**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

**PRINCIPAL INVESTIGATOR:** Rodney Chan, MD

**CONTRACTING ORGANIZATION:** The Metis Foundation, San Antonio, TX

**REPORT DATE:** July 2022

**TYPE OF REPORT:** Annual

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

# REPORT DOCUMENTATION PAGE

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|---|---|---|
| July 2022 | Annual | 01Jun2021-31May2022 |

**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; diaz@metisfoundationusa.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)**
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**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** | **18. NUMBER OF PAGES** | **19a. NAME OF RESPONSIBLE PERSON** |
|---|---|---|---|---|---|
| **a. REPORT** | **b. ABSTRACT** | **c. THIS PAGE** | | | USAMRDC |
| Unclassified | Unclassified | Unclassified | Unclassified | 12 | **19b. TELEPHONE NUMBER** *(include area code)* |

**Standard Form 298 (Rev. 8-98)**
**Prescribed by ANSI Std. Z39.18**

Table of Contents

## 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: Completed

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

*Milestone Achieved:* HRPO approval. Month 5.
STATUS: Completed Y3Q4

**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 dermato-pathologist. 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)**

During this reporting period the IRB approved protocol was revised and approved by the IRB. The approved protocol and all supporting documents were submitted to and approved by HRPO. Device training by the manufacturer, Medline, has been scheduled for 12 July 2022.

**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. Also, to complete device training for all study personnel. Methodist hospital system has a new research operations committee in which we will obtain approval from to commence enrollment at the site.

Following commencement of enrollment at the Methodist site, we will move forward with CRADA, IRB and HRPO approval for added ISR as another enrollment site.

## 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

Nothing to report.

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

The Methodist hospital has a new research operations committee in which IRB approved protocols must be submitted to prior to commencement of research activities at the hospital. Since this is a new process, we anticipate that this will cause a delay in initiating enrollment.

## 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

**Amendment approval**
**-06 January 2022**
**-15 April 2022**

**CR approval**
**-15 April 2022**

**HRPO approval**
**-23 May 2022**

## Significant changes in use or care of vertebrate animals

N/A

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

N/A

## 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?**

| | |
|---|---|
| *Name:* | Rodney Chan, MD |
| *Project Role:* | PI |
| *Researcher Identifier:* | P-6422-2017 |
| *Nearest person month worked:* | 12 months |
| *Contribution to Project:* | Dr. Chan has performed work in the areas of overall oversight of study design, preparations and communications for study progress. |

| | |
|---|---|
| *Name:* | Victoria Diaz, RN |
| *Project Role:* | Research Coordinator |
| *Researcher Identifier:* | |
| *Nearest person month worked:* | 12 months |
| *Contribution to Project:* | Ms. Diaz has performed the work in protocol design, regulatory preparations, IRB and HRPO submissions, preparation of study agreements and communications with all involved parties (IRB, HRPO, Manufacturer, Study team). |

**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 CHART**

## 9. APPENDICES