

**AWARD NUMBER:** W81XWH-21-2-0003

**TITLE:** Clinical Translatability of Reactive Hyperemia Measurements That Can Monitor Adaptation of Residual Limb Skin to Socket Wear

**PRINCIPAL INVESTIGATOR:** Walter Lee Childers

**CONTRACTING ORGANIZATION:** Henry M. Jackson Foundation, Bethesda, MD

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Fort Detrick, Maryland 21702-5012

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<b>14. ABSTRACT</b> The subject of the research is to compare direct measurements of reactive hyperemia (RH) response using OCT to indirect measurements using thermal images to confirm that changes in thermal imaging do represent changes in skin vascular flow. 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 three aims. The first aim is to define the relationship between skin temperature and microvascular response during reactive hyperemia. The second aim is to determine the differences in reactive hyperemia between normal skin and residual limb skin exposed to transtibial and transfemoral prosthesis use. The third aim is to evaluate the associations between reactive hyperemia response and clinical outcomes.					
<b>15. SUBJECT TERMS</b>  Reactive hyperemia, OCT, skin health, residual limb, lower limb loss					
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## 1. INTRODUCTION:

The subject of the research is to compare direct measurements of reactive hyperemia (RH) response using OCT to indirect measurements using thermal images to confirm that changes in thermal imaging do represent changes in skin vascular flow. 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 three aims. The first aim is to define the relationship between skin temperature and microvascular response during reactive hyperemia. The second aim is to determine the differences in reactive hyperemia between normal skin and residual limb skin exposed to transtibial and transfemoral prosthesis use. The third aim is to evaluate the associations between reactive hyperemia response and clinical outcomes.

## 2. KEYWORDS:

Reactive hyperemia, optical coherence tomography (OCT), forward-looking infrared imaging (FLIR), residual limb health

## 3. ACCOMPLISHMENTS:

### What were the major goals of the project?

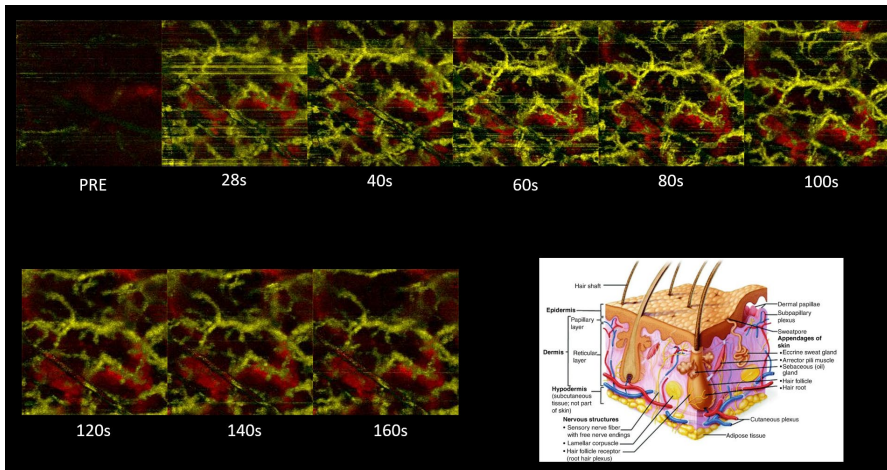
	Timeline	Progress	Completion Date
<b>Major Task 1: Gain Regulatory Approval</b>	Months		
Main protocol submitted to BAMC IRB	1-3	100%	11 Aug 2021
Site specific addendums to WRNMMC and UW	1-3	100%	5 OCT 2021/ 15 FEB 2022
Requisite data sharing documents filed	3-5	20%	
BAMC IRB Approval	6	100%	03 Nov 2021
WRNMMC IRB Approval	7	50%	
UW IRB Approval	7	100%	11 Oct 2021
MRDC HRPO review and approval	8-10	100%	1 Feb 2022
<i>Milestone Achieved: Regulatory approval</i>	10	70%	
<b>Major Task 2: Data Collection Preparation</b>	Months		
Develop and test load applicator system	1-6	90%	
Deliver load applicator systems to CFI and WRNMMC	7	50%	CFI delivered 08 AUG 2022, WRNMMC scheduled 20 SEP 2022
Train staff from CFI and WRNMMC on load applicator system in conjunction with OCT measurements	8	50%	
CFI and WRNMMC collect test data and confirm data quality with UW	9-10	10%	
<i>Milestone Achieved: UW can successfully reduce data collected at CFI and WRNMMC.</i>	11	50%	

