The Toronto experience with the Argus II retinal prosthesis: new technology, new hope for patients

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ABSTRACT • RÉSUMÉ

Surgical restoration of vision with retinal prostheses is a new and developing technology currently available in a select group of countries, Canada among them. The Argus II retinal prosthesis is the first commercially available device for restoration of vision in patients with Retinitis Pigmentosa or with similar retinal pathology who still have minimal residual native vision. The surgery is complex and requires training however it is within the abilities of any experienced retina surgeon. Surgical experience builds up with each case and in our patients length of surgery constantly went down. Complications occurred however we experienced no catastrophic events. Most notable is that in our implanted cases the Argus II technology proved to be beneficial to most patients. In order to obtain optimal results with this surgical intervention it is absolutely required that the surgical work is complemented simultaneously with the work of a specialized rehabilitation team. A review of the technology, of our experience, comments and concerns is presented in this paper.

Le rétablissement chirurgical de la vision à l'aide de prothèses rétiniennes est une nouvelle technologie en développement dans un petit nombre de pays, dont le Canada. La prothèse rétinienne Argus II est le premier dispositif commercial qui permette de restaurer une certaine vision chez les patients atteints de rétinite pigmentaire ou d'autres affections rétiniennes et qui disposent d'un minimum de vision résiduelle. L'intervention est complexe et demande de la formation, mais demeure à la portée de tout chirurgien rétinologue d'expérience. La dextérité chirurgicale s'accroît avec l'expérience et, chez nos patients, la durée de l'intervention a systématiquement diminué. Il s'est produit des complications, mais aucun incident catastrophique n'a été déploré. Fait le plus notable, la technologie de l'Argus II s'est révélée bénéfique chez la plupart de nos patients qui ont reçu l'implant. Pour s'assurer d'obtenir des résultats optimaux, il est vital que le travail du chirurgien soit épaulé par celui d'une équipe de réadaptation spécialisée.

INTRODUCTION

Restoring useful, functional vision to patients with previously untreatable retinal diseases is a dream that is becoming a reality. Although in its infancy, the use of retinal prostheses to treat patients blinded by outer retinal degenerations is being performed in specialized centres. At the University Health Network Toronto Western Hospital, we were the first team in Canada to implant the Argus II retinal prosthesis (Second Sight Medical Products, Sylmar, Calif.) in patients with outer retinal degenerations. Our first patient was treated over the summer of 2014 as part of an observational study. Health Canada officially approved the device for regular use in December 2014. Since then, 11 patients have been implanted with the Argus II retinal implant at our centre. We want to share our experience with, concerns about, and comments on this new technology for this specific group of patients with minimal residual native vision.

METHODS

This is a retrospective review of cases. We followed a treatment protocol approved by the University Health Network Ethics Board. The Argus II device is an epiretinal prosthesis designed to electrically stimulate the visual system by bypassing the absent outer retina. Its goal is to provide restoration of functional vision in patients with outer retinal degenerations.[1]

The device and its works

The Argus II system[2] consists of 2 components. The first is a spectacle-mounted camera connected to a video processor and battery unit worn on a belt (Fig. 1). The second is an ocular component consisting of a receiving/transmitting coil, electronics case, and a 60-electrode implantable array (Fig. 2). The array is placed in an epiretinal location and is secured to the retina using a retinal tack (Fig. 3).The array is connected to the electronics housing via a ribbon cable inserted through a 5 mm pars plana incision. The electronics housing is secured to the sclera and is flanked by a receiving coil that sits on a band implanted under the rectus muscles like a scleral buckle (Fig. 4). Before closing the conjunctiva, a patch of donor pericardium is used to cover the electronics to reduce the risk of exposure and extrusion.

