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14. ABSTRACT Majority of limb loss incidents (~75%) among US Military Service members is in the lower limb. However, restoring sensorimotor function with advanced active prostheses that communicate directly with the intact nervous system falls far behind development of robotic prostheses for individuals with upper limb loss. The objective of this project is to develop and deploy a fully implantable, self-contained, neurally integrated bidirectional lower limb neuroprosthesis that can be readily incorporated into the body schema and utilized without cumbersome external components. In this project, a total of six subjects (three with trans-tibial and three with trans-femoral limb loss) will be enrolled. Electrical stimulation through nerve cuff electrodes directly excites the sensory nerves remaining in the residual limb while electromyography (EMG) signals from intramuscular electrodes are interpreted to intuitively control the actions of advanced robotic lower limb prosthesis. We examine the impact of integrating sensory feedback with EMG-controlled robotic prostheses on balance, gait, and performance during complex mobility tasks in laboratory and during use at home and in community.									
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1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The majority of limb loss incidents (~75%) among US Military Service members is in the lower limb. However, restoring sensorimotor function with advanced active prostheses that communicate directly with the intact nervous system falls far behind development of robotic prostheses for individuals with upper limb loss. The objective of this project is to develop and deploy a fully implantable, self-contained, neurally integrated bidirectional lower limb neuroprosthesis that can be readily incorporated into the body schema and utilized without cumbersome external components. Although state-of-the-art prosthetic technologies, such as microprocessor-controlled knees and powered ankles, restore some level of function to lower limb amputees, such wearable robotic devices still cannot provide natural somatosensory feedback related to the lost limb or respond seamlessly to the intent of the user in unexpected situations. Our bidirectional neuroprosthesis will allow users to directly control their prostheses by sensing and interpreting the activities of the intact muscles formerly associated with the desired movement, while simultaneously eliciting useful sensations that correspond to joint movements and limb loading to provide seamless sensory feedback about the motorized ankle/knee motion and foot-ground interactions. This project addresses a limitation in the current technology and will lay the foundation for a new generation of prosthetic devices that are fully integrated with the intact nervous system. A total of six subjects (three with trans-tibial and three with trans-femoral limb loss) will receive surgically implanted non-penetrating, high contact density peripheral nerve cuff electrodes on the sciatic and/or tibial nerves above the knee. Bipolar intramuscular recording electrodes will be implanted in the residual and intact upper thigh or gluteal muscles. Electrical stimulation delivered via the nerve cuff electrodes directly excites the sensory nerves remaining in the residual limb while electromyographic (EMG) signals from the implanted intramuscular electrodes are interpreted to intuitively control the actions of advanced robotic lower limb prosthesis. We examine the impact of integrating sensory feedback with EMG-controlled robotic prostheses on balance, gait, and performance during complex mobility tasks in the laboratory and during use at home and in community.

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

Bidirectional neuroprosthesis, lower-limb amputees, peripheral nerve stimulation, gait, balance, myoelectric control, robotic prosthesis, neurally integrated prosthesis

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.

The major goals of this project are to:

- 1) Amend the IRB study protocol at the Louis Stokes Cleveland VA Medical Center (LSCVAMC) to include EMG control and a fully implantable system and amend the IDE that currently regulates the fully implantable system for upper limb amputees to lower limb applications (35% Completed).
- 2) Procure critical components required for the implant surgery (75% Completed)

- 3) Identify six lower-limb amputees and complete the implant procedure with temporary percutaneous interface (35% Completed).
- 4) Design, prototype, verify, and produce electronic hardware and system software to access and control internal circuitry of robotic prostheses (Genium and Proprio) (45% Completed).
- 5) Determine the effects of bidirectional neuroprosthesis on static and dynamic measures of posture, balance, and gait mechanics (30% Completed).
- 6) Determine the effects of bidirectional neuroprosthesis during complex mobility tasks such as ascending/descending inclines or stairs, negotiating difficult changing terrain, dual tasks, and horizontal ladder walking task (35% Completed).
- 7) Install fully implantable bidirectional neuroprosthesis in two bidirectional neuroprosthesis recipients and establish reliable communications with INC and Hub (Not started yet).
- 8) Evaluate subjective perceptions of balance confidence, utility, comfort, satisfaction, and ease of use of the neuroprosthesis and measure its impact on overall mobility, incidence/severity of falls and phantom pain episodes during homegoing trials. (Not started yet).

