

 Confidential	<i>Pilot Study to Evaluate VelaShape III & UltraShape Power Combined Treatment for Thigh Circumference Reduction</i>			
	Protocol #	DHF24451	Rev. Date	October 6, 2017

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Title: *Pilot Study to Evaluate VelaShape III & UltraShape Power Combined Treatment for Thigh Circumference Reduction.*

Protocol Number: DHF24451

Study Type: Prospective Clinical Study

Date: October 6, 2017

Study Devices: VelaShape III and UltraShape Power

Sponsor: Syneron Candela
530 Boston Post Road
Wayland, MA 01778
United States

This document contains confidential information.

This study will be performed in accordance with applicable regulatory requirements and Good Clinical Practice (GCP). This clinical investigation will follow the principles outlined by the International Conference on Harmonization (ICH).

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GLOSSARY

ADE	Adverse Device Effect
AE	Adverse Event
BMI	Body Mass Index
CFR	Code of Federal Regulations
Cm	Centimeter
CRF	Case Report Form
FDA	Food & Drug Administration
FU	Follow-up
GCP	Good Clinical Practice
ICF	Informed Consent Form
IEC	Institutional Ethics Committee
IRB	Institutional Review Board
Kg	Kilogram
Min	Minute
wk	Weeks
PI	Principal Investigator
USAE	Unanticipated, serious adverse event
USADE	Unanticipated, serious adverse device effect
SAE	Serious Adverse Event
W	Watt (Output Electric Power)

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Table 1- Study Synopsis

Proprietary Name	VelaShape III and UltraShape Power Devices
Design	Prospective, one-arm, baseline-controlled pilot study for the evaluation of the VelaShape III combined with UltraShape Power treatment for non-invasive circumference reduction to the thighs.
Study Population	Up to 40 healthy adult volunteers seeking noninvasive circumference reduction of thighs. Male and females, 18 to 60 years of age enrolled at up to two investigational sites.
Treatment and Duration	Eligible subjects will receive 3 bi-weekly treatments to the thighs at 2-week intervals, with the VelaShape III and UltraShape Power devices according to the study protocol. Each subject will return for 3 follow up visits: four weeks (4wk FU), 8 weeks (8wk FU) and 12 weeks (12wk FU) after the last treatment (Tx.3), for total expected study duration of 16 weeks.
Objective	The objective of this trial is to evaluate the safety and efficacy of the VelaShape III combined with UltraShape Power for circumference reduction of the thighs.
Primary Objective	<ol style="list-style-type: none"> 1. Statistically significant circumference reduction post combined VelaShape III and UltraShape Power treatments at 12 weeks follow-up (12wk FU) versus baseline. 2. Evaluate the safety of the combined treatment with the VelaShape III and UltraShape Power devices.
Secondary Objectives	<ol style="list-style-type: none"> 3. Circumference reduction post combined treatments Pre-Tx.2, Pre-Tx.3 and all follow-up visits (4wk FU, 8wk FU and 12wk FU) versus baseline. Statistically significant reduction post combined treatment at the follow-up visits only. 4. Investigator satisfaction assessment will be performed independently, using a 5-point Likert scale questionnaire, at each follow-up visit (4wk FU, 8wk FU and 12wk FU). 5. Subject satisfaction assessment will be performed independently by the subject, using a 5-point Likert scale questionnaire, at each follow-up visit (4wk FU, 8wk FU and 12wk FU). 6. Comfort level during treatment: Comfort assessment will be performed independently by the subject using a 10-point NSR scale. The subjects will answer this questionnaire regarding each device separately and combined after each treatment (Tx.1, Tx.2 and Tx.3).
Efficacy Endpoints	Primary and secondary objectives will be assessed using the following efficacy endpoints:

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	<ol style="list-style-type: none"> 1. Circumference measurements of the treatment area 2. Investigator satisfaction 3. Subject satisfaction 4. Pain assessment 5. Photography
Safety Endpoints	Number, severity and type of any adverse events recorded throughout the study and post treatment (immediate and delayed response).
Statistical Methods	Descriptive statistics will be used to present changes in the assessments along the study course. Circumference measurements and subject assessments' and satisfaction data will be analyzed using two-tailed Wilcoxon Signed Rank test and/or paired t-test (alpha=0.05) to analyze the data difference from baseline and longitudinal change.

INTRODUCTION AND RATIONALE

Background

Adipose tissue is a loose type of connective tissue specialized to store lipids. The majority of lipids stored in adipose cells are triglycerides formed from imported free fatty acids and glycerol. It is not uniformly distributed in the body. The major adipose depot is subcutaneous (about 80% of all body fat).¹ In men, it normally represents 15-20% of body weight and in women, 20-25% of body weight. A certain amount of body fat is necessary for normal female reproduction and health. Subcutaneous adipose tissue helps to shape, cushion and insulate the body and provides padding to some organs.

Liposuction is a procedure that can help sculpt the body by removing unwanted fat from specific areas.^{2,3,4} The increasing popularity of this procedure is associated with the evolution of techniques and equipment for fat removal, body reshaping and cellulite treatments. Besides the traditional suction-assisted lipoplasty, other options include ultrasound-assisted and external ultrasound-assisted liposuction, power-assisted liposuction and laser lipolysis, as well as low-level laser-assisted liposculpture.⁵

The efforts in the search for alternative non-invasive or minimally-invasive techniques and new tools aim mainly at reducing downtime and facilitating treatment for reduction of the localized fatty tissue areas. New minimally-invasive technologies include subcutaneous injection of phosphatidylcholine. This drug was initially used in emergencies and in the treatment of atheroma plaques in cardiac diseases. Recently, it has also been used in the treatment of localized fat deposits, with mixed reviews.⁶

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The VelaShape device is a commercial device cleared by the Food and Drug Administration (FDA) under 510(k) K071872 indicated for the relief of minor muscle aches and pain, relief of muscle spasm, temporary improvement of local blood circulation, temporary reduction in the appearance of cellulite, and for temporary reduction of thighs circumferences. It combines controlled infrared (IR) light and conducted bipolar radiofrequency (RF) energies with mechanical manipulation. The VelaShape II, the next generation VelaShape, is a CE-cleared device since 2009, which also combines controlled infrared (IR) light and conducted bipolar radiofrequency (RF) energies with mechanical manipulation. The VelaShape II device has 65W RF energy.

The VelaShape III, the newest generation VelaShape, is a device based on the CE-cleared VelaShape II and FDA-cleared Transcend device (K120510). All devices combine controlled infrared (IR) light and conducted bipolar radiofrequency (RF) energies with vacuum. The VelaShape III device is indicated for relief of minor muscle aches and pain, relief of muscle spasm, temporary improvement of local blood circulation, temporary reduction in the appearance of cellulite, and for temporary reduction of thighs and abdomen circumference.

The VelaShape III device has 150W RF energy.

The UltraShape® Contour I VER 3.1 is a device cleared by the Food and Drug Administration (FDA – K133238) and Health Canada (HC). The UltraShape, the next generation of Contour I VER 3.1, is a commercial device cleared by the CE, Health Canada and by the Food and Drug Administration (FDA – K141708), which uses focused ultrasound to produce localized mechanical motion within fat tissues and cells for the purpose of producing mechanical cellular membrane disruption. It is intended for reduction in abdominal circumference. The newest generation UltraShape device, UltraShape Power, includes a small transducer (U-Sculpt Power), and is FDA-cleared (K170370) for lipolysis (breakdown of fat) to provide a non-invasive approach to achieve a desired aesthetic effect. It is intended for non-invasive reduction in abdominal circumference and fat reduction in the flanks and thighs.

