HIFEM® PROCEDURE FOR ARMS AND CALVES: A MULTICENTER ULTRASOUND STUDY

ASSESSMENT OF CHANGES IN ADIPOSE TISSUE AND MUSCLE MASS IN UPPER ARMS AND CALVES AFTER HIFEM PROCEDURE: ULTRASOUND STUDY.

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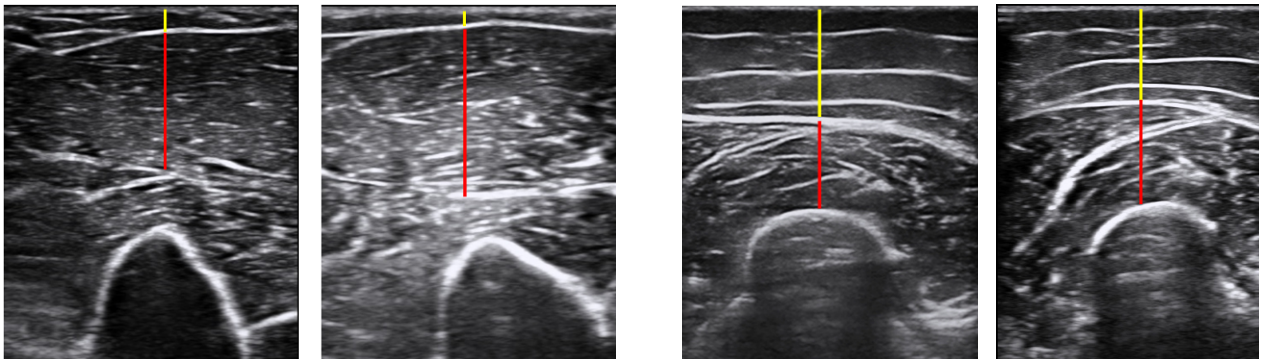
HIGHLIGHTS

- **21 subjects** (45.81±14.45 years; 24.10±3.27 kg/m^2) were treated by the **HIFEM procedure** over the **biceps**, **triceps**, and **calves**.
- The **thickness** in **m. biceps brachii** and **m. triceps brachii** increased by **16.38%** and **15.32%** respectively at **3-month follow-up**.
- The thickness of **m. gastrocnemius** was increased by **15.77% at 3-month follow-up**.
- The **arm fat thickness** was decreased by **14.55%** and **the fat thickness in calves** decreased by **14.93% at 3 months follow-up** respectively.



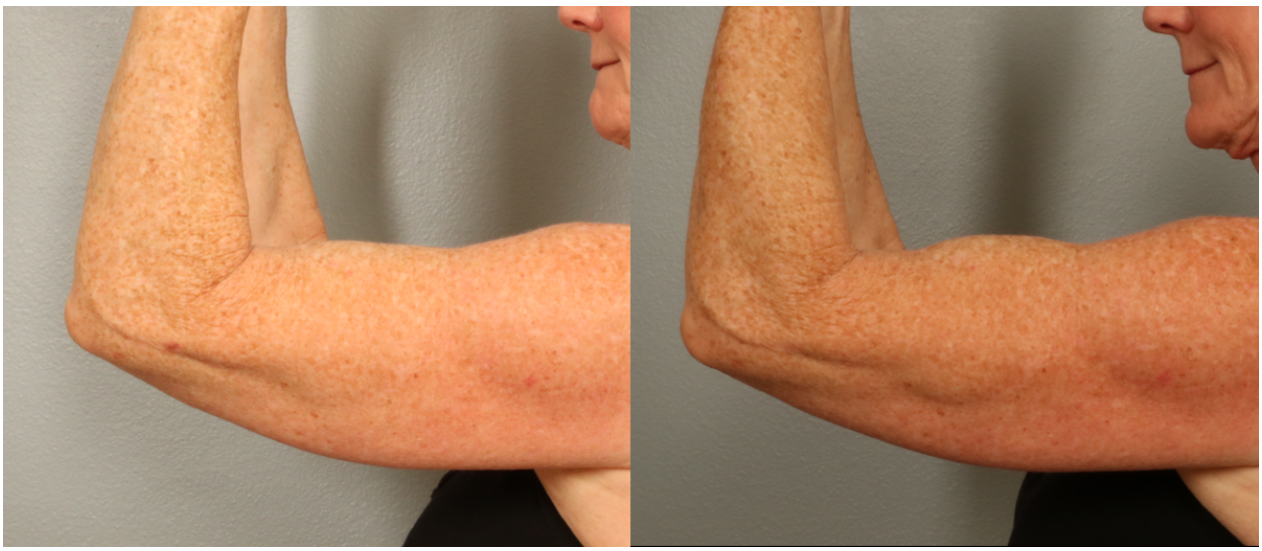
Ultrasound scans with highlighted biceps brachii (left) and triceps brachii (right) muscle before the treatments and at 1-month follow-up.

STUDY DESIGN

- Subjects underwent four 20-minute treatments of the arms and calves.
- Ultrasound images were taken at the baseline, 1 month, and 3 months after the last treatment.
- The m. biceps brachii, m. triceps brachii, m. gastrocnemius and adjacent fat tissue were independently assessed in the ultrasound images.
- Fat and muscle thickness was measured at predefined and equally spaced points on the arm and calves.

RESULTS

- **Increase** of muscle thickness and **reduction** of fat layer were **gradually improving** up to 3 months.
- Digital photographs revealed aesthetic improvement of the treated areas.
- The HIFEM procedure is beneficial for the treatment of calves and arms through toning, strengthening an increasing volume of the muscles.



Digital images of the female subject taken at baseline (left) and 1-month post-treatment (right).

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REVIEW ARTICLE

Review of non-invasive body contouring devices for fat reduction, skin tightening and muscle definition

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ABSTRACT

Non-invasive body contouring is a rapidly growing field in cosmetic dermatology. Non-invasive contouring devices improve the body's appearance through the removal of excess adipose tissue, particularly in areas in which fat persists despite optimal diet and exercise routine. The technology can also be used for skin tightening. This article reviews the five FDA-approved non-invasive body contouring modalities: cryolipolysis, laser, high-intensity focused electromagnetic field, radiofrequency and high-intensity focused ultrasound. These devices have emerged as a popular alternative to surgical body contouring due to their efficacy, favourable safety profile, minimal recovery time and reduced cost. Although they do not achieve the same results as liposuction, they are an attractive alternative for patients who do not want the risks or costs associated with surgery. When used appropriately and correctly, these devices have demonstrated excellent clinical efficacy and safety.

Key words: body contouring, fat reduction, lipolysis, liposuction, skin tightening.

In recent years, non-invasive body contouring has emerged as an increasingly popular and growing area of cosmetic medicine. The increasing pressure to meet the standards of idealised body figures and a desire for optimal health have rendered these novel treatments a valued adjunct to lifestyle measures such as diet and exercise.

Body contouring is defined as modification of the body's appearance through changes in size or shape. Fat reduction, a key component of body contouring, was previously only available through liposuction. However, liposuction requires some form of anaesthesia and is typically associated with a variety of surgical risks and significant downtime. These undesirable features have led to a shift in demand for effective, non-invasive treatments with a lower price point and reduced risks. Despite these advantages, expectations are lower than with liposuction, particularly in patients with higher BMI.[1] Moreover, the lipolytic responsiveness of adipose tissue has been found to be inversely proportional to an individual's BMI.

A number of different treatment options are now available, which allow for customised therapy that is tailored to the patient's personal preferences, body goals and body type. Currently, FDA-approved devices include cryolipolysis, laser, high-intensity focused electromagnetic field (HIFEM), radiofrequency (RF) and high-intensity focused ultrasound (HIFU). Studies of these modalities have demonstrated their clinical efficacy and safety for subcutaneous fat reduction and/or skin tightening (Table 1).

CRYOLIPOLYSIS BODY SCULPTING

Cryolipolysis is a popular non-invasive body contouring procedure that is moderately effective and generally well-tolerated. It uses controlled cooling to specifically target areas of adipose tissue whilst preserving surrounding structures such as the overlying skin, muscles and nerves.[2,3]

The most commonly used cryolipolysis device, Coolsculpt® (ZELTIQ Aesthetics, Inc., Pleasanton, CA, USA), first received FDA clearance for fat reduction in the flank area in 2010. Since this time, cryolipolysis has been approved for several other body areas, including the abdomen, flank, thighs, buttocks, submental area, bra fat, back fat and, less commonly, the upper arms.[4]

A vacuum is used to suction adipose tissue into an applicator cup in which the fat is frozen between two cooling panels. The cold-initiated damage triggers panniculitis,

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Table 1 Comparison of modalities for body contouring

	Fat reduction	Skin tightening	Muscle hypertrophy and tone	Downtime	Level of evidence
Cryolipolysis	++	0	0	0	IV
Laser	+/++	0	0	0	II
HIFEM	++	0	++	0	IV
RF	+	++	0	0	IV
HIFU	+	++	0	0	II
Liposuction	++++	+	0	+++	IV

HIFEM, high-intensity focused electromagnetic technology; HIFU, high-intensity focused ultrasound; RF, radiofrequency.

which selectively induces apoptosis of the adipocytes without damaging surrounding tissues. The destroyed fat is then cleared by macrophages. This inflammatory process peaks at 2 weeks, but lasts for approximately 3 months and is accompanied by a progressive decline in fat thickness.[3,5]

During the procedure, patients may experience tingling, stinging and aching associated with the intense cold. These unpleasant sensations tend to subside after 5–10 min as the area numbs. The device may also induce pulling and pinching sensations of the skin. After a cryolipolysis session, patients should expect some mild temporary bruising, swelling and sensory changes that usually resolve within days or weeks.[4,6] A small number of patients may complain of mild-to-moderate pain that subsides within a few days.[7] There are no reports of permanent skin or sensory disturbances, and other adverse effects are minimal.[3,4,6,7] Rarely, patients may develop a hardened, tender area of localised adipose tissue known as paradoxical adipose hyperplasia 2–3 months after treatment.[8,9] In some cases, it may require liposuction, although in others it may resolve spontaneously.

A typical treatment session applies controlled cooling at −10°C for 35–60 min; multiple sessions are recommended to optimise aesthetic results.[3] Overall duration of the treatment is tailored to the needs of the patient and depends on the number of areas treated per visit and total number of sessions.

Results may first be noticed 3 weeks after starting treatment, but improvements may continue for up to 6 months. In patients with an ideal body weight, typically 1–3 treatment sessions are required at least 2 months apart for optimal results. Clinical studies investigating this modality have documented significant patient satisfaction, which is largely attributable to minimal discomfort during treatment, limited side effects and substantial fat reduction.[3,10] A significant advantage of cryolipolysis is that results are permanent as demonstrated by long-term follow-up data. However, patients should be aware that results are still not as dramatic as liposuction.

The best candidates for this procedure are those with soft, discrete bulges of fat in localised areas that can be adequately pulled away from the body into the device. This poses a challenge when attempting to use cryolipolysis for the arms. Cryolipolysis is not recommended in patients who are obese, have amorphous fat, have had previous abdominal hernia surgery or suffer from cold-induced metabolic disorders.

Cryolipolysis may be used in conjunction with non-contact body contouring devices such as ultrasound and radiofrequency. Combination therapy helps maximise treatment efficacy by destroying more adipose cells and increasing overall fat reduction, and may also assist with skin tightening.

Possible leakage of fat contents from the apoptosed adipocytes raised concerns that serum lipid levels may become elevated and liver function may be compromised. Subsequent studies demonstrated no effect of cryolipolysis treatment on serum lipid levels or liver panel tests.[11,12]

LASER BODY CONTOURING

Laser therapy is a relatively new, efficacious and safe option for patients seeking modest non-invasive body contouring. Two types of device currently exist. These devices are particularly useful for non-pinchable areas of adipose tissue such as the outer thighs or slimmer abdomens.

The older version, low-level laser therapy, was FDA-cleared in 2010 for fat reduction in the abdomen, back, thigh and submental area. Low-level laser therapy uses a 635 nm wavelength to create temporary microscopic openings within the cell membrane of adipocytes, allowing lipids to leak out. This does not, however, induce the apoptosis seen with other non-invasive body countering modalities.[10] The lack of adipocyte cell death led to concerns regarding the permanency of low-level laser therapy-induced fat reduction.[13]

A 1060-nm diode laser has recently been developed that seeks to reduce adipose tissue through a thermally induced inflammatory process that is reminiscent of cryotherapy (SculpSure®; Cynosure, Westford, MA, USA). Fifteen minutes of prolonged hyperthermic exposure selectively raises adipose tissue temperature to between 42 and 47°C. This disrupts the cell membrane integrity to a degree that triggers apoptosis, after which the destroyed cells are eventually cleared from the interstitial space.[14,15] The specificity of the 1060 nm wavelength combined with the device's contact cooling system ensures preservation of the overlying skin and adnexae during treatment.[16]

Despite the leakage of fat associated with both lasers, there are no documented reports of changes in serum lipid levels associated with treatment.[13,15]

Low-level laser therapy sessions typically last up to 30 min. The 1060-nm laser treatments are slightly shorter, lasting between 20 and 25 min. Less than 20 min is

insufficient to produce adequate results, and longer than 25 min increases the risk of dermal injury and the formation of subcutaneous nodules.[16]

Both the low-level laser therapy and 1060-nm laser have a favourable safety profile with no serious adverse effects reported. Treatment with the 1060-nm laser is associated with mild-to-moderate pain, as the degree of tissue heating is gradually raised according to the patient's tolerance levels to maximise results.[16] Mild tenderness is the most commonly reported side effect of treatment. There are no reports of skin burns, scarring or pigmentation changes. Swelling, tenderness and induration may occur in some cases, but these undesirable outcomes typically resolve spontaneously within 1–3 weeks.[16] Results are best seen after 3 months, but improvements may be seen in half this time.[16,17] However, treatments have varying degrees of effectiveness, and anywhere from 2 to 12 sessions, are typically necessary for desired results, performed ideally 6–8 weeks apart. As with the other non-invasive devices, results are subtle compared with liposuction.

Laser treatment should be avoided in patients with a scar or tattoo at the treatment site, pregnant women and those with an abdominal hernia or implanted metal.

MAGNETIC RESONANCE CONTOURING

Magnetic resonance contouring with high-intensity focused electromagnetic technology (HIFEM) is the latest advancement for non-invasive body contouring. Magnetic stimulation has previously been used as an effective treatment for a variety of medical conditions, most commonly neuropsychiatric, musculoskeletal and urogynaecological disorders.[18–20] Unlike other currently available non-invasive fat reduction therapies, magnetic resonance may also help improve muscle thickness, strength and tone.

High-intensity focused electromagnetic field received FDA approval in 2018 for contouring of the buttocks and abdomen. The treatment uses electromagnetic energy to stimulate supramaximal muscle contractions of approximately 20 000 pulses within one 30-min session.[21,22] The physiological mechanism behind both the adipose and muscular benefits is incompletely understood; however, current data suggest that these contractions trigger intensive lipolysis within fat cells, which releases a large volume of free-fatty acids that damage surrounding adipose tissue.[23] Apoptosis ensues following adipocyte injury, as evidenced by the 91.7% increase in the apoptotic index of 120 histological samples.[21] This yields a desirable reduction in fat.

The stress of rapid nerve firing and muscle fibre contractions also leads to compensatory muscle thickening. Recent studies have demonstrated a gradual increase in muscle thickness and strength over the course of 6 months; however, further investigation of the long-term sustainability of muscular changes is warranted.[21] Another unique muscular benefit of HIFEM body contouring is a reduction in the distance between the large abdominal muscles. This outcome was observed in 91% of patients, regardless of whether diastasis recti was clinically present.[22]

Treatment involves at least four 30-min sessions spread evenly over the course of 2 weeks. Following this, one treatment every 3–6 months is recommended to maintain results. The strength of contractions can be adjusted from 0 to 100% with the Emsculpt® (BTL Industries, Inc., New York, NY, USA) device and is increased to the highest level tolerated by the patient to yield optimal effects. Stimulation intensities of 90 to 100% are commonly reached and sustained by a majority of patients.[21,22] The treatment is described as comfortable by most patients; however, some individuals report sensations of painful, gripping muscle contractions or brief electric shocks.

Complications following treatment with HIFEM are minimal, as transient, mild muscle soreness was the only side effect noted in a minority of patients.[21]

Subtle skin changes may be appreciated after one or two sessions, but considerable improvements should not be expected until at least 4 weeks after the last treatment. Three clinical trials found that HIFEM treatment significantly reduced patients' abdominal waist circumference, adipose tissue thickness, muscle thickness and diastasis recti.[21,22] Jacob and Paskova[22] reported a 92% patient satisfaction with abdominal appearance 3 months after completing treatment. Another study demonstrated HIFEM's ability to lift and tone the gluteal muscles; this leads to a significant improvement in buttocks appearance that was associated with a high degree of patient satisfaction.[24] These data, although promising, have been derived from studies with a maximum 6-month follow-up period. As such, the sustainability of abdominal and gluteal changes and long-term adverse outcomes is unclear.

Consensus regarding the ideal candidate for HIFEM non-invasive body contouring is lacking. The efficacy of treatment may be less significant in patients with a higher BMI, which may be attributed to impaired muscle contraction intensity due to increased distance between the magnetic coil and the target tissue.[21] Another study, however, found no such correlation.[22] The ideal candidate may, therefore, be one with a low or medium BMI and less than 2.5 cm of subcutaneous fat that can be pinched between two fingers.[22,23] Patients who fall outside of this demographic are still likely to see appreciable results. Again, results with this device are likely to be inferior to liposuction even in the best candidates. Contraindications for treatment with HIFEM include pregnancy and patients with metal or electronic implants.

RADIOFREQUENCY SKIN TIGHTENING AND BODY CONTOURING

Radiofrequency devices primarily cause skin tightening and can also cause mild fat reduction. Thermage® (Solta Medical, Pleasanton, CA, USA), the most commonly used radiofrequency device, was FDA-approved in 2002 for primarily tightening of skin but also fat reduction in a variety of locations, most commonly the face, abdomen, thighs and buttocks.[25,26]

Based on the principle of volumetric heating and the varied impedance of different skin layers, radiofrequency energy is used to generate heat that selectively targets the collagen-rich tissue layers to contract and denature collagen fibres, which results in immediate skin improvement. Long-term skin rejuvenation occurs secondary to stimulation of fibroblasts, which fuels gradual growth of new collagen and elastic fibres.[27] The thermal injury also induces apoptosis of adipocytes, which is responsible for the fat reduction component of the treatment.

Radiofrequency devices may have up to three settings: unipolar, monopolar and bipolar. The unipolar type is more difficult to control and more likely to cause deep tissue damage. Alternatively, the multipolar type allows for more uniform wavelength penetration, which yields superior skin contouring. It is, therefore, preferred by many practitioners. Low-to-medium BMI and significant skin laxity are two features used to identify favourable candidates.

Since Thermage®, many other radiofrequency devices have also emerged. Vanquish® (BTL Industries, Boston, MA, USA) is a monopolar radiofrequency device that has been developed primarily for fat reduction in the midsection including abdomen, back and flanks, and can cover very large treatment areas at one time through the unique use of extendable paddles. Patients who seek fat reduction in these sites may also benefit from truSculpt® (Cutera, Brisbane, CA, USA), another monopolar system with differently sized handpieces with maximal flexibility to target both large and smaller hard-to-reach treatment areas.

The Venus Legacy® (Venus Concept, Toronto, ON, Canada) device combines multipolar radiofrequency with pulsed electromagnetic fields to tighten skin and/or reduce adipose tissue depending on the applicator used. Pulsed electromagnetic fields is a non-thermal mechanism emitted through the applicator's electrodes to promote angiogenesis and growth factor release, resulting in increased collagen formation.

Radiofrequency sessions typically involve heating an area between 43 and 45°C over 20–30 min followed by air-cooling of the epidermis with the device's built-in cryogen spray which creates a reverse thermal gradient. This cooling process is critical to protect the skin from complications such as burns, infections, scarring and pigment changes.

Patients may experience mild heat-related pain during treatment. After sessions, most patients will experience transient, mild erythema and swelling that typically resolves within 24 h.[28] Less common adverse effects reported include facial tenderness, temporary dysesthesia, subcutaneous nodule formation and fat atrophy; these risks are minimised with high-pass treatment methods and use of bipolar settings.[29] Close monitoring of the skin appearance during treatment sessions is critical to identify any signs of epidermal injury. Some devices offer an additional safety feature in which a built-in temperature sensor helps to prevent burn-related superficial skin damage.

Numerous clinical trials have demonstrated this modality's efficacy in primarily tightening the skin and, to a lesser extent, reducing fat.[30–32] Some studies have reported improvement with skin tightening after a single treatment,[30] but in clinical practice, multiple treatments are needed, and gradual improvement is seen over the following 2–6 months. Permanency of these effects is still unknown; however, clinical studies demonstrated that 71–97% of patients were satisfied with the body improvements.

ULTRASOUND SKIN TIGHTENING AND BODY CONTOURING

Ultrasound devices for body contouring have been uniquely designed for skin tightening and mild fat reduction using acoustic energy.[33,34] They are broadly classified into two categories: high-frequency and low-frequency devices.

There are several different high frequency ultrasound devices that have garnered FDA approval, the most popular of which is Ultherapy® (Merz Aesthetics, Raleigh, NC, USA). High-frequency ultrasound energy generates heat at the target sites that are attached to the external transducer. This heat induces coagulative necrosis of the adipocytes and stimulates collagen remodelling within the tissue matrix.[35] Tissue temperatures above 56°C facilitate the necrotic process whilst sparing the surrounding nerves and vessels.[36] Targeting both fat and collagen leads to gradual skin tightening and reduced adipose tissue.[36] A short-duration approach helps ensure minimal epidermal damage. Alternatively, focus-pulsed ultrasound uses low-frequency waves to cause mechanical disruption of adipocytes and is usually better tolerated due to its non-thermal mechanism.

The focal depth and energy output on these devices can be adjusted based on the thickness of the patient's facial and body skin, which ultimately determines the treatment outcome.[37] Each procedure lasts for approximately 30–90 min, depending on the treatment location on the body. The high-frequency energy may be painful for some patients.[37]

This procedure is safe to perform with no serious adverse events. Common side effects include erythema, localised pain or tenderness, swelling and mild bruising, all of which typically resolve within hours to days.[37] Strict adherence to correct treatment technique minimises the risk of burning and scarring. Rare adverse outcomes include temporary muscle weakness, numbness and tingling due to the effect of high frequency ultrasound on local nerves. There is no evidence that high frequency ultrasound alters baseline serum lipid levels, liver function or inflammatory markers during or after treatment.[38]

Some studies have reported improvement after a single treatment,[39] but in clinical practice, multiple treatments are needed usually 3–4 weeks apart, and gradual improvement is seen over the following 2–6 months.[37,39,40] The ideal candidate for this procedure has mild-to-moderate skin laxity, but results will not be as impressive as ablative forms of skin tightening or surgical lifting procedures.

CONCLUSION

As the clinical evidence supporting non-invasive body contouring devices continues to build, patient demand will rise accordingly. These less invasive modalities may be preferred due to an improved safety profile and minimal or non-existent recovery time. However, patients should recognise the limitations of non-invasive methods, as results are much less dramatic than surgery. For this reason, liposuction remains the gold standard for body contouring, and non-invasive modalities should be reserved for patients with a low BMI who are physically fit and only require small areas of fat reduction. Treatment of obese patients is unwarranted as clinical trials have not adequately assessed the devices' effects in these individuals. Further high-quality studies are needed to better establish the role of these devices for body contouring and tightening.

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HIFEM® PROCEDURE FOR ARMS AND CALVES: MRI CASE STUDY

MRI ASSESSMENT OF ARM AND CALF MUSCLE TONING WITH HIFEM PROCEDURE: A CASE STUDY.

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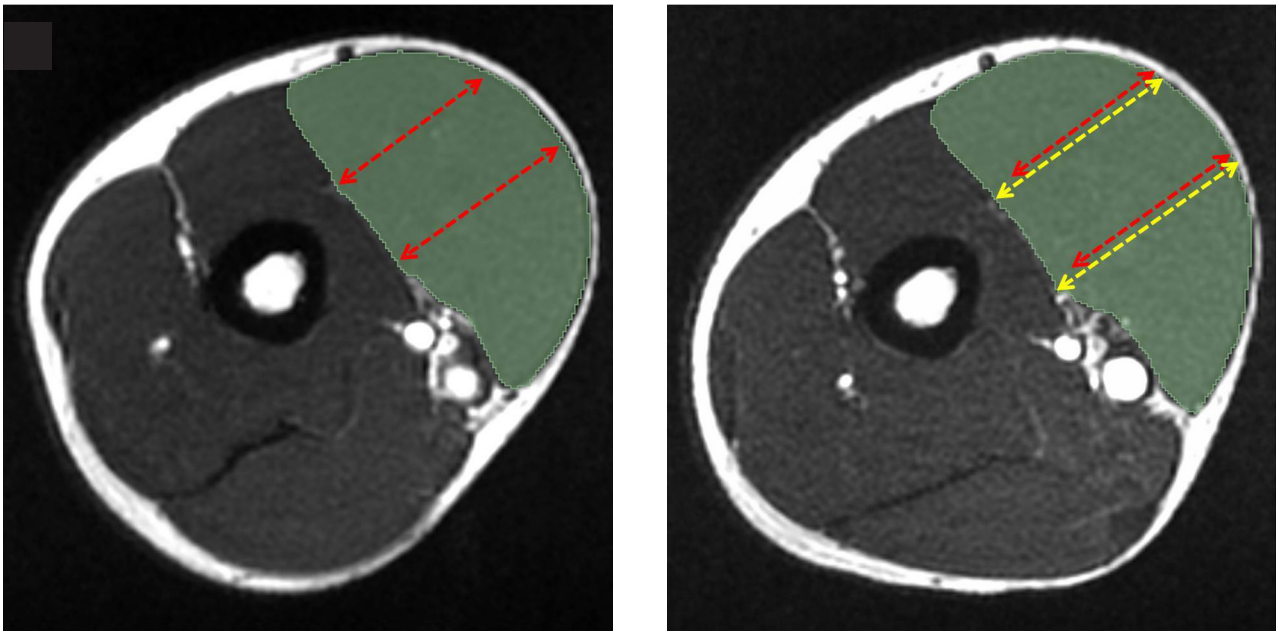
HIGHLIGHTS

- MRI evaluation showed an **increase in all three** treated muscles – **biceps, triceps, and calves**.
- The muscle mass of arm muscles in **the cross-sectional area** increased by **17.1%** for **biceps brachii** and by **10.2%** for **triceps brachii**.
- The **calves muscle mass** was increased by **14.6%** post- treatment.
- The **arm fat thickness** was decreased by **12.8%** and **calves fat thickness** decreased by **9.9%**.



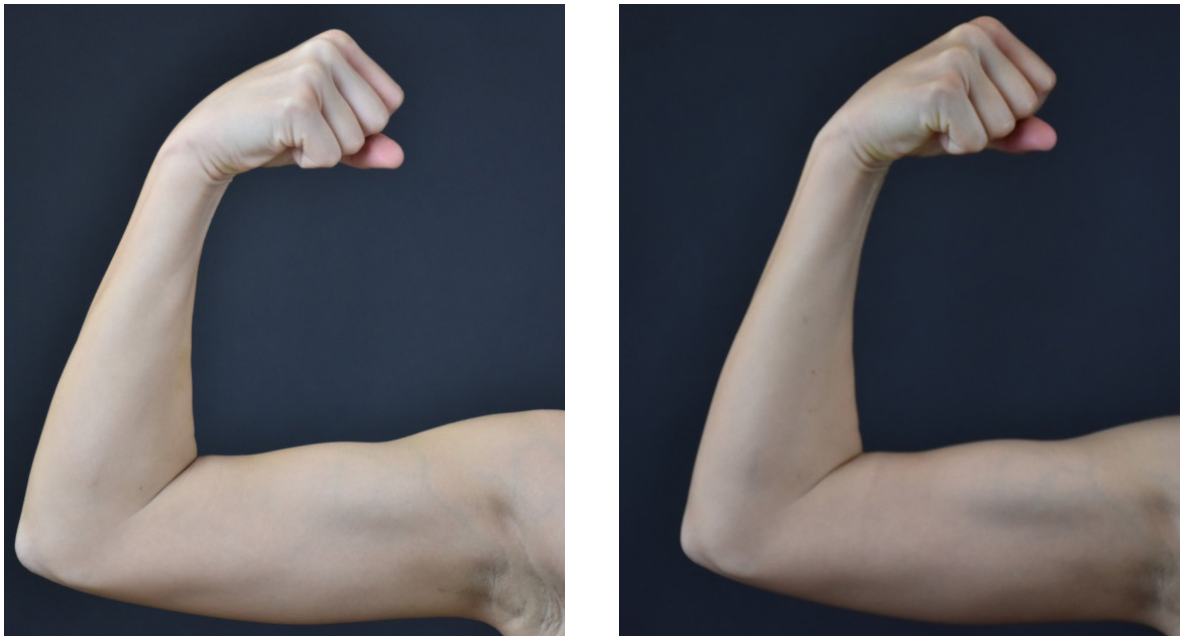
The MRI scans with highlighted biceps brachii muscle before (1919,4 mm^2) the treatments and 1-month post-treatment (2252,4 mm^2).

STUDY DESIGN

- Subjects underwent four 20-minute treatments of arms and calves.
- MRI images were taken at the baseline and 1 month after the last treatment.
- The biceps brachii m., triceps brachii m. and gastrocnemius m. were segmented in the MRI images and their cross-sectional area was measured.
- Fat thickness was measured at eight equally spaced points around the arm circumference and above the gastrocnemius m. of calves.

RESULTS

- Both subjects showed an increase in muscle mass and fat reduction in the treated body parts one month after the last treatment.
- HIFEM procedure is beneficial for the treatment of calves and arms through toning, strengthening an increasing volume of the muscles.
- This procedure can be an alternative tool to the current surgical as well as noninvasive procedures.



Digital images of the female subject taken at baseline (left) and 1- month post-treatment (right).

Preliminary Report

Noninvasive Induction of Muscle Fiber Hypertrophy and Hyperplasia: Effects of High-Intensity Focused Electromagnetic Field Evaluated in an In-Vivo Porcine Model: A Pilot Study

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Abstract

Background: High-intensity focused electromagnetic (HIFEM) field technology has been reported to increase muscle thickness and hypertrophy. However, this process has not yet been confirmed on a histologic level.

Objectives: The aim of this study was to evaluate in-vivo structural changes in striated porcine muscle tissue following HIFEM treatment.

Methods: Three Yorkshire pigs received four 30-minute HIFEM treatments applied to the biceps femoris muscle on 1 side only. The fourth pig served as a control subject. At baseline and 2 weeks after the last treatment, biopsy specimens of the muscle tissue were collected from the treatment site. The control pig underwent muscle biopsy from a similar but untreated site. Twenty-five histology slides were evaluated from each pig. A certified histopathologist analyzed sliced biopsy samples for structural changes in the tissue.

Results: Histologic analysis showed hypertrophic changes 2 weeks posttreatment. The muscle mass density increased by 20.56% (to a mean of 17,053.4 [5617.9] μm^2) compared with baseline. Similarly, muscle fiber density (hyperplasia) increased: the average change in the number of fibers in a slice area of 136,533.3 μm^2 was +8.0%. The mean size of an individual muscle fiber increased by 12.15% (to 332.23 [280.2] μm^2) 2 weeks posttreatment. Control samples did not show any significant change in fiber density or hyperplasia.

Conclusions: Histopathologic quantification showed significant structural muscle changes through a combination of fiber hypertrophy and hyperplasia. Control biopsies showed a lack of similar changes. The data correlate with findings of other HIFEM research and suggest that HIFEM could be used for noninvasive induction of muscle growth.

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Muscles have long been neglected in the body-shaping industry, which predominantly deals with subcutaneous fat deposits. However, strong and firm muscles significantly contribute to the overall aesthetic appearance. High-intensity focused electromagnetic (HIFEM) field technology has recently been introduced in the field of aesthetic medicine to provide physicians with a tool for muscle toning and strengthening beyond the capability of normal exercise.

Current noninvasive body-shaping devices are based on heating or cooling of subcutaneous fat tissue to levels that fat cells can no longer tolerate, consequently triggering programmed cell death—apoptosis.[1] The heating

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modalities of these radiofrequency devices are based on emitting electromagnetic waves of high frequencies (0.5-50 MHz)[2] which are predominantly absorbed in the subcutaneous fat tissue, where the energy of the waves is transformed into heat. HIFEM technology, on the other hand, does not deliver any heating through electromagnetic radiation, as it utilizes magnetic waves of very low frequencies (3-5 kHz) which propagate through the tissue without being absorbed. In this case, an interaction between the wave and human tissue occurs according to the principles of electromagnetic induction, first described by Michael Faraday in 1831. The law of electromagnetic induction says that any change in a magnetic field induces an electric current and vice versa. The HIFEM device comprises a circular coil located in the applicator, which is placed over the treatment area. During the treatment, an alternating electric current is sent into the circular coil. The alternations in the electric current induce rapidly changing magnetic waves which propagate into the underlying tissue, where they induce a secondary electric current. These electric currents within the tissue depolarize the muscle-innervating motor neurons and induce muscle contractions.[3]

Several studies have shown that humans are unable to fully activate muscles voluntarily as the power of muscle contraction is limited by the firing rates and conductivity of neural pathways.[4-7] Application of HIFEM bypasses the central and peripheral nervous system and directly stimulates the muscle-innervating motor neurons, allowing full muscle contraction. In addition, the frequency of delivered pulses does not allow the muscle to relax between 2 consecutive stimuli, which results in supramaximal tension within the muscle and thus supramaximal muscle contraction.

Multiple studies have investigated the effects of rapidly changing magnetic fields delivered through HIFEM technology.[8-13] The studies by Kent et al,[11] Katz et al,[12] and Kinney et al[8] employed computed tomography (CT), ultrasound, and magnetic resonance imaging (MRI), respectively, to investigate changes in abdominal composition post-HIFEM treatments. The thickness of abdominal muscles measured in CT and MRI images increased on average by 14.8% to 15.4%, indicating muscle hypertrophy. Although HIFEM technology directly affects muscles, the studies also found that the thickness of abdominal fat was reduced on average by 17.5% to 19%. The effect of the HIFEM procedure on adipose tissue was confirmed by a veterinary study,[13] which reported increased apoptotic index and apoptotic markers in the fat tissue post-HIFEM treatments.

Results from human trials suggest that HIFEM technology is a feasible modality for the aesthetic industry and could be widely used in body contouring for simultaneous fat reduction and muscle toning. Clinical trials are currently underway to assess the use of this technology to improve strength and tone in biceps, triceps, and gastrocnemius muscles. HIFEM has also been successfully used for strengthening the pelvic floor.[14]

Unlike fat apoptosis, which was confirmed on a histologic level, there is no histologic evidence for muscle hypertrophy. Because muscle thickness was found to be increased posttreatment, it might not necessarily indicate muscle fiber hypertrophy, but could be linked to swelling,[15] overall hydration, or increased water content in the muscle,[16] which may change with time. Therefore, histologic evaluation is necessary to confirm the observations on a cellular level.

The present study aimed to investigate the effect of an HIFEM-based procedure on muscle cells in a porcine model. The goal was to determine whether muscle hypertrophy is present on a cellular level.

METHODS

Four Yorkshire pigs served as subjects. Inclusion in the study required the animals to be in full physical health, which was assessed via blood samples collected 2 days before the treatment began. Three pigs received active treatment applied to the unilateral thigh, and the fourth untreated animal served as a control. The treatment procedure consisted of 4 sessions (30 minutes each) with a device that utilizes HIFEM technology (EMSCULPT; BTL Industries Inc., Boston, MA). The treatment sessions were scheduled twice a week for 2 weeks. The study was approved by the Institutional Animal Care and Use Committee (Bulgarian Food Safety Agency—BFSA committee, ID 195/2018). Animal care complied with the convention for the protection of vertebrate animals used for experimental and other scientific purposes. The experiment was conducted in July and August 2018.