<b>Major Task 3: Collect Experimental Data</b>	Months		
Collect data on 24 people with transtibial amputation after gaining informed consent	12-38		
Collect data on 24 people with transfemoral amputation after gaining informed consent	12-38		
Reduce OCT and Thermal data within 1 month of collection	12-39		
Gather data from the medical record associated with Aim 3	12-39		
Collect exploratory data on people with amputation considering osseointegration surgery after gaining informed consent	12-39		
Complete chart reviews	45		
<i>Milestone Achieved: Data collection complete</i>	45		
<b>Major Task 4: Data Analysis</b>	Months		
Reduce OCT and thermal imaging data within 1 month of collection	12-39		
Perform initial analysis on reliability data from CFI and WRNMMC	10-12		
Compile data and perform statistical analysis for Aims #1 & 2	12-41		
Complete statistical analysis for Aim #3	46		
<i>Milestone Achieved: Analysis complete</i>	46		
<b>Major Task 5: Dissemination</b>	Months		
MHSRS abstract on thermal imaging methodology	17		
MHSRS abstract on Hypotheses 1.1 and 1.2 based on data collected to that point	29		
MHSRS abstract on Hypotheses 2.3	41		
Abstract submission to major prosthetic and orthotic conference on Hypothesis 1.3	43		
Abstract submission to major orthopedic conference on Hypothesis 3.2	43		
Paper submitted to peer-reviewed journal on thermal imaging methodology	18		
Paper submitted to peer-reviewed journal on Hypotheses 1.1 and 1.2	44		
Paper submitted to peer-reviewed journal on Hypotheses 1.3	45		
Paper submitted to peer-reviewed journal on Specific Aim #2	46		
Paper submitted to physical medicine and rehabilitation focused peer-reviewed journal on Hypotheses 3.1	47		
Case series paper submitted to peer-reviewed orthopedic focused journal on Hypotheses 3.2	48		
Milestone Achieved: Abstracts and papers submitted	48		