Device Descriptions

VelaShape Device

The newest generation, VelaShape III, is composed of a console to which two applicators, VContour and VSmooth, are connected via an umbilical cable. Each applicator incorporates an operation panel to enable the operator remote control of the system in addition to the system's touch screen operation panel. Prior to treatment, the applicators are fitted with a replaceable cap, which keeps the skin from coming into direct contact with the applicator during the treatment. These caps can be cleaned between treatments for reuse for the same subject, since multiple treatments are typical. During treatment with the VelaShape III device, the applied

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suction repeatedly pulls the skin into a chamber in the middle of the cap. There, the skin is exposed to the combined **elōs** technology (electro optical synergy - IR light and RF) using gentle vacuum suction with or without mechanical manipulation.

The VSmooth applicator contains rotating elements that create a massaging motion. The system enables the user to adjust the RF energy, optical energy and vacuum levels, thereby utilizing the optimal treatment parameters for each subject/anatomical area.



Figure 1: VelaShape III Device

UltraShape Power Device

General: Tissue selectivity is achieved by a proprietary knowledge of ultrasound parameters ensuring specific destruction of the fat cells only within the target area. All other types of tissue, such as blood vessels, muscles and peripheral nerves remain intact. There are no thermal effects. Fat cell destruction is achieved by ultrasound-induced mechanical effects during a very short exposure time.

The Ultrasonic Transducer: The ultrasonic transducer is an electro-mechanical device that converts an electrical signal into mechanical (acoustical) energy. Its functionality is based on piezoelectric ceramics that has the property of changing size when a voltage is applied. Thus, applying an alternating voltage frequency across such piezoelectric element causes it to oscillate in the same frequency, producing sound waves. The spherical shape of that piezoelectric element enables the focusing of the ultrasound waves into a narrow focal region, which is the target region. The transducer is comprised of a Polyethylene membrane, which was approved by biocompatibility testing and in vitro and in vivo verification tests.

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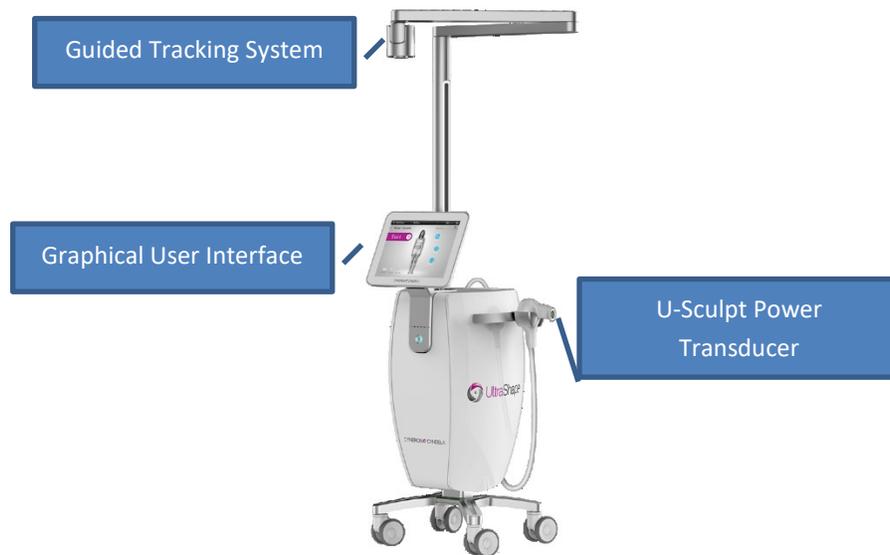


Figure 2: UltraShape Power System

Accessories needed for the UltraShape Power Treatment

Small transducer (U-Sculpt Power)

will be used to deliver the ultrasonic energy to the body.

Reusable Straps

Gather skin and fat in the area to be treated.

Parker Gel

Used as a coupler agent between skin surface and the ultrasonic transducer.

Calibrated Caliper

Assess fat thickness at treatment area prior to starting the treatment.

Circumference measuring tape

Assess circumference reduction.

Height Measuring Device(Seca)

Measure circumference at the same height in the subsequent visits.

A3 Transpaernt Paper (B ledger size)

Assure repeatable marking of treatment area at each treatment visit.

STUDY DESIGN OVERVIEW

This study is a prospective, baseline-controlled, pilot study to evaluate the performance and safety of the combined VelaShape III and UltraShape Power treatment for non-invasive circumference reduction of the thighs.

Up to 40 healthy subjects from up to two investigational sites will be enrolled in this study. All subjects will undergo an assessment of their general health. All subjects will receive treatment for circumference reduction with VelaShape III combined with UltraShape Power for the thighs. Eligible subjects will receive 3 bi-weekly treatments, at 2-week intervals, to thighs with the VelaShape III combined with UltraShape Power devices. Each of the three treatments (Tx.1, Tx.2 and Tx.3) include the following steps, as shown in Table 2.

Table 2: Combined Treatment by area

Step	Thigh Treatment
1	VelaShape III (VContour applicator to inner thigh) – 10 minutes at time on temperature
2	VelaShape III (VSmooth applicator to lateral thigh) – 10 minutes at time on temperature
3	Ultrashape Power to inner and outer thighs – FTZs applied per User Guide

The subject will return for 3 follow up visits: four weeks (4wk FU), 8 weeks (8wk FU) and 12 weeks (12wk FU) after last treatment (Tx.3). The total expected study duration for each subject is 16 weeks.

At baseline and before each treatment (Tx.1, Tx.2 and Tx.3) and at follow-ups (4wk FU, 8wk FU, 12wk), the subject’s weight, circumference and fat thickness (using caliper) will be measured. Photography will be performed under visible light conditions of the front, right and left sides of the thighs.

After each treatment (Tx.1, Tx.2 and Tx.3), the comfort assessment will be performed by the subject using the NSR scale. The subjects complete the questionnaire regarding each device separately and combined.

In addition, at each follow-up visit (4wk FU, 8wk FU, and 12wk FU), the subject and investigator questionnaires will be completed.

OBJECTIVE

The objective of this trial is to evaluate the safety and efficacy of the VelaShape III combined with UltraShape Power for circumference reduction of the thighs.

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Primary Endpoint

1. Statistically significant circumference reduction post combined VelaShape III and UltraShape Power treatments at 12 weeks follow-up (12wk FU) versus baseline.
2. Number, severity and type of adverse events following combined treatment with the VelaShape III and UltraShape Power devices (immediate and delayed response), as recorded throughout the study.

Secondary Endpoints

1. Circumference reduction post combined VelaShape III and UltraShape Power treatments at Pre-Tx.2, Pre-Tx.3 and all follow-up visits (4wk FU, 8wk FU and 12wk FU) versus baseline. Statistically significant circumference reduction post combined treatment at the follow-up visits only.
2. Investigator satisfaction assessment will be performed independently, using a 5-point Likert scale questionnaire, at each follow-up visit (4wk FU, 8wk FU and 12wk FU).
3. Subject satisfaction assessment will be performed independently by the subject, using a 5-point Likert scale questionnaire, at each follow-up visit (4wk FU, 8wk FU and 12wk FU).
4. Comfort level during treatment: Comfort assessment will be performed independently by the subject using a 10-point NSR scale. The subjects will complete this questionnaire regarding each device separately and combined after each treatment (Tx.1, Tx.2 and Tx.3).

