AWARD NUMBER: W81XWH-16-2-0009

TITLE: A Pilot Trial to Assess Implantable Myoelectric Sensors (IMES) to Improve Prosthetic Function for Transhumeral Amputees with Targeted Muscle Reinnervation

PRINCIPAL INVESTIGATOR: Dr. Paul F. Pasquina, MD

CONTRACTING ORGANIZATION: Henry M. Jackson Foundation for Advancement of Military Medicine

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Fort Detrick, Maryland 21702-5012

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A Pilot Trial to Assess Implantable Myoelectric Sensors (IMES) to Improve Prosthetic Function for Transhumeral Amputees with Targeted Muscle Reinnervation

5a. CONTRACT NUMBER
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5b. GRANT NUMBER
(W81XWH-16-2-0009)

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)

Henry M. Jackson Foundation for the Advancement of Military Medicine 6720-A Rockledge Drive, Suite 100
Bethesda, MD 20817

8. PERFORMING ORGANIZATION REPORT

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 NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES
N/A

14. ABSTRACT

The overall project goal is to investigate the functional performance of transhumeral amputees who have received targeted muscle reinnervation with EMG signals measured intramuscularly using a fully wireless implant. This year we have prepared a biocompatibility test plan, secured components, and submitted regulatory protocols to ACURO. We have received initial feedback and are in process of addressing the comments.

15. SUBJECT TERMS
Recruitment, infrastructure, patient identification, implants

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER**
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1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

The inadequacies of current prosthetic technologies severely limit rehabilitative options for upper limb amputees and contribute to the disability caused by upper limb loss. TMR presents new possibilities for control of upper limb prostheses, and, building on this success, our team has developed innovative technologies to address key remaining challenges in the design and control of advanced prosthetic systems. The overall objective of this grant is to improve functional independence for individuals with transhumeral amputees, who have had TMR using implantable MyoNodes. Our hypothesis is that chronic implants within reinnervated muscle will provide stable EMG recordings that will allow intuitive, simultaneous control of 3 DOF prosthesis system. Furthermore, we hypothesize that this technology will result in significant functional improvements for users as measured through the ACMC, SHAP, clothespin relocation, Jebsen Hand task, and box-and-block tasks.

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

Amputation; MyoNodes; Targeted Muscle Reinnervation, Electromyography

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: Obtain a feasibility study investigational device exemption for the MyoNode system. Extensive preliminary work has already been conducted to develop and test the MyoNode prototype, with demonstration of successful wirelessly powered and telemetered data from a tissue depth of 10 cm in an animal model. All design files have been transferred to Cirtec Medical Systems to create final form factor devices under GMP and are working with Med Institute Inc., to obtain a feasibility Investigational Device Exemption (IDE) from the FDA. The engineering, fabrication, and regulatory team has extensive experience in developing implantable medical devices.

Aim 2: Assess the accuracy with which transhumeral amputees can control isolated and simultaneous movements of a three DOF myoelectric prosthesis utilizing the MyoNode system after successful TMR surgery. TMR has proven very useful for enhancing prosthesis control. However, to date, subjects have been limited to using surface EMG signals to control a prosthesis. Surface EMG is often corrupted by muscle cross-talk and instability in the skin-electrode interface necessitates frequent recalibration of controllers. We will recruit three individuals with transhumeral amputations and who have had TMR surgery. As our basic control platform, we will use natively innervated biceps and triceps to provide direct proportional control of the elbow, and we will try both direct control and pattern recognition of EMG from reinnervated muscles to control the wrist and hand. Subjects will complete 3-DOF Fitt's Law virtual testing to measure throughput of discrete and simultaneous measurements. We will also measure subjects' control of a physical prosthesis as they complete movements which require discrete and simultaneous movements. A commercially available prosthesis with an elbow, a wrist rotator, and a hand will be used in conjunction with commercially available pattern recognition software (Coapt LLC). The

only variable will be the input signals; allowing us to compare performance using IM and/or surface EMG signals, and with data from other transhumeral TMR subjects using the pattern recognition controller with surface EMG (W81XWH 12-02-0072).
Aim 3: Determine the ability of transhumeral amputees to successfully perform functional activities using a three DOF myoelectric prosthesis control by the MyoNode system and TMR. We hypothesize that the MyoNode implant system will improve control of the prosthesis, and that this will subsequently improve functional activities. We will measure functional performance prior to implantation and during training with the MyoNode system, using the SHAP, ACMC, a clothespin relocation task, the Jebsen task, and the box and blocks task. We will also provide the subjects with a questionnaire for subjective feedback at the end of the study.

