The First Epiretinal Implant for Hereditary Blindness in the Asia-Pacific Region

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Abstract

In February 2013, the Argus® II Retinal Prosthesis System (Second Sight Medical Products, Inc., Sylmar, CA, US) became the first "bionic eye" approved by the FDA to restore useful vision in patients previously blinded by end-stage retinitis pigmentosa, a hereditary, progressive degeneration of the outer retinal photoreceptor cells. The system captures and converts an external optical input into an electrical signal that activates an epiretinal electrode array on the inner surface of the retina. This signal bypasses dysfunctional photoreceptors and directly stimulates the functional inner retina, thus transmitting information to the visual cortex and creating artificial vision. This article describes the first implantation of the Argus II Retinal Prosthesis System in the Asia-Pacific region, which occurred in a deaf and blind 72-year-old Japanese American woman with Usher syndrome. At 57 months after her operation, the patient uses the device daily to perform visual tasks, and the microelectrode array remains in the proper position on the macula. This case demonstrates the long-term safety and efficacy of the Argus II epiretinal implant, which allowed a functionally blind patient to gain meaningful vision.

Keywords

ophthalmology, Argus II, Visual Prosthesis, vision rehabilitation, artificial vision, Usher Syndrome, retinitis pigmentosa, retinal degeneration; low vision

Introduction

Hereditary retinal degenerative diseases result in progressive blindness due to progressive loss of the photoreceptors and retinal pigment epithelial scarring. Until recently, once the photoreceptors were lost, there were not any potential treatments to recover vision. Presently there has been a novel approach to stimulating the retina bypassing the damaged photoreceptors and using microelectrodes. The first artificial vision device approved for retinitis pigmentosa (RP) was the Argus II Retinal Prosthesis System (RPS) (Second Sight Medical Products, Sylmar, CA, USA).[1,2] Often referred to as the "bionic eye," it obtained the CE Mark (approval for use in Europe) in 2011, the US Food and Drug Administration (FDA) approval in 2013, and Health Canada approval in 2014. This device aims to allow potential recovery of visual tasks not possible to completely blind patients with end-stage RP.

RP is a hereditary condition characterized by gradual and progressive death of the photoreceptor cells, ultimately resulting in irreversible blindness. However, the inner retina and optic nerve remain relatively preserved, allowing for potential stimulation of functional ganglion and bipolar cells of the inner retina and transmission through the optic nerve to the visual cortex. Usher syndrome is a disease that presents with a spectrum of vision loss due to RP and varying degrees of hearing loss and vestibular abnormalities. In the literature, substantial clinical heterogeneity has been reported regarding the onset and severity of ocular, hearing, and vestibular function loss.[3–5] Usher syndrome type I is typically characterized by RP with profound deafness and vestibular abnormalities from birth, whereas Usher syndrome type II manifests as congenital RP with severe deafness but normal balance, and type III is characterized by late-onset RP, hearing loss, and deficits in balance. It has been proposed that there may be vestibulo-cochlear and cochlear subtypes of Usher syndrome type I, with or without vestibular abnormalities, respectively.[6]

The Argus II RPS is a sight-restoring analogue to a cochlear implant, which has similarly improved auditory capabilities and quality of life in patients with Usher syndrome.[7] The system is composed of a wearable external unit and a surgically implanted internal unit. Externally, a camera mounted on sunglasses captures real-time images (Figure 1A). A portable computer processes the video input and communicates digitized information to an external transmitting coil at the glasses earpiece. These data are wirelessly transferred from the transmitting coil to a surgically-placed subconjunctival receiving coil and electronics casing that delivers electrical pulses to the 60-channel (6x10) epiretinal microelectrode array (Figure 1B). The microelectrode directly contacts the macula and stimulates viable inner retinal cells, delivering the signal through the optic nerve to the brain where it is perceived as light.

This device has demonstrated improved functioning and quality of life in patients with RP.[8] The combination of deafness and blindness makes the use of the Argus II RPS particularly challenging in patients with Usher syndrome due to communication challenges during rehabilitation. Its long-term safety and efficacy in patients with Usher syndrome has been previously reported only twice in patients with Usher syndrome type II.[9,10] Herein, a 72-year-old woman with Usher syndrome type I and her long-term response to the Argus II RPS 57 months after initial surgery are reported.

