PROTOCOL **UC 26-2025**

Study Title:	**"Evaluation of the 2910 nm Erbium-Doped Fluoride Fiber Glass Laser for the Treatment of Advanced Perioral Lines and Wrinkles"**
Sponsor:	**Acclaro Corporation**
Protocol Number:	**UC 26-2025**
Protocol Date:	**17-FEB-2025**
Principal Investigator:	**Paul M. Friedman, M.D.**
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The study will be conducted according to the protocol and in compliance with the International Conference of Harmonization Good Clinical Practice Guidelines and all other applicable regulatory requirements[1].

CONFIDENTIALITY STATEMENT

THE INFORMATION PROVIDED IN THIS STUDY PROTOCOL IS INTENDED FOR REVIEW BY THE PRINCIPAL INVESTIGATOR, ALL RESEARCH RELATED PERSONNEL, ETHICS COMMITTEE(S) AND HEALTH AUTHORITIES. INFORMATION PROVIDED AND CAPTURED IN THIS PROTOCOL IS STRICTLY CONFIDENTIAL AND WILL ONLY BE DISCLOSED WITH WRITTEN CONSENT FROM THE SPONSORS.

[1] See Dixon JR Jr., The International Conference on Harmonization Good Clinical Practice guideline. Qual Assur. 1998

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SYNOPSIS
Study Objective:

The primary objective of this clinical trial is to assess the efficacy, safety and patient satisfaction associated with the resurfacing treatment of perioral lines and wrinkles with the 2,910 nm mid-infrared Fiber Laser (UltraClear, Acclaro Medical) using both superficial epidermis ablation capabilities and the deep ablative and coagulative capabilities into the dermis for rejuvenation.

Study Design:

This is a prospective, single-center clinical trial.

Study Population:

Male and female adult subjects of Fitzpatrick skin types I-IV and aged 50-80 years who meet all inclusion and no exclusion criteria.

Clinical Protocol:

Enrolled subjects will be treated with the UltraClear 2,910nm mid-infrared laser using both superficial epidermal ablation and deep ablative and coagulative capabilities in the dermis for rejuvenation addressing perioral lines and wrinkles. In order to participate in the study, subjects must provide written informed consent to have their photographs used for research, publication and/or commercial purposes. Subjects satisfying all inclusion and no exclusion criteria will be enrolled in this trial and will receive up to two UltraClear treatments. Prior to receiving any study treatment, mandatory digital photography will be captured. The primary endpoint of the study will be to evaluate the UltraClear laser device for its effectiveness defined as improvement addressing perioral lines and wrinkles utilizing multiple scales completed by the investigator and blinded Independent Photographic Reviewers (IPRs) Additionally, safety, subjective overall aesthetic improvement and satisfaction will be monitored and tracked.

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1. BACKGROUND AND RATIONALE

Fractional laser treatment was developed to address a high demand for a safe and effective skin resurfacing. By employing the principal of fractional photothermolysis, significant shortcomings in the two main laser treatment modalities available on the market, ablative skin resurfacing and non-ablative dermal remodeling, were addressed [2].

Acclaro Corporation currently marketing a new device that have received FDA clearance in December 2021, operating at mid-infrared wavelength, ablative fractional resurfacing devices for treatment of photodamaged skin. The UltraClear Laser Workstation with a nominal wavelength of 2,910 nm, is designed to create microscopic thermal wounds within the epidermis and dermis, with spatial separation between damaged tissue. UltraClear laser delivers thermal disruption in a microscopic grid pattern to safely result in the coagulation or remodeling of tissue.

Long-term exposure to sunlight (UVA or UVB) produces the visible signs associated with photoaging and photodamage, including freckles, wrinkling, actinic keratosis, skin cancer, and melasma. The current standard of care for photodamaged skin involves routine skin surveillance, including sun

avoidance and protection from UVA or UVB rays with appropriate sunscreens [3]. Other recognized treatment modalities include, but are not limited to, topical treatments with retinoids, alpha-hydroxy acids, hydroquinone (HQ), hyaluronic acid gel, tretinoin, chemical peels, and, more recently, fractional thermolysis.

Fractional photothermolysis is a popular treatment option for photodamaged skin. Ablative resurfacing removes thin layers of the epidermis to lead for natural renewal of the epidermis layer, and at the same time the ablative laser energy will penetrate into the dermis to produce dermal thermal injury to improve rhytids and photodamage while preserving most of the epidermis [4]. In a retrospective analysis, Robert Bowen, MD investigated the improvement of ultrastructural changes associated with photodamaged skin using the 2,940 nm ER:YAG Laser System [5]. Eight subjects with skin types III and IV were treated with a 2,940 ER:YAG laser for 1 treatment. The results of this study show that a single treatment with the ER:YAG laser device significantly reduces Fitzpatrick wrinkles scores of the perioral area, improvement is comparable to that obtained with the full-field Contour TRL.

The investigator hopes to demonstrate the safety and effectiveness of the UltraClear laser device in rejuvenation addressing perioral lines and wrinkles.

The UltraClear Mid IR Fiber Laser System is an FDA cleared device K210847 and K233803.

Indication for Use: The UltraClear Fractional Laser System with its accessories is intended for use in dermatological procedures requiring coagulation, resurfacing, and ablation of soft tissue. Procedures include skin resurfacing and treatment of wrinkles, rhytids, furrows, fine lines, textural irregularities, epidermal nevi, telangiectasia, spider veins, actinic cheilitis, keloids, verrucae, skin tags, anal tags, keratoses, scar revision, (including acne scars), benign pigmented lesions and vascular dyschromia.

UltraClear generates a fractional resurfacing regular pattern of microscopic treatment spots at the surface of the skin. The pattern created by fractional ablation in an isolated non-contiguous formation with the sparing of healthy tissue between the treatment zones, lends to rapid re-epithelialization and healing. Since the laser-tissue interaction of the UltraClear Mid IR Fiber Laser is similar to other Er:YAG lasers, similar wound healing profiles are expected.

2. STUDY OBJECTIVE

The primary objective of this clinical trial is to assess the efficacy, safety and patient satisfaction associated with the treatment addressing advanced perioral lines and wrinkles with the 2,910 nm mid-infrared UltraClear Fiber Laser Workstation using both superficial epidermis ablation capabilities and the deep ablative and coagulative capabilities into the dermis for rejuvenation.

The following endpoints will be assessed in this study:

- **Primary Endpoint: To evaluate the UltraClear laser device for its effectiveness:**
    - Defined as improvement addressing advanced perioral lines and wrinkles utilizing multiple assessment scales: Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS), Physician Global Aesthetic Improvement Scale (PGAIS) and Percent Improvement Evaluation completed by the investigator (Appendix A).
    - Defined as improvement addressing advanced perioral lines and wrinkles utilizing multiple scales: PGAIS and Percent Improvement Evaluation completed by Independent Photographic Reviewers (Appendix A).

- Comparison of the proportion of subjects (i.e., percentage of treatment responders) correctly identified by at least two out of three blinded Independent Photographic Reviewers (IPR).
- **Primary Safety Variable:** is the evaluation of adverse events up to the 3-month visit after treatment.

- **Secondary Endpoint: To evaluate the investigational device for its safety, subjective overall aesthetic improvement and overall satisfaction determined by study participants:**
  - Subjects with at least a self-reported "improved" rating on the Subject Global Aesthetic Improvement Scale (SGAIS) at follow up will be considered to have an aesthetically pleasing outcome. The SGAIS is a measure of aesthetic improvement relative to baseline, pre-treatment condition.
  - Subjects with a self-reported "satisfied" rating on the Subject Satisfaction Questionnaire.
  - **Secondary Safety Variable:** is the evaluation of the pain and discomfort after treatment as reported by the subject on a visual analog scale (VAS).

3. STUDY DESIGN

This is a prospective, single-center clinical trial. The study will consist of 20 subjects who will be treated with the UltraClear 2,910nm mid-infrared erbium-doped fluoride fiber glass laser (2,910 nm Fiber Laser) using both superficial epidermal ablation and deep ablative and coagulative capabilities in the dermis for rejuvenation addressing advanced perioral lines and wrinkles. The study will last approximately up to 8 months.

Prior to any study activities, the subject will be provided unlimited time to review the Informed Consent Form (ICF) document. All questions and concerns will be addressed. The ICF will be reviewed with the subject and signed if the subject understands and accepts the document. A copy of the signed ICF will be provided to the subject. The estimated time for the review and the explanation of the consent form is about 30 minutes. After signing the consent, the subject is enrolled.

Subjects interested in participation in the study will contact the clinical study team. During this first contact they will be informed regarding the goals of the study, history of the investigational device, inclusion/exclusion criteria, study procedures, potential benefits, risks, and duration of the study.

No treatment or data collection will be obtained before a subject is enrolled. Subjects will provide consent prior to providing HIPAA-regulated Protected Health Information and enrolled after informed consent materials, including the specifics of research participation, the potential risks and benefits of participation, and confidentiality concerns, are presented.

