Retinal Prosthesis for Degenerative Outer Retinal Disease

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Ventures in Translation features innovators in the field of vitreoretinal disease. Successful translation of scientific ideas to useful medical treatments and technologies requires many elements. Each of the innovators featured here has a story to tell that often combines an exceptional understanding of disease, foresight, perseverance, and an ability to obtain funding for an unrecognized technology. The stories featured here will provide a snapshot of what it has taken to bring these breakthroughs to our patients. The authors will range from scientists to clinicians to bankers to venture capitalists, and some will do a little of all.

In this installment, Mark Humayun, MD, and colleagues from the Doheny Eye Institute in Los Angeles discuss their work in collaboration with Second Sight Medical Products (Sylmar, CA) toward the effort of developing a retinal prosthesis. The first-generation retinal implant showed promising phase 1 clinical results. The second generation, which has been modified based on findings from the first phase, is currently in phase 2 clinical trials.

-Elias Reichel, MD

In the late 1960s, it was shown that electrical stimulation of the retina by means of contact lens electrodes could produce electrically evoked responses associated with phosphenes in normal subjects, as well as in some patients with retinitis pigmentosa (RP).[1] It was not until the early 1990s, however, that the notion of visual restoration with a retinal prosthesis for patients with retinitis pigmentosa and age-related macular degeneration (AMD) became strong enough to instigate serious investigations in this field. Morphometric analyses of postmortem eyes from RP and AMD patients, at this time, demonstrated the partial preservation of inner retinal cells.[2,3] Moreover, direct retinal stimulation in blind subjects suffering from degenerative outer retinal disease resulted in the perception of phosphenes in patients who had a visual acuity of little or no light perception.[4,5]

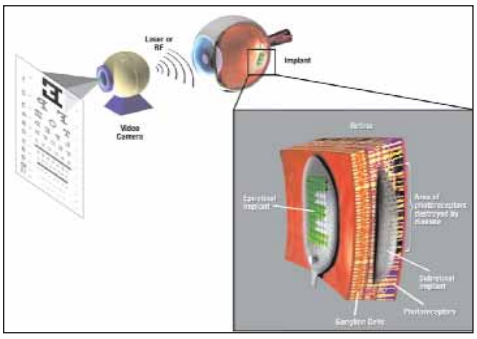
CURRENT EFFORTS

Currently, there are more than 35 centers working on different versions of a retinal prosthesis worldwide. Although the debate as to the target of electrical retinal stimulation continues, there is consensus that simple electrical retinal stimulation can result in perception of visual phenomena. Some laboratories have focused their efforts on the basic science behind electrical retinal stimulation, trying to answer fundamental questions, whereas others have moved more clinically and established collaborations with private companies in hopes of delivering this technology to patients in need.

Several configurations have been proposed for a retinal prosthesis. Common qualities of almost all of them, however, include a light sensitive device for capturing image data, an implanted microelectronic device for converting image data into a stimulus pattern, and a microelectrode array interface for delivering the stimulus current to the retina. Various approaches are being pursued for surgically placing the microelectrode array in relation to the retina, including epiretinal, subretinal, suprachoroidal, intrascleral, episcleral, and penetrating electrodes. The pros and cons of each of these approaches are related to both the efficacy of retinal stimulation and the potential for damage to ocular tissues.

At the Doheny Eye Institute, we have been fortunate to receive funding from the Department of Energy (DOE), National Science Foundation (NSF), National Institutes of Health (NIH), and the W. M. Keck Foundation. Most recently (2003-2008), funding from the DOE for basic science has been almost $6 million, with somewhat less in a comparable period from NSF directed to basic engineering aspects of developing the prosthetic device. Also, our collaborations with Second Sight Medical Products (SSMP, Sylmar, CA) and

several universities and national labs throughout the nation have been extremely helpful. In particular, collaboration with SSMP, led by CEO Robert Greenberg MD, PhD, has been crucial in each step of prosthesis development including design, testing and, most recently, the planning and execution of the clinical trial. SSMP funding has come from sources such as private investment, the NIH, etc. In general, companies are best suited for the rigorous engineering design and manufacturing required for a class III medical device. In addition, industrial partners usually have experienced regulatory affairs department to manage the relationship with the US Food and Drug Administration.



CHRONIC IMPLANTATION OF RETINAL PROSTHESIS DEVICES

In 2002, after obtaining FDA approval, we began chronically implanting a 16-channel microelectronic device (Argus I) made by SSMP in one eye of six blind subjects at the Doheny Eye Institute. In our study, all patients had degenerative outer retinal disease with preoperative vision of light perception or worse and a nonrecordable ERG. The surgery involved standard pars plana vitrectomy, followed by extension of the superotemporal sclerotomy and insertion of a 5x6 mm silicone-platinum electrode array into the eye, which was then tacked onto the retina. The microelectronic implant was placed in a recessed well created in the temporal skull behind the ear. Using a cable, a connection between the microelectronic implant and the electrode array was made through a shallow groove along the temporal skull.

The results of this phase 1 clinical trial were promising, and we learned a great deal. Both threshold and impedance values showed an inverse correlation with the distance of the array from the retina. Across all subjects, the majority of the electrodes had stimulation thresholds below the safe charge injection limit for platinum electrodes.

Tests of spatial vision (eg, maps of the perceived locations of phosphenes, two-point discrimination, and direction of motion discrimination) showed performance significantly above chance, indicating that our subjects can spatially resolve electrodes within the array. We also found that when input is provided via a head-mounted camera, subjects can use head scanning to localize objects and determine the orientation of test patterns.

Of a total of six, five patients have taken the devices home. Some subjects have reported that they find the device useful for certain activities (eg, orientation and mobility), which exceeded our original expectations for the device. We may not be able to fully explain these phenomena for years to come, but their presence may be an indication of the plasticity of the visual pathways and the complexity of the brain.

RECENT IMPLANTATIONS

We now have begun a phase 2 clinical trial by implanting the second generation of the retinal prosthesis, Argus II, in multiple centers in the United States as well as in several centers throughout the world. The Argus II has a 60-channel electrode array, and it is intended to provide higher resolution vision. In addition, the whole device is considerably smaller and can be implanted by a vitreoretinal surgeon without the need for surgical assistance from other disciplines.

In conclusion, restoration of useful vision has been the goal of retinal prosthesis efforts worldwide. Initially viewed as a "moon shot," retinal prosthesis research has made great strides and now is entering the commercial arena. If current clinical trials continue to bear out our initial successes, not only could protheses help restore useful vision to many who are otherwise blind but also possibly herald a new era of bioelectronics in ophthalmology. ■

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