PROSPECTIVE CLINICAL STUDY FOR THE EVALUATION OF THE EFFICACY AND SAFETY OF THE BESHAPE ONE DEVICE FOR NON-INVASIVE WAIST CIRCUMFERENCE REDUCTION.

BeShape Technologies Ltd.

Product: BeShape One™

Protocol Number: CTP-BSO-001

Development Phase: Clinical Validation

Sponsor: BeShape Technologies Ltd.
Hataas 20, Kfar Saba
Israel

Protocol Approval Date: 3-Nov-2022

Current protocol Version: 5.1

This clinical study will be conducted in accordance with current Good Clinical Practice (GCP) as directed by the provisions of the International Conference on Harmonization (ICH); Israel Ministry of Health; United States (US) Code of Federal Regulations (CFR) and the Sponsor's Standard Operating Procedures (SOPs).

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PROTOCOL SYNOPSIS

Protocol Number	CTP-BSO-001
Protocol Title	Prospective clinical study for the evaluation of the efficacy and safety of BeShape One device for non-invasive waist circumference reduction.
Location(s)	2 primary care clinics in Europe and North America
Study Design	Open-Label, prospective, multicenter, one arm, baseline-controlled study
Investigational Product	BeShape One
Device Description	The BeShape One Device is a non-invasive, high-intensity non focused ultrasound device intended for non-invasive waist circumference reduction. The device includes two treatment chambers which apply homogeneous, selective and uniform heating of the entire volume of fat cells.
Study overview	Study subjects will be consecutively screened and enrolled into the study. The study will consist of a single BeShape One treatment and a follow up period (12 weeks) Eligible subjects will receive 1 treatment with the BeShape One device. Treatment will take approximately 1 hour. Subjects will be followed for 12 weeks, FU visits occurring at 6- and 12-weeks post treatment.
Study Population	Adult volunteers, seeking non-invasive abdominal fat and circumference reduction, male and females, 18 to 65 years of age.
Study Objectives	To evaluate the safety and efficacy of the BeShape One device for non-invasive waist circumference reduction.
Inclusion Criteria	1. Female and male subjects ≥18 and ≤65 years of age. 2. Abdominal fat thickness of at least 1.5 cm. 3. 18.5 ≤ BMI ≤ 33 4. Women of childbearing potential (i.e., not post-menopausal or surgically sterilize) must have a negative urine

	pregnancy test. Participating women of childbearing potential must be using a medically acceptable form of birth control for at least 3 months prior to enrollment. 5. Understand the study and volunteer to sign the informed consent. 6. Willing to follow the treatment and follow up schedule and post-treatment care instructions. 7. Willing to refrain from a change in diet, exercise or medication regimen for the duration of the study. 8. Willing to have de-identified images of the treated areas taken for possible use in publications and presentations.
Exclusion Criteria	1. Pregnant women, intending to become pregnant during the study, less than 12 months after delivery, breastfeeding, or less than 6 weeks after completing breastfeeding; 2. Participation in a clinical study of another investigational device or drug involving the same anatomical site within the last 3 months, or, if it does not involve the same anatomical site, at the discretion of the researcher. 3. Subjects with significant systemic disease, such as ongoing hyperlipidemia, diabetes mellitus, hepatitis or other liver disease, HIV-positive status, blood coagulopathy or excessive bleeding, autoimmune or connective tissue disease, and malignant neoplasms; undergoing chronic steroid or immunosuppressive therapy. 4. Subject 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. 5. An implanted pacemaker or any other implantable active device anywhere in the body. 6. Subjects with thyroid disease and / or metabolic syndrome. 7. Unstable weight within the last 6 months (i.e. $\pm$ 3% weight change in the past six months). 8. Local skin pathologies or natural structure loss in the treated area (hernia) and / or loss of sensation or dysesthesia in the treated area. 9. Previous body contouring procedures in the treatment area within the past 12 months. 10. History of abdominal surgery, including laparoscopic procedures. 11. Caesarean section within 12 months. 12. Any permanent or temporary implant in the treatment area such as metal plates or an injected chemical substance

	such as silicone. 13. Actively expressed psychiatric or psychological state. 14. Abnormal kidney, liver or coagulation functions, abnormal lipid profile or blood count within the last 3 months. 15. Any condition that, at the researcher's discretion, renders the subject unsuitable for participation in a clinical research study.
Duration of Study	Up to 4 months (including screening period and two follow up visits at 6 and 12 weeks after the treatment)
Primary Endpoint	To evaluate the reduction in waist circumference following treatment with the BeShape One device at the final 12-week follow-up visit compared to baseline.
Secondary Endpoints	1. Waist circumference reduction at 6 week follow up visit compared to baseline 2. Subject improvements measured independently by the Global Aesthetic Improvement scale at each follow up visit (6 wk and 12 wk). 3. Subject satisfaction using a 5-point Likert scale at each follow up visit (6 wk and 12 wk). 4. Investigator satisfaction using the Clinical Global Aesthetic Improvement scale at each follow up visit (6 wk and 12 wk). 5. Subject comfort/pain level, assessed after treatment using a pain scale.
Exploratory Endpoints	To evaluate the reduction in abdominal fat thickness at 6- and 12-weeks post treatment.
Safety Endpoint	Number, severity and type of adverse events recorded throughout the study and post treatment phase (immediate and delayed response).
Study Sponsor	BeShape Technologies Ltd. Hataas 20, Kfar Saba Israel

