Prospective Clinical Study To Assess The Safety And Efficacy Of A Radiofrequency Diathermocontraction Device For Muscle Stimulation And The Treatment Of Abdominal Fat

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INVESTIGATIONAL PLAN

PROTOCOL #: MED4-PL01-2022

PROSPECTIVE CLINICAL STUDY TO ASSESS THE SAFETY AND EFFICACY OF A RADIOFREQUENCY DIATHERMOCONTRACTION DEVICE FOR MUSCLE STIMULATION AND THE TREATMENT OF ABDOMINAL FAT

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PROSPECTIVE CLINICAL STUDY TO ASSESS THE SAFETY AND EFFICACY OF A RADIOFREQUENCY DIATHERMOCONTRACTION DEVICE FOR MUSCLE STIMULATION AND THE TREATMENT OF ABDOMINAL FAT

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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1.0 PURPOSE

1.1 Name and Intended Use

The device used in this study is called the Brera/Med 400 device.

The intended use of the Brera/Med 400 device in this study to assess the safety and efficacy of the adhesive electrodes for muscle stimulation and the treatment of abdominal fat on the abdomen and/or flanks.

1.2 Objectives

1. Primary Objective:
   - Evaluation of adverse events and side effects throughout the study.
2. Optional Assessments:
   - Photographic evaluation with correct identification of pre-treatment 2D images when compared to the 30 and 90 day follow up images performed by three independent reviewers.
   - Abdominal circumference reduction evaluated using a tape measurement.
   - Principle Investigator assessment using the Global Aesthetic Improvement Scale Abdominal fat reduction evaluated using an ultrasound device
   - Principle Investigator assessment using the Global Aesthetic Improvement Scale (PGAIS) at the 30 and 90 day follow up visit.
   - Subject Questionnaire(s)
     - The Global Aesthetic Improvement Scale (SGAIS) at the 30 and 90 day follow up visit.
     - Subject satisfaction at the 30 and 90 day follow up visit.
     - Psychometric Questionnaire (muscle firmness, hardness, self-image, and well-being)
     - Subject Treatment Questionnaire
   - Collection of 3D Photography
   - Objective measurement of abdominal muscle strength.
   - Temperature monitoring.

3. Additional Safety Objectives:
   - Collection of Treatment Discomfort/Pain Evaluation

1.3 Duration of the Investigation

The sponsor anticipates that all subjects can be enrolled within 6 months. If subject participates in all required visits, then the subject's participation in this study may last up to 5 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 14 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 30 subjects will be enrolled at 1 study center. Subjects will be enrolled into 2

groups, Group A and Group B. Subjects will be enrolled in Group A if they present with abdominal fat and are able to be present for all visits as outlined in "Schedule of Visits and Procedures – Group A". Subjects will enroll in Group B for training and experience purposes only and will follow the visit schedule as outlined in "Schedule of Visits and Procedures – Group B". Randomization will not be required as each subject will be assigned to a group depending on the purpose of their treatment(s). All 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 8 treatments with the Brera/Med 400 device on their abdomen or flanks. 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 30 and 90 days post last treatment for efficacy and side effects assessments.

Subjects in Group B may receive up to 8 treatments with the Brera/Med 400 device on their abdomen and/or flanks. Subjects may receive a phone call 1 week (1-7 days) after each treatment to record side effects. Subjects may be asked return for follow up visits at 30 and 90 days 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.[i] 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.[ii] Radiofrequency technology used for muscle stimulation and fat reduction needs to be further investigated to optimize treatment parameters for safe and effective non-ablative aesthetic treatments.

Relevance:
Non-invasive fat reduction is a commonly sought out procedure and continues to increase in demand (+3% from 2018 to 2019)[iii] perhaps due to the fact that, according to the CDC, the prevalence of obesity in the U.S. was 42.4% in 2017-2018.[iv] Currently, the treatments available for non-invasive muscle building and fat reduction include, but not limited to, radiofrequency, HIFEM, and bio-electric current stimulation. The limitations of current products on the market include different side effect profiles and modes of administration.

