

AWARD NUMBER: W81XWH-19-2-0017

TITLE: “A Randomized, Prospective, Within-Patient, Controlled Clinical Study to Investigate Full Thickness Skin Tissue Columns As a Novel Skin Replacement Therapy”

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CONTRACTING ORGANIZATION: The Metis Foundation, San Antonio, TX

REPORT DATE: July 2021

TYPE OF REPORT: Annual Report

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

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1. REPORT DATE (DD-MMM-YYYY) July 2021		2. REPORT TYPE Annual Report		3. DATES COVERED (From - To) 01Jun2020-31May2021	
4. TITLE AND SUBTITLE "A Randomized, Prospective, Within-Patient, Controlled Clinical Study to Investigate Full Thickness Skin Tissue Columns As a Novel Skin Replacement Therapy"				5a. CONTRACT NUMBER W81XWH-19-2-0017	
				5b. GRANT NUMBER BA180250	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Rodney Chan, MD; Victoria Diaz, RN E-Mail: rodneykchan@gmail.com; diazmetisfoundationusa.org				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) The Metis Foundation 300 Convent Street, Suite 1330 San Antonio, Texas 78205				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S) USAMRDC	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT Split-thickness skin grafts (STSG), the current standard of care for wounds too large to heal effectively by linear closure, are typically harvested with a dermatome that TANGENTIALLY removes the epidermis and a thin layer of dermis from a donor site. Even though STSG have been the mainstay of skin replacement therapy since pinch grafts were described in 1869 by Reverdin, there are well-known limitations. In particular, STSG fail to adequately recapitulate some basic features of skin including pliability, uniform texture and color, and adnexal functions of lubrication and temperature regulation. Further, there is a finite number of possible re-harvests and donor sites from tangential harvests are not only painful (from exposure of nerve endings in the dermis) but also result in disfiguring scars in a previously uninjured region. Orthogonal skin harvest is a novel technique to obtain donor skin in the form of tissue columns for skin replacement therapy. The transfer of full thickness skin elements in columnar bits to a recipient wound bed may result in more functional skin and less donor site morbidity than conventional, tangentially-harvested, split thickness skin grafts. In this study, we propose to evaluate and compare tissue columns obtained from an FDA-cleared device, ART™ (Autologous Regeneration of Tissue), to split thickness skin grafts obtained from a conventional skin dermatome in a prospective, randomized, within patient, controlled study to determine quality and speed of healing as well as the need for re-grafting and donor site morbidity. The purpose of the study is to compare the efficacy and feasibility of skin harvest and replacement using: (1) Autologous Regeneration of Tissue (ART) device, which harvests FSTCs orthogonally to (2) conventional STSG harvested tangentially. The primary specific aim is to compare the quality of healing of the FSTC grafted recipient sites with the conventional STSG recipient sites. Secondary aims include evaluating the pain and healing of FSTC donor and recipient sites, the presence of adnexal structures and the need for reoperations for skin coverage.					
15. SUBJECT TERMS None listed.					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES 13	19a. NAME OF RESPONSIBLE PERSON USAMRMC
a. REPORT Unclassified	b. ABSTRACT Unclassified	c. THIS PAGE Unclassified			19b. TELEPHONE NUMBER (include area code)

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1. INTRODUCTION

Orthogonal skin harvest is a novel technique to obtain donor skin in the form of tissue columns for skin replacement. The transfer of full-thickness skin elements in columnar bits to a recipient wound bed may result in more functional skin and less donor site morbidity than conventional, tangentially-harvested, split-thickness skin grafts. In this study, we propose to evaluate and compare tissue columns obtained from an FDA-cleared device, ART™ (Autologous Regeneration of Tissue), to split-thickness skin grafts obtained from a conventional skin dermatome in a prospective, randomized, within-patient, controlled study to determine quality and speed of healing, as well as the need for re-grafting and donor site morbidity. The use of skin tissue columns as donor skin grafts presents a new paradigm for skin replacement, and this study is an important step to understanding how skin columns fit into our current surgical armamentarium for patients who have open wounds from surgery, trauma or burns.

2. KEYWORDS

Orthogonal skin harvest; donor site morbidity reduction; skin tissue columns; skin replacement.

3. ACCOMPLISHMENTS

What were the major goals of the project – (goals to be accomplished and status)

Specific Aim 1 and 2: Obtain all necessary IRB approvals to conduct the proposed clinical trial.

