Investigating the Efficacy of a Fractionated 1927nm Laser for Diffuse Pigmentation and Actinic Changes

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1. Background

Melasma is an acquired skin condition defined by symmetric hyperpigmentation, typically occurring on the face. It arises from hyperfunctional melanocytes that deposit excess melanin into the epidermis and dermis, resulting in irregular light to greyish brown macules on the skin.[1-3] Studies have shown that the estimated prevalence in the general population exists at about 1% while higher-risk populations can reach a prevalence of up to 50%.[4,5] The condition is also noted to have female predominance, particularly during reproductive years.[1,6,7] Pathogenesis is multifactorial and not yet fully understood; however common etiologic factors that play a role include sun exposure, genetic influences and female sex hormones. Hormonal influences play a significant role, most notably seen by the increased prevalence of melasma amongst pregnant women or those who use hormonal therapies such as hormonal contraceptives.[8-12] Melasma can occur in all skin types, however, more commonly affects darker skin types.[13] [redacted]

MOXI is a fractionated 1927 wavelength thulium non-ablative laser (f1927) developed to reduce unwanted pigment, improve skin texture and tone and promote new cell growth. The fractionated 1927 nm thulium non-ablative laser is suitable for targeting epidermal lesions and has been shown to be effective in resurfacing photoaged skin as well as addressing pigmented lesions without exacerbation.[18-25] Thus it is a very effective option for addressing pigment concerns and the treatment itself requires less downtime than more aggressive laser procedures.

This study intends to evaluate the clinical performance of f1927 for the treatment of diffuse pigmentation including melasma. We hypothesize that the treatment will produce a statistically significant improvement in the appearance of hyperpigmentation over the course of 30 days, followed by 1-month and 3-month post-treatment visits when compared to baseline.

2. Purpose

This single-center clinical trial is being conducted over the course of 30 days followed by 1-month and 3-month follow-up visits. The primary objective of this study is to assess the efficacy of f1927 when used by men and women with diffuse hyperpigmentation and/or melasma.

3. Concise Summary of Project

3.1. Clinical Study

This is a single-site, non-randomized, non-controlled study at UT Southwestern Medical Center at Dallas in the Department of Plastic Surgery designed to follow up to 30 qualified and consenting subjects receiving

f1927 treatments under an IRB approved protocol [redacted]

These patients will receive treatment using a f1927 device and will be treated twice over the affected areas, once each month for a total of two months, followed by two follow-up visits at 1-month and 3-months post-treatment [redacted] A quantitative assessment of the effects of treatment will be performed using VISIA and Vectra H2 3D facial skin analysis at 1-month and 3-months post-treatment.

[redacted]

3.2. Primary Endpoints

- Assessment of improvement in overall facial hyperpigmentation using quantitative measurements provided by VISIA and Vectra H2 3D analysis of photos obtained at Baseline, 1-Month and 3-Months post-treatment to evaluate the efficacy of f1927 treatments
    - Calculate percent change from baseline in visualization and numeric analysis of brown and red areas utilizing the Facial Skin Analysis on Canfield's Imaging Systems
- Clinician assessment of pigmentation improvement using the Physician's Global Assessment Scale

3.3. Secondary Endpoints

- Monitoring incidence, severity, and relatedness of adverse events throughout the study.

4. Test Material Information

4.1. Study Device Description

The following devices will be evaluated during the study:

Proprietary Name	Device Description	Regulatory Information
Sciton MOXI	Aesthetic device that utilizes a fractionated laser to treat uneven pigmentation and heal photodamaged skin	Class II 510(K) Number: N/A Regulation Number:878.4810

5. Study Population and Enrollment

5.1. Subject Enrollment

Healthy subjects who are interested in treatment for diffuse pigmentary changes will be recruited for the study through recruitment flyers and social media posts. [redacted] Potential subjects will have the study explained to them, will be asked about their willingness to be involved in the study, and their willingness to sign an informed consent form.