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.

Key Research Accomplishments
In consultation with NAMSA®, and in response to the FDA feedback from our IDE request, the following biocompatibility tests were completed to support the use of the MyoNode implant in an early feasibility study clinical trial:

- Sensitization testing – Approved/Passed
- Intracutaneous irritation testing – Approved/Passed
- Acute systemic toxicity testing – Approved/Passed
- Mediated pyrogenicity testing – Approved/Passed
- 4 Week implantation testing – Approved/Passed
- 26 Week implantation testing – Approved/Passed

Detailed Description
The FDA agreed using the same processes used in assembling the final implant, but also requested a chemical characterization and risk analysis to justify not testing for subchronic systemic toxicity, genotoxicity, chronic systemic toxicity, carcinogenicity. The FDA also recommended, but did not mandate a 6 month animal study. Once ACURO approvals were approved, the tests were run in parallel with one another if possible in order to maximize time. Thus, should the FDA deny the IDE on the basis of the 6 month animal study, it will minimize the overall impact. At this time, all 6 ACURO protocols were approved and passed.

Table 1. Material samples required to conduct biocompatibility testing.

Test	Surface Area Required (cm^2)			Number of Coupons	Test Durations (Days)
	Total	Zirconia	Pt/Ir		
Cytotoxicity	60	48	12	1	20
Sensitization	540	432	108	9	56
Irritation	120	96	24	2	28
Acute Systemic Toxicity	120	96	24	2	28
Pyrogenicity	900	720	180	15	28
2 week implantation	Not applicable, Use actual implants			15	56

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.

Nothing to report.

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.

Nothing to Report.

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.

NAMSA is now summarizing all results from the animal test protocols and preparing a biological risk analysis report which will be available in July. In the following quarter, we expect to receive the biological risk assessment from NAMSA for inclusion into the IDE.

To complete the IDE, we need to complete a validation of our sterilization protocol, which requires some completed test article. These were expected in January 2021; however, supply chain issues have delayed these several times. We expect them this quarter, and can have the articles built for testing within 3 weeks of receipt.

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).

Nothing to Report.

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:*

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.

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.

During the execution of award 64991 (W81XWH-16-2-0009), CRSR encountered an unexpected delay in obtaining FDA approval in order to initiate the study. We secured USAMRAA approval to collaborate with NAMSA and amend the protocol to implement animal testing. All of the required biocompatibility tests have been completed and all have passed.

COVID-19 did impact the project this year, as research and development was generally slower than an average year (long lead times associated with procuring materials, fewer people working in the laboratories, etc.).

It is possible there may be additional delays in procuring the materials, however, we have little control over this, as the issue is across multiple suppliers. We have done our best to source alternative components; however, we have not been successful in finding other suppliers.

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

The biocompatibility requirements required by the FDA necessitated animal testing. 6 ACURO protocols were approved and conducted to complete the animal tests.

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.*

Nothing to Report.

- **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.*

Nothing to Report.

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".

Example:

Name: *Mary Smith*
Project Role: *Graduate Student*
Researcher Identifier (e.g. ORCID ID): *1234567*
Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: Dr. Paul F. Pasquina
Project Role: PI
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.6
Contribution to Project: Dr. Pasquina is the PI for this protocol. He provides leadership and scientific oversight; and is responsible for the development, oversight, revision, and completion of this protocol. He will communicate with the Program Manager and Associate Investigator Dr. Levi Hargrove to ensure progress toward FDA approval and protocol development.

Name: Levi Hargrove, PhD
Project Role: PI
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 1.0
Contribution to project: Dr. Hargrove's focus has been associated with completing the technical developments of the implant and base-station, as helping to secure the FDA IDE.

