AWARD NUMBER**:** **W81XWH-19-1-0057**

TITLE**:** **A Microcoil-Based Cortical Visual Prosthesis**

PRINCIPAL INVESTIGATOR**:** **Shelley Fried, PhD**

CONTRACTING ORGANIZATION**:** **Boston VA Research Institute (BVARI)**

REPORT DATE**:** **FEBRUARY 2023**

TYPE OF REPORT**:** **Annual**

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
February 2023	Annual	1FEB2022 - 31JAN2022

4. TITLE AND SUBTITLE

A Microcoil-Based Cortical Visual Prosthesis

5a. CONTRACT NUMBER
W81XWH-19-1-0057

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Boston VA Research Organization (BVARI)
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8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
We are developing a cortical visual prosthesis that can restore vision to the blind. Our approach is based on the recent development of micro-coils, small implantable inductors that magnetically activate neurons. Much proof-of-concept testing has shown that coils are more selective and maintain consistency longer than conventional micro-electrodes. The Aims here focus on the design and development of a device that can be safely implanted into humans, the initial testing of the new prototypes, and then establishing safety and efficacy of the implants. Here, we describe our ongoing progress with the design of the device, a wide range of safety and performance testing as well as progress towards psychophysical testing in non-human primates.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
U	U	U	UU	22	19b. TELEPHONE NUMBER *(include area code)*

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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Despite some encouraging clinical results, progress with cortical visual prostheses has been limited. Phosphenes (light percepts) are reliably elicited by stimulation from single electrodes, but their assembly into complex spatial patterns is much less consistent, likely because of an inability to create specific patterns of neuronal activation. There are also questions about how foreign body responses impact long-term efficacy. Our goal here is to advance efficacy and reliability by developing a device based on implantable micro-coils. Much previous work has shown that coils are more selective and will remain stable over longer periods of time (vs. implanted electrodes). The Aims here focus on the design and development of the array, initial testing of the new prototypes and then establishing safety and efficacy of the implants.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Visual prostheses; cortical stimulation; magnetic stimulation; cortical implants

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Aim 1: Design and development of a micro-coil array suitable for implantation into human visual cortex

- Aim 1.1: Establish thresholds of human pyramidal neurons to magnetic stimulation
- Aim 1.2: Develop design specifications for the array
- Aim 1.3: Development of driving electronics optimized for use with coils
- Aim 1.4: Fabrication of prototype micro-coil devices

Aim 2: Establish efficacy of the WFCA via physiological testing

- Aim 2.1: Verify functionality of WFCA prototypes via physiological testing

Aim 3: Establish safety and efficacy of implanted devices

- Aim 3.1: Assess the effectiveness of device implantation into cortex.
- Aim 3.2: Evaluate long-term safety and efficacy of the implant via a conditioned avoidance paradigm.
- Aim 3.3: Establish the ability of WFCAs to elicit psychophysical percepts in non-human primates.
- Aim 3.4: Determine the spatial extent of activation in human cortex *in vivo*.

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and

negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Introduction:

We have made much progress and most of the Aims/sub-Aims are completed. We have demonstrated that manufactured coils reliably activate CNS neurons via in vitro, in vivo as well as in behavioral experiments. We have demonstrated performance is consistent and reliable during chronic implantation. We have demonstrated effectiveness via stimulation of primary visual cortex in awake behaving monkeys. We have performed much safety testing and revised several key design features to greatly reduce concerns about coil heating and/or temperature increases. A second NCE period was approved to help compensate for delays in the supply chain that adversely impacted our receipt of the final ASIC chip and thus our testing of the final device that would be used in human testing. The chip arrived at our sub-contract site (Sigenics) in late 2022 and the testing and associated software development is largely completed; the chip is functioning as expected. With approval of the Year 2 NCE, the final design with the chip will be implanted and tested in lab animals during this upcoming quarter. As mentioned previously, it is unlikely that we will complete Aim 3.4 (acute testing in human); approval of the IRB will require the testing of the final design and by the time we have such data, the grant period will be over. We are nevertheless continuing these efforts with a coil-based cortical visual prosthesis and have applied for additional (NIH) funds to move this forward. Progress and remaining challenges for all Aims are described below.

Aim 1.1 (thresholds of human PNs):

To evaluate the effectiveness of a given microcoil design, we measure the strength of the stimulus needed to activate individual neurons; we refer to the minimum strength needed for activation as the threshold and compare thresholds across designs. We have performed extensive threshold testing in mouse cortex but needed to better understand the sensitivity of human neurons, i.e., will the coils be similarly effective when tested clinically.

Fortunately, we were able to obtain small pieces of human cortical tissue, resected from medically necessary neurosurgical procedures, that allowed us to measure thresholds in individual (human) neurons. Using test protocols that were essentially identical to those performed in mice, we determined that thresholds for activating human cortical neurons are only about 15% higher than those from mouse. Note that in mouse we had access to all cortical regions and therefore could test a specific class of neurons, referred to as Layer 5 pyramidal neurons, from a portion of cortex referred to as V1 (or primary visual cortex). V1 is almost never resected during clinical surgery and so we worked with Layer 5 pyramidal neurons from other cortical regions (mostly the temporal lobe). Nevertheless, our experiments in mouse suggest that most L5 pyramidal neurons have similar thresholds, regardless of region, and so the similarity in threshold levels (between mouse and human) is encouraging because it suggests that our ongoing animal testing does indeed directly inform the design of clinical devices.

