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POST MARKET STUDY TO COLLECT EFFICACY DATA FOR THE TREATMENT OF WRINKLES WITH A RADIOFREQUENCY DEVICE
UNIQUE PROTOCOL ID: 7027-PM01-2021

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INVESTIGATIONAL PLAN

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POST MARKET STUDY TO COLLECT EFFICACY DATA FOR THE TREATMENT OF WRINKLES WITH A RADIOFREQUENCY DEVICE

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.

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POST MARKET STUDY TO COLLECT EFFICACY DATA FOR THE TREATMENT OF WRINKLES WITH A RADIOFREQUENCY DEVICE

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)

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ATTACHMENTS/REFERENCES

I. Operator Manual for the TempSure device
II. Clinical Reference Guide for the TempSure device
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 TempSure device. The study will be using the Mini Envi handpiece and may also use the Envi handpieces and Icon device (Max series).

The intended use of the TempSure device used in this study to assess the efficacy of the handpiece for the treatment of facial wrinkles. If the Icon device is used, the intended use will be for the treatment of benign pigmented and/or vascular lesions.

1.2 Objectives

1. Primary Objective:
   - Photographic evaluation with correct identification of pre-treatment 2D images when compared to the 12 week follow up images performed by three independent reviewers.
2. Assessments:
   - Photographic evaluation with correct identification of pre-treatment 2D images when compared to the 4 week follow up images performed by three independent reviewers.
   - Photographic evaluation with Fitzpatrick Wrinkle Severity Scale (FWSS) grading comparing pre-treatment images to the 4 and 12 week follow up images performed by three independent reviewers.
   - Principle Investigator assessment using the Global Aesthetic Improvement Scale (PGAIS) at the 4 and 12 week follow up visit.
   - Subject assessment using the Global Aesthetic Improvement Scale (SGAIS) at the 4 and 12 week follow up visit.
   - Subject Questionnaires
     - Pre-Treatment 1
     - Post Treatment 1
     - Follow Up
3. Safety Objectives:
   - Collection of Adverse Events
   - Collection of Treatment Discomfort/Pain Evaluation

1.3 Duration of the Investigation

The sponsor anticipates that all subjects can be enrolled within 3 months. If subject participates in all required visits, then the subject's participation in this study may last up to 6 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 12 months.

2.0 PROTOCOL

2.1 Protocol Methodology and Analysis

Methodology:
Subjects are to be enrolled in this clinical study if they are a healthy male or female 18 years of age or older. Up to 50 subjects will be enrolled at 3 study centers. Subjects will be enrolled into 2

groups, Group A for TempSure treatments only and Group B for TempSure and Icon treatments. Randomization will not be required as subjects will only be enrolled in Group B and treated with the Icon device if they present with pigment and/r vascular lesions. Subjects will attend a screening/pretreatment visit which may be performed on the same day as the treatment visit. Subjects in Group A will receive up to 4 treatments with the TempSure device on the face. Subjects in Group B will receive 2 treatments with just the TempSure device and 2 treatments with both the TempSure and Icon device. Some subjects may be asked to return for an optional 5th treatment (2 – 3 weeks post last treatment) with the Icon device (and/or TempSure device) after the completion of their 4 treatments at the discretion of the Investigator. Subjects may receive a phone call 1 week (1-7 days) after each treatment to record side effects. Subjects will return for follow up visits at 4 and 12 weeks post last treatment for efficacy and side effects assessments. 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 non-ablative aesthetic 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 technology for the treatment facial wrinkles and skin laxity needs to be further investigated to optimize treatment parameters for safe and effective non-ablative aesthetic treatments.

Relevance:
Over time, skin structure degrades due to a variety of internal and external conditions. As enzymes break down collagen and elastin, skin loses its suppleness and becomes loose. UV exposure, diet, and smoking among other behaviors all contribute to the skin becoming lax. Body wrinkles, particularly on the abdomen, are a sign of aging and are also a prevalent concern with postpartum women or subjects who have lost weight. It is estimated that adult skin loses approximately 1% of its dermal collagen content on an annual basis due to increased collagen degradation and decreased collagen synthesis.[2] Radiofrequency, ultrasound, non-ablative fractional technology, and ablative technology have all been used to varying degrees of success. The limitations of current products on the market include different side effect profiles and modes of administration.

