PROTOCOL #: CYN19-RF-MN-01

FEASIBILITY STUDY TO ASSESS A RADIOFREQUENCY MICRONEEDLING DEVICE FOR ELECTROCOAGULATION AND HEMOSTATIS OF SOFT TISSUES FOR DERMATOLOGIC CONDITIONS

Clinicaltrials.gov Identifier: NCT05097157

Document Date: December 7, 2020

INVESTIGATIONAL PLAN

PROTOCOL #: CYN19-RF-MN-01

FEASIBILITY STUDY TO ASSESS A RADIOFREQUENCY MICRONEEDLING DEVICE FOR ELECTROCOAGULATION AND HEMOSTATIS OF SOFT TISSUES FOR DERMATOLOGIC CONDITIONS

CONFIDENTIAL

THIS INVESTIGATIONAL PLAN CONTAINS CONFIDENTIAL INFORMATION FOR USE BY THE INVESTIGATORS AND THEIR DISIGNATED REPRESENTITIVES PARTICIPATING IN THIS STUDY. IT SHOULD BE HELD CONFIDENTIAL AND MAINTAINED IN A SECURE LOCATION. IT SHOULD NOT BE COPIED OR MADE AVAILABLE FOR REVIEW BY ANY UNAUTHORIZED ENTITY.

SPONSOR:
CYNOSURE, LLC
5 CARLISLE ROAD
WESTFORD, MA 01886
PHONE: 800-886-2966
FAX: 978-256-6556

FEASIBILITY STUDY TO ASSESS A RADIOFREQUENCY MICRONEEDLING DEVICE FOR ELECTROCOAGULATION AND HEMOSTATIS OF SOFT TISSUES FOR DERMATOLOGIC CONDITIONS

INVESTIGATOR AGREEMENT

I agree to conduct the study in accordance with the relevant, current protocol and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation.

I agree to inform any patients, or any persons used as controls if applicable, that the device(s) is/are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in and institutional review board (IRB) review and approval are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigations. I have read and understand the information in the device manual, including the potential risks and side effects of the device.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records and to make those records available for inspection. I further agree that Cynosure, Inc. or their designees shall have access to any source documents from which case report form information may have been generated.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators.

I will comply with the International Conference on Harmonization (ICH), Good Clinical Practice (GCP) guidance E6, FDA Good Clinical Practice Regulations (21 CFR parts 50, 56, and 812), Declaration of Helsinki (DoH) and the Health Human Service (HHS) Belmont Study Principals and Guidelines during the conduct of this study.

I have read the foregoing protocol and agree that it contains all necessary details for carrying out this study. I will conduct the study as outlined herein and will complete the study within the time designated.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the study device the conduct of the study.

I will disclose financial arrangements and interests in accordance with Financial Disclosure Rules (21 CFR part 54) and FDA Form 3455.

_____ _____

Investigator's Signature Date

_____

Name of Investigator (Typed or Printed)

_____

_____

_____

Address of Investigator (Typed or Printed)

SITE #1 CONTACT INFORMATION:
Principal Investigator Information:
Sean Doherty, M.D.
Phone: 617-735-8735
Email: info@seandohertymd.com

Location #1:
Cynosure, LLC
5 Carlisle Rd.
Westford, MA 01886

Location #2:
Boston Center for Facial Rejuvenation
1 Brookline Place, Suite 427
Brookline, MA 02445

SITE #2 CONTACT INFORMATION:
Robert Arnold Weiss, M.D., F.A.A.D., F.A.C.Ph
Maryland Dermatology Laser, Skin, & Vein Institute, LLC.
54 Scott Adam Rd Ste 301
Hunt Valley, MD 21030
Phone: 410-666-3960
Email: rweiss@mdlsv.com

SITE #3 CONTACT INFORMATION:
Christine Dierickx, M.D.
Résidence Blues
52 Rue Charles Martel
L-2134 Luxembourg
Phone number: +352 2740 6396
Email: info@skinperium.com

SITE #4 CONTACT INFORMATION: TBD
Principal Investigator Information:
Emil A. Tanghetti, M.D.
Center for Dermatology and Laser Surgery
5601 J Street Sacramento, CA. 95819
Phone: (916) 454-5922
Fax: (916) 454-2156
Email: et@dermatologyandlasersurgery.com

SITE #5 CONTACT INFORMATION: TBD
David H. McDaniel, M.D., F.A.A.D.
McDaniel Institute of Anti-Aging Research
125 Market Street
Virginia Beach, VA 23462
Phone: 757-437-8900
Email: dhm@drmcdaniel.com

SPONSOR CONTACT INFORMATION:
Jennifer Civiok
Director, Clinical Development
Cynosure, LLC
5 Carlisle Road
Westford, MA 01886
Phone: 800-886-2966
Fax: 978-256-6556
Email: jennifer.civiok@hologic.com

TABLE OF CONTENTS

1.0 PURPOSE
- 1.1 Name and Intended Use
- 1.2 Objectives
- 1.3 Duration of the Investigation

2.0 PROTOCOL
- 2.1 Protocol Methodology and Analysis
- 2.2 Protocol Study Design
- 2.3 Subject Selection Criteria
- 2.4 Screening
- 2.5 Informed Consent Process and Enrollment
- 2.6 Pre-Treatment Procedures
- 2.7 Treatment Procedures
- 2.8 Post Treatment Procedures
- 2.9 Follow Up
- 2.10 Biopsy Portion of the Study
- 2.11 Unscheduled Visits
- 2.12 Replacement of Subjects
- 2.13 Schedule of Visits and Procedures
- 2.14 Evaluation Methods
- 2.15 Adverse Event Recording
- 2.16 Statistical Analysis

3.0 RISK ANALYSIS AND MANAGEMENT
4.0 DEVICE DESCRIPTION AND SPECIFICATIONS
5.0 MONITORING PROCEDURES
6.0 LABELING
7.0 CONSENT MATERIALS
8.0 INSTITUTIONAL REVIEW BOARD INFORMATION
9.0 OTHER INSTITUTIONS
10.0 ADDITIONAL RECORDS AND REPORTS
11.0 PREGNANCY
12.0 SUBJECT WITHDRAWAL
13.0 PHOTOGRAPHY
14.0 ADVERSE REACTIONS DEFINITIONS AND REPORTING REQUIREMENTS
15.0 PROTOCOL DEVIATIONS
16.0 CONFIDENTIALITY AND DISCLOSURE OF MEDICAL INFORMATION
17.0 CLINICAL RESEARCH CONDUCT
18.0 REPORTING FOR THE STUDY
19.0 DISCLOSURE
20.0 RESPONSIBILITY OF THE INVESTIGATOR
21.0 PROCEDURE FOR AMMENDMENTS TO PROTOCOL
22.0 TERMINATION OF STUDY
23.0 DATA SECURITY
24.0 REPORT OF PRIOR INVESTIGATIONS

APPENDICES
- A. Protocol Revisions Tracker
- B. Universal Pain Assessment Tool

ATTACHMENTS/REFERENCES

I. Operator Manual for the Potenza™ device
II. Treatment Guideline for the Potenza™
III. Informed Consent Form
IV. Pre and Post Treatment Instructions

1.0 PURPOSE

1.1 Name and Intended Use

The device used in this study is called the Potenza™ device.