Name: Derek Soloway
Project Role: Program Manager
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.04
Contribution to Project: Mr. Soloway is the Program Manager for CRSR. He communicates with the PI and Investigators to understand the PI's/Investigator's needs, such as modifications to the protocol that would require award/subaward modification, and submits these modifications for consideration to stakeholders. He tracks budgets, approves expenses, and employee contributions. In addition, he supervises staff to ensure deliverables and milestones are completed on time and coordinates with other stakeholders to ensure the completion of all project and proposal aims.

Name: Delaney Dodd
Project Role: Program Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.03
Contribution to Project: Ms. Dodd is a Program Coordinator with HJF supporting the CRSR at USUHS. She provides research support, including regulatory guidance and collaborates with the program manager to assist with budgeting, reporting, and the research team to review research assistants' work.

Name: Shannon Fichter
Project Role: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.02
Contribution to Project: Ms. Fichter is a Clinical Research Coordinator with HJF supporting the CRSR at USUHS. She provides research support, including monitoring the progression of the research being conducted, and working with the Program Coordinator to ensure updates and reports are provided in a timely manner.

Name: Melissa Hewitt
Project Role: Clinical Research Assistant
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.02
Contribution to Project: Ms. Hewitt is a Clinical Research Assistant with HJF supporting the CRSR at USUHS. She assists with regulatory requirements, IRB compliance, and coordination between sites. She maintains biweekly communication with Dr. Hargrove to track progress, obtain FDA approval, and assists with submission for ACURO and IRB approval.

Name: Withney Altema
Project Role: Clinical Research Assistant
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 0.01
Contribution to Project: Ms. Altema is a Clinical Research Assistant with HJF supporting the CRSR at USUHS. She assists with regulatory requirements, IRB compliance, and coordination between sites.

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.

Since the last annual report, Todd Kuiken, MD, PhD has retired and a PI change was requested and approved for Levi Hargrove to assume the position as the subcontract PI for the Shirley Ryan AbilityLab.

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.*

Organization Name: Walter Reed National Military Medical Center
Location of Organization: Bethesda, MD
Partner's contribution to the project: Facilities, Collaboration

Organization Name: Henry Jackson Foundation
Location of Organization: Rockville, MD
Partner's contribution to the project: Collaboration

Organization Name: Shirley Ryan Ability Lab
Location of Organization: Chicago, IL
Partner's contribution to the project: In-kind support, Collaboration

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://ebrap.org/eBRAP/public/index.htm*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil/Pages/Resources.aspx) 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 Pilot Trial to Assess Implantable MyoNodes to Improve Prosthetic Function for Transhumeral Amputees after Targeted Muscle Reinnervation

W81XWH-16-2-0009

PI: Paul F. Pasquina, MD **Org:** Henry M. Jackson Foundation

Award Amount $2,622,160

Study Purpose / Deliverables

Current prosthetic technologies severely limit rehabilitative options for upper limb amputees and contribute to the disability caused by upper limb loss. Targeted muscle reinnervation (TMR) presents new possibilities and the overall objective of this grant is to improve functional independence for individuals with transhumeral amputees, who have had TMR using implantable MyoNodes.

Study Aims

Aim 1: Investigational device exemption for the MyoNode system.
Aim 2: Assess the accuracy and control of a 3 DOF myoelectric prosthesis utilizing the MyoNode system after TMR surgery.
Aim 3: Determine the ability of transhumeral amputees to successfully perform functional activities using a three DOF myoelectric prosthesis control by the MyoNode system and TMR.

Accomplishments: We received ACURO approvals from all animal protocols required to satisfy the FDA feedback and commenced the study activities. To date, we have received reports back on all 6 protocols. Each of the respective tests have passed.

Timeline and Cost

Activities / FY	16	17	18-20
Execute subaward agreements			
Complete development work			
Obtain IDE from the FDA			
Evaluate technology and publish findings			
Estimated Budget ($K)	**$2100**	**$250**	**$250**

Updated: May 24, 2022

Goals/Milestones

FY16 Goals

- ☑ Execute subaward agreements between institutions
- ☑ Technical Demonstration of MyoNode Technology

FY17 Goals

- ☑ Complete MyoNode Developmental Work

FY18-20 Goals

- ☐ Obtain investigational device exemption (IDE) from the FDA
- ☐ Complete the final study report and publish findings

Budget Expenditure to Date: $2,532, 814.29
Projected Expenditure: $2,622,160.00