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Preliminary 6 Month Results from the Argus™ II Epiretinal Prosthesis Feasibility Study

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***Abstract*— The Argus™ II 60 channel epiretinal prosthesis has been developed in order to provide partial restoration of vision to subjects blinded from outer retinal degenerative disease. To date the device has been implanted in 21 subjects as part of a feasibility study. In 6 month post-implantation door finding and line tracking orientation and mobility testing, subjects have shown improvements of 86% and 73%, respectively, for system on vs. system off. In high-contrast Square Localization tests using a touch screen monitor 87% of tested subjects performed significantly better with the system on compared with off. These preliminary results show that the Argus II system provides some functional vision to blind subjects.**

I. Introduction

Multiple research groups are investigating the feasibility of a retinal prosthesis for people suffering from outer retinal degenerative diseases such as retinitis pigmentosa (RP) or age-related macular degeneration (AMD) [1-5]. In these diseases while the photoreceptors degenerate, a percentage of inner retinal cells (ganglion cells and bipolar cells) remain viable [6]. It has been demonstrated that electrical stimulation of these cells can elicit percepts (phosphenes) in blind human subjects [4]. The goal of such an implant is to bypass degenerate photoreceptors and relay information via an array of electrical stimulating electrodes.

The Argus II™ retinal prosthesis system (Second Sight® Medical Products, Inc., Sylmar, CA) consists of a pair of glasses housing a miniature video camera, an external visual processing unit (VPU), and an intraocularly implanted stimulating electrode array and inductive coil for wirelessly relaying power and data. The VPU acquires and digitizes video input from the camera, applies various filters on the image (e.g. edge detection, contrast enhancement, difference of Gaussian), and downscales the resolution to a 6 x 10 grid. This 60 pixel image is then mapped to a stimulation intensity using customized look-up tables that have been derived from testing of individual subjects.

Here we report the ability of implanted subjects to perform orientation and mobility tasks (high-contrast line tracking and door finding), and results of Square Localization and Direction of Motion tests which use custom made software and a touch screen monitor.

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II. Methods

A. Subject selection and safety profile

Blind subjects with severe to profound RP have been surgically implanted as part of a phase 1 feasibility study (clinicaltrials.gov identifier: NCT00407602; active, recruiting) at multiple clinical sites worldwide: Doheny Eye Institute at the University of Southern California (Los Angeles, CA); Retina Foundation of the Southwest (Dallas, TX); Moorfields Eye Hospital (London, UK); University of California at San Francisco (San Francisco, CA); Wilmer Eye Institute at the Johns Hopkins School of Medicine (Baltimore, MD); Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts (Paris, France); Hôpitaux Universitaires de Genève (Geneva, Switzerland); Puerta de Hierro Centro Medico (Guadalajara, Mexico). The study was approved by Institutional Review Boards and Ethics Comittees at each site, and respected the tenets of the Declaration of Helsinki. Informed consent was obtained from all subjects.

To date 21 subjects (8 female, 13 male) have been implanted. The average age of at the time of surgery was 58 ± 11 years (range 27 – 77). The average time of implantation across all subjects is 15 ± 9 months (range 0 – 30). Only the 17 subjects implanted 6 months or more were included in the orientation and mobility and Square Localization testing described below.

Serious adverse events (requiring intervention or hospitalization) occurring within the first 6 months of implantation in the first 17 subjects were endophthalmitis (n=3), conjunctival erosion (n=3), hypotony (n=1), inflammation (n=1), re-tack (n=1), and retinal tear (n=1). All of these events are resolved, with the exception of

hypotony which is now stable. All of the events occurred in five subjects; 12 subjects had no serious adverse events.

B. Orientation and Mobility

The mobility tests were set up in a 20 foot by 20 foot empty room with at least one wall of uniform, light color. If such a room was not available, then the test was conducted in the best alternative. Subjects used both eyes (binocular vision) for these tests. The subject was instructed to walk each predefined course as quickly and safely as possible. The investigator walked near the subject to ensure the subject safely performed the tests.