During each treatment session, the animals were placed under general anesthesia to minimize their discomfort; this process was supervised by a veterinarian who chose the type and dosing of the anesthetic. A single applicator of the device was placed over the back thigh of the pig and secured by a fixation belt. All parameters used were identical to those commonly used in humans. Device settings were controlled by the operator. The intensity was gradually increased to 100% of the maximum device output, at which level it was maintained for the rest of the treatment time. For the 30 minutes of the treatment, the applicator was continuously delivering electromagnetic pulses with a magnetic field intensity of up to 1.8 T. The applicator position was adjusted during the treatment to ensure maximum contraction in the entire treatment area.

Punch biopsy specimens of muscle tissue were collected with a disposable biopsy punch (diameter, 5 mm)

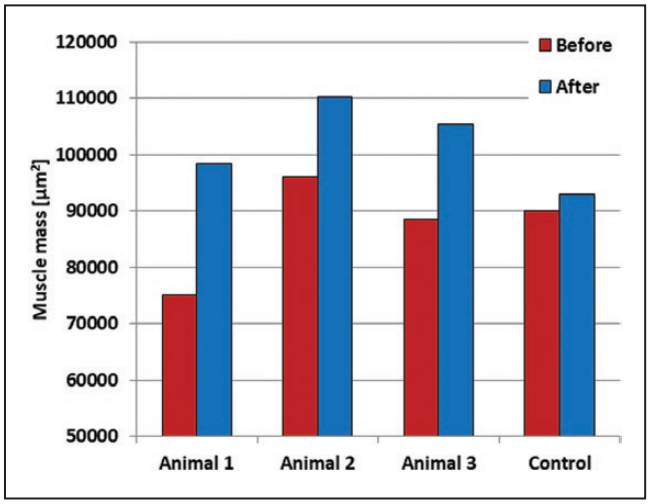

Figure 1. The average muscle mass per slice for each of the animals. All treated animals showed a significant growth in muscle mass. The muscle mass in the control animal did not change significantly.

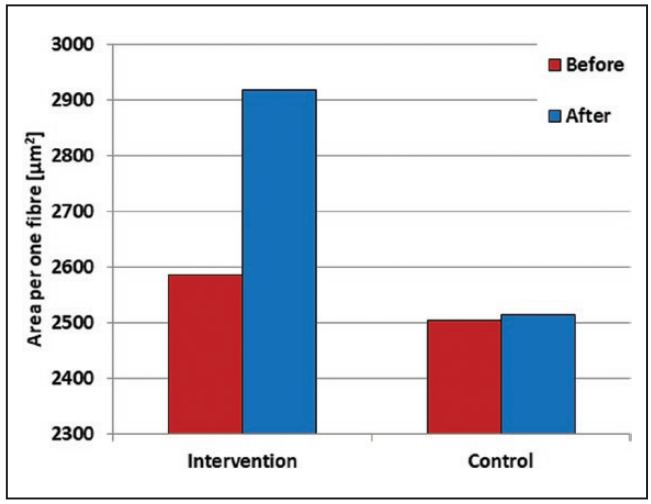

Figure 2. The average area per single muscle fiber in the treated (left) and control (right) animals at baseline (red) and posttreatment (blue).

before the first treatment and 2 weeks after the last treatment . The samples were fixed in 10% neutral buffered formalin and stained with hematoxylin and eosin. For microscopic evaluation, the samples were cut into 5-µm thick slices.

The slices were screened under a microscope (DFC295; Leica Microsystems Ltd, Germany) and an image of the entire slice was obtained for further analysis with Leica Application Suite (version 4.9.0) software. Each slice area was 136,533.3 µm^2. The analysis comprised the calculation of muscle fiber density, muscle mass density, and muscle fiber volume. Muscle fiber density was obtained as an average number of muscle fibers calculated individually in each slice. Muscle mass density was defined as the slice area occupied by muscle tissue. Muscle volume represents the area per single muscle fiber. ImageJ 1.52a software (National Institutes of Health, Bethesda, MD)[17] was used to calculate the muscle mass density and muscle fiber volume. Based on individual pixel color the software automatically segments the muscle tissue within the slices and calculates the area occupied by the muscle tissue.

In addition, the animals were monitored for any possible external manifestations of adverse events or side effects related to the procedure. The test animals were examined after every procedure to ascertain whether they exhibited any change in their condition compared with the baseline examination.

The sliced biopsy samples collected at baseline and 2 weeks posttreatment were compared for histologic changes. The statistical significance of possible changes was assessed by *t* test with a significance level set to 5%.

RESULTS

The 4 recruited Yorkshire sows (females) were between 1.5 and 2 years old (mean, 1.7 [0.2] years) and their mean weight was 74.6 [1.5] kg. All animals recovered from anesthesia without any complications or adverse events. The skin of test animals did not show any signs of adverse events such as erythema, scarring, ruptures, or skin texture change. The weights of all animals (treated and control) did not change after the treatments. In total 104 slices were obtained by slicing the punch biopsy samples (26 slices per subject). The statistical analysis showed a significant increase ($P < 0.01$) of muscle mass in the samples from treated animals.

In the treated animals, the muscle mass density increased on average by 20.56% (to a mean of 17,053.4 [5617.9] µm^2). An increase was observed in each of the treated animals, although the density remained constant in the control animal, with the change being within the standard deviation. The results for each animal are shown in Figure 1.

The change in the number of muscle fibers per slice was not statistically significant ($P > 0.05$), although a increasing trend was present in the treated animals as the average fiber density increased by 8.0% from 35.0 [6.8] to 38.2 [10.5]. The average muscle fiber density per slice in the control animal was 36.0 [9.1] at baseline and 37.0 [10.2] 2 weeks posttreatment. The difference was not statistically significant ($P > 0.05$).

Posttreatment, the average area per single muscle fiber increased significantly ($P < 0.05$) by 12.15% (to 332.23 [280.16] µm^2) in the intervention group. In the control animal the fiber area remained constant. See Figure 2 for the average results.

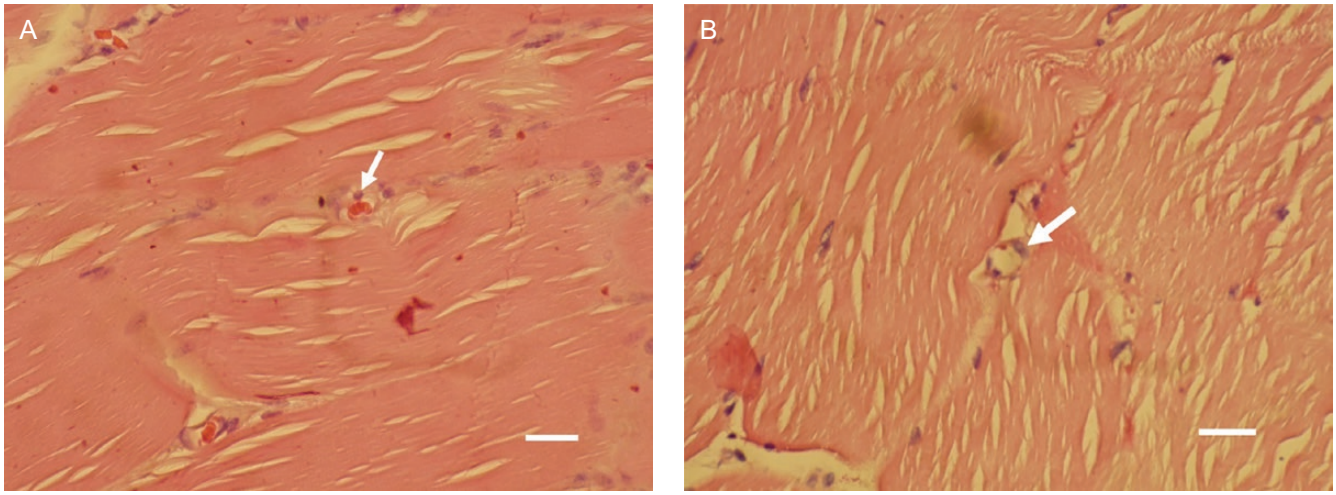

Figure 3. (A, B) The white arrows point to areas with the appearance of the endothelial cells with the onset of new capillary build-up in 2-week follow-up samples from the treated animals. White bar, 35 µm.

A further observation was neovascularization of the muscle tissue, which was widely seen in the 2-week follow-up histologic samples of the intervention group. Figure 3 shows samples exhibiting new capillary build-up.

DISCUSSION

Hypertrophy is normally seen in humans. There is, however, little evidence as to whether the overall muscle increase is simply due to increased thickness of individual muscle fibers (fiber hypertrophy) or due to a combination of fiber hypertrophy and multiplication of existing fibers/creation of new fibers (hyperplasia). Hyperplasia in humans is controversial among the scientific community, but existing studies have assessed this phenomenon after sets of ordinary exercises.[18] HIFEM, on the other hand, induces approximately 20,000 strong, supramaximal contractions within a time frame of 30 minutes, which cannot be achieved voluntarily, and the effects thus could be significantly higher, even leading to hyperplasia. Previous research on HIFEM technology showed an increase in muscle thickness in MRI, CT, and ultrasound images, providing evidence of muscle hypertrophy.[8,11] However, no study to date has looked at what happens to the muscle on a histologic level. The current study extends the scope of the existing literature by evaluating the effect of HIFEM treatments on individual muscle fibers, which has not been studied before.

This study aimed to determine whether HIFEM treatments can induce muscle hypertrophy on a cellular level. The histologic examination demonstrated that 4 HIFEM treatments induced prominent growth in the muscle tissue. The observed increase in total muscle mass by 20.56% appears to be mainly caused by a volumetric growth in individual muscle fibers, ie, muscle fiber hypertrophy (contributing 12.15%), and partially by an increase in the number of muscle fibers, ie, hyperplasia (contributing 8.0%), although the latter was not statistically significant.

The muscle growth observed in the current study correlates with previous research investigating the effect of HIFEM treatments on muscles. Kent et al[11] and Kinney et al[8] reported an increase in the muscle thickness by 14.8% and 15.4%, respectively. In comparison with these studies, the 20.56% increase on a cellular level seen in this study is larger, possibly due to densifying of the muscle tissue, as the connective tissue surrounding muscle fibers (endomysium) is compressed by increased muscle mass. This has indeed been observed in the histologic slices, and examples are shown in Figure 4. This is the first study investigating the hypertrophic effects of HIFEM technology on a histologic level, and hence there is no other histologic research with which the present results can be compared.

The lack of significant hyperplasia could be attributed to the short duration of the follow-up period. The posttreatment samples were collected 2 weeks after the last treatment and this period might not have been enough to fully manifest the hyperplastic changes as they might require more time to occur than fiber hypertrophy. A study by Crameri et al[19] found that it took 4 to 8 days to capture increased levels of myosatellite cells after a single bout of exercise. Therefore the terminal differentiation of these cells into clearly recognizable new muscle fibers might require more than 2 weeks.

The role of muscle fiber hyperplasia and muscle hypertrophy in humans is controversial because no evidence conclusively documents hyperplasia in human muscle.[20,21] Although the indications of hyperplasia observed in our study are not necessarily transferable to humans, it would be convenient to investigate whether the same pattern can be seen in human studies. Previous studies investigated

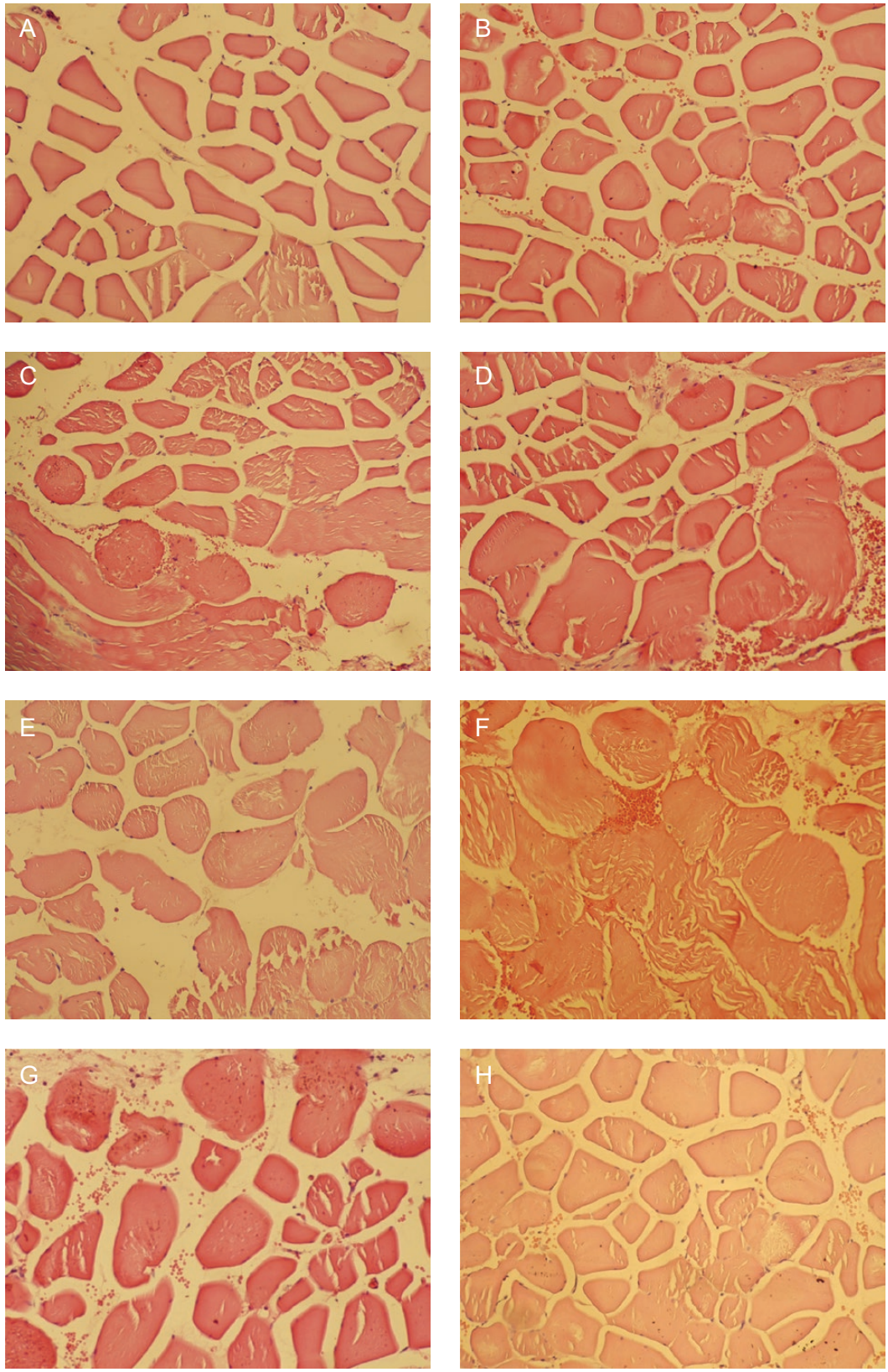

Figure 4. Example of histologic images of slices taken at (A, C, E, G) baseline and (B, D, F, H) 2 weeks posttreatment. The baseline images (A, C, E, G) show normal structure of muscle fibers, whereas the posttreatment images (B, D, F, H) show hypertrophy of muscle fibers with the muscle cell diameter being noticeably larger. The same magnification is used in all the images.

hyperplasia only postexercise, but HIFEM induced contractions of significantly higher strength and power than "exercise contractions" and could eventually trigger the terminal differentiation of myosatellite cells into new muscle fibers.

Besides HIFEM technology, which is based on magnetic stimulation, modalities based on electrical stimulation, such as electrical muscle stimulation (EMS) or transcutaneous electrical nerve stimulation (TENS), have been used in the past for muscle training.[22-24] Although TENS and EMS are predominantly used in rehabilitation and physiotherapy, HIFEM is the first muscle-affecting technology intended for body contouring. However, electromagnetic stimulation appears to offer a number of advantages over electrical stimulation: it induces 2 times higher peak torque[25] and, unlike with electrical stimulation, there is no pain[25] or risk of burns[26,27] with high stimulation intensities. Electromagnetic stimulation was further found to penetrate deeper into the tissue,[28] which is linked with the larger peak torques observed. The absence of adverse events in our study correlates with previous studies on humans. Due to the nonthermal nature of HIFEM technology, any risk of thermal tissue damage is eliminated. It might be assumed that rhabdomyolysis could occur following supramaximal contractions, but this has not been observed. Other expected complications or adverse events could be prolonged muscle soreness, swelling, bruising, cramping, or erythema of the overlying skin, but none of these were noted.

Observed neovascularization appears to be an adaptation response to the high load induced by HIFEM treatments when the growth of new capillaries is initiated to supply nutrition to the increased muscle mass.[29,30] Nevertheless, the level of neovascularization was not quantified and should thus not be considered as a definite conclusion. As such, this observation will be subjected to additional research in the future to provide objective evidence.

One of the limitations of the present study is the sample size; the study included only 4 animals (3 treated animals and 1 control) to minimize the number of animals in order to conform to the convention for the protection of vertebrate animals. However, to increase the statistical power of the study, over 104 histologic slices were examined and evaluated. Another limitation of the study is the short time period between the treatment and the muscle biopsy, because with longer terms larger hypertrophy and higher levels of hyperplasia may be noted, as discussed above. The use of animal subjects in the study may also be considered as a limitation because the observed results may not be fully transferable to humans. On the other hand, the porcine model is widely used as a suitable substitute due to its high biological similarity with humans.

The results suggest that HIFEM induces intense muscle contractions, causing a response of the muscle tissue in the form of muscle fiber hypertrophy, which correlates with previous studies reporting increased muscle thickness in CT[11] and MRI[8] images posttreatment. Future studies should focus on further verification of the observed hyperplastic effects via additional evaluation methods such as monitoring the levels of myosatellite cells.[31-33] In addition, longer follow-ups are required to capture potential terminal differentiation of the satellite cells.

To the best of our knowledge, no previous studies investigating changes in strength after HIFEM have been reported, although several studies have reported increased muscle mass posttreatment.[8,11,12] Anecdotally, patients often report increased strength during exercise after the treatment procedure, and one may infer that an increase in muscle mass is also linked with increased strength. Further studies should include strength assessment prior to and following HIFEM to document this hypothesized benefit.

CONCLUSIONS

Histopathologic evaluation found a hypertrophic effect of HIFEM application on a cellular level, which correlates to the muscle growth observed in previous studies. The results indicate that intense muscle activity is induced during the HIFEM treatments and suggests this technology could serve as a convenient tool for muscle toning.

Disclosures

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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MRI and CT Assessment of Abdominal Tissue Composition in Patients After High-Intensity Focused Electromagnetic Therapy Treatments: One-Year Follow-Up

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Abstract

Background: Several studies investigating high-intensity focused electromagnetic (HIFEM) treatments have recently been published. However, due to the novelty of the procedure, long-term data are still missing.
Objectives: The aim of this study was to evaluate changes in abdominal tissues on average 1 year after a series of HIFEM treatments, to determine the long-term durability of patients' original body responses.
Methods: Magnetic resonance imaging (MRI) or computed tomography (CT) scanning were performed on 21 patients a mean of 332.6 [88.5] days after their original HIFEM treatment series. The scans were evaluated by a blinded radiologist for abdominal muscle thickness, subcutaneous fat changes, and abdominal separation. The results were compared with the MRI/CT-assisted measurements taken at baseline and 6-week follow-up. Correlations between collected data sets were calculated and tested. The incidence of any adverse events related to earlier treatments was monitored.
Results: When comparing the 1-year follow-up measurements with the baseline, the MRI/CT-assisted calculations revealed mean reductions of 14.63% (2.97 [2.11] mm) in fat, 19.05% (1.89 [0.88] mm) in muscle thickening, and 10.46% (1.96 [1.71] mm) in diastasis recti. All changes were significant ($P < 0.05$) and not related to weight fluctuations ($P > 0.05$). The baseline width of diastasis positively correlated with the degree of improvement at follow-up. No adverse events were reported.
Conclusion: The HIFEM-induced muscle hypertrophy, fat reduction, and reduction in abdominal separation were maintained 1-year posttreatment. This suggests long-term durability of the original bodily response, which needs to be verified by continuing follow-up of this group and by further studies.

Level of Evidence: 4

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In the 1980s, aesthetic medicine, previously predominantly represented by surgical procedures such as liposuction, breast augmentation, and deep-layer facelifts, began to evolve. The emergence of new technologies, and the FDA's clearance of the first cosmetic hair-removal lasers in the 1990s, initiated a shift in trend; since then, noninvasive aesthetic procedures have been growing at a faster

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pace than their surgical peers.[1] The major advantages of nonsurgical, and especially noninvasive, body-shaping solutions are their relative safety, fast protocols, reduced (or even eliminated) downtime, and often the absence of any incision-induced permanent tissue damage. However, the physiologic response to various noninvasive technologies usually cannot compare to immediate appearance alterations caused by surgical interventions such as volumetric tissue removal or the insertion of implants. Another concern relates to the long-term efficacy of noninvasive body-shaping procedures. Long-term clinical trials remain scarce but are needed to minimize medical uncertainty.

High-intensity focused electromagnetic (HIFEM) technology is a noninvasive procedure that has been the subject of multiple recent studies.[2-5] The technology delivers rapidly changing alternating magnetic fields, with intensities of up to 1.8 T and frequencies of up to 3 kHz, which induce electric currents in the underlying tissue. Motor neurons are highly sensitive to propagating electric currents and are thus stimulated, which leads to muscle contraction. An appropriate combination of pulse parameters, such as frequency, pulse width, and pulse intensity, leads to supramaximal involuntary muscle contractions. HIFEM treatment has been found to simultaneously affect the muscle tissue as well as the subcutaneous fat. Its body-contouring effects are based on the principle of a supraphysiologic response of muscle[6] and consequent rapid boost of fat metabolism.[5] Subjects with fat deposits thicker than 3 cm are recognized not to be ideal candidates for this procedure. Peer-reviewed data so far report muscle hypertrophy,[3] core strengthening, subcutaneous fat reduction,[3,7,8] and reduced abdominal separation.[3,7] The most extended published or presented follow-up data are from 6 months posttreatment.[3,4]

The objective of this study was to collect 1-year follow-up data of patients who had undergone HIFEM treatment. In total, 21 subjects were recalled on average 1 year after their original treatment series to evaluate, by magnetic resonance imaging (MRI) or computed tomography (CT), the long-term effects of the procedure.

METHODS

Study Population

The original study included 44 patients. One year after the original treatment series the patients were telephonically contacted by the practice clinical coordinator; only those patients who had not undergone any other aesthetic procedures of the abdomen, had not experienced a >10-lb (4.5-kg) weight change, or had not started taking weight-affecting medication since the original follow-up were asked to participate in the 1-year follow-up visit.

In total, 23 out of the 44 original subjects were excluded from the study due to additional abdominal procedures (abdominal skin tightening/cellulite radiofrequency treatment, n = 4; additional HIFEM treatments, n = 3; not available, n = 1); weight change exceeding 10 lb (n = 5); weight-affecting medication (n = 4); having moved away (n = 3); or not expressing interest in the follow-up visit (n = 3).

Twenty-one patients (16 women, 5 men) met the inclusion criteria, and were successfully recalled for evaluation.

Study Design

The study was a multicenter, open-label, single-arm study conducted between March 2017 and August 2018. Historically, the patients underwent MRI/CT scans at baseline and 1-2 months (average, 6 weeks) post-HIFEM procedure. Our study did not include administration of any additional treatments and the patients did not receive any other body-shaping-related treatments in the meantime.

The subjects included in the follow-up examination underwent abdominal MRI or CT scanning on average 332.6 days after completing a series of four to eight 30-minute abdominal HIFEM treatments (EMSCULPT, BTL Industries Inc, Boston, MA). The original treatments were applied with the patient lying in a supine position. Initially, the center of the device applicator was positioned over the umbilicus in an upward-facing direction and stimulation of mild intensity was delivered (up to 15%). The position of the applicator was individually adjusted to create homogeneous contractions across the abdomen, and the intensity was then increased to therapeutic levels just below the patient's tolerance threshold. The intensity was further adjusted during the treatment according to the patient's feedback. A fixation belt served to prevent any applicator movements during the course of the treatment. The clinical protocol was approved by an institutional review board committee (Advarra, Columbia, MD) and conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Signed written informed consent was acquired from all patients. The individual follow-up length ranged from 231 to 509 days. MRI/CT scanning methodology was identical with the original baseline and posttreatment evaluation (T12 to S1 vertebrae determination, axial planning, and maximum spacing 50 mm).

Evaluation Methodology

Extracted MRI/CT images were evaluated by a single certified radiologist for the thickness of musculus rectus abdominis, abdominal subcutaneous fat, and the width of abdominal separation. Evaluation of matching bodily sections was then compared with the original baseline and posttreatment evaluation data. Cross-sectional

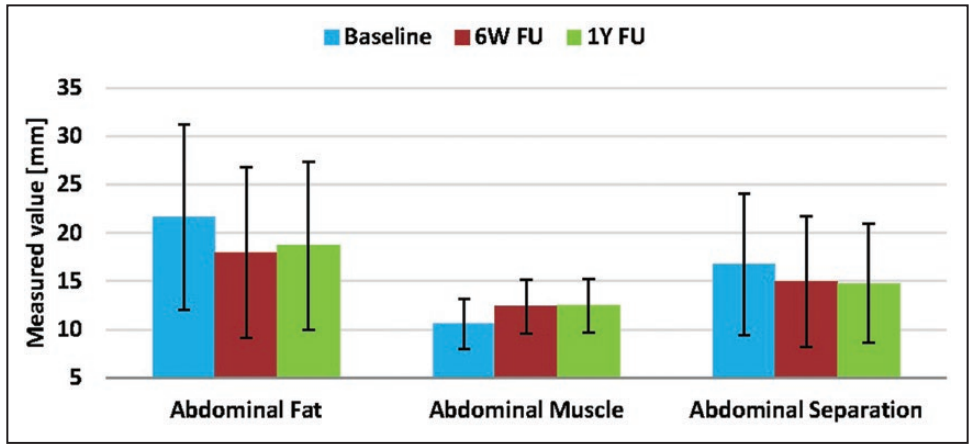

Figure 1. Magnetic resonance imaging/computed tomography–assisted measurements of abdominal fat, abdominal muscle, and abdominal separation (n = 21). Values are plotted in millimeters. The vertical lines represent standard deviations. 6W FU, 6-week follow-up; 1Y FU, 1-year follow-up.

dependence was statistically tested to reveal possible links among the different measurements taken. On the day of their MRI/CT scanning, patients were also screened for any adverse events and side effects that could relate to the initial treatment series, and their weight was measured.

The statistical difference between baseline and follow-up measurements was determined with a paired *t* test. Pearson's correlation tests were run to investigate the interdependence between the various sets of collected data; the significance of resultant *r* values was also tested.

RESULTS

The 21 patients who were successfully recalled for the follow-up and met the inclusion criteria had a mean age of 40.1 [10.4] years (range, 23-54 years), and a mean body mass index (BMI) of 24.1 [3.2] kg/m^2 (range, 18.4-30.4 kg/m^2).

Changes in Abdominal Tissue at 1-Year Follow-Up

At the 1-year follow-up, the MRI/CT-assisted measurements showed that the subcutaneous fat thickness remained reduced in 19 out of the 21 patients compared with baseline; 1 patient did not show any change (+0.3%) and the fat layer increased in another patient (+6.3%). Overall, the mean change was a 14.63% (2.97 [2.11] mm) reduction compared with baseline, which represents a minor, but not statistically significant, decline from the original 6-week measurements (17.46%, 3.67 [2.20] mm reduction).

At the initial 6-week follow-up, all 21 patients showed bulking of abdominal muscles when compared with their pretreatment evaluation, with the mean change measured from the MRI/CT scans being +17.66% (1.79 [0.73] mm). This muscle-thickening effect was maintained at the 1-year follow-up (+19.05%, 1.89 [0.88] mm). In all 21 patients the rectus abdominis thickness was increased on both sides at the 1-year follow-up compared with baseline; 11 patients further improved between the 6-week and the 1-year follow-ups, but the overall difference between 6-week and 1-year follow-ups was not significant.

A statistically significant narrowing in the abdominal separation was observed at the 6-week evaluation when compared with baseline (–10.76%, –1.82 [1.46] mm). When remeasured in the 1-year scans, this effect remained unchanged (–10.46%, –1.96 [1.71] mm). See Figure 1 and Table 1 for a summary of observed changes in all measured abdominal tissues.

All tissue changes between the baseline and the 6-week follow-up, as well as between the baseline and the 1-year follow-up, showed a high statistical significance through paired *t* tests ($P < 0.05$). However, no statistically significant difference between the 6-week and 1-year measurements was found for any of the assessed tissues ($P > 0.05$). In addition, no statistical difference was found between the patients who completed 4 vs 8 treatments.

Weight changes were insignificant in both the original as well as the 1-year follow-up. None of the patients reported any side effects or adverse events that could be linked to the original treatment.

Mutual Correlations

Statistically speaking, most variables proved to be unrelated to each other, yet the data suggest 3 significant correlation trends. See Table 2 for an overview of results.

A moderately strong positive correlation ($r = 0.53$; $P = 0.01$) was found between the baseline BMI and the absolute subcutaneous fat thickness at baseline. A weak

Table 1. Average Changes in Abdominal Tissues Over Time

	6 weeks to baseline	1 year to baseline	1 year to 6 weeks
Abdominal fat thickness	–3.67 mm; $P < 0.05$	–2.98 mm; $P < 0.05$	+0.7 mm; $P > 0.05$
Abdominal muscle thickness	+1.8 mm; $P < 0.05$	+1.9 mm; $P < 0.05$	+0.11 mm; $P > 0.05$
Abdominal separation width	–1.83 mm; $P < 0.05$	–1.96 mm; $P < 0.05$	–0.14 mm; $P > 0.05$
Weight	–0.36 lb; $P > 0.05$	+0.42 lb; $P > 0.05$	+0.78 lb; $P > 0.05$

A paired *t* test was used to test the significance of the changes.

Table 2. Correlations Between the Measured Parameters

	Baseline fat, mm	Fat reduction, mm	Baseline muscle, mm	Muscle growth, mm	Baseline abdominal separation, mm	Reduction in separation, mm	Weight loss, lbs
Fat reduction	0.18; 0.43	–	–	–	–	–	–
Baseline muscle thickness, mm	–0.26; 0.26	0.40; 0.07	–	–	–	–	–
Muscle thickness growth, mm	–0.14; 0.54	–0.10; 0.67	–0.48; 0.03	–	–	–	–
Baseline abdominal separation, mm	0.03; 0.91	–0.29; 0.21	–0.08; 0.72	–0.08; 0.72	–	–	–
Reduction in abdominal separation, mm	0.13; 0.59	0.26; 0.25	0.10; 0.66	–0.14; 0.54	–0.49; 0.02	–	–
Weight loss	0.07; 0.78	–0.10; 0.65	–0.04; 0.85	0.22; 0.33	–0.09; 0.69	–0.02; 0.93	–
Baseline BMI, kg/m^2	0.53; 0.01	0.34; 0.13	0.19; 0.42	–0.05; 0.84	–0.14; 0.54	0.21; 0.35	–0.17; 0.45
Length of FU, days	NR	–0.33; 0.14	NR	–0.35; 0.12	NR	–0.39; 0.08	0.15; 0.52
Number of treatments	NR	–0.32; 0.16	NR	–0.25; 0.27	NR	–0.22; 0.33	–0.30; 0.19

The first number in each cell is the Pearson correlation coefficient (*r*), and the second number is the value of significance (*F*). Fat reduction, muscle thickness growth, reduction in separation, and weight-loss parameters were calculated as the difference between the baseline measurement and the 1-year follow-up measurement. Duplicate calculations were omitted. BMI, body mass index; FU, follow-up; NR, not relevant.

yet statistically significant negative relation ($r = –0.48$; $P = 0.03$) was observed between the patients' muscle thickness before treatment and the percentage change in this thickness measured at the 1-year visit. Furthermore, a correlation ($r = –0.49$; $P = 0.02$) was measured between the initial size of the abdominal separation and its reduction at the 1-year follow-up visit.

DISCUSSION

In this study, we present data of the longest follow-up yet reported on patients treated with HIFEM for abdominal body shaping; previous studies have evaluated patients between 1 and 6 months posttreatment.

At the 1-year follow-up, 19 (90.5%) patients showed statistically significant lasting improvement in all 3 of the evaluated tissues (reduced fat, bulked muscles, shortened muscle separation); the remaining 2 patients had a lasting improvement in 2 out of the 3 measurements. The coefficient of variation of observed changes increased compared with the original 6-week follow-up measurements (from an average of 53.4% at 6 weeks to 68.7% at 1-year posttreatment).

This suggests that after the initial treatment series, patients are likely to preserve the induced changes over a span of many months, yet with a higher variability probably affected by individual lifestyle and physical/dietary habits. This also means that patients may maintain a visible aesthetic improvement in the long term. See Figures 2-4 for examples of patient images.

Although based on a limited-size sample, an interesting observation was the absence of any significant correlation

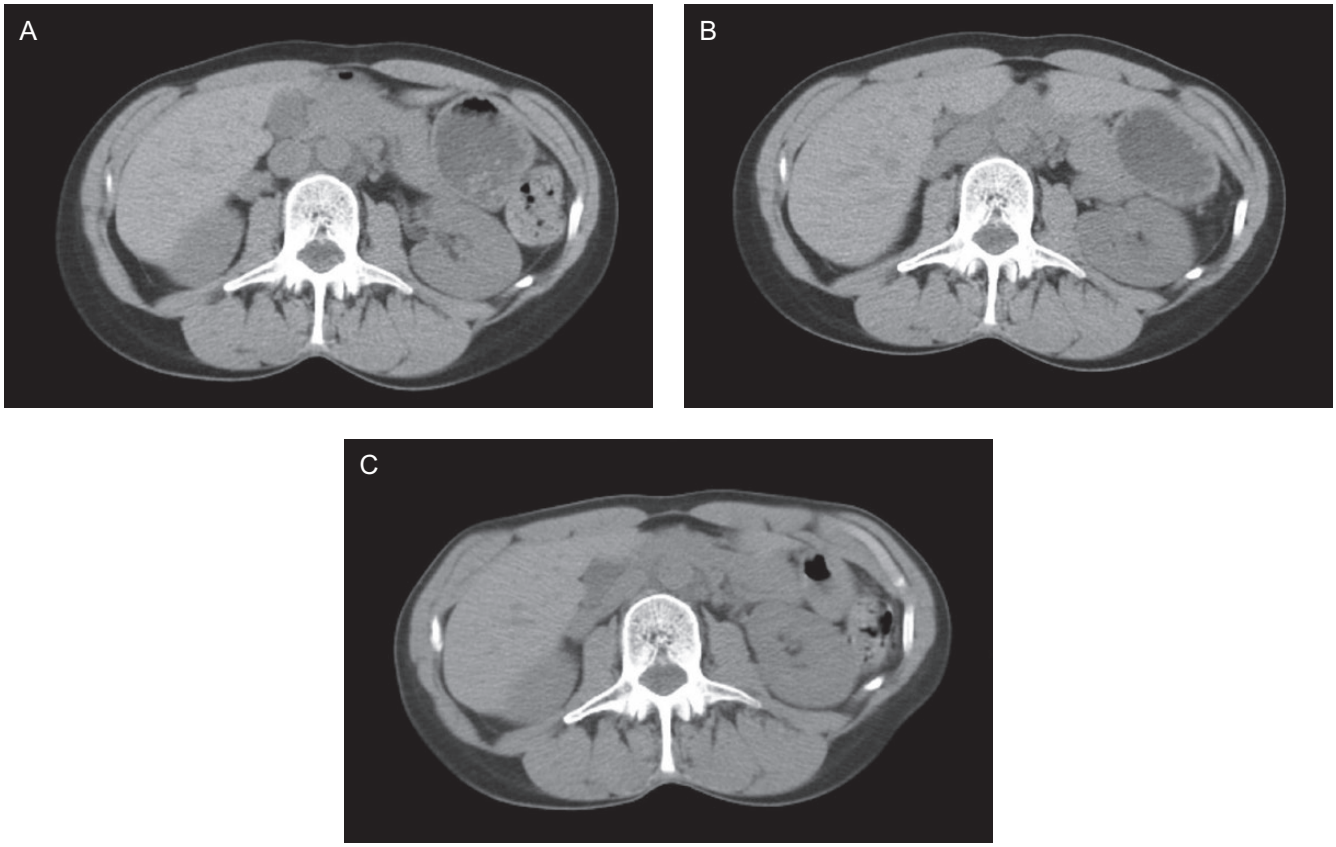

Figure 2. Computed tomography of a 37-year-old female patient at (A) baseline, (B) 1 month posttreatment, and (C) 1 year posttreatment. The fat reduction from 1 month (–10.7%) was improved at the 1-year visit (–40.5%). The thickening of the rectus abdominis muscle at 1 month (+32.0%) was slightly reduced to +26.1% at the 1-year follow-up.

between the exact length of the follow-up and the degree to which patients preserved their improvements. This suggests that the original changes in abdominal tissues do not follow a linear trend of decline, but larger-cohort studies will be needed to verify such a hypothesis.

