CLINICAL PROTOCOL

AN OPEN-LABEL, SINGLE-CENTER, SINGLE-TREATMENT, SAFETY AND EFFECTIVENESS EVALUATION OF PERCUTANEOUS RADIOFREQUENCY IN ACHIEVING SUBMENTAL LIFT

Investigational Device Name (if applicable):	ThermiRF
Regulatory Clearance No.:	K130689
Protocol Number:	Thermi_0005
Sponsor:	ThermiGen, LLC
Version and Date:	Final - 10 MAY 2016

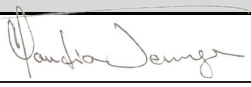
INTERNAL PROTOCOL APPROVAL FORM

Protocol Effective Date: *10 May 2016*

Protocol No.: **Thermi_0005**
Protocol Title: An Open-Label, Single-Center, Single-Treatment, Safety and Effectiveness Evaluation of Percutaneous Radiofrequency in Achieving Submental Lift

The above reference protocol was authored, reviewed and approved by the THERMI approving committee listed below.

Changes to the approved protocol will require issuance of an amendment /amended protocol and separate approval of such amendment.

SPONSOR REPRESENTATIVE *(Name and Title)*	FUNCTION	SIGNATURE OF APPROVAL	DATE
Claudia Jennings *Consultant Clinical*	Author		10-May-2016
Kevin O'Brien *President*	Reviewer & Approver		
Toni Fournier *VP Commercialization*	Reviewer & Approver		
Sam Dickson *Consultant Statistician*	Reviewer & Approver		
Carrie Eddings *Regulatory Manager*	Reviewer & Approver		

INVESTIGATOR SIGNATURE OF AGREEMENT

The signature below constitutes the investigator agreement to conduct the study in accordance to the stipulations and guidelines set forth in the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable United States Food and Drug Administration (FDA), the applicable Code of Federal Regulations (CFR), and International Conference on Harmonization (ICH).

Principal Investigator Name	Dr. Barry DiBernardo	**Signature**	Date:_____
Sub-Investigator Name	Dr. Maria DelVecchio	**Signature**	Date:_____
Sub-Investigator Name		**Signature**	Date:_____

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation/ Term*	Definition
AE	Adverse event
CIB	Clinical Investigator Brochure
CRF	Case report form
eCRF	Electronic Case Report Form
EOS	End of study
ESP	External service provider
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICF/ICD	Informed consent form/Informed consent document
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
ID	Investigational Device
IRB	Institutional Review Board
ITT	Intent-To-Treat
NSR	Non-Significant Risk
P-GAIS	Physician Global Aesthetic Improvement Scale
P-GSQ	Physician Global Satisfaction Questionnaire
PI	Principal Investigator
PPP	Per Protocol Population
PRA	Percutaneous Radiofrequency Ablation
QA	Quality Assurance
QC	Quality Control
SAE	Serious adverse event
S-GAIS	Subject Global Aesthetic Improvement Scale
S-GSQ	Subject Global Satisfaction Questionnaire
™	Trademark
MeDRA	Medical Dictionary for Regulatory Activities

1. ETHICS

1.1. Institutional Review Board (IRB)/Independent Ethics Committee (IEC)

It is the responsibility of the investigator to have prospective approval of the study protocol, protocol amendments, informed consent forms, and other relevant documents, e.g., recruitment materials, if applicable, from the IRB/IEC. All correspondence with the IRB/IEC should be retained in the Investigator File (Site Master File). Copies of IRB/IEC approvals should be forwarded to the Sponsor.

The only circumstance in which a protocol amendment may be initiated prior to IRB/IEC approval is where the change is necessary to eliminate apparent immediate hazards to the subjects. In that event, the investigator must notify the IRB/IEC and the Sponsor in writing within 5 working days after the implementation.

1.2. Ethical Conduct of the Study

The study will be performed in accordance with the protocol, International Conference on Harmonization Good Clinical Practice guidelines (ICH E6) and applicable local regulatory requirements and laws.

1.3. Subject Information and Consent

All parties will ensure protection of subject personal data and will not include subject names on any forms, reports, publications, or in any other disclosures. In case of data transfer, Sponsor will maintain high standards of confidentiality and protection of subject personal data.

The informed consent form must be agreed to by the Sponsor and the IRB/IEC and must be in compliance with ICH GCP, local regulatory requirements, and legal requirements.

The investigator must ensure that each study subject, or his/her legally acceptable representative, is fully informed about the nature and objectives of the study and possible risks associated with participation. The investigator, or a person designated by the investigator, will obtain written informed consent from each subject or the subject's legally acceptable representative before any study-specific activity is performed. The informed consent form used in this study, and any changes made during the course of the study, must be prospectively approved by both the IRB/IEC and the Sponsor before use. The investigator will retain the original of each subject's signed consent form.

2. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Details on the administrative structure of the study (e.g., investigator, coordinating, steering committee, administration, monitoring and evaluation committees, institutions, statistician, central laboratory facilities, external service provider (ESP or CRO), or clinical study supply management) will be maintained in the Sponsor's Study Master File throughout the study for inclusion in the clinical study report.

3. INTRODUCTION

3.1. Background and Rationale

Biochemical changes in dermal connective tissue lies at the foundation of skin laxity, often leading to the inevitable "Aging Face Syndrome." The appearance of a young and well defined neck is deemed to have cervicomental angle of 90 ° – 105 °, a good tone, a well-defined mandibular border, no accumulation of fat in the submental area, and no evidence of platysma bands [1].

In the course of aging, the neck serves as an indicator for the loss of collagen and elastin causing excessive skin laxity, an increase in submental fat and loose jowls along the mandibular border. A 2014 American Society for Dermatologic Surgery consumer survey found 68 percent of respondents were concerned about excess fat under the chin and neck. Data were obtained through a blind online survey conducted in April 2014 through the web-based Contribute service. The survey received 8,315 responses.

Laxity of submental area is therefore, a common cosmetic complaint of the aging population. As the "baby boomer" generation reaches later life, aesthetic surgical medical interventions are becoming increasingly sought after by patients to aid and improve the cosmetic profile of these persons.

Thermi plans to evaluate the safety and effectiveness of ThermiRF™ radiofrequency in the treatment of submental skin laxity using. The planned treatment uses targeted temperature controlled RF to achieve lifting in subjects with mild to moderate severity defined as normal muscle and mild to moderate skin laxity and mild to moderate fat on the submental area. Additionally biomechanical changes of the skin will be evaluated using the Cutomer® which may be evident as a result of the ThermiRF treatment [6].

The ThermiRF system uses radiofrequency to apply heat to target areas using electrocoagulation; this is a percutaneous minimally -invasive technique.

ThermiRF Device

The ThermiRF device is a minimally invasive radiofrequency solution, and an established therapeutic modality for the treatment of nerve tissue ablation and electrocoagulation. The use of radiofrequency in aesthetics is well published. [2-4]. the temperature controlled radiofrequency is less-invasive and provides a better safety profile (reduced risk) when compared to surgery, other more invasive treatments and non-temperature controlled energy devices. The ThermiRF device delivers a controlled thermal endpoint as a result of its proprietary software algorithm and feedback loop that consistently measures the tissue temperature at the tip of the treatment RF electrode.

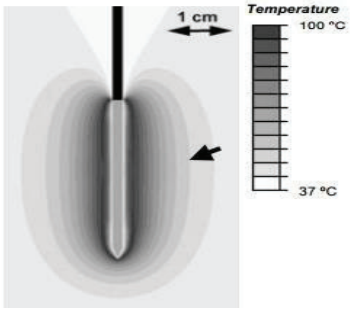
As the electric current permeates a tissue layer, ions found within that layer, deliver or carry the current. This, in turn, increases the kinetic activity of the ions. Increased ion kinetics and oscillations engenders resistive tissue thermogenesis.

Thermogenesis is calculable via the Specific Absorption Rate (SAR) equation, which assesses local electrical conductivity and magnitude of local electric current density generated around the electrode (Equation 1).

$$SAR = \frac{\sigma}{\rho}|E|^2 = \frac{1}{\sigma \cdot \rho}|J|^2$$

The electric field strength generated is capable of heating tissue in close proximity to the electrode. Thermal conduction attenuates the heating of tissue as you move further from the electrode. With proper controls, generating the ideal thermal endpoint will occur very close to the electrode, thereby affecting only the intended target tissue area (Figure 1).

Figure 1: Distribution of RF-induced heat



Regulation of tissue temperature derives from power control. Power (P) is equal to the voltage multiplied by the current; the Power is delivered via the radiofrequency electrode. Depending on the tissue impedance, the power will need further adjustment, ensuring the proper voltage/current is delivered to satisfy the tissue impedance. Finally, thermal sensors – thermocouples – integrated within the radiofrequency electrode to allow for accurate measurement of tissue temperature and the system will adjust power to maintain the physician selected therapeutic temperature. With these proper controls in place, selective thermogenesis serves as a viable treatment for numerous medical conditions.