Testability:
The TempSure device is currently cleared for use for non-ablative treatment of mild to moderate facial wrinkles and rhytids (K171262). The Icon device is currently cleared for used for the Max Series Intense Pulsed Light Handpieces for the treatment of benign pigmented epidermal and cutaneous lesions, including warts, scars and striae; removal of unwanted hair from skin types 1-VI, and to effect stable long-term, or permanent, hair reduction; treatment of benign pigmented lesions, including lentigines, nevi, melasma, and cafe-au-lait; and treatment of vascular lesions, including port wine stains, hemangiomas, angiomas, telangiectasias, rosacea, facial and leg veins (K103664). This study will utilize the collection of data and imaging to support current and additional marketing claims.

Compatibility:

In earlier stages of facial wrinkles and skin laxity, and therefore younger subjects, there is normally minimal appearance of those conditions, allowing for less aggressive and therefore safer overall treatments. Younger subject's bodies are also capable of responding to the treatment quicker due to their ability to produce more collagen quicker than an older subject. As a subject gets older their condition becoming more severe, this may result in the subject needing more overall treatment and more aggressive treatments to get their body to respond the same way that a younger subject may be able to respond.

Predictive power:
While this study will observe the efficacy of the device on the face, this treatment could potentially be applied to a variety of body areas and other potential applications. Assuming there an acceptable safety profile, it would be appropriate to expect results in different areas.

2.2 Protocol Study Design

This is a prospective, open label, multi-center clinical study to collect efficacy data on the TempSure device and may also collect data on the Icon device.

2.3 Subject Selection Criteria

Subjects will meet the criteria described below:

Inclusion Criteria:

- A healthy male or female 18 years of age or older.
- Agrees to be treated with the TempSure device.
- 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 has a cut, wound, or infected skin on the area to be treated.
- The subject is on local, oral, or systemic anesthetic agents.
- The subject has nerve insensitivity to heat in the treatment area.
- 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:

- 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 (or at the discretion of the Investigator) prior to entering this study.

- The subject has any embedded electronic device that gives or receives a signal, the device should be turned off or removed prior to treatment.
- The subject has an embedded pacemaker or implantable cardioverter defibrillator (ICD), the client's cardiologist must be consulted prior to treatment.
  NOTE: This device has not been tested on patients implanted with electronic devices that receive or emit signals, such as: Pacemakers, Implantable Cardiac Defibrillators (ICD), or Cardiac Resynchronization Therapy (CRT) devices.
- If the neutral pad would need to be placed on a subject that has a metal plate, rod, or any metal implant that could conduct heat from the Smart Handpiece or surgical handpiece.
- The subject is allergic to adhesives, such as glues on medical tape, they should be alerted that a rash may occur on the neutral pad site and an over the counter solution may be used to treat the area.
- The subject is allergic to gold, such as the metallic covering of the TempSure handpieces.
- The subject is allergic to corn, such as the corn derivative ingredient in Parker Aquasonic Gel.
- If the subject has an unhealthy expectation of the results – this is not plastic surgery and all subject should be fully informed of the treatment's expected results.
- The subject has severe laxity or sagging that causes redundant folds of tissue or hanging skin in the area to be treated – this treatment will be ineffective.
- The subject has used Accutane (Isotretinoin) six to twelve months prior to treatment, as this can thin the skin and make it brittle.
- Studies of the use of the RF generator on subjects that have any of the following conditions is unknown:
  - Autoimmune Disease
  - Diabetic
  - Herpes Simplex
- Use caution when treating areas that have scars, tattoos, permanent makeup, and permanent brows.

Exclusion Criteria for Icon Treatments Only:

- The subject is using systemic steroids (e.g. prednisone, dexamethasone) prior to or during the course of treatment.
- The subject has a medical condition or is receiving treatment that significantly compromise healing response.
- The subject has a history of light-induced seizures.
- The subject has a history of skin photosensitivity disorders.
- The subject has a history of hypertrophic scars or keloid formation.
- The subject has a history of radiation therapy in area to be treated.

Additional Cautionary Criteria for Icon Treatments Only:

- The subject is not allergic to medications, latex or other substances that may be used during treatment course.
- The subject's skin type is appropriate for the handpiece to be used.
- The subject is taking photosensitizing medication. Perform test spots 24 hours up to one week before considering treatment.

