AWARD NUMBER: W81XWH-22-2-0010

TITLE: The Relationship Between Residual Limb Skin Health Measurements and Clinical Outcome

PRINCIPAL INVESTIGATOR: W. Lee Childers

CONTRACTING ORGANIZATION: Henry M. Jackson Foundation for the Advancement of Military Medicine 6720-A Rockledge Dr. STE 100
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5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Henry M. Jackson Foundation for the Advancement of Military Medicine
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9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

The subject of the research is to compare measurements of residual limb skin health and to relate these measurements to clinical outcomes. The purpose is to provide evidence-based assessments to guide clinical care to enhance the quality of life of people with limb amputation. Findings could dictate treatment earlier on, helping Service Members return to duty more quickly and fully, while saving time, energy, and resources attempting a treatment regimen that will be less successful. There are two specific aims to this study. Aim 1 will establish the ability of skin health measurements to distinguish between residual limb skin and the contralateral limb skin. This will provide more information on the measurement techniques being used in this study, many for the first time on individuals with an amputation. Aim 2 will define the relationship between skin health measurements and long-term clinical outcomes and continued prosthetic socket use. This aims to relate these measurements to clinical outcomes in the hopes of predicting when skin breakdown will occur.

15. SUBJECT TERMS

skin health, residual limb, lower limb loss, barrier function, color, elasticity

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
U	U	U	UU	15	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.*

The subject of the research is to compare measurements of residual limb skin health and to relate these measurements to clinical outcomes. The purpose is to provide evidence-based assessments to guide clinical care to enhance the quality of life of people with limb amputation. Findings could dictate treatment earlier on, helping Service Members return to duty more quickly and fully, while saving time, energy, and resources attempting a treatment regimen that will be less successful. There are two specific aims to this study. Aim 1 will establish the ability of skin health measurements to distinguish between residual limb skin and the contralateral limb skin. This will provide more information on the measurement techniques being used in this study, many for the first time on individuals with an amputation. Aim 2 will define the relationship between skin health measurements and long-term clinical outcomes and continued prosthetic socket use. This aims to relate these measurements to clinical outcomes in the hopes of predicting when skin breakdown will occur.

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

Residual limb health, Mexameter, Cutometer, Frictiometer, Ultrasound, Semmes-Weinstein Filament, Tewameter, Corneometer, sensation, elasticity, barrier function, skin thickness, color

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 Tasks for Specific Aims 1 and 2	**Timeline**	**Progress**	**Completion Date**
Major Task 1 – Gain regulatory approvals	**Months**		
Submit an amendment to a current IRB protocol that will enable these measurements to BAMC IRB	1-2	100%	17 NOV 2022
Site specific addendums to WRNMMC	1-2	100%	27 JAN 2023
Requisite data sharing documents filed	2-3	90%	DSA-9 MAR 2023 WRNMMC CRADA-pending
BAMC IRB Approval	3	100%	11 JAN 2023

WRNMMC IRB Approval	3	100%	20 MAR 2023
MRDC HRPO review and approval	2-3	100%	22 FEB 2023
Milestone Achieved: Regulatory approval	3	95%	20 MAR 2023
Major Task 2 – Data collection preparation	**Months**		
Order necessary supplies and measurement equipment	1	100%	1 AUG 2022
Train staff from CFI and WRNMMC on measurement equipment operation	2-3	80%	
CFI and WRNMMC collect test data and confirm data quality with CFI	2-3	50%	
Milestone Achieved: CFI can successfully reduce data collected at CFI and WRNMMC.	3	75%	
Major Task 3 – Collect Experimental data	**Months**		
Collect data on 12 people (5-7 participants per site) with transtibial amputation after gaining informed consent	4-15	0%	
Collect data on 12 people (5-7 participants per site) with transfemoral amputation after gaining informed consent	4-15	0%	
Reduce data within 1 month of collection and send to CFI for analysis and processing	5-16	0%	
Gather data from the medical record associated with Aim 2	10-21	0%	
Complete chart reviews	21	0%	
Milestone Achieved: Data collection complete	21	0%	
Major Task 4 – Data analysis	**Months**		
Perform initial analysis on reliability data from CFI and WRNMMC	3	0%	
Compile data and perform statistical analysis for Aim #1	5-16	0%	
Complete statistical analysis for Aim #2	21	0%	
Milestone Achieved: Analysis complete	21	0%	
Major Task 5 – Dissemination	**Months**		
Abstract submission to MHSRS	21	0%	
Abstract submission to major prosthetic and orthotic conference	21	0%	
Paper submitted to peer-reviewed journal	24	0%	
Milestone Achieved: Abstracts and papers submitted	24	0%	

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.

