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COSMETIC SURGERY (JF SOBANKO)

Getting to the Bare Bones: A Comprehensive Update of Non-Invasive Treatments for Body Sculpting

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Abstract Liposuction is currently the "gold standard" for fat reduction offered by physicians. The growing demand for less invasive procedures has led to a sudden growth of noninvasive alternatives during the past 5 years. Despite being readily available, many of these noninvasive technologies have not been thoroughly evaluated for their short-term and long-term efficacy. To review the varying mechanisms and literature of the commercially available noninvasive body sculpting technologies, specifically radiofrequency, ultrasound, lasers and light, and cryolipolysis. A literature search was performed and evaluated for relevant studies regarding radiofrequency, ultrasound, laser and light, and cryolipolysis technologies for the treatment of body shaping. Patients treated with radiofrequency usually receive 2 months of treatments, with improvements decreasing after 6 months. Multiple studies using ultrasound treatments showed a statistical significant decrease in waist circumference. However, these improvements diminished after 6-month follow-up. Previous studies analyzing laser treatment show mixed results. Studies involving cryolipolysis are limited but show decrease in fat thickness. Noninvasive body sculpting technologies are still early in their commercial development. Additional research is needed to assess efficacy and safety. Early results thus far are encouraging for some of these technologies, but their commercial acceptance appears to have outpaced their scientific scrutiny.

Keywords Fat reduction · Cellulite · Body contour · Body sculpting · Cryolipolysis · Radiofrequency · Ultrasound · Laser · Light

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Since 1997, the number of cosmetic procedures in the United States has increased by 197% with a total of 9.2 million cosmetic procedures in 2011 according to the Aesthetic Plastic Surgery National Database [1]. Not surprisingly, liposuction remains the number one cosmetic surgical procedure. With popular culture's emphasis on body appearance and the public's attention to the worsening obesity epidemic, invasive and noninvasive options to treat unwanted fat have grown. Currently, liposuction remains the "gold standard" for fat reduction. In 2011, physicians in the United States performed 325,332 liposuction procedures with an average cost of $3,000, making it a nearly $1 billion industry. As with any surgical procedure, there remains a risk to the patient. Although rare, these risks include, but are not limited to complications from anesthesia, infection, hematoma, scar, and even death. Despite these risks, the number of liposuction procedures continues to rise. During the past 5 years, commercially available noninvasive fat reduction options have grown tremendously. Each modality utilizes a different approach to target adipose tissue and decrease unwanted fat. This article will review those recent studies for these noninvasive bodysculpting alternatives, including radiofrequency, ultrasound, laser and light, and cryolipolysis.

Radiofrequency

Mechanism of Action

Radiofrequency (RF) devices produce electromagnetic waves ranging from 1.0×10^5 nm to approximately $3.0X10^{13}$ nm. RF exploits the increased electrical resistance in adipocytes relative to adjacent tissue. When the electrical current reaches the fat containing pockets of subcutaneous tissue, it is converted to heat, thus acting as a distinct source of thermal damage. Thermal damage ultimately produces dermal contraction and remodeling [2]. Some studies have

demonstrated neocollagenesis and elastogenesis in RF thermally damaged tissue [3, 4••, 5]. RF technologies were the first energy-based devices used for body sculpting with Thermacool® (Thermage, CA) first being introduced in 2002 for wrinkle reduction. Since then, the FDA has approved a variety of other brands for the treatment of cellulite and circumference reduction.

Devices

There are various configurations used in RF devices: monopolar, bipolar, and unipolar. Monopolar systems use two electrodes that deliver current. One electrode is used as a grounding pad while the other produces the current when it touches the skin. This device is often employed in electrosurgery; however, there have been a few studies demonstrating its efficacy for skin tightening especially for rhytid reduction. On the other hand, bipolar configurations require multiple electrodes that contact the skin and limit the pathway of current, containing it between the electrodes. This often is fabricated into a hand piece that makes contact with the skin using a grid-like array of small pinpoint electrodes whereby the electromagnetic waves pass between (Fig. 1). The array of electrodes create a grid of small, thermally damaged foci, much-like fractionated resurfacing laser spots, which align themselves between the electrode pins and not directly beneath the pins. Rather than creating an electrical current, unipolar devices produce electromagnetic radiation with resultant oscillating water molecules creating thermal effects that drive many of the histological events described by the aforementioned devices. Multipolar devices utilize a combination of monopolar and/or bipolar configurations.