Subjects who believe they meet the exclusion and inclusion criteria and remain interested in the study will be invited to come in for their screening visit. During the screening visit, the investigator will ask the subject questions to determine if the inclusion and exclusion criteria are met. Following the investigator's determination that the inclusion and exclusion criteria are met, the subject will be invited to participate in the study.

The pain management plan will be discussed with the subject during the screening session. If the PI determines oral anxiolytics (ie. Ativan) and/or pain medications (Toradol) will be utilized, it will be confirmed that the subject will have a driver to transport them home following the treatment.

Upon enrollment and after a thorough review of the inclusion and exclusion criteria as well as obtaining written and informed consent, each subject will receive one laser treatment with an optional second (pending PI discretion) and up to six (6) study visits per the subject visit schedule below. Subjects may be treated on the same day that they are screened and provided with informed consent.

Prior to treatment at each visit, VISIA Imaging (Canfield Scientific, City, NJ) and IntelliStudio Photographs (Canfield Scientific, City, NJ) will be completed with identical photographic exposures (Appendix C) (left profile, left oblique, anterior, right oblique, right profile).

Following the appropriate photographs and evaluations, BLT topical anesthetic (consisting of 20% Benzocaine, 6% Lidocaine 6% Tetracaine) will be applied to the subject's entire treatment area for 45 – 60 minutes prior to the laser procedure. Injectable blocks (Lidocaine) to numb the area, oral anxiolytics (ie. Ativan) and /or pain medications (Toradol) may also be utilized per the PI discretion.

The treating investigator will determine the parameters used for treatment with the UltraClear 2,910nm mid-infrared laser based on their clinical discretion, keeping the subject's Fitzpatrick skin type in mind (Appendix D).

For additional comfort, cold air cooling (Zimmer MedizinSystems,; Irvine, CA) may be utilized throughout the treatment. After treatment subjects will be provided with post care instructions as well as the specific skin care regimen.

Treatment characteristics including treatment time and laser parameters will be recorded. Additionally, the Comfort Level Visual Analog Scale (VAS) will be completed by the study subject after the treatment using a 0 to 10 score, with 0 signifying no pain and 10 signifying significant pain (Appendix B). Procedure-related side effects and adverse events will be evaluated and recorded by the investigator following treatment and at each subsequent visit (Appendix A). Post-procedure care instructions will be reviewed and provided in writing to each subject after treatment (Appendix B).

Following treatment, subjects will have a 1-week follow up visit (virtual or in-person pending PI discretion) at Day 7 (± 3 days), 7-week follow-up (± 7 days) with potential 2nd treatment (pending PI discretion), 1-month follow-up (± 7 days) for subjects receiving a second treatment, and 3-month follow-up(± 7 days) for both treatment groups for post-procedure assessments and to complete questionnaires. Following the completion of the 3-month follow-up, subjects will be exited from the study. Assessment of Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) will be made at baseline and the 3-month follow-up, PGAIS and Percent Improvement will be completed at the 3-month follow-up by the investigator (Appendix A). Three sourced blinded, board-certified dermatologists or plastic surgeons or other qualified clinicians (Independent Photographic Reviewers [IPRs] using the PGAIS and Percent Improvement will assess randomized baseline and 3-month follow-up images (Appendix A).

4. STUDY POPULATION

Male and female adult subjects of Fitzpatrick skin types I-IV and aged 50-80 years who meet all inclusion and no exclusion criteria.

4.1. Number and Subject Compensation

20 subjects will be enrolled. No cost compensation will be provided to the enrolled participants. No remuneration will be offered for treatment visits.

4.2. Inclusion Criteria:

a. Fitzpatrick skin type I-IV.

b. Male or female.

c. Subjects must be between 50 and 80 years of age.

d. Subjects must have the ability to receive up to two full face resurfacing laser treatment with specific focus on advanced perioral lines and wrinkles.

e. Subjects must read, understand, and sign the Informed Consent Form.

f. Subjects must be willing and able to comply with all follow-up visit requirements.

g. Subjects must agree to refrain from using cosmeceutical agents or topical agents during the study, except as directed by study investigator.

h. Subjects must be rated as Class II or Class III based on the Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS).

i. Subject identified as an appropriate candidate for study treatment based on principal investigator's opinion.

j. Subjects of childbearing potential have been on an acceptable form of contraception for 30 days prior to enrollment and agree to continue using throughout the course of the study.

4.3. Exclusion Criteria:

a. Subjects must not have active localized or systemic infections.

b. Subjects must not have a compromised ability for wound healing, such as: malnutrition, steroid use, history of collagen vascular disease (e.g., lupus, scleroderma, history of keloid scar formation), atrophic dermatitis or immunologic abnormalities such as vitiligo.

c. Subjects must not have had treatments with 5FU, diclofenac, imiquimod, steroids, retinoids, or PDT within 1-month prior to enrollment.

d. Subjects must not currently be taking Accutane or have taken Accutane within the last 1-month.

e. Subjects must not have a known allergy to lidocaine or epinephrine, topical or injectable products containing lidocaine or any numbing medications.

f. Subjects must not have had previous surgery and/or fat transfer in the treatment area within the last 6-months.

g. Subject must not have had injectable soft tissue fillers within the last 12 months in the treatment area.

h. Subject must not have had Poly-L-Lactic acid (PLLA) fillers within the last 2 years in the treatment area.

i. Subject must not have had permanent filler i.e., Polymethylmethacrylate (PMMA) in the treatment area.

j. Subjects must not have had neurotoxins within the last 3-months in the treatment area.

k. Subject must not have a personal history of any facial threads i.e., PDO (Polydioxanone), PLLA (Polylactic acid), PCL (Polycaprolactone) in the treatment area within the last 12 months.

l. Subject must not have had a pulse dye or vascular laser, non-ablative laser, microneedling, or energy-based device treatment in the treatment area within the last 3 months.

m. Subject must not have had an ablative laser treatment in the treatment area within the last 6 months.

n. Subjects must not have a personal history of malignant melanoma, keloid scars, generalized psoriasis or systemic diseases that would preclude the use of topical anesthesia.

o. Subject must not have active sunburn or excessively tanned skin.

p. Subjects must not be pregnant or breastfeeding, think they may be pregnant or are trying to get pregnant during the study.

Subjects may not participate in the study if they are pregnant. If subjects are of childbearing potential, they will be asked to confirm they are not pregnant at screening, treatment visit(s) and day 90 (1 Treatment Group) or day 139 (2 Treatment Group), and that they do not plan to become pregnant for the duration of the study.

5. MATERIALS AND METHODS

5.1. Procedure Overview:

After completing the informed consent process as well as confirming fulfillment of all inclusion and no exclusion criteria, each subject will be enrolled in the trial.

1) A thorough review of the subjects' medical history and concomitant medications will be completed at each visit.
2) If applicable, a urinary pregnancy test will be completed at the screening/treatment day visit prior to application of topical numbing cream or any procedure.
3) Photographs will be completed at all visits. If a procedure will be completed during a visit, all photography will be completed prior to any procedure.
4) At the screening/treatment day visit as well as at the 3-month follow-up visit, the investigator will complete the Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) (Appendix A).
5) At the screening/treatment day visit and 3-month follow up visit, subjects will complete a Subject Perioral Questionnaire (Appendix B)
6) Following completion of the investigator and subject surveys, the treatment areas will be numbed with a thin coat of BLT topical anesthetic (consisting of 20% Benzocaine, 6% Lidocaine 6% Tetracaine) tetracaine for 30-45 minutes.
7) Prior to treatment, the topical anesthetic will be removed, and the skin surface will be cleansed with Hibiclens® (chlorhexidine gluconate solution 4% Mölnlycke Health Care AB; Gothenburg, Sweden) or 70% isopropyl alcohol at the discretion of the treating investigator.
8) UltraClear laser treatment: The treating investigator will determine the parameters used for treatment with the UltraClear 2,910nm mid-infrared laser based on their clinical discretion, keeping the subject's Fitzpatrick skin type in mind (Appendix A). To begin treatment, the handpiece will be brought into contact to the skin surface. The exposure will be performed holding the handpiece in one location steady with no movement for the entire duration of the laser emission delivery. Continuing treatment, the investigator will move the handpiece to next adjacent location with minimal space between the stamp for repeating the same cycle, until the entire treatment area is covered with the desired treatment coverage. For additional comfort, cold air cooling (Zimmer MedizinSystems, Irvine, CA) may be used throughout the treatment.