Testability:
Emsculpt Neo® is intended for non-invasive lipolysis (breakdown of fat) of the abdomen and thighs and reduction in circumference of the abdomen and thighs with Skin Type I to Skin Type VI. Emsculpt Neo® is also cleared for improvement of abdominal tone, strengthening of the abdominal muscles and development of firmer abdomen. Strengthening, toning, firming of buttocks, thighs, and calves. Improvement of muscle tone and firmness, for strengthening muscles in arms. TruSculpt device has been cleared for used for reduction in circumference of the abdomen and non-invasive lipolysis (breakdown of fat) of the abdomen (K180709). These devices

performed studies which utilized the following evaluation methods: circumferential measurements, histology, subject assessment of improvement and satisfaction.. This particular study will utilize the collection of before and after photography for blinded, independent review of clinical photographs, ultrasound and circumferential measurements, 3D quantification of volume reduction, satisfaction scores, and safety data to evaluate the safety and efficacy of the treatment.

Compatibility:
Due to such a high prevalence of obesity in the U.S. and the increasing demand for non-invasive muscle toning and lipolysis treatments, there is a need to treat unwanted fat in its earlier stages to optimize treatment outcomes. As a subject gets older or the condition worsens, their treatment may need to be more aggressive to get their body to respond the same way that a younger subject or less severe case may be able to respond.

Predictive power:
While this study will observe the effects of the device on muscle stimulation and fat reduction on the abdomen and 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, open label, single center clinical study to collect safety and efficacy data on the Brera/Med 400 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 Brera/Med 400 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.
- 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.
- Has injured (such as a cut, wound) or infected skin, or has presence of evident pathologies such as melanomas or other tumors of the skin, dermatitis, eczema, psoriasis, etc. in the area to be treated.
- Is on local, oral, or systemic anesthetic agents.

- Has nerve insensitivity to heat in the treatment area.
- Has received an organ transplant.
- Has any embedded electronic device that gives or receives a signal, the device should be turned off or removed prior to treatment.
- 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.
- Has an allergy to adhesives, such as glues on medical tape, they should be alerted that a rash may occur on the applicator and neutral pad site, and an over-the-counter solution may be used to treat the area.
- Has an unhealthy expectation of the results – this is not plastic surgery and all subjects should be fully informed of the treatment's expected results.
- 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.
- Has used Accutane (Isotretinoin) six to twelve months prior to treatment, as this can thin the skin and make it brittle.
- Is currently taking anticoagulants.
- The treatment area has scars and/or tattoos.
- Has any of the following conditions:
  - Thrombosis or Thrombophlebitis
  - Active Vascular Disease
  - Labyrinthitis and Tinnitus
  - Liver Disease or Dyslipidemias
  - Acute Sepsis
- 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:

- Has any of the following conditions:
  - Autoimmune Disease
  - Diabetic
  - Herpes Simplex

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.

The following Pre-Treatment instructions will be reviewed:

- Shave any visible hair on the area to be treated.
- Do not wear constrictive clothing. Your abdomen or flanks must be accessible for the neutral pad to be attached.
- Remove all makeup and lotions from the treatment area and all jewelry and metal objects from the body.
- 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.

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.

2.6 Pre-Treatment Procedures

If the subject is of childbearing potential (i.e. females not post-menopausal or not surgically sterile), pregnancy verification will be required. Pregnancy verification will be performed by asking the subject if they are pregnant, the date of their last menstrual cycle, and be required to perform a urine pregnancy test at the site. For Group A, pregnancy verification will be performed prior to the subject's first treatment and prior to their 5th treatment. Pregnancy verification will be performed by verifying the date of their last menstrual cycle at each subsequent treatment. For Group B, pregnancy verification will be performed prior to the subject's first treatment and prior to each treatment only if their treatment is 30 days past their last pregnancy verification. A urine pregnancy test may also be conducted at the Investigator/clinician'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.