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.

Scientific/Technical Accomplishments:

Our team successfully installed the implanted system in a 50-year-old Army veteran who lost his left leg at the knee due to trauma four years prior to enrolling in the study. The procedure took place on November 23, 2022 and involved the surgical installation of two 16-contact compliant flat interface nerve electrodes (C-FINEs) on the sciatic nerve in his residual limb. Additionally, the participant received 12 bipolar intramuscular (IM) recording electrodes in the hamstring, quadricep, and gluteal muscle groups (4 per group). A percutaneous interface provides access to the C-FINEs and IM electrodes, with lead wires to the implanted components exiting the skin in the lower abdominal area. External connectors were installed on the percutaneous leads to interface with custom sensory stimulation and myoelectric recording circuitry. The surgery spanned about six hours, and the participant was discharged the following day.

Preliminary observations suggest that electrical stimulation through about 70% of the tested C-FINE contacts elicited sensations referred to the missing limb. However, sensory thresholds seem to be higher compared to those obtained from system recipients with transtibial limb loss. This observation might be due to the participant's use of pregabalin, a medication intended to alleviate phantom pain but also known to affect nerve excitability. We presented a summary of these findings, including a comparison of the sensory thresholds between participants with transtibial and transfemoral limb loss, in a poster titled "Eliciting Plantar Sensation via Nerve Cuff Electrodes in Individuals with Transtibial versus Transfemoral Amputation" at the 11th International IEEE EMBS Conference on Neural Engineering (NER'23) in Baltimore, MD on April 25-27, 2023.

Throughout this reporting period our technical team has continued to work with Carroll Biomedical, an engineering firm in southeast Ohio, to develop an Electromyography Processing Module (EPM). We received a functional prototype of the EPM in May 2023 that is designed to integrate seamlessly into our existing neural stimulation unit. The EPM can acquire EMG signals from intramuscular electrodes, conduct onboard processing, and has the capability to generate corresponding motor commands for a robotic prosthesis. Integration of the EPM will elevate our neural stimulation unit to a fully independent, wearable, and untethered system that can operate as the primary controller for a bidirectional neuroprosthesis.

We conducted a comprehensive assessment of the EPM by comparing the EMG signals acquired with it to those of the Delsys Trigno wireless EMG system which is widely utilized in human movement studies by various research laboratories including our group at LSVAMC. Specifically, we acquired surface myoelectric signals from the lower-limb muscles of a transtibial amputee and an able-bodied participant and determined their signal to noise ratio (SNR), root mean square (RMS), Minimum Viable Contraction (MVC) timing, drift, saturation, and crosstalk. Initial results suggest comparable performance for the EPM and the Delsys Trigno system. The average ratio of EPM to Delsys was 88% for SNR and 99% for RMS. Additional performance indicators such as drift and crosstalk for EPM were negligible with no saturation observed. These results verified that the EPM could function as a portable system for processing EMG signals to control of a bidirectional neuroprosthesis moving forward. We will be presenting a summary of these findings at the *Biomedical Engineering Society (BMES) Annual Meeting* in Seattle, WA on October 11-14, 2023 in which we will acknowledge the DoD's contribution to these efforts.

To further the goal of a neurally integrated and bidirectional prosthesis, we also assembled the Open Source Leg (OSL) from Humotech LLC during the last reporting period and began designing a basic control system. The design of the OSL is state-of-the-art and provides the freedom to alter the hardware and software without the constraints often imposed by commercial prosthesis manufacturers. The device is customizable and equipped with fully accessible sensors that track loading, position, and other parameters of the prosthesis throughout ambulation.

