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TITLE: A Within-Scar, Randomized Control Trial Comparing Fractional Ablative Carbon Dioxide Laser to Non-Energy-Based, Mechanical Tissue Extraction and No Treatment

PRINCIPAL INVESTIGATOR: Jonathan Friedstat, MD

CONTRACTING ORGANIZATION: Massachusetts General Hospital, Boston MA

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Fort Detrick, Maryland 21702-5012

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Jonathan Friedstat, MD
E-Mail: jfriedstat@partners.org

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Massachusetts General Hospital
55 Fruit Street, Boston MA 02114-2621

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14. ABSTRACT
Survivors of burn injuries face many challenges in their recovery. One of those challenges they commonly face is the result of scarring from their injury. These particular scars can be quite debilitating as they can limit mobility of the skin, result in decreased movement to parts of the body, and also be associated with pain and itching. While there are non-surgical treatments for these scars, they can be very expensive, time consuming and uncomfortable for patients and have limited improvements. Surgical treatments for the scarring exist, but they have their own downsides including pain, risk of complications, and longer recovery. The introduction of fractional ablative carbon dioxide lasers has offered tremendous potential to help improve scars with minimal pain, downtime, and cost compared to the traditional approaches. Despite the promising studies we do not have clear data demonstrating whether the laser works, how it works, or more importantly how the impact of laser treatment changes people's quality of life or long-term outcomes. This study is designed to begin to address these gaps in our current knowledge.

15. SUBJECT TERMS Hypertrophic burn scar, carbon dioxide laser, patient reported outcome measures, randomized control trial

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
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1. INTRODUCTION:

This is a within-scar randomized control trial that compares fractional ablative CO2 laser, 0.5mm punch biopsies, and non-treated controls in the treatment of hypertrophic burn scars (HTBS). The study aims to utilize data collected from punch biopsies to examine changes in histology and gene expression. Patient reported outcome measures (PROMs) will be collected to detect changes in response to CO2 laser treatment/reconstructive procedures.

2. KEYWORDS:

Hypertrophic burn scar, carbon dioxide laser, patient reported outcome measures, randomized control trial

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Aim I: Conduct a randomized control trial comparing fractional ablative CO2 laser, 0.5mm punch biopsies, and control in the treatment of HTBS
Aim II: Evaluate whether PROMs detect changes in response to CO2 laser treatment/reconstructive procedures in burn patients

Goals:
-Initiate enrollment of patients and the RCT (7 patients have been enrolled)

What was accomplished under these goals?

Aim 1: Conduct a randomized control trial comparing fractional ablative CO2 laser, 0.5 mm punch biopsies, and control in the treatment of HTBS (months 1-48)

We have been working to increase enrollment in the study. As of last year we had 2 patients enrolled and are now up to 7 patients enrolled with 5 patients completing their treatments. We have obtained approval to share flyers with regional burn centers and also are in discussion with Brigham and Woman's hospital, which part of our healthcare system to help with referring patients that would be eligible for the trial. Several iterations of screening and enrollment have occurred and now we are working on at least biweekly review of cases scheduled so we can review patient cases with their respective provides and further increase enrollment

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

Nothing to Report

How were the results disseminated to communities of interest?

With flyer approval we have partnered with Harvard Burn Model System to disseminate information about the study to burn survivors communities in the New England area.

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

The main goal is to increase enrollment. By screening every patient that is booked for surgery, it should help us avoid missing patients for the study. These cases will be discussed at the biweekly at our weekly burn staff meetings and individual providers will contact the patients to see if they would be interested.

4. **IMPACT:**

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

This trial has led to other studies on patient reported outcomes in burn survivors. While there are limitations to the study, it does suggest that simply administering a PROM (generic or burn specific), may not be specific enough to detect changes in patients before and after certain reconstructive procedures. It raises the question of whether more specific outcome measures need to be designed to address changes before and after reconstructive procedures

What was the impact on other disciplines?

There are impacts within our burn model system (funded by NIDLRR) and a growing awareness that patient reported outcome measures might need to be more specific to detect changes before and after reconstructive procedures. We have been a little delayed in getting the publication out on that subject but it is generating discussions of future PROM design an

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

The results of this study if positive, would help improve access to care for burn survivors across the county as with level 1 evidence it would be difficult for insurance companies to deny access to laser treatment for burn survivors. This continues to be a problem across the country despite several studies demonstrating the positive impact of laser treatment on burn scars.

5. CHANGES/PROBLEMS:

We obtained fliers and IRB/HRPO approval for them to share with regional burn centers to try and increase recruitment.

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

The main challenge remain recruitment of patients. I have tried several methods to increase awareness among the clinic staff, NP, and physicians, but that effort wanes and has not been successful. What we have switched to now is reviewing our scheduling list for all reconstructive surgeries with our clinic manager and then going into epic to screen them myself with her input. Since starting that method 2 weeks ago, we identified 5 patients to approach and have called those that expressed an interest. The plan will be to discuss these patients at least biweekly at our weekly staff meetings with all providers to try and avoid missing eligible patients.

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

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to Report

Books or other non-periodical, one-time publications.

Nothing to Report

Other publications, conference papers and presentations.

Building a Successful Burn Program, American Society of Plastic Surgery, The Meeting. Atlanta, GA. 2021.

- **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:	Jonathan Friedstat, MD
Project Role:	Principal Investigator
Nearest person month worked:	No change
Contribution to Project:	Dr. Friedstat is overseeing the study, participating in regularly scheduled conferences on the progress of the study as well as data analysis, and preparation of reports and manuscripts.