Efficacy and Safety

During the past few years, little clinical research has been published on these emerging technologies. Mlosek et al. recently conducted a placebo-controlled study that involved 45 women using a novel tripolar device [6••]. The women received treatment once a week for 8 weeks with sequential increases in fluence. Ultrasound imaging demonstrated a >2 mm decrease in subcutaneous tissue thickness. When the dermal tissue was taken into account, patients presented with almost a 3 mm loss of tissue thickness. Thigh circumference was reported to have decreased with statistical significance among those who received treatment.

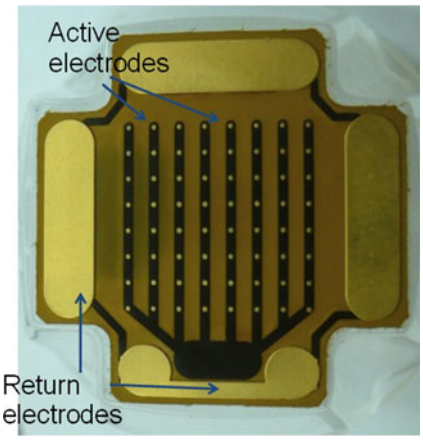

Fig. 1 Sublative™ (Syneron®, Irvine CA) radiofrequency tip

Previous studies suggested that mechanical massage might augment the electromagnetic mechanisms for the improvement cellulite [7, 8]. These findings led Gold et al. to investigate the first device combining RF and vacuum for the treatment of wrinkles and elastosis [9]. Sixteen of 46 subjects experienced side effects, including pain, erythema, burn/blistering, edema, purpura, crusting, and transient hyperpigmentation. All of these adverse events resolved within 4 weeks, and none resulted in permanent complications. Facial rhytides were reduced in a statistically significant manner using a bipolar electrode. Belenky et al. evaluated 27 females for cellulite and skin tightening using a bipolar RF combined with vacuum [10]. After 8 weekly sessions, 55% improvement in cellulite was recorded for all participants. At the 3-month follow-up, an average reduction of 3.31 cm, 2.94 cm, and 2.14 cm was seen for the buttocks, thighs, and abdomen, respectively. However, maintenance was a problem when at 6 months follow-up, a slight loss in the gains made was observed. Of note, this study did not provide any side effects encountered by participates nor any statistical analysis to determine if the results were significant but did correlate an increase in vacuum strength with penetration depth. Increasing the vacuum strength permitted treatment depths of more than 7 mm. Furthermore, they concluded that lower frequencies penetrated deeper into the dermis and subcutaneous tissue allowing for more user control.

Contraindications include pregnancy, implanted electronic devices, artificial joints, metallic devices capable of interfering with the electrical current, active or recent malignancies, collagen vascular disease, autoimmune disease, history of diseases associated with heat, recent use of isotretinoin, or blood coagulopathies. Of note, the companies also advise against using their devices over areas with tattoos because of possible metal ingredients in the dye.

Early experience with RF for noninvasive fat reduction has generated excitement for its utility and safety, but it does come with some risks. Overheating can occur, creating depressions and scarring. This often is felt to be due to pulse stacking, grid overlap, or user error. Pain also is a major limitation. Finally, the inability to reliably reproduce good results has been an obstacle to a broader professional acceptance.

Ultrasound

Mechanism of Action

Ultrasound (US) technology has been used in a variety of medical fields for imaging, shock wave therapy of renal calculi, tumors, and musculoskeletal disorders. Ultrasound affects the adipocytes in two ways: mechanical compression causing destructive cavitation of adipocytes and thermogenesis secondary to cellular absorption. There is an inverse relationship between frequency and depth of penetration. As frequency increases, penetration depth decreases, allowing the user greater control of treatment depths. There are two types of US categories reported in the literature for the use of cellulite therapy and fat reduction. Low-frequency devices use cavitation but cannot generate heat and can cause more unwanted side effects. Additionally, because low-frequency devices do not generate heat, they do not tighten skin. In contrast, high intensity focused ultrasound (HIFU) combines both mechanisms to destroy adipose tissue. HIFU treatment applies enough focal energy to raise tissue temperature above 56 °C for at least 1 second, leaving the surrounding tissue unaffected [11].