We conducted a set of experiments with system recipients with transtibial limb loss involving split-belt treadmill walking with the goal of analyzing the impact of elicited plantar sensation on both motor adaptation and speed perception. Findings indicate that these elicited plantar sensations not only increased stance time and propulsive force on the prosthetic side but also improved gait symmetry and enhanced the perception of prosthetic leg movement during walking. These outcomes suggest that restoring plantar sensation can make the locomotor adaptation response of lower limb amputees resemble that of able-bodied individuals. Furthermore, they indicate that a peripheral nerve-based approach to elicit plantar sensation directly affects central nervous system pathways involved in locomotion and motor adaptation during walking. These results have important functional implications on highlighting the role of plantar sensation in increasing mobility, improving walking dynamics, and possibly reducing fall risk in amputees. Our manuscript, "Plantar Somatosensory Restoration Enhances Gait, Speed Perception, and Motor Adaptation," summarized these results and was just published in vol. 8, issue 83 of *Science Robotics* for October 2023.

A manuscript describing our recent findings titled "Neural Sensory Stimulation Does Not Interfere with the H-Reflex in Individuals with Lower Limb Amputation," was recently published in vol. 17 of *Frontiers in Neuroscience – Neuroprosthetics* in late September 2023. This article highlights an experiment that characterized the effects of electrically elicited sensations on the sensorimotor control system of individuals with lower limb loss by probing H-reflex excitability in the triceps surae muscles. We found that delivering electrically elicited plantar sensations did not interfere with reflex pathways while participants maintained static postures and loading conditions mimicking gait. This means that individuals with lower limb loss can receive the benefits of our neural sensory stimulation technology, such as improved gait symmetry, without the stimulation interfering with reflex pathways that are important for smooth and stable walking.

We conducted a dual-task experiment with three system recipients to elucidate how restored sensation affects cognitive load during ambulation. Participants were asked to walk on a self-paced, instrumented treadmill while engaging in a cognitive task. In this series of experiments we applied a color-word matching Stroop task, where participants were presented with two rows of words and were asked to respond to the question: "Does the color of the upper word match the meaning of the lower word?" The lower word was consistently shown in a black font color, and the upper word was adjusted to increase the task difficulty allowing us to probe changes in speed and gait outcomes based on the difficulty of the cognitive task. We expected gait performance in terms of self-selected walking speed and other measures to decrease with increasing difficulty of the cognitive task, and expected the sensory neuroprosthesis to reverse or mitigate this degradation. Interestingly, we found that two participants increased their gait speed as the difficulty of the cognitive task increased. Reports in the literature document that walking becomes more automatic above a certain speed threshold, leading us to hypothesize that walking faster may decrease the cognitive load of walking for these participants and thereby freeing up resources to be applied to the cognitive task at hand that may mask any effects of the sensory neural prosthesis. Preliminary findings from this study were presented in a poster presentation at the 11th *International IEEE EMBS Conference on Neural Engineering (NER'23)* in Baltimore, MD, on April 25-27, 2023.

We began data collection on a new experiment to assess how plantar sensation affects the perception of uprightness. This sensation is affected by various sources including vestibular, visual, and proprioceptive inputs. Previous work utilized a paradigm known as subjective visual vertical (SVV) to assess how the sense of uprightness is affected by changes such as tilting the head. A visual red line stimulus was displayed to system recipients as the radius of a circle at angles ranging from 0 to 360 degrees. The participant was instructed to answer whether the line appeared to the right or left of their perceived centerline, with the range of responses narrowing as the stimulus was repeated. The resulting data were used to construct a psychometric curve of correct responses with the point of 50/50 accuracy termed the SVV. Changes to this value, as well as to other aspects of the curve, indicate a change in the perception of uprightness. By performing trials with and without elicited plantar sensation, this experiment will inform how the implanted system integrates with other sensory inputs to inform more complex perceptions, such as the perception of uprightness.

We have begun data collection on a new assessment that investigates the impact of the Sensory Neuroprosthesis (SNP) activation on stair negotiation. Since individuals with lower limb loss often rely heavily on visual feedback when walking, stairs can pose a unique challenge, especially when their view is obstructed while carrying items. We are utilizing kinetic and kinematic data from a Bertec Instrumented Staircase and a Vicon motion capture system to understand how the SNP influences factors such as safety, toe clearance, and strategy when negotiating stairs with varying levels of visual feedback.

