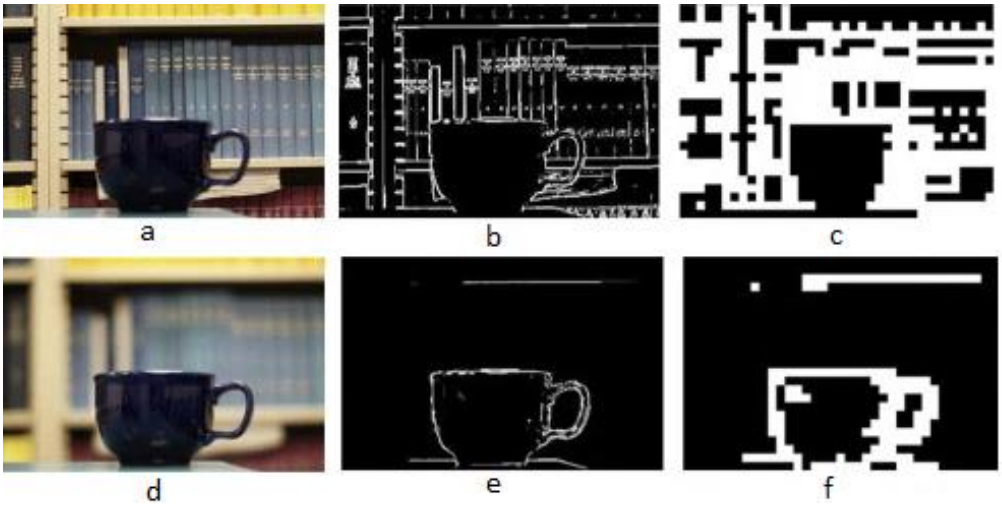


Figure 10 Composed of Fig. 2 and Fig. 3 (Jung et al., 2015), but with new letter notations. A and D represent the same motive, but a confocal technique has been used in picture D to blur the background. The effect of high-pass filtering in E is much better than in B because of the blurred background. Image C and F is the compressed version with low resolution. From "Active confocal imaging for visual prostheses", by Jae-Hyun Jung et al., 2015, *Vision Research*, 111(1), p.185, Copyright 2014 by Elsevier Ltd.

Despite the effectiveness of their system the resolution in current visual prostheses are not adequate. They performed tests where the image was compressed to match the resolution of the prostheses, and then gradually increasing the resolution. The test subjects struggled to identify the object of interest with the low resolution. Figure 11 illustrates what the images presented to the participants looked like. The tests estimated that 3000 to 5000 electrodes are needed to acquire the resolution where users recognize the image 50% of the times. Unfortunately, it is not expected that the next generation of electrode arrays will have that many electrodes (Jung et al., 2015).