Regulatory

- IRB and OHRO approval has been achieved at both CFI and WRNMMC.
- Data Sharing Agreement is in place.

Equipment

- Equipment was all ordered and delivered.
- Equipment has been tested at each site.
- Several pieces of equipment had to be sent back to the manufacturer for repair/recalibration. We are still waiting on the return of one more system at CFI.

Data Collection

- SOPs have been developed for each measurement including the parameters that will be used for data collection.

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.

In the next year we plan to begin and complete recruitment. While we are behind on recruitment goals (see Actual Problems section), we intend to recruit one individual with a transtibial and one with a transfemoral amputation at each site each month which will allow us to recruit fully in 6 months. We will develop abstracts for submission to MHSRS and a prosthetics conference in the next year. We will begin work on a manuscript for publication of relevant results.

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.

The CRADA at Walter Reed is still pending. It is with HJF for their review from the WRNMMC business office and we hope it will be approved shortly.

Despite ordering measurement equipment prior to the start date, there was a delay in receiving equipment. Additionally, two pieces of equipment at CFI were defective when received and required extensive troubleshooting with the company to determine the cause of the issue. One device (Mexameter) was returned for a re-calibration and is still pending repair and shipment back. One device (Ultrascan) was returned to the manufacturer with a new device shipped to expedite the process. Research staff are now familiarizing themselves with this device.

This has delayed data collection; however, we are prepared to begin data collections by end of August 2023. We will shift recruitment goals to recruit one individual with a transtibial amputation and one individual with a transfemoral amputation at each site each month. This will allow for all recruitment to occur within 6 months and allow for 6 month follow-ups before August 2024, the end of period of performance.

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

No significant changes to care of human subjects have been made. No RDT&E, education or training activities involving human cadavers will be performed to complete the Statement of Work (SOW).

Significant changes in use or care of vertebrate animals

No animal use research will be performed to complete the Statement of Work.

Significant changes in use of biohazards and/or select agents

None.

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: Lee Childers, PhD
Project Role: PI
Researcher Identifier (ORCID ID): 0000-0002-6119-983X
Nearest person month worked: 1
Contribution to Project: Dr. Childers manages IRB and other administrative issues, and study personnel at the CFI. He oversees the entire project.

Name: Molly Baumann, PhD
Project Role: Research Scientist – Co-I
Researcher Identifier (ORCID ID): 0000-0002-5462-405x
Nearest person month worked: 2
Contribution to Project: Recruitment, materials prep, data collection, study execution

Name: Alyssa Salazar
Project Role: Research Assistant
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Recruitment, materials prep, data collection

Name: Bradford Hendershot
Project Role: Site-PI
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: IRB and administrative issues, oversees data collections at site

Name: Julian Acasio
Project Role: Research Assistant
Researcher Identifier (ORCID ID): N/A
Nearest person month worked: 1
Contribution to Project: Recruitment, materials prep, data collection

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.

This proposal for Dr. Childers has moved from current to past.
Title: Assessing Rehabilitation Outcomes after Severe Neuromusculoskeletal Injury
Dr. Childers was site-PI at 7.5% effort from 8/1/2017-7/31/2022.

The following proposals for Dr. Childers have moved from pending to current.
Title: Validation of military-relevant assessments to predict successful return to duty following lower limb injury
Dr. Childers is Co-I at 3.75% effort from 8/1/2021-7/31/2023.

Title: Exoskeletons for rapid return to duty after tibial stress fracture
Dr. Childers is PI at 10% effort from 8/1/2021-8/1/2025.

Title: Personalizing MPK Prescription for Individuals with Transfemoral Amputation
Dr. Childers is a consultant at 2.5% effort from 10/1/2022-9/30/2026.

Title: Development of the Intrepid Battlefield Exoskeleton to enable continued battlefield lethality during prolonged field care scenarios
Dr. Childers is Site PI at 7.5% effort from 10/1/2022-9/30/2024.

Title: Impact of Technologies that Personalize Robotic Leg Prostheses for Individuals with Transfemoral Amputation of Varying Mobility
Dr. Childers is Co-I at 5% effort from 8/1/23-7/31/27.