The intended use of the Potenza™ device is to collect clinical data for a wide array of dermatologic conditions in which electrocoagulation and hemostasis is a viable mechanism for means of improvement.

1.2 Objectives

1. Primary Objectives:
   - Assessment of safety of the study device through the collection of side effects throughout the study.
   - Assessment of the efficacy of the study device through Investigator and subject satisfaction.
   - Evaluation of baseline photographs compared to post treatment images.
2. Assessments:
   - Treatment discomfort evaluation
   - Subject treatment experience questionnaire
   - Clinician ease of use questionnaire
   - Clinician and subject satisfaction questionnaire
   - Treatment area photograph blinded evaluation
   - Baseline and short-term histological tissue response as seen in biopsies.

1.3 Duration of the Investigation

The sponsor anticipates that all subjects can be enrolled within 6 months. If subject participates in all required visits, then the subject's participation in this study may last up to 9 months. It is anticipated that it will take approximately 3 months to analyze the data collected during this study. The total duration of this study is anticipated to last approximately 18 months.

2.0 PROTOCOL

2.1 Protocol Methodology and Analysis

Methodology:
Subjects are to be enrolled in this clinical study if they are 18 - 55 years old. Up to 120 subjects will be enrolled at 5 study centers. Subjects may receive up to 5 treatments with the Potenza™ device if they present with conditions such as, but not limited to; Wrinkles, fine lines, crepey skin, acne scars, active acne, enlarged pores, stretch marks, or loose skin on the face, neck and/or body.

Subjects will attend a screening/pretreatment visit which may be performed on the same day as the treatment visit. Subjects will receive up to 5 treatments. All subjects may receive a phone call or attend a visit 24 hours post each treatment and will receive a phone call or attend a visit 1 week (2-10 days) after each treatment to record side effects. Subjects will be required to return for a follow-up visit 30 days after the final treatment. Subjects may also attend an optional follow up visit 90 days after the final treatment. An unscheduled visit or phone call may be performed at any time during the study at the request of the subject or as deemed necessary by the site Investigator.

Analysis:
Upcoming generations are proving to have an interest in aesthetic dermatology treatments and will drive demand for innovated products, procedures, and practice design.[1] Due to this shift in patient base, practices need to evolve to adapt to the newer generational ideologies. There have been rapid advances in RF technology over the past few years and the nonsurgical treatment using this energy source offers great promise to our aging population.[2] Radiofrequency micro needling technology for the treatment of dermatologic conditions needs to be further investigated to optimize treatment parameters for safe and effective non-ablative treatments.

Relevance:
Does not apply to this study – feasibility study.

Testability:
Does not apply to this study – feasibility study.

Compatibility:
Does not apply to this study – feasibility study.

Predictive power:
Does not apply to this study – feasibility study.

2.2 Protocol Study Design

This is a prospective, open label, multi-center clinical study

2.3 Subject Selection Criteria

Subjects will meet the criteria described below:

Inclusion Criteria:

- A healthy, non-smoking male or female between the age of 18-55 years old.
- Fitzpatrick skin type I to VI.
- Understands and accepts obligation not to receive any other procedures on the treatment area through the length of the study.
- Understands and accepts the obligation and is logistically able to be present for all visits.
- Is willing to comply with all requirements of the study and sign the informed consent document.

Exclusion Criteria:

- Is pregnant or of childbearing potential and not using medically effective birth control, or has been pregnant in the last 3 months, currently breast feeding or planning a pregnancy during the study.
- The subject is currently enrolled in an investigational drug or device trial or has received an investigational drug or been treated with an investigational device within in the area to be treated 6 months prior to entering this study.

- The subject has physical problems such as cardiovascular disorders.
- The subject has a pacemaker.
- The subject had previous use of gold thread skin reju venation.
- The subject has skin infections.
- The subject has any of the following conditions:
  - Diabetes
  - Epilepsy
  - Acute disease
  - Dermatitis
- Subjects with electronic implants such as cardiac defibrillator. It may interfere with operation of electronic implants or damage the implants, causing risks.
- The subject has any condition or is in a situation which in the investigators opinion may put the subject at significant risk, may confound study results or may interfere significantly with the subject's participation.

Cautionary Criteria:

- Subjects taking medications for heart disease, hyperlipidemia, and hypertension and patients taking NSAIDs, aspirin, and fish oil. They may have more bleeding than others.
- Malignant disease (excluding skin malignancies)
- Subjects with herpes.
- Hemangioma
- Subjects with autoimmune disease
- Subjects with keloids

Be sure to list all concomitant medications or procedures permitted before, during and after the trial.

Subjects will be recruited for the study through existing patient database and advertisements.

Subject populations will not be eligible to participate in the study if they are vulnerable populations such as; children, pregnant women, prisoners, institutionalized individuals, and any persons requiring a legally authorized representative as part of the consenting process.

Subject population characteristics that will not be eligible to participate in participate in the study include non-English speaking individuals and people who cannot read or comprehend English. Employees of the Investigator will may participate in the study.

2.4 Screening

Subjects will be asked questions about their medical history, may have a limited physical and their inclusion/exclusion criteria will be verified. Discontinuation of any concomitant medications, pretreatment instructions and post treatment instruction will be reviewed with the subject.

Procedure for the Limited Physical Exam:

If the investigator determines that a limited exam is necessary, the exam will be like a basic annual physical exam performed by a primary care doctor to determine general overall health. The limited medical exam may include all or any of the following; vital signs such as blood pressure, heart rate, respiratory rate and body temperature, general appearance, listening to the heart, lungs and abdomen with a stethoscope, head and neck exam, in addition to examining the throat, tonsils, teeth, ears, eyes and nose as well as a neurological exam such as testing muscle strength, reflexes, balance, sensory changes of the extremities and mental state.

2.5 Informed Consent Process and Enrollment

Subjects will be asked to review the pre and post treatment instructions prior to signing the informed consent and their involvement in the study. Subjects who sign the informed consent will be screened to confirm eligibility and if eligible, will be assigned a subject identification number. Subjects will be de-identified through their subject identification number, which will be stored in a secure location. Subject identification numbers will be generated chronologically and assigned only to subjects who have met all the study selection criteria and have signed the informed consent form. The informed consent will be obtained prior to a subject's involvement in any study related procedures. A subject will be considered enrolled in the study once they have signed the informed consent form. Employees of the Sponsor will be required to sign both the main informed consent form as well as an employee consent form.

