Engineering 2015, 1(3): 288–291
DOI 10.15302/J-ENG-2015080

Research

Medical Instrumentation—Perspective

Visual Prostheses: Technological and Socioeconomic Challenges

John B. Troy

ABSTRACT Visual prostheses are now entering the clinical marketplace. Such prostheses were originally targeted for patients suffering from blindness through retinitis pigmentosa (RP). However, in late July of this year, for the first time a patient was given a retinal implant in order to treat dry age-related macular degeneration. Retinal implants are suitable solutions for diseases that attack photoreceptors but spare most of the remaining retinal neurons. For eye diseases that result in loss of retinal output, implants that interface with more central structures in the visual system are needed. The standard site for central visual prostheses under development is the visual cortex. This perspective discusses the technical and socioeconomic challenges faced by visual prostheses.

KEYWORDS neuroprostheses, vision, eye disease, restoration of function, rehabilitation

1 Visual prosthesis development

1.1 The beginning

Technology intended to restore vision to blind people dates back to the late 1960s, when G. S. Brindley and W. S. Lewin of the University of Cambridge in the United Kingdom tested a visual cortical prosthesis on a 52-year old female blind patient. Brindley and Lewin sought to create visual sensations in this patient by electrically stimulating that part of the cerebral cortex known to represent visual information in sighted people. At that time, the occipital lobe of the human brain was known to be a center for the higher processing of visual signals, and it was known that electrical stimulation of this part of the visual system could evoke visual sensations called phosphenes; that is, the perception of spots of light, localized within the visual field. It was also known that such phosphenes could be evoked after years of blindness. The results obtained with the first visual prosthesis were so encouraging that Brindley and Lewin predicted in the conclusions section of their paper that improvements to their prototype should "permit blind patients not only to avoid obstacles when walking, but to read print or handwriting, perhaps at speeds comparable with those habitual among sighted people."

1.2 Waxing and waning

The field of visual prostheses has waxed and waned over the decades since this pioneering effort, and its history might thus serve as a case study in how challenging the development of medical technology can be. The failure of Brindley and Lewin to deliver on the bold prediction made in their conclusions section had a dampening effect on enthusiasm for the field, and we should learn from this. A developer of medical technology needs to tread a fine line between promoting a product enthusiastically in order to garner the financial support needed to bring it to market and avoiding the damaging effect of overstating its likely short-term impact. One needs to become adept at defining realistic milestones and, at the same time, portraying the larger significant long-term impact. The investment community is attuned to the course of technological development. The patient population is hungry for therapies and is therefore both more susceptible to accepting overstated claims and less forgiving when the outcomes fall short of expectations. Today, nearly half a century later, the visual capacities that Brindley and Lewin predicted would be soon provided by a visual prosthesis seem distant. Current visual prostheses fall far short of providing the level of visual performance proposed, and many technical challenges, unappreciated by Brindley and Lewin, remain to be addressed.

1.3 Recent developments

We are currently experiencing an upswing in interest in visual prostheses, following some major recent successes. Retinal implants, developed by Second Sight in the US and Retinal Implant AG in Germany, are now available as clinical products. Initially targeted to patients rendered blind through retinitis pigmentosa (RP), in July of 2015, a retinal implant was for the first time given to a patient suffering from dry age-related macular degeneration (AMD): 80-year old Ray

Biomedical Engineering Department, Northwestern University, Evanston, IL 60208-3107, USA
E-mail: j-troy@northwestern.edu
Received 2 August 2015; received in revised form 27 August 2015; accepted 6 September 2015

Flynn, at the Manchester Royal Eye Hospital in the United Kingdom. Both RP and AMD are eye diseases that lead to blindness through the loss of photoreceptors. The incidence of the former disease is significantly lower than AMD and affects a younger group of patients. It made good sense therefore to target patients with RP as the initial recipients for a retinal implant, leaving those with AMD to follow. Certainly, for investors, the potential for a technology to be applied to the population of AMD patients is enticing, since this population is already large and is sure to grow significantly in coming decades as the populations of developed countries age. Indeed, the potential to apply new technologies to AMD patients may be essential. The cost of developing technology to interface with the central nervous system, of which the retina is a displaced part, is immense and unthinkable from a commercial perspective without the prospect of it being of use to a substantial patient population.

