Visual Performance Using a Retinal Prosthesis in Three Subjects With Retinitis Pigmentosa

DOUGLAS YANAI, JAMES D. WEILAND, MANJUNATHA MAHADEVAPPA, ROBERT J. GREENBERG, IONE FINE, AND MARK S. HUMAYUN

PURPOSE: To assess visual task performance in three blind subjects implanted with epiretinal prostheses.

DESIGN: Prospective, investigational device exemption trial.

METHODS: Three subjects with light perception or no light perception vision were enrolled at a single center. All subjects had retinitis pigmentosa (RP). Main inclusion criteria: light perception or worse vision in one eye and some visual experience as an adult before blindness. Main exclusion criteria included other ophthalmic problems. A prototype retinal prosthesis was implanted in the eye with worse light sensitivity. The prosthesis had a 4 × 4 array of platinum electrodes tacked to the epiretinal surface. The prosthesis was wirelessly controlled by a computer or by a head-worn video camera. Visual function testing was performed in single masked or double masked fashion. Scores from the visual task were compared to chance to determine statistical significance.

RESULTS: The subjects performed significantly better than chance in 83% of the tests. Using the video camera, subjects scored as follows on simple visual tasks: locate and count objects (77% to 100%), differentiate three objects (63% to 73%), determine the orientation of a capital L (50% to 77%), and differentiate four directions of a moving object (40% to 90%). A subset of tests compared camera settings using multipixels vs single pixels. Using multipixel settings, subjects performed better (17%) or equivalent (83%) in accuracy and better (25%) or equivalent (75%) in reaction time.

CONCLUSIONS: Three RP implant subjects used epiretinal prostheses to perform simple visual tasks. Multipixel settings proved slightly more effective than single pixel settings. (Am J Ophthalmol 2007;143:820–827. © 2007 by Elsevier Inc. All rights reserved.)

HEREDITARY RETINAL DEGENERATIVE DISEASES, such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD), result in blindness for a significant number of people.1,2 Ten years from now, the incidence of AMD among people older than age 65 may be as high as 5.5%.3 Although RP is less common, it has an incidence rate of approximately one in 3,500 births in the United States, and therefore affects more than 100,000 people.4 Increasing lifespans within the United States and other countries mean these progressive, degenerative diseases will affect more and more individuals.

Implantable microelectronic prostheses designed to stimulate the neural retina, optic nerve, or visual cortex have been proposed as a therapy for patients with AMD and RP.5,6 In both these diseases, degeneration occurs within the outer retina with subsequent remodeling of the inner retina. Cell morphometry studies have shown that the cells of the inner retina survive at a higher rate vs those of the outer retina.7–11 However, in response to the loss of the sensory retina, the inner retinal cells are significantly modified both in their synaptic organization and their location.12 Although acute and chronic studies have both demonstrated that electrical stimulation can reliably produce visual percepts, it still needs to be determined to what extent these prostheses can be used as a substitute for natural vision in improving the daily lives of blind people.13–16 Here we show that three blind test subjects, chronically implanted with epiretinal stimulators, can successfully make simple visual discriminations in a controlled environment.

METHODS

This study protocol was granted an investigational device exemption by the US Food and Drug Administration and was approved by the Institutional Review Board at the University of Southern California. This research adhered to the tenets of the Declaration of Helsinki. The trial is registered at the National Institutes of Health (trial identifier NCT00279500).

SUBJECT SELECTION: Three subjects with severe retinitis pigmentosa participated in the study (Table 1). One of the subjects had no light perception (S1), and two of the subjects had light perception only (S2 and S3). After
TABLE 1. Age and Visual History of the Three Retinal Prosthesis Test Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age, Gender</th>
<th>Diagnosis</th>
<th>VA Implanted/ Fellow Eye</th>
<th>Years With Lowest VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>74, M</td>
<td>RP</td>
<td>NLP/LP</td>
<td>20 years</td>
</tr>
<tr>
<td>S2</td>
<td>55, F</td>
<td>RP</td>
<td>LP/LP</td>
<td>5 years</td>
</tr>
<tr>
<td>S3</td>
<td>71, F</td>
<td>RP</td>
<td>LP/LP</td>
<td>15 years</td>
</tr>
</tbody>
</table>