A moderately strong positive correlation ($r = 0.53$; $P = 0.01$) between the baseline BMI and the baseline absolute subcutaneous fat thickness was expected, on the basis that larger BMI values are usually associated with accumulation of abdominal fat. Data processing also revealed a weak, yet statistically significant, negative relation between muscle thickness before treatment and the percentage change in thickness measured at the 1-year visit. This suggests that patients with initially more severe abdominal muscle disuse atrophy are likely to respond with more profound hypertrophic effects. Another significant weak correlation was measured between the initial size of abdominal separation and its reduction at the 1-year visit. This again shows that patients with more severe separation are more likely to see a better improvement 1 year after treatment.

Although the differences in muscle (+19.05%) and fat (–14.63%) are nearly the same and the patients' fat loss might seem to be compensated by muscle gain, we can still see circumferential reduction in these patients due to the correction of abdominal muscle laxity. Because the fat layer is reduced and muscle mass increased, the muscle definition below the skin is much more visible, which contributes to the athletic look that many patients desire. However, it is true that in patients with large fat deposits, the muscle effect cannot be seen very well because the muscles are hidden below the fat layer. In these patients only a reduction in fat can be seen. It should be noted, however, that patients with high fat deposits are not considered ideal candidates for HIFEM treatment.

A minor decline in the original fat reduction over time was expected as any lifestyle alterations may stimulate abdominal fat redeposition and lipolysis, and a subsequent adipocyte resizing effect may also play a role. Regarding muscle, not only preservation but even a minor continuous improvement is a result that does not correlate with previous research on muscle response to exercise, especially when our patients reported an unchanged lifestyle. Although no direct evaluation of hypertrophy has been reported, various studies have observed a decline in muscle strength, which starts between 1 and 6 months after the last

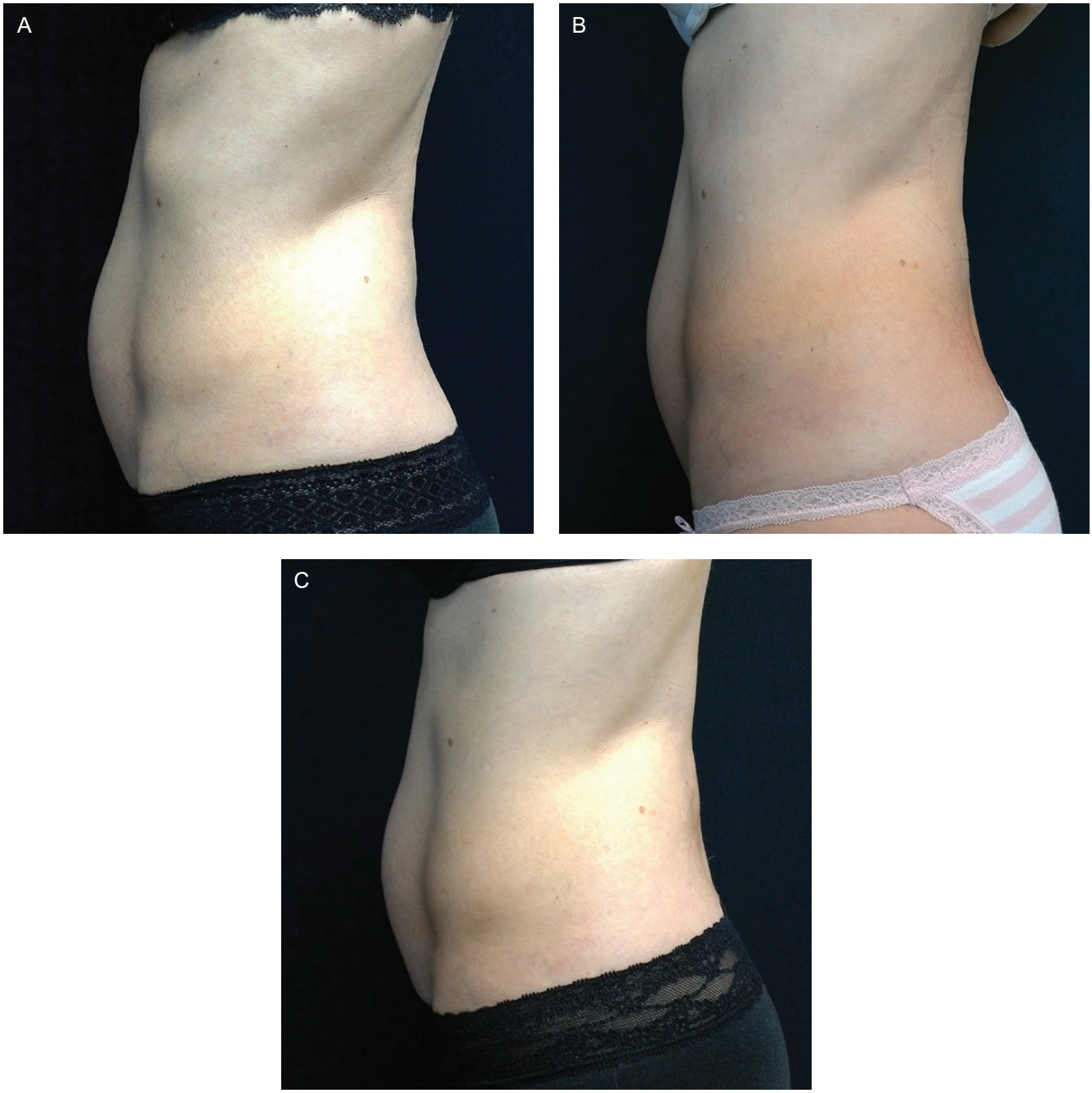

Figure 3. Digital photographs of a 37-year-old female patient (the same patient featured in Figure 2) at (A) baseline, (B) 1-month posttreatment, and (C) 1-year posttreatment.

exercise.[9-11] Duncan and Dinev[6] evaluated porcine muscle histology after HIFEM application and proposed a possible hyperplasic effect of the treatments. Their data are not conclusive, but if true, could explain that even without lifestyle changes, long-lasting muscle bulking occurs due to a higher number of muscle fibers in the patient's tissue. Any future research on human muscle biopsies could also provide better insights as to whether there is any effect of the treatments on myosatellite cells.

Based on circumferential measurements, Kent and Jacob[7] suggested that the application of 8 HIFEM treatments does not necessarily result in more profound changes in abdominal tissues compared with the application of 4 treatments. In this study group no significant

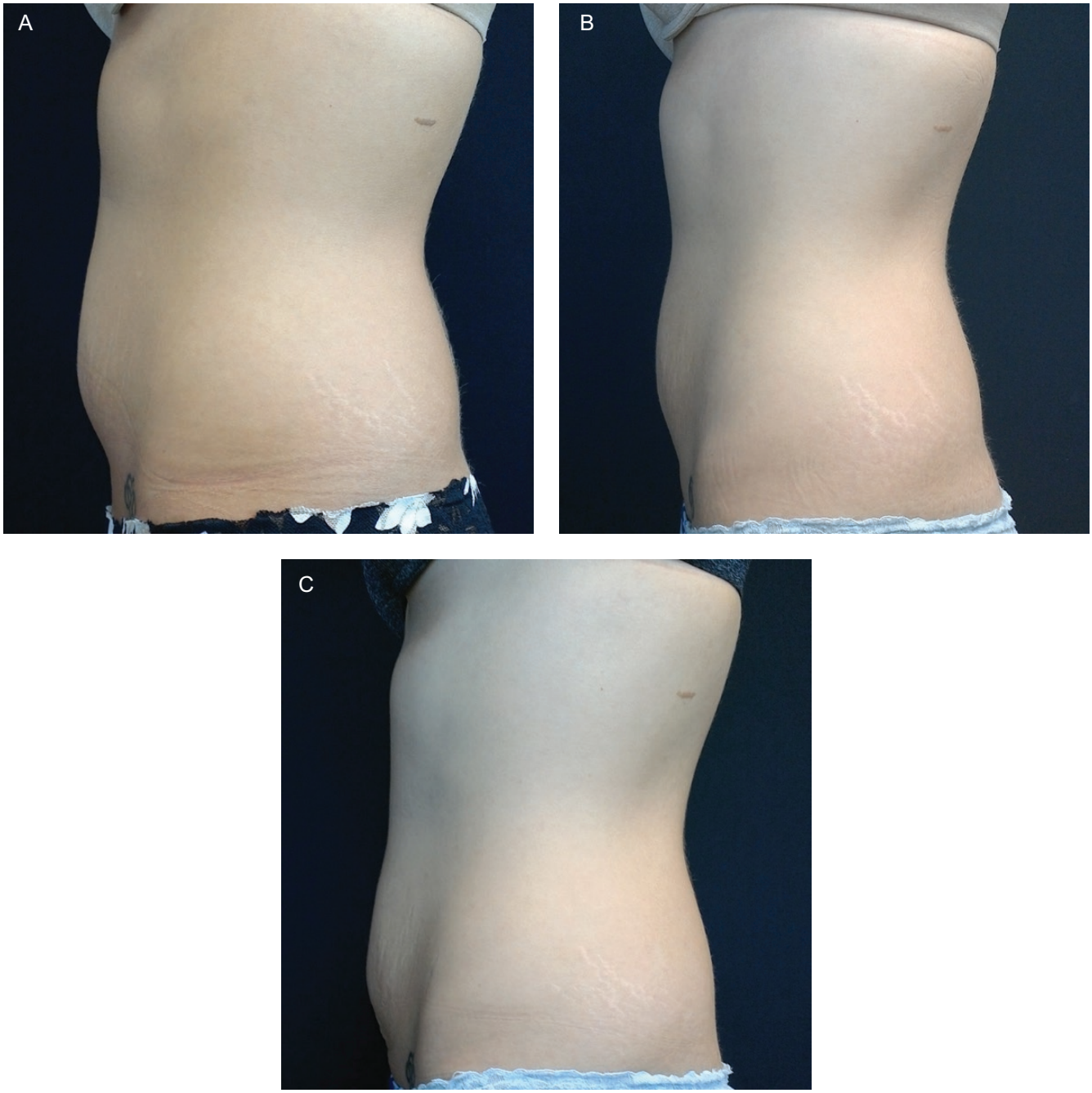

Figure 4. Digital photographs of a 51-year-old female patient at (A) baseline, (B) 1 month posttreatment, and (C) 1 year posttreatment.

relation was found between the number of treatments received and the degree of change in evaluated tissues at the 1-year follow-up. An explanation for this observation remains unknown, and future research may focus on investigating why there is a higher potential for HIFEM-induced changes in abdominal tissues in the first few sessions rather than following any additional treatments.

One limitation of such long follow-up is the inability to control the patients' lifestyles. After this long period of time the results may thus not be solely attributed to the treatment itself. It could be a combined effect of the treatments, following a balanced and healthy diet, together with incorporating exercise into their daily activities. Although our inclusion criteria were intended to reduce such bias, the effect of lifestyle cannot nevertheless be entirely ruled out. A lack of patient

satisfaction evaluation can also be considered a limitation of this study as patient satisfaction is a crucial outcome in aesthetic medicine. However, the current study was focused solely on objective evaluation free of subjectivity, which is high according to satisfaction questionnaires. Another limitation of the study is associated with the MRI/CT interslice spacing. The spacing between the individual slices was 5 mm. Because the MRI/CT scans were obtained at different times, the exact slice location could have moved slightly relative to the baseline scans, resulting in a maximum of 5 mm difference between the compared slices. However, we believe that a difference of up to 5 mm does not affect the final results. Furthermore, the study included only 21 patients out of the original patient group (n = 44) and this sample may not be representative of the entire general population. It is necessary to collect data from a larger group of patients post-HIFEM procedure to investigate whether the same patterns are also present on a larger scale.

CONCLUSIONS

Twenty-one patients who received HIFEM treatment were evaluated on average 1 year after their procedure in order to understand trends in the long-term evolution of their original body responses. Our results show that in those patients, HIFEM-induced muscle hypertrophy, fat reduction, and reduction in abdominal separation are maintained for at least 1 year posttreatment. Maintenance treatments can be used to prevent decline in individual patients.

Disclosures

Drs Kinney and Kent are medical advisors for BTL Industries Inc (Boston, MA).

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Preliminary Report

Noninvasive Induction of Muscle Fiber Hypertrophy and Hyperplasia: Effects of High-Intensity Focused Electromagnetic Field Evaluated in an In-Vivo Porcine Model: A Pilot Study

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Abstract

Background: High-intensity focused electromagnetic (HIFEM) field technology has been reported to increase muscle thickness and hypertrophy. However, this process has not yet been confirmed on a histologic level.

Objectives: The aim of this study was to evaluate in-vivo structural changes in striated porcine muscle tissue following HIFEM treatment.

Methods: Three Yorkshire pigs received four 30-minute HIFEM treatments applied to the biceps femoris muscle on 1 side only. The fourth pig served as a control subject. At baseline and 2 weeks after the last treatment, biopsy specimens of the muscle tissue were collected from the treatment site. The control pig underwent muscle biopsy from a similar but untreated site. Twenty-five histology slides were evaluated from each pig. A certified histopathologist analyzed sliced biopsy samples for structural changes in the tissue.

Results: Histologic analysis showed hypertrophic changes 2 weeks posttreatment. The muscle mass density increased by 20.56% (to a mean of 17,053.4 [5617.9] μm^2) compared with baseline. Similarly, muscle fiber density (hyperplasia) increased: the average change in the number of fibers in a slice area of 136,533.3 μm^2 was +8.0%. The mean size of an individual muscle fiber increased by 12.15% (to 332.23 [280.2] μm^2) 2 weeks posttreatment. Control samples did not show any significant change in fiber density or hyperplasia.

Conclusions: Histopathologic quantification showed significant structural muscle changes through a combination of fiber hypertrophy and hyperplasia. Control biopsies showed a lack of similar changes. The data correlate with findings of other HIFEM research and suggest that HIFEM could be used for noninvasive induction of muscle growth.

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Muscles have long been neglected in the body-shaping industry, which predominantly deals with subcutaneous fat deposits. However, strong and firm muscles significantly contribute to the overall aesthetic appearance. High-intensity focused electromagnetic (HIFEM) field technology has recently been introduced in the field of aesthetic medicine to provide physicians with a tool for muscle toning and strengthening beyond the capability of normal exercise.

Current noninvasive body-shaping devices are based on heating or cooling of subcutaneous fat tissue to levels that fat cells can no longer tolerate, consequently triggering programmed cell death—apoptosis.[1] The heating

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modalities of these radiofrequency devices are based on emitting electromagnetic waves of high frequencies (0.5-50 MHz)[2] which are predominantly absorbed in the subcutaneous fat tissue, where the energy of the waves is transformed into heat. HIFEM technology, on the other hand, does not deliver any heating through electromagnetic radiation, as it utilizes magnetic waves of very low frequencies (3-5 kHz) which propagate through the tissue without being absorbed. In this case, an interaction between the wave and human tissue occurs according to the principles of electromagnetic induction, first described by Michael Faraday in 1831. The law of electromagnetic induction says that any change in a magnetic field induces an electric current and vice versa. The HIFEM device comprises a circular coil located in the applicator, which is placed over the treatment area. During the treatment, an alternating electric current is sent into the circular coil. The alternations in the electric current induce rapidly changing magnetic waves which propagate into the underlying tissue, where they induce a secondary electric current. These electric currents within the tissue depolarize the muscle-innervating motor neurons and induce muscle contractions.[3]

Several studies have shown that humans are unable to fully activate muscles voluntarily as the power of muscle contraction is limited by the firing rates and conductivity of neural pathways.[4-7] Application of HIFEM bypasses the central and peripheral nervous system and directly stimulates the muscle-innervating motor neurons, allowing full muscle contraction. In addition, the frequency of delivered pulses does not allow the muscle to relax between 2 consecutive stimuli, which results in supramaximal tension within the muscle and thus supramaximal muscle contraction.

Multiple studies have investigated the effects of rapidly changing magnetic fields delivered through HIFEM technology.[8-13] The studies by Kent et al,[11] Katz et al,[12] and Kinney et al[8] employed computed tomography (CT), ultrasound, and magnetic resonance imaging (MRI), respectively, to investigate changes in abdominal composition post-HIFEM treatments. The thickness of abdominal muscles measured in CT and MRI images increased on average by 14.8% to 15.4%, indicating muscle hypertrophy. Although HIFEM technology directly affects muscles, the studies also found that the thickness of abdominal fat was reduced on average by 17.5% to 19%. The effect of the HIFEM procedure on adipose tissue was confirmed by a veterinary study,[13] which reported increased apoptotic index and apoptotic markers in the fat tissue post-HIFEM treatments.

Results from human trials suggest that HIFEM technology is a feasible modality for the aesthetic industry and could be widely used in body contouring for simultaneous fat reduction and muscle toning. Clinical trials are currently underway to assess the use of this technology to improve strength and tone in biceps, triceps, and gastrocnemius muscles. HIFEM has also been successfully used for strengthening the pelvic floor.[14]

Unlike fat apoptosis, which was confirmed on a histologic level, there is no histologic evidence for muscle hypertrophy. Because muscle thickness was found to be increased posttreatment, it might not necessarily indicate muscle fiber hypertrophy, but could be linked to swelling,[15] overall hydration, or increased water content in the muscle,[16] which may change with time. Therefore, histologic evaluation is necessary to confirm the observations on a cellular level.

The present study aimed to investigate the effect of an HIFEM-based procedure on muscle cells in a porcine model. The goal was to determine whether muscle hypertrophy is present on a cellular level.

METHODS

Four Yorkshire pigs served as subjects. Inclusion in the study required the animals to be in full physical health, which was assessed via blood samples collected 2 days before the treatment began. Three pigs received active treatment applied to the unilateral thigh, and the fourth untreated animal served as a control. The treatment procedure consisted of 4 sessions (30 minutes each) with a device that utilizes HIFEM technology (EMSCULPT; BTL Industries Inc., Boston, MA). The treatment sessions were scheduled twice a week for 2 weeks. The study was approved by the Institutional Animal Care and Use Committee (Bulgarian Food Safety Agency—BFSA committee, ID 195/2018). Animal care complied with the convention for the protection of vertebrate animals used for experimental and other scientific purposes. The experiment was conducted in July and August 2018.

During each treatment session, the animals were placed under general anesthesia to minimize their discomfort; this process was supervised by a veterinarian who chose the type and dosing of the anesthetic. A single applicator of the device was placed over the back thigh of the pig and secured by a fixation belt. All parameters used were identical to those commonly used in humans. Device settings were controlled by the operator. The intensity was gradually increased to 100% of the maximum device output, at which level it was maintained for the rest of the treatment time. For the 30 minutes of the treatment, the applicator was continuously delivering electromagnetic pulses with a magnetic field intensity of up to 1.8 T. The applicator position was adjusted during the treatment to ensure maximum contraction in the entire treatment area.

Punch biopsy specimens of muscle tissue were collected with a disposable biopsy punch (diameter, 5 mm)

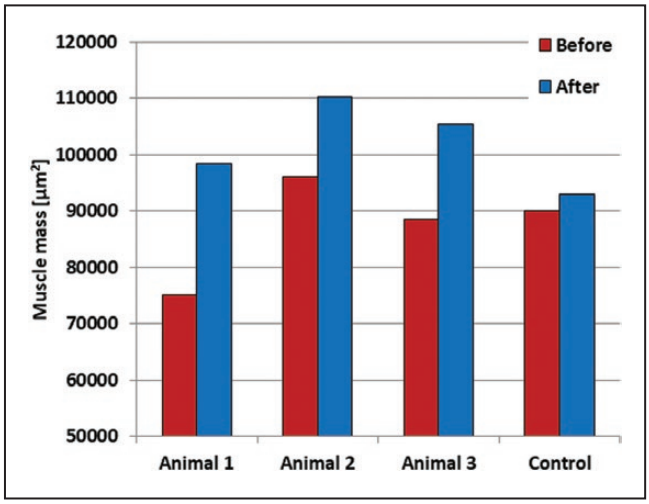

Figure 1. The average muscle mass per slice for each of the animals. All treated animals showed a significant growth in muscle mass. The muscle mass in the control animal did not change significantly.

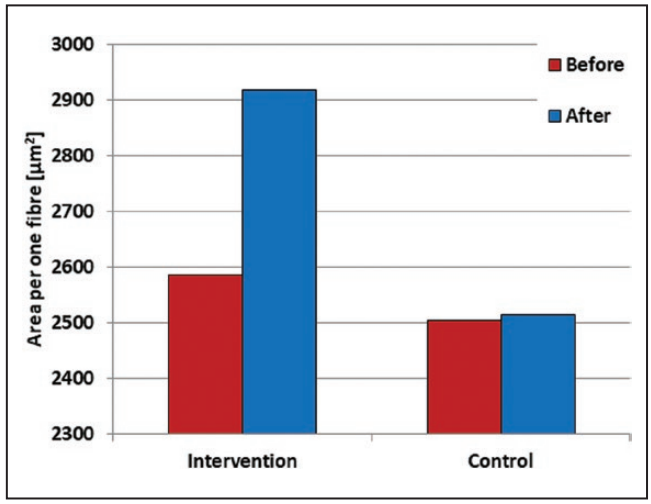

Figure 2. The average area per single muscle fiber in the treated (left) and control (right) animals at baseline (red) and posttreatment (blue).

before the first treatment and 2 weeks after the last treatment . The samples were fixed in 10% neutral buffered formalin and stained with hematoxylin and eosin. For microscopic evaluation, the samples were cut into 5-µm thick slices.

The slices were screened under a microscope (DFC295; Leica Microsystems Ltd, Germany) and an image of the entire slice was obtained for further analysis with Leica Application Suite (version 4.9.0) software. Each slice area was 136,533.3 µm^2. The analysis comprised the calculation of muscle fiber density, muscle mass density, and muscle fiber volume. Muscle fiber density was obtained as an average number of muscle fibers calculated individually in each slice. Muscle mass density was defined as the slice area occupied by muscle tissue. Muscle volume represents the area per single muscle fiber. ImageJ 1.52a software (National Institutes of Health, Bethesda, MD)[17] was used to calculate the muscle mass density and muscle fiber volume. Based on individual pixel color the software automatically segments the muscle tissue within the slices and calculates the area occupied by the muscle tissue.

In addition, the animals were monitored for any possible external manifestations of adverse events or side effects related to the procedure. The test animals were examined after every procedure to ascertain whether they exhibited any change in their condition compared with the baseline examination.

The sliced biopsy samples collected at baseline and 2 weeks posttreatment were compared for histologic changes. The statistical significance of possible changes was assessed by *t* test with a significance level set to 5%.

RESULTS

The 4 recruited Yorkshire sows (females) were between 1.5 and 2 years old (mean, 1.7 [0.2] years) and their mean weight was 74.6 [1.5] kg. All animals recovered from anesthesia without any complications or adverse events. The skin of test animals did not show any signs of adverse events such as erythema, scarring, ruptures, or skin texture change. The weights of all animals (treated and control) did not change after the treatments. In total 104 slices were obtained by slicing the punch biopsy samples (26 slices per subject). The statistical analysis showed a significant increase ($P < 0.01$) of muscle mass in the samples from treated animals.

In the treated animals, the muscle mass density increased on average by 20.56% (to a mean of 17,053.4 [5617.9] µm^2). An increase was observed in each of the treated animals, although the density remained constant in the control animal, with the change being within the standard deviation. The results for each animal are shown in Figure 1.

The change in the number of muscle fibers per slice was not statistically significant ($P > 0.05$), although a increasing trend was present in the treated animals as the average fiber density increased by 8.0% from 35.0 [6.8] to 38.2 [10.5]. The average muscle fiber density per slice in the control animal was 36.0 [9.1] at baseline and 37.0 [10.2] 2 weeks posttreatment. The difference was not statistically significant ($P > 0.05$).

Posttreatment, the average area per single muscle fiber increased significantly ($P < 0.05$) by 12.15% (to 332.23 [280.16] µm^2) in the intervention group. In the control animal the fiber area remained constant. See Figure 2 for the average results.

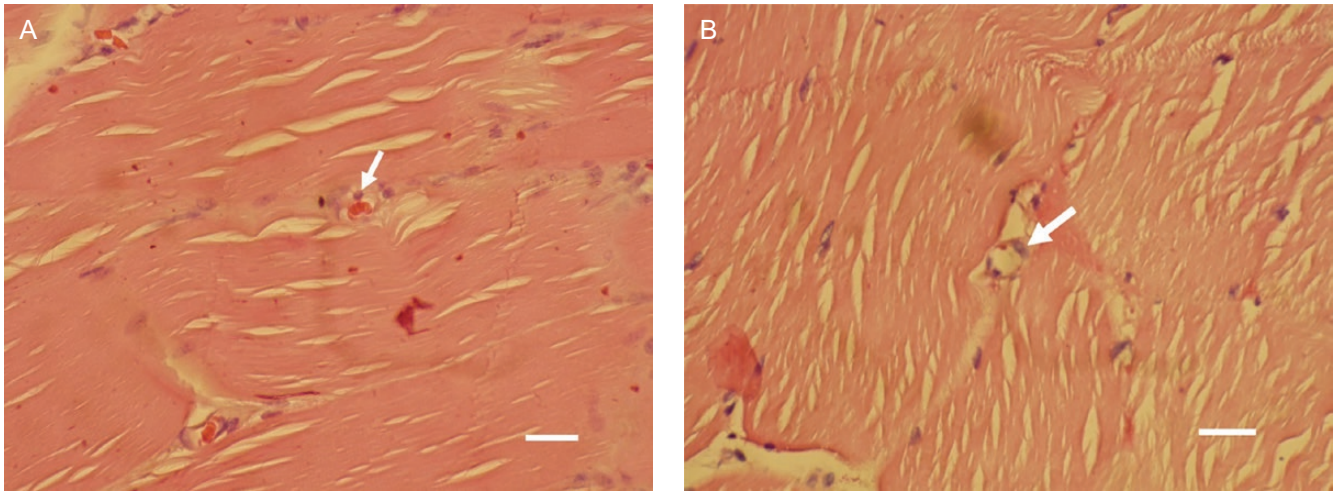

Figure 3. (A, B) The white arrows point to areas with the appearance of the endothelial cells with the onset of new capillary build-up in 2-week follow-up samples from the treated animals. White bar, 35 µm.

A further observation was neovascularization of the muscle tissue, which was widely seen in the 2-week follow-up histologic samples of the intervention group. Figure 3 shows samples exhibiting new capillary build-up.

DISCUSSION

Hypertrophy is normally seen in humans. There is, however, little evidence as to whether the overall muscle increase is simply due to increased thickness of individual muscle fibers (fiber hypertrophy) or due to a combination of fiber hypertrophy and multiplication of existing fibers/creation of new fibers (hyperplasia). Hyperplasia in humans is controversial among the scientific community, but existing studies have assessed this phenomenon after sets of ordinary exercises.[18] HIFEM, on the other hand, induces approximately 20,000 strong, supramaximal contractions within a time frame of 30 minutes, which cannot be achieved voluntarily, and the effects thus could be significantly higher, even leading to hyperplasia. Previous research on HIFEM technology showed an increase in muscle thickness in MRI, CT, and ultrasound images, providing evidence of muscle hypertrophy.[8,11] However, no study to date has looked at what happens to the muscle on a histologic level. The current study extends the scope of the existing literature by evaluating the effect of HIFEM treatments on individual muscle fibers, which has not been studied before.

This study aimed to determine whether HIFEM treatments can induce muscle hypertrophy on a cellular level. The histologic examination demonstrated that 4 HIFEM treatments induced prominent growth in the muscle tissue. The observed increase in total muscle mass by 20.56% appears to be mainly caused by a volumetric growth in individual muscle fibers, ie, muscle fiber hypertrophy (contributing 12.15%), and partially by an increase in the number of muscle fibers, ie, hyperplasia (contributing 8.0%), although the latter was not statistically significant.

The muscle growth observed in the current study correlates with previous research investigating the effect of HIFEM treatments on muscles. Kent et al[11] and Kinney et al[8] reported an increase in the muscle thickness by 14.8% and 15.4%, respectively. In comparison with these studies, the 20.56% increase on a cellular level seen in this study is larger, possibly due to densifying of the muscle tissue, as the connective tissue surrounding muscle fibers (endomysium) is compressed by increased muscle mass. This has indeed been observed in the histologic slices, and examples are shown in Figure 4. This is the first study investigating the hypertrophic effects of HIFEM technology on a histologic level, and hence there is no other histologic research with which the present results can be compared.

The lack of significant hyperplasia could be attributed to the short duration of the follow-up period. The posttreatment samples were collected 2 weeks after the last treatment and this period might not have been enough to fully manifest the hyperplastic changes as they might require more time to occur than fiber hypertrophy. A study by Crameri et al[19] found that it took 4 to 8 days to capture increased levels of myosatellite cells after a single bout of exercise. Therefore the terminal differentiation of these cells into clearly recognizable new muscle fibers might require more than 2 weeks.

The role of muscle fiber hyperplasia and muscle hypertrophy in humans is controversial because no evidence conclusively documents hyperplasia in human muscle.[20,21] Although the indications of hyperplasia observed in our study are not necessarily transferable to humans, it would be convenient to investigate whether the same pattern can be seen in human studies. Previous studies investigated

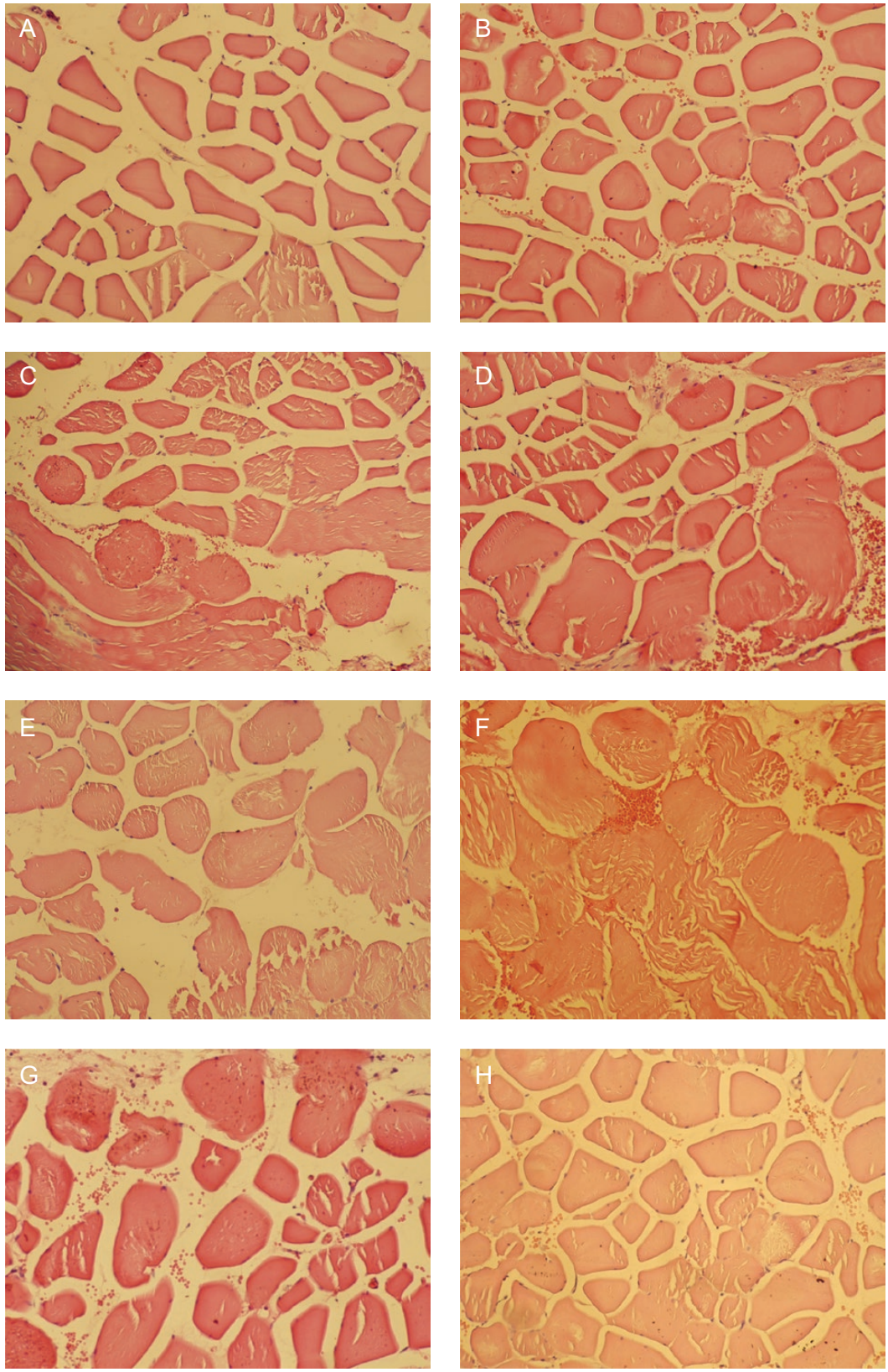

Figure 4. Example of histologic images of slices taken at (A, C, E, G) baseline and (B, D, F, H) 2 weeks posttreatment. The baseline images (A, C, E, G) show normal structure of muscle fibers, whereas the posttreatment images (B, D, F, H) show hypertrophy of muscle fibers with the muscle cell diameter being noticeably larger. The same magnification is used in all the images.

hyperplasia only postexercise, but HIFEM induced contractions of significantly higher strength and power than "exercise contractions" and could eventually trigger the terminal differentiation of myosatellite cells into new muscle fibers.

Besides HIFEM technology, which is based on magnetic stimulation, modalities based on electrical stimulation, such as electrical muscle stimulation (EMS) or transcutaneous electrical nerve stimulation (TENS), have been used in the past for muscle training.[22-24] Although TENS and EMS are predominantly used in rehabilitation and physiotherapy, HIFEM is the first muscle-affecting technology intended for body contouring. However, electromagnetic stimulation appears to offer a number of advantages over electrical stimulation: it induces 2 times higher peak torque[25] and, unlike with electrical stimulation, there is no pain[25] or risk of burns[26,27] with high stimulation intensities. Electromagnetic stimulation was further found to penetrate deeper into the tissue,[28] which is linked with the larger peak torques observed. The absence of adverse events in our study correlates with previous studies on humans. Due to the nonthermal nature of HIFEM technology, any risk of thermal tissue damage is eliminated. It might be assumed that rhabdomyolysis could occur following supramaximal contractions, but this has not been observed. Other expected complications or adverse events could be prolonged muscle soreness, swelling, bruising, cramping, or erythema of the overlying skin, but none of these were noted.

Observed neovascularization appears to be an adaptation response to the high load induced by HIFEM treatments when the growth of new capillaries is initiated to supply nutrition to the increased muscle mass.[29,30] Nevertheless, the level of neovascularization was not quantified and should thus not be considered as a definite conclusion. As such, this observation will be subjected to additional research in the future to provide objective evidence.

One of the limitations of the present study is the sample size; the study included only 4 animals (3 treated animals and 1 control) to minimize the number of animals in order to conform to the convention for the protection of vertebrate animals. However, to increase the statistical power of the study, over 104 histologic slices were examined and evaluated. Another limitation of the study is the short time period between the treatment and the muscle biopsy, because with longer terms larger hypertrophy and higher levels of hyperplasia may be noted, as discussed above. The use of animal subjects in the study may also be considered as a limitation because the observed results may not be fully transferable to humans. On the other hand, the porcine model is widely used as a suitable substitute due to its high biological similarity with humans.

