Post Excision/Mohs Fractional CO2 Resurfacing: A Quantitative and Qualitative Scar Analysis Study
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	Principal Investigator Name/Contact Info:	Hooman Khorasani MD hooman.khorasani@mountsinai.org
	Primary Contact Name/Contact Info	212-731-3311 (office) 212-731-3395
	Date Revised:	2/27/2019
	Study Number:	**IF# 2430986 HS# 14-00132 GCO# 14-0387**

MSSM Protocol Template HRP-503a

Instructions:

1. *Prepare a document with the following sections. Note that, depending on the nature of your research, certain sections below may not be applicable. Indicate N/A as appropriate, explaining where possible.*
2. *For any items described in the sponsor's protocol, grant application or other source documents submitted with the application, you may reference the title and page numbers of these documents rather than cutting and pasting into this document.* ***Do NOT refer to any derived documents, such as the Sample Consent document, or other internal documents required with the submission.***
3. *If you reference page numbers, attach those pages to this protocol.*
4. *When you write a protocol, keep an electronic copy. You will need to modify this copy when making changes.*

Brief Summary of Research (250-400 words):

The purpose of this study is to evaluate the benefits and the ideal timing of treating a surgical scar of the skin with an ablative fractionated CO2 laser. An attempt to quantify the amount of collagen that gets deposited during the healing process after being treated with the fractionated CO2 laser as compared to an untreated area of the scar will be performed through a spilt scar study. Subjects will be placed in one of three categories, based on the timing of when their scar will receive intervention after the excisional surgery. The clinical appearance of the scar will then be documented over several office visits and at week 16 of the scar having been treated with the CO2 laser, a biopsy will be taken of the treated half of the scar and also one from the untreated half. These samples will be evaluated by confocal microscopy and H+E staining to quantify the amount of collagen deposition as well as the architectural changes in both the treated and untreated areas of the surgical scar.

1) Objectives:

The purpose of this study is to evaluate the potential benefits of treating a surgical scar post excision with an ablative fractionated CO2 laser with the goal of decreasing the appearance and size of the scar. The hypothesis of the study is that the portion of the scar treated with laser will have an improved appearance and texture. An attempt will be made to quantify the difference in collagen deposition and architecture with the theory being that the treated portion of the scar will have an architectural change similar to normal "scar-less" tissue. A secondary objective of the study is to try and determine the ideal time to treat the surgical scar post-excision.

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2) Background

Improvement of scar appearance after surgery has been a concept that has been looked at for many years. Katz et al. showed in the early 90's through a split scar study that mechanicaFel dermabrasion improved the clinical appearance of excision scars of the skin when performed 8 weeks after the surgery. Recently, there has been a great interest in fractional ablative resurfacing to improve the appearance of scars that resulted from either trauma or burns. Previous studies have indicated that a noticeable clinical improvement can be achieved when treating these types of scars with a fractionated CO2 laser. Fractional photothermolysis produces a unique thermal damage pattern known as microthermal treatment zones. These zones can be characterized as multiple columns of thermal damage surrounded by areas of untreated tissue. It is this intervention pattern that has revolutionized the arena of ablative laser therapy and enabled laser platforms such as the erbium:YAG (2,940 nm) and the carbon dioxide (10,600) lasers to provide effective results with significantly less side effects and much shorter recovery time. A study published in the Feb. 2010 Archives of Dermatology by Weiss et al. looked at treating atrophic surgical and traumatic scars with ablative fractional resurfacing and found it to be a safe and effective intervention for improving the clinical appearance of scars. It is felt that the zones of ablation and coagulation that are created produce dermal remodeling, tissue tightening, new collagen formation and thus lead to a clinical improvement in atrophic scars. While the study by Weiss et al. attempted to quantify the subjective improvement of the treated scars with objective topographical skin imaging, there has not been an established methodology for quantitatively assessing dermal collagen architecture. This pilot study will attempt to quantify the difference in collagen architecture of the treated area of the surgical scar compared to the untreated area by using methodology involving confocal microscopy established by Khorasani et al. in the Feb. 2011 article in The American Journal of Pathology titled "A Quantitative Approach to Scar Analysis"

3) Setting of the Human Research

Subjects will attend their study visits in the outpatient offices at the85th street FPA clinic, 5th floor, Department of Dermatology

4) Resources Available to Conduct the Human Research

Meeting the recruitment goals of this project will be feasible as the surgical division of Mount Sinai's Dermatology Department performs over 500 surgeries in a six month time period and the study is looking to recruit 45 patients, thus the study needs to recruit less then 10% of the patients having surgery.

