Title: Object Finder for a Retinal Prosthesis

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JHM IRB - eForm A – Protocol

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1. Abstract

In outer retinal degeneration, such as retinitis pigmentosa (RP), the photoreceptors and their supporting retinal pigment epithelium are gradually damaged and destroyed. In RP (incidence 1:4000) legal blindness is reached after 25 years. In many RP patients over sixty years of age, rudimentary vision with only gross movement or bright light perception remains, with little or no appreciable peripheral vision. Eventually, even light perception may recede. Currently, there is no treatment that stops or reverses the loss of photoreceptors in retinitis pigmentosa.

The Argus II Retinal Stimulation System developed by Second Sight is a second generation system following the first generation Argus 16. The main differences are that the Argus II provides more independent channels for stimulation and that the Argus II Implant antenna and electronics are attached to the outside of the eye. Like the Argus 16 System, the Argus II system comprises three sub-system components: the internal Implant, the external Video Processing Unit (VPU) and Glasses, and the supporting Clinical Fitting System. The critical steps leading to the present application are provided below. The device was approved by the FDA in February 2013.

Patients being implanted with the Argus II at JHU will be invited to join the FDA-mandated, SSMP-sponsored post-approval study (PAS; NA_00087968). The FDA and SSMP have authorized participating centers to supplement the FDA protocol with their own ancillary research protocols aimed at improved understanding of the Argus II and the potential benefits obtained by implantees, who choose to enroll in the PAS (NA_00087968) and ancillary studies.

In this ancillary study we are asking Argus II users to perform visual activities under different experimental conditions, created by modifying either the settings on the VPU or the imagery provided to the VPU.

In an amendment (July 2017) we are inviting sighted individuals to perform experiments similar to those of the Argus II users, viewing simulated prosthetic imagery in a video headset.

2. Objectives

The objective of this study is to supplement the FDA-mandated post-approval study (PAS; NA_00087968) with additional functional tests and image manipulations that will help us gain a better understanding of Argus II use, and potential benefits for the implantees. We will be presenting the same visual information (in simulated form to sighted individuals, to compare their performance to that of Argus II users.

3. Background

The Argus II System was developed to provide electrical stimulation of the retina to induce visual perception in blind individuals with retinitis pigmentosa. The Argus II System was extensively studied in 30 clinical trial subjects who met this indication for use. Subjects were implanted between June 2007 and August 2009. As of November 2012, all subjects had been implanted for more than 3 years (with exception of one subject whose device was explanted after 14 months), and half of the subjects were followed for over 4 years. Collectively these subjects have been implanted (as of November 2012) for a total of over 125 implant-years. Data collected from this trial through March 2012 were reported to the FDA in a Humanitarian Device Exemption (HDE) application. The Argus II device was granted HDE status by the FDA in Feb 2013.

4. Study Procedures

In addition to the outlined testing in the post-approval study (PAS; NA_00087968) participants who have previously been implanted with an Argus II will be asked to practice specific tasks using their Argus II retinal prosthesis system, and perform multiple other functional tests to gain better understanding of their use of the device and potential benefits for future implantees. These practice tasks and tests may be carried out in the laboratory, at Johns Hopkins Hospital (JHH), at participant's home or in the participant's community. Typical examples include object localization and manipulation, interaction with stationary or moving individuals and obstacles, wayfinding in familiar and unfamiliar settings, and self-care. The imagery provided to implantees may be filtered or enhanced with the objective to improve the understanding by the prosthesis wearer. Two specific changes made to the imagery will be the use of a thermal camera that enhances human bodies and warm objects in the image, and the use of a distance-filtering mechanism that allows us to reduce image clutter by suppressing information coming from closer or farther away than the user's range of interest.

In order to test the performance of these systems in realistic situations it is important that they are tested in environments where other people are present, such as public spaces around the East Baltimore campus. This raises the issue of video recordings, needed for post-hoc analysis of the study participant's interaction with the environment, in terms of correct detection and identification of events, but also of timing, e.g., how long it takes a subject to respond to a person passing by, or to a potential collision while walking. In order to avoid inadvertent disclosure of JHM patients through such recordings we propose the following measures:

- All video recordings made in JHH areas accessible to patients will avoid recording faces by lowering the camera angle
- Any videos that inadvertently do capture identifiable 3rd persons will be promptly analyzed for participants' performance data, and destroyed
- Any videos that will be saved for later analysis will be stored on a server that is not network connected
- Videos to be shown at scientific gatherings will be carefully selected so no identifiable features of 3rd persons are shown

We will recruit a small cohort of sighted individuals and ask them to perform the same experiments as the Argus II users, albeit with simulated rather than real prosthetic vision.