- The subject is currently taking blood thinning medications or anti-coagulants. The subject should discontinue the use of these medications if determined to be safe to do so by their prescribing physician. With the prescribing physician's approval, the subject should stop taking the medication at least 2 weeks prior to and throughout the treatment course.
- The subject has a condition or is taking medications that alters the ability of the blood to coagulate.
- The subject is currently using Tretinoin and topical retinoids, e.g., Retin-A®, Renova® and exfoliating products. Although use in the area to be treated is not absolutely contraindicated, it is known to make skin more sensitive and prone to exfoliation. Candidates for Icon™ treatment should be advised to discontinue the use of exfoliating creams and other exfoliating products two (2) weeks prior to and during the entire treatment course.
- The subject has a history of heat urticaria. They may develop hives with exposure to light pulses.
- The subject has Herpes I or II within the treatment area. Before a treatment, candidates should consult their primary care physician for medical evaluation and possible prophylaxis to minimize the chance of a herpetic breakout. A small percentage of persons may experience an activation of oral herpes simplex virus infection within 5-10days after the procedure, even with appropriate prophylaxis.
- The subject has received Botulinums treatments in the treatment area. There is the possibility for increased diffusion of Botulinums, such as Botox®, as a result of edema associated with facial light-based treatment, which may result in facial asymmetry when these procedures are performed at the same visit. Many physicians recommend waiting for a minimum of 2 weeks after a Botox injection before performing facial light-based treatments. Cynosure has conducted no clinical trials and cannot recommend any specific waiting time.
- The subject has Pigmented Lesions in treatment area. If treating over a pigmented lesion, the lesion must be diagnosed as benign by a qualified practitioner prior to treatment. Inaccurate diagnosis and inadvertent treatment of a skin cancer may lead to a delay in the person receiving proper medical care.
- Th subject has Cosmetic Dermal Fillers/Implants in treatment area. This Handpiece has not been evaluated or tested on areas with cosmetic dermal fillers, neurotoxins, or implants.
- The subject has had unprotected sun exposure or use of tanning beds or creams in areas to be treated. Protected sun exposure means wearing protective clothing and the daily use of a SPF-45 or greater sunscreen. Those being treated should be advised to discontinue indoor and outdoor tanning at least four (4) weeks prior to treatment, during the treatment course, and four to six (4 to 6) weeks after treatment. This will reduce the chance of skin color changes and manifestation of new pigmented lesions.
- The subject has a history of Menstrual dysfunction/Polycystic Ovarian Syndrome (PCOS). Those with menstrual dysfunction, such as PCOS and/or ovarian hyperandrogenism, may have unpredictable results. These subjects tend to have hirsutism secondary to their disease and should consult a primary care physician before a light-based treatment.
- The subject has a history of vitiligo, eczema, psoriasis, allergic dermatitis, any diseases affecting collagen including Ehlers-Danlos syndrome, and scleroderma may affect response to treatment.

- The subject is of Middle Eastern and Mediterranean descent. They may have an ill-defined hair line with no obvious transition of the hairline to the face which may put them at risk of paradoxical hair growth. These clients are at a high risk for hair stimulation and should be advised of this phenomenon before treating.

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

Subjects will be recruited for the study through the existing patient database and may also be recruited through 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 be participating 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 will be discussed, and 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 form and their involvement in the study. Subjects will be informed of site's COVID-19 procedures that adhere to federal and state guidelines at this time. 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.

2.6 Pre-Treatment Procedures

If the subject is of childbearing potential (i.e. females not post-menopausal or not surgically sterile), they will be asked if they are pregnant, the date of their last menstrual cycle, and perform a urine pregnancy test at the site prior to their first treatment. Pregnancy verification will be performed by verifying the date of their last menstrual cycle at each subsequent treatment. A urine pregnancy test may also be conducted at the Investigator's discretion at any time 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.

- Photographs will be taken prior to the first treatment and may be taken prior to each subsequent treatment.
- The following Pre-Treatment instructions will be reviewed:
  - Shave any visible hair on the area to be treated.
  - Do not wear constrictive clothing. Your back must be accessible for the neutral pad to be attached.
  - The treatment area must be free of any open lesions or infections.
  - 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 24 hours in advance.

