

**Health Policy Advisory Committee on  
Technology**

**Technology Brief Update**

**Argus II Retinal Prosthesis System**

**August 2016**



**Australian  
Safety  
and Efficacy  
Register  
of New  
Interventional  
Procedures –  
Surgical**



**Royal Australasian  
College of Surgeons**

**HealthPACT**  
*emerging health technology*

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This Brief was commissioned by Queensland Health, in its role as the Secretariat of the Health Policy Advisory Committee on Technology (HealthPACT). The production of this Brief was overseen by HealthPACT. HealthPACT comprises representatives from health departments in all States and Territories, the Australian and New Zealand governments and MSAC. It is a sub-committee of the Australian Health Ministers' Advisory Council (AHMAC), reporting to AHMAC's Hospitals Principal Committee (HPC). AHMAC supports HealthPACT through funding.

This brief update was prepared by Mr Ning Ma from the Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S).

## **2016 Summary of findings**

Since the 2013 publication of the original technology brief four, clinical trials on the use of Argus II Retinal Prosthesis System for patients with retinitis pigmentosa (RP) have been published; each of these level II clinical studies are included in this update. Of these, three studies updated clinical data for the 30 patients reported in the original brief. These studies were a part of ongoing clinical trials, sponsored by the manufacturer. They all showed clinically significant improvement in patients' functional vision compared to not using the device. The remaining study showed no comparative improvement, suggesting improved navigational capabilities may be due to non-visual information and training.

One cost-effectiveness study was identified. The Argus II Retinal Prosthesis System appeared to be cost-effective compared to not using the device, with an average \$22,665 per quality adjusted life years (QALYs) gained.

Six ongoing clinical trials were identified and the earliest completion expected in May 2016. Conflict of interest still remains an issue with the evidence base. Currently there are no competing devices for Argus II Retinal Prosthesis System but experimental retinal implants (e.g. Alpha-IMS, Germany) are being developed.

## **2016 HealthPACT assessment**

Several new studies have been published since the original brief in 2013, which have demonstrated that the Argus II retinal prosthesis system improved visual function, functional outcomes and quality of life in patients with severe vision loss from advanced retinitis pigmentosa at 3-year follow-up. Although the Argus II retinal prosthesis system continues to evolve, the costs for the technology remain high.

Due to the lack of long-term patient outcome data HealthPACT does not support public investment in the Argus II retinal prosthesis system in clinical practice at this time, and recommends no further review of the evidence is warranted.

## **Technology, Company and Licensing**

<b>Register ID</b>	<b>WP173</b>
<b>Technology name</b>	<b>Argus® II Retinal Prosthesis System</b>
<b>Patient indication</b>	<b>Adults (25 years or older) with severe to profound retinitis pigmentosa and bare light or no light perception in both eye</b>

### **Reason for assessment**

In 2013, a Technology Brief investigated the Argus® II Retinal Prosthesis for use in blind adults (25 years or older) with severe to profound retinitis pigmentosa and bare light or no light perception in both eyes. In light of developing evidence on the subject, the Brief recommended that this technology be monitored for further evidence in 24 months. In line with this recommendation, the purpose of the current Update is to consider the evidence that has emerged since 2013 and determine whether this new evidence may provide additional information to inform policy decisions.

### **Description of the technology**

The Argus II Retinal Prosthesis System is designed to restore some functional vision to the blind. The system consists of both surgically implanted and externally worn equipment. The external component consists of a miniature video camera and transmitter mounted on a pair of glasses, as well as a small computer (video processor unit) and battery worn on a belt or shoulder strap. The implanted portion, which is designed to be implanted into a single eye (typically the poorer), consists of a receiving and transmitting coil and an electronic case fixed to the outside of the sclera (white of the eye), and an electrode array (60 electrodes) that is surgically attached to the surface of the retina. The electrode array is connected to the electronic case by a ribbon cable that passes through the sclera.<sup>1</sup> The camera housed within the glasses captures images that are sent to the video processing unit and converted to electronic signals. These signals are then sent to the transmitter coil on the glasses. The implanted receiving coil wirelessly receives data and sends signals via the ribbon cable to the implanted electrode array which emits small pulses of electricity to stimulate the remaining bipolar or ganglion cells in the retina. These electrical signals pass through the optic nerve to the brain creating a light sensation that patients interpret as visual patterns.<sup>2</sup>



**Figure 1 Argus II Retinal Prosthesis System. Copyright © 2013 Second Sight Medical Products, Inc.**

Implantation of the Argus II Retinal Prosthesis System can be performed by a single surgeon in a two-hour outpatient procedure under general anaesthesia.<sup>3</sup> Details regarding the surgery are as follows:

- At commencement of the implant procedure, antibiotics and steroids are administered by intravenous injection.
- In phakic eyes (eyes with a lens) the lens is removed.
- An incision is made into the conjunctiva surrounding the cornea, exposing the underlying sclera and extra-ocular muscles (peritomy).
- The transmitting coil is placed on the eyeball and centred under the lateral rectus muscle.
- The electronics package is centred in the superior temporal quadrant of the eye and the implant is then fixed to the eye with sutures.
- The vitreous gel in the middle of the eye is removed (vitrectomy), along with any epiretinal membrane in the area where the surgeon intends to attach the array.
- The microelectrode array is inserted through an incision in the sclera (sclerotomy) and affixed to the retina in the macula with a retinal tack.
- The extraocular portion of the ribbon cable is then sutured to the sclera and all incisions are sutured.
- A transplanted scleral tissue graft (or alternative) is sutured over the electronics package to reduce the likelihood of conjunctival irritation.
- At completion of the surgery, steroids, antibiotics and an anaesthetic are injected under the conjunctiva.

For approximately two weeks after the operation, patients are given antibiotics (oral and eye drops), steroids (oral and eye drops) and atropine to dilate the pupil.<sup>1</sup> The implant is activated one week after surgery.<sup>3</sup>

Patients with the following characteristics are eligible for the procedure:

- At least 25 years old
- Bare light or no light perception in both eyes (if there is no light perception, the eye must respond to electrical stimulation)
- Previous ability to see objects, shapes and lines
- Implanted eye must have an artificial lens or no lens at all
- The patient must be willing and able to follow the recommended schedule of clinical follow-up, device programming and visual rehabilitation.<sup>4</sup>

Contraindications for the Argus II Retinal Prosthesis System are:

- An eye disease or condition that could prevent the device from working
- An eye structure or condition that could make it difficult to successfully implant the device or recover following surgery
- Eye diseases or conditions that make it difficult for the doctor to see inside the eye
- Inability to undergo general anaesthesia
- Inability to take the antibiotic and steroid medications required prior to and following surgery
- Presence of metallic or active device implants in the head
- Presence of a disease or condition that prevents a patient giving informed consent
- Any disease or condition that prevents medical follow-ups or having the video processing unit programmed
- Constant eye rubbing.<sup>4</sup>