Major Task 1: Prepare study protocol and associated regulatory documents for proposed study.
STATUS: COMPLETED, Y1Q1

Subtask 1: Coordinate with site for cooperative research and development agreement as needed (i.e. CRADA) for submission. Months 0-4.
STATUS: PENDING

Subtask 2: Coordinate with site for nondisclosure agreements (NDAs). Months 0-4
STATUS: COMPLETED, Y1Q1

Subtask 3: Submit study protocol (including: eligibility, screening protocol, consent forms etc.)
STATUS: COMPLETED, Y2Q1

Subtask 4: Military 2nd level IRB review (HRPO). Months 3-5
STATUS: PENDING

Subtask 5: Submit amendments, adverse events and protocol deviations. As needed.

STATUS: YET TO START

Subtask 6: Annual IRB/REB report for continuing review. Annually.

STATUS: COMPLETED, Y2Q4

Milestones Achieved: Local IRB/REB approval at MRDC IRB. Month 3.

STATUS: PENDING

Milestone Achieved: HRPO approval. Month 5.

STATUS: PENDING

Major Task 2: Patient screening and enrollment, treatment, sample collection and assessments

STATUS: YET TO START

Subtask 1: Subject recruitment. Months 6-18.

STATUS: YET TO START

Subtask 2: Subject screening and consent. Months 6-18.

STATUS: YET TO START

Subtask 3: Subject treatment. Months 6-18.

STATUS: YET TO START

Subtask 4: Subject follow-up visits; complete study measurements for study endpoints. Months 6-24

STATUS: YET TO START

Subtask 5: Enter and maintain all data in established database. Months 6-24.

STATUS: YET TO START

Subtask 9: Perform regular QA checks of database. Months 6-24.

STATUS: YET TO START

Milestone(s) Achieved: First subject recruited. Month 6.

STATUS: YET TO START

Milestone(s) Achieved: Last subject recruited. Month 18.

STATUS: YET TO START

Milestone(s) Achieved: Final sample and clinical data collection completed. Month 24.

STATUS: YET TO START

Major Task 3: Data analysis

STATUS: YET TO START

Subtask 1: Send stained tissue sections of biopsies to be graded by single blinded dermatopathologist. Months 3-18.

STATUS: YET TO START

Subtask 3: Perform statistical analysis on all obtained data. Months 12-24.
STATUS: YET TO START

Milestone(s) Achieved: Complete analysis of all data. Months 24.
STATUS: YET TO START

Milestone(s) Achieved: Complete statistical analysis. Months 24.
STATUS: YET TO START

What was accomplished under these goals – (detailed progress and results)

Major Task 1: Prepare study protocol and associated regulatory documents for proposed study.
The study protocol and supporting regulatory documents have been created for this project and submitted to the local IRB.

Subtask 1: Coordinate with site for cooperative research and development agreement as needed (i.e. CRADA) for submission. Months 0-4.
Agreement established with Methodist hospital system to conduct the study. A master CRADA between the Metis Foundation and USAISR has been established.

Subtask 2: Coordinate with site for nondisclosure agreements (NDAs). Months 0-4
The Metis Foundation master CRADA with the USAISR encompasses NDA.

Subtask 3: Submit study protocol (including: eligibility, screening protocol, consent forms etc.)
The study protocol and supporting regulatory documents were submitted and approved by the Methodist IRB. An amendment will be submitted to update with the new FDA status, device sponsor non-significant risk determination and to add the ISR as a site. The Methodist IRB will serve as the Single IRB.

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.

Plans for the next reporting period to accomplish the goals

The plans for the next reporting period are to obtain the devices and cartridges from the manufacturer, Medline and to amend the IRB protocol to update the FDA status of the device and add the ISR as a site. Following IRB approval of the updated protocol, HRPO approval will be sought. Once materials and approvals are obtained, we plan to commence enrollment at the sites.

4. IMPACT

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

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS

Changes in approach and reasons for change

The Metis Foundation has applied for support from Medline to provide approval for use of the device to be utilized in this study after the device re-design and change in FDA status. With the re-design of the device we are slightly changing the manner in which we have defined high and low density of the full-thickness skin grafting technique. Previously we proposed controlling the distance in which the columns were distributed to obtain different densities. The new proposed way is to one harvest for low density or 3 harvest for high density to the two sites that will receive FTSG.

