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Pattern electrical stimulation of the human retina

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Abstract

Experiments were conducted to study if electrical stimulation of the retinal surface can elicit visual sensation in individuals blind from end-stage retinitis pigmentosa (RP) or age-related macular degeneration (AMD). Under local anesthesia, different stimulating electrodes were inserted through the eyewall and positioned over the surface of the retina. Subjects' psychophysical responses to electrical stimulation were recorded. Subjects perceived simple forms in response to pattern electrical stimulation of the retina. A non-flickering perception was created with stimulating frequencies between 40 and 50 Hz. The stimulation threshold was dependent on the targeted retinal area (macular versus extramacular). © 1999 Published by Elsevier Science Ltd. All rights reserved.

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1. Introduction

Different electronic devices have been proposed to convey visual information to blind patients. Some convert visual information and present it as an auditory or tactile input (i.e. sensory substitution devices) (Brabyn, 1986). Others hope to restore vision by electrically stimulating the visual cortex or optic tract (Brindley & Lewin, 1968; Pollen, 1977; Normann, Maynard, Guillory & Warren, 1996; Schmidt, Bak, Hambrecht, Kufta, O'Rourke & Vallabhnath, 1996). However, each device has had its limitations preventing the development of a visual prosthesis that could help a large subset of blind patients.

Our group as well as others has taken a new approach (Humayun, de Juan Jr., Dagnelie, Greenburg, Propst & Phillips, 1996; Wyatt & Rizzo, 1996; Chow & Chow, 1997; Eckmiller, 1997; Zrenner, Miliczek, Gabel, Graf, Guenther, Hammerle et al., 1997). This approach proposes the development of an electronic device that would stimulate the remaining retinal neurons of patients who are blind from end-stage photoreceptor degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) (Heckenlively, Boughman & Friedman, 1988). Post-mortem RP eyes with bare or no light perception vision prior to death were analyzed morphometrically (Stone, Barlow, Humayun, de Juan Jr. & Milam, 1992; Santos, Humayun, de Juan, Greenburg, Marsh, Klock et al., 1997). This analysis showed that only 4% or less of the nuclei remaining in the outer nuclear layer. In contrast, the ganglion cell layer contained 30% and the inner nuclear layer 80% of its nuclei. Given this limited transneuronal degeneration, the retinal implant could electrically stimulate the remaining retinal neurons and provide useful vision.

A drawing of an electronic retinal prosthesis as envisioned by our group is shown in Fig. 1. The external part of the system would be a camera and an electronic image-processing chip mounted on an eyeglass frame. These electronics would capture and convert a visual scene into pixels. Then the image data would be sent via a telemetry link (laser or radio frequency modulated signal) to a retinal microchip implanted intraocularly. The retinal chip would convert the transmitted image data and produce an appropriate pattern of small electrical currents to be applied through a two dimensional grid of electrodes positioned closely over the retina. Each electrode site would thus stimulate underlying retinal neurons, which would result in the perception of

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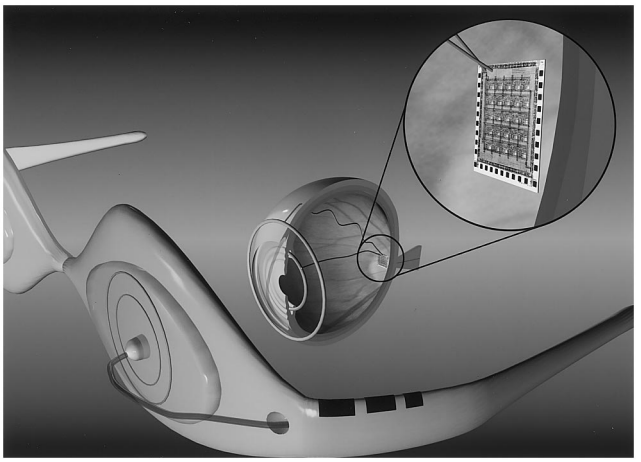

Fig. 1. Conceptual Drawing of the Retinal Prosthesis System. Extraocular electronics residing in a glass frame would capture an image and transmit a signal containing image information to the implanted electronics. The implanted electronics would decode the signal and produce the commanded electrical output at the electrode array on the retinal surface (computer illustration by Mr Jerry Lim, B.F.A).