Abbreviations

Abbreviation	Description
CRF	Case Report Form
FDA	US Food and Drug Administration
GCP	Good Clinical Practice
BMI	Body Mass Index
SAT	Subcutaneous Adipose Tissue
US	Ultrasound
TD	Transducers
TEC	Thermoelectric Coolers
VAS	Visual Analogue Scale
AE	Adverse Event
SAE	Serious Adverse Event
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
IEC	Independent Ethics Committee
IRB	Institutional Review Board
PE	Physical Examination
PI	Principal Investigator
SOP	Standard Operating Procedure
WHO	World Health Organization
W	Watt (Output Electric Power)

1 INTRODUCTION

A growing number of people seek cosmetic solutions for the removal of excess weight. These solutions include surgical trends of abdominoplasties, Brachioplasty and liposuction procedures. The latter is used for the removal of excess fat tissues in specific body areas for body shaping, combined with several modifications including ultrasound (US) and laser (Brown SA, 2009). Due to limitations and complications resulting in death, there has been a significant decrease in the performance of these procedures (Garcia O, 2013), and during this period, a significant number of noninvasive body contouring devices have been introduced to the aesthetic surgery market. Many 21st-century aesthetic surgery patients now seek noninvasive or minimally invasive procedures with minimal downtime in exchange for limited aesthetic outcomes. Current nonsurgical procedures employ mechanical vacuum massage, lasers, radiofrequency, ultrasound, or low-level energy infrared light (Sasaki GH, 2014). Some of these devices may create a temporary effect but are unable to present any scientific or preclinical evidence (histology or gross pathology) of fat cell disruption.

Currently, a significant number of noninvasive in-use devices are ultrasonic energy-based. The use of ultrasonic energy in aesthetic body contouring, dating back to the late 1980s, popularized the concept of ultrasound-assisted liposuction (UAL), and introduced the techniques to the USA in 1993 (Garcia O, 2013; Manstein D L.H., 2008).

US used for body sculpting can be divided into two broad categories: relatively low-frequency nonthermal ultrasound and high intensity focused thermal ultrasound. With nonthermal US, a low frequency is chosen to increase the likelihood of cavitation while generating little heat through absorption mechanisms. The high-intensity focused ultrasound (HIFU) can be highly focused to confine the cavitation effects to the focal zone of the ultrasonic beam. Thermal HIFU delivers high frequency (2MHz) ultrasonic energy to subcutaneous tissue, producing heat capable of disrupting adipose tissue and thermally modifying collagen (Jewell, 2011).

The early generations of US devices for use in body contouring were associated with increased complication rates, which were mostly attributed to the high ultrasonic energy output associated with these devices (Garcia O, 2013; Manstein D, 2008).

The ultrasonic energy used by the LipoSonix system (Solta Medical, Inc., Hayward, CA, USA) is an example of High-Frequency Thermal Ultrasound, which is generated by an internally focused transducer and focuses the ultrasonic waves so they converge at a specified depth and location (Ter Haar G, 2007) at temperatures reaching 60-65^{0}C. Clinical trials conducted with the LipoSonix device explored its effects on waist circumference utilizing a standardized waist measuring technique. Results showed statistically significant decrease in waist circumference reduction. Safety of the device was also evaluated. There were no unanticipated adverse device events, and clinical laboratory tests did not reveal any abnormalities (Mark L. Jewell, 2011)

In contrast to HIFU technology, the BeShape technology makes use of high intensity non-focused US, utilizing continuous wave (CW) ultrasonic energy to the adipose tissue at a temperature of 48^0C. There is far less information regarding the effects of non-focused and weakly focused US on adipose tissue and its ability to disrupt fat cells. Non-focused US has typically been used for US physiotherapy, where changes in cellular activity and cell membrane permeability have been reported (Garcia O, 2013).

A unique feature of the BeShape One™ is the vacuum feature. The activated vacuum effectively fixes the target tissue in the treated area inside the cup-shaped chamber of the device applicator. This tissue fixation in the applicator allows the transmission of the ultrasound energy parallel to the body surface, rather than perpendicular, thereby reducing US energy exposure to the underlying muscles and internal organs.

An example of a device utilizing vacuum to achieve its desired affects in lipolysis (breakdown of fat) is the Zeltiq CoolSculpting System (Allergan + Zeltiq Aesthetics, Pleasanton, CA USA). It is a thermoelectric cooling and heating device using Cryolipolysis technology to target fat cells. Similar to BeShape's technology, the device includes a cup-shaped applicator with two cooling panels that is applied to the treatment area. The tissue is drawn into the handpiece under moderate vacuum and the selected temperature is modulated by thermoelectric elements and controlled by sensors that monitor the heat flux out of the tissue (Nils Krueger, 2014). The vacuum applicator draws tissue into the applicator cup and holds the tissue against the cooling surfaces of the applicator. Clinical findings with the Zeltiq CoolSculpting system utilizing vacuum and surface applicators demonstrated that use of the device safely and effectively induced cold-assisted lipolysis with colder temperatures down to -15°C, resulting in shorter duration treatment.

The purpose of the current clinical study is to evaluate the safety and effectiveness of treatment with the investigational high-intensity non-focused BeShape One US device on waist circumference reduction.

2 DEVICE DESCRIPTION

2.1 General Device Description

The BeShape One™ system consists of hardware and software, these elements are integrated in the BeShape One™ console and applicator/handpiece. BeShape One™ is supplied as a kit, with a console and 2 applicators.

The console is floor-standing and portable. It is controlled by a touch screen.

The BeShape One device applicator is a mechanical hand piece with an internal rectangular bathtub-shaped chamber and contains the US transducers. The applicator uses a vacuum during the procedure that draws adipose tissue into the inner cup-shaped chamber, thereby providing heating of the subcutaneous adipose tissue.

