AWARD NUMBER: W81XWH-20-2-0062

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

PRINCIPAL INVESTIGATOR: David Tulsky, PhD

CONTRACTING ORGANIZATION: University of Delaware, Newark, DE

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**6. AUTHOR(S)**

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**5e. TASK NUMBER**

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UNIVERSITY OF DELAWARE
220 HULLIHEN HALL
NEWARK DE 19716-0099

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**14. ABSTRACT**

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.

**15. SUBJECT TERMS**

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

| 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 | 11 | 19b. TELEPHONE NUMBER *(include area code)* |

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## 1. INTRODUCTION

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

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** |
|---|---|
| **Major Task 1: Prepare Regulatory and Administrative Documents for Data Collection** | |
| Subtask 1.1: Finalize study procedures, consent form(s), and human subjects protocol | 100 |
| Subtask 1.2: Coordinate IRB protocol submission at UD | 100 |
| Subtask 1.3: Coordinate IRB protocol submission at WR | 50 |
| Subtask 1.4: Coordinate IRB protocol submissions at other recruitment sites | 50 |
| Subtask 1.5: Coordinate protocol submission to HRPO at UD | 50 |
| Subtask 1.6: Coordinate protocol submission to HRPO at WR | |
| Subtask 1.7: Coordinate protocol submission to HRPO at other sites, as necessary | |
| Subtask 1.8: Coordinate administrative approvals (e.g., Data Sharing Agreements) among all sites, as necessary | 20 |
| **Major Task 2: Conduct Baseline Interviews with Participants (n = 100)** | |

| | |
|---|---|
| Subtask 2.1: Develop data collection platform (i.e., REDCap) and finalize interview procedures | |
| Subtask 2.2: Recruit and screen participants | |
| Subtask 2.3: Enroll and interview participants | |
| **Major Task 3: Analyze Data from Baseline Interviews** | |
| Subtask 3.1: Conduct thematic qualitative analyses | |
| Subtask 3.2: Conduct descriptive analyses of data from baseline interviews | |
| Subtask 3.3: Evaluate and summarize results from Aim 1 analyses | |
| **Major Task 4: Conduct Longitudinal Interviews with Participants (n = 100)** | |
| Subtask 4.1: Develop longitudinal data collection platform and finalize interview procedures | |
| Subtask 4.2: Re-contact and interview participants from Aim 1 data collection | |
| **Major Task 5: Analyze Data from Longitudinal Interviews** | |
| Subtask 5.1: Conduct thematic qualitative analysis from longitudinal interviews | |
| Subtask 5.2: Conduct descriptive analysis of data from longitudinal interviews | |
| Subtask 5.3: Evaluate and summarize results from Aim 2 analyses | |
| **Major Task 6: Identify and Disseminate a Set of Recommended Outcome Variables for VCA of the Hand** | |
| Subtask 6.1: Develop a proposed set of outcome variables based on results from prior research and the Aim 1 results | |
| Subtask 6.2: Share recommendations with partnering VCA collaborators and gather feedback | |
| Subtask 6.3: Revise recommendations based on feedback | |
| Subtask 6.4: Summarize recommendations and prepare for dissemination to VCA clinical sites | |

**What was accomplished under these goals?**

Major Task 1: Prepare Regulatory and Administrative Documentation

During year 1, a comprehensive multi-site study protocol has been reviewed and approved by the University of Delaware IRB and is under review with HRPO. Following the UD IRB's request to confirm that all sites were amenable to a single IRB model for this project, in light of the current DoD guidelines, we have approached all of the involved recruiting sites to gather information on the opportunity for a reliance agreement with the University of Delaware IRB. All sites have confirmed their willingness to have UD be the IRB of record. We have held meetings individually with Walter Reed, Johns Hopkins, UCLA, Brigham and Women's, and Massachusetts General teams to review each site's and UD's regulatory and administrative documentation requirements, and created follow-up plans for each site. The University of Pennsylvania and the University of Louisville teams are planning to participate in the activities for this grant by amending their existing IRB protocols, which were established for our initial grant (W81XWH-18-2-0068). Staff at Walter Reed 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. **Since we have not yet received full regulatory approval, no grant funds have been used during this period (that is, since this is the initial year of the project, no grant funds have been spent to date).**

**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 2 of this project, we will obtain HRPO approvals for conducting individual patient participant interviews at the University of Delaware, obtain 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 TORCH Consortium (Transplant Outcomes Research Collaborative for the Hand). 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 hand transplantation research and clinical care. This consortium will also allow our research team to recruit and enroll many the available hand transplant participants in the U.S., as well as osseointegration participants, both of which are relatively 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 longer than anticipated. 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.

