# Protocol Summary

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| **Study Title:** | Dualsculpting The Abdomen Using Cryolipolysis |
| **Protocol Number:** | ZA16-004 |
| **Study Device:** | Zeltiq CoolSculpting System with Vacuum Applicator |
| **Sponsor:** | Zeltiq Aesthetics<br>4410 Rosewood Dr.<br>Pleasanton, CA 94588 |
| **Date:** | 05 June 2020 |
| **Date of IRB Approval:** | 06 October 2016 |

# 1. Introduction

## *1.1 Background*

ZELTIQ Aesthetics has developed and commercialized a technology to non-invasively reduce subcutaneous fat. The ZELTIQ technology, termed CoolSculpting and generically referred to as cryolipolysis, enables a non-invasive alternative for subcutaneous fat reduction through cellular apoptosis. The CoolSculpting System, which is FDA-cleared for use in the United States for an indication of fat layer reduction in the submental area, thighs, flanks, abdomen, bra fat, and banana roll, has been clinically proven to reduce fat bulges, allowing patients to achieve noticeable and measurable aesthetic results without the pain, expense, downtime, and risks associated with existing invasive and minimally-invasive procedures.

The purpose of this study is to evaluate the safety and efficacy of the ZELTIQ CoolSculpting System using vacuum applicators for non-invasive subcutaneous fat reduction in the abdomen. Slightly different size vacuum applicators will be used in this study.

## *1.2 Device Description*

The study treatments will be performed using the ZELTIQ CoolSculpting System. The ZELTIQ CoolSculpting System is comprised of a control unit which houses the system controller and power source, and a detachable vacuum applicator used to apply the cooling to the treatment site.

This study will evaluate the safety and efficacy of the vacuum applicators to treat the abdomen. The subjects will receive 4-6 cooling cycles during each of two treatment visits The treatment cooling cycle on the abdomen will be up to (REDACTED) minutes in duration with a temperature of (REDACTED)°C. At the investigator's discretion, an additional cooling cycle may be delivered to cover the treatment area..

## *1.3 Regulatory Status*

The ZELTIQ CoolSculpting System has been cleared in the United States for use as an aesthetic treatment to affect the appearance of the flanks (DEN090002), the abdomen (K120023), the thighs (K133212) the submental area (K151179), and bra fat, back fat, and banana roll (K160259). Additionally, the System has been cleared for flexible treatment parameter ranges (K142491).

The ZELTIQ CoolSculpting System can also provide localized thermal therapy (hot or cold) to minimize pain for post-traumatic and/or post-surgical pain and to temporarily relieve minor aches and pains and muscle spasms. The optional massage function can also be used for temporary:

- Relief of minor muscle aches, pain, and spasm
- Improvement in local circulation

This study will investigate the use of the FDA cleared ZELTIQ CoolSculpting System and (REDACTED) applicators for DualSculpting the abdomen.

# 2. Study Protocol

## *2.1 Design*

Prospective, non-randomized interventional cohort

## *2.2 Study Duration*

Enrollment and follow-up is expected to take up to six (6) months for each subject.

## *2.3 Physician Participants*

Study investigators must be practicing medical physicians with experience in the use of the Zeltiq System.

## *2.4 Site Requirements*

Study investigators must have at least one study coordinator with experience in conducting aesthetic research and with sufficient time to conduct the study.

## *2.5 Subject Recruitment*

Subjects who seek reduction of fat in the abdomen and who the investigator has assesses to be eligible for multiple CoolSculpting treatments will be recruited from the general population.

## *2.6 Sample Size*

A maximum of twenty (20) subjects will be treated at up to 2 investigational sites.

## *2.7 Patient Eligibility*

To be eligible to participate, subjects must meet all of the inclusion criteria and none of the exclusion criteria listed in **Table 1**.

**Table 1. Eligibility criteria.**

| **Inclusion Criteria** |
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| a) Male or female subjects > 22 years of age and < 65 years of age. |
| b) Subject who has been assessed to be eligible to receive multiple DualSculpting treatments on the abdomen using the (REDACTED) and/or (REDACTED) applicator. |
| c) No weight change exceeding 5% in the preceding month. |
| d) Subject agrees to maintain his/her weight (i.e., within 5% of total body weight) by not making any major changes in their diet or exercise routine during the course of the |

study.
e) Subject has read and signed the study written informed consent form.