Vision in a healthy patient is achieved when light is refracted and focused on the retina so that photoreceptors can be stimulated. In normal cases, through photochemical

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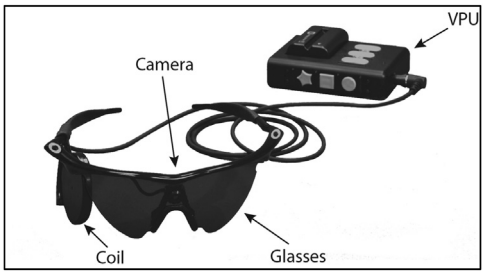

Fig. 1—Argus II system component 1: spectacle mounted camera connected to a video processor and battery unit worn on a belt.

transduction, a signal is sent from the photoreceptors through the bipolar cells to the ganglion cells, whose axons form the nerve fibre layer that become the optic nerve and synapse in the lateral geniculate body in the brain. In patients with outer retinal degenerations, the photoreceptors do not function or do not exist, but connections throughout the ganglion cells remain relatively intact. The Argus II retinal prosthesis bypasses the absent photoreceptors and hooks into the functioning downstream cells required for vision processing.

With the Argus II retinal prosthesis, the head-worn camera captures an image that is sent to the video processor worn on a belt clip. The processor converts the image into a pixelated artificial image that is transmitted to the glasses system where, in turn, it is wirelessly transmitted to the receiver coil on the bulbar encircling band. The signal is sent through the electronics housing and down the transmitting coil to the epiretinal electrode array sitting on the retina. The electrodes on the array stimulate the ganglion cells with which they are in contact, and impulses perceived are sent via the visual pathway to the brain. The patient perceives an artificial vision image, which needs interpretation by the visual cortex.

The surgery

The surgical implantation of the Argus II device involves many steps, most of which are familiar to experienced retinal surgeons. Unique aspects involve the use of retinal tacks, the use of donor pericardium and the creation of a large sclerotomy. In the interim clinical trial (clinicalTrials.gov NCT00407602), the median surgical time was 4 hours and 4 minutes (range, 1 hour 53 minutes to 8 hours 32 minutes).[3] We have found that the procedure takes 1.25–2 hours (median surgical time 1.5 hours, 10 cases). The surgical team consists of the surgeon, an assistant, nursing staff, an anesthetist, and engineers who test the device in the operating room just before the conclusion of the surgery.

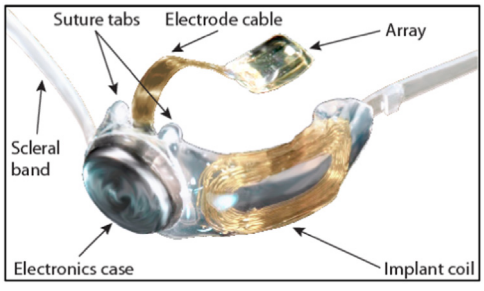

Fig. 2—Argus II system component 2: ocular component consisting of a receiving/transmitting coil, electronics case, and a 60-electrode implantable array.

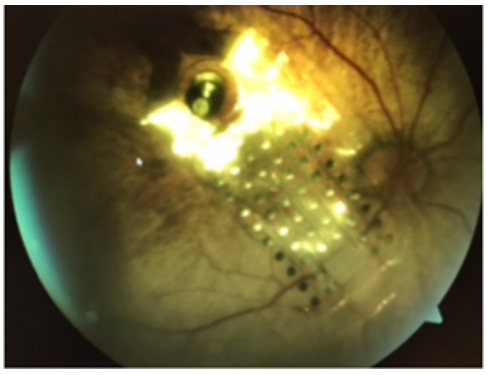

Fig. 3—Argus II. The implantable array is placed in an epiretinal location and is secured to the retina using a retinal tack.