3 INTENDED USE AND INDICATIONS FOR USE

The BeShape One Device is a high-intensity non-focused ultrasound device intended for non-invasive waist circumference reduction in adult population.

4 RATIONALE FOR STUDY

A growing number of people seek cosmetic solutions for the removal of excess weight. Surgical solutions such as abdominoplasties, Brachioplasty and liposuction procedures are available but these include limitations and complications sometimes even resulting in death. Therefore, there has been a significant decrease in the performance of these invasive procedures (Garcia O, 2013) and nonsurgical solutions are at need.

Although no nonsurgical procedure has been accepted as the gold standard as of yet, cryolipolysis is considered to be both safe and effective, with a high patient satisfaction rate of up to 73% after one treatment. This rate is comparable with that of HIFU and acoustic wave therapy (62.3% and 64%, respectively). However, the latter modalities are associated with either a higher rate of adverse events and pain or a high number of up to eight treatments necessary to achieve the desired effect (Nils Krueger, 2014) .

The noninvasive BeShape One device offers an alternative approach for waist circumference reduction using a high intensity non-focused US technology. The current proposed study will evaluate the safety and efficacy of the BeShape One device in effectively reducing waist circumference in adult population.

5 STUDY OBJECTIVES AND ENDPOINTS

The objective of the study is evaluating the safety and efficacy of the BeShape One device for non-invasive waist circumference reduction.

5.1 Primary Endpoint

To evaluate the reduction in waist circumference following BeShape treatment at the final follow-up visit compared to baseline.

5.2 Secondary Endpoints

The secondary objectives of the study are as follows:

- Waist circumference reduction at 6 week follow up visits compared to baseline,.
- Subject improvement as measured independently by the Global Aesthetic Improvement scale at each follow up visit (6 wk and 12 wk).
- Subject satisfaction using a 5-point Likert scale at each follow up visit (6 wk and 12 wk).
- Investigator satisfaction using the Clinical Global Aesthetic Improvement scale at each follow up visit (6 wk and 12 wk).
- Subject comfort/pain level, assessed after treatment using a pain scale.

5.3 Exploratory Endpoint

To evaluate the reduction in abdominal fat thickness at 6- and 12-weeks post treatment.

5.4 Safety Endpoint

Number, severity and type of adverse events recorded throughout the study and post treatment phase (immediate and delayed response), including skin reactions (erythema, edema, irritation, etc.).

6 SELECTION OF STUDY POPULATION

The intention is to enroll 70 patients who meet all eligibility criteria. Evaluation of the study participant inclusion/exclusion criteria will be based on the review of clinical medical records and documented patient interviews conducted by the investigator or under the direction of the investigator.

To be enrolled in the study, patients must meet ALL of the inclusion criteria and NONE of the exclusion criteria designated below.

6.1 Inclusion Criteria:

1. Female and male subjects ≥18 and ≤65 years of age.
2. Abdominal fat thickness of at least 1.5 cm.
3. 18.5 ≤ BMI ≤ 33
4. Women of childbearing potential (i.e., not post-menopausal or surgically sterilize) must have a negative urine pregnancy test. Participating women of childbearing potential must be using a medically acceptable form of birth control for at least 3 months prior to enrollment.
5. Understand the study and volunteer to sign the informed consent.
6. Willing to follow the treatment and follow up schedule and post-treatment care instructions.
7. Willing to refrain from a change in diet, exercise or medication regimen for the duration of the study.
8. Willing to have de-identified images of the treated areas taken for possible use in publications and presentations.

6.2 Exclusion Criteria

1. Pregnant women, intending to become pregnant during the study, less than 12 months after delivery, breastfeeding, or less than 6 weeks after completing breastfeeding;
2. Participation in another clinical study of another investigational device or drug involving the same anatomical site within the last 3 months, or, if it does not involve the same anatomical site, at the discretion of the researcher.
3. Subjects with significant systemic disease, such as ongoing hyperlipidemia, diabetes mellitus, hepatitis or other liver disease, HIV-positive status, blood coagulopathy or excessive bleeding, autoimmune or connective tissue disease, and malignant neoplasms; undergoing chronic steroid or immunosuppressive therapy.
4. Subject 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.
5. An implanted pacemaker or any other implantable active device anywhere in the body.
6. Subjects with thyroid disease and / or metabolic syndrome.
7. Unstable weight within the last 6 months (i.e. ± 3% weight change in the past six months).
8. Local skin pathologies or natural structure loss in the treated area (hernia) and / or loss of sensation or dysesthesia in the treated area.
9. Previous body contouring procedures in the treatment area within the past 12 months.
10. History of abdominal surgery, including laparoscopic procedures.
11. Caesarean section within 12 months.
12. Any permanent or temporary implant in the treatment area such as metal plates or an injected chemical substance such as silicone.
13. Actively expressed psychiatric or psychological state.
14. Abnormal kidney, liver or coagulation functions, abnormal lipid profile or blood count within the last 3 months.

15. Any condition that, at the researcher's discretion, renders the subject unsuitable for participation in a clinical research study.

6.3 Informed Consent

Written informed consent will be obtained from each study patient prior to enrollment into the study. A written informed consent (approved by BeShape Technologies Ltd. and the Ethics Committee) must be signed and dated by the patient (or legally authorized representative, if appropriate), and the investigator. Patients will be given a copy of the signed informed consent document. The signed informed consent will be retained with the study records at the site. It is the responsibility of the Investigator to assure that informed consent is obtained from each patient in accordance with GCP guidelines. Subjects may withdraw their consent to participate in the study at any time without prejudice. The investigator may withdraw a subject if, in his clinical judgement, it is in the best interest of the subject or if the subject cannot comply with the protocol.

