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TITLE: Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient-Reported Outcome Metrics and the Candidate Screening Process

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CONTRACTING ORGANIZATION: University of Delaware, Newark, DE

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Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient-Reported Outcome Metrics and the Candidate Screening Process

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Hand transplantation (also known as upper extremity vascularized composite allotransplantation, or UE VCA) can potentially restore function and improve quality of life (QOL) for affected individuals. Over the last two decades, science has focused on improving this treatment, and people are finding more success with this surgery. However, the science is less clear on who are the best candidates for this type of surgery. Also, so far doctors have focused mostly on the medical parts of the surgery but have focused less on how recipients feel about their QOL with their new hands/arms. UE VCA is different from solid organ transplantation (e.g., kidney transplant). Patients who want UE transplants must be resilient, highly motivated, and determined to succeed in ways that are not required of solid organ transplant recipients. Psychological evaluation before the surgery is important, but scientists do not yet know the most important questions to ask patients. The proposed research intends to take what we know from studying amputees and other organ transplant patients to study people who receive hand transplants. This will also help doctors know what makes someone a good candidate for hand transplantation. The purpose of this project is to understand QOL before and after UE VCA, and to understand what factors make someone a good candidate for this surgery. This project addresses the FY17 Reconstructive Transplant Research Program (RTRP) Qualitative Research Award Focus Area: "Psychosocial considerations and challenges associated with VCA." To date, 13 focus groups with VCA stakeholders from a wide variety of specialties and backgrounds have been completed. Individual interviews have been completed with seven patient participants, including both bilateral and unilateral UE VCA recipients and one candidate. Qualitative analysis was used to identify the most important QOL outcome domains for UE VCA, which included several topics mentioned that were unique to the UE transplant patient experience. New items were written to cover these new topics. Expert item review has been completed and cognitive debriefing has been initiated with UE VCA recipients to finalize the new items. This research represents a vital first step in developing a qualitative framework for understanding QOL after UE VCA.

15. SUBJECT TERMS

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

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1. INTRODUCTION

The psychosocial outcomes of hand transplantation remain elusive to clinicians and researchers. Little effort has been devoted to understanding these outcomes over the past 20 years. The purpose of this project is to understand quality of life (QOL) before and after hand transplant, and to understand what factors make someone a good candidate for this surgery. This project addresses the FY17 Reconstructive Transplant Research Program (RTRP) Qualitative Research Award Focus Area: "Psychosocial considerations and challenges associated with VCA." Through the use of focus groups and patient interviews, we are 1) actively determining the QOL domains most important to individuals involved in the VCA process, to enhance the creation and validation of standardized, psychometrically robust, and clinically useful patient reported outcome (PRO) measures for individuals with upper extremity amputation who have received or have been screened for hand transplantation; (2) evaluating the candidate screening process for reconstructive hand transplantation to identify the most important characteristics for successful transplantation.

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?

Note: on August 30, 2020, USAMRAA approved a modification to this project's Statement of Work (SOW), partly as a result of a second, complementary grant being awarded to the same team of investigators. All accomplishments and information provided in this annual report reflect this new SOW.

Major Tasks		Estimated % Complete
1.1	Obtain IRB approvals	100
1.2	Obtain HRPO approvals	100
1.3	Conduct focus groups at ASRT conference	100
1.4	Recruit and enroll patient participants for study inclusion from participating sites nationwide	100
1.5	Conduct initial interviews with transplant recipients and candidates (n = 30-35)	100
1.6	Conduct in-person focus groups with clinician participants from participating sites nationwide	100
1.7	Conduct thematic qualitative analysis from clinician and patient interviews	100
2.1	Develop new VCA-specific PRO items	100
2.2	Conduct 2nd telephone interviews with patient participants (n = 30-35) to administer PRO items	67
2.3	Analyze cognitive debriefing interview feedback	0
2.4	Revise new VCA-specific items as needed	80
2.5	Develop new VCA-specific PRO items to fill any identified domain gaps	100
2.6	Finalize VCA item pools	0
2.7	Analyze all PRO data to evaluate HRQOL of HT recipients	80

Major Tasks	Estimated % Complete
3.1 Discuss candidate screening process with clinician participants from participating sites nationwide as part of focus groups	100
3.2 Conduct Thematic Qualitative Analysis from focus group data on candidate selection process	20
3.3 Discuss screening process with investigators at each TORCH Consortium site; verify and systematically review procedures for candidate screening	0
3.4 Finalize screening process findings summary and recommendations	0
3.5 Disseminate best-practice recommendations for screening process	0

What was accomplished under these goals?