All procedures were performed under general anesthesia. Usually, the patient is given a preoperative dose of intravenous dexamethasone and cefazolin. After anesthesia and sterile prepping and draping, the surgeon begins as if starting a scleral buckle by performing a 360-degree conjunctival peritomy and isolating the rectus muscles with 2-0 silk sutures. The receiver coil is centered underneath the lateral rectus muscle, and the electronics package is placed in the superotemporal quadrant and secured with sutures, similar to placing a glaucoma valve. The encircling band is then placed under the remaining recti and secured with a standard Watzke sleeve in the superior-nasal quadrant. If the patient is phakic, the lens is removed. Core and peripheral vitrectomy is performed, and any epiretinal membranes are peeled if needed. A 5 mm pars plana incision is made in the superior-temporal quadrant with a microvitreoretinal blade. The precise location of this incision is calculated based on the individual anatomy and axial length of the eye. The sclerotomy is placed such that

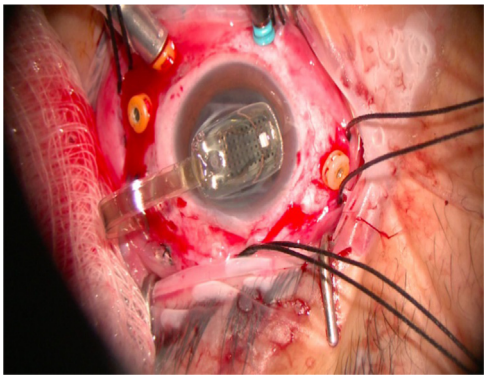

Fig. 4—Implantable array before intraocular implantation.

the implanted array lies precisely over the macula, with no twisting or tension on the ribbon cable.

The array, which is connected to the electronics box by the ribbon-cable, is introduced into the vitreous cavity through the incision. It is tacked down to the retina using a retinal tack, which is essentially a sharp miniature tack introduced through the array, retina, choroid, and sclera. The impedance of each electrode of the implanted array is then tested by an engineering team present in the operating room while the surgical team stands by. After confirmation that most electrodes on the implant are technically working, the electronics package is covered by pericardium to prevent conjunctival erosion. The eye is closed, and the surgical procedure is concluded. The surgical team evaluates the patient on postoperative day 1, week 1, and months 1, 3, 6, 9, and 12. Visits include full eye examinations, optical coherence tomography to verify implant location, and fundus photographs. In our protocol, the visual rehabilitation process begins on postoperative day 10.

Visual function assessment

About 3 weeks after surgery, visual functional assessment takes place in our clinic. In our practice, we used the following 3 high-contrast, objective, computer-based outcome measures developed by SecondSight[2]: square localization (SL), moving grating visual acuity (MGVA), and grating visual acuity (GVA). Visual function tests were performed at baseline, 3 months, 6 months, and 1 year. SL measures the ability to locate and touch a target (white square on a black touchscreen monitor). Forty trials were performed, and response error (the distance between the subject's response and the center of the target square in centimeters) was recorded and averaged. MGVA measures the ability to perceive the direction/trajectory of a moving object (white bar on a black touchscreen), and the subjects were asked to draw the direction of the bar movement. Eighty trials were performed, and response error (the difference between the subject's response angle and the target bar's angle in degrees) was recorded and averaged. GVA measured visual acuity in the range of 1.6 to 2.9 logMAR (20/796 to 20/15887 in Snellen notation) using black and white gratings displayed for 5 seconds. Four alternative answers were given (horizontal, vertical, diagonal left/right) and the program adaptively reduced or increased the spatial frequency of the gratings on the basis of the number of correct and incorrect answers. Qualifications could be worse or better than 2.9 logMAR units.

The rehabilitation protocol

The vision rehabilitation protocol includes assessment of residual vision and vision-related skills, establishment of a rehabilitation plan and goals, vision rehabilitation training supporting individual goals, progress notes, and discharge summary.[4,5] The main goal of the rehabilitation program is to maximize the benefit of the Argus II system in the patient's daily life. The rehabilitation process is a significant time commitment for the patient, medical team, and engineering team, with multiple sessions lasting up to 6 hours each. The central focus of the vision rehabilitation program is to maximize visual ability and foster meaningful use of vision throughout the day at work and at home.