Clinical/Outreach Accomplishments:

To date our participant with transfemoral limb loss has experienced no clinical issues following the surgery. All incision sites healed as expected, and the participant has reported no complications in using his prosthesis. We began delivery of electrical stimulation to the C-FINEs at four weeks post-surgery, as outlined in our IRB protocol. Since then, he has attended regular laboratory visits where we conduct experiments to characterize sensations elicited by electrical stimulation delivered through the implanted nerve cuff electrodes.

Co-Investigators Drs. Gilles Pinault and Hamid Charkhkar attended the *Advances in Amputation Surgery International Conference* on January 27, 2023, at the Hospital for Special Surgery in New York, NY. Dr. Pinault presented the surgical technique for installing the implantable

neural interfaces to restore sensorimotor function by highlighting the recent surgery with our participant with transfemoral limb loss as a case study. Following the talk, both Drs. Pinault and Charkhkar participated actively in the Q&A session. The Department of Defense's contribution to the project was duly acknowledged during the presentation. Additionally, Dr. Hamid Charkhkar disseminated our work across various platforms, reaching audiences from clinicians to researchers. He presented at the *Bioengineering Seminar at George Mason University* in Fairfax, VA, on April 13th, 2023. On May 20th, he gave a presentation at the *Orthotic and Prosthetic Innovative Technologies (OPTech) Conference* in Minneapolis, MN and engaged in a panel discussion with neuroprosthetics experts following the presentation to address the challenges and recent advancements in neuroprosthesis research. Additionally, On June 14th, Dr. Charkhkar delivered a lecture in the *Musculoskeletal Research Training Program* at Case Western Reserve University School of Medicine to communicate our latest findings. In all presentations, the DoD contribution was acknowledged.

Four members of our team participated in the *Biomedical Engineering Society (BMES) Annual Meeting* in San Antonio, TX from October 12 to 15, 2022. Graduate students delivered two oral presentations titled "Enhancing Gait Symmetry and Perception through the Restoration of Plantar Sensation in Lower-Limb Amputees" and "Investigating the Impact of Electrically Elicited Sensations on Spinal Reflex Pathways." Additionally, we showcased two undergraduate poster presentations. Members from our team are slated to give two podium presentations and two poster presentations at this year's *BMES Annual Meeting* on October 11-14, 2023 as well. Three of our team members presented at *NER '23* in Baltimore, MD on April 25-27, 2023. These podium presentations were titled "Sensory Neuroprosthesis Reduces the Cognitive Load During Dual-task Walking in Individuals with Lower Limb Loss," "Eliciting Plantar Sensation via Nerve Cuff Electrodes in Individuals with Transtibial versus Transfemoral Amputation," and "Sensory Neuroprosthesis Improves Recovery from Treadmill-induced Stumbles." DoD contribution was acknowledged.

In our ongoing effort to increase awareness about the project, members of our team attended the annual *Veterans Wheelchair Games* in Portland, OR from July 4-9, 2023 as exhibitors representing the Advanced Platform Technology Center. Our participant with transfemoral limb loss competed in the games, attaining medals in multiple events. In addition, we continued our engagement at the *Amputee Coalition* meeting in Orlando, FL, from August 2-5. The same participant conducted a live demonstration of the SNP, providing attendees with firsthand experience of the life-changing potential of our technology.

Our work at the LSCVAMC on sensory restoration in amputees was also featured in a **CBS 60 Minutes** segment titled "Feeling of Feeling." This story focused on the ongoing developments in prosthetic technology that can potentially restore a sense of touch to persons with limb loss. Interviews were conducted with our implant recipients at LSCVAMC, and showcased the work of Co-Investigator Dustin Tyler, who uses the identical technology to restore sensation in upper limb amputees.