The results suggest that HIFEM induces intense muscle contractions, causing a response of the muscle tissue in the form of muscle fiber hypertrophy, which correlates with previous studies reporting increased muscle thickness in CT[11] and MRI[8] images posttreatment. Future studies should focus on further verification of the observed hyperplastic effects via additional evaluation methods such as monitoring the levels of myosatellite cells.[31-33] In addition, longer follow-ups are required to capture potential terminal differentiation of the satellite cells.

To the best of our knowledge, no previous studies investigating changes in strength after HIFEM have been reported, although several studies have reported increased muscle mass posttreatment.[8,11,12] Anecdotally, patients often report increased strength during exercise after the treatment procedure, and one may infer that an increase in muscle mass is also linked with increased strength. Further studies should include strength assessment prior to and following HIFEM to document this hypothesized benefit.

CONCLUSIONS

Histopathologic evaluation found a hypertrophic effect of HIFEM application on a cellular level, which correlates to the muscle growth observed in previous studies. The results indicate that intense muscle activity is induced during the HIFEM treatments and suggests this technology could serve as a convenient tool for muscle toning.

Disclosures

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MRI QUANTIFICATION OF HIFEM® EFFECTS ON BUTTOCKS

MAGNETIC RESONANCE IMAGING EVALUATION OF CHANGES IN GLUTEAL MUSCLES AFTER TREATMENTS WITH THE HIGH-INTENSITY FOCUSED ELECTROMAGNETIC PROCEDURE

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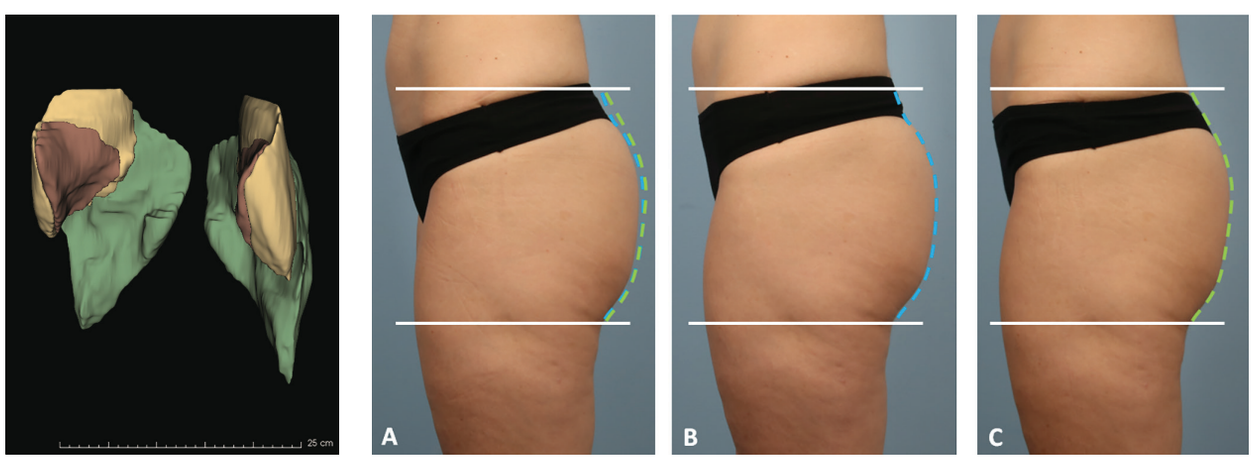
HIGHLIGHTS

- 7 female subjects received four 30-minute HIFEM treatments on the buttocks.
- **3D volumes** of gluteal muscles were **reconstructed from MRI scans**.
- Simultaneous **enhancement (P<0.001) of all three gluteal muscles** was found at 1-month (**+10.81%**, 197.98 cm^3) and 3-month (**+13.23%**, 241.45cm^3) follow-ups.
- The appearance of buttocks was improved with a **visible lifting effect**.
- The thickness of gluteal adipose tissue was not affected.



On the left: 3D reconstruction of the muscle volumes; musculus gluteus maximus (green), medius (yellow) and minimus (red).
On the right: standardized patient photography that shows a change in the buttock contour at 1 month (B, blue-dotted line) and 3 months (C, green-dotted line) relative to the baseline (A).

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DRUGS • DEVICES • METHODS

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC TECHNOLOGY (HIFEM) FOR NON-INVASIVE BUTTOCK LIFTING AND TONING OF GLUTEAL MUSCLES: A MULTI-CENTER EFFICACY SAFETY STUDY

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J Drug Dermatol. 2017;17(11):1129-1132.

High Intensity Focused Electro-Magnetic Technology (HIFEM) for Non-Invasive Buttock Lifting and Toning of Gluteal Muscles: A Multi-Center Efficacy and Safety Study

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ABSTRACT

Objective: Surgical intervention has been the only method to improve the aesthetic appearance of buttocks apart from physical exercising. This study evaluates the efficacy of high intensity focused electro-magnetic (HIFEM) treatments as a non-invasive solution for improvement of buttocks through toning and lifting of gluteal muscles.

Materials and Methods: A total of 75 patients (aged 22-59) were treated using a device with HIFEM technology which stimulates gluteal muscles (EMSCULPT, BTL Industries, Boston, MA). The protocol included four 30-minute treatments. Patients' weight was monitored throughout the study. Standard photographs were taken at the baseline, after the 4th treatment, and at the 1-month follow-up. Two 7-point Likert scale questionnaires were used to evaluate patients' buttock and treatment satisfaction. Total score of buttock satisfaction was calculated as a sum of all individual questions to reflect the overall perception of patients' buttocks. The level of comfort during procedures was assessed on a visual analog scale (VAS).

Results: The overall buttock satisfaction score (range, 4-28) of all subjects improved from 13.1±5.7 at baseline to 18.4±5.2 after the treatment and 18.9±5.1 at follow-up. For subjects with initial buttock dissatisfaction the scores improved from 8.7±1.6 to 16.3±3.1 after the treatment and to 17.3±3.1 at follow-up. The average score of all treatment satisfaction questions (range, 1-7) was 5.2±1.2 immediately after the treatments and 5.1±1.3 at follow-up. In total, patients initially dissatisfied with the appearance of their buttocks reported a significant 85% improvement after the fourth treatment. Immediately after the fourth treatment, all the subjects reported that their buttocks felt more lifted and toned. Results were maintained at one-month follow-up. Weight of the patients didn't change significantly. Digital photographs showed aesthetic improvements of the buttocks for most of the patients. No adverse events were reported.

Conclusion: The results show that the investigated device safely and effectively improves the aesthetic appearance of buttocks non-invasively. The treatments not only resulted in a significant visual improvement but also increased patient confidence and satisfaction. The procedure is suitable for patients seeking improvement in tone, shape, lift, and tightness of the buttocks.

J Drugs Dermatol. 2018;17(11):1229-1232.

INTRODUCTION

The popularity of surgical butt lifting, and augmenting procedures is rapidly growing. Since 2015, the number of performed procedures increased on average by 25% each year,[1] while the increase over the past two decades totals 342%,[2] with the total expenditures for these type of procedures reaching 120 million USD in 2016.[2] The most popular methods are represented by buttock augmentation using silicone implants, autologous fat grafting, and a traditional butt lift done by cutting out an ellipse of excess skin and suturing the remaining skin back together. In general, these procedures are associated with one to four weeks of downtime.[2]

Surgical procedures are associated with risk of complications. The rate of complications related to buttock augmentation using silicone implants were reported to be as high as 21.6%[3] and 38.1%,[4] while for autologous fat grafting complications were reported to occur in 9.9% of all cases.[3] The most common complications are wound dehiscence, seroma, and infection.[3] Further-

FIGURE 1. A photograph of a patient during an ongoing treatment.

more, all surgical procedures focus on artificially increasing the subcutaneous volume of buttocks, yet they do not target the underlying gluteal muscles, which play a crucial role in the buttock shape definition and overall aesthetic appearance of buttocks.

Magnetic stimulation has been widely and successfully used before, eg, in the treatment of incontinence by strengthening the pelvic muscles,[7] in cough restoration,[8] or in augmentation of resistance training.[9] This study investigates the efficacy and safety of a high-intensity focused electro-magnetic (HIFEM) technology (EMSCULPT, BTL Industries, Boston, MA) when used for non-invasive improvement of the appearance of buttocks. The device delivers magnetic impulses into the tissue where it stimulates the gluteal muscles (gluteus maximus, medius, and minimus) and induces supramaximal contractions of all these muscle groups simultaneously. The muscle tissue is forced to adapt to the supramaximal load, which then leads to muscle hypertrophy and hyperplasia.[5,6] As a result, the gluteal muscles responsible for the aesthetic appearance of buttocks increase in size and become firmer. This application has been shown to lead to an improvement of buttock shape.

MATERIALS AND METHODS

In total, 76 subjects (74 females and 2 males) participated in the study. The age of recruited subjects ranged between 22 and 59 years (average, 36.6±8.3) with average BMI 21.5±2.2 kg/m^2. The participants received bilateral treatments of buttocks with a novel device based on the HIFEM technology (EMSCULPT, BTL Industries, Boston MA). The therapy protocol consisted of 4 treatment sessions which were spaced by 2-3 days, each session including 30 minutes of application. During the treatment, subjects were placed in a prone position and the applicator of the device was placed over the buttocks to simultaneously affect all the gluteal muscles as seen in Figure 1. A fixation belt was used to avoid any movements of the applicator during the treatment. The output intensity was kept just below each patient's tolerance threshold in order to maintain the supramaximal contractions throughout the entire treatment.

Patients were evaluated at the baseline, after the last treatment, and at 1-month follow-up. Digital photographs of the treated area were taken, and patients' weight were measured as a control indicator. Two different non-standardized questionnaires based on 7-point Likert scales were used to assess the effects of the treatment. The buttock satisfaction questionnaire focused on measuring if the treatments can change the way patients perceive and/or think about the appearance of their buttock area. The total possible score ranged from 4 points (lowest possible satisfaction) to 28 points (highest possible satisfaction). See Table 1. The responses were compared between the baseline, post-treatments, and the follow-up. After the last treatment and at the follow-up, the second questionnaire was used to evaluate patients' satisfaction with the results of the treatments. See Table 2. Average scores were calculated, and a paired t-test was used for statistical analysis.

A visual analogue scale (0-10) was used to assess the level of comfort during the treatments. Any side effects or adverse events were monitored.

RESULTS

In total, 75 subjects (73 females and 2 males) completed the full treatment protocol; four subjects withdrew before the follow-up for reasons unrelated to the study. The results presented herein thus include data from 71 subjects.

FIGURE 2. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). Female, 31 years old.

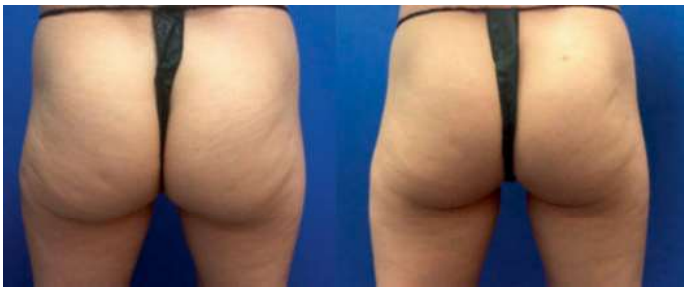

FIGURE 3. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). The demarcation line shows the improvement and lifting of the gluteal fold.

The average buttock satisfaction scores significantly improved (P<0.01) after the last treatment and at the one-month follow-up, both when measured as a total and individually for each question. The total average score increased by 40.5% from 13.1±5.7 at the baseline to 18.4±5.2 post-treatments, and further improved to 18.9±5.1 at the follow-up. The most significant improvement was seen in patients who were initially dissatisfied with the appearance of their buttocks prior to the treatments, with the average score increasing by 83% from 8.7±1.6 to 16.3±3.1 after the treatment, and on to 17.3±3.1 at the follow-up. See Table 1.

Statistical analysis of the results revealed that 69% of patients who initially reported buttock laxity improved to a higher degree of buttock tightness post-treatments and at the follow-up. In total, 85% of the patients initially dissatisfied with the appearance of their buttocks reported a significant improvement immediately after the fourth treatment, which was maintained over the course of one-month follow-up. Furthermore 80% of the patients initially dissatisfied with the shape of their buttocks reported a significant improvement immediately after the fourth treatment and during the follow-up. 79% of patients with low confidence while wearing the bikini at baseline felt significantly more confident after the fourth treatment and continued to feel confident during one-month follow-up.

In the patient satisfaction questionnaire, 76% of patients reported that the appearance of their buttock area has been improved after the treatments and during the one-month follow-up, while 80% of all the patients reported that their buttocks felt more lifted and toned right after the fourth treatment as well as at the follow-up. In total, 71% of all patients were satisfied with the treatment results immediately after the fourth treatment as well as during the one-month follow-up. The average scores can be seen in Table 2.

Patients found the treatments comfortable with an average VAS score of 2.01 (corresponding to none or very mild discomfort).

The analysis of weight did not show significant changes. No adverse events were observed during the treatments nor as a consequence of the treatments. Digital photographs showed improvements in aesthetic appearance of the buttocks. See Figures 2 and 3 for examples of patient images.

DISCUSSION

As of today, there are no standardized measurement tools that could be used for evaluation of a non-invasive improvement of buttocks. This can primarily be attributed to the fact that most currently used methods are surgical by nature. The study presented focused mainly on the evaluation of the subjective perception of the treated patients. This subjective satisfaction assessment was then further supported by visual improvement captured in digital images.

The results show a statistically significant positive trend in all of the measured criteria. This suggests that the treatments can have a positive effect on the way patients perceive the ap-

TABLE 1.

Buttock Satisfaction Questionnaire Results					
Question (Score range, 1-7)	Baseline	After	Change	1M FU	Change
Please rate your subjective perception of your buttock laxity/tightness[1]					
Total (n=75)	3.4±1.6	4.6±1.5	+1.2 (P<0.01)	4.8±1.3	+1.4 (P<0.01)
Baseline score <4 (n=42)	2.2±0.7	4.0±1.6	+1.8 (P<0.01)	4.5±1.4	+2.3 (P<0.01)
I am satisfied with the overall aesthetic appearance of my buttocks[2]					
Total (n=75)	3.2±1.5	4.8±1.3	+1.6 (P<0.01)	5.0±1.5	+1.8 (P<0.01)
Baseline score <4 (n=46)	2.2±0.7	4.4±1.5	+2.2 (P<0.01)	4.6±1.6	+2.4 (P<0.01)
I am satisfied with the shape of my buttocks[2]					
Total (n=75)	3.4±1.6	4.7±1.6	+1.3 (P<0.01)	4.9±1.4	+1.5 (P<0.01)
Baseline score <4 (n=45)	2.3±0.7	4.1±1.6	+1.8 (P<0.01)	4.5±1.5	+2.2 (P<0.01)
I feel confident about my buttock area when wearing the bikini[2]					
Total (n=74)	3.1±1.6	4.4±1.5	+1.3 (P<0.01)	4.3±1.6	+1.2 (P<0.01)
Baseline score <4 (n=48)	2.0±0.7	3.8±1.4	+1.8 (P<0.01)	3.7±1.6	+1.7 (P<0.01)
Total score	13.1±5.7	18.4±5.2	+5.3 (P<0.01)	18.9±5.1	+5.8 (P<0.01)
Total score (Baseline score < 4)	8.7±1.6	16.3±3.1	+7.6 (P<0.01)	17.3±3.1	+7.2 (P<0.01)

[1]1 – Very loose, 2 – Moderately loose, 3 – Slightly loose, 4 – Neither loose/tight, 5 – Slightly tight, 6 – Moderately tight, 7 – Very tight.
[2]1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

TABLE 2.

Treatment Satisfaction Questionnaire Results		
Question (range, 1-7)[1]	After	1-month FU
The appearance of my buttock area has been improved after the treatments	5.0±1.4	5.2±1.4
My buttocks feel more lifted and toned after the treatments	5.3±1.3	5.2±1.4
I am satisfied with the treatment results	5.2±1.3	5.1±1.4
I would recommend the treatment to a friend	5.1±1.5	4.9±1.5
AVERAGE SCORE	5.2±1.2	5.1±1.3

[1]1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

pearance of their buttocks, their level of confidence and overall satisfaction.

For the analysis of subjects' buttock satisfaction, the data was adjusted for patients who initially had a negative perception of their buttocks (score <4) as this would likely be the primary target group of the treatments. This group showed greater improvements than the total study population, which suggests that this sub-group of initially dissatisfied patients are the ideal profile that can most benefit from the treatments.

Visual inspection of digital photographs showed visible aesthetic improvement in most patients. The best results were seen in patients with lower BMI and in patients who reported a more active lifestyle. However, patient expectation management is crucial as the changes to the buttocks should not be compared to any surgical intervention. Rather than large volume augmentation, the patients in this study showed a lifting effect coupled with an improvement in their gluteal folds, as well as an increase in the overall buttock tightness. We thus suggest that the investigated device should not be considered a replacement for a surgical butt lift procedure yet brings a new alternative to patients seeking more toned and athletically appearing buttocks.

CONCLUSION

The EMSCULPT device proved to be effective and safe for non-invasive improvement of the aesthetic appearance of the buttocks. Future research should focus on bringing more evidence based investigational methods for the evaluation of non-invasive buttock treatments.

DISCLOSURE

Carolyn Jacob MD and Brian Kinney MD are medical advisors for BTL. Mariano Busso MD and Suneel Chilukuri MD are speakers for BTL. The other authors have no financial interest to declare in relation to any of the products or device mentioned in this article.

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WAIST CIRCUMFERENCE **REDUCTION** TESTED IN A MULTICENTRIC STUDY

A NOVEL NON-INVASIVE TECHNOLOGY BASED ON SIMULTANEOUS INDUCTION OF CHANGES IN ADIPOSE AND MUSCLE TISSUES: SAFETY AND EFFICACY OF A HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC FIELD DEVICE USED FOR ABDOMINAL BODY SHAPING

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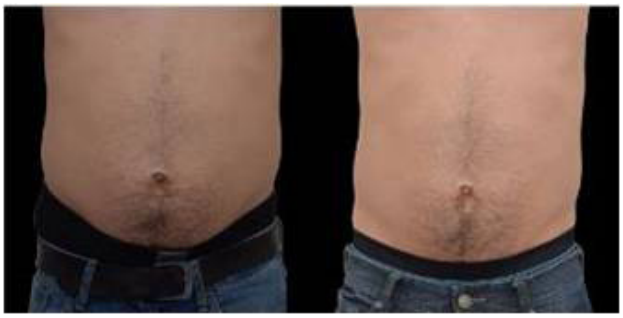
Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

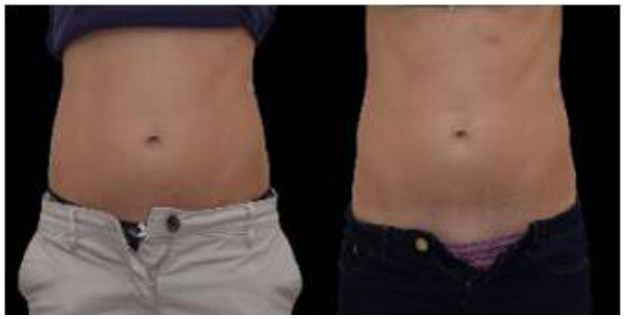
- **22 patients** (lower BMI profile - average 23.8kg/m2) were treated in 4 sessions within 2 weeks.
- Patient **waist** size **was reduced** on average **by 4.37 cm** at **3 month post-treatments**.
- Patient photography captured a combination of **muscle toning and fat reduction.**
- **96 % patients** were **satisfied with** treatment **results**.

Higher-BMI patient



BASELINE 1 MONTH FU

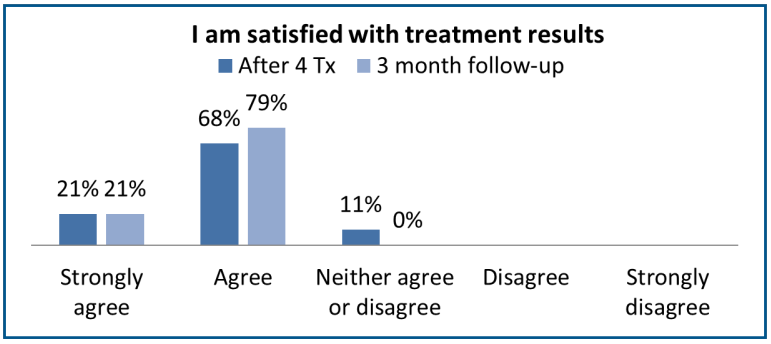
Lower-BMI patient



BASELINE 1 MONTH FU

DETAILED RESULTS

- 19 patients completed the study; no adverse events.
- **16 out of 19 subjects** (84%) showed >**2.5 cm circumferential reduction** 3-months post-treatment (independent of weight changes).
- A significant portion of the **reduction** (75%) was measured **already after the last treatment**, further improving at 3-months.
- Two patients (11%) didn't have any waist size change, but their aesthetic appearance improved in digital photographs.
- The **overall recognition** rate of digital photographs (before and 3-months post) averaged **89.47%**. Images of 15 subjects were uniformly recognized by all 3 reviewers.
- At 3-months all patients expressed some level of satisfaction with treatment results, there were **no dissatisfied patients**.



BASELINE 1 MONTH FU

Digital images before (left) and 3-months after last procedure (right). Subject 04, age 36, BMI 20.4, waist circumference -4 cm (-5.3%), weight change +1.1 lbs (+0.7%).

COMPUTED TOMOGRAPHY STUDY: SIMULTANEOUS FAT AND MUSCLE EFFECT

SIMULTANEOUS CHANGES IN ABDOMINAL ADIPOSE AND MUSCLE TISSUE FOLLOWING TREATMENTS BY HIGH-INTENSITY FOCUSED ELECTROMAGNETIC (HIFEM®) TECHNOLOGY-BASED DEVICE: COMPUTED TOMOGRAPHY EVALUATION.

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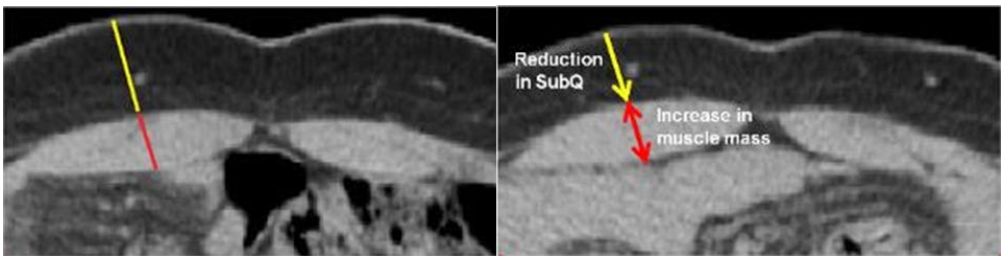
HIGHLIGHTS

- 22 patients received 5–8 treatments to evaluate effects of an extended protocol. Subject were evaluated 1 month post-treatments.
- Abdominal **fat thickness** was **reduced** on average by **17.5% (-3.1±1.9 mm)**.
- Simultaneously a **14.8% (+1.5±0.8 mm) increase in abdominal muscle thickness** was observed, coupled with a 9.5% (-2.0±1.7 mm) reduction in diastasis recti.
- **Waist circumference decreased on average by 3.9±3.1 cm** (after 4th Tx).
- Data suggest **4 treatments as the optimal protocol**.

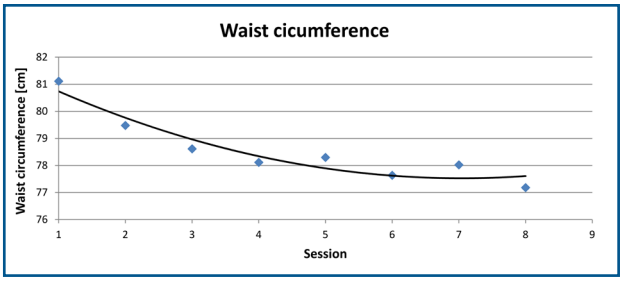


BASELINE 1 MONTH FU

RESULTS

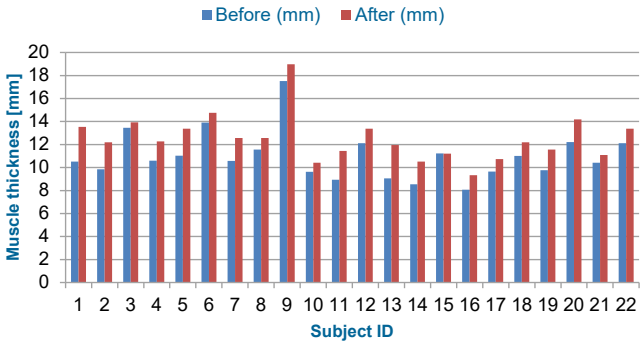
UMBILICAL CIRCUMFERENCE

- Additional treatments didn't show any significant circumference decrease.

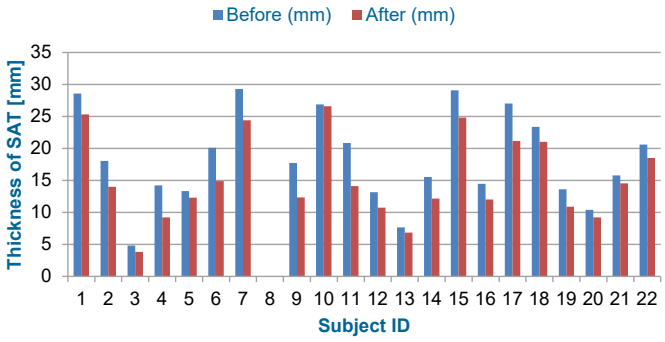


CT MEASUREMENTS

CT calculated thickness of rectus abdominis at baseline and 1 month post treatments.

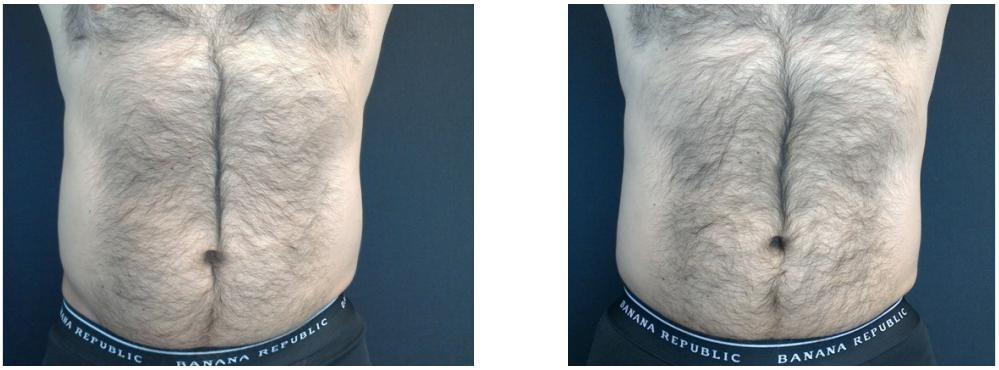


Subcutaneous fat thickness at baseline and 1-month post treatments. Patient ID8 fat measurements could not be objectively made due to close-to-zero baseline fat thickness.



BASELINE

1 MONTH FU



CT scans of patient ID9 at baseline (left) and 1-month post treatments (right). The scan shows reduction of subcutaneous fat (-30.3%) and thickening of rectus abdominis muscle (+8.4%).

Magnetic Resonance Imaging Evaluation of Changes in Gluteal Muscles After Treatments With the High-Intensity Focused Electromagnetic Procedure

Melanie Palm, MD, MBA

BACKGROUND High-intensity focused electromagnetic (HIFEM) field procedure induces changes in the gluteal muscles and improves the aesthetic appearance of the buttocks.

OBJECTIVE This study aims to objectively assess the hypertrophic response of the gluteal muscles after HIFEM treatments.

MATERIALS AND METHODS Seven subjects (40.00 ± 6.68 years) received 4, 30-minute HIFEM treatments of the buttocks. Magnetic resonance imaging of the pelvic region was obtained at baseline, 1-month, and 3-month follow-up to reconstruct 3D volumes of *musculus gluteus maximus*, *medius,* and *minimus*. Volumetric changes were calculated and statistically analyzed. Standardized photographs, weight measurements, patient satisfaction, treatment comfort, and adverse events were also documented.

RESULTS Volumetric analysis revealed a significant increase ($p = .001$) in the size of the examined muscles at 1-month (+10.81 ± 1.60%) and 3-month (+13.23 ± 0.91%) follow-up. A more profound hypertrophic effect was seen in the upper buttock region. This translated into a visible buttock lifting, also captured by patient photography. Gluteal adipose tissue was insignificantly affected. Patients were satisfied, and they found the treatments comfortable. No adverse events were observed.

CONCLUSION Simultaneous enhancement of gluteal muscles was documented. This represents the first objective evaluation of the HIFEM-induced structural changes in the gluteal muscles and physiologic documentation of the aesthetic improvement previously reported by other authors.

This was an investigator-initiated study. The author received financial support from BTL and serves on the medical board of BTL.

Aesthetic appearance of the buttocks is one of the essential attributes of beauty. Not surprisingly, the interest in buttock augmentation has increased over the past decade. According to 2018 statistics of the American Society of Plastic Surgeons (ASPS), more than 29,000 buttock augmentation surgeries are performed annually.[1] The most frequent buttock augmentation procedures include silicone implant placement; local flaps or tissue rearrangement; autologous fat grafting; and injections of various filler materials (although not FDA approved), such as hyaluronic acid gels, polymethyl methacrylate, or polyacrylamide.[2,3] These techniques, however, are accompanied by a relatively high complication rate.[2] The spectrum of observed complications is broad and includes both minor and major postoperative sequelae, such as prolonged pain, seroma, or occasional infection. Because of the inherent risks and postoperative complications after invasive buttock enhancement procedures, a safe, noninvasive and no downtime approach for buttock enhancement would be an attractive alternative to high-risk surgical procedures.

High-intensity focused electromagnetic (HIFEM) field procedure may represent an effective treatment alternative to riskier surgical procedures. High-intensity focused electromagnetic field procedure works

Art of Skin Maryland, Solana Beach, California

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through noninvasive stimulation of the gluteal muscles (gluteus maximus, medius, and minimus). It depolarizes peripheral motor neurons and elicits intense supramaximal contractions that impose the muscle to an extensive load. After several applications, muscles are expected to increase in size due to the muscle fiber hypertrophy and hyperplasia.[4–6] Recent studies found HIFEM as an effective and safe tool for buttock lifting with a lack of any significant adverse events.[7,8] However, the treatment outcomes were based on patient satisfaction and visual improvement. Therefore, an accurate, quantitative, and objective evaluation is needed to validate the treatment-induced changes apparent in previous studies.

A convenient tool for the objective evaluation of muscle changes is magnetic resonance imaging (MRI). Magnetic resonance imaging is the gold-standard method for the evaluation of skeletal muscles in terms of its shape or three-dimensional (3D) volume reconstruction.[9] Previously, MRI has been used for 3D volumetric examination of the gluteal muscles and was deemed to be a feasible objective measurement tool of muscle changes.[10,11]

This study aims to provide an objective evaluation of the expected hypertrophic response of gluteal muscles after HIFEM treatments by using MRI.

Materials and Methods

This was a prospective open-label single-arm study approved by the institutional review board (IRB). All procedures were performed with regard to ethical principles stated in the Declaration of Helsinki. Seven healthy and physically active women (mean age 40.00 ± 6.68 years; body mass index [BMI] 21.16 ± 2.08 $kg \cdot m^{-2}$) participated in the study. Written informed consent was obtained from all participating subjects.

Study subjects aged ≥21 years were physically active and recommended to maintain at least minimum physical activity between the treatments to enhance muscle regeneration and thus facilitate its structural changes. Patients with large amount of fat deposits (BMI ≥30 $kg \cdot m^{-2}$), previous surgery in the buttock/thigh area or any other concurrent treatments applied on the treated area during the study, pronounced skin laxity in the treated area, pregnancy, metal implants, and any of the contraindications listed in the operator's manual of the used HIFEM device were excluded.

In compliance with the IRB-approved protocol, each subject received 4 bilateral treatments with the HIFEM device (EMSCULPT; BTL Industries Inc., Boston, MA). Thirty-minute treatments were performed biweekly over 2 weeks. During the therapy, patients rested in a prone position. The applicators were placed on the buttocks and equally centered, to achieve simultaneous contractions of the gluteus maximus (gmax), medius (gmed), and minimus (gmin). A fixation belt was used to ensure the stable position of the applicators. Intensity of the HIFEM field was set to a maximum tolerable level (range of 0%–100%), and it was continuously adjusted according to the subject's feedback.

The primary outcome was to document hypertrophic changes of the gluteal muscles. Magnetic resonance imaging was performed at baseline, 1 month, and 3 months after treatment. Using a conventional system Philips Infinion 1.5T (Philips medical systems Inc., Andover, MA), the transverse, T1-weighted spin-echo images (from the iliac crest to the upper third of thighs) were acquired. Scanning protocols were set with regards to the optimal distinction of muscle tissue[12–14] as follows: time to repetition 600 ms, time to echo 13 ms, section thickness 3 mm, matrix size 512 × 512 and a field of view sufficient to cover the entire pelvic region. The obtained MRI scans in the Digital Imaging and Communications in Medicine format were slice-by-slice manually segmented to define 3D volumes of all 3 gluteal muscles (Figure 1). Evaluated slices at the baseline and follow-ups were chosen to be equivalent for further comparison of outcomes. The volume changes (in cm^3) between the follow-ups and baseline were calculated.

Standardized photographs of the subject's gluteal area (back and side view) were taken at the baseline, after the last treatment, at 1 month, and 3 months to evaluate changes in the physical appearance of buttocks.

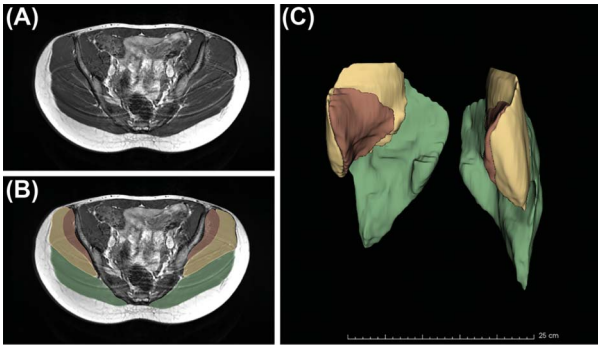

Figure 1. Example of the manual segmentation (B) of gluteal muscles in the transverse plane (A). Musculus gluteus maximus (green), medius (yellow), and minimus (red) are highlighted in colors. Three-dimensional reconstruction of muscle volumes can be seen on the right (C).

Weight and height measurements were also recorded. The occurrence of any adverse events was documented at each subject visit.

The patient's satisfaction and therapy comfort were assessed by using a 5-point Likert scale questionnaires. The satisfaction questionnaire consisted of 3 questions, and it was completed after the last treatment, at 1 month, and 3 months. Subjects reported their level of satisfaction with the appearance of the treated area, whether their buttocks felt tighter and more lifted as well as their overall satisfaction with treatment results. The therapy comfort questionnaire was assessed immediately after the last treatment.

Results of the volumetric muscle analysis were statistically analyzed using the two-tailed Wilcoxon signed-rank test for matched samples. p-values less than 0.05 ($\alpha = 5\%$) were considered as statistically significant.

Results

All subjects completed scheduled treatment sessions and study visits. The baseline weight of treated group was 57.99 ± 7.35 kg, and it insignificantly changed at 1 month (−0.25 kg; $p = .20$) and 3 months (+0.41 kg; $p = .69$). No adverse events were reported during or after the procedure or during the follow-up period.

Results of the 3D volumetric analysis at the 1-month follow-up revealed a highly significant ($p = .001$) increase in the size of the examined muscles when compared with baseline (Figure 2). The average muscle volume enhancement was 10.81 ± 1.60% (197.98 ± 40.93 cm^3; 6.69 oz). Also, it was seen a highly significant ($p = .001$) increase in each of the 3 gluteal muscles individually. In specific, gmax increased by 11.15 ± 1.91% (134.19 ± 31.58 cm^3; 4.54 oz), gmed by 10.21 ± 2.53% (47.35 ± 14.21 cm^3; 1.60 oz), and gmin by 9.92 ± 2.27% (16.44 ± 4.94 cm^3; 0.56 oz). The detailed data are shown in Table 1.