During year 4, major accomplishments were achieved in data collection, item development, and analysis of HRQOL results of transplant recipients.

Major Tasks 1.4, 1.5, and 2.2

During year 4, data collection for patient interviews was continued. As of the end of this annual reporting period, we have completed all of the patient participant interviews for Major Task 1.5 and cognitive debriefing interviews were initiated and are nearly complete for Major Task 2.2. For Major Task 1.5, we have completed seven interviews. For Major Task 2.2, four participants have been interviewed and two additional recipient participants have been scheduled for interviews, to be conducted at the start of Year 5. No additional recruitment is planned, as this number of participants has been deemed sufficient for the qualitative aims of the study.

Major Task 1.7

During year 4, major progress was made on the thematic qualitative analysis of the focus groups and patient interviews. A manuscript reporting on these results was completed and is under peer review in a leading rehabilitation journal.

Major Task 2.1

During year 4, we gathered expert feedback and winnowed the newly developed PRO items specifically for hand transplant recipients down to 76 from the 191 originally developed for this purpose. A manuscript was written on new HRQOL PRO domain development and was submitted and accepted for publication in a peer-reviewed journal, as part of a special research topic on VCA.

Major Task 2.7

During year 4, we have been analyzing results from applicable PRO measures of recipients' HRQOL. We are examining existing PRO measures that were administered to all 7 participants in this study and to a sample of 191 individuals who have upper limb injury and/or amputation in a parallel DoD-sponsored study. Results showed initial evidence of construct validity in a sample of individuals with upper limb injury and/or amputation. We believe this evidence for the validity of using this set of measures will generalize for use with hand transplant recipients until further validation can be performed in a hand transplant population in future research.

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

Nothing to report

How were the results disseminated to communities of interest?

See section 6. Products below for additional information.

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

We have formally submitted a request for a second no-cost extension (NCE) to complete the few remaining project major tasks. During our second NCE year (year 5) of this project, we will complete the final two cognitive debriefing interviews in October (Major Task 2.2). We will then analyze this cognitive debriefing interview feedback (Major Task 2.3) and work to revise the VCA item pools (Major Task 2.4).

To ensure that items are linguistically appropriate, we will engage with PRO linguistic experts to conduct a translatability analysis of these newly developed items. In doing so, we will assure that we remove any colloquialisms, idiomatic phrases, or American-only word meanings that would cause the measures to be confusing if translated to another language in the future. By conducting this analysis, we will assure the final item sets can be successfully translated to common languages (e.g., Spanish, French) as well as non-American English. After this step is completed, we will finalize the item banks (Major Task 2.6). We will then draft and submit a manuscript describing the item development process.

To further disseminate our work, we will draft and submit a manuscript describing the analytical work we have completed on existing PRO measures and the potential for use in evaluating HRQOL after UE VCA. Our work examining the construct validity of relevant existing PRO measures in a large sample of individuals with moderate to severe upper extremity injury and/or amputation should generalize to a UE VCA population, as described under Major Task 2.7 above.

In a parallel effort, we will analyze and evaluate the data collected from sites regarding their candidate screening process, request any supplemental information from sites as needed, and then verify, review, and summarize our findings for Major Tasks 3.3, 3.4, and 3.5.

4. IMPACT

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

To date, qualitative analysis of focus group and patient interview transcripts has been used to identify 33 domains across the areas of physical function, physical symptoms, emotional well-being, and social participation as relevant to the HRQOL of individuals who have undergone UE VCA. We identified that several of these areas of functioning can be examined through existing measures, and we have leveraged data from a “proxy” sample of participants with upper limb injury and/or amputation from a parallel study—with the assumption that the results would generalize to UE VCA—to begin to evaluate the validity of these existing measures for use in this population.