The generation of heat is enough to promote tissue necrosis within a defined area. Accordingly, percutaneous radiofrequency can be administered for destruction of terminal fibers, which in turn, contracts tissue. Overall, percutaneous radiofrequency administers energy in a highly selective manner to induce the desired clinical outcome; "lift" achieved through tissue contracture and tightening.

3.2. Regulatory Status

The ThermiRF® Device is classified by the FDA/IEC as a Class 2 radiofrequency device. The device used in this study was cleared by the Food and Drug Administration (FDA) for dermatological and general surgical procedures for electrocoagulation and hemostasis **[K130689]**.

4. STUDY OBJECTIVES

4.1. Primary Objective/Endpoint

- Improvement in overall lift of the submental area at Day 90, as determined by:
    - Quantitative assessment based on 3D photography

4.2. Secondary Objective/Endpoint

- Overall aesthetic improvement of the submental area and jawline definition at Days 90 and 180 evaluated by the investigator and subject, using the following subjective assessment:
    - Qualitative assessment based on 2D photography performed by blinded panel
    - Physician - Global Aesthetic Improvement Scale Scores (P-GAIS)
    - Subject – Global Aesthetic Improvement Scale Scores (S-GAIS)
    - Physician - Global Satisfaction Questionnaire (P-GSQ)
    - Subject - Global Satisfaction Questionnaire (S-GSQ)

Each individual endpoint will be based on study subject population response for each individual endpoint.

- Safety will be evaluated using the following measures:
    - Numerical Rating Scale (NRS) a 10-point pain scale
    - Self-reported and observed adverse event

4.3. Exploratory Endpoint

- Elasticity measurement at Days 90 and 180.

5. OUTCOMES MEASURE

5.1. Primary Outcomes measure

Overall tissue lift at the submental area as determined by quantitative assessment at Day 90 compared to baseline based on 3D photography.

5.2. Secondary Outcomes Measure

Overall improvement in submental area as determined by qualitative assessment at Day 90 compared to baseline based on 2D photography and subjective questionnaire.

6. INVESTIGATIONAL PLAN

6.1. Overall Study Design and Plan

This is an open-label, single-center, single-treatment prospective evaluation of the ThermiRF device in the treatment of submental skin laxity. The purpose of this prospective study is to determine the effectiveness and safety of the ThermiRF device in achieving overall submental lift.

In this study, "Lift" is defined as a ≥ 20 mm^2 lift of the submental area after the ThermiRF treatment.

A total of 70 male and female healthy volunteers between the age of 35 and 65 will be considered for this study. Subjects who sign the informed consent form and meet all entry criteria will be enrolled in this study and will be assigned a unique number/code to preserve confidentiality.

A total of six study visits are planned as described below:

- Visit 1: Screening visit – (Day 1)
- Visit 2: Single Treatment visit
- Visit 3: Day 30 safety assessment *(± 7 to 14 days)*
- Visit 4: Day 60 safety and Image capture for validation exercise *(± 7 to 14 days)*
- Visit 5: Day 90 safety and effectiveness follow-up visit *(± 7 to 14 days)*
- Visit 6: Day 180 safety and effectiveness follow-up visit - *(± 7 to 14 days)*

Photo images (2D and 3D) will be collected at Visits 1, Visit 4 (on first 30 subjects only), and at Visits 5 and 6 using a standard camera (2D) and the Vectra XT system (3D). The purpose of the photos are to quantitatively and qualitative evaluate treatment effectiveness using objective and subjective assessments to measure physical changes to the skin's microstructure and aesthetic skin features over time.

A skin elasticity assessment using the Cutomer® will be collected at Visits 1 (screening), 5 (Day 90) and 6 (Day 180) to assess if any biomechanical changes of the skin occurred as a result of the ThermiRF treatment.

Safety assessments will be collected using the Numerical Rating Scale (NRS) a 10-point scale, and adverse events reports (observed or reported).

The overall study duration is approximately 12 months (i.e., 5-6 month recruitment period and 6 month study visits).

6.2. Discussion of the Study Design and Subject Selection

The study design represents a prospective evaluation of the ThermiRF system effectiveness in the treatment of submental laxity through electrocoagulation and neocollagenesis towards achieving Lift. Submental laxity is a common occurrence of the aging population affecting not only the submental area near the upper part of the neck but also the jawline. For the purposes of this study, subjects between the ages of 35 and 65 years old, are likely to show architectural changes of aging on the submental area, with a clearly noticeable

"mild to moderate" severity defined as having *"normal"* muscle, *"mild to moderate"* skin laxity and *"mild to moderate"* fat. Subject's skin laxity severity will be confirmed by the investigator at the screening visit to ensure appropriateness in subject selection. In an effort to eliminate variance across the group and with respect to treatment response, each subject will serve as his/her own control

The application of RF treatment on this category of subjects is "superficial" in nature with no adjuvant therapies needed. It is anticipated the benefits will be "lift" of the treated (submental) area following a minimally invasive approach resulting in less adverse outcomes such as swelling, bruising, and pain.

6.3. Selection of Study Population

The following eligibility criteria are designed to select subjects for whom protocol requirements are considered appropriate. All relevant medical and non-medical conditions should be taken into consideration when deciding whether this protocol is suitable for a particular subject.

6.3.1 Inclusion Criteria

- Male or female between the age of 35 and 65 inclusive;
- Mild to Moderate Skin Laxity Severity on the submental area defined as: *"normal"* muscle, *"mild to moderate"* skin laxity and *"mild to moderate"* fat;
- Desire to improve jawline definitions and/or submental skin lift
- Body mass index (BMI) ≤30;
- Females of childbearing potential who are sexually active must be willing to use an approved method of birth control during study participation.
- Cooperative, reliable, and able to read and comprehend English;
- Able to read, understand, sign and date the informed consent document (English only);
- Able and willing to comply with the schedule visit(s) and study requirements.

6.3.2 Exclusion Criteria

Subjects presenting with any of the following will not be included in the study:

- Excessive subcutaneous fat on the submental area
- Use within 24 hours preceding surgery of ibuprofen, acetaminophen, any other analgesics, anti-inflammatory products, or any products including herbals and supplements that could interfere with the clinical assessments of this study (other than drugs used for anesthesia);
- History of cosmetic treatments on the face and neck including but not limited to: facial skin tightening procedures within the ***past year***, injectable fillers of any type, Botox on the lower face, ablative resurfacing laser treatment, none ablative, rejuvenative laser or light treatment within the *past six months*, deep facial peels, dermabrasion, face lift, neck lift, blepharoplasty or brow lift, contour threads or other.
- History or current injury to the Head and Neck.
- Severe solar elastosis

- Clinically significant facial wounds, lesions or acute infections including cystic acne, dermatitis, lupus or other immunodeficiency affecting the dermis
- Presence of metal stents or facial implants
- Pregnant or planning pregnancy prior to the end of study participation
- Current or past history of smoking
- History or current diagnosis of cancer of any type
- History of uncontrolled cardiovascular disease(i.e. myocardial infarction, hypertension, hypercholesterolemia, peripheral vascular disease, other)
- Known hypersensitivity to local anesthetic medications
- History, or current bleeding disorders (i.e. hemophilia or von Willebrand disease), or anticipated treatment with prescription anticoagulants
- Possesses a surgically implanted electronic device (i.e. pacemaker)
- History of AIDs/HIV
- Serious mental health illness such as dementia or schizophrenia; psychiatric hospitalization in the past two years
- Developmental disability or cognitive impairment that would preclude adequate comprehension of the informed consent form and/or ability to follow study subject requirement and/or record the necessary study measurements
- A family member of the investigator or an employee of the investigator.
- Participation in any other investigational study **within 30 days prior to consent**;

In addition to the above restrictions, subject selection must be consistent with all the warnings, precautions, and contraindications associated with the ThermiRF procedures. The investigator will thoroughly familiarize him or herself with the approved labeling or manual of operations for the ID and devices used in this study.

7. TREATMENTS

7.1. Treatment Administration

The single ThermiRF treatment to the neck (right/left) will be administered by the investigator in accordance with the protocol requirements, and with adherence to Good Clinical Practices (GCP) and standard of practice for surgical procedures.

Only study subjects who signed the informed consent and meet all entry criteria, will be enrolled and treated.

7.2. Modification of Study Intervention/Investigational Product for a Subject

The output dosage is pre-determined based on the ThermiRF software algorithm. Therefore, no adjustments are planned nor anticipated.