9) Following the UltraClear laser treatment, the subject will be provided with cooling packs for additional comfort to cool the skin surface post procedure at PI discretion.
10) After treatment the subject will complete a Comfort Level Visual Analog Scale for the treatment area.
11) After the treatment session, the subject will be provided post-procedure instructions.
12) After treatment and at each of the following coinciding visits, the investigator will evaluate for any anticipated post treatment responses and/or adverse events.
13) Scheduling of follow-up visits will be confirmed for the following treatment groups:
    a. 1 Treatment Group: 1-week (virtual or in-person), 7-week, 3-month follow up.
    b. 2 Treatment Group: 1-week (virtual or in-person), 7-week + 2nd Treatment, 1-month follow up, 3-month follow up.
14) At the 3-month follow-up visit the following will be completed (Appendix A & Appendix B):
    a. Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) by investigator
    b. Physician Global Aesthetic Improvement Scale (PGAIS) by investigator
    c. Percent Improvement Evaluation by investigator
    d. Subject Perioral Questionnaire by subject
    e. Subject Global Aesthetic Improvement Scale (SGAIS) by subject
    f. Subject Satisfaction Questionnaire by subject
15) Following the 3-month follow-up visit, study photos will be compiled, randomized, and sent to blinded IPRs and appropriate study assessments will be completed.

5.2. Study Photography:

Prior to treatment, VISIA Imaging and IntelliStudio photographs (Canfield Scientific, Parsippany, NJ) will be taken, capturing five (5) views: left profile, left oblique, anterior, right oblique, right profile (Appendix C). Subjects must remove all makeup and the face must be thoroughly cleaned at least 15 minutes prior to having photographs taken to ensure makeup, lotions, and/or sunscreens will not interfere with any evaluations. Subjects must remove all jewelry prior to photos. Subjects' hair must be secured away from the face with a black headband ensuring any stray hairs are not on the face). Standard high resolution 2D photography will be taken at every visit.All photography will be compared from baseline pre-treatment photos to treatment photos throughout the study.

5.3. Concomitant Medications:

Systemic and topical medications being used at baseline are considered necessary for the subject's welfare and will not interfere with the study or interact with the study treatment may be used. Administration of these drugs must be reported on the appropriate case report form and any alterations in the use of medication during the study should be carefully noted. All systemic and topical medications that the subject receives during the study will be recorded. Any alterations will be noted.

5.4. Publication Plan:

Manuscripts and abstracts may be prepared by the investigator. Publication of the study results in scientific journals will be pursued following completion of the study report and submission of the report to the appropriate regulatory authorities. It is the interest of the principal investigators to publish or present the study results.

6. CLINICAL ASSESSMENT

6.1. Schedule of Visits and Measurements

The length of enrollment period for all subjects will be 2-months. The length of treatment period (time in which the single treatment may be scheduled and performed) for one subject will be approximately 1-month. The follow-up period for one subject will be 3-months following the 1st or 2nd Treatment (number of treatments pending PI discretion).

Visit Procedures	Visit 1 Screening Visit	Visit 2 Day 0 1st Tx Day	Visit 3 Day 7 (± 3 days) 1-Week Follow-Up (Virtual or In-Person)	Visit 4 Day 49 (± 7 days) 7-Week Follow-Up *2nd Tx Day (pending PI discretion)	Visit 5* Day 79 (± 7 days) 1-Month Follow Up *2 Tx Group Only	Visit 6 Day 90* Day 139** (± 7 days) 3-Month Follow-Up *1 Tx Group **2 Tx Group
Informed Consent	X					
Review Inclusion / Exclusion Criteria	X					
Review Medical History and Concomitant Medications	X	X	X	X	X	X
Urinary Pregnancy Test (if applicable)	X	X		X * If Treatment Performed		X
Perioral Questionnaire by Subject	X	X				X
Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS)	X	X		X * If Treatment Performed		X
VISIA Imaging & IntelliStudio Photography	X	X	X	X	X	X
UltraClear Laser Treatment		X		X* Pending PI Discretion		
Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator		X	X	X	X	X

Comfort Level Visual Analog Scale Post-Procedure by Subject		X		X* If 2nd Tx Performed		
Subject Post-Procedure Instructions & Post Care Products Dispensed		X		X* If 2nd Tx Performed		
Physician Global Aesthetic Improvement Scale (PGAIS)						X
Percent Improvement Evaluation by Investigator						X
Subject Global Aesthetic Improvement Scale (SGAIS)						X
Subject Satisfaction Questionnaire						X

Visit 1 (Screening): Day 0 or -30 Days:

1) Informed consent form
2) Review inclusion/exclusion criteria; subject will be enrolled in the study upon verification of meeting inclusion/no exclusion criteria
3) Review medical history and concomitant medications
4) Urine pregnancy test (if applicable)
5) Fitzpatrick Wrinkle Scale FWS by investigator
6) Perioral Questionnaire by subject
7) Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured

Visit 2 – Treatment (Day 0, can be same day as screening visit):

*If treatment occurs on Day 0, the forms/activities below do not need to be duplicated

1) *Review of medical history and concomitant medications
2) *Urine pregnancy test (if applicable)
3) *Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) by investigator
4) *Perioral Questionnaire by subject
5) * Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured
6) UltraClear Laser Treatment
7) Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator
8) Comfort Level Visual Analog Scale post-procedure by subject
9) Subject Post-Procedure Instructions and post-care products provided

Visit 3 – 1-week follow up Day 7 (± 3 days)

1) Review medical history and concomitant medications
2) Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured if in person
3) Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator

Visit 4 – 7-week follow-up Day 49 (± 7 days) & 2nd Treatment Pending PI Discretion**

1) Review medical history and concomitant medications
2) Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured
3) **UltraClear Laser Treatment (pending PI discretion)
4) Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator
5) **Comfort Level Visual Analog Scale post-procedure by subject
6) ** Subject Post-Procedure Instructions and post-care products provided

****Visit 5 – 1-month follow-up Day 79** (± 7 days) **for 2 Tx Group Only**

1) Review medical history and concomitant medications
2) Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured
3) Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator

Visit 6 – 3-month follow-up, 1 Tx Group Day 90 / 2 Tx Group Day 139 (± 7 days)

1) Review medical history and concomitant medications
2) Clinical Photography: VISIA Imaging and IntelliStudio Photographs captured
3) Evaluation of Anticipated Post Treatment Responses and Adverse Events by investigator
4) Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) by investigator
5) Physician Global Aesthetic Improvement Scale (PGAIS) by investigator
6) Percent Improvement Evaluation by investigator
7) Perioral Questionnaire completed by subject
8) Subject Global Aesthetic Improvement Scale (SGAIS) by subject
9) Subject Satisfaction Questionnaire by subject

Blinded Independent Photographic Reviewers (IPRs)

Assessment of each subjects' baseline and follow-up images viewed simultaneously will be performed by the IPRs who will be blinded to the study subject's visit (baseline and follow-up). Each IPR will view each set of randomized images and assess which set represent the subject's post treatment images. A subject will be considered a success if at least 2 out of the 3 IPRs correctly identify the follow-up image. The following assessments will be completed by the IPRs for each study subject:

- Physician Global Aesthetic Improvement Scale (PGAIS)
- Percent Improvement Evaluation

6.2. Study Period

Enrollment and follow-up are expected to take up to 8 months. The follow-up period for one subject will be three (3) months.

6.3. Study Completion / Exit Criteria

Subject Completion of Study

If a subject has completed the final study visit: 1 Tx Group (Day 90) or 2 Tx Group (Day 139), they are considered to have completed the study.

Subject Discontinuation
Each subject may voluntarily discontinue the study at any time if they choose. Subjects who cannot complete the study for administrative reasons (e.g., non-compliance, failure to meet visit schedule, etc.) will be discontinued from the study. Subjects discontinued during the enrollment period of the study will be replaced.

Subject Termination
Subjects experiencing moderate to severe adverse events of definite, probable, or unknown relationship to UltraClear laser treatment may be discontinued at the discretion of the investigator.

A subject will receive appropriate treatment at the discretion of the investigator and will be terminated from using the treatment. Notification of termination will be clearly documented on the appropriate case report form. These subjects will be immediately moved to visit 5 for follow-up.

Study Termination
The investigator, with appropriate notification to the Sponsor and subjects, may terminate the study. If, after clinical observations, the investigator feels that it may be unwise to continue the study, he or she may stop the study after discussion with the Sponsor.

Study Completion
The study will be complete when 20 subjects have completed study visit 6: 1 Tx Group (Day 90) or 2 Tx Group (Day 139), thereby exiting or have been terminated from the study.

7. POTENTIAL RISKS AND BENEFITS

7.1. Side Effects

To evaluate the safety of the treatment, side effects (prolonged erythema, prolonged edema, post-inflammatory hyperpigmentation, etc.) are scored, as appropriate, using a scale of 0 to 4. (0 = none; 1 = trace; 2 = mild; 3 = moderate; 4 = severe) – Appendix A.

7.2. Potential Risks

Risks and discomforts for subjects who participate in this study are the same as for subjects undergoing any dermatological laser treatment. Eye injury due to use of the laser system is a risk to the subject and the operator. Appropriate eye protection will be used to minimize that risk.

