

AWARD NUMBER: W81XWH-20-2-0061

TITLE: Assessing the Comparative and Longitudinal Benefits of Vascularized Composite Allotransplantation of the Hand

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<b>14. ABSTRACT</b> Hand transplantation can restore physical functions, including movement and sensation, and qualitative evidence from our ongoing research suggests that hand transplantation can also improve well-being and quality of life (QOL). However, there are risks to receiving hand transplant surgery and patients and doctors need valid information on QOL outcomes to weigh the risks and benefits of hand transplantation. This project will address the FY19 RTRP Focus Areas to (1) define/assess the benefits or value of hand transplant, including the relative value of hand transplantation compared to other treatment options and the benefits to social participation and satisfaction, and (2) to determine how psychosocial functioning changes over time within hand transplant recipients. We will conduct qualitative interviews with participants from four different clinical groups: (1) individuals who have undergone hand transplantation, (2) individuals with severe upper extremity injuries who have undergone limb reconstruction surgery, (3) individuals with upper-extremity amputation who use prosthetic devices, and (4) individuals with upper-extremity amputation who use osseointegrated prosthetic devices. Furthermore, we will develop a set of consensus standardized outcomes measures that can be used at all clinical sites. The overall goal of this qualitative research study is to improve the methods used for evaluating outcomes after hand transplant surgery, leading to improved clinical decision-making and improved outcomes overall. This information may help hand transplant become a more feasible option for those with hand or arm amputations, which would allow more individuals to resume productive lives as a result. To date, a comprehensive multi-site study protocol has been reviewed and approved by the University of Delaware IRB and is under review with HRPO. We have worked with participating sites to establish reliance agreements for single IRB review. Paperwork for a CRADA with Walter Reed was initiated, with the goal of engaging all sites.				
<b>15. SUBJECT TERMS</b> Hand Transplant, Patient reported outcomes, quality of life, vascularized composite allotransplantations, amputation, upper extremity				
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**1. INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Hand transplantation can restore physical functions, including movement and sensation, and qualitative evidence from our ongoing research suggests that hand transplantation can also improve well-being and quality of life (QOL). However, there are risks to receiving hand transplant surgery and patients and doctors need valid information on QOL outcomes to weigh the risks and benefits of hand transplantation. This project will address the FY19 RTRP Focus Areas to (1) define/assess the benefits or value of hand transplant, including the relative value of hand transplantation compared to other treatment options and the benefits to social participation and satisfaction, and (2) to determine how psychosocial functioning changes over time within hand transplant recipients. We will conduct qualitative interviews with participants from four different clinical groups: (1) individuals who have undergone hand transplantation, (2) individuals with severe upper-extremity injuries who have undergone limb reconstruction surgery, (3) individuals with upper-extremity amputation who use prosthetic devices, and (4) individuals with upper-extremity amputation who use osseointegrated prosthetic devices. Furthermore, we will develop a set of consensus standardized outcomes measures that can be used at all clinical sites. The overall goal of this qualitative research study is to improve the methods used for evaluating outcomes after hand transplant surgery, leading to improved clinical decision-making and improved outcomes overall. This information may help hand transplant become a more feasible option for those with hand or arm amputations, which would allow more individuals to resume productive lives as a result.

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

Hand Transplant, Patient reported outcomes, quality of life, vascularized composite allotransplantation, amputation, upper extremity

**3. ACCOMPLISHMENTS:**

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

Study Specific Aims: (1) Assess the benefits of upper extremity (UE) vascularized composite allotransplantation (VCA) across emotional, social, physical, and functional domains. (1a) Understand the relative value of UE VCA compared to other treatment options (e.g., prosthetics, reconstruction, osseointegration). (1b) Document how UE VCA affects social roles, interactions, and functioning, including sense of self and wholeness. (2) Explore how psychosocial functioning and QOL change over time for UE VCA recipients. (3) Develop a consensus set of psychosocial and QOL outcome variables that can be assessed longitudinally across VCA clinical centers.

