



First implantation of retinal prosthesis in a patient with high myopia after surgery and rehabilitation program in Taiwan

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Abstract: The implantation of the Argus II retinal prosthesis system in a 54-year-old woman with retinitis pigmentosa who presented with an eye of long axial length at 26.82 mm was successful. Postoperative examination revealed a gap of 700 μ m between the electrode array and the retina, which caused decreased visual perception. A modified strategy with quad and quinary electrode stimulation was introduced to generate higher perceptual thresholds. The patient experienced visual functional changes during the first half of the year after surgery, although no remarkable difference was observed in terms of implant–retina distance. Fibrosis around the tack developed and extended between the gap with the retina elevated from the tack toward the center array, 8 months after the surgery. Schisis of the retina developed and filled the gap, resulting in decreased threshold, and the strategy was then shifted back to single electrode stimulation mode. Rehabilitation program is an evolving process that depends on the distance between the array and the retina in the eye with staphyloma. This study first showed the implantation in a patient with high myopia who presented with long axial length after surgery and rehabilitation program in Taiwan.

Keywords: Case Report; Long ocular axial length; Retina prosthesis; Retinitis pigmentosa; Visual rehabilitation

1. INTRODUCTION

Retinitis pigmentosa (RP) is a disease that is characterized by hereditary and progressive degeneration of the eye. The degeneration of the photoreceptor layer of the retina leads to the loss of visual function that starts with night blindness, followed by peripheral and central visual field loss in later life, and finally total blindness.¹

Various treatments for the restoration of visual perception in patients with end-stage RP were developed in the past decades. Among them, retinal prosthesis is considered a promising treatment to date. The Argus II retinal prosthesis system (Second Sight Medical Products, Sylmar, CA, USA) is an epiretinal prosthesis that contains an array of 60 electrodes. The concept of epiretinal prosthesis is to directly stimulate the remaining inner retinal cells that survived, including the bipolar cells, and horizontal and ganglion layers and ultimately induce a visual perception.²

The Argus II retinal prosthesis was successfully implanted in the eyes of hundreds of patients with RP after the approval of the U.S. Food and Drug Administration in 2013 and European

(CE Mark) in 2011. The safety and efficacy of the Argus II retinal prosthesis were reported in various trials in different countries, and data have suggested that such system had a safe profile.^{3–5} In long-term follow-ups, the visual function tests and orientation and mobility tests showed positive outcomes.³

The Argus II retinal prosthesis was designed with a fixed-length cable to connect the epiretinal electrodes with the extraocular portion of the eye. Based on the range of the human ocular axial length (OAL), the recommended parameters of OAL for the implantation of the Argus II retinal prosthesis were between 20.5 and 26.0 mm. A previous study has shown a successful procedure in a patient with a short OAL of 19.95 mm,⁶ which was lesser than what is recommended for Argus II implantation. Herein, we present the successful implantation of the Argus II retinal prosthesis in a patient with a long OAL of 26.82 mm.

2. CASE REPORT

A 54-year-old woman without any systemic diseases was diagnosed with RP at the age of 20 years. She relied on her residual central field for visual perception in daily activities and first used low vision assistive devices when she was in her 30s. Her visual acuity has dropped to only light perception and worsened in both eyes 5 years before this surgery. Comprehensive ophthalmic examinations revealed normal cornea and anterior chamber as well as normal intraocular pressure in both eyes. Bilateral dense cataracts were noted. Based on electroretinogram results, the responses of rods and cones were flat in both eyes. Fundus photograph showed bony spicule and diffuse atrophy of the retina in both eyes (Fig. 1A). The degree of refractive error in both eyes could not be measured due to the presence of cataract. The

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Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

Journal of Chinese Medical Association. (2019) 82: 599–602.

Received February 21, 2019; accepted February 27, 2019.

doi: 10.1097/JCMA.0000000000000091.