In addition to the above indications and contraindications, the manufacturer provides information outlining general precautions, precautions regarding other medical procedures, possible interference from other electronic devices, air travel, general travel and international use, electromagnetic interference and adverse events.<sup>4</sup>

#### 2016 Stage of development in Australia

- |  |   |
|--|---|
| <input type="checkbox"/> Yet to emerge           | <input type="checkbox"/> Established  |
| <input checked="" type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational         | <input type="checkbox"/> Should be taken out of use   |
| <input type="checkbox"/> Nearly established      |   |

## 2016 Licensing, reimbursement and other approval

The Argus II Retinal Prosthesis System (Second Sight Medical Products, Inc. California, United States of America) received a CE mark in February 2011 and a Humanitarian Device Exemption from the United States Food and Drug Administration (FDA) in February 2013 on the proviso that two post-approval studies are conducted, one of which must provide 10-year follow-up data on patients who have received the device.<sup>5</sup> The device has also received regulatory approval from Health Canada.<sup>6</sup> Additionally, the Argus II Retinal Prosthesis System has been approved by the Centres for Medicare & Medicaid Services in the United States for both a new technology add-on payment (inpatient setting) and a transitional pass-through payment (outpatient setting) beginning October 1, 2013.

## 2016 Australian Therapeutic Goods Administration approval

- Yes                                  ARTG number (s): Not applicable
- No
- Not applicable

## 2016 Diffusion of technology in Australia

The Argus II Retinal Prosthesis System is not listed on the Australian Register of Therapeutic Goods and is yet to emerge in Australia.

## 2016 International utilisation

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
United States of America		✓	
Canada		✓	
Mexico	✓		
France	✓		
Switzerland	✓		
Germany		✓	
Italy		✓	
UK		✓	
Austria		✓	
Turkey		✓	

## 2016 Evidence and Policy

### Safety and effectiveness

Since the publication of the 2013 Technology Brief, there have been a number of new studies on the Argus II Retinal Prosthesis System: one systematic review published in 2014 on retinal implants (all types) and several narrative reviews (on case series or other low-level evidence data) for Argus II Retinal Prosthesis System (summarised in Table 1 below). This update includes the four most recently published comparative studies, three of which are ongoing.

**Table 1 Study profile of included studies**

Study/design	Population	Comparison	Clinical/other outcome	Length of follow-up & number of patients	Conflict of interest
Geruschat et al 2016 <sup>7</sup> Level III-2 evidence Multicentre prospective crossover trial United States, France, Mexico, Switzerland and United Kingdom	Patients with confirmed history of retinitis pigmentosa and low visual acuity.	Patients served as their own controls to compare baseline and post-implant measurements with the device turned on and off.	Visual acuity	36 months N = 26	Sponsored by the manufacturer
Garcia et al 2015 <sup>8</sup> Level III-2 evidence Single centre prospective clinical trial United Kingdom	Patients with retinitis pigmentosa and choroideremia with only bare light perception	Adults with the Argus Prosthesis compared with normal-sighted, age-matched individuals wearing goggles to mimic blindness	Path reproduction and triangle completion tasks	Duration not specified Argus: N = 4 Control: N = 11	The authors declared no competing interests
Ho et al 2015 <sup>9</sup> Level III-2 evidence Multicentre prospective crossover trial United States, France, Mexico, Switzerland and United Kingdom	Patients with confirmed history of retinitis pigmentosa and low visual acuity or outer retinal degeneration.	Patients served as their own controls in comparisons of the device turned on or off	Safety: Adverse events Effectiveness: square localisation, direction of motion and grating acuity	36 months N = 30	Sponsored by the manufacturer
Dorn et al 2013 <sup>10</sup> Level III-2 evidence Multicentre prospective crossover trial United States, France, Mexico, Switzerland and United Kingdom	Patients with confirmed history of retinitis pigmentosa and bare light perception or worse in both eyes.	Patients served as their own controls in comparisons of the device turned on or off	Direction of motion test, including identification of visual patterns in motion	6 months N = 28	Sponsored by the manufacturer

Studies by Geruschat et al (2016), Ho et al (2015) and Dorn et al (2013) are from the same clinical trial NCT00407602 of 30 patients (more detail see below).



Three of the four included studies report results for the same group of 30 patients enrolled in a worldwide, multicentre (10 centres), phase II clinical trial (NCT00407602)<sup>11</sup> sponsored by Second Sight Medical Products, Inc. and reported in the original brief. Information regarding targeted patients, eligibility criteria and outcome measures remains unchanged. Briefly, all patients received the Argus II System and all patients acted as their own control (outcomes were compared in each patient with the device activated and deactivated). The trial, which is no longer recruiting, is expected to be completed in August 2019. As similar safety results were reported among the included studies, these are collated into one entry following study effectiveness.

The fourth study,<sup>8</sup> which is not part of the aforementioned clinical trial, enrolled four patients in the United Kingdom who received the Argus II Prosthesis. Normal sighted individuals were given goggles to mimic blindness and served as simulated controls. Due to limited reporting of safety outcomes and inter-relatedness of efficacy outcomes for the three studies above, safety and effectiveness is reported below.

### *Safety*

Geruschat et al (2016) reported one case of device removal; however, this was noted in the original brief. Dorn et al (2013) did not report any safety-related outcomes. Ho et al (2015) monitored serious adverse events (SAE), which were defined as “adverse events that required medical or surgical interventions or hospitalisation to prevent permanent injury”, throughout the study period (36 months). There were 23 SAEs over the 36 months reported in 2015, compared with 17 SAEs reported by the 2013 Technology Brief. However, it is unclear what the six additional SAEs were. The reported categories of all SAEs included low fluid pressure in the eye, splitting or erosion of the conjunctiva (mucous membrane covering the front of the eye) and presumed inflammation of the inside of the eye (endophthalmitis).<sup>1, 7</sup>

### *Effectiveness*

#### Geruschat et al 2016<sup>7</sup>

This latest publication on the clinical trial NCT00407602 reported functional visual ability in a series of observer-rated tasks performed by patients with the Argus II Retinal Prosthesis System turned on and off. Functional visual ability was measured using the Functional Low-Vision Observer Rated Assessment (FLORA) instrument, which assesses how patients perform while using a retinal prosthesis to complete activities of daily living.<sup>7, 12, 13</sup> A total of 35 tasks were categorised into four groups: visual orientation, visual mobility, daily life and interaction with others.<sup>13</sup> Testing was done an average of 36 months after device implantation.