2.7 Treatment Procedures

- Prior to treatment 1 only, subjects will be asked to complete a Pre-Treatment 1 Questionnaire.
- The defined study area will be identified and may be marked with a surgical marker.
- Procedures for the TempSure treatment:
  - A neutral pad will be placed on the back in an area determined by the Investigator to maintain standard energy settings and to require less power from the device during the treatment.
  - The subject may be required to wear eye shields at the discretion of the Investigator.
  - Gel will be applied to the treatment area.
  - The handpiece will be placed in contact with the skin.
  - The entire defined treatment area will then be treated by delivering energy to the skin.
  - Temperature will be continuously monitored and recorded during treatment.
- Procedures for the Icon treatment:
  - All operators and subjects will wear appropriate protective eyeglasses during the pulse-light treatments.
  - The Skintel Melanin Reader may be used for objective measurement of the melanin content of skin. The Skintel Reader may provide guidance to help select test spot settings.
  - Test spots will be performed prior to treatment in an area in or close to the treatment area in order to determine safe parameters for treatment.
  - The handpiece will be placed in contact with the skin.
  - The entire defined treatment area will then be treated by delivering adjacent pulses with minimal overlap of 20% or less.

- An air-cooling system may be used during treatment. The air-cooling system allows for the continuous flow of cold air on the treatment area to ease the sensation from the pulse.

- Parameters may be adjusted throughout the treatment to increase subject comfort.
- 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.
- The additional treatments will follow the same procedure.
- Subjects will receive up to 4 treatments on the face. Subjects in group B may be asked to return for an optional 5th treatment with the Icon device (and/or TempSure device) at the discretion of the Investigator.

2.8 Post Treatment Procedures

- Adverse events will be documented after treatment.
- Photographs may be taken post treatment.
- After treatment 1 only, subjects will be asked to complete a Post Treatment 1 Questionnaire.
- The following post treatment instructions will be reviewed:
  - If the skin is slightly pink or red in areas following the treatment, avoid hot water when washing or showering until any erythema (redness) has subsided.
  - Soothing creams or moisturizers, such as Aveeno, may be used.
  - Gently massage the treated area daily for 5 minutes for the duration of your involvement in the study.
  - Use a sun block with UVA and UVB protection with SPF of 30 or greater to prevent sun damage.
  - Maintain the same weight and exercise routine throughout the study.
- If the subject is treated with the Icon device, the following post treatment instructions will also be reviewed:
  - A mild sunburn-like sensation is expected. This usually lasts two to twenty-four (2-24) hours but can persist up to seventy-two (72) hours. Mild swelling and/or redness may accompany this, but it usually resolves in two to three (2-3) days. Apply wrapped ice or gel packs to the treatment area for ten to fifteen (10-15) minutes every hour for the next four hours, as needed. Never apply ice directly to skin. An oral, over-the-counter anti-inflammatory (ibuprofen such as Advil®) or an analgesic (acetaminophen such as such as Tylenol®) may be taken to reduce discomfort. Use medicine according to manufacturer's recommendations.
  - Until redness has resolved, it is recommended to avoid the following:
    - Applying cosmetics to treated areas.
    - Swimming, especially in pools with chemicals, such as chlorine.
    - Hot tubs, Jacuzzis, and saunas.
    - Activities that cause excessive perspiration or any activity that may raise core body temperature.
    - Sun exposure and tanning in treated areas. Apply a SPF 45 or greater sunscreen to prevent skin color changes.
    - Aggressive scrubbing and use of exfoliants on the treated area.
  - Bathe or shower as usual. Treated areas may be temperature-sensitive.

- Pigmented lesions may initially look raised and/or darker with a reddened perimeter.
- Pigmented lesions will gradually turn darker over the next twenty-four to forty-eight (24-48) hours. It may turn dark brown or even black.
- Pigmented lesions will progress to darkening and/or crusting and will start flaking off in an average of seven to twenty-one (7-21) days.
- Vascular lesions may undergo immediate graying or blanching, or they may exhibit a slight purple or red color change. The vessels will fully or partially fade in about ten to fourteen (10-14) days.
- Do not pick or pull at darkened lesions as scarring may occur.