a dot of light at each stimulation point. Multiple activated electrodes would create a visual pattern composed of individual dots of light recreating the image akin to how printed dots are combined by a dot-matrix printer to form a letter. At first glance, it may seem ideal to design a one-piece implantable device with light detection, image processing, current generation, and an electrode array on one intraocularly implanted electronic chip. This design would simplify the engineering by placing all system components in one package. The optics of the eye would need to be used to focus an image on the light detector. Such a device would also be the easiest to implant surgically. However, we envision that the prototype device would consist of discrete subsystems with a majority of the electronics outside the eye because: (a) we do not know if enough power can be transmitted wirelessly without raising the temperature of the retina to harmful levels and; (b) we are unsure as to the extent of the image processing that maybe required to regenerate the image when groups of neurons are stimulated by extracellular electrical field patterns. Keeping some electronics extraocular (such as the camera and image processing electronics) will allow upgrades without subjecting the implant patient to further surgery.

Prior work has shown that direct electrical simulation of the retina in animal experiments can produce localized retinal responses at low current levels (Humayun, Sato, Propst & de Juan Jr., 1995; Greenberg, 1998; Katona, 1998). We have shown that controlled electrical stimulation of the retina by intraocular electrodes residing on the retinal surface results in focal visual percepts (dots of lights) in individuals blind from end-stage RP and AMD (Humayun et al., 1996). Using a two-point discrimination test, we obtained resolution compatible with a Snellen visual acuity of 4/200 (crude ambulatory vision). While these results lent credence to the retinal prosthesis concept, critical questions remained about whether the small dot-like visual percepts produced by electrical stimulation of the retina can be combined to form an image that both has a recognizable pattern and is continuously present. In this report, we describe our results from pattern electrical stimulation experiments designed to generate form vision using stimulating arrays with as many as 25 individual electrodes. We also present data on tests aimed at determining the optimum site for electrode implantation. This report expands on our previous report that described results from five tests with devices containing at most three stimulating electrodes (Humayun et al., 1996).

2. Methods

2.1. Patient selection

The electrical stimulation tests involved nine subjects with bare or no light perception vision due to end-stage RP and one patient with 20/400 vision due to extensive geographic atrophy involving the entire macular region (AMD) (Table 2). The subjects for these tests are different from our last human test report except patient HC, who for this report underwent additional testing with more complex stimulating electrodes. As a control, one patient with no light perception vision due to giant cell arteritis optic neuropathy was tested with extraocular stimulating electrodes only. All tests were performed after obtaining informed consent under a protocol approved by the Institutional Review Board at Johns Hopkins University, School of Medicine. Methods for patient selection and testing have been described previ-

Table 1
Stimulating probe specifications

Probe type	Number of electrode	Diameter of disk electrode (μm)	Electrode spacing edge-to-edge (μm)
3×3 Array	9	400	200
5×5 Array	25	400	200
Wire	3	25–125	250

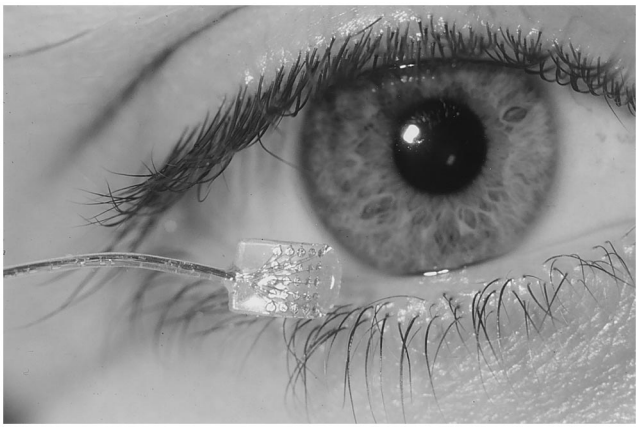

Fig. 2. Multi-electrode (5 × 5 array) held near a human eye.

ously (Humayun et al., 1996). Two patients were tested with multielectrode arrays. Electrode arrays consisted of nine or 25 individual 400 μm diameter platinum disks. The disk electrodes were arranged in either a 3 × 3 or 5 × 5 square array and supported in a silicone matrix. The edge-to-edge electrode spacing was 200 μm. Connection was made to the array via a multi-lead silicone coated cable (diameter < 0.6 mm) composed of nine or 25 individual wires. A multi-electrode array held next to a human eye is shown in Fig. 2. Most patients were tested with simpler devices, consisting of no more than three platinum wires (25–125 μm diameter) packaged as a surgical instrument in a handpiece. The cross section of the wire formed the electrode and the rest of the wire was electrically insulated. Specifications for each electrode used are listed in Table 1.