Of the 30 recruited patients, only 26 patients were included in this study. One patient had the prosthesis removed after 14 months (reason not provided) and three other patients did

not consent to the use of FLORA. Of the 35 FLORA tasks, results for 24 (69%) showed a statistically significant improvement when the device was turned on; results for two (6%) showed better performance with the device turned off; and results for the remaining nine (26%) tasks showed no statistically significant difference. Although results for 11 tasks identified no significant result with the device turned on, when these tasks were grouped into their respective domain, a significant result was identified. The performance changes by domain are tabulated in Table 2.

**Table 2 Change in FLORA score with the Argus II Retinal Prosthesis turned on versus off**

Domain	Number of tasks	OFF mean performance (SEM)	ON mean performance (SEM)	p-value
Orientation	6	3.6 (0.11)	2.2 (0.17)	<0.05
Mobility	5	3.7 (0.10)	2.9 (0.18)	<0.05
Daily life	17	3.1 (0.09)	2.5 (0.14)	<0.05
Interaction with others	7	3.9 (0.06)	3.1 (0.16)	<0.05

FLORA: Functional Low-Vision Observer Rated Assessment; SEM: standard error of mean; Scores range from 4 (impossible) to 1 (easy); The *p* values were reported by post-hoc Bonferroni adjustment.

The study observed significant improvements in all four domains. In particular, the most significant improvements were among five tasks<sup>7</sup>, which shared common features of using light projection and contrast to identify objects.

#### Ho et al 2015<sup>9</sup>

The author reported 36-month follow-up data on all 30 patients. The study investigated improvement in visual function with the Argus II System turned on or off. Benefits were assessed using objective, computer-based tests including “square localisation”, “direction of motion”, “grating visual acuity”, “find the door” and “follow the line”.<sup>9</sup> Details of these tests are mentioned in the 2013 brief. Instead of measuring time to complete a task as per previous publications,<sup>1, 10</sup> response errors were recorded and analysed (see Table 3).

**Table 3 Percentage reduction in error with the ArgusII prosthesis turned on at 1 and 3 years post-implantation**

Outcome measures	Year 1		Year 3	
	Number of patients	% improvement	Number of patients	% improvement
Square localisation	16	94%*	28	89%*
Direction of motion	16	63%*	27	56%*
Grating visual acuity	19	48%*	27	33%*
Find the door	28	22%	28	35%*
Follow the line	28	56%*	28	54%*

\*Statistically significant improvement ( $p < 0.05$ ).

#### Dorn et al 2013<sup>10</sup>

This study investigated the ability to detect a rectangular object moving across a screen in random angles and errors of responses. Although also reported by Ho et al (2015), this study

conducted multiple regression analyses to investigate effects of the following patient-related co-variants on error rates: age at implantation; age of implant; duration of self-reported blindness, and speed/tilt angle of the object in the experiment. None of the covariates were statistically significant. These results demonstrate that these patient-related factors did not contribute to patient performance. Therefore, the improvement in performance was more likely enabled by the device.

#### Garcia et al 2015<sup>8</sup>

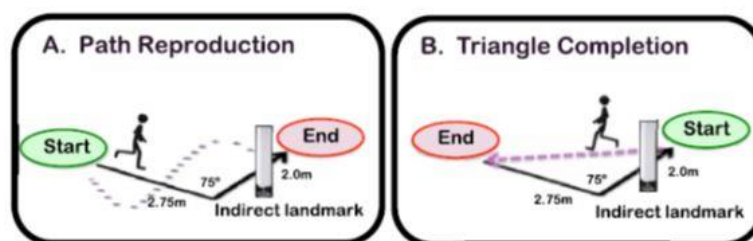
This study investigated whether patients treated with the Argus II Retinal Prosthesis System could navigate using both visual and non-visual information in controlled situations. Four patients who had the Argus II system for at least seven years and 11 adults with normal vision were recruited for the intervention and control group, respectively. The mean age of the four patients in the intervention group was 66 years; three were diagnosed with retinitis pigmentosa and one with choroideremia. In the control group, the mean age of six young adults was 25.7 years and the mean age of the five age-matched adults was 63 years. These normal-sighted individuals simulated a control group by wearing goggles that mimicked the bare light perception of the Argus recipients and were asked to complete the same tasks as the Argus patient group.

#### *Safety*

No safety related outcomes were reported by this study.

#### *Effectiveness*

All participants were asked to complete two tasks: path reproduction and triangle completion. In the first task the person is guided to walk along a path and then asked to retrace the path without guidance. The path includes one turn and an obstacle placed midway. The second task uses the same path as the first, but the person must return to the starting position without guidance (see Figure 2). All participants undertook the two tasks with vision (device on for patients and wearing goggles for controls) and without vision (blindfolded for all subjects). Errors of path deviations were recorded and analysed.



**Figure 2** The experimental tasks illustration, provided by the study<sup>8</sup>

To investigate the impact of age on navigation performance the study included age-matched subjects in the control group. No statistical significance differences were identified. The control participants showed better precision when navigating with reduced vision than

without vision ( $p = 0.003$ ). This was not true for the Argus patients ( $p$  value = 0.3), although two patients did show improvement in the triangle completion task. Additionally, all of the Argus patients showed greater precision than the controls in both tasks when navigating without vision (1<sup>st</sup> task,  $p = 0.003$ ; 2<sup>nd</sup> task,  $p = 0.02$ ). These results indicate that the Argus II Prosthesis may not provide sufficiently reliable visual information to improve the precision of patients on tasks for which they have learnt to rely on non-visual senses.

## 2016 Economic evaluation

One cost-effective analysis was identified. In this European multi-centre trial, Vaidya et al (2014) used a multi-state transition Markov model to establish the cost-effectiveness for the Argus II Retinal Prosthesis System in comparison with usual care.<sup>14</sup>

**Table 4 Economic study details**

Study/design	Population	Comparison	Clinical/other outcome	Length of follow-up	Conflict of interest
Vaidya et al 2014 Cost-effectiveness analysis The Netherlands	A hypothetical cohort of 1000 retinitis pigmentosa patients aged 46 years	Usual care (without Argus II system)	Quality adjusted life years (QALYs) and direct healthcare costs and incremental cost effective ratio (ICER)	25 Years (simulation)	None identified

A simulated cohort of 1,000 patients followed up over a 25-year time horizon was used. Probabilistic sensitivity analysis was performed to take account of underlying uncertainties in model inputs.

