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RESEARCH ARTICLE

HIGH-INTENSITY FOCUSED ULTRASOUND WITH SURFACE COOLING NON-INVASIVE ABDOMINAL SUBCUTANEOUS ADIPOSE TISSUE REDUCTION

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ARTICLE INFO	ABSTRACT
Article History: Received 19 th May, 2016 Received in revised form 23 rd June, 2016 Accepted 11 th July, 2016	Background: High-intensity focused ultrasound (HIFU) quickly raises local temperature of subcutaneous adipose tissue, resulting in instantaneous cell death within the targeted area; higher temperatures can be safely applied using contact cooling. Objective: Evaluate safety and performance efficacy of HIFU with surface cooling for Non-Invasive reduction of the subcutaneous adipose tissue (SAT) in the abdomen.
Published online 20th August, 2016	Methods: A new HIFU device (LIPOcel TM , Jeisys Medical, Inc. Seoul, Republic of Korea) with
Key words:	 contact cooling was used to reduce abdominal circumference adipose tissue in 3 treatment modalities. Results: 30 subjects, mean age of 35.4 years underwent one or 2 HIFU treatments. Mean total energy dose was 509.4 J/cm², 495 J/cm², and 374 J/cm² for Groups A. B. and C respectively; whole study
Body sculpting, HIFU, High-intensity focused ultrasound, Surface Cooling, Noninvasive Fat reduction.	mean total fluence was 459.47 J/cm ² . Mean waist circumference reduction was 2.95 cm, 2.4 cm, and 3.8 cm for Groups A, B, and C respectively. A significant mean waist circumference reduction of 3.05 cm from baseline was observed. Most subjects (63.3%) reported being satisfied or very satisfied with the results; 80% of the investigators reported satisfactory results. Conclusions: HIFU with surface cooling using high fluence, assessed by standardized waist circumference measurement, is safe and effective for abdominal SAT reduction and noninvasive body sculpting.

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INTRODUCTION

Non-invasive Procedures for fat reduction are becoming increasingly popular. (Sarwer and Crerand, 2004) The demand for cosmetic procedures targeting subcutaneous adipose tissue (SAT) has rapidly increased over the past decade. Nowadays, more than half of individuals interested in cosmetic procedures are most interested in "body sculpting". (Friedmann et al., 2014) The greater willingness of individuals to seek out cosmetic treatments, advances in technology and limited adverse events have contributed in this development. (http://www.asds. net/ Media.aspx?id=7204) SAT deposits in the abdominal region are a particularly common area of aesthetic concern for male and female patients of all demographic groups. Currently, many therapeutic options are available for the aesthetic treatment of the abdomen. (Lian and Avram, 2012) Existing procedures rely on either ablation (cooling, heating, or adipocyte disruption or dissolution), non-

**Corresponding author: Hector Leal Silva* Universidad de Monterrey, Mexico. ablative effects (adipocyte lipolytic stimulation or modification), physical ultrastructural and removal (liposuction) of SAT. (Kennedy et al., 2015) High-intensity focused ultrasound (HIFU) is a recent, safe and effective noninvasive therapeutic option. It uses high-frequency acoustic energy (2 MHz, >1,000 W/cm²) to ablate focal areas of SAT, sparing any damage to surrounding connective tissues, blood vessels, nerves, and overlying skin. (Fatemi, 2009) The thermal effects of HIFU rapidly raise adipose temperature above 55°C, producing coagulative necrosis, whereas the mechanical (cavitational) effects of this technology lead to adipocyte membrane disruption secondary to negative acoustic pressure. (Haar and Coussios, 2007; Kyriakou et al., 2011) There is currently one HIFU device cleared by the Food and Drug Administration (August 16, 2011) for noninvasive waist circumference reduction (LipoSonix™, Solta Medical, a division of Valeant Pharmaceuticals North America, LLC. Quebec, Canada), it targets SAT at a focal depth of 1.3 cm. Several studies (Solish et al., 2012; Shek et al., 2014; Jewell et al., 2011; Robinson et al., 2014; Jewell et al., 2011; Gadsden