In Test 1 (door finding) the subject was either placed in the center, offset left 3 feet, or offset right 3 feet, and was instructed to walk to, and place their hand on, a 3' x 7' (1 m x 2.1 m) rectangular target "door" 20 feet away (Figure 1). 6 trials were run (two from each position, chosen randomly). The distance from the subject's hand to the edge of the door was recorded; a trial was determined to be "successful" if the subject touched any part of the door.

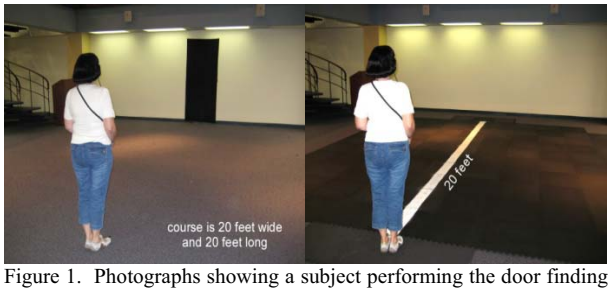

Figure 1. Photographs showing a subject performing the door finding (left) and line tracking (right) tasks.

In Test 2 (line tracking), 6" wide tape was used to make a high contrast 20 foot line on the floor. The subject was placed at the start location in one of the three directions (left, center, or right), selected in random order and instructed to walk to the end of the line. Six trials were run (two from each position, chosen randomly). The distance from the subject's feet to the end of the line was recorded; a trial was determined to "successful" if the subject was standing on the line at the end.

C. Square Localization and Direction of Motion

A spatial vision test (Square Localization) was developed to provide an objective measure of spatial vision. In both tests the subject was seated 12" away from the center of a 20" touch screen monitor.

In this test, a high-contrast white square (200 x 200 pixels, 2.8") was presented in random locations on the monitor. When prompted, the subject scanned the monitor and attempted to locate the square, touching the screen at the location of the square center (Figure 3). Forty trials were administered with the system on and off for a total of 80 trials.

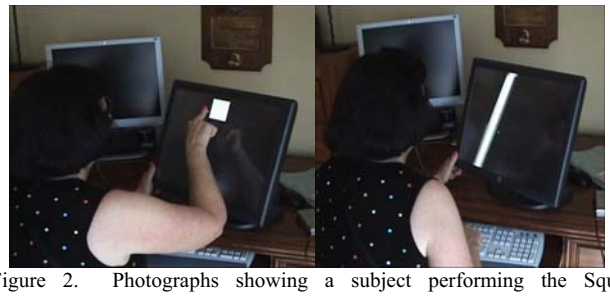

Figure 2. Photographs showing a subject performing the Square Localization (left) and Direction of Motion (right) tests.

III. Results

In the door finding task the average success rates of touching the door with the system on were 55% and 59% at the 3 and 6 month follow up testing points, respectively. This is an improvement in performance compared with the system off where the average success rates were 33% and 32% at the 3 and 6 month follow up testing points, respectively (Figure 3).

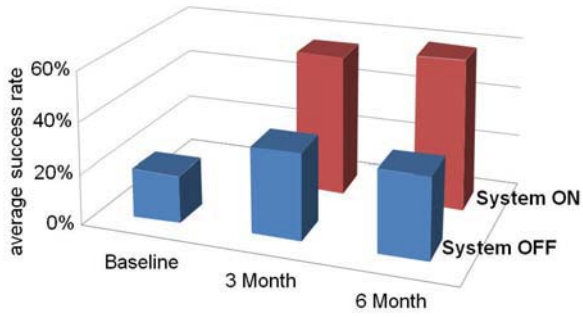

Figure 3. Average success rate measured at baseline, 3 months post-op, and 6 months post-op for the door finding task (n=17).