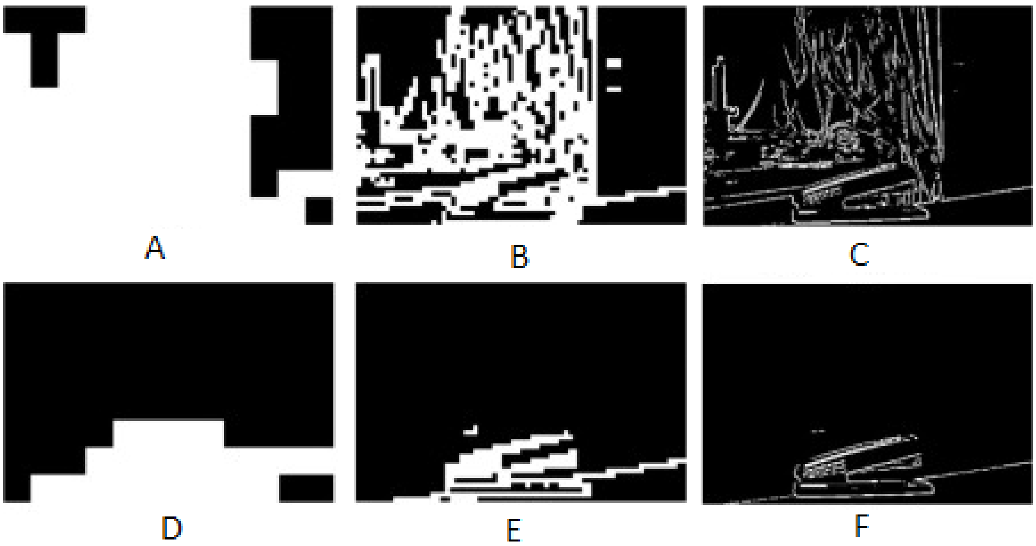


Figure 11 Composed of Fig. 6 and Fig. 7 (Jung et al., 2015), but with new letter notations. Picture A is the compressed low resolution of picture D where the background is not removed. Similarly, Picture C is the compressed version of picture D where the background is taken away. B and E represents the gradually increasing resolution presented if the subject could not identify the object. Although C contains less information that A, it is still difficult to recognize what the image represents. From "Active confocal imaging for visual prostheses", by Jae-Hyun Jung et al., 2015, *Vision Research*, 111(1), p.187-188, Copyright 2014 by Elsevier Ltd.

Several other effective advanced attention models been demonstrated as well. However, a group of scientists from China suggests that visual prosthetic users would benefit more from a simpler algorithm. They argue that many of the more advanced algorithms are not performing well, or are incapable of performing, in real-time processing. A fundamental of visual prostheses is that the user can perceive the images immediately. The concept of their algorithm is to scan the images from bottom to top to locate and highlight objects that is in contact with the ground surface. Thus, they will detect objects present in the foreground. Their enhanced solution can be seen in Figure 12 (Li et al., 2017).

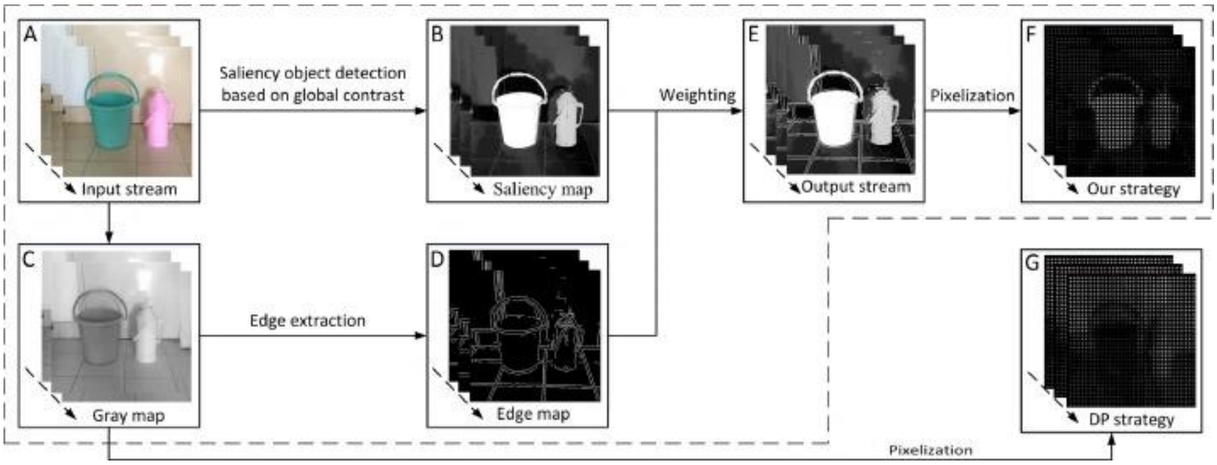


FIGURE 12 A SCHEMATIC PRESENTATION OF THE SIMPLER ATTENTION MODEL. A COMPARISON OF THE ENHANCED IMAGE AND DIRECT PIXELIZATION STRATEGY IS SHOWN AT THE RIGHT. FROM "A REAL-TIME IMAGE OPTIMIZATION STRATEGY BASED ON GLOBAL SALIENCY DETECTION FOR ARTIFICIAL RETINAL PROSTHESES", BY HENG LI ET AL., 2017, *INFORMATION SCIENCES*, 415-416(1), P.4, COPYRIGHT 2017 ELSEVIER INC.