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REVIEW

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High-intensity focused ultrasound for noninvasive body contouring: current perspectives

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Abstract: Noninvasive devices for fat reduction have become increasingly popular over the past decade. High-intensity focused ultrasound (HIFU), already in use for nearly half a century for the noninvasive treatment of tumors, has only recently been evaluated as a method for the selective ablation of adipose tissue. HIFU works by focusing high-intensity ultrasonic waves at the level of the subcutaneous adipose tissue, causing focal coagulative necrosis with contraction and thickening of adjacent collagen bundles while sparing the overlying tissue. Several studies reveal the safety and efficacy of HIFU for fat reduction in the abdomen and flanks. These studies show a consistent reduction in the abdominal circumference of at least 2 cm after a single treatment. Adverse events are limited to mild, transient procedural and postprocedural discomfort, erythema, bruising, and edema. HIFU is a safe and effective method for focal fat reduction. **Keywords:** body sculpting, HIFU, lipoplasty, high-intensity focused ultrasonography

Introduction

Mankind has been pursuing body contouring since at least the 16th century by way of the corset. Today, the technology has changed but the goal remains the same: to optimize the smoothness, definition, or silhouette of the human physique, particularly the torso.¹ Lipoplasty is the fourth most popular cosmetic surgical procedure performed in the US.² However, it is expensive, invasive, and associated with significant downtime, morbidity, and mortality.^{3,4} For this reason, there is a strong demand for noninvasive body sculpting technologies such as cryolipolysis, radiofrequency, external low-level laser therapy, injection lipolysis, low-frequency nonthermal ultrasound, and high-intensity focused ultrasound (HIFU). As one of the newest of these technologies, HIFU will be the focus of this article.

HIFU is a method of noninvasive tissue heating and ablation currently used for treating a variety of disorders, including shock wave lithotripsy, uterine fibroids, and solid organ tumors.⁵ It reduces focal adiposity by delivering high-energy ultrasonic waves across the skin at a low intensity before sharply focusing them at the level of the subcutaneous adipose tissue (SAT). At the skin surface, the intensity of the waves is low enough to avoid tissue damage. However, at the level of the SAT, the waves are focused to a high enough intensity to induce focal coagulative necrosis. This fat ablation is achieved by two mechanisms: hyperthermia and inertial cavitation.⁵ HIFU causes molecular vibration of the targeted adipocytes and subsequent rapid heating to temperatures exceeding the upper limit of protein denaturation (60°C–65°C), resulting in coagulative necrosis. The mechanical ultrasound wave also travels through the adipocytes, creating cycles of increased and reduced pressure, which draw gas out of

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Review Article

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/m²) 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 bodycontouring 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

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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).

In a randomized, single-blind, sham-controlled study in 2012, 180 males and females (18 - 65 years) participated with BMI of \leq 30 kg/m² 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/cm² (three passes at 0 J/cm²; 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 fallowup. Mean energy level of the HIFU device was 134.8 J/cm² 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/m² 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/cm² and the energy was increased up to patient's tolerance level (mean 161 J/cm²). Initial measures included weight, BMI, and waist circumference. Statistically, a significant decrease in waist circumference at four, eight and twelveweek 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 ≥ 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

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Semin Cutan Med Surg. 2009 Dec;28(4):257-62. doi: 10.1016/j.sder.2009.11.005.