Initial experiments with human tissue were performed prior to the start of this CDMRP award. However, since human tissue becomes available on a regular basis at MGH, we proposed to continue our *in vitro* testing and applied for HRPO approval (received March 2020). The additional measurements add to existing cell counts for basic threshold measurements (Aim 1.1) and also help to evaluate whether other response characteristics, identified in rodent neurons, persist in human neurons (Aim 2). The additional experiments have been completed and final analysis is underway.

HRPO reviewed and approved the most recent Continuing Review from the MGH IRB on November 27,

2022 although no additional experiments are anticipated.

Aim 1.2 (Design optimization of coils):

We have established design specifications for several types of wired devices and one wireless version. Multiple samples of all versions have been produced (Aim 1.4, described below) and physiological testing continues (Aim 2, in vitro and Aim 3, *in vivo*); summaries of this testing are reported in the corresponding sections below.

Although originally confined to months 1-6 in the original SOW, design efforts to enhance the efficacy, enhance selectivity and reduce power consumption will continue for the duration of the project. In general, this effort consists of computational modeling of coil efficacy, e.g., how do changes to coil shape, change stimulation waveforms and the addition of specialized cores influence the field strength and gradients produced by the coil, followed by fabrication of prototypes (for promising designs) and then physiological testing. This ongoing effort does not adversely impact progress on the rest of the Aims.

Aim 1.3 (Development of electronics):

There has been much additional testing of the new chip and there are no functional concerns which is very encouraging. The software and additional hardware needed to help us interface with the chip is still in progress and will not be completed until January. A summary of the Technical Update from Sigenics is below.

To recoup some of the time lost due to the pandemic and to the transfer of NHP testing from HMS to ASU, the initial ASIC testing will operate with wired devices. Use of wires (vs. the wireless design) will enable more precise temporal control of all channels and also enable a wider range of stimulus amplitudes to be tested. In addition, much less design refinement will be needed with a wired device, allowing us to quickly establish proof-of-principle for the multi-channel chronic implant. This will also allow us to focus more narrowly on evaluating the performance of the chronic implant rather than on the development of wireless technology.

The chip was received by Sigenics and testing completed in Q16. The chip is now at MGH and its performance will be assessed via a series of in vitro and in vivo experiments.

Aim 1.4 (coil fabrication):

- The first 4 steps in the SOW (Develop coil fabrication processes; Fabrication of 1st generation coils; Develop coil testing procedures; Fabrication of 2nd generation coils) have all been completed. We continue to refine the designs and to develop and test new coils (see details below).
- There are now two versions of the wired device – one for use in *in vitro* experiments and one for use in *in vivo* (chronic) testing. Devices produced by MicroProbes for Life Sciences (MLS, one of the sub-contracts sites for this award) reliably meet design specifications and perform consistently. To date, MicroProbes has made over 100 *in vitro* devices and ~40 *in vivo* devices. They continue to refine the production process and coils are now made reliably and repeatedly.
- Quality checks remain in place to ensure that key elements of the design (e.g., impedance, lead integrity, tip orientation, etc.) are all consistent (validated by testing at the vendor and at MGH). Additional improvements in the fabrication process continue to be implemented on an ongoing basis.
- The wired device for use in acute NHP testing (Aim 3.3) had been completed previously. Our decision to move the NHP experiments to a new site (Greger lab at ASU) necessitated some additional design changes that were worked on in Q8. Samples for the first NHP experiments were developed in Q8 and revised in Q9; they have been tested in >40 experiments to date. Results indicated that the acute, single channel device effectively elicits percepts in awake, behaving monkey (more details in Aim 3.3). These findings were presented at the recent SfN conference.
- The final device that will be fabricated is the chronic, multi-coil implant. The design has been completed and 2-, 4- and 8-channel devices have been prototyped. All were tested for penetration and worked well. Individual channels have been functionally tested *in vitro* and function as expected and we are

assembling the chronic design with 16-channels; we were hoping to have it ready in Q13, but a new fabrication run of the SU-8 inserts was required and has run into significant delays. We received the additional prototypes in mid-November and are currently assembling them into devices. Testing has begun and the inserts work fine. The final testing was held up pending arrival of the final chip and power supply from Sigenics; it will resume in Q17 now that the final package is in place.

Aim 2 (establish efficacy via physiological experiments)

- Much testing of effectiveness using *in vitro* experiments in mice has been completed (MGH). The results are encouraging in that devices consistently drive neuronal activation, impedance levels are low (and consistent), the devices are robust, e.g., they are used in many consecutive experiments with no loss of function so far.
- Power levels remain higher than we would like, and so effort continues to refine the coil design (Aims 1.2 and 1.4). Note that higher power levels do not impede progress with these Aims or even testing up to and including clinical trials. If the quality of artificial vision arising from coil-based devices exceeds that of conventional electrode devices, the engineering design of the coil and power supply can be overhauled to incorporate advanced electromagnetic design features.
- Much of our focus now has shifted to psychophysical testing in awake behaving NHPs. Results are summarized in Aim 3.3. Encouragingly, thresholds appear to be significantly lower than those from anesthetized rodent experiments (~17 mA vs. >300 mA in rodent experiments). We continue to explore ways to reduce thresholds further.
- In parallel experiments to the Aims of this grant, we have begun exploring ways to reduce threshold using a narrow-pitch multi-electrode array. The fine pitch allows us to assess how thresholds vary with fine movements. Experiments to date with electrodes indicate that the 'sweet spot' (region of lowest threshold) for some behavioral responses can be confined to a region as narrow as 250 microns. In the upcoming period, we will repeat these experiments with our microcoil.