2 Retinal and visual cortical prostheses

There are a number of reasons why retinal prostheses have reached the clinic ahead of visual prostheses that interface with the visual cortex or other areas of the visual system. Anyone considered a candidate for a visual prosthesis today must be blind in both eyes and must hope for just partial restoration of monocular vision. Partial restoration can be accomplished with a single retinal implant, while a visual cortical prosthesis would likely require two implants, one for each hemisphere, since the left visual field is represented in the right visual cortex and the right visual field is represented in the left visual cortex. Another advantage of the retinal implant is that the full visual field is exposed across the retinal surface. For the visual cortical prosthesis, a significant fraction of the visual field is not represented on the brain surface but is instead buried in sulci (infoldings of the cerebral cortex), making it more difficult to access for electrical stimulation. A third advantage of the retinal implant follows from the fact that these implants are more resistant to tissue rejection than cortical implants are. Adverse tissue responses are greater when an implant damages blood vessels. The retina has two blood supplies: the choroid and the retinal circulation. Both varieties of retinal prosthesis—the subretinal implant, which is positioned where degenerated photoreceptors once resided, and the epiretinal implant, which is situated adjacent to the retina's inner limiting membrane—make no contact with blood vessels. In contrast, visual cortical prostheses that employ penetrating electrodes invade the rich capillary bed and larger blood vessels that feed the cerebral cortex. Hence cortical implants are more prone to generate a significant adverse tissue response.

A number of the technological challenges that affect visual prostheses are the same as those affecting many other brain implants: for example, how to minimize damage to tissue and electrodes through implantation and electrical stimulation; how to protect electronics from the electrolyte environment of the brain; how to better match the mechanical properties of the implant, which is generally rigid, with the mechanical properties of the brain, which is soft; how to transfer power to and signals to and from the implant; how to ensure that the implant does not interfere with the flow of nutrients to brain cells; how to minimize the heating of tissue during stimulation; and so forth. There are also some challenges that are specific to visual prostheses. Accomplishing Brindley and Lewin's goal of creating a visual prosthesis permitting a patient to read at a speed comparable to a sighted person would require considerably more electrodes than are available in current retinal prostheses. In fact, accomplishing this goal will likely require the development of electrodes made of novel materials, which have yet to obtain regulatory sanction. A number of investigators have studied materials with a superior charge-transfer capacity to standard platinum electrodes and, as electrode-tip size decreases in order to achieve the goal of higher electrode density, one or more of these materials is likely to be essential.

It is with regard to the goal of attaining good reading performance that the advantage shifts from the retinal prosthesis to the visual cortical prosthesis. The fact that the representation of central vision is magnified in the visual cortex relative to peripheral vision means that good acuity is attainable with reasonable electrode spacing. For the retinal implant, the task of stimulating the central retina is daunting. The retinal ganglion cells—the output cells—are packed tightly, stacked and displaced from the fovea. It is hard to imagine how these important drivers of central vision, essential for the detailed viewing of objects and for reading, can be effectively driven with a retinal prosthesis.

Visual cortical prostheses have one other important advantage: They offer a solution to restoring vision to those rendered blind through the loss of retinal ganglion cells—such as would occur in the event of eye loss or with the disease glaucoma, which is the leading cause of incurable blindness in the world and the cause of blindness for Brindley and Lewin's patient. However, technical challenges are perhaps not the major obstacles to the development of visual prostheses. There are many social and economic factors that potentially stand in the way of success and it is prudent to consider them also.

2.1 Economic considerations

The economics of visual prostheses raises concern about the distribution of medical care. It is perhaps too early in the development cycle to put a price on the cost of a visual prosthesis, but one imagines that the same kinds of concern that have been raised for the implementation of cochlear and deep brain stimulation (DBS) implants will apply. Both of these technologies have seen an uneven distribution of application across the world's population, reflecting in a large part the uneven distribution of medical care generally. Europe, North America, and developed Asia and Oceania have been early beneficiaries. Rapidly developing countries like China are also benefiting, often first from donation units with the expectation that a commercial market will follow. Within the developed world, inequity in delivery also exists. In a study of more than 500 000 Medicare beneficiaries with Parkinson's disease in the US, it was found that men were more likely to receive DBS implants than women and that white patients

were more likely to receive them than African-American or Asian patients.

There is also the issue of cost effectiveness. Both the cochlear and DBS implants have been the subject of studies seeking to evaluate the benefit of these treatments in relation to cost. Placing a monetary value on the restoration of vision, hearing, or improved motor performance is obviously not something that will be without disagreement, but it is necessary if we are to evaluate the effectiveness of brain-implant technology. Studies seeking to evaluate the effectiveness of DBS implants for Parkinson's disease have demonstrated improvements in quality of life for patients. Unfortunately, as far as I have been able to tell, no economist has been involved in the assessment of outcomes, so one must question the rigor with which economic value has been determined. Another problem is that there are many measures of quality of life in existence. The World Health Organization (WHO) has WHO Quality of Life-BREF (WHOQOL-BREF), the US Center for Disease Control has Health-Related Quality of Life (HRQOL), and the US HealthyPeople.gov has HRQoL. There are also various measures crafted for specific medical subgroups: ① the Eastern Cooperative Oncology Group's metric, ② the New York Heart Association scale, and ③ the stroke-specific quality of life (SS-QOL) measure. For auditory performance, there is the Glasgow Benefit Inventory. So, in summary, there is no generally accepted measure that could be used to assess how much benefit a visual prosthesis would provide a patient and no economically justifiable means thus far established to assign a monetary value to that benefit, against which the cost of the treatment could be evaluated.