High-intensity focused ultrasound effectively reduces adipose tissue

Afschin Fatemi¹

Affiliations PMID: 20123425 DOI: 10.1016/j.sder.2009.11.005

Abstract

Liposonix is considered to be a nonsurgical treatment for body contouring that uses high-intensity focused ultrasound (HIFU) to disrupt adipocytes percutaneously. We wanted to find out about its efficacy, effectiveness, and so forth. The technique delivers energy across the skin surface at a relatively low intensity, but brings this energy to a sharp focus in the subcutaneous fat. At the skin surface, the intensity of the ultrasound energy is low enough so that no damage occurs. The focusing of the ultrasound beam at specific depths beneath the epidermis, combined with proprietary application techniques, results in adipose tissue disruption. Once adipocytes have been disrupted, chemotactic signals activate the body's inflammatory response mechanisms. Macrophage cells are attracted to the area to engulf and transport the lipids and cell debris. This results in an overall reduction in local adipose tissue volume. Our clinical and histologic studies will show exactly what happens under the skin. We did a series of studies on gross pathology and histology, and we tried to correlate these with the clinical results. The histologies show clearly that adipocytes are disrupted by HIFU. The pathologies show the lesions, but they are always at a safe distance from dermis or the epidermis. The correlation between focal depth, energy levels, and clinical results is evident. The average circumference reduction after treatment of the abdomen and waist is 4-5 cm. Liposonix turns out to be a safe and effective technique for nonsurgical body sculpting by reduction of fat deposits.)

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Clinical Trial Aesthet Surg J. 2011 May;31(4):401-10. doi: 10.1177/1090820X11405027.

Evaluation of a novel high-intensity focused ultrasound device for ablating subcutaneous adipose tissue for noninvasive body contouring: safety studies in human volunteers

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Affiliations PMID: 21551431 DOI: 10.1177/1090820X11405027

Abstract

Background: High-intensity focused ultrasound (HIFU) is an energy-based medical technology with many clinical applications. A device under clinical investigation in the United States (LipoSonix; Medicis Technologies Corporation, Bothell, Washington) uses HIFU to reduce localized deposits of abdominal adipose tissue.

Objectives: The authors describe the results from their clinical trial investigating the safety of this HIFU device in human patients.

Methods: Over the course of three studies evaluating the safety of the HIFU device for ablating human subcutaneous adipose tissue (SAT), 152 healthy patients were treated with total HIFU energy doses of 47 to 331 J/cm(2)), including patients who presented for elective abdominoplasty and underwent treatment to areas identified for subsequent excision. The safety of each treatment regimen was confirmed before the energy levels were raised. Abdominoplasty was performed up to 14 weeks following the HIFU procedure, and a pathologist performed histopathological analyses of excised tissues. Safety evaluations included an assessment of clinical chemistry and hematology profiles, physical examinations, and adverse events.

Results: Posttreatment ultrasound confirmed that the HIFU effects were limited to targeted SAT layers. Histopathology revealed well-demarcated disruption of adipocytes within the targeted SAT. Phagocytosis of released lipids and cellular debris occurred after 14 to 28 days. Phagocytized lipids underwent normal hepatic metabolism. Healing progressed normally and was 95% complete after eight to 14 weeks. Adverse events consisted primarily of temporary treatment discomfort, edema, erythema, dysesthesia, and ecchymosis. There were no changes in clinical laboratory parameters, and no serious device-related adverse events occurred. Optimal clinical outcomes were achieved with lower energy levels, which provided beneficial effects with the least amount of discomfort.

Conclusions: HIFU appears to provide a safe means for removing and remodeling unwanted deposits of abdominal SAT.

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Review Aesthetic Plast Surg. 2011 Oct;35(5):901-12. doi: 10.1007/s00266-011-9700-5. Epub 2011 Apr 1.

Noninvasive body sculpting technologies with an emphasis on high-intensity focused ultrasound

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Abstract

Background: Body-sculpting procedures are becoming increasingly popular in the United States. Although surgical lipoplasty remains the most common body sculpting procedure, a demand exists for noninvasive alternatives capable of reducing focal adiposity without the risks of adverse events (AEs) associated with invasive excisional body-sculpting procedures.

Methods: This report describes the mechanism of action, efficacy, safety, and tolerability of cryolipolysis, radiofrequency ablation, low-level external laser therapy, injection lipolysis, low-intensity nonthermal ultrasound, and high-intensity focused ultrasound (HIFU), with an emphasis on thermal HIFU. The articles cited were identified via a PubMed search, with additional article citations identified by manual searching of the reference lists of articles identified through the literature search.

