

Artificial vision moving from science fiction to science fact

Competition heats up in quest to deliver first commercially available retinal chip

Dermot McGrath
in Paris

A QUICK Internet search of the terms “artificial vision” and “bionic eye” confirms what everyone working in this area of research already knows – namely, that the field of artificial vision is very much in the news these days.

While media hype will always run ahead of the reality, there is nevertheless a real sense that a certain critical mass has been attained and that the means are now in place to finally realise Benjamin Franklin’s 18th Century prediction of an artificial vision system.

The reason for the recent upsurge in interest in artificial vision is down to a combination of factors, according to Joseph Rizzo MD, co-director of the Boston Retinal Implant Project and director of the Centre for Innovative Visual Rehabilitation at the Boston VA Medical Centre.

“The first reason I think is just the natural desire to try to restore vision to the blind. Ophthalmologists as a general rule go into this discipline in order to help people who are visually impaired and yet the means for being able to do this for patients with neural damage or damage to the retina or optic nerve are severely limited or non-existent. So the notion that there is now an opportunity to be able to help patients with neural visual impairment is very compelling. Also, the availability of very sophisticated technology makes it feasible and credible that vision could be restored to these patients,” he said.

Dr Rizzo highlighted three principal accomplishments: the development of advanced engineering technology, the evolution of relatively safe surgical procedures to implant the devices and finally, the demonstration that the devices are relatively well tolerated by the human eye.

A race to market

With several research groups and companies around the world now working on retinal prostheses, there is increasing pressure on the interested parties to be the first to gain market approval for their devices.

While the regulatory approval process is long and expensive, most observers believe that a two to three year time frame is a reasonable expectation to see the first commercially available devices on the market. At least four companies to date – Intelligent Medical Implants AG, Optobionics, Second Sight Medical Products Inc and Retina Implants AG – have successfully implanted retinal devices in human subjects.

In the US, the FDA recently gave approval to Second Sight to enrol up to 20 retinitis pigmentosa (RP) patients to participate in three-year feasibility trials of the Argus II Retinal Implant, and studies of the device are ongoing in several centres in Europe and Mexico.

The Argus II consists of 60 independently controllable electrodes attached to the retina in the macular region and used in conjunction with an external camera mounted on a pair of eyeglasses and video processing system to provide a basic level of vision for implanted patients. The data from the camera and power are transmitted wirelessly in real-time to the implant.

At the ARVO meeting this year, lead investigator Mark Humayan MD presented six months’ follow-up on 17 patients implanted with the Argus II. There were no device failures and no explants. Major adverse events included conjunctival erosion in five patients, hypotony in four and endophthalmitis in three patients, all of which occurred within one month postoperatively and all of which resolved by the six-month endpoint. In terms of efficacy, 100 per cent of the subjects were reported as seeing phosphenes and significant improvements were reported in spatial localisation, motion detection, orientation and mobility and other measures.

In France, four patients have been implanted with the Argus II device and the early results have been encouraging, according to José-Alain Sahel MD.

“After about one year, the tolerance is good, the surgery is complex but feasible and there have been no serious complications. The device has provided patients with some ambulatory vision. They are now able to recognise a door or window, follow a white stripe on the ground and there are several tasks that they are able to perform. The results have also been improving over time as there is a learning curve with this device and the brain has to learn how to ‘see’ with it,” he said.

Learning Retinal Implant System

The Learning Retinal Implant System developed by IMI Intelligent Medical Implants GmbH is a three-part device comprising an epiretinal implant of 50 electrodes, special eyeglasses with integrated mini-camera and transmitter components for wireless signal and energy transmission, and a processor worn at the patient’s waist to replace the information processing function of the formerly healthy retina.

Early tests of the system in three RP patients demonstrated that the device was safe and well tolerated in the eye

up to six months after implantation and enabled participants to discriminate specific objects, distinguish light and recognise simple patterns such as a horizontal bar.

More extensive trials of the Learning Retinal Implant System are currently under way at several European centres and the initial results are encouraging, according to Gisbert Richard MD, one of the lead investigators of the study.

Dr Richard cautioned, however, against unrealistic expectations of the quality of vision that the current generation of retinal implants can deliver.

“The medical possibilities of retinal chip implantation are limited mainly due to retinal cell demise, as well as the shortcomings in the relaying of information, optic nerve atrophy and in the processing through the primary and secondary visual centres. There are also technical limitations regarding the number of electrodes, the processing of information and the fact that encoder technology, which processes, adapts and relays the received signal, is not yet far enough advanced. There are many aspects of this field that require intense research and will be receiving our full attention in the near future,” he said.

1,500 photodiodes on new subretinal chip

Another European group, Retina Implant AG, has developed a subretinal prosthesis drawing on the experience gained from over 14 years of work by a consortium led by Eberhart Zrenner MD from Tübingen. The core of the implant is a microchip of about 3.0mm diameter and 50µm thickness, in which 1,500 light-sensitive photodiodes amplifiers and electrodes are arranged. The microchip is connected to an external energy supply through a power connection that is implanted subdermally.

