

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

R. Stephen Mulholland, MD, FRCS(C)<sup>a</sup>,  
Malcolm D. Paul, MD<sup>b,\*</sup>, Charbel Chalfoun, MD<sup>c</sup>

## 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

Noninvasive body contouring is perhaps one of the most alluring areas of esthetic surgery today. Driven by strong public demand for safer procedures with quicker recovery, fewer side effects, and less discomfort, while supported by media attention and economic appeal, new modalities have been developed to address body contouring from a less-invasive perspective. Current surgical options carry the drawbacks of hospitalizations, anesthetics, pain, swelling, and long recovery, as

well as inherent risks associated with surgery. Even standard surgical lipectomy methods have progressed from power-assisted liposuction, to ultrasound or laser-assisted modalities, to radiofrequency (RF) methods with a focus on gaining improved results, shorter postoperative recovery, and adjunctive benefits, such as less bruising and more skin tightening. Patients, however, are still seeking safer alternatives and are excited by the thought of losing fat quickly without having

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<sup>a</sup> Private Plastic Surgery Practice, SpaMedica® Clinics, 66 Avenue Road, Suite 4, Toronto, ON M5R 3N8, Canada

<sup>b</sup> Aesthetic and Plastic Surgery Institute, University of California, Irvine, CA, USA

<sup>c</sup> The Plastic Surgery Group, 37 North Fullerton Avenue, Montclair, NJ 07042, USA

\* Corresponding author. 1401 Avocado Avenue, Suite 810, Newport Beach, CA 92660.

E-mail address: mpaulmd@hotmail.com

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to undergo surgery. Several technologies have emerged to attempt to address these concerns and propose a noninvasive, transcutaneous delivery of energy for lipolysis.

## CELLULITE REDUCTION AND FAT CELL REDUCTION

Plastic surgeons have had a long and pioneering history in the art and science of body contouring. From the advent of liposuction in the late 1970s and early 1980s, the practice of body contouring has seen the growth of less-invasive and more-effective liposuction techniques. When one combines men and women together, liposuction is still the most common surgery performed by esthetic plastic surgeons in North America<sup>1</sup> and liposuction remains the number one esthetic procedure performed by plastic and cosmetic physicians worldwide. In 2009, it was estimated that there were 700,000 liposuction procedures performed in the United States (approximately 500,000 by board-certified plastic surgeons and the rest by cosmetic physicians) or 4% of all elective surgeries.<sup>2</sup> The number of liposuctions is anticipated to double over the next 4 years to 1.5 million procedures or 8% of all elective operations in United States.<sup>3</sup> This growth in body-contouring surgery is reflective in general of the expansion in the body mass index (BMI) of the average North American. The BMI and average weight of North Americans is increasing at an alarming rate; in fact, obesity is one of the most challenging epidemics facing North American health care. Fully 30% of Americans have a BMI higher than 30 and another 30% have a BMI between 27 and 30, making more than 200 million Americans candidates for weight loss programs and focal or generalized body-contouring procedures when weight loss has been achieved.<sup>4</sup> Some experts project that by 2015, 75% of adults will be overweight, with 41% obese.<sup>5</sup>

Increasing numbers of consumers desiring esthetic body-contouring changes are seeking less-invasive, less-traumatic, and more-effective procedures than traditional suction-assisted liposuction (SAL). Although, SAL is still perceived as the gold standard in nonexcisional body-contouring techniques by most plastic surgeons, recent developments in energy-based liposuction, including third-generation ultrasound (UAL), laser-assisted lipolysis (LAL), and RF-assisted liposuction (RFAL) may offer reduced ecchymosis, swelling, pain, and enhanced skin contraction when compared with SAL.<sup>6-9</sup>

However, as popular as the various forms of liposuction remain, the fastest growth market segment in esthetic medicine is in the area of

noninvasive body contouring.<sup>10</sup> This reflects the underlying paradigm of many patients: that any surgery, no matter how “minimally invasive,” is not what they want. As this timely issue in *Clinics in Plastic Surgery* is devoted to noninvasive and minimally invasive esthetic techniques, it is important that the modern plastic surgeon and the specialty of plastic surgery in general, be well versed in the various nonsurgical procedures and technologies that patients may use to enhance their figure and form, or, increasingly, offer these modalities in conjunction with their surgical body-contouring practice. In 2009, the global market for all body-shaping platforms was expected to reach \$361.9 billion with more than 9 million procedures performed.<sup>10</sup> The annual growth in noninvasive body-contouring procedures is estimated to expand by 21% per year.<sup>10</sup>

This article focuses on the noninvasive body-contouring modalities that have become available in the US and North American markets over the past few years, as well as those that are imminent (selling worldwide but pending approval by the Food and Drug Administration [FDA]). We review the basic science and peer-reviewed articles on clinical outcomes. At the conclusion of the article, some basic business models on incorporating noninvasive body-contouring procedures into an esthetic plastic surgery practice are discussed.

It is an exciting time in esthetic plastic surgery and the growth in noninvasive plastic surgery techniques affords the forward-thinking plastic surgeon the opportunity to treat many more patients who either are not ready for invasive techniques or will never consider incisional plastic surgery. We hope this article provides a solid basis for understanding the noninvasive body-contouring options available in 2010.

## CLASSIFICATION OF NONINVASIVE BODY-CONTOURING TECHNOLOGY

Over the past 5 to 10 years, there has been considerable growth in body size and patient BMI, both in North America and worldwide, which has coincided with market growth and advances in the technology devoted to the nonsurgical management of fat and body contouring. Just as liposuction is the number one cosmetic plastic surgery procedure performed worldwide, noninvasive body-contouring technology is the fastest growing segment of the esthetic capital equipment space.<sup>10</sup> In classifying the technologies related to noninvasive body contouring, we have decided to classify on the basis of the type of energy delivered by a particular technology in modifying the adipocyte. There are many exciting advances in body-contouring technology involving

the transepidermal delivery of energy targeting the adipocyte.

