# A feasibility study addressing the frequency of Low Level Laser Therapy for reducing central adiposity and weight in overweight individuals.

NCT02877004

10/28/16

Currently in the United States about 97 million adults are overweight, accounting for about 33% of the American adult population[1]. Low level laser therapy (*LLLT*) is a new novel non-invasive procedure that removes excess fat without the negative side effects associated with surgical methods. *LLLT* also has the potential to enhance motivation for weight management as *LLLT* treatment can provide immediate feedback to the patient or study participant in the form of lost inches which can be seen by the individual. *LLLT* has been associated with reductions in waist circumference of 6-12 inches with 6 treatments.

Clinically, the LLLT treatments can vary from 6 to 28 treatments and a frequency of 1-3 times per week depending on the patients' preference and ability to pay. Our research team conducted a previous feasibility study of 45 overweight/obese subjects looking at the use of 12 LLLT treatments over the course of 12 weeks (one treatment per week) with the end goal of reducing central adiposity. In this prior study (IRB 14-002370), subjects were randomized to 1 of 3 conditions (LLLT, lorcaserin, and LLLT + lorcaserin). This study demonstrated feasibility by recruiting the goal of 45 obese subjects within 3 months. The subjects assigned to LLLT did not have any adverse events reported during the 6 months of the trial and although the sample size was too small for any significant findings, the LLLT did show a reduction in body circumference (2.3 to 4.0 cm reduction) and a reduction in weight (1 to 3.5 kg reduction). At this point, the question still remains on the ideal frequency of LLLT treatments which are needed to see a significant loss in weight and reduction in body circumference. Significant weight loss is defined as a reduction of 5% or more of the baseline weight.

For the purposes of this study we will define overweight as having a body mass index [BMI] 25-29.9. In this pilot study we will randomize 60 overweight individuals to one of three LLLT treatment schedules:

1. 12 treatments of LLLT - 3 times per week
2. 12 treatments of LLLT - 2 times per week
3. 12 treatments of LLLT - 1 time per week

The overarching purpose of this study is to obtain preliminary evidence regarding the most efficacious frequency of LLLT treatments to obtain at least a 5% weight loss and to produce reduction in body circumference.

Hypothesis: We hypothesize that an increase frequency of LLLT treatments will produce a greater weight loss and greater reduction in body circumference when compared to a less frequent schedule of LLLT:

**Group 1 weight loss > Group 2 weight loss > Group 3 weight loss**

**Group 1 reduction in body circumference > Group 2 reduction in body circumference > Group 3 reduction in body circumference**

Aims, purpose, or objectives:

1. To compare the % of weight loss and reduction in body circumference at the end of 4 weeks for overweight individuals undergoing LLLT treatments at different frequencies

## Study Design and Methods

**Methods:**

**Study Design -** This will be an open label clinical trial with all study participants receiving *LLLT*. We will obtain preliminary data on the efficacy of *LLLT* based on varying frequency of the *LLLT* treatments. We will focus this study on 60 overweight adults with a BMI of 25 to 29.9. We will assess changes in weight and waist circumference at end of treatment for group 1 (week 4) and group 2 (week 6) and group 3 (week 12). Participants will be randomized to receive *LLLT* treatments either 3 times a week for a duration of 4 weeks (group 1); 2 times a week for a duration of 6 weeks (group 2); or once a week for a duration of 12 weeks (group 3).

**Study Procedures:** We will use standardized procedures to ensure that uniform instructions are provided to all participants and that recruitment and screening result in the enrollment of appropriate study participants. All Study Case Report Forms are paper documents and also function as study source documents. The data will be entered into an online electronic data program (Redcap) by research staff within 7 days of the completed study visit. Study participant data on this system will be identified using unique subject IDs, not personal identifiers. This data entry system will provide immediate feedback on the majority of data integrity issues, including implausible entries, and checks of consistency between variables.

**Study Processes and Procedures**

*Intervention*

*LLLT:* Each LLLT device consists of a multiple-head low-level diode laser with 6 independent diode laser heads (**Figure 2**). Each diode emits 532 nm (green) laser light. In the active device (Erchonia1 LipoLaser, Erchonia Medical, Inc., McKinney, TX)[2] each diode generates a 17 mW output. The average number of treatments can vary, depending on the adipose make up on the patient.[3] In this trial*, subjects will undergo 12 treatments of LLLT at varying frequencies.*

The *Erchonia® Zerona™ 2.0 Laser* (which will be used in this study) has been approved by the FDA (K123237) as a non-invasive dermatological aesthetic treatment which can be used by individuals intending to reduce circumference of hips, waist, and thighs. Justification for the assertion of anticipated safety and effectiveness of the Erchonia® Zerona 6 Headed Scanner (EZ6) for application to reducing body circumference is found through several FDA clearances for Erchonia® Low Level Laser devices for body circumference reduction indications. For all of the 510(k) clearances, the assigned Product Code is OLI, defined as follows:

Figure 2. LLLT device - Zerona® by Erchonia

- ✓ *Device:* Fat reducing low level laser
- ✓ *Regulation Description:* Low level laser system for aesthetic use
- ✓ *Definition:* Non-invasive reduction in fat layer for body contouring
- ✓ *Technical Method:* Use of low level laser energy to create pores in adipocyte cells to release lipids (triglycerides)
- ✓ *Target Area*: Adipocyte cells within the subcutaneous fat layer of the body, this could include abdomen (waist), thighs and hips

Under 21 CFR 878,5400, the FDA identifies this generic type of device as: "A Low Level Laser System for Aesthetic Use is a device using low level laser energy for the disruption of adipocyte cells within the fat layer for the release of fat and lipids from these cells for non-invasive aesthetic use."