In the line task the average success rates of tracking the line until the end with the system on were 47% and 44% at the 3 and 6 month follow up testing points, respectively. This is an improvement in performance compared with system off where the average success rates were 20% and 26% at the 3 and 6 month follow up testing points, respectively (Figure 4).

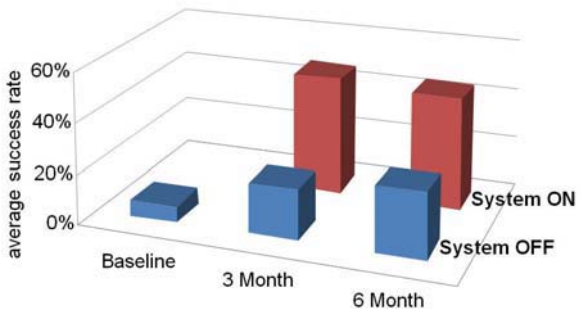

Figure 4. Average success rate measured at baseline, 3 months post-op, and 6 months post-op for the line tracking task (n=17).

The results of the Square Localization test are presented in figure 5. The mean distance from the square center in pixels was determined for both system on and system off conditions. There was a significant improvement with the system on compared with off in 13 of 15 subjects (87%).

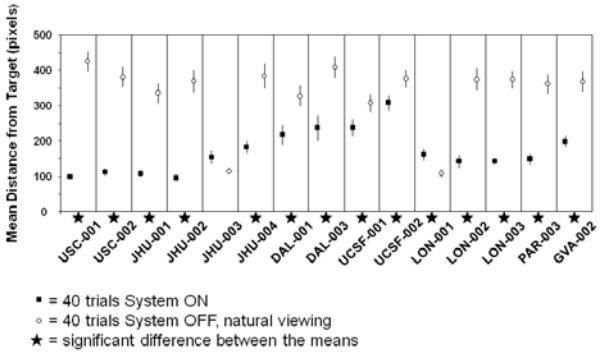

Figure 5. Mean distance from square center (in pixels) for each subject with the system on (dark circles) and off (light circles). Cases in which there is a significant difference between the means in these two cases is demarcated with a star.

IV. Discussion

For this initial cohort of 17 subjects at the 6 month time point, some visual function has been restored by the Argus II™ system in blind individuals. Furthermore, the safety profile is acceptable.

References

[1] E. Zrenner, A. Stett, S. Weiss *et al.*, "Can subretinal microphotodiodes successfully replace degenerated photoreceptors?," *Vision Res,* vol. 39, no. 15, pp. 2555-67, Jul, 1999.

[2] A. Caspi, J. D. Dorn, K. H. McClure *et al.*, "Feasibility study of a retinal prosthesis: spatial vision with a 16-electrode implant," *Arch Ophthalmol,* vol. 127, no. 4, pp. 398-401, Apr, 2009.

[3] J. F. Rizzo, 3rd, J. Wyatt, M. Humayun *et al.*, "Retinal prosthesis: an encouraging first decade with major challenges ahead," *Ophthalmology,* vol. 108, no. 1, pp. 13-4, Jan, 2001.

[4] M. S. Humayun, E. de Juan, Jr., G. Dagnelie *et al.*, "Visual perception elicited by electrical stimulation of retina in blind humans," *Arch Ophthalmol,* vol. 114, no. 1, pp. 40-6, Jan, 1996.

[5] G. Richard, M. Keserue, M. Feucht, N. Post, R. Hornig "Visual Perception after long-term implantation of a retinal implant," *Invest Ophthalmol Vis Sci,* vol. 49, pp. 1786, 2008.

[6] J. L. Stone, W. E. Barlow, M. S. Humayun *et al.*, "Morphometric analysis of macular photoreceptors and ganglion cells in retinas with retinitis pigmentosa," *Arch Ophthalmol,* vol. 110, no. 11, pp. 1634-9, Nov, 1992.