The possible side effects and risks associated with the UltraClear laser treatment of the skin are as follows:

a) Pain (during or immediately following treatment)
b) Erythema (redness) of treated skin
c) Edema (swelling) and inflammation of treated skin
d) Dryness, itchiness, and desquamation (sloughing) of treated skin
e) Dyspigmentation/skin color changes of treated area (hyperpigmentation, hypopigmentation)
f) Blistering
g) Burn
h) Scarring
i) Skin crusting
j) Bruising/petechiae or a purple discoloration of the treated area
k) Bleeding
l) Infection
m) Delayed wound healing
n) Acne flare

o) Herpes simplex virus (HSV) flare
p) Eye injury
q) Melasma exacerbation
r) Allergic reaction to topical and injectable anesthesia

If hyperpigmentation occurs, hydroquinone or a brightening agent will be provided. Investigators may instruct subjects to apply twice per day in addition to re-applying SPF 50+ daily.

Though unexpected, there is a risk of infection whenever the skin is wounded, e.g., during laser treatment. In cases of possible infection, the study investigator may provide topical antibiotics (erythromycin, bacitracin or similar ophthalmic ointment) for management of the symptoms.

7.3. Unknown / Unforeseeable

In addition to the risks listed above, there may be some unknown or infrequent and unforeseeable risks associated with the use of the UltraClear laser system and subjects will be informed both verbally and in writing in a timely manner of any new information, findings, or changes to the way the research will be performed that might influence their willingness to continue their participation in this study.

Pregnancy/Fetal Risks: The effects of the UltraClear laser system, use of topical anesthetics, as well as the post-treatment skincare regimen have not been studied in pregnancy and therefore may be hazardous.

If a subject thinks they may be pregnant or have become pregnant during the study, the subject is to inform the study investigator immediately. If a subject becomes pregnant or thinks they may be pregnant, they will be removed from the study, the study investigator will refer the subject to seek obstetric care, will request to track their pregnancy, and will report the pregnancy to the Sponsor and the Institutional Review Board (IRB).

Subjects may or may not benefit from the laser treatment. It is possible that no significant reduction in the number of actinic lesions will be observed. If that is the case, other treatment modalities will be recommended by study investigators.

8. RESPONSIBILITIES OF THE INVESTIGATOR

8.1. Site / Investigator Criteria

The study will be conducted at Dermatology & Laser Surgery Center – Paul M. Friedman, M.D. (Houston, TX). This site was chosen due to the established expertise of the clinical investigator and site staff with fractional technology, laser resurfacing, treatment of photodamaged skin, and their committed interest in developing new technologies. Several investigators may contribute to the research taking place at this site, and, as such, are listed as sub-investigators for the study.

Principal Investigator: Paul M. Friedman, M.D. (Houston, TX)
Curriculum vitae for the investigator will be provided to the Institutional Review Board as required.

8.2. Adherence to the Study Protocol

The investigator must ensure adherence to the procedures outlined in this Study Protocol. The procedures set out in this study protocol, pertaining to the conduct, evaluation, and documentation of this study are designed to ensure that the investigator abides by Good Clinical Practice (GCP) as described in the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guidelines Topic E6 “Guideline for Good Clinical Practice.”

Compliance with these regulations also constitutes compliance with the ethical principles described in the current version of the Declaration of Helsinki. The study will also be carried out in keeping with local legal and regulatory requirements.

The investigator is obligated to follow the protocol without departure from the requirements written in the protocol. If the investigator deviates from the protocol requirements, the Sponsor will make the determination as to whether the subject will continue in the study. The Sponsor also has the right to discontinue the subject for protocol violations. The IRB may also have to be contacted if safety to the subject or if the scientific soundness of the study is involved. All protocol deviations must be documented in the CRFs and reported to the Sponsor as soon as possible.

8.3. Data Handling and Record Keeping

All study documentation at the investigation site will be archived in accordance with ICH GCP E6.

The designated clinical monitor is:

Shlomo Assa
President and CTO
Acclaro Corporation
333 George Washington Hwy
Smithfield, RI 02917

9. REGULATORY OBLIGATIONS

This study is to be conducted in accordance with the specifications of this protocol and in accordance with principles consistent with the Declaration of Helsinki, Good Clinical Practice (GCP), 21 CFR 312, ICH E6, HIPPA regulations in 45 CFR Part 164, and the Belmont Principles of respect for persons, beneficence, and justice. No protocol changes will be implemented without the prior review and approval of the IRB, except where it may be necessary to eliminate an immediate hazard to a research subject. In such a case, the change will be reported to the IRB as soon as possible, in accordance with IRB regulations. Additionally, all study products used in this study are manufactured, handled, and stored in accordance with applicable Good Manufacturing Practices (GMP) and the products provided for this study will be used only in accordance with this protocol.

Institutional Review Board: The study protocol, informed consent forms (all versions), and any specific advertising will be submitted to and approved by the IRB before the start of the study. A form must be signed by the chairman or designee of the IRB noting the approvals. This notification will be provided to the sponsor for informational purposes. It is the investigator's responsibility to submit reports to the IRB per the IRB's requirements.

Protocol: The investigator signing the protocol signature page will act as the principal investigator. Protocols will be noted as approved by the investigator by placement of his or her signature on the investigator's signature page. Copies of the IRB approved protocol and informed consents should be provided to the funding Sponsor for informational purposes.

Informed Consent Form: An Informed Consent Form (ICF) document that includes all the relevant elements currently required by FDA and/or state regulations will be provided to each prospective study subject at screening and before enrollment into the study. The type and method of study, any potential or possible hazards, and the subject's right to withdraw from the study at any time will be explained to the subjects by the investigator or designee.

In obtaining and documenting informed consent the investigator must comply with applicable regulatory requirements and must adhere to GCP. Evidence of GCP training is required for all investigators. The investigator, or designee, must fully inform subjects of all pertinent aspects of the study. Before informed consent may be obtained, the investigator, or a person designated by the investigator, must provide the subject ample time and opportunity to inquire about details of the study and to decide whether to participate in the trial. All questions about the trial must be answered to the satisfaction of the subject. Prior to the subject's participation in the trial, the written informed consent must be signed and personally dated by the subject and by the person who conducted the informed consent discussion.

A copy of the IRB approved ICF form will also be provided to the Sponsor for informational purposes.

Protocol and Informed Consent Changes: Changes to the protocol or informed consent form(s) will be implemented as amendments to the original document following discussion with the Sponsor and approved by the IRB. The approval will be processed in accordance with the established IRB procedures. Copies of all protocol and informed consent form(s) amendments/revisions, along with letters noting IRB approval, should be submitted to the Sponsor, as this may affect safety. Any addenda, amendment, or revision that substantially alters the study design or increases potential risk to the subject requires the subject's consent to continue in the study.

Investigational Product Accountability: The investigational product to be used for this study is the sole property of the Sponsor. All provided products to be used for this study and their receipt, inventory, dispensing, and reconciliation records will be maintained in compliance with Federal Regulations. The study supplies will be dispensed by the investigator or designee to qualified study subjects according to established procedures. Upon completion or termination of the study, the site will be responsible for retaining all partial and unused products under FDA regulations.

Study Monitoring: All monitoring activities are the responsibility of the clinical site. Monitoring is for the purpose of confirming adherence to the protocol and to verify complete and accurate data collection. The site will be responsible for internal verification of data throughout the study.

10. CONFIDENTIATIY OF RECORDS

Information about the subject's health taken during this study may be used and given to others by the study coordinators, the medical staff, and the respective study center and by the subject's physician and their other health care providers (together, called "providers"). These providers may share health information about the subject with the study coordinator. The study coordinator and the providers may share that information with researchers participating in this study and laboratories conducting tests for this study. A final study report will be shared with the Sponsor, FDA; Department of Health and Human Services (DHHS) agencies; other U.S. and foreign government agencies that watch over quality, safety, and effectiveness of research.

11. DELEGATION OF INVESTIGATOR RESPONSIBILITIES

The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, any amendments to the protocol, the study treatments, and their trial-related duties and functions. The investigator should maintain a list of co-investigators and other appropriately qualified persons to whom he or she has delegated significant trial-related duties, and this list should be provided to the Sponsor and updated regularly.

12. DIRECT ACCESS TO SOURCE DATA / DOCUMENTS

The investigator must ensure that institutional regulations, the Informed Consent Form, and the HIPAA Authorization clearly permit study-related monitoring, audits, IRB review, and regulatory inspections providing direct access to source data and documents.

13. ADVERSE EVENT AND REPORTING

An adverse event (AE) is defined as any unfavorable or unintended sign, symptom, or disease that occurs or is reported by the subject to have occurred, or a worsening of a pre-existing condition. An AE may or may not be related to the treatment regimen. All AEs and intercurrent illnesses must be recorded in the subject's medical records and case report form (CRF).

The investigator is responsible for assessing the relationship of the adverse event to the treatment, and the seriousness and expectedness of the adverse event at the time of occurrence. A medically qualified person appointed by the Sponsor will also assess this, once the Sponsor has been notified of an AE. All AEs that occur during the trial will be documented on the supplied adverse event forms. When possible, relevant hospitalization summaries (admission and/or discharge summaries), diagnostic reports, and laboratory reports should be obtained.

