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Review Article

Non-invasive body contouring: A review

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Abstract Non-invasive body contouring modalities optimize the cosmesis of the human body safely and effectively and represent a fast-expanding domain of cosmetic dermatology. There are currently five approved modalities including cryolipolysis, radiofrequency, high-intensity focused ultrasound, laser therapy and high-intensity focused electromagnetic field. This article provides a brief overview of these modalities in the light of the recent literature.

Key words
Obesity; Body contouring; Lipolysis; Laser; Radiofrequency; High frequency focused ultrasound; High-intensity focused electromagnetic field.

Introduction

Obesity has attained pandemic proportions over the last few decades owing to a massive change in lifestyle with increasing reliance upon the widely available calorie-dense fast food and reduction in physical activity. And with obesity, has come the expanding evidence about the detrimental effects of obesity and the desired to appear youthful, smart and healthy. This desire to attain a flawless-appearing body has got heightened by wide publicity of the images of idealized bodies and models in the media. The popularity of social networking services (like Instagram, Snapchat, TikTok and Facebook) and a global trend to click, upload and share selfies/ videos has only enhanced the desire to look good. It is in this context, the concept of body contouring has been evolving to optimize the definition, aesthetics, smoothness, and shape of the human body.[1]

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Body contouring may be achieved by invasive surgical operations or else by adopting non-invasive tools. The results with surgical methods are dramatic and immediate but there is an increasing demand for non-invasive options as they are not associated with the risks and adverse effects that are otherwise always possible with the surgical options.[2]

There are currently five approved modalities used for non-invasive body contouring as shown in **Figure 1**, but none of the procedures has yet been accepted as the gold standard or deemed as the most effective one.[3]

In this article, a brief overview of these modalities is presented in light of the recent literature.

Methods

The articles in the English language, dealing with non-invasive body contouring were reviewed in PubMed, ResearchGate, EMBASE, CINAHL, Google Scholar and Web of Science after search on the keywords: Body contouring, Non-invasive. Additional cross-references from the source bibliographies were used to further

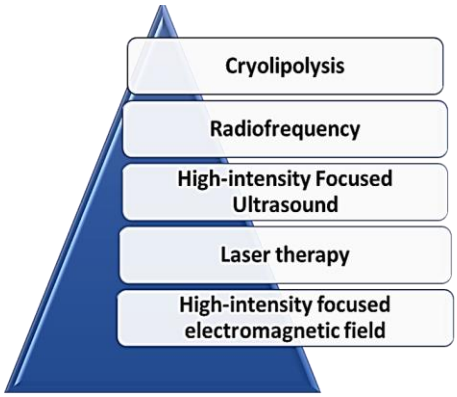

Figure 1 Current modalities of non-invasive body contouring.

Figure 2 Cryolipolysis device over anterior abdomen (Image courtesy: Ryan Towart, RT Aesthetics).

supplement this review. Time limits were set from January 2008 to August 2021.

1. Cryolipolysis

Cryolipolysis (synonym: CoolSculpting) is conducted by a device that is based upon the principle that adipocytes due to the higher content of lipids are more liable to freezing and damage than the cells from other adjoining tissues that have abundance of water content **(Figure 2)**. Accordingly, lobular panniculitis is induced by freezing followed by selective apoptosis of the damaged adipocytes while the rest of the normal structures stay preserved. The apoptotic adipocytes end up getting digested by macrophages and that translates clinically into reduction of subcutaneous adipose tissue volume over the subsequent 2 to 3 months.[4]

Manstein et al.[5] in 2008 conducted extensive experiments upon the black Yucatan pigs wherein the selected test sites were given exposure to pre-set temperatures ranging from 20^{o}C to -7^{o}C. This was followed by histopathological studies on the same day and then at intervals up to 4 weeks for four pigs, and 14 weeks in one pig. Furthermore, in six pigs, the test sites that covered 15% of the total body surface area were exposed to temperature between −5°C and −8°C for 10 minutes. The study led to a conclusion with controlled exposure to low temperature, subcutaneous fat loss can be achieved without inflicting any appreciable damage to the overlying.