The incremental cost-effectiveness ratio for Argus II was \$22,665<sup>a</sup> per quality-adjusted life-year (QALY). Probabilistic sensitivity analysis of uncertainties in the model inputs (including transition probabilities of health status and costs associated with retinitis pigmentosa related injuries) showed an increased ICER of \$22,477 per QALY. Two additional scenarios showed that the ICER increased to \$49,496 assuming that the visual acuity of the patients does not change over time. The ICER increased to \$77,246 when the life-span of the device was reduced to 10 years. Overall, this economic evaluation showed that the Argus II is a cost-effective intervention compared with usual care of patients with retinitis pigmentosa.

<sup>a</sup> A AUD = 0.727 USD, currency conversion performed on 13 May 2016, source XE Currency Converter

## 2016 Ongoing research

A search of ongoing clinical trials for Argus II Retinal Prosthesis System was performed in Clinicaltrial.gov identified six ongoing trials Table 5.

**Table 5 Ongoing clinical trials**

Trial Identifier / site details	Trial status	Interventions	Indication	N	Study design	Outcomes	Estimated completion date
NCT02227498 <sup>15</sup> Single centre (UK)	Recruiting	Argus II retinal prosthesis	Age-related macular degeneration	5 <sup>11</sup>	Non-randomised, open label comparative study	Adverse events, visual function	June 2019
NCT02303288 <sup>16</sup> Multicentre (France)	Recruiting	Argus II retinal prosthesis	Retinitis pigmentosa	18	Prospective cohort post-market surveillance	The impact of the Argus II measured by FLORA; incidence of procedure- and device-related adverse events	November 2018
NCT00407602 <sup>9</sup> Multicentre (France, Mexico, Switzerland, United Kingdom, United States)	Ongoing, not recruiting	Argus II retinal prosthesis	Retinitis pigmentosa	30	Non-randomised comparative study European multi-centre trial performing	Visual acuity, safety, activities of daily living, quality of life, orientation and mobility, spatial vision, stability of implant, system functionality	August 2019
NCT01860092 <sup>17</sup> Multicentre (US)	Recruiting	Argus II retinal prosthesis implantation	Retinitis pigmentosa	53	Prospective cohort post-approval study	Safety, visual function, and device reliability	August 2018
NCT01490827 <sup>18</sup> Multicentre (Germany, Italy)	Recruiting	Argus II retinal prosthesis implantation	Outer retinal degeneration and retinitis pigmentosa	45	Prospective cohort post-market surveillance	Adverse events, visual function	May 2016
NCT01999049 <sup>19</sup> Single centre (Canada)	Recruiting	Argus II retinal prosthesis implantation	Retinitis pigmentosa	10	Prospective case series	Safety, visual function	January 2017

FLORA: Functional Low-Vision Observer Rated Assessment.

## 2016 Other issues

As identified in the original 2013 HealthPACT Technology Brief, conflicts of interest are present in the included studies. All the three studies from the same clinical trial (NCT00407602) were sponsored by Second Sight Medical Products, Inc., the manufacturer of the Argus II Retinal Prosthesis System. This conflict of interest was reported in each study. Additionally, there was significant author overlap between the included studies in this update and the 2013 Technology Brief. While Garcia et al (2015) seems to be independent,

patients from this study had the Argus implant for at least seven years and previously received rehabilitation training sponsored by the manufacturer. Therefore, it is unclear whether the recruited four patients were involved in the ongoing clinical trial (NCT00407602).

Similarly, Geruschat et al (2015)<sup>13</sup> reported patient outcomes using a tool developed as part of this clinical trial to assess outcomes for the Argus II Prosthesis system. A target literature search did not identify any validity studies on this tool.

Surgical implantation of the device requires a high level of precision to ensure an appropriate level of stimuli to the optic nerve.<sup>21</sup> Patients are still going through a learning process to cope with the device and they need to have dedication and persistence to training for the best use of the device.<sup>22</sup> While competing devices are still emerging,<sup>21, 23</sup> the Alpha IMS (Retina Implant AG, Germany) is the only similar technology that has received a CE mark.

### **2016 Updated search**

Literature searches were performed in PubMed and Embase using “Argus II” and “retinitis pigmentosa” as the key words.

### **2016 Number of studies included**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the [HealthPACT web site](#).

Total number of studies 4

Total number of Level III-2 studies 4

### **Date searched**

6/5/2016

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## **Technology, Company and Licensing**

<b>Register ID</b>	<b>WP173</b>
<b>Technology name</b>	<b>Argus II Retinal Prosthesis</b>
<b>Patient indication</b>	<b>For use in blind adults (25 years or older) with severe to profound retinitis pigmentosa and bare light or no light perception in both eyes</b>

## **Description of the technology**

The Argus II Retinal Prosthesis System is designed to restore some functional vision to people who are blind. The system consists of surgically implanted and external equipment. The external component consists of a miniature video camera and transmitter mounted on a pair of glasses, as well as a small computer (video processor unit) and battery which are worn on a belt or shoulder strap (Figure 3). The implanted portion, which is designed to go in a single eye (typically the worse seeing), consists of a receiving and transmitting coil and an electronic case which are fixed to the outside of the sclera (white of the eye), and an electrode array (60 electrodes) that is surgically attached to the surface of the retina. The electrode array is connected to the electronic case by a ribbon cable that goes through the sclera.<sup>1</sup> The camera housed within the glasses captures images which are sent to the video processing unit and converted to electronic signals. These signals are then sent to the transmitter coil on the glasses. The implanted receiving coil wirelessly receives these data and sends the signals via the ribbon cable to the implanted electrode array which emits small pulses of electricity to stimulate the remaining bipolar or ganglion cells in the retina. These electrical signals pass through the optic nerve to the brain allowing light sensation which patients learn to interpret as visual patterns.<sup>2</sup>



**Figure 3 Argus II Retinal Prosthesis System. Copyright © 2013 Second Sight Medical Products, Inc.**

Implantation of the Argus II Retinal Prosthesis System can be performed by a single surgeon in a two-hour outpatient procedure done under general anaesthesia.<sup>3</sup> Details regarding the surgery are as follows. At the start of the implant procedure, antibiotics and steroids are administered by intravenous injection. In phakic eyes (eyes with a lens), the lens is removed. An incision is made of the conjunctiva surrounding the cornea exposing the underlying sclera and extra-ocular muscles (peritomy). The transmitting coil is placed on the eyeball and centred under the lateral rectus muscle. The electronics package is centred in the superior temporal quadrant of the eye, and the implant is then fixed to the eye with sutures. The vitreous gel in the middle of the eye is removed (vitrectomy), along with any epiretinal membrane in the area where the surgeon intends to tack the array. The microelectrode array is inserted through an incision in the sclera (sclerotomy) and affixed to the retina in the macula with a retinal tack. The extraocular portion of the ribbon cable is then sutured to the sclera and all incisions are sutured. A transplanted scleral tissue graft (or alternative) is sutured over the electronics package to reduce the likelihood of conjunctival irritation. At the end of surgery, steroids, antibiotics and an anaesthetic are injected under the conjunctiva. For approximately two weeks after the operation, patients are given antibiotics (oral and eye drops), steroids (oral and eye drops) and atropine to dilate the pupil.<sup>1</sup> The implant is activated one week after surgery.<sup>3</sup>