Our work has also identified several important measurement gaps that are unique to the UE VCA population. A major focus of our work has been to define these topics and to develop items to fill these measurement gaps. We have developed new item content specific for UE VCA HRQOL outcomes in several areas. In the physical/medical realm, new items have been written regarding UE VCA-specific hand function as well as satisfaction with post-transplant hand function, sensation, and aesthetics. Items were also written covering post-transplant challenges

(e.g., post-transplant medication and therapy regimens), medical complications, and treatment compliance. In the social and emotional realm, new domains and items were developed for UE VCA on the topics of post-transplant expectations, fitting in, and integration and assimilation of the transplant (i.e., restoring "wholeness"). This research represents a vital first step in advancing outcomes measurement of HRQOL after UE VCA. New items will be evaluated using qualitative and linguistic review to maximize the impact of this work for widespread use in UE VCA research and practice.

This work will set the stage for a quantitative examination of existing measures and newly developed items for understanding HRQOL in the UE VCA population.

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

As noted in section 3 above, the SOW for this project was changed during an earlier reporting period, in consultation with the project's Science Officer. The SOW change was approved on August 30, 2020, by USAMRAA. All reporting herein is based on this revised SOW.

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

Given the several scientific steps in our process for readying the newly developed items, we needed to obtain additional IRB approval during this reporting period to be able to recontact participants and conduct cognitive debriefing interviews. This regulatory requirement lengthened our timeline; however, we have managed costs effectively and will be able to complete this work in the first half of our second requested NCE year.

Changes that had a significant impact on expenditures

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

Journal publications.

One peer-reviewed manuscript was accepted for publication during the reporting period. The article is currently in press.

1. Tyner, CE, Slotkin, J, Kisala, PA, Tintle, SM, Levin, LS, Tulsky, DS (*in press*). Assessment of quality of life after upper extremity transplantation: Framework for patient-reported outcome scale domains. *Frontiers in Psychology - Health Psychology.* doi: 10.3389/fpsyg.2022.989593

An abstract for this accepted publication is provided in Appendix A.

Books or other non-periodical, one-time publications. Nothing to Report

Other publications, conference papers, and presentations.

Two conference presentations were accepted during the reporting period. These presentations are scheduled for October 2022.

1. Tulsky DS, Boulton A, Slotkin J, Tyner CE. Validating PRO measurement scales in individuals with major upper extremity trauma and amputation. Abstract accepted for oral presentation at the 29th annual conference of the International Society for Quality of Life Research (ISO-QOL), Prague, Czechia.
2. Tyner C, Slotkin J, Kisala P, Tintle S, Levin L, Tulsky D. Quality of life assessment for hand transplant outcomes: New item domain development. Abstract accepted for oral presentation at the 29th annual conference of the International Society for Quality of Life Research (ISO-QOL), Prague, Czechia.

Abstracts for these presentations are provided in Appendix A.

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: none
Nearest person month worked: 1
Contribution to project: CDR Tintle oversaw all aspects of the project-related activities, including weekly team teleconferences, facilitation of the recruitment of patient participants, data analyses and manuscript preparation.

Name: **Christopher L. Dearth, PhD**
Project Role: Co-Investigator at WR
ORCID ID: none
Nearest person month worked: 1
Contribution to project: Dr. Dearth participated in the weekly team teleconferences and assisted CDR Tintle with efforts related to recruitment and manuscript preparation.

Name: **Toby Perkins, CCRP**
Project Role: Clinical Research Manager/Program Manager at WR
ORCID ID: none
Nearest person month worked: 1
Contribution to project: Ms. Perkins participated in the weekly team teleconferences and assisted CDR Tintle with efforts related to recruitment and manuscript preparation.

University of Delaware (UD)

Name: **David Tulsky, PhD**
Project Role: Collaborating PI
ORCID ID: none
Nearest person month worked: 1
Contribution to Project: Dr. Tulsky oversaw all aspects of the project-related activities at UD, including weekly team teleconferences, supervision of data collection, data analyses and manuscript preparation

Name: **Jerry Slotkin, PhD**
Project Role: Co-I
ORCID ID: none
Nearest person month worked: 1
Contribution to Project: Dr. Slotkin participated in weekly team teleconferences, oversaw project planning, data collection, analyses, and manuscript preparation.

Name: **Callie Tyner, PhD**
Project Role: Co-I
ORCID ID: 0000-0003-2945-392X
Nearest person month worked: 5
Contribution to Project: Dr. Tyner participated in weekly team teleconferences, contributed to overall project planning, trained and supervised call center staff, oversaw data collection, and participated in data analyses and manuscript preparation.