## What was accomplished under these goals?

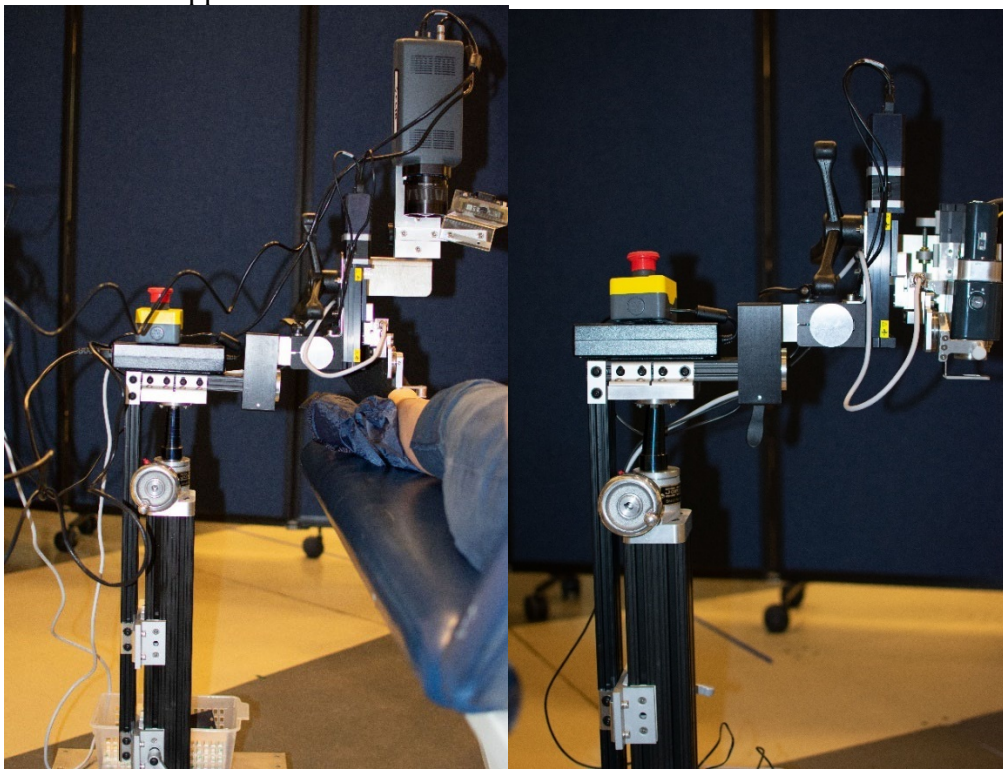
### Load Application Design

1. Designs are complete for load applicator design. Minor alterations to the user interface are being made after initial testing at CFI.
2. Full load applicator tests completed at University of Washington ensuring load applicator maintains load even if the leg shifts slightly.
3. OCT and load applicator run in parallel – demonstrate ability to successfully capture OCT images after load application.



OCT test images provided below showing vascular dilating after the load was removed, reaching a peak, and then subsiding.

4. Successful tests with OCT and FLIR after load application.
5. Load applicator has been delivered and built at CFI.



Built Load Applicators for FLIR and OCT Imaging

6. Training with load applicators has commenced at CFI.
7. Parts ordered to fabricate devices for Walter Reed and fabrication has begun.

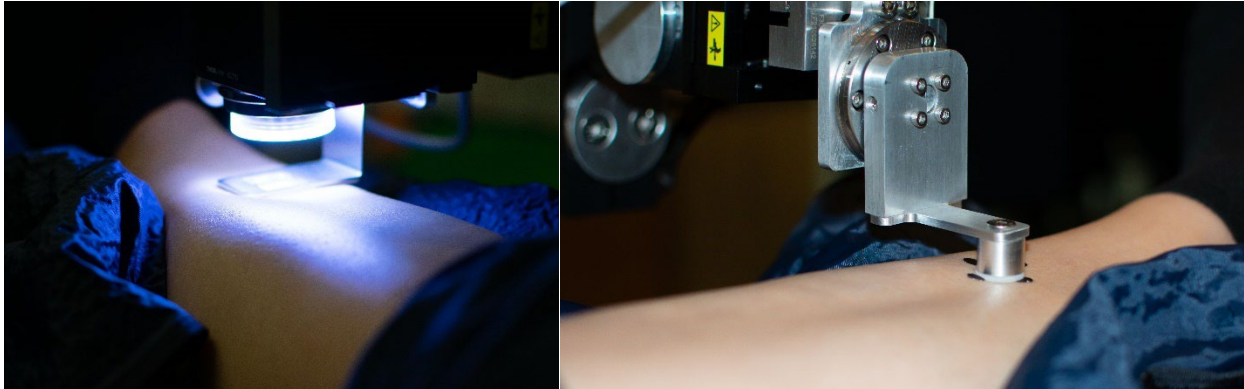
### Regulatory

1. San Antonio IRB Approval for Core Protocol achieved (C.2021.112, 3 NOV 2021)
2. University of Washington IRB defer to San Antonio achieved (11 OCT 2021)

3. HRPO approval achieved (E02261.1a – 1 FEB 2022)
4. WRNMMC SSA submitted (ref. 947729, IRB C.2021.112, 15 FEB 2022)
5. CURRENT STATUS: We are approved and can collect data at the CFI once we are comfortable using the load applicator. Waiting on WRNMMC's IRB to approve their site.

### Data Collections

1. FLIR cameras arrived at both WRNMMC and CFI
2. FLIR camera and software successfully tested at CFI
3. Set up with FLIR, OCT, and load applicators successfully tested at CFI



Example of OCT imaging after load application and load application prior to imaging.

### What opportunities for training and professional development has the project provided?

Nothing to report.

### How were the results disseminated to communities of interest?

Nothing to report.

### What do you plan to do during the next reporting period to accomplish the goals?

- Gain approval for data collections at WRNMMC
- Finalize and submit data sharing agreements based on new DHA guidance that now require DSA to share identifiable information pulled from the medical record between MTFs.
- Ship and build load applicators at WRNMMC
- Continue training for data collections, collect test data, and confirm data quality at CFI and WRNMMC.
- Establish SOP for data collection and data processing.

**4. IMPACT:**

**What was the impact on the development of the principal discipline(s) of the project?**

Nothing to report.