#### Classification

1. Suction: Massage Devices
  - a. Endermologie
2. Suction-Massage: Thermal Devices
  - a. TriActive (Cynosure, Inc., Westford, MA, USA)
  - b. Smoothshapes (Cynosure, Inc., Westford, MA, USA)
3. Radiofrequency Energy Devices
  - a. VelaSmooth, VelaShape (Syneron, Inc., Irvine, CA, USA)
  - b. Thermage™ (Solta Medical, Hayward, CA, USA)
  - c. Accent (Alma Lasers Inc, Buffalo Grove, IL, USA)
  - d. TiteFX (Invasix, Inc., Yokneam, Israel)
4. High-Frequency Focused Ultrasound Energy Devices
  - a. UltraShape (UltraShape Ltd., Yoqneam, Israel)
  - b. LipoSonix (Medicis, Scottsdale, AZ, USA)
5. Cryolipolysis Energy Devices
  - a. Zeltiq (Zeltiq Aesthetics, Pleasanton, CA, USA)
6. Low-Level Light Laser Therapy Devices
  - a. Zerona (Erchonia Medical, McKinney, TX, USA)

With the classification of noninvasive body contouring based on the kind of energy delivered to the adipocyte, we focus on the following: basic science, clinical results, and complications for those technologies that are the most relevant, peer reviewed, market proven, or exciting.

### BASIC SCIENCE

The basic science of noninvasive body contouring is really the basic science of the adipocyte, its storage of triglyceride, and the aggregate number of adipocytes as they relate to the focal and generalized excess of adipose tissue, the convex distension that forms the focal “bulges,” and more superficially, clinical cellulite topographically. The adipocyte is a very important cell involved in energy storage, hormonal regulation, and a host of other endocrinological functions. The adipocyte has a large amount of cytoplasm that serves as a storage depot for triglycerides, which are composed of glycerol and free fatty acids. The adipose cell is our intermediate and long-term energy storage depot. When caloric intake exceeds caloric output, adipocytes then swell with triglycerides. As adipocytes continue to enlarge within their intralobular and interlobular fascial compartments, they create “bulges” or convex distensions of soft tissue that then modify our contours. Typical convex distensions that one sees in the female

topography are “out-pouching,” “bulges,” or convex distensions of the hips, lower abdomen, outer thighs, inner thighs, inner knees, arms, and bra line. For men, the typical android distribution of subcutaneous adipose-derived convex distensions commonly include the flanks (love handles), lower abdomen, “spare tire,” male fatty breast tissue, and the submentum.

Historically and currently, the gold standard for body contouring still remains the various techniques of liposuction. Great advances of liposuction have made this a much less invasive procedure, and this issue of *Clinics in Plastic Surgery* deals with some of the newer energy-based liposuction technologies such as RF-assisted liposuction and laser lipolysis. However, even though liposuction has become less invasive and more amenable to outpatient procedures, it is still a procedure that requires surgical instrumentation under the skin and has risk and morbidity in recovery. Many patients, no matter how less invasive liposuction may appear, will not submit, nor are they interested in a liposuction procedure. Many patients seek mild to moderate body contour improvements through diet and exercise and adjunctive noninvasive body-contouring procedures. We focus on the technologies that have the most peer-reviewed data and literature, and appear the most promising for long-term management of focal convex distension of adipose tissue, as well as for generalized figure and shape.

The basic science of the noninvasive modulation and modification of the adipocyte involves one of several mechanisms (which will be dealt with in more detail in the Clinical Results and Outcomes of Specific Technologies section). In one mechanism, the adipocyte experiences a periadipocyte thermal environment induced by transepidermal delivery of some energy and this heat increases the localized metabolic rate of the fat, evacuating, enhancing, and augmenting the natural egress of triglyceride out of the fat cell, resulting in a diminishment of the convex distension. Overlying this, there is also some thermal-related dermal tightening with these transepidermal body-contouring heating devices and a measurable circumferential reduction in fat. Most of these thermal technologies do not, in fact, kill the fat cell. Some technologies deploy energy, either a pulse of high-voltage RF current, or a focused high-frequency ultrasound energy experience that disables or destroys the adipocyte by permanently damaging the cell membrane, or coagulating or disrupting and releasing the adipocyte cell contents. And yet other technologies, such as low-level light laser therapy, create temporary disruptions in the cell membrane of the adipocyte allowing a temporary egress

of the triglyceride from the cytoplasm, but the cell membrane then rights itself again. So, through these mechanisms, either thermal augmentation of normal metabolic pathways, thermal destruction, cavitation destruction, or an energy cascade and creation of a temporary adipocyte cell membrane pore, the final result is that the sizes of the adipocytes are either temporarily or permanently reduced and/or the number of adipocytes are reduced, which when translated over hundreds of thousands or millions of fat cells, will result in a measurable reduction of fat and a circumferential reduction of the body contour area in the treated area.

## INDICATIONS AND CONTRAINDICATIONS OF NONINVASIVE BODY CONTOURING

In general, all the noninvasive body-contouring technologies share the same relative indications and contraindications for treatment.

Indications include realistic expectations of a modest reduction of localized fat, modest cellulite improvement, compliance with multiple visits, reasonable BMI and lifestyle, and are opposed to a surgical procedure, which would get a better result.

Contraindications include if the patient is pregnant, has a pacemaker, is medically unwell, has unrealistic expectations, or has a large BMI.

### *Proper Patient Preparation*

With all body-contouring technologies, it is important to take consistent before-and-after photographs, make circumference measurements, and record weight change at each follow-up visit to document results and ensure the patient is not gaining weight because of a poor diet or lack of exercise. A proper consent should be executed.

