

# Feasibility Study of a Retinal Prosthesis

## Spatial Vision With a 16-Electrode Implant

Avi Caspi, PhD; Jessy D. Dorn, PhD; Kelly H. McClure, MS; Mark S. Humayun, MD, PhD; Robert J. Greenberg, MD, PhD; Matthew J. McMahon, PhD

**Objective:** To demonstrate that an epiretinal prosthesis can produce patterned visual perception in patients blinded by photoreceptor degeneration who have no other treatment options.

**Methods:** A totally blind subject with retinitis pigmentosa had a 16-electrode epiretinal prosthesis implanted. The implant is controlled wirelessly by an external computer or a head-mounted video camera. Spatial vision was assessed by measuring the subject's response to direct stimulation of patterns and by comparing the ability of the subject to identify the orientation of gratings with the system on and off.

**Results:** In response to stimulation of 2 orthogonal rows of electrodes, the subject drew 2 lines with a mean (SEM)

angle of 87.4° (1.8°) between them. With the system on, the subject identified the orientation of the grating target up to a spatial resolution that matches the spacing between the adjacent electrodes. In contrast, with the system off, the subject could not detect or identify the target's orientation.

**Conclusion:** Synchronized stimulation of different retinal locations with an epiretinal prosthesis implanted long-term can produce spatial vision with an acuity level determined by the distance between the electrodes.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00279500

*Arch Ophthalmol.* 2009;127(4):398-401

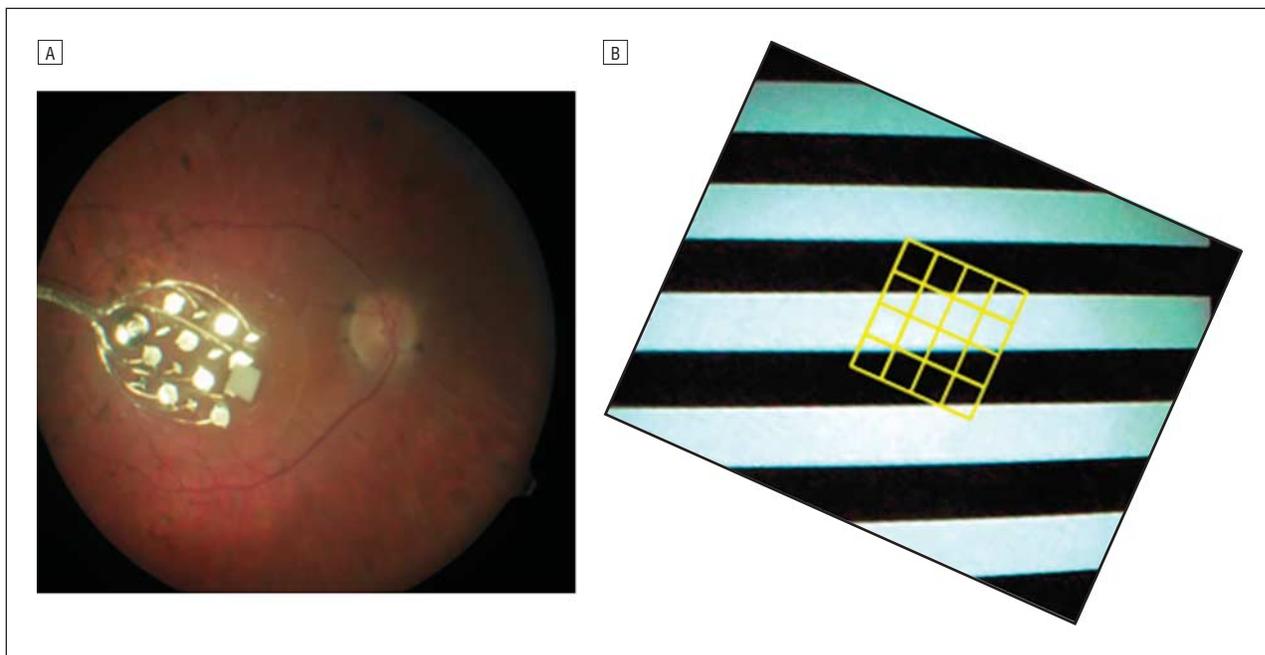
**E**LECTRICAL STIMULATION OF the retina can restore light perception to subjects blinded by degenerative retinal diseases that damage the photoreceptors, such as retinitis pigmentosa or macular degeneration.<sup>1</sup> To generate a patterned image, such an implant uses an array of independently controllable electrodes, each stimulating a different area of the retina to create the perception of light in different locations in the visual field. Although retinal prosthesis research and development have progressed greatly over the years,<sup>2-4</sup> owing to the small number of subjects with visual prostheses implanted long-term, it had previously not been shown that the brain can perceive a useful spatial image through stimulation of different retinal locations.