2.6 Pre-Treatment Procedures

If the subject is of childbearing potential (i.e. females not post-menopausal or not surgically sterile), then they will be asked if they are pregnant, the date of their last menstrual cycle, and perform a pregnancy test. If the treatment is on the abdomen, a urine pregnancy test must be performed before each treatment. A urine pregnancy test may be conducted at the Investigators discretion during the study. If a urine pregnancy test is conducted, then a negative result must be obtained within 24 hours prior to the treatment.

Urine Pregnancy Test Procedure:

1. A urine sample is tested mid-stream or by cup sample with an indicator stick.
2. Negative results are indicated on the indicator stick.

- The following Pre-Treatment instructions will be reviewed:
  - Remove all jewelry and makeup, including eye makeup, lotions or sun block and wash facial area prior to treatment.
  - For an optimum treatment, keep hydrated by drinking water (at least 8 cups daily) or hydrating fluids, such as Gatorade, and avoid drinking alcohol for several days in advance.
  - For five to seven days prior to treatment, at the physician's discretion, avoid therapies that may cause erythema (redness) or irritation such as Retin A or products containing Isotretinoin, glycolic and or salicylic acid.
  - Shave visible hair from the treatment area. Male beards should be shaved day of treatment. RF follows the path of least resistance and the hair will receive the energy.
- Photographs will be taken prior to the first treatment.

2.7 Treatment Procedures

- Procedure for the Potenza™ device:
  - The treatment area will be identified and may be marked with a surgical marker.
  - Anesthesia (such as a topical or local), air cooling, and/or Nitronox will be used at the discretion of the Investigator.
  - A neutral pad will be placed in an area determined by the Clinician to maintain standard energy settings and requires less power from the device during the treatment.
  - Test spots may be performed prior to the first treatment. Test spots may be performed prior to the first treatment. It will follow a similar procedure to treatment but only in an inconspicuous place, such as behind the ear, in an area no larger than 2in x 2in.
  - The tip will be placed in contact with the skin.
  - The entire defined treatment area will then be treated as instructed by the Operator's Manual.
  - Parameters may be adjusted throughout the treatment and will determined by the Clinician.
  - Subjects will be asked to report the general level of treatment discomfort/pain on a scale of 0 (none) to 10 (maximum intolerable pain).
- Photographs may be taken during treatment.
- Subjects may receive up to 5 treatments every 4 weeks (+/- 2 weeks) which will be determined by the Investigator.
- The additional treatments will follow the same procedure.

2.8 Post Treatment Procedures

- Adverse events will be documented after treatment.
- Photographs may be taken post treatment.
- Clinician ease of use and subject treatment experience questionnaires may be performed.
- The following post treatment instructions will be reviewed:
  - Be careful not to expose area of treatment to external stimulation for at least 2 days after treatment.
    - Avoid ultraviolet rays and apply sunscreen.
    - Do not to scrub the skin or exfoliate for several days after treatment.
  - Refrain from high intensity exercise (such as running, weightlifting, aerobics), hot bath or saunas that may cause increase in skin temperature for 5 days after treatment.
  - Refrain from drinking alcohol or taking medicine that interferes with blood coagulation such as aspirin for 2 weeks after treatment.
  - If heat sensation or erythema (redness) after treatment is bothersome, use an ice pack to the treated area at home.
  - If the skin in the treatment area feels tight or dry, apply plenty of moisturizing cream, such as Neutrogena.
  - After the procedure, inflammation or edema (swelling) may block the pores and acne can temporarily worsen (about 7 days). If acne worsens, do not pick or squeeze as pigmentation changes may occur.
  - Sleep in a semi reclined position for the first 2-3 nights to minimize facial swelling.
  - Apply soothing facial mask as needed.

2.9 Follow Up

- All subjects may receive a 24 hour phone call or attend a visit post each treatment and will receive a phone call or attend a visit 1 week (2-10 days) after each treatment to record side effects.
- The study subjects are required to return to the investigative site for a follow-up evaluation at 30 days post last treatment.
- Subjects may be asked to return for an optional follow up visit 90 days post last treatment.
- Photographs will be taken, subject and physician questionnaires will be performed, and adverse events will be documented at all follow up visits.
- Some subjects may have an incomplete response or no response by the end of the study. At the end of the study, treatments using an FDA approved/cleared treatment method may be discussed with the subject and obtained at the cost of the subject.

2.10 Biopsy Portion of the Study

- Up to 6 subjects will enroll in the biopsy portion of this study. If the subject has enrolled, the following will also be performed:
  - Biopsies will be taken from the test spot area day of treatment and may be taken 0-24 hours, 25-48 hours, 3-7 days, and 30 days post treatment.
  - Biopsy subjects may receive up to 2 biopsies at each visit, totaling 10 biopsies.
  - A local anesthetic, such as lidocaine, may be injected to the area prior to biopsy.
  - A 2 mm or 3mm punch biopsy (based on Physician assessment) will be taken from the treatment area.
  - Sutures will be uses to close the incision site.
  - The subject will be required to attend a 1 week (7-14 days) post the 7 day biopsy visit and a 1 week (7-14 days) post 30 day biopsy follow up visit to remove the sutures and assess side effects.
- The following post biopsy treatment instructions will be reviewed:
  - Slight redness, initial tenderness to the wound site is normal; however, if you experience more redness, swelling, pain, pus, or drainage contact the study site immediately.
  - If the biopsy site begins to bleed, apply direct pressure for 10-20 minutes. If it continues to bleed, call the study site immediately.
  - Keep the wound dry today and remove bandage in 24 hours and leave off.
  - Avoid hot tubs, pools, and ocean until sutures are removed. Avoid soaking in water until 14 days after your biopsy.
  - When showering, wash carefully and do not scrub or traumatize the treated skin, or allow spray of shower to strike the skin directly. If the skin is treated harshly, this can increase the risk of scarring.
  - After showering, lightly pat dry the wound or let it air dry, then cover the biopsy site with an application of Vaseline (or petroleum jelly) at least 1-2 times daily. Keeping the wound moist reduces infection, minimizes scarring, and prevents crust formation over the wound.
  - Band-Aids (or any generic Adhesive Bandages) may be used for sleeping or in daily routines where the area may be rubbed/irritated. Whenever possible, keep Band-Aid (or generic Adhesive Bandage) off of the area and keep the area moist with Vaseline (or petroleum jelly) as previously described but do not allow drying out and forming a hard scab.

- For any wound discomfort, you may take Tylenol as needed, or use cold compresses for up to 20 minutes hourly as needed. If using ice, it should be wrapped in a plastic and then a cloth to avoid burning your skin and wetting your bandage.
- Avoid picking at the wound site, which increases risk of infection and scarring.
- In order for the wound to heal properly and not leave bumpy scars, be careful not to overstretch the wound site area. As a wound heals, it will be weaker than the surrounding skin and can even "pop open" the sutures (stitches) if stretched too much. Sport or strenuous exercises that can pull at the wound site are best avoided for at least the next 3 days and up to one week.
- Return for suture removal within 7 - 14 days as instructed per study protocol. If applied, Steri-strips must be kept dry as they are more likely to separate when wet. Steri-strips will usually fall off by themselves or you may be advised by the study doctor to remove them when the wound healed.
- ONCE SUTURES ARE OUT: To minimize sore formation and to improve the final appearance of your skin, it is very important to keep the wound site area covered with the Vaseline for the next few days, until there is no more crust forming and the skin has completely healed.
- Temporary discoloration at the wound site is normal and should gradually fade over the next few months. Please protect newly healed biopsied area with SPF and avoid sunburn.