2.2. Baseline visual function assessment

In order to assess subjects' remaining vision beyond the routine clinical examination parameters (i.e. light perception, hand motion), we recorded (in each eye) psychophysical dark-adapted flash threshold sensitivities, dark adapted, full field single bright flash electroretinogram (ERG), and a dark adapted, bright flash, flicker ERG. For both tests we used a ganzfeld bowl with a Grass PS22 photo strobe and computer controlled ND filters (LKC UTAS 2000 system, Gaithersburg, MD, USA). A photographic flash unit was used if the unattenuated PS22 flash was below the subject's threshold, increasing the range to + 34 dB. To determine flash thresholds, a method of limits was used; ascending in intensity until flashes were first seen and then descending until flashes were no longer seen. The last perceived intensity level was recorded as the threshold. Exceptions to the protocol are as follows. The photographic flash was not available for subject HC. For AB, a visual acuity value is given rather than a flash threshold; a focal rather than a full-field ERG was performed for this subject.

Burian–Allen contact lens electrodes were used for ERG recordings. ERG flicker responses were recorded at full flash intensity, at 20, 25, 30, 35, and 40 Hz, filtered around 30 Hz with a bandwidth of 1.8 octaves. The 30 Hz first harmonic amplitude in the Fourier spectrum of the ERG was used as the flicker response value, provided it exceeded the background noise at neighboring frequencies by at least a factor of 2, and provided similar response value were obtained at the other stimulus frequencies. Details of the psychophysical testing are provided elsewhere (Dagnelie 1998).

2.3. Extraocular electrical stimulation

Prior to surgery, patients were tested in the clinic with extraocular stimulation, to ensure that their retina would respond to electrical current. A Burian–Allen (concentric, bipolar) contact lens electrode was placed on the cornea. A dipolar stimulating probe positioned extraocularly on the sclera was also used in a limited

Table 2
Patient histories, charge thresholds for electrical stimulation, and percepts[a]

Subject	Diagnosis	Flash threshold	ERG (μV)	Stimulating probe type	Percept shape	Percept color	Threshold charge (μC)
H.C.	RP	NPL[b]	NA	(2)	Letter H	White	0.4
B.C.	RP	−12	NR	(3)	Pin	Yellow	1.6
R.J.	RP	−28	NR	(3)	Pin	Yellow	1.8
B.H.	RP	+11	NR	(3)	Pin	White	1.1
A.B.	AMD	20/400	NR	(3)	Pin	White	0.3
C.S.	RP	−28	NR	(3)	Pin	Blue	2.4
V.O.	RP	−30	1.0	(3)	Pin	Yellow	1.0
H.W.	RP	−18	NR	(3)	Dot	White	0.4
J.T.	RP	+18	NR	(3),(1)	Dot, box[c]	White	0.6
J.L.	RP	−14	NR	(3)	Firefly	White	0.2

[a] VA, visual acuity; ERG, full field, bright flash, flicker electroretinogram; AMD, age-related macular degeneration; RP, retinitis pigmentosa; NR, not recordable; NA, not applicable.

[b] photographic flash not available for HC.

[c] Dot seen with probe type (3), box seen with probe type (1)

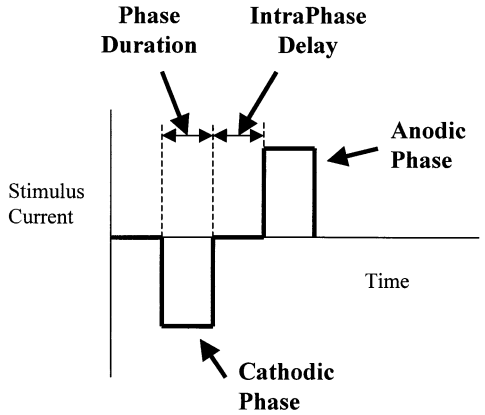

Fig. 3. Diagram of stimulating current pulse. The first phase of the pulse (cathodic current) depolarizes nearby cell membranes and elicits a neural response. The second phase (anodic current) balances the first phase so that no net charge accumulates on the electrode. The intraphase delay separates the pulses slightly so that the second pulse does not reverse the physiological effect of the first pulse.

number of subjects. The probe had two platinum ball electrodes (diameter 200 μm) and adjustable electrode spacing. Patients were asked to describe their perceptions to the electrical stimulation. By giving them experience with the experimental setup and with the sensation of electrically produced vision, extraocular testing prepared patients for the intraocular stimulation in the operating room.