The feasibility of a retinal prosthesis to restore vision is currently under investigation in 5 clinical trials. The 16-electrode epiretinal implant from Second Sight Medical Products, Inc, Sylmar, California, has been implanted long-term in 6 subjects in the United States for more than 5 years, and this is the only study with subjects using the full system in their homes (clinicaltrials.gov identifier: NCT00279500; active, not recruiting). Intelligent Medical Implants GmbH, Bonn, Germany, described 4 subjects with an implanted 49-electrode epireti-

nal array in a trial designed to last 18 months<sup>5</sup> (clinicaltrials.gov identifier: NCT00427180; recruiting). The EPI RET3 25-electrode epiretinal array was implanted for 4 weeks in 6 blind subjects<sup>6</sup> (clinical trial: DE/CA21/A07). A subretinal implant composed of a 1550-microphotodiode array and a 4 × 4-electrode array from Retina Implant AG, Reutlingen, Germany, was implanted in 8 subjects for 4 weeks<sup>7</sup> (clinicaltrials.gov identifier: NCT00515814; recruiting). Second Sight is conducting another long-term clinical trial of a new-generation permanent implant that consists of 60 electrodes (clinicaltrials.gov identifier: NCT00407602; recruiting).

We report the visual performance of a totally blind subject with an implanted first-generation 16-electrode Second Sight retinal prosthesis<sup>1,8</sup> to determine whether his spatial vision could approach the level expected from the spacing between the electrodes in this early prototype. Subjects with the implant experience visual perception as a result of electrical stimulation and are able to perform simple visual tasks such as locating and counting objects.<sup>9</sup> We describe a novel measurement of the visual acuity subserved by the retinal prosthesis and quantify the increase in visual acuity performance obtained by stimulating the retina with higher numbers of electrodes.

**Author Affiliations:** Second Sight Medical Products, Inc, Sylmar (Drs Caspi, Dorn, Humayun, Greenberg, and McMahon and Mr McClure) and Doheny Eye Institute, Los Angeles (Dr Humayun), California.



**Figure 1.** Implanted 16-electrode array. A, Fundus image of the implanted 16-electrode array. The 260- and 520- $\mu\text{m}$  diameter electrodes were arranged in a checkerboard pattern with center-to-center spacing of 800  $\mu\text{m}$ . B, A frame captured from the video camera during the grating acuity experiment. The yellow lines mark the visual field mapped to each of the electrodes.

## METHODS

This study was granted an investigational device exemption by the US Food and Drug Administration and was approved by the institutional review board of the University of Southern California, Los Angeles. This research adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained, which explicitly stated the investigational nature of both the system and the surgery.

Measurements were carried out on a single subject who had severe retinitis pigmentosa with no light perception and was aged 55 years on the date of the implantation (the only subject active in the follow-up study who was available for testing). Prior to implantation, the subject's level of vision was determined to be no light perception based on a failure to detect any targets during dark-adapted static and kinetic confrontation perimetry and nonrecordable full-field visual evoked potentials and electroretinograms (flash and flicker) in both eyes. The subject received the implant on June 23, 2004, and the results described here were collected between January and August 2007.