7.3. Identity of Investigational Device and Supplies

ThermiRF is an FDA cleared device. The device is provided as a system and it includes a rectangular unit consisting of a front and rear panels, and single-use procedure kits. The system is designed to precisely deliver RF energy to target tissue. The system continuously monitors tissue temperature for patient safety using temperature controlled technology.

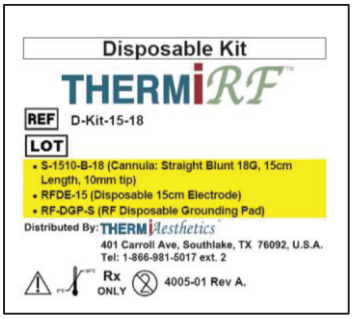
7.3.1 Single Use Procedure Kits

The investigator will be provided with single use procedure kits to be dispensed as one kit per study participant. The single used procedure kit consist of:

DESCRIPTION OF PROCEDURE KIT	
MODEL/ID	**DESCRIPTION**
S-1510-B-18	RF Disposable Cannula 15 CM length, 18 gauge, 10mm exposed tip
RFDE-15	Disposable 15 CM RF Electrode
RF-DGP-S	RF Disposable Grounding Pad

The RF Cannula and RF Electrode are sterile products and are individually packaged under sterile conditions and labeled with the commercially available label (Figure 2).

Figure 2: Primary Label Sample



For the purposes of this study, a secondary label will be applied to separate the study supplies, from the commercial product (Figure 3).

Figure 3: Secondary Label Sample

THERMI_0005

"FOR INVESTIGATIONAL USE ONLY"

7.3.2 Other Supplies

The investigator will be permitted to use the following:

- ***Urine Pregnancy Test Kits:*** Commercially available/marketed urine pregnancy test kits and anesthesia of his/her choice.
- ***Cutometer® MPA 580:*** Commercially available standard device used to measure elasticity and other biomechanical parameters of the skin.
- ***Vectra XT System:*** a handheld 3D imaging system that delivers precision optics for high-resolution 3D images to measure contouring and area differences.

7.4. Investigational Device Storage and Accountability

The investigator must maintain adequate records documenting the receipt, use, loss, or other disposition of the ID(s). All study related supplies must be stored in a secured area or locked location and shall be accessible to the investigator or designee responsible for the conduct of this study. Used materials will be discarded by the investigator while unused materials will be returned to the sponsor at the conclusion of the study.

7.5. Blinding

This study is open-label however, photo images collected during the study will be evaluated qualitative by a panel of three qualified raters whom will be blinded (i.e., will not know) to the date and time when the photo images were collected. Each rater will evaluate the images independent of each other and will provide their respective photo image qualitative assessment for analysis.

7.6. Blinded Rater Reliability Assessment

Prior to the completion of the study, the panel of raters will undergo a validation process as defined by the sponsor using photo images collected at Day 60. The method used to evaluate and validate the reliability of the blinded panel (Appendix 10), will follow the approach taken by Kim, et al. [5], where a range of possible outcomes can be detected from "no improvement" to "some improvement" to "significant improvement" at the specified time point. The approach implemented by Kim, et. al., is deemed consistent with ICH guidelines for validation of analytical procedures.

7.7. Expected / Unexpected Risk

The anticipated risks and/or discomforts associated with the procedure are described below:

General Statement:

The device has risk of burns or fire, and therefore, cannot be used near conductive materials such as metal bed parts, inner-spring mattress, etc.

A disposable grounding pad is used to ground/neutralize the electrical current. Subjects undergoing radiofrequency treatment will be kept away from contact with metal parts which are grounded or which have appreciable capacitance to earth.

The device cannot be used in subjects with a pacemaker, implantable defibrillators, or monitoring equipment.

Risk Associate with the PRD Procedure

Known risks associated with the use of ThermiRF include:

- Erythema
- Edema
- Electric shock: operator risk only: mitigated through electrical safety testing.
- Postoperative pain and edema that resolved within three days
- Second-degree burn treatment
- Treatment induced ulcers and fistulas

Although no immediate risks are anticipated, all aspects of this clinical investigation will be conducted under the direct supervision and oversight of the investigator and designated study staff. Adverse events whether spontaneous, or self-reported, will be collected and analyzed.

Other Risk

Surgical shock, pulmonary complications, irregular surface area. Proper pre and post treatment safety precautions will reduce the risk of these complications.

Any unexpected or unforeseen complications will be managed by the investigator throughout the conduct of the study. Unforeseen or unexpected side effects not listed above will be reported to the sponsor and regulatory representatives (IRB) as they occur.

7.8. Prior and Concomitant Medications and Therapies

7.8.1 Permitted

Subjects will be allowed to continue with their usual necessary medical therapies, with no medically unnecessary changes in their diet or overall lifestyle. If medical conditions exist at the start of the study that require drug therapy during the study, those conditions and any concomitant medications prescribed should be recorded in the subject's source documents and the appropriate section of the CRF.

Subjects must abstain from exclusionary procedures/medications/therapies as listed under the Exclusion Criteria for the duration of the study.

8. STUDY PROCEDURES

Study procedures as described in this section are depicted in the schedule of evaluations (Appendix 1).

8.1. VISIT 1 (Screening) - (*Day 1)*

Subjects who signed the informed consent at Visit 1 will have the following assessments performed:

- Inclusion and exclusion criteria
- Medical and Medication History
- Demographic and baseline characteristics
- Brief physical exam and Medical Clearance
- Vitals including height and weight
- Photography (2D and 3D)
- Confirmation of "Skin Laxity Severity" by the investigator
- Elasticity measurement

Subjects who meet all required entry criteria will be enrolled in the study, and will be a **subject ID** starting with **"0116"** and continuing in sequential order until enrollment is met (i.e., 7016). The first two digits represent the subject number and the last two digits represent the year when the study is initiated.

Enrolled subjects will be scheduled for Visit 2 promptly after Visit 1. A prescription slip for an antibiotic and an analgesic medication will be dispensed at the discretion of the investigator with instructions as follow:

INSTRUCTION

"Begin taking the antibiotics the day before the procedure at Visit 2, and continue taking as prescribed until the dose regimen is completed. The analgesic should be brought to the research site at which time, the first dose will be taken"

"*Make arrangements to have a legal representative drive to and from the research site."*

8.2. VISIT 2 (Treatment)

Upon arrival, subjects will have the following assessments performed:

- Verify conformance with eligibility criteria
- Urine pregnancy test *(must be performed prior to treatment at V1 or V2)*

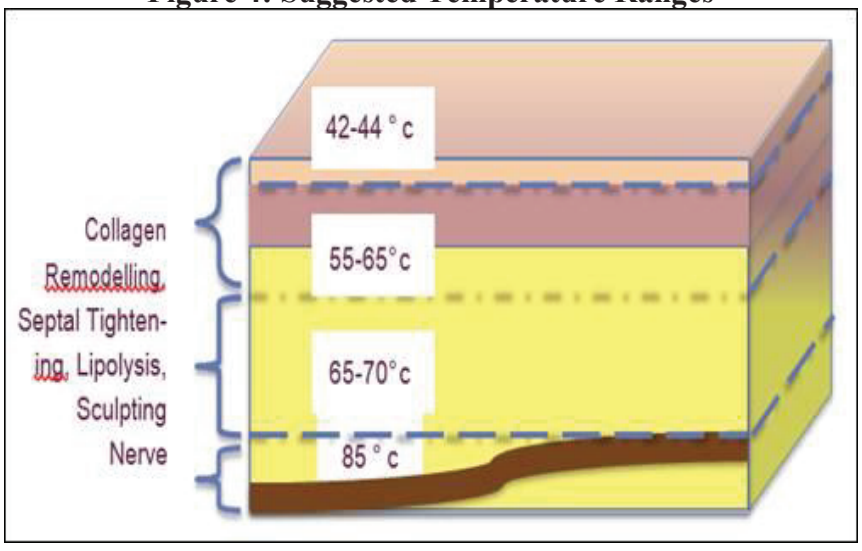
Provided the subject conforms to all entry criteria, the subject will be prepared for surgery and the visit will proceed as follow:

The subjects will be placed in a sitting or supine position. Using a surgical pen or marker the investigator will outline the treatment area and the area will be anesthetized using tumescent solution containing lidocaine and epinephrine. Sufficient time will be allowed for the anesthesia to take effect prior to the surgical procedure

Up to three small incisions measuring approximately 2 mm in length will be made to the right and left of the jaw line below the ear lobe, and below the chin. Each incisions will act as the point of entry for the investigational device probe.

The depth of penetration is approximately 2 mm below the dermis. The affected area of the neck will be infused with standard tumescent Hunstad formula (50-100cc). The investigator will proceed with the treatment by inserting the electrode to the distal portion of the first pass. Once in position, and the electrode temperature will be brought to the "procedure set temperature" in accordance with the suggested temperature ranges below (Figure 4).

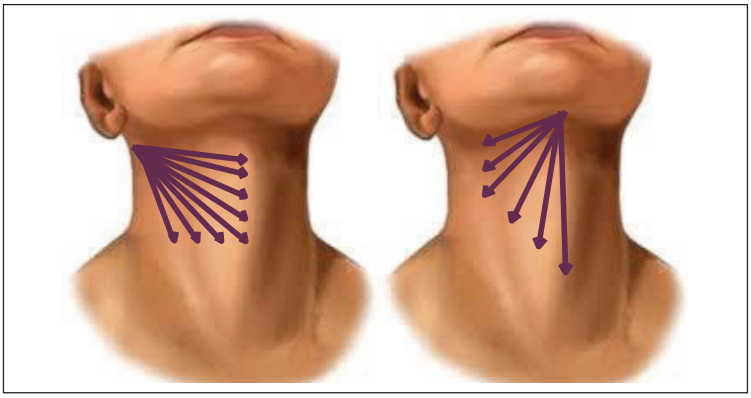
Figure 4: Suggested Temperature Ranges



The investigator will begin to slowly withdraw the electrode to ensure the temperature achieves the level of the set temp.

The pass is repeated in a "fanning" manner to ensure treatment of the entire neck area is achieved (Figure 5).

Figure 5: Treatment Passes



The surface of the skin must reach a temperature between 45-47^{0}C.

At the conclusion of the treatment, hypoallergenic tape may be applied and the use of a neck garment required in support of tissue repair post treatment. The duration of garment use is approximately 3-5 days or as directed by the investigator.

Subjects will be sent home and will be instructed on the following:

"Do not drive, engage in physical exercise or operate heavy machinery the day of the procedure at Visit 2 and for approximately 14 to 21 days for physical exercise including heavy lifting."

8.3. Visit 3 (Day 30) - *(± 7 to 14 days)*

The following assessments will be performed:

- NRS
- AE and ConMed assessment

8.4. VISITS 4 (Days 60) - *(± 7 to 14 days)*

This visit applies to the first 30 subjects enrolled in the study. During this visit, the following assessments will be performed:

- NRS
- Photography (2D and 3D)
- Questionnaires
  - P-GAIS (Appendix 2)
  - S-GAIS (Appendix 3)
  - P-GSQ (Appendix 4)
  - S-GSQ (Appendix 5)
- AE and ConMed assessment

8.5. VISIT 5 and 6 Follow-Up (Days 90 and 180 "EOS") - *(± 7 to 14 days)*

During these follow-up visits, the following assessments will be performed:

- NRS
- Photography (2D and 3D)
- Elasticity measurement
- Questionnaires
    - S-GAIS
    - P-GAIS
    - SGSQ
    - PGSQ
- AE and ConMed assessment

8.6. Subject Withdrawal and Early Termination

Subjects may withdraw from the study at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or Sponsor for safety, behavioral, or administrative reasons. Every effort should be made to document subject outcome, if possible. The investigator should inquire about the reason for withdrawal, request the subject return for a final visit, and if applicable, follow-up with the subject regarding any unresolved adverse events.

If the subject withdraws from the study and also withdraws consent for disclosure of future information, no further evaluations will be performed and no additional data will be collected. The Sponsor may retain and continue to use any data collected before such withdrawal of consent.

8.6.1 Protocol Deviations

Protocol deviations will be tracked and managed during the conduct of the study. A protocol deviation is defined as a non-conformance from the protocol which occurs at any time during the conduct of the study. Exceptions will not be granted by the sponsor for any planned or unplanned deviation. All protocol deviations will be tracked.

8.6.2 Status Classification

Classification	Criteria
Screen Failure	Signs the ICD but does not meet entry criteria or withdraws prior to Visit 2.
Enrolled	Signs the ICD and met all inclusion/exclusion criteria
Treated	Signs the ICD and successfully completes V2
Discontinued/Withdrawal	Signed the ICD but does not successfully complete any visits
Completed	Signs the ICD and successfully completes all study visits

9. ASSESSMENTS

9.1. Clinical Evaluations

The following clinical evaluations will be conducted during the study review:

- **Medical and medication history** – An assessment of the participant's health status prior to enrollment to ascertain appropriateness for study participation based on inclusion/exclusion criteria.

- **Brief Physical Examination –** A brief physical exam of the major organ systems will be performed at Visit 1 (screening) to assess the subject's physical/medical state prior to Visit 2. Adverse events reported during the conduct of the study will be evaluated by organ system with respect to the baseline physical evaluation.

- **Vital Signs -** Collected at Visit 1 (screening) and will include pulse, respiration, heart rate (systolic and diastolic), temperature, height and weight. The height and weight will be used to calculate and confirm the body mass index (BMI) requirement.

- **Urine Pregnancy Assessments -** Urine pregnancy test will be collected (for females of child bearing potential) at Visit 2 prior to treatment. Subjects with a positive result will be excluded from the study.

- **Adverse Event Reporting –** Investigator examination of the treatment area and surrounding anatomy and notation of any observations made by the study investigator of a potential adverse event.

- **Cutometer Elasticity Measurement** – an elasticity measurement use to determine skin pliability prior to, and post treatment. This measurement may serve as an indicator for how the subject's dermis will behave after exposure to RF treatment (Appendix 6).

- **Numerical Rating Scale (NRS)** – a unidimensional 10-point scale used to measure pain intensity from "no pain" to "worst pain possible" (Appendix 7).

- **Photography** - Standard photo images (2D) and 3D photography using the Vectra XT will be collected for study visits as defined in the protocol. The subject positioning is planned to deliver the following views:

    - "frontal view";
    - "lateral Right and Left view";
    - " 45^0 angle Right and Left".

For reproducibility of the subject's positioning during the photo session, every effort will be made by the investigator to replicate the same position and facial expressions from

baseline at every required time point. Additionally, every effort will be made by the investigator to ensure the same person (study staff member) will take all photos on the same subject during their participation.

- **Submental Skin Laxity Confirmation:** This assessment integrates three features: skin fat and muscle neck structures and redundancy (horizontal and vertical folds). This assessment will be performed by the investigator to ensure the subject's eligibility at Visit 1.
- **Global Assessment of Improvement Questionnaires:** A subject and physician appraisals of treatment outcomes.

9.2. Effectiveness Assessments

- Objective:
    - 3D Photography
    - Standard 2D Photography
    - Blinded panel assessment on 2D photography
    - Elasticity Measurement

- *Subjective:*
    - S-GAIS
    - P-GAIS
    - SGSQ
    - PGSQ

9.3. Assessment of Safety

Safety assessment will include an evaluation of the treatment area to assess overall quality and integrity of tissue layers for subjects that have completed treatment. All known and unknown events including known risks (see below) will be collected during the conduct of the study regardless of causality.

- Edema
- Infections
- Thermo-injury (i.e. Burns)
- Scarring
- Erythema
- Postoperative pain
- Second-degree burn treatment
- Transient paresthesia

Sensory assessment will be collected using the Numerical Rating Scale (NRS) a 10-point scale to measure pain after treatment.

10. ADVERSE EVENT REPORTING

10.1. Introduction

All observed or volunteered adverse events regardless of treatment group or suspected causal relationship to the ID(s) will be reported as described in the following sections.

For all adverse events, the investigator must pursue and obtain information adequate both to determine the outcome of the adverse event and to assess whether it meets the criteria for classification as a serious adverse event requiring immediate notification to the sponsor or its designated representative. For all adverse events, sufficient information should be obtained by the investigator to try to determine the causality of the event. For adverse events with a suspected causal relationship to the ID, follow-up by the investigator is required until the event or its sequel resolve or stabilize at a level acceptable to the investigator, and Sponsor concurs with that assessment.

10.2. Reporting Period

Serious adverse events require immediate notification within **24 hours** to the Sponsor or its designated representative. When reporting a serious adverse event, the investigator or designee completes the SAE form with as much information as possible however, at a minimum the Subject ID, Name of ID, SAE, and Name of person reporting the event. The completed form must be:

- Emails to the sponsor:

  Attention: Toni Fournier __ (Vice President Commercialization)

  PH: 617- 216-8211

  Email: Tfournier@thermi.com

  And,

  Attention: Claudia Jennings __ (Study Manager-Thermi Consultant)

  Phone: 973-222-8335

  Email: Cjennings@Thermi.com

All adverse events (serious and non-serious) must be collected on the subject's CRF from the time the subject signed informed consent through last subject visit.

10.3. Definition of an Adverse Event

An adverse event is any untoward medical occurrence in a clinical investigation associated with the use of an investigational product in human subjects. The event need not necessarily have a suspected causal relationship with the treatment or usage.

Examples of adverse events include but are not limited to:

- Abnormal test findings
- Clinically significant symptoms and signs
- Changes in physical examination findings
- Hypersensitivity
- Progression/worsening of underlying disease

Additionally, they may include the signs or symptoms resulting from:

- Product misuse
- Product dependency
- Extravasation
- Study related procedure

10.4. Serious Adverse Events

A medical device adverse event is serious when both of the following criteria are fulfilled:

- The event involves patient/subject/consumer contact
- The event results in:
  - Death
  - Serious deterioration in state of health. This includes:
    - Life-threatening illness or injury
    - Permanent impairment of a body function
    - Permanent damage to a body structure
  - Requires medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure
  - Requires inpatient hospitalization or prolongation of existing hospitalization

10.5. Severity Assessment

If required on the adverse event case report forms, the investigator will use the adjectives MILD, MODERATE, or SEVERE to describe the maximum intensity of the adverse event. For purposes of consistency, these intensity grades are defined as follows:	
MILD	Does not interfere with subject's usual function.
MODERATE	Interferes to some extent with subject's usual function.
SEVERE	Interferes significantly with subject's usual function.

Note the distinction between the severity and the seriousness of an adverse event. A severe event is not necessarily a serious event. For example, a headache may be severe (interferes significantly with subject's usual function) but would not be classified as serious unless it met one of the criteria for serious adverse events, listed above.

10.6. Causality Assessment

The investigator's assessment of causality must be provided for all adverse events (serious and non-serious). An investigator's causality assessment is the determination of whether there exists a reasonable possibility that the ID caused or contributed to an adverse event. If the investigator's final determination of causality is unknown and the investigator does not know whether or not ID caused the event, then the event will be handled as "related to ID" for reporting purposes. If the investigator's causality assessment is "unknown but not related to ID", this should be clearly documented on study records.

In addition, if the investigator determines a serious adverse event is associated with study procedures, the investigator must record this suspected causal relationship in the source documents and CRF, as appropriate, and report such an assessment in accordance with the serious adverse event reporting requirements, if applicable.

11. STATISTICAL METHODS AND DETERMINATION OF SAMPLE SIZE

All data collected on CRFs will be presented in data listings. The safety analyses will be carried out using the safety population. All efficacy analyses will be analyzed using the Intent-to-Treat (ITT) population. Any formal statistical tests will be performed at α = 0.05 and will be two-sided, unless otherwise specified. All statistical analyses will be conducted in a validated instance of SAS 9.1 or higher. Other analyses, including the creation of figures, may be performed in SAS 9.1 or higher or R 3.2.4 or higher.

11.1. Study Hypothesis

The aim of this study is to evaluate the safety and effectiveness of the ThermiRF™ in the treatment of submental skin laxity with respect to "Lift". The study design assumes that at least 70% of the population that consists of the target demographic (those that meet the inclusion/exclusion criteria) will have 20 mm^2 or more of lift. The null hypothesis is that subjects have a response rate of 45% or lower.

11.2. Sample Size Determination

The sample size calculation is based on the following assumptions:

- The true response rate for subjects that do not drop out will be 70%.
- The null response rate is 45%, so a successful trial will reject the null hypothesis that the true response rate is less than or equal to 45%.
- The dropout rate will be approximately 12.5%. While some subjects that drop out may have data from Day 60 that can be carried forward in the primary effectiveness analysis, the sample size calculation assumes that none does and will therefore be treated as non-responders.
- The primary effectiveness analysis is based on a one-sided binomial proportion test that compares the null proportion to the alternative proportion.

Based on these assumptions, a minimum of 68 subjects is required to achieve 80% power at one-sided α = 0.05, so a sample size of 70 subjects provides greater than 80% power.

Additionally based on the rule of three, sample size of at least 60 makes it possible to observe any adverse event that occurs with a frequency > 5% with 95% confidence.

11.3. Analysis Populations

- **Intent-to-Treat (ITT):** The ITT population includes all subjects that meet inclusion/exclusion criteria, have a signed informed consent form, and are enrolled in the study. The primary effectiveness analysis will be on the ITT population.
- **Safety:** The safety population will include all randomized subjects who received at least one treatment.

- **Per-Protocol Population (PPP):** The PPP will include all subjects who:
    - Completed the Day 90 visit
    - Have an evaluable photograph to estimate area of lift from the Day 90 visit
    - Have not used an excluded medication

11.4. Demographics and Baseline Characteristics

Demographic data and baseline characteristics will be summarized for the Safety population. Demographic data (age, gender, ethnicity and race) and baseline characteristics (height, weight, BMI, heart rate, respiration, blood pressure, and temperature) will be summarized in a table and presented in a listing. A summary of all prior and concomitant medications will be presented.

11.5. Analyses

11.5.1 Primary Effectiveness Analysis

The primary effectiveness analysis will compare the proportion of subjects who respond to treatment by achieving at least 20 mm^2 of lift of the submental region to a null proportion 45% using a one-sided binomial proportion test at $\alpha = 0.05$. Responders will be determined based on change from baseline of area as measured by Vectra XT 3D photography in standard lighting conditions. The primary effectiveness analysis will be based on the ITT population, so any missing data, including withdrawn consent and lost to follow up, will be treated as non-response.

11.5.2 Secondary Effectiveness Analyses

Analysis of all effectiveness endpoints will be conducted on the ITT population and on the PP population. Continuous endpoints will be tested using the paired *t*-test, ordinal endpoints will use the Wilcoxon-Pratt signed rank test, and binary endpoints will be tested using the binomial proportion test.

Raters' assessment of improvement will be validated based on a comparison of the blinded raters' assessments to unblinded raters' assessments at Day 60 as outlined in Kim et al. (Kim et al. 2004) using 30 subjects at Day 60 selected at random. Two unblinded clinicians, who know which photos are baseline and which are Day 60, will assess the 2D photography at baseline and Day 60. Three blinded clinicians, who do not know which photos are baseline and which are Day 60, will assess the same photos. The assessments of the unblinded and blinded raters will be compared using Cohen's unweighted kappa statistic (Fleiss et al. 1969). The assessments will be considered validated according to the scale detailed by Landis et al. (Landis & Koch 1977), where <0.00 is considered poor agreement, 0.00-0.20 is slight agreement, 0.21-0.40 is fair agreement, 0.41-0.60 is moderate agreement, 0.61-0.80 is substantial agreement, and >0.80 is almost perfect agreement. Accordingly, any score greater than 0.60 will validate the method.

11.5.3 Interim Analysis

N/A

11.5.4 Safety Analysis

All safety analyses and summaries will be based on the Safety population. The number and percentage of subjects reporting AEs during the study will be tabulated by MedDRA system organ class (SOC) and preferred term within each SOC. SOCs will be listed in order of descending frequency. Preferred terms will be listed in order of descending frequency within each SOC. Summaries and listings will be provided for subjects reporting SAEs, subjects experiencing AEs related to study medication and subjects withdrawing due to an AE.

Subjects experiencing serious adverse events, treatment-related adverse events and discontinuation from the study due to adverse events will also be summarized.

Treatment-related adverse events will include events marked as being at least possibly or probably related to the study treatment. Adverse events will be presented by severity and by relation to treatment.

Subject disposition at Visit 1 will be presented. Enrollment status with respect to number of subjects enrolled, completed, lost-to-follow and discontinuation regardless of reason will be presented.

Concomitant medications will be summarized.

11.6. Statistical Analysis Plan

A separate statistical analysis plan (SAP) will contain all details needed to carry out the statistical analysis, including specific statistical tests for all effectiveness endpoints, adjustments for multiple testing, specific derivations, and specifications for the tables, listings, and figures.

12. QUALITY CONTROL AND QUALITY ASSURANCE

During study conduct, the sponsor or its agent will conduct periodic monitoring reviews (in person or remote) to oversee the progress of the clinical trial and to ensure that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs) as applicable, Good Clinical Practice (GCP), and the applicable regulatory requirement(s).

The sponsor representative may review source documents to confirm that the data recorded on CRFs/eCRF is accurate. The investigator and institution will allow Sponsor's representative or its agents, and appropriate regulatory authorities, direct access to source documents to perform this verification.

The study site may be subject to review by the institutional review board (IRB)/independent ethics committee (IEC), and/or to quality assurance audits performed by Sponsor, and/or to inspection by appropriate regulatory authorities.

It is important that the investigator(s) and their relevant personnel are available during any in-person monitoring visits and possible audits or inspections, and that sufficient time is devoted to the process.

13. ADMINISTRATIVE REQUIREMENTS

13.1. Protocol Amendments and Administrative Changes

Amendments and administrative changes are not to be made to this protocol without consultation with and the agreement of the Sponsor. The investigator and Sponsor should discuss amendment or administrative change. If agreement is reached, such amendment or administrative change will be developed in writing by the Sponsor and submitted to the investigator.

The investigator will be responsible for ensuring that all protocol amendments are approved in writing by the appropriate IRB or IEC before the institution of the changes specified in the amendment (except when necessary to eliminate an immediate hazard to the subjects). The investigator will also ensure that the Sponsor receives a copy of the written IRB or IEC approval of these changes.

The investigator will be responsible for ensuring that the IRB or IEC receives written notification of all administrative changes to the protocol prior to institution of the specified changes. The investigator will ensure that the Sponsor receives a copy of these written notifications.

13.2. Data Handling and Record Keeping

The investigator will document all study related procedures directly on the source record or medical chart as the primary source of data collection. Study related information/data points required by the sponsor for analysis will be transcribed by the investigator or designee from the source record, onto the CRF/eCRF (data collection tool) for this study using good documentation practices.

In some instances, the sponsor will provide a CRF template for use as the primary source of data collection.

The investigator is encouraged, however not required to maintain additional source records on matters respective to the subject's safety and wellbeing not already captured on the CRFs/eCRF or source template.

Black or blue ink must be used on all data collection requirements. All errors and omissions must be crossed out by means of a single line, and the date and initials of the correction or addition of correct information must be provided. Use of white-out or write-overs will not be permitted. All study related records will be kept in a secure and locked location, and shall only be accessible to the assigned study personnel during the conduct of the study, and to the regulatory authorities in the event of an inspection.

13.3. Case Report Forms / Electronic Data Record

As used in this protocol, the term case report form (CRF) should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this study.

A CRF is required and should be completed for each enrolled subject. The completed original CRFs are the sole property of the sponsor and should not be made available in any form to third parties, except for authorized representatives of the sponsor or appropriate regulatory authorities, without written permission from the sponsor.

It is the investigator's responsibility to ensure completion, review and approve all CRFs. CRFs must be signed by the investigator or by an authorized staff member. These signatures serve to attest that the information contained on the CRFs is true and accurate.

At all times, the investigator has final personal responsibility for the accuracy and authenticity of all clinical and laboratory data entered on the CRFs. In cases where the source documents are the hospital or the physician's chart, the information collected on the CRFs must match those charts.

13.4. Record Retention

To enable evaluations and/or audits from regulatory authorities or the Sponsor, the investigator agrees to keep records including the identity of all participating subjects (sufficient information to link records, e.g., CRFs and hospital records), all original signed informed consent forms, copies of all CRFs, serious adverse event forms, source documents, and detailed records of treatment disposition. The records should be retained by the investigator according to ICH guidelines, local regulations, or as specified in the Clinical Study Agreement, whichever is longer.

If the investigator relocates, retires, or for any reason withdraws from the study, the Sponsor should be prospectively notified of the event, and the location of study records.

The study records must be transferred to an acceptable designee, such as another investigator, another institution, or to the Sponsor.

The investigator must obtain Sponsor's written permission before disposing of any records, even if retention requirements have been met.

14. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this clinical study may occur because of a regulatory authority decision, change in opinion of the IRB/IEC, device safety problems, or at the discretion of the sponsor. In addition, the sponsor retains the right to discontinue development of the device at any time.

If a study is prematurely terminated or discontinued, the sponsor will promptly notify the investigator. After notification, the investigator must contact all participating subjects within 2 weeks from study termination. All study materials must be collected and all CRFs completed to the greatest extent possible.

15. PUBLICATION OF STUDY RESULTS

Publication of study results by the investigator is discussed in the Clinical Study Agreement, as appropriate. Results from this study may be published in the form of oral or written presentations at scientific meetings or as one or more peer-reviewed journal articles. In these cases, no information on individual subjects will be revealed.

16. REFERENCES

1 DiBernardo B. The Aging Neck: A diagnostic approach to surgical and nonsurgical options. Journal of Cosmetic and Laser Therapy 2013; 15: 56-64
2 J. Multicenter study of noninvasive radiofrequency for periorbital tissue tightening. Lasers Surg Med. 2003; 33(4):232-42.
3 Hernandez-Zendejas G, et al. Percutaneous selective radiofrequency neuroablation in plast surgery. Aesth Plast Surg 1994;18:41-48
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5 Kim EJ, Reeck JB, Maas CS. A validated rating scale for hyperkinetic facial lines. Arch. Fac. Plast. Surg. 2004, Vol. 6 July/Aug., 253-256.
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APPENDIX 1 SCHEDULE OF EVALUATIONS

	Visit 1 Screening	Visit 2 (Treatment) (n=70)	Visit 3 Day 30	Visit 4 (F/U)[4] Day 60 *(n=first 30)*	Visit 5 (F/U) Day 90	Visit 6 (F/U) Day 180 (EOS)
Informed consent	X					
Medical /Medication History	X					
Demographics and Baseline Characteristics	X					
Inclusion/Exclusion criteria/conformance	X	X[1]				
Urine Pregnancy Test		X[1]				
Brief Physical Evaluation and Medical Clearance	X					
Vital Signs (incl. Height & Weight)	X					
Photography – 2D (Left, Right and Front views)	X[2]			X[2]	X[2]	X[2]
Photography 3D	X[3]			X[3]	X[3]	X[3]
Elasticity measurement	X				X	X
Treatment Administration		X				
NRS pain scale			X	X	X	X
S-GAIS, S-GSQ				X	X	X
P-GAIS, P-GSQ				X	X	X
Concomitant Medications		X	X	X	X	X
Adverse events		X	X	X	X	X

[1] Urine pregnancy test must be conducted prior to treatment

[2] All 2D images must be collected using standard camera and lighting. Positioning of images must be ***Front View, Right and Left Lateral view and Right and Left views at a 45^0 angle.***

[3] All 3D images must be collected using the Vectra XT camera.

[4] Visit 4 only applies to the first 30 subjects enrolled in the study.

APPENDIX 2 PHYSICIAN GLOBAL AESTHETIC IMPROVEMENT SCALE (P-GAIS)

PHYSICIAN GLOBAL AESTHETIC IMPROVEMENT SCALE (P-GAIS)		
Compared to baseline photography, how would you rate the appearance of the subjects neck laxity with respect to ***"lift"***	5. ☐ Very Much Improved	Optimal cosmetic result for this volunteer.
	4. ☐ Much Improved	Marked improvement in appearance from the initial condition, but not completely optimal for this volunteer. A touch-up would slightly improve the result.
	3. ☐ Improved	Obvious improvement in appearance from the initial condition, but a touch-up or retreatment is indicated
	2. ☐ No Change	The appearance is essentially the same as the original condition
	1. ☐ Worse	The appearance is worse than the original condition

APPENDIX 3 SUBJECT- GLOBAL AESTHETIC IMPROVEMENT SCALE (S-GAIS)

SUBJECT GLOBAL AESTHETIC IMPROVEMENT SCALE (S-GAIS)		
Compared to baseline how would you rate the appearance of your neck with respect to ***"lift"***	5. ☐ Very Much Improved	Optimal cosmetic result for this volunteer.
	4. ☐ Much Improved	Marked improvement in appearance from the initial condition, but not completely optimal for this volunteer. A touch-up would slightly improve the result.
	3. ☐ Improved	Obvious improvement in appearance from the initial condition, but a touch-up or retreatment is indicated
	2. ☐ No Change	The appearance is essentially the same as the original condition
	1. ☐ Worse	The appearance is worse than the original condition

APPENDIX 4 PHYSICIAN- GLOBAL SATISFACTION QUESTIONNAIRE (P-GSQ) OF THE NECK

STUDY NO.: THERMI_005 **SUBJECT ID:_____**	**VISIT DAE:_____** **VISIT DAY: ☐ 90 ☐ 180**
PHYSICIAN GLOBAL SATISFACTION QUESTIONNAIRE (P-GSQ) OF THE NECK	
1. When looking at the photo images and respective to your clinician assessment during this visit, do you see any change on the treated area with respect to "improvement" of the skin and overall area?	☐ Yes, *if "yes" please check all that apply:* ☐ Less sagging on the jawline and cheeks ☐ Tighter/lift under the chin area ☐ Smoother skin texture ☐ Jaw line more defined ☐ less wrinkles/lines ☐ Other (specify);_____ ☐ No
2. Compared to "BEFORE" treatment how does the subject's skin ***feel*** today (check all that apply?	☐ Tighter ☐ Firmer ☐ Smoother ☐ Make-up application easier ☐ Shaving easier ☐ No change from prior to treatment
3. How satisfied are you with the results of the treatment.	☐ Very Satisfied ☐ Satisfied ☐ Neutral ☐ Dissatisfied ☐ Very dissatisfied
4. How likely are you to recommend the treatment to your patients?	☐ Very likely ☐ Likely ☐ Neutral ☐ Unlikely ☐ Vert unlikely

APPENDIX 5 SUBJECT- GLOBAL SATISFACTION QUESTIONNAIRE (S-GSQ) OF THE NECK

STUDY NO.: THERMI_005 **SUBJECT ID:_____**	**VISIT DAE:_____** **VISIT DAY: ☐ 90 ☐ 180**
SUBJECT GLOBAL SATISFACTION QUESTIONNAIRE (S-GSQ) OF THE NECK	
Instruction: • *Provide a copy of the before and after photo to the study participant PRIOR to administering the G* • *Direct the subject to the photo and review the lower part of the face using the "jawline", "upper neck – under the chin" and "lower neck"* • *Have the subject provide responses to the following questions.*	
1. Have you noticed any change with respect to "improvement" of the skin appearance of your neck?	☐ Yes, *if "yes" please check all that apply:* ☐ Less sagging on the jawline and cheeks ☐ Tighter/lift under the chin area ☐ Smoother skin texture ☐ Jaw line more defined ☐ less wrinkles/lines ☐ Other (specify);_____ ☐ No
2. Compared to "BEFORE" treatment how does your skin ***feel*** today (check all that apply?	☐ Tighter ☐ Firmer ☐ Smoother ☐ Make-up application easier ☐ Shaving easier ☐ No change from prior to treatment
3. How satisfied are you with the results of your treatment.	☐ Very Satisfied ☐ Satisfied ☐ Neutral ☐ Dissatisfied ☐ Very dissatisfied
4. How likely are you to recommend this treatment to family and friends?	☐ Very likely ☐ Likely ☐ Neutral ☐ Unlikely ☐ Vert unlikely

APPENDIX 6 CUTOMETER BROCHURE

CUTOMETER® DUAL MPA580 - MECHANICAL PARAMETERS OF THE SKIN

What does it measure?

The Cutometer® MPA 580 is a worldwide acknowledged standard device to measure elasticity and other biomechanical parameters of the skin. The Multiprobe Adaptor function allows to connect further probes additionally to the two Cutometer® probes.

The Measuring Principle

The measurement is based on suction. Negative pressure is created in the device and the skin is drawn into the aperture of the probe. Inside the probe the penetration depth is determined by a non-contact optical measuring system consisting of a light source and a light receptor, as well as two prisms facing each other, which project the light from transmitter to receptor. The light intensity varies due to the penetration depth of the skin.
The resistance of the skin to be sucked up by negative pressure (firmness) and its ability to return into its original position (elasticity) are displayed as curves.

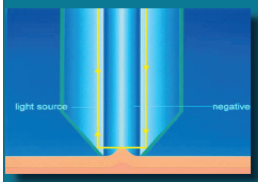
Fields of Application

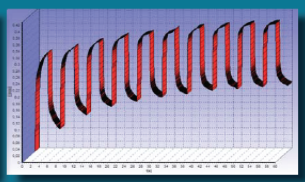
The measurement with the Cutometer® is used as standard in dermatology and cosmetology

- It is indispensable for formulation, efficacy testing and claim support for all kinds of cosmetic products (especially anti-ageing products, firmness enhancing products).
- It is used for research and clinical diagnosis, e.g. measurement on scars. Also special applications like in gynaecology are possible.
- Other materials like food can also be assessed.

Advantages

- The modern, high quality electronics of the prob allow a very quick measurement.
- Several probe aperture sizes for different skin s tes and study requirements available.
- Two probes with different aperture sizes can b connected at the same time.
- A spring in the measuring head provide constant pressure on the skin.
- The low weight of the probe ensures easy han ling. A multitude of elasticity related parameter can be calculated from the curves.
- The settings in the programme are very flexibl and can be selected by the user according to di ferent applications.
- All data of the curves can be transferred t spreadsheets (Microsoft Excel®) for further indiv dual evaluation (up to four curves per sheet).
- Available solely as C+K MPA -System.




hnical Data
ensions: Device: 39 x 22.5 x 7.6 cm, Probe:10.7 cm x Ø 2.4 cm , Aperture: Ø 2 mm standard, (4, 6 or 8 mm on uest), Weight: Device: 3.9 kg , Probe:165 g incl. air tube, Power supply: ext.100-240 VAC, 47-63 Hz, DC 12V/9A
s: µm penetration depth into the probe opening, expressed as curves
hnical changes may be made without prior notice.

Courage+Khazaka electronic GmbH since 1986
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CUTOMETER® DUAL MPA580 - MECHANICAL PARAMETERS OF THE SKIN

Software & Parameters

The software of the Cutometer® dual MPA 580 allows to calculate a lot of interesting parameters. Here a short overview:

R-Parameters

- R0: This parameter represents the passive behaviour of the skin to force.
- R1: The ability of the skin to return to its original state.
- R2: Gross elasticity, the closer the value is to 1 (100 %) the more elastic the curve, very important parameter.
- R3: Last curve, compared to the maximum amplitude of the first curve. „Tiring effects" of the skin are visible, as the amplitude increases with each new suction.
- R4: Last minimum amplitude compared to the first curve, „tiring effects" of the skin are visible, as the ability of redeformation decreases with each new suction.
- R5: Net elasticity, the closer the value is to 1 (100 %) the more elastic the skin.
- R6: Portion of the visco-elasticity on the elastic part of the curve. The smaller the value the higher the elasticity.
- R7: Portion of the elasticity compared to the complete curve, the closer the value is to 1 (100 %) the more elastic the skin.
- R8: The closer Ua of the first curve is to 0 the greater the ability of the skin to return into its original state.
- R9: Represents tiring effects of the skin after repeated sucking in of the skin. The smaller R9 the smaller the tiring effects.

F-Parameters

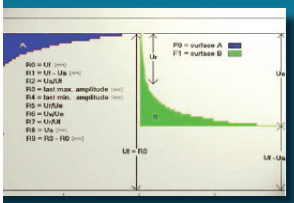
These area parameters can only be taken in mode 1 and some will need 10 repetitions.

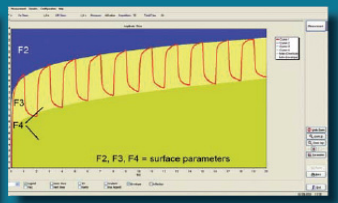
- F1: This area is deducted from the total area. A completely elastic material will show no area at all, the closer the value to 0 the more elastic the material.
- F2: Area above the upper envelope-curve.
- F3: Area within the envelope curves.
- F4: The smaller F4 the more the skin resists t the suction (skin firmness).

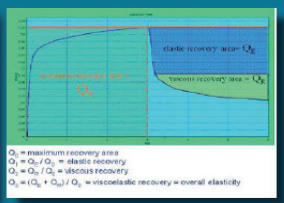
Q-Parameters

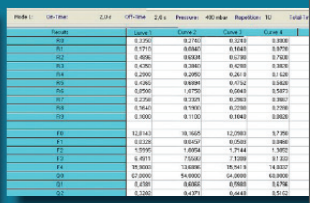
A set of parameters developed by the scientist D Qu* has recently been added, showing interesting correlations between skin age and the elastic an viscous recovery of the curves.

- Q0: Maximum recovery area, will go down wit more firmness of the skin.
- Q1: Elastic recovery, will be higher with mor firmness of the skin.
- Q2: Viscous recovery
- Q3: Viscoelastic recovery (overall elasticity) will be higher with more firmness of the skin.









hnical Data
nputer: Windows® XP, Vista or 7, 32 bit (not 64 bit!), performance must meet system requirements, USB 2.0

nical changes may be made without prior notice.

Qu, Senior Research Scientist, R&D Skin Care, Amway Corporation, Ada, Michigan, USA

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APPENDIX 7 NUMERICAL RATING SCALE

APPENDIX 8 APPLICATION OF NON-SIGNIFICANT RISK

THERMIAGEN, LLC LETTER OF APPLICATION FOR NONSIGNIFICANT RISK DETERMINATION FOR THE THERMIRF® DEVICE (V0.1 12.07.14)

Description of Investigational Product:

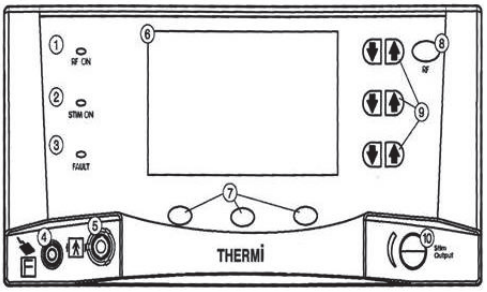
Name of the device: ThermiRF

Description of the device: The ThermiGen, LLC ThermiRF is a non-invasive, transcutaneous radiofrequency device that is FDA cleared for dermatological and general surgical procedures for electrocoagulation and hemostasis (K130689).

The ThermiRF has been tested by a third party (Intertek Testing Services NA Inc.) for conformance to IEC 60601-1-2 (EMC) and IEC 60601-1 (electrical safety). Third party verification of IEC 60601-1-4 and IEC 60601-1-6 Collateral Standards was performed as well.

The ThermiRF is a 20 watt electrothermal RF generator that continuously monitors temperature and impedance. It provides controlled temperature tissue heating as its mechanism of action.

Name: ThermiRF



Control/Connections	Function
1. RF ON (blue light)	Illuminated when generator is delivering RF power
2. STIM ON (yellow light)	Illuminated when generator is delivering Stimulate Power
3. FAULT (red light)	Illuminated when a fault condition is detected
4. Neutral electrode connection port	Used to connect a neutral electrode (grounding pad) to the generator
5. Device connection port	Used to connect RF electrode accessories to generator
6. Display window	Displays generator information, modes, and operating parameters.
7. Soft Keys	STIM: Motor; ThermiTight, ThermiSmooth, ThermiRase, Help/Exit, Start, Reset, and OK
8. RF ON Button	Start or stops RF power delivery
9. Up/down buttons	Used to increase or decrease function settings
10. Stim output knob	Adjusts the stimulate output voltage. Push and release the knob to turn Stimulate power on/off.

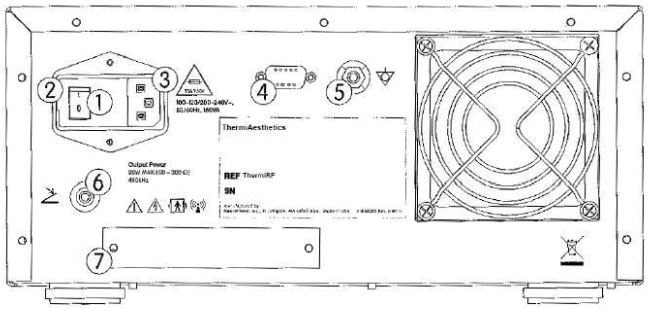


Figure 2. ThermiAesthetics™ ThermiRF™ System rear panel.

Control/Connections	Function
1. On/Off rocker switch	Turn the generator main power on/of
2. Fuse access door	Access for fuse replacement
3. Power cord connector	Input module
4. RS-232 connector	For service use only
5. Equipotential compensator terminal (case ground)	Bring equipment into the same case potential as the generator
6. Footswitch connector	Connect pneumatic footswitch to the generator
7. Security door	Access for software upgrades (Authorized user only)

ThermiRF is a main powered device; the specifications of which are:

Height: 5.75”
Width: 12.5”
Depth: 13.0”
Weight: 12.6 lbs.

SPECIFICATIONS

Parameters	ThermiRF
Dimensions ThermiRF Generator	W:12.5 * D:13.0 * H:5.75
Internal Display	LCD Display
ThermiRF Generator Specifications	
Input Power	100-120/200-240 + 10%, 50/60 Hz
Output Power	20 watts (maximum) into 50-300Ω
Output Voltage in Stimulate Mode	0-10 V
Output Voltage in RF Lesion Mode	0-20 V
Operating Frequency	460 kHz (+5 kHz)
Power Delivery Modes	Stimulate Mode, ThermiTight Mode, ThermiRase Mode, ThermiSmooth Mode Pulsed RF Mode, Biomed (calibration-test) Mode

Set Temperature Range	35-90oC, this range varies for each Power Delivery Mode

Waveform	Sine wave for RF Lesion and Pulsed RF Modes, Square wave for Stimulate Modes
Protection (per IEC 60601-1)	Class I, Type BF Applied Part- defibrillator proof, IXP0, Continuous Operation. Not suitable for use in the presence of a flammable anesthetic mixture.
Controls	Line Power On/OFF, RF On/OFF, Stimulate Output, Front Panel Soft Keys (Start, Set Temp, Set Profile, Reset, Width, Frequency, and Mode Selection)
Displays	Impedance, Actual Temp, Elapsed Time, Paused, Volts, Frequency
Electrode surface	180 mm^2
Subject contacting part	Yes
Subject contacting materials	Surgical Stainless Steel

Device Preparation and Administration of Study Intervention/Investigational Product:

The device will administer up to 20 Watts of radiofrequency energy.

DETERMINATION OF DEVICE SAFETY

RISK AND PREVENTION

The ThermiRF® Device is classified by the FDA/IEC as a Class 2 radiofrequency device. The device has risk of burns or fire, and therefore, cannot be used near conductive materials such as metal bed parts, inner-spring mattress, etc. A disposable grounding pad is used to ground the electrical current. Furthermore, the subject will not be placed into contact with metal parts which are grounded or which have appreciable capacitance to earth. The device cannot be used in subjects with a pacemaker, implantable defibrillators, or monitoring equipment.

FDA DETERMINATION OF NON-SIGNIFICANT RISK (NSR) STATUS

The ThermiGen LLC ThermiRF is a radiofrequency device that is FDA cleared for dermatological and general surgical procedures for electrocoagulation and hemostasis (K130689).

N.B.; The ThermiRF is technically identical to the Symphony RF, the marketing name of the device was changed from Symphony RF to ThermiRF. No technical modifications were made. (K130689).

1. 510(k)# 130689
   Device Name: SymphonyRF Generator (ThermiRF)
   Indication for use: dermatological and general surgical procedures for electrocoagulation and hemostasis; and to create lesions in nervous tissue

2. 510(k) #: K-033981
   Device Name: Smith and Nephew ElectroThermal 20S Spine Generator
   Indication of use: Intended to create lesions in nervous tissue, and to coagulate and decompress disc material when used in combination with Smith and Nephew thermal/coagulating probes.

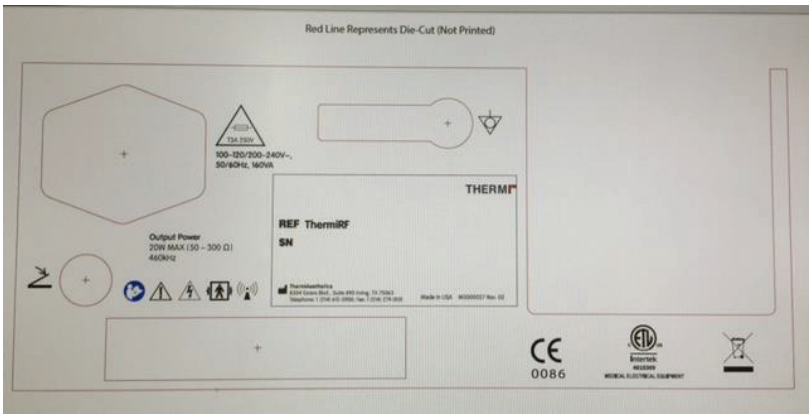
3. 510(k) #: K121858
   Device Name: The Acessa System

Indication of use: Percutaneous use for laparoscopic coagulation and ablation of soft tissue

4. 510(k) #: K121481
   Device Name: The INFINI Radiofrequency System
   Indication of use: For use in dermatologic and general surgical procedures for electrocoagulation and hemostasis, and the percutaneous treatment of facial wrinkles
5. 510(k) #: K082391
   Device Name: Primaeva Medical
   Indication for use: For use in dermatologic and general surgical procedures for electrocoagulation and hemostasis, and the percutaneous treatment of wrinkles
   IRB approved study: The protocol was reviewed and approved by the local ethics committee (Independent Investigational Review Board, Inc, Plantation, FL, USA Millheiser LS, Pauls RN, Herbst SJ, Chen BH. Radiofrequency treatment of vaginal laxity after vaginal delivery: non-surgical vaginal tightening. J Sex Med. 2010; 7(9):3088-95.

DEVICE LABELING

The ThermiRF is manufactured in accordance with the Good Manufacturing Procedures set forth by the FDA. Per CE (Certified European) standards and testing results and has been validated by a third party (Intertek Testing Services NA Inc. Report Reference No. 100584146BOX-004) for conformance to IEC 60601-1-2 (EMC) and IEC 60601-1 (electrical safety). Third party verification of IEC 60601-1-4 and IEC 60601-1-6 Collateral Standards was performed as well.



In addition, the device used in this clinical study shall be labeled with the following statement: NON-SIGNIFICANT RISK STATEMENTS
"CAUTION – Investigational device. Limited by United States law to Investigational use."

Do you contend that this device as used in this protocol is an NSR device?
_✓_ Yes ___No
Has another IRB decided this device is SR?
___ Yes _✓_ No
Does this type of device appear as SR on the FDA Information Sheet?
____Yes _✓_ No

APPENDIX 9 THERMI_RF USER MANUAL 4002-01 REV C.PDF (1MB)

The User Manual is on-file in the sponsor Trial Master File (TMF), and a copy provided to the investigator in the Site Master File.

APPENDIX 10 BLINDED RATER VALIDATION GUIDELINES

The blinded-rater validation guidelines can be found in the sponsor Trial Master File (TMF)