A feasibility study addressing the adjunct use of Low-Level Laser to Mayo Lifestyle Modification Education and Wellness Coaching for Reducing Central Adiposity and Fat Mass

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General Study Information

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Study Title: A feasibility study addressing the adjunct use of Low-Level Laser to Mayo Lifestyle Modification Education and Wellness Coaching for Reducing Central Adiposity and Fat Mass

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Research Question and Aims

Hypothesis: We hypothesize that the addition of Lifestyle Modifications as well as Wellness Coaching counseling during **LLLT** treatments targeting central adiposity body regions will produce a **greater fat mass loss** when compared to Lifestyle Modifications and Wellness Coaching alone:

GROUP 1		***GROUP 2***
Lifestyle Modifications		***Lifestyle Modifications***
+		+
Wellness Coaching	>	***Wellness Coaching***
+		+
LLLT		***Sham LLLT***

Aims, purpose, or objectives: The overarching purpose of this study is to obtain preliminary evidence regarding the efficacy of LLLT treatments for obtaining fat mass loss and to produce a reduction in waist circumference by week 6 (end of treatment).

Primary Aim:

To compare the amount of fat mass loss at the end of week 6 (end of LLLT treatment) for people who are overweight and obese who are receiving Wellness Coaching with lifestyle modifications, with and without adjunct LLLT.

Secondary Aim:

To compare the change in waist circumference from baseline, at the end of week 6 (end of LLLT treatment) for people who are overweight and obese who are receiving Wellness Coaching and lifestyle modification instruction, with and without adjunct LLLT.

Background: Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health, leading to reduced life expectancy and/or increased health problems[1], and results from an energy imbalance. In basic terms, *obesity* is defined as having more body fat than is considered healthy[2], which, in turn, is defined as a body mass index (weight (kg)/height $(m)^2$) of 30.0 or higher[3]. Currently in the United States, about 38% of the American adult population is considered obese[3-7], which translates to one in three Americans being obese.

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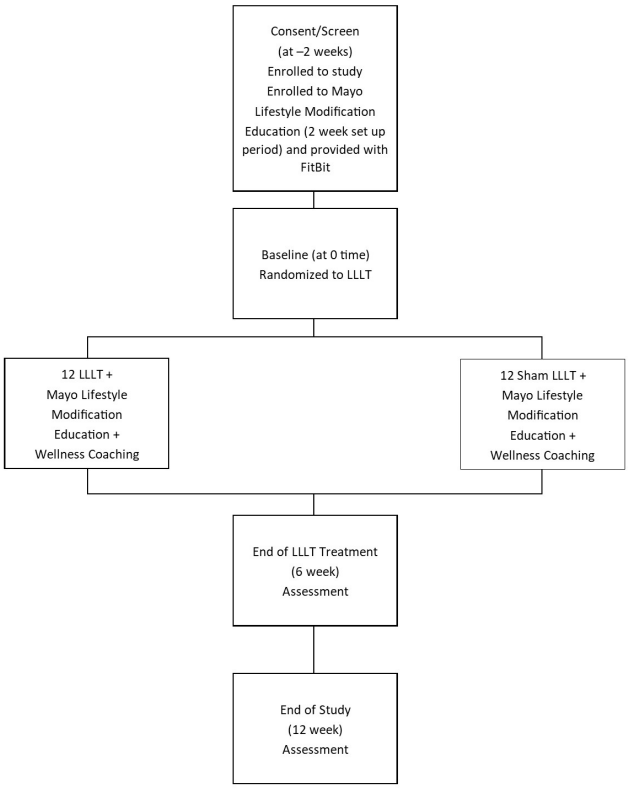
Low level laser therapy (LLLT) is a new novel non-invasive procedure that removes excess fat without the negative side effects associated with surgical methods. LLLT also has the potential to enhance motivation for weight management as LLLT treatment can provide immediate feedback to the patient or study participant in the form of lost inches which can be seen by the individual. LLLT has been associated with a reductions in waist circumference of 6 inches as reported in prior studies, with some noting more extensive reductions of up to 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). This 2014 study was followed by another study (IRB 16-004817) in which our study team compared different frequencies of administering 12 LLLT. The compared frequencies were 12 treatments administered once per week, twice per week or 3 times per week. This latter study found that 12 treatments delivered twice per week (for up to 6 weeks) was the most optimal[8] frequency when considering maintenance of the weight loss post treatment. Although weight loss and inches lost were significant with LLLT, a theory does exist that when LLLT is accompanied by lifestyle modification, including a reduction in dietary intake as well as an increase in caloric expenditure through moderate-intensity activity, the impact of the weight and inches lost will be greater. The overarching goal of this study is to test this hypothesis.