The implant consisted of an electronic case and an intraocular stimulating array. The implanted electronic case, a modified version of the Clarion C-1 (Advanced Bionics, Valencia, California), was surgically implanted into the temporal bone as in the cochlear implant.<sup>10</sup> Data and power were transmitted to the implant via a 49-MHz inductive wireless link using an external antenna magnetically aligned over the electronic implant. A 16-wire cable ran from the electronic case along a channel drilled along the skull to the orbit. The cable then passed into the orbit through the sclera to the electrode array on the surface of the retina. The intraocular stimulating array contained 16 platinum electrodes in a 4  $\times$  4 arrangement fixed in a clear silicone rubber platform.

The array was positioned over the macula and attached to the surface of the retina using a retinal tack (**Figure 1**). The stimulation signal sent to each electrode is independently controlled by an external video processing unit. Real-time video captured by a miniature video camera mounted on the subject's glasses is continuously sampled by the video processing

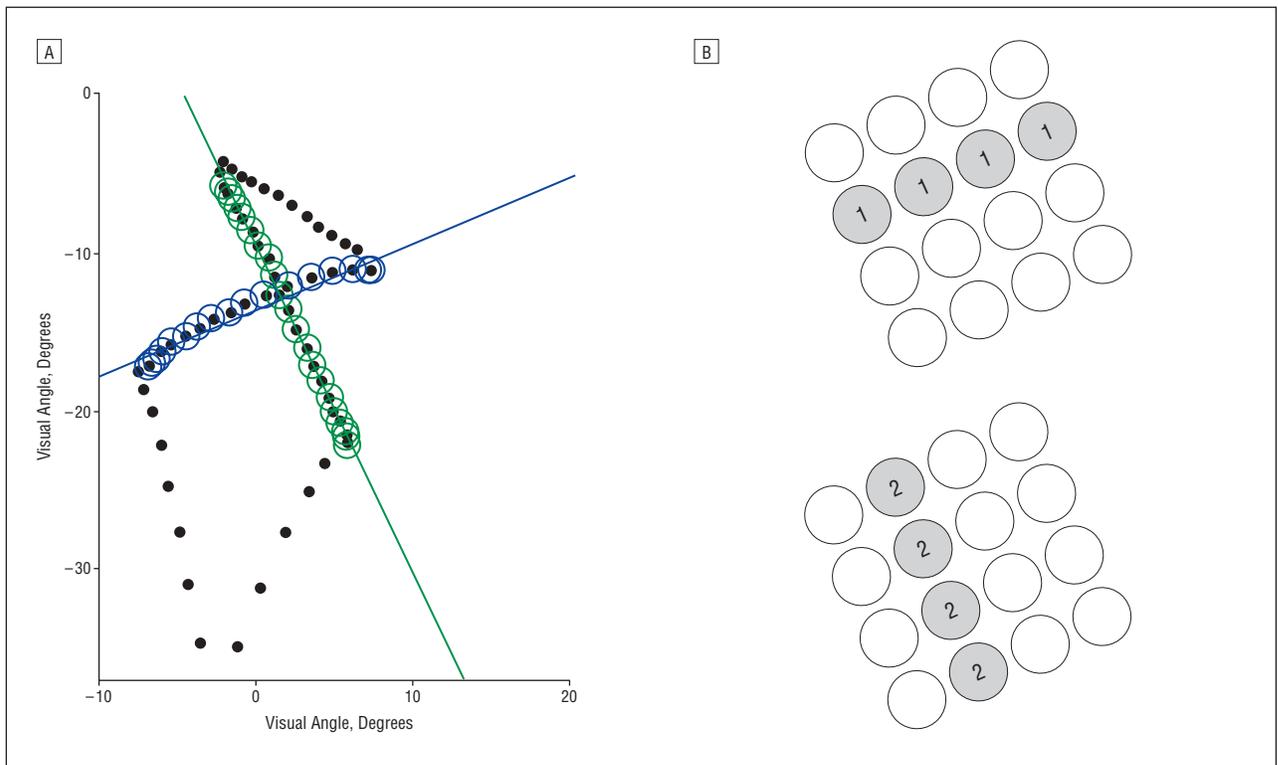
unit and the stimulation current amplitude in each electrode is matched to the brightness at the corresponding area of the scene. The sensitivity of subjects to stimulation of individual electrodes is affected by many factors<sup>9</sup>; this subject's stimulation threshold for the most sensitive electrode was 16 microcoulombs ( $\mu\text{C}$ ) and the threshold for the least sensitive electrode was 28  $\mu\text{C}$ . The camera zoom is set so that the field of view approximates the angle subtended by the electrode array on the retina. The system can also be operated in direct stimulation mode, where the stimulation pattern sent to each electrode in the array is determined by an external computer instead of by the acquired video image.