Rehabilitation starts with instruction on usage of the device components. The rehabilitation training then aims at training patients in the following skills: eye, head, and camera position awareness and movement; small-scale light localization/micro scanning; large-scale light localization/macro-scanning; tracking; luminance; discrimination; and shape recognition. After approximately 4 in-clinic sessions, most patients acquire basic abilities that could be retested and enhanced in a home and outdoor environment. Most skills acquired will be used to enhance further orientation and mobility and other abilities during another 6 training sessions. During and after the rehabilitation program, the patients receive intense technical assistance with the device from the local team and from SecondSight personnel. This includes, among other things, intraoperative, postoperative, and repeat calibration of impulse reaching the retinal electrodes during the life of the device.

Results

A total of 11 patients (55% male and 45% female) with a diagnosis of retinitis pigmentosa (RP) were implanted. Average patient age was 62.8 years, and average intraocular pressure preimplantation was 11.3 mm Hg OD and 11.8 mm Hg OS. Average axial length of the implanted eyes was 23.49 mm. All implanted eyes had light perception visual acuity. Seven left and 4 right eyes were implanted. There were no intraoperative complications. No serious adverse events were reported; 4 nonserious adverse events were reported and treated with standard ophthalmological care. One patient presented hyphema at 6 months after implantation and underwent anterior chamber washout. All patients are still on a follow-up schedule; the longest follow-up is 3 years, and the shortest is 3 months.

Visual function tests performed in 6 cases (SL and MGVA) showed twice as good improvement on performance (number of correct from total trials) with the implanted device ON compared with OFF at 3, 6, and 12 months compared with baseline on SL and MGVA. Patients reported visual acuity worse than 2.9 logMAR in 83.34% of eyes (5 of 6) when tested with the MGVA; 1 eye was better than 2.9 logMAR when tested with GVA on baseline. Visual acuity (GVA) remained worse than 2.9 logMAR in the eyes with this level reported at baseline (5 of 6 eyes). The eye with reported levels of GVA better than 2.9 logMAR on baseline also persisted with the same score. When testing with SL, there was statistical significance on mean error distance in pixels ($p < 0.05$) and in centimeters ($p < 0.05$) when comparing performance with the implanted device OFF and ON.

Discussion

The idea of a bionic eye was once science fiction, but with advances in retinal prostheses it is becoming a reality. The Argus II retinal prosthesis is currently available for general use in cases with RP, and the first cases were implanted in Canada with the device in 2014. To date, 11 cases have been implanted in Toronto, all with vision less than 20/2000. One case was implanted at the University of Montreal.

Selection of cases for this procedure involves presurgery assessment by the surgeon and the rehabilitation team. Patients suitable for this technology are those with residual vison of less than around 2.8 logMAR units, those with no additional ocular structural impairments, those with priority tasks for rehabilitation that may benefit from vision provided by the Argus II retinal prosthesis, those with physical and cognitive abilities sufficient to enable optimal use of the device, and those with declared expectations matching the expected output of vision the device provides.

The surgical procedure involves many steps and requires significant training even for an experienced vitreoretinal surgeon. Most surgical maneuvers, however, are all familiar to vitreoretinal surgeons, with the exception of the use of retinal tacks. In addition, extra care needs to be taken during implantation so as to not damage the sensitive electronics of the implant.

The introduction of prosthetic devices for vision rehabilitation in cases with minimal residual native vision required the usage of suitable outcome measures for assessment of such cases. The SecondSight set of tests for SL, MGVA, and GVA used in our cases is a proprietary approach to provide a measure of utility in such cases with regard to visual functions. Other similar proprietary measures with other devices have been publicized as well. From our results, we see that SL and MGVA were significantly better with the device turned ON, but these results did not correlate accurately in some cases with the initial impressions we collected on actual functional vision obtained. Furthermore, these results cannot be compared for equivalency with results from other studies using different technologies because other studies also use specific proprietary outcome measures. This is probably the biggest challenge that minimal residual native vision rehabilitation faces today. We still need to define, standardize, and validate outcome measures for assessment of visual functions and functional vision in cases with minimal residual native vision that can be used in all instances and with all procedures.

