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AWARD NUMBER: W81XWH-17-2-0060

TITLE: **Transfemoral Amputee Osseointegration Study (TFAOS)**

PRINCIPAL INVESTIGATOR: Jonathan Forsberg, MD, PhD

RECIPIENT: Henry M Jackson Foundation,
Bethesda, MD 20817

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

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Transfemoral Amputee Osseointegration Study (TFAOS)

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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 Adv. of Mil. Med.
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8. PERFORMING ORGANIZATION REPORT NUMBER

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

U.S. Army Medical Research and Materiel Command
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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

This is a 5-year, prospective multisite cohort study, evaluating a device that is FDA approved under a Humanitarian Device Exemption. The study is being conducted at Walter Reed National Military Medical Center and The University of California San Francisco. This non-randomized, longitudinal study will use each study participant as his or her own control, and test the hypothesis that osseointegration results in improvements in the primary and secondary outcomes. In year 1, nineteen patients have been enrolled at WRNMMC. Functional outcomes, and patient reported outcomes continue to be collected as scheduled.

15. SUBJECT TERMS

Osseointegration, transfemoral, amputee, OPRA, functional outcomes, titanium implant, amputation

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		**19b. TELEPHONE NUMBER** ***(include area code)***

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

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

Transfemoral Amputation Osseointegration Study (TFAOS) This is a 5-year, prospective multisite cohort study, evaluating a device that is FDA approved under a Humanitarian Device Exemption. Transfemoral amputees will be recruited using an existing, robust, network of combat related upper extremity amputees maintained at the Military Advanced Training Center, Walter Reed National Military Medical Center (WRNMMC), and at University of California San Francisco (UCSF). This non-randomized, longitudinal study will use each study participant as his or her own control, and test the hypothesis that osseointegration results in improvements in the primary and secondary outcomes listed below. In conducting this study, we will measure a comprehensive set of physiologic parameters, and collect outcome measures that ensure the results of this trial and safety profile of the OPRA implant system are comparable to previous studies, which is important when applying this FDA-approved—but emerging—technology to a new, predominately military, patient population. The study will investigate the function, health related quality of life, and safety outcomes following placement of the OPRA device in patients with transfemoral amputations

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

Osseointegration, implant, titanium, OPRA, functional outcomes, transfemoral, amputee, amputation

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.

Major Task 1: Study Preparation	Timeline (mnths)	Status
subtask 1: Initiate subaward contract	1-4	complete
Subtask 2: Obtain local IRB Approval (UCSF)	1-8	complete
Subtask 3: Obtain local IRB Approval (WRNMMC)	1-8	complete
Subtask 4: Obtain secondary approval (HRPO) for WRNMMC site	3-12	complete
Subtask 4a: Obtain secondary approval (HRPO) for UCSF site	3-12	Pending
Major Task 2: Project Initiation and enrollment	Timeline (mnths)	Status
subtask 1: Enroll patients at WRNMMC (15 patients)	3-24	complete/ongoing**
Subtask 1a: Enroll patients at USCF (15 patients)	3-8	pending HRPO approval
Subtask 2: Conduct surgeries (S1)	3-36	ongoing
Subtask 3: Conduct surgeries (S2)	6-36	ongoing
Major Task 3: Patient Rehabilitation and Prosthetic fitting	Timeline (mnths)	Status
subtask 1: Patient rehabilitation	3-60	ongoing
Subtask 1a: Establish weight bearing protocol and fit new prosthetics	3-60	ongoing
Major Task 3: Patient Rehabilitation and follow-up	Timeline (mnths)	Status
subtask 1: Conduct patient rehabilitation and collect functional outcomes data (Pre., 3,6,9,12,24 months)	3-60	ongoing*
Subtask 1a: Collect AE and infection rate data on all patients	3-60	ongoing
Major Task 4: Project Analysis and reporting	Timeline (mnths)	Status
subtask 1: Conduct analysis of surgical outcomes and expected infection rates	36-60	
Subtask 2: Conduct analysis of functional outcomes and compare to pre osseointegration functional status	3-8	
Subtask 3: Publish results in peer -reviewed journals and present at MHSRS.	36-60	

* For patient safety and to allow full recovery, 3 month functional outcomes will no longer be collected.
** Due to overwhelming interest, WRNMMC has increased project enrollment to 35 patients

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.