2.4. Intraocular electrical stimulation

Intraoperatively, after local anesthesia (4% Lidocaine) was administered at the intended sites of scleral incisions, the stimulating electrodes were introduced via the pars plana and were hand-held on the retinal surface under the guidance of a surgical microscope. The electrodes were used in a dipolar or monopolar configuration. The ground electrode for monopolar stimulation was a Ag–AgCl skin electrode pasted on the subject's ipsilateral shoulder. An optically and transformer isolated current generator under computer control provided stimulus current. Stimulating pulses were biphasic, with phase duration up to 2 ms and intraphase delay up to 2 ms (Fig. 3). When multiple electrodes were activated, the stimulating pulses were routed through a custom-built, isolated demultiplexor, which serially connected multiple electrodes to the stimulator. While this caused a short time delay (approximately 3 ms) between pulses on multiple electrodes, this short delay was imperceptible to the subjects. No subject reported any delay or scrolling effect when multiple electrodes were used. The stimulating electrodes were positioned over the macular and extramacular regions in the patients with RP and only in the area of geographic atrophy (i.e. macula) in the AMD patient. Attempts were made to record electrically evoked potentials from the visual cortex. This recording was unsuccessful due to a host of complications including: the small retinal areas being stimulated, the inherent electrically noisy environment of the operating room, and the inability to record using a Faraday cage without jeopardizing the sterile operating field. We circumvented this problem by asking the subjects to count out loud each time they saw a visual percept. We were assured that the visual percept was electrically elicited only when patients could track the electrical stimulation by counting along accurately with the varying frequencies of stimulation.

Once the patient recognized the visual percept created by the electrical signal we asked the patient questions regarding the nature of the percept. Care was taken not to lead the patient, but instead to ask open-ended questions. After changing the stimulus parameters, the first question we asked was typically 'What do you see?' These were followed up by more specific questions, such as 'What color is the percept?' 'Where is it located?' 'How bright is it?' and for pattern stimulation 'Does it have a shape'? If the patient was having difficulty relating the size or brightness of the visual percept, we gave options. For example, if the subject had difficulty describing the brightness of the stimulus, we would ask 'Is it as bright as a flashlight or as bright as the moon?' However, in experiments in which electrical stimulation was used to elicit the visual perception of shapes or letters, the patients were asked what shape or letter they saw without giving them a choice of shapes or letters.

3. Results

The subjects' clinical histories, the threshold charge densities to elicit a visual percept, a description of their visual percepts, and the type of stimulating electrode used are shown in Table 2.

3.1. Pattern stimulation

A multi-electrode array was used in two experiments. In the first test, H.C. was able to distinguish between a row of active electrodes (identified as a horizontal line) and a column of active electrodes (identified as a vertical line). These percepts appeared as continuous lines and not as a series of individual dots aligned linearly. Next, two columns and one row were stimulated in a 'U' shape, but the patient described an 'H'. There was no color to the letter and it was described as white against a dark background whereas a blue colored dot was elicited with one electrode earlier in the same session. There was no persistence of the image after the termination of the electrical stimulus. J.T. was the second of the two patients tested with a multi-electrode

array. The perimeter electrodes of a 3×3 electrode array were activated. Initially, she described the percept as larger. When asked to describe the shape of the percept, she identified a box shape, describing the percept as 'the size of a matchbox'. The visual perception was that of an outline of a matchbox and was not filled in the center.