STUDY POPULATION

Number of Subjects

This study will enroll and be comprised of up to 40 subjects, who meet all the inclusion and none of the exclusion criteria, from up to two investigational sites. The subject will receive treatment for circumference reduction of thighs.

Subject Withdrawal and Replacement

Subjects enrolled in the study can discontinue their participation at any time for any reason without prejudice or reduction in the quality of their medical care. The investigators or sponsor can terminate a subject's participation in this study to protect the subject's health or if the subject fails to follow directions resulting in noncompliance to study procedures. Subjects who withdraw or are terminated from the study may be replaced to ensure at least 60 subjects have completed the study. Subjects who fail to complete the treatment may be replaced and will not be evaluable.

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Inclusion Criteria

A subject is eligible to participate in the study if he/she meets all the following inclusion criteria:

1. Signed informed consent to participate in the study.
2. Female and male subjects, ≥ 18 and ≤ 60 years of age at the time of enrollment.
3. Fitzpatrick Skin Type I to VI.
4. Fat thickness of at least 1.5 cm (measured by calibrated caliper).
5. BMI interval: $22 \leq \text{BMI} \leq 30$ (normal to overweight, but not obese).
6. Female subjects must be either post-menopausal, surgically sterilized, or using a medically acceptable form of birth control at least 3 months prior to enrollment (i.e., oral contraceptives, contraceptive implant, barrier methods with spermicide or abstinence).
7. In addition, negative urine pregnancy test as tested before each treatment and at the last visit for women with child-bearing potential (e.g. not menopausal).
8. General good health confirmed by medical history and skin examination of the treated area.
9. Willing to follow the treatment and follow-up schedule and post-treatment care instructions.
10. Willingness to refrain from a change in diet/ exercise/medication regimen for the entire course of the study.
11. Willing to have photographs and images taken of the treated areas to be used de-identified in evaluations, publications and presentations.

Exclusion Criteria

A subject is not eligible for participation in this study if he/she meets any of the following exclusion criteria:

1. History of hypertension, ischemic heart disease, valvular heart disease, congestive heart failure, pacemaker/defibrillator, abdominal aortic aneurism.
2. Known hyperlipidemia, diabetes mellitus, hepatitis, liver disease, HIV positive status, blood coagulopathy or excessive bleeding, autoimmune or connective tissue disease.
3. Having or undergoing any form of treatment for active cancer, or having a history of skin cancer or any other cancer in the areas to be treated, including presence of malignant or pre-malignant pigmented lesions.
4. Having any active electrical implant anywhere in the body, such as a pacemaker or an internal defibrillator.

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5. Having a permanent implant in the treated area, such as metal plates or an injected chemical substance such as silicone.
6. Having undergone any other surgery in the treated areas within 12 months of treatment or during the study, including liposuction.
7. Previous body contouring procedures in the treatment area within 12 months.
8. History of skin disease in the treatment area, known tendency to form keloids or poor wound healing.
9. Known photosensitivity.
10. Suffering from significant skin conditions in the treated areas or inflammatory skin conditions, including, but not limited to, open lacerations or abrasions and active cold sores or herpes sores prior to treatment (duration of resolution as per the Investigator's discretion) or during the treatment course.
11. Skin lesions in the treatment area other than simple nevi on physical examination (e.g., atypical nevus, tattoo, abrasions) including depressed scars in the treatment area.
12. Very poor skin quality (i.e., severe laxity).
13. Abdominal wall diastasis or hernia on physical examination.
14. Abnormal kidney, liver or coagulation functions, abnormal lipid profile or blood count within the last 3 months.
15. Obesity (BMI > 30).
16. Pregnant, childbirth within the last 12 months or breastfeeding women.
17. Any acute or chronic condition which, in the opinion of the investigator, could interfere with the conduct of the study.
18. Unstable weight within the last 6 months (i.e., \pm 3% weight change in the prior six months).
19. Inability to comply with circumference measurement procedure (e.g., inability to hold breath for the required duration).
20. Abdominal fat thickness lower than 2.5 cm after strapping.
21. Participation in another clinical study within the last 6 months.
22. As per the Investigator's discretion, any physical or mental condition which might make it unsafe for the subject to participate in this study.

STUDY PROCEDURES

Enrollment and Screening

During the first visit, the research staff will screen the subject for eligibility to participate. The inclusion/exclusion criteria will be reviewed, the subject's medical history, an examination of the subject's skin in the treatment areas will be conducted.

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The subject will review the informed consent form and the study will be explained to the subject including all risks, potential benefits, procedures, visit requirements, and other alternative treatment options. If the subject qualifies and wishes to participate they will complete the ICF with a signature and date. The original will be retained with subject's records and a copy will be provided to the subject.

The following measurements will be performed and recorded at the specified times throughout the study (Table 3).

Table 3- Clinical Evaluation Measurements and Tools

Measurement	When to conduct	Method
Height	Baseline	Scale
Weight	Prior to all treatments and at all follow-ups visits (Tx.1, Tx.2, Tx.3. 4wk FU, 8wk FU and 12wk FU)	Scale
BMI		Calculation
Circumference measurements		Standardized circumference measuring tape
Fat thickness: Caliper measurement		Caliper
Photographs		Standardized digital photographs
Urine pregnancy test	Prior to each treatment, and at the last follow-up visit (Tx.1, Tx.2, Tx.3, 12wk FU)	Urine pregnancy test
Pregnancy inquiry	At each visit (at treatments visits- prior to treatment)	Pregnancy inquiry
Treatment-associated pain	Immediately after treatment (Tx.1, Tx.2, Tx.3) the subject will be asked to assess the pain level during treatment	Numerical Scale Response (NSR)
Immediate Response Assessment	Immediately after treatment the investigator should assess the post-treatment immediate response	Post-treatment Side Effect Severity Scale (Table 9)
Subject satisfaction	At all follow-up visits: 4wk FU, 8wk FU and 12wk FU	Subject Satisfaction Questionnaires (Table 10, Table 11)
Investigator satisfaction		Investigator Satisfaction Questionnaire (Table 10)
Safety	During treatment and throughout study	Examination of skin in the treated area, interview subjects, Adverse Events form, Occurrence and Severity Ratings, as well as relation to treatment, action taken and outcome

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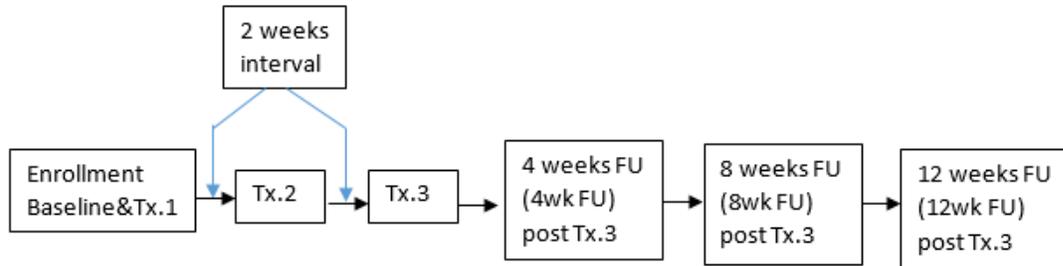


Figure 3: Study Flow-Chart (Visits at the Clinic)

Pre-Treatment Procedures

It is expected that the screening and baseline procedures will be conducted during the same visit as the treatment. All visit procedures should take up to 2 hours.