2.11 Unscheduled Visits

An unscheduled visit may be performed at any time during the study at the subject's request or as deemed necessary by the site Investigator. The date and reason for the unscheduled visit will be recorded in the source documentation.

2.12 Replacement of Subjects

Replacement of subjects who have withdrawn or been withdrawn from the study will be allowed to be replaced with prior approval from the sponsor and/or IRB.

2.13 Schedule of Visits and Procedures

	Visit #1	Visit #2-6	Call #1 or Visit (optional)	Call #2 or Visit #7	Visit #8	Visit #9 (optional)
Procedure	Screening and Pretreatment Procedures*	Treatment Visit(s) 1-5 Every 4 Weeks (+/- 2 weeks)	Phone Call 24 Hours Post Each Tx	Phone Call or Visit 1 Week Post Each Tx (2-10 Days)	Follow Up 30 Days Post Last Tx (+/- 1 Week)	Follow Up 90 Days Post Last Tx (+/- 2 Weeks)
Medical History	X					
Pregnancy Verification	X	X**				
Informed Consent	X					
Photographs	X	X	X	X	X	X
Treatment		X				
Treatment Discomfort/ Pain Evaluation		X				
Subject Questionnaires		X		X	X	X
Clinician Questionnaires		X		X	X	X
Adverse Events Assessment		X	X	X	X	X

*Screening and Pretreatment Procedures may occur at the same time as the first Treatment Visit. Must be performed at least 30 days prior to first treatment.
**Pregnancy verification will only be required to be performed prior to each treatment if the treatment is on the abdomen.

Biopsy Schedule of Visits and Procedures:

	Biopsy #1	Biopsy #2	Biopsy #3	Biopsy #4	Post Biopsy Visit #1	Biopsy #5	Post Biopsy Visit #2
Procedure	Treatment Visit (control)	0-24 Hours Post Treatment	25-48 Hours Post Treatment	3-7 Days Post Treatment	Follow Up 1 Week Post Biopsy #4 (7-14 Days)	Follow Up 30 Days Post Tx (+/- 1 Week)	Follow Up 1 Week Post Biopsy (7-14 Days)
Biopsy	X	X	X	X		X	
Suture Removal					X		X
Photographs	X	X	X	X	X	X	X
Adverse Events Assessment	X	X	X	X	X	X	X

2.14 Evaluation Methods

Photographs:
Photographs will be taken at all visits and will be used to assess safety and efficacy of treatment.

Treatment Discomfort/Pain Evaluation:
Subjects will be asked to report the general level of treatment discomfort on a scale of 0 (none) to 10 (maximum intolerable pain) using the universal pain assessment tool (Appendix B)

Subject Questionnaire:
The subject will be asked their level of satisfaction using a 6-point Likert scale that ranges from "extremely satisfied" to "extremely unsatisfied."

Subject Satisfaction	
Rating	Description
6	Extremely Satisfied
5	Satisfied
4	Slightly Satisfied
3	Slightly Unsatisfied
2	Dissatisfied
1	Extremely Unsatisfied

Physician Questionnaire:
The Clinical Global Aesthetic Improvement Scale (CGAIS) ranging from "worse" to "very much improved" will be used to judge the improvement as seen by the treating Investigator.

Global Aesthetic Improvement Scale Assessment	
Rating	Description
1	**Very Much Improved-** Optimal cosmetic result in this subject
2	**Much Improved-** Marked improvement in appearance form the initial condition, but not completely optimal for this subject.
3	**Improved-** Obvious improvement in appearance from initial condition, but a re-treatment is indicated.
4	**No Change-** The appearance is essentially the same as the original condition.
5	**Worse-** The appearance is worse than the original condition.

Blinded Evaluation:
Three blinded independent reviewers will perform a photographic evaluation in which they will be asked to identify pre-treatment images when compared to post treatment images. The reviewers will be Board Certified Dermatologist and be chosen based on availability and have relevant clinical experience. They will attend a training session prior to grading.

Skin Biopsies:
Biopsies will be obtained to examine the effects on the skin following radiofrequency treatment. Sections of skin will be removed using the punch biopsy technique to render a microscopic

diagnosis. Each specimen will first be preserved with a fixative and then stained using Hemotoxylin & Eosin, Verhoeff and Masson Red/Fast Green or nitroblue tetrazolium chloride (NBTC) staining methods. If using Hemotoxylin & Eosin, Verhoeff and Masson Red/Fast Green staining, samples will be assessed and evaluated by the amount of collagen and elastin stained. If using NBTC staining, samples will be assessed and evaluated to differentiate between the blue-stained viable cells and the unstained thermally damaged cells. A histological analysis will be provided by the Investigator.

2.15 Adverse Event Recording

All data captured must be supported by the Investigator's timely assessment and documentation of the adverse event in the case report forms or source documents. All documented adverse events will be reviewed by the Sponsor or designee to determine whether the adverse event meets regulatory reporting requirements and to ensure timely adverse event reporting to meet local and global regulatory requirements. All adverse events must be followed until their resolution.

Adverse Events Pertaining to the Potenza™ Device:

- Temporary erythema: area of treatment may turn red right after treatment, but this symptom disappears within 48 hours after treatment
- Temporary tingling: slight edema may occur right after treatment, but this symptom disappears within 48 hours after treatment.
- Burning sensation: patients may feel uncomfortable temporarily while receiving treatment.

Other possible adverse effects may include pain/tenderness, pinpoint bleeding, folliculitis, skin burn, hypopigmentation, hyperpigmentation, infection, paresis, scarring, bruising, acne, dryness, eye twitching, eye tearing, petechiae, skin textural irregularity, and allergic reaction which may be transient and resolve over time.

Adverse Events Pertaining to Neutral Pad:

Mild heat or hot spots may be felt during treatment by the subject. If the subject reports heat at the pad site, evaluate the site, check for epidermal injury. Skins burns may occur if subject does not report if the pad becomes too hot.

Adverse Events Pertaining to Anesthesia:

Topical anesthesia, such as but not limited to; EMLA, LMX and Lidocaine/Tetracaine, or a local anesthetic will be used. The most common side effects for most anesthetics include redness, blanching, swelling and application site reaction.

Less common side effects include; large swellings that look like hives on the skin or in the mouth or throat. Pain, burning, paleness and altered temperature sensation. Subjects may be allergic to the contents of any anesthetic which may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

Adverse Events Pertaining to Nitronox:

May experience nausea, vomiting, excessive sweating, euphoria, excitement, deep sedation, drowsiness, sleep, dizziness, lightheadedness, dysphoria, amnesia, and headaches.