The patient's target treatment areas are assessed and marked in a similar way as for patients undergoing liposuction. When assessing and marking the targeted treatment area, the patient should stand straight up and look forward. Soft tissue deformities (unwanted fat deposits) should be evaluated from multiple views for best assessment. Palpate the perimeter of the area to identify exactly where the deformity begins and mark the precise area for treatment with a single line. Only soft tissue deformities with at least 1.5 cm of fat thickness should be treated and not the adjacent flat or concave areas.

## CLINICAL RESULTS AND OUTCOMES OF SPECIFIC TECHNOLOGIES

### *Suction/Massage Devices*

The first class of body-contouring technology emerged approximately 15 to 20 years ago.

Endermology is a suction/massage device manufactured in France. The device uses a mechanical suction and roller applicator used to pass over fatty areas of the body and cellulitic regions. There are peer-reviewed articles in the literature that show that in selected patients, particularly those with edematous type fatty tissue, endermology can result in measurable circumferential reduction. Endermology is often combined with increased exercise, caloric restriction, and increased water intake.<sup>11</sup> Although endermology is popular in the day spa environment, it has very mild, modest clinical effects and has had minimal penetration in the physician market. The indications are rather limited and more than 16 treatments are required, which last longer than 30 minutes, and thus it is not proven to be an optimal revenue generator nor successful in plastic surgery and physician offices.

### *Suction/Massage and Energy Devices*

Augmenting the concepts of endermology are devices from several companies that use suction rollers in combination with transepidermal thermal energy. These devices will deploy diode arrays or diodes/nonfocused ultrasound around the applicator head that is then passed over the fatty areas of the body, such as TriActive and SmoothShapes (Cynosure, Inc., Westford, MA, USA) (**Fig. 1**). Again, results are mild to modest in effect and generally have not been incorporated into many practices for full-scale noninvasive body contouring.

### *Radiofrequency Energy Devices*

The RF energy devices currently dominate the worldwide noninvasive body-contouring device market.<sup>10</sup> The first serious noninvasive body-contouring device that was widely incorporated in physicians' practices was the VelaSmooth (Syneron), followed 2 years later by the VelaShape. This was followed by other RF body-contouring devices, including Thermage™ (Solta Medical, Hayward, CA, USA), Accent (Alma Lasers), TriPollar (Pollogen, Tel Aviv, Israel), Freeze (Venus Concepts, Karmiel, Israel) and most recently TiteFX (Invasix).

### *VelaSmooth and VelaShape*

In 2005, the VelaSmooth became the first energy-based medical device to be approved by the FDA for reducing the appearance of cellulite. In September 2007, VelaShape became the first FDA-approved noninvasive device for both cellulite and circumference reduction.

**Device description** Both VelaSmooth and VelaShape systems combine controlled 700-nm to 2000-nm infrared (IR) light and suction couple-



**Fig. 1.** TriActive device. (From Cynosure; with permission.)

conducted bipolar RF (1 MHz) energies with mechanical manipulation. Conductive RF energy is applied externally by suction coupling 2 electrodes to the skin surface. Both the geometry of the electrodes and the conductive RF pulse duration are optimized for safe heating of the skin. The use of conductive RF allows for a reduction in the necessary optical energy applied to the skin. Furthermore, this form of energy is not sensitive to skin pigmentation and therefore its use is advantageous in treating all skin types.

These systems are composed of a base unit to which 2 different applicators (large and small) may be connected (**Fig. 2**). The applicators are equivalent in their power density and each is fitted to the base unit via a replaceable cap. During treatment, the applied suction repeatedly pulls the skin into a chamber in the middle of the treatment cavity, where the skin is exposed to IR light and RF while its surface temperature is being monitored. The system enables the user to adjust the RF energy



**Fig. 2.** VelaShape VSII device. (From Syneron and Candela Science; with permission.)

and optical energy levels, thereby using the optimal treatment parameters for each subject/anatomic area.

**Mechanism of action** The VelaSmooth and VelaShape mechanism of action is based on a novel combination of suction-coupled bipolar RF and optical energies delivered to the dermis/hypodermis zones. Optical IR energy targets mainly the dermal water, whereas the RF energy targets the hypodermis by controlled thermal stress. Applying thermal energy to the dermis causes dermal tightening and contraction but also activates a cascade of physiologic responses inside

the dermal fibroblasts (the cells that produce collagen) to stimulate and promote neocollagenesis (new collagen formation). Neocollagenesis is further potentiated by increased dermal vascularity secondary to the thermal stress induced. The vacuum potentiates neocollagenesis via the mechanical stress imposed on dermal fibroblasts. Neocollagenesis and collagen contraction further contribute to enrichment and strengthening of the otherwise loose connective tissue fibrous septae. Applying the bipolar RF energy to the hypodermis increases fat cells' metabolism and accelerated triglyceride egress from the cell. Increased tissue temperature increases vascular perfusion, which further enhances lipid turnover owing to increased oxygen content. Increased lipid turnover results in fat cell shrinkage and reduced fat tissue volume, a circumferential reduction, and an esthetic reduction in the convex distension. Vacuum and mechanical massage increase blood vessel and lymphatic circulation and lymphatic drainage, which further contribute to lipid turnover and fat cell redistribution throughout the body. The resulting simultaneous increase in the dermal collagen and ground substance content, connective tissue architecture, and the decrease in subcutaneous fat tissue volume allow for optimal circumferential reduction and improvement in cellulite appearance.

As the VelaShape and VelaSmooth have long-term placements in the physician market, there is good peer-reviewed evidence of their efficacy for both the treatment and temporary reduction of cellulite and fat.

**Clinical VelaSmooth and VelaShape results** In the largest study of VelaSmooth to date, Sadick and Mulholland<sup>12</sup> evaluated 35 patients who completed either 8 or 16 treatments with VelaSmooth. Clinical improvement as evaluated by a blinded dermatologist revealed an average of 40% improvement in the appearance of cellulite and a measurable circumferential reduction in all.

