Noninvasive Body Contouring with Radiofrequency, Ultrasound, Cryolipolysis, and Low-Level Laser Therapy

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KEYWORDS
- Body contouring
- Noninvasive body contouring
- Nonsurgical liposuction

Key Points
- Discuss current noninvasive body-contouring modalities, including suction massage devices, radiofrequency energy, high-frequency focused ultrasound, cryolipolysis, and low-level light laser therapy devices.
- Discuss imminent technologies awaiting approval by the Food and Drug Administration.
- Review the basic science and clinical effects behind each of these existing and emerging technologies.
- Address patient selection and clinical applications of each modality.
- Discuss the applicability and economics of providing noninvasive lipolysis services in office.

Low-Level Laser Therapy (Zerona)

Although lasers are often used in various aspects of medicine with success, their role in lipolysis is only starting to be delineated. Low-level laser therapy (LLLT) is defined as treatment with a dose rate that causes no immediate detectable temperature rise of the treated tissue and no macroscopically visible changes in tissue structure. Laser dosage is a magnitude used to define the laser beam energy applied to the tissue. Units are expressed as joules per centimeter squared, and the dosage is calculated as the laser power measured in milliwatts, multiplied by treatment time in seconds, and divided by the area of the laser spot directed toward the tissue.

The Zerona (Erchonia Medical) is a low-level laser device emitting a wavelength at 635 nm with an output power that distinguishes Zerona as a class IIIB laser. In recent years, LLLT has emerged as an efficacious adjunct therapy for numerous cosmetic procedures, including breast
augmentation and lipoplasty. However, the completion of numerous histologic investigations and a placebo-controlled, randomized, double-blind, multicenter study resulted in Zerona emerging, on its own, as a viable, independent, therapeutic strategy for the circumferential reduction of the waist, hips, and thighs.

The histologic and basic science research behind LLLT is very solid, perhaps more so than most technologies in the noninvasive body-contouring market. Multiple histologic examinations were performed to assess how laser light, with well-defined parameters, was able to modulate adipocyte function. Neira and colleagues \(^{49}\) in 2002 reported on the effect of low-level laser energy on adipose tissue, demonstrating that a 6-minute exposure of 635-nm 10-mW laser diode energy created a 99% release of fat from adipose tissue taken from abdominoplasty samples. These samples were evaluated by transmission electron microscopy after irradiation, which revealed a transitory pore in the cell membrane opening, which thereby permitted the fat content to leak out of the cell into the interstitium. The laser does not destroy or lyse the adipocyte completely, which is a differentiation from the proposed mechanism for ultrasound-induced changes. Brown and colleagues \(^{50}\) in 2004, reported a completely opposite conclusion from previous findings using a similar laser. Histologic and electron microscopy data from their porcine model and human subjects revealed no significant difference between laser-treated and nonexposed treatment sites, nor could they demonstrate disruption to adipocyte membranes.

Despite this dichotomy, a few small clinical series have demonstrated promising results. Jackson and colleagues \(^{47}\) demonstrated in a 35-patient double-blind, placebo-controlled trial, a significant reduction in treatment area circumference after 2 weeks, at 3 sessions per week. Patients underwent treatment of their hips, thighs, and waist. After completing all sessions, there was an overall reduction of 3.51 inches in all 3 sites collectively. Participants had a 0.98-inch reduction at the waist, 1.05 inch at the hip, and 0.85 inch in the thighs. Similarly, Caruso-Davis and colleagues \(^{51}\) demonstrated a 2.15-cm cumulative reduction in waist circumference over a 4-week treatment course in 44 patients.