Adverse Events Pertaining to the Surgical Marker:
Using surgical marker has minimal risks and may produce effects on the body such as redness or a rash. Markings may remain visible for a few days or may be removed with alcohol.

Biopsies
Complication with biopsies can include pain, redness, swelling, infection, bleeding, scarring and skin texture irregularities.

Other Cautions:
Incomplete response or no response may occur since some subjects may not respond to treatment.

2.16 Statistical Analysis

2.16.1 Hypothesis
For this study to be considered a success, the Investigator and subject satisfaction rates will be ≥80% and if the side effect profile is acceptable to the Physician as it relates to this type of treatment. In cases where the subject's improvement is being graded on a scale, such as the GAIS scale, we will test the statistical significance of our results against a hypothetical population that would have no change (average score of 4).

For secondary objectives to be considered a success, the results from any assessments will need to be statistically significant or have ≥80% response rate.

2.16.2 Sample Size Rationale
Based on the need for the data collected from this study, it was determined that a total of 120 patients would be required for the study, including departures.

2.16.3 Patient Populations
Interim results may be collected and reported. All data will be analyzed at the end of the study. The primary analysis will be performed by the intention-to-treat approach. Everyone who begins the treatment is part of the study whether he or she completes the study or not. Additional per-protocol analysis may also be performed on subjects who complete the entire clinical trial according to the protocol. The most appropriate method of handling missing values will be chosen based on the individual trial goals, endpoints and context.

The analysis of demographic, medical history, and efficacy variables will be based on all patients who are randomized and receive at least one treatment. The analysis of safety data will be based on all patients who are randomized, receive at least one treatment, and have at least some safety data.

2.16.4 Analysis of Demographic and Medical History Variables
Summaries will be prepared for all important demographic and medical history variables. For quantitative variables summaries will include the sample size, mean, median, standard deviation, minimum, and maximum. For these variables the treatment groups will be compared using either a t-test or a Wilcoxon Rank Sum test, as appropriate. For categorical variables the summaries will

include the sample size and the number and percent of patients for each outcome. For these variables the treatment groups will be compared using Fisher's Exact test. Statistical significance will be declared if the two-sided p-value is < 0.05.

2.16.5 Analysis of Efficacy Variables

The primary efficacy variable is the change from baseline to visit 8 (30 days post last treatment) with respect to the treated condition evaluated by physician grading with CGAIS. Baseline is defined as the last assessment prior to the first treatment. The change from baseline to visit 8 will be analyzed using a Mixed Model Repeated Measures Analysis of Variance. A pairwise treatment group comparison at visit 8 will be performed using the results of this analysis. If a patient has no post-baseline assessment of the primary efficacy variable the patient data will be excluded from the statistical analysis of the improvement. Statistical significance with respect to the treatment group comparison at visit 8 will be declared if the two-sided p-value is < 0.05. For each treatment group summaries will be prepared for both the observed assessment and the change from baseline. Subject satisfaction results from Visit 9 will also be included in the summary. The summaries will include the sample size, mean, median, standard deviation, minimum, and maximum. Categorical variables will also include a summary which will include the number and percent of patients for each outcome. The statistical significance of the mean change from baseline for each treatment group will be determined using a student's paired t-test.

The secondary efficacy variables will be determined at a later date based on image grading. As with the primary efficacy variable the assessment at Visit 8 (30 days post last treatment) will be primary. The analysis and summaries for any secondary efficacy variables will be the same as that described for the primary efficacy variable. Statistical significance with respect to the treatment group comparison at visit 8 will be declared if the two-sided p-value is < 0.05.

2.16.6 Analysis of Safety Variables

Safety will be assessed through the degree of pain/discomfort related to the procedure (universal pain scale) and the collection of Adverse Events throughout the course of the study. For each treatment group these variables will be summarized. The summaries will include the number and percent of patients for each outcome. No statistical comparisons will be performed for any of these variables.

3.0 RISK ANALYSIS AND MANAGEMENT

3.1 Risk Determination

This device study used in this study does not meet the FDA definition for a Significant Risk Device study per 21 CFR 812.3(m). Therefore, the sponsor determines that this is a non-significant risk device study.

Significant risk device means an investigational device that:
(1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
(2) Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

(3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
(4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

3.2 Risk Management

The Investigator in this clinical trial has been invited to participate based on his/her previous experience with the use of the system and/or similar systems and industry experience. Experience with treatments is the most critical element in managing subject risk in this trial.

In addition, as with any study, there is a risk of bias. Objective evaluation methods may be used in conjunction with subjective evaluation methods when feasible. The value of the compensation to the clinical investigator for conducting the study is not influenced by the study outcome. If photographic results are listed as the primary objective, they are to be evaluated by blinded evaluators who did not partake in the study. If information concerning investigator assessment of improvement or investigator satisfaction is collected, then it is not listed as an objective for the study.

All other known risks will be disclosed to the subject via the informed consent process. Since this is an elective procedure and the subjects are volunteers, it can be assumed that their signature on the informed consent is indicative of their agreement to accept the risks involved.

The risks to the subjects who participate in this study are the same as those for the subject undergoing similar ablative radiofrequency treatments. It is possible to have an adverse reaction to the Potenze™ device use. There may be some side effects that we don't know about yet.

3.3 Risk Analysis

CONTEXT OF THE PROPOSED INVESTIGATION:
Radiofrequency (RF) technology is commonly used in surgery, noninvasive treatments and aesthetic applications. RF technology combined with micro needling is a safe method for non-ablative (A non-wounding device treatment which heats underlying skin) treatment because energy can be precisely delivered through the skin to the dermal tissue beneath with minimal injury to the epidermis.

Aging skin shows decreased collagen synthesis and alteration of fiber networks. By gently heating dermis tissue (which is comprised of collagen, elastic fibers and ground substance), both immediate effects (collagen contraction) and long-term effects (wound-healing response with neocollagen production) will occur. RF-induced thermal injury to the dermal tissue will produce a microinflammatory response to induce collagen denaturation, contraction, and subsequent synthesis as well as elastin and ground substance production.[iii] Microneedling will cause discrete coagulative injury in the dermis while sparing the epidermis. This allows for a faster healing time and fewer complications in the treatment area.

The extent of collagen shrinkage, fibroblast activation, fibroplasia and neocollagenesis in the different skin layers is based on a complex multivariate mechanism, which depends on the

temperature distribution and timing.[2] Further investigation of parameter optimization is necessary to achieve safe and efficacious results.

ASSESSMENT OF RISKS OF THE PROPOSED INVESTIGATION:
There are two risks identified with the Potenza™ device used in this study. The first risk identified is the efficacy of the treatment. There is a lack of clinical data for evidence of effectiveness when treating with the Potenza™ device. The second risk identified is the safety profile of the device.

The risk identified with the overall clinical investigation is the integrity of the data collected.