Alster and Tanzi<sup>13</sup> conducted a self-control study, including 20 women patients who received 3 biweekly VelaSmooth treatments for thigh and buttock cellulite. Ninety percent of the patients noticed overall clinical improvement and side effects were limited to transient erythema in most patients.

A longer follow-up study performed by Kulick<sup>14</sup> evaluated the degree of improvement 3 and 6 months after the last session of treatment. According to the blinded physician evaluators, all patients were improved at both posttreatment periods with an average of 62% and 50% improvement at the 3-month and 6-month follow-up, respectively.

Another long follow-up study conducted in an Asian population found a significant reduction in thigh and abdomen circumferences up to 1 year after treatment. At 4 weeks after the last treatment, the average circumference reductions of the abdomen and thigh were sustained at  $3.17 \pm 2.75$  cm and  $3.50 \pm 2.04$  cm, respectively. At the 1-year follow-up visit, the average circumference reductions of the abdomen and thigh were maintained at  $3.83 \pm 0.76$  cm and  $3.13 \pm 3.54$ , respectively. The average clinical improvement scores of the abdomen and thigh after the series of treatments were 0.75 (corresponding to ~25% improvement) and 1.75 (corresponding to ~50% improvement), respectively.<sup>15</sup>

More recently, Sadick and Magro<sup>16</sup> found a statistically significant decrease in thigh circumference at 4 weeks after VelaSmooth treatments, but no immediate change or a persistent decrease at 8 weeks after the procedure. Nevertheless, it should be noted that the main indication for using VelaSmooth is improving cellulite appearance, and of all available RF devices, only VelaSmooth has been approved by the FDA specifically for cellulite treatment.

Winter<sup>17</sup> evaluated the performance of the higher-power version of this technology (VelaShape with 50 W as opposed to VelaSmooth with 25 W) for body reshaping and improvement of skin texture/laxity in postpartum women. In this study, 20 women received 5 weekly treatments to the abdomen, buttocks, and thighs with the VelaShape system. The overall mean circumference reduction was  $5.4 \pm 0.7$  cm ( $P < .001$ ). Significant ( $P < .02$ ) improvement in skin laxity and tightening was noted by both the physician and patients. Treatments were well tolerated with no major safety concerns (1 purpura, 1 mild burn).

In a recent study, Brightman and colleagues<sup>18</sup> revealed the clinical efficacy and the molecular mechanisms underlying treatments with VelaShape. Nineteen subjects underwent 5 weekly treatments of the upper arms, and 10 subjects underwent 4 weekly treatments of the abdomen and flanks. Change in arm circumference, at the fifth treatment was statistically significant with a mean loss of 0.625 cm. At 1-month and 3-month follow-ups, mean loss was 0.710 and 0.597 cm respectively. Reduction of abdominal circumference at the third treatment was statistically significant with a 1.25 cm mean loss. At 1-month and 3-month follow-ups, average loss was 1.43 and 1.82 cm respectively. Furthermore, the sustainable reduction in circumferences and the significant improvement in the appearance of the arms and abdomen correlated with significant morphologic and histologic changes observed in biopsies obtained in vivo from the treated areas.

In summary, there are many peer-reviewed articles to support the clinical efficacy and safety of using the combined bipolar RF, IR, and mechanical manipulation technology for cellulite improvement and circumference reduction in a wide variety of patient populations. The clinical and molecular data presented here further support the concept that the underlying mechanism of action for improved skin laxity and volume reduction is based on controlled RF and IR thermal modification of the dermal/hypodermal layers.

### ***Thermage™ body and accent***

There are 2 common monopolar RF devices sold in the marketing place, Thermage™ (Solta Medical, Hayward, CA, USA) and Accent (Alma Lasers). Both of these devices are discussed extensively in the RF for Skin Tightening article by Mulholland elsewhere in this issue. Thermage™ has had an FDA-cleared body tip since 2006 and Accent has had body clearance for more than 2 years. The monopolar RF in these systems is not suction coupled and there is no adjunctive optical energy source as in the VelaShape. Thermage™ RF body treatments have been shown in the animal and human biopsy model to result in lysis of the adipocyte membrane when high enough energies are deployed.<sup>19</sup> Thermage™ has been assessed in the treatment of cellulite with improvement scores of 30% to 70% and in treatment of stretch marks with improvement scores of 20% to 80%, when measured at least 6 months following treatment, depending on the study.<sup>20–22</sup> Thermage™ monopolar RF body treatment has also demonstrated moderate average circumferential reduction and fat-thickness reduction at 6 months following one or more treatments.<sup>20</sup> Accent is another monopolar RF system that operates at a high frequency and has shown improvement with noninvasive monopolar RF treatments of cellulite and fat reduction.<sup>23,24</sup> TriPollar (Pollogen, Tel Aviv, Israel) and Freeze (Venus Concepts) have 3 to 8 RF electrodes and show early promise for temporary adipocyte reduction and skin tightening.<sup>25</sup>

### ***TiteFX: RF and high-voltage pulse electroporation***

The TiteFX is an interesting emerging body-contouring technology that differentiates itself from other RF technologies, which (except in animal studies) use lower tissue levels of RF to metabolically enhance the triglyceride processing out of the adipocyte but not permanently kill or damage the fat cell and so the focal lipodystrophy or cellulite is more prone to recurrence. TiteFX uses suction-coupled RF to preheat the dermis and first 15 to 20 mm of fat and uses a precise thermistor built

inside the suction cavity to monitor the uniform and even skin temperature and suction distribution. When the epidermal temperature reaches the desired level, usually 43 to 45°C, a high-voltage, electroporation pulse is generated through the adipose tissue resulting in a high voltage electroporation apoptosis, or death of the fat cell over the following week.<sup>26</sup>

The device is very fast and the temperatures very uniform, making the treatment more tolerable than other RF systems that develop thermal “hot spots” and pain. With the TiteFX, like the high-intensity focused ultrasound (HIFU) family, a significant portion of the adipocyte population is targeted for cell death and thus the body-contouring circumferential reductions and cellulite improvements are more long term or permanent than other RF technologies.<sup>26</sup> TiteFX comes with a noninvasive fat-contouring and cellulite applicator, as well as a noninvasive face-tightening hand piece.