Patients with the following characteristics are eligible for the procedure:

- at least 25 years old
- bare light or no light perception in both eyes (if there is no light perception, the eye must respond to electrical stimulation)
- previous ability to see objects, shapes and lines

- implanted eye must have an artificial lens or no lens at all
- the patient must be willing and able to follow the recommended schedule of clinical follow-up, device programming and visual rehabilitation.<sup>4</sup>

Contraindications for the Argus II Retinal Prosthesis System are:

- an eye disease or condition that could prevent the device from working
- an eye structure or condition that could make it difficult to successfully implant the device or recover following surgery
- eye diseases or conditions that make it difficult for the doctor to see inside the eye
- inability to undergo general anaesthesia
- inability to take the recommended antibiotic and steroid medications required prior to and following surgery
- presence of metallic or active device implants in the head
- presence of a disease or condition that prevents a patient from giving informed consent
- any disease or condition that prevents medical follow-ups or having the video processing unit programmed
- constant eye rubbing.<sup>4</sup>

In addition to the above indications and contraindications, the company that produces the Argus II Retinal Prosthesis System provides information outlining general precautions, precautions regarding other medical procedures, possible interference from other electronic devices, air travel, general travel and international use, electromagnetic interference and adverse events.<sup>4</sup>

### **Company or developer**

Second Sight Medical Products, Inc. (Sylmar, CA, United States of America).

### **Reason for assessment**

The Argus II Retinal Prosthesis System is a novel device that can assist blind people with severe to profound retinitis pigmentosa and bare or no light perception in both eyes. There is currently no cure for this condition and no treatment that will stop or slow its progression.

### Stage of development in Australia

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established  |
| <input type="checkbox"/> Experimental             | <input type="checkbox"/> Established <i>but</i> changed indication or modification of technique |
| <input type="checkbox"/> Investigational          | <input type="checkbox"/> Should be taken out of use   |
| <input type="checkbox"/> Nearly established       |   |

### Licensing, reimbursement and other approval

The Argus II Retinal Prosthesis System received a CE mark in February 2011. It also received a Humanitarian Device Exemption from the United States Food and Drug Administration (FDA) in February 2013 on the proviso that two post-approval studies are conducted, one of which must provide 10-year follow-up data on patients who have received the device.<sup>5</sup> The Argus II Retinal Prosthesis System is available at two National Institute for Health Research centres in the United Kingdom. In Germany and Italy, two to four patients per month are currently receiving the device.<sup>2</sup>

### Australian Therapeutic Goods Administration approval

- |   |                                |
|---|--------------------------------|
| <input type="checkbox"/> Yes            | ARTG number (s) Not applicable |
| <input checked="" type="checkbox"/> No  |                                |
| <input type="checkbox"/> Not applicable |                                |

**Technology type**

**Device**

**Technology use**

**Assistive**

### Patient Indication and Setting

#### Disease description and associated mortality and morbidity

Peripheral degeneration of the retina is caused by many diseases, the most common being a family of diseases known as retinitis pigmentosa (RP). RP is a heterogeneous group of inherited retinal disorders characterised by progressive damage to and loss of the light receptor (photoreceptor) cells in the retina, with subsequent degeneration of the retinal pigment epithelium.<sup>24</sup> The retina contains two types of photoreceptors: rods and cones. Rods are responsible for peripheral vision and vision in low light, while cones provide vision in bright light, including colour vision. In most cases, the rods degenerate first, followed by the cones. Consequently, the first symptom patients experience is impaired night vision; loss of daytime vision occurs later in life.<sup>25</sup>

There are two forms of RP: syndromic and non-syndromic. The non-syndromic form, in which the signs and symptoms of RP are limited to loss of vision, is the most common. In the

less common syndromic forms of RP, one or more other organs are affected as well. The typical non-syndromic form of RP slowly progresses over several decades, although some patients experience rapid onset over two decades or a slow disease progression that never leads to blindness. In the early stages of the disease, the main symptom is loss of the ability to see at night (night blindness) or in very low light. This symptom is often experienced in childhood, but may also appear during the second decade of life or later. In the middle stage of the disease, night blindness is obvious and results in difficulty driving and walking at night. Patients also become aware of a loss in peripheral vision in daylight (tunnel vision). Other symptoms include light intolerance (photophobia), colour vision deficiency (dyschromatopsia) and difficulty reading. In many cases, these severe vision problems do not occur until early adulthood. In the advanced stage of the disease, patients can no longer move independently as a result of peripheral vision loss, reading is difficult and photophobia is intense. Some individuals may retain limited central vision whereas others experience complete vision loss.<sup>26</sup> The rate and degree of disease progression varies among individuals. Complications associated with RP include cataracts and macular oedema.<sup>25</sup>

Clinical diagnosis of RP is based on the presence and progressive worsening of night blindness and peripheral visual field defects, lesions in the fundus, and hypovolted electroretinogram traces. Currently there is no therapy that stops the progression of the disease or restores lost vision.

### **Number of patients**

No New Zealand data could be found on the incidence or prevalence of RP, the most common of the retinal degenerative diseases. It is estimated that one in every 3,000 Australians is affected by RP and that five to seven per cent of newly diagnosed blindness in Western countries is attributable to this family of diseases.<sup>27, 28</sup> According to a report on vision loss in Australia from the Centre for Eye Research Australia (CERA), RP was the cause of 769 cases of blindness (1.5%) in people older than 40 years in 2004.<sup>29</sup>

### **Speciality**

**Ophthalmology**

### **Technology setting**

**Specialist hospital**

### **Impact**

### **Alternative and/or complementary technology**

The Argus II Retinal Prosthesis System is neither an alternative nor a complementary technology. It is the world's first and only United States FDA approved (humanitarian device exemption) device for restoring some functional vision in people suffering from blindness as a result of severe to profound RP.

### **Current technology**

There is currently no cure for RP, the most common cause of peripheral retinal degeneration, and there are no treatments that stop the condition from gradually worsening over time.<sup>30</sup> Therapy aimed at slowing the degenerative process includes protecting the eyes from sunlight (wearing dark glasses outdoors), taking vitamins A and E to protect the photoreceptors and treating complications. Psychological and genetic counselling is used to help patients cope with the social and psychological impact of blindness.<sup>25</sup>

### **Diffusion of technology in Australia**

The Argus II Retinal Prosthesis System is not listed on the Australian Register of Therapeutic Goods and is yet to emerge in Australia.