Three months after treatment, the gluteal muscles showed a further significant increase of 21.96% (+43.47 cm^3; 1.47 oz; $p = .001$) on average when compared with 1 month. The most noticeable improvement was observed in gmed and gmin, and the muscle growth was evident in each evaluated subject. The gmax increased on average by an additional 25.52 cm^3, gmed by 13.41 cm^3, and gmin by 4.54 cm^3 (Table 1). Compared with the baseline, the overall increment of muscle mass was equal to 13.23 ± 0.91% (241.45 ± 28.78 cm^3; 8.16 oz). Individually, the gmax improved by 13.33 ± 1.50% (159.71 ± 25.43 cm^3; 5.40 oz), gmed by 13.20 ± 1.62% (60.76 ± 9.93 cm^3; 2.05 oz), and gmin by 12.67 ± 1.45% (20.98 ± 4.03 cm^3; 0.71 oz).

An example of the comparison of 3D volumes is shown in Figure 3. Reconstructed baseline and follow-up volumes were positioned at the same coordinates to visualize its intersections. All displayed muscles are visibly thicker at the follow-up (red = muscle enlargement) in comparison with baseline (blue). The gmax showed the most noticeable enlargement (+13.02%), although gmed (+14.34%) or gmin

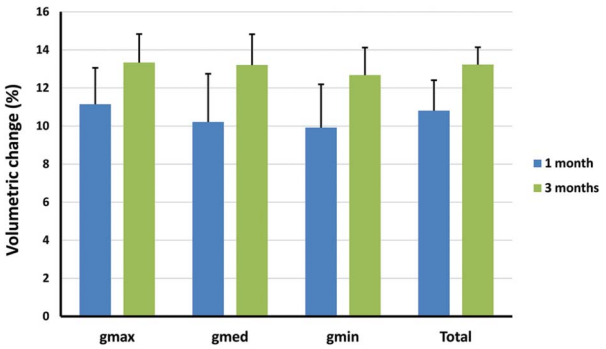

Figure 2. Volume enhancement at the 1-month and 3-month follow-ups (mean ± SD). gmax, gluteus maximus; gmed, gluteus medius; gmin, gluteus minimus.

TABLE 1. Results of the Volumetric Evaluation (Mean ± SD)

Muscle	*Baseline*	*1 mo*	*3 mo*
Muscle Volume (cm^3), $n = 7$			
gmax	1,197.26 ± 130.98	1,331.45 ± 155.49	1,356.97 ± 150.14
gmed	459.67 ± 46.38	507.02 ± 56.40	520.44 ± 53.68
gmin	165.56 ± 24.14	181.99 ± 28.22	186.53 ± 28.42
Total	1822.49 ± 133.48	2020.47 ± 168.00	2063.94 ± 158.61

gmax, gluteus maximus; gmed, gluteus medius; gmin, gluteus minimus.

(+14.45%) demonstrated relatively greater improvement against the baseline.

Standardized digital photographs showed improvement in aesthetic appearance (lifted and firmer buttock), which coincided with the muscle enlargement observed in MRI scans. Horizontal fragmentation (slice-by-slice evaluation) of the muscle changes revealed a more profound hypertrophic effect in the upper buttock region. As shown in Figure 4, the enlargement of gluteal muscles peaked approximately between the slices 23 to 36, which correspond to the anatomical area at the level of/above the femoral head. This translated into a visible buttock lifting, also captured by patient photography (Figure 5).

Magnetic resonance imaging scans did not reveal any visible changes in other underlying tissue structures, including gluteal fat layer. For instance, as can be seen in Figure 6, the fat deposits remained unaffected while the gluteal muscles are visibly thickened. To be more specific, the linear measurements of adipose tissue taken at 5 specified locations depicted in the figure showed a clinically insignificant reduction of 1.45%.

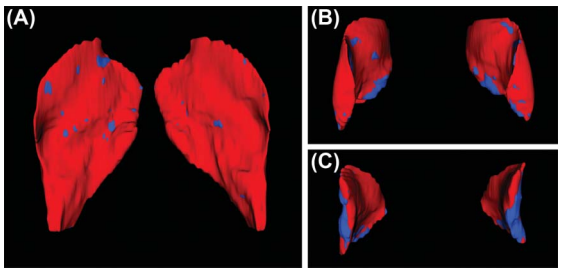

Figure 3. Comparison of reconstructed 3D volumes (gmax (A), gmed (B), and gmin (C)). Baseline volumes are highlighted in blue and 1-month follow-up volumes in red (an increase in volume). The average improvement is equal to 13.37%, front view.

Immediately after the last treatment, the patients reported a high level of satisfaction with achieved results, which further improved with time. At 3-month follow-up, all subjects agreed or strongly agreed that the aesthetic appearance of their buttocks improved, achieving a high score range of 4.6 to 4.9 on the 5-point Likert scale. The treatments were well tolerated (average score of 3.9) as 5 of the 7 patients found the treatments comfortable.

Discussion

Nonsurgical options for body rejuvenation are of increased value and interest when considering public awareness and risks associated with surgical options. By using the MRI examination, this study documented a significant change in the volume of gluteal muscles induced by a noninvasive HIFEM procedure. The volume enhancement showed to be uniform across the investigated muscles (Figure 2), and results were found to be continuously improving. The consistency of results among subjects may be attributed to the body constitution of participants because they were of similar BMI.

Muscle growth after the series of HIFEM treatments was previously documented by Kent and Jacob[5] and Kinney and Lozanova,[4] who reported increased thickness of rectus abdominis, reduction of abdominal separation, and a decrease of adipose tissue thickness. The muscle mass increase observed in this article corresponds with aforementioned

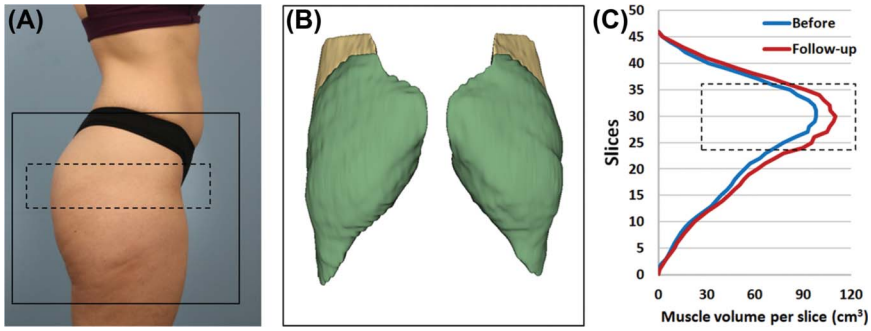

Figure 4. Horizontal fragmentation of overall muscle volume enhancement slice-by-slice at the 3-month follow-up (average improvement of 14.15%). The 3D volumes (B) are assigned to the standardized patient photography (A, side view). The more profound hypertrophic effect was observed in the upper buttock region (C, highlighted with a dotted line).

findings; however, the clinically significant reduction of fat thickness was not detected in this study (Figure 6). This may be attributed to the differences between the metabolism of adipose tissue in the buttock and abdominal region. It was documented that adipose tissue in the buttocks is metabolically less active and shows a significantly lower lipolytic rate.[15,16] Nevertheless, future studies should verify if any changes occur in the gluteal adipose tissue at the cellular level in response to HIFEM treatment, as was performed for abdomen.[17]

Until now, the application of HIFEM on the buttocks was studied only by subjective methods (quantification of visual appearance and patient satisfaction). According to the previously published multicenter study,[8] as much as 80% of patients reported that they felt more lifted and toned in the buttock region, and 71% of them were satisfied with the results immediately after the last treatment. Because of the simultaneous evaluation of MRI scans and standardized photographs presented in this article, one can infer that a noninvasive buttock-lifting effect is primarily associated with increment of muscle mass that peaked in the upper buttock region. Although Jacob and colleagues[8] noticed that patients with a lower BMI achieved a higher degree of visual improvement, sample size in this study was not large enough to reliably determine the correlation between BMI and the level of muscle volume enhancement.

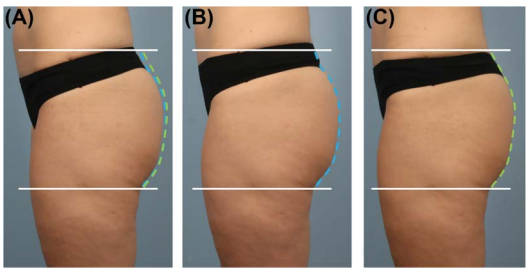

Figure 5. The baseline (A), 1-month (B), and 3-month follow-up (C) photographs. The dotted lines indicate a change in the buttock contour (improvement in muscle mass of 9.80% at 1 month and 12.67% at 3 months).

Gluteal enhancement is used to address aging changes of the muscle tissue or to improve gluteal contour and projection. Peak physical muscular capacity occurs in the second and third decade, and it then decreases with time,[18] a physiologic and predictable age-related muscular change referred to as sarcopenia.[19] Sarcopenia leads to a dramatic decrease in muscular mass and strength.[20] Also, the maintenance of lean mass has important consequences on slowing the increase in fat deposits and changes in body composition with age.[19,21] Fortunately, the age-related effects on skeletal muscle are mostly reversible[18] as seen after the strength training.[21] Nonetheless, noninvasive hypertrophic technologies could represent an alternative and possibly more efficient method of reversing muscle mass changes. In comparison to the voluntary exercise, HIFEM-induced supramaximal contractions forces muscles to contract selectively and under the greater load than possible voluntarily. This is beneficial for muscle hypertrophy response because it increases with tension of the contraction.[22]

Results of this study suggest that HIFEM-induced muscle fiber hypertrophy may represent advancement

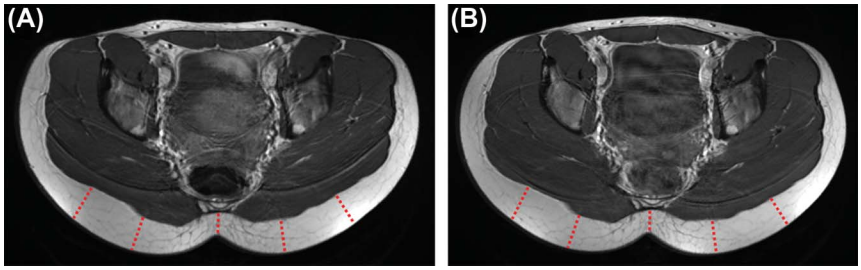

Figure 6. Baseline (A) and 3-month follow-up (B) MRIs of an HIFEM-treated patient. No structural changes in fat deposits were observed. The thickness of the subcutaneous layer was not significantly affected by the treatments (see the equally sized dotted red lines). The enlargement of gluteal muscles at the 3-month follow-up is visible. HIFEM, high-intensity focused electromagnetic; MRI, magnetic resonance imaging.

in the treatment of gluteal ptosis and volume loss. An average muscle volume increased by 197.98 cm^3 after 1 month and by 241.45 cm^3 at 3 months (Table 1). This amount is roughly equivalent to 8.2 ounces and is comparable but slightly lower than average volumes of injected fat during micro fat grafting procedures.[23] The greatest advantage of HIFEM therapy is that it achieves noninvasive buttock augmentation by using physiologic stimulation of the targeted muscle with no downtime. More importantly, HIFEM caused no adverse events during or after the treatment. It eliminates the risk of long-term postoperative adverse sequelae, such as muscle atrophy,[24] silicone implant migration,[25] or pulmonary fat embolism.[26]

One possible limitation of this study is relying on manual assessment of MRI slices. Slice-by-slice segmentation is limited because it is a time-consuming process. It is preferably used in specific case scenarios or as a reference for some easy method of evaluation.[10,27] To shorten processing time, it can be simplified by reducing the number of segmented slices or by use of automatic methods. However, reducing the number of slices may lead to a higher level of error in volume estimation and reconstructed muscle may also lose its inherent shape and contour. On the other hand, automated methods encounter issues with separation of gluteal muscles, especially the gmed and gmin, where the border is far from clear.[11] Despite the possible disadvantages, manual segmentation still produces the best possible results.

The major limitation of this study is the sample size. In addition, the subject group consisted predominantly of low BMI and physically active women without excessive fat deposits in the treated area. It is unclear whether these findings would be similar in subjects with a higher BMI (<30 $kg \cdot m^2$) who may have a significant amount of gluteal fat. Furthermore, a detailed physiologic explanation for the stability of the gluteal fat layer may be subject to further research efforts.

Conclusion

HIFEM application to the buttocks is safe, comfortable, and effective as a means of increasing volumetric muscle mass of the gluteal muscles. Patient satisfaction was high, and no adverse events were observed. Magnetic resonance imaging analysis revealed simultaneous enhancement of all 3 gluteal muscles at 1 month and 3 months after the HIFEM procedure. The gluteal fat layer was not affected by the treatment. The overall muscle mass increase peaked in the upper gluteal area; this corresponds with digital photographic documentation of a visible lifting effect on the ptotic buttocks region. This study had documented the first objective evaluation of structural changes of gluteal muscle tissue induced by an HIFEM procedure, which may explain the aesthetic improvement previously reported by other authors.

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Ultrasound Assessment of Subcutaneous Abdominal Fat Thickness After Treatments With a High-Intensity Focused Electromagnetic Field Device: A Multicenter Study

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BACKGROUND High-intensity focused electromagnetic (HIFEM) technology is intended for muscle toning, firming, and strengthening.

OBJECTIVE The goal of this study is to quantify the effect of HIFEM treatments on subcutaneous fat.

MATERIALS AND METHODS A total of 33 patients participated in the study. Each subject underwent 4 treatments on the abdomen with the HIFEM device. Ultrasound images were obtained measuring the thickness of the subcutaneous fat from 4 standardized measurement points. Ultrasound images were taken before treatment and at 1-month and 3-month follow-up visits. Photographs were captured using both 2D and 3D cameras. Weight measurements were taken, as well as surveys assessing both patient comfort, satisfaction, and adverse events.

RESULTS A significant reduction in the subcutaneous fat thickness across the abdomen was observed, averaging 19.0%/4.47 ± 3.23 mm ($p < .01$) at 1 month after treatment and 23.3%/5.78 ± 4.07 mm 3 months after treatment. At 1 month, the most significant reduction in subcutaneous fat was measured subumbilically (26.6%/6.25 ± 4.70 mm; $p < .01$) and epiumbilically (21.6%/5.08 ± 3.69 mm; $p < .01$). No discomfort was reported, and 91% of study participants were satisfied with their result.

CONCLUSION Based on the ultrasonographic and photographic observations, the authors conclude that the application of an HIFEM field is an effective option for the noninvasive treatment of subcutaneous fat.

B. Katz is a medical advisor for BTL Industries, Inc.

As adult obesity rates have increased, so has the number of people considering fat-reducing procedures. In 2016, 58% of the US population considered a body-sculpting procedure.[1] There are various surgical[2] (e.g., abdominoplasty and liposuction) and noninvasive[3] options to consider that offer a permanent solution to fat reduction.

Such procedures may or may not necessarily lead to an overall increase in patient satisfaction. Many patients remain unsatisfied with their aesthetic appearance after abdominal fat removal due to bulging and/or flaccidity around their midsection, which, in most cases, result from weak abdominal muscles and/or diastasis recti. The removal of excess fat does not solve the problem of muscle flaccidity developed through increased intra-abdominal pressure and reduced muscular and aponeurotic tension.[4]

There have been surgical attempts to treat this condition with the submuscular application of alloplastic mesh,[4] but physical exercise before the procedure is

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normally recommended to prevent muscle laxity. In addition to physical exercise, both electrical[5,6] stimulation and low-level magnetic[7–9] stimulation have been used to try and assist muscle strengthening. It has been observed that a high-intensity magnetic stimulation penetrates deeper into the tissue without a risk of burns or nociceptive activation, which is often associated with electrical stimulation methods.

Recent studies suggest that a high-intensity focused electromagnetic (HIFEM) field based on focused magnetic stimulation can simultaneously induce muscle growth and reduce subcutaneous fat (Kent DE, presented at ASLMS, Dallas TX, April 2018; Kinney BM, presented at ASLMS, Dallas TX, April 2018) when applied to the abdomen. Although the effects of magnetic stimulation on muscle are well established and have been described in several studies,[7–10] its effects on fat tissue have not yet been thoroughly investigated.

This study investigates the effects of HIFEM technology treatment on subcutaneous fat using ultrasound imaging evaluation. Simultaneous muscle strengthening and the magnetic field's effect on fat could help avoid abdominal bulging and flaccidity, which most patients find aesthetically unsatisfactory.

Methods

The subject group was composed of 33 subjects (mean age 40.8 years and mean body mass index [BMI] 24.5 kg/m^2). For the study, the following inclusion criteria were respected: BMI 20.0 to 30.0 kg/m^2, age 21 to 65 years, stable weight (maximum weight change 2.2 kg in the preceding month), and sufficient thickness of the abdominal fat layer (0.5–3 cm). The exclusion criteria included previous abdominal surgery or other aesthetic procedures in the abdominal area, use of medications known to affect weight levels, and any of the contraindications stated in the device manual. Patients were instructed to maintain their daily routines. Basic biometric data were also collected before the treatment.

Each subject received 4, 30-minute treatments using the HIFEM device (Emsculpt; BTL Industries, Inc., Boston, MA). The treatments were performed over a 2-week period, spaced by a minimum of 2 days between each session as outlined in the Institutional Review Board-approved protocol and as conforming to the ethical guidelines of the 1975 Declaration of Helsinki. The patients were placed in a supine position, and the treatment was administered on the abdomen.

For the study, a single applicator was used over the treatment area. The applicator itself consists of a focused circular coil that generates electromagnetic pulses with intensities reaching up to 1.8 Tesla. The magnetic field can penetrate to depths of 7 cm. The center of the applicator was centered directly over the umbilicus to stimulate the musculus rectus abdominalis. All clothing and jewelry were removed from the treated area. During the treatment, the intensity of the magnetic field was gradually increased until the patient's tolerance threshold was reached. Most patients were able to tolerate 100% intensity of the stimulator output by the end of the first 30-minute treatment. All the patients reached 100% intensity by the end of the second treatment and were able to tolerate this intensity during the remaining treatments. Abdominal muscle stimulation was closely monitored to ensure equal stimulation bilaterally. A fixation belt was used to secure the single applicator during all treatments.

Patients were evaluated at the baseline, 1 month, and 3 months after the final treatment.

The primary evaluation of the subcutaneous fat layer thickness was measured with a diagnostic ultrasound. The ultrasound devices GE Voluson E8 with linear probe SP10-16-D (General Electric; GE Healthcare, Chicago, IL) and Sonosite Micromax Turbo with linear probe HFL50x (Sonosite, Bothell, WA) were used for this study. An external template was used on all patients to ensure the consistency of the 4 different measurement points. The template measuring points were at a distance of 5 cm from the umbilicus: epiumbilical, subumbilical, lateral right, and lateral left (Figure 1). To avoid any fat compression errors, the ultrasound probe was placed above a given site without any pressure by using a thick layer of ultrasound gel between the probe and the skin. All ultrasound scans were evaluated by a board-certified radiologist.

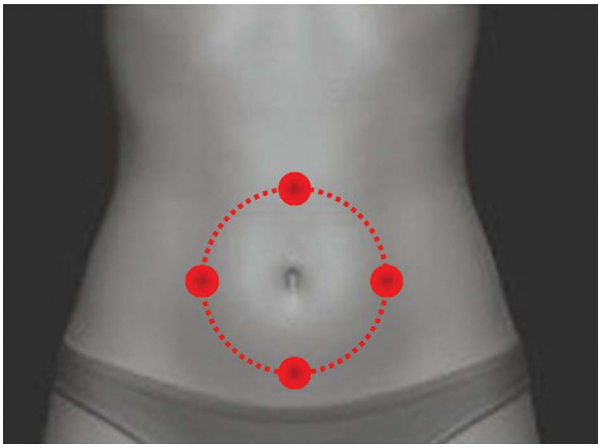

Figure 1. Visualization of ultrasound measurement points.

Standardized 2D and 3D digital photographs were taken to document any further changes in the appearance of the abdominal area. Patient satisfaction was assessed at the 1-month and 3-month follow-up evaluations with a standardized 5-point Likert scale questionnaire. A visual analog scale (0—no discomfort and 10—unbearable discomfort) was also used to evaluate the patient's comfort during treatments.

Patients were monitored and encouraged to report any adverse events related to the treatment.

The significance of the obtained data/results was verified by paired *t*-tests. The significant level α was set to 5%.

Results

All patients completed the study protocol and underwent evaluation during the 1-month follow-up visits. In total, 21 of 33 patients attended the 3-month follow-up visits. During the 1- and 3-month follow-up evaluations, the data showed a significant reduction in the subcutaneous fat thickness of the treated area. Weight change for all patients was insignificant. The digital photographs showed aesthetic improvement in the abdominal area, which correlated with relatively high patient satisfaction.

Ultrasound Measurements

When compared with the baseline, a statistically significant reduction in subcutaneous fat was observed in each of the 4 measurement points at 1 month and at 3 month after treatment (all $p < .01$). At 1 month, the most significant reduction was observed in the epiumbilical and subumbilical regions (21.6% and 26.6%, respectively), with a lower reduction observed in the lateral regions (12.9% and 14.8%). The total average reduction across all patients and all measurements totaled 19.0% (4.47 ± 3.23 mm; $p < .01$). An average reduction exceeding 10% was observed in 25 of 33 patients (76%). See Figure 2 for a histogram of the changes.

During 3-month evaluations, the fat thickness measurement of the 21 evaluated patients was further reduced (Table 1), ranging from 18.2% (left lateral point) to 30.8% (subumbilical point). The total average reduction across the whole abdomen was 23.3% (5.78 ± 4.07 mm; $p < .01$). Changes observed in individual patients were rather consistent, as the average abdominal fat thickness decreased in each of the treated patients at both follow-up visits. None of the patients had an increase in the average fat thickness.

All presented data were compared with the baseline (Table 1).

Digital Photographs

The evaluation of digital photographs showed a volumetric reduction and visual aesthetic improvement, which correlated with the changes documented by the ultrasound measurement. See Figure 3 for an example of 2D and 3D photographs and corresponding ultrasound images.

Patient Comfort and Satisfaction

Patient satisfaction questionnaires showed relatively high patient satisfaction with the results of the therapy at 1 month after treatment. In total, 30 of 33 subjects (91%) reported they were satisfied or strongly satisfied with the results ($\geq$4 on the Likert scale), 2 patients (6%) were unsure about their satisfaction, and 1 patient (3%) expressed dissatisfaction. See Table 2. The visual analog scale showed that the patients found the treatments highly comfortable, with the average score across all patients totaling 1.05 (little to no discomfort). As a general observation, besides mild

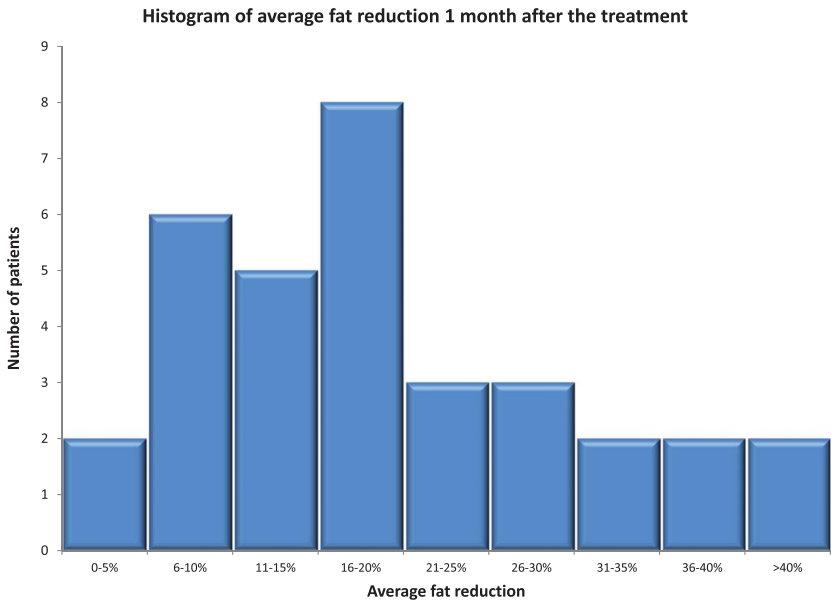

Figure 2. The distribution of the average fat reduction calculated from the 4 measurement points obtained during the 1-month follow-up.

muscle fatigue and soreness on the day after the treatment, no adverse events were recorded or observed during the treatments or during the 3 months of follow-up.

Discussion

The effects of HIFEM treatments on subcutaneous tissue were recently investigated by Weiss and colleagues, who studied the apoptotic and biochemical processes associated with intense magnetic stimulation in a porcine model (Weiss R, presented at ASLMS, Dallas TX, April 2018). In the histology evaluation, they observed a statistically significant increase of 91.7% in the number of apoptotic nuclei in fat tissue after a single HIFEM treatment. This observation was coupled with an increased presence of RNA proapoptotic markers as a response to the treatment.

The data presented herein show a substantial reduction in subcutaneous fat in comparison with the baseline. The ultrasonography revealed that 1 month after 4 treatments, every single patient showed a reduction in the fat layer (average 19.0%), and this reduction was retained at the 3-month evaluation (average 23.3%). These results strongly correlate with other recent research that used the HIFEM technology: Kent and colleagues (Kent DE, presented at ASLMS, Dallas TX, April 2018) found an average

TABLE 1. Changes in Fat Layer Thickness Measured by Ultrasound (Average ± SD)

		1-Month Data		*3-Month Data**		
Measurement	*Baseline Fat Thickness (mm)*	*Reduction in mm*	*Reduction in %*	*Reduction in mm*	*Reduction in %*	*Significance*
Epiumbilical	23.72 ± 8.9	5.08 ± 3.69	21.6	5.47 ± 3.18	22.2	$p < .001$
Subumbilical	22.96 ± 9.9	6.25 ± 4.70	26.6	7.54 ± 4.89	30.8	$p < .001$
Left lateral	17.75 ± 10.1	3.17 ± 4.57	12.9	4.93 ± 5.32	18.2	$p < .001$
Right lateral	17.77 ± 10.0	3.38 ± 4.53	14.8	5.19 ± 5.92	21.9	$p < .001$
Average	20.55 ± 10.01	4.47 ± 3.23	19.0	5.78 ± 4.07	23.3	$p < .001$

*3-month calculations are based on data from 21 subjects.

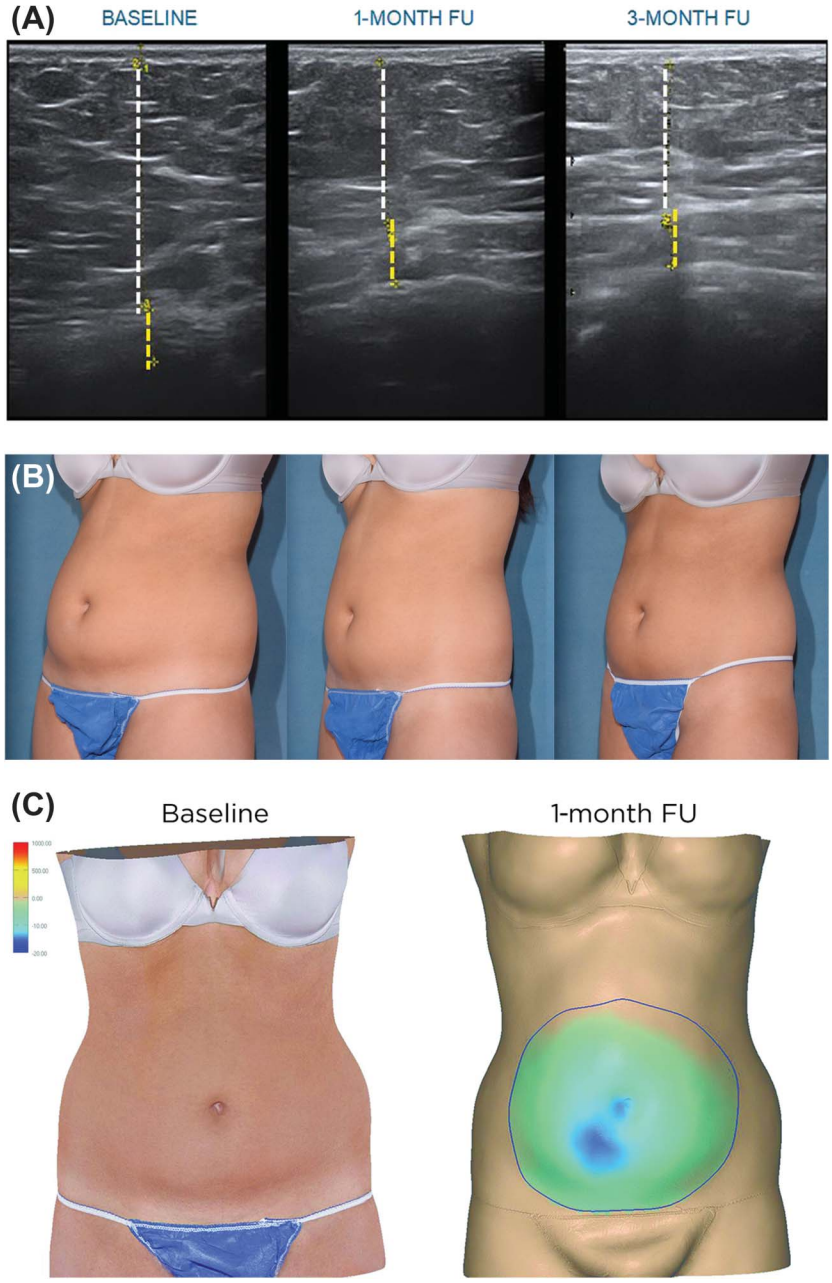

Figure 3. Example of results (Patient ID3, 24 years old). (A) Ultrasound images showing the subumbilical fat layer thickness. The white lines mark the fat layer, and the yellow lines represent the muscle layer. The fat layer thickness reduced by 10 mm (32%) from 31 mm at baseline to 21 mm at the 1-month follow-up and to 20 mm at the 3-month follow-up. (B) 2D photographs captured at baseline (left), 1 month (center), and 3 months (right) after treatments. (C) 3D images obtained at the baseline and at 1-month follow-up. The volumetric changes in the abdominal area are shown on the right image. Courtesy of Bruce Katz, MD. FU, follow-up.

reduction of 19.2% in fat thickness 1 month post-HIFEM treatments when using computed tomography (CT) evaluation, and Kinney and colleagues (Kinney BM, presented at ASLMS, Dallas TX, April 2018) also reported an average reduction of 18.6% in abdominal fat at 2 months after four HIFEM treatments evaluated by magnetic resonance imaging (MRI). Similar results from different clinical trials and evaluation methodologies suggest that the treatments can cause a consistent and repeatable localized reaction in adipose tissue. The difference between 1-month data (19.0%) and 3-month data (23.3%) was not

TABLE 2. Patient Satisfaction Data

Level of Satisfaction	*No. of Patients* N *(%)*
Strongly satisfied	7 (21%)
Satisfied	23 (70%)
Neither satisfied nor dissatisfied	2 (6%)
Dissatisfied	1 (3%)
Strongly dissatisfied	0 (0%)
Average	4.09

statistically significant ($p > .05$); however, the tendency suggests a continuation of fat reduction. This phenomenon could be attributed to the lingering effects of the apoptotic process, since fat cells can continue to flush out for up to 4 months.[11] An additional possible mechanism could be explained by an increase in the basal metabolism, due to the increase in the abdominal muscle mass/tissue, which was found to have occurred in the MRI and CT studies by Kinney and colleagues and Kent and colleagues Finally, this tendency could also be explained by the patients' enhanced motivation to maintain a healthier lifestyle, including maintaining dietary and workout routines after seeing significant post-treatment improvements.

The observed changes in the fat tissue are comparable with thermal-based technologies, which routinely report reductions ranging between 20% and 29%.[12–16] Yet, contrary to heating or cooling devices that externally affect the cellular membrane of a fat cell to cause an apoptotic effect, HIFEM works from within, on the muscle, causing supramaximal contractions, which affects fat internally through an extreme hypermetabolic reaction. This rather natural process of affecting fat can potentially explain the absence of nonresponding patients in the authors' study; yet, such a hypothesis will require further investigation.

The reduction of the fat layer measured by ultrasonography was also coupled with changes observed in abdominal body contours by 2D/3D photographs. Patients were treated with a single-applicator prototype, which did not cover the entire abdomen, particularly in larger patients. This may help to further explain the more significant reduction observed in the central abdomen (epiumbilically and subumbilically) compared with the lateral measurements. Future research is expected to further explore this technology using dual-applicator protocols.

Conclusion

Based on ultrasonographic observations, the authors conclude that the application of an HIFEM field is a unique, safe, and effective alternative for the noninvasive reduction of subcutaneous fat thickness. This study confirms and conforms to other recent HIFEM research observations; however, to assess the full clinical potential of this technology, further research is required.

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HISTOLOGICAL IN VIVO STUDY: THE MECHANISM OF ACTION

INDUCTION OF FAT APOPTOSIS BY A NON-THERMAL DEVICE: MECHANISM OF ACTION OF NON-INVASIVE HIGH-INTENSITY ELECTROMAGNETIC TECHNOLOGY IN A PORCINE MODEL

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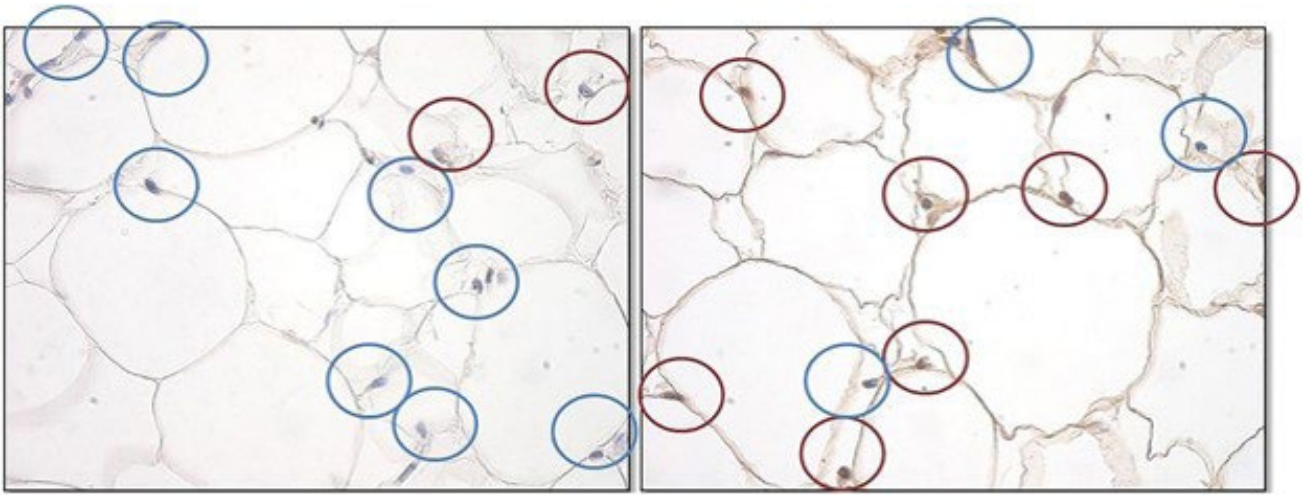
HIGHLIGHTS

- **92 % increase in average apoptotic levels** in fat cells from 18.75 % at baseline to 35.95 % 8 hours post 1 treatment (levels in the control subject remained stable).
- The results show link between **fat cells apoptosis** and elevated levels of free fatty acids released during **supramaximal muscle contractions** induced by the treatment.
- Blood analysis confirmed a rapid metabolic reaction after the treatment as supporting evidence of changes in the subcutaneous fat tissue. **No safety risks were identified**.

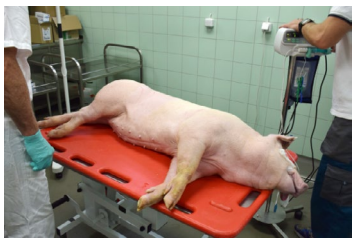


Histological examination of apoptosis in pig fat tissue (TUNEL method). Apoptotic nuclei are marked brown, while the intact nuclei are marked blue. There was an increase in the number of apoptotic nuclei after the treatment.