### ***High-Frequency Focused Ultrasound Energy Devices***

The HIFU noninvasive body-contouring devices, UltraShape and LipoSonix, have received a lot of media attention and both have been sold in many markets around the world, including Canada, but are awaiting FDA clearance. They are exciting technologies and, like Zeltiq and TiteFX, they both result in noninvasive adipocyte death, rather than just metabolic amplification of the fat cell metabolism and, as such, may offer long-term noninvasive body-contouring results. Many physicians around the world are achieving good body-contour results and have profitable body-contour programs using HIFU.

However, there are many noninvasive, nonfocused ultrasound devices on the market, such as Proslimelt (Medical Care Consulting, Murten, Switzerland), Medcontour (General Project, Florence, Italy), Ultracontour (Medixsysteme, Nimes, France), Novashape (Ultra Med, Milton, ON, Canada), Accent Ultra (Alma, Buffalo Grove, IL, USA), VaserShape (Sound Surgical Technologies, Louisville, CO, USA), or the so-called “Ultracavitators,” that claim to have an effect on the fat cell, but there is no known published scientific, preclinical, or clinical data to support such claims. Most of these devices use a variation of standard physiotherapy ultrasound technology indicated for diathermy, combined with some type of massage or vacuum. The nonfocused ultrasound simply heats the underlying skin and tissue just as any standard physiotherapy ultrasound device. These devices do not meet the requirements to produce focused

ultrasound; therefore, they cannot increase maximal pressure deep without causing skin damage. The likelihood for cavitation is characterized by the mechanical index (MI), and based on the ultrasound specifications of these devices, they do not meet the minimum MI and pressure threshold for cavitation in fat; therefore, they do not disrupt fat cells. These physiotherapeutic ultrasound devices are not new to plastic surgeons, as they are similar to the external-assist UAL technologies of the early 1990s. These devices may create a temporary effect but there is no known scientific or preclinical evidence (histology or gross pathology) of fat cell disruption. Most of these devices are sold in Europe or Asia to beauty spa markets where there are fewer regulations and/or enforcement of unsubstantiated or nonapproved marketing claims, but they are also finding their way into US markets. We focus our attention on the HIFU technologies with peer-reviewed evidence of fat disruption.

### **UltraShape**

The UltraShape Contour I system (UltraShape Ltd.) was the first HIFU system launched commercially in the world and UltraShape has the most basic science, peer-reviewed articles, and worldwide clinical experience of the HIFU systems. It uses nonthermal selective focused ultrasound to produce localized, mechanical motion within fat tissues and cells for the purpose of producing mechanical cellular membrane disruption.<sup>27</sup> The Contour I operating parameters are designed to deliver concentrated pulsed energy through the skin into a focal volume at a precise depth to disrupt subcutaneous fat cells without harming neighboring tissues (eg, nerves, blood vessels, and connective tissue).

Peer-reviewed published preclinical research demonstrates that fat tissues and cells are disrupted and surrounding structures exposed to these effects are not damaged.<sup>28</sup> Tissue selectivity is achieved by using a pulsed ultrasound wave, limiting temperature increases in the target tissue and differential susceptibility to mechanical (nonthermal) stresses induced by the ultrasound energy in these tissues and the ultrasound focal distance. Precision and safety are further reinforced by an integrated acoustic contact sensor, which provides real-time feedback on acoustic contact, thus ensuring proper transducer-to-skin contact and efficient energy delivery to the treatment area. The Contour I device is composed of the following subsystem components: the system console, the therapeutic ultrasound transducer, and a real-time video-tracking and guidance system. The video-tracking and guidance system ensures that the treatment is performed

homogeneously only within the designated area. Peer-reviewed published clinical studies show that UltraShape is safe and effective for circumference reduction and reduction of localized fat deposits on the abdomen, flanks, and thighs.<sup>27,29</sup>

Experimental and clinical studies have been performed to demonstrate significant reduction in subcutaneous fat. Brown and colleagues<sup>28</sup> studied the physics of focused external ultrasound using the UltraShape Contour I device and attempted to validate its efficacy in a porcine model. Gross and histologic evaluations of porcine adipose tissue after treatment with the device confirmed cavitation induced zones of injury in the adipose tissue with sparing of nervous and vascular structures as well as skin.

Several studies have extrapolated these results to the clinical setting. A prospective study conducted in Spain by Moreno-Moraga and colleagues<sup>29</sup> involved 30 patients. Each patient underwent 3 treatments at 1-month intervals. Areas treated were the abdomen, inner and outer thighs, flanks, inner knees, and male breasts. Ultrasound measurements and circumference measurements were used to assess changes in fat thickness. They found that the mean reduction in fat thickness after 3 treatments was  $2.28 \pm 0.80$  cm, whereas the circumference was reduced by a mean of  $3.95 \pm 1.99$  cm. No significant changes in weight were identified to suggest changes as secondary to weight loss. Serum triglyceride levels and liver ultrasound evaluations for steatosis were also performed for safety profiles, all of which showed no significant abnormalities.<sup>29</sup> The group reports treating more than 400 patients outside of the clinical study with successful reduction in localized adiposity and great patient satisfaction.

Teitelbaum and colleagues<sup>27</sup> performed a multicenter study (2 centers in the United States, 1 in the United Kingdom, 2 in Japan) involving 164 patients, 137 of whom had undergone a single treatment of focused external ultrasound lipolysis, whereas 27 served as controls. Follow-up was performed on days 1, 3, 7, 14, 28, 56, and 84. They reported a single contour treatment produced a mean reduction of approximately 2 cm in treatment area circumference and approximately 2.9 mm in skin fat thickness. No adverse effect was noted on lipid profiles or liver sonography. Complications were mild and included erythema, mild blistering in 2 patients, and mild dermal erosion in 1 patient that resolved by the end of the follow-up period.

