Retinitis pigmentosa (RP) is an inherited disorder affecting an estimated one in 4,000 people worldwide. Symptoms, such as difficulty seeing in dim light, can appear in childhood. Although some individuals retain central vision with restricted visual field past their 50s, many people with RP may progress to lose considerable amounts of sight.

RP is a group of conditions caused by mutations in the genes responsible for making proteins that are needed in cells (predominantly photoreceptors) in the retina. The mutations can cause the genes to stop making these proteins, to produce abnormal proteins, or to produce proteins that are toxic to the cell, resulting in damage or loss of function to the photoreceptors. With nonfunctioning photoreceptors, the visual system is disrupted and cannot transform light into images.

There are no proven treatments for patients with RP, but artificial vision devices such as the Argus II Retinal Prosthesis System (Second Sight Medical Products) are offering hope for those affected by the disorder. This article briefly describes the Argus II and provides highlights from a recently published 5-year dataset from the international multicenter regulatory clinical study using the device.

THE NUTS AND BOLTS

The Argus II is indicated for use in patients with profound vision loss from RP. It functions by bypassing damaged photoreceptors to provide electrical stimulation directly to the remaining functioning inner retina. This is achieved via an epiretinal electrode array that is surgically implanted in the eye (Figure 1).

When the device is turned on, images of the surroundings are captured by a tiny video camera housed in a pair of glasses. This video information is sent via cable to a small video processing unit worn by the patient, which in turn creates a pixelated brightness map in real-time of the scene that is being viewed (Figure 2). The brightness map is transmitted wirelessly to a hermetically sealed receiver and computer chip attached to the back surface of the eye (Figure 3), which decodes it into a series of graded currents. The currents travel to the epiretinal electrode array, which emits small pulses of electricity that bypass the damaged photoreceptors and directly stimulate the remaining inner retinal cells. The optic nerve transmits this visual information to the brain, and the patient experiences the perception of discrete light patterns.

With practice and training, patients learn to interpret the light perceptions as useful visual information and to integrate the grayscale images with additional sensory perception, such as sound and touch.

AT A GLANCE

- Genetic mutations that lead to loss of photoreceptors in RP can disrupt the visual system and cause diminished vision and blindness.
- The Argus II Retinal Prosthesis System bypasses dysfunctional photoreceptors to provide electrical stimulation directly to the residual inner retina via an epiretinal electrode array that is surgically implanted in the eye.
- At least 5 years after implantation in a cohort of 30 patients from the Argus II regulatory trial, patients’ visual function and functional vision were better when using the Argus II system than with their residual vision when the device was turned off.
THE SURGICAL TECHNIQUE

Implantation of the Argus II requires meticulous surgical technique. To implant the device, a 360° limbal conjunctival peritomy is first performed. The rectus muscles are isolated, and the induction coil, which provides the power for the device, is inserted temporally on the globe, passing under the lateral rectus muscle and centered in the inferotemporal quadrant. The hermetically sealed electronics package is then fixed in the superotemporal quadrant via associated suture tabs. The encircling scleral band that is attached to the coil and electronic package is passed under the remaining rectus muscles, linked together with a Watzke sleeve and secured with mattress sutures or scleral tunneling.

Core and peripheral vitrectomies are then performed using standard 23-gauge, three-port technique. A temporal sclerotomy is made at a set distance from the limbus to allow the cables to be passed into the eye and to fall smoothly onto the retina. The electrode array is tacked directly onto the central macula using a spring-loaded retinal tack. The extracocular portion of the cable is sutured to the sclera, and all sclerotomies are closed. An allograft, or a suitable alternative in countries where allografts are not permitted, is fixed over the device to reduce the likelihood of conjunctival erosion, and then the Tenon capsule and conjunctiva are closed.

There is limited ability to reenter the eye and perform maintenance on the Argus II, so it is critical that the surgical placement and closure be optimal. The 5-year results from the Argus II clinical trial are now available, and they demonstrate not only that surgeons can successfully complete the delicate surgery, but also that the device is stable and safe, with the majority of implants still functioning 5 years after initial implantation.

STUDY DESIGN

The clinical trial was a prospective, single-arm, nonrandomized study. Because of the rarity of RP, a sample size of 30 patients was deemed sufficient for an analysis of safety and efficacy. Patients received one Argus II implant, typically in their worse-seeing eye. The primary endpoint for efficacy was visual function as measured by three objective assessments performed with the device turned on and again with it turned off. Square localization measured the ability to locate and touch a high-contrast white square of light on a black background on a touchscreen monitor. Direction of motion assessed patients’ ability to determine and indicate the direction of a high-contrast bar that moved across the monitor. Grating visual acuity measured patients’ visual acuity using square-wave gratings of different spatial frequencies presented on a computer monitor.

Secondary endpoints included the door task, a real-world
assessments in which patients attempted to walk to and touch a large piece of contrasting felt in the shape of a door; the line task, in which patients followed a white line painted on black tiles; and several questionnaires and assessments designed to measure changes in functional vision and assess quality of life.

**STUDY RESULTS**

More than 200 patient-years of data on the 30 original patients implanted with the Argus II Retinal Prosthesis System demonstrate that this therapy is a safe option for patients with RP that may allow stable and reliable restoration of some basic visual function.

The longest implant duration to date is 8.4 years. This device and 23 others continue to function. The device stability remains good, with two device failures, both of which remain safely implanted but nonfunctional, and three explanted devices from among 30 implanted patients. Of the three explantations, one was carried out to resolve recurrent conjunctival erosion and chronic hypotony. The other two explantations were elected by the patients to avoid further surgeries to address recurrent serious adverse events (SAEs). One patient died during the trial due to causes unrelated to the device or the trial. No eyes were lost and no residual vision was damaged in the study; however, one should remember that the trial patients had no light perception or bare light perception at implantation. Although there were no catastrophic events involving these eyes, there were a series of SAEs reported in the trial over the 5 years. It goes without saying that any chronic implant in the eye carries a risk of long-term SAEs.

Five years after implantation, visual function and functional vision, for patients as a group and individually, were better using the Argus II system as compared with their residual vision with the device turned off (Table). Only one new SAE (a rhegmatogenous retinal detachment) occurred between 3 and 5 years after device implantation, and it was treated successfully and resolved. This was reassuring to the investigators, as it showed that the onset of new SAEs was decreasing with time and that, overall, the device remained safe in the long term. The results of the assessment tests at 3 and 5 years are shown in the Table. Improvement was measured against residual vision.

**LOOKING AHEAD**

The outcomes of the functional tests and safety profile of the Argus II based on earlier results from this clinical trial led to its regulatory approval in the European Union, the United States, and Canada. In many countries, the Argus II is the only available treatment for profound vision loss resulting from RP and outer retinal dystrophy. Year-5 data reinforces the findings of long-term efficacy and safety of this device. The original study patients will continue to be followed and monitored to see what, if any, long-term effect there is on the stimulated nerves and how the device interacts with the human body.

New patients continue to be implanted with the Argus II, and more than 150 patients worldwide are using the retinal prosthesis system. Patient-driven data will serve as a critical resource to help scientists understand how the device is used by patients. This knowledge will serve to drive further development and improve upon its limitations.


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- financial disclosure: Second Sight provides institutional funding to Moorfields Eye Hospital for the trial of the Argus II retinal prosthesis system; however, the author has no financial interest in the sale of the device.
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