3.2. Electrode position

The position of the electrically elicited percept reported by each subject corresponded accurately to the location of the stimulating electrode relative to the underlying retina (i.e. retinotopically correct). In all our previous patients, we confined our sites of stimulation to the macula. In this study, we tested extramacular sites but were only able to elicit a response in one patient (P.S.) who described the percept as 'way out there like on the edge of a visual field test'. The electrical charge threshold for this response was twice that required to elicit a response from the macular region. The lower threshold for electrical stimulation in the macular region was further demonstrated in patient J.L., in whom we maintained a constant stimulating current, but moved the electrode from the peripheral retina towards the macula and then back out towards the periphery. When the electrode was closer to the macula, the percept would appear, indicating a lower threshold in the macula. This was evident when approaching the macula from several directions. Typically, the larger electrodes (125 μm diameter) were used for stimulation with the wire electrode. No difference was noted when the smaller electrodes (25 μm) were used, but this variable was not studied systematically.

The extraocular focal electrical stimulation performed using a dipole electrode on the sclera was markedly less effective in eliciting a visual percept than either of the two intraocular locations (i.e. the macular or the extramacular regions). Electrical currents up to a level of 6 mA resulted in eliciting a visual percept in only one patient (i.e. $12\times$ higher than those required when the electrodes were close to the retinal surface in the same patient). Currents greater than 6 mA were not used because of extraocular muscle twitching that is triggered by these high current levels. The one patient (V.O.) in whom extraocular stimulation resulted in a visual percept described round percepts larger than those obtained when he was tested with intraocular electrodes. The patient also described the percepts elicited by the extraocular electrodes as if 'a row of light bulbs were lit sequentially', whereas, those produced by the intraocular electrodes were discrete spots of light.

The threshold stimulating currents were also increased by the distance between the stimulating electrode and the retinal surface. However, we were unable to quantify this in our setup. The eye remains fully mobile precluding the use of a micromanipulator to carefully study the distance between the electrode and the retina. In general, when the distance between the hand-held stimulating electrode and the retina was much greater than 0.5 mm, the current requirements increased dramatically often more than doubling.

Threshold stimulating currents also varied between patients. RP patients with less marked bone spicule change and less atrophic maculas had lower thresholds than those with more advanced disease. For example, patient (J.L.) had thresholds that were $12\times$ less than patient (C.S.). However, lower electrical thresholds did not correlate with greater light sensitivity as measured by flash intensity. Table 2 shows the psychophysical flash thresholds, flicker ERG response amplitudes, and electrical stimulation threshold for the test subjects. Note that only one of the subjects (V.O.) had a recordable flicker ERG response. No patient had a recordable single flash ERG (A.B. not tested). Also note that more sensitive (i.e. more negative dB values) do not correlate with low charge thresholds in column 8. In fact, the most sensitive flash thresholds are found in subjects R.J., V.O., and C.S. These subjects had charge thresholds at or above 1 μC. The highest flash threshold (about 50 000 times brighter) was found in J.T., whose charge threshold was 0.6 μC. One of the lowest threshold currents was required in patient A.B. with severe geographic atrophy due to AMD. In this patient, the stimulating electrode was positioned only in the center of the area of geographic atrophy and the patient localized the visual percept directly in front of her. Lastly, we were unable to elicit an electrically elicited visual perception using the Burian–Allen electrode in the patient with optic neuropathy due to giant cell arteritis.

3.3. Flicker fusion

The point of flicker-fusion for electrical stimulation was measured in four patients. The stimulation rate that produced a continuous spot of light was 50 Hz in two subjects (H.C. and J.T.) and 40 Hz (H.W. and J.L.) in the other two subjects. The stimulation current was set at the perception threshold measured using a 1 Hz stimulation rate, but all subjects described the visual percept as growing brighter with increased frequency.

4. Discussion

The success of a retinal implant will depend on whether or not extracellular stimulation of groups of neurons can produce a usable image in individuals blind from photoreceptor loss. In prior tests, we have shown that electrical stimulation delivered through two electrodes separated by 435 μm created the visual per-

ception of two distinct closely spaced dots of light. The ability of the subject to discriminate between the two dots of light approximated a Snellen visual acuity of 4/200 (Humayun et al., 1996). But a usable image requires more than two dots of light being turned on once a second. In the current experiments, we built on earlier results and created a recognizable, continuous image using pattern electrical stimulation of the retina.