Zelickson et al.[6] also conducted a similar type of experiments on three Yucatan pigs and evaluated the test sites using photography, ultrasound, and histopathology. They also reached a similar conclusion that cryolipolysis significantly decreases the subcutaneous fat and modifies the contour of the body contour without changes in serum lipids or the overlying skin.

Coleman et al.[7] in 2009 studied the impact of cryolipolysis on function of sensory nerves. They devised a cooling device and subject test areas in ten subjects to cryolipolysis. Ultrasound assessed the changes in subcutaneous fat volume whereas neurologic evaluation (n=9), and biopsies (n=1) assessed the sensory nerves. The study concluded that cryolipolysis causes a in substantial reduction in subcutaneous fat. Furthermore, the procedure leads to modest changes in the function of peripheral sensory nerves that are short-term and reversable. Biopsies also ruled out any sort of long-term change in the structure of nerve fibers.

After successful animal-based experiments, cryolipolysis has been gradually introduced into clinical practice and has been gaining public

acceptance. The Food and Drug Administration (FDA) of the United States, awarded approval for its application for fat reduction over the flanks in 2010 and subsequently, over the previous decade, other areas of the body have been brought under the permission that includes the abdominal wall, thighs, arms, submental area, back, and the gluteal region.[4] The device creates a vacuum over the area to be treated and holds the tissue between the two cooling panels for about 30 to 60 minutes.

In a recent study published in 2020,[8] a split-body trial was conducted by Hwang et al., to explore if a single session of cryolipolysis could induce changes in the visceral and subcutaneous fat. They enrolled 15 subjects and applied cryolipolysis once but only to the left half of the abdomen while keeping the right half of abdomen untreated to serve as a control. The cross-sectional areas of the abdominal fat were calculated by computed tomography (CT scan) before and at 3 months post-treatment. Similarly, the waist circumference was measured and body fat percentage was calculated by bioelectrical impedance analysis before the treatment and then at 6 weeks and 3 months follow-up. From this study, it was found that a single session of cryolipolysis led to reduction in the waist circumferences by 10%, and the percent body fat, by 0.6%. Decrease on the side that received cryolipolysis was 15.6% and that of the control half was only 3.6%. The levels of visceral fat tissue also decreased in a significant manner. Thus, a conclusion was drawn that a single application of cryolipolysis can safely and effectively reduce the magnitude of subcutaneous as well as visceral fat.

Lipner[9] in 2018 reviewed the literature related to use of cryolipolysis for submental adipose tissue reduction. A total of 101 patients from four clinical trials and one case series were reviewed and, it was found that significant submental fat was attained, leaving the patients highly satisfied. There were side-effects of mild and self-resolving nature. Suh et al.[10] also reported satisfactory outcomes of cryolipolysis in submental region. They applied cryolipolysis contact device (CoolMini applicator, Zeltiq Aesthetics) in 10 Korean origin subjects and achieved submental fat reduction attaining favourable facial features. The change was objectively demonstrable with ultrasound studies conducted at 2-months post- treatment. Kilmer et al.[11] and Bernstein et al.[12] have also reported visible neck contour improvement and submental fat reduction.

In a recent study published in 2020, Rodopoulou et al.[13] reported the use of three dimensional (3-D) cryolipolysis over the neck in 39 subjects . Posttreatment, 95% of the cases marked the results of fat reduction as r very improved or as improved and only 5% were dissatisfied. Satisfied patients also noted a skin tightening effect that enhanced the cosmesis. No serious adverse reactions are reported. Multiple studies have reported a very favourable role of cryolipolysis in the reduction of thigh region. Boey and Wasilenchuk[14] in 2014 treated inner thigh fat with a cryolipolysis flat cup vacuum applicator. 11 patients were enrolled and treatment was delivered to the one thigh while the contralateral thigh was left untreated to serve as a control. 10 patients (91%) displayed satisfaction at the cosmetic results at surveys conducted after 2 months and 4 months after treatment. The results were clearly distinguishable in the clinical images clicked pre and post treatment. Subsequently, the control sides were treated on similar lines and symmetry attained.

