

AWARD NUMBER: **W81XWH-15-1-0669**

TITLE: **The Use of Quantitative SPECT/CT Imaging to Assess Residual Limb Health**

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CONTRACTING ORGANIZATION: **HENRY M. JACKSON FOUNDATION FOR  
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<b>14. ABSTRACT</b>  The objective of the study was to translate SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate the utility of non-invasive imaging for evaluating the impact of next-generation socket technologies on the health of the residual limb. It was hypothesized that SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and that acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes.					
<b>15. SUBJECT TERMS</b> Prosthetics, residual limb health, imaging, extremity trauma, amputation					
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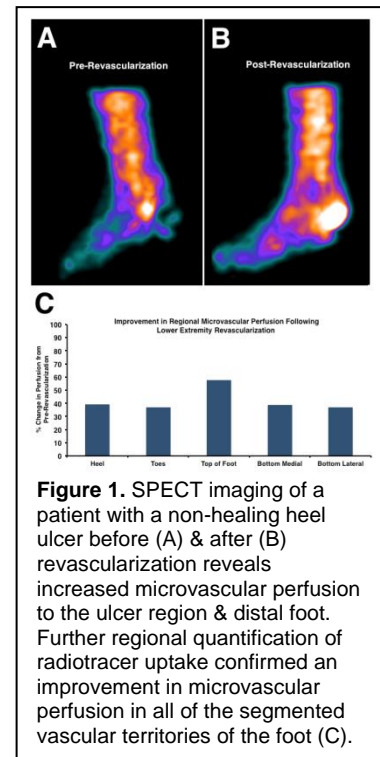
## INTRODUCTION:

Prosthetic devices aim to restore the appearance and/or function of the affected extremity for patients with amputations. The socket is a critical feature of a prosthetic device as it acts as the interface between the prosthesis and residual limb. Numerous residual limb health issues have been associated with traditional socket technologies. Accordingly, the DoD has invested significant effort and funding in recent years to facilitate the development of improved socket technology to aid in the maintenance of tissue health in the residual limb. While these efforts are beginning to yield exciting next-generation socket technologies (e.g., ‘smart’ sockets), limited technologies are available to assess the impact of these sockets on the underlying physiological response in the residual limb.

The health of residual limb tissue in persons with lower-limb amputation is of critical importance. Breakdown of tissue viability of the residual limb can negatively impact the progress of the patient’s rehabilitation and/or lead to prosthesis abandonment, thus reducing their mobility, function, and overall quality of life. To date, the ability to accurately assess tissue viability within the residual limb of individuals with amputations while the socket is on has been challenging. Therefore, a non-invasive, sensitive, and quantitative imaging modality that could provide an objective assessment of the overall health of the residual limb would advance the standard of care for affected patients, as well as improve selection of the most effective socket technologies at promoting overall limb health.

In accordance with the intent of the OPOP award mechanism, the goal of the current research study is to provide outcomes data to inform and improve the care of military service members with lower extremity amputation(s). This will be accomplished by utilizing a validated SPECT/CT imaging technique to assess which prosthetic socket technologies will generate the best patient outcomes (i.e., residual limb health) for service members with limb loss. Successful completion of this study would significantly improve our understanding and advance the implementation of the prosthetic socket devices most effective at promoting the overall health of the residual limb, thereby greatly benefiting patient care.

**KEYWORDS:** Prosthetics, residual limb health, imaging, extremity trauma, amputation



**ACCOMPLISHMENTS:**

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

The objective of the proposed study was to translate SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate the utility of non-invasive imaging for evaluating the impact of next-generation socket technologies on the health of the residual limb. It was hypothesized that SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and that acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes.

<b><i>Specific Aim 1 - To quantify basal microvascular perfusion and perfusion reserve of the residual limb in patients with lower extremity amputation using SPECT/CT imaging.</i></b>	<b>Percentage Completion</b>
<b>Major Task 1:</b> To evaluate SPECT/CT imaging as a means to assess limb health in patients with amputation.	
Subtask 1.1 – IRB Approval -- WRNMMC	0%
Subtask 1.2 – IRB Approval -- Yale University (ended upon departure)	100%
Subtask 1.2 – IRB Approval -- Research Institute at Nationwide Children’s Hospital	100%
Subtask 1.3 – HRPO Approval	0%
Subtask 1.4 – Human subject testing of SPECT/CT imaging	0%
Subtask 1.5 – Image analysis and quantification	0%
Subtask 1.6 – Dissemination of results describing SPECT/CT imaging in an amputee population	0%
<b><i>Specific Aim 2 - To evaluate the efficacy of next-generation (e.g., breathable socket) prosthetic socket technologies at promoting tissue health of the residual limb of patients with lower extremity amputation using SPECT/CT imaging.</i></b>	<b>Percentage Completion</b>
<b>Major Task 2:</b> To use SPECT/CT imaging to evaluate new socket technologies on the long term limb health in patients with amputation.	
Subtask 2.1 – Long term follow up SPECT/CT imaging of 40 subjects	0%
Subtask 2.2 – Image analysis and quantification of long term follow up imaging	0%
Subtask 2.3 – Dissemination of results describing use SPECT/CT imaging to evaluate new socket technologies on the long term limb health in patients with amputation.	0%