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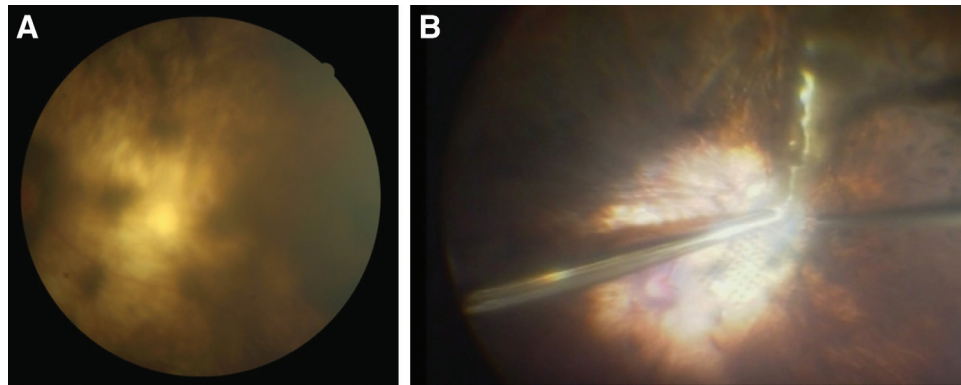


Fig. 1 The fundusoscopic image of the implanted eye before, during, and after surgery. A, Before surgery; B, During surgery.

OAL was 26.82 mm in the left eye and 26.26 mm in the right eye. The left eye was randomly chosen for implantation because both eyes had an ultra-low vision.

She underwent a smooth implant surgery without complication and tolerated the whole procedure well. After removing the cataract with phacoemulsification, conjunctival peritomy was performed, and the extraocular portion of the device was sutured on the exact planned position of the sclera with a 360-silicon buckle. A 23-gauge vitrectomy was performed, and the posterior hyloid membrane was removed completely. The implant coil and electrode were gently positioned and tacked in the superotemporal quadrant of the retina. Minimal wound leakage despite suturing the wound in the sclera was observed probably due to the elongated OAL, and the pulling strength of the relatively insufficient core length was noted during surgery (Fig. 1B). The impedance test performed at the end of the surgery showed that 58 out of 60 electrodes were accurately working with low impedances. The remaining two electrodes were disabled.

The patient's intraocular pressure was 5 to 8 mmHg during the first week of the postoperative follow-up. Optical coherence tomography (OCT) image showed a gap of 700 μm between the center of the electrode array and retinal surface. For customized basic measurements and setting of the device, system customization (fitting) was performed 4 weeks after the surgery. Considering the long OAL and the space between the array and underlying retina, the electrical stimulation mode was modified in terms of quad stimulation (where four adjacent electrodes were grouped in one unit instead of a single electrode) to increase the intensity.

Thresholds for each quad were measured for the amount of electrical current necessary to produce visual percepts. In 11 of 15 quads, a low current amplitude (below 233 μA) could induce a visual perception. For the four remaining quads, the thresholds for visual perception ranged from 250 to 306 μA (Fig. 2).

During the first two rehabilitation training sessions, she learned the skills in keeping her eyes positioned in line with her head. She could also apply micro-scanning strategy to detect the gross shapes of items on a magnetic board. However, in the second month, she complained of decreased visual perceptions when the Argus II system was operating. The OCT image showed that the distance between the electrode array and underneath the retina was similar to that in the first week after surgery, and no structural or device abnormalities were observed. The square localization test, a visual function test that is performed to detect the patient's capability in localizing the target, was applied to compare the differences in visual functions (Fig. 3). The result of the first square localization test, which included a number of corrections and mean error of distance between real target and patient's pointing position, showed no significant improvement after the Argus system was operating (2 compared with 1 in a total number of 40, as shown in Table 1). Therefore, a second array adjustment and threshold examination were performed due to her complaints such as decreased visual perception. Results showed increased threshold for each quad unit; therefore, an adjustment using quinary unit was carried out to increase the stimulation intensity. She had improved light perceptions and was able to localize objects on the magnetic board after the second fitting procedure.

In the fifth month, she complained of progressive deteriorated light perception. The examinations showed increased threshold in each quad electrode compared with the results in the second month after surgery. To generate stronger intensities of current to stimulate the optic nerve, another modification offering two modes (quinary and hexad units) was performed. The patient was asked to compare light perception and comfort of use. After the daily use of Argus II, she reported increased comfort and response when using quinary unit. When using hexad unit stimulation, prolonged residual red-light perception was reported. The second square localization test was arranged using the quinary electrode stimulation, which is a more comfortable mode, to determine whether the modification can lead to improvement in visual perception. Results revealed that the patient could localize a higher number of correct numbers (14 compared with 5 in a total number of 40, as shown in Table 1) with the use of the Argus II system.

After 2 months of quinary and hexad unit stimulations, she reported intolerable brightness in her visual field. We then performed the third array scanning and adjustment and found a remarkably reduced stimulation threshold. Therefore, the stimulation intensity was adjusted to a quad unit stimulation mode.

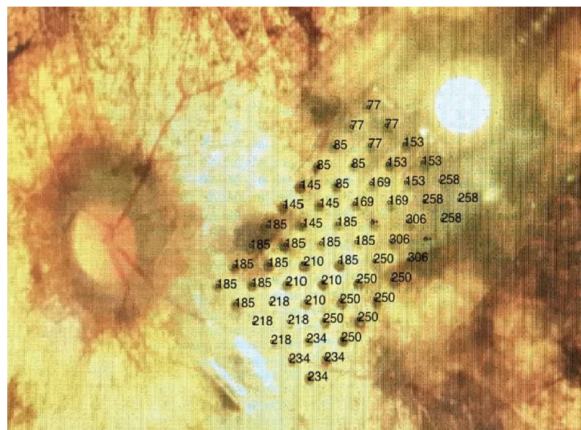


Fig. 2 The threshold of each electrode during the first fitting. The measurement of threshold was tested in quads.

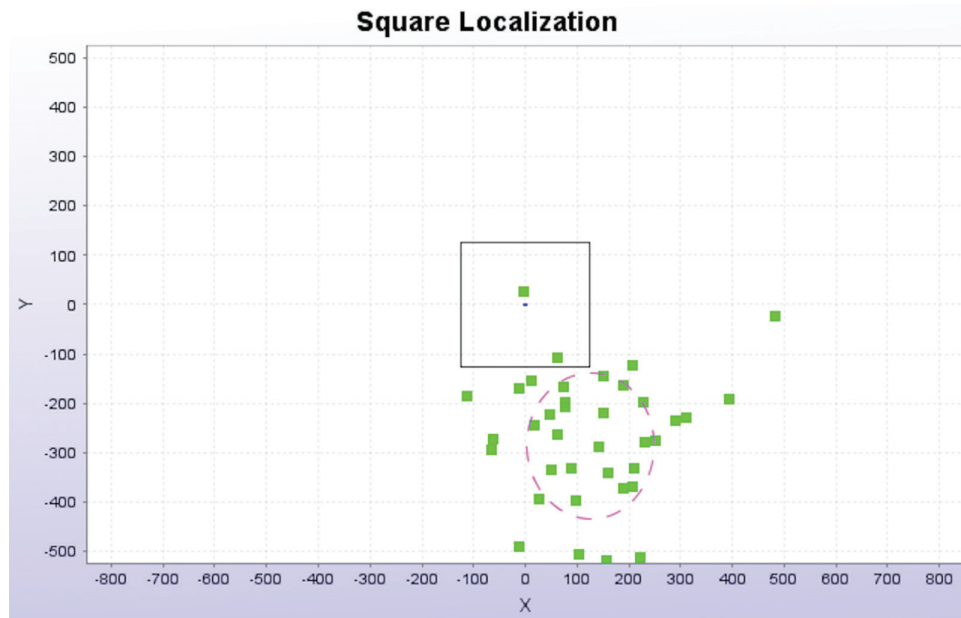


Fig. 3 Result of square localization test to demonstrate the relation between the patient’s pointing (green dot) and actual target zone (square).