5.2. Informed Consent Form

An IRB-approved informed consent form (ICF), explaining the purpose, design, risks and duration of the study, will be given to each candidate subject before participation in any study procedures. The candidate subject will be given as much time as needed to read the ICF and will have the opportunity to have any study-related questions answered to their satisfaction prior to signing the ICF [redacted]

5.3. Subject Identification

[redacted]

5.4. Eligibility Criteria

Inclusion Criteria

1. Healthy male and female adults between 20-75 years of age.
2. Fitzpatrick skin type I-IV.
3. Individuals deemed by the Investigator to have a significant amount of pigmentation/melasma and that desire correction of this condition.
4. Individuals willing to withhold aesthetic therapies, or other therapies judged to potentially impact results to the treatment areas for the duration of the study.
5. Women of childbearing potential who agree to take a urine pregnancy test at the Screening visit or when deemed by Investigator. Women of childbearing potential must have a negative urine pregnancy test and must not be lactating at Screening. Women must be willing and able to use an acceptable method of birth control (see below) during the study. Women will not be considered of childbearing potential if one of the following is documented – postmenopausal for at least 12 months prior to study, without a uterus and/or both ovaries, bilateral tubal ligation at least 6 months prior to study enrollment.

[redacted]

7. Individuals who can read, speak, write and understand English and who are willing to provide written informed consent.
8. Individuals willing to sign a photography release.
9. Individuals willing and able to cooperate with all study requirements for the duration of the study.

<u>Exclusion Criteria</u>

1. Fitzpatrick skin type V-VI.
2. Known allergies to general skin care products.

[redacted]

[redacted]

18. Individuals undergoing concurrent therapy that, in the Investigator's opinion, would interfere with the evaluation of the safety or efficacy of the study devices.

[redacted]

25. Individuals who are unable to understand instructions or give informed consent
26. Individuals who have physical or psychological conditions which, in the opinion of the Investigator, makes them unable to complete the study per protocol (e.g., not likely to avoid other cosmetic treatments to area; not likely to stay in study for entire duration due to other commitments; or those with concomitant conditions that may develop symptoms that might confuse or confound study treatments or assessments).

6. Subject Instructions

Subjects will be asked to wash off all skincare products at least 30 minutes prior to each scheduled clinic visit using a cleanser of your choice. [redacted]

[redacted]

Subjects will be asked to avoid extended periods of sun exposure and all use of tanning beds for the duration of the study. Extra care should be taken to wear protective clothing and avoid sun exposure from 10 AM to 4 PM.

Subjects will be encouraged to consistently use face wash, moisturizer, and sunscreen of their choosing. Subjects will be asked to refrain from using any new anti-aging, acne, and acne scar products or devices and beginning the use of any new skincare products or devices other than the assigned test material for the duration of the study.

7. Study Design

7.1. *Outline of Procedures*

Procedures/ Time Points:	**Visit 1** **Screening** (-30 to 0 days)	**Visit 2** **Baseline/ Treatment #1*** (Day 0 ; ± 3 days)	**Visit 3** **Treatment #2** (Day 30; ± 3 days)	**Visit 4** **1-month post-treatment** (± 3 days)	**Visit 5** **3-months post-treatment** (± 3 days)
Informed Consent	X				
Enrollment Paperwork	X				
Medical History/ Concomitant Medications	X	X	X	X	X
Pregnancy Test	X				
MOXI Treatment		X	X		
Standard Photography	X			X	X
H2 3D and VISIA Photography	X			X	X
Physician's Global Assessment Scale				X	X
Safety Assessment		X	X	X	X

* Treatment #1 (Visit 2) activities may be conducted at the Screening visit (Visit 1)

7.2. *Pre-Study Procedures*

Prior to the start of the study, potential subjects will be screened for eligibility requirements via chart review on EPIC. [redacted]

7.3. *Screening: Visit 1 (Day 0; -14 to 0 days)*

The purpose of the study, eligibility criteria and potential risks will be discussed with the potential subject.

This visit will take 30-45 minutes. Screening (Visit 1) may be combined with Visit 2.

7.4. Treatment Visits: Visit 2 (Day 0; +/-3 days) and Visit 3 (Day 30; +/-3 days)

A member of the study team will record concomitant medications and will ask subjects if they have experienced any changes in their health since the previous visit. If an adverse event (AE) is reported than the Investigator will be informed, and an AE log will be completed/updated for PI review.

The procedure will then be performed in our Plastic Surgery clinic following standard of care procedures. A trained staff member will apply a topical triple anesthetic (benzocaine, lidocaine, tetracaine) to anesthetize the areas being treated.

Appropriate post-treatment care instructions will be provided as deemed appropriate by the Investigator or study staff.

[redacted]

These visits will take approximately 1 hour.