We routinely distribute our IRB approved recruiting materials to local prosthetists, physical therapists, and amputee support groups. Moreover, we redesigned our ad from the last half of 2022 for the Amputee Coalition's magazine, *inMotion*. The updated content just appeared in the October 2023 issue. We have significantly increased our recruitment efforts locally and nationally. Accordingly, we created an advertisement that runs daily on the Digital Announcement Network boards throughout the LSCVAMC. Our team also continues to regularly search for any eligible candidates in the Amputee and Endocrine/Diabetic Clinics at the LSCVAMC on a weekly basis, and routinely attends Amputee Clinic at nearby MetroHealth Medical Center.

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.

All team members are up to date on the safety training and *VA Human Subjects Protection and Good Clinical Practices* through The Collaborative Institutional Training Initiative (CITI Training).

Three undergraduate students joined the study team during summer 2023 as interns. These students, ranging from sophomore to senior, trained with the existing established Investigators and graduate students. They assisted with technical development, experimental setup, and data collection and analysis while being encouraged to develop their own small undergraduate research projects. Two of these students submitted abstracts to the *2023 BMES Annual Meeting* and will be presenting posters at the event on October 11-14, 2023, in Seattle, WA.

Our graduate and undergraduate students have given presentations at scientific meetings around the country during this reporting period. These included presentations at the *BMES Annual Meeting* and *NER '23*. More details on these are provided below in the presentations section.

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.

Co-Investigators and students from the project team actively disseminated results of our studies by presenting at professional scientific meetings including *BMES*, the *Bioengineering Seminar at George Mason University*, the *Orthotic and Prosthetic Innovative Technologies (OPTech) Conference*, the *Musculoskeletal Research Training Program* at Case Western Reserve University School of Medicine, and the *Advances in Amputation Surgery International Conference*. In addition, our work on sensory restoration in amputees was featured in a **CBS 60 Minutes** segment titled "Feeling of Feeling." The segment focused on the ongoing developments in prosthetic technology that can restore a sense of touch to persons with limb loss and included interviews with our implant recipients at LSCVAMC that showcased the work of Co-Investigator Dustin Tyler, who uses the identical technology to restore sensation in upper limb amputees.

We were an exhibitor at the *Amputee Coalition National Conference* and annual *Veteran's Wheelchair Games*. In addition to our team members, our transfemoral amputee participant attended both of these events and provided a live demonstration of our sensory neuroprosthesis at the *Amputee Coalition National Conference*.

We published three journal articles over the course of the reporting period. These publications encompassed three different aspects of our work including the impact of the SNP on reflex modulation, user experiences with the SNP at home, and the biomechanical effects of the SNP on gait adaptation and speed perception. All appeared in high impact journals such as *Frontiers* and a special issue of *Science Robotics* focused on human-robot interaction.

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.

- Intensify efforts to identify, recruit, screen, and enroll subsequent candidates with transfemoral and transtibial limb loss
- Verify EPM functionality with participants during over ground walking
- Fully integrate the EPM with our existing neurostimulator
- Develop a prosthesis control scheme for the OSL based on EMG signal and complete benchtop testing
- Continue data collection with participants to determine the impact of the SNP on stair negotiation, cognitive load, and recovery from slips and trips

4. **IMPACT:** *Describe 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).

Our findings show that electrically elicited plantar sensations with our implanted cuff electrodes did not interfere with reflex pathways while participants maintained static postures and loads representative of gait. This means that individuals with lower limb loss can receive the benefits of our neural sensory stimulation technology, such as improved gait symmetry, without it interfering with reflex pathways that are important for smooth and stable walking. A manuscript with these was published in the September 2023 issue of *Frontiers in Neuroscience*.

We have shown that individuals with lower limb amputation achieved higher gait symmetry and stability with the sensory neuroprosthesis. In addition, we demonstrated elicited plantar sensations from the missing foot improved locomotor adaptation, suggesting integration of this new input in the central nervous system. These results were just published in the October 2023 issue of *Science Robotics*.