Aim 3.1 (Establish efficacy of implanting)

- Coils have been safely and reliably inserted into mouse, rat and NHP cortex. A large number of acute mouse experiments have been performed without significant problem. Testing of insertion into rat cortex (n=~30) has also been relatively straightforward to date. Prior to the start of this grant, coils were inserted into visual cortex of anesthetized monkeys (after craniotomy and removal of dura); insertion was relatively easy, and we were able to detect surface responses (ECoG) arising from stimulation of the coils.
- Initial implantation of single channel devices into NHP cortex has been successful in >30 experiments to date. The design has worked well and we are now putting together a final summary of our progress (see Aim 3.3). While much of the Aim has been completed, final testing will extend beyond the date in the SOW; this is largely due to issues with the original NHP site (see below for details). It is not expected to adversely affect any of the key milestones or other goals of this grant.
- The multi-channel chronic design was also successfully inserted into mouse cortex. Devices containing 2-, 4- and 8-channels have all been inserted successfully and are not impacted by the presence of the dura, i.e., insertion works well regardless of whether the dura is removed. 16-channel devices are currently under development; these will be tested once the final ASIC chip is completed – we will perform this in Q17.
- We resolved the previously reported bending of the coil shaft. After investigation, it turns out that small etches we made in the coil housing (used to allow insertion depth to be estimated), were causing weakness during insertion. These marks were removed, and the bending has stopped. Insertion depth is now estimated via the manipulator readout.

Aim 3.2 (Evaluate long-term safety and stability)

- Preliminary psychophysical testing of chronic (wired) coils took place in collaboration with Kevin Otto and his lab at the University of Florida. As per the testing plan, responses to chronic implantation of electrodes were completed first and included measurement of thresholds, dynamic range, signal-to-noise ratio, etc. Repeated capture of these measurements allowed the stability of responses over time to be evaluated. The results convincingly show that thresholds do indeed vary over time, i.e., the performance of implanted electrodes is not stable. Two studies have been published (Urdaneta et al. 2021 and Urdaneta et al. 2022). A third study is currently under review.
- Stability testing is ongoing at MGH with implants that have performed consistently for more than 100 days. Our initial immunochemical analysis was positive but we need more samples to complete and publish the study. Consistent with our physiological findings, markers of activity are largely confined to focal regions around each coil. Also, as expected, markers of gliosis are qualitatively similar with coils (as with microelectrodes); the additional testing is to help improve our statistical analysis.
- We have made considerable progress towards the safety component of this sub-Aim. The design protocol has been completed and experiments to evaluate coil function and tissue integrity over time have been performed. This includes measuring temperature, pressure waves, tissue response, etc. in response to chronic implantation. The tissue response consists of a number of immunochemical markers analyzed in the immediate vicinity of the coil implant and findings will be compared to those from electrodes. This testing will provide much of the safety validation as we prepare for human testing.
- The temperature measurement portion of the study is largely complete, and a manuscript is largely developed. We found that coil-based stimulation could induce relatively large temperature changes but that neural responses arose from parameter sets that did not induce large temperature changes, i.e., observed neuronal responses are not mediated through a temperature-related mechanism. Pressure waves also do not appear to play a significant role in the activation process. A manuscript on this work is largely completed and will be submitted in Q17.
- Additional recent analysis of the model created as part of the temperature study, revealed a potential flaw in the coil design. There are a few air pockets surrounding the coil that could overheat, i.e., temperature increases of more than 2 degrees Celsius on the outer coil surface. We have changed the design of the coil to eliminate the air pockets and are running final simulations to verify that temperature changes remain minor. New coils have been assembled and the final experiments have been completed. Additional use of the model led us to change the coil material from platinum-iridium (Pt-Ir) to gold. The higher conductivity of gold produces much less heat and our latest samples have temperature rises less than 1ºC, well below the threshold for existing safety standards.

Aim 3.3 (Psychophysical testing in non-human primates)

- All of the delays, both prior to moving to ASU, as well as the minor delays after starting at ASU, have been described in previous reports and are not repeated here.
- Results from ongoing experiments with implanted coils were encouraging although additional testing is desirable. Our analysis of recent experiments strongly suggested that the animal is detecting stimulation from the implanted micro-coil. Also encouragingly, the stimulus amplitudes required are much less than those required in the experiments with anesthetized rodents, e.g., our estimate of threshold from the psychometric curve fit to the monkey results is ~17mA while thresholds from rodent experiments were sometimes >300 mA.
- We were not able to get good experiments every time we run. Some of this is the nature of psychophysical work with NHPs and some is that the specific animal we are using is probably not the best for this type of work. As explained in previous report, part of the attraction in moving to ASU was that they had an animal available in house, allowing us to be up and running in a few short months. It is unfortunate that this animal turned out to be sub-optimal and

we regularly lose days when the animal is not cooperative or where we only get a short window of cooperation. After much discussion, we decided to stop the experiments as we felt we went as far as we could with this particular animal. These findings were presented at the Society for Neuroscience meeting in San Diego. Responses to my talk and Bradley Greger's poster were both very encouraging.

