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TITLE: “Implantation of full-thickness skin columns to decrease hypertrophic scar formation after deep partial thickness burns”

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14. ABSTRACT

PURPOSE: The purpose of this study is to provide proof-of-concept, pre-clinical evidence for use of autologous full-thickness skin column implantation for the treatment of deep partial-thickness burn injury to prevent hypertrophic scar formation. This evidence will support a pivot into clinical trials of this strategy.

OBJECTIVES: The long-term objective is to develop autologous full-thickness skin column implantation as an improved, low-morbidity methodology for the treatment of deep partial-thickness burn. The scientific objective of this proposal is to evaluate the early (pre-epithelialization) and late (post-epithelialization) efficacy of three different seeding ratios of implanted full-thickness skin columns in reducing hypertrophic scar formation by accelerating wound closure, improving skin quality parameters, reducing wound contraction and minimizing donor-site morbidity in a porcine model of deep partial thickness burn.

Study Aims:

1. Identify optimal implanted FTSC seeding density and treatment modality for early treatment of open, debrided deep partial-thickness burn

1a. Optimization of FTSC seeding density for early treatment of deep partial-thickness burn.

1b. Comparative evaluation of early treatment of deep partial-thickness burn with implanted versus topical FTSCs

2. Identify optimal implanted FTSC seeding density for late treatment of epithelialized deep partial-thickness burn

3. Determine donor skin quality after FTSC harvests

Study Design: Pre-clinical, porcine deep partial thickness burn model. The design of this research is to identify the most favorable time for treatment with implanted FTSC, determine the optimal FTSC seeding ratio and to evaluate FTSC implantation for use as a novel treatment of DPTB. The successful completion of these three Specific Aims is expected to produce an optimal FTSC treatment algorithm and provide evidence for FTSC implantation as a low-morbidity, high-quality approach to the treatment of DPTB that can be further evaluated in clinical trials.

Relevance: Deep partial thickness burns are common among combat related traumatic and burn wounds as are civilian burn injuries. Development of an efficacious treatment for DPTB lacking significant donor site morbidity would be a major advance for the treatment of burn injuries.

15. SUBJECT TERMS: Burn wound healing, skin graft, skin replacement therapy, skin substitute

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Table of Contents

1. INTRODUCTION

SINGLE HYPOTHESIS: Autologous full-thickness skin columns implanted into the residual dermis of debrided deep partial-thickness burns will decrease hypertrophic scar formation with minimal donor site morbidity.

PURPOSE: The purpose of this study is to provide proof-of-concept, pre-clinical evidence for use of autologous full-thickness skin column implantation for the treatment of deep partial-thickness burn injury to prevent hypertrophic scar formation. This evidence will support a pivot into clinical trials of this strategy.

OBJECTIVES: The long-term objective is to develop autologous full-thickness skin column implantation as an *improved, low-morbidity* methodology for the treatment of deep partial-thickness burn. The scientific objective of this proposal is to evaluate the early (pre-epithelialization) and late (post-epithelialization) efficacy of three different seeding ratios of *implanted* full-thickness skin columns in reducing hypertrophic scar formation by accelerating wound closure, improving skin quality parameters, reducing wound contraction and minimizing donor-site morbidity in a porcine model of deep partial thickness burn.

PREDICTED OUTCOME: The predicted outcome of this study is the identification of an optimal seeding ratio and harvest density for full-thickness skin column treatment of deep partial-thickness burns.

2. KEYWORDS

Burn wound healing, skin graft, skin replacement therapy, skin substitute

3. ACCOMPLISHMENTS

What were the major goals of the project? (Goals to be accomplished and status.)

Specific Aim 1: Identify optimal implanted FTSC seeding density and treatment modality for early treatment of open, debrided deep partial-thickness burn

Aim 1a: Optimization of FTSC seeding density for early treatment of deep partial-thickness burn

Aim 1b: Comparative evaluation of early treatment of deep partial-thickness burn with implanted versus topical FTSCs

Subtask 1: Obtain approval of local IACUC for porcine study

Subtask 2: Obtain 2nd level ACURO approval

Subtask 3: Perform analysis of primary endpoint for Aim 1a

Subtask 4: Perform analysis of secondary endpoints for Aim 1a

Subtask 3: Perform analysis of primary endpoint for Aim 1b

Subtask 4: Perform analysis of secondary endpoints for Aim 1b

Milestones Achieved: Local IACUC approval at USAISR

Milestone Achieved: ACURO approval

Milestone Achieved: Optimized seeding ratio for early implantation

Milestone(s) Achieved: Question of topical vs. anatomic implantation

- STATUS: COMPLETE

Specific Aim 2: Identify optimal implanted FTSC seeding density for late treatment of epithelialized deep partial-thickness burn

Subtask 1: Perform analysis of primary endpoint for Aim 2

Subtask 2: Perform analysis of secondary endpoints for Aim 2

- STATUS: NOT COMPLETED

Specific Aim 3: Determine donor skin quality after FTSC harvests

Subtask 1: Perform analysis of primary endpoint for Aim 3

Subtask 2: Perform analysis of secondary endpoints for Aim 3

Milestone(s) Achieved: donor skin quality of FTSC harvests

Milestone(s) Achieved: Complete statistical analysis of all data

- STATUS: COMPLETE

What was accomplished under these goals? (Detailed progress and results.)

Specific Aim 1a: Optimization of FTSC seeding density for early treatment of deep partial-thickness burn.

Key Findings:

- Wounds treated with FTSC implantation densities of 1:1 and 1:2 were significantly more re-epithelialized at PBD 28 as compared to the burned, untreated control. These wounds also appeared to contract less than the burned, untreated control; however, these results were not significant.
- The 1:4 and 1:9 implantation densities showed no significant differences in re-epithelialization and contraction as compared to the burned, untreated control.
- **For this reason, we have concluded that a minimum of 1:1 and 1:2 ratios are the optimal FTSC implantation densities.**