**Exclusion Criteria**
a) Subject has had a surgical procedure(s) in the area of intended treatment.
b) Subject has had an invasive fat reduction procedure (e.g., liposuction, mesotherapy) in the area of intended treatment.
c) Subject has had a non-invasive fat reduction and/or body contouring procedure in the area of intended treatment within the past 12 months.
d) Subject needs to administer, or has a known history of subcutaneous injections into the area of intended treatment (e.g., heparin, insulin) within the past month.
e) Subject has a known history of cryoglobulinemia, cold urticaria, cold agglutinin disease or paroxysmal cold hemoglobinuria.
f) Subject has a known history of Raynaud's disease, or any known condition with a response to cold exposure that limits blood flow to the skin.
g) Subject has a history of bleeding disorder or is taking any medication that in the investigator's opinion may increase the subject's risk of bruising.
h) Subject is taking or has taken diet pills or supplements within the past month.
i) Subject has any dermatological conditions, such as moderate to excessive skin laxity, or scars in the location of the treatment sites that may interfere with the treatment or evaluation (stretch marks is not an exclusion).
j) Subject has an active implanted device such as a pacemaker, defibrillator, or drug delivery system or any other metal containing implant.
k) Subject is pregnant or intending to become pregnant during the study period
l) Subject is lactating or has been lactating in the past 6 months.
m) Subject has a history of hernia in the areas to be treated.
n) Subject is unable or unwilling to comply with the study requirements.
o) Subject is currently enrolled in a clinical study of any other unapproved investigational drug or device.
p) Any other condition or laboratory value that would, in the professional opinion of the investigator, potentially affect the subject's response or the integrity of the data or would pose an unacceptable risk to the subject.

## *2.8 Informed Consent*

Study candidates shall receive an explanation of the study objectives, possible risks and benefits of the study, and be given adequate time to read the information included in the informed consent document. Candidates will be given an opportunity to ask questions about any of the information contained in the informed consent. Candidates must verbally acknowledge understanding of the informed consent, and sign the consent form accordingly. This form must have prior approval of the Institutional Review Board (IRB) or Ethics Committee (EC).

### *2.9 Study Procedures*

#### 2.9.1 Screening

Subjects will undergo screening to determine eligibility for study participation. Screening procedures include the collection of demographic information medical history and examination, concomitant medications, and pre-treatment imaging of the intended treatment area. All female subjects of childbearing potential will be asked to take a pregnancy test (urine) prior to being treated. If the subject is pregnant, she will be excluded from participation.

#### 2.9.2 Treatment

Treatment will be performed in accordance with Zeltiq Aesthetic's Instructions for Use for the CoolSculpting System and vacuum applicator. Cooling will be delivered to the abdomen using two (2) applicators simultaneously. Treatment parameters such as cooling temperature and duration of cooling will be preset by Zeltiq Aesthetics.

#### 2.9.3 Follow-up Schedule

Follow-up will occur at 1, 6 and 12 weeks post-treatment with the CoolSculpting System. Post-treatment images will be collected at all in-office follow-up visits.

## 3. Study Endpoints

The primary endpoints of the study will be defined as follows:

- **Safety endpoint:** measurement of device- or procedure-related adverse events
- **Efficacy endpoint:** Correct identification of pre-treatment vs. 12-week post-final treatment images by two out of three blinded independent reviewers. Success will be defined as at least 70% correct identification of the pre-treatment images.

The secondary endpoint of the study is defined as subject satisfaction as assessed by questionnaire administered at 12-weeks post-treatment.

### *3.1 Statistical Analysis Plan*

#### 3.1.1 Statistical Methods: Overall Plan

Data will be summarized based on the nature of the data. Dichotomous (e.g., gender, independent photographic review) and ordinal (e.g., Fitzpatrick Skin type) data will be tabulated by category. The mean, standard error, maximum and minimum will be tabulated for continuous data (e.g., age,). The significance level will be two-sided 0.05 for all statistical tests.