- We were hoping to start additional experiments in a new animal however there simply isn't enough time to get a new animal up and running before this grant ends in early 2023. Regardless, we continue to believe that the results obtained so far provide convincing evidence that magnetic stimulation from a microcoil implanted in V1 can indeed elicit visual percepts in an awake behaving primate.
- A grant proposal to perform follow-up testing has been submitted to NIH and will be reviewed in early Q17.

Aim 3.4 (Spatial extent of activation in humans)

- We will not be able to complete this sub-Aim by the time this award ends. It had always been an optimistic timeline, especially with all of the delays arising from the pandemic, but we were making good progress and had lots of encouraging results. Much safety and efficacy data has been compiled but the lack of availability of the 'chip' has prevented us from running the final necessary set of experiments. The chip arrived in late January and functional testing in animals won't be completed until March 2023; it will take an additional 2-3 months before the IRB package is reviewed and approved. We will still pursue this – it just won't be completed before this grant runs out.
- As mentioned previously, initial discussions with neurosurgeons were encouraging in that they support the support the project and do not see any significant challenges with the proposed testing. The focus will be on intrasurgical testing, e.g., in pieces of cortex slated for resection in human neurosurgical patients at MGH.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

There are several opportunities for Training as well as for Professional Development

- Sang Baek Ryu, PhD is working with Seung Woo Lee (site-PI for the MGH sub-

contract) to obtain greater proficiency with micro-coil design, development and testing. He has become quite adept in all of these and has completed 3 first-author studies to date and is proceeding with additional work. He was recently promoted from post-doctoral fellow to Research Associate.

- Aditya Datye, M.S. is a research assistant in the lab and has been trained on how to model the effectiveness of coil-based stimulation; his efforts are contributing to the goal of optimizing coil design. Drs. Lee and Fried provided most of the training but are also making additional resources available, e.g., electromagnetic experts. Aditya was accepted into a Master's Program at Boston University and is now back in school.
- Andrew Whalen is a post-doc in the lab and is working with Drs. Fried and Lee to learn how to perform *in vitro* and *in vivo* electrophysiological experiments. He has performed much of the temperature and stability testing of Aim 3.2. Andrew was offered a Senior Scientist position at Yale University (Dept of Neurosurgery) and is now running his own studies.
- Jae-Ik Lee is a post-doc in the lab and was trained on how to perform coil-based electrophysiological experiments. He is now part of a collaboration between the PI (Fried) and Julie Arenberg, PhD (along with Christian Brown and Dan Lee, all at MEE) to develop a coil-based cochlear implant and learned how to perform the complex *in vivo* measurements needed to test such a device. Results from the first study are encouraging, e.g., they show that coil-based stimulation of the cochlea is effective and further, that it better confines activation than electric stimulation, thus offering the potential for narrower spectral channels. A manuscript on this work has been published and we have received notice that our NIH grant will be funded through NIDCD.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Dissemination has been achieved through publications, conference presentations and abstracts. A full list of presentations and abstracts is provided below.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Aim 1.4 (Fabrication of prototype devices). Most tasks have been completed. The design of the final device, the multi-channel implant for chronic use, is largely complete. The chip has been delivered to MGH and testing will be completed this Quarter.
- Aim 2 (Verify functionality of prototypes). Testing of the original Aims is largely completed at MGH

but we continue to test devices, evaluating efficacy, consistency, stability, functionality, power usage and selectivity. Modeling efforts are being incorporated to help optimize design. This effort focuses on continuous improvement of the designs and will continue throughout the course of this project.

- Aim 3.1 (Implant testing in rodents). As described above, we have initial results from implant testing (electrodes) in S1 (somatosensory cortex) and the same testing with coils continues at MGH with implants in both primary visual cortex (V1) and superior colliculus. We are very encouraged by the fact that thresholds with implanted coils have remained stable for 10+ months. We determined some inconsistency in performance across animals was caused by the length of our experiments and have reduced them accordingly. New results are more consistent, i.e., coil performance is stable, and we are beginning to assemble our test results for publication.
- Aim 3.2 (evaluate long-term safety). The hot spots discovered during modeling were verified experimentally and a new coil design developed to eliminate the air pockets that cause the heating. The new samples arrived; along with the change to gold wire, the potential for excessive heating has been greatly reduced.
- Aim 3.3 (NHP testing). We no longer feel we have adequate time to work with a second (and/or third) animal as part of this project. Our application for a new R01 grant to the NIH/NEI, to continue this portion of the study has been resubmitted and will be reviewed in March of 2023.
- Aim 3.4 (evaluation in humans). We no longer feel we can complete this within the grant period but we continue to develop the IRB application and will submit it for review once all tested is completed (with the final design including the chip).

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Implantable micro-electrodes have been the standard for delivering artificial stimulation to targeted regions of the CNS. The micro-coils we are developing as part of this project represent an alternative to conventional electrodes and may have some important advantages, e.g., enhanced performance stability over time as well as the ability to more precisely target specific neuronal populations. We continue to present our work at meetings focused on the development of neural prostheses so that those in the field can learn of the potential benefits of this approach.