All participants will be asked to agree to having their tests audio and/or video recorded.

5. Inclusion/Exclusion Criteria

Only those enrolled in the Argus II post-approval study(PAS; NA_00087968) or other interested post FDA-approval Argus II retinal implantees or the Argus II Retinal Implant System feasibility study (NA_00008133) will be enrolled in this study. In the sighted comparison group we will enroll adults with normal vision who are in good general health. JHU undergraduates and employees may be included.

6. Drugs/ Substances/ Devices

ARGUS II SYSTEM DESCRIPTION:

The Argus II Retinal Prosthesis System consists of the following main parts:

- *Argus II Retinal Prosthesis (referred to as the "Implant")*
- *Argus II Video Processing Unit (referred to as the "VPU")*
- *Argus II Glasses*

How Does the Argus II System Work?

Patients will have the Argus II Retinal Prosthesis implanted in and around their eyeball. To turn on and use the implant, patients need to wear the glasses and VPU.

When patients are using the system, a miniature video camera on the glasses captures images in real time. The glasses send these images to the VPU. The VPU converts these video images into electrical signals and send them back to the glasses. The coil on the glasses sends the signals wirelessly to the implant. The implant then sends out small pulses of electricity to the retina in the patient's eye. These pulses stimulate their surviving secondary cells in the retina. The retina sends the nerve signals along the optic nerve to the brain, and the prosthesis wearer perceives these pulses as patterns of light. Over time, they may learn how to interpret these visual patterns as objects and shapes.

Argus II Retinal Prosthesis System(Implant)

The implant consists of four parts: (1) the electronics case, (2) the implant coil, (3) the electrode array, and (4) the scleral band.

Only the electrode array goes inside the eye. The electronics case, the implant coil and the scleral band sit on the outside of the eye. The scleral band wraps around patient's eye and holds the implant in place. The conjunctiva, a thin layer of tissue that covers the white part of the eye also covers the parts of the implant that sit on the outside of the eye.

A ribbon cable connects the electronics package to the electrode array. This cable enters patient's eye through an incision made during surgery. At the end of cable is the electrode array. The electrode array is fastened over the surface of the retina with a retinal tack.

The electrode array provides electrical stimulation to patient's retina. It has 60 electrodes arranged in a rectangular grid. Fifty-five of these electrodes are turned on at the time of implant. Up to 5 of the remaining electrodes may be functional and could be turned on to replace an electrode that is not working.

Video Processing Unit (VPU) – External Equipment

The VPU allows wearers to turn stimulation on and off. Using the buttons on the VPU, they can change the stimulation program to suit their current environment.

The VPU keeps track of when wearers turn it on and off, and it keeps a record of how well their implant and VPU are functioning. The VPU also records when there is a disruption in the wireless link between the implant and glasses. The clinician can check all of this information when the wearer visits the clinic.

Glasses– External Equipment

The glasses have a miniature video camera in the bridge above the nose. The glasses also have a coil on one of the earpieces. The coil sends power to the implant and communicates wirelessly with it. The glasses connect to the VPU with a cable. Patient must wear both the VPU and glasses for the system to work.

Equipment for simulations in sighted individuals

Instead of the Argus II glasses and implant, sighted volunteers will be fitted with a pair of video goggles and an external graphics processor that will generate video imagery closely resembling the prosthetic iimagery perceived by the Argus II users. The same image capture systems used to capture the scene for the Argus II users will be used in simulations with sighted individuals.

7. Study Statistics

NA

8. Risks

Similar to the Post-Approval Study (NA_00087968) and Argus II retinal Implant Feasibility Study (NA_00008133) , all practice and testing will take place under immediate supervision of study team members. Moreover, these activities will be no different from those undertaken by blind and partially sighted individuals. Therefore, the study will not add appreciable risk to that of being blind and having a retinal prosthesis system.

No additional risks will exist for sighted participants, who will also be closely supervised.

9. Benefits

The direct benefits of participation in this study may include greater proficiency in the operation and use of the Argus II retinal prosthesis system. There will be no benefit to sighted participants.

10. Payment and Remuneration

Sighted participants will receive a modest remuneration ($10/hr), while Argus II users will not be paid for this study. Travel reimbursement/lunch vouchers will be offered to all participants.

11. Costs

Tests will be at no cost to the participants. No additional costs anticipated.