2.9 Follow Up

- Subjects may receive a phone call 1 week (1-7 days) after each treatment to record side effects.
- Subjects will return for follow up visits at 4 and 12 weeks post last treatment.
- Photographs will be taken, adverse events will be documented, and subject questionnaires will be performed at all follow up visits.
- Any subject affected by COVID-19 that is not able to attend their follow up visits to complete the study will be asked to return to the site for a final follow up visit within 1 year of last treatment.
- 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 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.

2.11 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.

2.12 Schedule of Visits and Procedures

	Visit #1*	Visit #2 - 5	Treatment Visit*** (Optional)	Call (Optional)	Visit #6	Visit #7
Procedure	Screening and Pretreatment Procedures	Treatment Visits 1-4 (1 - 2 weeks apart)	Treatment Visit #5 (2 - 3 weeks post last treatment)	Phone Call 1 Week Post Each Tx (1-7 Days)	Follow Up 4 Weeks Post Last Tx (+/- 1 Week)	Follow Up 12 Weeks Post Last Tx (+/- 1 Week)
Medical History	X					
Pregnancy Verification**	X	X	X			
Informed Consent	X					
Photographs	X	X	X		X	X
FWSS	X				X	X
Subject Pre-Treatment 1 Questionnaire		X				
Treatment		X	X			
Treatment Discomfort/ Pain Evaluation		X	X			
Subject Post Treatment 1 Questionnaire		X				
PGAIS					X	X
SGAIS					X	X
Subject Follow Up Questionnaire					X	X
Adverse Events Assessment	X	X	X	X	X	X

*Screening and Pretreatment Procedures may occur at the same time as the first Treatment Visit.
**Pregnancy verification required before each treatment only for women of childbearing potential.
***Group B only

2.13 Evaluation Methods

Photographs:
Photographs will be taken at baseline and at the 4 and 12 week follow up visit, and may be taken at eat treatment visit to assess the efficacy and safety 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)

Fitzpatrick Wrinkle Severity Scale
The Fitzpatrick Wrinkle Severity Scale will be used to evaluate outcomes. Live evaluation will be performed at Baseline and the 4 and 12 week follow up visits. The results will be compared to determine improvement.

Class	Wrinkling	Score	Degree of Elastosis
I	Fine wrinkles	1-3	Mild (fine textural changes with subtly accentuated skin lines)
II	Fine to moderate-depth wrinkles, moderate number of lines	4-6	Moderate (distinct papular elastosis [individual papules with yellow translucency under direct lighting] and dyschromia)
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 cutis rhomboidalis)

Subject Treatment Questionnaire:
Subject treatment questionnaires may be collected from each subject to obtain feedback on their treatment experience.

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 Dermatologists and/or Surgeons and will be chosen based on availability and have relevant clinical experience. They will attend a training session prior to grading.

Physician and Subject Questionnaire:
The Global Aesthetic Improvement Scale (GAIS) ranging from "worse" to "very much improved" will be used to judge the improvement as seen by the subject and 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.

2.14 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 TempSure Device:
Mild discomfort during treatment may be experienced by the subject. Typically, the discomfort is temporary and localized within the treatment area. Mild edema (swelling) and erythema (redness) may occur. Initial studies indicate that these side effects typically resolve within 2 to 24 hours.

Other anticipated side effects may include; pain, skin burns, bleeding, scarring, crusting, bruising, infection, itching, prolonged edema (swelling) and erythema (redness), hardness, and nodules. Loss of hair pigment may also occur within and adjacent to the treatment area.

Adverse Events Pertaining to the Icon Device:
Adverse effects can include discomfort/pain, redness, swelling, pinpoint bleeding, skin peeling, itching, scabbing, crusting, purpura, and bruising, which are usually transient and resolve without intervention.

Possible adverse effects include pustules (such as ingrown hairs), skin burns, hypopigmentation, hyperpigmentation, removal or lightening of freckles, scarring, infection and allergic reaction (such as a rash). There is also risk of incidental hair reduction or removal in the treated areas.

People of Middle Eastern and Mediterranean descent and those who have an ill-defined hair line with no obvious transition of the hairline to the face are at a high risk for hair stimulation (paradoxical hair growth).

