Independent Evaluation of Low-Level Laser Therapy at 635 nm for Non-Invasive Body Contouring of the Waist, Hips, and Thighs

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Introduction: The non-invasive body-contouring segment continues to exhibit uninhibited growth, a trend that has provoked the emergence of numerous body-contouring devices. One particular device, low-level laser therapy at 635 nm (LLLT-635), has exhibited promising clinical results. We performed an independent, physician-led trial to evaluate the utility of LLLT-635 nm for non-invasive body contouring of the waist, hips, and thighs.
Methods: Eighty-six participants were retrospectively assessed at an individual clinic in the United States. A multi-head laser device was administered every-other-day for 2 weeks. Each treatment consisted of 20 minutes of anterior and posterior treatment. Patients received concurrent treatment of the waist, hips, and bilateral thighs. Circumferential measurements were evaluated at baseline and one week following the 2-week treatment administration phase.
Results: Compared with baseline, a statistically significant 2.99 in. (7.59 cm) mean loss was observed at the post-procedure evaluation point ($P < 0.0001$). When analyzed individually, the waist, hips, and thighs each reported a statistically significant reduction of -1.12, -0.769, and -1.17, respectively. Furthermore, linear regression analysis revealed a weak linear dependence ($r = 0.179$) between the reported weight and circumference change.
Conclusion: These data further validate the clinical efficacy and safety of LLLT at 635 nm. Lasers Surg. Med. 45:1–7, 2013. © 2013 Wiley Periodicals, Inc.

Key words: non-invasive body contouring; low-level laser therapy; photochemistry; subcutaneous adipose; adipocyte; photobiomodulation

INTRODUCTION

Current non-invasive body-contouring devices have helped foster the growth of aesthetic medicine's non-invasive segment, as evidenced by a 20% increase in the total number of non-invasive tightening procedures, which includes body-contouring devices, performed from 2010 to 2011 [1]. One technology that has arguably contributed to this growth is low-level laser therapy. To date, the most studied low-level laser treatment for non-invasive body contouring uses a monochromatic 635 nm wavelength with an estimated output dosage of 1.0 J/cm^2 [2–19]. Studies have delineated these specific output parameters—when applied to adipocytes—activate intracellular secondary cascades causing the formation of transitory pores, or transmembrane openings, within the adipocyte membrane [2–9]. Newly formed pores increase membrane permeability and engender the release of stored intracellular lipids—primarily as triglycerides [2–9]. As a result, hypertrophic adipocytes collapse. This basic outcome has fostered the use of LLLT-635 for non-invasive body contouring.

LLLT-635 nm subtle effect on adipocyte structure derives from a photochemical mechanism [12–16]. Photochemistry is a scientific discipline that applies specific patterns of light energy to affect intracellular biochemical cascades in a non-destructive manner [20]. To activate intracellular cascades, photoreceptors, which are chemical structures capable of absorbing monochromatic light, must be present to absorb the applied light energy [21]. An important photoreceptor believed to incite many of the reported clinical outcomes is cytochrome *c* oxidase (CCO) [22–30]. CCO is the terminal enzyme of the respiratory chain responsible for establishing the electrochemical gradient required for adenosine triphosphate (ATP) synthesis [31]. Laser therapy excites CCO, which, in turn, accelerates electron transport upregulating ATP synthesis and affecting the cell's bioenergetics [32]. Upregulating cell bioenergetics initiates the secondary messenger system sending an amplifying signal that diffuses throughout the cell to influence cell activity. The subtle effect laser therapy has on the secondary messenger system shares similarities with agonist drugs. Light energy, like a drug agonist, activates cell signal transduction by, first, stimulating a specific receptor; second, triggering a secondary

signal that affects secondary cascades and overall cell physiology. Believed to activate signal transduction within adipocytes, LLLT-635 nm collapses hypertrophic adipocytes by exerting a subtle mechanism in a non-destructive, non-thermal manner.