7 STUDY DESIGN

This study is a prospective, baseline controlled, multi-center, one arm clinical study aimed to assess the efficacy and safety of the BeShape One^{TM} device for waist circumference reduction.

All subjects will undergo an assessment of their general health. A single treatment utilizing the BeShape One^{TM} device will be administered.

During the follow-up period, visits will be conducted as follows: 6 weeks (6wk FU), and 12 weeks (12wk FU) post treatment. Subject's waist circumference will be measured at baseline (before treatment) and at each of the follow up visits. Circumference reduction will be assessed at each post baseline visit. Additionally, investigator and subject assessments will be completed at each follow up visit. Photography of the treatment areas will be performed under visible light conditions of the front, right, left and back view of the subjects at the baseline visit (before first treatment) and at the last follow-up visit (12wk FU).

8 ADMINISTRATION OF TREATMENT

Subjects will receive one treatment with the BeShape One^{TM} device on the anterior abdomen. Prior to the treatment, measurements of weight and waist circumference will be performed.

Before starting the procedure using the BeShape One^{TM} device, the administrator should clean the entire treatment area with a wet wipe and hairs should be shaved. Conductive castor oil will be applied to the treatment areas to ensure full contact between the applicator and the skin. Prior to treatment, it is necessary for the operator to ensure that all treatment areas are in close contact with the cup-shaped applicator chamber. Following visual confirmation of proper contact with the tissue, the skin will be marked as a

treatment area using a skin marking pen. Subjects will receive treatment on at least 4 abdomen/flanks treatment areas and up to 6 treatment areas, at the discretion of the investigator. During the procedure, subjects will lie in the supine position in order to provide the best access to the treatment area.

Upon completion of treatment, the treated area will be freed from the applicator. The administrator should check for any immediate skin reaction and record any outstanding findings on the CRF before proceeding to the next area of treatment.

Immediately after completion of the procedure (after all treatment areas have been treated), the following evaluations and measurements will be performed:

* Assessment of adverse events, including any skin reaction (erythema, edema, irritation, etc.) or any other side effects;
* Pain assessment.

All findings will be recorded on the Adverse Events form.

9 STUDY PROCEDURES

9.1 Overview

Patient visits may occur within a $\pm$ 2 days deviation from the scheduled time.

Efficacy rating scales to be used in the study include:

- Waist circumference measurement
- Abdominal fat thickness measurements
- Global Aesthetic Improvement scale (GAI)
- Clinical Global Aesthetic Improvement scale (CGAI)

Safety evaluations will include a pain scale and adverse event monitoring throughout the study. Number, severity and type of adverse events will be recorded throughout treatment and follow-up phases.

9.2 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 and a physical examination of the subject's general health including vital signs will be performed. In addition, there will also be an examination of the subject's skin in the treatment area.

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.

9.3 Baseline

Baseline assessments will include height, weight and waist circumference measurements and obtaining photographs of the treatment area.

9.4 Treatment

A single treatment will be administered at the baseline visit, following completion of baseline measurements and photographs. Clinical and safety assessments will be administered prior to and following the treatment.

9.5 Follow-Up

Follow up visits will occur 6- and 12-weeks post treatment. Clinical and safety assessments will be performed at each of the follow up visits.

9.6 Clinical Assessments

9.6.1 Patient Improvement using the Global Aesthetic Improvement Scale

Patient improvement assessment will be performed independently by the subject using pre-defined scale questionnaire. The subjects will answer this questionnaire at each follow-up visit (6wk FU, and 12wk FU).

9.6.2 Patient Satisfaction using a 5-point Likert Scale

Patient satisfaction assessment will be performed independently by the subject using pre-defined scale questionnaire. The subjects will answer this questionnaire at each follow-up visit (6wk FU, and 12wk FU).

9.6.3 Investigator Satisfaction using the Clinical Global Aesthetic Scale

Satisfaction assessment will be performed by the study investigator using a pre-defined scale questionnaire. The investigator will answer this questionnaire at each follow-up visit (6wk FU, and 12wk FU)

9.6.4 Pain Rating Scale

The subjects will rate their pain at the treatment visit.

9.6.5 Abdominal Fat Thickness Measurements

Abdominal fat thickness will be assessed at the treatment area prior to starting the treatment and following the treatment.

10 PATIENT COMPLETION / WITHDRAWAL

10.1 Completion

A subject will be considered to have completed the study if the they complete the treatment as well as both follow up visits.

10.2 Withdrawal from the study

A subject will be withdrawn from the study for any of the following reasons:

- Withdrawal of consent
- Subject is not compliant with requirements of the study, including inclusion and exclusion criteria.
- The investigator believes that for safety reasons (e.g. an adverse event) it is in the best interest of the patient to stop the study.
- The study is prematurely stopped or halted (e.g. clinical halt)

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 fail to complete the study will be replaced and will not be considered evaluable.

11 STATISTICAL CONSIDERATIONS

11.1 Study Design and Objectives

This study is a prospective, baseline controlled, multi-center, one arm study. The purpose of this study is to evaluate the performance and safety of the BeShape One device for waist circumference reduction.

11.2 Study Endpoints

11.2.1 Primary Endpoint

The primary endpoint is the change from baseline to 12 weeks after treatment in waist circumference.

11.2.2 Secondary Endpoints

The secondary endpoints are

- Change from baseline to 6 weeks after treatment in waist circumference.
- Global Aesthetic Improvement scale at 6 weeks and 12 weeks following treatment measuring subject rated improvement.
- Satisfaction scale at 6 weeks and 12 weeks following treatment measuring subject rated satisfaction.
- Clinical Global Aesthetic Improvement scale at 6 weeks and 12 weeks following treatment measuring investigator rated improvement.
- Pain score after treatment measuring subject comfort/pain level.