In Jung's experiments of the multi-camera system, they noticed that the test participants who struggled to identify the object of interest started to tilt and turni their head. This could be a natural reflex that normal sighted use to try to distinguish the object from the background. By moving the head, the observer can see the object from different perspectives. However, it was unsuccessful in the experiment because the participants were looking at static images. Jung implies that in a live video system lateral head movements could help to distinguish the object and make it easier to recognize (Jung et al., 2015).

It is common knowledge that training in how to use visual prostheses improves its performance (The Lasker/IRRF Initiative for Innovation in Vision Science, 2014a). It is therefore possible that different movement techniques can increase the functionality in certain situations. A study with origin in the observations from Jung's experiment seek to understand the effect of lateral head movements to distinguish an object of interest from the background. Lateral head movements changes the position of viewpoint which might give rise to motion parallax (Qiu et al., 2018), which is a physical phenomenon that can occur due to change in the position of view. It makes objects close to the viewpoint move faster than objects in the background (John H. Krantz & Schwartz, 2015). For instance, if a passenger looks out the window on a train traveling through a beautiful mountain landscape, rocks and bushes next to the railway tracks will fly past the window while the majestic mountains in the background will move slowly across the field of view. The different behaviour of foreground objects opposed background objects can possibly be detected. The outcome of the study was that decluttering of the background by utilizing motion parallax in a visual prosthesis system with a head-mounted video camera had a positive effect. They performed a simulation of motion parallax which increased the recognition rate from 10% to 20% as opposed to static images. The results implies that lateral head movements can aid visual prosthetic users to identify objects, but further investigations are necessary (Qiu et al., 2018).

The previous mentioned methods seek to optimize the input information of visual prostheses which can provide better functionality for the user. Others put an effort into researching different electrode stimulation strategies to increase the amount of information produced by the implant. Positive outcomes of this research are not only better functionality in everyday life, but it might also increase the resolution of the visual prosthesis and provide the user with better vision. The resolution is ultimately determined by the user experienced phosphene pattern, which is dependent on several factors. Such as how few neurons is it possible to trigger at the same time. Different electrode design parameters have a central role in this matter, like the thickness of the electrodes. Thinner electrodes can trigger fewer neurons which in turn can trigger smaller phosphenes and potentially result in better resolution because of the smaller pixels. However, decreasing the diameter is not so simple, because it results in an increase in the electrode's electrical impedance which in turn require higher currents to trigger the neurons, and can put the patient in danger. Being able to control where the currents flow in the retina is another parameter that seems to be essential. The return currents produced by the electrical stimulation in the implant must be controlled, or else the current will flow through several neurons and produce distorted phosphenes in the patient's visual (Tong et al., 2020). The characteristics of the signal is also determining how the phosphenes forms. Researchers are therefore experimenting with different frequencies, amplitudes and pulse length etc.(Tong et al., 2020).

Future

The visual prostheses market is in growth and we are most likely to experience an increase in the amount of visual prosthetic users. The technology has proven itself valuable as the only alternative to restore visual perception, and it has not yet fulfilled its true potential. Tomorrow we might all know someone whose parent has been blessed and can see how their silhouetted grandchild is running around. Or two friends that yet again can go to the movies together. This is merely a prediction, but the progress of visual prostheses is most likely to accelerate. Web searches in relevant journals reveals an increase in number of publications containing phrases related to visual prostheses. The trends indicate that there is an increased attention to the field, although there was a stagnation the last five years. The data is presented in Figure 14.