Stevens and Bachelor[15] reported the safe reduction in undesirable "saddlebag" bulges by treatment of "non-pinchable" fat in the lateral thighs. They utilized custom made conformable-

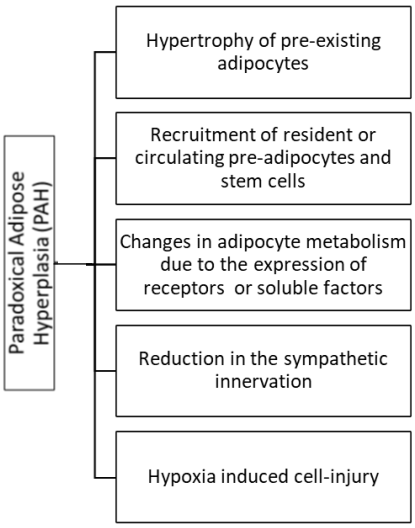

Figure 3 Mechanism of paradoxical adipose hyperplasia.

surface applicator. Zelickson et al.[16] applied a flat cup vacuum applicator (CoolFit applicator, CoolSculpting System) and attained significant fat reduction over the inner thighs of 45 subjects. Satisfaction rate was 93% and there were no recorded side effects. Meyer et al.[17] in 2018 presented the results of a modified version of cryolipolysis termed 'Contrast Cryolipolysis. This modification relies on heating-cooling-heating method. They recruited two volunteers who were assessed, before and after the intervention with tools including cirtometry, ultrasonography, and the anthropometric analysis. Right flank was treated with conventional cryolipolysis, whereas the left with contrast cryolipolysis. Satisfactory cosmetic results were attained with both the versions; however, the flanks treated with Contrast Cryolipolysis showed greater loss of fat tissue, reducing waist measurements and demonstrated with ultrasonography. It was concluded that the contrast cryolipolysis is superior in attaining fat reduction than the conventional cryolipolysis.

Cryolipolysis is contraindicated in patients who have history of cold-induced disorders like cryoglobulinemia and cold urticaria. This modality should also preferably be not offered if patient has varicose veins (severe) or atopic dermatitis.[18] The adverse effects with Cryolipolysis at any site are usually mild and include erythema, edema, bruises, paraesthesia, dysesthesia, skin hyperpigmentation, motor neuropathy, and pain.[4,19,20] These adverse effects are self-limiting and resolve within a few weeks.

However, over the past several years, reports regarding a phenomenon named paradoxical adipose hyperplasia (PAH) post-cryolipolysis, with a reported incidence of 0.025% to 1%, have been increasing published though it used to be previously identified as a "rare" adverse effect.[21-23]

The pathogenesis of this PAH is still not clearly known but certain possible mechanisms have been hypothesised in the recent literature[22-24] as depicted in **Figure 3**.

Nikolis and Enright[25] after an evaluation in 2114 patients, proposed that certain individuals may be predisposed to the development of PAH due to unknown factors. They also cautioned that the usage of older version of tools might have some contributory role in this complication. Keaney and Naga[26] on the basis of analysis of literature observed despite the fact that even though a far lesser number of men opt for cryolipolysis as compared to women but proportionately greater number of the cases have been reported in men, suggesting thereby that PAH may have a possible predilection for men and that this predilection may have some link to the sexual dimorphism in adipose anatomy. They, thence, cautioned that a proper patient selection criterion be properly applied and men with visceral abdominal fat and firm, non-distensible, fibrous adipose tissue be not offered cryolipolysis.

Treatment of PAH must be ideally delayed until the affected area softens after the initial cryolipolysis and this normally occurs in about 6 to 9 months. The preferred method of treatment

Figure 4: Radiofrequency device over face (Image courtesy: Ryan Towart, RT Aesthetics).