Case Report

A 72-year-old Japanese American woman presented with end-stage RP due to Usher syndrome. She was born with complete bilateral deafness and developed adult-onset nyctalopia at 57 years of age. She had no history of vestibular abnormalities. Her presentation was suggestive of Usher Syndrome type I,

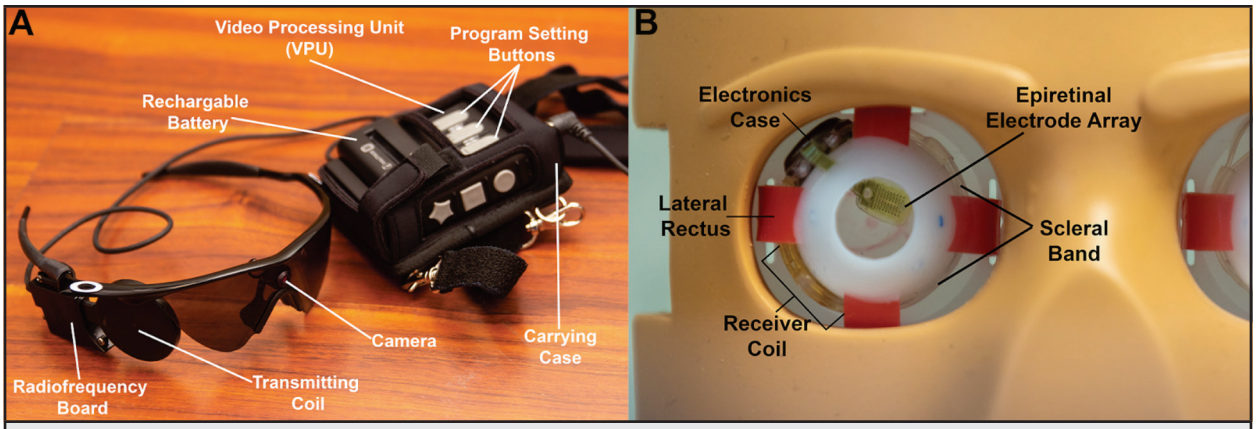

Figure 1. Labeled photograph of the Argus II Retinal Prosthesis System. The external component (A) is composed of a camera mounted on sunglasses and a visual processing unit (VPU). Optical data from the camera are transformed into an electrical signal in the VPU, which is worn on a belt or in a purse. The internal component (B) consists of the receiving coil, electronics casing, scleral band, and the epiretinal microelectrode array. The electrical information from the VPU is transmitted via wireless radiofrequency telemetry to the receiving coil, which is placed under the lateral rectus muscle. The elements of the electronics casing are activated, triggering epiretinal microelectrode activation and retinal nerve fiber layer and ganglion cell stimulation.

although her preserved vestibular function was suggestive of the proposed cochlear subtype.[6] Due to progression of RP, she eventually became functionally blind with no light perception in her right eye and a very minimal ability to sense any light in her left eye. With complete loss of vision, she could no longer communicate through American Sign Language. This required her to converse through tactile sign language, necessitating continuous hand-to-hand contact with a highly skilled interpreter to convey messages. Realistic visual outcomes were discussed with the patient using a professional tactile sign language interpreter who was essential in conveying the device risks and limitations. The patient consented to surgery in the right eye.

Although the Argus II RPS was approved by the FDA in 2013 and in Europe and the Middle East in 2011, there were not any cases of bionic eye surgery throughout the Asia-Pacific region through 2015. The first Argus II surgery in the Asia-Pacific region was performed at the Eye Surgery Center of Hawaii on March 24, 2015. The surgical team included the primary surgeon and author (GK), assistant surgeon, Dr. Troy Tanji, and surgical consultant, Dr. Mark Humayun, who invented the Argus II RPS and was present throughout the surgery. A 360-degree peritomy was performed, and the rectus muscles were isolated. The coil and the sealed electronics case were stabilized on the outside of the eye, the vitrectomy was completed, and the 60-microelectrode implant of the Argus II was positioned over the macula and held in place with a single tack. Pericardial graft material (Innovative Ophthalmic Products, Inc., Costa Mesa, CA) was used to cover the electronics case and coil, and the conjunctiva was carefully closed.[2] Post-operatively, the implant was well positioned over the macula without optic nerve overlap (Figure 2A) and was in close contact with the retinal surface on spectral-domain optical coherence tomography (Figure 2B-2C). The patient recovered well and initiated rehabilitation, which was guided heavily by a tactile sign language interpreter.