VA = visual acuity; M = male; F = female; RP = retinitis pigmentosa; NLP = no light perception; LP = light perception.

informed consent, we carried out a series of standard preoperative ophthalmologic tests to confirm each of the subject’s visual acuity and assess their general ophthalmologic health. The informed consent explicitly stated the investigational nature of both the study and the surgery and emphasized that there was no expected short- or long-term benefit. The preoperative evaluation included a regular eye exam, an electroretinogram, a visual-evoked potential, bright flash detection, kinetic perimetry, and electrically evoked responses, fluorescein angiography, and fundus photography. In all three subjects, the worse eye had a bright flash detection threshold greater than ambient indoor lighting. Using the worse eye, the subjects could not localize a bright light source in the kinetic perimetry task. The prosthesis was always implanted in the worse of the subjects’ two eyes. Details of the surgical procedure have been described previously. At the time of data analysis, S1 had been implanted for 18 months, S2 for 15 months, and S3 for seven months. A thorough data analysis was performed at this point in the clinical trial to evaluate the testing protocols and to consider expanding the trial. The trial has since been expanded to an additional three subjects and the testing tools were updated to improve the efficiency of the testing. This expansion of the trial provided a logical point at which to report the initial testing results from specific experiments in the first three subjects, because subsequent testing has used different tools and methods.

During the study period delineated previously, one complication did occur in S2, who underwent surgery twice on the same eye because her retinal array became separated from her retina 11 months after initial surgery because of falling and bumping her head. No retinal detachment occurred at the time of her accident and in the second surgery, the array was reattached. Data collected before and after the incident had similar results.

Visits for testing lasted a maximum of four hours each with frequent rest breaks. The number of visits was limited by the subjects’ availability and by the protocol. For geographic reasons, S1 could have only limited participation for some experiments (the subject lives on the East coast, approximately 5,000 km from the test site in Los Angeles, California, USA). In general, the subjects were tested at five to 10 visits per month.

OPERATION OF THE PROTOTYPE RETINAL PROSTHESIS SYSTEM: A custom camera system or a custom computer interface was used to wirelessly transmit image data to an implanted stimulator. The implanted stimulator consisted of an electronics case, an intraocular stimulating array, and a cable connecting these two components. The intraocular stimulating array had 16 platinum electrodes in a 4 × 4 arrangement (Figure 1) fixed in a clear silicone rubber platform. For all subjects, the center-to-center electrode spacing (Figure 1, Right) was 800 μm. In S1 and S2, the electrode diameter (Figure 1, left) was 520 μm (1.6 degree) and in S3, the electrode diameter was 260 μm (0.8 degree). The electrodes covered a 2.9 H × 2.9 W (S1, S2) or 2.65 H × 2.65 W (S3) mm² area of the retinal surface. The electronics case, which converts a wireless signal from the camera into electrical stimulation patterns, was surgically implanted into the temporal bone, similar to that of a cochlear implant. A 16-wire cable ran from the electronics case in a channel drilled along the skull to the orbit. The cable passed into the orbit, through the sclera, and to the electrode array.

The impedance and detection thresholds for individual electrodes were measured frequently to confirm device integrity and interface stability. These data have been reported previously. False-positive rates for threshold testing were very low for these subjects (approximately 5%, as reported by Mahadevappa M, et al. IOVS 2003;44: ARVO E-Abstract 5059). In the functional tests that used more than one electrode, an effort was made to make the stimulation produced by each electrode as comparable as possible with respect to brightness, color, and size. Percepts were yellow or white, and were small round or oblong shapes. The subjects’ unoperated eye was patched during all tests to ensure that their performance was not being aided by residual vision in that eye. The implant was only activated in the clinic.

For all experiments described in the following section, the subjects were first given training with auditory and tactile feedback and then tested on their ability to perform the task. During training, the subjects were told what they were viewing and encouraged to find and touch objects when applicable. During training, small adjustments were made to the brightness of each electrode. In all experiments described, the subjects were trained to only give answers from a limited number of alternative choices, so a two choice test is labeled as 2altFC, which means a two alternative forced-choice test.