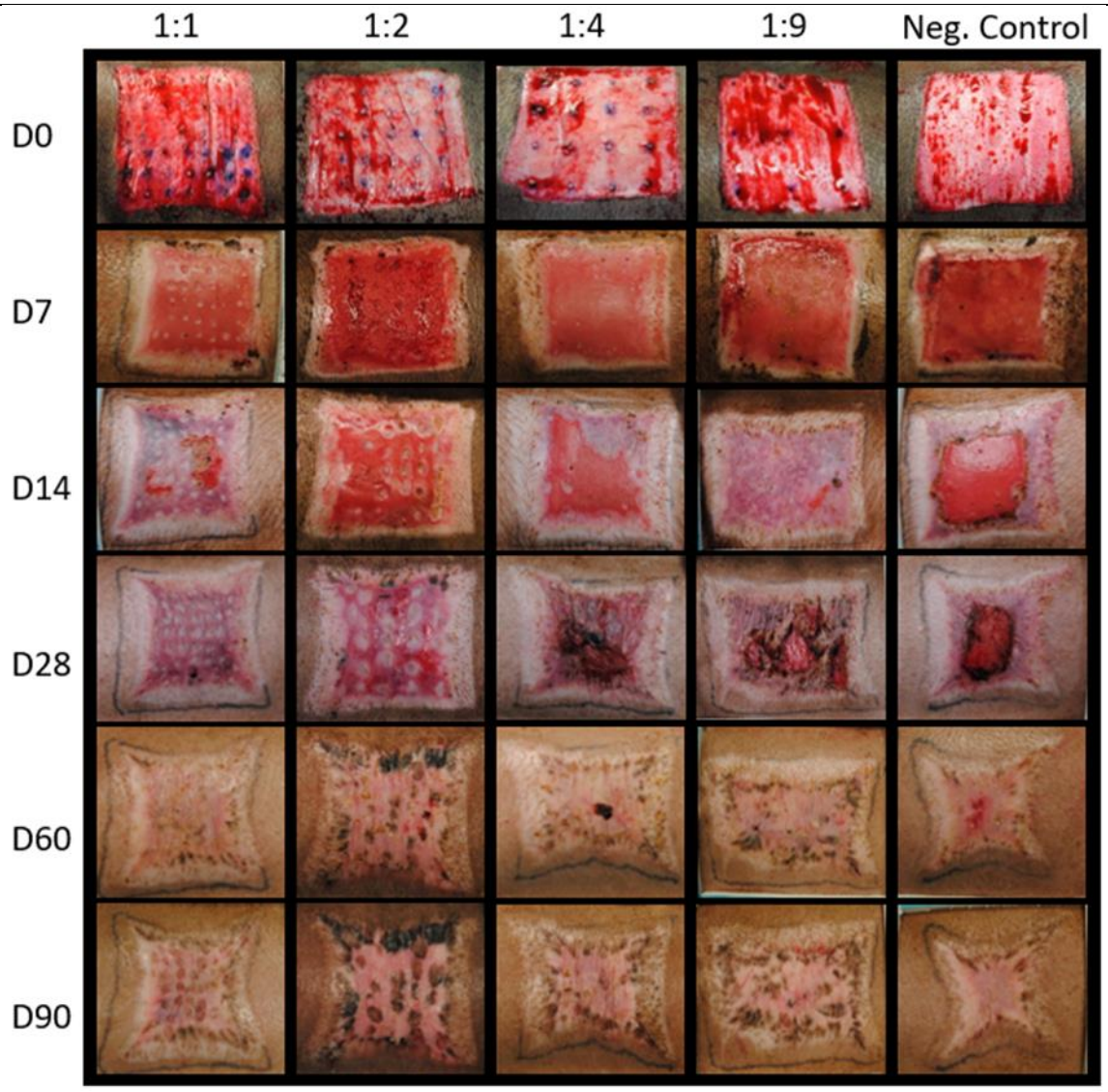


Figure 1. Visualization of FTSC implanted wounds at ratios 1:1, 1:2, 1:4, 1:9 and untreated control over 90 days. Briefly, deep-partial thickness burns were debrided and implanted with FTSC at different ratios. Wounds treated with FTSC implantation densities of 1:1 and 1:2 were significantly more re-epithelialized at PBD 28 as compared to the burned, untreated control.

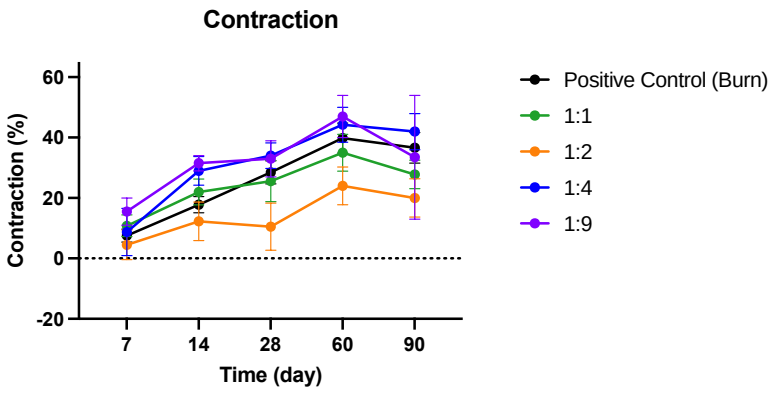


Figure 2. Contraction over time. At post-burn day (PBD) 90, wounds treated with 1:1 and 1:2 implantation densities appeared to contact less than the burned, untreated control (1:1, 28%; 1:2, 20%; control, 37%); however, these results were not significant (p=0.71 and 0.33, respectively). Implantation densities of 1:4 and 1:9 showed no significant difference as compared to burned, untreated control at PBD 90 (42%, p=0.95; and 34%, p=1.00, respectively).

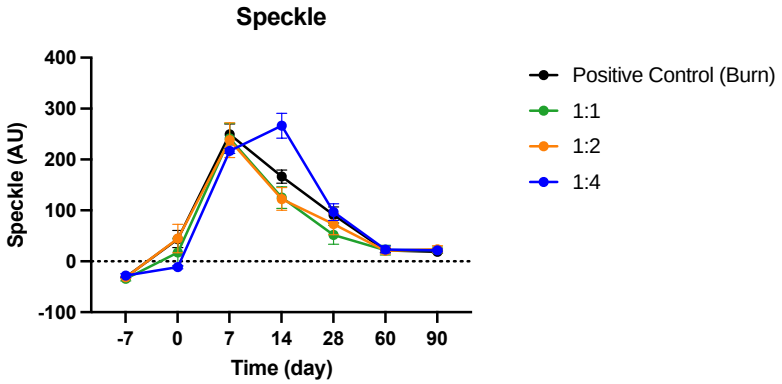


Figure 3. Superficial blood flow over time, as measured by laser speckle imaging (LSI). There were no significant differences between groups at any assessment day in terms of superficial blood flow.

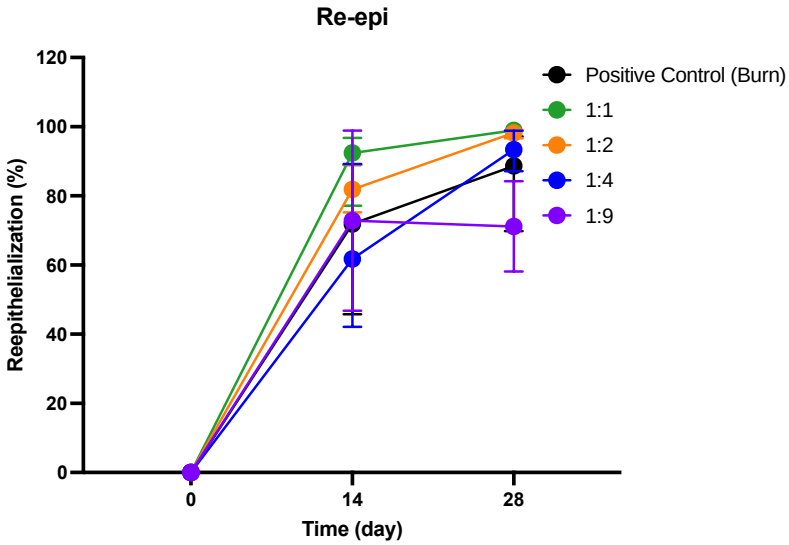


Figure 4. Re-epithelialization over time. At PBD 28, wounds treated with the 1:1 and 1:2 implantation densities had a mean re-epithelialization of 99% and 98%, respectively. Both were significantly more re-epithelialized as compared to the burned, untreated control, with mean re-epithelialization of 84%, at PBD 28 (p=0.02 and 0.03, respectively). Implantation densities of 1:4 and 1:9 showed no significant difference as compared to burned, untreated control in terms of re-epithelialization on PBD 28 (93%, p=0.45; and 71%, p=0.85, respectively).

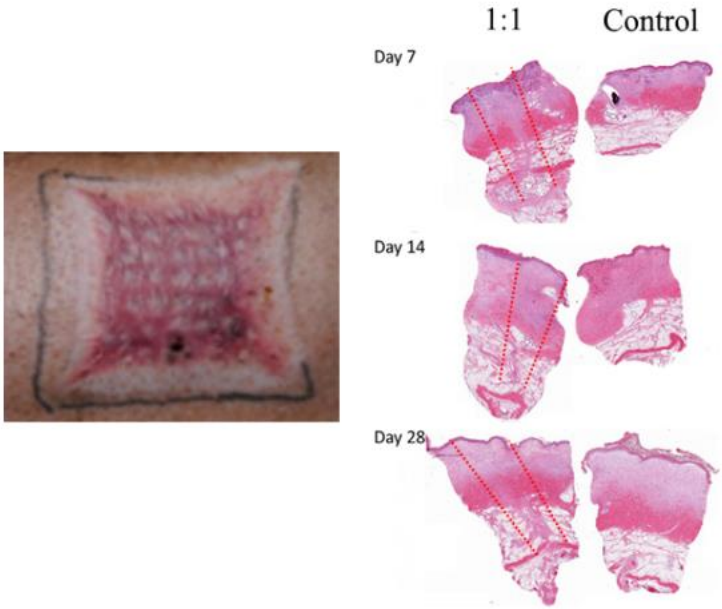


Figure 5. Representative H&E histology of burns that have received FTSCs at a 1:1 ratio, and their burned, untreated locational controls. Implanted skin columns are visualized using red dotted lines. The figure shows detectable skin columns in the healing burn wound from day 7, 14, and 28.

Specific Aim 1b: Comparative evaluation of early treatment of deep partial-thickness burn with implanted versus topical FTSCs.