Assessment of functional abilities also is essential, and this is done in conjunction with assessment of visual functions, as described above. Functional abilities also improved in this group of patients, as reported in a separate article by our vision rehabilitation team.[7] The surgical remedies available today for those with minimal residual native vision are truly revolutionary in scope and practice; however, intensive vision rehabilitation after the surgery is an indispensable part of the process required to ensure a successful outcome. Some of our patients can now ambulate independently, navigate doorways, and recognize objects and people. Patients are very pleased and continue to work diligently on their rehabilitation.

Several studies reported results following implantation of the Argus II retinal prosthesis. Most reports indicate that patients had visual functions and functional vision with the Argus II retinal prosthesis similar to what we show in our report. In a few cases, the implant was removed after surgery for various reasons.[6,8]

This technology is under constant review for additional refinement and redevelopment. Future improvements in the technology will include software to enhance facial recognition and colour perception, as well as new high-definition v ideo cameras and more powerful processors. Additionally, software to create hundreds of "virtual electrodes" between the 60 physical electrodes is being developed. Other possible applications of this technology are considered for other pathologies, mainly involving macular function loss. Such considerations are at a very initial research stage.

The Argus II retinal prosthesis is exciting because we are able to give hope to patients with previously untreatable degenerative retinal diseases. The Argus II retinal prosthesis has shown early, promising outcomes, but it is vital to manage patient expectations. The Government of Ontario recently gave initial approval to funding the device via health care budgets. Of note, patients with the Argus II implant have undergone 1.5T MRI safely without movement of or damage to the device, although the device does create artifact, which makes orbital imaging problematic.[8] The technology is not at a point where we can operate, flip a switch, and give people their sight back. What we can do is offer them the latest technology, comprehensive visual rehabilitation, and a chance at a seemingly modest improvement in their functional vision. To some this may seem small, but to a patient with bare light perception vision, this is a gigantic, positive, transformative, and life-changing outcome.

References

1. Dorn JD, Ahuja AK, Caspi A, et al. The detection of motion by blind subjects with the epiretinal 60-electrode (Argus II) retinal prosthesis. *JAMA Ophthalmol*. 2013;131:183-9.
2. Second Sight Medical Products Inc. *Argus II Retinal Prosthesis SystemVisual Rehabilitation Guide*. Available at: www.secondsight.com. Accessed December 5, 2017.
3. Humayun MS, Dorn JD, da Cruz L. Interim results from the international trial of Second Sight's visual prosthesis. *Ophthalmol*. 2012;119:779-88.
4. Markowitz SN. Principles of modern low vision rehabilitation. *Can J Ophthalmol*. 2006;41:289-312.
5. Markowitz M. Occupational therapy interventions in low vision rehabilitation. *Can J Ophthalmol*. 2006;41:340-7.
6. da Cruz L, Coley BF, Dorn J, et al. The Argus II epiretinal prosthesis system allows letter and word reading and long-term function in patients with profound vision loss. *Br J Ophthalmol*. 2013;97:632-6.
7. Markowitz M, Rankin M, Devenyi RG, et al. Vision rehabilitation with the Argus II retinal prosthesis. *Can J Ophthalmol*. 2018;53:15-23.
8. Luo YHL, Davagnam I, da Cruz L. MRI brain scans in two patients with the Argus II retinal prosthesis. *Ophthalmol*. 2013;120:1711.

Footnotes and Disclosure:

The authors have no proprietary or commercial interest in any materials discussed in this article.

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