There are multiple clinical mitigation strategies for the risks identified. Proper training on the device and protocol will be performed. Data from other comparable devices, such as the Lutronic Genius and Infini and Genius Vivace, will be utilized to minimize side effects and optimize treatment outcomes. Monitoring of the study will be implemented to minimize subject and data risks.

ASSESSMENT OF BENEFITS OF THE PROPOSED INVESTIGATION:
The subject may or may not have a reduction in the condition they present with.

CONSIDERATION OF PATIENT PREFERENCE INFORMATION:
Many physicians support the use of radiofrequency devices minimally invasive cosmetic treatments due to current patient satisfaction of cosmetic results with the currently available devices. However, there is still a level of interest in novel technologies that could reduce the need for future treatments.

ASSESSMENT OF UNCERTAINTY:
There is uncertainty of the safety and efficacy of the treatment with Potenza™ since it is not cleared for use by the FDA.

CONCLUSION:
The Potenza™ device is intended for electrocoagulation and hemostasis of soft tissues for dermatologic conditions. This device is determined to be a non-significant risk study. The risks posed to the subjects and integrity of data are acceptable.

Patient population to be enrolled in this clinical study:
Total anticipated population: 120 Subjects
Age Range years old: 18 – 55 Years Old
Gender: Male or Female
Condition: Such as, but not limited to; Wrinkles, fine lines, crepey skin, acne scars, active acne, enlarged pores, stretch marks, or loose skin on the face, neck and/or body.

4.0 DEVICE DESCRIPTION AND SPECIFICATIONS

The Potenza™ device was FDA cleared for use on February 20th, 2020 (K192545). The Potenza device is intended for use in dermatologic and general surgical procedures for electrocoagulation and hemostasis.

This study is considered investigational because this device may not be used within its currently cleared instructions for use.

The Potenza™ Device Specifications are:

Model/Class	POTENZA / IIb
Input Rating	100-240V, 50/60Hz, 500VA
Applied Frequency	1 & 2MHz
Maximum Power	**MOTOR Handpiece** Min1~Max50Watt, Rf Time=5~990ms, Output Voltage:0~100V(Load 200Ω) **SOLENOID Handpiece** Min1-Max50Watt, Rf Time = 5~400ms, Output Voltage:0~100V(Load 200Ω) **AC Handpiece** Min1-Max40Watt, Rf Time = 5~990ms, Output Voltage:0~80V(Load 200Ω)

The Potenza™ device Operator Manual: Attachment I

The Potenza™ consumables are: Tips, NEM Pads

5.0 MONITORING PROCEDURES

The Sponsor Standard Operating Procedure (SOP) for monitoring the investigative site will be followed. The sponsor will train the site following sponsor SOP's and may be present at initiation of treatment. The sponsor will also monitor the site periodically. The Investigator/Institution will permit trial-related monitoring, audits, IRB/IEC review, and regulatory inspections by providing direct access to source documents. The sponsor may request intermediate data following each visit to evaluate treatment progress. Case Report Forms will be reviewed for current data and Regulatory Binders will also be reviewed for correct documents. The sponsor will collect data at the end of the follow up period. The sponsor will list the study on clinicaltrials.gov when required by FDA regulations.

The monitoring plan for this study is outlined in the Cynosure Monitoring Plan.

ASSIGNED CLINICAL RESEARCH MONITOR:
Monitor #1
Name: Lisa Tocci
Institution: Cynosure, LLC
Address: 5 Carlisle Rd. Westford, Ma

6.0 LABELING

Sample labeling will follow FDA regulations and the sponsor standard operating procedure. If applicable, the Potenza™ device label will include, (in accordance with 801.1):

Statement: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use."

Additionally, the label or other labeling will describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings, and precautions.

Directions for use are contained in the Potenza™ Operators Manual

7.0 CONSENT MATERIALS

Forms and informational materials which are provided to the subject during the informed consent process are listed below:

Form/Informational Material Description
Pre and Post Treatment Instructions
Informed Consent Form

8.0 INSTITUTIONAL REVIEW BOARD INFORMATION

This protocol, informed consent forms, and any amendments to the protocol will be reviewed by the appropriate Institutional Review Board prior to initiation. The study will not be initiated without the approval from the Institutional Review Board.

IRB Contact Information:
IRB Name: Allendale Investigational Review Board
IRB Chairperson: Robert Staab
IRB Address: 30 Neck Rd. Old Lyme, CT 06371
Phone: 860-434-5872
Fax: 860-434-5892
Email: Rta1ali1@aol.com

9.0 OTHER INSTITUTIONS

If a part of the study is conducted by an institution that has not previously been identified within the Investigational plan each institution's contact information will be documented below;

No other institutions will be part of this study.

10.0 ADDITIONAL RECORDS AND REPORTS

If this is an IDE study, additional records and reports will be maintained on the investigation in addition to those prescribed in 21 CFR 812 sub-part G. If this is a non-IDE study, the study summary will be maintained on the investigation and may include those prescribed in 21 CFR 812 sub-part G.

Additional Records and Reports:

Report	Submit To	Description/Constraints
N/A	N/A	This is a non-IDE study; no additional records or reports will be maintained.

11.0 PREGNANCY

Females may not participate in this study if they are pregnant, breastfeeding, were pregnant within the last three months or are planning a pregnancy during the study.

If the subject thinks they have become pregnant during the study, it is important that they inform the Investigator immediately. If she becomes pregnant or thinks that she may be pregnant, she will be removed from the study and will be asked to perform a final evaluation similar to that of the final follow-up visit. The Investigator may request to track the pregnancy and will report the pregnancy to the Sponsor.

12.0 SUBJECT WITHDRAWAL

The subject is free to withdraw from this study at any time. The subject must inform the Investigator immediately if they intend to withdraw. To terminate the subject's participation in this study, they must contact the Investigator at the contact information listed on page one of the informed consent form. They will be asked to come to the study clinic or Investigators office to complete a final follow up visit and may be asked to perform end of study procedures. Their decision to participate in this study or to withdraw from this study will not influence the availability of their future medical care and will involve no penalty or loss of benefits to which they are otherwise entitled.

The Investigator in charge of the study can remove the subject from this study without their consent for any reason, including, but not limited to:

a) His/her judgment that any condition or circumstance may jeopardize their welfare or the integrity of the study.
b) Their failure to follow the instructions of the Investigator(s).
c) If the study is stopped by the sponsor and/or Investigators participating in the study prior to completion.

Data collected prior to withdrawal will be used in data analysis but after withdrawal no further data will be collected.

13.0 PHOTOGRAPHY

Standardized photographs will be taken of the treatment area. If the photograph is located on the face the subject will be asked to remove jewelry and make up and lotions prior to each photo session. Photographs will be taken with an appropriate high-resolution digital camera. Camera settings

(lighting, distance, background, polarization, etc.) will be reproduced at each visit, so that photographs are suitable for comparison. Photographs will be taken of the treatment area for study purposes. If the subject does not wish to have their photographs taken, they cannot be in the study.