Shek and colleagues<sup>30</sup> attempted to validate the results of prior studies in the Asian population, but found strikingly different results. Fifty-three patients had up to 3 treatments 1 month apart. Efficacy was assessed by changes in abdominal circumference,

ultrasound fat thickness, and caliper fat thickness. A patient questionnaire was also used to assess satisfaction. Weight loss-induced measurements were also monitored. Shek and colleagues<sup>30</sup> found that there were no significant changes in any of the measurements before and after treatment. Patient satisfaction was also poor, because results were suboptimal. Shek and colleagues<sup>30</sup> attribute the discrepancy in results to body frame size of Southern Asians compared with Caucasians, suggesting that a modification in the transducer may alleviate the difficulties in delivery of ultrasonic energy on a smaller body habitus.

The UltraShape procedure is guided by a proprietary real-time tracking and guidance system designed to deliver smooth, uniform body-contouring results. The tracking and guidance system consists of a video camera, frame grabber, and software package all together capturing, processing, and displaying in real time, the location of the treatment area with an overlay dictating to the operator where to place the transducer for each pulse of energy. The software calculates and maps the treatment area in 3 dimensions, which guarantees adherence to a predetermined computer-controlled treatment algorithm.

Key parameters of the computer-controlled treatment algorithm include the following:

1. Treatment is performed only within the marked treatment area.
2. Each point (node) is treated only once.
3. Each pulse of energy is delivered immediately adjacent to the prior pulse, ensuring complete uniform coverage over the entire treatment area.

This algorithm ensures complete and uniform energy delivery over the entire treatment area, minimizing the risk of contour irregularities, a common side effect of liposuction.

The tracking system also addresses the dynamic nature of the treatment area, as it monitors and synchronizes patient position in real time, enabling the patient to move freely without affecting the treatment.

**Second-generation UltraShape technology** After 3 years of clinical experience outside the United States, UltraShape launched its new, improved, and faster system in January of 2008. This advanced-generation system includes upgraded software and an improved transducer that offers reduced treatment time, lower treatment cost, and an enhanced operator and patient experience. A summary of the Contour II upgrades includes the following:

1. Reduced the average treatment time to between 40 and 60 minutes, depending on

the treatment area, a reduction of more than 35% over the prior version.

2. The transducer emits 50% more ultrasonic pulses for the same price as the previous one, thus reducing treatment cost by 35%.
3. Clinical studies conducted in France, Canada, and Israel demonstrated that 3 successive UltraShape treatments at 2-week intervals are safe and effective, and show significant treatment area reduction—3 treatment series can be completed within 1 month without compromising results.<sup>31,32</sup>

**Third-generation UltraShape technology** The newest UltraShape model, the Contour I Ver3 multiapplication platform was launched in January 2010, includes an advanced focused ultrasound technology and vacuum-assisted radio frequency, all in an upright mobile-upgradeable device (**Fig. 3**).

Some of the new features of the UltraShape Ver3 include the following:

1. New software featuring an intuitive “TOUCH” graphic user-interface for shorter treatment set-up and treatment time; 3-dimensional treatment mapping for improved treatment area coverage; and advanced proprietary tracking and guidance software for enhanced treatment efficiency.
2. Digital ultrasound pulsar designed to deliver higher energy more consistently to target tissue, further improving efficacy and reproducibility.
3. Two complementary energy-based technologies: advanced nonthermal selective focused ultrasound and vacuum-assisted RF combined in one platform. These 2 technologies support same-session combination therapy, allowing for a synergistic treatment effect for a complete body-contouring solution.<sup>32,33</sup>

Step 1: Tightening and tissue preparation with suction-coupled RF. The theory is that preheating the tissue increases local blood circulation and creates mild edema producing a more “wet environment” in the target tissue, which may enhance the cavitation mechanical effects of focused ultrasound treatment.

Step 2: Immediate fat cell destruction to reduce localized fatty areas with the focused ultrasound.

Step 3: Tightening and expedited fat clearance with the focused ultrasound. The theory is that treating with vacuum-assisted RF after the focused ultrasound treatment can increase blood circulation and stimulate localized lymphatic drainage and accelerate fat clearance for even better and more consistent results.

4. Planned 2010 upgrades include a patent-pending Vertical Dynamic Focus (VDF)



**Fig. 3.** UltraShape Contour v3 device. (From UltraShape NA Inc., and Global Sales; with permission.)

ultrasound technology. VDF is designed to treat multiple depths in a single pulse, allowing the flexibility to treat focal depths from superficial to deep. This new technology will deliver higher acoustic peak pressure and treat more fat volume per pulse, which should increase the amount of fat reduction achieved with each patient session.

The UltraShape Contour I System is designed to target and selectively disrupt (lyse) fat cells so that any released triglycerides can be processed by the body's natural physiologic and metabolic

pathways that handle fat during weight loss. UltraShape's published multicenter-controlled clinical study and other independent clinical trials have shown that triglycerides do not accumulate to any clinically significant extent in the blood or liver.<sup>28</sup>

The safety and effectiveness of the UltraShape Contour I is backed by scientifically demonstrated results from clinical trials performed on hundreds of patients worldwide. Since UltraShape received the CE (European Conformity) Mark from the European Commission and a Medical Device License from Health Canada, more than 200,000 commercial patient treatments have been performed through August 2010 with no reported treatment-related serious adverse events.