Numerous studies have evinced the photochemical mechanism exerted by LLLT-635 nm to modulate hypertrophic adipocytes; this includes two placebo-controlled, randomized, double-blinded, multi-centered clinical studies [12–16]. Jackson et al. [12] reported a combined circumferential loss of 3.5 in. (8.9 cm) for the waist, hips, and thighs after 2 weeks. Nestor et al. [13] treated upper extremities with LLLT-635 nm and reported a combined loss of 3.7 cm after 2 weeks. Additionally, a retrospective study evaluated 689 subjects and demonstrated a total combined loss of 3.21 in. (8.15 cm) after 2 weeks [14]. Accordingly, these studies have demonstrated the clinical utility of LLLT-635 nm.

Regardless of the total number of studies completed, further clinical validation is an essential tenet of evidence-based medicine. To further validate the utility of LLLT-635 nm, or any non-invasive body-contouring device for that matter, physician-directed studies must be performed as they provide an unbiased analysis. Accordingly, we performed an independent, retrospective investigation to examine the objective findings of 86 subjects who underwent LLLT-635 nm for non-invasive body contouring of the waist, hips, and bilateral thighs (WHT).

METHODS

Eighty-six participants were retrospectively assessed at an individual clinic in the United States. All participants were deemed eligible following the completion of a basic medical history questionnaire. Participants were excluded if they presented with one of the following comorbidities: active cancer or within one year remission, severe progressive cardiovascular disease (i.e., congestive heart failure and cardiac arrhythmias), renal failure, liver failure, active infection, pregnant or breast feeding, serious mental illness (dementia or schizophrenia), and uncontrolled diabetes type I and II. The inclusion/exclusion criteria were selected to restrict the treatment of subjects with chronic, progressive disorders or conditions that may affect their basal metabolic rates.

All participants were not recruited; they actively sought body-contouring services and responded to marketing advertisement that discussed the services offered at the clinic. All subjects were informed that the treatment device was cleared by the Food and Drug Administration (FDA) for non-invasive body contouring of the waist, hips, and thighs, and signed an informed consent form that obtained permission to disseminate aggregated clinical data and images for scientific purposes only. Subjects were not offered any financial compensation and all participants were required to pay for the treatment. Additionally, the provider purchased the device used in the study and was not provided any financial compensation to conduct the study.

Randomization and Blinding

The clinical study was a retrospective, non-randomized, non-controlled single-site study. All 86 participants received concurrent treatment of the waist, hips, and thighs.

INTERVENTION

All subjects received treatment with a multiple head low-level diode laser consisting of five independent diode laser heads with each emitting a 635 nm wavelength with each diode producing an output intensity of 17.5 mW (The Erchonia® Zerona Laser, McKinney, TX).

Study Design

Prior to the treatment administration phase, all subjects had their baseline waist, hip, and individual thigh circumference recorded. To aggregate precise and accurate measurements, patients stood adjacent to a height chart to ascertain the exact position of the greatest subcutaneous fat pocket for the waist, hips, and individual thighs—in lieu of using anatomical landmarks (i.e., iliac crest, navel, or pubis). Subject tissue was palpated to denote areas of greatest subcutaneous fat accumulation, which was then, documented according to its position on the height chart. Accordingly, when patients assumed the same anatomical position adjacent to the height chart the greatest point of subcutaneous fatty material is documented directly, rather than, measuring from another anatomical region with an unfixed ruler. This method seemed to have greater reproducibility than attempting to identify a measurement point and defining its position in reference to an anatomical demarcation like the iliac crest or navel. Additionally, the natural curvature of the body could distort the measurement between the region of greatest subcutaneous fat and local anatomical feature. Once the measurement points were identified, a self-adhering tape measure was placed around the patient at the exact point identified on the height chart; the tape measure was activated and the circumferential measurement for each anatomical area was recorded. A self-adhering tape was used to mitigate the risk of inconsistent pressure applied when obtaining subject circumference. Participant circumference was measured at two different times: pre-procedure and 1-week post-procedure. The same clinic representative collected all measurements. Forty-two participants had a separate measurement point reported across their mid-abdomen, waist, hips, and thighs (MWHT). In addition to the circumferential measurements, pre-procedure and post-procedure weights were also recorded.