We provided an account of a first-hand user experience with the SNP from one of our participants in a recent publication titled “The Experience of Sensorimotor Integration of a Lower Limb Sensory Neuroprosthesis: A Qualitative Case Study,” which was published in *Frontiers in Human Neuroscience* in January 2023 following a long-term home use study with the SNP. Results suggest that integration of the SNP into the user’s motor plan occurs over time, showing the benefits of long-term, continuous use.

Our participant with transfemoral limb-loss who underwent implant surgery in November 2022 reported a noticeable decrease in phantom pain since the start of sensory neural stimulation. This observation suggests that sensory input perceived as arising from the amputated limb may affect phantom pain perception. We continue to actively investigate this phenomenon.

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.

Nothing to Report.

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.*

Nothing to Report.

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:*

Nothing to Report

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.

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.

We are still encountering delays in scheduling OR time for our implant surgery due to a backlog of elective procedures at LSCVAMC. Recently, we enrolled a participant with diabetic peripheral neuropathy resulting in transtibial limb-loss to help us complete the SOW in this and another VA funded project. We coordinated with the OR staff and scheduled a time to surgically install the system; however, unforeseen health complications related to his diabetes prevented this procedure from taking place. Our clinical team is addressing his health issues and identifying other potential volunteers with diabetic limb loss.

Our plans to upgrade two participants to the fully implantable system, *iSens*, have been delayed due to supply chain issues and shortage of system components. We are working hard to continue to procure the required components as soon as possible. This delay in availability of *iSens* components will not affect the planned experiments with existing or new implant recipients because the percutaneous interface provides full access to the stimulating nerve cuffs and intramuscular recording electrodes.

To accelerate subject recruitment, we have increased our presence locally and nationally, including a plan to specifically target potential participants in the waiting areas for the Prosthetics Service in addition to Amputee Clinic. This will allow a study staff member to meet personally with individual prosthesis users who may not have medical issues, provide study materials, and answer questions following their standard appointments. Furthermore, our nationwide recruitment efforts have been bolstered by the recent re-airing of the **CBS 60 Minutes** episode which resulted in contact with another candidate who we will be screening in the near future.

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

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).*

- 1) S. Li, R. Triolo, H. Charkhkar. “Neural Sensory Stimulation Does Not Interfere with the H-Reflex in Individuals with Lower Limb Amputation.” *Frontiers in Neuroscience*, vol. 17, 2023. DoD support is acknowledged in the manuscript.
- 2) D. Kim, R. Triolo, H. Charkhkar. “Plantar somatosensory restoration enhances gait, speed perception, and motor adaptation.” *Science Robotics*, vol. 8, issue 83, 2023. DoD support is acknowledged in the manuscript.
- 3) M. Schmitt, J. Wright, R. Triolo, H. Charkhkar, E. Graczyk. “The Experience of Sensorimotor Integration of a Lower Limb Sensory Neuroprosthesis: A Qualitative Case Study.” *Frontiers in Human Neuroscience*, vol. 16, 2023. DoD support is acknowledged in the manuscript.

Books or other non-periodical, one-time publications.

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.*

- 1) H.Morgan, R. Triolo, H. Charkhkar. Quantifying cutaneous vasodilation reflexes in lower limb amputees. *2023 Biomedical Engineering Society (BMES) Annual Meeting*. Seattle, WA, Oct. 2023 (Accepted for podium presentation).
- 2) L.Hauck, R. Triolo, H. Charkhkar. Quantifying peripheral nerve stimulation sensations through pressure matching. *2023 Biomedical Engineering Society (BMES) Annual Meeting*. Seattle, WA, Oct. 2023 (Accepted for podium presentation).
- 3) A. Khot, D. Noble, R. Triolo, H. Charkhkar. Advancing bidirectional neuroprosthetics with the Open Source Leg. *2023 Biomedical Engineering Society (BMES) Annual Meeting*. Seattle, WA, Oct. 2023 (Accepted for poster presentation).