Statement of Work – Tasks and Subtasks	% Complete
<b>Major Task 1: Prepare Regulatory and Administrative Documents for Data Collection</b>	
Subtask 1.1: Finalize study procedures, consent form(s), and human subjects protocol	100
Subtask 1.2: Coordinate IRB protocol submission at UD	100

<b>Statement of Work – Tasks and Subtasks</b>	<b>% Complete</b>
Subtask 1.3: Coordinate IRB protocol submission at WR	100
Subtask 1.4: Coordinate IRB protocol submissions at other recruitment sites	75
Subtask 1.5: Coordinate protocol submission to HRPO at UD	100
Subtask 1.6: Coordinate protocol submission to HRPO at WR	0
Subtask 1.7: Coordinate protocol submission to HRPO at other sites, as necessary	0
Subtask 1.8: Coordinate administrative approvals (e.g., Data Sharing Agreements) among all sites, as necessary	50
<b>Major Task 2: Conduct Baseline Interviews with Participants (n = 100)</b>	
Subtask 2.1: Develop data collection platform (i.e., REDCap) and finalize interview procedures	0
Subtask 2.2: Recruit and screen participants	0
Subtask 2.3: Enroll and interview participants	0
<b>Major Task 3: Analyze Data from Baseline Interviews</b>	
Subtask 3.1: Conduct thematic qualitative analyses	0
Subtask 3.2: Conduct descriptive analyses of data from baseline interviews	0
Subtask 3.3: Evaluate and summarize results from Aim 1 analyses	0
<b>Major Task 4: Conduct Longitudinal Interviews with Participants (n = 100)</b>	
Subtask 4.1: Develop longitudinal data collection platform and finalize interview procedures	0
Subtask 4.2: Re-contact and interview participants from Aim 1 data collection	0
<b>Major Task 5: Analyze Data from Longitudinal Interviews</b>	
Subtask 5.1: Conduct thematic qualitative analysis from longitudinal interviews	0
Subtask 5.2: Conduct descriptive analysis of data from longitudinal interviews	0
Subtask 5.3: Evaluate and summarize results from Aim 2 analyses	0
<b>Major Task 6: Identify and Disseminate a Set of Recommended Outcome Variables for VCA of the Hand</b>	
Subtask 6.1: Develop a proposed set of outcome variables based on results from prior research and the Aim 1 results	0
Subtask 6.2: Share recommendations with partnering VCA collaborators and gather feedback	0
Subtask 6.3: Revise recommendations based on feedback	0
Subtask 6.4: Summarize recommendations and prepare for dissemination to VCA clinical sites	0

### **What was accomplished under these goals?**

#### Major Task 1: Prepare Regulatory and Administrative Documentation

During year 1, a comprehensive multi-site study protocol was reviewed and approved by the UD IRB. UD confirmed with all participating sites that they were amenable to a single IRB model for this project, given the current DoD guidelines, and we approached all of the involved recruiting sites to gather information on the opportunity for a reliance agreement with the UD IRB.

In year 2, we obtained approval of our multi-site protocol by HRPO. We have held multiple meetings individually with teams at all participating sites [Walter Reed (WR), University of Pennsylvania (Penn), the University of Louisville (UL), Johns Hopkins (JH), UCLA, Brigham and Women's Hospital (BWH), and Massachusetts General Hospital (MGH)], confirmed each site's willingness to have UD be the IRB of record, reviewed each site's and UD's regulatory and administrative documentation requirements, and created follow-up plans for each site. All steps between WR and UD have been completed, including UD IRB approval, and the formal reliance agreement awaits final signature at WR.

. At BWH, cede approval was submitted and approval at the site is expected at the start of year 3. MGH, JH, and Penn have each received local approval for reliance agreements; paperwork submission from them to UD IRB is pending. UL and UCLA reliance reviews are pending. In addition, staff at WR have begun the paperwork for a cooperative research and development agreement (CRADA) that will cover all involved sites and will include the necessary data sharing agreement(s). All subawards have been established with participating sites

**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?**

In year 3 of this project, we will obtain all remaining IRB and HRPO approvals for recruiting patient participants from the involved sites, finalize site-specific agreements for data sharing and other administrative concerns, develop the data collection procedures and platform, train data collectors, and initiate the patient participant interviews.

**4. IMPACT:**

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

We have brought together many of the clinical sites involved in hand transplantation in the United States by forming the Transplant Outcomes Research Collaborative for the Hand (TORCH). Forming this consortium will have a major impact on the field because it will allow for improved synchronization of efforts for standardizing outcomes measures for upper extremity transplantation research and clinical care. This consortium will also allow our research team to recruit and enroll many of the available upper extremity transplant participants in the U.S., as well as osseointegration participants, both of which are extremely small populations nationwide.

**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**

Regulatory and administrative approvals have taken significantly longer than anticipated, due in part to the complexity of obtaining reliance agreements across seven sites, all of which have idiosyncratic review and procedures for participant safeguards. To address this, we have delayed expenditures to assure funds are available to accomplish all project goals. We are working closely with representatives from all sites to establish single IRB reliance agreements as well as a CRADA that will cover all sites. In addition, we are exploring additional partnerships with upper extremity transplant centers with English-speaking participants, to help ensure we meet enrollment targets. For example, we have had initial discussions with Leeds Teaching Hospitals in the United Kingdom, and they have expressed interest in potentially joining our consortium. The Leeds site has completed upper extremity transplants on eight patients, so their potential inclusion would meaningfully augment the participant pool.