The treatment administration phase commenced 1-week after the initial patient consultation. Prior to the first treatment, patients were asked to consume 2.0 L of water per day to maintain proper hydration. Additionally, patients were provided and asked to consume supplements: 100 mg of niacin, 100 mg of niacinamide, 100 mg of L-carnitine, 880 mg of omega-3 fish oil, 60 mg of ginkgo biloba, and 200 mg of decaffeinated green tea extract.

The treatment administration phase consisted of six total laser treatments evenly spaced across 2 weeks: Monday, Wednesday, and Friday. Each treatment consisted of 20 minutes of anterior stimulation and 20 minutes of posterior stimulation.

The device was positioned over the patient's waist, hips, and thighs. The center diode was positioned above the greatest fatty accumulation positioned along the patient's midline: either below or above the navel. Two diodes were positioned above the left and right lateral waist subcutaneous fat pockets. Finally, two diodes were positioned above the left and right lateral thighs and hips. Each diode was positioned in a manner that resulted in the formation of a 3.0 in. line-generated beam, generating an output intensity of $\sim$0.95 J/cm^2.

Statistical Analysis

A paired t-test compared the two independent group means. Additionally, a repeated-measures ANOVA was performed to evaluate the combined WHT pre-procedure and post-procedure mean values. A non-parametric histogram was used to estimate the probability of distribution for the WHT mean difference. Finally, a scatterplot (linear regression) evaluated the linear dependence between weight and total WHT circumference loss.

RESULTS

Comparison of the two independent group means for the continuous variable of mean change in total combined circumference for WHT was -2.99 in. (or -7.59 cm) (Table 1).

The estimated probability distribution, which is the probability that a clinical observation takes a particular value, for the mean change in total combined circumference for WHT exhibited the greatest probability density between -4.0 and -2.0 in. (Fig. 1).

Compared with baseline, a statistically significant mean change for the independent waist, hips, and thigh variables was observed (Table 2).

Compared with baseline, the mean change in patient weight was—1.24 lb (2-tailed $P < 0.0001$). Comparison of the independent mean weight change and the independent WHT mean circumferential change reported a correlation coefficient of 0.179, which indicates the linear dependence between the two variables is weak (Fig. 2). The measure of the shared variance (r^2) was 0.032, which demonstrates that body weight accounts for 3.2% of the variance in the change in body circumferential measurement. The reported slope of 0.15 indicates the average change in circumference (inches) is 0.15 in. per each 1.0 lb change in patient body weight.
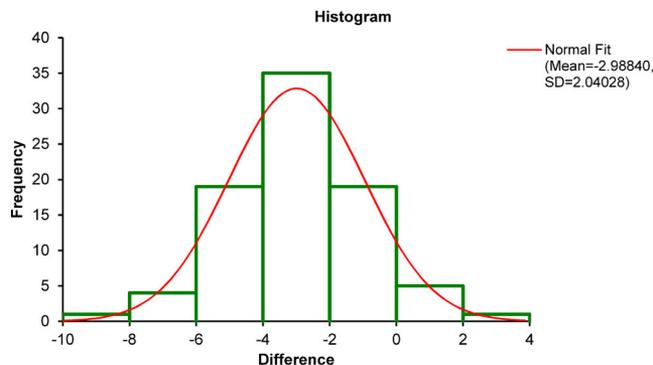

Fig. 1. Probability distribution for the mean change in total combined circumference for WHT.