**What was accomplished under these goals?**

During the project period of performance, considerable effort was devoted towards completion the current project, specifically towards the pursuit of regulatory (IRB) approval. To that end, the study team worked tirelessly for over 3 years, including countless rounds stipulations from the IRB, to obtain regulatory approval; however, much to our surprise, on 25JAN2019 the protocol was “disapproved” by the WRNMMC IRB citing “the board could not justify the risk-benefit ration for this study as currently designed.” Additionally, the letter stated that the design of the

study was not appropriate and required a modification / addition of additional groups / aims, etc. Furthermore, the outcome letter goes on to state “the study employs an unproven techniques to test an unproven hypothesis”. It is not clear why the WRNMMC IRB decided to opine on the scientific merit of the study, particularly considering the study had previously undergone extensive scientific and programmatic review from the funding agency. Importantly, it is the opinion of the entire study team that the conclusions drawn by the IRB are patently inaccurate and contrary to numerous published studies. However, we were informed that once a disapproval decision has been rendered, it is not possible to be overturned. Due to this misguided decision, regulatory approval for this study was not possible and thus the study was unable to be accomplished.

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

This project provided training and professional development for several of our team members related to regulatory considerations for non-minimal risk studies.

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

The general concept of this study – i.e., utilizing next generation imaging technologies to generate novel, quantitative outcome assessments for the field of O&P – has been disseminated to our communities of interest (e.g., Military Medicine) via both manuscripts in peer reviewed, scientific journals and presentations at an internationally renowned conference. The specifics of the knowledge products are listed below:

- Accepted Abstract -- “*Evaluating Traumatic Extremity Injuries Using Multimodality Imaging: Emphasis on SPECT/CT Imaging and Implications for Military Medicine*”. 2017 Military Health System Research Symposium (MHSRS).
- Published Article – Stacy MR, Dearth CL. *Multimodality imaging approaches for evaluating traumatic extremity injuries: implications for military medicine*. *Adv Wound Care* (New Rochelle). 2017 Jul 1;6(7):241-251. doi: 10.1089/wound.2016.0716.

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

n/a (final report)

**IMPACT:**

The general concept of this study – i.e., utilizing next generation imaging technologies to generate novel, quantitative outcome assessments for the field of O&P – hold the potential to improve the overall health of the residual limb, thereby greatly benefiting patient care.

**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.

**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**

See above – i.e., inability to gain regulatory approval from the WRNMMC IRB.

**Changes that had a significant impact on expenditures**

Due to the regulatory associated delays and subsequent inability to conduct the study, the overall project expenditures were significantly less than the original projection.

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

Nothing to Report.

**PRODUCTS:**

**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.

**PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS**

**What individuals have worked on the project?**

Name:	Christopher L. Dearth, PhD
Project Role:	Principle Investigator
Organization:	Extremity Trauma & Amputation Center of Excellence

Walter Reed National Military Medical Center &  
Uniformed Services University of the Health Sciences

Name: Mitchel R. Stacy, PhD  
Project Role: Co-Principle Investigator  
Organization: The Research Institute at Nationwide Children's Hospital

Name: CDR Grant H. Bonavia, MD PhD  
Project Role: Associate Investigator  
Organization: Nuclear Medicine Service, Department of Radiology  
Walter Reed National Military Medical Center

Name: Michael Valerio, PhD  
Project Role: Associate Investigator  
Organization: Extremity Trauma & Amputation Center of Excellence  
Walter Reed National Military Medical Center &  
Uniformed Services University of the Health Sciences

Name: Elizabeth Husson, CCRC  
Project Role: Protocol Coordinator  
Organization: Extremity Trauma & Amputation Center of Excellence  
Walter Reed National Military Medical Center &  
Uniformed Services University of the Health Sciences

Name: Heidi Mahatan, MA, LCPC  
Project Role: Protocol Coordinator  
Organization: Henry M. Jackson Foundation for the Adv. of Mil. Medicine  
Walter Reed National Military Medical Center

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

Nothing to Report. No changes have been made to efforts on this project.