A serious adverse event (SAE) is any untoward medical occurrence, that, at any dose:

s) Results in death;
t) Is life-threatening;
u) Requires in-subject hospitalization or prolongation of existing hospitalization;
v) Results in persistent or significant disability/incapacity;
w) Is a congenital anomaly/birth defect;
x) Or is an important medical event

An unexpected adverse event is any treatment-related adverse event, which is not identified in nature, severity, or frequency in current literature on the test product.

Any serious adverse event occurring in this study must be reported to the IRB and the Sponsor within 24 hours of awareness of the event. Initial reports must be made by telephone, followed by the completion of a Serious Adverse Event Report and submission by facsimile.

Throughout the study, subjects will be monitored for signs and symptoms of adverse events. An adverse event is any pathological or unintended change in structure, function, or chemistry of the body that occurs during the study, irrespective of causality, including any illness, injury, toxicity, sensitivity, or sudden death. The condition must either not be present pre-study or must worsen in either intensity or frequency during the study.

All adverse events, including serious and treatment related or unexpected adverse events, must be recorded by the investigator. Serious and unexpected device-related adverse events should be reported immediately to the Sponsor.

Subjects who have had a serious adverse event must be followed clinically until a
parameters, including laboratory values, have either returned to normal or are otherwise explained.

If death was the outcome of the event on the initial SAE Report, a follow-up/final report including autopsy report, when performed, must be completed.

Adverse events will be assigned a relationship (causality) to the treatments. The investigator will be responsible for determining the relationship between an AE and the treatment. The type of event,

organ system affected, and timing of onset of the event will be factors in assessing the likelihood that an AE is related to the treatment. Relationship of AEs to study products will be classified as follows:

A. Not related: No relationship exists between the AE and the treatment. The event is attributed to a pre-existing medical condition or an intercurrent event unrelated to the study product.
B. Possibly related: Follows the treatment but may have developed as a result of an underlying clinical condition or treatments/interventions unrelated to the study product.
C. Probably related: Follows the treatment but is unlikely to have developed as a result of the subject's underlying clinical condition or other treatment or other interventions.
D. Definitely related: Follows the treatment and physical evidence shows a convincing relationship to the treatment.
E. Unknown: Follows the treatment, but unable to determine the relationship to the treatment.

14. REFERENCES

1) Dixon JR Jr. The International Conference on Harmonization Good Clinical Practice guideline. Qual Assur. 1998 Apr-Jun;6(2):65-74. doi: 10.1080/105294199277860. PMID: 10386329.
2) Manstein D, Herron GS, Sink RK, Tanner H, Anderson R. Fractional Photo: A New Concept for Cutaneous Remodeling Using Microscopic Patterns of Thermal Injury. Lasers Surg Med 2004. 34(5): 426-38.
3) Hegedus F, Diecidue R, Taub D, Nyirady J. Non-surgical treatment modalities of facial photodamage: practical knowledge for the oral and maxillofacial professional. Int J Oral Maxillofac Surg. 2006 May;35(5):389-98.
4) Alexiades-Armenakas MR, Dover JS, Arndt KA. The spectrum of laser skin resurfacing: nonablative, fractional, and ablative laser resurfacing. J Am Acad Dermatol. 2008 May;58(5):719-37.
5) ROBERT BOWEN, MD. Periorbital Rejuvenation with the Contour TRL™and ProFractional-XC™ Laser Devices

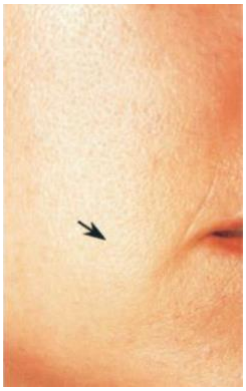
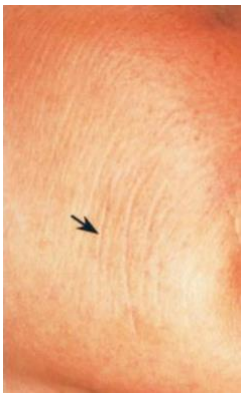
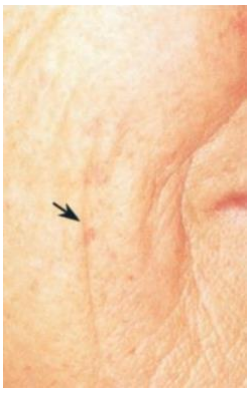
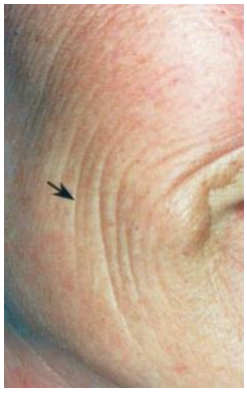
APPENDIX A – INVESTIGATOR SURVEYS / ASSESSMENTS

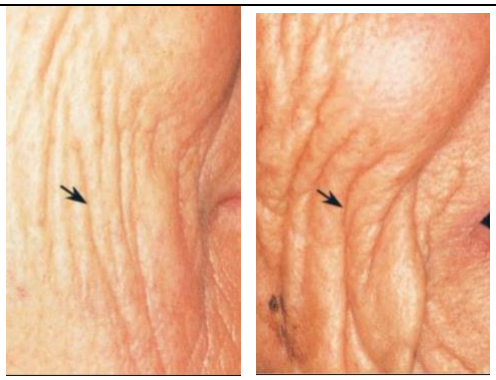
1. Fitzpatrick Skin Type Assessment (FST)

Fitzpatrick Skin Type (circle one)	Description
Type I	Always burns, never tans
Type II	Usually burns, tans less than average (with difficulty)
Type III	Sometimes burns, tans about average
Type IV	Rarely burns, tans more than average (with ease)
Type V	Very rarely burns, tans very easily
Type VI	Does not burn, tans very easily

Investigator Signature: _____ **Date:** _____/_____/_____
MM DD YYYY

2. **Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS)**

Fitzpatrick Wrinkling and Degree of Elastosis Scale (FWS) **For each subject, select ONE class and ONE score based on the scale below:**				
Class	**Wrinkling**	**Score**	**Degree of Elastosis**	**Photographic Examples**
I	**Fine Wrinkles**	**1-3**	**Mild (fine textural changes with subtly accentuated skin lines)**	**Score: 1**  **Score: 3** 
II	**Fine to moderate deep wrinkles, moderate number of lines**	**4-6**	**Moderate (distinct popular elastosis (individual papules with yellow translucency under direct lighting and dyschromia)**	**Score: 4**  **Score: 6** 
III	**Fine to deep wrinkles, numerous lines with or without redundant skin folds**	**7-9**	**Severe (multipapular and confluent elastosis (thickened yellow and pallid) approaching or consistent with**	**Score: 7** **Score: 9**

			cutis rhomboidalis)	

Adapted from: Fitzpatrick RE, Goldman MP, Satur NM, et al. Pulsed carbon dioxide laser resurfacing of photo-aged facial skin. Arch Dermatol. 1996;132(4):395-402. And Lemperle G, Holmes RE, Cohen SR, et al. A classification of facial wrinkles. Plast Reconstr Surg. 2001;108(6):1735-1750.

3. Evaluation of Anticipated Post Treatment Responses and Adverse Events Assessment

Evaluation of Anticipated Post Treatment Responses and Adverse Events To be completed by treating investigator	
Rating	**Description**
0	**NONE:** Normal
1	**TRACE:** Barely visible and localized
2	**MILD:** Somewhat visible and diffuse
3	**MODERATE:** Visible and diffuse
4	**SEVERE:** Extremely visible and dense
SCORES (check a box for each anticipated post treatment response):	
ERYTHEMA	
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)	
EDEMA	
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)	
HYPERPIGMENTATION	
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)	

HYPOPIGMENTATION
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
BLISERING
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
BURN
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
SKIN CRUSTING
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
SCARRING
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
BLEEDING
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
BRUISING / PETECHIAE
☐ 0 (None) ☐ 1 (Trace) ☐ 2 (Mild) ☐ 3 (Moderate) ☐ 4 (Severe)
Investigator Signature: _____ **Date:** _____/_____/_____ **MM DD YYYY**

4. **Physician Global Aesthetic Improvement Scale (PGAIS)**

Physician Global Aesthetic Improvement Scale Assessment (PGAIS) **To be completed by investigator and Independent Photographic Reviewer(s)**	
Rating	**Description**
4	Very much improved, optimal cosmetic result, very significant (76%-100% improvement)
3	Much improved, marked improvement in appearance from the initial condition, but not completely optimal, marked (51%-75%)
2	Improved, obvious improvement in appearance from the initial condition, but a retreatment is needed, moderate (26%-50%)
1	Mild improvement, some mild improvement in appearance from the initial condition is noted, minor (1%-25%)
0	No change, the appearance is essentially the same as the original condition, no improvement (0%)
PERIORBITAL SCORE (check a box below)	
☐ **4 (Very Much Improved)** ☐ **3 (Much Improved)** ☐ **2 (Improved)** ☐ **1 (Mild Improvement)**	