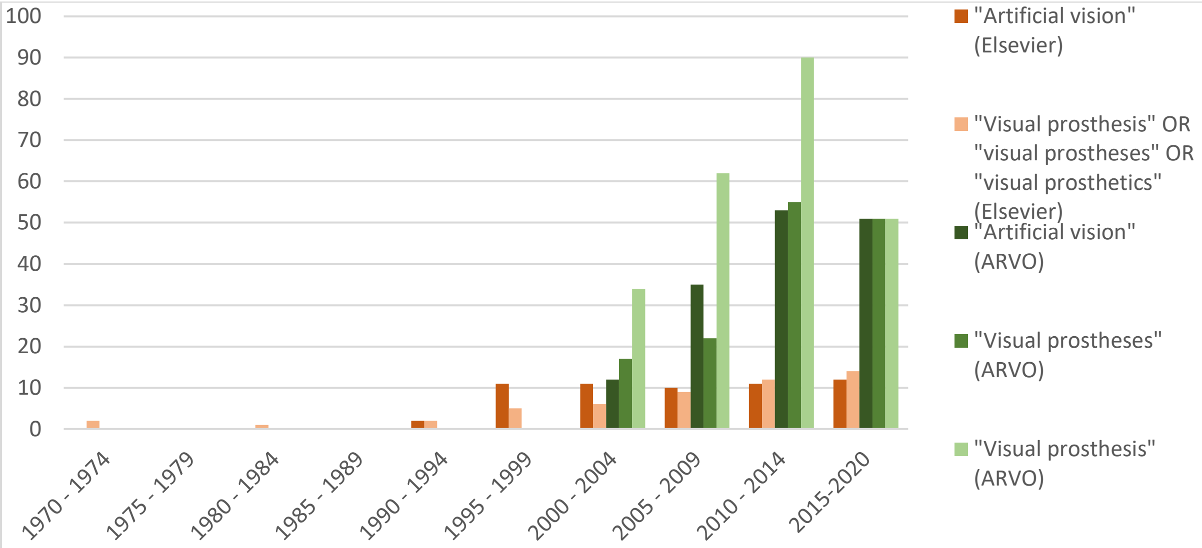


Figure 13 The amount of journal publications related to search phrases relevant to visual prostheses.

The same trends can be seen in Figure 15 where data from Google Scholar is displayed. The large number of articles containing “artificial vision” is most likely related to computer science, which is not included in the journals. Computer vision can possibly aid in the evolution of visual prostheses, because object recognition algorithms and other image processing techniques may be adaptable.

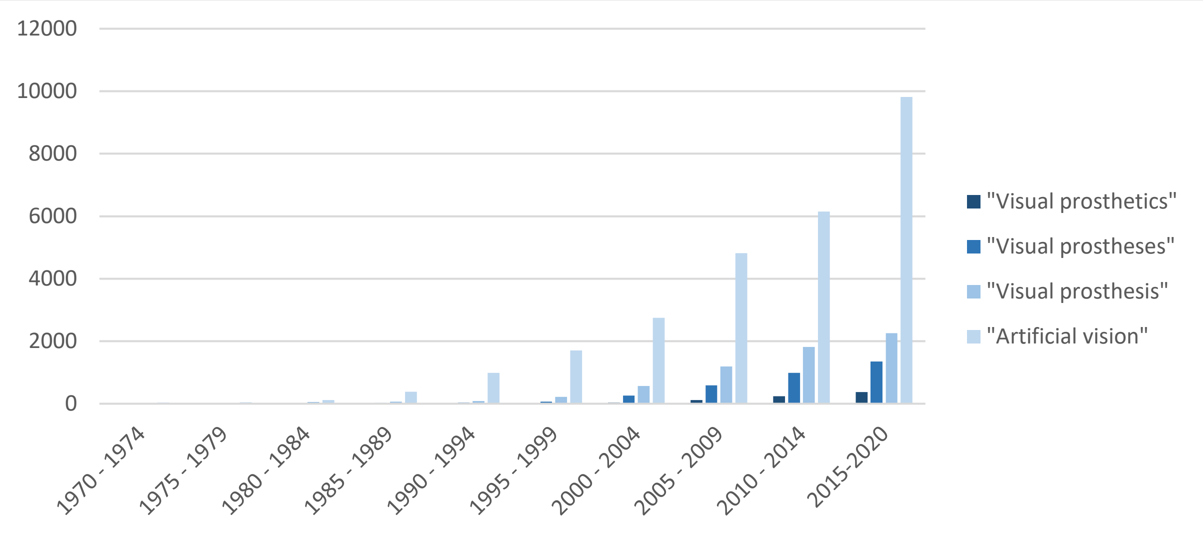


FIGURE 14 THE AMOUNT OF PUBLICATIONS IN GOOGLE SCHOLAR CONTAINING SEARCH PHRASES RELATED TO VISUAL PROSTHESES.