Name:	Benjamin Levi, MD
Project Role:	Co-Investigator (Principal Investigator, Subaward)
Nearest person month worked:	0.1
Contribution to Project:	Dr. Levi is overseeing study preparation to begin single cell analysis once samples are available.

Name:	Domenic Annand
Project Role:	Clinical Research Coordinator
Nearest person month worked:	4.8
Contribution to Project:	Mr Annand is taking over Angela Man, who has returned home to NYC to pursue interests in medical research working on clinical trial monitoring.

Name:	Joshua Tam, PhD
Project Role:	Investigator
Nearest person month worked:	No change
Contribution to Project:	Dr. Tam is involved in the histologic evaluation/data analysis, and is participating in regularly scheduled conferences on the progress of the study

Name:	Jermaine Henderson
Project Role:	Research Technician
Nearest person month worked:	No change
Contribution to Project:	Mr. Henderson performs histology/immunohistochemistry related tasks, including embedding and sectioning of biopsy samples, processing and staining of tissue sections using the various staining methods described in the proposal, and data collection.

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

Over the past year:

Dr. **Jeremy Goverman** received new support from PolyNovo Limited, for a clinical trial entitled *A Pivotal Study to Assess the Safety and Effectiveness of NovoSorb® Biodegradable Temporizing Matrix (BTM) in the Treatment of Severe Burn Skin Injuries.* He also received funding from Medline Industries for a clinical trial entitled *A Prospective Pilot Study on the Use of Full Thickness Micro Skin Tissue Columns in Burn Care.* He does not have a dedicated level of effort to either of those studies, but serves as Principal Investigator.

Dr. **Colleen Ryan** received new support as a Co-Investigator on Dr. Rahme's R56 from the NIH (R56AI155505-01A1, PI: Rahme). Dr. Ryan's dedicated level of effort to the project is 3%.

What other organizations were involved as partners?

Dr. **Jeffrey Schneider** received new support through The Stepping Strong Foundation.

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES:

A Within-Scar, Randomized Control Trial Comparing Fractional Ablative Carbon Dioxide Laser to Non-Energy-Based, Mechanical Tissue Extraction and No Treatment

MB170043, W81XWH-18-1-0608

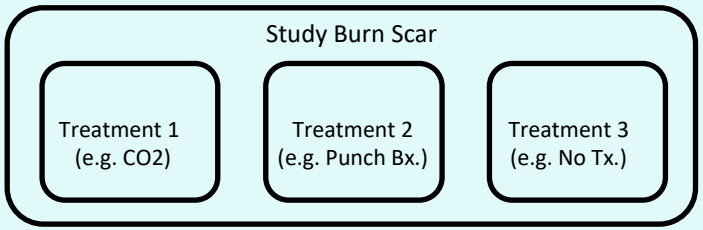
PI: Jonathan Friedstat, MD **Org:** Massachusetts General Hospital **Award Amount:** $1,749,178

Study/Product Aim(s)

- Aim I: Conduct a randomized control trial comparing fractional ablative CO2 laser, 0.5mm punch biopsies, and control in the treatment of HTBS
- Aim II: Evaluate whether PROMs detect changes in response to CO2 laser treatment/reconstructive procedures in burn patients

Approach

A within scar, randomized control trial will be performed to compare laser treatment to 0.5 mm punch biopsy and no treatment (controls). Evaluation of each of the three treated areas will be conducted with histology, photography, cytometry all with blinded assessors. Gene expression will also be performed before and after laser treatment. Since the procedures will be performed concurrently with other reconstructive procedures, PROMs will be administered to evaluate whether our procedures change patients' PROM scores.



Burn scar study area with three treatments that will be randomly assigned. Each treatment area is 16cm^2 and there is 3cm space between treatment areas to minimize interaction between treatments. Bx=biopsy, Tx=Treatment

Accomplishment: We are slowly increasing enrollment and have enrolled 6 patients. We have obtained HRPO approval for use of flyers to increase recruitment from other regional burn centers and have shared them with the burn model systems group at Harvard..

Timeline and Cost

Activities CY	18	19	20	21	22-
Major Task 1: Preparatory work for Initiation of RCT					
Major Task 2: (Aim I): Conduct RCT of Laser to punch biopsy and no treatment					
Major task 3: (Aim II): Evaluate PROM changes following reconstructive procedures					
Major task 4: Data analysis					
Estimated Budget ($K)	**42**	**178**	**184**	**213**	**1132**

Updated: 10/30/21

Goals/Milestones

CY18 Goal – Preparatory work for Initiation of RCT
- ✓ Start IRB Approval
- ✓ Hire and train study staff

CY19 Goals – Obtain approval from MGH IRB, HRPO, and start RCT
- ✓ IRB Approval
- ✓ HRPO Approval
- ✓ Initiate enrollment and the RCT

CY20 Goal – Enroll patients in the trial
- ✓ Collect PROM DATA
- ✓ Continue to enroll patients for the RCT

CY21-CY22 Goal – Complete enrollment and analyze data
- ☐ Complete enrollment in the trial
- ☐ Evaluate the data

Comments/Challenges/Issues/Concerns
- IRB approval took longer than expected
- COVID-19 Pandemic stopped all non-urgent surgical procedures

Budget Expenditure to Date

Projected Expenditure: $583,375

Actual Expenditure: $583,375