Group A:

- Photographs will be taken prior to the 1st and 5th treatment, and may be taken prior to each subsequent treatment.
- Prior to treatment 1 and 5 only, circumference measurements and abdomen strength measurement will be taken, and ultrasounds may be performed.
- Prior to treatment 5 only, subjects will be asked to complete a Subject Treatment Questionnaire.
- For treatment 5 only, pre-treatment procedures and treatment may be separated into 2 visits.

Group B:

- Photographs will be taken prior to their first treatment and may be taken prior to each subsequent treatment.
- Circumference measurements and abdomen strength measurements may be taken, and ultrasounds may be performed at any treatment visit.
- Subjects may be asked to complete a Subject Treatment Questionnaire prior to any treatment visit.

2.7 Treatment Procedures

- The defined study area will be identified and may be marked with a surgical marker.

- Procedures for the Brera/Med 400 treatment:
  - The applicators will be placed in contact with the skin.
  - The entire defined treatment area will then be treated by delivering energy to the skin.
  - Temperature may be continuously monitored and recorded during treatment.
- 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.

2.8 Post Treatment Procedures

- Adverse events will be documented after treatment.
- Photographs may be taken post treatment.
- Post treatment instructions will be reviewed with the subject.

2.8 Follow Up

Group A:

- 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 30 and 90 days post last treatment.
- Photographs will be taken, adverse events will be documented, and subjects will be asked to complete questionnaires, objective measurements will be taken, and ultrasounds may be performed.
- 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.

Group B:

- Subjects may receive a phone call 1 week (1-7 days) after each treatment to record side effects.
- Subjects may return for follow up visits at 30 and 90 days post last treatment.
- Photographs will be taken, adverse events will be documented, and subjects may be asked to complete questionnaires and objective measurements may be taken and ultrasounds may be performed.

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

Group A:

	Visit #1*	Visit #2-9	Call (optional)	Visit #10	Visit #11
Procedure	Screening and Pretreatment Procedures	Treatment Visit(s) 1-8 (1 Week Apart ± 4 Days)	Phone Call 1 Week Post Tx (1-7 Days)	Follow Up 30 Days Post Last Tx (± 10 Days)	Follow Up 90 Days Post Last Tx (± 10 Days)
Medical History	X				
Weight/BMI	X	X**		X	X
Pregnancy Verification	X	X**			
Informed Consent	X				
Photographs (2D)	X	X		X	X
Photographs (3D)	X	X**		X	X
Ultrasounds	X	X**		X	X
Circumference Measurement	X	X**		X	X
Abdomen Strength Measurement***	X	X**		X	X
Treatment		X			
Treatment Discomfort/ Pain Evaluation		X			
Subject Treatment Questionnaire		X**		X	X
Subject Satisfaction				X	X
SGAIS				X	X
PGAIS				X	X
Adverse Events Assessment	X	X	X	X	X

*Screening and Pretreatment Procedures may occur at the same time as the first Treatment Visit.
**Performed pre-treatment 5, optional at other treatment visits.
***Optional

Group B:

	Visit #1*	Visit #2-9	Call (optional)	Visit #10 (optional)	Visit #11 (optional)
Procedure	Screening and Pretreatment Procedures	Treatment Visit(s) 1-8 (At least 3 days apart)	Phone Call 1 Week Post Tx (1-7 Days)	Follow Up 30 Days Post Last Tx (± 10 Days)	Follow Up 90 Days Post Last Tx (± 10 Days)
Medical History	X				
Weight/BMI	X	X		X	X
Pregnancy Verification	X	X***			
Informed Consent	X				
Photographs (2D)	X	X**		X	X
Photographs (3D)**	X	X		X	X
Ultrasounds**	X	X		X	X
Circumference Measurement **	X	X		X	X
Abdomen Strength Measurement**	X	X		X	X
Treatment		X			
Treatment Discomfort/ Pain Evaluation		X			
Subject Treatment Questionnaire**		X		X	X
Subject Satisfaction**				X	X
SGAIS**				X	X
PGAIS**				X	X
Adverse Events Assessment	X	X	X	X	X

*Screening and Pretreatment Procedures may occur at the same time as the first Treatment Visit.
**Optional.
***Pregnancy verification only required prior to each treatment if their treatment is 30 days past their last pregnancy verification.