**What was the impact on other disciplines?**

Nothing to report.

**What was the impact on technology transfer?**

Nothing to report.

**What was the impact on society beyond science and technology?**

Nothing to report.

**5. CHANGES/PROBLEMS:**

**Changes in approach and reasons for change**

Nothing to report.

**Actual or anticipated problems or delays and actions or plans to resolve them**

1. Supply chain shortages resulted in delay of building load applicators to distribute to CFI and WRNMMC. This has since been resolved and WRNMMC will be receiving their load applicators soon. In the meantime, CFI continues training with load applicator and FLIR and OCT devices we received from Univ of Washington.
2. There have been some changes in data sharing and cooperative agreements with the transition of MTFs to DHA delaying their completion. We have a path forward and these agreements are all in process.
3. Shifting to having a single IRB has delayed the process of getting Walter Reed approved. This however will save time over the duration of the project as amendments will only need to be made once. This has not delayed the start of data collection as we are awaiting load applicator builds.

**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**

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:**

- **Publications, conference papers, and presentations**

**Journal publications.**

Nothing to report.

**Books or other non-periodical, one-time publications.**

Nothing to report.

**Other publications, conference papers and presentations.**

Nothing to report.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### What individuals have worked on the project?

*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:* Joan Sanders, PhD  
*Project Role:* Co-PI  
*Researcher Identifier (ORCID ID):* 0000-0002-8850-243X  
*Nearest person month worked:* 1  
*Contribution to Project:* Dr. Sanders coordinates the project at UW including design and fabrication, communicating regularly with Dr. Childers on study-related issues

*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:* Noel Guerrero  
*Project Role:* Research Coordinator  
*Researcher Identifier (ORCID ID):* 0000-0002-5129-1763  
*Nearest person month worked:* 1

*Contribution to Project:* IRB Management, ordering  
*Name:* Ciera Price, CPO  
*Project Role:* Research Prosthetist  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 1  
*Contribution to Project:* Recruitment, prosthetic support, materials prep, data collection

*Name:* Alyssa Salazar  
*Project Role:* Research Assistant  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 3  
*Contribution to Project:* Recruitment, materials prep, data collection

*Name:* Mathew Weissinger  
*Project Role:* Research Engineer  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 2  
*Contribution to Project:* Mechanical design

*Name:* Bailey Ramesh  
*Project Role:* Research Engineer  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 3  
*Contribution to Project:* Control system design

*Name:* Conor Lanahan  
*Project Role:* Research Assistant  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 3  
*Contribution to Project:* Mechanical design, data collection procedures

*Name:* Christopher Dearth  
*Project Role:* Chief R&S Division  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 1  
*Contribution to Project:* Walter Reed oversight

*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:* Heidi Mahatan

*Project Role:* Program Manager  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 1  
*Contribution to Project:* Project Management and regulatory approval

*Name:* Julian Acasio  
*Project Role:* Research Assistant  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 2  
*Contribution to Project:* Recruitment, materials prep, data collection

*Name:* Megan Loftsgaarden  
*Project Role:* PM&R Doctor  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 1  
*Contribution to Project:* Clinical advisor and support

*Name:* John Fergason  
*Project Role:* Prosthetist  
*Researcher Identifier (ORCID ID):* N/A  
*Nearest person month worked:* 1  
*Contribution to Project:* Clinical advisor and support

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

This proposal for Dr. Childers has moved from pending to current.  
Title: Validation of military-relevant assessments to predict successful return to duty following lower limb injury  
Co-Investigator at 5% from 08/01/2022-07/31/2023

This proposal for Dr. Childers and Dr. Baumann has moved from pending to current.  
Title: The relationship between residual limb skin health measurements and clinical outcomes  
Dr. Childers is PI at 5% effort from 08/01/2022-07/31/2024  
Dr. Baumann is Co-I at 20% effort from 08/01/2022-07/31/2024

**What other organizations were involved as partners?**

University of Washington:  
Seattle, Washington:

- Collaboration – Development of load applicator, assistance on imaging SOP development.

WRNMMC:  
Bethesda, Maryland

- Collaboration – Assistance on imaging SOP development, eventual data collection site

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS:**

Please see attached.

**9. APPENDICES:**

Nothing to attach.