Many efforts to develop a neural prosthesis that targets the CNS are faced with similar challenges: maintaining stability and enhancing selectivity of stimulation. We have started a collaboration on a coil-based cochlear implant. Results have been highly successful so far and we have 1 publication and have received notification of intent to fund a grant from the NIH (NIDCD). We have recently been contacted by a group studying artificial stimulation of the peripheral nervous system for help evaluating coils in their animal and clinical research programs.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

N/A

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Interest in microcoil based stimulation of the CNS continues to grow and the number of citations of our previous publications continues to increase. Several additional groups have requested collaborations. Nevertheless, the technology is still new, and it will take additional testing before it is adopted into standard practice.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Supply chain issues negatively impacted our ability to complete and test the electronic chip as part of Aim 1.3. We were able to divert some funding so that we could request an additional

NCE to complete this testing. The chip and control board finally arrived and will be tested at MGH starting February 2023.

As described above, we tried to obtain a new monkey to resume the psychophysical experiments at ASU. Unfortunately, there isn't enough time to complete all the preliminary steps and still have enough time to obtain meaningful results. We resubmitted our R01 application to NIH – the original application had many good scores and we felt we could directly respond to all concerns.

Even without the ongoing testing, we believe we have enough 'efficacy' data to justify the human experiment and discussed this previously with IRB staff in a preliminary meeting. Our findings were presented at SfN and comments there were encouraging. Nevertheless, we do not think it is likely that we will complete this sub-Aim before the NCE period expires. Even though the ASIC chip and software are now at MGH, the safety testing will take some time and development of the package to the IRB will not occur before the grant expires. However, we have applied applying for additional funding to non-DoD sources and we expect to complete the result beyond the end of this (CDMRP) project.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Detailed above

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to report

Significant changes in use or care of vertebrate animals

N/A

Significant changes in use of biohazards and/or select agents

Nothing to report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

1. Liu, X., Whalen, A.J., Ryu, S.B., Lee, S.W., **Fried, S.I.**, Kim, K., Cai, C., Lauritzen, M., Bertram, N., Chang, B., Yu, T., Han, A., (2023), MEMS micro-coils for magnetic neurostimulation, Biosensors and Bioelectronics. PMID: 36805270.
2. Kim, T., Kadji, H., Whalen, A.J., Ashourvan, A., Freeman, E., **Fried, S.I.**, Tadigadapa, S., Schiff, S.J., (2022), Thermal Effects on Neurons During Stimulation of the Brain. J. Neural Eng. PMID: 36126646.
3. Lee, J.I., Seist, R., McInturff, S., Lee, D.J., Brown, M.C., Stankovic, K.M., **Fried, S.I.** (2022), Magnetic stimulation allows focal activation of the mouse cochlea. eLife 11:e76682. PMID: 35608242
4. Urdaneta, M.E., Kunigk, N.G., Currlin, S, Delgado, F., **Fried, S.I.**, Otto, K.J., (2022), The long-term stability of intracortical microstimulation and the foreign body response are layer dependent. Front. Neurosci, PMID: 35769707.
5. Raghuram, V., Werginz, P., **Fried, S.I.,** Timko, B., (2021), Morphological factors that underlie neural sensitivity to simulation in the retina, Advanced NanoBiomed Research 2021, PMID: 34399546.
6. Lee, S.W., **Fried, S.I.**, (2022), Micro-magnetic stimulation of primary visual cortex induces focal and sustained activation of secondary visual cortex, Phil. Trans. R. Soc. A. PMID: 35658677.
7. Lee, K., Paulk, A.C., Ro, Y.G., Cleary, D.R., Tonsfeldt, K.J., Kir, Y., Pezaris, J.S., Tchoe, Y., Lee, J., Bourhis, A.M., Vatsyayan, R., Martin, J.R., Russman, S.M., Yang, J.C., Baohan, A., Richardson, R.M., Williams, Z.M., **Fried**, **S.I.**, Hoi Sang U, Raslan, A.M., Ben-Haim, S., Halgren, E., Cash, S.S., Dayeh, S.A., (2022) Flexible, Scalable, High Channel Count Stereo-Electrode for Recording in the Human Brain, BioRxiv (on-line).
8. Lee, J.I., Werginz, P., Im, M., Fried, S.I., (2023), Exploring the Underlying Mechanism of Neuronal Responses to High-Frequency Stimulation: Membrane Depolarization Mediates Inhibition of Neuronal Activity as well as Response Variability across Types, (Submitted).

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of*

publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Other Publications:

1. Han, A., Le, H., Haque, R., Ouyang, Z., Lee, S.W., Fried, S.I., Zhao, D., and Min, Q, (2021), MEMS inductor fabrication and emerging applications in power electronics and neurotechnologies, Nature Microsystems and Nanoengineering. PMID: 34567771.
2. Moleirinho, S. Whalen, A.J., Fried, S.I., Pezaris, J.S. (2021), The impact of synchronous versus asynchronous electrical stimulation in artificial vision, J.Neural Eng. PMID: 33900206.
3. Paulk, A.C., Yang, J.C., Cleary, D.R., Soper, D.J., Lee, S.H., Ganji, M., Ro, Y.G., Oh, H., Hossain, L., Rogers, N., Kilic, K. Ryu, S.B., Lee, S.W., Hermiz, J., Gilja, V., Lee J.W., Maus, D., Devor, A, Fried, S.I., Jones, P.S., Nahed, B.V., Ben-Haim, Sharona, Raslan, A.M.T., Siler, D.A., Cahill, D.P., Williams, Z.M., Cosgrove, G.R., Dayeh, S.A., Cash, S.C., (2021), Microscale physiological events on the human cortical surface detected with PEDOT:PSS Electrodes, Cerebral Cortex, PMID: 31369283.
4. Ryu, S.B., Paulk, A.C., Yang, J.C., Ganji, M., Dayeh, S.A., Cash, S.C., Fried, S.I., Lee, S.W. (2020), Spatially confined responses of mouse visual cortex to intracortical magnetic stimulation from micro-coils, J. Neural Eng. PMID: 32998116.
5. Otgondemberel, Y., Roh, H., **Fried, SI**, Im, M (2021), Spiking Characteristics of Network-Mediated Responses Arising in Direction-Selective Ganglion Cells of Rabbit and Mouse Retinas. IEEE-Trans Neural Syst Rehabil Eng. 2021. PMID: 34784280.
6. Urdaneta, M.E., Kunigk, N.G., Delgado, F., **Fried, S.I**., Otto, K.J. (2021), Layer-Specific Parameters of Intracortical Microstimulation of the Somatosensory Cortex, J.Neural Eng. PMID: 33706301.
7. Werginz, P, Raghuram, V, **Fried, S.I.** (2020), Tailoring of the axon initial segment underlies reliable conversion of synaptic inputs into spiking output in OFF-Alpha T retinal ganglion cells, Science Advances, 2020 Sep 11;6(37):eabb6642. doi:10.1126. PMID: 32917708.
8. Werginz, P, Raghuram, V, **Fried, S.I.** (2020), The relationship between morphological properties and extracellular electric stimulation in alpha RGCs, J.Neural Eng., 2020;10.1088/1741-2552. PMID: 32736374.
9. Yoon, Y.J., Lee, J.I., Jang, Y.J. An, S., Kim, J.H., **Fried, S.I.**, Im, M. (2020), Retinal Degeneration Reduces Consistency of Network-mediated Responses Arising in Ganglion Cells to Electric Stimulation, IEEE-Trans Neural Syst Rehabil Eng. PMID: 32746297.
10. Muralidharan, M. Guo, T., Shivdasani, M.N., Tsai, D., **Fried, S.I.**, Cameron, M., Morley, J.W., Dokos, S., Lovel, N.H. (2020), Towards controlling functionally-distinct retinal ganglion cells in degenerate retina, Conf Proc IEEE Eng Med Biol Sci. PMID: 33018781.
11. Hadjinicolaou, A., Werginz, P., Lee, J.I., **Fried, S.I.** (2020), Differential responses to high-frequency stimulation in brisk transient and delta ganglion cells, Conf Proc IEEE Eng Med Biol Sci. PMID: 33018765.

12. Lee, J.I., Hadjinicolaou, A.E. **Fried, S.I.** (2020), Response profiles of retinal ganglion cells to sinusoidal electric stimulation vary for low and high frequencies, Conf Proc IEEE Eng. Med Biol Sci. PMID: 33018766.
13. Muralidharan, M., Guo, T., Shivdasani, M.N., Tsai, D., **Fried, S.I.**, Li, L., Dokos, S., Morley, J.W., Lovel, N.H. (2020), Neural activity of functionally different retinal ganglion cells can be robustly modulated by high-rate electrical pulse trains, J. Neural Eng., 2020 Jun 8, doi: 10.1088/1741-2552. PMID: 32512555.
14. Yu, H., Enayati, S., Chang, K., Cho, K., Lee, S.W., Talib, M., Zihlavnikova, K., Xie, J., Achour, H., **Fried, S.I.**, Utheim, T.P., Chen, D.F. (2020), Noninvasive electrical stimulation improves photoreceptor survival and retinal function in mice with inherited photoreceptor degeneration, IOVS Apr 9;61(4):5. PMID: 32271885.
15. Rathbun, D, Shivdasani, M, Guo, T, **Fried, SI**, Lovell, N, Hessburg, P (2020), The eye and the chip 2019 – Conference report." Journal of Neural Eng., 2020: 17 (1), 010401. PMID: 31965978.
16. **Fried, S.I.**, Shivdasani, M.N., (2020), News and Views: Selective activation of the visual cortex, Nature Biomed. Eng. https://doi.org/10.1038/s41551-020-0419-8. PMID: 32051575.
17. Lee, SW, Thyagarajan, K, **Fried, SI**, (2019), Micro-coil design influences the spatial extent of responses to intracortical magnetic stimulation. IEEE-Trans BioMedical Engineering. PMID: 30369434. **** Featured cover****.
18. Ryu, SB, Werginz, P, **Fried, SI**, (2019), Response of visual cortical neurons in the mouse to electric stimulation of the retina, Frontiers in Neuroscience, 04 April 2019 https://doi.org/103389/fnins.2019.00324. PMID: 31019449.
19. Guo T, Tsai D, Yang CY, Al Abed A, Twyford P, **Fried SI**, Morley JW, Suaning GJ, Dokos S and Lovell NH (2019), Mediating Retinal Ganglion Cell Spike Rates Using High-Frequency Electrical Stimulation, Front. Neurosci., 13:413. doi: 10.3389/fnins.2019.00413. PMID: 31114476.
20. Werginz, P, **Fried, SI** (2019), Comparison of electrically elicited responses in rabbit and mouse retinal ganglion cells, Conf Proc IEEE Eng Med Biol Sci., 2019 Jul; 2019:1813-1816. Doi: 10.1109/EMBC.2019.8857504. PMID:31946249.
21. Ganji, M., Paulk, A., Yang, J., Vahidi, N., Lee, S.H., Liu, R., Hossain, L., Arneodo, E., Thunemann, M., Shigyo, M., Tanaka, A., Ryu, S.B., Lee, S.W., Tchoe, Y., Marsala, M., Devor, A., Cleary, D., Martin, J., Oh, H., Gilja, V., Gentner, T., **Fried, S.**, Halgren, E., Cash, S., Dayeh, S. (2019), Selective Formation of Porous Pt Nanorods for Highly Electrochemically Efficient Neural Electrode Interfaces, Nano Letters Article ASAP. DOI: 10.1021/acs.nanolett.9b02296. PMID: 31369283. PMCID: 7174248.
22. Raghuram, V, Werginz, P, **Fried, SI** (2019), Somatodendritic and AIS scaling in retinal ganglion cells helps to regulate spike properties and maintain response consistency, Front. Cell. Neurosci, https://doi.org/10.3389/fncel.2019.00436. PMID: 31611777

