Identifiers: NCT04881149
Unique Protocol ID: CYN20-FIRM-LIPO-ROLLOVER

# Title: Rollover Study to Evaluate Histological Results of Radiofrequency Device Treatments on the Flank

**Document Date: February 2, 2021**

# INVESTIGATIONAL PLAN

## PROTOCOL #: CYN20-FIRM-LIPO-ROLLOVER

## ROLLOVER STUDY TO EVALUATE HISTOLOGICAL RESULTS OF RADIOFREQUENCY DEVICE TREATMENTS ON THE FLANKS

**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**

**ROLLOVER STUDY TO EVALUATE HISTOLOGICAL RESULTS OF RADIOFREQUENCY DEVICE TREATMENTS ON THE FLANKS**

## 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, LLC 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:**
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Email: DHM@miaar.com

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**Principal Investigator Information:**
Bruce Katz, M.D.
JUVA Skin & Laser Center
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Phone: 888-729-6399

**SITE #3 CONTACT INFORMATION:**
**Principal Investigator Information:**
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ATTACHMENTS/REFERENCES

I. Informed Consent Form
II. Post Treatment Instructions

# 1.0 PURPOSE

## 1.1 Name and Intended Use

The purpose of this study is to evaluate histological results of the treatments with the TempSure Firm handpiece on the flanks performed in the CYN20-FIRM-LIPO study.

## 1.2 Objectives

Primary Objective:

- Evaluate histological tissue response as seen in biopsies.

## 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 1 month. 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 7 months.

## 1.4 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.[1] This, in turn, creates a tightening effect that helps to eliminate skin wrinkles and is used also for other cosmetic treatments on the body.[2]

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.

# 2.0 PROTOCOL

## 2.1 Protocol Methodology and Analysis

Methodology:

Subjects are to be enrolled in this clinical study if they have completed their participation in the CYN20-FIRM-LIPO study. Up to 10 subjects will be enrolled at up to 4 study centers. Subjects will receive 2 biopsies, 1 biopsy in the treatment area on the flank and 1 biopsy on the contralateral side to serve as a control.

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.[3] 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.[4] Radiofrequency technology for the treatment of abdominal wrinkles 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 improvement in the appearance of skin has been previously linked to a histological evaluation of the treatment area and can be used to verify an increase in collagen after a radiofrequency treatment. Dr. Neil Sadick in 2008 published an article titled *Tissue Tightening Technologies: Fact or Fiction* which discusses the link between changes in collagen and improvement in skin tightening, including wrinkles. The collection of biopsies will allow a histological evaluation of the treatment area to confirm the device is safely and effectively affecting the collagen in the dermis.

Compatibility:
Not applicable – feasibility study.

Predictive power:
While this study will observe the effects of the handpieces on the flanks, results could potentially be applied to a variety of body areas and other potential applications. Assuming that there is significant improvement, it would be appropriate to expect results in different areas where other products and devices have significant results.

## 2.2 Protocol Study Design

This is a prospective, multi-center clinical study to evaluate histological results of treatments with the TempSure™ Firm handpiece.

## 2.3 Subject Selection Criteria

Subjects will meet the criteria described below:

Inclusion Criteria:

- Subject has completed their participation in the CYN20-FIRM-LIPO study no more than 6 months prior.

Exclusion Criteria:

- The subject has not had any other treatment in the treatment area after their involvement in the CYN20-FIRM-LIPO study.
- 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.

## 2.4 Screening

Subjects will undergo the screening procedures in the CYN20-FIRM-LIPO study.

## 2.5 Informed Consent Process and Enrollment

Subjects will be asked to review the post treatment instructions prior to signing the informed consent form and their involvement in the study. Subjects will be informed of standard COVID-19 procedures that adhere to federal and state guidelines at this time. 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-Biopsy 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. A urine pregnancy test will be performed on all women of childbearing potential prior their biopsies. 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.

- The biopsy area will be identified and may be marked with a surgical or permanent marker.
- Photographs will be taken prior to the biopsy and may be taken during and/or after treatment.

