AWARD NUMBER: W81XWH-15-2-0068

TITLE: Ambulatory and Non-Ambulatory Benefits of Lower Limb Exoskeleton Use, with and without FES, in Clinical and Community Settings

PRINCIPAL INVESTIGATOR: Michael Goldfarb

CONTRACTING ORGANIZATION: Vanderbilt University
Nashville, TN 37235-0002

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6. AUTHOR(S)

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Vanderbilt University
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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This research investigates the extent to which regular walking in an exoskeleton will provide mobility, health, and recovery benefits to individuals with spinal cord injury. The research is comprised of three sub-studies. The first investigates prospective benefits while walking in an exoskeleton; the second investigates prospective additional benefits when the exoskeleton is supplement with lower limb functional electrical stimulation; and the third investigates prospective benefits during home and community use. As of this first annual report, the first study is underway, with two of 24 subjects enrolled. Although all sites have received exoskeleton training and IRB approval, only the Mayo Clinic has received HRPO approval. HRPO review has taken much longer than expected, in part due to an unexpected change in the Human Subjects Protections Scientist at HRPO assigned to review the study.

15. SUBJECT TERMS
spinal cord injury, paraplegia, exoskeleton, physical medicine and rehabilitation, rehabilitation research, legged mobility, neuromuscular impairment, neural and functional recovery

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
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Unclassified	Unclassified	Unclassified	Unclassified	16	**19b. TELEPHONE NUMBER** *(include area code)*

TABLE OF CONTENTS

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

This research investigates the extent to which regular walking in an exoskeleton will provide mobility, health, and recovery benefits to individuals with spinal cord injury. The research is comprised of three sub-studies. The first investigates prospective benefits while walking in an exoskeleton; the second investigates prospective additional benefits when the exoskeleton is supplement with lower limb functional electrical stimulation; and the third investigates prospective benefits during home and community use. The respective studies will characterize effects of exoskeleton walking on pain, spasticity, bowel and bladder function, body-mass index (BMI), bone mineral density (BMD), cardiovascular health, well-being, potential neurological recovery, and level of mobility. The research is being conducted at three sites – Vanderbilt Medical Center, Mayo Clinic, and the Tampa VA – each of which is conducting the same study protocol. The first two studies, each of which are conducted in a clinical setting, will enroll 24 subjects total (8 per study site), while the third, which is a take-home study, will enroll 6 subjects total (2 per study site). The first study is expected to be completed by 3/31/2017; the second by 03/30/2019; and the third by 09/30/2019.

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

spinal cord injury; paraplegia; exoskeleton; physical medicine and rehabilitation; rehabilitation research; legged mobility; neuromuscular impairment; neural and functional recovery

3. **ACCOMPLISHMENTS:** The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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 following narrative provides a description of progress:

This research entails three sub-studies. The major goal of the first year was to approve and initiate the Study 1 protocol at all study sites. The intent of Study 1 is to determine the extent to which regular walking in an exoskeleton provides health benefits, functional or neurological recovery, and legged mobility to non-ambulatory or poorly-ambulatory individuals with SCI. Study 1 is expected to enroll 24 subjects, 8 at each study site. Each subject is expected to be involved in the study for 2 months of active intervention (i.e., walking with the exoskeleton), with an additional follow-up measurement of outcomes 2 months later. As per the SOW, Study 1 was expected to begin enrolling subjects 04/01/2016, and to complete the protocol on all 24 subjects by 12/30/2017.

The following table outlines the major tasks there were scheduled to start and be in progress during previous reporting periods:

Task/Milestone	Description	Target Completion Date/Quarter	Status
Major Task 1	Finalize Protocol and Obtain IRB/HRPO Approval	Apr 2016 or Y1Q3	COMPLETED
Major Task 2	Conduct Study 1	Jan 2018 or Y3Q2	IN PROGRESS (40% COMPLETE)
Major Task 3	Finalize Protocol and Obtain IRB/HRPO Approval	Jan 2018 or Y3Q2	IN PROGRESS (25% COMPLETE)
Major Task 4	Conduct Study 2	Jan 2019 or Y4Q2	NOT YET STARTED

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.