11.2.3 Exploratory Endpoint

Change from baseline to 6 weeks and 12 weeks after treatment of abdominal fat thicknes.

11.2.4 Safety Endpoints

The incidence, severity and type of adverse events recorded throughout the study and post treatment phase, including skin reactions (erythema, edema, irritation, etc.).

Safety will also be assessed with vital signs.

11.3 Statistical Hypothesis

The null hypothesis of this study is that there is no difference between the mean decrease from baseline of waist circumference 12 weeks after treatment.

The alternative hypothesis is that there is a difference in the mean decrease from baseline of waist circumference 12 weeks after treatment.

11.4 Sample Size Determination

A total samples size of 70 subjects should be enrolled into the study.

11.5 Analysis Data Sets

11.5.1 Safety Analysis Set

All subjects who received treatment will be included in the safety analysis set. The safety analysis set will be used for the summary and analyses of all safety endpoints.

11.5.2 Full Analysis Set (FAS)

The full analysis set (FAS) includes all eligible subjects who are enrolled in the study, received treatment and have at least one post treatment waist circumference measurement. The FAS will be used for the summary and analyses of the primary, secondary and exploratory endpoints.

11.5.3 Per Protocol (PP) Analysis Set

The per protocol (PP) analysis set will consist of all subjects from the FAS without any major protocol violations. The PP analysis set will be used for a sensitivity analysis of the primary endpoint.

11.6 Statistical Methods

11.6.1 Randomization

This is a one arm study thus no randomization will be performed.

11.6.2 Disposition of Subjects/Data

The numbers of subjects who were enrolled will be provided. A list of discontinued subjects together with the reasons for discontinuation will be presented.

11.6.3 Demographic and Baseline Characteristics

Demographic and baseline characteristics including age, gender, race, ethnicity, height, weight and BMI will be tabulated. Continuous variables will be summarized by a mean, standard deviation, minimum, median and maximum, and categorical variables by a count and percentage.

11.6.4 Efficacy Analyses

All efficacy analyses will be performed on the FAS. All efficacy endpoints will be listed by subject and presented descriptively.

11.6.5 Safety Analyses

All safety analyses will be performed on the Safety Analysis Population. The safety assessment will be based on the incidence, severity and relationship to treatment of the adverse events.

All Serious Adverse Events (SAEs) will be listed and discussed on a subject-by-subject basis.

Vital signs will be presented descriptively by visit.

12 SAFETY, ADVERSE EVENT AND DEVICE DEFICIENCY REPORTING

Timely, accurate, and complete reporting and analysis of safety information from clinical studies are crucial for the protection of subjects, investigators, and the sponsor and are mandated by regulatory agencies worldwide. The sponsor has established Standard Operating Procedures (SOPs) in conformity with regulatory requirements worldwide to ensure appropriate reporting of safety information. All clinical studies conducted by the sponsor or of its affiliates will be conducted in accordance with those procedures.

12.1 Definitions

The definitions provided below are in compliance with ISO 14155 (2020-07 third edition) and 21 CFR 812.3

- **Adverse Event (AE)**

An adverse event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

This definition includes any occurrence that is new in onset or aggravated in severity or frequency from the baseline condition, or abnormal results of diagnostic procedures, including laboratory test abnormalities.

This definition also includes events related to the control and to the procedures involved.

Note: The sponsor collects adverse events starting with the signing of the informed consent.

- **Adverse Device Effect (ADE)**

An adverse event related to the use of an investigational medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation or operation or any malfunction of the investigational device.

This definition includes any event resulting from use error or from intentional misuse of the investigational device.

- **Serious Adverse Event (SAE)**

An adverse event that led to any of the following:

- death
- serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
  - a life-threatening illness or injury or a permanent impairment of a body structure or
  - a body function including chronic diseases or
  - in-patient or prolonged hospitalization or
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or function
- foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment

Note: Medical and scientific judgment should be exercised in deciding whether expedited reporting is also appropriate in situations other than those listed above. For example, important medical events may not be immediately life threatening or result in death or hospitalization but may jeopardize the subject or may require intervention to prevent one of the outcomes listed in the definition above. Any adverse event is considered a serious adverse event if it is associated with clinical signs or symptoms judged by the investigator to have a significant clinical impact.

- **Serious Adverse Device Effect (SADE)**

An adverse device effect (ADE) that has resulted in a ny of the consequences characteristic of a serious device event (SAE).

- **Unanticipated Serious Adverse Device Effect (USADE)**

A serious adverse device effect (SADE) which by its nature, incidence, severity or outcome has not been identified in the current version of the risk assessment.

Note: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the current version of the risk assessment.

- **Device Deficiency (DD)**

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety and performance.

This definition includes malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labeling.

This definition includes device deficiencies related to the investigational device or control.

12.2 Definition of Adverse Event Severity

For all adverse events, the severity of the adverse event will be determined by the investigator, using the following terms:

- **Mild**

A mild adverse event is one in which the subject is aware of the event, but it is easily tolerated without intervention.

- **Moderate**

A moderate adverse event is one that causes sufficient discomfort to interfere with usual activities.

- **Severe**

A severe adverse event is one that results in the inability to perform usual activities.

12.3 Definition of Relationship to Investigational Device

For all adverse events, the relationship to study device and/or procedure will be determined by the investigator, using the following terms:

- **Probably related:**

Follows a reasonable temporal sequence from study device delivery / retrieval, and cannot be reasonably explained by known characteristics of the patient's clinical data or the surgical procedure applied.