Efficacy and Safety

In 2011, Jewell et al. evaluated 180 patients in a randomized, placebo-controlled trial that included three groups: two receiving a single treatment, and one receiving a sham treatment [12•]. At 12-week follow-up, both groups receiving treatment had a statistically significant difference in waist circumference, although the intent to treat group saw a statistically significant improvement for the higher fluence treatment group only. Additionally, Solish et al. applied three different treatment settings to a total of 45 patients with all three groups exhibiting a statistically significant decrease in waist circumference [13••]. Ferraro et al. evaluated 50 patients for localized fat and cellulite with a 12-month follow-up [14••]. The authors combined cryolipolysis with shock waves ultrasound therapy (Proshockice™ - PromoItalia Group S.p.A, Naples, Italy). Patients had an average of 6.86 cm, 5.78 cm, 2.75 cm, and 5.00 cm, and 2.75 cm in reduction of circumference in abdomen, thighs, arms, buttocks, and ankles respectively. The reduction in circumference and fat thickness were significant compared with their baseline. After treatments, cholesterol levels were measured and were mildly increased but remained within normal limits. Unfortunately, the authors did not adequately explain why it was mandatory for their patients to drink 2 liters of water per day and maintain a high protein diet, thus making these results difficult to interpret or practically implement. In a study by Alster and Tanzi [15], 18 women received a single pass along the arm, knee, or thigh with a 4.0 MHz (4.5 mm depth) transducer as well as a dual pass using the 4.0 MHZ and 7.0 MHz (3.0 mm depth) on the contralateral side. The mean global assessment score (GAS) was used to analyze effectiveness. The GAS for the arms, knees, and thighs for the single-pass treated areas were 1.83, 2.33, and 1.3 respectively after 3 months and 2.05, 2.45, and 1.48 after 6 months. The GAS for the arms, knees, and thighs for the dual pass treated areas were 1.92, 2.75, and 1.4 respectively after 3 months and 2.25, 2.78, and 1.47 after 6 months. There were no significant differences between the two treatments. Adverse effects in this study included erythema and tenderness.

No study to date has reported any significant increase in baseline laboratory values, particularly lipid profile. However, some adverse effects noted include erythema, ecchymosis, edema, discomfort during treatment, and dysesthesias. Pain is a significant limiting factor for these procedures, and it is not uncommon for patients to require pain control during treatment, often deterring patients as well as practitioners from using this modality.

Lasers

Mechanism of Action

Currently the majority of commercially available lasers for fat reduction are used in the setting of laser assisted liposuction (LAL). While the FDA approved the use of low-level laser therapy (LLLT) for fat reduction in 2010, the use of lasers for noninvasive fat reduction is still in its research phase.

LLLT devices emit wavelengths in the range of 635–680 nm. This spectrum directly damages the adipocytes, creating pores and an egress of the cell contents. Currently the pathophysiology is not entirely understood; however, the laser is thought to photochemically induce damage to adipocytes.

Efficacy and Safety

Using an experimental laser (Lipex 2000 lipolaser, Meridian Company Ltd, Korea), Carruso-Davis et al. examined 40 subjects with a body mass index (BMI) <30 in a randomized, controlled study [16•]. Whereas their results demonstrated the treatment group to have had a reduction in girth by approximately 2 cm, the difference compared with the controls was only significant before the third treatment. Additionally, prior studies have not been convincing. Elm et al. failed to demonstrate any statistical significant difference of waist or thigh circumferences between the treated and control groups [17•]. Mixed published results suggest more research is needed to determine the efficacy of this device.