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

During the study period of performance, Dr. Stacy relocated from Yale University to The Research Institute at Nationwide Children's Hospital / Ohio State University (Columbus, OH)

**SPECIAL REPORTING REQUIREMENTS**

**QUAD CHART:**

(See next page)

# The Use of Quantitative SPECT/CT Imaging to Assess Residual Limb Health



Orthotics and Prosthetics Outcomes Research Award - W81XWH-15-1-0669

**PI:** Christopher L. Dearth, PhD    **Org:** Walter Reed National Military Medical Center    **Award Amount:** \$484,210

**Objective:** The objective of the proposed proof of concept, pilot clinical study is to translate <sup>99m</sup>Tc-tetrofosmin SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate its effectiveness as a means to evaluate the impact of next generation socket technologies on the health of the residual limb. This objective will be evaluated by the following specific aims:

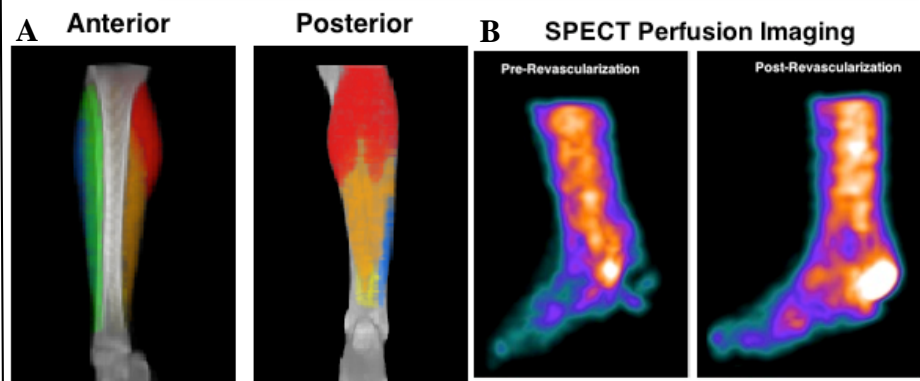
**Specific Aim 1:** To quantify basal microvascular perfusion and perfusion reserve of the residual limb in patients with lower extremity amputation using <sup>99m</sup>Tc-tetrofosmin SPECT/CT imaging.

**Hypothesis:** It is hypothesized that evaluation of microvascular perfusion via <sup>99m</sup>Tc-tetrofosmin SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to use during the assessment of residual limb tissue health beyond traditional limb health outcome measures.

**Specific Aim 2:** To evaluate the efficacy of current (e.g., VASS) and next-generation (e.g., breathable socket) prosthetic socket technologies at promoting tissue health of the residual limb of patients with lower extremity amputation using <sup>99m</sup>Tc-tetrofosmin SPECT/CT imaging.

**Sub Aim 2.1 -** To determine if acute changes in microvascular perfusion are predictive of long term residual limb health outcomes.

**Hypothesis:** It is hypothesized that <sup>99m</sup>Tc-tetrofosmin SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and these acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes.



**A)** Anterior & posterior views of 3-D calf muscle regions segmented from a CT attenuation scan. Gastrocnemius (red), soleus (orange), tibialis anterior (green), tibialis posterior (yellow), and fibularis longus (blue) muscles are displayed and overlaid on a bone only CT image. **B)** <sup>99m</sup>Tc-tetrofosmin SPECT perfusion imaging in a patient with a non-healing heel ulcer prior to and following lower extremity revascularization demonstrates increased radiotracer uptake in the site of the heel ulcer and distal foot following treatment.

## Timeline and Cost

Activities	Calendar Year	2016	2017	2018	2019
IRB creation / submission / approval		[Progress bar spanning 2016-2019]			
Begin subject recruitment / enrollment					
Specific Aim #1					
Specific Aim #2					
Study Completion / Data Dissemination					

## Goals / Milestones

### CY16-18 Goals – Initiation / IRB / Personnel

- Study kickoff meeting
- Generation & posting of position description for research personnel
- CRADA & DSA document creation & submission
- WRNMMC IRB SRC submission & approval
- Yale University IRB submission & approval
- WRNMMC IRB submission
- Initiation of knowledge dissemination

### CY18-19 Goals – Study Initiation / Data Collection / Study Completion

- IRB submission at Nationwide Children's Hospital
- WRNMMC IRB Approval
- HRPO Approval
- Begin subject recruitment / enrollment
- Begin data collection for SA 1 & 2
- Complete data collection for SA 1 & 2
- Manuscript(s) submission / publication
- Conference abstract submission / presentation