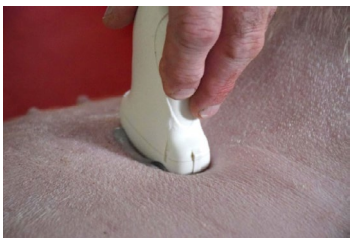
STUDY DESIGN

- Evaluation of changes in the levels of **programmed cell death of adipocytes** in a porcine model in vivo **following a single** EMSCULPT® **treatment**.

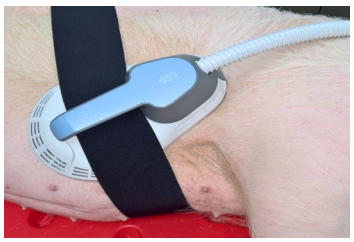
- Two Yorkshire pigs were treated for 30 minutes. One pig was recruited as a control subject.



Animal care was in compliance with the convention for the protection of vertebrate animals used for experimental and other scientific purposes.



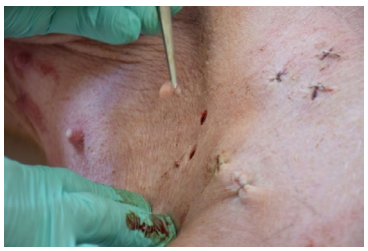
The fat thickness was checked before the experiment using the linear probe of a diagnostic ultrasound device (Mindray M5Vet).



The abdomen was treated for 30 minutes using the EMSCULPT applicator secured by a fixation belt.

- **Punch biopsy** specimens of fat tissue together with **blood samples** were taken before the treatment, after 1 hour and 8 hours post-treatment.

- **TUNEL assay** was applied on **histological samples** and the blood samples were tested for biochemical and hematological parameters.



An image of a biopsy sample being taken 8 hours post-treatment.

RESULTS

- The apoptotic index was calculated from **120 histological samples**. Data were statistically analyzed using rANOVA.

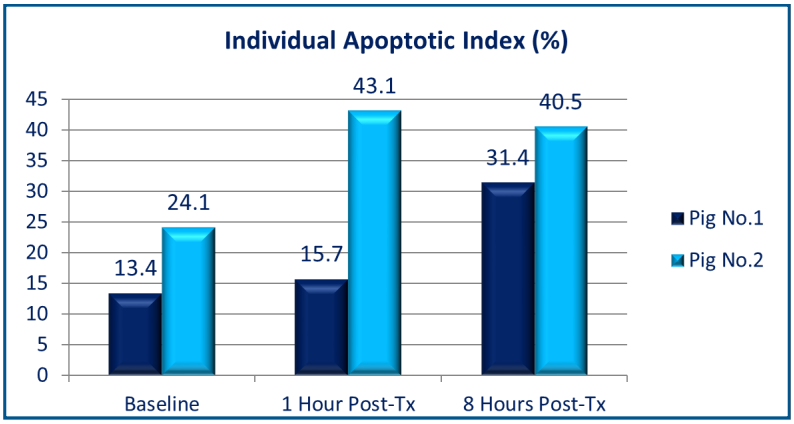


Figure 1: Average apoptotic index (%) evaluated in each pig individually.

MECHANISM OF ACTION: EFFECT OF HIFEM® ON FAT

MECHANISM OF NONTHERMAL INDUCTION OF APOPTOSIS BY HIGH-INTENSITY FOCUSED ELECTROMAGNETIC PROCEDURE: BIOCHEMICAL INVESTIGATION IN A PORCINE MODEL

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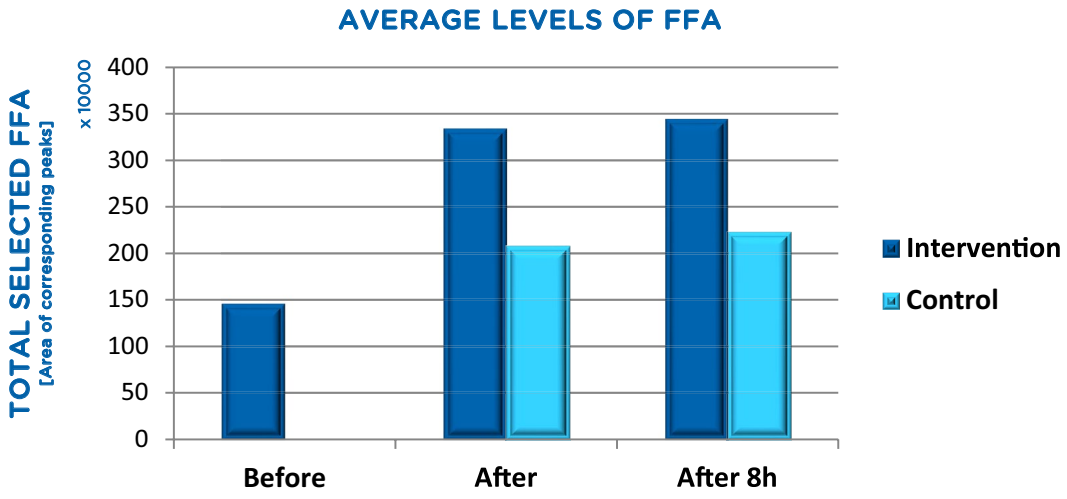
HIGHLIGHTS

- **The levels of FFA** (free fatty acids) in the treated area **increased by 127.1%** immediately post-treatment and **by 134.1%** 8h post-treatment. High levels of FFA indicate **strong metabolic response** in the fat tissue.
- The levels of four out of five analyzed DNA **pro-apoptotic markers increased significantly** after application, providing evidence of **enhanced apoptosis in the subcutaneous adipose tissue**.
- The average fat **pH decreased from 7.30±0.12 to 6.60±0.07** immediately post-treatment and to **7.11 ± 0.11** 8h post-treatment.

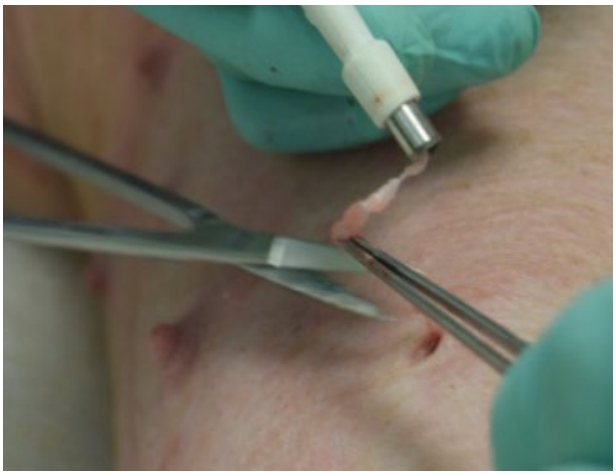


Results of total FFA amount in specimens (mean ± SD) at baseline, immediately after treatment (after Tx), and 8 h after treatment (after 8 h). Values correspond to the overall area under the peaks obtained by mass spectrometry

STUDY DESIGN

- The aim was to investigate the mechanism of apoptosis induced through saturation of FFA in the fat cells.
- Two Large White pigs received a **single 30-minute** long treatment of thigh.
- **Punch biopsies** were collected **before, immediately after and 8 hours after treatment**. Control samples were obtained from the abdomen at the baseline and 8 hours post-treatment.

Measurements of pH were performed immediately after the punch biopsy directly in the fat tissue.



Collection of control punch biopsies of the fat tissue from the abdomen. The bioptate was pulled out by tweezers.

CONCLUSIONS

- **Levels of pro-apoptotic markers** in histological samples were **increased post-treatment**, indicating enhanced **apoptosis** in the tissue.
- **FFA concentrations increased and pH decreased significantly post-treatment**, suggesting that HIFEM induces a strong metabolic response in the fat tissue which leads to **the breakdown of fat**. High levels of FFA may saturate the fat cell and trigger fat cell apoptosis.
- Results of this study **correlate with previous research** reporting elevated apoptotic levels post HIFEM treatments as well as with fat reduction observed in human studies.
- **The results support the proposed MOA** stating that HIFEM contractions evoke a strong metabolic reaction and trigger cascade effect leading to FFA saturation, the stress of endoplasmic reticulum and fat cell apoptosis.

EMSCULPT® MECHANISM OF ACTION GLOSSARY AND COMMONLY USED TERMS

Adenosine triphosphate (ATP): Considered the "energy currency", it is the molecule that stores energy we need.

Adipocyte: Also known as a lipocyte or fat cell. These cells specialize in storing energy as fat.

Anabolic: "Think Anabolic Steroids". It is a building/growth phase. This growth state requires energy from the catabolic reaction.

Apoptosis: The death of cells which occur as a normal and controlled part of an organism's growth or development. Also called programmed cell death.

Apoptotic: Adjective of apoptosis, please see above.

Brown Adipose Tissue (BAT): Unlike white fat cells, these cells have a considerably thicker cytoplasm (outer shell), with lipid droplets scattered throughout. The nucleus is round and has a large quantity of mitochondria, giving it its color. Brown fat, is also known as "baby fat", and it is used to generate heat. As an example, animals that hibernate have larger quantities of brown fat.

Catabolic: "Think Catastrophe". It is a breaking down into smaller units, breakdown of molecules to gain energy.

Cellular Dysfunction: An inflammatory condition. Impaired energy production (related to mitochondrial inhibition, damage and reduced protein turnover) appears to be the core mechanism underlying the development of cell and organ dysfunction.

Creatine Phosphate and Glycogen: A secondary fuel source to fuel the muscles.

Depolarization of neurons: Depolarization is a change within the neuron, during which the cell undergoes a shift in electric charge. It works as a communication tool among cells. Due to depolarization, the nerve signals to the muscle that it should contract.

Diastasis Recti: (also known as abdominal separation) is commonly defined as the gap of roughly 2.7 cm or greater between the two sides of the rectus abdominis muscle.

Free Fatty Acids (FFA) and Glycerol: These released molecules usually act as an energy source for the needed muscle activity and body metabolism.

Gauss: (G) is the (small) unit of measure of magnetic flux density (or magnetic induction). Named after Carl Friedrich Gauss.

HIFEM: High-Intensity Focused Electro-Magnetic.

Hormones that help induce lipolysis: Glucagon, epinephrine, norepinephrine, growth hormone, atrial

natriuretic peptide, brain natriuretic peptide, and cortisol.

Lipid: Fat-like substance that is insoluble in water. Cholesterol and triglycerides are lipids.

Lipolysis: is the breakdown of lipids and involves the hydrolysis of triglycerides into free fatty acids and glycerol. Lipolysis is used to mobilize stored energy during fasting and exercising.
Maximal Voluntary Contraction (MVC): Under normal conditions, the highest amount of tension that could be developed and held physiologically is called maximal voluntary contraction (MVC).

Muscle hyperplasia: Hyperplasia means an increase in cell number. Muscle Hyperplasia is thus creation of new protein strands and muscle fibers.

Muscle hypertrophy: Hypertrophy means an increase in cell size. Muscle Hypertrophy is thus growth of existing myofibrils.

Myocytes: Tubular cells known in striated muscles, these cells in turn contain many chains of myofibrils.

Myofibril: The basic rod-like unit of a muscle cell.

Neuron: A nerve cell. It is an electrically excitable cell that receives, processes, and transmits information through electrical signals.

Paracrine substances: Paracrine signaling is a form of "cell to cell" communication in which a cell produces a signal to induce changes in nearby cells, altering behavior of those cells. Paracrine factors diffuse over a relatively short distance (local action), as opposed to endocrine factors (hormones) which travel considerably longer distances via the circulatory system.

Skeletal Muscle: Called striated muscle because of the light and dark striped fibers. These muscles are voluntary, meaning you control them. The sarcolemma is the cell membrane of the muscle fibers. The sarcolemma acts as a conductor for electrochemical signals that stimulate muscle cells.

Smooth Muscle: Sometimes called visceral or involuntary muscles. They are controlled by the involuntary part of the brain and usually in the form of sheets or layers. They form the walls of veins and arteries, line your stomach and digestive system. The bladder is made up of smooth muscles and these relax when it's time for you to pee.

Supramaximal Contractions: Contractions with a tension higher than MVC are defined as supramaximal.

Supramaximal Lipolysis: A part of an extreme catabolic reaction, which brings about a dramatic release of FFA. When the amount of released FFA exceeds normal levels, they start accumulating intracellularly in surrounding adipocytes.

Tesla: (T) is the standard (large) unit of measure for magnetic flux density (or magnetic induction). Named after Nikola Tesla. Note: 1 Tesla is equal to 10,000 Gauss ($1\ T = 10^4\ G$).

Triglycerides: The most common form of fat in the body. In a catabolic state, triglycerides break down into Free Fatty Acids and Glycerol.

White Adipose Tissue (WAT): White fat cells contain large lipid droplet surrounded by a thin layer of cytoplasm and a flat nucleus. The fat is stored in a semi-liquid state and primarily composted of Free fatty acids and cholesteryl ester. An average human has 30 billion fat cells.

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AN INITIAL STUDY INVESTIGATED THE **EFFECTS ON BUTTOCKS**

HIGH-INTENSITY FOCUSED ELECTROMAGNETIC (HIFEM) FIELD THERAPY USED FOR NONINVASIVE BUTTOCK AUGMENTATION AND LIFTING: FEASIBILITY STUDY

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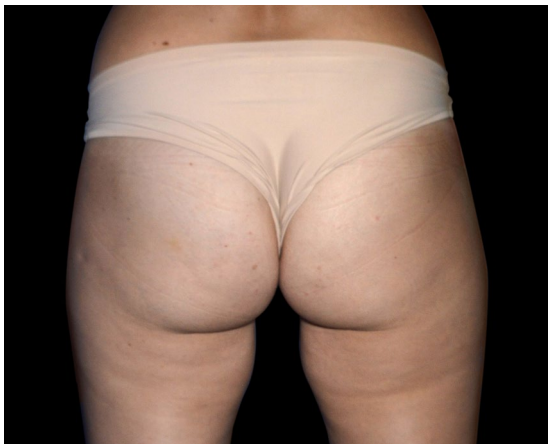
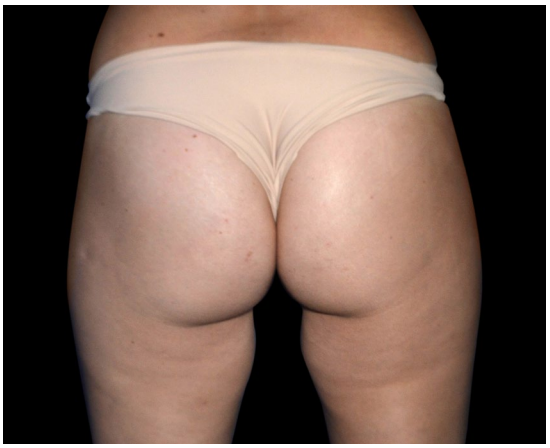
HIGHLIGHTS

- **21 women** received **4 bilateral treatments on** their **buttocks**.
- The treatments caused **significant changes** to gluteus muscles which translated into **overall aesthetic improvement**.
- Digital photographs showed **overall buttock lifting** and **reduction in muscle laxity**.
- **High levels of satisfaction** with treatment results **(7.3/10)**.
- The **results triggered a** following **large-scale multicentric study** to bring further evidence.



BEFORE



AFTER

DESIGN AND METHODOLOGY

- Evaluation at baseline, after last treatment, 1-month post, and 3-month post:
  - Weight measurement, standardized digital photography.
  - Patient comfort and satisfaction with results.

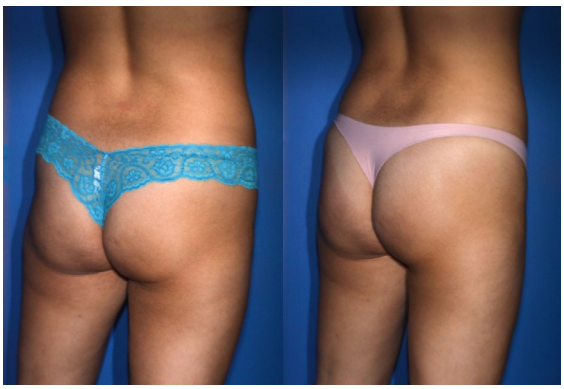
RESULTS

Satisfaction with results (0-10)	After treatment	1 month follow-up	3 month follow-up
Average (n=21)	7.2±1.8	7.4±1.8	7.8±2.0

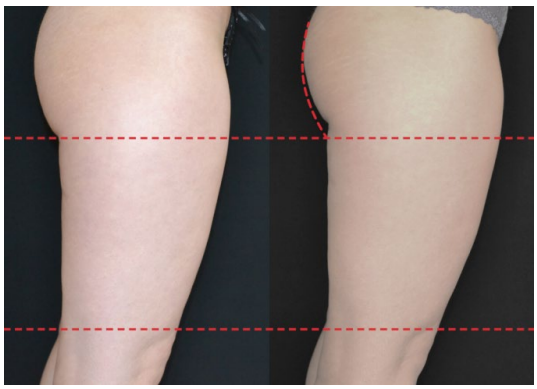
Chronologic evaluation of patient satisfaction with the treatment results using a VAS scale (10 = Complete satisfaction, 0 = Complete dissatisfaction). Average satisfaction was high and increased over time.

Treatment comfort (0-10)	1st session	4th session
Average (n=21)	7.0±2.3	8.3±1.9

VAS scale patient comfort during the treatment (10 = Complete comfort, 0 = complete discomfort).



BEFORE AFTER



BEFORE AFTER

Digital images of two patients showing overall lifting of their buttock coupled with elevation of the gluteal fold and a tighter and more sporty look after HIFEM® treatment (4x30min).

Research Article

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High-Intensity Focused Electromagnetic (HIFEM) Field Therapy Used for Non-Invasive Buttock Augmentation and Lifting: Feasibility Study

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[2]Aesthe Clinic Beauty, Sofia, BG

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Abstract

Although latest trends indicate increasing demand for aesthetic improvement of buttocks, there is currently no alternative to injectable or surgical buttock augmentation. We aimed to investigate the feasibility of the High-Intensity Focused Electromagnetic field (HIFEM) therapy for buttock shaping. 21 women received 4 HIFEM sessions (lasting 30 minutes) focused on gluteal muscles. Subjects were evaluated at baseline, after the last treatment, and at 1-month/3-month follow-ups. The evaluation comprised weight measurement, level of treatment comfort and satisfaction (Visual Analogue Scale, 0-10 range) questionnaire. Visual improvement in digital photographs was assessed by three independent evaluators using the Global Aesthetic Improvement Scale (GAIS). The average satisfaction score after the last treatment was 7.2 ± 1.84 and increased at 1-month (7.4 ± 1.79) and 3-month (7.8 ± 1.95) follow-ups. The comfort level after the last treatment was 8.3±1.9. Weight change was insignificant. None of the subjects reported discomfort. GAIS score for the after photos was 1.56 ± 0.68 and was maintained at 1-month (1.51 ± 0.65) and 3-month (1.53 ± 0.66) follow-up. Digital photographs showed aesthetic improvement in most patients through improved shape and volume of the treated area, overall buttock lifting and reduction in muscle laxity. We suggest the device is suitable for non-invasive buttock augmentation as an alternative to surgical procedures.

Keywords: Field therapy; Buttock augmentation; Gluteal muscles

Introduction

High-Intensity Focused Electromagnetic (HIFEM) field technology utilizes the principles of magnetic stimulation. It is based on application of rapidly changing magnetic fields that generate electrical currents in the underlying tissue where it depolarizes motor neurons and causes muscle contractions [1]. If the frequency of the stimulation is higher than the time needed for the muscle relaxation, the muscle is forced into tetanic contraction which is a highly stressful condition triggering changes in the muscles as an adapting response to these conditions [2]. Published studies showed its' efficacy in increasing the muscle mass [3,4] accompanied with apoptosis [5] and consequent fat reduction [3-7]. However, all conducted studies applied the treatment on the abdomen, and the effects on other body parts have not yet been documented.

As the HIFEM technology directly stimulates muscles, it could very well be used for toning and strengthening of muscular body parts such as buttocks. By volume, gluteus maximus is one of the largest muscles in the human body, and its' stimulation could provide beneficial results for the patient. The number of buttock shaping procedures is increasing every year as people desire to augment and tone their buttocks [8]. Currently, the most popular procedures such as fat grafting, silicone implant or traditional butt lift are, however, invasive and carry a high risk of complications [8].

HIFEM technology, on the other hand, could be potentially used for noninvasive toning of buttocks as a safe alternative to current buttock shaping procedures. We hypothesize that use of the HIFEM technology on the gluteal muscles may induce hypertrophy of these muscles, as it has been seen on the muscles of the abdomen, and as such it could lead to aesthetic improvement of the buttocks by lifting the gluteal fold and firming the structure of gluteal muscles. The goal of this study is to perform an initial investigation of the feasibility, safety, and efficacy of buttock treatments by a device utilizing the HIFEM technology (EMSCULPT, BTL Industries, Boston, MA).

Methods

The subject group was composed of 21 females, with a mean age of 32.5 ± 7.5 and mean BMI of 22.0 ± 2.6. Subjects with metallic implants and any other contraindicated conditions were excluded from the study.

The treatment protocol was composed of four sessions administered during two consecutive weeks with a minimum of two-day rest between two sessions. Emsculpt device (BTL Industries, Boston MA) was used for the treatments. Subjects were lying down on their abdomen and a coil applicator

inducing magnetic fields was placed over the buttock to stimulate the left and right gluteus maximus muscles. Positioning the applicator above the inferior gluteal nerve was crucial for homogenous stimulation, the intensity was therefore initially set to 15% of the device output, and the position of the applicator was adjusted for inducing contractions of the entire gluteal area. Once the proper position of the applicator was found, the intensity was increased up to the patients' tolerance threshold and was further adjusted throughout the treatment based on the patient's feedback.

The treatment time of each side of the buttock was 30 minutes.Weight measurements and digital photographs were taken immediately after the last treatment, during 1-month follow-up and 3-month follow-up. In addition, subjects were asked to fill patient satisfaction and comfort questionnaires. Clinical efficacy was evaluated using the Global Aesthetic Improvement Scale (GAIS). It is a photograph-based instrument for grading the overall improvement by comparing the after intervention photographs to the baseline photographs (**Table 1**).

Table 1: The Global Aesthetic Improvement Scale.

Score	Rating	Description
3	Very much improved	An excellent corrective result
2	Much improved	Marked improvement of the appearance
1	Improved	Improvement in the appearance, better compared with the original condition
0	No change	The appearance substantially remains the same compared with the original condition
-1	Worse	The appearance has worsened compared with the baseline condition

Three independent evaluators were presented pairs of "before–after", "before-follow - up" photographs which they visually examined and graded according to the GAIS.

A visual analog scale (VAS) with a score ranging from 0 to 10 (0=absolutely dissatisfied, 10=absolutely satisfied) was used to assess the patient satisfaction with the treatments after the last treatment, and during one-month and three-month follow-ups. Patients' comfort with the treatments was assessed after the last treatment using VAS questionnaire with a score range 0-10, where 0 stands for unbearable discomfort and 10 for no discomfort. During each treatment and follow up visit patients were monitored for any side effects and adverse events.

Ethics

All subjects received oral instructions and information after which they signed informed consent.

Statistics

Fluctuation of the subject's weight was statistically analyzed using the paired t-test with significance level set as 5%.

Results

All recruited subjects completed the 4 treatments with a device utilizing HIFEM technology, after treatment follow-up visits and phone call evaluation. GAIS score showed that patients significantly improved post-treatment. The patients found the treatments comfortable and showed high satisfaction which was gradually increasing.

Photo evaluation using the GAIS grading system resulted in a score of 1.56 ± 0.68 when the baseline photographs were compared to the ones taken immediately after the last treatment. For the photo pairs, baseline and 1-month follow-up, the average score of the three evaluators was 1.51 ± 0.65. The improvement score at three months was 1.53 ± 0.66 indicating that the improvement seen immediately after the last treatment was maintained over the course of 3 months. Example of a set of patient photographs can be seen in **Figure 1**.

The figure shows mild improvement in the buttock shape and volume immediately post-treatment. The more dramatic change in comparison to baseline can be seen in the photo taken 1 month post-treatment showing lifted and more toned buttocks with significantly increased volume. The three month follow-up photo shows that the lifted buttock shape was preserved and the volume continued to increase.

Evaluation of VAS satisfaction questionnaires resulted in high patient satisfaction with the treatment outcomes as the average VAS score was 7.2 ± 1.84 after the last treatment. The satisfaction increased during the 1-month follow-up to 7.4 ± 1.79 and was further enhanced to 7.8 ± 1.95 during the 3-month follow-up. The histogram representing the distribution of patient satisfaction during the 3-month follow-up is displayed in **Figure 2**.

It shows that there was one dissatisfied patient (score<5), while 10 patients reported satisfaction higher than 8.

Furthermore, subjects found the treatments comfortable with VAS score of 8.3 ± 1.9. None of the patients reported discomfort during the treatments (score<5). Average weight change did not exceed 1 lb during the study and was not statistically significant ($p>0.05$). Mild muscle soreness was present on the day after the treatment session in several subjects but resolved within 24 hours. No adverse events or side effects were reported.

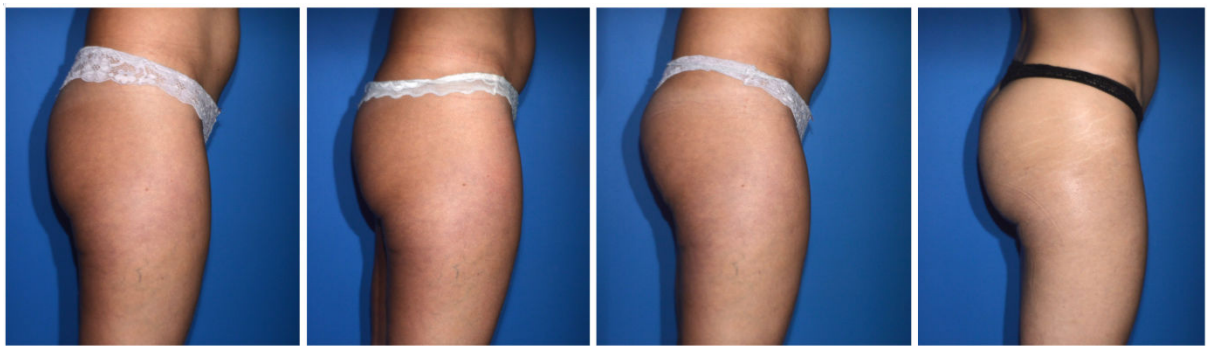

Figure 1: Digital photographs of subject ID 6 taken at baseline (left), after the 4th treatment (middle left), during the one-month follow-up (middle right) and three-month follow-up (right). The photographs illustrate gradual progress in the shape of the buttocks.

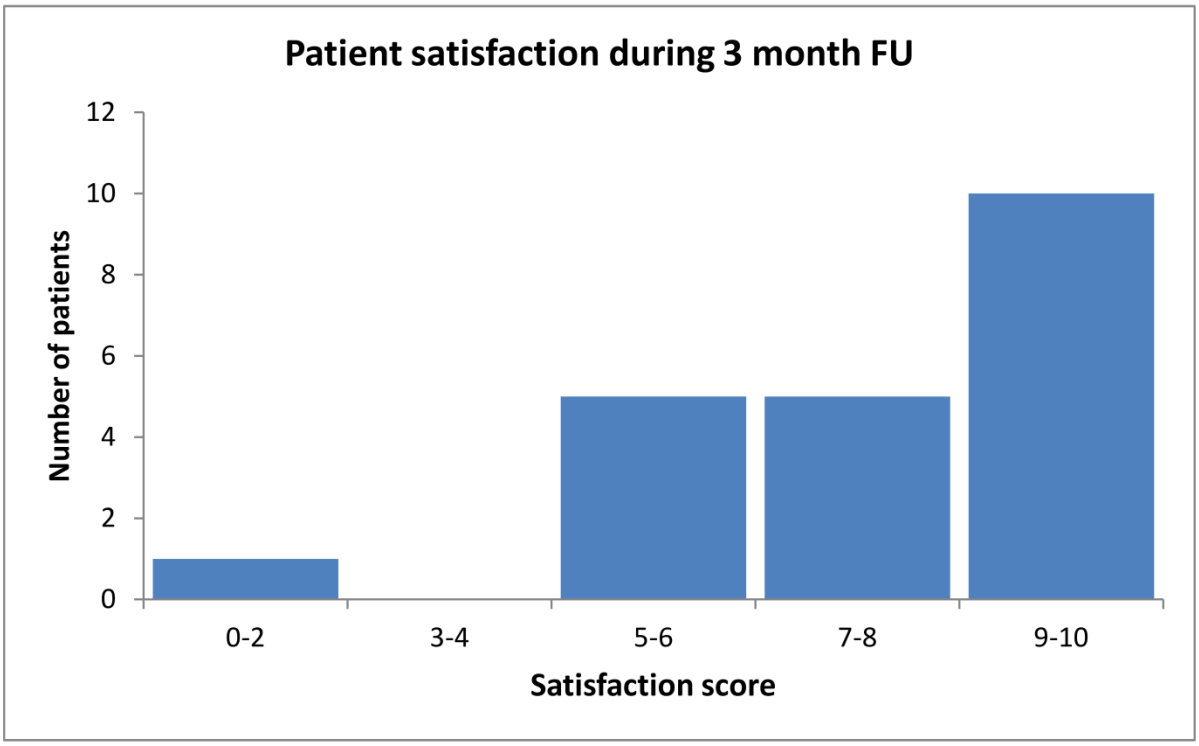

Figure 2: Distribution of patient satisfaction score during the 3-month follow-up.

Discussion

The analysis of the study outcomes suggests that the HIFEM technology is feasible for aesthetic improvements of buttocks, with the treatments being safe and comfortable for the patient. The GAIS scores for all analyzed pairs of photos ("before-after" and "before-follow up") were on the scale in between "Improved" and "Much improved," indicating that the appearance of buttocks was significantly enhanced. The patient satisfaction continued to grow throughout the study (score = 7.2 after the last treatment, score = 7.4 during the 1 month fu) with a peak during the 3-month follow-up (score = 7.8) suggesting that the appearance continued to improve even after 3 months since the last treatment.

The visual examination of the photographs indicates that the treatment with HIFEM technology may not induce large volumetric changes as seen with fat grafting or silicone implants, but rather induces firming effect which corrects the unpleasant sagging look into lifted and sporty appearance. A demonstrative example of this effect is displayed in **Figure 3**.

The figure shows the toning effect of the treatments, at baseline the buttock is saggy in comparison to post-treatment photos. The main difference can be seen when focusing on the gluteal fold and intergluteal cleft, the buttock at post-treatment

photos is lifted, firmer and gives the impression of fuller look. In addition, a slight volumetric enhancement can be seen in the 3-month photograph.

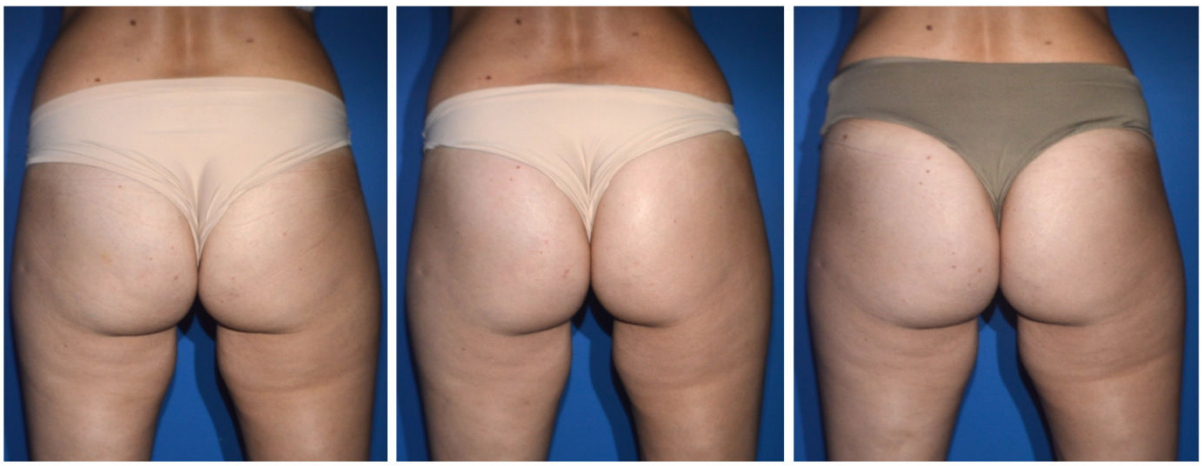

Figure 3: Photographs of a 25-year-old female (Subject ID 7) taken at baseline (left), after the 4th treatment (middle) and after 3 months (right).

Photographs demonstrate the firming effect of the treatments as the gluteal fold is lifted in the after intervention photograph. Previous abdominal studies [3,4,7] documented reduction in subcutaneous fat thickness after treatments by HIFEM technology device. This effect, however, may be an undesirable outcome of the buttock treatments for most of the patients, as fat deposits on buttocks may contribute to its fuller look. We did not measure the fat deposits, but it has been documented before, that the fat tissue of buttocks is much less metabolically active when compared to fat tissue of the abdomen. It can, therefore, be assumed that the fat layer of buttocks is not significantly affected during the treatments [9,10].

We thus link the observed aesthetic improvement solely to the HIFEM effect on muscles as previous studies [3,4] report approximately 16% increase in muscle thickness. Since the muscle laxity plays crucial role in the sagging look of buttock the correction of muscle laxity is the key for improving the buttock appearance and creating the desired sporty look. The HIFEM technology allows treatment of muscle laxity through induction of supramaximal muscle contractions.

Even though the used evaluation methodologies give promising results of the HIFEM technology for the buttock shaping, a quantitative evaluation is missing. Future studies should bring a quantitative and more objective evaluation of the buttock treatments e.g., MRI measurements of muscle thickness, MRI muscle volume assessment or 3D photograph volumetric assessment. Extended protocol with an increased number of treatments including long-term monitoring of the patient should also be considered for future research.

Conclusion

The HIFEM technology showed its capability in improving aesthetic improvement of buttocks which was demonstrated by the positive GAIS ratings given by three independent evaluators and high patient satisfaction. Marked improvements observed in the digital photographs suggest the HIFEM treatments for buttocks as a suitable alternative to current procedures. Further research including quantitative assessment is necessary.

Acknowledgments

None. No funding to declare.

Conflict of Interest

Mariano Busso MD is a speaker for BTL. Radina Denkova MD has no relevant conflicts to declare.

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Body shaping with high-intensity focused electromagnetic technology

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Body shaping with high-intensity focused electromagnetic technology

Introduction

Current surgical as well as noninvasive body shaping procedures are effective for fat elimination, but require patients with well-defined bulges for successful and safe treatment. Many patients, especially those with lower BMI, are not considered suitable candidates for established body shaping procedures such as cryoadipozytolisis (membrane defect to subcutaneous white adipose tissue, sWAT), radiofrequency (heat = apoptosis in sWAT), or high-intensity focused ultrasound (HIFU) [1] ("cooking" of sWAT).

Furthermore, while there are many ways of targeting subcutaneous fat, none of the established procedures deals with the underlying musculature. However, it is the shape, volume, and firmness of the underlying muscles that is highly responsible for a toned and aesthetically pleasing visual appearance. Physical exercise has long been the only option for muscle toning. Although various electrical stimulation-based modalities have been introduced for muscle strengthening [2, 3], their efficacy has been considered controversial. The electric current induced by electrical stimulation depolarizes motor neurons, which results in muscle contraction [4]. However, during electrical stimulation, most of the energy is concentrated superficially, which leads to skin overheating and the risk of burns [5, 6]. Moreover, nociceptors are activated, making the procedure highly painful at higher intensities [7] and thus limiting the use of efficient settings. When using low intensities, the stimuli are not strong enough to trigger any muscle structure changes or growth.

A true advancement for aesthetic use came with the introduction of the high-intensity focused electromagnetic (HIFEM) procedure based on electromagnetic field technology, which overcomes the disadvantages of electrical stimulation. Without any risk of burns or pain [7], the HIFEM procedure can induce supramaximal involuntary contractions that have been found to result in muscle growth and even in a reduction of subcutaneous fat in (but not limited to) lower-BMI patients. With dual effects of this kind, the procedure complements the fat reducing set of tools for practitioners to cover the entire patient spectrum and offers a completely new approach to body shaping by targeting muscle tissue.

HIFEM technology

- HIFEM technology utilizes low frequency magnetic waves (3–5 kHz), which propagate through the tissue without being absorbed. Thus, an interaction between the wave and human tissue occurs according to the principles of electromagnetic induction first described by Michael Faraday in 1831.
  A distinction is made between the following frequencies:
  430–750 THz *(between infrared/ ultraviolet <laser>)*
  = light spectrum visible to the human eye
- ***1–30 MHz*** *(high frequency)*
  = most non-invasive radiofrequency-based devices for skin/fat
- ***3–30 kHz*** *(very low frequency)*
  = HIFEM

Thus we are looking at the very low frequencies. The law of electromagnetic induction says that any change in a magnetic field induces an electric current and vice versa. The HIFEM device comprises a circular coil located in the applicator, which is placed over the treatment area. During the treatment, an alternating electric current is passed through the wire of the circular coil. The alternations in the electric current induce rapidly changing magnetic waves, which propagate into the underlying tissue, where they induce a secondary electric current. These electric currents within the tissue depolarize the muscle-innervating motor neurons and induce muscle contractions [8].

Several studies have shown that humans are unable to fully activate muscles voluntarily, since the power of muscle contraction is limited by the firing rates and conductivity of neural pathways [9, 10]. The application of HIFEM bypasses the central nervous system and directly stimulates the muscles, thereby allowing their full contraction. In addition, the frequency of delivered pulses does not allow the muscle to relax between two consecutive stimuli, which results in supramaximal tension within the muscle and thus supramaximal muscle contraction.

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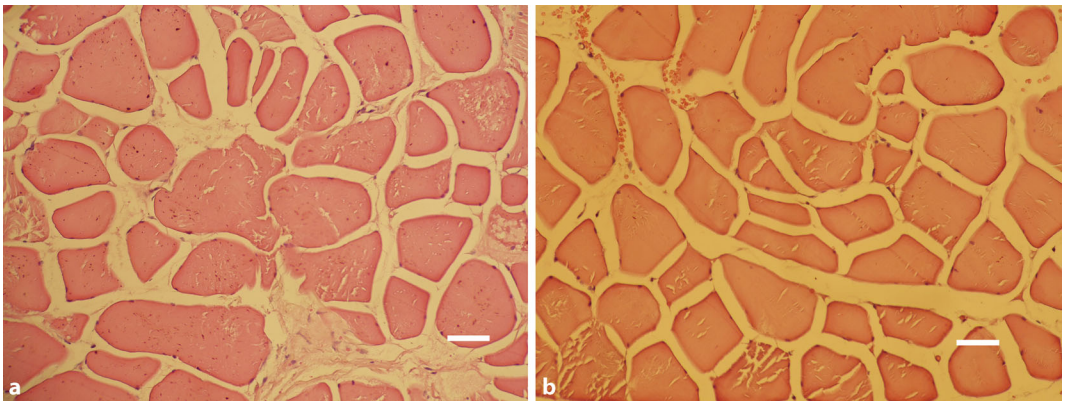

Fig. 1 ◀ Examples of histological images of slices taken at baseline (**a**) and 2 weeks post treatment (**b**). The baseline image shows the normal structure of muscle fibers, while the post-treatment image shows hypertrophy of muscle fibers with the muscle cell diameter being noticeably larger. (With permission from © BTL Medical Technologies s.r.o. All rights reserved)

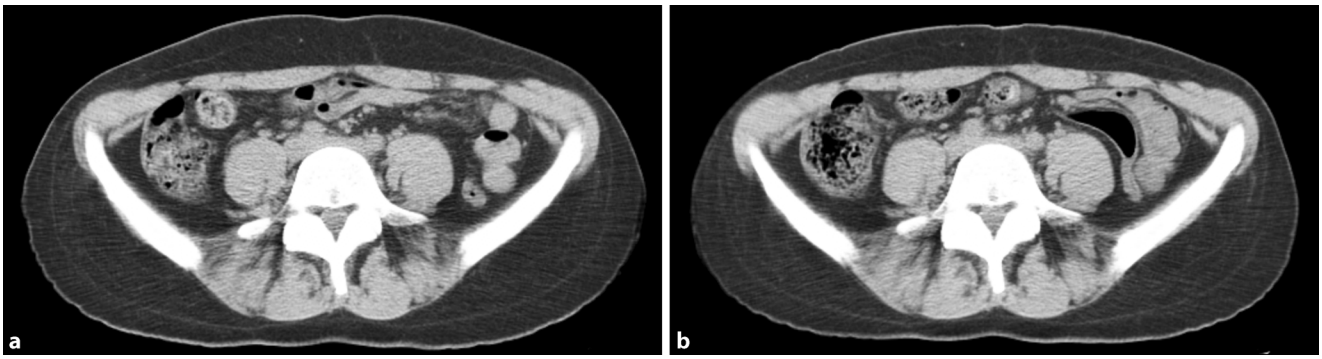

Fig. 2 ▲ Computed tomography scans taken at baseline (**a**) and 1 month post treatment. The measurements showed a 30.3% reduction in thickness of subcutaneous fat, a thickening of abdominal muscle by 8.4%, and a reduction in waist circumference by 2.0 cm. (With permission from © BTL Medical Technologies s.r.o. All rights reserved)

The HIFEM field directly targets the fibers of peripheral motor nerves in the stimulated area and thus leads to a contraction of the whole muscle group innervated by the specific nerve or nerve plexus.

Mechanism of action

Effect on muscle

The intensity of muscle contractions has a very powerful impact on deep muscle remodeling and firm toning of the muscles. The muscle structure is directly modified through the specific conditions to which the muscles need to adapt. HIFEM technology utilizes a unique combination of various field intensities, frequencies, and contraction lengths to induce optimum changes in muscle tissue. The supramaximal nature of the HIFEM-induced contractions puts a high load on the muscle tissue, which results in muscle fiber micro-damage, much like during resistance exercise [11], but to a greater extent. This triggers biochemical processes aimed at strengthening the muscle in order to adapt to such high-load stimuli. Physiologically, the adaptation response manifests as a highly efficient growth of myofibrils—muscle fiber hypertrophy, creation of new protein strands, and possibly new muscle fibers—muscle fiber hyperplasia [12, 13]. ◘ **Fig. 1** provides an example of a histological image. According to previous research, the first results of muscle structural improvements can be seen as early as 14 days after the last systematic muscle contractions, when tissue growth, thickening, and regeneration are fully completed [14].

Effect on subcutaneous fat

HIFEM-induced supramaximal muscle contractions create a high demand for energy supplies, which cannot be provided solely from glycogen storage. Lipolysis is thus initiated by an intracellular cascade reaction, which is activated by catecholamine epinephrine (adrenaline) to supply the muscle with the energy stored in fat. During the process, triglycerides are broken down into free fatty acids (FFA) and glycerol [15, 16]. Released molecules normally act as the primary energy source for muscle and body metabolism. However, when the amount of released FFAs exceeds a certain level, they start accumulating intracellularly in adipocytes, and eventually cause their dysfunction [17, 18].

Lipolysis starts primarily in the area around the muscles undergoing contractions. This is due to increased adipose tissue blood flow (ATBF) and paracrine substances released from contracting muscles, which diffuse to the adipose tissue and stimulate blood flow and adipose tissue lipolysis [15].

During HIFEM therapy, the mechanism that leads to adipocytes' death is endoplasmic reticulum (ER) stress-induced apoptosis [17, 18]. This reaction is triggered by an increased intracellular concentration of FFA due to an exag-

gerated lipolytic reaction to the supramaximal contractions. The ER is central for protein folding, secretions, calcium homeostasis, and lipid synthesis. With regard to adipocytes, the ER is directly involved in lipid droplet (LD; reservoir for cholesterol and triglycerides) formation and maintenance of lipid homeostasis [19].

The cell reacts to the FFA overflow by initiating an ER stress response to restore homeostasis. However, one of the additional cell responses to the ER stress is lipolysis itself, creating a continuous flow of FFA through lipolysis caused by the supramaximal muscle contractions and lipolysis triggered by the ER stress [20, 21].

At some point, the cell can no longer regulate homeostasis and enters apoptosis—programmed cell death. The apoptotic response to the fatty acid treatments has been confirmed by the measurement of cytoplasmic histone-associated DNA fragments. The results confirmed that the ER stress contributes to apoptosis induced by increased intracellular levels of FFA [22]. The fat cell apoptosis following a HIFEM procedure was proven in an animal study [23], where the apoptotic index increased by 91.7%.

The best aesthetic improvement after non-invasive fat reduction treatments has been widely claimed to appear between 1 and 3 months after the actual treatment [24], when the body fully processes and clears the cell debris and other metabolic waste. The visible fat reduction captured by computed tomography (CT) can be seen in **Fig. 2**.

Clinical application

The HIFEM procedure is currently used for strengthening and toning the entire abdominal area, for lifting and toning buttocks and thighs, as well as for toning arms and calves. Ideal patients for the HIFEM procedure are males and females with a fat layer of up to 2–3 cm. Exclusion criteria include pregnancy, breastfeeding, heart disorders, unhealed wounds in the treatment area, and any medical condition contraindicating the application of an electromagnetic field.

The recommended treatment protocol for the abdominal, thigh, and buttock HIFEM procedure consists of four treatments, each lasting 30 min, while the individual treatments should be spaced at 2–3 days. For arm and calf procedures, 20-min treatments are recommended due to the smaller volume of these muscle groups.

For abdominal treatments, one or two applicators are placed over the treatment area according to patient size. Bilateral placement is used for the buttock, thigh, arm, and calf procedures. Prior to the treatment, the device applicator is positioned over the treatment area and should be secured by a fixation belt to prevent it from shifting with the movements of contracting muscles. Low intensities should be used at the beginning of the treatment, as it is necessary to adjust the applicator position to a location resulting in the strongest and most evenly distributed contractions across the entire muscle group. During the ongoing treatment, the intensity should be continuously increased according to patient

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Body shaping with high-intensity focused electromagnetic technology

Abstract

The field of non-invasive body shaping has long been represented solely by fat reducing technologies, and the condition of the underlying muscles could be altered only by physical exercise. In 2018, high-intensity focused electromagnetic (HIFEM) technology was introduced to simultaneously tone and strengthen muscle and reduce fat. The technology is based on delivering focused electromagnetic fields into the treatment area, causing supramaximal muscle contractions. Clinical studies showed a significant reduction in subcutaneous white adipose tissue (sWAT) and an increase in muscle thickness (e.g., abdominal muscle) after a series of HIFEM treatments. The effect on both types of tissue was also confirmed by histological studies and was present in all imaging techniques (ultrasonography, magnetic resonance imaging, computed tomography). With an effect of this kind, HIFEM technology has opened up a completely new segment in body contouring.

Keywords

HIFEM · Electromagnetic stimulation · Muscle building · Fat removal · Muscle atrophy

Körperformung mit hochintensivem fokussiertem elektromagnetischem Feld

Zusammenfassung

Das Fachgebiet der nichtinvasiven Körperformung beinhaltete lange Zeit nur fettreduzierende Techniken. Der Zustand der darunter liegenden Muskeln konnte ausschließlich durch körperliches Training beeinflusst werden. Im Jahr 2018 wurde die sogenannte High-intensity-focused-electromagnetic(HIFEM)-Technik eingeführt, um zugleich eine Formung und Kräftigung der Muskulatur sowie eine Fettreduktion zu erreichen. Die Technik basiert auf der Erzeugung fokussierter elektromagnetischer Felder im zu behandelnden Gebiet, wodurch supramaximale Muskelkontraktionen ausgelöst werden. Klinische Studien zeigten eine signifikante Reduktion von weißem Unterhautfettgewebe und eine Zunahme der Muskeldicke (beispielsweise des M. rectus abdominis) nach einer Serie von HIFEM-Anwendungen. Der Effekt auf beide Gewebetypen wurde in histologischen Studien bestätigt und ließ sich mit sämtlichen bildgebenden Verfahren darstellen (Sonographie, Magnetresonanztomographie, Computertomographie). Mit einer derartigen Wirkung eröffnet die HIFEM-Technik ein vollkommen neues Arbeitsfeld im Bereich der Körperformung.

Schlüsselwörter

HIFEM · Elektromagnetische Stimulation · Muskelaufbau · Fettentfernung · Muskelatrophie

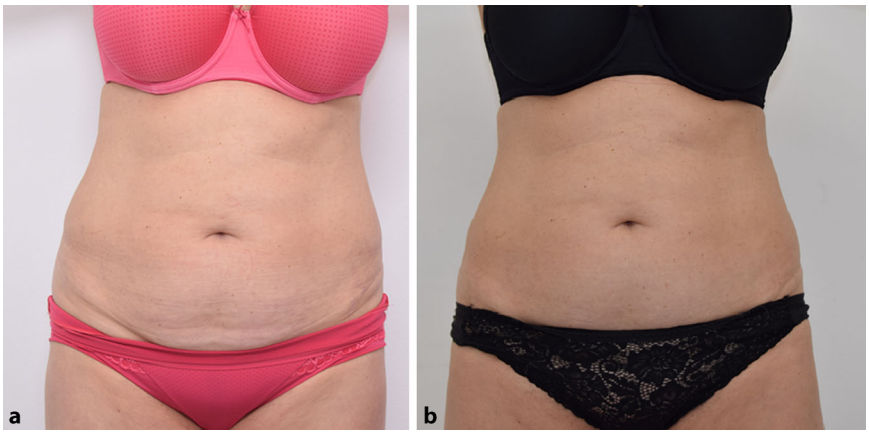

Fig. 3 ▲ An example of the result of abdominal treatment in a 52-year-old female patient. Photographs taken at baseline (**a**) and 2 months post four treatments (**b**). (With permission from © BTL Medical Technologies s.r.o. All rights reserved)

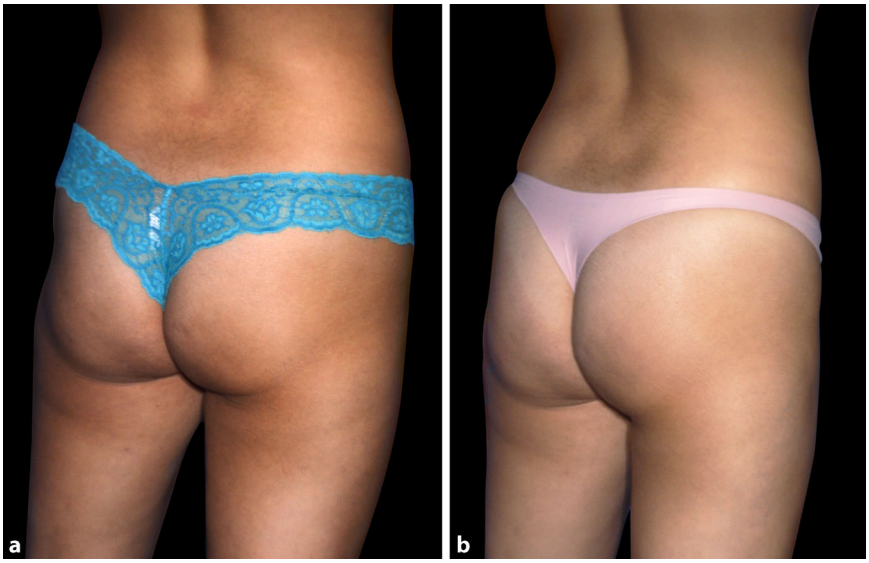

Fig. 4 ▲ An example of buttock treatment outcome in a 31-year-old female patient. Photographs taken at baseline (**a**) and 1 month post four treatments (**b**). (With permission from © BTL Medical Technologies s.r.o. All rights reserved)

feedback to induce challenging but not painful muscle contractions.

Immediately after the treatment, patients experience firming of the treated area, but the results fully manifest approximately 2 weeks to 2 months after the final procedure. For some patients seeing declines in the achieved outcomes, it may be beneficial to perform maintenance treatments 8–12 months post treatment in order to preserve the results.

Clinical evidence

Numerous clinical studies [13, 23, 25–30] investigating HIFEM technology have been published to date in peer-reviewed journals. The studies comprising hundreds of test subjects focused on determining the safety and efficacy of HIFEM for abdominal body shaping, buttock shaping, and histological evaluation.

A histological study by Weiss et al. [23] focusing on fat tissue demonstrated levels of apoptosis elevated by 92% through an apoptotic index following HIFEM treatment. The study also found increased levels of pro-apoptotic markers, further indicating the apoptotic response of subcutaneous fat to the treatment. The muscle histology study performed by Duncan et al. [13] confirmed HIFEM-induced muscle hypertrophy on a cellular level. The investigators acquired muscle biopsies prior to and after four HIFEM treatments and found a significant increase in the cross-sectional muscle mass of 20.56%. Individual muscle fibers increased by 12.15% on average and, although not statistically significant, the number of muscle fibers also increased by 8%, indicating that muscle fiber hyperplasia may also play a role in addition to muscle fiber hypertrophy.

Besides histology, the effects of the treatment on the abdomen were assessed using various imaging techniques: CT [29], magnetic resonance imaging (MRI) [27], and ultrasound imaging (US) [28]. The results from the different studies were seen to be consistent in terms of both subcutaneous fat and muscle thickness. The average subcutaneous fat reduction seen in these studies was 19.6% (17.5–23.3%), while muscle thickness was increased by 15.1% (14.8–15.4%) on average. Some of the studies also measured abdominal separation, which was found to be reduced by 9.95% on average due to the muscle thickening effect. In addition, the waist circumference measured in these studies was found to be decreased by 3.85 cm on average. ◘ **Fig. 3** provides an example of the abdominal treatment outcome.

The studies [25, 30] investigating the HIFEM procedure for shaping, toning, and lifting of buttocks were based primarily on a satisfaction assessment and an evaluation of digital photographs. In general, the studies found high patient satisfaction and a significant improvement in the aesthetic appearance of the buttocks, as documented by the digital photographs. An example of treatment outcome can be seen in ◘ **Fig. 4**.

To summarize, the HIFEM procedure is supported by strong clinical evidence based on a variety of investigating methodologies. The studies found the procedure to be effective for body shaping through fat reduction and muscle thickening while being safe, since none of the studies reported any adverse events or side effects.

Conclusion

Through its dual effect on fat and muscles, HIFEM technology represents a novel approach in the field of non-invasive body shaping. It should not be confused with electrical muscle stimulation (EMS),in which a current runs over the muscle fascia but does not penetrate the muscle in a comparable way to HIFEM. The procedure is convenient for patients that are not ideal candidates for established technologies and thus extends the target patient pool for practitioners. As muscle laxity is a common problem that has not been targeted as yet, the combination of HIFEM with other modalities complements the set of tools for body shaping to achieve complete non-invasive body reconstruction. Wide clinical evidence provides a strong and clear overview of the outcomes that can be expected and gives the practitioners the confidence to use the technology to achieve high patient satisfaction.

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Compliance with ethical guidelines

Conflict of interest. K. Hoffmann, S. Soemantri, K. Hoffmann, and K.K.P. Hoffmann declare that they have no competing interests. K. Hoffmann recurringly holds lectures for CYNOSURE (Westford, USA), the company distributing the STIMSURE device, as well as for BTL (Prague, Czech Republic), the company distributing the EMSCULPT device. Both devices have been regularly purchased by the university dermatology clinic. The author declares that he has no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

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ORIGINAL CONTRIBUTION

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Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping

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Abstract

Background: Thermal fat reduction technologies are leading the market for nonsurgical abdominal contouring. However, they are ideal principally for patients with fat bulges.

Objectives: Our study investigates the effects of a novel nonthermal technology affecting the abdominal musculature and subcutaneous adipose tissue.

Materials and Methods: A total of 22 patients (avg. BMI 23.8 kg m^{-2}) underwent 4 treatments on abdomen with high-intensity focused electromagnetic (HIFEM) field device. Treatments took 30 minutes and were spaced apart by 2-3 days. Photographs, weight, and waist measurements were taken at the baseline, after the last treatment, and at month 3 follow-up. Patient satisfaction was noted. Photographs were evaluated by blinded evaluators.

Results: The study protocol was completed by 19 patients. At month 3, the average waist size reduction was 4.37 ± 2.63 cm ($P < 0.01$). The evaluators identified the before image from the 3-month image 89.47% of the time. About 91% of patients reported their abdominal appearance improved, and 92% stated they are satisfied with treatment results at month 3. No adverse events occurred.

Conclusion: Observed waist size reduction and aesthetic improvement appear to be a combination of fat reduction and increased muscle definition of abdominal wall. In lower BMI patients, the increased abdominal muscle definition was largely responsible for the improvement. This novel energy device provides an additional tool for body contouring with primary application for lower and medium BMI patients.

KEYWORDS
body, contouring, electromagnetic, HIFEM, muscle, toning

1 | INTRODUCTION

The media-driven images of thin and muscular bodies lead to a high dissatisfaction rate of nonideal body type patients which may result in chronic depression.[1] Currently, up to 60.7% of men and 71.6% of women in US population are dissatisfied with their body size.[2] The desire for an easy solution to reduce fat and to improve the appearance of the abdomen is driving the market for body shaping procedures.

In 2017, liposuction was the most common surgical cosmetic procedure, after breast augmentation, with over 300 000 conducted procedures that year.[3] Due to the risk of complications (eg, infection, scarring or hematoma[4]), related downtime and substantial financial

cost associated with surgical procedures, there has been a rapid increase in the demand for noninvasive solutions. Since 2012, noninvasive procedures have grown by 217.3%.[3] The leading technologies in the noninvasive body shaping are low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF), and high-intensity focused ultrasound (HIFU).[5]

Surgical as well as noninvasive body shaping procedures are effective for fat disruption but require patients with well-defined bulges for successful and safe treatment. Many patients, especially those with lower BMI, who desire body shaping procedure, are not suitable candidates. Furthermore, none of the procedures focus on the underlying musculature, which is highly responsible for toned and aesthetically pleasing abdominal appearance.

Besides physical exercise, electric and electromagnetic stimulation has been used for muscle training.[6–8] Electromagnetic stimulation appears to dominate over the electrical stimulation as it induces double the peak torque,[9] penetrates deeper into the tissue[10] and is not associated with any pain[9] or risks of burns.[11,12] As electromagnetic stimulation has been shown to strengthen the muscles,[9,13,14] and an intensive muscle training was shown to induce lipolysis,[15,16] we hypothesize that the concept of electromagnetic stimulation can be applied for body shaping. Utilization of this technology would open possibilities for the patients not suitable for other procedures since the penetration of the magnetic field is not restricted by fat deposits.

Recently, there has been an introduction of a novel device (EMSCULPT, BTL Industries, Boston, MA) utilizing a high-intensity focused electromagnetic (HIFEM) field with frequencies inducing tonic muscle contractions. The study aims to examine the effect of the HIFEM technology on patients' waist circumference, the effect on abdominal appearance, the treatment satisfaction, and the safety of the procedure and to investigate the suitability of the treatment for lower BMI patients.

2 | MATERIALS AND METHODS

A total of 22 patients (avg. BMI 23.8 ± 3.3 kg m^{-2}) desiring aesthetic improvement of the abdomen voluntarily participated in this study. The patients' age ranged from 20 to 47 years with an average of 32 ± 7.1 years. Exclusion criteria included pregnancy, cardiac pacemakers, implanted electronic devices, metal implants, heart disorders, and any medical conditions contraindicating the use of the electromagnetic field. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Boards (IRB).

The patients underwent treatment of the abdomen by a device utilizing high-intensity focused electromagnetic field (EMSCULPT, BTL Industries, Boston, MA). The entire procedure consisted of 4 sessions distributed across two weeks (twice weekly, separated by 2-3 days). Each session lasted for 30 minutes during which the operator monitored the patients. Prior to treatment, informed consent was obtained from each patient.

The treatment was applied in a supine position with the device applicator positioned over the umbilicus. The targeted muscles were the rectus abdominis, external and internal obliques. The applicator position was being adjusted at the beginning of the treatment to ensure homogenously distributed contractions. The applicator was secured by a fixation belt to avoid any movement of the applicator during the treatment. The initial stimulation intensity was set according to patients' tolerance threshold and was further increased during the treatment once the patients got used to the muscle contractions. Over the course of a single session, most patients were able to reach an intensity of 90%-100%. No anesthesia was required.

To evaluate the treatment, weight, and waist circumference measurements, as well as frontal and lateral digital photographs, were taken before treatment, after the last treatment, and during a 3-month follow-up. Randomized digital photographs taken at baseline and during 3-month follow-up were given to three blinded evaluators for recognition. Furthermore, patient satisfaction with the treatment results was assessed using a 5-Likert scale questionnaire after the last treatment and during a 3-month follow-up. All data were tested by *t* test.

3 | RESULTS

The full study protocol was completed by 19 subjects (3 men, 16 women); 3 subjects opted out for reasons unrelated to the study. The results presented herein therefore comprise data from 19 patients.

Immediately after the last treatment, the waist circumference was significantly ($P < 0.01$) reduced on average by 3.29 ± 1.9 cm. This further improved three months after the last treatment, with the average reduction reaching 4.37 ± 2.63 cm compared to baseline. The total average circumference can be seen in Figure 1.

Circumferential reduction in 16 out of 19 subjects (84%) exceeded 2.5 cm at month 3 post-treatment. These results were independent of weight changes ($P > 0.05$). A significant portion of the reduction (75%) was measured after the last treatment, further improving at month 3. The waist circumference of 1 patient increased immediately post-treatment number 4, and 2 patients (10.5%) did not have any waist size change at the follow-up. The waist reduction was found to be independent of the baseline BMI ($P < 0.05$). The individual results can be seen in Figure 2. Patients' weight did not change significantly ($P > 0.05$) throughout the measurements.

On average, the evaluators successfully recognized the before images from the 3-month images in 89.47% of cases. In 15 patients (79%), the images were uniformly recognized by all 3 evaluators. The successful recognition rate was positively correlated with the amount of circumference reduction ($P < 0.01$). Example of patient photographs can be seen in Figures 3 and 4.

Analysis of the patient questionnaire revealed that 89% of patients were satisfied with the treatment results immediately after the last treatment. During the 3-month follow-up visit, the satisfaction increased as all patients reported a certain degree of satisfaction. The patient satisfaction was independent of the amount of waist size reduction. After the last treatment, 95% of the patients

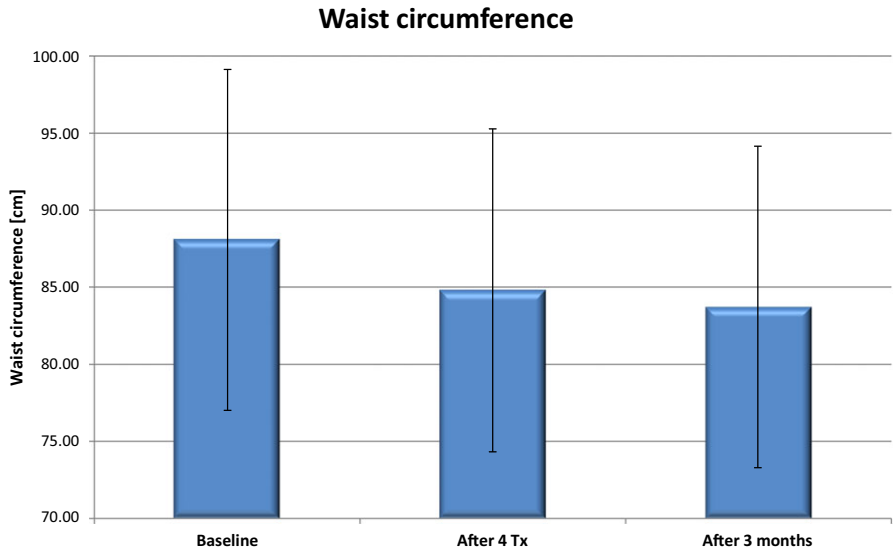

FIGURE 1 Average waist circumference at baseline, after fourth treatment and 3 months after last treatment

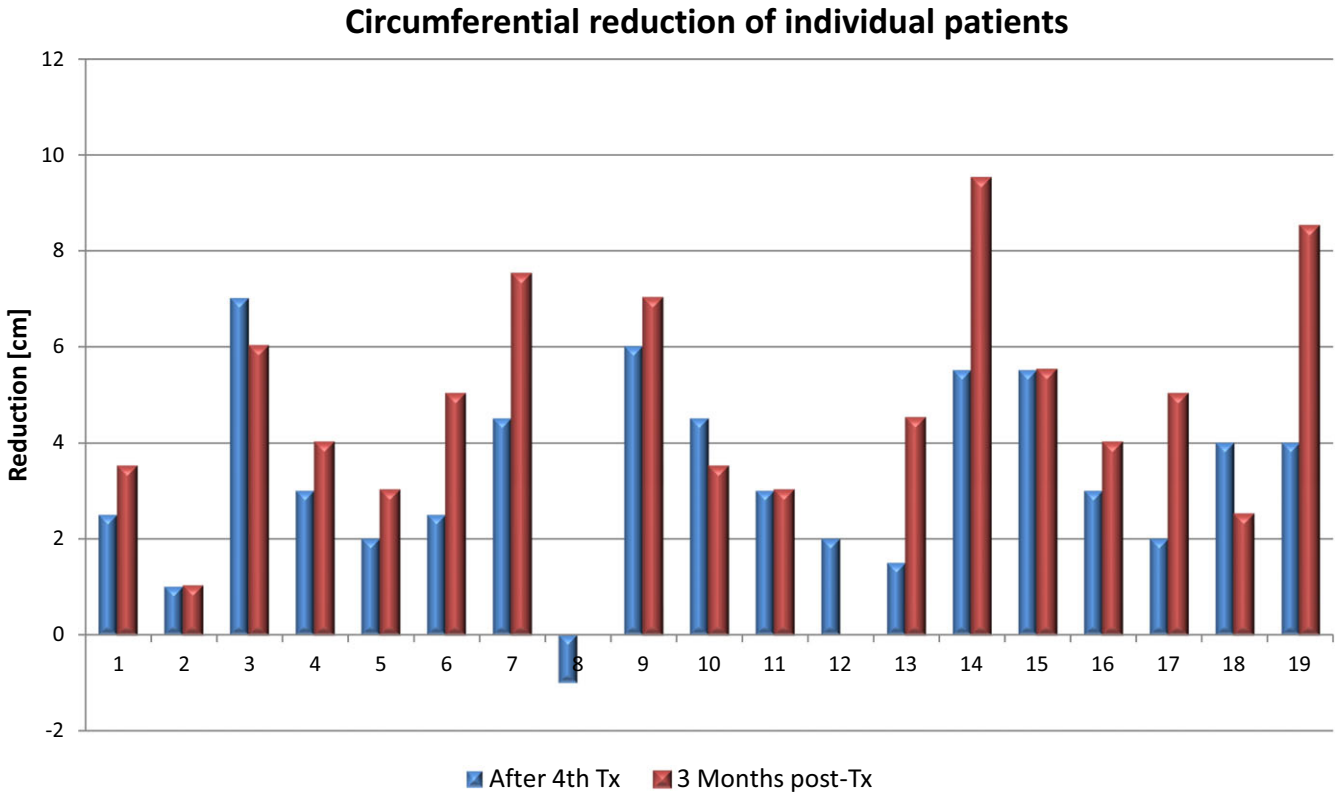

FIGURE 2 The individual waist circumference reduction measured immediately after the last treatment and during the 3-month follow-up

reported that they would recommend the treatment to a friend, while this decreased to 90% during the 3-month follow-up. Also, 89% of patients reported that their abdominal appearance improved immediately after the last treatment and this self-report further increased to 95% at month 3 follow-up. In general, the patient satisfaction improved at month 3 compared to evaluation after their last treatment, showing a similar trend as the measured waist reduction.

Muscle fatigue was a relatively frequent side effect that resolved within 12-48 hours. No adverse events were observed.

4 | DISCUSSION

Fifteen out of the 19 subjects had a BMI lower than 25, and the total average BMI was 23.8 ± 3.3 kg m^{-2}. Many of the subjects

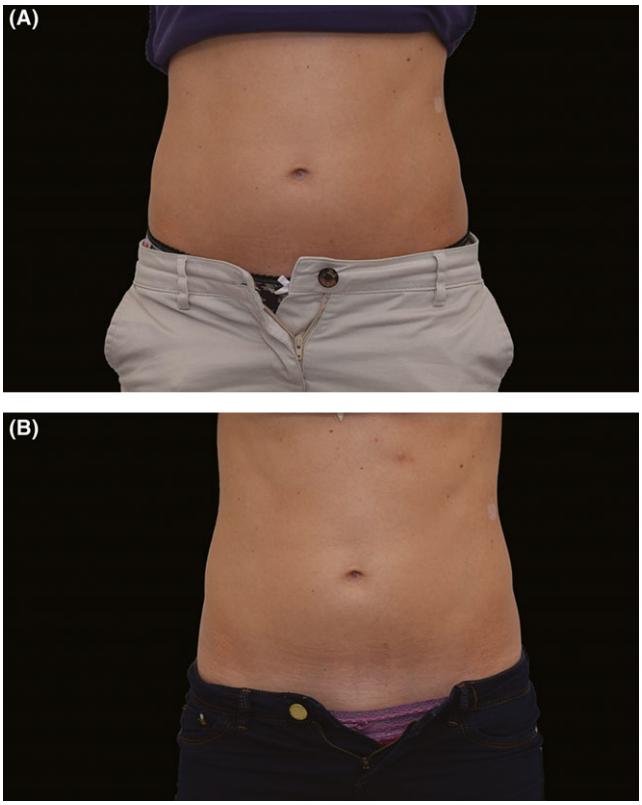

FIGURE 3 Digital images before (A) and 3 months after last procedure (B). Subject 13, age 30, BMI 18.9, waist circumference −3 cm (−4.0%), weight unchanged

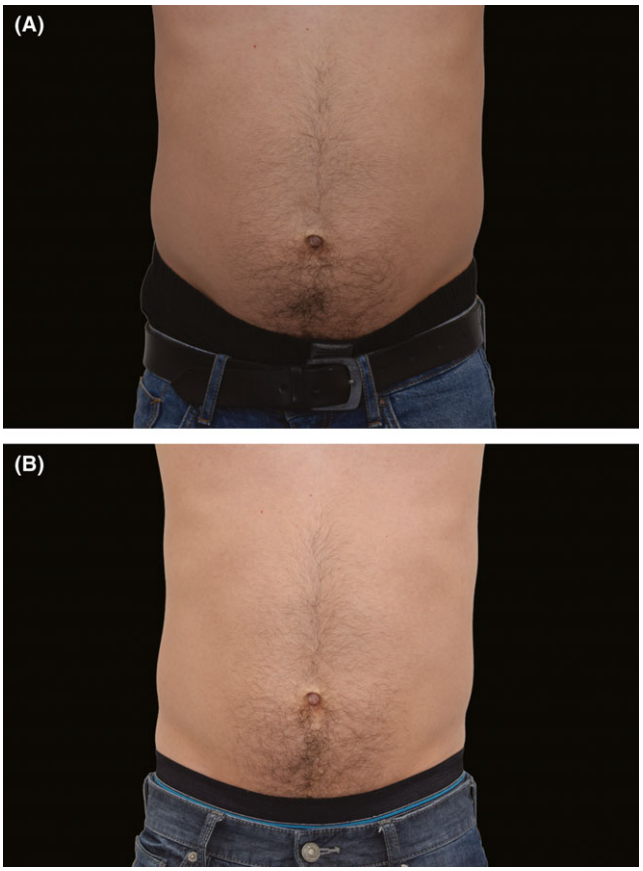

FIGURE 4 Digital images before (A) and 3 months after last procedure (B). Subject 11, age 33, BMI 25.2, waist circumference −7 cm (−7.7%), weight change −1.8 kg (−2.2%)

would not be suitable candidates for fat debulking treatments, such as suction based or stamping fat reduction devices. The primary goal was to understand if HIFEM can be used for lower BMI patients who are not ideal candidates for other available technologies.

The presented results showed that the treatment of the abdomen utilizing the HIFEM technology was effective in reducing the patients' waist circumference and in improving the aesthetic appearance of the abdomen. This was accompanied with high patient satisfaction. The waist size reduction was present already after the fourth treatment and continued to further reduce over the course of 3 months in most patients. The fact that the amount of waist size reduction was not correlated with the baseline BMI, suggests that the treatment was effective at the same level for the study patients' BMI range (18.8-33.3). The patients were satisfied with the results, and the treatment was generally perceived as comfortable.