Name: **Pamela Kisala, MA**
Project Role: Co-I
ORCID ID: 0000-0003-3234-795X
Nearest person month worked: 1
Contribution to Project: Ms. Kisala completed qualitative analyses of interviews and spearheaded manuscript preparation.

Name: **Aaron Boulton, PhD**
Project Role: Co-I
ORCID ID: none
Nearest person month worked: 4
Contribution to Project: Dr. Boulton participated in data collection platform (REDCap) design and oversaw data collection quality assurance.

Name: **Alyssa Griffith, EdS**
Project Role: Research Assistant
ORCID ID: none
Nearest person month worked: 1
Contribution to Project: Ms. Griffith completed data collection interviews.

Penn Medicine (PM)

Name: **L. Scott Levin, MD**
Project Role: Collaborating PI
ORCID ID: 0000-0001-9108-5182
Nearest person month worked: 1
Contribution to Project: Dr. Levin oversaw all aspects of the project-related activities at PM, including weekly team teleconferences, facilitation of the recruitment of patient participants, data analyses and manuscript preparation.

Name: **Annamarie Horan, PhD**
Project Role: Co-I
ORCID ID: 0000-0003-3000-5841
Nearest person month worked: 1
Contribution to Project: Dr. Horan participated in weekly team teleconferences and oversaw project planning and execution at PM.

Name:	**Ellen Stinger, MS**
Project Role:	Clinical Research Coordinator
ORCID ID:	none
Nearest person month worked:	1
Contribution to Project:	Ms. Stinger participated in weekly team teleconferences and oversaw project planning and execution at PM.

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:

- Title: iManage-Sexual Wellness: Development of a symptom-monitoring/self-management program to enhance sexual wellness after SCI and TBI
  Funding Agency: National Institute on Disability, Independent Living, and Rehabilitation Research
  Project dates: 2/4/2022-08/31/2025
  Effort: 1.2 academic, 0.66 summer
  Description: The goal of this five-year project is to create and evaluate a web-based symptom-monitoring/self-management system to improve sexual wellness in individuals with SCI or TBI.
- Overlap: none

Previous funding:

- Online Symptom-Monitoring/Self-Management for Pandemic-Related Emotional Distress (ACCEL), ended 06/30/2022

Jerry Slotkin, Ph.D.

New funding:

1. Title: iManage-Sexual Wellness: Development of a symptom-monitoring/self-management program to enhance sexual wellness after SCI and TBI
   Funding Agency: National Institute on Disability, Independent Living, and Rehabilitation Research
   Project dates: 2/4/2022-08/31/2025
   Effort: 0.48 calendar
   Description: The goal of this five-year project is to create and evaluate a web-based symptom-monitoring/self-management system to improve sexual wellness in individuals with SCI or TBI.
   Overlap: none
2. Title: ARMADA: Advancing Reliable Measurement in Alzheimer's Disease and cognitive Aging
   Funding Agency: Northwestern University/National Institutes of Health
   Project dates: 5/1/2022-12/31/2022
   Effort: 0.70 calendar
   Description: Cognitive decline and dementia due to Alzheimer's Disease, both associated with advancing age over 65, are increasing in the US due to the reduction of

other illnesses that, in the past, limited life expectancy. This project will provide a brief, comprehensive assessment tool (in English and Spanish versions), applicable to diverse populations, to screen for a decline in cognitive health and associated neurological functions. The burden of age-related cognitive decline and dementia on older adults and the health care system make their early identification a critical public health goal in order to pave the way for prevention trials.
Overlap: none

Previous funding:

- Online Symptom-Monitoring/Self-Management for Pandemic-Related Emotional Distress (ACCEL), ended 06/30/2022

Callie Tyner, Ph.D.

1. Title: iManage-Sexual Wellness: Development of a symptom-monitoring/self-management program to enhance sexual wellness after SCI and TBI
   Funding Agency: National Institute on Disability, Independent Living, and Rehabilitation Research
   Project dates: 2/4/2022-08/31/2025
   Effort: 0.48 calendar
   Description: The goal of this five-year project is to create and evaluate a web-based symptom-monitoring/self-management system to improve sexual wellness in individuals with SCI or TBI.
   Overlap: none

Previous funding:

Nothing to report

Aaron Boulton, Ph.D.