STIMULUS GENERATED DIRECTLY BY COMPUTER: In these experiments, the desired stimulation pattern was generated using the computer interface, thus permitting precise control over the stimulation presented to the subject. These tests were conducted in a double-masked
fashion by two researchers/operators. The computer operator (who did not speak to the subjects during testing) knew the trial sequence during each test session (e.g., whether a row or column was presented). The data recorder instructed the computer operator and subject to start the trial, and gave the subject verbal encouragement to complete the task, but did not provide feedback with respect to the subject’s performance in the task.

Experiment 1: electrode discrimination. For each trial, the subjects were asked to discriminate between two electrodes based on the percept location in the visual field. Two electrodes that were either vertically or horizontally aligned were used in this task, but only one was activated during each trial. Subjects were asked to make a 2AltFC decision as to which one of the two electrodes had been stimulated (e.g. “up” or “down”).

Experiment 2: sequential activation of paired electrodes. For each trial, two neighboring electrodes were activated in sequence to simulate a moving spot of light. Subjects were asked to make a 4AltFC decision as to whether they saw movement up, down, left, or right. The two pulses were separated by a one-second delay. A portion of the data from S1 in experiments 1 and 2 has been published previously and are included here (with permission) for easier comparison with data from later testing in S1 and with testing in S2 and S3.

Experiment 3: rows vs columns. For each trial, four electrodes were simultaneously stimulated in either a row or a column configuration. The subjects were asked to make a 2AltFC decision as to whether they saw a row or a column.

STIMULATION BASED ON VISUAL INPUT RECEIVED VIA A HEAD-MOUNTED VIDEO CAMERA: For these experiments, subjects performed visual tasks using the video camera, which was mounted on the nosepiece of a pair of spectacles. The combined weight of the camera and spectacles was negligible (approximately 100 g), allowing natural head-scanning motions. Because the camera’s field of view was approximately 45 degrees of the visual angle and the implant covered 15 degrees of visual angle, the visual angle subtended by any object on the retina was reduced by a factor of three. Visual angles reported in the text are those subtended at the camera and are therefore three times the value of the stimulation patterns on the retina.

For single pixel camera testing, a single central electrode or group of electrodes was activated under camera control. For multipixel camera testing, the camera pixel to electrode array mapping was similar to how light is projected onto the retina. For example, camera pixels that detected light in the upper visual field mapped to electrodes inferior on the retina, camera pixels that detected light in the left visual field mapped to temporal electrodes in right eye implants and nasal electrodes in left eye implants. In some cases, electrodes were turned off or used in combination, as described in Table 2.

TABLE 2. Retinal Prosthesis Electrode Limitations for Camera Testing

<table>
<thead>
<tr>
<th>Subject</th>
<th>Electrodes Modified for Camera Testing</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1</td>
<td>Electrodes used in groups of four</td>
<td>High stimulus thresholds on</td>
</tr>
<tr>
<td></td>
<td></td>
<td>some single electrodes</td>
</tr>
<tr>
<td>S2</td>
<td>Four electrodes turned off</td>
<td>Produced uncomfortably bright</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sensation when activated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>with other electrodes</td>
</tr>
<tr>
<td>S3</td>
<td>Two electrodes turned off</td>
<td>High stimulus thresholds</td>
</tr>
</tbody>
</table>

Figure 1. Retinal prostheses stimulating electrode array dimensions. Fundus photograph of an electrode array in S3 (Left), and diagram of the epiretinal electrode array with 16 platinum electrodes arranged in a 4 x 4 distribution (Right). For all arrays, H = 5.5 mm, L = 6 mm, and B = 0.8 mm. For S1 and S2, A = 520 μm; for S3, A = 260 μm. The white rectangle to the right of the electrodes is a handle that allows the surgeon to hold and manipulate the electrode array.
processing and camera settings for testing (see Supplementary Figure available at AJO.com).

All tests were carried out using white test shapes on black background with typical indoor lighting. For experiments 5 to 8, head movement (camera scanning) was permitted, whereas in experiment 4, head movement was restricted because we wanted the subject to detect motion and head movement may confound the perception of motion.