Key Findings:

- There were no significant differences in re-epithelialization at PBD 14 or contraction at PBD 60 between implanted and topical FTSCs.
- There was no significant improvement seen in POSAS at PBD 120 seen with either topical or implanted FTSCs.
- **There is no obvious benefit to either implantation or topical application of FTSCs. Clinically, topical application may be preferred as implantation requires a small incision.**

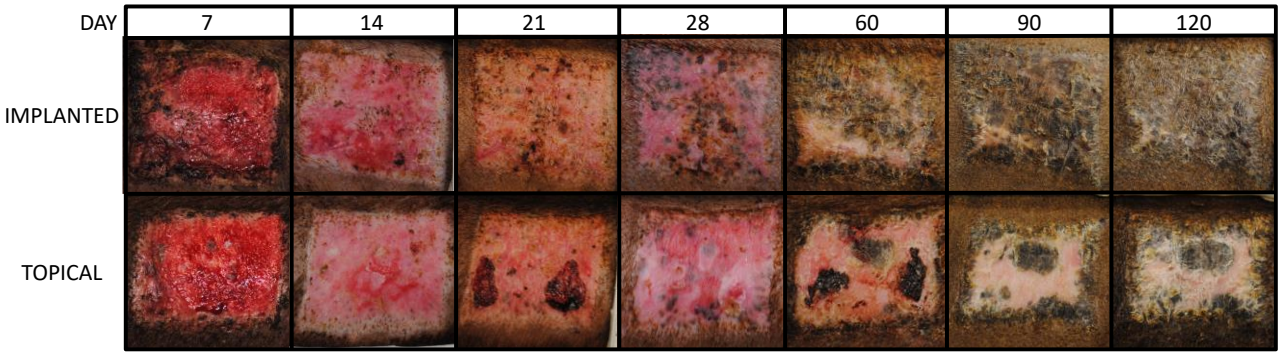


Figure 6. Digital photographs of implanted (top) and topical (bottom) FTSC administration over time, from day 7 post-FTSC application to day 120.

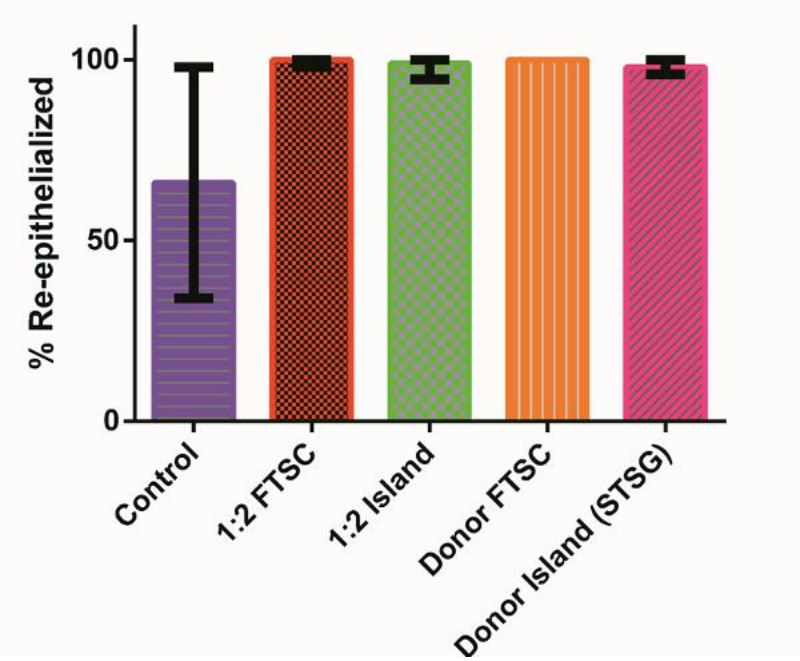


Figure 7. Re-epithelialization at PBD 14. There were no significant differences between implanted (1:2 FTSC) FTSCs and topical (1:2 Island) FTSCs (p=0.78). Donor FTSC and Donor Island (STSG) groups represent FTSC and STSG donor sites, respectively.

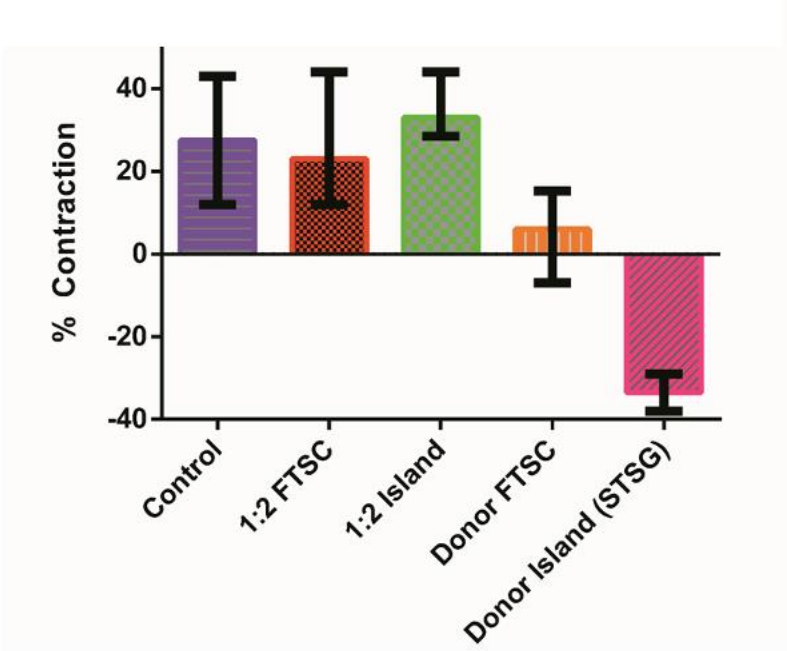


Figure 8. Contraction at PBD 90. The topical (1:2 Island) FTSCs appeared to contract more than implanted (1:2 FTSC) FTSCs. However, this result was not significant (p=1.0). Donor FTSC and Donor Island (STSG) groups represent FTSC and STSG donor sites, respectively.

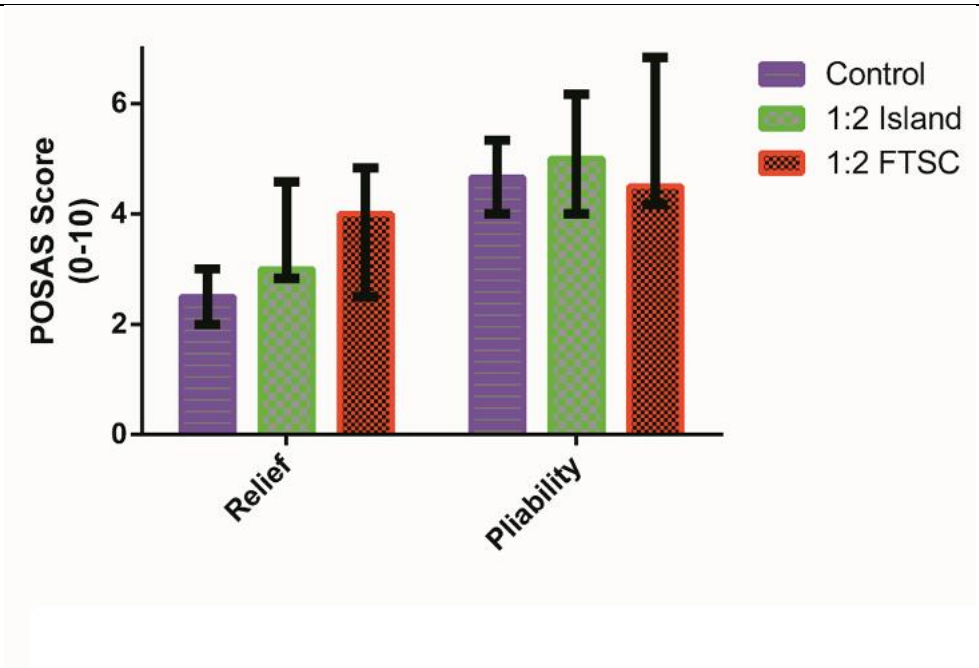


Figure 9. POSAS at PBD 120. Neither the topical (1:2 Island) or implanted (1:2 FTSC) FTSCs improved POSAS at day 120 as compared to burned, untreated control (Relief: p=0.50, 0.50, respectively; Pliability: p=0.20, 0.87, respectively).

Specific Aim 3: Determine donor skin quality after FTSC harvests.