Posters (last 12 months):

1. J.I. Lee, R. Seist, …, S.I. Fried, “Magnetic stimulation allows focal activation of the mouse cochlea”, ARO, February, 2023.
2. J.I. Lee, R. Seist, …, S.I. Fried, “Magnetic stimulation of the cochlear nerve”, SfN 2022, November 16, 2022.
3. B. Greger, J. Tanner, J.S. Pezaris, S.B. Ryu, S.W. Lee, S.I. Fried, “Micro-scale magnetic stimulation of primary visual cortex for evoking visual percepts”, SfN 2022, November 16, 2022.
4. P. Werginz, S.I. Fried, [2022], “Cellular properties and their influence on action potential

waveform in retinal ganglion cells", BRAIN Initiative Investigators Meeting, Virtual.
5. J.I. Lee, P. Werginz, S.I. Fried, [2022], Changes in baseline membrane potential underlie the non-monotonic responses of RGCs to high frequency stimulation as well as the response variability across types, BRAIN Initiative Investigators Meeting, Virtual.
6. M. Yunzab, A. Datye, V. Turnbull, G. Rosen, P. Werginz, J.I. Lee, A.J. Whalen, B.R. Huber, S.I. Fried, [2022], "Evaluating different morphometric methods in measurement of immunolabelling of axon initial segment in layer V pyramidal neurons of mouse primary visual cortex, BRAIN Initiative Investigators Meeting, Virtual.

Presentations (last 12 months):

1. Technical University of Vienna, "Micromagnetic stimulation of the CNS", Invited speaker, December 6, 2022.
2. Univ. Goettingen (Germany), "A microcoil-based cochlear implant", Invited speaker, December 5, 2022.
3. Society for Neuroscience, "Microcoil-based magnetic stimulation of the CNS", Invited Speaker, November 13, 2022.
4. FDA Workshop – Expediting Innovation of Bioelectronic Implants for Vision Restoration, Panelist: Effectiveness of Bioelectronic Implants, October 25, 2022
5. MOMRP Meeting on Neurosensory Prevention and Treatment, Virtual, Invited Talk, "A Microcoil-based Cortical Visual Prosthesis, July 27, 2022, Invited Speaker

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities.

friedlab.mgh.harvard.edu
(the web-site of the PI)

A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

N/A

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

1. Patent issuance reported previously:

   Application #: 11,007,372
   Title: Selective activation of cortex using bent micro-wires to magnetically stimulate neurons

Publication date: May 18, 2021
Inventors: Lee, Fried
Summary
The design consists of one or more bends in a micro-wire and can be used to magnetically stimulate cortical neurons. Precise arrangements of the bends can facilitate the creation of stronger field gradients in one direction with much smaller gradients in orthogonal directions, thus allowing for selective targeting, or avoiding, of specific cell types within a targeted region. In exemplary versions, a micro-wire stimulator may be implanted into the cortex of the brain to selectively stimulate nearby neural cells having a particular orientation relative to the stimulator. The micro-wire design results in a reduced cross-sectional surface area of the micro-wire stimulator; the smaller area helps to minimize both the trauma arising from implantation as well as the level of biological response that arises over time.

2.