Screening

1. ICF - Prior to any study-related activities, informed consent will be obtained. When the subject fully understands the possible benefits and risks of the study, the subject will be asked to sign and date the informed consent form (ICF). The subject will be given a copy of the signed ICF.
2. Medical History - A medical history will be obtained to determine if the subject meets the study criteria, including a list of all prescribed and over-the-counter medications.
3. Skin Exam - The subject will undergo a routine skin exam to determine if he/she meets the study criteria including the presence of fatty tissue deposits in the treatment area.
4. BMI – the volunteers' height and weight will be taken for calculation of BMI.
5. Pregnancy Screen – female subjects who can become pregnant will undergo a urine pregnancy test. This will be repeated prior to all treatments, and at the end of the study (last FU visit). If the Screening and Treatment procedures are not conducted on the same day, the urine pregnancy test will be repeated on the treatment day.
6. Scheduling: Subjects will be scheduled to return for the baseline and treatments visit within 14 days following the screening visit. It is preferable that the baseline procedures and Tx.1 will be conducted immediately after the Screening visit.

Baseline

1. Subject ID - Prior to treatment, subjects will be assigned a study subject number.
2. Photography – Baseline photographs will be obtained using a digital imaging system with standardized consistent camera settings.
3. BMI – the subject weight and height will be taken if baseline visit is a different day than the screening visit.

Measurements

Measure the Fat Thickness at the Area to be treated

The procedure can be performed only in areas where the fat thickness is ≥ 1.5 cm as measured by a skin fold caliper (or ≥ 3.0 cm as measured by a pinch test), and ≥ 2.5 cm as measured by a skin fold caliper after strapping.

Marking Area for UltraShape Power Treatment

The mark of the area to be treated should be copied to a transparent template (for each side: Right and Left) to ensure consistent marking of the same area for same patient during the subsequent visits.

During copying the treatment area to the transparent template, the following signs will be marked on transparency according to the following table (Table 4):

Table 4- Marking the intended area to be treat by UltraShape

Step	Thigh Treatment
1	The thigh area will be marked on the transparency. Each thigh (left and right) will be marked separately.
2	Mark the Subject's identification code on the transparency for each thigh (left and right) separately.
3	Define the thigh (right or left) on the transparency. Separate transparency for each side.

At the subsequent treatment sessions, this transparent template will be placed according to these signs on the treated area, and the line of treatment area will be re-marked.

Marking height circumference and circumference measurement

Patients should stand up straight when arms are placed at the rear of the neck and the head is positioned towards the horizon. Elbows will be positioned in front of the body (Figure 4).



Figure 4: Body positioning during marking height for circumference measurements

The height of midsection will be measured using the height measuring device (supplied by Syneron Candela). The marking pencil will be placed horizontally at the edge of the measurement device during the marking procedure (Table 5).

Table 5- Thigh Circumference Measurements

Step	Measurement
1) Mark the midsection for circumference (=Midline) measurement for left and right thighs separately.	

Step	Measurement
2) The height for the circumference measurement will be marked for each thigh separately.	
3) Measure the circumference of each thigh separately with the Circumference Measuring Tape.	

For each treatment area, the measurements will be taken at 2 cm above midsection (=2cm above Midline) measurement and 2 cm below midsection (=2cm below Midline) measurement.

The height of the midsection thigh (will be used as a reference for all study visit measurements) and the circumference measurements will be recorded in the CRF.

VelaShape - General Treatment Procedure

1. Ensure that the subject is in a comfortable position for the procedure.
2. Remove any jewelry in the treatment area.
3. Ensure that the treatment area skin is clean. The skin should be cleaned with water and soap, and hair in the treatment area should be shaved.
4. Ensure that the treatment applicator/ applicator cap is clean. If not, it should be wiped with 70% alcohol and allowed to dry.

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5. Prior to treating the entire area, a test should be performed in a small section within the area to assess the skin for unwanted affects.
6. The choice of treatment settings should take into consideration not only the severity of the treated condition (fat layer), but also the subject's skin type, tendency to bruise, the specific anatomical location (i.e. thigh), and comfort.
7. There should be a complete seal between the applicator and the skin during the treatment session. In curved or bony areas, careful attention is required when treating. A slight change in the orientation of the applicator may solve the problem.
8. Always hold the applicator perpendicular to the skin surface, so that the compression/contact with the skin is consistent for each application.
9. Full operating procedure, software screens and parameters are described in the device User Manuals. Instructions will be provided prior to the start of the study.
10. Always hold the applicator so that both electrodes have equal compression/contact with the skin to ensure safe and effective RF delivery.
11. Before the treatment, apply a thin layer of the commercial VelaEase treatment lotion (Appendix 5). You may need to re-apply the lotion, if the indicators on the applicator blink continuously for more than a few pulses, indicating bad coupling.

Treatment Using the VContour Applicator to the Inner Thigh

1. Select the appropriate zone for treatment of circumference reduction using the Medium Cover; define the size of the targeted sub-area, large, medium or small, And divide it into segments:
 - Large size sub-area (25 x 20 cm) will be divided into 20 segments.
 - Medium size sub-area (15 x 20cm) will be divided into 12 segments.
 - Small size sub-area (10 x 20 cm) will be divided into 8 segments.
2. Each segment of the sub-area is the size of the Medium Cover (5 x 5cm).

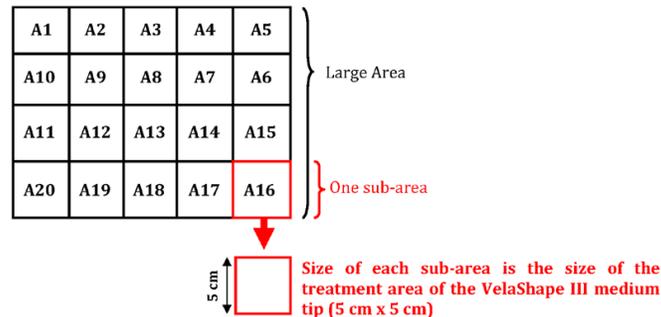


Figure 5: Sub-Area Divided into Segments

3. Set the following parameters:
 - The target RF level is level “3”. If safety concerns arise or if the subject reports too much pain, use lower RF levels.
 - The target vacuum level start is “1” gradually increased to level “2” and then to “3” over the treatment course.
 - In some cases, the skin is very lax and is pulled deep into the treatment chamber of the replaceable cap; to prevent adverse effects, use level vacuum “1” in these cases. The treatment will be performed with the large VelaShape applicator size (45_{mm} x 25_{mm}) or the small VelaShape applicator size with the appropriate tip size.
4. Cycle 1:
 - a. Starting with Section A1 to A20, each segment will undergo 5 consecutive stacking pulses in a “*horizontal snake-like*” treatment technique (see illustration below).
 - b. After all segments are pulsed 5 times, another cycle of 4 consecutive pulses, then 3 consecutive pulses and then 2 consecutive pulses should be performed.
 - c. Continue treating each sub-area from A1 to A20 with 2 consecutive stacking pulses until the surface temperature reaches 45°C or the patient is unable to tolerate more heat, whichever comes first.