Key Findings:

- FTSC donor sites between 2-10% harvest density showed less dyspigmentation and faster re-epithelialization as compared to STSG donor sites.
- At day 14 -21 the 2-10% harvest donor sites were fully healed and after that point it also became very hard to distinguish the donor sites by histology.
- As the 2-10% donor sites showed very little morbidity we tried to harvest as many skin columns as possible – the maximum harvest density 28% or 16 skin columns per cm^2.
- There were no significant differences seen in re-epithelialization and contraction between FTSC and STSG donor sites at the maximum 28% harvest density.
- At the maximum, 28% harvest density, STSG were hypopigmented as compared to uninjured skin and FTSC donor sites until PBD 60. By PBD 90, there was no significant difference in pigmentation between STSG donor sites and uninjured skin.
- At 28% harvest density, FTSC donor sites were initially hypopigmented and then significantly hyperpigmented by PBD 60 and 90 as compared to uninjured skin.
- At 28% harvest density, FTSC donor site scars were significantly thicker than STSG donor site scars at PBDs 28 and 60. This significance was lost by PBD 90.
- **FTSC donor sites at 2-10% harvest density have minimal to no associated morbidity. However, donor site morbidity in terms of scar hyperpigmentation and thickness was seen at the maximum 28% harvest density unlike at the lower harvest densities. For this reason, we conclude that harvest density of 28% likely exceeds the optimal harvest density.**

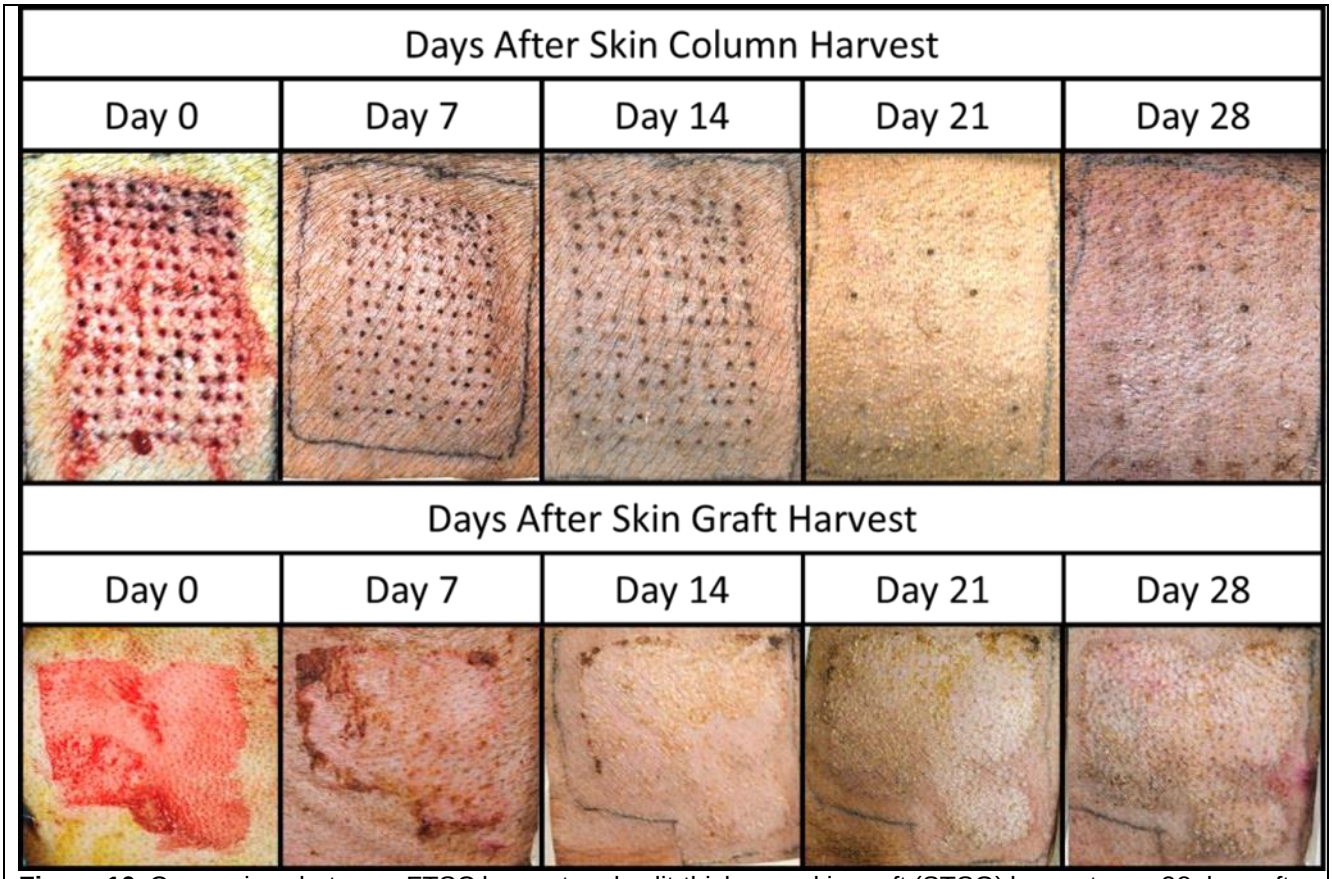


Figure 10. Comparison between FTSC harvest and split-thickness skin graft (STSG) harvest over 28 days after harvest. FTSC donor sites healed *quickly* and without obvious morbidity. See **Figure 11** and **12** for Histology and verification of findings.

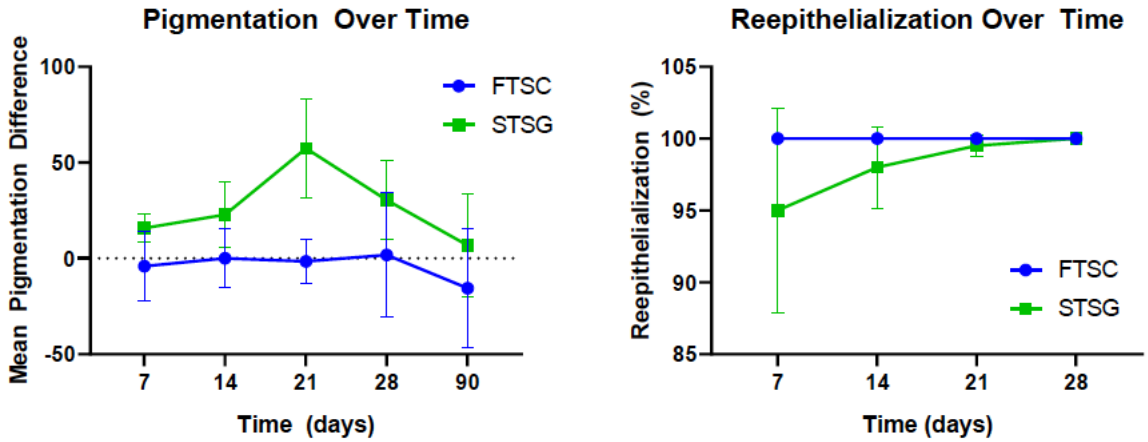


Figure 11. FTSC donor sites at about 2-10% harvest densities showed less dyspigmentation and re-epithelialized more quickly as compared to STSG donor sites. All FTSC donor sites were completely re-epithelialized by PBD 7. Whereas STSG donor sites were not fully re-epithelialized until day PBD 28.