Video was recorded with a video splitter (Video Accessory Corp, Boulder, Colorado) and a digital video recorder (Archos 704; Archos, Igny, France). In the grating acuity experiment, images were presented on a 20-in liquid crystal display monitor (Dell 2007FP; Dell, Inc, Round Rock, Texas).

## RESULTS

### EXPERIMENT 1: ORIENTED PATTERNS

The first experiment tested whether the retinal prosthesis could generate a percept of oriented contours. In each trial, direct stimulation mode (sending stimulation directly to the electrodes from a computer, bypassing the camera) was used to stimulate a single row of 4 electrodes for 1 second followed by a 1-second blank interval and then stimulation of a single column of 4 electrodes for 1 second while the subject maintained fixation straight ahead. Immediately after the second stimulus ended, the subject was instructed to use a bright marker to draw the pattern that he perceived on a board placed at arm's length in front of him. Using the system's head-mounted camera, we recorded video of the subject moving the marker on the board. An off-line single-particle



**Figure 2.** Measured visual percept as drawn by the subject after stimulation of a row of electrodes followed by stimulation of a column of electrodes (A), with the schematics of the electrodes stimulated during the experiment (B).

tracking program located the position of the marker in each video frame. Because the camera is fixed to the subject's head, the resulting measurements track the subject's description of the 2-dimensional spatial position of the percepts in head-centered coordinates. **Figure 2** shows the stimulation pattern and the results of a single trial. In all of the trials ( $n=14$ ), the subject drew 2 lines with a mean (SEM) angle of  $87.4^\circ$  ( $1.8^\circ$ ) between them. These results clearly demonstrate that the brain can identify spatial forms that are determined by the retinotopic organization of electrical stimulation of electrodes in the stimulating array. Furthermore, this pattern recognition is possible without the benefit of head scanning.

#### EXPERIMENT 2: VISUAL ACUITY

In a second experiment, we measured the resolution limit of the prosthesis by requiring the subject to report the orientation of high-contrast square-wave gratings. In this experiment, the electrode stimulation pattern was determined in real time using the image acquired by the head-mounted video camera. In each session, high-contrast gratings of different spatial scales (2.77-2.00 logMAR; Snellen equivalent 20/11 777-20/2000) were randomly interleaved. Each grating was presented on a computer monitor for 5 seconds, during which time the subject could scan the image using head movements. The subject was then required to choose 1 of the 4 possible orientations (4 alternative forced choice: horizontal, vertical, diagonal to the right, or diagonal to the left). The detection probability was calculated separately for each spatial scale and a logistic psychometric function was fit to the data with 2 free para-