Multiple electrodes were jointly activated to create simple forms in two subjects. The devices used in our tests had either a 5×5 or a 3×3 array of electrodes. We do not know how many electrode sites will be necessary to provide useful vision, vision for mobility, or vision for reading, but at least two different lines of evidence suggest that the number could be significantly less than the 100 million photoreceptors or even the 1.2 million retinal ganglion cells. First, there is the cochlear implant experience. The cochlear implant is a device in many ways analogous to the retinal prosthesis in that the function of hair cells (conversion of sound to a neural signal) is replaced by an implant that delivers electrical pulses directly to spiral ganglion cells. In so doing, the cochlear implant effectively bypasses damaged hair cells and restores a sense of hearing in the profoundly deaf. Cochlear implant patients can converse over the phone with only six input channels (electrodes), a number that is far less than the 30 000 auditory nerve fibers emanating from spiral ganglion cells. This shows that a combination of redundant input and the plasticity in higher neural centers can be exploited to teach an individual to process sensory input with less information to regain a significant level of sensory function. A similar redundancy in the visual information from the eye and plasticity of the visual cortex may decrease the number of required stimulating electrodes and allow the electrodes to be larger than the target retinal elements.

More direct evidence concerning visual acuity with a reduced input comes from the work of Cha, Horch and Normann, 1992. Using a custom made video display, an image was degraded into pixels and then projected onto the retina of seeing individuals. The results of these tests showed that a 25×25 pixel array placed over the macula allowed patients to read at a Snellen acuity level of 20/25 and a coarser array with similar pixel numbers allowed individuals to navigate around an obstacle course with equal speed as subjects with normal field of vision. These results and the experience with cochlear implants provide us with crude estimates of how many individual electrodes will be required to display a useful image. Yet, we believe that the required number of electrodes will be established only when implants can be chronically implanted over the retinal surface and the subjects are allowed an extensive training period.

The ability of our subjects to identify crude forms in the short test period within the operating room is very encouraging. The artificial sound created by electrical stimulation delivered via a cochlear implant is sometimes initially incomprehensible but eventually becomes intelligible after several weeks of training. The human auditory system adapts to this new form of input to a level where patients can understand speech without lip-reading (Clark, Tong & Patrick, 1990). Our blind subjects had only 45 min to recognize the visual percept created by pattern electrical stimulation of the retina. Moreover, the eye remained fully mobile during the procedure because we could not administer anesthetics into the muscle cone, without risking blocking optic nerve conduction. Motility of the eye resulted in movement of the hand-held electrode array relative to the underlying retina. This unstable positioning could have resulted in a 'blur' effect that might explain the perception of the letter 'H' instead of the expected 'U'. When an unambiguous shape like a box was presented with a 3×3 array, the subject identified the image correctly.

Our electrode arrays typically used fairly large electrode diameters (diameter > 125 μm) compared to the diameter of typical retinal neurons ganglion cell (diameter ~ 10–20 μm). We used large electrodes to keep current density below safe thresholds established for long-term stimulation of neural tissues (Brummer, Robblee & Hambrecht, 1983). Undoubtedly, the electrode size results in the simultaneous stimulation of a population of bipolar and ganglion cells. This mass recruitment of neurons will reduce the resolution of the electrically elicited image compared to activation of a single photoreceptor, as can be the case in normal vision. In order to decrease the size of the stimulating electrodes, future investigations could focus on different electrode geometries, bringing the electrodes closer to the retina, and more efficient stimulating paradigms. For example, trains of short pulses have been found to be more efficient than single longer pulses for electrically stimulating the cochlear neural elements (Parkins & Colombo, 1987).

In this study, we only evaluated planar stimulating electrodes that were either placed on the inner retinal surface or on the sclera. The electrically elicited visual percepts were very sensitive to the location of the stimulating electrode. The amplitude of stimulation currents needed to elicit a visual percept increased dramatically with an increase in the distance between the stimulating electrode and the retina. There was also a marked difference in thresholds between the macular and extramacular regions. In all cases, thresholds were higher in the extramacular than in the macular region. This was clearly demonstrated in subject J.L. The stimulating current pulse was continuously applied and the stimulating electrode was moved several times between the extramacular to macular region, essentially provid-

ing a spatial map of responsiveness to electrical current. As the stimulating electrode was moved over the macular region the subject would perceive a spot of light. The light disappeared when the electrode was moved outside the macula. We believe that higher current threshold is required for the extramacular regions because the inner retina is more damaged in those areas in retinitis pigmentosa. We base this on a study in which we performed a morphometric analysis on the extramacular regions using the same set of blind RP eyes in which we had earlier studied the macular regions (Humayun, Prince, de Juan Jr., Barron, Moskowitz, Klock et al., 1999). The extramacular analysis showed that, although there was some preservation of the inner retina, this preservation (expressed as a percentage of the number of cells normally found in these areas) was half that seen in macular regions (40% extramacular, 80% macular) (Santos et al., 1997; Humayun et al., 1999). This result may explain the increased electrical stimulation threshold observed in extramacular regions and is also consistent with the clinical progression of RP.