☐ **0 (No Change)**
Investigator Signature: _____ Date: _____/_____/_____ **MM DD YYYY**

5. Percent Improvement Evaluation

Percent Improvement Evaluation **To be completed by investigator and blinded investigator**
Degree of improvement from clinical evaluation, compare to baseline using a 1-10 scale. ☐ **1** (0-10%) ☐ **2** (10-20%) ☐ **3** (20-30%) ☐ **4** (30-40%) ☐ **5** (40-50%) ☐ **6** (50-60%) ☐ **7** (60-70%) ☐ **8** (70-80%) ☐ **9** (80-90%) ☐ **10** (90-100%)
Investigator Signature: _____ Date: _____/_____/_____ **MM DD YYYY**

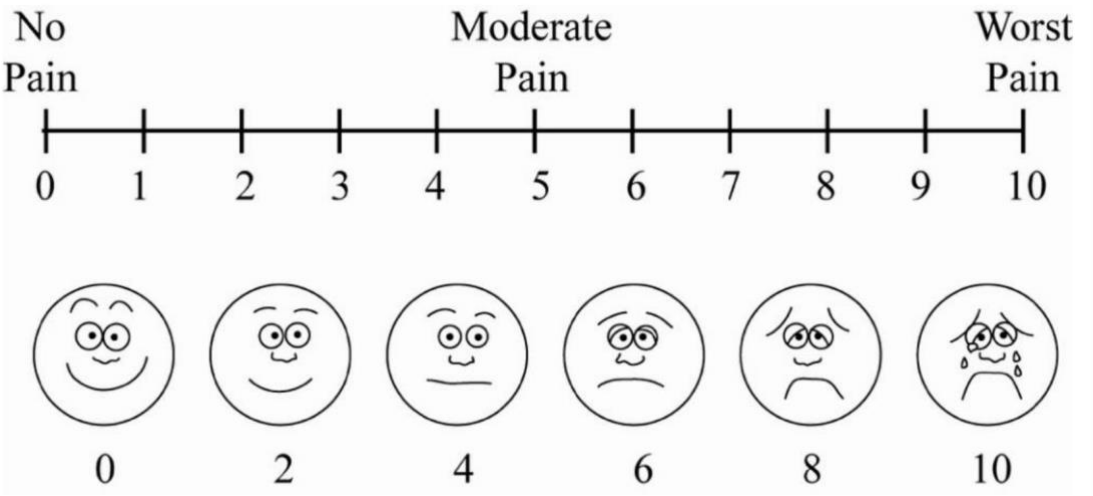
APPENDIX B – SUBJECT SURVEYS / ASSESSMENTS

1. Perioral Questionnaire

Subject Perioral Questionnaire Questionnaire to be completed by subject at Baseline (Day 0) and 3-Month Follow-Up				
When thinking of how your perioral regions (area around your mouth) look NOW, rate how BOTHERED you are by the following:				
	Not At All	A Little	Moderately	Extremely
Crepey (wrinkled) skin around my mouth	1	2	3	4
Vertical lip lines above upper lip	1	2	3	4
Deep lines and wrinkles around my mouth	1	2	3	4
Jowls / facial sagging around my mouth	1	2	3	4
The downward shape of mouth	1	2	3	4
When thinking about how your perioral regions (area around your mouth) looks NOW, answer the following question:				
	Not At All	A Little	Moderately	Extremely

How YOUTHFUL does the area around your mouth makes you look?	1	2	3	4
Subject Initials: _____ Date: _____ /_____/ _____ MM DD YYYY				

2. Comfort Level Visual Analog Scale Post Treatment

Visual Analog Scale **To be completed by subject**
Instructions: Pain at the treatment site is assessed immediately after treatment and 15 minutes after the treatment. Please use a VAS plastic ruler with a 100 mm long line with the left end representing "no pain" and the right end representing "unbearable pain" and a slider. Using the VAS plastic ruler, please report a vertical mark to show the location on the line that represents your level of pain. Please enter the units below in millimeters noted on the ruler at each time point for the treatment area.


Immediately after treatment	_____	_____	_____/_____/_____			___:___
		Patient Initials	MM	DD	YY	HH:MM
15 mins after treatment	_____	_____	_____/_____/_____			___:___
		Patient Initials	MM	DD	YY	HH:MM

3. Subject Global Aesthetic Improvement Scale (SGAIS)

Subject Global Aesthetic Improvement Scale Assessment (SGAIS) How would you rate the improvement of the treatment area? ***To be completed by subject***	
Rating	**Description**
4	Very much improved, optimal cosmetic result, very significant (76%-100% improvement)
3	Much improved, marked improvement in appearance from the initial condition, but not completely optimal, marked (51%-75%)
2	Improved, obvious improvement in appearance from the initial condition, but a retreatment is needed, moderate (26%-50%)
1	Mild improvement, some mild improvement in appearance from the initial condition is noted, minor (1%-25%)
0	No change, the appearance is essentially the same as the original condition, no improvement (0%)
PERIORBITAL SCORE (check a box below)	
☐ **4 (Very Much Improved)** ☐ **3 (Much Improved)** ☐ **2 (Improved)** ☐ **1 (Mild Improvement)**	

☐ **0 (No Change)**
Subject Initials: _____ Date: _____ /_____/ _____ MM DD YYYY

4. Subject Satisfaction Questionnaire

Subject Satisfaction Questionnaire How would you rate your satisfaction of your treatment? ***To be completed by subject***	
Rating	**Description**
5	**Very Satisfied**
4	**Satisfied**
3	**Somewhat Satisfied**
2	**Slightly Satisfied**
1	**Not Satisfied**
PERIORAL SCORE (check a box below)	
☐ **5 (Very Satisfied)** ☐ **4 (Satisfied)** ☐ **3 (Somewhat Satisfied)** ☐ **2 (Slightly Satisfied)** ☐ **1 (Not Satisfied)**	

Subject Initials: _____	Date: _____ /_____/ _____ MM DD YYYY

ULTRACLEAR PRE AND POST PROCEDURE PATIENT INSTRUCTIONS

Please bring a big hat and sunglasses to your appointment

- Hydrate well by drinking water prior to your procedures (ideally 6-8 (8oz) cups per day).
- Preventatively to reduce the risk of cold sores, antiviral prophylaxis medication (ie. Valtrex or similar) has been prescribed please take this medication day of procedure. This medication is for patients undergoing a deeper treatment or having a history of herpes simplex (cold sores) to avoid outbreaks.
- Avoid any prolonged (over 30 minutes) direct sun exposure for at least 1 month before your procedure. If unable to avoid sun, seek shade, wear large hats and reapply SPF 30+ multiple times daily.
- Removal all substances from the intended treatment area, including topical anesthetics, makeup, lotions, self-tanning products, and ointments.
- Remove all jewelry prior to your visits and consider wearing comfortable clothing.

INTRAOPERATIVE CARE

- Safety considerations are important during the laser procedure. Protective eye wear will be worn by the patient and all personnel during the procedure to reduce the chance of damage to the eye. Your provider will take all necessary precautions to ensure your safety.
- A smoke evacuator will be used to remove any smoke or debris from the air.
- Cooling air may be utilized after the procedure to soothe the skin.

POST TREATMENT CARE

- The treatment area should be cared for delicately until healing is complete. Care should be taken to prevent additional disruption to the treated area for the first 7-days following the treatment as this may prolong the healing process.

Provided Post-Care Products:

- Alastin Recovery Balm

- Gentle Cleanser (CeraVe or similar)
- Moisturizer (La Roche Posay Cicaplast Balm or similar)
- Patient responsible for purchasing and applying SPF 30+ to be used after day 4 post

Evening of Treatment:

- Apply barrier ointment (insert product) provided if skin is dry
- Do not sleep with pets and confirm sheets and pillowcases are freshly cleaned
- Sleep with head slightly elevated (ie. two pillows for support) to reduce swelling
- You may start vinegar soaks (instructions below) if it is comfortable to do so

Morning after Treatment:

- Start twice daily vinegar soaks if you did not start the day of treatment (instructions below)
- Cleanse skin using fingertips and gentle cleanser 1-2 times daily (avoid abrasive towels)
- Gently pat face to remove excess water using a soft gauze provided
- Apply barrier ointment (Alastin Recovery Balm) to entire treatment area
- You can shower starting 24 hours after your treatment. When showering avoid letting the water directly hit the treatment area. It is fine if the shower water runs down and over one's head and onto the treated skin surface.