Results: Each of the noninvasive treatments reviewed can be administered on an outpatient basis. These treatments generally have fewer complications than lipoplasty and require little or no anesthesia or analgesia. However, HIFU is the only treatment that can produce significant results in a single treatment, and only radiofrequency, low-level laser therapy, and cryolipolysis have been approved for use in the United States. Early clinical data on HIFU support its efficacy and safety for body sculpting. In contrast, radiofrequency, laser therapy, and injection lipolysis have been associated with significant AEs.

Conclusions: The published literature suggests that noninvasive body-sculpting techniques such as radiofrequency ablation, cryolipolysis, external low-level lasers, laser ablation, nonthermal ultrasound, and HIFU may be appropriate options for nonobese patients requiring modest reduction of adipose tissue.

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Review Semin Cutan Med Surg. 2013 Mar;32(1):26-30.

New waves for fat reduction: high-intensity focused ultrasound

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Affiliations PMID: 24049926

Abstract

With the rising demand for body contouring, noninvasive devices for fat reduction have become increasingly popular and have grown dramatically over the past decade. High-intensity focused ultrasound (HIFU) has been used for nearly half a century for the noninvasive treatment of tumors of various organs, but has only recently been evaluated as a method for the selective destruction of adipose tissue. HIFU works by ablating subcutaneous adipose tissue and causing molecular vibrations that increase the temperature of local tissue and induce rapid cell necrosis. Several studies reveal the safety and efficacy of HIFU for fat reduction in the abdomen and the flanks. These studies indicate consistent reduction in abdominal circumference > 2 cm after a single treatment. The adverse events are limited to transient tenderness, bruising, and edema. Increased utility of HIFU for fat reduction will likely increase over time.

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Case Reports Lasers Surg Med. 2016 Nov;48(9):878-886. doi: 10.1002/lsm.22576. Epub 2016 Aug 23.

Evaluation of a novel device, high-intensity focused ultrasound with a contact cooling for subcutaneous fat reduction

Heun Joo Lee¹, Mi-Hye Lee¹, Su Gun Lee², Un-Cheol Yeo³, Sung Eun Chang⁴

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Abstract

Background: Non-invasive devices for fat reduction involving high-intensity focused ultrasound (HIFU) are attracting attention. HIFU can deliver energy to the desired depth and can ablate subcutaneous adipose tissue (SAT), but purpura and pain may still limit its use.

Objectives: The aim of this study was to investigate the effects of a novel HIFU device for fat destruction with a contact cooling system compared to HIFU without contact cooling.

Methods: A group of three pigs were administered a series of four HIFU treatments with or without contact cooling over a period of 12 weeks. Energy fluence parameters ranged from 60 to 300 J/cm². Immediately after the treatment and at 1, 4, and 12 weeks, the tissue was studied by hematoxylin and eosin (H&E), Masson-trichrome, toluidine blue, CD68 staining, and transmission electron microscopy. Three human volunteers also received treatment with this HIFU device with cooling and were evaluated subjectively and objectively by computed tomography (CT).

Results: HIFU treatment with a contact cooling decreased the skin surface temperature and prevented epidermal damage. Ecchymosis was observed on the non-cooled area immediately after HIFU treatment, but not on the cooled area. Histological analyses on both areas (cooled and non-cooled) revealed disrupted adipocytes in the treatment area immediately, at 1 and 4 weeks following treatment. Lipophagic histiocytic fat necrosis was evident at 4 weeks. Finally, at 12 weeks all inflammation subsided, and the lobules were markedly atrophied with reduced SAT thickness. The human volunteers experienced reduction of a few centimeter-range reduction in waist circumference after 4 weeks and pain was tolerable without bruising.

Conclusions: HIFU treatment with a cooling system efficiently destroyed adipocytes. This novel HIFU device with an added contact cooling system may provide an effective, safe and less painful treatment as a non-invasive device for fat reduction. Lasers Surg. Med. 48:878-886, 2016. © 2016 Wiley Periodicals, Inc.

Keywords: contact cooling; fat reduction; high-intensity focused ultrasound (HIFU).

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