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TITLE**:** **A Micro-Coil Based Cortical Visual Prosthesis**

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

CONTRACTING ORGANIZATION**:** **Boston VA Research Institute (BVARI)**
WEST ROXBURY, MA 02132

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Shelley Fried, PhD

E-Mail: fried.shelley@mgh.harvard.edu

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5 Post Office Square, 16-28
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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 are 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. At the completion of the first year, we describe here our progress with the design and testing of the device as well as our plans to begin the safety testing as well as the efficacy 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
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Despite some early clinical success, progress with cortical visual prostheses has been limited by an inability to selectively target specific neuronal sub-populations as well as by the foreign body responses that can compromise long-term efficacy. Our goal here is to advance efficacy and reliability by developing an array of 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 are 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.

General Overview:

As described in the original proposal, our design efforts consist of two parallel approaches. The first is to develop and test an implant in which the coil is directly wired to the power supply ('wired' approach); this approach is technologically simpler and will be useful for much proof of principle testing, up to and including the human intrasurgical (acute) experiments we are hoping to do in the final year of this proposal. The second approach is to develop a version in which power and data are transmitted wirelessly to the device ('wireless' approach); this approach is more technologically complex but will be advantageous as we move towards chronic implantation of clinical devices. The Aims and SOW describe efforts to advance both approaches and are referred to as 1st generation and final generation, respectively. Here, and in future summaries, we will try to clarify which efforts are devoted to each approach

Aim 1.1 (thresholds of human PNs):

We are able to obtain small pieces of human cortical tissue, resected from medically-necessary neurosurgical procedures at MGH, that allow us to measure in vitro responses to stimulation from our coils (as well as from electrodes, i.e. for comparison). This work is currently performed outside the scope of the CDMRP funding since we do not have HRPO approval for that work. The funding that supports the work will end in June of 2020 and so we have submitted an application to HRPO, that will hopefully allow this work to continue. Our original IRB-approved protocol was returned from HRPO because it comprised an amendment to a larger protocol, i.e. one that contained Aims beyond the scope of our proposal. We have since obtained IRB approval for a stand-alone IRB and have resubmitted to HRPO. Note that even though we already have established thresholds from human PNs, additional human tissue becomes available on a regular basis and we want to expand our in vitro testing as well as add to existing cell counts. The additional experiments will not interfere with any of the other Aims.

Aim 1.2 (design specifications):

- We have established design specifications for the 1st and final versions. We have largely completed the design specification for the both the 1st (wired) and final (wireless) versions and samples have been produced (Aim 1.4, below). Physiological testing is ongoing (Aim 2, below).
- Efforts to revise the design will continue indefinitely. Although originally confined to months 1-6 in the original SOW, efforts to enhance efficacy and reduce power consumption will continue on an ongoing basis for the duration of the project. Such efforts include the PIs efforts to support computational modeling of coil efficacy, e.g. how do changes to coil shape, change stimulation waveforms and the addition of specialized cores all influence the field strength and gradients produced by the coil. This effort has almost no impact on the rest of the Aims. Efforts also include the behavioral testing of Aim 3 (see below) in which we are testing whether thresholds are reduced in awake behaving animals, i.e. does the anesthesia we use for ECoG (electrocorticography) experiments contribute to high thresholds?

Aim 1.3 (power supply):

- The hardware for wireless power delivery were completed in late December (Sigenics) and have since been tested at MGH. Tests were successful, i.e. neural responses can be reliably elicited in brain slices. In vivo physiological testing is scheduled to begin in March of 2020.
- Design efforts are now ongoing to further enhance the wireless system. This included reducing the size of the transmission and receive coils as well as integrating the wireless transmission into the existing micro-coil design. Incorporation of wireless power into the coil housing will greatly reduce the overall size of the implant; reducing the size of the supply leads should greatly reduce the power needed to drive activation. The next generation concept designs have begun but finalization of the design won't occur until we have some preliminary in vivo measurements with the first-generation wireless design.

Aim 1.4 (coil fabrication):

- Coil production for 1st generation devices remains stable and samples continue to perform consistently. There are now two versions of the wired device – one for in vitro experiments and one for in vivo. MicroProbes continues to refine the production process and coils are now made reliably and repeatably.
- 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 MGH). Additional improvements in the fabrication process will be implemented over time.
- A 2nd generation design was completed in late 2019 but took some time to develop the fabrication processes; the goal of the design revision was to stabilize the coil assembly to help ensure reliable insertion into primate cortex. The first samples arrived in late January (2020) and initial efficacy has been demonstrated via in vitro and in vivo (mouse) experiments. The first primate insertion experiments are expected to begin in Summer 2020.