Days 3-5 Post Procedure:

- Cleanse skin using fingertips and gentle cleanser 1-2 times daily
- Continue vinegar soaks twice daily or as needed to soothe the skin
- Apply barrier ointment (Alastin Recovery Balm) to the entire treatment area
- Transition to a unscented gentle moisturizer (ie. CeraVe). Your skin should not be dry as it prolongs healing
- Sunscreen (SPF 30+) should be applied every morning and every 1.5 hours if outdoors
- Apply ointment, such as Alastin Recovery Balm, CeraVe Healing Ointment, Aquaphor, or La Roche Posay Cicaplast Balm, as needed for dry scabby skin areas

Days 5-7 Post Procedure:

- Cleanse skin using fingertips and gentle cleanser 1-2 times daily
- Keep moisturizing and continued use of sunscreen per instructions above.
- Continue use of Alastin Recovery Balm or other such as CeraVe Healing Ointment, Aquaphor, or La Roche Posay Cicaplast Balm, as needed for dry scabby skin areas

See additional healing tips and soothing techniques on next page.

Additional Healing Tips & Soothing Techniques
• Acetic Acid Soaks (Distilled White Vinegar/Water): Mix 1 Tablespoons of distilled white vinegar with 160z of **bottled** cold water. Soak gauze (provided) with the mixture and place gently on face for 15 minutes as needed to soothe the skin. *You may repeat this process 2-3 times per day. Following soaks, re-apply the Alastin Recovery Balm.
• Swelling WILL occur and peak at 1-3 days. This is normal. • Take Zyrtec (in AM) and Benadryl (in PM) as needed for active swelling or itching. Please consult with your physician regarding associated risks including drowsiness and dry mouth.
• The redness can last much longer (sometimes weeks depending on treatment intensity). • The crusts will flake off over a period of 5 – 10 days. Do NOT scrub to remove. • As the skin heals, use a mineral sunscreen with a minimum of (SPF 30+) daily.
THINGS TO AVOID DURING THE HEALING PROCESS
• Avoid sun exposure to reduce the chances of hyperpigmentation (darker pigmentation). Always protect with sunscreen and reapply throughout the day.
• MAKE-UP: The use of makeup during the first few days is not recommended. The removal of makeup can disrupt the skin, increasing the chance for infection.
• EXERCISE / SAUNA: Excessive perspiration and heat in the treated area may cause tissue disruption. Physical exercise and excess heat (hot tubs, saunas, treadmill, yardwork etc.) should be discontinued for the first 2 – 3 days to reduce the risk of infection and discomfort.
• BATHS / SHOWERS: There are no restrictions on bathing except to treat the skin gently, avoid long hot showers or baths, avoid scrubbing or trauma to the treated areas, as if you had a sunburn. To prevent infection, regular gentle cleansing of the area is important.
• Avoid scrubs, picking at crust, exfoliating, retinoid topical creams, peels, facials, masks, and use only gentle washes for treated areas while you are healing.

- Avoid kissing pets. Wash hands well after touching pets to avoid increased risk of infection while your skin is healing. Especially, if pets are present in the home, wipe down all highly touched surfaces with disinfectant before your procedure.

Additional Notes:

_____
_____
_____
_____
_____

APPENDIX C – PHOTOGRAPHY

2D Photography

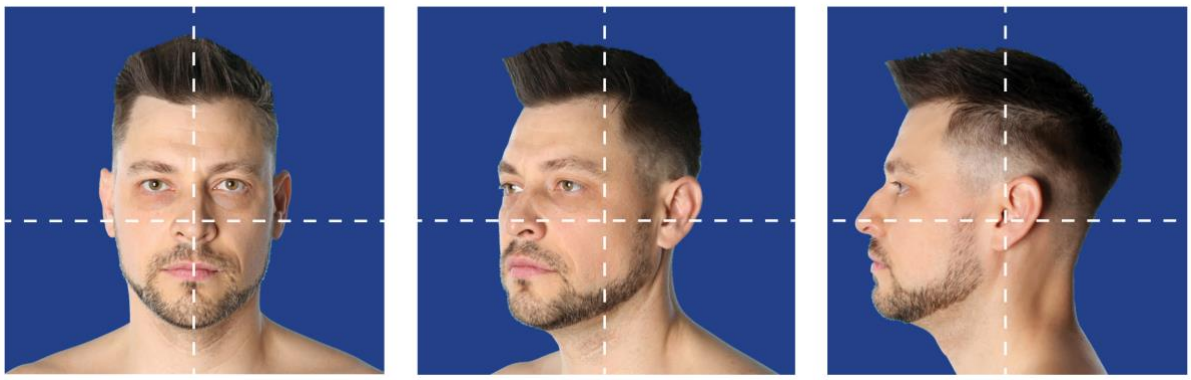
2D digital photos will be done in a standardized fashion capturing five (5) views. Subjects will stand in front of a black backdrop. Photographs will capture five (5) views: left profile, left oblique, anterior, right oblique, right profile of the face and perioral area. The camera that will be used is VISIA Skin Analysis and IntelliStudio (Canfield Scientific, Parsippany, NJ).

Please ensure the following for consistent before and after photos:

1) Subjects must remove all makeup and the face and neck must be thoroughly cleaned at least 15 minutes prior to having their photograph taken to ensure makeup, lotions and/or sunscreens will not interfere with any evaluations. Subjects will be instructed to clean with a baby wipe and dry the entire area of the face and neck.
2) Subjects must remove all jewelry on the face and neck prior to photos.
3) Subjects' hair must be pushed back away from the face with a black headband (ensure any stray hairs are not on the face).

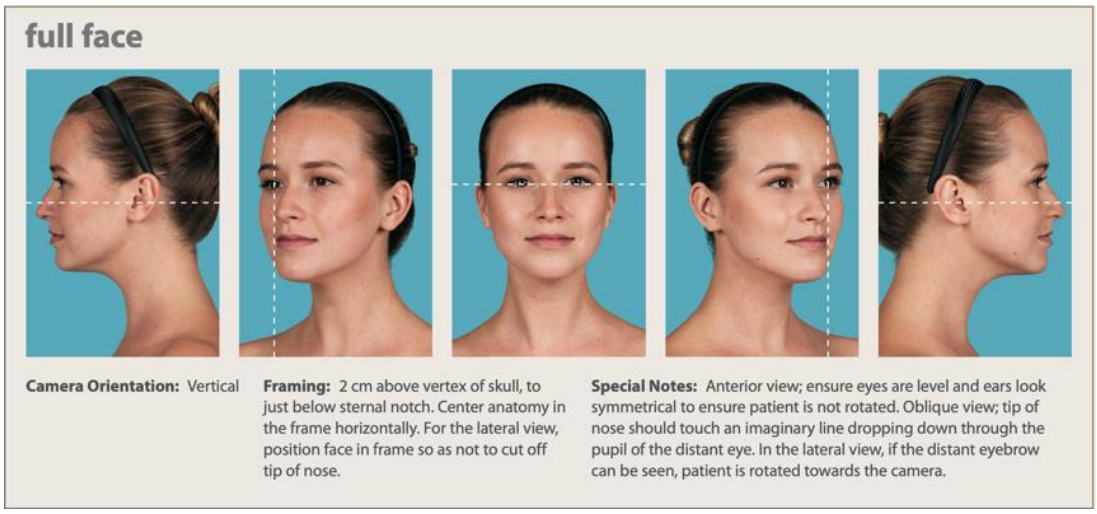
High resolution 2D photography will be taken at every visit. All photographs will be compared from baseline pre-treatment photos to treatment photos throughout the study.

Example of proper subject alignment:
Adapted from: Acclaro Medical Photography How-To-Guide



Anterior **Left Oblique** **Left Profile**

Adapted from: Photographic Standards in Plastic Surgery ©2013 Canfield Scientific, Inc. 1305-11



APPENDIX D – DEVICE DESCRIPTION, LABELING & TREATMENT PARAMETERS

Device Description

UltraClear Mid IR Fiber Laser includes a laser source with wavelengths of 2,910 nm. A Beam Delivery system collimated the Mid IR Fiber Laser Radiation and combines it with visible red aiming beam diode emitting red laser light at 635±15nm, (**Figure 1**.) An optical Scanner assembly deflection and focusing system converges the beam onto the skin (**Figure 2**).

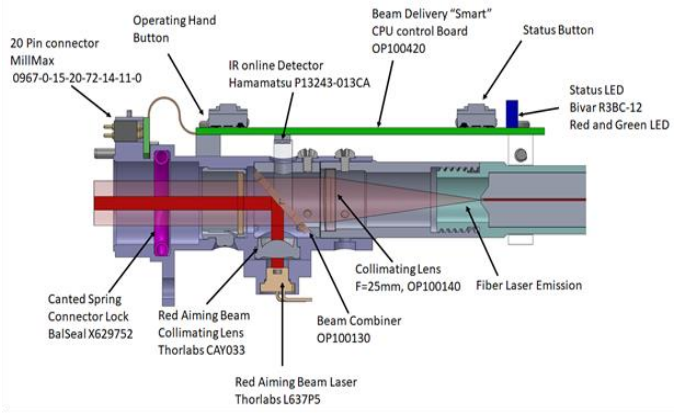


Figure 1. UltraClear Mid IR Fiber Laser Beam Delivery Schematic

An optical dual axis Scanner Assembly deflecting and focus the laser beam onto the working plan that is the treated skin (**Figure 2**) The Scanner Assembly is connected mechanically and locked in place to the Beam Delivery Mounting Shaft.