- IRB approval WRNMMC-2017-0091; received 11/11/2017.
- HRPO Log Number A-20341.a secondary approval received 11/21/2017.
- WRNMMC has COMPLETED the initial enrollment target of 15 total patients enrolled.
- Ten patients have completed Stage II at WRNMMC as of Sept, 2018.
- IRB approval UCSF 15-16764; received 2/6/2018.
- IRB proposals UCSF 18-25404 and 18-25641; submitted 7/2/2018 as per HRPO request to split 15-16764 into separate Study (research) and Non-Study (HUD surgical) arms.
- IRB approval UCSF 18-25404 approval received 10/1/2018 and 18-25641 approval received 9/17/2018.
- UCSF protocols pending final HRPO approval.
- WRNMMC submitted an amendment to increase the number of patients at WRNMMC to 35 given the overwhelming demand from patients interested in participating in the research arm. Approved July 2018.
- Patient follow-up ongoing.

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."

- 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.

- Poster Presentation: 2018 MHSRS. Early Outcomes of Osseointegrated Implants in Transhumeral and Transfemoral Amputations. Harrington CJ, Polmear MM, Melendez-Munoz A, Gomez Y, Nordstrom MJ, Beachler MD, Brånemark R, O'Donnell R, Potter BK, Forsberg JA

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.

- Begin enrollment of patients at UCSF, Q1Y2 expected
- Continue to conduct Osseointegration surgeries.
- Continue to track rehabilitation, functional outcomes and infection rates.
-

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

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."

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:

- It was determined that the 3 month evaluation post S2 surgery should eliminate the functional (gait and biomechanics) components as patients seemed to require additional time to be comfortable and safe on their new prosthetic set up.
- Due to overwhelming interest from the combat wounded population, WRNMMC has increased the enrollment to 35 patients up from 15. UCSF enrollment targets remain the same.
-

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.

Nothing to report

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

- It was determined that the 3 month evaluation post S2 surgery should eliminate the functional (gait and biomechanics) components as patients seemed to require additional time to be comfortable and safe on their new prosthetic set up.

Significant changes in use or care of vertebrate animals

Not applicable

Significant changes in use of biohazards and/or select agents

Not applicable

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).*

Interim results reported at the Musculoskeletal Tumor Society Meeting on 11 October 2018, in New York, NY.

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.

Early Outcomes of Osseointegrated Implants in Transhumeral and Transfemoral Amputations. Harrington CJ, Polmear MM, Melendez-Munoz A, Gomez Y, Nordstrom MJ, Beachler MD, Brånemark R, O'Donnell R, Potter BK, Forsberg JA. MHSRS 2018 –Poster

- **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.

- **Other Products**

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Jonathan Forsberg, MD
Project Role: Principle Investigator and Director
Researcher Identifier (e.g. ORCID ID): 0000-0003-3835-0615
Nearest person month worked: 2
Contribution to Project: CDR Forsberg responsible for consenting patients and performing surgeries and overall project management.

Name: Benjamin K. Potter, MD
Project Role: Associate Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2
Contribution to Project: LTC Potter responsible for consenting patients and performing surgeries.

Name: Yessenia Gomez
'Project Role: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 4
Contribution to Project: Ms. Gomez is responsible for coordinating patient appts, administering survey questionnaires.

Name: Angelica Melendez-Munoz
'Project Role: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 8
Contribution to Project: Ms. Melendez-Munoz is responsible for coordinating patient appts, administering survey questionnaires

Name: Richard J. O'Donnell, MD
Project Role: UCSF – subaward Site PI
Researcher Identifier (e.g. ORCID ID): 0000-0002-6366-2701
Nearest person month worked: 1
Contribution to Project: Dr. O'Donnell responsible for consenting patients and performing surgeries and oversight of subaward site.

Name: Veronica Andaya
'Project Role: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 4
Contribution to Project: Ms. Andaya is responsible for UCSF regulatory coordination, patient appts, administering survey questionnaires.

Dr. Rickard Brånemark resigned his position at UCSF, effective 5/1/2018. The partial FTE has been reassigned to Dr. O'Donnell, who will assume his workload.

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.*

Nothing to report

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.