Aim 2 (establish efficacy via physiological experiments)

- Much extensive testing of effectiveness using in vitro experiments in mice has been completed already (MGH). The results are encouraging in that devices can effectively drive neuronal activation, impedance levels are low (and consistent), the samples 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 (Aim 1.2).
- We were also able to test a few of the new (wired) coils in the visual cortex of a single non-human primate. This work was done outside the scope of this project, but the opportunity was unique and we spent a considerable amount of effort getting the coil (and hardware) ready for this test. Encouragingly, the performance of the coil in NHP was almost identical to that of mouse, e.g. we were able to activate focal regions of the visual cortex with coils while the use of electrodes resulted in activation of much broader regions (see figure in Quad Chart). Importantly, the coil could be inserted into the cortex of the NHP without bending or causing any other damage to the coil. Coil performance remained stable, even after multiple insertions into cortex and several hours of use. Post-experiment evaluation of the coil confirmed that the coil was damage free. The similarities of physiological results in NHP and mouse are encouraging because they suggest that the extensive testing we have performed in rodents (and will continue to do) will be informative for our translational efforts.

Aims 3.1 & 3.2 (Implant testing in rats)

The IACUC protocol for rat in vivo testing has now been approved by MGH as well as by ACURO. Animals have been ordered and testing is slated to begin in March of 2020. Start-up of this protocol took slightly longer than our original estimates; some of the delay was caused by administrative delays in implementing the sub-contract at MGH. Those issues have been resolved and we are now working to catch up.

- Outside the Aims of this grant, we have provided coils to a colleague (Kevin Otto, U. Florida) that also want to test the stability of coils via a conditioned avoidance paradigm. Our coil design was implanted by their team in mid-November and preliminary psychophysical testing began in December. They have observed conditioned behavioral responses to coil-based stimulation and are gearing up to run a formal study. Although their efforts focus on somatosensory cortex (i.e. not visual), we anticipate that their results will be useful to our experiments as well as to the final coil design.

Aim 3.3 (Psychophysical testing in non-human primates)

- This work was slated to begin in Q1 of Year 2 but due to the delays in sub-contract implementation, the actual start date will be sometime in Q2. Much effort is currently ongoing to ensure that the IACUC protocol and experimental requirements are all in place so that we are set to go on schedule.

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, a post-doc in the lab is working with Seung Woo Lee (site-PI for the MGH sub-contract) to obtain greater proficiency with micro-coil design, development and testing.
- Aditya Datye, M.S. is a research assistant in the lab and is being 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 are providing most of the training but are also making additional resources available, e.g. electromagnetic experts.
- 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.
- Vineeth Raghuram, M.S., is a graduate student at Tufts University who is working with Drs. Fried and Lee to learn how to perform in vitro and in vivo electrophysiological experiments. He is a student in the lab of Brian Timko (Tufts, Department of Biomedical Engineering) and they are collaborating with Dr. Fried on the development of coil arrays; Vineeth will be testing the arrays and his results will help to optimize the array features of the clinical device.

- 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 Konstantina Stokjovic, MD/PhD to develop a coil-based cochlear implant and is receiving additional training as to how to test the device.
- Drs. Ryu and Lee (Jae-Ik), along with Vineeth Raghuram, attended the 2019 Eye and the Chip meeting in Detroit. The meeting brings together leading experts in the field of visual prostheses and each attendee was able to present their work. Drs. Fried and Lee (Seung Woo) attended and presented their work as well.

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 so far has been limited to conference presentations and abstracts.

- Presentations have been made at conferences that have less of a focus on bionic vision, e.g. Neurotechnology for Dementia Workshop (Buckinghamshire, England), Electronics and Information Technology (Osaka, Japan) and the Bioelectronic Medicine Forum (NYC, NY).
- 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.

Our plan is largely guided by the SOW. We will (1) continue to refine the coil design and test efficacy, (2) continue to develop the wireless design and validate efficacy, (3) begin the conditioned avoidance testing and confirm safety via histology, (4) prep for the psychophysical experiments in NHP, and (5) evaluate multi-coil efficacy.

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).

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. We are currently collaborating with a group in the University of Florida to develop implants for their work on stimulation of the somatosensory cortex and a group at the Massachusetts Eye and Ear Infirmary focused on development of a next-generation cochlear prosthesis.

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.