Adverse Events Pertaining to Gel:
The gel is a water-based gel that may be placed on the skin during the TempSure® treatment. No known adverse events are documented. However, an allergic reaction is always possible when placing a topical gel onto the skin. Allergic reaction may include a mild reaction such as skin redness, irritation, or hives.

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 Cooling:
Anticipated transient side effects associated with forced air/contact cooling may include tingling, itching, decreased sensation, numbness, redness and pain.

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.

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

2.15 Statistical Analysis

2.15.1 Hypothesis

For this study to be considered a success, of pre-treatment images when compared to post treatment (90 day) images will be ≥80%.

For the additional assessments to be considered a success, the following must be true:

- In cases where the subject's improvement is being graded on a scale, such as the FWSS and GAIS scale, we will test the statistical significance of our results against a hypothetical population that would have no change (average score of 4).
- Subject treatment and clinician usability questionnaires are collected.
- The side effect profile (adverse events) and the average pain score is acceptable to the Physician as it relates to the type of treatment.

2.15.2 Sample Size Rationale

Based on the need for data collected from this study, it was determined that a total of 50 subjects will be required, including departures.

2.15.3 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.

2.15.4 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.

2.15.5 Analysis of Efficacy Variables
Additional efficacy variable is the change from baseline to Visit 7 (12 week follow up visit). Baseline is defined as the last assessment prior to the first treatment. The change from baseline to visits 6 and 7 will be analyzed using a Mixed Model Repeated Measures Analysis of Variance. A pairwise treatment group comparison at visit 7 will be performed using the results of this analysis. If a patient has no post-baseline assessment of the primary efficacy variable it will be assumed that the change from baseline to visit 7 is zero. The changes to visits 6 and 7 will be left as missing. Statistical significance with respect to the treatment group comparison at visit 7 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. The summaries will include the sample size, mean, median, standard deviation, minimum, and maximum. The statistical significance of the mean change from baseline for each treatment group will be determined using a paired t-test.

2.15.6 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 non-ablative radiofrequency treatment. It is possible to have an adverse reaction to the TempSure 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 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 without damaging 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.[3] This, in turn, creates a tightening effect that helps to eliminate facial wrinkles, and is also used for other cosmetic treatments on the body.[4]

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:

The risk identified with the overall clinical investigation is the integrity of the data collected. There are multiple clinical mitigation strategies for the risk identified. Proper training on the protocol will be performed. 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 improvement in their facial wrinkles.

CONSIDERATION OF PATIENT PREFERENCE INFORMATION:
Many physicians support the use of radiofrequency devices for non-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 efficacy results while using the TempSure device in this study.

CONCLUSION:
This device is determined to be a non-significant risk study and will be using a handpiece not cleared for use by the FDA. The Icon device is cleared for use by the FDA but may not be used within its currently cleared instructions for use. The risks posed to the subjects and integrity of data are acceptable.

Patient population to be enrolled in this clinical study:
Total anticipated population: 50 Subjects
Age Range: 18 years of age or older
Gender: Male or Female
Condition: Facial Wrinkles (TempSure) and benign pigmented and/or vascular lesions (Icon)

4.0 DEVICE DESCRIPTION AND SPECIFICATIONS

The TempSure® device used in this study is currently cleared by the U.S. Food and Drug Administration (the FDA). The TempSure® device received 510(k) clearance under K171262 on September 22, 2017 for:

- The 10mm, 15mm, and 20mm TempSure Envi handpieces are indicated for non-ablative treatment of mild to moderate facial wrinkles and rhytids.
- The 18mm, 25mm, and 30mm TempSure Envi handpieces provide heating for the purpose of elevating tissue temperature for selected medical conditions such as temporary relief of pain, muscle spasms, and increase in local circulation.
- The Massage device is intended to provide a temporary reduction in the appearance of cellulite.
- Coagulation/Hemostasis: Using the surgical handpieces and accessories, general surgical procedures including urologic, thoracic, plastic, reconstructive, and gynecological procedures where electrosurgical coagulation of tissue is performed.