Figure 1 – Study Flow



For the purposes of this study, we will define overweight as having a body mass index [BMI] of 25-29.9 kg/m^2 and obesity as a BMI of 30-39.9 kg/m^2. In this pilot study we will randomize 60 overweight and obese individuals to one of two treatment arms:

- LLLT + Lifestyle Modifications and Wellness Coaching (GROUP 1),
- Sham LLLT + Lifestyle Modifications and Wellness Coaching (GROUP 2).

Study Design and Methods

Methods:

Study Design: This will be a randomized clinical trial. We will obtain preliminary data on the efficacy of LLLT as an adjunct to Lifestyle Modification and Wellness Coaching. We will focus this study on 60 overweight and obese adults with a BMI of 25 to 39.9. We will assess changes in weight, waist circumference, A1C and CRP at end of LLLT treatment (week 6) and end of Lifestyle Modification/Wellness Coaching intervention (week 12). Participants will be randomized to one of the following groups:

- LLLT biweekly for 6 weeks + Lifestyle Modification and Wellness Coaching (GROUP 1),
- Sham LLLT biweekly for 6 weeks + Lifestyle Modification and Wellness Coaching (GROUP 2).

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 will be administered online using REDCap and will also function as study source documents. 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 data integrity issues, including implausible entries, and checks of consistency between variables.

Study Process

Study Visit:

- Each visit will have a window from midpoint of prior visit to midpoint of latter visit.
- If a subject cannot reschedule their visit within the study visit window, that visit is categorized as "missed".
- A subject is allowed 3 consecutive missed visits before "drop" procedure is commenced.

Post Baseline, *data collection options* for all self-assessments (i.e. surveys and questionnaires):

- E-mailed via REDCap program one week prior to the visit. Subject will be asked to complete and submit back to the site prior to the visit.
- In person/on paper at the clinic visit, if the email data was not received by the site prior to the visit.

	Screening Phase		Treatment Phase						Post Treatment Follow-up	
	Pre-screen	Consent/Screen/ Baseline								
Visit No.	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**S**	**8**
Visit Type	**P**	**C**	**C**	**C**	**C**	**C**	**C**	**C**	**P**	**C**
Visit Week	**-2**	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**12**
Allowable window (in days)			**±14**	**±2**	**±2**	**±2**	**±2**	**±2**	**±3**	**±14**
Study Entry/Screening										
Informed Consent		X								
Inclusion/Exclusion	X	X								
Demographics/Weight Loss History		X								
Safety										
Adverse Events (5) & Concomitant Medications (6)		X	X	X	X	X	X		X	
Medical History & Urine Pregnancy Test		X								
Vitals (weight, height, Body Mass Scale, blood pressure, and pulse)		X	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]		X
Depression (PHQ2)		X				X[2]		X[3]		X
Blood specimens (A1C, Lipid Panel, Leptin, Adiponectin, CRP, IL-6, fasting insulin)		X						X		X
Surveys										
Body Image Questionnaire (BASS)		X				X[2]		X[3]		X
Body Appreciation Scale (BAS)		X				X[2]		X[3]		X
Perceived Stress Scale (PSS)		X				X[2]		X[3]		X
Quality of Life - LASA		X				X[2]		X[3]		X
Sleep Impact (ASCQ)		X				X[2]		X[3]		X
End of Study Interview (Was It Worth It – WIWI)										X
Intervention										
Low-Level Laser Therapy/Sham (7) – twice/week			X	X	X	X	X	X		
Lifestyle Modification Introduction and Enrollment		X								
Wellness Coaching Consult, goal setting		X			X			X		
Enrollment into Fitbit® & My Fitness Pal®		X								
Fitbit® and My Fitness Pal® Set up and tutorial for recording steps, activity, and water intake		X								
Fitbit® Data Download (8)			X	X	X	X	X	X		X
Outcome										
WMA, WC, BMI, WHR (4)		X	X[1]	X[1]	X[1]	X[1]	X[1]	X[3]		X
InBody Analysis (1) (2) (3) (4)		X	X	X	X	X	X	X		X
Check in on adherence to Lifestyle Modifications			X	X	X	X	X	X		