New funding:

- Title: iManage-Sexual Wellness: Development of a symptom-monitoring/self-management program to enhance sexual wellness after SCI and TBI
  Funding Agency: National Institute on Disability, Independent Living, and Rehabilitation Research
  Project dates: 2/4/2022 – 08/31/2025
  Effort: 0.12 calendar
  Description: The goal of this five-year project is to create and evaluate a web-based symptom-monitoring/self-management system to improve sexual wellness in individuals with SCI or TBI.
  Overlap: none

Previous funding:

Nothing to report

Pamela Kisala, M.A.

New funding:

1. Title: iManage-Sexual Wellness: Development of a symptom-monitoring/self-management program to enhance sexual wellness after SCI and TBI
   Funding Agency: National Institute on Disability, Independent Living, and Rehabilitation Research
   Project dates: 2/4/2022 – 08/31/2025
   Effort: 1.6 calendar
   Description: The goal of this five-year project is to create and evaluate a web-based symptom-monitoring/self-management system to improve sexual wellness in individuals with SCI or TBI.
2. Overlap: none

Previous funding:

- Online Symptom-Monitoring/Self-Management for Pandemic-Related Emotional Distress (ACCEL), ended 06/30/2022

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

Collaborative Awards

n/a

Quad Charts
See Appendix B

9. APPENDICES

See Appendix A for the attached abstracts from the manuscript in press and the conference abstracts described in question 6.

See Appendix B for Quad Chart.

Appendix A: Publication and Presentation Abstracts

One peer-reviewed manuscript was accepted for publication during the reporting period. The article is currently in press.

1. Tyner, CE, Slotkin, J, Kisala, PA, Tintle, SM, Levin, LS, Tulsky, DS (*in press*). Assessment of quality of life after upper extremity transplantation: Framework for patient-reported outcome scale domains. *Frontiers in Psychology - Health Psychology.* doi: 10.3389/fpsyg.2022.989593

Abstract

Upper extremity transplantation offers the promise of restored function and regained quality of life (QOL) for individuals who have sustained hand or arm amputation. However, a major challenge for this procedure becoming an accessible treatment option for patients is the lack of standard measures to document benefits to QOL. Patient-reported outcomes (PRO) measures are well-suited for this kind of intervention, where the perspective of the patient is central to defining treatment success. To date, qualitative work with experts, clinicians, and patients has been used to identify the most important domains of QOL for PRO item development. Specifically, our group's qualitative work has identified several domains of QOL that are unique to individuals who have received upper extremity transplants, which are distinct from topics covered by existing PRO measures. These include emotional and social aspects of upper extremity transplant, such as Expectations and Perceived Outcomes, Integration and Assimilation of Transplant, Fitting in, and Post-Surgical Challenges and Complications. The broad topic of Satisfaction with Transplant was subdivided into three subtopics: Function, Sensation, and Aesthetics. Satisfaction with Sensation was also identified as a unique domain not evaluated by existing PRO measures. This report operationalizes these eight QOL domains by presenting scoping definitions. This manuscript describes the work that has been completed for domain characterization as an early step toward developing standardized PRO measures to evaluate these important outcomes specific to upper extremity transplantation.

Two conference presentations were accepted during the reporting period. These presentations are scheduled for October 2022.

1. Tulsky DS, Boulton A, Slotkin J, Tyner CE. Validating PRO measurement scales in individuals with major upper extremity trauma and amputation. Abstract accepted for oral presentation at the 29th annual conference of the International Society for Quality of Life Research (ISO-QOL), Prague, Czechia.

Abstract

Aims: Upper extremity (UE) amputation or severe, sudden-onset UE injury is life-changing and profoundly impacts several areas of functioning, yet, there is a dearth of research on this population. This study examines the construct validity of several patient reported outcomes (PRO) item banks (from PROMIS, Neuro-QOL, and those developed for rehabilitation populations like spinal cord (SCI-FI/SCI-QOL) and traumatic brain injury (TBI-QOL) for use in an UE population. The study also examines the factor structure underlying a comprehensive assessment of multiple domains of health-related quality of life (HRQOL).