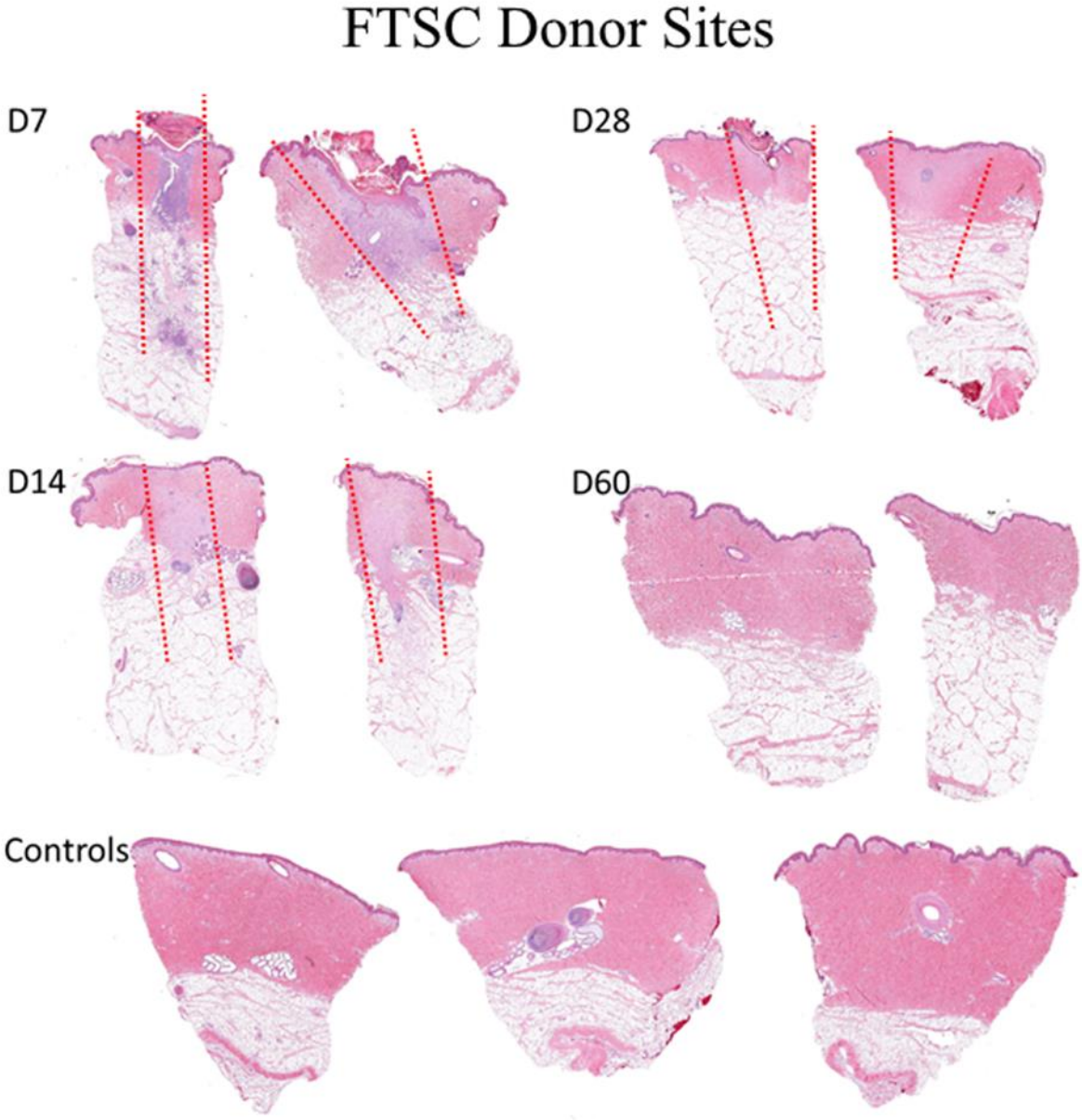


Figure 12. H&E stained histology from 2 different donor sites and unburned, not harvested controls over 60 days after harvest. FTSC donor sites healed well. At day 7, the dark purple areas visualize areas where skin columns have been harvested. At day 28, some minor dermal re-modulation can be observed. The histology confirms the findings that the donor sites heal quickly and without obvious morbidity.

As harvest densities of 2-10% showed minimal to no donor site morbidity (**Figure 10-12**), this aim was expanded further. The goal was to determine the highest harvest density possible in order to get the most out of the FTSC donor site. The maximal harvest density ratio was calculated ex vivo by determining the maximal number of full-thickness skin columns that could be harvested while leaving an intact skin bridge between columns and leaving enough room that there was no overlap of the columns at deeper layers of tissue.

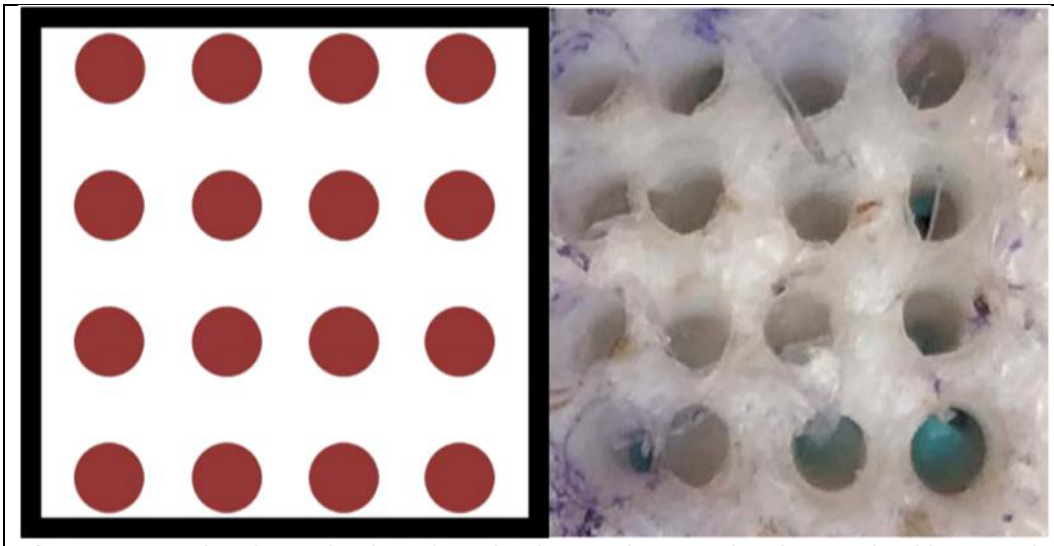


Figure 13. Ex vivo determination of maximal FTSC harvest density. Maximal harvest density was determined to be sixteen 1.5mm-diameter skin columns/1cm^2 (28% harvest density).

Figure 14. Overview from Day 14. Every other wound is a STSG or FTSC donor site. The donor site missing pigmentation are STSG and the ones with more retained pigmentation are FTSC donor sites.

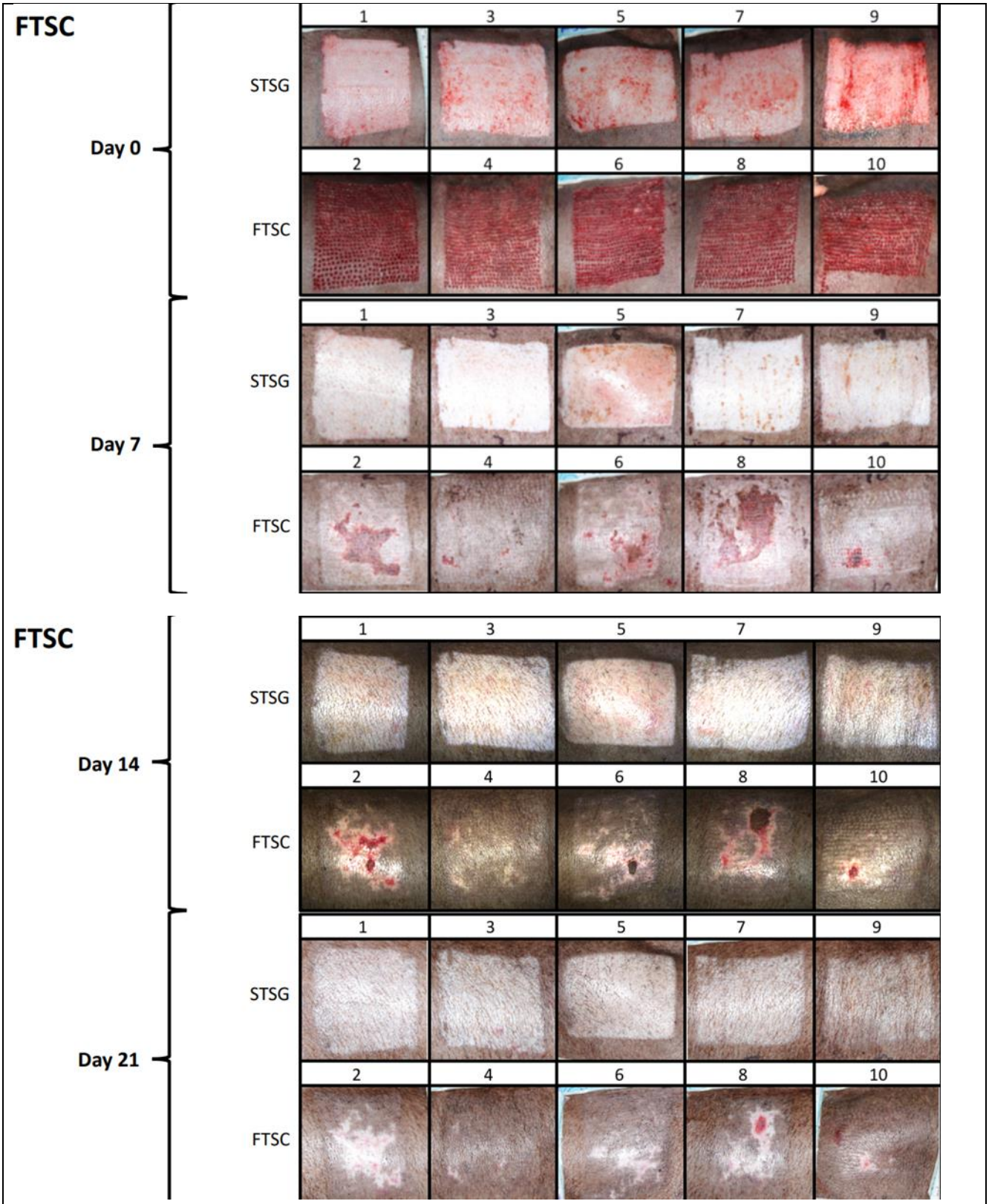


Figure 15. Overview of all donor sites over time from day 0 - 21. Wound numbers and type of donor site are indicated.