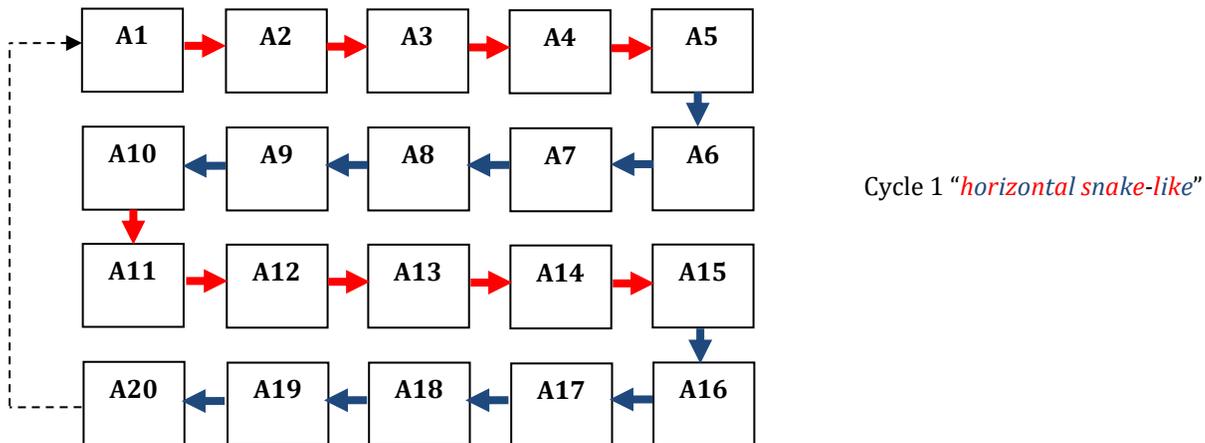


Figure 6: Cycle 1 treatment order

5. Cycle 2:

- d. In this cycle, the same sub-area set (A1-A20) will be started and continued with two consecutive stacking pulses using the “*vertical snake-like*” treatment technique (see illustration below) until the surface temperature reaches 45°C or the patient is unable to tolerate more heat.

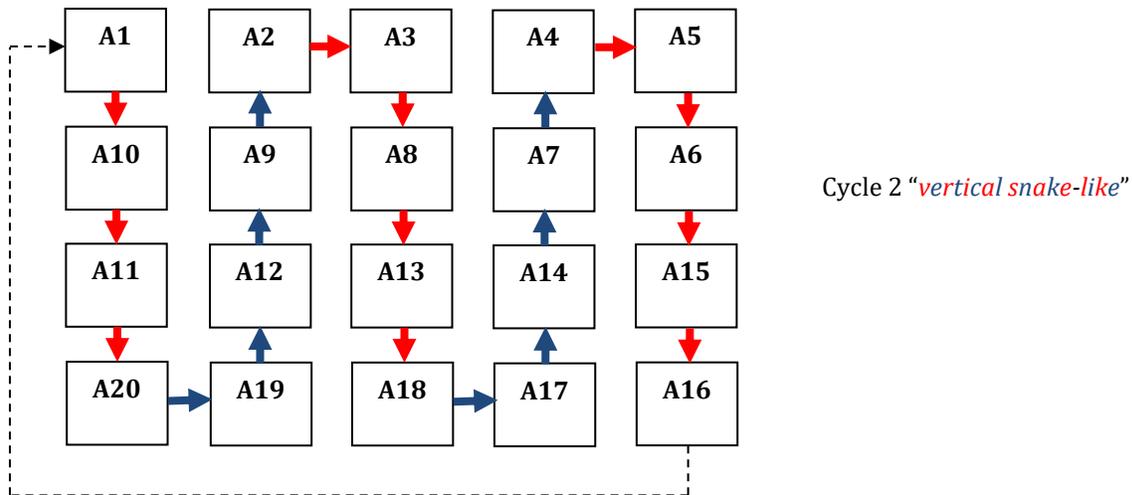


Figure 7 : Cycle 2 treatment order

6. Cycle 3:

- e. In this cycle, the same sub-area set (start from sub-area A1 to A20) will be started and continue with 2 consecutive stacking pulses using the “*horizontal snake-like*” treatment technique until the surface temperature reaches 45°C or the patient is unable to tolerate more heat.

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7. Cycle 4:
 - f. If the total time duration of Cycles # 1, 2 and 3 is less than 10 minutes at time on temperature (450C), then continue with the “Vertical Snake-Like” treatment technique (see Figures 4-7) and apply one pulse per sub-area until the 10-minute treatment duration for all four cycles is reached.

8. Treatment time: The large size sub-area (25 x 20 cm) set includes 20 segments (A1-A20), the medium size sub-area (15 x 20 cm) set includes 12 segments (A1-A12) and the small size sub-area (10 x 20 cm) set includes 8 segments (A1-A8). The 3-4 consecutive cycles should take at least 12 minutes (2 minutes to temperature + 10 minutes treatment time at temperature).

Treatment Using the VSmooth Applicator to the Lateral Thigh

1. Mark treatment areas that are 20 x 25 cm in size. Within each of these areas mark four elliptical overlapping segments according to the following illustration below

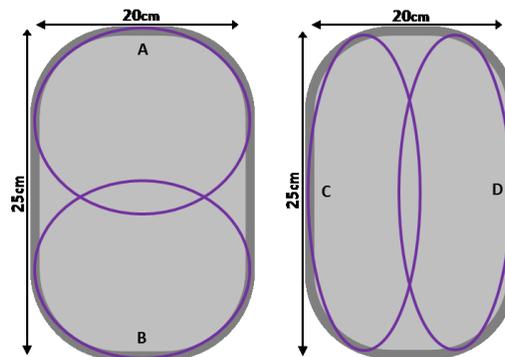
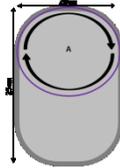
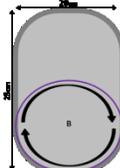
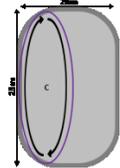
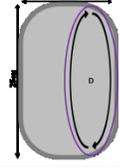
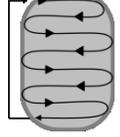
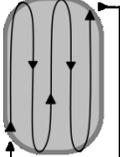


Figure 8: VSmooth Treatment Area Segmentation

2. Attach the Large Electrode cover to the VSmooth applicator.
3. Select treatment parameters on the screen or on the applicator:
 - a. IR = 1
 - b. RF =3
 - c. Vacuum = 1
4. It is recommended to maintain the RF level at 3 in all cycles to achieve optimal results.
5. You may increase the IR and Vacuum levels from 1 -> 2 -> 3 based on patient tolerance, and only in areas with minimal laxity.
6. Apply a thin, lightly visible layer of VelaSpray Ease lotion at the beginning of each cycle.
7. Start treating according to Table 6 below.

Table 6 - Cellulite Mode Protocol

Step	Segment	Mode/ Routine	Illustration
Step 1	A	Circular horizontal <i>Clock-Wise</i> manner in gliding technique until temperature reached.	
Step 2	B	Circular horizontal <i>Clock-Wise</i> manner in gliding technique until temperature reached.	
Step 3	C	Circular vertical <i>Clock-Wise</i> manner in gliding technique until temperature reached.	
Step 4	D	Circular vertical <i>Clock-Wise</i> manner in gliding technique until temperature reached.	
Step 5	All	Treat all sub-areas in <i>“Horizontal Snake-Like”</i> manner using gliding technique.	
Step 6	All	Treat all sub-areas in <i>“Vertical Snake-Like”</i> manner using gliding technique.	

UltraShape Power General Treatment Procedure

Thigh treatment: The subject treatment area will be gathered using taping, to gather the fat area for treatment according to the instructions provided in the User Manual.