Methods: A battery of 33 scales from PROMIS, Neuro-QOL, SCI-QOL, SCI-FI, and TBI-QOL were administered to a sample of 191 individuals with a major UE injury (n= 87 Amputation; n=96 UE Surgically Treated; n=8 had amputation and UE transplantation). The PROMIS, Pain Interference, Pain Intensity, Fatigue, Anger, Anxiety, and Depression and Neuro-QOL Upper

Extremity Function, Mobility, Positive Affect and Well-Being, and Ability to Participate score were compared with a general population control sample (n=191) that was extracted from the calibration samples of the measures. Propensity matching on key demographic variables (age, gender, race, education level, and household income) identified the control sample and scores between the UE and control group were compared using t-tests and examining effect size. Factor structure was evaluated by developing multiple models of HRQOL and examining common fit statistics (CFI, TLI, RMSEA) to determine the best-fitting model.

Results: Known group comparisons indicated that there were significant differences and effect sizes for physical variables like upper extremity function ($p < .01$; Cohen's $d = -1.64$) and Pain Interference ($p < .01$; Cohen's $d = 0.59$) between the UE sample and the general population control sample but small effect sizes for emotional variables. The factor structure indicated a complex structure with multiple domains including positive and negative affect, social, physical medical, and physical functioning.

Conclusion: The results are similar to those obtained in recent analyses of similar HRQOL data with individuals with traumatic brain and spinal cord injuries and these data collectively offer evidence of the construct validity of several PRO item banks for use in individuals with major UE injury and amputation.

2. Tyner C, Slotkin J, Kisala P, Tintle S, Levin L, Tulsky D. Quality of life assessment for hand transplant outcomes: New item domain development. Abstract accepted for oral presentation at the 29th annual conference of the International Society for Quality of Life Research (ISO-QOL), Prague, Czechia.

Abstract

Aims: Upper limb amputation affects multiple domains of physical, emotional, and social quality of life (QOL). Hand transplant (HT) offers an advanced surgical treatment option that can potentially ameliorate these challenges and improve QOL. However, there is currently no systematic approach to measuring outcomes from HT, and thus the evidence for the QOL benefits of this procedure is limited. This study seeks to (1) document the important domains of QOL that are impacted by HT, (2) identify existing patient-reported outcome (PRO) instruments that are relevant for HT, and (3) to articulate domain definitions for any unique content areas where there are no existing PRO instruments. This research is an important step toward developing PRO assessments for QOL after HT, which will be critical to have HT accepted as a treatment for limb loss.

Methods: A grounded-theory-based qualitative approach was used; individual interviews were conducted with HT recipients and focus groups were held with transplant experts. These were audio-recorded and transcribed. Systematic thematic analysis of interview transcripts was done using Open Coding to identify major content areas, Axial Coding to develop code hierarchy, and Selective Coding to tally the frequency of mention of each code using NVivo software. The resulting themes were linked with existing PRO measures as possible. Domain definitions were articulated for novel themes.

Results: In total, five HT recipients and 59 experts participated. Qualitative analysis identified HT QOL subdomains across the areas of emotional wellbeing and mental health difficulties, social participation and independence, medical complications, and physical abilities. Eight novel domains were detected, four in the emotional realm (Expectations & Perceived Outcomes, Fitting in, Integration & Assimilation of Transplant, and Post-Surgical Challenges & Complications) and four in the physical realm (Satisfaction with Hand Function, Sensation, and Aesthetics, as well as Satisfaction with Sensation).

Conclusion: Assessment of QOL after HT should involve both existing and novel PRO assessments across physical, emotional, and social domains. This qualitative research identified eight new domains for PRO item development that will be important to develop as part of standardizing comprehensive assessment of HT outcomes.

Appendix B: Quad Chart. Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient Reported Outcome Metrics and the Candidate Screening Process

Log Number: RT170101P3; Award Number: W81XWH18-2-0068

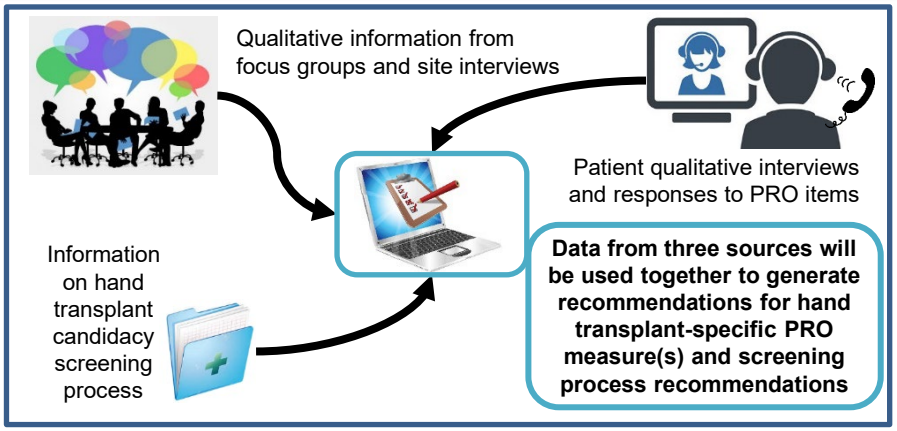
PI: David Tulsky, Ph.D. **Organization:** University of Delaware **Award Amount:** $1,084,330