## International utilisation

Country	Level of Use		
	Trials underway or completed	Limited use	Widely diffused
United States of America		✓	
Mexico	✓		
France	✓		
Switzerland	✓		
Germany		✓	
Italy		✓	
UK		✓	

## Cost infrastructure and economic consequences

The cost<sup>2</sup> of the device is estimated to be A\$112,724. Additional costs estimated by the company include A\$10,513 for surgery and A\$6,104 for follow-up.<sup>2</sup> However, actual follow-up costs may be significantly higher as they would include weekly training in a specialised setting by specialised staff for a 6 to 12 month period.

## Ethical, cultural or religious considerations

No ethical, cultural or religious considerations were identified in the published literature.

## Evidence and Policy

### Safety and effectiveness

Three studies were included in this Technology Brief. All three studies included the same group of 30 patients enrolled in a worldwide, multicentre (10 centres), phase II clinical trial (NCT00407602) sponsored by Second Sight Medical Products, Inc.<sup>31</sup> All patients received the Argus II Retinal Prosthesis System and all patients acted as their own control, that is outcomes were compared in each patient with the device activated and deactivated. The trial, which is no longer recruiting, is expected to be completed in August 2019. The median age of the 30 patients was 57 years (range 27–77) at the time of implantation and 30 per cent of patients were women. All patients were followed up for a minimum of six months, with some patients having follow-up data up to 2.7 years after surgery. Inclusion criteria for patients entering the trial were as follows:

- a confirmed history of RP (all centres) or outer retinal degeneration (France, Mexico, Switzerland and the United Kingdom only), with remaining visual acuity of bare light perception (all centres) or visual acuity of 2.3 logarithm of Minimum Angle

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<sup>2</sup> Costs converted from British pounds to Australian dollars where £1= A\$1.6956 (source ozforex.com.au, 19 August 2013)

Resolution (logMAR) or worse in both eyes (France, Mexico, Switzerland and the United Kingdom only);

- functional ganglion cells and optic nerve;
- a history of former useful form vision in the worse-seeing eye;
- at least 18 (France, Mexico, and the United Kingdom) or 25 (Switzerland and the United States of America) years old;
- resides within two (Mexico, the United Kingdom and the United States of America) or three hours (France and Switzerland) travel time (by ground transport) of the investigational site; and
- willing and able to comply with the protocol testing and follow-up requirements.

Patients were excluded from the trial if they had the following:

- disease of the optic nerve or ocular surface;
- diseases or conditions that affect retinal function, prevent adequate visualisation of the retina or prevent adequate performance of the physical examination;
- an ocular condition that predisposes the patient to eye rubbing;
- any disease or condition that prevents understanding or communication of informed consent, study demands, and testing protocols;
- pregnancy;
- another active implanted device;
- conjunctival thinning;
- any health concern that would preclude anaesthesia;
- unrealistic expectations of the implant;
- known allergy or contraindication to anticipated preoperative, intraoperative or postoperative medications;
- conditions likely to limit life to less than one year from the time of screening;
- diseases or conditions that impede the ability to implant the device or would prevent the system from functioning for the duration of the study; or
- an axial eye length less than 20.5 mm or more than 26.0 mm in the implanted eye.<sup>31</sup>

Ahuja and Behrend, 2013<sup>32</sup>; Humayun et al, 2012<sup>1</sup>

Results for the 30 patients from the phase II clinical trial (NCT00407602) were reported in the studies by Ahuja and Behrend (2013)<sup>32</sup> and Humayun et al (2012)<sup>1</sup> and are discussed together here. Outcomes from these studies included safety (serious and non-serious adverse events), outpatient use of the device and tests on direction of motion, real-world utility (door and line tests), full-field light stimulus light threshold, square localisation, visual acuity and the ability to read letters. Descriptions of tests on efficacy are provided in Table 6.



**Table 6 Tests conducted to assess the efficacy of the Argus II Retinal Prosthesis System conducted by Ahuja and Behrend (2013)<sup>32</sup> and Humayun et al (2012)<sup>1</sup>**

Test name	Description of test	Number of patients who completed the test and time (post-implantation) when test was conducted
Direction of motion	Patients were required to draw a line on a touch screen indicating the direction of motion of a white bar which swept across the screen at random angles ranging from 0° to 360°.	n=28, time=ns
Door test	Patients were required to find a door on the other side of a room.	Baseline (n=29), 3 months (n=29), 6 months (n=30), 12 months (n=14), 18 months (n=13), 24 months (n=8)
Line test	Patients were required to follow a white line on the floor.	Baseline (n=30), 3 months (n=27), 6 months (n=29), 12 months (n=14), 18 months (n=13), 24 months (n=8)
Square localisation	Patients were required to touch the centre of a square (2.3 x 2.3 inches) displayed in random locations on a monitor after being given an auditory prompt. Accuracy was determined by calculating the mean distance between individual responses and the square's centre.	n=27, time=ns
Visual acuity	Visual acuity was tested by presenting square-wave gratings of varying spatial frequency in one of four directions (horizontal, vertical, diagonal to the upper right or diagonal to the upper left) for five seconds.	n=ns, time=ns
Reading letters	<p>Three different tests were conducted: letter recognition, letter size reduction and word reading. Tests increased in difficulty and only those who performed well in one test moved on to the next.</p> <p>Test 1 (letter recognition): Patients had to identify letters in a force-choice closed-set test. There were three different test groups. Group A consisted of the letters L, T, E, J, F, H, I and U. Group B consisted of the letters A, Z, Q, V, N, W, O, C, D, and M. Group C consisted of the letters K, R, G, X, B, Y, S, and P. Letters were presented four times in random order.</p> <p>Test 2 (letter size reduction): Patients who correctly identified at least 50% of the letters in 60 seconds in all letter groups in test 1 were included in test 2. Patients were required to identify letters randomly presented from a closed set. Letters were grouped in lines of 5 that reduced in size equivalent to one log unit to mimic standard acuity testing. The test was stopped when the time limit expired, five incorrect responses were given in single line, or the patients were unable to guess at the end of the forced-choice test. Testing was carried out twice for each patient on separate days. The total number of letters correctly identified and the size of the smallest correct letter were recorded.</p> <p>Test 3 (word recognition): Patients who performed best in test 2 were included in test 3. Patients were presented with two-, three- and four-letter words and given the equivalent time to guess them.</p>	<p>Test 1 (group A: n=24, group B: n=22, group C: n=21)</p> <p>Test 2 (n=7)</p> <p>Test 3 (n=4)</p> <p>Time=ns for all tests</p>
Full-field light threshold	Patient's residual native light perception (without the use of the prosthesis) was measured before and 2 years after implantation	n=ns, time=2 years post-implantation

ns: not stated

Serious adverse events were defined according to the International Organization for Standardization (ISO) 14155 standard<sup>33</sup> as medical occurrences that: caused death, were life threatening, caused permanent impairment of a body function or permanent damage to body structure, necessitated medical or surgical intervention to preclude such impairment or damage, or required hospitalisation or prolonged hospitalisation. Non-serious adverse

events were defined as those related to the device or surgery that did not require surgical intervention (resolved with topical or oral medications or did not require treatment).