Note: Make sure that the gel remains are removed from the treatment area prior to the UltraShape Power treatment.

The UltraShape Power device will determine the total number of FTZs to be delivered during treatment according to the size of the treatment area. The recommended minimal number of ultrasound FTZs to be delivered per subject at a whole single treatment will be defined / determined by the system according to the subject physical characteristic and treated area size.

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Prior to applying the FTZs, Parker acoustic gel will be applied on the treated area and used as a coupling agent between the ultrasonic transducer and the skin surface.

UltraShape Power treatment should be performed according to treatment instruction in the UltraShape Power User Manual.

Expected post treatment side effects are limited to erythema (blanchable/non-blanchable), edema, heat and/or pain sensation.

Treatment Procedure

Eligible subjects will receive 3 bi-weekly treatments, at 2-weeks interval, to the thighs with the VelaShape III and UltraShape Power devices. Each of the three treatments (Tx.1, Tx.2 and Tx.3) includes the following steps, as shown in Table 7.

Table 7- VelaShape III and UltraShape Power Treatment to the Thighs

Step	Thigh Treatment
1	Pretreatment Measurements: weight, circumference, fat thickness (caliper) and photos of the treated area
2	~12 minutes/lateral thigh of VelaShape III using VSmooth applicator
3	~12 minutes/inner thigh of VelaShape III using VContour applicator
4	Clean the thigh treatment area from VelaShape spray
5	Gathering method: Taping
6	Ultrashape Power using small U-Sculpt Power transducer to the lateral and inner thigh
7	Clean the thigh treatment area from the gel
Comments	Move to other thigh only after completing all steps for one thigh

Post-treatment Procedures

Pain assessment – immediately after each treatment subjects will be asked to assess the pain sensation experienced during treatment using a Numerical Scale Response (NSR; see

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Appendix III - Pain assessment) for each treatment phase:

- a. VelaShape III
- b. UltraShape Power
2. Clinical effects - All visible and palpable immediate response will be recorded for the entire treatment area using a 4-point severity scale (Table 9).
3. Safety aspects will be assessed before and after each treatment:
 - a. Adverse Events – Record the number, severity and type of any adverse event occurring before, during and after treatments.
4. Subject will also be provided with the following instructions for care of the treated areas in the informed consent form.
 - a. Temporary skin erythema (redness) and edema (swelling), as well as heat and tightening sensations, may occur up to a few hours after the treatment, but normally do not last longer. If the subject feels significant discomfort longer than that time, cool/cold compress (but not ice packs) may be applied for relief. Over-the-counter pain medication such as Tylenol may be used.
 - b. On the evening after the treatment, subjects should wash the treated areas gently with lukewarm water and avoid very hot or cold water in these areas. Generally, subjects may use their regular soaps after treatment, as long as these are not scrub soaps or exfoliants.
 - c. The treated areas should also not be exposed to potential mechanical damage (e.g., kickboxing, massage) at least 48 hours post-treatment.
 - d. Tanning of any sort (sun exposure, tanning beds, and artificial sunless tanning lotions) is not allowed in the treated areas during the entire course of the study since it might cause hyperpigmentation.
 - e. Subjects will be instructed to use a high factor sunscreen with SPF of at least 30 and to protect the treated areas from direct sunlight for the entire period of the study.

Return Visits

All subjects will be requested to return to the clinic at the following time-points during the study to assess the clinical performance of the device:

- Visit 4: FU1 – 4 weeks (± 7 days) post last treatment.
- Visit 5: FU2 - 8 weeks (± 7 days) post last treatment.
- Visit 6: FU3 - 12 weeks (± 7 days) post last treatment.

At each return visit the following procedures will be conducted and data recorded:

- Weight.

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- Caliper measurements.
- Circumference measurements.
- Photographs as conducted at baseline visit.
- Completion of study questionnaires:
 - Investigator satisfaction using the 5- Point Likert Scale.
 - Subject satisfaction using the 5- Point Likert Scale.
- Pregnancy inquiry prior to each treatment and at the final follow-up visit, a urine pregnancy test will be performed for women with child-bearing potential.

DATA ANALYSIS

Recording

All data will be recorded on site source documents and transcribed onto Case Report Forms (CRFs). The site will be monitored by Syneron staff or designees to assure adherence to the clinical trial requirements, subject safety, protocol procedures, and for data accuracy. The Case Report Forms and images will be reviewed and retrieved during the monitoring visit. All source documentation will remain in the subject's files at the site.

Review and Analysis of all data collected will be conducted by the Sponsor or designee as described for this protocol with the following data:

Demography and Baseline Measurements

Demographic and baseline/screening measurements (e.g., weight, height and digital images) will be collected and descriptively presented.

Treatment Visit

Skin assessment by the PI, photographs of the treated region, and pain scores will be collected used to document any adverse events to assess the device performance.

Follow-up Visit Measurements

Follow-up measurements for weight, circumference and digital images will be used for comparative measurements with their respective measurement at baseline. Primary endpoints will be evaluated 12 weeks post last treatment (Tx.3). Secondary endpoints may be evaluated at all visits.

Safety

Safety of device procedure will be evaluated through skin assessments by the PI and research staff. The occurrence and severity of all complications from the start of the study will be recoded.

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Protocol Revisions and/or Deviations

Except for emergency situations, no changes or deviations in the conduct of this protocol will be permitted without the prior approval of the Sponsor.

The IRB/IEC that granted original approval for the study must be notified of all changes in the protocol, and will approve any change or deviation that may increase risk to the subject, and/or that may adversely affect the rights of the subject or validity of the investigation.

In the event of an emergency, the Investigator will institute any medical procedures deemed appropriate. However, all such procedures must be promptly reported to the sponsor and the IRB/IEC.

ADVERSE EVENTS (AE)

An adverse event (AE) is any adverse change in health or side effect that occurs in a study participant during their participation in the study.

Anticipated Adverse Effects

Following treatment with the VelaShape III and/or UltraShape Power the following local adverse effects could occur (anticipated):

- | | |
|---|-------------------------------------|
| ➤ Purpura | ➤ Hyperpigmentation |
| ➤ Blister | ➤ Hypopigmentation |
| ➤ Bruising | ➤ Soreness |
| ➤ Bullae | ➤ First-degree burn |
| ➤ Erosion | ➤ Second-degree burn |
| ➤ Pain | ➤ Excessive skin redness (erythema) |
| ➤ Damage to natural skin structure (scratching, crusting) | ➤ Hair removal (pulling) |

An adverse event (AE) is any undesired clinical occurrence in a study subject as indicated by signs, symptoms, illnesses, events that develop or worsen in severity in association with the study when deemed by the Investigator to be related to use of the device or study procedures. The Investigator will document all adverse signs and symptoms regardless of severity or frequency that are either volunteered by subjects or observed during the study that are related to the device. The Investigator will also record adverse experiences of subjects resulting from concurrent illnesses, reactions to concurrent medications, or progression of disease states that the Investigator deems related to the device. Included in the description will be the nature of the sign or symptom, the date of onset, whether the event was serious, the severity, the relationship

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to study procedures or investigational device, the action taken, the date of resolution, and the outcome. The Principal Investigator will determine the relationship of the adverse device effect to the investigational device.

Unanticipated Adverse Device Effects

For device studies, part 21 CFR 812.3(s) uses the term unanticipated adverse device effect which is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with the device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Significant device failure may constitute an adverse event if an undesirable experience occurs. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device, or any event that is a result of a user error.