The membrane invagination or transitory "pore" was found to be unique to those adipocytes receiving laser therapy at 635 nm and is believed to serve as the primary passage by which the stored triglyceride and fatty debris are removed from the cell. The wealth of basic science research and histologic evidence certainly points to the concept that adipocyte membrane disruption is secondary to light stimulation at 635 nm and is responsible for the egress of triglyceride, evacuation of cells, and the ultimate slimming event observed following a Zerona treatment series.\(^ {45,49}\)

Photobiomodulation via an external light delivery system represents a unique and misunderstood sector of medicine; yet, studies continually affirm that light has the capacity to penetrate the skin barrier and trigger real and measurable biochemical responses within the targeted tissue.\(^ {45,49}\)

Early utility of LLLT was found as an adjunct therapy to liposuction improving the ease of extraction and reducing postsurgical pain. A 700-patient report was published documenting improved contour and skin retraction, with an overall improved postoperative recovery when lipoplasty was coupled with LLLT.\(^ {47}\)

**Mechanism of action**

The 635-nm LLLT Zerona laser penetrates the first few millimeters of fat and, through a cytochrome oxidize enzyme interaction, results in the creation of a temporary pore in the adipocyte lipid belyad. Liberation of intracellular fat transitions into the interstitial space that is regulated by the lymphatic system and possesses the capacity to hydrolyze triglycerides into nonesterified free fatty acids (NEFAs), which is important for fat catabolism. As the fluid passes along the anastamosing network of lymphatic vessels, it ultimately arrives at lymph nodes where the extraneous materials are filtered out via macrophages that contain enzymes capable of degrading triglycerides and cholesterol. It is postulated that the fatty debris released after laser therapy is transported to lymph nodes where lysosomal acid lipase (LAL) hydrolyzes the released triglycerides to generate NEFAs.\(^ {45,49}\)

**Clinical results**

A placebo-controlled, randomized, double-blind, multicenter clinical study was conducted to evaluate the efficacy of the Zerona for noninvasive body slimming.\(^ {47}\) There were 67 participating subjects, of which 35 were randomized to the active treatment group and 32 were randomized to the sham-treatment group. Subject randomization was performed by a third party and was computer generated. Subjects assigned to the test group were treated with a multiple-head low-level diode laser consisting of 5 independent diode laser heads, each with a scanner emitting 635-nm (red) laser light with each diode generating 17 mW output (Zerona, manufactured by Erchonia Medical). Sham-treatment group participants were treated with a multiple-head nonlaser red light-emitting diode (LED) consisting of 5 independent red diode light heads each with a scanner emitting 635-nm (red) light with each diode generating
2.5 mW power. Both the sham-treatment light and real-laser devices were designed to have the same physical appearances, including the appearance of any visible light output. The primary success criterion was established by the FDA, which was defined as at least a 35% difference between treatment groups, comparing the proportion of individual successes in each group. Further, it was determined by the FDA that a reduction of at least 3 inches was clinically meaningful and patients were determined successful if that reduction was revealed in 2 weeks.

Comparison of the 2 independent-group means for the continuous variables of mean change in total combined circumference (total number of inches) from study baseline to end point demonstrated a mean difference of -2.837, a deviation found to be statistically significant ($t = -7.30; df = 65; P < .0001$). Treatment participants produced a reduction of 3 inches or greater in 2 weeks, compared with 2 subjects within the sham light group revealing a similar outcome. The difference was determined to be significant at $P < .0001$ (Table 1).

Compared with baseline, the changes in total circumference measurements between groups were statistically significant at all 3 subsequent evaluation points: -1.794 inches at week 1 ($t = -3.83; df = 65; P = .00029 [P < .0005]$), -2.838 inches at week 2 ($t = -7.30; df = 65; P < .0001$), and -2.593 inches at 2 weeks after the procedure ($t = -6.66; df = 65; P < .0001$). Zerona test subjects responded to the satisfaction survey. Thirty of the 35 test subjects and 31 of the 32 sham light–treated subjects recorded their satisfaction level subsequent to the treatment administration phase. Twenty-one test group participants (70%) and 8 sham-light group participants (26%) recorded a “satisfied” rating (see Table 1).

Moreover, 1 test group participant and 11 control group participants recorded a “dissatisfied” rating (see Table 1). The difference of the rating score between the 2 treatment groups was found to be statistically significant ($P < .0005$).