1. *Vitals will be collected once a week PRIOR to 2nd treatment of each week (Treatments 2, 4, 6, 8, and 10)*
2. *These assessments will be collected BEFORE last LLLT intervention of the week.*

3. *These assessments will be collected AFTER last LLLT intervention.*
4. *WMA, Weight Motivational Assessments; WC, waist circumference; BMI, body mass index; WHR, waist-to-hip ratio. In order to control for any variance in WC, BMI, or WHR, the visits will be at approximately same time of the day (± 2 hours). These measures will take place at each study visit (once a week during treatment phase).*
5. *Adverse events (AEs) will be collected at EVERY visit, referencing "since last visit".*
6. *Concomitant medication information will be collected at EVERY visit, referencing "since last visit".*
7. *TWICE a week for 6 weeks for a total of 12 treatments.*
8. *Download weekly data.*

Study Measures

*Safety Measures**:***

- Patient Health Questionnaire-2 (PHQ-2):[9,10] The PHQ-2, comprising the first 2 items of the PHQ-9 by asking about the degree to which an individual has experienced depressed mood and anhedonia over the prior two weeks. The scoring ranges from 0 to 6. A cut-off score of 3 as the optimal cut point for screening purposes and a determination will be made if the participant should be referred for mental health services (see DOM CRO Standard Crisis Policy in the DSMB section of the IRBe application).

- Pregnancy tests: A self-report of negative pregnancy status will be required at screen for all female participants who are of childbearing potential. In addition, a pregnancy test will be available at the patient's request during the study.

- InBody Measurements: The InBody bioelectrical impedance scale will measure the subject's weight, height, BMI, body composition analysis (total body water, proteins, minerals, and body fat mass), visceral fat area and lean balance (*http://www.e-inbody.com/global/product/InBody770.aspx*).

- Safety Phone Visit: Study team member will contact Subjects by phone 1 week after completion of their *Erchonia® EMERALD Laser* randomized treatment (LLLT or sham LLLT) (week 7).

- Adverse Events/Concomitant Medications: IRB policy will be adhered to for the collection and reporting of all Adverse Events and Concomitant medications as well as all adverse events determined to be Reportable Events and Serious Adverse Events as defined by the IRB and the FDA. These are standard safety collection measures which will be collected at every patient contact, by the coordinator. (*http://mayocontent.mayo.edu/irb/DOCMAN-0000182833?qt=reportable%20event*)

*Outcome Measures**:***

- Weight Motivation Assessments (MVA): Likert Scale to assess participants' motivation to reduce their weight (on a scale of 0 to 10, where 10 is the most motivated and 0 is not motivated at all), follow a healthy diet (0 to 10) and have a physically active lifestyle (0 to 10) will be assessed weekly during the study.
- Linear Analogue Self-Assessment (LASA):[11-13] A six-item measure of quality of life (QOL), in which QOL is conceptualized as a multidimensional construct with five domains (physical, functional, emotional, spiritual, and social). This data will be collected at screen (prior to any treatment), week 4, week 6, week 12 and at end of study (6 weeks post last treatment).