All unanticipated adverse effects will be graded as follows:

- Mild:** Sign or symptom, usually transient, non-life-threatening requiring no special treatment and generally not interfering with usual activities.
- Moderate:** Sign or symptom, non-life-threatening which may be ameliorated by simple therapeutic measures, and may interfere with usual activity.
- Major:** Sign or symptom that is intense or debilitating but non-life-threatening and that interferes with usual activities. Recovery is usually aided by therapeutic measures and the discontinuation of the study device may be required.
- Severe:** Any untoward medical occurrence that at any time results in death or life-threatening illness, resulting in persistent or significant disability/incapacity.

The relationship of the adverse effect to the study is defined as follows:

- Probable:** An adverse event has a strong temporal relationship to study device, and another etiology is unlikely or significantly less likely.
- Possible:** An adverse event has a strong temporal relationship to the study device, and an alternative etiology is equally or less likely compared to the potential relationship to study device.

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Probably not: An adverse event has little or no temporal relationship to the study device and/or a more likely alternative etiology exists.

Not related: An adverse event has no temporal relationship to study device or has a much more likely alternative etiology.

Reporting Adverse Events (AE) and Serious Adverse Events (SAE)

Anticipated Adverse Events: Anticipated adverse events in this study include Purpura, blistering, bruising, bullae, erosion, hyperpigmentation, hypopigmentation, soreness, pain, erythema, damage to natural skin structure and burn. If an unanticipated adverse event occurs at any time during or after the use of the VelaShape III and UltraShape devices, the Investigator must report it to Syneron.

The Investigator must report all unanticipated adverse device effects that are serious in nature to the clinical study monitor immediately or within twenty-four hours by telephone (see below). If such an unanticipated adverse device effect is reported after normal working hours, the Investigator will leave a voice message at the monitor's telephone number with accompanying report of the unanticipated adverse device effect emailed to the address below:

Mark Lakernik, M.D., Clinical Consultant
Cell Number: 1-416-456-9330
Fax Number: 1-877-597-5640
E-mail: markl@syneron-candela.com

A written report prepared by the Principal Investigator must follow within five working days to both the IRB and to Syneron Candela and should include a full description of the event and sequence.

Measures taken to protect the rights and welfare of subject

Research records will be available to study personnel, the sponsor, Ethics Review Committee and regulatory agencies as required. Research records may be used for purposes of medical education, after removal of subject names or other identifying information. In the ICF the subjects will be informed that the photographs and video taken of them during the study may be made available to the sponsor for marketing and instructional purposes, after removal of identifying information. All images collected will be stored without personal subject identifiers at the site and at Syneron.

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RISK/BENEFIT ANALYSIS

Risks

Syneron has determined that the *VelaShape III* and the *UltraShape Power* systems are non-significant risk devices. As indicated in the AE section, the anticipated risks associated with the use of both of the systems are:

- Purpura
- Blister
- Bruising
- Bullae
- Erosion
- Pain
- Hair pulling
- Hyperpigmentation
- Hypopigmentation
- Soreness
- First-degree burn
- Second-degree burn
- Erythema
- Damage to natural skin structure (scratching, crusting)

Over 2,000 subjects worldwide participated in clinical research and underwent treatment with the different *VelaShape* or *UltraShape* devices. The *VelaShape III* and *UltraShape Power* devices that will be used in this study were previously used in clinical studies and emitted the same RF or acoustic energy, respectively. To date, no serious adverse events or unanticipated AEs have been reported. The reported AEs relate to skin and subcutaneous tissue confined to the treatment area and were all mild or moderate in nature and resolved within the study period.

Potential benefits to participating individuals and to society

Subjects may or may not benefit from circumference reduction, reduction of subcutaneous fatty tissue in the treated area via a non-invasive technique resulting in body contouring, or from skin laxity and texture improvement. All subjects in the treatment groups are expected to have some benefit from the treatment procedures as would be expected for the commercial devices (*VelaShape III* and *UltraShape Power*). Subject will receive all treatment procedures at no cost. This study will benefit the advancement of medicine by generating data on safety and efficacy that will aid in the development of an alternative treatment options to procedures with higher potential risks subjects, such as liposuction. The results of this study will help to determine whether this device is safe and effective for improvement of localized subcutaneous fat.

Conclusion:

Considering the potential benefits of non-invasive circumference and fat reduction relative to its risks, the potential benefits associated with the use of the *VelaShape III* and *UltraShape Power* Systems outweigh its risks, supporting study initiation.

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ETHICS AND GOOD CLINICAL PRACTICE

This study will be carried out in compliance with the following:

- Syneron Standard Operating Procedures.
- Declaration of Helsinki, concerning medical research in humans (Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects, Helsinki 1964, amended Tokyo, 1975, Venice 1983, and Hong Kong 1989).
- US Code of Federal Regulations (Title 21CFR including parts 50, 56 and 812 governing informed consent and IRB regulations).
- International Conference on Harmonization (ICH) Harmonized Tripartite Guideline for Good Clinical Practice (GCP), 1996.

QUALITY ASSURANCE AND STUDY MONITORING

Study Monitoring/Auditing/Inspection

The Study Monitor will be responsible for monitoring the study sites to review the data being collected. The sponsor shall implement and maintain quality control and quality assurance procedures with written standard operating procedures (SOPs) to ensure that the trial is being conducted and data are generated, documented and reported in compliance with the protocol, Good Clinical Practice (GCP) and applicable regulatory requirements. Visits will be made prior to the initiation of the study, at scheduled intervals throughout the study, and at termination of the study.

Once enrollment and treatments have begun, monitoring visits will take place more frequently pending enrollment and study activities.

The sponsor and site will maintain regular phone and e-mail correspondence throughout the study to confirm compliance of study procedures.

The investigator/institution agrees to allow the monitor and other authorized personnel direct access to source data/documents for trial related monitoring, the clinical supplies storage/dispensing area and to provide all documents in the Investigator Regulatory Binder for review, and to assist site auditors in their activities if requested. Requests by the Health Canada or regulatory agencies of other countries to inspect the study site may be made after adequate notification. The investigator may be required to assist the regulatory inspectors in their duties, if requested.

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ADMINISTRATIVE PROCEDURES

Supply and Disposition of Study Device

If required the *VelaShape III* device, *UltraShape Power* device, and VelaSpray ease lotion, Parker Gel (coupling agents) will be supplied to the participating clinic. The device will be maintained by the Sponsor, as needed. Unused equipment or coupling agents will be returned to the Sponsor at the end of the study. At the end of all planned treatment sessions, the devices will be returned to Syneron Candela.

Control & Disposition of the Investigational Device

The *VelaShape III* and *UltraShape Power* devices will be used according to the instructions of the manufacturer, Syneron Medical Ltd. At the end of this study, any materials provided specifically for use in this study may be returned to the Sponsor, as described in the Clinical Trial Agreement and study budget.

Informed Consent

The Study Personnel will obtain written Informed Consent prior to the subject's participation in any study procedures. The Study Personnel will inform the subjects of the experimental procedure to be utilized and assure the subjects that their decision regarding participation in the study will have no bearing on the quality of medical care received and that their decision whether to participate in the study is strictly voluntary.

During the initial interview, the subject will be assured that they are free to change their mind and will be allowed to participate in the study or withdraw from the study with no adverse effect on their standard medical care.