At this time there will be 2 staff members involved in this research and each member has already participated in IRB approved protocols at Mount Sinai and currently work at the only

study site involved in the research. All investigators have extensive experience operating the Lumenis Ultrapulse CO2 fractional laser. The pathology specimens will be reviewed by a board certified dermatopathologist with extensive experience in evaluating specimens with confocal microscopy. Any additional members that will be added to assist in the study will be required to review the initial protocol that was submitted to the IRB and any further revisions required by the IRB. The PI will ensure that all personnel that are added after initial IRB approval disclose any financial interests and complete their education requirements prior to beginning the study.

5) Study Design

a) Recruitment Methods

Study subjects will be recruited through referrals from dermatologists at Mount Sinai's Department of Dermatology Faculty Practice

b) Inclusion and Exclusion Criteria

Inclusion criteria

1. Must understand and voluntarily sign an informed consent form 2. Must be male or female and aged >18 years at the time of consent 3. Must be able to adhere to the study visit schedule and other protocol requirements 4.Patients undergoing skin excisions and Mohs surgery of the face/trunk/extremities

Exclusion criteria

1.Inability to provide voluntary informed consent 2.Use of laser or light based interventions to affected areas in past year 3. Fitzpatrick Skin types 3-5. 4.Surgical lesions located on the central chest 5.History of keloid formation 6. History of Accutane use in the last 6 months

c) Number of Subjects

We intend to recruit and enroll 45 patients for this pilot study

d) Study Timelines

The duration of an individual subject's participation in this study will be carried out over six months. Enrollment completion will be scheduled for April 2019.

e) Study Endpoints

For primary end point refer to pg.17 , section 7.2.2.1 and for secondary end point refer to pg. 17, section 7.2.2.2

f) Procedures Involved in the Human Research

All patients participating in this investigator initiated split-scar study will receive ablative fractional resurfacing with the Deep and Active FX™ platforms of the Lumenis Ultrapulse CO2 laser. The settings for interventions of scars on the face with the Deep platform will be 15% coverage, 15mJ at 150 Hz and 15% coverage, 12.5 mJ at 150 Hz for off the face. The Active platform settings will be 90 mJ with a density of 3 for the face and 70 mJ and a density of 2 for off the face. The DeepFX™ platform will be applied to the scar prior to the ActiveFX™ platform. Half of the excision scar will be treated with the appropriate settings and half will go untreated. Subjects will be randomized to receive laser intervention at the time of the excision, ten days post-op or 8 weeks post-op. There will be a total of 15 subjects in each study group. Each study group will consist of 5 subjects with excisions on the face, 5 subjects with excisions on the trunk and 5 subjects with excisions on the extremities. General wound care for post surgical excision and laser therapy will include a topical antibiotic cream as well as a topical skin moisturizer and gauze dressing.