The commercial Zerona unit has an array of 6 x 635-nm diodes, each with a source fluence of 15 W and all 6 are adjusted to within 6 inches of the patient’s body (Fig. 4). The patient is treated for 20 minutes on the front and then 20 minutes on the back. It is important that the treatments are conducted 48 hours apart to optimize the transitory pore. Between treatments, patients are asked to walk 30 minutes per day, drink 1 L of water, and take a supplement called Curva that contains niacin and some homeopathic substances, all of which is designed to increase lymphatic flow and “wash out” the interstitial triglyceride. Minimization of inflammatory processes like alcohol and smoking should be attempted. The current Zerona protocol calls for 6 to 12 treatments, depending on the adipose make up on the patient. The “average” Zerona patient undergoes a treatment every 48 hours for a total of 9 treatments over 2 weeks. The lead author (RSM) has deployed Zerona in his practice for 10 months. A review of 110 consecutive, well-selected patients shows that the minimum

![Fig. 4. Zerona device. (From Zerona Science and Media Images; with permission.)](image)
"guarantee" of 3-inch to 9-inch reduction measured over 10 pinch locations occurred in 80% of patients. The company stands by their "guarantee" of 3 to 9 inches and we offer a second complimentary set of treatments (6 treatments over 2 weeks) to nonresponders. In the 20% of initial nonresponders, we salvaged 50% and were left with 10% of patients who did not hit the minimum guaranteed of 3-inch pinch reduction. Our patient happiness index remains very high, as we under promote and guarantee our minimum. It is possible to combine Zerona with other more focal, ablative, fat-reduction technologies to gain a generalized slimming and enhanced focal fat reduction.

Zerona truly occupies a unique position in the noninvasive body-contouring space, as it is the only generalized laser-slimming technology. Further, the departure from adipocyte ablation positions, the Zerona is in a unique and beneficial category as it exemplifies a truly noninvasive approach inducing slimming without cell death or upregulation of inflammation. Well-selected patients are generally very satisfied with their treatment.

CELLULITE

As cellulite is such a common presenting complaint of our body-contouring patients, it is important to mention some of the exciting new frontiers in the management of this pathology. Cellulite is the phenotypic description of lumpy, bumpy, irregular "peau d’orange" or "cottage cheese"-like skin. The etiology and pathophysiology in the basic science of cellulite are still poorly understood and debated, but various hypoxic, ischemic, hereditary, hormonal, and multifactorial theories are postulated. Over time, the cellular skin progresses from lymphedema to a lipedema, then to mild fibrous retraction bands and exacerbated hypoxia and matrix sclerosis. Herniated edematous fat lobules move up into the reticular dermis, creating lumpy, bumpy, irregular skin.

Of the noninvasive body-contouring technologies that are used to treat convex and focal distension of fat, some can also be used for the treatment of cellulite. The VelaSmooth and VelaShape have perhaps the greatest reported experience in the treatment of cellulite and improvements of 60% after multiple sessions have been reported. Thermae and the Acaent monopolar RF devices have also shown some success with multiple treatments for cellulite.

Because cellulite is so ubiquitous, it can affect patients with higher and lower BMI. It is going to be a continued area of growth. New minimally invasive technologies that have been developed by Invasix that use a bipolar RF device with 1 electrode on the skin and 1 RF electrode under the skin immediately in the subdermal and hypodermal areas are used to treat cellulite. This application of RF energy results in adipocyte destruction and the external electrode moves smoothly along the surface of the skin delivering a monopolar, gentle dermal tightening effect. Recent BodyTite (Invasix, Inc., Yokneam, Israel) studies on cellulite show that increased collagen at the subdermal hypodermal junction may act as a barrier, which, together with the adipocyte RF coagulation and dermal tightening, accounts for the RFAL cellulite improvement with the RF Cellulite™ applicator. This minimally invasive technology has shown tremendous long-term improvement in cellulite in early studies with 70% to 80% improvement with Grade 3 cellulite followed for greater than a year.