Unit of electrode stimulation	First		Second	
	Quad	Quinary	Quad	Quinary
Argus II system	On	Off	On	Off
Number of correction (correction rate)	2/40(5%)	1/40 (2.5%)	14/40 (35%)	5/40 (12.5%)
Mean error of distance between real target and patient’s pointing position, cm	9.98	7.63	6.59	6.92

Since the seventh month, she has been complaining of persistent pink light in the mid-upper visual field region that blocked her visual percepts. The OCT image showed decreased distance between underneath the retina and electrode, which may be attributed to the traction of the peripheral fibrotic tissue. An adjustment was carried out according to the new testing results in the ninth month. Due to the fact that the overall threshold of the electrodes decreased, we changed the stimulation mode to single unit electrode stimulation. She no longer observed the pink light immediately after adjustment and could perceive light in the current setting.

Currently, the patient’s surgical wound completely healed, with an intraocular pressure of 16 mmHg. The patient had significant improvement in visual function. She could localize the light source when performing the mobility training. Her luminance discrimination in a dark room also improved. She reported seeing the shapes of television, cellphones, motor cycles, and furniture. Overall, no significant adverse effect was observed when using the Argus II implant after the surgery and series of adjustments. Furthermore, low vision rehabilitation will be continued.

3. DISCUSSION

In relation to the implantation of the Argus II system, the most common adverse effects after surgical implantation were

conjunctival erosion and hypotony.⁷ One concern regarding the device is the fixed-length cable that connects the intraocular retinal array to the extraocular portion. As mentioned earlier, the recommended OAL is between 20.5 and 26 mm. In our case, the disadvantage of using the Argus II system in the eye with long OAL was the increased distance between the epiretinal electrode array and the inner retinal layer. We aimed to address this special consideration and to discuss the adjustments that may be correlated to long OAL in our case presentation.

Montezuma et al.⁶ have presented the modification of the surgical implantation technique for Argus II retinal prosthesis in a patient with an eye with short OAL. Unlike the implantation in an eye with short OAL with modification that was primarily carried out during the surgical procedure, the main limitation in implantation in an eye with long OAL was correlated to the longer distance between the electrode array and inner retinal layer. A farther distance could attenuate the electric field, as described by Coulomb’s law, and lead to a higher current that induces visual perception. Few data have validated the theory stating that the square of distance between the electrode and retina was inversely associated with the threshold charge in a model using macaque retina.⁸ A significant correlation between perceptual threshold and electrode–retina distance and a weaker but significant inverse correlation between light perceptual threshold and electrical spike stimulation were observed in another study on patients with RP who underwent Argus II implantation.⁹

In the standard protocol, device fitting was performed in each individual electrode to obtain a definite threshold for setting the stimulation parameters. Regarding the long distance between the electrode array and underneath the retina, the device fitting process was modified. Stimulation by quinary electrodes was introduced in our patient to send stronger currents to overcome the attenuation of the electric field. Our results validated that this adjustment was successful and could lead to visual perception to conquer the effect of the long distance between the retina and retinal prosthesis.

Quad/quinary stimulation is not a standard choice for Argus II fitting. In our case, due to the patient’s long OAL, this unusual stimulation mode may be unavoidable, and it ultimately

provided good results in her visual percepts. Moreover, quad/quinary stimulation mode may compromise the resolution because spatial resolution in retinal prosthesis is correlated to the selectivity of activation neurons and electrode density.¹⁰ Theoretically, a lower spatial resolution was expected in quad/quinary electrode stimulation. However, no head-to-head comparison trial that elucidates a more compelling proof has been conducted. Moreover, whether the difference in spatial resolution caused by a single electrode vs quad/quinary electrode stimulation mode is enough to affect the visual function of a patient is not elucidated.

