

A New Treatment Pathway for Retinitis Pigmentosa

An artificial vision prosthesis has been commercially available in Europe since 2011.

BY STANISLAO RIZZO, MD

Retinal diseases can affect different layers of the retinal tissue. A retinal prosthesis that is commercially available in Europe has recently offered a treatment pathway for retinitis pigmentosa (RP) and other diseases of the outer retinal layers—the retinal pigment epithelium (RPE) and photoreceptors—for which few if any therapeutic options previously existed.

There are an estimated 1.2 million people worldwide with RP, including 100 000 in the United States. Numerous strategies to treat RP have been investigated, including intravitreal injection of growth factors, genetic therapy, vitamin A supplementation, surgical transplantation of the neural retina and RPE, ozone therapy, and electrical stimulation. Unfortunately, none of these have been effective.

An artificial visual prosthesis has for many years been a hope of ophthalmology, and numerous approaches have been tried, including epiretinal and subretinal prostheses, an optic nerve prosthesis, and a cortical prosthesis. The visual pathway can be stimulated at various levels, whether in the eye, the optic nerve, or the brain. Numerous centers continue to investigate multiple potential approaches to artificial vision, but only 1 group has successfully commercialized a product in this category to date. That product is the Argus II Retinal Prosthesis System (Second Sight Medical Products Inc.), originally developed by Mark Humayun, MD, PhD, and colleagues at the Doheny Eye Center of the University of Southern California.

The Argus II system consists of a surgically implanted, 200- μ m diameter, 60-electrode stimulating microelectrode



Figure 1. The Argus II system consists of a surgically implanted, 200- μ m diameter, 60-electrode stimulating microelectrode array and an inductive coil link used to transmit power and data to the internal portion of the implant.



Figure 2. A miniature camera mounted on a pair of glasses is connected to an external video processing unit worn on the subject's belt.



Figure 3. The implant is ready to use.



Figure 4. The electrode array and cable are implanted using a pars plana approach, and the electrode array is positioned epiretinally on the macula.

array and an inductive coil link used to transmit power and data to the internal portion of the implant (Figures 1 and 2). A miniature camera mounted on a pair of glasses is connected to an external video processing unit worn on the subject's belt (Figure 3). Image data from the external camera is transmitted wirelessly to the implant, which stimulates electrodes in an array on the retina to produce vision.

The array, in which each electrode is individually programmable, uses electrical stimulation to bypass defective photoreceptors and stimulate the remaining viable retinal cells. The dimensions of the array are equivalent to a visual field of approximately 20°. Because the camera is external to the eye, the implant is not affected by media opacities. In the surgical implantation procedure, the electronic stimulator and antenna are sutured to the sclera with an encircling silicone band. The electrode array and cable are then implanted using a pars plana approach, and the electrode array is positioned epiretinally on the macula (Figure 4). No silicone oil tamponade, large choroidal incision, or hypotensive anesthesia is needed.

Patients indicated for the Argus II are adults with severe to profound outer retinal degeneration, residual light per-

ception, and a previous history of useful vision. The principal contraindications are ocular diseases or conditions that could prevent the Argus II System from working, such as optic nerve diseases. The potential patient population for this type of retinal prosthesis must have an intact optic nerve and inner retina in order for the device to function.

MULTICENTER TRIAL

To assess the safety and effectiveness of the Argus II system, an international prospective, multicenter, single-arm nonrandomized study was conducted at centers in North America and Europe (<http://clinicaltrials.gov/show/NCT00407602>). The 6-month results of this study, with a planned 3-year follow-up, were published last year.¹

The indicated population at all centers included patients with a confirmed history of RP with remaining visual acuity of bare light perception or worse in both eyes.

The study enrolled 30 patients between June 2007 and August 2009. Mean age at enrollment was 58 (range, 28–77) years. Follow-up at the time of the published report ranged from 6 months to 2.7 years. Almost all patients had advanced RP (97%; n=29) and visual acuity of bare light perception (defined as 2.9 logMAR or worse with the ability to detect a photographic flash; 97%; n=29). One patient had choroideremia and 1 had no light perception.