LLLT is also being investigated for the treatment of cellulite. Although various creams, mechanical manipulation of tissues, mesotherapy, and others have been attempted, treatment of cellulite remains a challenge. Low-level laser energy may have a role. Lach reported the use of a vacuum/massage and dual-wavelength (850 and 915 nm), low-level laser energy device to improve the appearance of cellulite. One thigh was treated circumferentially with massage alone, whereas the other circumferential thigh was treated with dual-beam laser energy. Sixty-five patients received an average of 14 treatments, 1 to 3 per week over 4 to 6 weeks, and were followed with magnetic resonance imaging measurements, which were obtained before and after the last treatment. The fat thickness decreased over time by 1.19 cm² in the leg treated with laser and massage, whereas the leg treated with massage alone increased by 3.82 cm².

Kulick demonstrated the efficacy of a noninvasive laser-suction device using a low-level dual-energy laser in the treatment of cellulite. Twenty women with mild to moderate cellulite underwent treatment of their lateral thighs and were evaluated with body weight measurements, digital photographs, 3-dimensional images, and questionnaires. Two treatments per week for 4 weeks were performed using a commercially available machine emitting a 1-W, 650-nm and 10-W, 915-nm dual-laser combined with suction. The treatments resulted in 76% improvement in cellulite reduction based on 3-dimensional imaging and patient satisfaction surveys.

Management and treatment of cellulite is a very common problem in North America and Europe, and less common in the Asian skin type. The complications in the management of cellulite can include thermal skin injury and safety and efficacy
protocols need to be followed. The complications, however, are rare. The biggest complication again is patient dissatisfaction from unrealistic expectations. With the ability to pass RF heat across and now under the skin, cellulite may become a surgically manageable process with good long-term improvements.

**NONINVASIVE BODY-COUNTURING COMPLICATIONS**

All of the noninvasive body-countering technologies described in this article are extremely safe. Rare reports of focused ultrasound thermal injuries over thin bony prominences can be avoided by following the recommended techniques and protocol set out by the companies. The thermal injuries from the RF devices can occur but, again, are very rare with instances far less than 1%. With the cryolipolysis technology, a reported temporary, but annoying, dysesthesia can happen in up to 20% of patients, but there are no reports of permanent sensory loss.

Although the safety and efficacy of these noninvasive body-counturing devices have been proven and documented in peer-reviewed literature, by far the most common complication is patient dissatisfaction. Patients who present to the plastic surgeon's office for noninvasive body contouring are often thinking they will receive "liposuction"-like results and it is critical to educate patients on the modest significance of 2 to 4 cm of circumferential improvement in body contour. With noninvasive and minimally invasive facial rejuvenative procedures, we can achieve remarkable results with a combination of Botox, soft tissue fillers, subdermal RF, laser heating, and fractional resurfacing. Such results are comparable with more aggressive surgical interventions. However, the same cannot be said of noninvasive or minimally invasive body-counturing technologies. Although it is impressive that we can achieve 4-cm or more reductions with most of the technologies in the truncal region, those patients who present for noninvasive body contouring with large BMIs, or individuals with large focal fatty deposits, will see limited benefit. Reductions of 4, 5, or 6 cm still leave behind most of the fatty tissue causing the convex distention. Patients wanting noninvasive body contouring need to be judiciously selected and the procedures should not be overpromoted. The best candidates and indications for noninvasive body contouring are those patients who are very accepting of a mild to moderate result; in fact, the best candidates are those who state they will be happy with any measurable reduction in fat. These well-selected patients are not willing to undergo any form of liposuction or body-counturing surgery, as these will invariably give the best results.

With proven safety and efficacy, the future of noninvasive body contouring looks bright. Plastic surgeons who incorporate these technologies into their practices will be able to offer noninvasive as well as invasive body contouring and offer synchronous programs that can move patients from noninvasive to invasive and back again. Again, like purchasing expensive facial skin-tightening and rejuvenation technologies, a business model and an appreciation of the marketing behind the business model for patients wanting noninvasive body contouring is an important part of this emerging area of noninvasive plastic surgery.