eters, maximum performance level and threshold (cut-off) spatial frequency. The results are reported in both logMAR and units scaled to the horizontal field of view of the array. With the system off, the subject's performance was not significantly better than chance for all of the spatial frequencies tested (11 of 40 correct for 1.6 logMAR, 14 of 40 correct for 2.0 logMAR, and 14 of 40 correct for 2.5 logMAR;  $P > .05$  for all of the conditions). With the system on, the subject performed significantly above the chance level of 25% (69 of 108 trials correct;  $P = 1.4 \times 10^{-17}$  according to the binomial distribution) for grating spatial frequencies up to the critical sampling frequency (Nyquist limit) of the  $4 \times 4$  electrode array (2.21 logMAR or 2 cycles/array) (**Figure 3A**). When analyzed separately, performance for all of the 4 orientations was above chance for all of the trials up to 2.21 logMAR (95% for horizontal, 63% for diagonal left, 93% for diagonal right, and 93% for vertical). At the critical sampling frequency, each black and white bar of the grating falls on 1 row of electrodes. The resolution limit was therefore well matched to the spacing of the electrodes and performance dropped to chance levels for finer gratings (Figure 3).

To test whether the spatial resolution provided by the system was determined by the fineness of the spacing of the electrodes, we artificially reduced the resolution of the array by stimulating groups of 4 electrodes together while keeping the field of view constant. This effectively created a  $2 \times 2$  array (4 "pixels" total), reducing the resolution of the system by half and the corresponding sampling frequency to 1 cycle/array. The performance of the subject for the simulated  $2 \times 2$  array is shown in Figure 3B. As expected, the subject's performance with the reduced resolution mapping

dropped to chance levels at a spatial frequency twice as low as the original  $4 \times 4$  array. When analyzed separately, performance for all of the 4 orientations with the simulated  $2 \times 2$  array was above chance for all of the trials up to 2.52 logMAR (86% for horizontal, 73% for diagonal left, 68% for diagonal right, and 69% for vertical).

Finally, when the structure in the stimulation pattern was decoupled from the video image entirely by arbitrarily associating an area in the image to an electrode in the array (ie, scrambling the video image to the electrode map), performance decreased to chance for all of the spatial frequencies tested (Figure 3C). Because the field of view is identical for all 3 conditions, a specific video input stimulus will stimulate the retina with equal total current levels in the 3 conditions. The only difference between the 3 conditions is the spatial modulation within the electrode array. Arbitrarily mapping the electrodes to areas of the video image reduces the performance to chance, whereas mapping the retinotopic location of each electrode to the corresponding section of the video image results in visual acuity well matched to the retinal prosthesis electrode spacing.

### COMMENT

We have demonstrated that stimulation of different retinal locations by a long-term epiretinal prosthesis results in the perception of spatial patterns without the benefit of head scanning. The finding that the resolution limit is well matched to the spacing of electrodes in the stimulating array provides strong evidence that the brain perceives a patterned image and not the average brightness resulting from the overall level of stimulation and further suggests that the development of retinal prosthesis systems with more electrodes should provide higher-spatial-resolution vision to blind subjects.

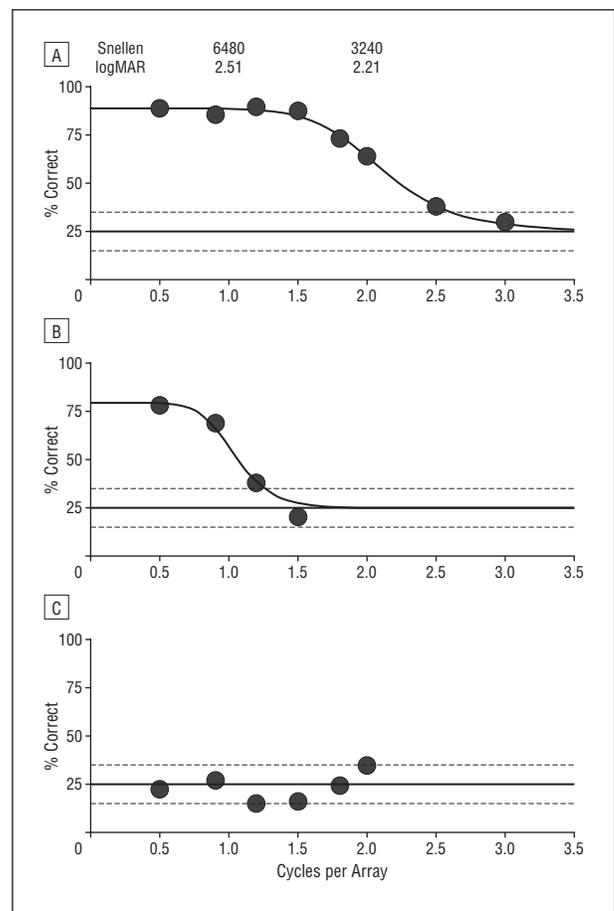
Although the experimental results reported here are from a single subject with a prototype system implanted, these psychophysical measurements conclusively illustrate the spatial capabilities of an epiretinal prosthesis. As additional subjects receive implants of higher-resolution devices, these results will be confirmed and extended to determine how factors such as the state of disease progression, perceptual learning, and improvements in surgical technique and system design contribute to prosthesis-based visual perception.