2.13 Evaluation Methods

Photographs:

Photographs 2D and 3D will be taken at baseline, pre-treatment 5 and at the 30 and 90 day follow up visit, and may be taken at each additional treatment visit to assess the efficacy and safety of treatment. 2D photography may be taken at any time during treatment to document treatment performance and/or adverse events.

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

Subject 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.

Abdominal Muscle Strength Evaluation:
Abdominal muscle strength will be evaluated using the manometer to sternum method. This method measures the amount of pressure on the sternum when the subject is in a sit-up position (back 20cm off the table both hips at a 30° angle and both feet secured down), and then pressure is exerted on the manometer by the observer to the maximum the subject can sustain.

Circumference Evaluation:
Abdominal circumference measurements is a tool used to measure abdominal fat by wrapping a tape measurer around the waist. Measurements may be taken at baseline, pre-treatment 5, and at the 30 and 90 day follow up visits.

Temperature Monitoring:
An infrared thermometer may be used for temperature monitoring to measure temperature on the skin before, during, and after treatment.

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.

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

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

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 Brera/Med 400 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), pain/soreness, cramping, and erythema (redness) may occur.

Other possible anticipated side effects may include; numbness, muscle twitching (which may last days), 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 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, the side effect profile is acceptable to the Physician as it relates to this type of treatment.

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

- Pre-treatment images when compared to post treatment (90 day) images will be ≥80%

- In cases where the subject's improvement is being graded on a scale, such as the GAIS scale, we will test the statistical significance of our results against a hypothetical population that would have no change (average score of 4).
- 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 20 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 assigned to Group A 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 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 11 (90 day follow up visit). Baseline is defined as the last assessment prior to the first treatment. The change from baseline to visits 10 and 11 will be analyzed using a Mixed Model Repeated Measures Analysis of Variance. A pairwise treatment group comparison at visit 11 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 11 is zero. The changes to visits 10 and 11 will be left as missing. Statistical significance with respect to the treatment group comparison at visit 11 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 Brera/Med 400 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) diathermocontraction technology has shown to be a non-invasive effective treatment method for aesthetic applications (such as abdominal fat). RF diathermocontraction technology is a safe method for non-invasive treatment because energy can be precisely delivered through the skin to the subcutaneous fat beneath and contract muscle fibers without damaging the epidermis.

ASSESSMENT OF RISKS OF THE PROPOSED INVESTIGATION:
There are two risks identified with the Brera/Med 400 device used in this study. The first risk identified is the safety of treatment with the Brera/Med 400 device. Since the Brera/Med 400 device has not been cleared for use and has limited safety data, optimizing the safety profile is necessary. The second risk identified is the lack of clinical data for evidence of effectiveness of Brera/Med 400 device for muscle stimulation and the treatment of lipolysis. Parameters need to be further investigated to be optimized for efficacious results.

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

There are multiple clinical mitigation strategies for the risks identified. Proper training on the device and protocol will be performed. Data from prior investigations will be utilized to minimize side effects and optimize treatment outcomes. Monitoring of the study will be implemented to minimize subject and data risks.

ASSESSMENT OF BENEFITS OF THE PROPOSED INVESTIGATION:
The subject may or may not have improvement in muscle strength and fat reduction.

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 the safety profile and efficacy results while using the Brera/Med 400 device in this study.