Specific Aims & Approach

Aim 1: Determine the psychosocial/QOL outcome domains most important to individuals involved in the VCA process. We will conduct focus groups with VCA clinicians and interviews with patients involved in the VCA process to identify the most critical psychosocial and QOL domains to be assessed in individuals at all stages of the VCA process (e.g., screening, candidacy, transplantation, rehabilitation).

Aim 2: Enhance the selection and validation of standardized, psychometrically robust, and clinically useful patient-reported outcome (PRO) measures for traits and symptoms that are of critical importance to VCA patients. Individuals currently or formerly involved in the VCA process will review items from the ExTrA-QOL measurement system to evaluate 1) the relevance/appropriateness of included constructs and 2) the wording, construct representativeness, and content coverage of the ExTrA-QOL items.

Aim 3: Optimize the VCA candidate screening process by identifying and standardizing the most important clinical and psychosocial characteristics to consider for successful transplantation. We will conduct another series of clinician focus groups and individual patient interviews to understand, evaluate, and optimize the current VCA screening process. We will utilize ExTrA-QOL and other current measures and variables as needed to recommend a standardized and data-supported method for screening.



Accomplishments: During year 4 (NCE), two manuscripts were written and submitted. Item development included item writing, expert review, and cognitive debriefing interviews.

Timeline and Cost

Major Tasks	Sites	Year 1	Year 2	Year 3	NCE
1.1 Obtain IRB approvals	WR, UD, PM				
1.2 Obtain HRPO approvals	WR, UD, PM				
1.3 Conduct focus groups at ASRT conference	WR, UD, PM				
1.4 Recruit and enroll patient participants from sites nationwide	WR, PM				
1.5 Conduct initial interviews with transplant recipients and candidates	UD				
1.6 Conduct in-person focus groups with clinician participants	UD				
1.7 Conduct thematic qualitative analysis from clinician and patient interviews	UD				
2.1 Develop new VCA-specific PRO items	UD				
2.2 Conduct second round of interviews with participants	UD				
2.3 Analyze cognitive debriefing interview feedback	UD				
2.4 Revise new VCA-specific PRO items as needed	UD				
2.5 Develop new VCA-specific PRO items to fill any identified gaps	UD				
2.6 Finalize VCA item pools	UD				
3.1 Discuss candidate screening process with clinician participants	UD				
3.2 Conduct Thematic Qualitative Analysis from interviews	UD				
3.3 Discuss screening process with clinician participants, verify and review procedures for candidate screening	WR				
3.4 Finalize screening process findings summary and recommendations	WR, UD, PM				
3.5 Disseminate best-practice recommendations for screening process	WR, UD, PM				
Estimated Budget ($K)		**$353**	**$383**	**$348**	

Updated: 28-Oct-2022 NOTE: WR = Walter Reed, UD = University of Delaware; PM = University of Pennsylvania Medicine

Goals/Milestones

Year 1 Goals

- ☑ Obtain regulatory approvals (IRB & HRPO)
- ☑ Conduct focus groups at ASRT conference
- ☑ Engage with partnering sites for recruiting patients
- ☑ Identify most important domains for hand transplant outcomes

Year 2 Goals

- ☑ Conduct expert groups and interviews at participating transplant sites
- ☑ Develop new hand transplant-specific items

Year 3 Goals

- ☑ Enroll transplant recipients and candidates (n = 30-35) ***in process***
- ☐ Finalize hand transplant-relevant item pools
- ☐ Finalize and disseminate screening process observations and recommendations

Comments/Challenges/Issues/Concerns

Timeline updated to reflect NCE; expenditure differential relates in part to timing.

Budget Expenditure to Date Projected Expenditure: ***$1,084,330***
Actual Expenditure: ***$1,014,728***