For 42 subjects, an additional abdominal circumferential measurement was recorded across the mid-abdomen, and when this point was combined with the total circumferential mean change of the WHT, the total combined circumferential mean change was a 4.42 in. (or 11.23 cm) (Table 3).

DISCUSSION

These data further substantiate the preceding clinical reports that have examined the efficacy of LLLT for non-invasive body contouring, and with no adverse events reported, this trial also corroborates the safety of this procedure. Furthermore, since all preceding *in vivo* studies have reported a total mean circumferential change for single points collected across the WHT, our study—with the additional measurement point collected across the mid-abdomen—has reported the greatest total mean WHT circumferential loss of 4.42 in. (or 11.23 cm). The addition of a fourth measurement point reflected the design of the application device. The study device administers a line-generated laser beam that rotates, and as a result, treats a much larger area outside of a single point. Therefore, we randomly selected a small portion of the population to assess an additional measurement point to elucidate its clinical relevance. Accordingly, the circumferential reduction reported in previous studies may not accurately quantify the total inch loss produced by LLLT-635 nm. Nevertheless, with only 42 of the 85 subjects reporting additional measurement point data, the total combined mean change for this sub-population is an inchoate observation. Additionally, there are inherent limitations in retrospective studies; this includes the lack of a control population. However, the purpose of a retrospective study is not elucidating the efficacy and

TABLE 1. Mean Total Circumference Change for WHT ($n = 84$)

	Mean (ins.)				
	Pre-procedure	Post-procedure	Difference	2-Tailed P	Pr $> |t|$
WHT	123.38	120.39	2.99	$P < 0.0001$	<0.0001
Standard deviation	12.03	11.89	2.04		

TABLE 2. Mean Circumference Change for Individual Anatomical Regions ($n = 84$)

	Mean (ins.)			
	Pre-procedure	Post-procedure	Difference	2-Tailed P
Waist only	37.28	36.16	−1.12	$P < 0.0001$
Standard deviation	4.97	4.9355	1.11	
Flanks only	40.955	40.186	−0.769	$P < 0.0001$
Standard deviation	4.156	4.420	1.051	
Thighs only (left + right)	45.28	44.11	−1.17	$P < 0.0001$
Standard deviation	4.97	4.44	1.42	

safety of a therapy: that is the responsibility of a randomized, controlled study. Instead, retrospective studies ascertain the reproducibility of results outside of a clinically controlled environment. Nestor et al. [13] and Jackson et al. [12] completed randomized, controlled studies absent of lifestyle modifications; these studies substantiated the utility of LLLT-635 nm. Accordingly, our study evaluated the reproducibility of their reported outcomes within a broader, indefinite patient base. An additional limitation was our use of supplementation, which introduces a confounding variable. Jackson et al. [14] described the use of supplements as a means to equate a multifarious population that may possess varying degrees of nutritional deficiencies. In fact, studies have reported nutritional deficiencies increase the likelihood of being overweight

and obese by 80% [33,34]. Nevertheless, the studies completed by Nestor et al. [13] and Jackson et al. [12] reported statistically significant circumferential changes without the use of supplements. Accordingly, the role supplements play in facilitating lipid metabolism remains elusive. And finally, both the Nestor et al. [13] and Jackson et al. [12] studies reported significant differences concerning subjective evidence, with more test subjects generally "satisfied" or "very satisfied" with their results. Satisfaction data were not collected in this study, but future studies should combine both objective and subjective data to better appreciate the overall clinical utility of a body-contouring application.

