Retinal Prosthesis Technology

Clinical trials demonstrate that both epiretinal and subretinal approaches provide visual function to blind patients.

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Two approaches to retinal prothesis implants are currently being studied by investigators: epiretinal and subretinal implants. The epiretinal approach involves placing a chip on top of the macular region of the retina and requires additional extraocular equipment, such as cameras or special glasses. The subretinal approach involves implanting the chip underneath the retina, specifically in the macular region. This article provides an overview of these approaches, with a focus on two retinal prosthesis technologies currently being studied in clinical trials.

EPIRETINAL APPROACH: SECOND SIGHT

The Argus II (Second Sight Medical Products, Inc., Sylmar, CA) is the second generation of an electronic retinal implant designed for the treatment of blindness due to retinitis pigmentosa (RP). The implant consists of a 60-electrode grid that is attached to the retina and used in conjunction with an external camera mounted in eyeglasses to provide a rudimentary form of sight to implanted patients. A wireless microprocessor and battery pack worn on the patient's belt powers the device. The implant is reportedly designed to last a lifetime but can be safely removed if necessary.

The camera on the glasses captures an image and sends the information to the video processor, which converts the image to an electronic signal and sends it to the transmitter on the spectacles. The implanted receiver wirelessly receives this data and sends the signals through a tiny cable to the electrode array, stimulating it to emit electrical pulses. The pulses induce responses in the retina that travel through the optic nerve to the brain, which perceives patterns of light and dark spots corresponding to the electrodes that are stimulated. Although the restored vision is not normal, patients learn to interpret the visual patterns produced into meaningful images.

"For normally sighted people, photoreceptors convert light into an electrical signal for the rest of the retina," Brian Mech, PhD, MBA, Vice President of Business Development for Second Sight, said in an interview with *Retina Today*. "For these [RP] patients, the photoreceptors are dead, so we are supplying the electrical signals directly, based on what the camera is seeing.

"The major advantage of the epiretinal device is that it is a very safe surgical approach to the retina," Dr. Mech continued. "Also, because we capture the video signal with a camera, we have the ability to do image processing, in order to enhance the functional vision outcome. Examples of this include zoom, edge detection, contrast enhancement, and many other more complex algorithms."

In 2002, Second Sight launched a trial of the company's first generation epiretinal prosthesis, the Argus I, under an Investigational Device Exemption at the Doheny Eye Institute at the University of Southern California. This 16-electrode device was implanted in six patients with RP between 2002 and 2004. The prosthesis enabled these patients to detect when lights were on or off, describe an object's motion, count discrete items, and locate and differentiate basic objects in an environment. Five of the six patients went on to use the retinal prosthesis at home.

In 2006, Second Sight began a study of the Argus II, a second-generation retinal prosthesis with 60 electrodes. The trial is currently under way. Thirty-two patients, including 14 in the United States, have been enrolled at 11 sites in five countries (France, Mexico, Switzerland, and the United Kingdom). It is the only clinical study of a chronically implanted active prosthesis that is used routinely, even out of the clinic and in the homes or places of business of the users. Other such studies so far have been only of short duration with relatively infrequent use, and then only in the clinic, Dr. Mech told *Retina Today*.

Interim results showed significant improvements in orientation and mobility measures for the trial participants, including their ability to walk in outdoor environments. Individuals were frequently able to locate a door up to 20 feet away and walk to the end of a 20-foot line drawn on the floor. Recent data also indicated that the majority of the trial participants were able to identify large letters and some could even read words with the Argus II.

Perhaps more important, the device has had an impact on the participant's lives in ways that were not even imagined prior to the study and are difficult to quantify. "We have subjects that have watched fireworks, and Christmas lights, and their grandchildren playing sports," Dr. Mech said. "Some subjects use the device to walk in the park, shoot baskets, find the bus stop, and avoid collisions with people and objects. Until you get these devices to people for them to use in their everyday life, you just don't realize what they can do. The comment that we hear most often is that our Argus II users feel 'more connected' to their environment."

Second Sight intends to launch the Argus II commercially in Europe later this year.

SUBRETINAL APPROACH: RETINA IMPLANT AG

Retina Implant AG (Reutlingen, Germany), a start-up company founded in 2003, is developing a subretinal prosthesis for visually impaired patients who have lost their photoreceptors due to diseases such as RP. The chip is placed underneath the retina in the macular region at the point where light-sensitive photoreceptor cells are found in normally sighted individuals. A wireless power supply is implanted below the skin behind the ear. All of the implant is embedded in silicone except for the stimulating chip. The right half of the implant is placed beneath the retina; the left, thicker part is sewn from the outside onto the eye and is covered by the conjunctiva.

The core of the implant is a 1,500-pixel microchip approximately 3 mm in diameter and 50 µm thick. The size of one pixel is approximately 70 x 70 μm^2, yielding a visual field of 10° and allowing mobility and object recognition in space. Each pixel field contains a photocell, an amplifying circuit, and a stimulating electrode. The photocells absorb light falling into the eye and transform it into electrical energy. This energy serves to control external source energy and stimulate the intact nerve cells in the retina. The nerve impulses from these cells are then led via the optic nerve to the visual cortex, leading to impressions of sight. The chip is light sensitive within 5 decades of illumination, allowing patients the ability to adapt to relatively dim light.

Retina Today recently interviewed Walter G. Wrobel, PhD, President and CEO of Retina Implant, about the company's first human trial with this technology. According to Dr. Wrobel, Retina Implant initiated its first clinical pilot study of the subretinal implant in 2005. At present, 11 patients have been implanted with the subretinal prosthesis for periods of time ranging from 4 weeks to several months. Dr. Wrobel said that in the future the device would be implanted permanently, meaning for several years.

"The first patients were able to see a single phosphene, an electrically excited visual sensation," Dr. Wrobel said. "Interestingly, the phosphenes were remarkably similar among the patients, small spots in the distance of about 50 cm. The first patients were also able to see horizontal or vertical bars. In later patients, the 1,500-pixel chip was used. These patients were able to identify objects, such as an apple and a banana, see the difference between a knife and a spoon, locate a plate or a pencil on the table, and tell time from a clock."

Additionally, patients considered totally blind according to German law distinguished white letters 4 to 8 cm high at a distance of 30 to 40 cm on a black background, Dr. Wrobel said. Also, patients were able to see objects and shapes so clearly that they could combine letters to form words and recognize foreign objects. One patient, who had been blind for 15 years, promptly told investigators that his name was misspelled when asked to read it.

Dr. Wrobel attributes this success to the position and placement of the device. "Our implant is positioned subretinally, where there is a retinotopically correct excitation. This means that if there is light falling onto this area, at the same position electric excitation is generated because the photoreceptors are normally below the retina. From the photoreceptors, all of the ganglion cells and bipolar cells are then going to the surface of the retina and are bundled into the optic nerve, creating electrically excited visual sensations. The electrical excitation is then a 1:1 replacement of the lost photoreceptors."

Retina Implant has started a second trial, Dr. Wrobel noted. "The pilot study is finished, and we are starting a new main clinical study in five centers in Europe with a device that does not require a cable-bound external power supply like the one we have used up to now," he told *Retina Today*. The trial will involve several phases, beginning with six patients, and advancing to 10 and then 15, with milestones in between each phase in which the company will decide if the results are acceptable.

"We have learned from our patients, that they consider these visual results as a major breakthrough to a really useful device, and they call me regularly asking for a date for the next implantation." ■