14.0 ADVERSE REACTIONS DEFINITIONS AND REPORTING REQUIREMENTS

All adverse events that occur, starting from the time of the first treatment, will be recorded in the source documents and Case Report Forms (CRF).

Adverse Events (AE) occurring will be captured and followed until the condition resolves, stabilizes, is otherwise explained, or the subject is lost to follow-up. Subjects will be instructed that they may contact the Investigator at any time throughout the course of the study.

The Investigator and/or designated study staff will review each event and assess its relationship to the study device (not related, unlikely, possible, probable, and highly probable). The following definitions will be used for rating relationship to the Potenza™ treatments:

- Not related – The event is clearly related to other factors such as the subject's clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Unlikely – The event was most likely produced by other factors such as the subject's clinical state, therapeutic interventions, or a concomitant medication administered to the subject; and does not follow a known response pattern to the investigational product.
- Possible – The event follows a reasonable temporal sequence from the time of investigational product administration; **and/or** follows a known response pattern to the study sampling sessions; **but** could have been produced by other factors such as the subject's clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Probable – The event follows a reasonable temporal sequence from the time of investigational product administration; **and** follows a known response pattern to the investigational product; **and** cannot be reasonably explained by other factors such as the subject's clinical state, therapeutic interventions, or concomitant medications administered to the subject.
- Highly Probable – The event follows a reasonable temporal sequence from the time of investigational product administration; **and** follows a known response pattern to the investigational product; **and** cannot be reasonably explained by other factors such as the subject's clinical state, therapeutic interventions, or concomitant medications administered to the subject; **and** either occurs immediately following investigational product administration, **or** improves on stopping the investigational product, **or** reappears on repeat exposure, **or** there is a positive reaction at the application site.

  Each adverse event reported will be graded on a 3-point severity. Using the following definitions for rating severity will be used:

- Mild – easily tolerated, causing minimal discomfort, and not interfering with normal everyday activities.
- Moderate – sufficiently discomforting and may interfere with normal everyday activities.
- Severe – incapacitating and/or preventing normal everyday activities.

A Serious Adverse Event (SAE) is any adverse device experience that results in any of the following outcomes: death, a life-threatening adverse device experience, in-patient hospitalization or prolongation of hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may or may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse device experience when, based upon appropriate medical judgment, they may jeopardize the subject or subject may require medical or surgical intervention to prevent one of the outcomes listed in this definition

If any of the above adverse events are serious as defined by the FDA Code of Federal Regulations (CFR), Title 21, special procedures will be followed. All serious adverse events will be reported within 24 hours of acknowledgment to the Sponsor whether or not the serious events are deemed sampling session related. All serious event reporting will adhere to 21 CFR part 812 and the IRB will be notified accordingly.

The SAE information will be entered into the database and a desk copy of the complete SAE report will be submitted to the study file.

Adverse events, whether serious or non-serious, will be followed until the condition is resolved, stabilized, otherwise explained or the subject is lost to follow-up. Adverse events will be captured throughout the study and where appropriate, medical tests and examinations will be performed to document the resolution of event(s). Outcomes may be classified as resolved, improved, unchanged, worse, fatal, unknown or lost to follow-up. Following the resolution of any study-associated adverse events there will be no further adverse event reports for that subject.

Reporting Adverse Events:

Report	Submit To	Description/Constraints
Adverse Events, Unanticipated Adverse Device Effect	IRB and Sponsor	If an unforeseen complication is determined to be an unanticipated adverse device effect, the investigator's report must be submitted within 10 working days after the investigator first learns of the effect.
Serious Adverse Events	IRB and Sponsor	The sponsor must be notified within 24 hours of serious adverse events. The IRB must be notified within 10 working days of serious adverse events as defined by FDA guidelines.

15.0 PROTOCOL DEVIATIONS

All requests for protocol deviations by the Investigator have to be communicated to the sponsor in writing and if accepted by the Sponsor must be approved by the IRB. If a deviation occurs, the

Investigator must inform the Sponsor as soon as possible. The Sponsor will notify the IRB in accordance with IRB specific policies.

16.0 CONFIDENTIALITY AND DISCLOSURE OF MEDICAL INFORMATION

As part of this study the Investigator and the team at the research facility will keep records of subject participation in the study. These study records will include personal information that the subjects provide including age, sex, etc., the results of the study, information about response to treatments, photographs taken during the study and other medical information relating to participation in the study.

Under federal law the study records cannot be used or disclosed by the Investigator for research purposes unless subjects sign the informed consent authorization.

Some or all of the test results, photographs and other information will be reported to Cynosure, Inc. the manufacturer of the test device (Sponsor), and consultants that are helping conduct the study. The Sponsor and its consultants will analyze and evaluate these results and information and may report them to the U.S. Food Administration and the FDA, Institutional Review Board or other regulatory agencies in the United States and/or foreign countries. The subject's study records will be assigned a code number by the study team and they will ordinarily not be identified by name in the study records that are sent to the Sponsor and its consultants. However, The Sponsor, the Institutional Review Board and its consultants will have the right to see the complete study records, including the subject's name, and might choose to do so. If reports or articles are written about the study, the subject will not be identified by name in them however your study information and photographs may be used.

The research facility will review and use the study records only for purposes of this study. They will keep the subject's identity confidential and, except for the disclosures described above, will not disclose the study records to other parties unless disclosure is required by law. Once the research facility discloses information in the study records, photographs or medical records to the Sponsor or its consultants, the information will no longer be protected by federal law. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed. However, the Sponsor and its consultants will only use information for purposes of the study and will not disclose your study records to parties other than; the FDA or other regulatory agencies in the United States and/or foreign countries, unless disclosure is required by law. If reports or articles are written about the study, subjects will not be identified by name in them however, subject study information and photographs may be used.

Study records will be kept at the research facility according to applicable regulations and policies and may be kept indefinitely following the completion of the study. Subjects will not have the right to review their records while the research is in progress. However, they will be able to review their records after the research has been completed.

17.0 CLINICAL RESEARCH CONDUCT

The study will be conducted in accordance with the protocol, International Conference on Harmonization (ICH) GCP guidelines, applicable regulations and guidelines governing clinical study conduct and ethical principles that have their origin in the Declaration of Helsinki. The investigator must ensure that the study is conducted in accordance with the provisions as stated in the FDA regulations and complies with the applicable local or regional regulatory requirements.

18.0 REPORTING FOR THE STUDY

A study summary report will be generated. It will include a description of the clinical conduct of the study and results.