- Body Areas Satisfaction Scale (BASS): [14-16] 10 questions concerning self-perceived body image and the body satisfaction (excerpt from MBSRQ). The Multidimensional Body-Self Relations Questionnaire (MBSRQ) has been used to assess body image satisfaction. Respondents are asked how satisfied they are with 8 specific body areas using a 5-point Likert scale. It has a test-retest reliability of 0.81 and consistency of 0.88. This data will be collected at screen (prior to any treatment), week 4, week 6, week 12 and at end of study (6 weeks post last treatment).
- Body Appreciation Scale (BAS):[17] This is a 13-item validated questionnaire assessing positive body image. This data will be collected at screen (prior to any treatment), week 4, week 6, week 12 and at end of study (6 weeks post last treatment).
- Sleep Quality (*ASCQ-Me® v2.0 Sleep Impact - Short Form*[18]): is an effective instrument used to measure the impact sleep has on overall health in adults. The ASCQ-Me Sleep Impact SF is equivalent to the PROMIS Sleep Disturbance and Sleep-Related Impairment Surveys except the scoring is reversed.[18] The PROMIS surveys indicate greater symptom burden as the score goes higher and the ASCQ-ME survey indicates better health as the score goes up. The Sleep Impact Scale consists of 5-item, likert scale, validated, scoring system.[19] The 5 questions focus on experiences in the prior 7 days. Self-efficacy (*Short Form 4a – 4 items*)[20]: This PROMIS Self-efficacy Scale defines self-efficacy as confidence in one's ability to successfully perform specific tasks or behaviors. It assesses confidence in one's ability to successfully perform specific tasks or behaviors related to one's health in a variety of situations. Each item on the measure is rated on a 5-point scale (1=I am not at all confident; 2=I am a little confident; 3=I am somewhat confident; 4=I am quite confident; 5=I am very confident).This data will be collected at screen (prior to any treatment), week 4, week 6, week 12 and at end of study (6 weeks post last treatment).

- Perceived Stress Scale (PSS): The PSS is a 10-item Likert scale that measures global life stress by assessing the degree to which experiences are appraised as uncontrollable or unpredictable.[21] Scores can range from 0 to 40, with higher scores indicating greater perceived stress. Reliability is reported as 0.85, with Cronbach alphas ranging from 0.75-0.86. [22]
- Anthropomorphic Measurements: Measurements will be performed on all participants during all study clinic visits. BMI and WHR will be derived from measurement of weight, height, and waist and hip circumference. The measurements will be as follows: *Height* and *Weight* will be measured using the InBody standiometer scale. *Body Mass Index (BMI)* will be calculated by InBody. *Waist circumference* (WC) will be measured while participants are upright. A soft measuring tape will be placed in a horizontal plane at the level of the superior border of the iliac crest. The tape will be snug but not compressing the skin and parallel to the floor. The measurement will be made at the end of a normal expiration.
- Biomarkers: Levels of A1C, CRP, Lipid Panel, Leptin, CRP, IL-6, Adiponectin, fasting insulin will be collected at baseline, week 6 (end of treatment) and week 12 (end of study).
- Was it Worth it Questionnaire (WIWI)[23]: This a satisfaction survey will be administered to the participants at the end of the study, probing their satisfaction with the research study. These data could be used to assess the feasibility of the intervention by asking the patient if the entire research experience was worth it for them.

Adherence to Intervention:

- Diary to collect Calorie Intake and Water Intake: My Fitness Pal® will be utilized as an online diary log which the participants can use to record calorie and water intake. This program is linked to the FitBit® (see below). The study staff will educate and assist the participant in setting up a study ID, enrollment and use of both online apps for study purposes. Data from Diary collected on weekly basis.
- Steps: Fitbit® Data from these devices will be collected on weekly basis to download activity levels. A Fitbit® account will be created by each study participant with the help of the research coordinator to allow us to track activity level per week. A weekly report will be sent to their email and this will be logged into the database.
- Treatment Tracking: the study staff will log in the days and times each patient attended an LLLT intervention session during the clinical trial and record the self-report on the lifestyle modifications by the participant.

Intervention:

- Lifestyle Modifications: At Baseline, the study assistants will complete an additional brief (10-minute) individual behavioral intervention. Introduce and review the key tenets of lifestyle modification utilizing the "My Weight Solution©" manual and motivate the patient toward a steps goal using Wellness Coaching Approaches. Topics to be covered will include: motivational strategies, social support, goal setting strategies, nutritional recommendations and strategies for physical activity. A copy of "My Weight Solution©" will be given to the study participant to keep and to be used by the study participant at their convenience. The book chapters include: Introduction [Not just another diet, Getting started, Are you Ready]; Part 1: Lose It! [Add 5 Habits, Break 5 Habits, Adopt 5 Bonus Habits], Part 2: Live It! [Your Live It! Strategies, Strategy 1: Set Realistic Goals, Strategy 2: Follow the pyramid, Strategy 3: Burn calories by being active], Bonus section: How to stick with your commitment [Change Behaviors, Change Your Mind, Stay Connected, Overcome Challenges].
- Wellness Coaching: Study Staff, who are trained as Wellness Coaches (SF and SL) will introduce the patient to Lifestyle Modification approaches, and review and discuss the different chapters of the book "My Weight Solution©", at the baseline visit. Lifestyle modification will consist of caloric reduction of 500 -750 calories from current needs depending on BMI. Additionally, subjects will be advised to target 150 minutes of moderate intensity activity with the type of activity varying by patient's current degree of mobility. This visit will be approximately 20-30 minutes in duration. During each week the Wellness Coaches will meet with the participants for a short education session on another aspect of the lifestyle modifications utilizing "My Weight Solution©". Each of these follow up sessions can last anywhere from 10-15 minutes. During the first 6 weeks of study participation (during the LLLT/Sham LLLT treatments) the sessions will be individualized and in person.