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

The delays in regulatory approvals have caused corresponding delays in spending for this project. However, we anticipate that the effect of this will be neutral on the budget over the life of the project.

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

Nothing to report.

### **Significant changes in use or care of human subjects**

Nothing to report.

### **Significant changes in use or care of vertebrate animals**

Nothing to report.

### **Significant changes in use of biohazards and/or select agents**

Nothing to report.

## **6. PRODUCTS:**

### **Publications, conference papers, and presentations**

Nothing to report.

### **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?**

<b><u>Walter Reed National Military Medical Center (WRNMMC)</u></b>	
Name:	CAPT (sel) Scott Tintle, MD
Project Role:	Initiating PI at WR
ORCID ID:	0000-0003-0887-7600
Nearest person month worked:	1
Contribution to project:	no change
Name:	Christopher L. Dearth, PhD
Project Role:	Co-Investigator at WR
ORCID ID:	0000-0003-3701-0950
Nearest person month worked:	1
Contribution to project:	no change
Name:	Toby Perkins
Project Role:	Regulatory
ORCID ID:	none
Nearest person month worked:	1
Contribution to project:	no change
<b><u>University of Delaware (UD)</u></b>	
Name:	David Tulsy, PhD
Project Role:	Collaborating PI
ORCID ID:	0000-0002-4335-4509
Nearest person month worked:	1
Contribution to Project:	no change

Name: Jerry Slotkin, PhD  
Project Role: Co-I  
ORCID ID: 0000-0001-8199-3056  
Nearest person month worked: 1  
Contribution to Project: no change

Name: Callie Tyner, PhD  
Project Role: Co-I  
ORCID ID: 0000-0003-2945-392X  
Nearest person month worked: 1  
Contribution to Project: no change

**Massachusetts General Hospital (MGH)**

Name: Curtis L. Cetrulo, MD  
Project Role: Collaborating PI  
ORCID ID:  
Nearest person month worked: 1  
Contribution to Project: Dr. Cetrulo oversees all aspects of the project-related activities at MGH.

**Brigham and Women's Hospital (BWH)**

Name: Simon G. Talbot, MD  
Project Role: Collaborating PI  
ORCID ID:  
Nearest person month worked: 1  
Contribution to Project: Dr. Talbot oversees all aspects of the project-related activities at BWH.

**The Johns Hopkins University (JHU)**

Name: Gerald Brandacher, MD  
Project Role: Collaborating PI  
ORCID ID:  
Nearest person month worked: 1  
Contribution to Project: Dr. Brandacher oversees all aspects of the project-related activities at JHU.

**University of Louisville (UL)**

Name: Christina L. Kaufman, PhD (CK)  
Project Role: Collaborating PI  
ORCID ID:  
Nearest person month worked: 1  
Contribution to Project: Dr. Kaufmann oversees all aspects of the project-related activities at UL.

**University of California Los Angeles (UCLA)**

Name: Kodi Azari, MD, FACS (KA)  
Project Role: Collaborating PI  
ORCID ID:  
Nearest person month worked: 0.2  
Contribution to Project: Dr. Azari oversees all aspects of the project-related activities at UCLA

**University of Pennsylvania (UPenn)**

Name: L. Scott Levin, MD  
Project Role: Collaborating PI  
ORCID ID: 0000-0001-9108-5182  
Nearest person month worked: 0.2  
Contribution to Project: Dr. Levin oversees all aspects of the project-related activities at PM.

Name: Annamarie Horan, PhD  
Project Role: Co-I  
ORCID ID: 0000-0003-3000-5841  
Nearest person month worked: 0.2

Name: Mary Dooley, PhD  
Project Role: Co-I  
ORCID ID: 0000-0002-0647-6187  
Nearest person month worked: 0.2

**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

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

Nothing to report.