An important parameter assessed was the correlation between weight change and the observed circumferential
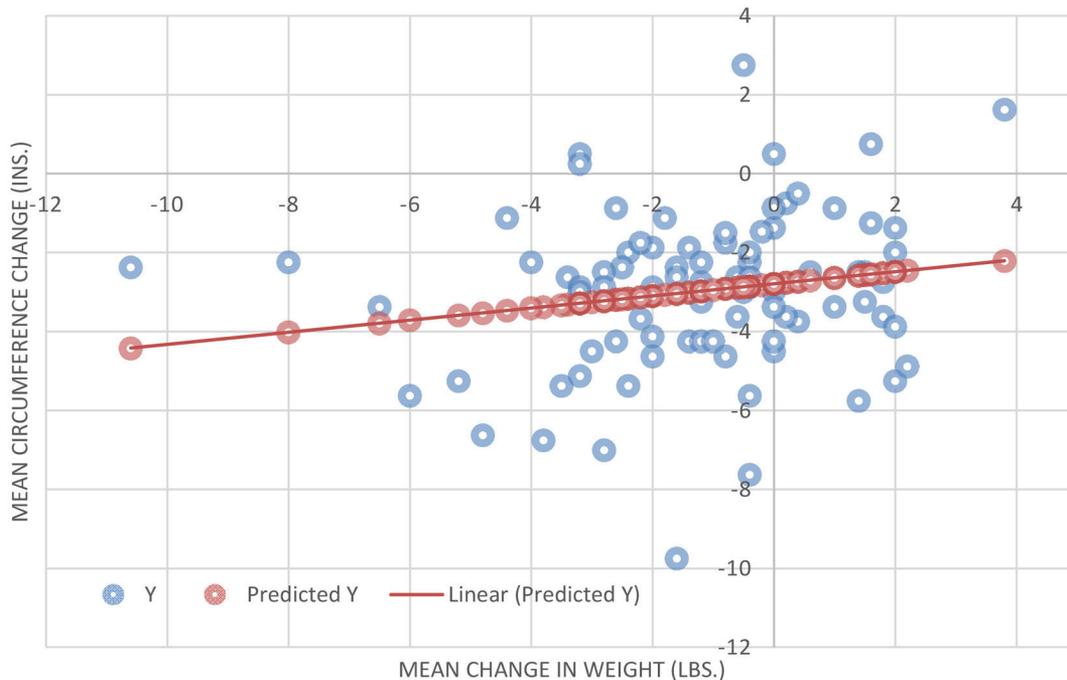

Fig. 2. Comparison of the independent mean weight change and the independent WHT mean circumferential change. Blue data points indicate individual subject reported mean circumference and weight change. Red data points represent predicted linear dependence.

TABLE 3. Circumferential Mean Change for MWHT Combined ($n = 42$)

	Mean (ins.)			
	Pre-procedure	Post-procedure	Difference	2-Tailed P
MWHT	161.02	156.59	4.42	$P < 0.0001$
Standard deviation	17.35	16.90	2.12	

change. A marked weight loss, inherently, may promote a marginal circumference loss. Valsamakis et al. [35] treated patients for weight loss with Sibutramine, an appetite suppressant, for 6 months and reported a loss of 7.1 kg (15.65 lb) and a 4.5 cm waist circumference reduction. However, the displacement of only lipid material, which accounts for 95% of adipocyte volume, would generate a larger volume reduction than weight reduction. This occurs because lipids purport approximately 56–80% of adipocyte weight, but 95% of adipocyte volume [36–40]. In turn, lipid displacement, for non-invasive body-contouring procedures, would disproportionately reduce volume. Accordingly, circumference loss should have a weak linear dependence with weight change.