- **Possibly related:**

Follows a reasonable temporal sequence from study device delivery / retrieval, but could have been produced by the patient's clinical state or by the surgical procedures regardless of the study device.

- **Probably not related:**

Temporal association is such that the study device is not likely to have had any reasonable association with the observed event.

- **Not related:**

No relationship to study device activation is perceived.

12.4 Management of Adverse Events

12.4.1 Adverse Events Assessments

Should the subject experience an adverse event, an assessment of the situation will be initiated by the study staff, the PI will be notified and appropriate course of action will be determined. The sponsor will be contacted as appropriate. The AE will be documented and reported per the sponsor SOPs, IRB and regulation requirements.

12.4.2 Adverse Event Documentation

The adverse event will be recorded in the Case Report Forms and will include the following information:

- Type of effect (AE, ADE, SAE, UADE, ASADE, SADE)
- Date of onset and resolution
- Severity
- Seriousness (yes/no)
- Relationship to device/procedure
- Anticipated (yes/no)
- Treatment given and/or action taken

12.4.3 Reporting of SAE and/or UADE

All SAE's, SADE, ASADE and UADE will be reported in writing to the PI, sponsor and IRB within 72 hours of knowledge of the event.

If the event resulted in death of a subject, the event will be reported to the PI, sponsor and IRB within 24 hours of knowledge of the event.

In case of an UADE, the sponsor will immediately conduct an evaluation. The results of the evaluation will be reported to the regulatory authorities, IRB and PI within 10 days after the sponsor first receives notice of the effect.

12.5 Management of Device Deficiencies

12.5.1 Device Deficiency Assessment

All DD of an investigational device will be documented throughout the study and managed by the sponsor in accordance with written SOPs for the control of a non-conforming product. The sponsor will take, where applicable, appropriate corrective and preventive actions to protect the safety of subjects, users and other persons. Device deficiencies of the control, if applicable, will also be documented.

12.5.2 Device Deficiency Documentation

The PI will record any observed device deficiency on a device deficiency form. The form may or may not be part of the CRFs.

The sponsor will review all device deficiencies and determine and document in writing whether they could have led to a serious adverse device effect.

12.5.3 Reporting of Device Deficiencies

The PI will report to the sponsor, IRB and regulatory authorities (if applicable) device deficiencies that could have led to a serious adverse device effect within 72 hours of knowledge of the event.

13 RISK / BENEFIT ANALYSIS

13.1 Risks

The BeShape One Device is a high-intensity non focused ultrasound device intended for non-invasive waist circumference reduction in adult population. The risks to patients resulting from potential device hazards and associated with the study procedures/devices have been analyzed using the Risk Management Standard - ISO 14971. The different types of hazards were identified and evaluated using risk assessment numerical parameters. Applicable controls for the risks were analyzed. After the implementation of appropriate risk control measures, the level of risk was re-evaluated and found to be acceptable. Below is a summary of some of the key hazards and applicable control measures.

Patient Injury Risk: The BeShape One device may cause over-heating related patient injuries such as skin burns, blistering and erythema.
Patient Injury Risk Mitigation: The over-heating related injuries are mitigated by an inherent device design cooling mechanism and controlling mechanism that stops activation of the device at a predetermined time. In addition, mitigation is achieved by comprehensive software validation ensuring correct device algorithm output, including constant monitoring of the energy level during treatment and cooling water and therapeutic heating temperature control. The device has also been tested in pre-clinical settings, demonstrating and proving the safety of the device.

Biocompatibility Risk: The device components and/or materials may present a biocompatibility risk (irritation, allergic reaction, etc.) if they contact the patients' body.
Biocompatibility Risk Mitigation: The risk of biocompatibility is mitigated as all the materials that come in contact with the skin human are known to be biocompatible. The device is non-invasive and only comes in contact with the outer skin surface.

Use Risk: The operator may perform the treatment incorrectly (due to use error or SW bug) and/or apply excessive treatment duration, potentially causing patient injury.
Use Risk Mitigation: The BeShape One device includes a floor standing portable console and touch screen which indicates if the acoustic energy is turned on or off. The user can stop the acoustic energy transmission at any time by pressing the on/off button or the emergency button. Furthermore, prior to each treatment a system test is performed. Comprehensive software validation, proper operator training, proper instructions for use and electrical safety testing are additional mitigations for this use risk.

Performance Risk: The BeShape One device may lead to ineffective treatment due to vacuum mechanism failure.
Performance Risk Mitigation: This risk is mitigated by real time monitoring of the vacuum level and software control on energy transmission coupled to vacuum formation. The system is configured to stop its operation if good skin contact is not established. Further mitigations include pre-clinical studies and SW validation.

System Failure Risk: The BeShape One device may fail to operate due to system malfunction.
System Failure Risk Mitigation: The BeShape Once device is calibrated during manufacturing. In addition, the manufacturer supplies it with a tissue-mimicking phantom for periodic user tests.

In summary, there are no anticipated severe risks or serious adverse device effects. There are no contraindications for use in the proposed study or study population. There may be other risks to the subject that are associated with the device or procedure which are unforeseeable at this time.

13.2 Benefits

Subjects may or may not benefit from circumferential waist reduction of the treated area resulting in body contouring improvement via the investigational device. Subjects 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, such as liposuction. The results of this study will help to determine whether this device is safe and effective for improvement of waist circumference reduction.

14 ETHICAL ASPECTS

14.1 Study-Specific Design Considerations

Subjects/cases will be carefully screened using the study eligibility criteria prior to enrollment in the study.