Many efforts to develop a neural prosthesis that targets the CNS are faced with similar challenges: maintaining stability and enhancing selectivity of stimulation. We are presenting this work to those in the broad field of stimulation with the hope that others will find the approach advantageous to their project. This work is not likely to have a significant impact outside the field of neural prostheses other than the human interest aspect if we can restore function to a non-working part of the CNS.

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.*

We have begun discussion about forming a company. Efforts are still in the initial stages and the company is not likely to get started until reports from the first clinical tests are complete. However, the goal is to be able to rapidly move the technology forward at that point. Preliminary discussions about a company to develop a next-generation cochlear prosthesis are also underway.

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:*

Nothing to report.

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.

- It took some time to get the individual sub-contracts issued and the corresponding research started. All sites are now up and running and we do not anticipate additional delays. The onset delays resulted in delays in some of the Aims; this does not really reflect actual problems or delays with the proposed work but many of the sub-Aims that involve subs were delayed between 3 and 6 months.
- There was a delay in developing and getting approval for a second IACUC protocol related to testing of implant insertion (Aim 3.1). This occurred because of a misunderstanding between the site PI at MGH (Lee) and myself – an approval had been granted for a different study and I was asking about this study and he answered about a different one. The new protocol has since been issued and was approved by ACURO after their review. The Aim is back on schedule and first implants are scheduled to begin in March of 2020.

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 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).*

Nothing to report

  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:

- Fried, S.I., Shivdasani, M.N., (2020), News and Views: Selective activation of the visual cortex, Nature Biomed. Eng (2020). https://doi.org/10.1038/s41551-020-0419-8. PMID: 32051575.
- 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.
- 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
- 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.
- Lee, SW, Thyagarajan, K, Fried, SI, (2019), Micro-coil design influences the spatial extent of responses to intracortical magnetic stimulation. IEEE-Trans BioMedical Engineering. DOI: 10.1109/TBME.2018.2877713. PMID: 30369434.
    - Publication featured on the Journal cover.
- 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.

Talks:

1. 11th World Congress on Visual Prostheses, Detroit, MI, Invited Talk, “Towards the development of a micro-coil based cortical implant”, November 11, 2019.
2. Society for Neuroscience, Chicago, IL, Tools and Techniques Session, “Micro-coils for cortical stimulation”, October 20, 2019,
3. Electronics and Information Technologies for Bionic Human (collaboration with BioCAS2019), Osaka, Japan, Invited Talk, “Implantable micro-coils for neural modulation”, October 16, 2019
4. Neurotechnology for Dementia (Workshop), Buckinghamshire, England, Invited Talk, “Implantable microcoils for neurorehabilitation”, May 15, 2019
5. Bioelectronic Medicine Forum, New York, NY, ‘A cortical visual implant to restore vision to the blind’, April 4, 2019.

Posters / Abstracts:

- S.W. Lee, S.B. Ryu, S.I. Fried [2019]. Optimization of Micro-Coil Designs for Selective Cortical Stimulation. The Eye and the Chip World Congress on Artificial Vision. Detroit, MI.
- S.B. Ryu, S.I. Fried, S.W. Lee [2019]. Spatially Confined Evoked Responses of Mouse Visual Cortex by Magnetic Stimulation Using Micro-Coils. The Eye and the Chip World Congress on Artificial Vision. Detroit, MI.

Posters / Abstracts (continued):

- V. Raghuram, P. Werginz, S.I. Fried [2019]. The Spike Initiation Zone in Mouse ON and OFF Alpha sustained RGCs Scales with Cell Size. The Eye and the Chip World Congress on Artificial Vision. Detroit, MI.
- P. Werginz, V. Raghuram, S.I. Fried [2019]. Location-Dependent AIS variations and Their Influence on Preferential Activation of RGC Subclasses. The Eye and the Chip World Congress on Artificial Vision. Detroit, MI.
- S. I. Fried, S. W. Lee, S. B. Ryu, [2019], Development of a Micro-Coil Based Visual Prosthesis. Military Health System Research Symposium, Kissimmee, FL.
- S.I. Fried, S.B. Ryu, A.C. Paulk, J.C. Yang, M. Ganji, S.A. Dayey, S.S. Cash, S.W. Lee, [2019]. Spatially confined evoked responses of mouse visual cortex by magnetic stimulation using micro-coils. Association for Vision in Research and Ophthalmology Annual Meeting, Vancouver, BC, Canada.
- S. B. Ryu, S. I. Fried, S. W. Lee, [2019], Focal activation of mouse visual cortex by magnetic stimulation using micro-coils, International IEEE EMBS Conference on Neural Engineering, San Francisco, CA.
- S. W. Lee, S. B. Ryu, S. I. Fried, [2019], Optimizing micro-coil designs for precise activation of primary visual cortex, International IEEE EMBS Conference on Neural Engineering, San Francisco, CA.
- S. B. Ryu, S. I. Fried, S. W. Lee [2019], Spatially confined evoked responses of mouse visual cortex by magnetic stimulation using micro-coil, 71st Annual MGH Scientific Advisory Committee Meeting.
- S. W. Lee, K. Thyagarajan, S. I. Fried [2019], Optimization of micro-coil designs for precise activation of primary visual cortex,71st Annual MGH Scientific Advisory Committee Meeting. Notable Poster Award.
- S. B. Ryu, S. I. Fried, S. W. Lee [2019], Focal activation of mouse visual cortex by magnetic stimulation using micro-coils, IEEE NER Meeting.
- S. W. Lee, K. Thyagarajan, S. I. Fried [2019], Optimizing micro-coil designs for precise activation of primary visual cortex, IEEE NER Meeting.
-