Median surgery time in the study was 4 hours. The cumulative implant time for all 30 subjects was more than 105 (average 3.6 ± 1.0 , range 2.6–4.9) years. Only 1 device has been explanted, 14 months after implantation, due to recurrent conjunctival erosion. There was a communication failure with 1 device, which remains implanted.

Adverse events were typically categorized as serious if they required treatment by a surgical intervention or procedure (eg, intravitreal injection of antibiotics). In 70% of patients, no serious adverse event (SAE) occurred. Endophthalmitis was seen in 3 cases, all at the same center. The most common SAE reported was conjunctival erosion or dehiscence over the extraocular implant, and this was successfully treated in all but 1 patient, who required explantation.

Table 1 illustrates that device- or surgery-related SAEs decreased with greater experience, with no endophthalmitis and no conjunctival erosion in the latter half of the total patient cohort.

Visual performance, from bare light perception to a quantifiable visual acuity below the ETDRS chart, was assessed with the system turned on or off using a series of tests: light detection, object localization, motion discrimination, discrimination of grating orientation, and Landolt C.

Subjects performed statistically better with the system on than off in object localization (96% of subjects), motion

TABLE 1. DEVICE- OR SURGERY-RELATED SERIOUS ADVERSE EVENTS

Complication	Argus II All Subjects (n=30)	Argus II Later Enrollees (n=15)
Conjunctival erosion	6.7%	0%
Endophthalmitis	10.0%	0%
Hypotony	10.0%	6.7%
Iatrogenic retinal tear/detachment	10.0%	5.7%
Wound dehiscence	10.0%	6.7%
Dislodged tack	6.7%	6.7%

discrimination (57%), and discrimination of the orientation of gratings (visual acuity improved by more than 3 lines; 27%). The best recorded visual acuity to date is 20/1260. Subjects' mean performance on orientation and mobility tasks (identifying a door, following a line) was significantly better when the system was on vs off.

A quality-of-life questionnaire was administered by independent, certified, trained low-vision rehabilitation experts.² The Functional Low-Vision Observer-Rated Assessment (FLORA) was developed specifically for patients with low vision in collaboration with experienced low-vision rehabilitation experts and the US Food and Drug Administration. This 3-part assessment included an in-depth interview with the subject, performance of observer-rated tasks in and around the subject's home, and a written case-study narrative. The assessments took approximately 3 to 4 hours to complete and were scored by independent review.

In these assessments, 77% of patients (n=26) reported a broadly positive impact on their quality of life.

In our hospital in Pisa we implanted 8 Argus II implants. With experience, the surgery time decreased from an initial duration of 3 hours, 40 minutes, to a final 2 hours, 40 minutes for our last patient. There were no major complications in our series. One postoperative intraocular pressure spike of 40 mm Hg was resolved with medical therapy, and 1 shallow choroidal detachment resolved spontaneously in 1 week.²

In a recent further investigation, the potential for color vision perception was assessed using 2 experiments.

The first experiment examined whether subjects with the Argus II system (n=14) could consistently perceive colors. Different groups of electrodes were stimulated with cathodic-anodic pulses with different parameters, and subjects reported the color they perceived after each stimulation. In this evaluation, subjects reported perceiving 9 different colors.

The second experiment examined whether Argus II subjects (n=4) could consistently perceive 2 different colors simultaneously with the system. Pairs of electrodes were

stimulated with different parameters, and subjects reported the color or colors they perceived. In this experiment, subjects reported perceiving 7 different color combinations.

CONCLUSIONS

The Argus II Retinal Prosthesis System is the only treatment for RP currently available. The manufacturer, Second Sight, has received regulatory approval to sell the device in Europe, and commercial implants in Europe began October 2011. Application for FDA marketing approval has been submitted and is under review with more than 2 years of follow-up on all 30 subjects. An advisory panel to the FDA last year recommended approval of the device.³

Clinical results with this system to date demonstrate that the Argus II can reliably withstand long-term implant (greater than 4 years) with an acceptable safety profile. Using the system, blind subjects are able to detect light and improve performance on visual tasks including orientation and mobility. These results are sustained over time.

In addition, subjects report that they use the Argus II in their daily lives and the system has had a positive impact on their well-being. In the course of day-to-day living, this positive effect on quality of life is potentially much more important than purely functional results. ■

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