The progress of previously mentioned research such as electrode design, stimulation strategies will most probably lead to improved performance in visual prostheses. But other modern tools can also be beneficial, such as machine learning or feedback loops. Implementing machine learning is expected to increase the functionality of the visual prostheses depending on the purpose of the algorithm. For instance it could be designed to help in specific daily encountered situations and assist the user in those situations(Niketeghad & Pouratian, 2019). Resolving how to implement closed-loop feedback from the implants are also expected to increase the effectiveness significantly. The researchers of current visual prostheses are depending on feedback from the visual experience of the user. This information might be inaccurate and improving the devices can therefore be time consuming (Tong et al., 2020). Feedback from the implant can also be further used in machine learning or predictive algorithms to enhance performance by reducing noise.

The first commercialized cortical prostheses will eventually come into existence. There are several teams working on devices that share features with the Dobelle implant, like using a camera to capture the images. However, these novel cortical prostheses have adapted the wireless principle of Brindley’s devices to minimize the danger of infections. Some of the upcoming prostheses are in the process of planning clinical trials, but there is one that has already started: The Orion I (Niketeghad & Pouratian, 2019).

Orion I

Orion I is a cortical implant under development by Second Sight that also launched the Argus II retinal implant. Much of the technology is transferable between the two approaches and Orion I has therefore adopted several features from its cousin. They share the same external components, such as a head-mounted camera, video processing unit and a similar transmitter coil for wireless communication with the internal components. The internal components, as seen in Figure 15 (Patel et al., 2019), consist of a receiver coil, circuitry responsible for triggering impulses and an array of 60 electrodes stimulating the occipital lobe(Niketeghad & Pouratian, 2019).

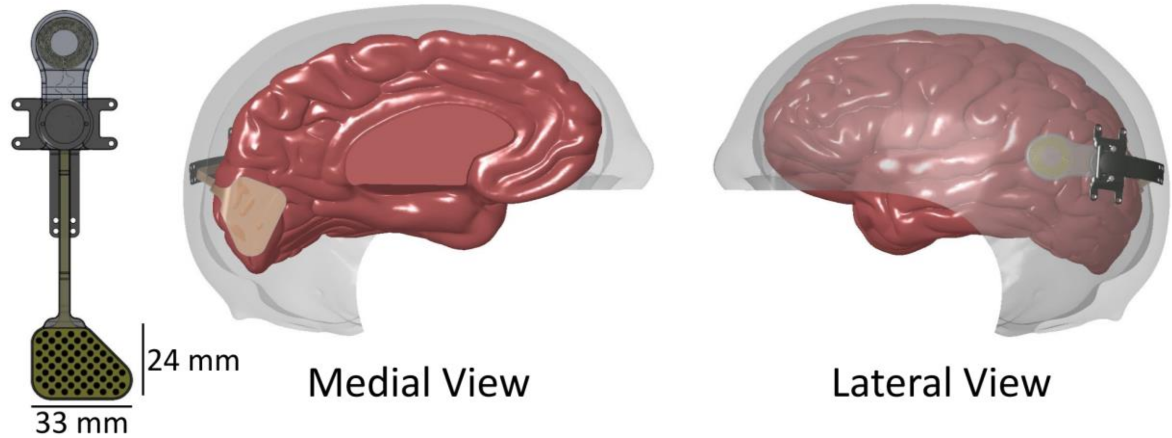


Figure 15 Overview of the Orion implant(Patel et al., 2019). Adapted From "Early Feasibility Study for the Orion® Visual Cortical Prosthesis: from thresholds to visual function", by U. K. Patel et al., 2019, Second Sight *press releases*, copyright 2019 Second Sight Medical Products Inc.

The device is currently being studied in a clinical trial to evaluate the safety and function where six patients are being followed for five years. The one-year clinical trial was completed last year and were presented 11/11 at The Eye and The Chip World Research Conference 2019. The results are promising for the Orion I as a therapeutic procedure for patients where the visual system before the visual cortex is non-functional. Relevant patient groups for the Orion I is burn or head trauma patients. In the visual tasks the patients were able to detect motion and locate a square presented on a computer screen (Dorn et al., 2020).