#### **3.1.2 Endpoint Analysis**

#### *3.1.2.1 Primary Safety Endpoint*

The primary safety endpoint is measurement of all device- or procedure-related adverse events. All adverse events reported during and following the treatment will be included in the safety analysis.

#### *3.1.2.2 Primary Efficacy Analysis*

The primary efficacy endpoint is the correct identification of pre- vs 12-week post-treatment images. Since weight change will affect the image, the analysis will be based on the evaluation of the PP population, (i.e. treated subjects followed for 12 weeks who did not became pregnant, and with weight change of no more than 5% at the 12-week visit). Success will be defined as at least 70% correct identification of the pre-treatment images.

#### *3.1.2.3 Secondary Endpoint Analysis*

The secondary endpoint of the study is subject satisfaction as assessed by questionnaire administered at 12-weeks post treatment. The number and percentage of subjects will be summarized for each possible point grade of the satisfaction questionnaire at 12-weeks post-treatment. The percentage of subjects with moderately or very satisfied will be provided, and the corresponding exact 95% confidence interval (per binomial distribution) will be calculated. The percentage and the exact 95% confidence interval of unsatisfied response (very, moderately, or mildly) will also be calculated.

# 4. Adverse Events

Adverse events (AE) will be assessed continuously throughout the study. An adverse event is defined as any untoward medical occurrence in a subject, regardless of whether the event is related to the device.

**Adverse Device Effect (ADE)**
Any sign, symptom, or disease in a study subject that occurs during the course of a clinical trial that is determined by the investigator to have a causal relationship or possible causal relationship with the device under investigation.

**Serious Adverse Event (SAE)**
Any untoward medical occurrence in a subject, regardless of whether the event is related to the device that:
a. results in death;
b. results in a life threatening illness or injury;
c. results in a permanent impairment of a body structure or body function;
d. requires in-patient hospitalization or prolongation of existing hospitalization
e. results in medical or surgical intervention to prevent impairment to body structure or function;
f. results in fetal distress, fetal death, or a congenital abnormality/birth defect.

**Unanticipated Adverse Device Effect (UADE)**
Any serious adverse effect on health and safety or any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational

plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

The Sponsor is responsible for the ongoing safety evaluation of the product(s). The Sponsor shall be responsible for adjudication of all reported adverse events to determine whether the event is reportable under federal regulations (i.e., 21 CFR 812.150[b][1]). The Sponsor will promptly notify all participating investigators and regulatory authorities, as appropriate, of findings that could affect adversely the safety of subjects, impact the conduct of the trial or alter the IRB's approval opinion to continue the trial.

# 5. Study Conduct

## *5.1 Confidentiality*

All information and data concerning study subjects will be considered confidential, and handled in compliance with all applicable regulations including the requirements of the Health Information Protection Act (HIPAA) of 2004.

Only authorized site staff, the study Sponsor or the Sponsor's designee and IRB will have access to these confidential files and case report forms. A unique identification code will be assigned to each subject participating in this trial. All data used in the analysis, reporting and publication of this clinical trial will be maintained without identifiable reference to the subject. Any data that may be published in abstracts, scientific journals, or presented at medical meetings will reference a unique subject code and will not reveal the subject's identity.

## *5.2 Ethics and Good Clinical Practice*

The Investigator will ensure that this study is conducted in full conformance with the principles of the "Declaration of Helsinki" (as amended in Tokyo, Venice, Hong Kong, Somerset-West and Edinburgh).

Additionally, all Investigators and staff must follow the ICH Guidelines for Good Clinical Practice and the applicable Code of Federal Regulations (21 CFR 50, 56 and 812).

## *5.3 Institutional Review Board*

The Investigator will submit this protocol and any related documents to be provided to the subject (such as subject informed consent form) to an IRB with jurisdiction for his/her site. Approval from the IRB must be obtained before starting the Study, and should be documented in a dated letter to the Investigator, clearly identifying the trial, the documents reviewed and the date of approval. A list of members participating in the meeting must be provided.

Modifications made to the protocol after receipt of the IRB approval must also be submitted as amendments by the Investigator to the IRB.

Since this study will be conducted as a non-significant risk trial, the IRB must also grant its concurrence with non-significant risk status before the study can begin at that site.