- Major activities during Y2:
  - Finalized Study 1 IRB/HRPO approval for all sites.
  - Actively enrolling subjects and conducting Study 1 at all sites.
  - Conducted pilot testing of Study 2 intervention (i.e., exoskeleton with FES)
  - Prepared Study 2 protocol for IRB/HRPO approval.

- Specific objectives:
  - Conduct Study 1.
  - Complete pilot testing of Study 2 intervention.
  - Initiate protocol approval for Study 2.

- Significant results or key outcomes:
  - Obtained IRB/HRPO approvals at all sites.
  - Nine (of 24) subjects completed or near completed Study 1.
  - Completed pilot testing of Study 2 intervention (i.e., exoskeleton with FES)
  - Prepared Study 2 protocol for IRB/HRPO approval.

- Other achievements: None yet.

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.

Clinical staff at all study sites attended a 3-day course and obtained training and certification to use exoskeletons in clinical practice.

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.

No results yet to disseminate.

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.

1) Complete Study 1. This is expected to be completed in Q2 of 2018.
2) Obtain IRB/HRPO approval of the Study 2 protocol. This is expected to be completed in Q2 of 2018.
3) Update exoskeletons to support supplemental FES for Study 2. This will require sending the devices back to the manufacturer for an equipment upgrade, and will also entail additional training sessions for the site physical therapists on use of the FES feature.
4) Initiate Study 2. This is expected to start in Q3 of 2018.

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).

Nothing to report at this point.

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 at this point.

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 at this point.

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 Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer 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.

No changes in objectives or scope.

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.

HRPO approval took much longer than expected, and as result our study is several months behind schedule. Now that all sites have approval, the study enrollment and protocol is proceeding smoothly and at the rate originally planned. We hope to partially recover the original schedule. If the original schedule cannot be recovered, we will either slightly reduce the number of subjects in Studies 1 and 2, and/or will request a no cost extension to complete.

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.

Approval delays reduced the rate of personnel expenditures during Y1 and some of Y2, although the exoskeletal devices were erroneously paid in Y1 and Y2 rather than over the entire project period, so those issue offset each other, such that the rate of expenditures is currently right at the originally expected rate, and should remain as such for the remainder of the project, assuming the schedule proceeds as expected.

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

None to report.

Significant changes in use or care of vertebrate animals.

None to report.

Significant changes in use of biohazards and/or select agents

None 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).*

None yet 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).*

None yet 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.*

None yet 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.

None yet to report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

None yet to report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. 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.

None yet 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;*
  - *biospecimen 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.*

None yet 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. Michael Goldfarb
Project Role: PI, Vanderbilt lead researcher
Researcher Identifier: ORCID ID 0000-0002-6622-095X
Nearest person month worked: 3
Contribution to Project: Dr. Goldfarb is coordinating the research effort.

Name: Ms. Sheri Dixon
Project Role: Vanderbilt study coordinator
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Ms. Dixon is the Vanderbilt study coordinator, has been assembling IRB and HRPO applications for Vanderbilt and all sites, has set up the REDCap database, and the overall project (i.e., multi-site) study coordinator.

Name: Ms. Christina Durrough
Project Role: Vanderbilt lead physical therapist
Researcher Identifier: n/a
Nearest person month worked: 1.5
Contribution to Project: Ms. Durrough has been assisting with design and assembly of the protocol and data recording notebooks, and is responsible for exoskeleton use and oversight.

Name: Dr. Kristin Zhao
Project Role: Mayo lead researcher
Researcher Identifier: ORCID ID 0000-0001-7598-8197
Nearest person month worked: 2
Contribution to Project: Dr. Zhao is leading the research effort at the Mayo Clinic.

Name: Ms. Megan Gill
Project Role: Mayo Clinic lead physical therapist
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Ms. Gill has been administering the study protocol on the two subject currently enrolled at Mayo.

Name: Mr. Tyson Scrabeck
Project Role: Mayo study coordinator
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Mr. Scrabeck has authored and assembled IRB and HRPO applications for the Mayo site.

Name: Mr. Daniel Veith
Project Role: PT
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to Project: Mr. Veith oversees treatment for some subjects.

Name: Mr. Michael Boyd
Project Role: PT assistant
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to Project: Mr. Boyd oversees treatment for some subjects.