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

1. An animation that conceptually describes the coil approach has been developed
2. Microprobes for Life Sciences, LLC (Gaithersburg, MD) is a for-profit electrode manufacturing company; they are now developing coils for use as an alternative to electrodes.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: Shelley Fried, PhD
No change

Name: Seung Woo Lee, PhD
No change

Name: Adita Datye
Project Role: Research Assistant
Researcher Identifier (e.g. ORCID ID): ecommons ID: adatye
Nearest person month worked: *6*
Contribution to Project: computational modeling, coil design
Funding support *DoD Grant (and other grants)*

Name: Jae-Ik Lee, PhD
Project Role: Post-doctoral research fellow / Instructor
Researcher Identifier (e.g. ORCID ID): ecommons ID: jiklee
Nearest person month worked: *8*
Contribution to Project: animal testing of implanted coils, protocol development
Funding support *DoD Grant (and other grants)*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Dr. Seungwoo Lee, a long-time collaborator of Dr. Fried (PI), was offered a very prestigious faculty position in South Korea (his home country) and is starting in March of 2023. He was PI on an R01 award from the NIH and the award has approximately 1 year of funding left. Dr. Lee could not remain as PI but the NIH allowed Dr. Fried to take over as PI for the final year of funding. The Aims of Dr. Lee's grant were devoted to coil-based stimulation of visual cortex, but they did not include any of the translational efforts involved in this (DoD) award and hence, there is no overlap between the 2 awards. (NIH/NEI R01-029022, "Optimization of micro-coil arrays for precise stimulation of visual cortex.")

In addition, the PI (Fried) has received "Intent to Fund" notifications for 2 new awards. Both awards are pending receipt of the funding documents:

1) Dept of Veterans Affairs, BX005959, "Functional analysis of an LGN-based visual

prosthesis", Role: PI, 2023-2027, Annual direct amount: (est.)

2) NIH/NIDCD, R01-DC019916, "Development of a microcoil based cochlear implant", Role: PI, 2023-2028, Annual direct amount: (est.)

There is no overlap between either of the new awards and the current award discussed here.

Previously reported:
The PI (Fried) has received 2 new-subcontracts: one is from an NIH R01 award to Tatjana Jakobs at Schepens Eye Institute ("Cell biology of astrocyte-ganglion cell interactions") – our role is to perform physiological recordings from retinal ganglion cells in the PI's animal model of glaucoma. There is no overlap with the present work. The second is from a foundation from NovoNordisk, a Danish Foundation, to Anpan Han PhD, a PI at the Danish Technical Institute in Copenhagen ("Micro-coil-based cortical implant for restoration of vision to the blind"). Dr. Han is trying to develop next-generation coils in which intensifying cores are used to enhance the effectiveness of stimulation. This could help to reduce thresholds and would enable many more channels. Even though the titles are similar, there is no overlap with the present work.
The PI (Fried) received a new award from the BRAIN Initiative (NINDS; R01-NS110575) to investigate the fundamental biophysics of neuronal activation. Aims include study capturing detailed anatomy of retinal and cortical neurons, including a new technique we've developed to study the axon initial segment, and incorporating the measurements into realistic biophysical models. Model predictions will be verified by *in vitro* measurements.

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*

- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

- Sub-contracts have been issued to the same four organizations listed in the original proposal (Illinois Institute of Technology, Sigenics Inc., Massachusetts General Hospital and MicroProbes for Life Sciences).

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

A micro-coil based cortical visual prosthesis

ERMS/Log Number: N/A
Award Number: W81XWH1910057

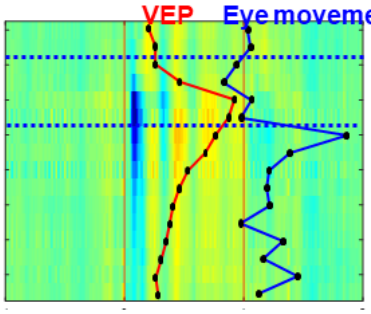
PI: Shelley Fried **Org:** Boston VA Research Institute (BVARI) **Award Amount: $2.1 MM**

Study/Product Aim(s)

- Design and development of a micro-coil array suitable for implantation into human visual cortex
- Establish functionality of the device via physiological testing
- Establish safety and efficacy of implanted devices

Approach

The use of magnetic stimulation from coils offers several important advantages over conventional electrode-based stimulation and we think our approach overcomes many of the limitations that have hindered progress with electrode-based prostheses in the past. We target visual cortex because it makes treatment available to the widest range of blind subjects, including soldiers and others that have suffered traumatic eye injury and/or damage to the optic nerve or optic radiation. The Specific Aims focus on optimizing the device design, establishing manufacturing processes that will consistently produce high-quality devices, and safety and efficacy testing in preparation for clinical trials.



Comparison of visually-evoked potentials (VEP) vs. eye movement, both as a function of electrode location. Each point represents the response from a different electrode of a multi-electrode array (MEA); pitch 50 um. Tests are helping us to better understand the size and location of the 'sweet spot' to stimulation. Ongoing experiments will test responses to microcoil-based stimulation once the electrode testing is complete.

Timeline and Cost

Activities / CY	19-20	21	22	23
Dev. of human device				
Prototype testing				
Safety and Effectiveness				
IRB / IDE Development				
Estimated Budget ($K)	**$800k**	**$500k**	**$600k**	**$200k**

Updated: (February 28, 2023)

Goals/Milestones

CY19-21 Goals – Development of human device

- ☐ Human in vitro testing; develop design specifications
- ☐ Prototype fabrication
- ☐ Chronic implantation study
- ☐ Psychophysical testing of coils in NHPs

CY22-23 Goals – IRB/IDE Development

- ☐ Psychophysical testing in NHPs
- ☐ IRB & IDE preparation
- ☐ Human testing (acute); behavioral activation and spatial spread

Comments/Challenges/Issues/Concerns

Testing of final device underway

Budget Expenditure to Date

Projected Expenditure: $2.1 MM
Actual Expenditure: $1.973 MM