Experiment 4: direction of motion discrimination. The camera was pointed toward a black background, and subjects were asked to keep their head and the camera stationary. A rectangular white bar (5 × 30 cm; 14 × 73 degree of the visual angle) was then passed in front of the camera at a distance of 20 cm from the camera. Subjects were asked to discriminate (4altFC) whether the bar was moving up, down, left, or right. The object was moved one time across the visual field. The object was moved sufficiently far from the subjects’ faces for air movement and any associated sound to have been imperceptible.

Experiment 5: object detection. Subjects were asked to respond whether a white object (6 × 10 cm; 11 × 19 degree of visual angle) approximately 30 cm from the camera was in the left visual field, right visual field, or absent (3altFC). Subjects were encouraged to scan the visual field by moving their head. The alternative of “object absent” in this experiment served as a control against spontaneous perceptions unrelated to stimuli.

Experiment 6: counting objects. Subjects were asked to respond whether there were zero, one object to the left, one object to the right, or two objects present in the visual field (4altFC). Objects from experiment 5 were used. If two objects were present, they were separated by approximately 30 cm (56 degrees of visual angle). Subjects were encouraged to scan the visual field by moving their head. The alternative of “object absent” in this experiment served as a control against spontaneous perceptions unrelated to stimuli.

Experiment 7: form discrimination I. The subjects were asked to discriminate the orientation of two white bars (30 × 5 cm; 40-cm viewing distance; 7 × 41 degree of visual angle) in an “L” configuration. The subjects were asked to respond whether the corner of the L was positioned up-left, up-right, lower-left, or lower-right (4altFC). The subjects were encouraged to scan the visual field by moving their head.

Experiment 8: form discrimination II. The subjects were asked to discriminate among three white objects (a dessert plate, a coffee cup, and a plastic knife). The plate was a circle with 16 cm (26 degrees of visual angle) in diameter, the cup approximately 6 cm in diameter and 10 cm in height (10 × 16 degree of visual angle), and the plastic knife was 2 cm in width and 12 cm in height (3 × 19 degree of visual angle). In each test, one of the three objects was placed in front of the subjects (30 to 40 cm distant). The long axis of the knife was oriented away from the subject. The plate and cup were symmetric and therefore insensitive to orientation. The objects were each mounted on a piece of black cardboard to ensure the subjects did not get an auditory clue when the object was set on the table. They were asked to identify which of the three objects was present (3altFC). Subjects were encouraged to scan the visual field by moving their head.

Data for each of the experiments described were accumulated from multiple tests performed on several days within the delineated period. Data from all tests are reported in the results. We measured percent correct in all subjects, and reaction time in subjects S2 and S3. The number of trials per test was typically 10, but ranged from between four and 12. Differences in the number of trials across subjects were due to limited subject availability in the case of S1 and that, occasionally, a subject became tired, which forced termination of the test session. Differences were considered significant if P values were less than .05.

RESULTS

- EXPERIMENTS USING COMPUTER INPUT: Subjects scored better than chance in eight of nine computer-controlled experiments (see Figure 2). When asked to
identify which of two electrodes had been presented (experiment 1), all of the subjects performed significantly better than chance (S1 = 72%, S2 = 100%, S3 = 67%; P < .01). This suggested that the percepts elicited by individual electrodes remain reasonably consistent over short periods. In experiment 2 (sequential activation of paired electrodes), all three subjects performed significantly better than would be expected by chance in a 4altFC task (S1 = 67%, S2 = 93%, S3 = 50%). In Experiment 3 (distinguishing rows and columns), S2 and S3 (though not S1) performed significantly better than would be expected by chance (S2 = 97%, S3 = 77%; P < .001). S2 scored better than the other subjects in experiments 1 to 3.

● EXPERIMENTS USING VIDEO-CAMERA INPUT: The subjects had difficulty with experiment 4 (motion detection), in which they were not allowed to carry out head scanning. Only S2 was able to correctly identify the direction of motion at a percentage higher than chance (S2 = 87%, P < .001).