Following device programming and fitting, the implant was activated 2 weeks after surgery. The patient immediately reported perceiving "lines of bright lights." She successfully tracked a light source by pointing and walking towards it. She distinguished and identified dark and bright utensils on a table and read large letters from a high-contrast screen. Nine months post-operatively, she followed a pathway of lights on the floor of a dark room with minimal assistance. She was able to distinguish patterns to perform her craft work and locate a person in a room. Rehabilitation continued for 24 months. At 57 months post-implantation, the patient continues to use the device daily to assist her in navigating throughout her house, localizing and sorting light and dark colored items, and identifying fruits on the ground. It remains in excellent position, securely positioned to the retina with a single tack, as noted on ultrawide fundus photography (Figure 3A), and remains in close contact with the retinal surface on spectral-domain optical coherence tomography (Figure 3B-3C).

Discussion

This patient was the first to receive the Argus II RPS in the Asia-Pacific region, including all of Asia, Australia, New Zealand, and the Pacific Islands. She is also the first reported patient with suspected Usher syndrome type I to receive the implant. Given the end-stage nature of her condition, genetic testing was not pursued. Nevertheless, only a few reports of Argus II RPS implantations in patients with Usher syndrome of any subtype are found in the literature. Nadal and Iglesias placed an Argus II RPS into a patient blinded for 20 years by RP due to Usher syndrome type II who demonstrated visual

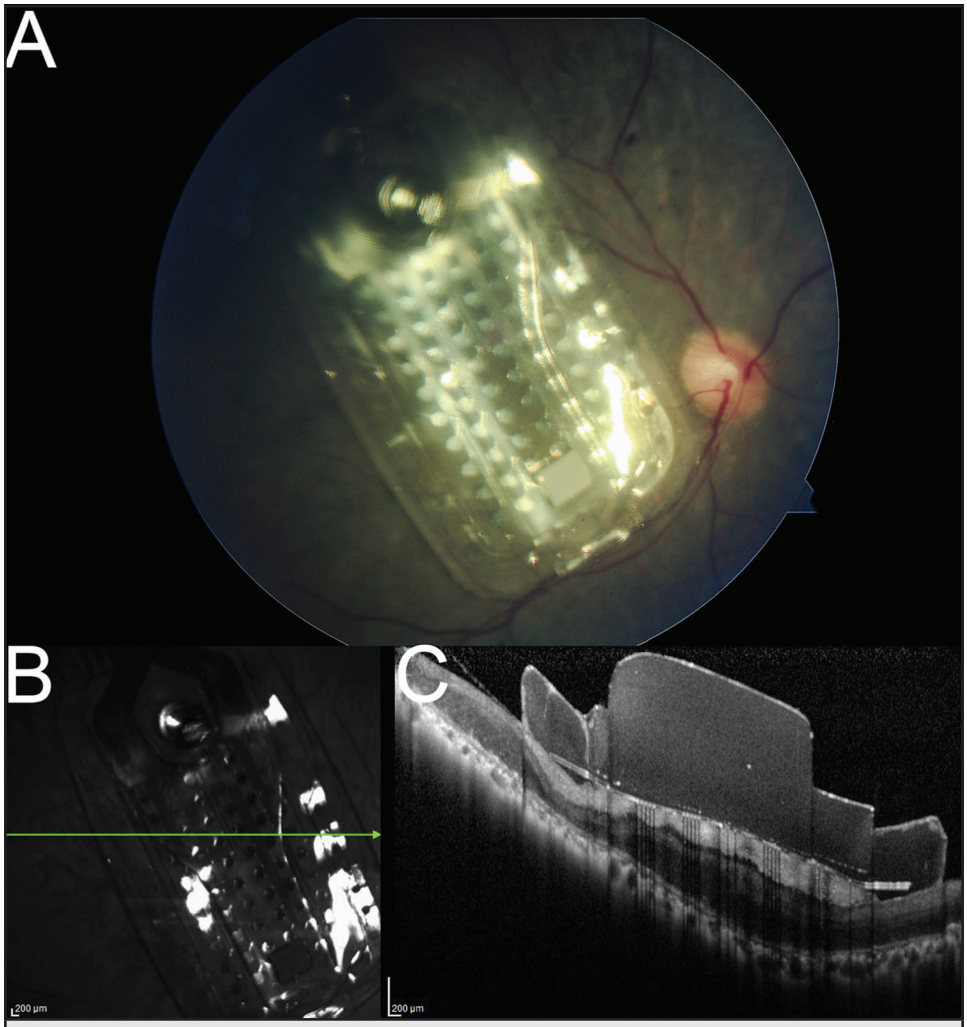

Figure 2. Postoperative images of the Argus II Retinal Prosthesis System in the current patient. Color fundus photograph (A) demonstrates the epiretinal microelectrode array well-positioned over the macula without overlay over the optic nerve head. Photograph (B) shows a green line through the microelectrode array corresponding to the B scan spectral-domain optical coherence tomography (C), which demonstrates stable and close approximation of the microelectrode array to the retinal surface.