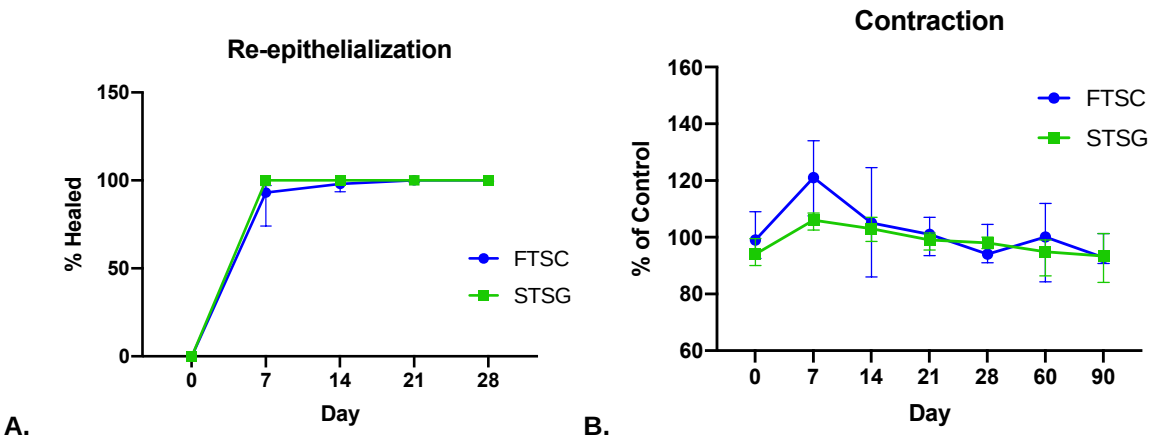


Figure 16. A. Re-epithelialization over time as represented as a percent of total wound area healed. Although STSG appeared to have a slightly faster rate of re-epithelialization by day 7, this result was not significant. There was no significant difference in re-epithelialization at PBD 14 between FTSC and STSG donor sites (p=0.35). All wounds were completely re-epithelialized by day 21. Results are shown as median with IQR and were analyzed with a two-way ANOVA. **B.** Contraction over time as represented as a percentage of untreated control in order to account for the growth of the animal. Both donor sites appeared to contract slightly but there was no significant difference between groups. There was no significant difference in contraction at PBD 90 between FTSC and STSG donor sites (p=0.10). Results are shown as median with IQR and were analyzed with a two-way ANOVA.

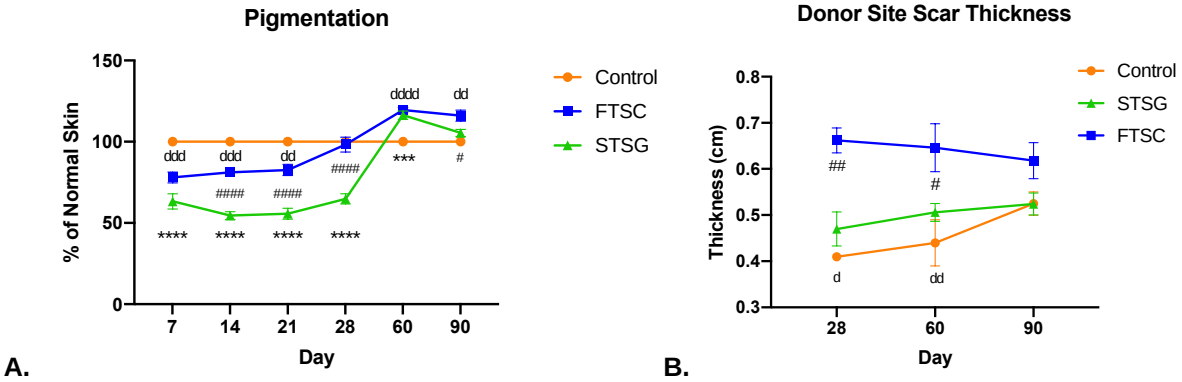


Figure 17. A. Pigmentation over time as represented as a percentage of surrounding uninjured skin compared to uninjured controls at each assessment timepoint. Both FTSC and STSG donor sites were significantly hypopigmented as compared to control, although this significance was lost for the FTSC donor sites at day 28, after which they became hyperpigmented in relation to uninjured skin. STSG donor sites followed a similar pattern: initially hypopigmented, then hyperpigmented on day 60, and finally with no significant difference as compared to control on day 90 (p<0.0001, <0.0001, <0.001, <0.0001, =0.003, =0.080, respectively). STSG donor sites were also significantly hypopigmented as compared to FTSG donor sites until day 28 after which this significance was lost (p<0.0001). Pigmentation was decreased for FTSC donor sites up to PBD 21 (p=0.0003, 0.0005, 0.0018) but significance was lost by PBD 28 (p=0.93), when compared to uninjured skin. Results are shown as mean with SEM and analyzed with a mixed-effects model with Tukey's multiple comparisons test. **B.** Donor site dermal (scar) thickness measured by ultrasound over time. FTSC donor sites were significantly thicker than both control and STSG donor sites on days 28 and 60 (FTSC v. control: p=0.01 and 0.01, respectively; FTSC v. STSG: p=0.001 and 0.02, respectively). This significance was lost by day 90 (FTSC v. control: p=0.33; FTSC v. STSG: 0.14). Results are shown as mean with SEM and were analyzed with a mixed-effects model with Tukey's multiple comparisons test.

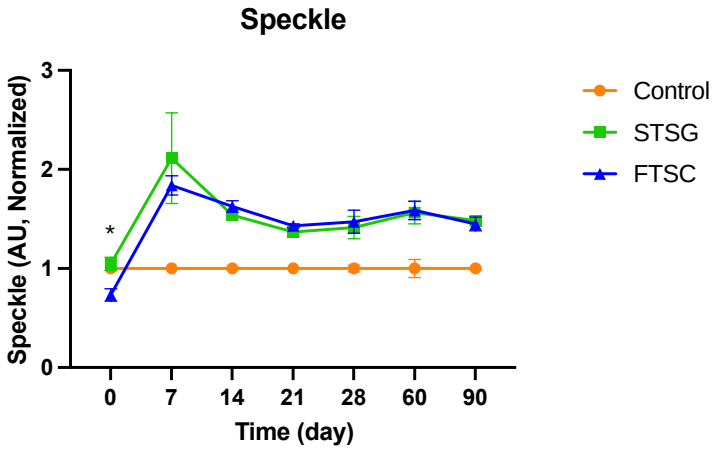


Figure 18. Superficial blood flow as measured by laser speckle imaging (LSI). On injury day (day 0), FTSC showed significantly less blood flow as compared to STSG (p=0.83). From day 7, 90, FTSC and STSG were significantly more vascular as compared to intact skin control; however, there was no significant difference in vascularity between FTSC and STSG.