**Submitted for Publication:** August 29, 2008; final revision received December 23, 2008; accepted December 31, 2008.

**Correspondence:** Matthew J. McMahon, PhD, Second Sight Medical Products, Inc, 12744 San Fernando Rd, Bldg 3, Sylmar, CA 91342 (mm@2-sight.com).

**Financial Disclosure:** Drs Caspi, Dorn, Greenberg, and McMahon and Mr McClure are employees of Second Sight Medical Products, Inc, and Dr Humayun is a consultant for Second Sight Medical Products, Inc. All have stock options. Drs Humayun and Greenberg are also investors in Second Sight Medical Products, Inc.

**Funding/Support:** This work was supported by grant EY012893 from the National Institutes of Health.



**Figure 3.** The percentage correct for the grating acuity task is well matched to the spatial sampling of the electrode array. A, Standard mapping. The stimulation current sent to each electrode is determined by the corresponding area in the video image. B, Reduced-resolution mapping. The video image is mapped to groups of 4 electrodes that are identically stimulated, creating a  $2 \times 2$  array with half of the sampling frequency. C, Arbitrary mapping. The current level sent to each electrode is mapped to a random pixel in the image. A solid line indicates the chance level (25%) and the dashed lines indicate the 95% confidence interval for 72 trials according to the binomial distribution.

### REFERENCES

- Humayun MS, Weiland JD, Fujii GY, et al. Visual perception in a blind subject with a chronic microelectronic retinal prosthesis. *Vision Res.* 2003;43(24):2573-2581.
- Tassiker GE, inventor. *Retinal stimulator*. US patent 2,760,483. August 28, 1956.
- Zrenner E. Will retinal implants restore vision? *Science.* 2002;295(5557):1022-1025.
- Wickelgren I. Biomedical engineering: a vision for the blind. *Science.* 2006;312(5777):1124-1126.
- Richard G, Keserue M, Feucht M, Post N, Hornig R. Visual perception after long-term implantation of a retinal implant. *Invest Ophthalmol Vis Sci.* 2008;49:E-abstract 1786.
- Walter P, Mokwa W, Messner A; EPI RET3 Study Group. The EPI RET3 wireless intraocular retina implant system: design of the EPI RET3 prospective clinical trial and overview. *Invest Ophthalmol Vis Sci.* 2008;49:E-abstract 3023.
- Gekeler F, Sachs H, Szurman P, et al. Surgical procedure for subretinal implants with external connections: the extra-ocular surgery in eight patients. *Invest Ophthalmol Vis Sci.* 2008;49:E-abstract 4049.
- de Balthasar C, Patel S, Roy A, et al. Factors affecting perceptual thresholds in epiretinal prostheses. *Invest Ophthalmol Vis Sci.* 2008;49(6):2303-2314.
- Yanai D, Weiland JD, Mahadevappa M, Greenberg RJ, Fine I, Humayun MS. Visual performance using a retinal prosthesis in three subjects with retinitis pigmentosa. *Am J Ophthalmol.* 2007;143(5):820-827.
- Papsin BC, Gordon KA. Cochlear implants for children with severe-to-profound hearing loss. *N Engl J Med.* 2007;357(23):2380-2387.