Greater inner retinal preservation more than likely also explains the lower thresholds in the non-neovascular AMD patient relative to the RP patients. Unlike the patient with neovascular AMD and a large subretinal hemorrhage in our first report who required very high current thresholds, current levels required by the patient with non-neovascular AMD were among the lowest. In a morphometric analysis of AMD patients, the greater inner retinal preservation was found in non-neovascular AMD than in neovascular AMD. Retinas with non-neovascular AMD also had a greater inner retinal preservation than RP retinas (Curcio, Millican, Sloan & Medeiros, 1997). This is an important finding because lower thresholds would allow smaller electrodes with closer electrode spacing, both of which could contribute to greater resolution. This greater resolution may enable reading and not mere ambulatory vision, as needed by patients with AMD.

Extraocular stimulation (i.e. using a Burian–Allan electrode) is part of our patient screening protocol prior to intraocular testing. If a prospective subject cannot see a response with this diffuse stimulus then it is unlikely that (s)he will see a response with localized electrical stimulation of the retina. This led us to investigate the possibility of using extraocular electrodes to elicit localized visual percepts. We envisioned the development of a multi-electrode array that would be sutured to the sclera and envelop the eyeball like a glove. The advantages of such an approach are the less invasive nature of the implant, as it remains extraocular, and the ease of implantation. Using dipole and monopole electrodes placed on the sclera, we were successful in eliciting visual percepts in only one patient. The perception threshold for this patient, however, was $12\times$ greater than that needed with an intraocular electrode (12 μC extraocular, 1 μC intraocular). With extraocular stimulation, the visual percepts corresponded to the area of stimulation but were described as a string of beads and not as a single percept. Moreover, electrical pulses often resulted in an involuntary eye movement as the higher currents began to stimulate the extraocular muscles. The high currents, lack of resolution, and involuntary muscle twitch has led us to abandon this approach.

One might have expected RP subjects with better light sensitivity to have both more preserved photoreceptors and better preservation of inner retinal cells. This greater preservation of the retina should have resulted in lower charge thresholds. There are, however, at least two reasons why such a correlation was not found: (1) A low flash threshold requires no more than a small number of relatively healthy photoreceptors and these are most likely to occur in or very near the fovea. Electrical stimulation was never directed at the fovea hence these few areas could have never been tested. (2) Charge thresholds also depend on a host of configuration and conductance factors such as the condition of the vitreous and inner limiting membrane and the precise distance and orientation of the probe relative to the retina. One noteworthy consequence of these findings is that RP subjects who can detect the dimmest light flashes (i.e. at least using our protocol) are not necessarily better candidates for a retinal prosthesis than others who performed poorly on the visual function tests.

Flicker fusion was another important feature we needed to delineate. A strobe-like flashing image would be of limited value and bothersome. Our results show that using stimulation rates between 40 and 50 Hz, the patients begin to perceive the flashing stimulus as continuously on. There is no persistence of the image or negative after image following cessation of stimulation. The frequency of electrical pulse stimulation required to elicit a continuous percept was similar to flicker fusion rates in normally sighted observers, and was higher than that for light stimulation in advanced RP (Dagnelie & Massof, 1993).

In conclusion, retinal electrical stimulation results in discrete, non-flickering visual percepts and pattern electrical stimulation results in form vision. Macular regions in RP patients exhibit the lowest electrical current thresholds to elicit visual perceptions and remain the site of choice for the implantation of a retinal electrode arrays. Without the ability to test patients while engaged in their activities of daily living, it is hard to say if we have created usable vision. However, we believe that with the results of these latest experiments, we have taken significant steps towards demonstrating the feasibility of providing useful vision via pattern electrical stimulation of the retinas of individuals blinded by

outer retinal degeneration. What is needed now is a prototype implantable retinal prosthesis in order to evaluate if long-term electrical stimulation will confirm the expectations raised by the short-term results presented here.

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