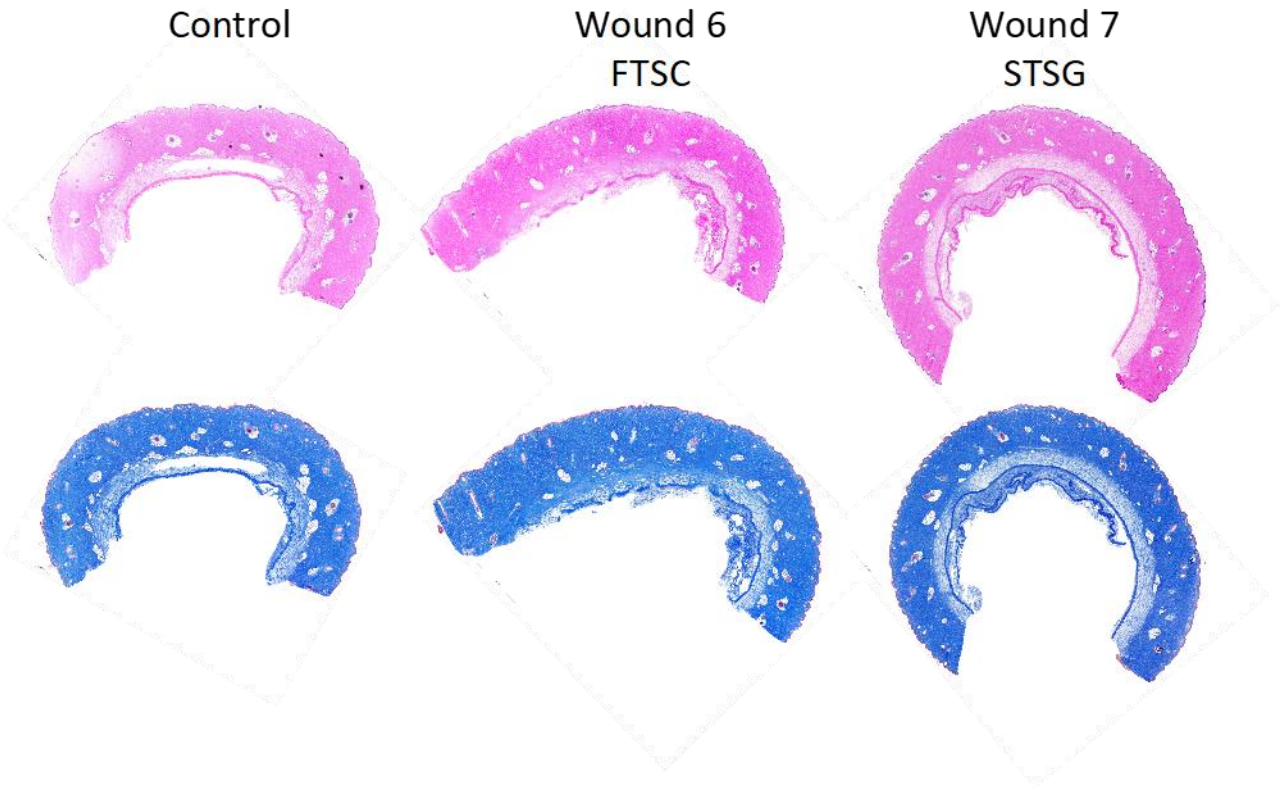


Figure 19. Masson's Tricrome and H&E staining of donor site biopsies on day 90. Strip biopsies were taken following euthanasia from areas of normal skin (left), FTSC donor sites (middle), and STSG donor sites (right).

Other achievements:

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

This project allows for several opportunities of training and professional development. Most opportunities are in smaller study groups or at the individual level. Examples of training opportunities for residents, post-docs and techs include; 1) Animal ethics & porcine animal studies, 2) Porcine pain assessments and pain management in research animals, 3) Porcine burns and how to conduct dressing changes, wound & scar assessments etc. 4) The importance of adherence and maintenance of IACUC/ACURO protocols. 5) Opportunities to present data (Posters and oral presentations) at conferences.

How were the results disseminated to communities of interest?

Nothing to Report.

Plans for the next reporting period to accomplish the goals

Work is completed.

4. IMPACT

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

The results of this study have provided the pre-clinical data needed to move forward with the study of this technique in the clinical setting. As the FTSC implantation method is a novel skin replacement therapy with essentially no donor site, we anticipate that if future clinical studies show the promising results we have observed in our porcine models, this method could revolutionize burn and chronic wound care.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Given the promise of manual FTSC harvest and treatment, efforts are being made to develop a device that can automate the process. Automating this method of skin replacement would allow a larger number of medical providers to adopt this technique in a variety of practice settings (office, operating room).

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS

IMPORTANT REMINDER – Award recipient organization is required to obtain prior written approval from the awarding agency Contracting/Grants Officer whenever there are significant changes in the project or its direction such as significant change in scope or the Statement of Work (e.g. removal, change, or addition of aims/tasks or animal model change), change in PI or key personnel, reduction of 25% FTE, or significant change in budget.

Changes in approach and reasons for change

Approved no cost extension. We have received an approved no cost extension of the performance period of this project. The SOW remains the same – no changes has been done to the project or it's direction.

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

1. Long wait for histopathologic assessment/scoring. The renovations of the core histology laboratory have delayed processing and analysis of our samples. Although the renovations are complete the core histology laboratory is now working on the backlog resulting in that the turnaround time for the ISR core

histopathology assessments is very slow. The core lab should soon be all caught up and our samples processed faster. (- see previous quarterly report for details)

2. Shortage of red Duroc and Duroc hybrid with ISR porcine vendor. The ISR vivarium vendor for red Duroc and purebred Durocs have not had sufficient supply of Durocs. A new contract have been initiated. The new vendor should be able to provide a sufficient number of Durocs that adhere to the ISR vivarium quality standards.

3. Delayed software update of the Research Management System, RMS. A planned update to RMS was intended to be performed at the end of the 2019 fiscal year. The update took longer than anticipated. As RMS is used to order animals and for orders on core services, this incurred some delay in our progress. However, since the timing coincided with the new pig vendor contract, there was no additional delay.

4. COVID-19 pandemic. The COVID-19 pandemic have had severe impact on the ISR animal facility. A decision to stop all animal activities, sanitize and prepare the large animal facility for human clinical overflow was made in the spring of 2020. On-post personnel has been and still is limited but with improvements in sight as the majority of personnel have received the vaccine and COVID-19 numbers in San Antonio are decreasing. The animal facility is now open to active experiments, however, there is a limitation to one animal shipment per months due to personnel restrictions and training of new vivarium staff. There is now a substantial backlog of research that needs to be conducted and the research directorate is discussion a priority list. Intramural projects will likely be prioritized.

5. ISR reorganization and shift of priorities. ISR has gone through a change of research director and reorganization. Our former Burn and Soft Tissue Repair department has now merged with other departments to form Combat Wound Care. ISR has also implemented a narrower field of research to align with its mission resulting in a larger focus on shorter research experiments related to prolonged field care and less on longer studies with scar amelioration focus.

Specifically, both #4 (COVID restrictions) and #5 (shift of ISR priorities) have made the performance of Aim #2 substantially delayed and then no longer feasible to perform and ultimately absent from this final report. During the pandemic period, personnel were still paid and no one was put on furlough or with decreased effort per CDMRP guidance. Thus, the total budget has been spent without the completion of Aim #2.

Changes that had a significant impact on expenditures

Nothing to report.

Significant changes in use or care of human subjects

Not applicable.

Significant changes in use or care of vertebrate animals

TOTAL PROTOCOL(S): 1

PROTOCOL (X of Y total):
IACUC Protocol Number: A-14-042-TP, TS-2
ACURO Protocol Number: BA160416
Protocol PI: Dr. Rodney Chan
Protocol Site: USAISR
Protocol Title: "Modulation of Deep Partial-Thickness Burn Wounds Using Autologous Skin Tissue Columns in a Porcine Animal Model - A Type Study"
Number of Animals Approved for Use: 9
IACUC INITIAL APPROVAL DATE: 04/20/2016 (expired 04/20/2019)
ACURO INITIAL APPROVAL DATE: 06/23/2017
RENEWAL APPROVAL DATES:
- 9/29/2017 EXPIRED 09/29/2020

AMENDMENTS:
- 09/29/2017
- 02/26/2018
- 04/19/2018

- 02/13/2020

ADVERSE EVENTS OR UNANTICIPATED PROBLEMS:

- 07/31/2016 – 08/10/2016

  On July 31 and August 1, 2016, pig #8720 showed symptoms of dermatitis (inflammation of the skin) which was unrelated to our study and could possibly confound our research wherein skin wound healing and scarring are studied. The animal was given Rimadyl on August 1, 2016 and closely examined by the AIs and ISR veterinary staff on August 3 during a scheduled assessment. Skin cultures were taken for bacterial and fungal analysis, and tissue biopsies were sampled for histological assessment. The impact of the dermatitis on the experiment was determined to be severe, however, all parties agreed to treat the animal starting on 4 August 2016 with Benadryl, Baytril and continue Rimadyl until the next assessment on August 10, 2016. On August 10, 2016, the animal was euthanized due to the likely impact the dermatitis would have on the study. A replacement animal was authorized.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS

Journal publications

Nothing to report – yet ☺

Books or other non-periodical, one-time publications

Nothing to report.