**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.**

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**

***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?**

**Walter Reed National Military Medical Center (WR)**

| | |
|---|---|
| **Name:** | **CDR Scott Tintle, MD** |
| Project Role: | Initiating PI at WR |
| ORCID ID: | 0000-0003-0887-7600 |
| Nearest person month worked: | 1 |
| Contribution to project: | CDR Tintle oversaw all aspects of the project-related activities, including teleconferences and initial planning activities. |

**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: Dr. Dearth participated in project coordination activities.

**Name:** **Toby Perkins**
Project Role: Regulatory at WR
ORCID ID: none
Nearest person month worked: 1
Contribution to project: Ms. Perkins has been working on the IRB/CRADA/DSA.

**University of Delaware (UD)**

**Name:** **David Tulsky, PhD**
Project Role: Collaborating PI at UD
ORCID ID: 0000-0002-4335-4509
Nearest person month worked: 1
Contribution to Project: Dr. Tulsky oversaw all aspects of the project-related activities at UD, including planning teleconferences and creation of IRB protocol at UD.

**Name:** **Jerry Slotkin, PhD**
Project Role: Co-Investigator at UD
ORCID ID: 0000-0001-8199-3056
Nearest person month worked: 1
Contribution to Project: Dr. Slotkin participated in planning teleconferences, UD IRB protocol creation, and CRADA development.

**Name:** **Callie Tyner, PhD**
Project Role: Co-Investigator at UD
ORCID ID: 0000-0003-2945-392X
Nearest person month worked: 1
Contribution to Project: Dr. Tyner participated in planning teleconferences, led the UD IRB protocol development, and assisted with CRADA development.

**Name:** **Emily Forth, BA**
Project Role: Research Assistant at UD
ORCID ID: none
Nearest person month worked: 1
Contribution to Project: Ms. Forth contributed to IRB protocol development.

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

**University of Delaware (UD)**

David Tulsky, Ph.D.

**New funding:**

1. Title: Online Symptom-Monitoring/Self-Management for Pandemic-Related Emotional Distress (ACCEL)
   Funding Agency: NIH/NIGMS
   Project dates: 7/1/2021-6/30/2022
   Effort: 0.60 academic
   Description: To adapt an existing, web-based "ehealth" symptom-monitoring/self-management system, iManage, to the needs of the general population in the wake of the COVID-19 crisis.
   Overlap: none
2. Title: Relations between motor social and social communication impairments as well as repetitive behavior severity in children with autism spectrum disorder (ASD)
   Funding Agency: NIH
   Project dates: 6/1/2021-3/31/2024
   Effort: 0.24 academic
   Description: We will determine the risk for motor impairment and how that changes with increasing social communication impairment, repetitive behavior severity, comorbidities, and levels of impairment using parent report measures.
   Overlap: none

**Previous funding:**

- Development of Psychosocial Symptom Monitoring and Self-Management System for individuals with SCI (CNF), ended 2/28/2021
- Stakeholder Determination of Patient-Reported Outcomes for Adults with Communication Disorders (NIH/NIGMS), ended 11/30/2020
- Women's Health & Disability: Building a Clinically Relevant Outcome Measure (Univ Mich/NIH), ended 5/31/2021

Jerry Slotkin, Ph.D.

**New funding:**

1. Title: Online Symptom-Monitoring/Self-Management for Pandemic-Related Emotional Distress (ACCEL)
   Funding Agency: NIH/NIGMS
   Project dates: 7/1/2021-6/30/2022
   Effort: 0.24 calendar
   Description: To adapt an existing, web-based "ehealth" symptom-monitoring/self-management system, iManage, to the needs of the general population in the wake of the COVID-19 crisis.
   Overlap: none

**Previous funding:**

- Development of Psychosocial Symptom Monitoring and Self-Management System for individuals with SCI (CNF), ended 2/28/2021

Callie Tyner, Ph.D.

Nothing to report

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

Nothing to Report

## 8. SPECIAL REPORTING REQUIREMENTS

### Collaborative Awards

n/a

### 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: RT190094P1; Award Number: W81XWH-20-2-0062

**PI:** David Tulsky, PhD **Organization:** University of Delaware **Award Amount:** $1,000,152

## 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.

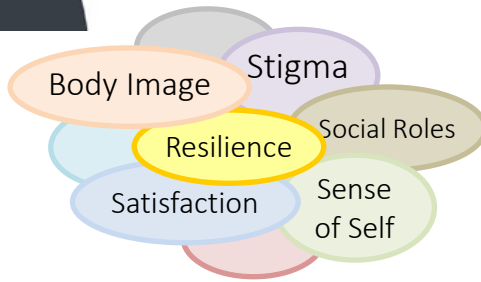
**Aim 2:** Explore how psychosocial functioning and QOL change over time for UE VCA recipients.

**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 Year 1, we worked on the regulatory and administrative documentation to launch the study. The study protocol was approved by the University of Delaware IRB and is under review with HRPO. We worked with participating sites to establish reliance agreements. 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 | | | |
| Estimated Budget | *$280k* | *$384k* | *$336k* |

Updated: 21-Oct-2021

## 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: **$279,920**
Actual Expenditure: **$0**