

AWARD NUMBER: W81XWH-18-1-0608

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

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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									
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1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

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: *Provide a brief list of keywords (limit to 20 words).*

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

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

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:
-Obtain HRPO approval for beginning recruitment (completed 10/25/2019)

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

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)

During this reporting period, we have obtained MGH IRB approval and HRPO approval as of 10/25/1019. We look forward to beginning recruitment of patients.

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

If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to Report

How were the results disseminated to communities of interest?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report

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

If this is the final report, state “Nothing to Report.”

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We plan to start enrollment of patients into the study. Additionally, a methods paper will be worked on and ideally have it published to share our plans in advance of the study and increase our chances to permit it to be published in a higher impact factor journal at the conclusion.

4. IMPACT: *Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

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

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research

in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Turnover in study staff caused some delay in IRB approval. A new study coordinator had to be hired and trained on study protocol. IRB approval also took longer than expected due to technological upgrades/issues both at our institution and with HRPO.

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

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report.

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report.

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

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

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: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”*

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

Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

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 during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

Name: Mary Smith
Project Role: Graduate Student
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: 5
Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.
Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)

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: Kristina Chang
Project Role: Clinical Research Coordinator
Nearest person month worked: 3
Contribution to Project: Ms. Chang assisted the study team in overall coordination of the project.

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?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Over the past year:

Dr. Jeremy Goverman received new support from XenoTherapeutics, Inc. for a Phase I clinical trial.

Dr. Colleen Ryan received new support through the MGH Center for Disaster Medicine (1HITEP180042-01-00, PI: Biddinger).

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- Financial support;
- In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);
- Facilities (e.g., project staff use the partner’s facilities for project activities);

- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.*

- 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.*

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

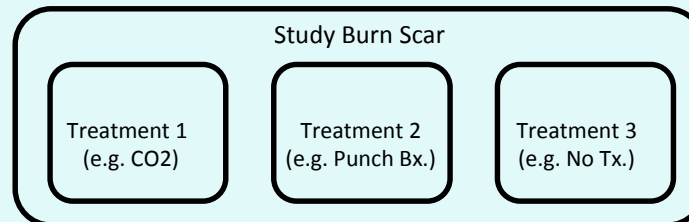
Award Amount: \$1,749,178

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 16cm² and there is 3cm space between treatment areas to minimize interaction between treatments. Bx=biopsy, Tx=Treatment

Accomplishment: We have received IRB approval at MGH and are working toward HRPO approval, which we anticipate during the next quarter.

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	177	747	445	338

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

- Continue to enroll patients for the RCT
- Collect PROM data

CY21-CY22 Goal – Complete enrollment and analyze data

- Complete enrollment in the trial
- Evaluate the data

Comments/Challenges/Issues/Concerns

- IRB approval is taking longer than expected

Budget Expenditure to Date

Projected Expenditure: \$173,955

Actual Expenditure: \$173,955

Updated: October 24, 2019