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Review of the Mechanisms and Effects of Noninvasive Body Contouring Devices on Cellulite and Subcutaneous Fat

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Abstract

Context: Today, different kinds of non-invasive body contouring modalities, including cryolipolysis, radiofrequency (RF), low-level laser therapy (LLLT), and high-intensity focused ultrasound (HIFU) are available for reducing the volume of subcutaneous adipose tissue or cellulite. Each procedure has distinct mechanisms for stimulating apoptosis or necrosis adipose tissue. In addition to the mentioned techniques, some investigations are underway for analyzing the efficacy of other techniques such as whole body vibration (WBV) and extracorporeal shockwave therapy (ESWT). In the present review the mechanisms, effects and side effects of the mentioned methods have been discussed. The effect of these devices on cellulite or subcutaneous fat reduction has been assessed.
Evidence Acquisition: We searched pubmed, google scholar and the cochrane databases for systemic reviews, review articles, meta-analysis and randomized clinical trials up to February 2015. The keywords were subcutaneous fat, cellulite, obesity, noninvasive body contouring, cryolipolysis, RF, LLLT, HIFU, ESWT and WBV with full names and abbreviations.
Results: We included seven reviews and 66 original articles in the present narrative review. Most of them were applied on normal weight or overweight participants (body mass index < 30 kg/m^2) in both genders with broad range of ages (18 to 50 years on average). In the original articles, the numbers of included methods were: 10 HIFU, 13 RF, 22 cryolipolysis, 11 LLLT, 5 ESWT and 4 WBV therapies. Six of the articles evaluated combination therapies and seven compared the effects of different devices.
Conclusions: Some of the noninvasive body contouring devices in animal and human studies such as cryolipolysis, RF, LLLT and HIFU showed statistical significant effects on body contouring, removing unwanted fat and cellulite in some body areas. However, the clinical effects are mild to moderate, for example 2 - 4 cm circumference reduction as a sign of subcutaneous fat reduction during total treatment sessions. Overall, there is no definitive noninvasive treatment method for cellulite. Additionally, due to the methodological differences in the existing evidence, comparing the techniques is difficult.

Keywords: Body Contouring, Subcutaneous Fat, Cellulite

1. Context

In the recent years, noninvasive body contouring techniques have become one of the most widespread procedures and are growing fast in areas of esthetic medicine (1, 2). The vast majority of surgical body contouring methods has inherent risks and complications such as pain, swelling, prolonged recovery, scarring, hematoma or infection, which make noninvasive procedures increasingly popular (3-5). According to reported data by the American society for aesthetic plastic surgery in 2013, the significant risk of invasive body contouring procedures has led to 521% growth of noninvasive techniques since 1997 (6). In addition, it has been estimated that noninvasive body-contouring procedures are growing 21% annualy (7). Even for shortening postoperative recovery, decreasing bruising and more skin tightening, surgical lipectomy techniques are combined with noninvasive methods (7).

1.1. Cellulite and Subcutaneous Fat

Cellulite is a skin discomfort developed by multiple factors (8) but the main etiology is not completely understood (9). The appearance of skin changes and it becomes like an "orange peel". Cellulite is commonly found on the thighs and buttocks (8, 10, 11). Cellulite is more common in adult females than males. Up to 98% of females are concerned about their skin changes due to cellulite and the changes decrease their self-esteem (12).

The Nurnberger and Muller scale is the most commonly used classification for cellulite (9, 13). According to this scale, three grades were defined: I- visible changes with skin clamping or muscle contraction; II- visible changes without manipulation; and III- visible changes associated with nodules. In addition to Nurnberger and Muller grading-score, recent classification includes four additional variables: (i) the number of evident depres-

sions; (ii) the depth of visible depressions; (iii) appearance alterations of skin surface and (iv) laxity grade. According to these items, cellulite is classified with three degrees: mild, moderate and severe (9). Estimating accurate results of anti-cellulite therapies is not easy but there are some practical methods for measuring the outcomes such as real-time scanning ultrasound image, three-dimensional optical skin surface measurement, clinical photographing, histological findings, personal questionnaires, etc. (14-18).

Subcutaneous fat is different from cellulite. As mentioned before, cellulite is defined by focused and topographic skin changes with an orange-peel look, yet subcutaneous fat is an indicator of peripheral fat mass, which could be evaluated by circumference and skin fold measurements and variation in these parameters could be considered as an indicator of cellulite changes. However, other cellulite indices such as skin elasticity and dermal thickness should be considered besides these measurements (11).

In the past, different methods of body contouring were assessed in order to specify their safety and influence on subcutaneous fat reduction and the treatment of cellulite. Patient satisfaction in the short-term and medium-term, durability of the results and time to obtain maximum outcomes, common complication and recovery time were considered in these studies. The objectives of this paper were to review and evaluate prominent methods on noninvasive subcutaneous fat removal and improvement of cellulite and comparing their clinical results. Since, there is physiological and biochemical diversity between subcutaneous fat tissue and cellulite, both were included in the review.

2. Evidence Acquisition

We used pubmed, google scholar and the cochrane review database websites to find relevant articles in the English language (abstract and/or full-text). Systematic reviews, review articles, meta-analyses and randomized clinical trials (published up to February-2015) were considered. The keywords used for our research were as the following: noninvasive body contouring, subcutaneous fat, obesity, cellulite, cryolipolysis, radiofrequency (RF), low-level laser therapy (LLLT), infrared light and high-intensity focused ultrasound (HIFU), extracorpeal shockwave therapy (ESWT) and vibration exercise. To increase the inclusiveness of our search strategy, authors also studied the texts to find other relevant cited manuscripts that were not retrieved in the initial search. Given the narrative nature of the review, no formal quality assessment was done.

3. Results

In the primary search, we found 2024 articles with the keywords. Non-English papers, and articles that did not mention clinical efficacy measures or used invasive methods were excluded. Further, articles, which focused on the effects of various methods on weight loss or percentage body fat, were omitted. We included seven reviews and 66 original articles in the present narrative review. Most of them were applied on normal weight or overweight participants (body mass index (BMI) < 30 kg/m^2) of both genders with broad range of ages (18 to 50 years on average). Six of the articles evaluated combination therapies and seven compared the effects of different devices. The summary of the results is mentioned in Figure 1.

Below, we discuss the common noninvasive body contouring methods:

3.1. High Intensity Focused Ultrasound

The concept of applying HIFU for therapeutic aims was introduced in 1942 and for more than 50 years HIFU has been used for treating organ tumors, kidney stones and uterine fibroids to decrease the need for aggressive procedures (19-21). Recently, attention was drawn to HIFU devices for reducing adipose tissue and body contouring (7).

By using an external transducer, HIFU energy cuts off targeted adipose tissue. However, it has no effects on surrounding tissues. Due to high convergence of ultrasound energy at high frequencies, tissue damage is limited to a small focal point. ultrasound energy makes molecular vibrations at the zone, that leads to increasing temperature at targeted tissue above 56°C and coagulative necrosis of fat cells (20, 22, 23).

There are various types of HIFU devices in the market such as LipoSonix (Medicis Technologies Corporation, Bothell, Washington), which are approved by the food and drug administration (FDA), yet there are also other ultrasound devices developed for noninvasive body contouring not yet approved by the FDA such as Proslimelt (medical care consulting, Murten, Switzerland), Medcontour (general project, Florence, Italy), Ultracontour (Medixsysteme, Nimes, France), Novashape (UltraMed,Milton,ON, Canada), Accent Ultra (Alma, Buffalo Grove, IL, USA and Vaser-Shape (sound surgical technologies, Louisville, CO, USA) (7, 22).

In 2011, a preclinical animal research on 26 pigs was performed. Treatment was applied by HIFU in one session for each site (25 × 25 mm for each site) and energy levels varying from 85.3 to 270 J/cm^2. The study showed successful decrease of subcutaneous fat. In addition, no adverse effects were seen on the skin, fascia, or other surrounding tissues. No systemic abnormalities in blood chemistry parameters or fat emboli were reported during necropsy (22).

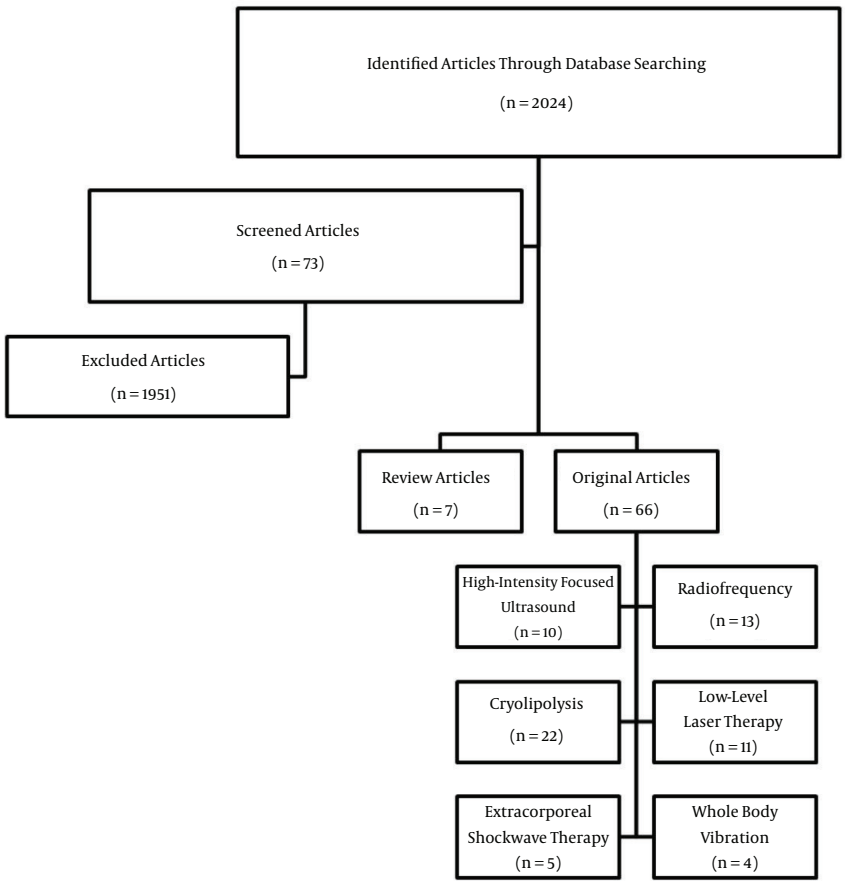

Figure 1. The Flowchart of the Search Strategy

In a randomized, single-blind, sham-controlled study in 2012, 180 males and females (18 - 65 years) participated with BMI of $\leq$ 30 kg/m^2 and Subcutaneous adipose tissue (SAT) thickness of $\geq$ 2.5 cm in the treatment region (anterior abdomen and flanks). During the study, participants continued their usual diet and physical activity. Patients were divided to three groups and received HIFU treatment at one of the three total doses of energy: 177 J/cm^2 (three passes at 59 J/cm^2), 141 J/cm^2 (three passes at 47 J/cm^2), or 0 J/cm^2 (three passes at 0 J/cm^2; sham group) for nearly one minute for each targeted zone and 15 minutes for the total treatment session. No abnormalities in blood lipids or inflammatory markers were reported. The most adverse effects of treatment were pain, ecchymosis and swelling. Post-treatment follow-up at 12 and 24 weeks revealed no significant changes in cholesterol, triglycerides, free fatty acids, markers of inflammation and liver or renal function (24). Moreover Jewell et al. confirmed HIFU as a useful method for reducing waist circumference. After 12 weeks, significant reduction in waist circumference in the two study groups was reported. The mean decrease in waist circumference was more than 2 cm. However, no changes in weight or BMI were reported (25).

Likewise, a retrospective study in 2010 with 85 participants (57 females and 28 males with a mean age of 43.8 years), showed similar findings at $\leq$ 16-week fallow-up. Mean energy level of the HIFU device was 134.8 J/cm^2 and treatment session duration varied from 60 to 90 minutes. The most common adverse effects of this study were edema, tenderness, ecchymosis, and hard lumps, and only one participant experienced major pain. No significant change on blood lipids was reported. The average decrease in waist circumference was 4.6 cm, 12 weeks after treatment (26).

Shek al. published a single center prospective study on 12 Chinese participants (nine females and three males, with a mean age of 39.5 years), who underwent single treatment on their anterior abdominal wall. Subjects with BMI

$\leq$ 30 kg/m^2 and subcutaneous adipose tissue $\geq$ 2.5 cm in the targeted zone were recruited in the study. The minimum energy level for the treatment session was 150 J/cm^2 and the energy was increased up to patient's tolerance level (mean 161 J/cm^2). Initial measures included weight, BMI, and waist circumference. Statistically, a significant decrease in waist circumference at four, eight and twelve-week fallow-up was reported. The average decrease of waist circumference was 1 cm at the 12th week follow-up. However, there was no significant change in weight or BMI (20).

In a clinical trial in Paris, HIFU technique was applied on 25 Caucasian subjects (females with a mean age of 38.9 years) and this treatment was shown to be a safe procedure for body contouring, which had a significant effect on abdominal circumference. Mean BMI of patients was 24.5 and mean baseline abdominal fat thickness was 3.24 cm. Each patient received three treatment sessions at 14-day intervals. According to the reported data, mean changes in circumference from baseline were -2.47 $\pm$ 0.44, -3.52 $\pm$ 0.46 and -3.51 $\pm$ 0.56 cm on days 14, 28 and 56, respectively (27).

To sum up, it seems that HIFU is a safe and efficient technology for reducing subcutaneous adipose tissue without any significant effect on blood lipid or inflammatory markers and with no local adverse effects such as burns or scarring. Studies based on the use of HIFU for body contouring showed that self-reported patient's satisfaction is approximately 47% to 86%. These treatment effects are not dependent on diets or daily physical activity. In addition to the above-mentioned benefits of HIFU, the recovery time of the procedure is minimal, which can be considered as an important advantage. However, according to available evidences no considerable influence was reported on BMI or body weight (20, 22, 25, 26, 28).

3.2. Radiofrequency

Radiofrequency is an electromagnetic wave that was initially used for treating periorbital wrinkles, rhytids and skin laxity (29, 30). Today, RF is extensively used for body contouring, skin tightening and cellulite reduction (31).

Radiofrequency is commonly used for increasing deeper skin temperature without any epidermal or dermal ablation. It is not only used as an efficient method for contracting or inducing skin tightening but also as an effective method for reducing fat in repetition (31, 32). However, there is no standard protocol for treatment time with RF, and the range of therapeutic sessions were widespread between 1 and 24 weeks (30). However, higher temperature at shorter time could be lethal for adipose tissue but it is not necessarily comfortable for patients; longer time, for example eight to ten minutes, with lower temperature, leads to intended adipose cells damage (32). Former researchers insisted that different parameters in addition to time are related to the success of RF, such as power and the frequency of treatment sessions, yet the exact protocols in this area are unavailable (30).

Radiofrequency generates heat in different tissues by transforming energy through three basic mechanisms from electromagnetic field (32). These mechanisms include (i) orientation of electric dipoles that already exists in the atoms and molecules in the tissue; (ii) polarization of atoms and molecules to produce dipole moments; and (iii) displacement of conduction electrons and ions in the tissue. The frequency of an RF device ranges between 3 kHz and 24 GHz, and the monopolar and the bipolar configuration are used commonly in medicine (31).

Vela Smooth was the first RF device, which was used widely for body contouring. Now, there are various types of RF devices in the market such as Thermage (SoltaMedical, Hayward, CA, USA), Accent (Alma Lasers), TriPollar (Pollogen, TelAviv, Israel), Freeze (Venus Concepts, Karmiel, Israel) and most recently TiteFX (Invasix).

A variety of studies demonstrate smoothening of the cellulite exposure using RF and reduction of subcutaneous tissue, which leads to circumference reduction (16, 17, 33-36). Manuskiatti and colleagues evaluated the effects of a TriPollar RF technology on abdomen and thigh circumferences and cellulite appearance in 39 female subjects with cellulite grade $\geq$ 2 (Nurnberger-Muller scale). The subjects received eight treatment sessions, seven days apart, without any change in their physical activity and diet. Four weeks after the last treatment session, the study showed significant circumference reduction of the abdomen and thigh regions. Nevertheless, there was no significant reduction in buttocks and arms. In addition, the study showed that TriPollar RF improved the appearance of cellulite (16). For assessing treatment procedure's outcomes, circumference measurements of treated region were done along with taking real-time scanning images and measuring skin elasticity. The cellulites condition was evaluated in each patient according to the Nurnberger-Muller scale (16).

Del Pino et al. assessed the effects of applying unipolar RF [the Accent RF System (Alma Lasers Inc)] on subcutaneous fat of the buttocks and thighs of 26 female subjects (ages 18 to 50 years) with visible cellulite (grade 1 to 3). Two treatment sessions, two weeks apart, were considered. They used real-time scanning image ultrasound for measuring the distance between the dermis and the camper's fascia, and their findings showed that controlled tissue heating with RF could reduce the thickness between the dermis and fascia. The average reduction in thigh and buttocks were 2.64 and 1.8 mm, respectively. Understanding the effect of treatment sessions from changes on skin texture and clothing leads to patient's satisfaction with the

procedure and was assessed by the studying group (14).

Another study in Spain revealed that RF could improve upper thigh cellulite in females aged 24 - 58 years, and the positive effects remained at least for six months after treatment. Van Der Lugt et al. applied a unipolar, volumetric RF device (frequency between 0.6 and 2.4 MHz) for 12 sessions, one week apart. All of the fifty female subjects (with homogenous cellulite depositions) showed considerable amelioration in buttock skin conditions, which was completely noticeable by real-time scanning ultrasound image and comparing the distance between stratum corneum and Camper's fascia and from the stratum corneum to the muscle, before and two weeks after treatment sessions. Most of the patients were satisfied with the treatment. However, two months after the last session, slight return was seen in the favorable treatment results (17).

Another study in New Jersey revealed that utilization of unipolar RF (Alma Lasers, Buffalo Grove, IL) improved upper thigh cellulite in females. All the subjects were over the age of 30 years with upper thigh cellulite (grade 3 to 4, according to the Nurnberger-Muller scale). Their thigh circumference decreased 2.45 cm on average after six sessions of treatment, one week apart. However, there were no significant changes in body weight and blood lipids after the treatment (34).

Sadick and Mulholland (35) reported their experience on the use of RF energies in order to treat cellulite in 35 female subjects. Each patient received 8 to 16 treatment sessions one week apart and target zones were thighs and/or buttocks. Subjects were instructed to continue their normal lifestyle (including diet and fluid consumption). After eight treatment sessions, the mean reduction in circumference was 2.03 cm.

By reviewing related articles on RF therapeutic effects on skin laxity, Araujo et al. confirmed that up to 96% of former studies obtained positive outcomes with RF. These data were collected by before and after exposure pictures, patient's questionnaires, biopsy, etc. (30). Satisfaction for subcutaneous fat reduction with RF was approximately 71 - 97%, according to patients' self-reported data (4). However, significant statistical outcomes about the effects of RF on skin laxity and cellulite treatment were low and limited (30, 37).

In summary, it seems that RF is a safe and relatively effective method for improving skin appearance and decreasing subcutaneous fat, especially in the abdomen and thighs. In addition, safety and relatively lower time for applying the modality are important advantages.

3.3. Cryolipolysis

Cryolipolysis is one of the newest procedures for non-invasive fat reduction, which was introduced as a body contouring technique in 2007 (19, 38). It has a major difference from other modalities such as ultrasound, radiofrequency, etc. (11). The principle of cryolipolysis is based on higher sensitivity of adipocytes to cold in comparison with other water-rich cells (39).

In 2010, cryolipolysis received FDA clearance for love handles (Zeltiq). In 2012 and 2014, FDA clearance was obtained for fat removal by cryolipolysis at abdomen and thighs, respectively (7, 19, 40).

The efficiency of the method on reducing fat layer thickness without any physical damage to circumambient tissue has been proven clinically. Assessing the efficacy of cryolipolysis and its potential side effects in different subjects showed that not only the procedure was effective in reducing adipose tissue, but also patient satisfaction was high after the treatment session (4, 5, 38-48).

Jalian reported fat cells sensitivity to cold injury in 1902 (19). In 1941, the term "adiponecrosis e frigore" was used by Haxthausen for sores, which occurred due to exposure to exceeding cold (49). During the period between 1940 and 1970, case reports showed gradual fat reduction in the lower cheeks of children who suck on a popsicle and the effect was known as "popsicle panniculitis" (5, 50). Such findings led to the advancement of cryolipolysis as a body contouring method (5, 19).

A preclinical animal research to assess effects of controlled cooling on subcutaneous fat was performed in 2008. In this study, black Yucatan pigs were placed under general anesthesia and their target zones (10 sites for each pig) were exposed to exceeding cold temperature within 10 minutes (20, -1, -3, -5, and -7 degrees C). The four pigs were controlled on days 1, 2, 7, 14 and 28 after the treatment session and the fallow-up continued up to 3.5 months for one pig. The assessment showed approximately 40% decrease in fat layer thickness without any scarring or damage to surrounding tissues (51). In addition, it seems that the best results in fat damaging were obtained at lower degrees (5, 51). However, studies have demonstrated that under temperature conditions as high as 1°C, adipocytes are damaged and possibly their chances of survival decreases. Scientific evidence on the effects of temperatures below -7°C on dermis and epidermis is not available, owing to the fact that the majority of research has been carried out under conditions with temperatures over -7°C (43, 52). Similar to Manstein, Zelickson et al. reported their porcine experiment that underwent cryolipolysis for one session. Their findings showed that the thickness of the superficial fat layer decreased by 33% without any side effects (52).

In human studies, the protocol of cooling has been done by cup-shaped applicators with two cooling panels. A vacuum pulls the tissue and draws the target zone between cooling panels. The constriction of blood vessels ac-

celerates the cooling process. The treatment session usually takes one hour (5, 7). Despite the fact that there are not any considerable changes in body fat instantly after the treatment session, different studies proved the efficacy of the procedure on reducing subcutaneous adipose tissue over time (11). In a prospective human clinical study, Dover et al. revealed a decrease in lateral flank and back fat following cryolipolysis. In this study, 32 subjects underwent a 60-minute treatment session. At a four-month post treatment fallow-up, 84% of subjects showed some degree of fat thickness reduction by photographic assessment. In addition, significant reduction in fat layer (22%) was reported in ultrasound evaluation in ten participants. Furthermore, more than 90% of participants were satisfied with the process and no significant complication was reported (53).

In another study, ten subjects (older than 18 years old) underwent cryolipolysis for 30 to 60 minutes on their love handles. Two and six months after the treatment, fat layer thickness decreased by nearly 20% and 25.5%, respectively. In addition, weekly neurologic assessment showed that cryolipolysis could make mild reversible changes in a short period, but the changes returned within two months after the treatment (43).

Shek et al. reported their experience on Chinese subjects with visible central fat bulge (on the abdomen and/or love handles). Subjects (males and females, above 18 years old) were divided to two groups. Group A received one treatment session on the abdominal fat bulges and group B received two treatment sessions on two sites (abdomen and flank), 60 days apart on average. After two months, 14% abdominal adipose tissue reduction in group A, and 14 and 13.4% fat reduction in abdomen and flank region, respectively in group B, was shown by caliper measurement. Moreover, it was reported that increasing the number of treatment sessions to two, improved the positive results. In this study, the fat layer reduction in the abdomen region rose by 7.2%, two months after the last treatment, and 4.3% improvement was found in the flank. This was statistically significant for abdominal fat (48).

Zelickson et al. demonstrated that using cryolipolysis for treating inner thigh fat bulges could be safe and effective for male and female subjects. They assessed 45 patients (mean age 48.1 years and mean body mass index 24.6 kg/m^2), who underwent one treatment session with a flat cup applicator. At two- and four-month fallow up sessions, photographic evaluation, circumferential measurements and ultrasound imaging was performed. The results showed a 0.9-cm reduction in inner thigh fat bulges at a 16-week fallow up, and 93% of the participants were satisfied (39). In a similar study on subjects with BMI of up to 40kg/m^2, a single treatment session on inner thighs was performed. Comparing photographs and ultrasound imaging at a four-month fallow-up showed a 20% fat reduction (3.3 mm) on average (41).

The shape of the applicator has recently been changed to a new generation of sharply-contoured device. A clinical study, in 2014, assessed the effectiveness of this new applicator on flanks. In this study, 10 female subjects (mean age 42.2 years and mean body mass index 24.3kg/m^2) received two treatments for each flank with 50% overlap. Photographic evaluation showed 43% improvement in reducing fat bulges on average in a follow-up after three months without significant side effects (40).

In a multicenter study, 518 males and females received the treatment in different target zones, including abdomen, back, buttocks, inner thighs and knees. At the 12-week fallow up, treated sites were evaluated by skin fold thickness. Overall, 94% of subjects experienced fat reduction in comparison with the controlled side. In addition, a 23% decrease in adipose tissue at the treated sites was reported. Blind investigation with photographs revealed fat layer thickness reduction in 73% of the patients. In addition, the results suggested the greatest reduction on abdomen and flank and the least changes on thighs, knees, and buttocks (44).

A comprehensive review in Canada showed the efficacy and safety of cryolipolysis in reducing thigh, abdomen, arm, and back fat bulges. In this study, investigators assessed the treatment process at 464 sites, during three years. The major treatment zones were abdomen and flank but some treatments were performed on other zones. Skin texture, laxity and cellulite were improved after the treatment (42).

The long-term effect was not clear. In two case reports, it was mentioned that two males, who underwent cryolipolysis treatment sessions were successful in keeping the fat reducing results, two and five years after the procedure (54).

In summary, using cryolipolysis for body contouring is effective for patients with separate fat bulges. However, it seems that the procedure is not pronounced for obese patients with considerable skin flaccidity (55). cryolipolysis is not dependent on the operator and this should be considered as an advantage for the technique, yet long treatment sessions are an important disadvantage (7). Kennedy et al. also reported that in most studies, assessing effects of cryolipolysis were done by patient questionnaires, anthropometric measurements, clinical photographing, etc. Self-reported satisfaction on reducing subcutaneous fat in patients was more than 70% (4).

3.4. Low-Level Laser Therapy

Low-level laser therapy is another noninvasive method for reducing adipose tissue and received FDA clearance in

2010. Before that, LLLT was widely used for treating other problems such as neurologic, ophthalmic, dental and dermatologic diseases (56-58).

Although there are some evidences, which show the effects of LLLT on reducing fat in combination with liposuction, the evidences for the effects of this method as a stand-alone procedure, are not sufficient (56). Applying LLLT for fat removal has no observable consequence on surrounding tissues and does not increase tissue temperature. Moreover, it takes time to show its own effect on the treated zone. The laser beam energy is defined by the ray dosage that is emitted to the body (7).

The type of device available in the market, works at a wave-length of 635 nm and has four adjustable arms. One treatment session with LLLT lasts up to half an hour and six to eight sessions is required in order to obtain optimum results. In addition, manufacturers encourage consumers to use some supplements such as vitamin B5 and L-carnitine, Ginkgo biloba or green tea to reinforce circulatory and lymphatic systems (56).

Using LLLT for fat reduction and body contouring is based on experiences, which showed that applying 635-nm laser leads to deflation of temporary tiny openings within membrane of adipose cells and releasing fats into the interstitial space. The result of these changes is reduction of unwanted fat. However, the openings have no destructive effect on body cells but let lipids enter the interstitial space and excrete from the body. It seems that the above-mentioned mechanism is the consequence of photoexcitation process of cytochrome c oxidase in mitochondria's respiratory chain (56, 59, 60). The first experiments of using LLLT with the possible mentioned mechanism, demonstrated that applying 635 nm, 10 mw intensity for six minutes caused approximately 99% fat reduction (60), though later studies such as the experience of Brown et al. did not support the these findings (61).

In 2009 Jackson et al. reported that applying LLLT to reducing body fat could be effective on overall circumference. They assessed 67 overweight participants (BMI 25 to 30 kg/m^2), which underwent LLLT (635-nm light with 2.5 mW power) for two weeks (three treatment sessions in each week). After treatment by LLLT (Zerona lipolaser was the first device that received FDA clearance), a total of 891-mm fat reduction was observed across waist, hips, and thighs. Maximum fat reduction was reported across the waist (2.66 cm). However, two weeks after the last treatment session, a 7.8-mm increase in circumferences was seen in three treated zones (62). In another clinical study, Jackson et al. reported that treating 689 subjects with LLLT (12 treatment sessions within 14 days) leads to 13.13-cm circumferential reduction in waist, hips, thighs, arms, knees, neck and chest (63).

Caruso-Davis et al. used 635 - 680 nm LLLT (Meridian LAPEX 2000 lipolaser system, Meridian medical Inc. Anyang, Korea) for reducing adipose tissue. Forty subjects with BMI of < 30 kg/m^2 participated in their experiment and received eight treatment sessions (half an hour for each session) within one month. Average fat reduction on waist circumference after the last treatment session was equal to 2.15 cm (64). There were two studies, which measured patient's satisfaction after the treatment procedure. In the study of Nestor et al., satisfaction was reported up to 80% but in the research of Lach et al. reduction of subcutaneous fat in normal weight women was nearly 32% (1, 65).

In conclusion, while some studies introduced LLLT as an effective method for body contouring and fat removal, more studies are needed to prove efficacy and safety of this method.

3.5. Extracorporeal Shockwave Therapy

Extracorporeal shockwave therapy has been a method for treating kidney stones since 1980 (45). In addition, the procedure has been used for curing lesions and wounds. Nowadays, the device is being used for body contouring and treating cellulite (66, 67).

Although the full mechanism of ESWT is not clear yet, it seems that it is based on converting electrical energy to mechanical energy (68). The energy created in this process is limited to target zones by affecting acoustical interfaces and no significant changes in surrounding tissue are observed (66).

The power and effectiveness of the device is affected by shockwave energy, the frequency of the generated waves, the number of pulses, and the number and interval of retreatments (69).

The commonly used form of ESWT in treating soft tissue is defocused, low-energy shockwaves, which comes in contrast with focused, high-energy ESWT and is commonly applied for delay-union or non-union fractures (69).

It seems that applying extracorporeal shockwave could be an effective method for treating cellulite due to skin collagen remodeling (66). Angehrn et al. assessed the shockwave effects on cellulite of 21 women. The participants received 12 sessions of low-energy defocused ESWT (96000 shots for each person) during six weeks in the lateral thigh. After the last session, high-resolution ultrasound measurements and personal questionnaire showed some degrees of improvement on their skin elasticity (66).

Another randomized-controlled trial in 2013 was performed to investigate the effects of ESWT along with exercise on cellulite. The intervention group received six sessions of focused ESWT on gluteal and thigh areas (2000

impulses, 0.35 mJ/mm^2) every one to two weeks. Six sessions of SHAM-ESWT was performed on the control group. Daily gluteal strength trainings were prescribed for both groups. The results showed significant improvement in skin appearance and cellulite severity scale, but no effect on thigh circumference was reported (67).

It seems that ESWT could be considered as an effective method for body contouring and cellulite treatment, yet further studies are required to determine the effect of this technique on circumference reduction.

3.6. Vibration Exercise and Weight Reduction

Current ACSM guidelines for weight reduction suggest moderate-intensity aerobic exercise in addition to a moderate caloric restriction, which further improves weight loss. Other exercise modalities such as resistance training have received a lot of attention for weight loss. An exercise mode that needs little time and physical exertion but provides advantages to increase muscle function and possible weight loss would be of interest to most people. One such exercise mode is vibration exercise (70).

Vibration exercise kicks off a fast and repetitious eccentric-concentric activity that induces muscular work and increases metabolic rate (70). This is done by standing on a machine with an oscillating platform or some other devices such as vibrating slimming belt or handheld devices. Low frequency vibration (5 - 45 Hz) increases muscle activity via stimulating the muscle spindle, involving the spinal reflex apparatus, which may increase energy expenditure and might be favorable for weight reduction (70). In fact, the vibration transferred to the muscle-tendon complex results in a stretch-shortening action, which stimulates muscle spindles and evokes subsequent muscle contractions via monosynaptic and poly-synaptic reflexes. These reflexive muscle contractions increase local metabolic rate (71).

Vibration exercise is a very popular exercise mode and there are different types of vibration machines in fitness centers and gyms. There are many reports in the literature suggesting that vibration exercise is an efficient method for reducing workout time while improving muscular performance to increase energy expenditure and decrease body fat. It has been reported that a 10-minute vibration exercise is equal to a one-hour of conventional exercise (70). It has been suggested that increased fat oxidation both during and after exercise and catecholamine release may cause weight loss in lean people who engage in vibration exercise but the underlying mechanisms remain unequivocal (70).

Recently, the ability of vibration exercise to increase skeletal muscle perfusion in the lower limb has been reported in the literature. The amount of increase in muscle blood flow seems to be related to the vibratory load and is due to reflexive muscular contractions during vibration exercise (71). In some reports, there is a positive linear correlation between vibratory load and muscle perfusion (71). A systematic review by Fuller et al. in 2013 indicated that vibration exercise increases muscle perfusion, particularly in the lower extremities, with the amount of increase in perfusion being positively related to the vibratory load (71).

The effect of whole body vibration exercise on body composition has been evaluated in different studies. Milanese et al. explored the short-term effect of whole body vibration (WBV) exercise on anthropometric measurements. Fifty obese women were randomly allocated to a ten-week WBV training group or a non-exercise control group. Whole body vibration exercise consisted of 14 minutes of vibration training on the WBV device (Bioplate RF, BIOS, Milano, Italy) with amplitude of 2 - 5 mm and frequency of 40 - 60 Hz, twice a week. Before and after the ten-week experimental period, anthropometric assessments and dual-energy x-ray absorptiometry (DXA) were carried out. The results showed that compared to the control group, subjects submitted to WBV exercise had significantly lower BMI, total body and trunk fat, sum of skinfolds and body circumstances. These results suggested that WBV exercise improved body composition and might be a useful addition to lifestyle recommendations (72).

Another study in Belgium by Roelants et al. investigated the effects of 24 weeks of WBV training on body composition compared with fitness training on forty-eight untrained females. Vibration platform (35 - 40 Hz, 2.5 - 5.0 mm; Power Plate®) was used for WBV training. The fitness group performed a standard cardiovascular (15 - 40 minutes) and resistance training (leg press and leg extension exercises 20/8 RM). Body composition was determined by the underwater weighing method and 12-points skinfold thickness assessment. After 24 weeks, there were no significant changes in weight, percentage of body fat or skinfold thickness in any of the groups. A significant strength gain was observed in both groups. The results of the study showed that although WBV training didn't reduce weight and subcutaneous fat, it could increase muscle strength comparable to the strength gain following a standard fitness training program (73).

To sum up, the results of studies on vibration exercise are contradictory and it is difficult to draw any conclusion about its effects on body composition, especially on local fatness. Although vibration exercise has gained popularity for weight loss and body contouring, it does not have the capability to substitute aerobic exercise in terms of energy costs. However, it seems that like resistance training, vibration exercise does have a positive effect on blood flow (70, 71), which could increase metabolic rate in relevant areas

and can improve fat free mass and muscle strength without any significant effect on skinfold measurements (73).

3.7. Combination Therapy

For increasing positive results of body contouring methods, in some studies, combination treatment regimens were used such as combination of cryolipolysis and shockwave, RF and suction, etc. Moreover, in some cases, especially in the cellulite therapeutic approach, manual massage is considered (4, 18, 37). It seems that the results can improve by combining several techniques. For example, in one study the best abdomen circumference reduction was observed by using cryolipolysis in combination with ESWT, yet in another study, the best results in buttocks fat removal were gained by using 635-nm LLLT in combination with vibration therapy (45, 57). In another research, when the HIFU technique was combined with RF therapy, positive outcomes were nearly 72%, which was assessed by a satisfaction survey (74). However, the existing evidences in this field are very limited.

4. Conclusions

According to the existing evidences in animal and human studies, some of the noninvasive techniques such as cryolipolysis, RF, LLLT and HIFU have shown statistically significant effects on body contouring, removing unwanted fat and cellulite. However, the reported effects of such devices were mild to moderate and the mentioned methods have little or no effect on body weight reduction and total percentage of body fat. On average, circumference reduction after noninvasive methods was 2 - cm. Moreover, there were major differences in the investigation methods especially target zones, number and time of fallow-up sessions and type of measurements or outcomes. Therefore, comparing the effectiveness of these methods was too hard. The follow-up sessions in most studies were planned 6, 12 or 24 weeks after treatment sessions and evidence on long-term outcomes or recurrence of subcutaneous fat after 24 weeks is inadequate. One of the most important aspects of body countering methods is patient satisfaction following treatment, which is not noticeable in most cases because most of the participants expect similar outcomes to surgical procedures. Focusing on the role of noninvasive body contouring methods on cellulite or subcutaneous fat as a sole defining method is too challenging. As a former experiment showed, some methodological faults in studies, such as lack of an end-point for cellulite severity or absence of clinical statistical analysis, make it very difficult to obtain confirmed results and it seems there is no definitive treatment method for cellulite and subcutaneous fat.

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Footnote

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