The subjects scored better on tasks when they were allowed to scan the scene by moving their head. All three performed better than would be expected by chance in experiments 5 to 8 (with the exception of S1 in experiment 8). As before, S2 tended to perform better than S1 and S3. In experiment 5, object detection, all subjects scored above chance (S1 = 90%, S2 = 100%, S3 = 77%; P < .001). In experiment 6, object counting, all subjects scored above chance (S1 = 77%, S2 = 85%, S3 = 78%; P < .001). In experiment 7, object discrimination I (L orientation), S2 and S3 scored above chance (S2 = 73%, S3 = 63%; P < .001). In experiment 8, object discrimination II (plate, cup, or knife), all subjects scored above chance (S1 = 67%, S2 = 73%, S3 = 63%; P < .001).

● COMPARISON OF SINGLE VS MULTIPIXELS PERFORMANCE: Figure 3 compares accuracy using a single pixel vs multiple pixels for the four experiments in which subjects were allowed to scan objects using head movements. On the whole, the subjects’ accuracy was very similar across the two conditions. Of the 12 comparisons of multi- and single pixel performance (three subjects, four experiments), two experiments showed significantly better accuracy with more pixels (S2, experiment 5, multipixel 100%, single pixel 73%, P < .001; S3, experiment 7, multipixel 63%, single pixel 36%, P < .001), and 10 experiments showed no statistical difference (Figure 3).

Figure 4 compares the time taken to make a response using a single pixel and multipixels for S2 and S3 (this was not recorded for S1). Note that a shorter bar indicates a faster reaction time. Standard t tests were used to test whether subjects responded significantly faster when using multiple pixels than when using a single pixel (***P < .001; **P < .01; *P < .05). The number of trials performed for each subject on that task is in the box overlying the columns.
DISCUSSION

THE SAFETY AND FEASIBILITY OF MICROELECTRONIC IMPLANTS has been supported by several recent studies, and the relative merits of epiretinal and subretinal retinal implants vs other approaches such as optic nerve cuffs and cortical implants has been extensively discussed in the literature. Recent clinical trials of retinal implants have included a passive subretinal device, an active subretinal device (Zrenner E, et al. IOVS 2006;47: ARVO E-Abstract 1538), and an active epiretinal device (Hornig R, et al. IOVS 2006;47: ARVO E-Abstract 3216). Passive devices rely on incident light for power, whereas active devices have an external power source. Subjects in the passive subretinal trial do not report pixelized vision, as might be expected if each photodiode were acting as a photoreceptor. However, some of the subjects have reported increased visual fields away from the implant site, suggesting that the presence of the implant alone, or coupled with low-level electrical stimulation, induced a “neurotrophic effect” that improved the health of the retina and the visual function. In our trial, the visual function of subjects did not improve after implantation and testing. However, our subjects had worse baseline vision than most of the subjects in the passive subretinal trial (bare light perception vs reading Early Treatment Diabetic Retinopathy Study letters). The other human clinical trials with permanent retinal implants are in early stages, but the initial reports indicate that perceptual thresholds and form vision are similar to what has been shown in our trial.

The experiments in this article were designed to determine what visual tasks are enabled by a low-resolution epiretinal implant. When we examined performance for stimulation patterns directly controlled via computer, we found that the percepts elicited by individual electrodes remain reasonably consistent such that subjects could reliably discriminate which of two electrodes had been stimulated (experiment 1). Subjects could also easily discriminate the relative location of electrodes activated in sequence (experiment 2). Two of the three subjects (S2 and S3) could distinguish between rows and columns (experiment 3). These data suggest that percepts map (at least crudely) onto their expected location, consistent with earlier reported data on S1, and with earlier studies of least crudely) onto their expected location, consistent with (experiment 3). These data suggest that percepts map (at least crudely) onto their expected location, consistent with earlier reported data on S1.