The following proposals for Dr. Hendershot have moved from current to past.
Title: Gait Coordination and Stability of Individuals Living with Transtibial Limb Loss
Dr. Hendershot was Co-I at 5% effort from 9/2020-8/2022

Title: Transfemoral Amputee Osseointegration Study (TFAOS)
Dr. Hendershot was Co-I at 5% effort from 9/2017-9/2022

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.*

WRNMMC:
Bethesda, Maryland
- Collaboration – Assistance on SOP development, eventual data collection site.

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 CHART:

Attached.

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.*

Nothing to attach.

The relationship between residual limb skin health measurements and clinical outcomes

OP210044 W81XWH-22-2-0010 **PI**: Lee Childers, PhD **Org**: **Henry M. Jackson Foundation**

Award Amount: $302,105

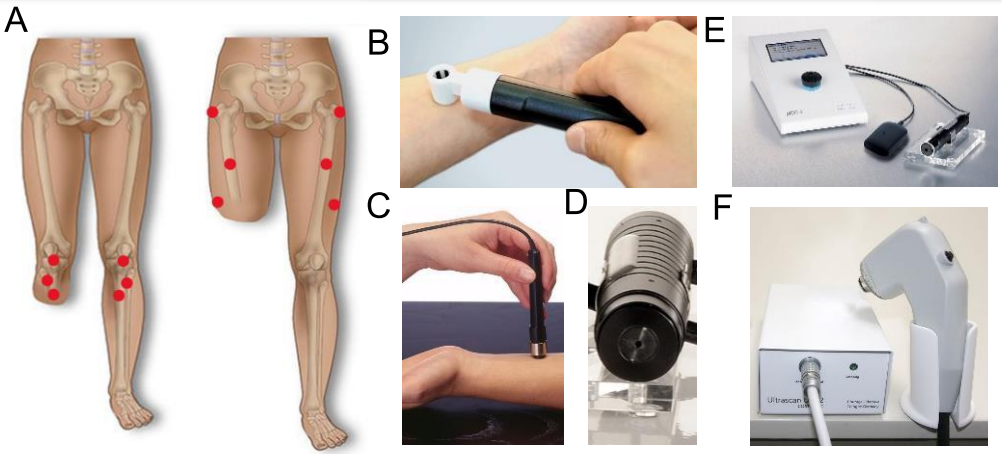
Study/**Product** Aim(**s**)

•Establish the ability of skin health measurements to distinguish between residual limb skin and normal skin

•Define the relationship between skin health measurements and long-term clinical outcomes and continued prosthetic socket use

Approach

We will collect measurements assessing transepidermal water loss, surface hydration, skin color (erythema and melanin), dermal thickness, and elasticity of both the residual limb and contralateral limb on individuals with transtibial (n = 12) and transfemoral amputation (n= 12, N = 24). We will compare contralateral/normal skin values to those of the residual limb which has been subjected to prosthesis wear over time to assess how we may best measure residual limb health. This will provide information on which properties may be more important to adaptation of the residual limb. For six months following data collection, participants will be tracked to assess any residual limb health concerns. Correlations between skin health measurements and clinical outcomes including continued socket wear will be evaluated.



The proposed study will measure three locations (A) each on the residual and contralateral limb utilizing a suite of instruments including transepidermal water loss (TEWL) (B), Corneometer® for skin hydration (C), Cutometer® for biomechanics (D), Mexameter® for erythema and melanin (E), and ultrasound for dermal thickness (F).

Timeline and Cost

Activities \ **Project Year**	1	2
Obtain IRB approval		
Successful data collection across sites		
Collect data on people with amputation		
Data analysis		
Disseminate study findings		
Estimated Budget ($341**K**)	$216	$125

Updated: 8 August 2023

Goals/**Milestones**

QTR 1 **Goals** – Study Preparation

☒ Obtain IRB approval for human subjects research

☒ Order and install testing equipment

☐ Demonstrate measurement repeatability across sites

QTR 2-7 **Goals** – Data Collection and Analysis

☐ Collect data on 12 people with transtibial amputation

☐ Collect data on 12 people with transfemoral amputation

☐ Complete chart reviews and patient follow-up calls to assess residual limb health

☐ Analyze data related to specific aims

QTR 8 **Goals** –Dissemination of Study Findings

☐ Brief study findings to site clinicians at the Brooke Army Medical Center and the Walter Reed National Military Medical Center

☐ Disseminate study findings through publications and presentations

Actual Expenditure:$39,441