2.2 Societal considerations

Another somewhat surprising challenge affecting medical technology has come from the patient population that the technology is intended to assist. Hearing impaired groups opposed the cochlear implant, fearing that this technology would splinter their community. Hearing impaired people are drawn together because of their disability. Sign language and lip reading are well-developed skills that permit easy communication, bonding, and the formation of a community. If participants of the community are to be removed and introduced to the broader hearing population, it is natural that those fearing abandonment may resist the technology that heralds the change. If a technology is revolutionary, it is disruptive; and this comes at a cost. There will be winners and losers, and it is not always easy to predict who will view themselves in which group.

Within this context, one should also look to resistance from the scientific community. None are better able to articulate the weaknesses of a new technology than those working in that field or in one closely related to it. To many visual neuroscientists, visual prostheses seem naively simplistic. When Brindley and Lewin built their visual cortical prosthesis, it was known that the amount of cortical tissue devoted to representing a region of the central visual field was disproportionately more than the amount of cortical tissue devoted to representing an equal area of the peripheral visual field. At that time, our understanding of the representation of information at the cellular level in the visual cortex had recently been advanced significantly by the work of future Nobel Laureates David Hubel and Torsten Wiesel. This knowledge was not incorporated into the prosthetic design, presumably because at that time it seemed to be unnecessarily detailed. Today, our understanding of how visual information is represented in the cerebral cortex is considerably more complex; it involves many distinct cortical areas, a vast array of distinct cell-types, and many recurrent connections between cortical areas and between cortical and sub-cortical areas. The designers of modern visual cortical prostheses, while producing devices that are more sophisticated than that of Brindley and Lewin, hardly seek to embrace our current knowledge base, and are probably right not to do so. The DBS implant for Parkinson's disease has been successful, in spite of researchers having a poor understanding of how it works, and in spite of it having been developed with minimal application of our understanding of the neural pathways that it affects. However, this approach will garner considerable resistance from members of the neuroscience community, who naturally feel that their discoveries should be embraced and factored into technologies to restore vision. The challenge for technology developers is to explain why much of our current knowledge base is at a level of detail for which current technology has no application. It should also be considered that knowledge evolves. Our understanding today of the visual cortex is richer than it was in the 1960s when Brindley and Lewin developed their visual prosthesis. Although our understanding will be better five years from now, blind patients have a right to expect us to develop technologies now that will improve their lives, even if these technologies are imperfect. The neuroscience of today may help to make vision restoration in 2115 better, but it should not inhibit the development of today's technology.

3 Brain plasticity and visual rehabilitation

Whatever visual prosthesis is developed, it is well understood that rehabilitation training on an individual-patient basis will be necessary in order to maximize its impact. When Brindley and Lewin developed their visual prosthesis, it was widely believed that there was minimal plasticity in adult human brains. However, the passage of time has changed our understanding of the visual cortex and brain plasticity significantly, and plasticity of the adult brain has been well established. Rehabilitation from stroke, for example, is founded on this principle. In retrospect, it is hard to imagine how the capacity for change in the adult brain could have been questioned; for example, while it is harder to learn a foreign language as an adult than as a child, it is possible. However, this disparity for learning between adults and children should not be forgotten when we consider how difficult it may be for recipients of visual prostheses in adulthood to learn how to make sense of the impoverished signals the prostheses provide, in comparison to those provided by an intact and functioning visual system. A number of groups working in the field of visual prostheses have already given considerable thought to training protocols. These are an important compo-

nent of the development of this technology that researchers are apt to overlook.

4 Concluding remarks

In summary, we may finally be at the true dawn of the era of visual prostheses, after a number of false dawns. Many challenges remain that must be addressed in order to ensure that the current situation is not another false dawn. While the engineering community remains focused on addressing the technological problems, we should remain vigilant in ensuring that expectations among the patient population are not raised to an unrealistic level. In addition, it is also essential that developers consider the path to success, which requires thought about the initial patient population to target and the economic benefit that would accrue from the technology. The development of sound outcome measures that would be considered valid by a group of economists would be a useful first step. Also, many have noted that with medical technology it is never too early to consider what steps one must take to obtain regulatory approval. It is a mistake to believe that regulatory agencies like the Food and Drug Administration (FDA) in the US exist to hinder the advance of medical technology. Their role is to serve the population, and this role has two components: to protect the population, and to bring therapies to patients as quickly as possible. Consultation with the FDA or equivalent agencies in other jurisdictions early in the design process would be prudent, as these agencies can advise developers on how best to demonstrate the efficacy and safety of a new technology.

Acknowledgement

This article was made possible by the National Priorities Research Program (NPRP) (NPRP 5-457-2-181) from the Qatar National Research Fund (a member of Qatar Foundation). The statements made herein are solely the responsibility of the author.