Pilot studies of the device were conducted in 11 RP patients between October 2005 and October 2008. The study period granted by the ethics committee was four weeks for the first eight patients and three months for the last three patients. The implants were well tolerated and there were no intraoperative or postoperative complications.

The implant yielded visual perceptions in eight of 11 patients through direct electrical stimulation, and in six of 11 patients through light-dependent stimulation on the photodiode, as reported by Prof Zrenner and his team at this year’s ARVO meeting in Florida. Investigators said that they were particularly impressed by the implant’s ability to restore useful vision to the

patients above and beyond that attained to date by rival devices. For the best case, a visual acuity exceeding legal limits of blindness was obtained.

“These experiments are the first proof of concept ever presented that electrical multi-local stimulation is able to restore useful vision up to reading capability,” said Florian Gekeler MD of the Tübingen group. “We noticed that the best results were obtained when the microchip was placed right under the macula where it can utilise all the power of the papillomacular bundle that is highly represented in the brain.”

“The Tübingen-study has proven that patients can regain useful vision with subretinal multielectrode arrays,” Prof Zrenner added and “that at least 1,000 electrodes in a 10-degree field are necessary to achieve such high spatial resolution to patients.”

He also said that research is currently ongoing to improve the longevity of the device in the eye so its benefits can be sustained beyond the time frame set by the ethics committee.

A stand-alone retinal device

A slightly different approach to the task of restoring vision to RP patients has been adopted by Alan Chow MD and his brother Vincent, an electrical engineer, co-inventors of the Artificial Silicon Retina (ASR). The ASR microchip contains approximately 5,000 micro-photodiodes each with its own stimulating electrode. These photodiodes are placed under the retina to convert light energy into electrochemical impulses that stimulate the remaining retinal cells.

Unlike other devices, the ASR microchip is self-contained, powered solely by incident light and does not require the use of external wires, batteries, headsets or ancillary computers. This has led to scepticism about the ASR chip from some quarters who believe that ambient light will never produce enough stimulation to provide a significant restoration of vision to blind patients.

The ASR chip has been implanted to date in 42 patients with RP. Although visual sensations have been noted by some patients at the location of the chip, Dr Chow told *EuroTimes* that the most exciting development has been the occurrence of what appears to be a neurotrophic rescue effect, resulting in a degree of vision recovery that has included visual acuity, contrast and colour perception, and expansion of the visual field.

“Additional animal studies have shown up-regulation of specific neurotrophic rescue factors resulting from ASR chip



José-Alain Sahel



Gisbert Richard



Eberhart Zrenner



Florian Gekeler



Alan Chow

stimulation. This begs the question of whether it is better to produce prosthetic vision using phosphenes like most of the devices currently being developed, or rather to use a prosthesis in order to stimulate the retina to recover vision that has been lost and to prevent further deterioration. While we were the first proponents of a prosthetic-phosphene type approach, based on what we have seen so far, the recovery of normal vision, such as colour vision, central visual acuity and contrast perception is really what patients prefer and that is what we are seeking to achieve," he said.

Facing financial problems, the original Optobionics Corporation has stopped operations. However, Dr Chow has acquired the Optobionics name and the Artificial Silicon Retina (ASR) implants and will be reorganising a new company under the Optobionics name.

The road ahead

Although researchers are optimistic about the future of retinal implants in the treatment of RP, as well as other diseases such as dry age-related macular degeneration, many issues remain to be resolved if the implants are to deliver on their promise.

"I do not believe that it is a foregone conclusion that vision will improve with further improvement in technology," warned Dr Rizzo. "I think it is likely, but I believe that the burden of proof remains on the researchers to demonstrate that greater visual capability can be delivered. Of course, to enable a blind person to distinguish light, shadows

or basic shapes is already a major accomplishment and that should not be underestimated. However, it is probably fair to say that the level of vision that has been reported from various groups is not at the level that had originally been hoped for," he said.

Looking further ahead, Prof Kevin Warwick, professor of cybernetics at the University of Reading, UK, said that the current generation of retinal chips and cochlear implants represent the vanguard of a broad spectrum of devices that will be implanted into the human body in the future. "The whole field is improving, whether it is power delivery, surgical techniques, miniaturisation, longevity of the device or biocompatibility, and that progress will continue. While the focus now is on solving problems – for instance, restoring eyesight to the blind or hearing to the deaf – I think in the future we'll see implants that will push the boundaries further and will seek to enhance our existing capabilities beyond the purely therapeutic applications that we are seeing today," he said.

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Key moments in the history of artificial vision

1751: Benjamin Franklin's famous "kite and key" experiment in 1751 leads him to predict the creation of artificial vision.

1929: German neurologist Otfried Foerster reports that stimulating the human visual cortex led to the perception of spots of 'light'.

1960s: Giles S Brindley of the University of Cambridge attached 80 electrodes to miniature radio receivers and implanted them into the brain of a blind patient. The patient reported seeing phosphenes (flashes of light).

1970s: William Dobbelle began experiments with cortical stimulation in human volunteers.

2000: First implantation of the Artificial Silicon Retina (ASR) device in humans by Alan Chow MD.

2008: First proof of letter reading capability in retinitis pigmentosa patient (subretinal implant with 1500 microphotodiodes, University of Tübingen, Germany).

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