In contrast, infrared laser may have a promising future for the use of body contouring. In 2006 Anderson et al. [18] reported the specific wavelength of 1,210 nm and 1,720 nm to selectively heat subcutaneous fat. Unlike LLLT, this device targets lipid molecules using selective photothermolysis rather than photochemical reactions. Since lipid-laden tissue has an increased amount of CH-CH2 bonds, the subcutaneous fat is susceptible to the infrared spectrum. In this study by Anderson et al., a laser emitting 1,210 nm destroyed adipose tissue up to 5 mm below the epidermis. A subsequent study by Wanner et al. [19] reported a pilot study that involved 24 subjects who received laser treatments followed by histological evaluation. Four weeks after treatment, laser-treated tissue exhibited fat changes and destruction. Unfortunately, pain was a major side effect with some subjects requesting medication for relief. Epidermal changes also were noted in some patients secondary to lack of cooling in the treated spot. To date, there are no randomized control studies investigating efficacy of pulsed lasers for selective fat destruction.

Cryolipolysis

Mechanism of Action

The mechanism for cryolipolysis stems from observations of "popsicle panniculitis," which was seen in infants and first described in the 1960s [20, 21]. To date, the exact mechanism for pathogenesis is unknown but is believed to be caused by a cryogenic lobular panniculitis. Cryolipolysis devices attach to the skin using a vacuum-assisted hand piece for localized fat cooling and fat reduction. This technique was introduced in 2007 and approved by the U.S. Food and Drug Administration (FDA) in 2010. Manstein et al. describe this mechanism as energy extraction [22]. The rate of this heat extraction is referred to as the cooling intensity factor (CIF), which is expressed in mW/cm^2. Cryolipolysis takes advantage of the increased sensitivity to cold by the adipocytes leaving the overlying dermis and epidermis unaffected, thus producing selective fat damage and subsequent loss.

Efficacy and Safety

In the seminal study by Manstein et al., 3.5 months after a cooling applicator was applied to black Yucatan pigs, histologic fat loss of 40% was evident in the treated area. There were no significant abnormalities in lipid levels throughout the study. They concluded that controlled cooling of fat initiates a cascade of cell-mediated inflammatory events that ultimately lead to selective destruction of adipocytes. Despite the pigmented skin, no scaring or ulcerations were observed. Following this study, a device by Zeltiq®, Coolsculpting® (Zeltiq, Pleasanton, CA), was created using a vacuum to draw up the tissue between two cooling panels. Until the development of this novel technology, most if not all prior technologies sought to manipulate the use of heat or the biochemical interactions of light with tissue. This is the first advancement that controllably employed heat extraction.

Peer-reviewed literature on this novel and evolving technology is limited, but early reports are very positive. In 2009 Dover et al. published a multicenter, prospective, nonrandomized study evaluating cryolipolysis for fat reduction of flanks and back. In this study, 32 patients were assessed and evaluated 4 months status after one treatment. The outcome was established by photographs, physician assessment, and subjective satisfaction. Twenty-seven (84%) patients exhibited fat reduction and contour changes. Ten of the subjects underwent ultrasound imaging that exhibited a 22% reduction in the fat layer 4 months after treatment [23].

Coleman et al. [24] followed nine patients during a 6-month course after receiving cryolipolysis in order to analyze side effects that occur with this treatment. Erythema and sensory defects were appreciated after treatment. For those who had erythema and numbness, these completely resolved within 6 weeks. Of the nine patients, three had no sensory deficits, four had decrease in light touch, which occurred 1–2 weeks after treatment and lasted for 1–2 weeks. Two point discrimination deficits also were noticed 1–3 weeks after treatment in four patients. Again, this symptom resolved within 3 weeks. One patient experienced changes in temperature sensation, which lasted up to 2 weeks. The most common side effects were pain and decreased pinprick sensation lasting up to 2 months. Biopsies for these patients 3 months following their procedure suggested that cryolipolysis does not permanently damage nerve fibers in the epidermis or nerve plexi in the dermis.