- 4) M. Koishida, S. Li, J. Schnellenberger, R. Triolo, H. Charkhkar. Integrated EMG processing module for bidirectional neuroprosthesis. *2023 Biomedical Engineering Society (BMES) Annual Meeting*. Seattle, WA, Oct. 2023 (Accepted for poster presentation).
- 5) E. Petros, R. Triolo, H. Charkhkar. Sensory Neuroprosthesis Reduces the Cognitive Load During Dual-task Walking in Individuals with Lower Limb Loss. *11th International IEEE EMBS Conference on Neural Engineering (NER'23)*. Baltimore, MD, Apr. 2023. (Poster presentation)
- 6) L. Hauck, R. Triolo, H. Charkhkar. Eliciting Plantar Sensation via Nerve Cuff Electrodes in Individuals with Transtibial versus Transfemoral Amputation. *11th International IEEE EMBS Conference on Neural Engineering (NER'23)*. Baltimore, MD, Apr. 2023. (Poster presentation)
- 7) S. Li, R. Triolo, H. Charkhkar. Sensory Neuroprosthesis Improves Recovery from Treadmill-induced Stumbles. *11th International IEEE EMBS Conference on Neural Engineering (NER'23)*. Baltimore, MD, Apr. 2023. (Poster presentation)
- 8) H. Charkhkar. The Integration of Ottobock Genium and Neural Interface to Restore Sensation to Lower Limb Amputees, *Internal presentation to the Ottobock R&D department*, Jun. 21, 2023. (Invited talk)
- 9) H. Charkhkar. The Power of Connection: Restoring Neural Pathways in Lower Limb Amputation, *Musculoskeletal Research Program 2023 Seminar Series*, Jun. 14, 2023. (Invited talk)
- 10) H. Charkhkar. Bidirectional Neuroprosthesis to Restore Sensory and Motor Function in People with Lower Limb Amputation, *Orthotic and Prosthetic Innovative Technologies (OPTech) Conference*, Minneapolis, MN, May 20, 2023. (Invited talk)
- 11) H. Charkhkar. A bidirectional neuroprosthesis for individuals with lower limb loss: technology development and functional impacts, *Bioengineering Seminar at George Mason University*, Fairfax, VA, Apr. 13, 2023. (Invited talk)
- 12) H. Charkhkar. Design, development, and deployment of a mobile app user interface for a sensory neuroprosthesis, *Advanced Platform Technology Monthly Town Hall*, Cleveland, OH, Feb. 6, 2023. (Invited talk)
- 13) G. Pinault, H. Charkhkar. Neural interface technology to restore sensory and motor functions in individuals with lower limb loss, *Advances in Amputation Surgery International Conference*, Hospital for Special Surgery (HSS), New York, NY, Jan. 27, 2023. (Invited talk)
- 14) Connecting Lower Limb Prostheses to the Nervous System: Benefits, Challenges, and Promises, *MetroHealth Center for Rehabilitation Research Seminar*, Cleveland, OH, Nov. 16, 2022. (Invited talk)
- 15) D. Kim, R. Triolo, H. Charkhkar. Restored plantar sensation in lower-limb amputees improves gait symmetry and perception. *2022 Biomedical Engineering Society (BMES) Annual Meeting*. San Antonio, TX, Oct. 2022 (podium presentation)
- 16) S. Li, R. Triolo, H. Charkhkar. Characterizing effects of electrically elicited sensations on spinal reflex pathways. *2022 Biomedical Engineering Society (BMES) Annual Meeting*. San Antonio, TX, Oct. 2022 (podium presentation)
- 17) M. Person, A. Hall, H. Charkhkar. Prosthetic smart liner for monitoring residual limb health and wound prevention. *2022 Biomedical Engineering Society (BMES) Annual Meeting*. San Antonio, TX, Oct. 2022 (poster presentation)
- 18) J. Baker, M. Person, H. Charkhkar. Wearable system for estimating energy expenditure in lower-limb amputees. *2022 Biomedical Engineering Society (BMES) Annual Meeting*. San Antonio, TX, Oct. 2022 (poster presentation)

- **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.

Nothing to Report.

- **Technologies or techniques**

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

Nothing to Report.

- **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.

Nothing to Report.