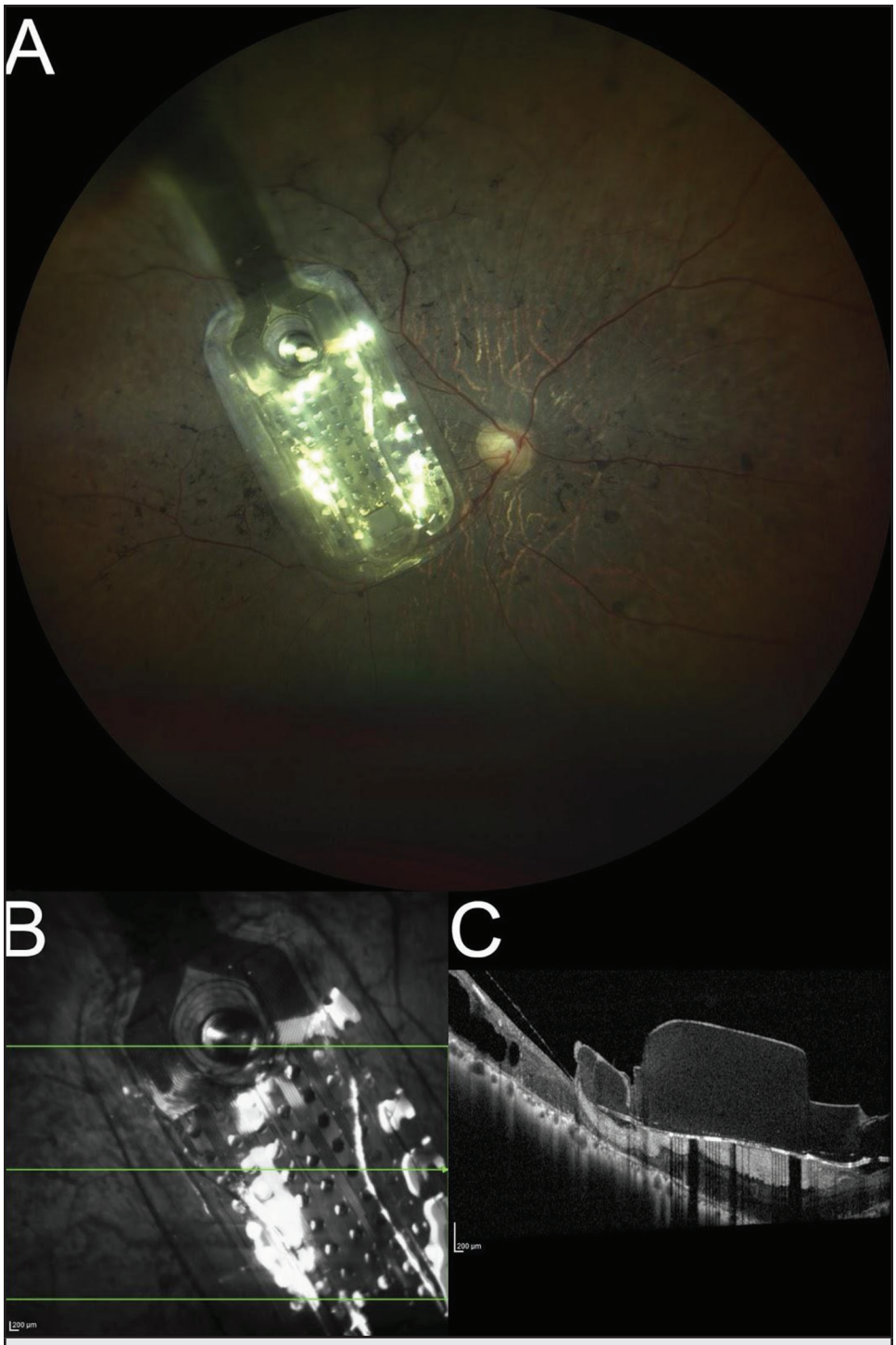

Figure 3. Month 57 postoperative images of the Argus II Retinal Prosthesis System in the current patient. Ultra-wide field fundus photograph (A) shows a stable and well-positioned microelectrode array over the macula without overlay over the optic nerve head using a single tack. Photograph (B) shows a green line through the microelectrode array corresponding to the B scan spectral-domain optical coherence tomography (C), which demonstrates stable and close approximation of the microelectrode array to the retinal surface.