Monitoring Plan

At least 3 monitoring visits are projected during the whole study. The frequency of which will be based on enrolment, study activities and the study visit scheduled. The first visit is scheduled at the initiation of the study prior to the first subject treatment in the study. The second visit is scheduled after enrolment and treatment has been initiated and a third visit will be for a close-out visit for the study. Interim visits may be conducted as needed to assure compliance to the study protocol and regulatory requirements. The number and frequency of monitoring visits may also be increased per the sponsor decision to collect data and images post treatment.

Case Report Forms

Paper case report forms will be used in this trial. All protocol-required information collected during the study must be entered in the appropriate field of the case report form (CRF). The

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investigator, or designated representative, should complete the appropriate CRF fields as soon as possible after information is collected. The information must match the information that exists as source documents in the clinic chart, hospital chart, and/or investigator's files. An explanation should be given for all missing data.

It is the investigator's responsibility to assure the accurate completion, review, and approval of all CRFs and the timely completion and submission of all adverse event forms.

Record Maintenance

The investigator shall retain a copy of all study documents in accordance with the FDA regulations which specify that records should be kept for a period of two years: 1) following the date a marketing application either is approved or disapproved for the use, or 2) following notification to FDA that no application is being filed and/or that the study has been discontinued.

If an investigator leaves the study site before record retention obligations have expired, the sponsor should be notified in writing of the person designated to retain the study documents during and after the study.

Handling of clinical data. The data are entered into a secure database that only the sponsor has access to. Admission to the database requires access to a password-protected network secured by the Sponsor. This database is maintained by Syneron that performs backups, data verification, and application upgrades. All equipment housing the clinical data is located in locked rooms or a secure computer network. The only individuals, who view, extract and analyze data for protocol reports and publications are physicians and nurses who are members of the study team or Sponsors. Only authorized personnel of the Sponsors have access to databases.

Any paper copies of subject medical records or research records are stored in secure cabinets at the study site.

PUBLICATION POLICY

The investigator will not publish the study results and will not disclose confidential information received from Syneron without prior written agreement from Syneron. Such confidential information shall include any and all information relating to this study as described in the Clinical Trial Agreement. In the event that Syneron consents to the publication of data from this study, the investigator will provide Syneron manuscripts for review thirty days before submission for publication. Syneron will have no editorial rights over manuscripts. The investigator will also provide Syneron with advance notice of at least (30) days, of any presentation, lecture, abstract session, etc., in which any results from the study will be disclosed.

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APPENDIX I – STUDY SUMMARY

Table 8 - Study Schematics

		Screening / Baseline Tx.1	Tx.2 2wk±4 days	Tx.3 4wk±4 days	4 weeks (±7 days) Follow-up from last Tx. (4wk FU)	8 weeks (±7 days) Follow-up from last Tx. (8wk FU)	12 weeks (±7 days) Follow-up from last Tx. (12wk FU)
	Informed Consent Process	X					
	Eligibility Screening & Medical History	X					
PERFORM BEFORE TREATMENT	Photography	X	X	X	X	X	X
	Height	X					
	Weight (BMI calculation)	X	X	X	X	X	X
	Caliper Measurement (without Strapping/Taping)	X	X	X	X	X	X
	Caliper Measurement (with Strapping/Taping)	X	X	X			
	Marking of the Treatment Areas	X	X	X			
	Reference height measurement	X					
	Circumference Measurements	X	X	X	X	X	X
	Treatment	X	X	X			
	Subject Pain Assessment	X	X	X			
	Safety Monitoring	X	X	X	X	X	X
	Investigator Satisfaction				X	X	X
	Subject Satisfaction				X	X	X
	Urine Pregnancy Test	X	X	X			X
	End of Participation (Termination)						X

APPENDIX II - SCALES

Table 9 - Post Treatment Side Effect Severity Scale

(0) Absent / None	<input type="checkbox"/>
(1) Mild	<input type="checkbox"/>
(2) Moderate	<input type="checkbox"/>
(3) Severe	<input type="checkbox"/>

Table 10 –Investigator and Subject Satisfaction Scale with Treatment Outcome

(2) Very Satisfied	<input type="checkbox"/>
(1) Satisfied	<input type="checkbox"/>
(0) No Opinion	<input type="checkbox"/>
(-1) Unsatisfied	<input type="checkbox"/>
(-2) Very Unsatisfied	<input type="checkbox"/>

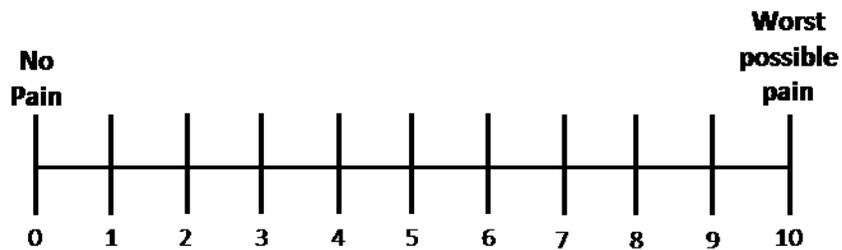
Table 11 –Subject Treatment Recommendation Scale

(2) Highly recommend	<input type="checkbox"/>
(1) Recommend	<input type="checkbox"/>
(0) No Opinion	<input type="checkbox"/>
(-1) Do not recommend	<input type="checkbox"/>
(-2) Definitely do not recommend	<input type="checkbox"/>

SYNERON CANDELA <i>Confidential</i>	<i>Pilot Study to Evaluate VelaShape III & UltraShape Power Combined Treatment for Thigh Circumference Reduction</i>			
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APPENDIX III - PAIN ASSESSMENT

Immediately after treatment the subject will be asked to rate treatment related pain. Pain will be assessed post treatment based on the Numerical Scale Response (NSR). The subject will be presented a scale (below) with words along a horizontal line and asked to make a mark along the scale to rate their pain from no pain to worst possible pain. A number will be derived by the research staff by measuring up to the point the subject has indicated versus the entire line.



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APPENDIX IV - PHOTOGRAPHY

At each of the specified time points; photographs of the treated areas should be taken by investigator or their designee.

- Photographs should be taken in a private room or area of the clinic under controlled conditions, including the distance from the camera to the subject, height of the camera, background, camera positioning, subject's positioning and lighting to achieve high-quality before & after sets.
- Consistent lighting- Lighting should be projected from about 45° angle in order to emphasize the body appearance.
- It is important to keep a constant distance between the subject's feet (use "sticky feet" or another way of marking) in order to properly present the effect of the treatment. The recommended distance between the feet is ~20 cm, but the main point is not to make this distance too small, so that the thighs touch each other, or too large.
- The disposable underwear should be used for all photographs of treatment areas at each study visit.
- For consistency purposes, the same person should ideally take all study photographs, particularly for the same area and subject.
- Small plain labels (with the date, subject ID, subject initials, Investigator name, and identity of the specific area photographed, if necessary) should be placed in the same location within each frame at each photography time point. The label should not cover the treated area.
- All digital files should follow a consistent standard naming scheme.

Specific photography details:

Four photographs of each thigh (angles below) should be taken at each specified time point:

- Front of the thigh
- 90° from the front (right side of the body)
- 90° from the front (left side of the body)
- Back of the thigh

Subjects' arms should remain out of the way; it is best to either cross them over each other in front of the chest or hold them up at a 90° angle to the body, ensuring that the arms do not rest on the chest or touch the body and that they do not cast a shadow in the photograph.