Study Summary Reporting:

Report	Submit To	Description/Constraints
Deviation from Investigational Plan	IRB and Sponsor	A deviation performed in an emergency to protect the life or physical well-being of a patient necessitates notification of the IRB and sponsor. The Investigator's report must be submitted within 5 working days after the emergency occurred. Deviations in a non-emergency situation require notification to sponsor prior to implementation
Failure to Obtain Informed Consent	IRB and Sponsor	The Investigator must make notification within 5 working days after device use, using the Protocol Deviation CRF. The report must include a brief description of the circumstances justifying the failure to obtain informed consent.
Final Report	IRB and Sponsor	The Investigator must submit a final report within 3 months after termination or completion of the investigation.
Withdrawal of IRB approval	Sponsor	The Investigator must report a withdrawal of the reviewing IRB approval within 5 working days.
Progress Report	IRB, Monitor and Sponsor	The Investigator must submit progress reports at regular intervals, and as required by the IRB, but in no event less than annually.

19.0 DISCLOSURE

The Principal Investigator and Cynosure employees and consultants have signed confidentiality agreements with the sponsor. This confidentiality agreement ensures that all information provided to the Investigator or Data Management and Statistics group dealing with the study and information obtained during the course of the study will be regarded as confidential.

20.0 RESPONSIBILITY OF THE INVESTIGATOR

The Investigator is responsible for ensuring that the clinical study is performed in accordance with the International Conference on Harmonization (ICH), Good Clinical Practice (GCP) guidance E6, FDA Good Clinical Practice Regulations, Declaration of Helsinki (DoH) and the Health Human Service (HHS) Belmont Study. Investigators will supply information to the sponsor such that the sponsor can comply with the Financial Disclosure Rules.

21.0 PROCEDURE FOR AMMENDMENTS TO PROTOCOL

No deviations from this protocol will be permitted, except in a medical emergency, without the approval of the Sponsor. Any amendment to this study will be discussed by the Investigator and the Sponsor. If agreement is reached concerning the need for modification, this will be made in a formal amendment to the protocol.

All revisions and/or amendments to the protocol must be approved in writing by the appropriate Institutional Review Board.

22.0 TERMINATION OF STUDY

The Sponsor reserves the right to discontinue this study for administrative reasons at any time. The Investigator reserves the right to discontinue the study for safety reasons at any time in collaboration with the Sponsor.

23.0 DATA SECURITY

To ensure the privacy and confidentiality of data for this protocol, the data will be stored on a restricted access location on a company server. Access to the project directory containing the data will be limited to the Investigators and research staff. Information about data security awareness is promoted through user training and education, supplemented by policies and procedures. Password protection will be used for all transactions that allow viewing, editing, and analysis of data, or that provide access to data fields derived from the original source documents.

24.0 REPORT OF PRIOR INVESTIGATIONS

The report of prior investigations or predicates are:

Protocol	Device	IRB Name	Determination	Initial IRB Approval Date
N/A	N/A	N/A	N/A	N/A

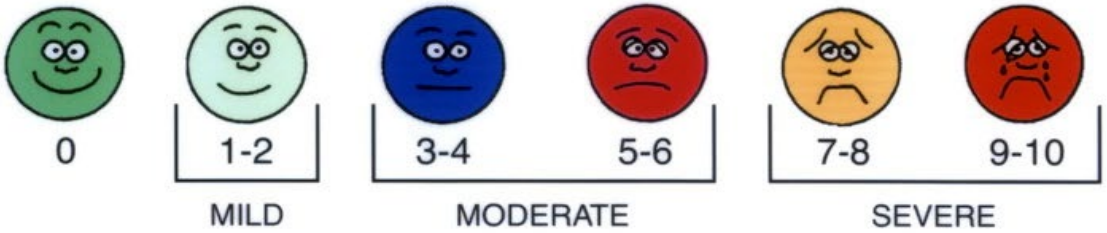
APPENDIX A:
Protocol Revisions Tracker

Version Date	Editor	Description
July 2, 2019	Kristy Luis	IRB Submission
July 26, 2019	Kristy Luis	IRB Response, Added Dr. Weiss and Dr. Dierickx
August 28, 2019	Kristy Luis	Reduced minimum age from 21 to 18. Revised follow-up schedule. Added folliculitis to possible adverse events and removed pustules. Other admin changes.
December 4, 2019	Kristy Luis	Increased number of treatments from 3 to 5 and changed intervals to 4 weeks (+/- 2 weeks). Added fish oil as cautionary criteria. Added the use of local anesthesia and air cooling during treatment. Updated post treatment instructions. Added questionnaires to 1-week phone call/visit. Updated Possible Adverse Events to include pinpoint bleeding and scarring and replaced paralysis with paresis. Other admin changes.
December 10, 2019	Kristy Luis	Added Dr. McDaniel and Dr. Tanghetti to protocol. Added biopsy portion of study.
February 4, 2020	Kristy Luis	Updated possible adverse events to include pain/tenderness, bruising, acne, dryness, eye twitching, eye tearing, petechiae, and skin textural irregularity.
July 31, 2020	Kristy Luis	Updated FDA clearance, added NBTC staining to biopsies, updated biopsy schedule
December 7, 2020	Kristy Luis	Increased number of subjects to 120. Changed optional 24hr phone call to a call or visit.

APPENDIX B:

UNIVERSAL PAIN ASSESSMENT TOOL

This pain assessment tool is intended to help patient care providers assess pain according to individual patient needs. Explain and use 0-10 Scale for patient self-assessment. Use the faces or behavioral observations to interpret expressed pain when patient cannot communicate his/her pain intensity.



ACTIVITY TOLERANCE SCALE	NO PAIN	CAN BE IGNORED	INTERFERES WITH TASKS	INTERFERES WITH CONCENTRATION	INTERFERES WITH BASIC NEEDS	BEDREST REQUIRED
SPANISH	NADA DE DOLOR	UN POQUITO DE DOLOR	UN DOLOR LEVE	DOLOR FUERTE	DOLOR DEMASIADO FUERTE	UN DOLOR INSOPORTABLE
FRENCH	AUCUNE DOULEUR	LÉGÈRE DOULEUR	DOULEUR MODÉRÉE	FORTE DOULEUR	TRÈS FORTE DOULEUR	DOULEUR EXTRÊME
GERMAN	KEINE SCHMERZEN	LEICHTE SCHMERZEN	MÄSSIGE SCHMERZEN	STARKE SCHMERZEN	SEHR STARKE SCHMERZEN	EXTREME SCHMERZEN
JAPANESE	痛みなし	軽い痛み	中程度の痛み	ひどい痛み	非常にひどい痛み	最悪の痛み

REFERENCES

[1] Sherber, N. S., MD FAAD. (2018). The Millennial Mindset. *Journal of Drugs in Dermatology, 17*(12), 1340-1342.
[2] Elsaie, M. (2009). Cutaneous Remodeling and Photorejuvenation Using Radiofrequency Devices. *Indian Journal of Dermatology, 54(3),* 201. doi:10.4103/0019-5154.55625
[iii] Levy, Adam S. et al. (2016). Radiofrequency Physics for Minimally Invasive Aesthetic Surgery. *Clinics in Plastic Surgery, 43(3)*, 551 – 556. doi: https://doi.org/10.1016/j.cps.2016.03.013