And received 510(k) clearance under K182365 on October 24, 2018 for:

- Cutting: snoring. submucosal palatal shrinkage, traditional uvulopalatoplasty (RAUP),

myringotomy with effective hemorrhage control, epistaxis treatment, turbinate shrinkage, skin incisions, biopsy, cysts, abscesses, tumors, cosmetic repairs, development of skin flaps, skin tags and blepharoplasty.

- Blended Cutting and Coagulation: snoring, submucosal palatal shrinkage, traditional uvulopalatoplasty (RAUP), myringotomy with effective hemorrhage control, epistaxis treatment, turbinate shrinkage, skin tags, papilloma keloids, keratosis, verrucae, basal cell carcinoma, nevi, fistulas, epithelidma, cosmetic repairs, cysts, abscesses, and development of skin flaps.
- Fulguration: basal cell carcinoma, papilloma, cyst destruction, tumors, verrucae, hemostasis.
- Bipolar: pinpoint precise coagulation, pinpoint hemostasis in any field (wet or dry). Snoring, submucosal palatal, shrinkage, traditional uvulopalatoplasty (RAUP), myringotomy with effective hemorrhage control, epistaxis treatment and turbinate shrinkage

The 60mm handpiece (under K190678 on July 24, 2019) and FlexSure applicators (under K200241 on March 25, 2020) of the TempSure® device received 510(k) clearance to provide heating for the purpose of elevating tissue temperature for selected medical conditions such as temporary relief of pain, muscle spasms, and increase in local circulation.

Changes to the TempSure® device are anticipated during the investigation as the Mini Envi handpiece is expected to receive clearance for use from the FDA.

The TempSure® Device Specifications are:

Surgical Connector	1 surgical monopolar port
Neutral Connector	One universal neutral connector compatible with Cynosure neutral electrodes
Smart Handpiece Connectors	One 4-pin circular connector for both RF energy delivery and temperature sensing (monopolar)
Modes of Operation	Select the Smart Handpiece or Surgical mode of operation
Maximum Power	**Temperature-Sensing Handpieces** ⚠ 10mm, 15mm, and 20mm handpieces have a maximum GUI setting of 70, which provides output power of 120 Watts (+/- 20%). ⚠ 18mm handpiece has a maximum GUI setting of 25, which provides output power of 25 Watts (+/-20%). ⚠ 25mm and 30mm handpieces have a maximum GUI setting of 80, which provides output power of 165Watts (+/- 20%). ⚠ 60mm handpieces have a maximum GUI setting of 100, which provides output power of 300 Watts (+/- 20%). ⚠ FlexSure applicators are controlled by setting the temperature. During treatment, power can reach a maximum output of 300 Watts (+/- 20%). Ensuring that the neutral pad recommended for use with the 60mm handpiece and flexible applicator has sufficient current carrying capacity so as to assure that there is no unacceptable temperature rise under the pad is an essential performance of the TempSure platform.

The TempSure® consumables are: Handpieces, NEM Pads

The Icon device used in this study is currently cleared by the U.S. Food and Drug Administration (the FDA). The Icon device received 510(k) clearance under K103664 on March 17, 2011 for:

The Max Series Intense Pulsed Light Handpieces are intended for the treatment of inflammatory acne (acne vulgaris) and for the treatment of benign pigmented epidermal and cutaneous lesions, including warts, scars and striae; removal of unwanted hair from skin types 1-VI, and to effect stable long-term, or permanent, hair reduction; treatment of benign pigmented lesions, including lentigines, nevi, melasma, and cafe-au-lait; and treatment of vascular lesions, including port wine stains, hemangiomas, angiomas, telangiectasias, rosacea, facial and leg veins.

The Icon Device Specifications for the Max G handpiece are:

The ***MaxG™ Handpiece*** is recommended for treatment of benign pigmented lesions and vascular lesions, e.g., telangiectasias, rosacea, port-wine stain, hemangioma, angioma, and spider veins, on skin types I-IV.

MaxG™ Pulsewidth (ms)	Minimum Fluence (J/cm²)	Maximum Fluence (J/cm²)	Fluence Increments
1	3	11	1
2	5	21	2
3	6	30	2
5	6	36	2
10	20	54	2
15	20	60	2
20	20	68	2
25	20	74	2
30	20	80	2
40	20	80	2
60	20	80	2
80	26	80	2
100	32	80	2

Handpiece	Spot size (mm)	Repetition Rate (Hz)	Spectral Range (nm)	Fluence Range* (J/cm²)	Application
MAXG	10 x 15	.2 – 2.0	500 – 670 & 870 - 1200	Up to 80	Pigmented and Vascular Lesions (skin types I-IV)

*The effective fluence may be higher due to photon recycling, wide spectrum, spot size, and skin contact. There is a ±7% maximum variation of the output from the mean value across the treatment area.