14.2 Regulatory Ethics Compliance

14.2.1 Statement of Compliance

The study will be conducted in compliance the Declaration of Helsinki, ISO 14155, 21 CFR 50 and 21 CFR 812 for non-significant risk device studies, applicable regulatory requirements and ICH Good Clinical Practice (GCP) guidelines. The study will be conducted in accordance with this protocol and any regional or national regulations, as appropriate. The study will not commence until the approval from the IRB has been

received and will be conducted in compliance with the conditions set forth in the IRB approval.

14.2.2 Investigators Responsibilities

The investigator is responsible for ensuring that the clinical study is performed in accordance with the protocol, current ICH guidelines on GCP, and applicable regulatory requirements.

GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the clinical study data are credible.

14.2.3 Independent Ethics Committee or Institutional Review Board

Before the start of the study, the investigator will provide the IEC/IRB with current and complete copies of the following documents:

- Final protocol and if applicable, amendments
- Informed consent form
- Investigator's Brochure (or equivalent information) and amendments
- Investigator's curriculum vitae or equivalent information (unless not required, as documented by IEC/IRB)
- Information regarding funding, name of the sponsor, institutional affiliations, and other potential conflicts of interest
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after IEC/IRB has given full approval of the final protocol, amendments (if any), and informed consent and after the sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the documents being approved.

During the study the investigator will send the following documents to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments
- Investigator's Brochure amendments or new edition(s)
- Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the IEC/IRB)
- Reports of any serious adverse events, if applicable
- Deviations from or changes to the protocol
- Notification if new investigator is responsible for the study at the site
- Any other requirements of the IEC/IRB

At least once a year the IEC/IRB will be asked to review and re-approve this clinical study. This request and approval should be documented in writing. At the end of the

study, the investigator (or sponsor where required) will notify the IEC/IRB about the study completion.

14.2.4 Informed Consent

Each subject must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form used must be approved by both the sponsor and by the reviewing IEC/IRB. The informed consent should be in accordance with principles set forth in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Before entry into the study, the investigator or an authorized member of the investigational staff must explain to potential subjects the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the subject will receive for the treatment for his/her disease. Subjects will be told that alternative treatments are available if they refuse to take part and that such refusal will not prejudice future treatment. Finally, they will be told that their records may be accessed by health authorities without violating the confidentiality of the subject, to the extent permitted by the applicable law(s) or regulations. By signing the informed consent form the subject is authorizing such access.

The subject will be given sufficient time to read the informed consent form and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by name of the subject, subject's signature and date of signature. After having obtained the consent, a copy of the informed consent form must be given to the subject. If the subject or legally acceptable representative is unable to read or write, an impartial witness should be present for the entire informed consent process (which includes reading and explaining all written explanations) and should personally date and sign the inform consent form after the oral consent of the subject or legally acceptable representative is obtained.

14.2.5 Privacy of Personal Data

The collection and processing of personal data from patients enrolled in this study will be limited to those data that are necessary to investigate the efficacy, safety, quality, and utility of the investigational product(s) used in this study. This data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations.

15 ADMINISTRATIVE REQUIREMENTS

15.1 Protocol Amendments

The investigator will not modify this protocol without a formal amendment. Protocol amendments must not be implemented without prior IEC/IRB approval, or when the relevant competent authority has raised any grounds for non-acceptance, except when necessary, to eliminate immediate hazards to the patients in which case the amendment must be promptly submitted to the IEC/IRB and relevant competent authority. When the change(s) involves only logistic or administrative aspects of the study, the IRB (and IEC where required) only needs to be notified.

15.2 Protocol Deviations

Investigators are not allowed to deviate from the protocol except under emergency circumstances. Deviations from the protocol to protect the rights, safety and well being of the subjects may proceed without prior approval of the sponsor and the IRB. Such deviations shall be documented and reported to the sponsor and the IRB as soon as possible but within 5 working days of the occurrence of such a deviation. In any other case, the investigator or other physician in attendance will contact the appropriate sponsor representative by fax or telephone regarding any situations requiring a departure from the protocol. If possible, contact will be made before implementing any departure from the protocol. In all cases contact with the sponsor must be made as soon as possible in order to discuss the situation and agree on an appropriate course of action. Any protocol deviation needs to be recorded in the CRF, source documents and protocol deviation form and should describe the deviation and the circumstances requiring it.

15.3 Regulatory Documentation

15.3.1 Regulatory Approval/Notification

This protocol and any amendment(s) must be submitted to the appropriate regulatory authorities in each respective country, if applicable. A study may not be initiated at a site until all local regulatory requirements are met.

15.3.2 Required Pre-study Documentation

The following documents must be available and maintained during the study:

- Approved Study Protocol and amendment(s)
- A copy of the dated and signed written IEC/IRB approval of the protocol and any amendments. This approval must clearly identify the specific protocol by title and number and must be signed by the chairman or authorized designee.
- An approved informed consent form
- Regulatory authority approval or notification, if applicable
- Documentation of investigator qualifications (e.g., curriculum vitae)
- Completed financial disclosure form
- Signed and dated clinical trial agreement, which includes the financial agreements
- Other documentation required by local regulations

15.3.3 Patient Identification Register and Patient Screening Log

The investigator agrees to complete a subject/case identification register to permit easy identification of each subject/case during and after the study. The subject/case identification register will be treated as confidential. To ensure patient confidentiality, no copy will be made. All reports and communications relating to the study will identify subject/case by initials and assigned number only. The investigator will also complete a subject/case enrollment log, which reports all subject/case who were determined eligible for inclusion in the study.