The clinical and histologic effects of UltraShape have been reported in peer-reviewed articles and national meetings. The highly selective, focused, nonthermal high-frequency UltraShape energy leaves nonadipose tissue undamaged, so the patient has no pain or swelling postoperatively and, with no edema, patients can start to see results in several weeks.<sup>27-33</sup> In general, an average of 2 to 4 cm of circumferential fat reduction<sup>30-33</sup> can be achieved over 3 sessions and 6 weeks from the abdominal and hip regions and about 2 to 3 cm from the inner and outer thighs.<sup>30-33</sup> With the VDF and combined suction-coupled RF, it is anticipated that this can occur after a single treatment.<sup>33</sup>

**UltraShape treatment protocol** Palpate the perimeter of the area to identify exactly where the deformity begins and mark the precise area for treatment with a single line. Only soft tissue deformities with at least 1.5 cm of fat thickness should be treated and not the adjacent flat or concave areas.

Proper patient positioning is a critical factor for a successful treatment. It is important to position the patient so that the treatment area is as flat as possible, enabling complete transducer-to-skin contact and preventing adjacent anatomy from interfering with the transducer movement throughout the treatment. Once the patient is positioned on the treatment bed with a flat area marked for treatment, it is important to lift and reposition the soft tissue around the treatment area with soft positioning blocks and medical tape to maintain maximum fat thickness in the zone of treatment. These positioning and taping techniques have been shown to increase efficacy and reproducibility of results.

After proper positioning, the treatment drapes and marker areas are applied. The intuitive graphic user interface will walk the operator through the final set-up. Once the treatment area and markers

have been acquired, the real-time tracking and guidance system will guide the operator through the treatment per a preprogrammed treatment algorithm. To optimize results, patients should undergo a series of 3 UltraShape treatments spaced 14 days apart. Maximum fat thickness and circumference reduction should be seen by 15 to 30 days after the final treatment.

The UltraShape procedure is performed during a convenient, “walk-in, walk-out” session performed in an office-based environment; it requires no anesthesia or sedation, and the vast majority of patients report no pain or discomfort. There is no bruising, swelling, or downtime associated with the UltraShape procedure. After treatment, patients immediately resume their daily routines with no need for maintenance treatments.

### **LipoSonix**

The LipoSonix system delivers HIFU energy that can disrupt subcutaneous adipose tissue to provide a noninvasive approach to body sculpting, such as a reduction in waist, abdomen, and thigh circumference.

**HIFU mechanism of action** LipoSonix HIFU, is highly convergent energy that is tightly focused in a manner analogous to focusing sunlight with a magnifying glass. Whereas UltraShape is focused, nonthermal, and cavitates only the adipose tissue, LipoSonix core HIFU technology enables its HIFU to be directed with very high intensity and in a very small volume at a specific location. At high energy levels, HIFU energy absorption within the focal zone induces high temperatures at the focal point, causing coagulative necrosis and almost instantaneous cell death.<sup>34,35</sup> The volume of destroyed cells is referred to as a “lesion”. Importantly, the intensity levels above and below the focal zone remain relatively low, keeping temperatures at levels that are not cytotoxic to the untreated, or nontargeted tissue.<sup>34,35</sup> An important feature of HIFU lesions is that the damage is spatially confined with no surrounding cellular damage in areas outside the focal zone. In summary, thermal tissue damage occurs at the focal point without causing injury to the skin and intervening tissues beyond the focal point.

After the treated adipose tissue has been thermally coagulated and destroyed, chemotactic signals activate the body’s normal inflammatory response mechanisms. Macrophage cells are attracted to the treated area where they engulf and transport the lipids and cellular debris. The lipids released from disrupted adipose tissue are ultimately metabolized and the lesion gradually heals in a normal fashion. This results in a volumetric

collapse of the treated tissues and an overall reduction in local adipose tissue volume.<sup>34,35</sup>

The LipoSonix system is equipped with a programmable system pattern generator that consistently and automatically directs HIFU energy over the entire treatment area. The preprogrammed movement of the transducer creates a continuous lesion. The amount of HIFU energy delivered by the LipoSonix system may be adjusted by changing the peak power and by changing the duration of each energy dose. In addition, the system has a user-adjustable focal depth of 1.1 to 1.8 cm. The LipoSonix system must be used with distilled water as a coupling agent to prevent the occurrence of significant acoustical reflections from air pockets at the HIFU treatment head/skin interface.

**LipoSonix preclinical trial results** Preclinical studies were conducted in a porcine model because their skin and subcutaneous adipose tissue closely resembles that of humans. During these studies, the placement of thermocouples in the skin and tissues surrounding the focal zone consistently demonstrated that the application of HIFU results in rapid increases in temperature exceeding 56°C (133°F).<sup>34,35</sup> These temperatures were confined to the focal zone and did not extend outside of the targeted subcutaneous adipose tissue. These results were confirmed by histologic analyses demonstrating that coagulative necrosis was confined to the targeted adipose tissue with no injury to nerves and arterioles outside the treatment area.

**Clinical trial results** Results from the preclinical studies were confirmed in human subjects during an early clinical study. This nonblinded trial enrolled 19 healthy female subjects who were scheduled to undergo elective abdominoplasty. Three patients were treated with 1 of 5 different HIFU energy levels (n = 16) or 2 treatments using 1 to 2 HIFU energy levels performed 4 weeks apart (n = 3). Patients were evaluated after 1, 2, 3, 4, 7, 28, and 56 days. Abdominoplasty was performed 1 to 18 weeks following treatment. Histologic examination of excised tissue showed well-demarcated adipocyte disruption. A normal inflammatory response with the presence of macrophages was observed and phagocytosis of released lipids occurred after 14 to 28 days. Healing progressed normally. Adverse events include swelling, ecchymosis, dysesthesia, and pain on treatment.<sup>35</sup>

Peer-reviewed studies published recently reveal that circumferential reductions of 2 to 5 cm can still be achieved after a single treatment session, but fluence and parameters used to achieve this may result in patient discomfort. Multiple treatments at modified settings are being studied.<sup>35–37</sup>