Ocular Hazard Distance = 3.3 meters.

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 TempSure® 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 TempSure® Operator's 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 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. The subject will be asked to remove jewelry, 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 TempSure® 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 1 working day of serious adverse events as defined by FDA guidelines.

15.0 PROTOCOL DEVIATIONS

All requests for protocol deviations by the Investigator must 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, LLC, 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 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:

Device	Determination	510(k)
TempSure	Meets the criteria for exemption from IDE regulations, non-significant risk	K200241
TempSure	Meets the criteria for exemption from IDE regulations, non-significant risk	K190678
TempSure	Meets the criteria for exemption from IDE regulations, non-significant risk	K182365
TempSure	Meets the criteria for exemption from IDE regulations, non-significant risk	K171262
Icon	Meets the criteria for exemption from IDE regulations, non-significant risk	K103664
Icon	Meets the criteria for exemption from IDE regulations, non-significant risk	K110907

Protocol	Device	IRB Name	Determination	Initial IRB Approval Date
7027-FS01-2021	TempSure	AIRB	Meets the criteria for exemption from IDE regulations, non-significant risk	04/01/2021
7027-FS01-2021	TempSure	AIRB	Meets the criteria for exemption from IDE regulations, non-significant risk	04/01/2021

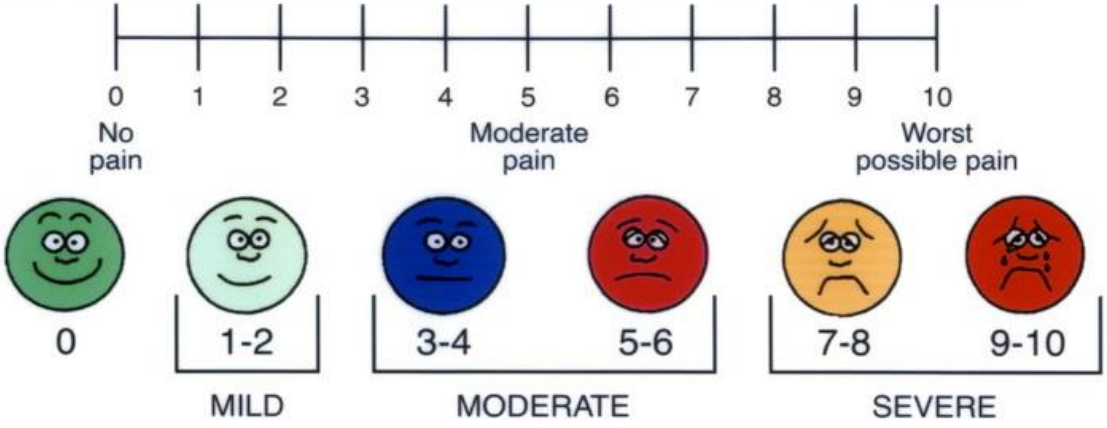
APPENDIX A:
Protocol Revisions Tracker

Version Date	Editor	Description
July 17, 2021	Kristy Luis	IRB Submission
August 23, 2021	Kristy Luis	Increased the number of patients from 30 to 50. Added Dr. Doherty as site #3. Added the use of the Icon device. Added 2 groups of subjects (Group A treated with only Tempsure, Group B treated with TempSure and Icon). Added Subject Questionnaires to be performed Pre-Treatment 1, Post Treatment 1, and at the Follow Up visits. Other Administrative edits.
September 10, 2021	Kristy Luis	Removed “pigmentation” as condition to be treated with Icon and replaced with “benign pigmented and vascular lesions”.
January 20, 2022	Kristy Luis	Added some subjects may be asked to return for an optional 5th treatment (2 – 3 weeks post last treatment) with the Icon device (and/or TempSure device) after the completion of their 4 treatments at the discretion of the Investigator to Group B. Other administrative changes.

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

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