15.3.4 Case Report Form Completion

All data relating to the study will be recorded on source documents/CRFs and then entered into an EDC with electronic CRFs (eCRFs). The case report forms and/or pre-templated source documents will only include a subject number and initials. Data will be collected in English. A black or blue pen will be used to record data on the source documents/CRFs. The source documents and eCRFs are to be completed at the time of the data collection. Recorded information should be legible and complete. Erroneous entries should be crossed out, corrected with the change, initialed and dated by the individual making the correction. Every effort should be made to ensure that all measures are recorded on the source documents and eCRFs. The investigator must verify that all data entries on the source documents and in the eCRFs are accurate and correct. The EDC will include electronic CRFs and will be used to process the data collected during the study. The development, validation, handling, maintenance, security measures, change control, data backup, retention, recovery, user access, blinding etc. will be performed per sponsor SOPs and regulatory requirements.

15.3.5 Record Retention and Storage

In compliance with the ICH/GCP guidelines, the investigator/institution will maintain all source documents and eCRFs that support the data collected from each patient, as well as all study documents as specified in ISO 14155 Annex E, Essential clinical investigation documents, and all study documents as specified by the applicable regulatory requirement(s). The investigator/institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained and stored for at least 2 years after the last approval of a marketing application ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational products. These documents will be retained for a longer period if required by regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.

If the responsible investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who

will accept the responsibility. The sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the investigator relocate or dispose of any study documents before having obtained written approval from the sponsor.

If it becomes necessary for the sponsor or the appropriate regulatory authority to review any documentation relating to this study, the investigator must permit access to such report.

15.3.6 Device Accountability

A Device Accountability Log will be maintained for the sponsor's equipment (smart phones and software) documenting date of receipt, description of device (including type, model#, serial number or unique code, quantity and software version) and date of return for used and unused products. Device usage will be recorded in the CRF for each subject.

15.3.7 Packaging and Labeling

This study will utilize an investigational device and FDA cleared devices as controls. The sponsor is responsible for packaging and labeling of the device for delivery to the study site. FDA cleared devices do not require special labeling. Investigational devices or its immediate package shall bear a label with the following statement:

"CAUTION – Investigational device. Limited by Federal (or United States) law to investigational use."

The label or other labeling shall describe all relevant contraindications, hazards, adverse effects, interfering substances or devices, warnings and precautions. It is the investigator's responsibility to ensure appropriate labeling is visible and remains intact throughout the life of the study. The instructions for use (IFU) will be provided as separate documents from this protocol.

15.4 Monitoring Procedures

The sponsor is responsible for all monitoring-related procedures. The monitoring activities will be performed based on a written monitoring plan and will include, but not be limited to, descriptions of monitor qualifications, training, visit reports and reviews, follow up on monitoring findings and corrective actions.

The monitoring requirements for an NSR device study is identified in 21 CFR 812.2(b) Abbreviated requirements. For monitoring an NSR device study, the requirement is to comply with 21 CFR 812.46 with respect to monitoring:

- Compliance to the signed agreement between the investigator and sponsor
- The study follows the protocol and any amendments that apply
- Compliance to any conditions of the approval imposed by the IRB or FDA

In addition, the monitor will verify that:

- The conditions for the study continue to be acceptable

- Accurate, complete and current records are maintained and required reports are written
- Any adverse effects are documented and reported to the sponsor and IRB as appropriate
- Source data is verified and corrections are made to any inconsistencies or missing data found
- Findings of non-compliance or required modifications are reviewed with the investigator and is presented in a written report or follow up letter
- A monitoring report is written at the end of each monitoring visit and/or the clinical study

15.5 Use of Information and Publication

All information, including but not limited to information regarding BeShape One TM or the sponsor's operation (e.g., patent application, manufacturing processes, basic scientific data, prior clinical data, and formulation information) supplied by the sponsor to the investigator and not previously published, and any data generated as a result of this study, are considered confidential and remains the sole property of the sponsor. The investigator agrees to maintain this information in confidence and use this information only to accomplish this study, and will not use it for other purposes without the sponsor's prior written consent.

The investigator understands that the information developed in the clinical study will be used by the sponsor in connection with the continued development of the BeShape One TM system, and thus may be disclosed as required to other clinical investigators or regulatory agencies. To permit the information derived from the clinical studies to be used, the investigator is obligated to provide the sponsor with all data obtained in the study.

The results of the study will be reported in a Clinical Study Report generated by the sponsor and will contain all data from all investigational sites. Any work created in connection with performance of the study and contained in the data that can benefit from copyright protection (except any publication by the investigator as provided for below) shall be the property of the sponsor as author and owner of copyright in such work.

The sponsor shall have the right to publish such data and information without approval from the investigator. If an investigator wishes to publish information from the study, a copy of the manuscript must be provided to the sponsor for review at least 30 days before submission for publication or presentation. Expedited reviews will be arranged for abstracts, poster presentations, or other materials. If requested by the sponsor in writing, the investigator will withhold such publication for up to an additional 90 days to allow for filing of a patent application. In the event that issues arise regarding scientific integrity or regulatory compliance, the sponsor will review these issues with the investigator. The sponsor will not mandate modifications to scientific content and does not have the right to suppress information. The investigator will recognize the integrity of a multicenter study by not publishing data derived from the individual site until the combined results from the

complete study have been published in full, within 12 months after conclusion, abandonment, or termination of the study publication. Authorship of publications resulting from this study will be based on generally accepted criteria for major medical journals.

15.6 Study Registration in a publicly accessible database

The description and information of the clinical study will be registered in a publicly accessible database prior to recruitment of the first subject and will be updated throughout the conduct of the study. Results will be entered at completion of the clinical study.