### *Safety*

A total of 17 device- or surgery-related serious adverse events (SAEs) were reported (Table 7). Eighty-two per cent of SAEs occurred within the first six months after implantation and 70 per cent occurred within the first three months. Seventy per cent of patients did not experience any SAEs.

Conjunctival erosion and dehiscence, which occurred in three and two patients respectively, were treated with additional sutures and/or placement of additional graft tissue in four patients and removal of the device due to damage in one patient.

Culture-negative presumed inflammation of the aqueous and vitreous cavity inside the eye (endophthalmitis), which occurred in three patients, was resolved with intravitreal, subconjunctival, topical and systemic antibiotics. The first incidence occurred in the immediate postoperative period. The second and third incidences developed approximately five and eight weeks postoperatively. None of the presumed endophthalmitis cases required device removal. No incidences of presumed endophthalmitis occurred after a protocol change was implemented that included the routine use of intraoperative broad-spectrum antibiotics, a reduction in the number of observers, stricter sterile techniques during implant and the use of a temporary sleeve to cover the array region before introducing it intraocularly.

All three cases of low intra-eye pressure (hypotony), two of which occurred within the first six months post-implantation and the third at one year, were successfully resolved. The patient who developed hypotony at one year post-implantation had the device removed because of device migration. With respect to the other two patients, one was treated with intraocular silicone oil tamponade, while the other, who had an associated rhegmatogenous retinal detachment requiring repair, was later also treated with silicone oil tamponade.

The two cases of retinal detachment, which occurred between the 5- and 6-month post-implantation period, required surgical intervention. One was associated with hypotony, as described above, while the other resulted from blunt trauma to the implanted eye. The retinal detachment was successfully repaired with vitrectomy, partial removal of the retina (retinectomy) and silicone oil.

In two patients, the electrode array had to be re-tacked to the retina shortly after surgery. In both cases, the reattachment was successful.

**Table 7**                      **Serious adverse events (device or surgery related) reported following surgery to implant the Argus II Retinal Prosthesis System.<sup>1</sup>**

Serious Adverse Event	Number of patients with event (%) (N=30)

Conjunctival dehiscence	3 (10)
Conjunctival erosion	2 (7)
Presumed endophthalmitis	3 (10)
Hypotony	3 (10)
Re-tack	2 (7)
Retinal detachment – rhegmatogenous	1 (3)
Retinal detachment – tractional	1 (3)
Retinal tear	1 (3)
Uveitis – inflammatory	1 (3)

Patients were followed up for a minimum of 6 months and up to 2.7 years

The types of non-serious adverse events and the number of patients in which they occurred are listed in Table 8. The exact number of patients who experienced each event was not reported other than that 10 patients developed conjunctival oedema that lasted longer than what is typically seen postoperatively. This was the most frequently reported non-serious adverse event.

**Table 8 Non-serious events (device or surgery related) reported following surgery to implant the Argus II Retinal Prosthesis System.<sup>1</sup>**

Number of patients who experienced the events listed* (N=30)	Types of non-serious adverse events
10	Conjunctival oedema <sup>†</sup>
5-7	Intraocular inflammation, hypotony without significant choroidal detachment, suture irritation and ocular pain
2-3	Inflammatory conjunctivitis, corneal filaments, epiretinal membrane, high intraocular pressure controlled by topical anti-glaucoma medication, epiphora, mild hyphema, inflammatory uveitis and mild vitreous haemorrhage.
1	Limited conjunctival dehiscence, corneal abrasion, mild peripheral corneal vascularisation, cystoid macular oedema, decrease in light perception, dry eye, transient headache, iris vessel engorgement that receded after surgery to resuture the sclerotomy (to treat hypotony), a stable tractional retinal detachment, transient nausea, transient increased nystagmus, scleritis, and transient vertigo

Patients were followed up for a minimum of 6 months and up to 2.7 years.

\* The exact number of patients who experienced each event could not be deduced from the data provided in the study

<sup>†</sup>Considered to be more extensive or longer lasting than what is typically seen postoperatively

## Efficacy

As of March 2010, 29 of the 30 patients had used the system at home for an average of 15.8 months. One patient's device was removed due to migration<sup>1</sup> (discussed above in safety). At 2-years' follow-up, there was no significant difference in full-field stimulus light threshold before and after surgery in either the implanted eye or the fellow eye in any patient ( $p>0.2$ ).<sup>32</sup>

Tests on visual acuity, where 20/20 vision is equivalent to 0.00 logMAR and the higher the logMAR the worse the vision, demonstrated that no patients had a recordable visual acuity prior to implantation or with the system off after implantation. Seven patients had a measurable acuity below the 2.9 logMAR test limit with the system on. The best result achieved was a score of 1.8 logMAR. With respect to the door and line test, patients performed significantly better with the system on than with the system off at all follow-up time points except at the 12-month time point for the door test ( $p<0.05$ ).<sup>1</sup> In the direction of motion test, 16 of the 28 (57%) patients performed better with the system on than off ( $p<0.05$ )<sup>1</sup>, whilst in the square localisation test 26 of 27 (96%) patients showed a statistically significant improvement in accuracy with the system on compared with the system off ( $p<0.05$ ).<sup>32</sup> Results of the letter reading tests are presented in Table 9.

**Table 9 Results from the letter recognition tests using the Argus II Retinal Prosthesis System.**<sup>32</sup>

Test	Number of patients tested	Results
1: letter recognition	24	21 patients (88%) were able to consistently identify letters. Among these 21, the correct response rate was 55% with the system on and 15% with the system off ( $p<0.001$ )
2: letter size reduction	7	Patients were able to consistently read letters of reducing size, the lowest to 0.9 cm, and could consistently identify previously unseen two-, three- and four-letter words correctly
3: word recognition	4	Four-letter words could be read with an accuracy of 61% (10 trials per patient)

The average implant duration time at the time of the tests was not reported in the study.