We did not consistently see better performance (either in speed or accuracy) for multielectrode performance than for single electrode performance, although we did see a trend in that direction. Most comparisons showed no statistically significant difference between single and multipixel, but in the few cases in which there was a significant difference, multipixel showed higher accuracy and faster reaction times. Further, S2 and S3 spontaneously reported that using the single electrode setting was difficult and frustrating. However, S1 reported multipixel stimulation to be more confusing. There are several possible reasons why we only found a trend towards better performance in the multipixel setting. First, the increase in the number of electrodes from one to four to 16 may not be enough of an increase in resolution to be helpful for the tasks we chose. The subjects were able to score better than chance in most tasks with a single pixel, so adding more information provided little benefit in these tasks. Second, the faster reaction times in some experiments with multipixel setting suggest that accuracy differences may be more apparent if the subjects were given a restricted period to respond. In the experiments reported here, the subjects did not have a time limit. That the reaction times decreased and that the subjects generally preferred the multipixel setting provides some evidence that increasing the number of electrodes may improve the capability of a retinal prosthesis. However, given the comparable results between one and multipixel settings in most of these experiments, a significant challenge facing a higher resolution implant will be to understand the complex interaction between the electric field and the degenerated retina, so that an increased number of electrodes can translate into increased visual performance for the patient.

S2 scored higher than the other subjects in two of three computer-controlled tests and in all of the camera tests. Many times, S1 and S3 described the patterns produced by the stimulation as being different from what they would expect for that task. In contrast, S2 consistently reported
percepts that matched the object being viewed with the camera. For example, S2 saw a white horizontal line as a horizontal line, and a white vertical bar as phosphenes aligned vertically. S2 also saw “L” shapes as “pieces” of the letter L that could be recognized if lines were imagined as connecting the points. However, even simple tasks such as discriminating between simple shapes such as horizontal and vertical lines and determining the orientation of a large “L” were difficult for S1.

There are several potential reasons for this inter-subject variability. It may have been easier for S2 to interpret the visual input because she was younger than the other two subjects (approximately 20 years younger than either S1 or S3), or because she had suffered form vision deprivation for significantly less time than the other two subjects (year since vision reduced to light perception: S1 = 50; S2 = 5; S3 = 15). It is also possible that S2 suffered less retinal degeneration than the other two subjects. Any of these alternatives would suggest that the time of implantation relative to the disease progression might play a role in the success of a retinal prosthesis. Other studies have also shown correlations between threshold and visual function. For example, acute stimulation studies found a correlation between the level of retinal degeneration and the electrical stimulus threshold, with normal retina being the most sensitive. Another study noted correlation between light sensitivity and electrical sensitivity in subjects with only light perception vision. These limitations are likely to be retinal rather than cortical, because even after long periods of blindness, subjects can still recognize simple two-dimensional shapes with little difficulty.

To conclude, three blind test subjects implanted with prototype retinal prostheses were generally able to perform simple visual tasks using the implanted device coupled to an external video source. Only three subjects were included in this initial study, so the results reported here need to be considered in light of the small study size. The findings will need to be confirmed through continued experimentation and comparison to other clinical trial results. Although far from normal vision, the results do suggest that a low-resolution epiretinal prosthesis can provide visual information that can be used to accomplish simple visual tasks that are impossible with the subject’s natural light perception vision. Continued progress in this field will rely on the availability of new technology as well as further understanding of the neurobiology of the degenerated retina. It is anticipated within the next five years, several clinical trials will be well under way to test the next generation of implants with up to several hundred electrodes. The utility of these more sophisticated devices will depend on the development of processing strategies that can transform an image into a stimulus pattern to effectively create form vision.20–21