The most recent study by Shek et al. involved 33 Chinese subjects [25••]. The authors used the Zeltiq device and compared the results of having one or two treatments 3 months apart. On average, it took 4 weeks after treatment for any noticeable changes, with 81% of subjects reporting a noticeable difference. Fat thickness using calipers found a 14.6% decrease in fat for the group 2 months after the single treatment. The group that received two treatments had a 14% reduction in fat after the first treatment and an additional 7% after the second treatment. Complications included redness (23.8%), bruising (9.5%), and numbness (28%) with all of these resolving within 1 month. This study is the first of its kind to report results after multiple treatments. Although improvement decreased with subsequent treatments, the authors concluded that there is benefit for multiple treatments. Caution should be advised for those with umbilical hernias for fear of possibly incarcerating herniated tissue. Additional areas of research could include the number of treatments needed to maximize benefit, the exact role of vacuum and massage, or time intervals between treatments. All of this

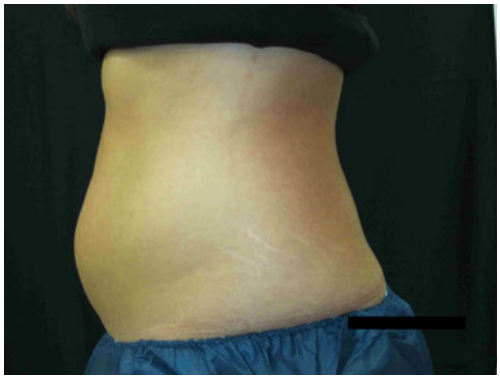

Fig. 2 View of patient's left flank pre cryolipolysis. Photo taken of a patient evaluated in clinic

Fig. 4 View of patient's lower back pre cryolipolysis. Photo taken of a patient evaluated in clinic

underlies the need for more information regarding the exact mechanism of cryogenic adipocyte injury. See Figs. 2, 3, 4 and 5 for results from our own clinical experience.

Conclusions

As public demand increases for the removal of unwanted fat, it is important that noninvasive treatments become better understood to provide a safe alternative to meet those public demands. Although liposuction remains the "gold standard," it presents with its own set of risks. When using noninvasive modalities, proper patient selection is critical for a successful treatment and patient outcome. Many trials performed have shown efficacy; however, long-term results are suspect and relapse is common. Despite statistical significance seen in many of these studies, it may not always translate to clinical significance. For instance with RF, a 2- to 3-mm loss of fat thickness may not be visible to the patient. Modest improvements, particularly compared with the more measurable benefits of liposuction, and the possibility for maintenance treatments, should be considered for disclosure during the cosmetic consultation. Unlike the immediate and obvious improvement following liposuction, many of these options take weeks to months before any benefit is appreciated.

Currently, there are no reports of any long-term damage aside from depressions and scarring seen with RF devices. Compared with liposuction, these options are safe and well tolerated. It appears that transient pain is a limiting factor but often is controlled with reassurance and treatment. Barring any future breakthroughs, ultrasound will likely end up as an adjuvant procedure used with other noninvasive techniques to produce the most efficacious outcome, whereas LLLT and laser devices are still very immature technologies that require some additional scientific development. The technology with the most promise appears to be cryolipolysis with its growing demand, high reproducibility, and excellent safety profile.

The notion of having an effective noninvasive option for fat and cellulite improvement is exciting. It should be noted that as often as new technologies develop a hasty euphoric adoption often is observed followed by

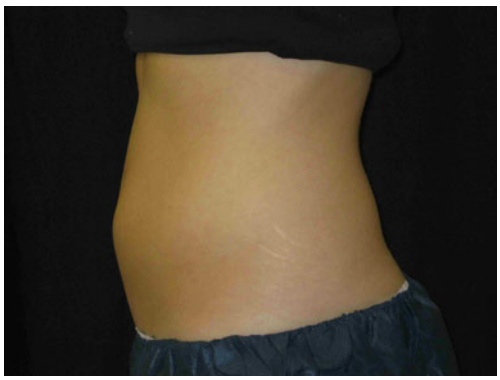

Fig. 3 View of patient's left flank Post treatment. Photo taken of a patient evaluated in clinic

Fig. 5 View of patient's lower backPost treatment. Photo taken of a patient evaluated in clinic

the realization of unexpected risks and unreliable results. Whereas this may be the case for some of the aforementioned technologies in this discussion, early reports strongly suggest that there will likely be a perseverance and successful development of niche applications for these technologies as they continue to develop. The future for these devices looks promising; however, the commercial availability should not replace proper study for improved patient care.

Conflict of Interest Brian A. Raphael declares that he has no conflicts of interest.

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