AWARD NUMBER: W81XWH-17-2-0060

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

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RECIPIENT: Henry M Jackson Foundation,
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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)

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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. As of year 3, there have been 38 patients enrolled at WRNMMC and 6 at the University of California San Francisco. Patient-reported outcomes continue to be collected as scheduled. We are doing our best to collect functional outcomes, although some pandemic-related clinical research restrictions remain in place.

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**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
Unclassified	Unclassified	Unclassified	Unclassified	13	**19b. TELEPHONE NUMBER** ***(include area code)***

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

TABLE OF CONTENTS

1.INTRODUCTION:

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 the 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 that the results of this trial and the safety profile of the (Osseoanchored Prosthesis for the Rehabilitation of Amputees) 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:

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?

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	complete
Major Task 2: Project Initiation and enrollment	**Timeline (mnths)**	**Status**
subtask 1: Enroll patients at WRNMMC (35 patients)	3-36	complete/ongoing**
Subtask 1a: Enroll patients at USCF (15 patients)	3-36	ongoing
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	In prep
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 up to 44 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.
- In Year two
  - UCSF received HRPO approval.
  - UCSF began recruitment and enrollment.
  - UCSF commenced stage 1 surgical procedures and scheduled stage 2 surgical procedures.
  - WR continued enrollment and patient follow up. Currently 30 patients enrolled. The remaining 5 patients are expected to be enrolled within first 6 months of Y3.
  - WR submitted IRB continuing review.
  - OI Program presented early findings at Blast Injury Conference (London, UK) and MHSRS (Orlando, FL)
- In Year three
  - Clinical Research activity paused, where necessary, due to COVID-19 pandemic beginning in March 2020. Although surgeries had resumed at WR by May 2020, many patients delayed surgery, and follow up appoints and continue to do so.
  - UCSF continued recruitment and enrollment though at a slower pace.
  - UCSF has resumed surgical procedures. Currently 6 patients enrolled.
  - Currently 38 patients enrolled at WR. Eleven patients have completed the 2 yr follow-up at WR
  - The remaining 6 patients are expected to be enrolled within first 4 months of FY 21 depending on COVID status and associated impacts.
  - IRB continuing reviews have been submitted.

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.

- Nothing to report due to curtailment of conferences secondary to the COVID-19 pandemic.

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.

- Continue enrollment of patients at UCSF (up to 12 patients – 50 total between sites)
- Complete enrollment at WR (up to 44 patients– 50 total between sites).
- Continue to track rehabilitation, functional outcomes, and infection rates.
- Present/ publish on interim results (TFAOS patients with at least 12-month follow-up).

4.IMPACT:

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.
- COVID 19 has impacted enrollment rate, surgical procedure timing and patient follow-up especially as most patients are not local to the study centers. Impact is expected to continue for the foreseeable future though both sites are able to conduct surgeries and follow-ups if patients are willing to travel/ and make appointments.

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.

The COVID-19 pandemic temporarily paused Clinical Research activities that were not essential to the health and well-being of subjects. Clinical Research Recovery is under way, such that we have been able to continue recruitment, enrollment, surgery, and patient-reported and surgical outcomes assessments, as well as many functional outcomes measures.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

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.
- No changes to report this period.
- Continuing Review was submitted on 10/15/2019 and approved November 7, 2019.

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:

- **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.

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.

https://orthosurgery.ucsf.edu/research/clinical-research/International.html
Details the UCSF international Center for Osseointegration Research, Education, and Surgery (iCORES) Program

https://orthosurgery.ucsf.edu/research/clinical-research/UCSF-Musculoskeletal-Research-Consortium-METRiCS.html
Describes the clinical and translational studies of the UCSF Musculoskeletal Research Consortium (METRiCS) Program.

- **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. .

- **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: 3
Contribution to Project: CAPT Forsberg responsible for consenting patients and performing surgeries and overall project management.

Name: Benjamin K. Potter, MD FACS
Project Role: Associate Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 3
Contribution to Project: COL 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: 9
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: 12
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: 6
Contribution to Project: Dr. O'Donnell responsible for consenting patients and performing surgeries and oversight of subaward site.

Name: Kristina Benirschke
'Project Role: Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 12
Contribution to Project: Ms. Benirschke is responsible for UCSF regulatory coordination, patient appts, administering survey questionnaires.

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."

- *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."

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);*
- *Other.*

•Nothing to report.

8.SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS: Attached

9.APPENDICES: N/A