**8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:**

**QUAD CHARTS: See Appendix A**

**9. APPENDICES: See Appendix A for Quad Chart.**

# Appendix A: Quad Chart: Assessing the Comparative and Longitudinal Benefits of Vascularized Composite Allotransplantation of the Hand

Log Number: RT190094 Award Number: W81XWH-20-2-0061



PI: CAPT(sel) Scott M. Tintle Organization: Walter Reed National Military Medical Center Award Amount: \$494,635

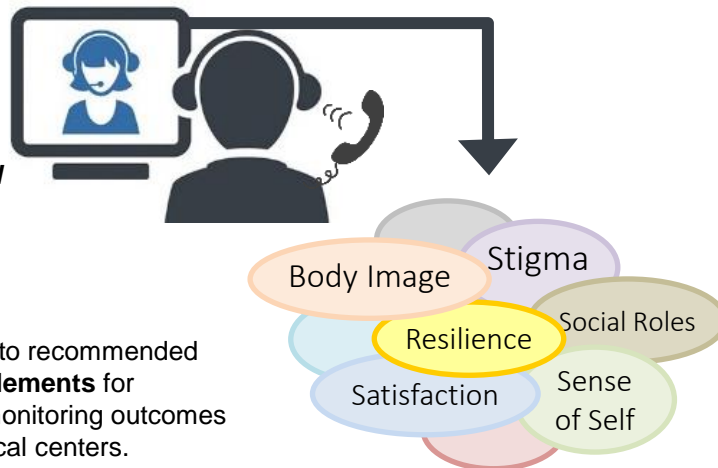
## Specific Aims

- Aim 1:** Assess the benefits of upper extremity (UE) vascularized composite allotransplantation (VCA) across emotional, social, physical, and functional domains. (1a) Understand the relative value of UE VCA compared to other treatment options (e.g., prosthetics, reconstruction, osseointegration). (1b) Document how UE VCA affects social roles, interactions, and functioning, including sense of self and wholeness.
- Aim 2:** Explore how psychosocial functioning and QOL change over time for UE VCA recipients.
- Aim 3:** Develop a consensus set of psychosocial and QOL outcome variables that can be assessed longitudinally across VCA clinical centers.

## Approach

These aims will be accomplished by using state-of-the-art qualitative and quantitative methods, employing both open-ended interviews and population-specific patient-reported outcomes (PRO) measurement items to assess quality of life (QOL) in four clinical groups: individuals who have undergone hand transplantation (n = 25), those with limb preservation or reconstruction (n = 25), traditional prosthesis users (n = 25, including myoelectric and body-powered), and those with osseointegrated prosthetics (n = 25).

Qualitative interviews will generate **comparative** and **longitudinal** information on psychosocial and QOL outcomes.



Results will lead to recommended **common data elements** for evaluating and monitoring outcomes across VCA clinical centers.

**Accomplishments:** During this quarter, we continued work on the regulatory and administrative documentation to launch the study. The study protocol has been approved by the University of Delaware IRB and HRPO, and regulatory and reliance agreement paperwork is either being prepared or is under review at all the partnering sites. Paperwork for a CRADA with Walter Reed was initiated, with the goal of engaging all sites.

## Timeline and Cost

Activities and Milestones	Year 1	Year 2	Year 3
Finalize study procedures and protocol	█		
Coordinate regulatory and administrative approvals	█		
Develop data collection platform and finalize interview procedures	█		
Recruit participants (n = 100) and complete baseline interviews	█	█	
Analyze qualitative baseline interview data and summarize Aim 1 results		█	
Develop longitudinal data collection platform and interview procedures		█	
Re-contact participants (n = 100) and complete longitudinal interviews		█	
Analyze qualitative longitudinal interviews and summarize Aim 2 results			█
Develop proposed set of consensus outcome measures			█
Share recommendations with VCA collaborators and gather feedback			█
Revise recommendations based on feedback			█
Summarize Aim 3 recommendations and disseminate to VCA clinical sites			█
<b>Estimated Budget</b>	\$	\$	\$

Updated: 25-Oct-2022

## Goals/Milestones

### Year 1 Goals: Regulatory and Administrative Approvals

- Milestone: IRB and HRPO approval obtained at University of Delaware
- Milestone: IRB and HRPO approval obtained at Walter Reed
- Milestone: IRB, HRPO & administrative approvals obtained at participating sites

### Year 2 Goals: Complete Baseline Interviews & Analyze Aim 1 Results

- Milestone: Participant interviews (n = 100) completed
- Milestone: Analyses for Aim 1 completed

### Year 3 Goals: Complete Longitudinal Interviews & Analyze Aim 2 Results; Develop and Finalize Recommended Common Data Elements

- Milestone: Longitudinal interviews (n = 100) completed
- Milestone: Analyses for Aim 2 completed
- Milestone: Final recommendations summarized and shared

### Comments/Challenges/Issues/Concerns

Some regulatory delays due to pandemic and gaining site reliance for unified IRB. Expenditures delayed to assure funds are available to accomplish all goals.

**Budget Expenditure to Date** Projected Expenditure: \$  
Actual Expenditure: \$ 251,224