Complete restoration?

There has been an extensive effort related to prototyping to uncover the mysteries of the visual system. And recently the prototypes have evolved to become a valid therapeutic procedure for rehabilitation of the blind. The technological improvements that followed enabled researchers to develop software methods to improve the performance of the existing prostheses, such as novel stimulation strategies or image processing techniques.

Considering the progression of cortical prostheses over a relatively short period of time, and that retinal implants have practically come into existence over the last decades. It is not incomprehensible that a futuristic visual prosthesis can fully recover the sight of a blind person. However, it is not necessarily a visual prosthesis as we know it that will seal the deal. Alexander Farnum has reviewed several novel technologies that can possibly improve the visual acuity beyond traditional electrode-based prostheses. He demonstrates how optogenetics can be used to increase the resolution by implementing light sensitive proteins into cells in the retina. The cells can then be triggered with light at a certain wavelength to produce phosphenes (Farnum & Pelled, 2020).

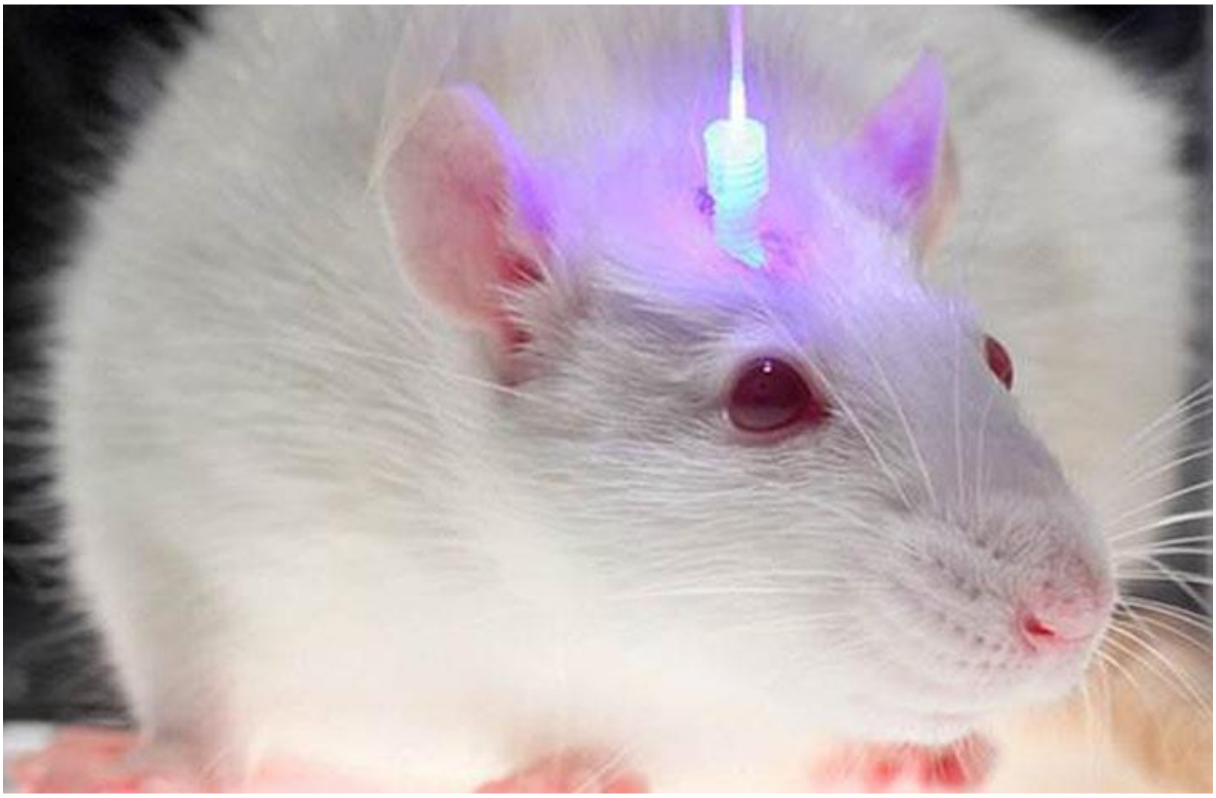


FIGURE 16 AS REPRINTED ON (SCIENTIFICA, N.D): THE IMAGE SHOWS A RAT WITH OPTICAL FIBERS CONNECTED TO NEURONS IN THE BRAIN. (HTTPS://WWW.SCIENTIFICA.UK.COM/LEARNING-ZONE/OPTOGENETICS-SHEDDING-LIGHT-ON-THE-BRAINS-SECRETS)

Magnetic stimulation is another innovative method that could potentially develop a non-invasive visual prosthesis. Non-invasive means that the skin remains intact, and is in many cases safer than invasive procedures, because it eliminates risk of infections. Magnetic stimulation can be utilized by inserting magnetic micro-coils into the brain or exploiting nano particles that has frequently been used in administration of drugs inside the body. Several types of nano particles have shown potential, but there is yet much that needs to be researched in this field, like long term effects. Researchers have also suggested to implement a magnetic gene found in different animals using the earth’s magnetic field for orientation. This technology is called magnetogenetics and the gene was named electromagnetic-perceptive gene (EPG). If scientists are able to discover the molecular structure of the gene it could be possible to implement it in cells and stimulate them with a magnetic field instead of using light or electric impulses (Farnum & Pelled, 2020). These technologies are still science fiction in the context of visual prostheses, but proof of principle has been established. Ethical questions arise in the wake of the potential of these technologies.

Ethical considerations