REFERENCES

OPERATION OF THE PROTOTYPE RETINAL PROSTHESIS SYSTEM


THE IMPLANTED STIMULATOR CONSISTED OF AN ELECTRONICS CASE, AN INTRAOCULAR STIMULATING ARRAY, AND A CABLE CONNECTING THESE TWO COMPONENTS. THE ELECTRONICS CASE, WHICH CONVERTS A WIRELESS SIGNAL (FROM THE EXTERNAL SYSTEM, DESCRIBED ABOVE) INTO ELECTRICAL STIMULATION PATTERNS, WAS SURGICALLY IMPLANTED INTO THE TEMPORAL BONE, SIMILAR TO THAT OF A COCHLEAR IMPLANT. A 16 WIRE CABLE RAN FROM THE ELECTRONICS CASE, ALONG A CHANNEL DRILLED ALONG THE SKULL TO THE ORBIT. THE CABLE THEN PASSED INTO THE ORBIT, THROUGH THE SCLERA, AND, FINALLY, TO THE ELECTRODE ARRAY ON THE SURFACE. DURING CAMERA TESTING, THE CAMERA WAS MAPPED IN A DIFFERENT WAY FOR EACH SUBJECT. THE CAMERA PIXEL TO ELECTRODE ARRAY MAPPING IS SUMMARIZED IN SUPPLEMENTAL FIGURE (SEE CAPTION). DURING CAMERA TESTING, NOT EVERY ELECTRODE WAS USED FOR EVERY SUBJECT FOR THE FOLLOWING REASONS:

1. IN S1, FOUR OF THE ELECTRODES REQUIRED VERY HIGH STIMULATION LEVELS (NEAR 1 mC/cm²) BEFORE ELICITING A PERCEPT. THIS SEEMED TO OCCUR MAINLY WHEN THE ELECTRODE WAS SEPARATED FROM THE RETINA. WHILE IT HAS BEEN SHOWN THAT NEURAL TISSUE CAN TOLERATE INTERMITTENT PULSING ABOVE 1 mC/cm² TO REDUCE RISK OF PERMANENT DAMAGE AND TO STAY WITHIN SAFE LIMITS FOR CHRONIC STIMULATION, ELECTRODES REQUIRING MORE THAN 0.35 mC/cm² STIMULUS WERE EITHER TURNED OFF DURING CAMERA USE OR USED IN COMBINATION WITH OTHER ELECTRODES TO REPRESENT THE SAME REGION OF THE VISUAL FIELD. DUE TO SUMMATION OF CURRENT, PERCEPTS COULD BE OBTAINED BY SIMULTANEOUSLY ACTIVATING ADJACENT ELECTRODES, EVEN WHEN THE ELECTRODES COULD NOT CREATE A PERCEPT WHEN ACTIVATED INDIVIDUALLY. IN THE TESTS DESCRIBED BELOW FOR S1, THE VISUAL FIELD WAS DIVIDED INTO FOUR QUADRANTS, AND EACH QUADRANT WAS IDENTICALLY MAPPED ONTO 4 ELECTRODES.

2. S2 HAD FOUR ELECTRODES THAT WERE NOT USED BECAUSE THEY COULD PRODUCE PERCEPTS THAT WERE UNPLEASNTLY BRIGHT WHEN STIMULATION LEVELS WERE INCREASED ABOVE THRESHOLD.

3. S3 HAD TWO ELECTRODES WITH HIGH STIMULUS THRESHOLDS THAT COULD NOT BE USED WITH OTHER ELECTRODES AS THEY TENDED TO INTERFERE WITH THE ABILITY TO SEE OTHER PHOSPHENES.

ALL THREE SUBJECTS WERE ALSO TESTED WITH A 1 PIXEL SETTING IN WHICH A CENTRAL CAMERA PIXEL WAS MAPPED TO A CENTRAL ELECTRODE OR GROUP OF ELECTRODES. THIS IS ALSO SHOWN IN SUPPLEMENTAL FIGURE.
SUPPLEMENTAL FIGURE. How the visual world was mapped onto individual electrodes for both multi- and single pixel testing in retinal prosthesis implant subjects. The empty circles represent the “natural” representation of each electrode in the subject’s visual field (i.e., upper electrodes represent those that were inferior on the retina. The electrodes on the right represent temporal electrodes in left eye-implanted subjects, and nasal electrodes in right eye-implanted patients). The camera and video processing unit reduces the visual field to 16 camera pixels. The grid inside each electrode shows which camera pixel was mapped onto that electrode. If no squares in the grid are highlighted, then this electrode was not used in camera testing for reasons described in the text. Light gray squares represent mappings where stimulation amplitudes used for the camera were sub-threshold when that electrode was stimulated in isolation. White squares represent mappings where stimulation amplitudes were above threshold when that electrode was stimulated in isolation.