Moreover, previous studies have reported adipocytes remain viable following treatment with LLLT-635 nm, and therefore, extraneous material contributing to weight—protein and water—would remain present. Therefore, substantial weight change could indicate confounding variables contributed to the reported circumference reduction. For most studies, monitoring weight's potential influence on the reported circumference reduction commonly includes reporting the mean weight change. However, this statistical model is not the ideal approach. For instance, the mean represents an average of all observed data points; therefore, errant points could inflate or conflate the mean misrepresenting the study population [41]. Instead, the preferred model is a linear regression that examines the linear dependence (or relationship) between weight and circumference change. A linear regression model plots a data point representing a subject's observed mean weight and circumference change. When data for the entire study population is plotted, a predicted linear trend delineates the relationship between the two variables (weight and circumference). For instance, if progressive weight loss corresponded with a proportional circumferential loss, the predicted linear trend would illustrate this trend with a steeper linear slope. The relationship between variables, also referred to as linear dependence, is determined by evaluating the correlation coefficient (r), which quantifies the relationship strength. The relationship between variables, also referred to as linear dependence, is determined by evaluating the correlation coefficient (r), which quantifies the relationship strength. The correlation coefficient ranges from -1 to 1, and the closer to -1 or 1, the stronger the relationship between two variables [41]. We reported a weak linear dependence ($r = 0.179$) between weight and circumferential change, which indicates

weight's infinitesimal effect on the circumferential loss shown. Disparately, the reported mean weight change of -1.24 lb was statistically significant, and therefore, without the linear regression model, could be misinterpreted as having influenced the results. Accordingly, linear regression data evidenced the limitations of reporting mean weight change to ascertain weight's role in patient circumference reduction; it also substantiated LLLT-635 nm, and not weight change, induced circumference reduction.

Although Jackson et al. [12] did not perform a linear regression to assess the linear dependence between weight and circumference change, they did restrict lifestyle adjustments and the use of ancillary therapies. Study protocol required all subjects record all lifestyle aberrations, and if a patient reported aberrant behavior, they were to be excused from the study. Both study groups—active and sham—were required to complete a daily lifestyle journal. From the placebo-controlled, randomized design to the dietary restrictions, Jackson et al. [12] made important steps to eliminate confounding variables.

Another important aspect of LLLT-635 has been the absence of reported adverse events. The absence of adverse events derives from LLLT-635 nm use of a photochemical pathway, and therefore, relies on a subtle therapeutic mechanism. Numerous peer-reviewed publications elucidate the core tenets of photochemistry [20–32]. Studies have demonstrated the photochemical mechanism stems from activating endogenous photoabsorbing structures within cells. These endogenous structures include porphyrins, cytochromes, flavoproteins, and many more [21,32]. Light-induced activation of the endogenous photoreceptors initiates the secondary messenger system, which, in turn, modulates cell physiology.

Jackson et al. [14] postulated that LLLT-635 nm activates CCO increasing ROS production. A consequence of increased ROS is lipid peroxidation, which is the deprotonation of the bilipid membrane resulting in the formation of transitory pores. However, alternative photoabsorbing structures—like nicotinamide adenine dinucleotide oxidase (NOX)—have been shown to respond to discrete parameters of light energy and may also be stimulated and disrupt the adipocyte membrane [42,43]. Specifically, NOX produces superoxide radicals mainly for destruction of foreign pathogens in phagocytic cells [44,45]. Activation of NOX with LLLT-635 nm could elevate intracellular superoxide levels initiating lipid peroxidation. Nevertheless, the exact mechanism of LLLT-635 nm remains

enigmatic, but numerous studies demonstrate the utility of this body-contouring application. Finally, Jackson et al. [14] proposed a pathway liberated lipids endure once liberated. They described triglyceride catabolism within lymph nodes, catalyzed by lysosomal acid lipase, and transportation of remnant free fatty acids to numerous tissues for further degradation via beta-oxidation, although the exact pathway remains elusive [14].

CONCLUSION

Histological and clinical data have substantiated LLLT-635 nm mechanism and efficacy for non-invasive body contouring of the waist, hips, and thighs. This independent, clinician-led study provided an unbiased assessment of LLLT-635 nm for non-invasive body contouring of the waist, hips, and thighs. Additionally, we provided empirical evidence that LLLT-635 nm produces statistically significant circumferential changes in 2 weeks without inducing an adverse event. However, the aggregate data in this study supports the previously published controlled studies assessing LLLT-635 nm for body contouring. Additionally, future physician-led studies should design controlled studies for a more rigorous evaluation.

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