and communicative improvements after device implantation.[9] Demchinsky et al successfully implanted the first Argus II RPS in Russia into a man with Usher syndrome who had bilateral sensorineural hearing loss with some preserved auditory function, although his hearing loss similarly limited rehabilitation methods.[10] However, both studies reported fewer than 16 months of follow-up, whereas the current patient has been monitored over 57 months.

Both of these previous cases, similarly to the current case, emphasized the importance of communication through tactile sign language to accomplish rehabilitation. Tactile signing involves the patient putting his or her hands over the signer's hands to feel the shape, movement, direction, and location of the signs. Initially, the current patient had difficulty understanding how to sweep her entire head from side-to-side when tracking objects and to not gaze straight ahead with her eyes. After a period of guiding the patient's head rotation, the patient understood and was able to identify objects faster and more consistently by using more dynamic motions of her head.

The 5-year safety results of the prospective Argus II RPS clinical trial, which is a similar time frame to the follow-up of the current patient, have been previously reported.[11] Conjunctival erosion or dehiscence was a commonly reported complication that occurred in 23% of cases. Conjunctival dehiscence can occur due to failure of peritomy closure, whereas erosion of the conjunctiva occurs over time with breakdown of the tissue covering the coil or the casing. To minimize this, Tutoplast pericardial tissue was used to cover the elements of the Argus II on the outside of the eye, and there has not been conjunctival erosion or dehiscence in the current patient. The current patient did not experience any of the other serious adverse events reported in the Argus II RPS clinical trial, including hypotony (13.3%), presumed endophthalmitis (10%), need for retack (6.7%), retinal detachment (6.6%), retinal tear, uveitis, keratitis, corneal melt or opacities (3.3% each).[11] Despite being held in place with a single tack, only 2 patients in the study required re-tacking at 5 years. The microelectrode array was also not displaced as evidenced on optical coherence tomography.[12]

Other treatment options for RP are being developed, such as gene therapy. Intravitreal voretigene neparvovec-ryzl (AAV2-hRPE65v2, Spark Therapeutics, Inc. Philadelphia, PA, USA) gene therapy is designed to deliver a normal copy of the *RPE65* gene to the retinal pigment epithelial (RPE) cells that lack a functioning *RPE65* gene. This genetic defect of *RPE65* mutations causes Leber's congenital amaurosis and autosomal recessive RP. Leber's congenital amaurosis is a heterogeneous group of diseases that results in severe vision impairment at a very early age.[13] Furthermore, the Argus II RPS is also being evaluated for people with other retinal conditions, including advanced non-exudative age-related macular degeneration (ClinicalTrials.gov Identifier: NCT02227498). These retinal implants may have potential applications beyond inherited retinal degenerations and may offer sight to a much broader demographic.

The recent expansion of the Argus II RPS into Asia offers a new therapy for patients with RP and other hereditary retinal degenerations. Subsequent to the case in Hawaii, Argus II implantations have been performed in Taiwan[14] and South Korea.[15] The current limitation is cost, as the $150 000 implant is prohibitive for patients and insurance companies.

The limitations of this study is that it only reports on one successful case of ARGUS II implantation and improvement in visual tasks. Larger studies have shown potential complications as noted above. In addition, it reports on an unusual case of implantation in a deaf and blind patient with Usher's syndrome, which may be less generalizable to retinitis pigmentosa patients without hearing loss.

In conclusion, this report documents the long-term efficacy and safety of the first retinal prosthesis in the Asia-Pacific region in a deaf-blind patient with RP due to Usher syndrome type I. The microelectrode array has been stable in position, and there has been no evidence of infection or exposure of the coil or the sealed electronics case. This previously completely blind patient is now able to distinguish dark and light and see people walking into a room. This device shows the potential of using epiretinal implants to stimulate the inner retina to transmit visual images to the optic nerve, even if the outer retina is damaged.

Conflict of Interest

None of the authors identify a conflict of interest.

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