### **Cryolipolysis**

Cryolipolysis refers to a novel noninvasive technology of using cold exposure to selectively and gradually lead to the reduction of subcutaneous fat. Although the mechanism of action is not fully understood, there is evidence to suggest the onset of an inflammatory reaction within the adipose tissue in response to cold exposure.<sup>38</sup> The mechanism for this phenomenon is a cold-induced apoptotic adipocyte cell death for those fat cells that have been exposed to a cold stimulus that is above freezing but below body temperatures for a defined duration.<sup>39</sup> Results also suggest that fat cells may be more sensitive to cold than other tissues. Manstein and colleagues<sup>40</sup> performed porcine experiments to evaluate the effect of controlled application of cold to skin and subcutaneous fat. Three complementary pig studies were completed: an initial exploratory study, a dosimetry study, and a follow-up safety study to assess the impact of such selective lipolysis on lipid levels. They used a copper plate that was cooled and regulated to  $-7^{\circ}\text{C}$  by an attached heat-exchanger chamber, and applied the plate to multiple sites on the animals. Exposures varied between 5 and 21 minutes and the pigs were observed for 3.5 months. No significant skin changes had manifested during the observation period, but selective fat absorption had occurred at treatment sites, as evidenced by contour indentations. On gross tissue observation, a 40% reduction in fat thickness had occurred, which was confirmed by histology to demonstrate reduction in distance between fat septae.

Originally, both Zeltiq and Zerona had both received limited FDA clearances for skin cooling and blood flow enhancement respectively, are now both FDA cleared for long reduction of subcutaneous fat (love handles for Zeltiq and multiple areas for Zerona). The success in the porcine studies led to human applications. The device consists of a control console and an umbilical cable connecting the cooling applicator cup or paddles to the console. The tissue to be treated, most commonly love handles and lower abdominal tissue, is drawn up with mild suction and the tissue is held between the panels of the treatment cup for 30 to 60 minutes. The amount of cooling (selected energy extraction rate) is controlled by the thermoelectric cooling cells powered by DC current and controlled by thermistors that monitor the skin temperature.

Clinical results from an early report show that consistent fat thickness and circumferential reductions occur that are competitive with other focal reduction technologies.<sup>41,42</sup> Dover and colleagues<sup>43</sup>

demonstrated the use of cryolipolysis for reduction of lateral flank and back adiposities. Thirty-two subjects underwent cryolipolysis with one side serving as the treatment side and the other as the control. Efficacy was determined by ultrasound measurements of fat-layer reduction, photograph comparisons, and physician evaluations. At 4 months, 22% fat reduction was demonstrated in 10 patients undergoing ultrasound evaluation. Visible contour changes were noted in the others, with the most pronounced in those with modest and discrete adiposities.

Coleman and colleagues<sup>42</sup> treated 10 patients to determine the effect of cold exposure on fat loss and sensory nerve function. At 6 months after treatment, there was a fat layer reduction of 25.5% with no long-term sensory disturbances. Six of 9 patients had mild transient reduction in sensation that returned spontaneously with 7 weeks of treatment. One patient underwent a nerve biopsy, which showed no significant changes. Klein and colleagues<sup>44</sup> evaluated the effect of cryolipolysis on serum lipid levels and liver function tests in 40 patients. No appreciable changes were noted in either test after a 12-week follow-up, suggesting the technology has unlikely adverse effects over lipid profiles and liver function.

There is a significant risk of temporary sensory nerve dysesthesia, which resolves over 2 to 3 months.<sup>41,42</sup> The disadvantages of the current device are its slow speed, ergonomics of cup application, and disposable cost, but these can be offset, as the device does not require a technician to operate.

### **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.<sup>45,46</sup> 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.<sup>46</sup>

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.<sup>47</sup> However, the completion of numerous histologic investigations and a placebo-controlled, randomized, double-blind, multisite 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<sup>45</sup> 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,<sup>46</sup> 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<sup>47</sup> 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<sup>48</sup> 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.<sup>45,49</sup>

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 photochemical responses within the targeted tissue.<sup>45,49</sup>

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.<sup>47</sup>

### ***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 belayed. 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 anastomosing 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.<sup>45,49</sup>

### ***Clinical results***

A placebo-controlled, randomized, double-blind, multicentered clinical study was conducted to evaluate the efficacy of the Zerona for noninvasive body slimming.<sup>47</sup> 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  $6 \times 635$ -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

**Table 1**  
Noninvasive body slimming subject ratings

	Respondents
	<ul style="list-style-type: none"> <li>• 35 Total test subjects</li> <li>• 32 Total control subjects</li> </ul>
<b>“Satisfied” Rating</b>	
Test group subjects	70% (21/30)
Control group subjects	26% (8/31)
<b>“Unsatisfied” Rating</b>	
Test group subjects	3% (1/30)
Control group subjects	35% (11/31)

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.



**Fig. 4.** Zerona device. (From Zerona Science and Media Images; with permission.)

“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 cellulitic skin progresses from lymphedema to a lipidema, 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.<sup>16</sup> Thermage™ and the Accent monopolar RF devices have also shown some success with multiple treatments for cellulite.<sup>19–23</sup>

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 Cellutite™ 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.<sup>8</sup>

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.<sup>50</sup> Low-level laser energy may have a role. Lach<sup>51</sup> reported the use of a vacuum/massage and dual-wavelength (650 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 cm<sup>2</sup> in the leg treated with laser and massage, whereas the leg treated with massage alone increased by 3.82 cm<sup>2</sup>.

Kulick<sup>52</sup> 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-CONTOURING COMPLICATIONS

All of the noninvasive body-contouring 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%.<sup>18</sup> With the cryolipolysis technology, a reported temporary, but annoying, dysethesia can happen in up to 20% of patients, but there are no reports of permanent sensory loss.<sup>42</sup>

Although the safety and efficacy of these noninvasive body-contouring 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-contouring 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-contouring 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.

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