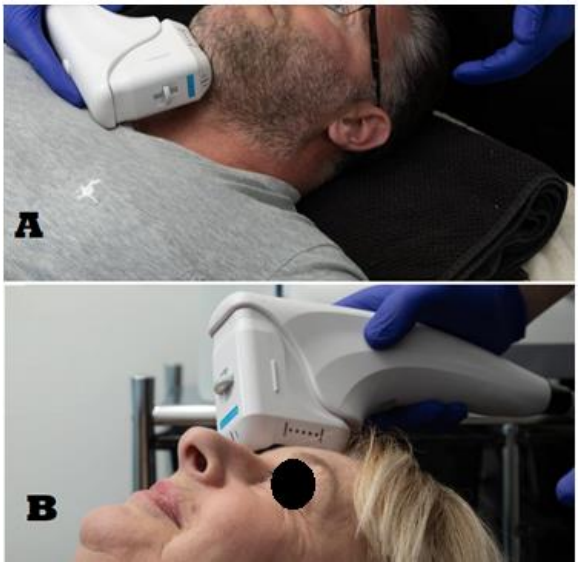

Figure 5 High-Intensity Focused Ultrasound (HIFU) device over A. Submental area, B. the forehead (Image courtesy: Ryan Towart, RT Aesthetics).

is power-assisted liposuction, but some cases may require surgical intervention in form of abdominoplasty.[27]

2. Radiofrequency

Radiofrequency (RF) is novel, safe and tolerable non-ablative recent technology that has attained wide popularity for non-surgical skin rejuvenation and body contouring.[28-29] In RF, electrical energy is utilized to force collisions between the charged molecules and ions due to which heat energy is generated **(Figure 4)**. Various tissues differ in impedance due to difference in their water content; fat tissue has high impedance and thermal energy gets focused there, leading to induction of cell death and apoptosis of adipocytes in the subcutaneous adipose tissue at exposure to temperatures of 43°C to 45°C (in first generation RF devices) over several minutes, without any significant risk of inflicting damage to the overlying skin layers or underlying muscle.[3] RF also denatures the collagen fibrils, which induces neocollagenesis, remodelling, and skin tightening.[30]

First generation RF devices have either monopolar or bipolar configuration and comprise of one RF generator linked to one or more skin electrodes. Bipolar version tends to require more frequent treatment sessions as compared to monopolar devices.[4] However recently, multisource radiofrequency (3DEEP) devices with six independently functioning RF generators have been successfully launched and these efficiently heat dermis to 52-55°C.[31] Bipolar and multipolar RF variants have minimal downtime and pain as compared with monopolar RF.

Sugawara et al.[32] treated the lower face in 14 Asian women with an average age of 44.6 years, using 1-MHz Monopolar with a stationary applicator, weekly for five consecutive weeks, by primarily concentrating on the nasolabial fold and buccal area. Adipose tissue reduction and skin tightening were assessed with three-dimensional (3D) volumetric studies, undertaken before each session and at 2 months post-treatment. In 90% of patients fat reduction could be documented and 60% were either "satisfied" or "very satisfied" with the cosmetic effects. The adverse effects included very mild discomfort and a minimal transient erythema. Taub et al.[33] applied 4-MHz monopolar RF in 17 patients with facial skin laxity, and found it to be safe and effective with no appreciable risks. Vega et al.[34] reported treated 31 female patients (median

age: 56 years) for laxity of skin over the hands and achieved cosmetic improvement in 89%.

Shemer et al.[35] in 2014 published the results of wrinkle reduction at one's home using a small, easy to operate, multisource phase-controlled RF device (3DEEP). 69 participants self-administered RF after having been taught the method of operating the device. None of the participants encountered difficulties in operating the RF device and 98% of the patients showed visible improvement in appearance of wrinkles. Gold et al. [36] also reported similar improvement in the appearance of periorbital wrinkles by self-administered RF.

RF have demonstrated a favourable adverse effect profile and the most common side effects are transient redness and edema at the treatment site that usually do not last more than 24 hours. However, few cases of Paradoxical adipose hyperplasia (PAH) have been reported recently. Agochukwu-Nwubah and Mentz[37] in 2019 reported PAH post- RF (Vanquish) in a 57-year-old male treated for abdominal skin laxity. The complication was managed by application of power-assisted liposuction.

3. High-intensity Focused Ultrasound

High-intensity focused ultrasound (HIFU) is a recent addition to the non-invasive body contouring tools and it had gained popularity for visible skin tightening and rejuvenation. HIFU resembles RF in its mechanism of action as it too relies on generation of heat energy which in turn induced adipocyte apoptosis. However, while RF is based on electric energy, HIFU utilizes acoustic energy.[38]

HIFU devices have the ability to focus energy at precisely targeted micro-coagulation zones (less than 1 mm in size) in the deeper portion of dermis and the subcutaneous connective tissue, and the underlying fibromuscular layers. Temperature greater than 65°C is reached within 1 to 3 seconds, creating cell protein thermal coagulation points (TCPs) to a depth of up to 5 mm without inflicting any damage to the superficially located papillary dermis or epidermis.[39-41] In addition, HIFU tends to mechanically disrupt the cell membranes and thereby enhances the coagulative necrosis and apoptosis. Furthermore, microcoagulation leads to collagen denaturation, contraction, remodeling and de novo collagen synthesis that translates into gradual skin tightening. HIFU has been found suitable for correction of mild to moderate skin laxity in young patients with normal wound healing and body mass index (BMI) of lesser than 30 kg/m^2. However, elderly patients with severe degrees of skin laxity or photoaging are not the fair candidates and should ideally be not offered this option, since the clinical response is partly linked to collagen neo-synthesis.[41-43]

The adverse effects profile is quite favourable. Mild pain is experienced during treatment and that gets relieved with oral nonsteroidal anti-inflammatory drugs (NSAID). Other side effects include erythema, edema, subcutaneous nodules, burning sensation, mild blisters and occasional bruising. Most of the adverse effects self-resolve by 4 weeks post-treatment, though very occasionally resolution may take up to 12 weeks.[40,44,45] There are no reports of derangements in serum lipid profile or liver functions as a result of HIFU.[40,46]

Fatemi and Kane[46] in 2010 described the results of a detailed retrospective chart review of patients who underwent HIFU treatment using a mean energy level of 134.8 J/cm^2 and a focal depth of 1.1 to 1.6 cm. 85 patients of both genders with a mean age of 43.8 years were treated with HIFU over the anterior abdomen and flank. Treatment was carried out in a single

session lasting approximately 1 to 1.5 hours. The patients, at 3 months post-treatment, has shown a decrease of 4.6 cm in waist circumference. Self-limiting adverse effects occurred in 10% of cases. Shek et al.[47] reported statistically significant decrease in waist circumference measured in 12 patients of Chinese origin. 60% of the cases had expressed satisfaction with the results. The study also pointed towards a direct relationship between the decrease in waist circumference with the dose of delivered fluence.

Fabi et al.[48] in their recent study have stressed concluded that the patient satisfaction with the results of HIFU is directly related to diligent patient selection and attention to patient comfort is directly related to satisfaction. Wrong selections and disregard for comfort lead to dissatisfied patients and sub-optimal outcomes. Gutowski[49] on the basis of his experiences noted that facial skin improvement can be attained in 60% to 90% of patients by 6 months post-treatment and that the outcome depends upon the patient characteristics and the treatment protocols that are adopted. Baumann and Zelikson[50] assigned 64 patients into groups and then treated the submental, submandibular, lower neck, and platysmal areas with microfocused ultrasound with visualization MFU-V (a variant of HIFU) at one or two depths. Treatment with MFU-V at two focal depths resulted in greater aesthetic improvement without any significant adverse effects. Hence, it was concluded that by application of treatment with MFU-V at two focal depths may potentially result in improved aesthetic impact.

Jones et al.[51] compared traditional HIFU with MFU-V for skin tightening over the neck region and found both the version to be equally effective though MFU-V resulted in greater discomfort levels. Kerscher et al.[52] used non-invasive biophysical measurements in 22 subjects to assess the skin physiology before and after MFU-V treatment. The parameters assessed included cutaneous temperature, transepidermal water loss, skin hydration, erythema, elasticity, skin thickness and skin density. The level of pain was scored using a numeric visual analog scale (VAS). It was concluded that even a single application of MFU-V treatment does not alter the skin physiology and is well tolerated. Saedi and Kaminer[53] foresees increased utility of HIFU for fat reduction over time due to safety and pleasant cosmetic outcomes.

4. Laser therapy

Laser technology has emerged in recent years as a non-invasive tool for body contouring. FDA has approved a 1060-nm diode laser with a non-suction applicator that uses hyperthermic treatment to destroy the adipocytes selectively and cause permanent reduction in stubborn fat. The device is applied externally and has an inbuilt contact cooling system that helps to prevent damage to the skin during the procedure [54].

Decorato et al.[55] conducted a three-part study to identify the parameters required for (i) safety and tolerability of treatment (ii) short- and long-term tissue response, and (iii) exploration of the possibilities of fat reduction with hyperthermic treatment using a 1,060 nm laser. The study showed that if 1,060 nm laser is applied while arranging for cooling of the skin surface, the hyperthermic temperature target of 42^{o} C to 47°C is safely achievable in subcutaneous adipose tissue. Post-treatment tissue responses evaluated by biopsy included inflammatory reactions, followed by macrophage infiltration starting at 2 weeks followed with evacuation of cellular debris by 6 months. Fat thickness reduction was approximately 14%, 18%, and 18% at 2, 3, and 6 months, respectively as

assessed by clinical examination and the average fat volume reduction demonstrated by imaging studies (MRI) at 3 and 6 months was 24% and 21%, respectively. Photo evaluation by blinded evaluators recorded improvement by only around 1-month post-treatment. No serious adverse events were encountered and few subjects experienced self-resolving mild tenderness. Bass and Dohenty[56] also confirmed the safety profile and utility of 1060 nm-based laser in consistent reduction of the abdominal fat contour.

Katz and Doherty[57] evaluated the safety and effectiveness of 1,060-nm Diode Laser for fat reduction over the flanks by single treatment in 49 subjects. Assessment by ultrasound and high-resolution images at baseline and 3-months post-treatment showed a significant fat reduction. 96% of subjects were satisfied with the results. The adverse effect was self-resolving mild to moderate pain. Sweeney et al.[58] tried by adopting a combination of options. They treated 5 subjects with hyperthermic 1060 nm diode laser and subsequently administered topical skin tightening concentrate of 5% yeast extract, 2% hydrolysed rice protein content, and 2.5% tripeptide, supplemented with hyperthermic diode laser lipolysis. They observed that the mentioned combination has the potential to achieve better aesthetic outcomes without any undue adverse effects.

Before the introduction of the above explained 1060-nm diode laser, the low-level laser therapy (LLLT), also termed as cold laser therapy was quite popular as a body contouring tool.[59] LLLT does not create any thermal tissue damage, but works by production of transient microscopic pores in adipocytes that led the lipids to leak out and thereby decrease the volume of fatty layer.[60] LLLT session requires about 30 minutes and results in immediate noticeable improvement. However, as this tool neither leads to necrosis nor apoptosis of the adipocytes, the results are only temporary and probability of recurrence of fatty deposition is great, rendering it to be a modality for a set of patients who may prefer immediate short-term cosmetic improvement despite later diminishment. Although the lipids are released during LLLT, there have been no reports of increase in serum lipid levels. Adverse effects are temporary and resolved spontaneously and include local edema, erythema, pain or paraesthesia, and increased urination.[59]