The dynamic change in the electrode–retina gap affected the threshold of the light perception in each electrode; therefore, a corresponding adjustment of the stimulation was performed to achieve an optimal visual function. The series of changes in the electrode–retina gap were discussed recently by Gregori et al.¹¹ in a study that included 33 participants. Approximately, half of the electrodes were completely apposed against the retina. Interestingly, the author has evaluated the correlation between electrode–retina gaps and OAL, which may explain the gap in our patient. However, the result did not support the hypothesis. The longest OAL in the cohort of the study conducted by Gregori et al.¹¹ was 25.9mm, and that of our patient was 26.82mm. Our study has shown that the length of the OAL may not be an absolute factor attributing to the electrode–retina gap, and a complete attachment of the electrodes is possible within months after the surgery.

In this study, Argus II retinal prosthesis implantation was conducted in a patient with long OAL. The modification of device fitting and electrical stimulation in quad/quinary is a useful and beneficial strategy. The patient has gained visual function in recognizing objects. It is worth noting that the change in perceptual thresholds may be dynamic, and a series of follow-up on the function of the electrodes must be conducted to gain an optimal visual function. This study first reported the use of the Argus II implant in Taiwan. Thus, long-term follow-up studies

with a larger number of patients must be conducted to compare the results of using the Argus II implant with the outcome of patients from other ethnic groups.

REFERENCES

1. Hartong DT, Berson EL, Dryja TP. Retinitis pigmentosa. *Lancet* 2006;368:1795–809.
2. Humayun MS, Dorn JD, Ahuja AK, Caspi A, Filley E, Dagnelie G, et al. Preliminary 6 month results from the Argus II epiretinal prosthesis feasibility study. *Conf Proc IEEE Eng Med Biol Soc* 2009;2009:4566–8.
3. da Cruz L, Dorn JD, Humayun MS, Dagnelie G, Handa J, Barale PO, et al. Five-year safety and performance results from the Argus II retinal prosthesis system clinical trial. *Ophthalmology* 2016;123:2248–54.
4. Rizzo S, Belting C, Cinelli L, Allegrini L, Genovesi-Ebert F, Barca F, et al. The Argus II retinal prosthesis: 12-month outcomes from a single-study center. *Am J Ophthalmol* 2014;157:1282–90.
5. Farvardin M, Afarid M, Attarzadeh A, Johari MK, Mehryar M, Nowroozzadeh MH, et al. The Argus-II retinal prosthesis implantation; from the global to local successful experience. *Front Neurosci* 2018;12:584.
6. Montezuma SR, Tang PH, van Kuijk FJ, Drayna P, Koozekanani DD. Implantation of the Argus II retinal prosthesis in an eye with short axial length. *Ophthalmic Surg Lasers Imaging Retina* 2016;47:369–71.
7. Ghodasra DH, Chen A, Arevalo JF, Birch DG, Branham K, Coley B, et al. Worldwide Argus II implantation: recommendations to optimize patient outcomes. *BMC Ophthalmol* 2016;16:52.
8. Sekirnjak C, Hottoway P, Sher A, Dabrowski W, Litke AM, Chichilnisky EJ. High-resolution electrical stimulation of primate retina for epiretinal implant design. *J Neurosci* 2008;28:4446–56.
9. Ahuja AK, Yeoh J, Dorn JD, Caspi A, Wuyyuru V, McMahon MJ, et al. Factors affecting perceptual threshold in Argus II retinal prosthesis subjects. *Transl Vis Sci Technol* 2013;2:1.
10. Fried SI, Hsueh HA, Werblin FS. A method for generating precise temporal patterns of retinal spiking using prosthetic stimulation. *J Neurophysiol* 2006;95:970–8.
11. Gregori NZ, Callaway NF, Hoepfner C, Yuan A, Rachitskaya A, Feuer W, et al. Retinal anatomy and electrode array position in retinitis pigmentosa patients after Argus II implantation: an international study. *Am J Ophthalmol* 2018;193:87–99.