- **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.*

- Popular Mechanics Article featuring an interview from Dr. Hamid Charkhkar: [Everything You Need to Know About Proprioception, Your Body's 'Silent' Sixth Sense](#)
- Podcast featuring Dr. Hamid Charkhkar: Biomechanics on our Minds, [Episode 55: Proprioceptive Prostheses and Clinical Impact | Hamid Charkhkar and Anna Smith](#)

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: Ronald Triolo

Project Role: PI

Researcher Identifier (e.g. ORCID ID): 0000-0003-0984-5803

Nearest person month worked: 1.8

Contribution to Project: Programmatic, administrative and scientific oversight of all aspects of the project

Name: Hamid Charkhkar

Project Role: Co-investigator (Technical)

Researcher Identifier (e.g. ORCID ID): 0000-0001-5485-5969

Nearest person month worked: 6

Contribution to Project: Conducting sensory stimulation tests, including stimulus calibration and parameter setting, psychometric testing, system integration and outcome measurement, supervising students and assisting the PI in project management

Name: Suzhou Li

Project Role: PhD Student (Technical)

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6

Contribution to Project: Designing and performing experiments to characterize effects of sensory neuroprosthesis in responding to slips and trips

Name: Eileen Petros

Project Role: PhD Student (Technical)

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6

Contribution to Project: Designing and performing experiments to characterize effects of sensory neuroprosthesis on cognitive load during ambulation

Name: Lindsey Hauck

Project Role: PhD Student (Technical)

Researcher Identifier (e.g. ORCID ID): N/A

Nearest person month worked: 6

Contribution to Project: Designing and performing experiments to determine stimulation thresholds

Name: Daekyoo Kim

Project Role: Postdoctoral Fellow (Technical)

Researcher Identifier (e.g. ORCID ID): 0000-0002-6123-2900

Nearest person month worked: 2

Contribution to Project: Designing and conducting balance and gait assessments and analyzing biomechanical data from participants using sensory neuroprosthesis

Name: Eileen Petros
Project Role: PhD Student (Technical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 6
Contribution to Project: Designing and performing experiments to characterize effects of sensory neuroprosthesis on cognitive load during ambulation

Name: Jeremy Dunning
Project Role: Electrical Engineer (Technical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Circuit design and software development for interfacing with Genium and Proprio prostheses

Name: Dakota Noble
Project Role: Biomedical Engineer
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 2
Contribution to Project: Assisting in Genium Technical Development, project management and report preparation

Name: Melissa Schmitt
Project Role: Nurse Coordinator (Clinical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.6
Contribution to Project: Medical monitoring and clinical services

Name: Aarika Sheehan
Project Role: Physical Therapist (Clinical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Subject recruiting, candidate screening, functional training and outcome assessment

Name: Alexandra Hutchison
Project Role: Study Coordinator (Clinical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 3.6
Contribution to Project: Subject Scheduling, Point of contact with Physicians

Name: Jessica Jarvela
Project Role: Study Coordinator (Clinical)
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: IRB Updates, Regulatory & Training Compliance

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.

Nothing to Report.

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);*
- *Other.*

Organization Name: Ottobock

Location of Organization: Vienna, Austria

Partner’s contribution to the project: Industrial partner and collaborator. Ottobock provided us with a *Genium Knee* prosthesis on loan without charge and will lend technical assistance with accessing internal circuitry of the device.

Organization Name: Ossur

Location of Organization: Reykjavik, Iceland

Partner’s contribution to the project: Industrial partner and collaborator. Ossur provided us with a two *Proprio* powered ankles on loan without charge and will lend technical assistance with accessing internal sensor data of the device.

Organization Name: Case Western Reserve University

Location of Organization: Cleveland, OH

Partner's contribution to the project: Access to microfabrication, electronic design and circuit testing facilities, and technical support required for external stimulator design modifications and fabrication.

Organization Name: Carroll Biomedical

Location of Organization: Jewett, OH

Partner's contribution to the project: Carroll Biomedical will design and fabricate a portable EPM which will be utilized to collect EMG from IM electrodes, perform onboard processing, and generate suitable commands to control the prosthesis.

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.*