Other publications, conference papers, and presentations

Cooper L*, Chapa J, Christy, S, Chan R, Carlsson A. April. 2021. Maximal Harvest Density of Full-Thickness Skin Columns in Skin Replacement Therapy. American Burn Association Annual Meeting. Virtual.

a. Correlative presentation
b. Presented
c. Directly related to SOW, Aim 3
d. DoD funding acknowledged

Cooper L*, Chapa J, Chan R, Carlsson, A. August. 2020. Reduction in Donor Site Morbidity: Full-Thickness Skin Columns vs. Split-Thickness Skin Grafts. Military City USA Trauma Collaborative Research Conference. Virtual.

a. Poster presentation
b. Presented
c. Directly related to SOW, Aim 3
d. DoD funding acknowledged

Cooper L*, Chapa J, Chan R, Carlsson, A. October. 2020. Reduction in Donor Site Morbidity: Full-Thickness Skin Columns vs. Split-Thickness Skin Grafts. American College of Surgeons Clinical Congress. Virtual.

a. E-poster presentation
b. Presented
c. Directly related to SOW, Aim 3
d. DoD funding acknowledged

Cooper L*, Chapa J, Chan R, Carlsson, A. December. 2020. Reduction in Donor Site Morbidity: Full-Thickness Skin Columns vs. Split-Thickness Skin Grafts. Southern Region Burn Conference. Virtual.

a. Poster presentation
b. Presented
c. Directly related to SOW, Aim 3
d. DoD funding acknowledged

Kemp Bohan P, Batchinsky M, Carlsson A, Chan R. August. 2019. Full-Thickness Skin Columns in the Treatment of Deep Partial-Thickness Burns. Military Health System Research Symposium. Kissimmee, FL.

a. Oral presentation
b. Presented
c. Directly related to SOW, Aim 1b
d. DoD funding acknowledged

Carlsson A*, Christy R, Chan R. June. 2019. Full-Thickness Skin Columns in the Treatment of Deep Partial Thickness Burns. European Wound Management Association Annual Conference. Gothenburg, Sweden.

a. Poster presentation
b. Presented
c. Directly related to SOW, Aim 1a
d. DoD funding acknowledged

Tassin D*, Haire T, Carlsson A, Everett T, Chapa J, Chan R. April. 2019. Full-Thickness Skin Columns in the Treatment of Deep Partial Thickness Burns. American Burn Association Annual Meeting. Las Vegas, NV.

a. Poster presentation
b. Presented
c. Directly related to SOW, Aim 1b
d. DoD funding acknowledged

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:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	https://orcid.org/0000-0002-5061-847X
	https://scholar.google.com/citations?user=Cu787kYAAAAJ&hl=sv

Nearest person month worked:	4
Contribution to Project:	Dr. Chan is the PI of the award.
Funding Support:	The Metis Foundation
Name:	Anders Carlsson, PhD.
Project Role:	Co-Principal Investigator
Researcher Identifier (e.g. ORCID ID):	https://orcid.org/0000-0002-4846-108X https://scholar.google.com/citations?user=WdVK3Z8AAAAJ
Nearest person month worked:	10
Contribution to Project:	Dr. Carlsson is the Co-PI of the award.
Funding Support:	The Metis Foundation

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: The Metis Foundation
Location of Organization: 300 Convent Street, Suite 1330. San Antonio, TX 78205
Partner's contribution to the project : In-kind support, Collaboration, Personnel exchanges

8. SPECIAL REPORTING REQUIREMENTS

QUAD CHART
Convert this report to a PDF file and append updated quarterly Quad Chart in PDF as an appendix.

9. APPENDICES

Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Full thickness Skin Columns (FTSC) Implantation to Decrease Hypertrophic Scar after Partial-Thickness Burn

W81XWH-17-2-0061

PI: Rodney Chan, MD/Anders Carlsson, PhD **Org:** **Metis Foundation/**USAISR **Award Amount:** $615,969

Study/Product Aim(s)

Study Goal: Accelerate wound closure and improve regenerated skin quality using FTSC implantation after deep-partial thickness burn (DPTB).

AIM 1: Establish optimal **early** FTSC seeding density for treatment of DPTB. This aim will simulate the treatment of acute burns before re-epithelialization.

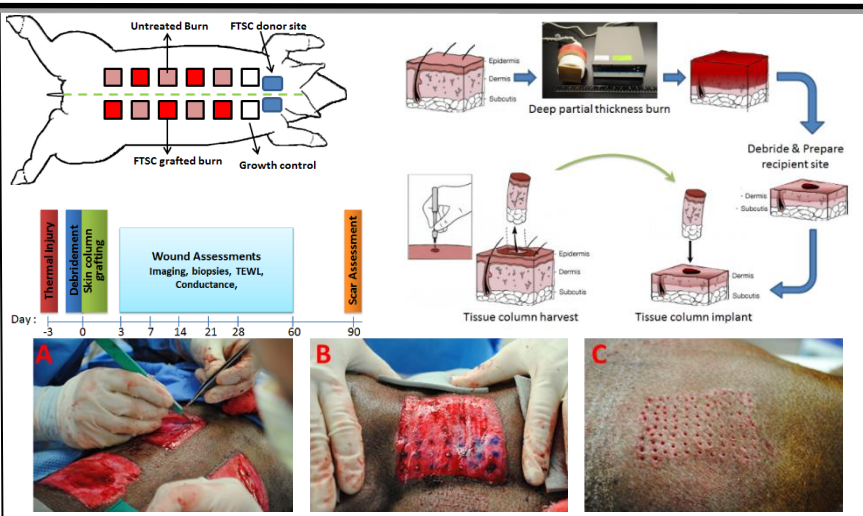
AIM 2: Establish optimal **late** FTSC seeding density for treatment of DPTB. This aim will simulate the treatment of burns after re-epithelialization.

AIM 3: Determine **donor site** morbidity related to harvest density of FTSCs as compared to split-thickness skin grafts (STSG).

Approach

Using established porcine models of DPTB we will compare wound kinetics, restoration integumentary function and regenerated skin quality after treatment with or without implanted FTSC. Treatment strategies will include three different ratios of FTSCs implantation in residual dermis following DPTB.

Comparisons between treatment groups will be made by assessing wound closure, degree of contraction, distribution of pigmentation, scar hypertrophy, transepidermal water loss and patient observer scar scale (POSAS). Histopathology and expression analysis will be investigated to establish mechanism of action



A) visualize the skin column implantation/technique. B) Shows a close up on a debrided partial-thickness burn after implantation of skin columns. C) Shows the skin column donor site on the shoulder/neck portion of the animal.

Timeline and Cost

AIM	TASKS AND MILESTONES	FY	18	19	20(NCE)
	Regulatory approvals (IACUC)				
1	**Evaluate FTSC treatment of DPTB** Establish seeding density for **early** FTSC treatment				
2	**Evaluate FTSC treatment of DPTB** Establish seeding density for **late** FTSC treatment				
3	**Evaluate FTSC donor site morbidity** Compare donor site morbidity of FTSC vs STSG				
	Data analysis, review, publication				
	Study close-out				
Proposal Budget ($K)	**TOTAL: $615**		$312.5	$303.4	**NCE**

Updated: April 16, 2021

Goals/Milestones

FY18 Goal – Begin FTSC seeding studies in DPTB.
- ✓ Obtain IACUC approval for and validate DPTB models
- ✓ Validate FTSC harvest technique and device
- ✓ Finalize protocol for FTSC treatment of DPTB
- ✓ **Begin AIM 1, early treatment** of DPTB seeding density experiments
- **X Begin AIM 2, late treatment** of DPTB seeding density experiments

FY19 Goals – Complete DPTB experiments, data collection/analysis, publish and close-out.
- ✓ **Complete AIM 1, early treatment** experiments
- **X Complete AIM 2, late treatment** experiments

FY20 Goals
- ✓ Complete data collection for AIM 1 data.
- ✓ Complete analysis of data

Comments/Challenges/Issues/Concerns: Delays due to ISR Histology core renovations, RMS update, Pig vendor contract and COVID-19 Pandemic impacted the timeline of this project and resulted in a NCE and non-completion of Aim 2.

Budget Expenditure to Date: September 30, 2017 – January 27, 2021

Projected Expenditure Years 01-03: $615,969.00

Actual Expenditure: $615,968.22