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

We have experienced delays due to device redesign and lack of availability. Medline now has FDA approval to use the device in an investigational use only capacity. We have communicated and worked with Medline representatives to obtain approval for use in this project and will continue to work with the company to obtain the devices and cartridges necessary for the study. We anticipate some further delays in amending the protocol as proposed as the single site IRB is unprecedented between the Methodist IRB and ISR site. We will continue to work with all parties involved to move the protocol forward towards milestone completion.

Changes that had a significant impact on expenditures

Nothing to report.

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

Significant changes in use or care of human subjects

IRB Protocol Number: **1586955-1**
HRPO Protocol Number: Pending assignment
Protocol PI: Rodney K. Chan, MD
Site: US Army Institute of Surgical Research Burn Center and San Antonio Methodist Hospital System
Title: Full-Thickness Microscopic Skin Tissue Column Grafting Technique Using the ART (Autologous Regeneration Tissue) System: An Interventional Clinical Trial
Target required for clinical significance: 40
Target approved for clinical significance: 40

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS

Publications, conference papers, and presentations

Journal publications

1. Authors names in format of Last Name First Initial followed by comma for each additional names (use et al if more than 10 authors). Title of paper. Journal Name Abbreviated Form. Year Month Date; Volume (Issue#):page numbers. doi: #. PubMed PMID: #; PubMed Central PMCID: #
 - a. List publication type (e.g. original manuscript, review, abstract, etc.)
 - b. State publication status (e.g. submitted, under review, accepted, or published)
 - c. Reference which specific aim (e.g. Directly related to SOW, specific aim 1)
 - d. State award funding acknowledgement (e.g. DoD funding acknowledged)

Nothing to report.

Books or other non-periodical, one-time publications

1. Authors names in format of Last Name First Initial followed by comma for each additional names (use et al if more than 10 authors). Chapter title if applicable. Title of the book. Edition. Publication. Publication date. (Chapter, page info if applicable). ISBN/doi: / PMID.
 - a. List publication type (e.g. book, dissertation, conference proceedings, supplemental, etc.)
 - b. State publication status (e.g. submitted, under review, accepted, or published)
 - c. Reference which specific aim (e.g. Directly related to SOW, specific aim 1)
 - d. State award funding acknowledgement (e.g. DoD funding acknowledged)

Nothing to report.

Other publications, conference papers, and presentations

Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made, including international, national, local societies, military meetings, etc. Use an asterisk () if presentation produced a manuscript. Follow the format:*

1. Authors names in format of Last Name First Initial followed by comma for each additional names (use et al if more than 10 authors), Speaker*. Month. Year. Title. Name of Meeting, Location of Meeting
 - a. List presentation type (e.g. invited, talk, poster, or government review, etc.)
 - b. State presentation status (e.g. submitted, under review, accepted, or presented)
 - c. Reference which specific aim (e.g. Directly related to SOW, specific aim 1)
 - d. State award funding acknowledgement (e.g. DoD funding acknowledged)

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

1. Inventors names in format of Last Name First Initial followed by comma for each additional names (use et al if more than 10 authors). Year. Title. US Patent No.
 - a. List patent type (e.g. provisional, international, etc.)
 - b. State patent status (e.g. filed, issued)
 - c. Reference which specific aim (e.g. Directly related to SOW, specific aim 1)
 - d. Anything else (e.g. filed before award)

Nothing to report.

Other Products

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Replace prompt and write per instructions above in this self-expanding table cell using the format/table below for each person (if necessary, copy and paste the below format/table for each additional person):

<i>Name:</i>	Rodney Chan, MD
<i>Project Role:</i>	PI
<i>Researcher Identifier:</i>	
<i>Nearest person month worked:</i>	12 months
<i>Contribution to Project:</i>	Dr. Chan has performed work in the areas of overall oversight of study design, preparation and communications for study progress.

<i>Name:</i>	Victoria Diaz, RN
<i>Project Role:</i>	Research Coordinator
<i>Researcher Identifier:</i>	
<i>Nearest person month worked:</i>	12 months

<i>Contribution to Project:</i>	Ms. Diaz has performed the work in the area of protocol design, regulatory preparation, IRB submissions, preparation of study agreements and communications with IRB, device manufacturer and study sites.
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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?

Organization Name:
 Location of Organization: (if foreign location list country)
 Partner's Contribution to the Project: (identify one or more, e.g. 1) financial support; 2) in-kind support

(e.g., partner makes software, computers, equipment, etc., available to project staff); 3) facilities (e.g., project staff use the partner's facilities for project activities); 4) collaboration (e.g., partner's staff work with project staff on the project); 5) personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); etc.

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS

QUAD CHART

9. APPENDICES