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

  Fried Lab web-site: friedlab.mgh.harvard.edu

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

BRAIN Initiative meeting: coils were presented at the Tools and Technologies workshop during the BRAIN Initiative Investigators Meeting (2019).

- **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.

- One existing patent has been obtained on coils prior to the onset of this grant and a second patent application is currently under review. These were developed prior to the onset of this award.
- Two additional patent applications are under development.

- **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.*

- An animation that conceptually describes the coil approach has been developed
- 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: Vineeth Raghuram, MS
No change

Name: Sang Baek Ryu, PhD
Project Role: Post-doctoral research fellow
Researcher Identifier (e.g. ORCID ID): ecommons ID: sangryu1
Nearest person month worked: *3*
Contribution to Project: in vivo testing of implanted coils, protocol development
Funding support *DoD Grant (and other grants)*

Name: *Aditya Datye*, MS
Project Role: Research Assistant
Researcher Identifier (e.g. ORCID ID): ecommons ID: N/A
Nearest person month worked: *2*
Contribution to Project: design improvements, modeling
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.

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).
- We continue to collaborate with Kevin Otto, PhD, in the Department of Biomedical Engineering at the University of Florida. Kevin is investigating the response of somatosensory cortex to electric stimulation and will perform some preliminary evaluations of coils to see how they compare to his electrode measurements. We supply Kevin with coils for this work and he has helped us to become more proficient with the process.

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)

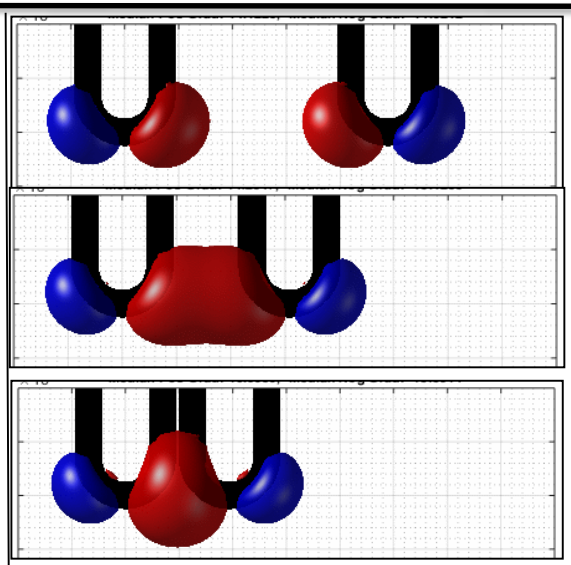
Award Amount: $2.1 MM

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.



Computer simulations of the activating force elicited by the flow of current through micro-coils. Excitatory (red) and suppressive (blue) fields are equal and opposite from isolated coils but combine in non-linear ways when the coils are brought close to one another. We are looking at the patterns, from these and other coil designs, to determine which will have the strongest reduction on thresholds and power consumption.

Timeline and Cost

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

Updated: (March 2020)

Goals/Milestones

CY19 Goal – Development of human device

☐ Human in vitro testing; develop design specifications

☐ Prototype fabrication

CY20 Goals – Prototype testing; proof of efficacy

☐ Chronic implantation study

☐ Phosphene generation

CY21 Goal – Safety and effectiveness testing

☐ Human testing (acute); behavioral activation and spatial spread

CY22 Goal – IRB/IDE Development

☐ IRB & IDE preparation

Comments/Challenges/Issues/Concerns

Psychophysical testing of coils in NHPs will begin in Q2 2020

Budget Expenditure to Date

Projected Expenditure: $2.1 MM

Actual Expenditure: ~$0.7 MM