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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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13. SUPPLEMENTARY NOTES

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
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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 (15 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 7 patients enrolled and are now up to 12 patients enrolled with 8 patients completing their treatments and 6 that have completed all their post-treatment follow-up. Recruitment has improved with more frequent screening of patients as a team as well.

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 and approached Brigham and Woman's hospital about referring patients, but this has not been successful at increasing enrollment.

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

Enrollment has increased because we are doing a better job screening patients, including screening patients toward the end of their inpatient stay to approach when they come to clinic for follow-up. It helps us better ensure we do not miss patients. Also, we have increased our clinic staffing to two medical assistants, so we have plenty of clinic appointment slots and this makes it easier to see more patients.

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. This is being worked on as a publication and is still in the draft stages. Also, a methods paper is in the draft stage and being worked on as well.

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. Greater interest in the outcomes following reconstructive surgery has resulted from this project.

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. Patients report this to us as do several insurance companies during peer reviews who simply are unaware of the benefits lasers seem to offer patients.

5. CHANGES/PROBLEMS:

Nothing to report

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

The main challenge remains recruitment of patients. We do appear to be on track to hit our goal of 20 patients, though will likely require an additional NCE to complete the data analysis. This has been discussed with our contacts at the DoD and we are starting the process early to request that as well as a plan for unused funding so that it can be utilized.

Changes that had a significant impact on expenditures

With revised power calculations, the number of patients needed to measure a reasonable effect size was decreased to 20. That extra funding is anticipated to be used for a second NCE to allow for analysis of the data.

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.

Future Trends in Burn Care, American Society of Plastic Surgery, The Meeting. Boston, MA. 2022.

- **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:	1
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:	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:	3
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:	1
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:	5
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, these co-investigators have obtained funding for additional projects, none that changed their effort on this project.

Dr. Levi:
1) Title: Novel, point of care biomarker to detect pre-clinical flares for people living with fibrodysplasia ossificans progressiva (FOP)
Performance Period: 02/2022- 01/2023
Project Goal: Define a series of novel blood-based biomarkers specific for monitoring FOP-associated heterotopic ossification
2) Title: Impacts of mechanosensation and matrix architecture on cell fate specification in traumatic heterotopic ossification - diversity supplement
Performance Period: 06/2022- 04/30/2024

Dr. Ryan:
1) Title: Predictive Approaches and Technology Development for Identification of Susceptibility to Multiple Independent Infections in Trauma Patients
Project/Proposal Start and End Date: 08/2021 - 07/2023
2) Title: The ACTUATE-CBC Study: ACcelerating The UptAke of TelemedicinE for Crisis Burn Care
Project/Proposal Start and End Date: 09/2021 - 09/2025

Dr. Schneider
1) Burn Model System Grant Renewal
Performance period: 2022-2027

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:
See attached

9. APPENDICES: