Title: Pilot Study: Clinical assessment of bipolar radiofrequency microneedling for improved laxity and wrinkles of the suprapatellar skin.

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The University of Texas Southwestern Medical Center at Dallas
Institutional Review Board

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1. Introduction and Purpose:

Purpose
The purpose of this study is to evaluate the safety and efficacy of bipolar fractional radiofrequency treatment for improving laxity and tightening of the suprapatellar skin.

Primary Objectives
To evaluate the effectiveness of the bipolar fractional radiofrequency device in improving laxity and tightening of the suprapatellar skin. Overall assessment of clinical outcome and safety will be based on clinic visits and evaluation of pre- and post-procedural photos. The subjects' assessment of satisfaction will be characterized using a non-parametric assessment scale at each follow up period.

2. Background:

The human skin aging process is characterized by thinning dermis, atrophy of the extracellular matrix, and reduced collagen synthesis[1]. Loss of collagen in the dermis is of aesthetic concern, as it is the main structural support in the dermis and its loss results in skin laxity. Photo-damaged skin, mostly due to UVR, causes degradation of elastic fibers. This is histologically seen as disorganized tangles of elastin. Additionally, as we age, skin tends to appear more dry due to its poor hydration and turgor capacity[1]. The use of minimally invasive aesthetic treatments in reducing signs of aging has been gaining in popularity over surgical treatments in recent years[2]. Several energy types including, laser, radiofrequency, infrared, and ultrasound, have been developed for facial rejuvenation[3]. These treatments induce controlled thermal damage into the dermis and cause collagen contraction and neocollagenesis resulting in skin tightening over several months[2]. For improving appearance of other anatomical areas, micro-focused ultrasound has been the preferred method, but has shown limited success in tightening the suprapatellar skin[3,4].

As with facial skin aging, the suprapatellar skin loses elasticity with age and begins to sag. Noninvasive treatments used for the face may also be used in other anatomical areas to produce the same effects of tightening. Minimally invasive bipolar radiofrequency produces a controlled thermal injury in a fractional manner without damaging the dermal-epidermal junction, epidermis or

subcutis[5]. Radiofrequency, unlike lasers, are chromophore-independent providing better penetration than lasers, and spare sweat glands, sebaceous glands, and hair follicles [5,6].

[redacted] is a bipolar fractional radiofrequency device which uses microneedles and thermal heat to stimulate neocollagenesis. Based on the its effect on facial skin, it can be hypothesized that bipolar fractional radiofrequency will stimulate similar effect on suprapatellar skin, lifting and reducing laxity of the skin in that region.

[redacted]

There are alternative treatments that have been shown to decrease laxity of the suprapatellar skin, however, the studies include a small and limited population, and have not produced the desired effects in practice. We feel that the [redacted] may be able to produce clinically significant improvement in laxity of the suprapatellar skin.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

3. Concise Summary of Project:

This is a pilot study to evaluate the safety, effectiveness, and time course of healing o [redacted] in improving laxity of the suprapatellar skin. Overall assessment of clinical outcome and safety will be based on clinic visits and evaluation of pre- and post- procedural photos. [redacted] The subject's assessment of satisfaction will be characterized using a non-parametric assessment scale at each follow-up period.

From these studies the improvement in laxity of the suprapatellar skin can be evaluated in comparison to pre-treatment assessments.

Clinical Study
[redacted] *treatment of suprapatellar skin*
This is a single-site, non-randomized, non-controlled investigator initiated study designed to follow a total of twenty qualified and consenting subjects treated with one bipolar fractional radiofrequency microneedling treatment during clinical practice.

[redacted]

Subjects will be identified from Dr. Jeffrey Kenkel's clinical practice at the University of Texas Southwestern Medical Center.

Follow-up for any identified adverse events will be reported to the IRB. During the treatment, subjects will be asked to rate any pain or discomfort on a 10-point scale of 0 = no pain to 10 = worst pain imaginable.

[redacted]

We will obtain standard and cross-polarized analyze skin texture and laxity. The time for imagine will take approximately 5 minutes.

High resolution ultrasound will be used to assess skin thickness and density. The standard time for use of high-resolution ultrasound should take approximately 5 minutes.

[redacted]

[redacted]

Other endpoints may include the appearance and disappearance of crusting, erythema, as well as the restoration of natural color and texture of the skin surface.

4. Study Procedures:

Screening Visit (Visit 1)

The purpose of the study and specific inclusion and exclusion criteria and potential risks will be discussed with the potential study subject. All interested subjects will be given the Consent Form with adequate time for review. The Investigator and/or his designee will address questions and concerns raised by the subject. Those subjects who elect to participate, will sign the Consent Forms prior to any study procedures.

Subjects will be screened to ensure that they meet all study criteria. A brief medical history will be taken, including but not limited to age, sex, skin type, recent sun exposure, allergies, current medications, major illnesses, etc. The location and approximate area of the treatment area(s) will be mapped. Pre-existing skin conditions will be evaluated for potential study impact.

The maximum amount of time for this visit will be 1 and 1 ½ hours.

Treatment Visit (Visit 2)

Prior to treatment, the knee area will be gently cleansed with an alcohol wipe. Any visible hair will be shaved before cleansing. [redacted]

Post-treatment care and precautions

Subject can shower beginning the next day after treatment and return to normal skin care regimen.

[redacted]

Follow-up Visits (Visits 3-6)

At a minimum, all subjects will return for follow-up at 7 days (+/- 1 day), 3 weeks (+/- 2 days), 3 months (+/- 7 days), 6 months (+/- 7 days) after treatment (with reasonable accommodation for scheduling). At all follow up visits, photographs will be taken [redacted]

[redacted]

Summary: Schedule of Study Activities

Visit 1: Enrollment/Screening Visit (Investigator or designee)

The following enrollment and screening activities will be performed

a. Discuss the bipolar fractional radiofrequency device with each patient presenting for treatment.
b. Obtain informed consent and HIPAA authorization.
c. Collect any appropriate medical and surgical history including current medications.
d. Urine pregnancy test for women of childbearing potential.
e. Examination of the treatment area by the physician.

This visit will take about 1 – 1 ½ 1hours

Visit 2 – Treatment Visit

[redacted]

This visit will take about 2 hours.

Visits 3, 4, 5, and 6: Follow-up Visits after treatment (Investigator or designee) – 1 day, 7 days (+/- 1 day), 3 weeks (+/- 2 days), 3 months (+/- 7 days), and 6 months (+/- 7 days)

The following activities will be performed:

A. Adverse Event Review
    1. Query the subject regarding any change in health since enrollment into the study.
    2. Perform a detailed cutaneous exam of the treatment area, review and record any local adverse events related to cutaneous changes.
B. Collect an updated surgical history and record any change in concomitant medications or treatments.
C. Collection of vital signs.

[redacted]

These visits will take about 45 minutes – 1 hour.

Follow-up Questionnaires

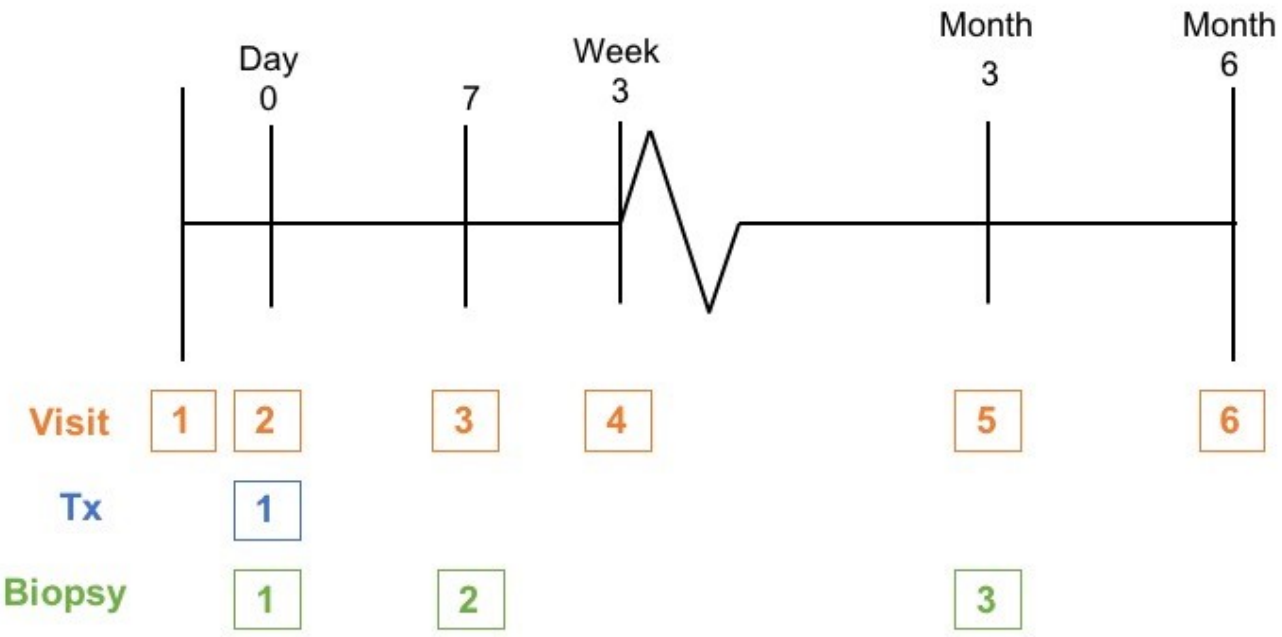
The following information will be collected:

a. Subject assessment of safety – potential adverse events (to be confirmed during office visit) occurring since last evaluation.
b. Information on any additional cosmetic treatments received in the facial treatment area.

Event Follow-up Visits (Investigator or designee)

If a potential adverse event is reported by the subject or identified during examination, the Investigator will contact the subject to schedule an Event Follow-up Visit. At this visit the Investigator or their designee will:

a. Obtain a complete history of the event in question as well as conduct an examination of the subject and determine if the reported event qualifies as an Adverse Event. If the event is determined to be an Adverse Event, an Adverse Event (AE) case report form and Event Follow-up (EF) Visit case report form must be completed. One AE case report form should be used to track the history of an individual AE throughout the period of the study.
b. Collect an updated medical and surgical history along with recording of concomitant medications or treatments.
c. Take photographs of the subject with attention to the area in question.
d. Render treatment for the event, if any, as determined by the medical judgment of the investigator.



5. Sub-Study Procedures: N/A

6. Criteria for Inclusion of Subjects:

a. Healthy male and female adults between ages 18-75 years of age.
b. Subjects who can read, understand, and sign the Informed Consent Form.
c. Subjects willing and able to comply with all study requirements
d. Fitzpatrick skin type I-III

7. Criteria for Exclusion of Subjects:

a. Subjects with active localized or systemic infections.
b. Immunocompromised subjects.
c. Subjects with coagulation disorder.
d. History of skin photosensitivity disorders, or use of photosensitizing drugs (e.g., tetracycline or sulfa drugs).
e. Pregnant and/or lactating (All female volunteers will be advised about using birth control during the period of study).
f. In the opinion of the trained clinician, subject is unwilling or unable to adhere to all study requirements, including application and follow-up visits.
g. Subjects with a history of radiation therapy to the treatment area.
h. Subject has a history of allergy to lidocaine or ester-based local anesthetics.
i. Subjects with any skin pathology or condition that could interfere with evaluation or with the use of typical ancillary medical treatments or care used before, during or after treatments.
j. Subjects have undergone dermatological procedures (e.g., laser or light treatments) for the treatment of wrinkles, skin resurfacing, or skin rejuvenation in the treatment area within 1 year of study participation.

8. Sources of Research Material:

Objective 1:

[redacted]

9. Recruitment Methods and Consenting Process:

Subjects will be recruited from the existing practice of the Investigators, Campus News postings, and flyers placed at UT Southwestern Plastic Surgery Clinics. Subjects who present for treatment with Profound System will have the study explained to them, will be asked about their willingness to be involved in the study, and their willingness to sign an informed consent form. Included in this interview will be questioning from the investigator or staff member about any privacy concerns the individual may have.

Prior to any study procedures each Subject will read and sign a Consent Form, explaining the purpose, design, risks and duration of the study. This consent will include a photography release that allows the investigator or his designee to take recognizable and non- recognizable photographs of the subject. If the subjects decline permission to be photographed, they may not participate in the study since the photographic documentation of treatment outcome is an important measure of evaluation.

[redacted]

10. Potential Risks:

Blistering, burning, scaling and infection: **(Rare < 1%)**

A crust, blister or superficial wound can occur at the treatment area. The risk of infection will be minimized by proper wound care.

Bruising: **(Rare < 1%)**

A mild bruising may occur at the treatment area as a result of radiofrequency exposure. This is usually transient and resolves in a few hours to few days.

***Transient edema and/or erythema*: (Occasionally < 3%)**
May develop within the irradiated areas but are usually temporary and fade within 24-72 hours. There is a 90% chance of transient edema and 99% chance of erythema to occur after treatment.

***Pigmentary changes:* (Rare < 1%)**
Radiofrequency exposure can cause pigmentary changes such as hyper- (3% chance) and hypo-pigmentation (<.5% chance). Although this is usually temporary, it may be permanent on rare occasions. Sun avoidance and/or the use of a total sun block (SPF 30 or higher) will help minimize the intensity and duration of any pigmentary changes.

***Scarring:* (Rare < 1%)**
As with any form of energy exposure, there is a small risk of scarring. However, this is minimized by proper technique and wound care.

***Allergic Reaction:* (Rare < 1%)**
There is a possibility of an allergic or toxic reaction to anesthesia used to numb the areas. Subjects will be questioned with regard to any history of allergies and carefully monitored for signs of allergic reaction.

Biopsy
Risks associated with biopsy include: 1) scarring - a small risk of scarring, which can be minimized by proper technique and wound care; 2) allergic reaction - there is a possibility of an allergic or toxic reaction to anesthesia used to numb the areas. Subjects will be questioned with regard to any history of allergies and carefully monitored for signs of allergic reaction.

Photography
The subject may be uncomfortable with sitting still for an extended period of time or from turning her body in various positions. Subjects may be sensitive to the bright and repeating flashes from the camera, which can sometimes cause headaches, irritation of the eyes, discomfort, after effects such as seeing spots, and in rare cases, could stimulate a migraine headache or epileptic seizure.

Photographs include a risk of identification. Privacy will be protected to the greatest extent possible. Photos will only be identified by a unique subject identification number that contains no personal identifying information. For research purposes photos may be used in scientific publications

11. Subject Safety and Data Monitoring:
For this protocol, which involves the use of a non-significant risk device, the Investigator will monitor accrual, subject experience, attrition, patterns of adverse events and/or unexpected adverse events, any protocol deviations or violations any changes in the risk/benefit analysis. This monitoring will be done at least monthly during the course of the protocol.

Subjects will be asked about any adverse events throughout the study. Subjects will be asked to contact the Investigator if adverse events develop between visits. An unscheduled visit will be arranged so that the Investigator can clinically evaluate and photograph these findings.

All study records and information will be identified by the subject number. All subject identifiers will be removed from all documents. The link between subject name and study ID number will be kept in separate password-protected files. Documents containing identifying information will be kept in locked files in the research staffs' locked office. All electronic study data will be password protected with access limited to members of the research team. No direct identifying information will be shared with any outside entities. Electronic data (electronic data entry - Case Report Forms) will be password protected.

In Objective 1, photographs of the subject's suprapatellar area will be taken at Enrollment/Treatment and Follow-Up visits. These photographs will be identified by subject numbers and will not include any identifying marks [such as tattoos]. Subject confidentiality will be protected to the greatest extent possible.

This study will be performed in accordance with Health Insurance Portability and Accountability Act. These guidelines will be followed specifically with regards to the privacy and confidentiality of patient care and study records.

Personnel associated with Investigator's office and the governing Institutional Review Board, have the right to review the data, including photographs, collected during this study.

12. Procedures to Maintain Confidentiality:

All study records and information will be identified by the subject number. All subject identifiers will be removed from all documents. The link between subject name and study ID number will be kept in separate password-protected files. Documents containing identifying information will be kept in locked files in the research staffs' locked office. All electronic study data will be password protected with access limited to members of the research team.

No direct identifying information will be shared with any outside entities. Electronic data (electronic data entry - Case Report Forms) will be password protected.

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This study will be performed in accordance with Health Insurance Portability and Accountability Act. These guidelines will be followed specifically with regards to the privacy and confidentiality of patient care and study records. Personnel associated with Investigator's office and the governing Institutional Review Board, have the right to review the data, including photographs, collected during this study.

13. Potential Benefits:

Subjects may benefit by having an overall improvement in the appearance of the suprapatellar skin, such as a reduction in skin folds and improved laxity or an overall improvement in skin tone or texture in the treated areas, but this is not guaranteed. There may be a benefit to the medical community by demonstrating the safety and effectiveness of a new technology in the management of skin laxity of the suprapatellar region. [redacted]

14. **Biostatistics:**

This pilot study will allow us to determine which statistical analysis will be most suitable based on the number of patients we are able to recruit.

[redacted]

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3. Alster TS, Tanzi EL. Noninvasive lifting of arm, thigh, and knee skin with transcutaneous intense focused ultrasound. *Dermatol Surg.* May 2012;38(5):754-759.
4. Gold MH, Sensing W, Biron J. Use of micro-focused ultrasound with visualization to lift and tighten lax knee skin (1.). *J Cosmet Laser Ther.* Oct 2014;16(5):225-229.
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