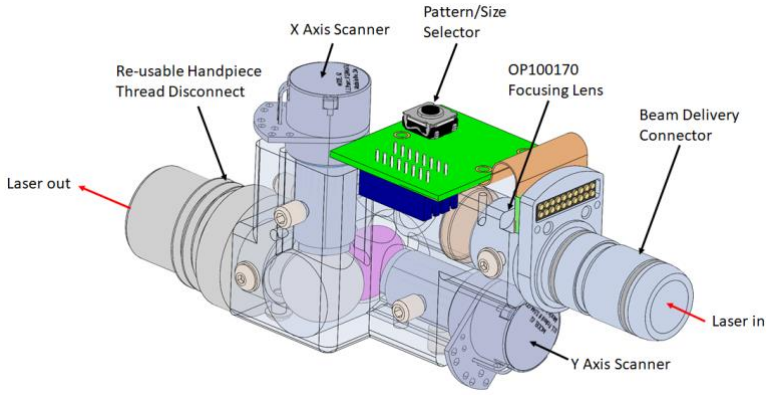


Figure 2. UltraClear Mid IR Fiber Scanner Assembly Schematic

Figure 3 illustrates the Mid IR Treating Applicator placement on subject's skin during the treatment.

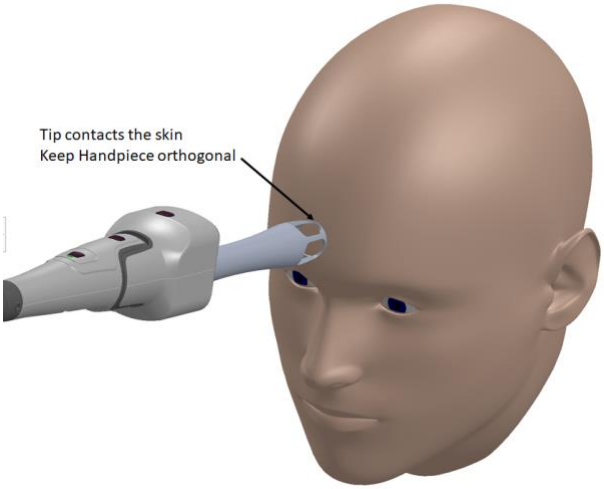


Figure 3 – UltraClear Applicator Treatment

UltraClear Handpiece is made of solid hollow metal that can be sterilized using Autoclave. Cleaning and Sterilization instructions are in UltraClear User's Manual.

UltraClear Resurfacing Laser's functional elements are equivalent to the CO2 systems, with the primary change being the laser source, and added Rejuvenation functionality. The system employs scanning optics and an electrically-controlled fiber-delivered Mid IR Fiber laser to create multiple spots within the treatment region, in a similar manner to other CO2 devices. The metal handpiece provides a guidance to the treating physician how to position the handpiece vertically to the skin and at the correct distance to achieve best results.

The user will interact with the UltraClear Mid IR Fiber Laser Workstation through the touch screen panel on the top of the unit. The foot pedal and key switch will provide redundant protection and must be activated to enable the laser. The device will plug into a standard 110 VAC wall outlet. Laser wavelength and treatment parameters, including treatment energy per pulse (mJ/pulse) and treatment density (% coverage) will be set by the user through the touch screen panel interface. These parameters will be used by software to set internal device

parameters, such as optical spot size which is adjusted internally using the same mode of operation as other CO2 Laser Systems. Optical output of the device will be calibrated by inserting the handpiece unit into a calibration port that consists primarily of an optical power meter.

UltraClear laser-tissue interaction is marked by peak water absorption within the tissue and by negligible absorption by other chromophores such as melanin and hemoglobin. The wavelength choice has a direct effect on depth of penetration because skin is composed of approximately 70% water. Other materials within the skin do not absorb significantly in the wavelength range of interest.

Product Labeling

The UltraClear Mid IR Fiber Laser Workstation will bear the required labeling information, including:

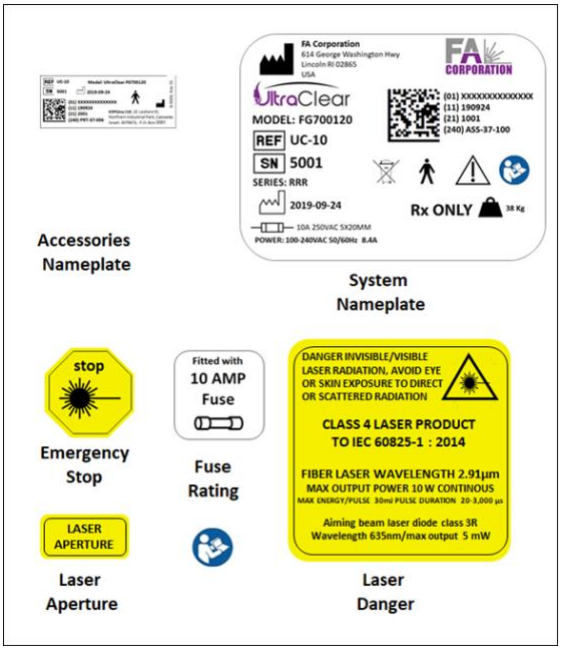


Figure 4- UltraClear Labels Content

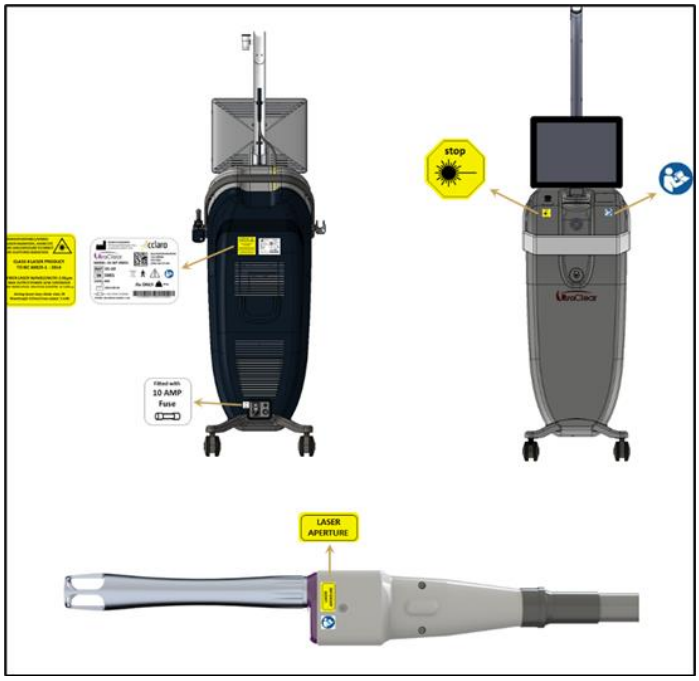


Figure 5 – UltraClear Label Placement

Treatment Parameters
Table 1 below illustrates the treatment parameters:

Table 1: UltraClear Treatment Parameter Selection

Mode	*Application*	*Energy Settings [mJ]*	*Fluence [J/cm²]*	*Fractional Density [%]*	*Est. Ablation Depth [µm]*
Clear	Light peel	0.6-0.93*	3.6 – 7.2	30 – 50	10 – 30
Clear+	Epidermal resurfacing	0.93-2.25*	7.2 – 21.6	20 – 40	40 –100
Ultra	Deep fractional resurfacing	3.6 – 25[2]	28 – 194*	1.5 – 5	50 – 1,500
UltraClear	Combination of **Clear+** and **Ultra** modes	0.93 – 2.25* 3.6 – 25*	7.2 – 21.6 28 – 194*	20 – 40	40 - 80 50 – 1,500
Laser-Coring	Deep fractional resurfacing	2.0**	125-500	0.5-3.0	500-2,000

- * *Note- Energy per micro-beam*

2

- *When the fractional density is set to higher than 20%, the energy on Skin Types IV and V should be lowered by 20%.*
- *On patients with Skin Type VI the energy should be lowered by 20% in all modes and energy settings.*

** Note- Energy per micro-beam in Laser Coring mode:
The energy per micro-beam is fixed at 2.0 mj per pulse, with 6 pulses delivered per ablation layer for approximate 36 microns ablation depth. For deeper ablation the UltraClear controller will add more layers (add more pulses) to achieve the results, same as adding more ablation locations when increasing % coverage density.

Laser exposure will be performed on the subjects' full face using UltraClear modes. The investigator can select from a range of settings around the treatment parameter settings shown below.

SIGNATURE PAGE

Principal Investigator(s): Paul M. Freidman, M.D.

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APPROVED BY:

_____ Date: _____/_____/_____

Paul M. Friedman, M.D. MM DD YYYY

Principal Investigator