*The procedure administration protocol for each session is as follows:*

- The study participant is correctly fitted with the safety glasses.
- The participant lies comfortably flat on his or her back on the procedure table such that the front area of the subject's body is facing upwards.
- The Erchonia® Zerona 6 Headed Scanner (EZ6) diodes are positioned at a distance of 6 inches above the subject's lower and upper abdomen, stomach, centered along the body's midline (the "line" that vertically "dissects" the body into two equal halves).
- The Erchonia® Zerona 6 Headed Scanner (EZ6) is then activated for 30 minutes over the subject's anterior (frontal) region. Each scanner emits to the subject a laser beam of approximately 17 mW with a wavelength of 532 nm, and creates a spiraling circle pattern that is totally random and independent from the others. These patterns overlap each other to guarantee total coverage within the target area of approximately 80 in²/516 cm².
- The participant then turns over to lie flat on his or her stomach such that the posterior treatment area of the subject's body encompassing the region spanning from the participant's back down though the central body region is facing upwards.
- The Erchonia® Zerona 6 Headed Scanner (EZ6) diodes are positioned at a distance of 6 inches above the posterior treatment area, centered along the body's midline, the same as for the anterior region.
- The Erchonia® Zerona 6 Headed Scanner (EZ6) is then activated for 30 minutes over the subject's posterior region. Each scanner emits to the subject a laser beam of approximately 17 mW with a wavelength of 532 nm, and creates a spiraling circle pattern that is totally random and independent from the others. These patterns overlap each other to guarantee total coverage within the target area of approximately 80 in²/516 cm².
- The participant's safety glasses are removed and the procedure administration session is over.

The Erchonia expert trained the DOM CRO staff in-person on the use and maintenance of the LLLT on December 12, 2013 for a prior study utilizing LLLT. This training session has been documented. They will be available for on the spot questions and for any online retraining, as needed. The study coordinators will be under the direction of the nurse coordinator/supervisor (DFR).

## Subject Information

**Target accrual:** We plan to enroll and screen a maximum of 75 overweight individuals with a BMI of 25-29.9 kg/ $m^2$ in order to accrue 60 research participants.

**Subject population:** Participants will be recruited from the local community through radio, internet postings, Mayo Clinic physician referrals.

Based upon our recruitment data from recent weight loss studies and a wait list of participants who are interested in this treatment, we estimate recruiting 3-4 study participants per week. Those who meet study criteria will be invited to participate in this open label study. In this study, all 60 study participants will receive

LLLT treatments. Everyone will be in the study for 6 months, but will be in treatment for varying periods of time based on the randomization group they will be assigned:

1. 12 treatments of LLLT 3 times per week (M W F) for a duration of 4 weeks
2. 12 treatments of LLLT 2 times per week (T Th) for a duration of 6 weeks
3. 12 treatments of LLLT 1 time per week for a duration of 12 weeks

**Inclusion Criteria:** Potentially eligible subjects must:

1. be over 18 years of age;
2. have a body weight of greater than 50 kg (110 pounds);
3. have a BMI 25–29.9 $kg/m^2$ ;
4. be able to participate fully in all aspects of the study; and
5. have understood and signed study informed consent.

**Exclusion Criteria:** Subjects will be excluded if they:

1. have used weight loss medications or participated in a weight loss program within the past 30 days;
2. are currently taking supplements known to affect weight, such as *garcinia cambrogia*;
3. have had weight fluctuations of 20 pounds or more in the past 6 months (self-report);
4. have an implanted device (including pacemaker or lap band) in the targeted area of LLLT;
5. have a known active eating disorder;
6. have a known, active, untreated clinically significant psychiatric condition (alcohol or substance abuse, psychosis, bipolar disorder, or depression);
7. have used an investigational drug within 30 days of study enrollment;
8. are currently pregnant or lactating, or are of child-bearing potential or are likely to become pregnant during the medication phase and are unwilling to use a reliable form of contraception; Acceptable forms include:
    a. Hormonal methods, such as birth control pills, patches, injections, vaginal ring, or implants
    b. Barrier methods (such as a condom or diaphragm) used with a spermicide (a foam, cream, or gel that kills sperm)
    c. Intrauterine device (IUD)
    d. Total hysterectomy or tubal ligation
    e. Abstinence (no sex)
9. have a history of any major cardiovascular events including heart valve disease, cardiac arrhythmias, congestive heart failure, acute coronary syndrome, stroke, transient ischemic attack, or peripheral vascular disease;
10. have current uncontrolled hypertension (systolic > 160 mm Hg or diastolic > 95 mm Hg) documented on 2 separate occasions;
11. have clinically significant acute or chronic progressive or unstable neurologic, hepatic, renal, cardiovascular, lymphatic, respiratory, or metabolic disease (such as diabetes) or active cancer or are within 1 year of cancer remission;
12. surgical intervention for body sculpting/weight loss, such as liposuction, abdominoplasty, stomach stapling, lap band surgery, etc. within 12 months prior to enrollment.
13. medical, physical, or other contraindications for body sculpting/weight loss;
14. any medical condition known to affect weight levels and/or to cause bloating or swelling;
15. a diagnosis of, and/or taking medication for, irritable bowel syndrome;
16. active infection, wound or other external trauma to the areas to be treated with the laser;
17. known photosensitivity disorder;