### Barry and Dagnelie, 2012<sup>34</sup>

Twenty-one of the 30 patients enrolled in the Argus II Retinal Stimulation System Feasibility Trial NCT00407602 participated in this study which investigated the capability of the prosthesis for guiding fine hand movement. Patients were required to trace white paths on black backgrounds on a touch screen without drawing outside its borders in up to three separate experiments with the prosthesis system switched on and off. Each successive experiment presented paths of increasing complexity and less predictability, and only those patients who showed significant improvement with the prosthesis over natural vision in the second experiment or whose system-off performance was comparable to the average system-on performance could move onto the third test. The paths the patients were

required to follow, in order of testing, included right-angle tests, mixed-angle single-turn tests and two-turn tests. Patients had training with the system on prior to each experiment. The study did not state the time after surgery when the tests were conducted.

### *Efficacy*

The Argus II Retinal Prosthesis significantly improved the patients fine hand movements. On average, across all subjects and trials, prosthesis use significantly reduced the error in tracing by 60 per cent ( $p < 0.001$ ) and increased trace time by 211 per cent ( $p < 0.001$ ). Results of individual tests are outlined in Table 10.

**Table 10** Reduction in tracing error, increase in trace time and within-patient reduction in error with the Argus II Retinal Prosthesis System.<sup>34</sup>

Test type	Reduction in tracing error with system on versus off (%)	<i>p</i>	Increase in trace time with system on versus off (%)	<i>p</i>	Number of patients showing significant reduction in error with system on (%)
Right-angle test n=21	63	<0.001	156	<0.001	43
Mixed-angle, single-turn test n=16	53	<0.001	184	<0.001	56
Two-turn test n=9	38	<0.001	252	<0.001	56

The average implant duration time at the time of the tests was not reported in the study.

### **Economic evaluation**

No cost evaluation studies on the Argus II Retinal Prosthesis System were identified in the literature. Investigations into the cost of the device compared with the cost of complete vision loss for both individuals and society are required.

### **Ongoing research**

Four ongoing trials concerning the Argus II Retinal Prosthesis System were identified through a search of [clinicaltrials.gov](http://clinicaltrials.gov) (Table 11). Eligible patients are adults aged at least 25 years with severe to profound RP and a confirmed history of RP or outer retinal degeneration, with remaining visual acuity of bare light perception or no light perception in both eyes. One trial (NCT00279500) included patients aged at least 18 years with a confirmed history of retinal degenerative disease in the worse-seeing eye and remaining vision that is no better than light perception.

**Table 11 Registered clinical trials underway for the Argus II Retinal Prosthesis System.**

Trial Identifier and site details	Trial status	Interventions	N	Study design	Outcomes	Estimated completion date
NCT00279500 Single centre (United States)	Ongoing, not recruiting	Argus retinal prosthesis (first generation device)	6	Non-randomised comparative	Medical and surgical risk, ability to resolve multiple percepts and patterns, optimize effectiveness of stimulus parameters	December 2014
NCT00407602 Multicentre (France, Mexico, Switzerland, United Kingdom, United States)	Ongoing, not recruiting	Argus II retinal prosthesis	30	Non-randomised comparative	Visual acuity, safety, activities of daily living, quality of life, orientation and mobility, spatial vision, stability of implant, system functionality	July 2014
NCT01860092 Countries not specified	Not yet open for recruitment	Argus II retinal prosthesis implantation	53	Case series	Safety, visual function, functional vision, device reliability	August 2018
NCT01490827 Multicentre (Germany, Italy)	Currently recruiting	Argus II retinal prosthesis	45	Case series	Nature and rate of adverse events, visual function	May 2016

Searched on 13 August 2013.

### Other issues

There are several conflicts of interest in the three studies included in this Brief. All three studies were derived from the same clinical trial sponsored by Second Sight Medical Products, Inc., the manufacturer of the Argus II Retinal Prosthesis System. Both authors of Barry and Dagnelie (2012)<sup>34</sup> disclosed affiliations with Second Sight Medical Products, Inc. The first author of Ahuja and Behrend (2013)<sup>32</sup> worked for Second Sight Medical Products, Inc. and later served as a consultant, and employees and consultants of Second Sight Medical Products, Inc. were involved with the design, data collection and analysis of this study. Finally, several of the authors of Humayun et al (2012)<sup>1</sup> have affiliations with the device manufacturer ranging from financial interests, stock options, receiving consulting fees, being employees of the company or being currently or previously employed by an institution that receives funding from Second Sight Medical Products, Inc.

There are several companies and academic institutions that are at various stages in the development of retinal prostheses with the aim of restoring light perception in blind individuals. Other devices being developed include: the Learning Retinal Implant (Intelligent Medical Implants AG, Zug, Switzerland), the Alpha IMS (Retina Implant AG, Reutlingen, Germany), the EPIRET3 retinal implant (Philipps University, Marburg, Germany), the Microelectrode-STIS (Osaka University, Osaka, Japan) and the Tübingen Retinal Implant

(University of Tübingen, Tübingen, Germany).<sup>35</sup> Of these devices, the Alpha IMS is CE marked; however, none have received United States FDA approval.

### **Summary of findings**

The evidence on the safety and effectiveness of the Argus II Retinal Prosthesis System considered in this Technology Brief is of a low level, being derived from the same group of 30 patients enrolled in the same phase two clinical trial. Given that the device is in its initial stage of assessment and the studies included in this Technology Brief are derived from the first clinical trial to assess the safety and efficacy of the device, the initial results are promising. All 30 patients who received the device have been using it at home, outside an outpatient clinical setting. In addition, patients performed significantly better in a range of tests concerned with orientation, navigation, guidance of fine hand movement and letter recognition when the system was on compared to when it was off, demonstrating that the prosthesis significantly improves visual acuity. Although, overall, a significant improvement in test results was observed with the system on compared to when it was off, there was a wide range in ability observed among the patients which indicates that the system may have more benefit for some patients than others. With respect to safety, the most common serious adverse events reported included conjunctival dehiscence and erosion, hypotony, retinal detachment and presumed endophthalmitis. The finding of no significant difference in full-field light stimulus light threshold at two years post-implantation between implanted and fellow eyes supports the notion that the Argus II implant has no harmful effect on remaining photoreceptor function, at least over the time period that was investigated in these studies (maximum follow-up of 2.7 years).

### **HealthPACT assessment**

Although the results from the studies included in this Technology Brief were promising, they were all derived from the same multicentre, phase II clinical trial of only 30 patients. HealthPACT therefore recommend that this technology be monitored for 24-months, in which time additional evidence may become available.

### **Number of studies included**

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the [HealthPACT web site](#).

Total number of studies 3

### **Search criteria to be used (MeSH terms)**

Retinitis pigmentosa (MESH) AND visual prosthesis (MESH) OR retinitis pigmentosa AND retinal prosthesis

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