Figure 2. LLLT device - Emerald® by Erchonia

- LLLT: In this trial, subjects randomized to receive LLLT or sham LLLT with Lifestyle Modification/Wellness Coaching will undergo 12 treatments – twice per week for 6 weeks.

- Each LLLT device consists of a multiple-head low-level diode laser with 10 independent Class 2 Line Generating Diode laser heads (**Figure 2**). This process produces a line 7 mm wide with a length of approx. 152 mm at 6 in (15.2 cm) away (rounded up to .0001 joules per cm^2 / second). With the treatment time being 30 minutes, the total fluence of all lasers is 288J and the total treatment area of all lasers is 5161.28cm^2.
- The Erchonia® Emerald emits a 532-nanometer (nm) wavelength with a tolerance of ±10 nmr, from each of the ten specially created and patented electronic diodes. In the active device (Erchonia Emerald Laser, Erchonia Medical, Inc., Melbourne, FL)[24] each diode generates a 16 mW ± 2mW output. The average number of treatments can vary, depending on the adipose make up on the patient.[25]
- *Erchonia® EMERALD Laser (*which will be used in this study) has been approved by the FDA (K192544) on January 13, 2020, 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® Emerald 10 Headed Scanner 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:
    - *Device:* Fat reducing low level laser
    - *Regulation Description:* Low level laser system for aesthetic use (878.5400)
    - *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 the lipids.
    - *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 study team will register the subject in the redcap database and once registered, the randomization program within the redcap patient record will identify the subject as being enrolled in Group 1 (LLLT) or Group 2 (Sham LLLT). The study team will then flip a switch on the LLLT machine to A or B depending on the group assigned and then follow the procedure administration protocol for the LLLT for each session (note, the same process is followed regardless of the group assigned to patient – after the switch is placed in the correct setting):

- The study participant is correctly fitted with the safety glasses (see manual for specifics of 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® Emerald 10 Headed Scanner diodes are positioned within 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® Emerald 10 Headed Scanner is then activated for 15 minutes over the subject's ***anterior*** (frontal) region. Each scanner emits to the subject a laser beam of approximately 16 mW ± 2mW 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 in^2/516 cm^2.
- 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® Emerald 10 Headed Scanner diodes are positioned at a distance of approximately 6 inches above the posterior treatment area, centered along the body's midline, the same as for the anterior region.
- The Erchonia® Emerald 10 Headed Scanner is then activated for 15 minutes over the subject's ***posterior*** (back) region. Each scanner emits to the subject a laser beam of approximately 16 mW ± 2mW 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 in^2/516 cm^2.
- The participant's safety glasses are removed and the procedure administration session is over.

The Erchonia experts (Steve Shanks and Travis Sammons) trained the study staff in-person on the use and maintenance of the LLLT on March 18, 2020. This training session has been documented. A refresher training zoom session is scheduled to take place two weeks prior to study start up. In addition, 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 study lead (SF).

Tracking Vitals:

Fitbit Tracker:

Participants will be asked to wear their Fitbit® 24/7 except during a time of recharging. Fitbit® Data will be collected weekly during intervention by the study team and from participants Fitbit® app that has been downloaded on their personal electronic device. The data collected will include Heart Rate, steps, water intake, and sleep quality. A Fitbit® account will be created by each study participant with the help of the research coordinator to allow us to track study participation. Information collected from the Fitbit® app will be logged into the database. This approach for working with the Fitbit has been successfully used in the past by Mayo investigators.