## 2.7 Biopsy Procedures

- Biopsy subjects will receive 2 biopsies, 1 in the treatment area and 1 on the contralateral side of the treatment area to serve as a control.
- A local anesthetic, such as lidocaine, will be injected to the area prior to biopsy.
- A 2 mm or 3mm punch biopsy (based on Physician assessment) will be taken.

- Sutures may be used to close the incision site.

**2.8 Post Biopsy Instructions**

- Slight redness, initial tenderness to the wound site is normal; however, if you experience more redness, swelling, pain, pus, or drainage contact the office 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 - 10 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.

**2.9 Follow Up**

- The subject may be asked to attend a 1 week (7-10 days) post biopsy follow up visit to remove the sutures.

- Photographs may be taken, and adverse events will be documented at this follow up visit.

## 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 not be allowed to be replaced without prior approval from the sponsor and/or IRB.

## 2.12 Schedule of Visits and Procedures

| | Visit #1 | Visit #2 (optional) |
|---|---|---|
| Procedure | Biopsy | Follow Up 1 Week Post Biopsy (7-10 Days) |
| Pregnancy Verification* | X | |
| Biopsy | X | |
| Suture Removal | | X |
| Photographs | X | X |
| Adverse Events Assessment | X | X |

*Pregnancy verification required before biopsy only for women of childbearing potential.

## 2.13 Evaluation Methods

**Skin Biopsies:**

Biopsies will be obtained to examine the effects on the skin following radiofrequency treatments. 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 and/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 report will be provided for each sample by the pathologist or the Investigator.

## 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.

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

**Lidocaine**
1% lidocaine (Lidocaine) Injection with or without Epinephrine
You may experience pain and numbness at the site of the injection. You may also experience redness, rash, infection, skin damage or nerve damage at the site of the injection. You may experience temporary loss of sensation and muscle function at the site of injection.

Lidocaine with epinephrine contains the preservative sodium metabisulfite 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 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.

## 3.0 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 biopsies 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 will be used. The value of the compensation to the clinical investigator for conducting the study is not influenced by the study outcome.

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 most subjects undergoing biopsies when enrolled in a non-ablative radiofrequency study.

## 4.0 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: Kristy Luis
Institution: Cynosure, LLC
Address: 5 Carlisle Rd. Westford, Ma

## 5.0 CONSENT MATERIALS

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

| Form/Informational Material Description |
|---|
| Post Treatment Instructions |
| Informed Consent Form |

## 6.0 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

## 7.0 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.

## 8.0 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. |

## 9.0 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.

## 10.0 PHOTOGRAPHY

Standardized photography may be taken of the biopsy site. 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.

## 11.0 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 10 working days of serious adverse events as defined by FDA guidelines. |

## 12.0 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.

## 13.0 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.

## 14.0 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.

## 15.0 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. |

## 16.0 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.

## 17.0 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.

## 18.0 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.

## 19.0 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.

## 20.0 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.

## 21.0 REPORT OF PRIOR INVESTIGATIONS

The report of prior investigations or predicates are:

| Protocol | Device | IRB Name | Determination | Initial IRB Approval Date |
|---|---|---|---|---|
| CYN20-FIRM-LIPO | TempSure | NEIRB | Meets the criteria for exemption from IDE regulations, non-significant risk | 07/21/2020 |

APPENDIX A:
Protocol Revisions Tracker

| Version Date | Editor | Description |
|---|---|---|
| December 10, 2020 | Kristy Luis | IRB Submission |
| February 2, 2021 | Kristy Luis | IRB Response, Removed Weiss and replaced with Brauer, Added site #4 (Griffin), Added to inclusion criteria that subjects must be enrolled within 6 months of completion of prior study. |
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## REFERENCES

[1] 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
[2] Stampar, M. (2011). The Pelleve Procedure: An Effective Method for Facial Wrinkle Reduction and Skin Tightening. Facial Plastic Surgery Clinics of North America, 19(2), 335-345. doi:10.1016/j.fsc.2011.05.012
[3] Sherber, N. S., MD FAAD. (2018). The Millennial Mindset. *Journal of Drugs in Dermatology, 17*(12), 1340-1342.
[4] Elsaie, M. (2009). Cutaneous Remodeling and Photorejuvenation Using Radiofrequency Devices. *Indian Journal of Dermatology, 54(3),* 201. doi:10.4103/0019-5154.55625