CONCLUSION:
This device is determined to be a non-significant risk study and will be using a device not cleared for use by the FDA.

Patient population to be enrolled in this clinical study:
Total anticipated population: 30 Subjects
Age Range: 18 years of age or older
Gender: Male or Female
Condition: Muscle stimulation and abdominal fat.

4.0 DEVICE DESCRIPTION AND SPECIFICATIONS

The Brera/Med 400® device used in this study is currently not cleared by the U.S. Food and Drug Administration (the FDA).

Changes to the Brera/Med 400® device are not anticipated during the investigation.

The Brera/Med 400® Device Specifications are:

Radiofrequency Specifications

Parameter	Specification
Effective Treatment Area	RF MULTIPOLAR™: Three electrodes of 0,785 cm^2 RF SELECTIVE™: Two electrodes of 3 cm^2 RF ELECTROPORATOR: Six electrodes of 0,031 cm^2 RF T-POINT™: 0,126 cm^2 RF- CAPACITIVE™: 19,00 cm^2 RF- RESISTIVE™: 19,00 cm^2 RF- MULTIACTION™ - Resistive : 14,32 cm^2 Capacitive: 4,9 cm^2 FPC MATRIX™: 1.2 X 1.2 cm by means of 125 points RF THERMOGYM™: Fixed electrodes - Large 132 cm^2 Medium 78 cm^2 Small 36 cm^2 BQUAD™: 4 electrodes 7cm^2
Radio Frequency Power	Up to 400W ± 10%
Output Voltage	137 V_{RMS} @ 47Ω
Mode(s) of Operation	CW/PW or combined
Polarization	Multipolar (multiplex Bipolar), Bipolar, Unipolar
Carrier Frequency	in the range 350kHz -1MHz
Modulation frequency	In the range 1Hz-250Hz
Duty cycle	In the range 1-100%
Combination Treatment	Vibration Massage

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: Kristy Luis
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 Brera/Med 400® 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 Brera/Med 400® 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 Brera/Med 400® 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)
TruSculpt	Meets the criteria for exemption from IDE regulations, non-significant risk	K180709
EmSculpt Neo	Meets the criteria for exemption from IDE regulations, non-significant risk	K213344

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

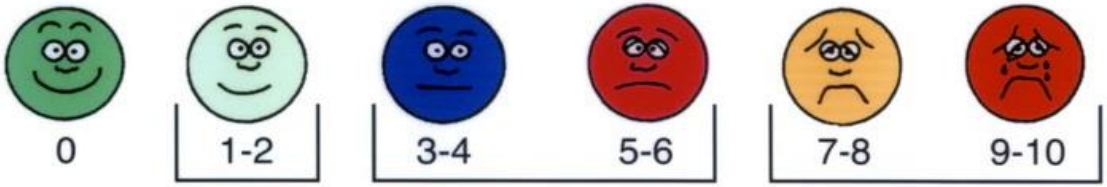
APPENDIX A:
Protocol Revisions Tracker

Version Date	Editor	Description
April 8, 2022	Kristy Luis	IRB Submission
April 18, 2022	Kristy Luis	IRB response. Added treatment 5 may be divided into 2 visits, one for pre-treatment procedures and one for treatment. Reduced amount of procedures to be performed for Abdominal Muscle Strength. Administrative edits.
June 9, 2022	Kristy Luis	Added muscle cramping and twitching as possible side effects. Removed the use of a neutral pad.

APPENDIX B:

UNIVERSAL PAIN ASSESSMENT TOOL

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



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

REFERENCES

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[ii] Elsaie, M. (2009). Cutaneous Remodeling and Photorejuvenation Using Radiofrequency Devices. *Indian Journal of Dermatology, 54(3),* 201. doi:10.4103/0019-5154.55625

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[iv] Centers for Disease Control and Prevention. (2020) Adult Obesity Facts. Available at https://www.cdc.gov/obesity/data/adult.html.