Participant Retention: All participants will also be provided with parking vouchers if they park in a Mayo parking lot (Damon or Graham). Each visit is estimated to be up to 2 hours. The cost of the vouchers can as much as $72 per person based on the number of study visits attended (14 in person visits, 2 hours each, $3/hour). This breaks down to a consent/baseline visit, 2 visit per week for 6 weeks during treatment and one final study visit thereafter (N=14). At the end of the study, participants that complete the study will be allowed to keep the Fitbit® for their continued use.

Subject Information

Target accrual: We plan to enroll and screen up to 80 people with a BMI of 25-39.9 kg/ m^2 in order to accrue 60 research participants.

Subject population: Participants will be recruited from the local community through internet postings, Mayo Clinic physician referrals, and word of mouth.

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 on average 3-4 study participants per week. Those who meet study criteria will be invited to participate in this study. In this study, all 60 study participants will receive some form of treatment and be in the study for 3 months. The following is a listing of interventions each participant will receive and the LLLT/sham LLLT aspect is based on the randomization group assigned:

1. 12 individual treatments of LLLT or sham LLLT (twice per week for 30 min each), while also utilizing Lifestyle Modification/Wellness Coaching.
2. Weekly sessions Lifestyle Modification discussion during the 6 weeks of individual treatments.
3. Three Goal setting discussions with Mayo Trained Wellness coaches during 6 weeks of treatments.

Inclusion Criteria: Potentially eligible subjects must:

1. be 18 years of age or older.
2. have a BMI 25–39.9 kg/m^2.
3. be able to participate fully in all aspects of the study; and
4. 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 medications or supplements known to affect weight, such as insulin or sulfonylurea, prednisone or *garcinia cambrogia*.
3. have had weight fluctuations of 5 pounds or more in the past month.
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. Reports being currently pregnant, lactating, or are of child-bearing potential or are likely to become pregnant during the LLLT treatment 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, ongoing angina, 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 uncontrolled diabetes type 2) 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.

Biospecimens

Collection of blood samples.

a. **From healthy, non-pregnant, adult subjects who weigh at least 110 pounds**. For a minimal risk application, the amount of blood drawn from these subjects may not exceed 550ml in an 8-week period and collection may not occur more frequently than 2 times per week.

   Volume per blood draw: 20 ml (total of 40 ml in the first 6 weeks (2 draws) and 20 ml at week 12)

   Frequency of blood draw -- 3 (time 0, week 6 and week 12)

Review of medical records, images, specimens

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.

Examples

- The study plans to conduct a retrospective chart review (study entry criteria) and ask subjects to complete study specific questionnaires.
- The study plans to include subjects previously diagnosed with a specific disease and add newly diagnosed subjects in the future.

Data Analysis

Statistical Considerations

The aim of this study is to assess the feasibility and potential efficacy of using LLLT combined with Lifestyle Modification/Wellness Coaching to reduce fat mass and WC in people with obesity or overweight.

The purpose is to decide whether additional studies of the experimental regimen are warranted and to provide preliminary data for designing a larger 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. Nonetheless, for the present study, a two-sided test with a false-positive (type I error) rate of 0.05 will be used for the primary comparison.

The primary endpoint of the current study is the change in fat mass from baseline. For the primary analysis, the change in WC and fat mass from baseline to week 6 will be compared between groups.

Data Analysis Plan:

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

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 person by calculating the percentage of treatment sessions attended. 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 the change in fat mass from baseline to week 6. For the primary analysis, the change in fat mass from baseline to week 6 will be compared between treatment groups using analysis of covariance (ANCOVA) with the baseline value included as the covariate. For this analysis, a two-tailed p-value of 0.05 will be considered statistically significant. Similar analyses will be performed for all secondary outcomes. In all cases, findings will be summarized by presenting the point estimate and 95% confidence interval for the difference between treatment groups.

Sample-size Justification:

From our pilot study, the mean ± standard deviation (SD) body fat mass change from baseline to 6 weeks was -1.1±1.6 kg for patients who received LLLT 2 times per week for 6 weeks. Under the assumption that the standard deviation is 1.6 kg, a sample size of N=30 per group will provide statistical power (two-tailed, alpha=0.05) of 75% to detect a difference of 1.1 kg for the comparison of LT vs. sham. Therefore, a total sample size of N=60 (N=30 per group) is proposed.

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