The screening visit will consist of reviewing inclusion/exclusion criteria and obtaining informed consent. There will be a total of 7 study visits to include the day of the excision, post-op day number 10 for suture removal as well as laser therapy if the subject has been randomized to that intervention group, 4 weeks post-op, 9 weeks post-op and laser intervention for subjects randomized to this time frame for intervention, 12 weeks post-op, 17 weeks post-op and 24 weeks post-op. Each visit will last approximately 30-45 minutes each in which clinical photos of the surgical scar will be taken and any wound care or side effects of the laser therapy or surgery will be addressed. Subjects will have a 3 mm punch biopsy taken from both the treated and untreated half of the scar at the post-op visit that correlates approximately with 8 weeks after having been treated with the laser (weeks 9 for two of the subject groups and week 17 for the final study group). These biopsy samples will be taken for the purpose of analyzing the ultrastructure of the collagen architecture. To evaluate this ultrastructure, confocal microscopy using fractional dimension and lacunarity analysis will be used. Further scar analysis will be performed by H&E staining photographs captured on an Olympus BX51 microscope (Olympus America Inc. Center Valley, PA) equipped with MicroFire 2.2 digital camera (Optronics, Goleta, CA) using PictureFrame 2.0 software at 40X magnification. Image analysis will then be performed using NIH's shareware program, ImageJ and the Scar index will be determined. Subjects will have the option of having the untreated portion of their scar treated at no charge at the end of the study if the subject is satisfied with the results of the study

g) Specimen Banking

N/A

h) Data Management and Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. Only the subject number will be recorded in the CRF, and if the subject name appears on any other document, it must be obliterated before a copy of the document is supplied to the sponsor. Study findings stored on a password protected computer will be encrypted and stored in accordance with local data protection laws. As part of the informed consent process, the subjects will be informed in writing that representatives of the IRB, or regulatory authorities may inspect their medical records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. If the results of the study are published, the subject's identity will remain confidential. Only the investigator will maintain a list to enable subjects to be identified. The biopsy specimens will be sent directly to the dermatopathology lab as per standard operating procedure of the department. The specimens will be analyzed then destroyed immediately as per hospital procedures for disposing biologic waste. Photographs will be taken of the scar. If the scar is present on the face, we will focus the picture in a manner that the subject's facial features are not identifiable to maintain their privacy. These photographs will be labeled with the patient ID number and the date. The pictures will not have any subject's name on them. They will be stored on a password protected computer until the study is over at which time they will be transferred onto a disc or USB drive and stored with the rest of the study documents. We will use the study photographs to study the effects of the laser on scars. The photographs will be used for documentation of the study and for the purpose of being viewed by the blinded third party to evaluate the scars and rate them. The camera will be stored in a locked filing cabinet in the PI's office which has a 24 hour keypad lock. All photos will be deleted from the camera after being loaded on to an encrypted and password protected desktop computer located in the PI's office. Only investigators and co-investigators will have access to the photo files

i) Provisions to Monitor the Data to Ensure the Safety of subjects

N/A

j) Withdrawal of Subjects

If a patient develops an infection while on the study that is serious, he or she will be terminated from the study. If the infection is not serious, and is mild to moderate in severity, then the patient and the investigator will decide, based on whether the infection resolves and whether it is reasonably related to study drug, whether or not to keep the subject on the study. Severe infections will most likely result in termination from the study.

6) Risks to Subjects

The potential risks of this study include erythema post-laser intervention. Some patients may be at risk for potential pigmentation loss while hyperpigmentation can also be a risk; however, laser settings will be adjusted according to the particular area of the body being treated. In addition Fitzpatrick skin types III-V will be excluded from the study in order to minimize this risk. Common minor side effects may include crusting, mild swelling, redness or brown discoloration at the intervention site. In rare cases, hypertrophic scarring or infection may occur. The potential risks of having a biopsy include pain, local swelling, bleeding and/or infection. A small scar may result at the biopsy site. To minimize the appearance of scarring from the biopsy the size of the punch biopsy will be limited to 3 mm.

7) Provisions for Research Related Injury

In the event of related harm or injury the patient will be clinically evaluated by the treating physician. If harm is deemed to have occurred the patient will be triaged and treated in clinically standard treatment protocols. In the case of worsening scar then may consider other modalities (e.g. surgery with a z plasty, dermabrasion, intralesional kenalog, other lasers) or discoloration (other lasers to correct color or topical therapies).

8) Potential Benefits to Subjects

Potential benefit for the subjects will be improved cosmetic appearance of the excision scar that is treated with the laser. In order to minimize any worsening of the scar appearance from the biopsy performed in the study, the size of the biopsy will be limited to 3 mm and will be taken from the center of the scar as opposed to the edge. All subjects will be offered an additional intervention with the fractionated CO2 laser of the biopsy sites scars at the completion of the study if the subject and investigators feel the intervention will improve the appearance of the biopsy site

9) Provisions to Protect the Privacy Interests of Subjects

N/A.