5. High-intensity focused electromagnetic field (HIFEM)

High-intensity focused electromagnetic field (HIFEM) is a novel modality introduced in recent years to reduce the fat and strengthening the muscles.[60] This tool works on the principles of magnetic induction and relies upon the creation of electrical currents in the tissues by rapidly changing the magnetic fields, leading to depolarization of nerve fibres and thereby the contraction of muscle **(Figure 6)**. If a muscle is stimulated at frequencies that exceed the muscle relaxation time, the muscle goes into tetanic spasms that lead to adaptive changes in form of increase in the muscle mass and decrease in adipose tissue by apoptosis of adipocytes.[61]

Halaas and Bernardy[62] in 2020 published the results of biochemical investigation that they had undertaken to understand how apoptosis

Figure 6 EMS Sculpt device over anterior abdomen using High Intensity Focused Electro-Magnetic Field (Image courtesy: Ryan Towart, RT Aesthetics).

gets induced by HIFEM. They worked on porcine adipose tissue models and detected the changes in the levels of the pro-apoptotic markers, along with an increase in the levels of free fatty acids, and reduction in the pH levels.

Kinney and Lozanova[63] enrolled 22 patients and administered HIFEM over abdominal region in four sessions, using the EMSCULPT device (BTL Industries Inc., Boston, MA). Assessment was done at presentation and subsequently up to 6 months post-treatment with the aid of anthropometric studies, high-resolution digital photography and MRI. The study revealed growth in muscle mass, reduction in fat and reduction in abdominal separation in all the participants.

Jacob et al.[64] delivered HIFEM in 75 patients for toning up the gluteal muscles and lifting the buttocks over four 30-minute treatment sessions. Aesthetic appearance of buttocks was significantly enhanced and the procedure was proposed as a safe modality for improving the gluteal tone, shape, lift, and tightness.

Giesse[65] evaluated the efficacy of HIFEM in reducing fat and strengthening the muscles in the abdominal and gluteal areas by enrolling 14 German patients. Using the Global Aesthetic Improvement Scale, the patients were rated as 100-percent improved with no relevant side effects. Jacob and Rank[66] in 2020 presented the results of abdominal remodeling in ten postpartum women by HIFEM. HIFEM led to increase in abdominal muscle thickness and reduction in the adipose layer. The observed results improved over the three months post-procedure and then remained stable thereafter, thereby indicating towards a potential role of HIFEM in the correction of altered body shape.

An advisory board meeting of senior aesthetic physicians was conducted in November 2020, via a virtual mode, to discuss various aspects related to use of HIFEM devices in the field of aesthetic medicine.[67] From the analysis of cumulative data related to 500 cases and derived from multiple studies from 30 investigators, it was found that HIFEM+ results in 30% reduction in fat, 25% increase in muscle mass, 19% reduction in abdominal layer separation and up to 5.9 cm decrease in waist circumference. Moreover, HIFEM+ leads to a 30% enhancement in satellite cell content, which is the almost the same as achieved after 3 months of exercise.

HIFEM+ is a technology that combines HIFEM and radiofrequency and the devises designed are aimed at both build-up of muscle mass as well as elimination of adipocytes. The advisory board unanimously agreed on several factors related to HIFEM, including the observation that the pairing of HIFEM and radiofrequency in form of HIFEM+ technology, be preferred over HIFEM alone as it achieves a greater magnitude of muscle stimulation and lipolysis.[67]

Conclusion

The demand for non-invasive body contouring is growing globally in the affluent sections. Various effective treatment options have been devised over the last decade and improvised to enhance efficacy and safety. The five leading options, currently in use include Cryolipolysis, Radiofrequency, High-intensity Focused Ultrasound (HIFU), Laser, and High-intensity focused electromagnetic field (HIFEM). Their usage is likely to become more widespread as the costs are contained and protocols standardized.

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