18. current active cancer or currently receiving treatment for cancer; or
19. have a known history of any condition or factor judged by the investigator to preclude participation in the study or which might hinder adherence

**Will a Certificate of Confidentiality be obtained?** *No*.

## Research Activity

1. ☒ **Drug & Device**: Drugs for which an investigational new drug application is not required. Device for which (i) an investigational device exemption application is not required; or the medical device is cleared/approved for marketing and being used in accordance with its cleared/approved labeling. (Specify in the Methods section)

2. ☒ **Survey, Interview, Focus Group**: Research on individual or group characteristics or behavior, survey, interview, oral history, focus group, program evaluation, etc. (Specify in the Methods section)

## Data Analysis

Statistical Considerations

The primary aim of this study is to assess the feasibility and potential efficacy of using LLLT at varying frequencies to reduce central adiposity in overweight individuals.

The purpose of a phase II trial is to decide whether additional studies of the experimental regimen are warranted and to provide preliminary data for designing a larger phase III trial to confirm efficacy. Although there has been debate about the value of formal statistical comparisons in phase II trials, we agree with those who propose that formal comparisons are appropriate under the caveat that phase II studies are not expected to provide reliable definitive comparisons using a traditional two-sided type I error rate of 0.05.(references). For a randomized phase II trial, a one-sided test with a false-positive (type I error) rate of 0.20 is considered appropriate for the primary comparison to assess whether additional studies of the given regimen are warranted.

For the current study the primary endpoint is change in waist circumference (WC) from baseline. For the primary analysis, the change in WC from baseline to week 4 will be compared across frequency groups.

**Data Analysis Plan:**

Data related to subject recruitment will be summarized, including the frequency of calls and the reasons for failing screening criteria.

Baseline characteristics and treatment compliance of the enrolled participants will be presented overall and also separately for each of the treatment groups. In all cases, data will be summarized using mean ± SD for continuous variables and frequency percentages for nominal variables. Treatment adherence will be quantified for each individual by calculating the percentage of treatment sessions attended and the percentage of medication used. The percentage of subjects who discontinue study participation and the reasons for discontinuing study participation will be summarized. Changes in measures of central adiposity and weight from baseline will be summarized at each study visit. The primary outcome of interest is change in waist circumference from baseline to week 4. For the primary comparison, the group receiving one LLLT session per

week will be the control group and the groups receiving two and three sessions per week will be considered the experimental groups. The mean change from baseline WC for each of the experimental groups will be compared to control using the two-sample t-test. For these comparisons, a one-tailed p-value of 0.20 or less will be considered evidence suggesting that studies utilizing increased frequency of LLLT sessions are warranted.

**Sample-size justification:**
The primary endpoint for the current investigation is change in WC from baseline to week 4. The group having one LLLT session per week will be considered the control group. From our previous study, the mean ± SD change in WC from baseline in those receiving 1 LLLT session per week was -1.1±1.9 cm. In order to be considered meaningful, we would expect an increased frequency of LLLT sessions to result an additional reduction of approximately 1.0 cm. Under the assumption that the SD is 1.9cm, a sample-size of N=20 per group will provided statistical power (one-tailed, alpha=0.20) of approximately 80% to conclude that additional studies are warranted (i.e. detect a difference between groups of 1.0 cm). Therefore, a sample-size of N=20 per groups will be used for the present study.

## References

1. Ogden CL, Carroll MD. Prevalence of Overweight, Obesity, and Extreme Obesity Among Adults: United States, Trends 1960–1962 Through 2007–2008. *Health E-Stat* [Web Page]. 2010; http://www.cdc.gov/NCHS/data/hestat/obesity_adult_07_08/obesity_adult_07_08.pdf. Accessed 01 Nov 2011.
2. Erchonia Corporation. Zerona. [Web Page]. 2011; http://www.myzerona.com/professional. Accessed 01 Sept 2011.
3. Mulholland RS, Paul MD, Chalfoun C. Noninvasive body contouring with radiofrequency, ultrasound, cryolipolysis, and low-level laser therapy. *Clin Plast Surg.* 2011;38(3):503-520, vii-iii.