7.5. Follow-Up Visits: Visit 4 (1-Month Post Treatment) and Visit 5 (3-Months Post Treatment)

At a minimum, all subjects will return for follow-up visits at 1 month (+/- 3 days) and 3 months (+/-3 days) after treatment.

The following activities will be performed on all study subjects during the follow-up visits:

1. The physician or study staff will ask subjects if they have experienced any changes in their health since the previous visit. Changes will be recorded accordingly. If an adverse event (AE) is reported than the Investigator will be informed, and an AE form will be completed.
2. Subjects will acclimate to ambient temperature and humidity conditions for 15 minutes prior to any procedures being done.
3. The physician or study staff will perform an examination of the skin in the treatment area
4. Obtain post-treatment close up and standard photography as described in section 8.1.
5. Obtain post-treatment photographs and measurements using the Vectra H2 3D Imaging System and VISIA Imaging System as described in section 8.1.

These visits will take about 30 minutes.

8. Assessments

8.1. Photography Procedures

[redacted]

1. NIKON D7200

Standard, close up and cross-polarized photography of the face will be utilized for evaluation of pigmentation. [redacted]

2. Vectra H2 3D Imaging System

Subjects will be instructed to adopt neutral, non-smiling expressions for each photograph. [redacted]

3. VISIA Imaging System

Subjects will be instructed to adopt neutral, non-smiling expressions with their eyes gently closed for each photograph. [redacted]

8.2 Physician's Global Assessment

Trained clinician reviewers will use the Physician's Global Assessment Scale to evaluate subject's clinical photography and assess melasma response to f1927 laser treatment. [redacted]

Table 1. Physician's global assessment

Score	Description
0	Clear, except for possible residual discoloration
1	Almost clear, very significant clearance (*c.* 90%); only minor evidence of hyperpigmentation remains
2	Marked improvement, significant improvement (*c.* 75%); some disease evidence of hyperpigmentation remains
3	Moderate improvement, intermediate between slight and marked improvement; *c.* 50% improvement in appearance of hyperpigmentation
4	Slight improvement, some improvement (*c.* 25%); significant evidence of hyperpigmentation remains
5	No improvement; hyperpigmented condition unchanged
6	Worse; condition worse than at week 0

9. Statistical Methods of Analysis

[redacted]

The primary outcome of effectiveness will be a paired comparison of baseline to all applicable post-baseline time points for hyperpigmentation and melasma severity using data obtained from Vectra H2 3D imaging results.

A descriptive statistical summary will be provided the VISIA, Vectra H2, and Physician's Global Assessment Scale. The descriptive statistical summary includes the number of observations (N), mean, median, and standard deviation (SD), minimum (MIN) and maximum (MAX) values at all applicable time points.

The following will be calculated and reported for each evaluation parameter at the applicable post-baseline time point(s):

$$\text{Percent Mean Change from Baseline} = \frac{(\text{Visit Mean Score} - \text{Baseline Mean Score}) \times 100}{\text{Baseline Mean Score}}$$

For each new measurement set we will conduct a repeated measures of analysis of variance to detect difference between sample distributions. If differences are detected, we will subsequently evaluate specific pairwise comparisons among the post treatment visit times using a paired T-test or Wilcoxon signed-rank tests. All statistical tests will have a significance level alpha =0.05. P-values will be reported to 3 decimal places (0.000).

10. Potential Risks

Blistering, burning, scaling and infection (Rare)

[redacted]

Bruising (Rare)

[redacted]

Transient edema and/or erythema (Common)

[redacted]

Skin roughness and/or peeling (Common)

[redacted]

Pigmentary changes (Rare)

[redacted]

Eye injury (Rare)

[redacted]

Scarring (Rare)

[redacted]

Allergic reaction (Rare)

[redacted]

Photography

[redacted]

[redacted]

[redacted]

[redacted]

11. Adverse Events

At each visit, the Investigator will question the subject about adverse events using an open-ended question. If a potential adverse event is reported by the subject or identified during examination, directed questioning and examination will be performed when appropriate. [redacted]

[redacted]

[redacted]

Photographs will be taken to document any AEs if possible.

[redacted]

[redacted]

12. Subject Safety and Data Monitoring

12.1. Research Standards/Good Clinical Practice

[redacted]

12.2. Data Monitoring

[redacted]

[redacted]

12.3. Procedures to Maintain Confidentiality

[redacted]

[redacted]

[redacted]

13. References

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