Name: Dr. Walter Kremers
Project Role: Statistician
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Dr. Kremers is the study statistician.

Name: Mr. Zachary Pohlkamp
Project Role: PT assistant
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Mr. Pohlkamp oversees treatment for some subjects.

Name: Dr. Sam Phillips
Project Role: Tampa VA lead researcher
Researcher Identifier: n/a
Nearest person month worked: 2
Contribution to Project: Dr. Phillips leading the research effort at the Tampa VA.

Name: Mrs. Padmaja Ramaiah
Project Role: Tampa VA study coordinator
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to Project: Mrs. Ramaiah has authored and assembled IRB and HRPO applications for the Tampa site.

Name: Mrs. Lisa Goff
Project Role: PT
Researcher Identifier: n/a
Nearest person month worked: 1
Contribution to Project: Mrs. Goff is the lead PT at Tampa.

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.

For PI Goldfarb, the following grant ended during the year covered by this annual report:
1R21HD076124-01A1 (Goldfarb) 01/15/2014 - 12/31/2016 1.25 Cal

For PI Goldfarb, the following grant started during the year covered by this annual report:
1R01HD088959-01A1 (Goldfarb) 09/01/2017 – 05/31/2022 1.0 Cal

There has been no significant net change in active other support for the study PI or co-PIs.

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: Mayo Clinic
Location of Organization: Rochester MN
Partner's contribution to the project (identify one or more)

- Collaboration: Mayo is one of the three study sites conducting the study protocol.

Organization Name: Tampa VA
Location of Organization: Tampa Bay FL
Partner's contribution to the project (identify one or more)

- Collaboration: Tampa is one of the three study sites conducting the study protocol.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating 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.

Ambulatory and Non-Ambulatory Benefits of Lower Limb Exoskeleton Use, with and without FES, in Clinical and Community Settings

Log no. SC140121

Award no. W81XWH-15-2-006

PI: Michael Goldfarb **Org:** Vanderbilt University **Award Amount:** $2,344,016

Study Aims

- Study 1: Determine extent to which regular walking in an exoskeleton provides health benefits, functional or neurological recovery, and legged mobility to non-ambulatory or poorly-ambulatory individuals with SCI.
- Study 2: Determine extent to which regular exoskeletal walking, when supplemented with functional electrical stimulation (FES) of leg and trunk muscle groups, will result in enhanced therapeutic and neurological benefits relative to exoskeleton use without FES.
- Study 3: Determine extent to which regular use of an exoskeleton in the home and community will result in enhanced therapeutic and neurological benefits relative to exoskeleton use in a clinic, to determine the extent to which the level of mobility provided by the exoskeleton will be amenable to home and community use, and to characterize the level of compliance of exoskeleton use.

Accomplishments and status: Study 1 underway at all sites; study has enrolled 11/24 subjects; completed 5/24 subjects through follow-up; completed 8/24 through treatment; currently conducting protocol on 2/24 subjects; 1 subject withdrew from study during protocol due to medical issue unrelated to study.

Timeline and Cost

Budget Year	15/16	16/17	17/18	18/19
Activity/Dates	09/30/15-09/29/16	09/30/16-09/29/17	09/30/17-09/29/18	09/30/18-09/29/19
IRB/HRPO				
Enrollment				
Study 1				
Study 2				
Study 3				
Publication				
Estimated budget ($k)	$597	$578	$593	$581

Updated: 11/07/2017

Budget Year 1 Goals

- ✓ IRB/HRPO approval for Study 1
- ✓ Study 1 underway

Budget Year 2 Goals

- ❑ Study 1 complete
- ❑ IRB/HRPO approval for Study 2

Budget Year 3 Goals

- ❑ Study 2 underway and 80% complete (~18 subjects complete)
- ❑ Study 3 IRB/HRPO review initiated

Budget Year 4 Goals

- ❑ Study 2 complete
- ❑ Study 3 complete

Comments/Challenges/Issues/Concerns

Study 1 is underway at all sites. Project is currently behind schedule due to delays in approval process.

Budget Expenditure to Date

Projected Expenditure: $1170k (assuming even burn rate through project)

Actual Expenditure: $1160k (reflects full cost of all exoskeleton kits).