There are always ethical concerns related to technology, especially in medical research, and the following paragraph contains the writers own reflections. The safety of the patients must be of high priority. For instance, recruiting a patient to a cortical prosthesis is not ethical if the patient’s profile is benefiting from a retinal prosthesis. Another issue is the use of animal models in preclinical trials to verify if it is safe to enter human trials. Mice used in retinal prosthetic experiments are often bred with a genetic error leading to rapid degeneration of the retina. We are evaluating our quality of life over another living creature’s by exposing it to the suffering we so badly want to cure. Animal models are essential in medical and other research, and perhaps it is a necessity. At least the human population seem to think so. We are committing to the practice by accepting treatments in any health-related discipline. A possible counterweight to animal testing is simulation methods since they allow safely testing of the solution on humans. Unfortunately, it is not applicable to all research.

Another ethical problem is the uncertainty of the outcome of the visual prostheses. We can think that the outcome will only be positive, because the person is getting visual perception back! However, that may not be true. Since the restored visual of the person is so limited it may be that the patient misinterprets the physical world. If he wants to take care of his own economy, it may be that he fails to do so by reading the wrong number and pays too much or miss the due date because he read it wrong. Awkward social situation might occur if the patient thinks he sees someone he knows. In worst case he can also hurt himself if he is unable to spot changes in the ground level. Many of the patients that get an implant have been blind for a long time and the newly acquired ability can lead to a change in personality (Slattery, 2017).

Bigger philosophical questions arise when complete restoration is achieved, because that is when we may restore the vision to beyond what the person had before the illness. That is also when we are at the boundary of becoming superhumans. At that point there is no technical issue to implement cameras that can enable sight outside the region of what is presently known as the region of visible light.

Conclusion and remarks

The reader has been taken on a visual journey through the timeline of the development of the visual prostheses. The chapter icons are representing the performance of the current visual prostheses. The images are modified from Chen's illustration of a visual prosthesis principle in Fig.1 (Chen et al., 2009).

Visual prostheses are only to some extent valuable as a therapeutic procedure with the current limitations and challenges. Most of the research in the field of visual prostheses concerns cortical and retinal implants and both approaches have shown promising potential to rehabilitate the blind. Performance of the only currently commercialized prostheses, as well as other upcoming prototypes, are limited. However, other methods such as image processing, stimulation strategies and movement strategies seek to improve their performance. Prototypes of the 2.0 electrode arrays are expected to improve the resolution but are currently only being tested in clinical trials. It is important to have established a standardization for psychophysical tests by then.

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