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MSSM Principal Monitor:

Last Name: Khorasani
First Name: Hooman
Academic Title: Chief
Department: Dermatology: Division of Mohs and Reconstructive Surgery

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MSSM Additional Monitor:
Last Name: Lin
First Name: Matthew
Academic Title: Procedural Fellow
Department: Dermatology

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2. The principal monitor is the principal investigator, and the additional monitor is the sub-investigator. Please refer to respective curriculum vitae for further information.
3. Adverse events and subject compliance to the protocol will be monitored for safety

4. Safety and accumulated adverse events will be reviewed at least quarterly.
5. The PI is the only entity that can amend the protocol for administrative or safety reasons. Any changes will be submitted to the IRB for approval prior to implementation.
6. As per the protocol, the energy setting for treating scars on the trunk and extremity will be reduced to minimize the risk of hyperpigmentation. In addition, subjects with Fitzpatrick skin types III-V will be excluded from the study to minimize the risk of a subject developing hyperpigmentation from the laser intervention.
7. N/A
8. Please see attached protocol page 18 sections 8 and 9.

9. Should a temporary or permanent suspension of the study occur, the PPHS and IRB will be contacted

10) Economic Impact on Subjects

Methods of protecting the rights and welfare of subjects include: not preferentially enrolling vulnerable subjects (those that are economically disadvantaged will not be financially induced because no compensation is being provided for participation in this study, providing information to subjects in terms that they can fully understand (the consent form is specifically written such that an individual with a 6th grade education can understand), not exerting any overt or covert coercion, not offering any financial incentives or if offered, not giving an amount that could be considered coercive, and using a consent document that the subject will be asked to sign that is written in the language that the potential subject understands. We will also make sure that the subject understands that there are other options for intervention available to them outside of our study.

11) Payment to Subjects

none

12) Consent Process

Consent will be obtained prior to any study procedures and administered by the Principal Investigator or delegates. The consent process will be performed either at the first visit to the study site (not necessarily the first study visit as specified in the protocol) or should the subject prefer to take the consent home to read at leisure, at a subsequent visit. Methods of protecting the rights and welfare of subjects will be taken: not preferentially enrolling vulnerable subjects (those that are economically disadvantaged will not be financially induced because they will be appropriately paid for time and expenses occurred). SOP HRP-090 Informed Consent Process for Research will be followed

13) Process to Document Consent in Writing

The standard PPHS consent template will be used for this research study. The consent process and date that the consent is signed is documented in our source notes.

14) Vulnerable Populations

Indicate specifically whether you will include or exclude each of the following populations:

Include	*Exclude*	*Vulnerable Population Type*
	X	*Adults unable to consent*
	X	*Individuals who are not yet adults (e.g. infants, children, teenagers)*
	X	*Wards of the State (e.g. foster children)*
	X	*Pregnant women*
	X	*Prisoners*

15) Multi-Site Human Research (Coordinating Center)

N/A

16) Community-Based Participatory Research

N/A

17) Sharing of Results with Subjects

During participation in this study, subjects will not be able to access their research records. This will be done to prevent the knowledge of study results from affecting the reliability of the study. Subjects' information will be available should an emergency arise that would require their treating physician to know this information to best treat them. Subjects will have access to their research record and any study information that is part of that record when the study is over or earlier, if possible. The investigator is not required to release to subjects research information that is not part of their medical record. Subjects will always have access to their own clinical medical records while participating in this study.

18) IRB Review History

Approved through 4/15/2019. Seeking continuation for one year

19) Control of Drugs, Biologics, or Devices

Ablative fractional carbon dioxide laser is stored in a combination-locked room accessible only by clinical trials personnel

Note: The IDS has its own forms that must be completed and a review process that must be followed before the IDS representative will sign off on Appendix B for submission to the PPHS.