The visual aesthetic improvement was confirmed by a high rate of successful photograph recognition done by blinded independent evaluators. The rate of successful recognition was correlated with the amount of waist size reduction, indicating that the higher the waist size reduction, the more the aesthetic improvement of the subject.

The study found that a significant weight loss did not accompany the waist size reduction. The device delivers pulses in a frequency that produces supramaximal contractions not achievable voluntarily. The muscle does not have time to relax between the 2 consecutive stimuli and is exposed to the extreme condition, which triggers a stress response in the tissue. Energy for supplying the contractions is taken from the fat cells presumably through lipolysis. The same effect, when muscles begin to use lipolysis as an energy supply, has already been seen during intense acute resistance exercise.[15,16] Further, when regularly exposed to these conditions, the muscle needs to adapt to them, which leads to a volumetric growth of muscle (hypertrophy)[17,18] and possibly hyperplasia.[19] The waist circumference reduction can therefore result from both fat reduction and strengthening and tightening of the abdominal wall. The lack of weight loss after the treatment thus appears to be logical effect since the weight of lost fat tissue is compensated by the weight of gained muscle volume.

In comparison to other technologies for noninvasive body shaping, the HIFEM showed competitive results regarding the waist circumference reduction. A study by Ferraro et al[20] on cryolipolysis reported circumference reduction of 6.86 cm, an LLLT study by Savoia et al[21] reported waist reduction as much as 6.83 cm, and RF study by Fajkosova et al[22] showed 4.93 cm. Studies on HIFU[23–25] showed a reduction of 4.1-4.7 cm. Looking at these results, the average waist reduction of 4.37 cm observed in the present study is highly competitive. However, the reduction presented in the mentioned studies is attributed to the fat loss, while the reduction in the present study appears to be a combined effect of a fat loss and strengthening of the abdominal wall muscles.

5 | CONCLUSION

The overall results are competitive in the noninvasive field of abdominal aesthetic improvement. The waist size reduction and improvement seen in photographs were driven by a combination of reduced fat and strengthened abdominal muscles. HIFEM treatments are effective for body shaping in both lower and medium BMI patients due to its effect on 2 tissues, showing high levels of patient satisfaction coupled with visible aesthetic improvement. We conclude the technology is ideal for treating patients who might not be candidates for other exiting technologies or whose problem is driven by a combination of fat deposits and underlying muscle laxity.

DISCLOSURE

Carolyn I. Jacob MD is medical advisor for BTL. Katya Paskova MD has no financial interest to declare in relation to any of the products or device mentioned in this article.

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ORIGINAL CONTRIBUTION

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Mechanism of nonthermal induction of apoptosis by high-intensity focused electromagnetic procedure: Biochemical investigation in a porcine model

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Abstract

Background: Multiple studies have reported adipose tissue reduction after the application of the High-Intensity Focused Electromagnetic (HIFEM) field technology, yet cellular level evidence of the mechanisms has remained scarce.

Objectives: This study aims to verify or refute previous single-study histological evidence and further investigates the proposed mechanism of apoptotic induction.

Methods: The thigh of two Large White pigs was treated with HIFEM for 30 minutes. Fat punch biopsies were collected from the application area before, immediately after, and 8 hours post-treatment. Control samples were taken from the abdomen immediately after and 8 hours post-treatment. Samples were analyzed for pro-apoptotic DNA markers (BAX, BCL-2, TXNIP, MMP9, TNF-α), the levels of free fatty acids (FFA), and the pH levels of the adipose tissue.

Results: The levels of FFA in the treated adipose tissue increased on average by 127.1% immediately post-treatment and by 134.1% 8 hours post-treatment, indicating a rapid breakdown of lipids. The average recorded adipose pH changed from 7.30 ± 0.12 at baseline to 6.60 ± 0.07 immediately post-treatment (P = .001) and to 7.19 ± 0.12 8 hours post-treatment. The levels of BAX, TXNIP, MMP9, and TNF-α increased post-treatment while BCL-2 decreased. Control samples showed constant levels of pH and pro-apoptotic markers. The FFAs in the control samples were increased by 41.6%-51.4%.

Conclusion: The changes in the levels of the pro-apoptotic markers conformed to the previously reported elevated fat apoptosis post-HIFEM treatments. These effects were accompanied by an increase in FFA levels, and by reduced pH levels, due to the increased acidity in the adipose tissue. Further research is required to explore the potential of nonthermal induction of apoptosis.

KEYWORDS

apoptosis, ER stress, fat disruption, high-intensity focused electromagnetic field technology, non-thermal

1 | INTRODUCTION

Too many calories consumed versus too little energy expended due to low levels of physical activity is considered the main cause of fat accumulation, especially in the lower body,[1] resulting in an undesirable aesthetic appearance. In an effort to improve their aesthetic appearance, patients often attempt to reduce this excess fat by dietary restraint, lifestyle modification, or increased physical activity. However, achieving a sustainable fat reduction requires a considerable commitment and dedication, while the desired results take significant time to manifest. Patients often seek help through aesthetic medicine to help further bolster their effort.

Aesthetic medical procedures can yield a volumetric reduction of fat, either invasively through surgical removal of fat deposits or noninvasively by the elimination of cells forming the subcutaneous tissue—the adipocytes. The noninvasive elimination of fat occurs through the action of various physical, chemical, and biological factors, resulting in adipocyte necrosis or apoptosis.[2]

Fat necrosis is a pathological and unregulated process. Apoptosis, on the other hand, is a highly regulated physiological process where the affected cell actively destroys itself (programmed cell death).[3] The induction of an apoptotic response in fat cells above normal physiological levels has long been considered temperature-dependent only, achievable by the heating of subcutaneous tissue[4] or its cooling below the freezing point.[5] The effectiveness of such approaches has been investigated by multiple studies.[6-8]

Recently published research unveiled that it is also possible to achieve similar fat reduction through apoptosis of adipocytes in a nonthermal manner with the application of the High-Intensity Focused Electromagnetic field (HIFEM) technology.[9] This novel technology utilizes the principles of electromagnetic induction to depolarize motor neurons, thus stimulating intense involuntary muscle contractions, by bypassing the central nervous system. Such intense muscle recruitment/load appears to be able to trigger an exaggerated need for energy at the cellular level. This perceived extreme energy need, hormonally signaled by the muscle, then leads to the adipocytes dysfunction and consequently to apoptosis. A similar study by Weiss et al, conducted on a porcine animal model, showed objective histological data and increased levels of fat apoptosis accompanied by elevated concentrations of free fatty acids (FFA), creatine kinase, and various apoptotic markers in the blood plasma after the HIFEM treatment.[9] The authors proposed that stress of endoplasmic reticulum could have been the mechanism for the observed apoptotic acceleration.

Several additional studies demonstrated that increased levels of extracellular FFA have the potential to induce endoplasmic reticulum (ER) stress reaction.[10,11] The ER is a central cellular organelle responsible for lipid, glucose, and protein metabolism, and it is also highly responsive to cellular nutrient and energy status.[12] The efficient functioning of the ER is essential for cell survival. However, ER is highly sensitive to stresses that perturb cellular energy levels. Such stress reduces the protein folding capacity of this organelle, which results in the accumulation and aggregation of unfolded proteins, referred to as ER stress. The cells themselves have developed various protective strategies to resist the deleterious effect of ER stress, referred to as an unfolded protein response (UPR). Nonetheless, when protein aggregation cannot be resolved through a cellular reparative processes, the pro-survival signaling mechanisms alter the pro-apoptotic and ER stress responses ultimately leading to apoptotic cell death.[12]

This study aims to build on the previous research, providing further evidence of increased apoptotic levels post-HIFEM treatments.[9] The proposed mechanism of adipocyte apoptosis is based on ER stress through the overflow of FFA, though previously no study measured the FFA levels directly in the treated tissue. A primary goal of this study is to further investigate the underlying mechanism of nonthermal apoptotic effect of the HIFEM procedure. Assessing the levels of FFA and ER stress markers in the porcine fat tissue should bring valuable insight into the nature of this process and provide supportive or refuting evidence for the proposed ER-stress-based mechanism of apoptosis.

2 | MATERIALS AND METHODS

The study protocol was approved by the institutional review board (IRB) of The Ministry of Agriculture of the Czech Republic, which also supervised the experiment.

2.1 | Description of animal model

Two Large White pigs (approximately 1 year old, 80-90 kg of weight) were used for the experiment. The pigs were clinically examined during the recruitment phase to ensure only those in the proper health conditions were recruited. A 1-week acclimation period was established for stabilization of the animals in the new environment. Prior to treatment, animals received anesthesia, dosed by a veterinarian who supervised the procedure, to minimize any pain or discomfort to the animals during the treatment and biopsy sampling. The general anesthesia was achieved by inhalation of anesthetic agents (tiletamine 2 mg/kg; zolazepam 2 mg/kg; ketamine 2 mg/kg; xylazine 2 mg/kg); thereafter, it was sustained by the intravenous continuous influx of 2% propofol (1-2 mg/kg) through a cannula inserted into a vein in the pig's ear. Both animals were intubated to prevent respiratory arrest.

2.2 | Treatment procedure

Both animals underwent one 30-minute treatment of the thigh with the investigated device (EMSCULPT; BTL Industries Inc), utilizing HIFEM technology. The circular coil, located at the distal end of the

device's applicator, generates alternating dynamic magnetic fields of intensities of up to 1.8 Tesla. During the treatment, the device's applicator was attached to the animal's thigh, secured by a fixation belt. The intensity of the stimulus was set to 100% of the device's possible output.

After the completion of the experiment, the studied animals were painlessly euthanized while under general anesthesia (described earlier) through the injection of an approved and certified veterinary euthanasia drug (T-61; dosed according to the instructions of the manufacturer).

2.3 | Collection of biopsy specimen

In total, five punch biopsies (6 mm in diameter) containing subcutaneous tissue with the adjacent skin tissue were obtained from each pig and prepared for evaluation. Three biopsies were obtained from the treated region, and two were taken from a nontreated abdominal area, which served as a control (taken immediately after treatment and then again after 8 hours). The biopsies were preserved for further analysis in an RNA solution, required for PCR analysis and deep freezing for detection of FFA.

2.4 | pH meter analysis

Local pH in subcutaneous tissue was measured in vivo by GRYF 259 digital-microprocessor pH meter (GRYF HB) with combined electrode FC430B (Hanna Instruments). The device was calibrated before each session. The pH measurements involved the insertion of the pH electrode into the wound. To minimize tissue traumatization, measurements (N = 3) were performed only once at each biopsy site. The pH was obtained at baseline, immediately after, and 8 hours post-treatment to document any fluctuation above/below its physiological baseline levels.

2.5 | RNA markers expression

The relative expression of apoptotic biomarkers in the taken samples of tissue was investigated to document hypothesized stress reaction. At the beginning of this procedure, the total RNA was isolated using the Tri RT Reagent (MRC) and purified in the RNeasy Mini Kit columns (Qiagen). The purity of RNA was expressed as the ratio of absorbances at 260 and 280 nm. M-MLV reverse transcriptase and oligo (dT) primer specific mRNA were used for cDNA generation. The expression of five genes of interest that are involved in ER stress apoptotic processes (TNF-α, MMP9, BAX, TXNIP, and BCL-2) was calculated relative to the expression of the reference gene TBP1,[13] which was chosen as stably expressed using the NormFinder algorithm (2004, Aarhus University Hospital). A qPCR analysis was performed on a LightCycler 480 device (Roche) using QIAGEN QuantiTect SYBR Green PCR MasterMix (Qiagen). Polymerase Chain Reaction plates were automatically filled by the Nanodrop II liquid dispensing robot (BioNex Solutions Inc). Gene-specific primers were partly adopted or designed using the NCBI primer designing software Primer-BLAST (see Table 1). The chain reactions were triplicated and were run under the following conditions: denaturation at 95°C for 15 minutes and 50 amplification cycles at 95°C for 15 seconds, followed by 58°C for 30 seconds and 72°C for 30 seconds. A melt curve analysis using the LightCycler 480 software (Roche Molecular Systems Inc; version 1.5.0.39) was performed to test the specificity of PCR products. A 10-fold serial dilution of DNA template was used to create a standard curve. Amplification efficiency (E) of each primer set was determined, and since the *E*-values fluctuated in the range from 1.892 to 2.245, an optimal efficiency of 2.0 was used to calculate the gene expression.

2.6 | FFA quantification

The total amount of FFA released from adipocytes was examined. The examination included (but was not specific to) palmitic acid, palmitoleic acid, stearic acid, oleic acid, and arachidonic acid. First, adipose tissue samples (approx 0.2 g) were homogenized in methanol. Nonpolar lipids, together with FFA, were extracted into a nonpolar solvent from a weakly acidic environment. The separation of FFA from co-extruded nonpolar lipids was performed by normal-phase liquid chromatography. A triple quadrupole mass spectrometer was used to detect mass spectra of ionized FFA. Its ionization was performed by an atmospheric pressure photoionization method (APPI). From the resulting relative intensities of the ions in mass spectra, we calculated areas under the peaks related to FFAs, which referred to the total amount in the studied specimens.

2.7 | Macroscopic analysis

Any signs of observable side effects or adverse events (bruising, redness or changes of skin texture) caused by treatment were immediately addressed after the therapy and during the housing. Also, any changes in behavioral pattern, gait, or movement stereotypes were monitored by the veterinarian.

2.8 | Statistical analysis

The results are expressed as mean ± standard deviation (SD). The levels of pH before and after the treatment were statistically evaluated. Analysis was performed using two-tailed Wilcoxon signed-rank test (α = 0.05) to identify any significant difference between means of dependent samples.

TABLE 1 PRC primers used in the study for an indication of ER-stress-induced apoptosis

Gene Acc. No[a]	5′- Forward primer- 3′ 5′- Reverse primer- 3′	Product length[b]/E[c]/ characterization of gene
TNF-α	CCCCCAGAAGGAAGAGTTTC	92/2.079/Pro-apoptotic
NM_214022.1	CGGGCTTATCTGAGGTTTGA	
MMP9	CCTTGAACACACACGACATCTTC	111/1.971/Pro-apoptotic
NM_001038004.1	CCACATAGTCCACCTGATTCACC	
BAX	AACATGGAGCTGCAGAGGATG	96/1.956/Pro-apoptotic
XM_003127290.5	GTTGCCGTCAGCAAACATTTC	
TXNIP	GATGACACAGATGGCTCTCAAGAC	99/1.925/Pro-apoptotic
NM_001044614.2	GGATGCAGGGATCACCTCAC	
BCL-2	AGTACCTGAACCGGCACCTG	110/1.892/Anti-apoptotic
XM_021099593.1	CAGCCAGGAGAAATCAAATAGAGG	

[a]Accession number in GenBank National Center for Biotechnology Information (NCBI).
[b]Size of the PCR product of adopted primers was derived using Primer-BLAST software based on the current nucleotide sequences available in the NCBI GenBank.
[c]Efficiency of specific primer set.

3 | RESULTS

3.1 | General observations

The animals were in good condition during the acclimation phase, as well as after the treatment procedure. We observed no side effects or adverse events while the treated area demonstrated no visible erythematous cutaneous reaction to the HIFEM application.

3.2 | pH levels

The average pH of the treated area at baseline (7.30 ± 0.12) corresponded to normal physiological values and did not differ from the measurements at the control site. Immediately after the treatment, pH significantly decreased by 0.70 points on average ($P = .001$), showing a slightly acidic value of 6.60 ± 0.07. The control measurements demonstrated a similar pattern but to a lesser extent. Although the pH mildly and insignificantly decreased, still it remained at near levels, indicating a more natural environment (7.11 ± 0.11). After 8 hours, pH levels returned back to nearly the original baseline levels (see Figure 1).

3.3 | RNA markers

The results of PCR analysis are summarized in Table 2. The relative expression of the examined genes show to be more upregulated (TNF-α, MMP-9, BAX, TXNIP) rather than downregulated (BCL-2) in response to the external stimulus delivered by the HIFEM fields. Conversely, the control samples did not manifest any significant fluctuations among the examined markers, and their expression immediately post-treatment and 8 hours post-treatment was comparable to the baseline.

In general, we observed a greater response in the levels of studied markers at 8 hours post-treatment. The highest fold change was observed in the TNF-α (2.14-fold increase) followed by TXNIP (2.01-fold increase) and MMP9 (1.62-fold increase). Conversely, the BAX marker reached its maximum immediately after treatment (1.43-fold change), while the BCL-2 production was attenuated by 26% in comparison with the baseline.

3.4 | FFA total amount

The assessment of free fatty acids demonstrated a dramatic variation in time, which coincided with the pH measurements (see Figure 2). The post-treatment biopsies of the treated tissue showed significantly increased levels of FFA's, by 127.10%, while control samples demonstrated change to a lesser extent, with FFA levels equal to 41.60%. Moreover, the FFA overflow showed to be sustained even 8 hours post-treatment, reaching an increment change of 134.10% in treated samples and 51.40% in the control samples when compared to baseline.

4 | DISCUSSION

One of the major finding of our study was the documented evidence of elevated levels of FFA in subcutaneous tissue after single HIFEM treatment. The release of FFA was followed by a decrease in pH levels and was accompanied by considerable fluctuations in the expression of important apoptotic markers, such as TNF-α, MMP9, TXNIP, BAX, and BCL-2. The presence of FFA was confirmed and proven by mass spectrometry analysis and a transient increase of acidity in subcutaneous tissue.

The levels of FFA and the pH values measured immediately after the treatment followed a similar complementary trend. As a result of dramatic lipid breakdown, FFAs were released and consequently caused a decrease of the physiological pH levels to slightly acidic

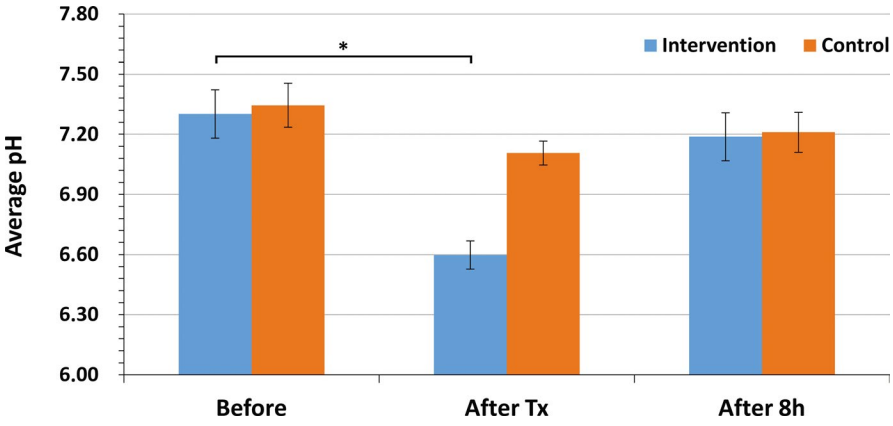

FIGURE 1 Results of pH measurements in subcutaneous tissue (mean ± SD) at baseline, immediately after treatment (after Tx), and 8 h after treatment (after 8 h). The statistically significant difference (P = .001) between baseline and post-treatment measures is depicted by an asterisk (*)

values. Although the levels of FFA remained highly elevated 8 hours post-treatment, the pH returned close to its original values, as the body seeks to restore itself to a more neutral pH to protect the internal cellular environment.

The control samples also showed increased FFA levels in post-treatment measurements and followed the same linear relationship, as the samples taken from the treatment site, although not to the same extent. We hypothesize that it is due to the complexity of the response to the HIFEM treatment. The initiation of triglyceride breakdown into FFA, triggered by intense muscle activity, is often linked to the hormonal release of epinephrine into the bloodstream.[14] Due to bloodstream transport, the epinephrine cannot be selectively delivered to only the localized treatment area, but creates more of a systemic response. This helps to explain the increase in FFA levels in the control area, though not high enough to trigger adipocytes apoptosis. This was also documented by the nonchanged RNA markers in the control area.

It has also been shown that elevated levels of FFA may trigger ER stress apoptotic pathways.[9-11,15] In our study, we observed considerable upregulation of studied ER stress markers in the treated animals, indicating a severe stress reaction. Similar to our findings, it was previously evidenced that during the ER stress in adipose tissue, the TNF-α mRNA expression is increased as the adipocytes enter the mechanism of programmed cell death.[16] In addition, Bouloumilé et al[17] documented that MMP9 could also be a key regulator of adipocytes differentiation, in terms of inhibition of adipose tissue growth. Based on the results of the qPCR analysis, the application of the HIFEM treatment resulted in upregulation of MMP9, indicating the possible contribution to ER stress in the treated adipose tissue.

The BAX is also a factor. It is a member of the BCL-2 family of proteins, and it exhibits pro-apoptotic activity. In resting conditions, BAX is kept inactive by its interaction with anti-apoptotic BCL-2. When severe stress of the ER occurs, the anti-apoptotic effect of the BCL-2 protein is eliminated, and its expression is blocked. This allows the activation of BAX, which leads to the initiation of ER-stress-induced apoptosis.[18] The following patterns have indeed been observed in our study when the BAX levels were upregulated while the BCL-2 levels were considerably decreased.

Furthermore, recent studies have demonstrated that TXNIP upregulation coincides with ER stress and can be induced at the transcriptional and post-transcriptional levels.[19,20] Our results revealed a gradually increasing expression of TXNIP reaching 2.01-fold at the 8 hours post-treatment, which implies an upcoming apoptotic change in the adipose tissue.

The first documented evidence of HIFEM-induced adipocyte apoptosis was recently performed by Weiss et al[9] in a porcine animal model. In addition to the evaluation of RNA markers, they also examined various recognized blood parameters related to both fat and muscle metabolism. One of the major contributions of this study is that it further describes the association between intense muscle load induced by supramaximal contraction and the subsequent stress reaction of the adjacent adipose tissue, caused by the increased levels of FFA. It has been shown that such extensive muscle load resulted in an increased catalytic activity of lactate dehydrogenase (LDH) and creatinine kinase (CK) 8 hours post-treatment. Although their qPCR values are not equally comparable to ours, due to the different reference gene chosen (HPRT1), the observed results revealed similar tendencies. In response to the excessive overflow of FFA measured

TABLE 2 Relative expression of studied apoptotic biomarkers including control samples (C) at baseline, immediately after treatment (after Tx) and 8 h after treatment (after 8 h)

Sampling	TNF-α	MMP-9	BAX	TXNIP	BCL-2
Before	0.050 ± 0.002	0.088 ± 0.023	0.12 ± 0.01	28.89 ± 1.36	0.54 ± 0.13
After Tx	0.052 ± 0.001	0.083 ± 0.022	0.17 ± 0.01	35.43 ± 2.05	0.42 ± 0.07
After 8 h	0.107 ± 0.002	0.142 ± 0.027	0.14 ± 0.02	58.08 ± 8.50	0.40 ± 0.08
After Tx (C)	0.057 ± 0.007	0.081 ± 0.017	0.13 ± 0.02	24.31 ± 6.46	0.52 ± 0.07
After 8 h (C)	0.053 ± 0.003	0.083 ± 0.035	0.13 ± 0.01	26.07 ± 5.14	0.49 ± 0.10

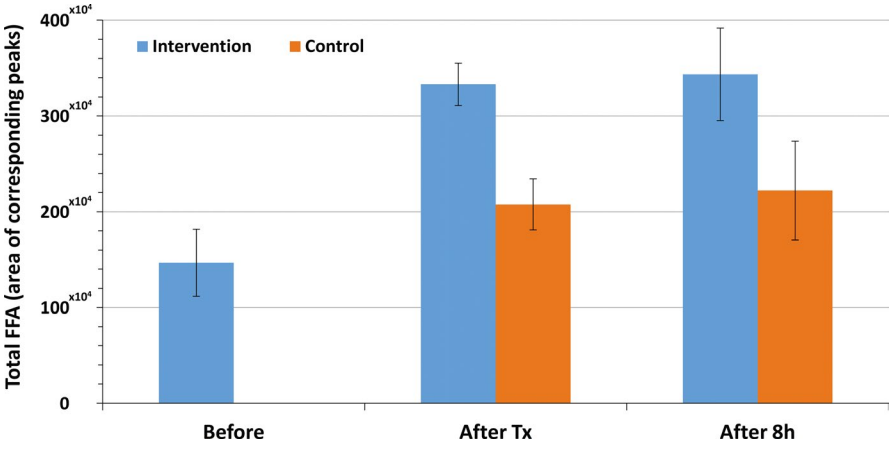

FIGURE 2 Results of total FFA amount in specimens (mean ± SD) at baseline, immediately after treatment (after Tx), and 8 h after treatment (after 8 h). Values correspond to the overall area under the peaks obtained by mass spectrometry

in the bloodstream right after the HIFEM application, the fat biopsies showed a strong pro-apoptotic reaction, as indicated by (but not limited to) the upregulated expression of TNF-α and MMP9, accompanied by a documented decrease in the levels of BCL-2. Examination of apoptotic markers and blood plasma was also complemented with the TUNEL analysis which showed an elevation of apoptotic index (ratio of apoptotic cells in the specimens) up to 35.95% at 8 hours after the treatment.

High-Intensity Focused Electromagnetic technology has proven itself to be safe. There were no adverse events, such as erythema, no change in epidermal/dermal integrity, or changed behavioral patterns in the treated animals. This observation is in line with previous research,[9,21,22] as no adverse events were reported in any of the previous studies.

This study provides novel findings that support the previously documented induction of ER stress apoptosis in subcutaneous tissue. Our investigation benefited from three different quantitative methods of evaluation, accompanied by control site measurements, utilized to further verify a link between the increased concentration of FFA and fat apoptosis.

Conversely, we are aware that these evaluation methods do come with limitations. One of the shortcomings is a relatively small sample size of only two animals, which did not allow us to perform a robust statistical analysis. Additionally, due to the short-term nature of studied treatments, we established the length of the follow-up examination up to 8 hours. This timeframe was similar to the previous study by Weiss et al[9] In future, a higher number of data points should be used, with an increased period of follow-up to determine and further understand the dynamics of this investigated phenomenon. Finally, we also need to consider that although the results of qPCR analysis coincided with the previous findings, the association between levels of BAX and BCL-2 might be a subject for a more detailed investigation. Also, the use of a porcine model, instead of a human trial, could be considered a limitation. Porcine models are widely recognized as an acceptable model for studies investigating digestion, diet, and fat metabolism, due to its similarities in gastro-intestinal tract, organ-size, genetics, dietary habits, and metabolism.[23-25] Due to the high similarity with humans, porcine subcutaneous fat is even often used as a model for studying RNA of subcutaneous adipose tissue.[26]

5 | CONCLUSION

Results of this animal study support the previously published findings, stating that HIFEM-induced contractions evoke a strong metabolic reaction, which can trigger a cascade effect resulting in FFA oversaturation. This rapid elevation of FFA levels appears to lead to the apoptosis of adipocytes, mediated through an endoplasmic reticulum stress reaction. We fully recognize, this studied phenomenon may not be the only mechanism involved and that other factors may play a role as well. Further research should be conducted to provide additional evidence and to test other hypotheses as well, as it is possible the outcome is a result of several other biochemical processes. Our research is only another piece into the puzzle which needs to be resolved, but our findings strongly indicate that FFA overflow plays significant a role.

CONFLICT OF INTEREST

Dr Bernardy and Dr Halaas have nothing to disclose.

ETHICAL APPROVAL

This prospective animal study was approved by the Institutional Animal Care and Use Committee (IACUC). The procedures were carried out according to the Good Laboratory Practices (GLP) standards, and animal care complied with the convention for the protection of vertebrate animals.

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CASE REPORT

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MRI Assessment of Arm and Calf Muscle Toning With High-Intensity Focused Electromagnetic Technology: Case Study

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ABSTRACT

Arms and calves have long been a subject of interest in aesthetic medicine. Current surgical and non-invasive procedures focus on sagging skin and fat deposits without targeting the muscles. The aim of this study is to investigate the feasibility of high-intensity focused electromagnetic (HIFEM) technology for arm and calf toning through simultaneous fat reduction and muscle strengthening. In this case study, two subjects received four 20-minute HIFEM treatments of biceps, triceps, and calves, with the outcomes assessed by MRI. The analysis of MRI images showed an average increase in all three muscle groups, biceps muscle mass 17.1%, triceps muscle mass 10.2%, and gastrocnemius muscle mass increased by 14.6%. In addition, the arm fat thickness was decreased by 12.8% on average and the calf fat thickness decreased by 9.9%. The results suggest that HIFEM technology is a feasible modality for both arm and calf toning. However, it will be necessary to continue to validate this outcome in a larger sample size study.

J Drugs Dermatol. 2020;19(5): doi:10.36849/JDD.2020.4546

INTRODUCTION

In terms of our daily lives, arms and legs play an important functional role. Interestingly, they also play a significant role in our perception of beauty. Many surgeons and physicians have thus been looking for ways of correcting or altering the forms and volumes of calves and upper arms.[1–3]

In fact, the popularity of arm lifting (brachioplasty) has grown rapidly in previous years, with a 2017 top 5 ranking for the fastest growing surgical procedures with more than 18,000 performed procedures in a single year.[4] Similarly, for calves, the most popular procedure is surgery, specifically the insertion of calf implants or autologous tissue transfer.[5] Although the surgical procedure shows effective results, they are inextricably linked with downtime, pain, scarring, and risk of complications. Furthermore, the arm procedures only deal with sagging skin and excess fat, while neglecting the role of underlying muscles in the resulting overall appearance. Currently, there are only moderately effective non-invasive arm lifting alternatives such as cryolipolysis[6,7] or radiofrequency[8,9] devices, which focus on skin tightening and reducing arm fat while the muscles remain untouched. However, to maximize the treatment outcome and results it is necessary to take into account both muscle and fat. An innovative tool for this purpose appears to be a high-intensity focused electromagnetic (HIFEM) technology, which has already been successfully used for the simultaneous abdominal muscle strengthening and reduction of abdominal fat.[10,11] Applicability of such an effect on arms would bring new treatment possibilities for both physicians and patients. Due to its effect on muscle, HIFEM could also be beneficial for the treatment of calves through toning the calf muscle and increasing its volume.

The goal of this case study is to investigate the efficacy of HIFEM technology for toning of arms and calves as an alternative tool to the current surgical as well as noninvasive procedures.

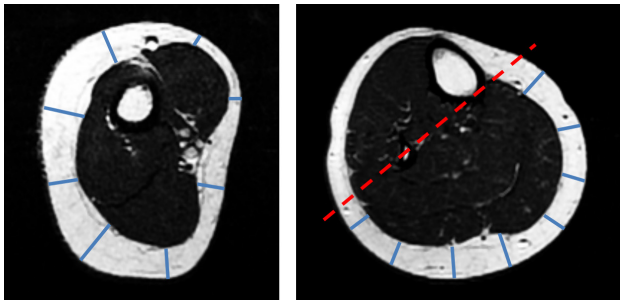
METHODS

One male (26 years) and one female (47 years) patients were recruited into the study. Both patients underwent the treatment of both calves and arms with a device utilizing HIFEM technology (EMSCULPT, BTL Industries Inc., Boston MA).

The treatment protocol consisted of 4 sessions scheduled twice a week for a two-week period. During each session, the patients received a 20-minute bilateral treatment for each muscle group, biceps/triceps, and calves. The calves and triceps treatments were administered in a prone position while the biceps treatment was applied in a supine position. The applicators were placed just under the treated muscle structure and the exact position was adjusted individually for the best muscle response. The applicators were always secured by a fixation belt.

To evaluate the treatment outcomes, the patients underwent MRI screening at baseline and 1 month after the last treatment. The scanned area for calves was defined by the knee and ankle and the scanned area for arms was defined by the shoulder and

FIGURE 1. Schematic illustration of measurement points used for the analysis of fat tissue (left – arm; right – calf).

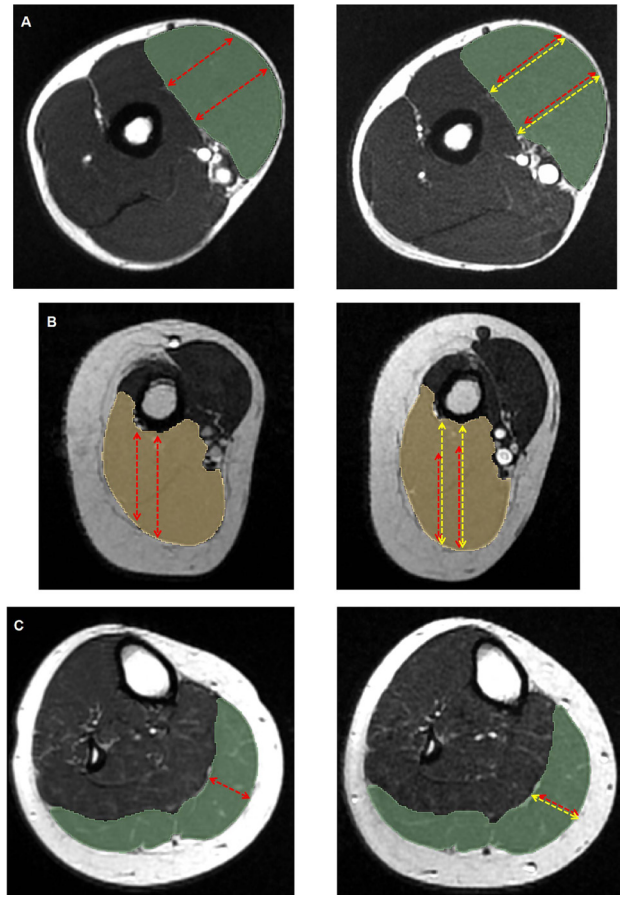


elbow joints. The MRI images for both treatment areas were acquired in the axial plane using the T1 fast spin-echo sequence with a slice thickness of 3 mm, matrix size 320x320, FOV 26, TR 200 ms. For each calf scan, the leg was bolstered under the ankle and the knee to avoid the suppression of the muscle. Similarly, for the arm scans, each arm was bolstered under the elbow.

To best analyze the changes in arm and calf muscle tissue, the biceps brachii m., triceps brachii m. and gastrocnemius m. were segmented in the MRI images. For each muscle, the slice with the largest cross-sectional area (CSA) was identified and was used for analysis along with two slices approximately 0.5 cm and 1 cm above and below this point (N=5 measurements). CSA for each of the slices and for each muscle was obtained and the average values were calculated. Segmented muscles can be seen in Figure 2.

To assess the changes in fat tissue, the fat thickness was measured in the same images which were used for muscle tissue analysis. For arms, the measurements were done at eight points equally sampled all around the arm circumference. For calves, the measurements were done only above the gastrocnemius m. at eight equally spaced points. Then, the average values were calculated. The points for fat measurements are displayed in Figure 1.

FIGURE 2. The B/A MRI images for biceps (A), triceps (B) and gastrocnemius (C).



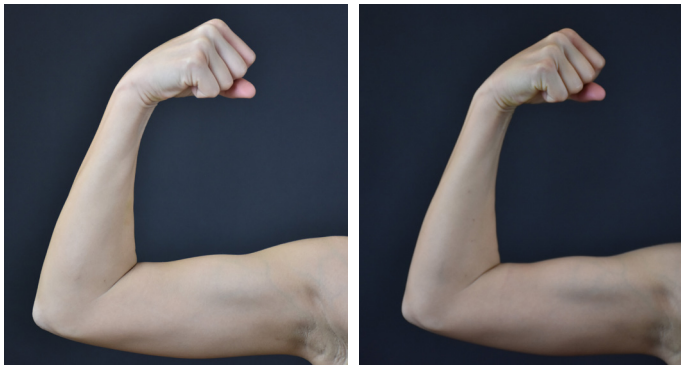
RESULTS

A single male and a female subject were recruited for the study to examine the HIFEM effects on different body compositions. Interestingly, it should be noted that the male subject had more than three times the muscle mass in comparison to the female subject. Both patients showed an increase in all three examined muscles; biceps brachii m., triceps brachii m., gastrocnemius m.

TABLE 1.

The Average Muscle CSA for Each Subject and Muscle (mean ± standard deviation)				
	Before (mm^2)	1M After (mm^2)	Diff. (mm^2)	Diff. (%)
Biceps_Male	1929.3 ± 37.2	2253.8 ± 5.0	324.4	16.8 %
Biceps_Female	589.4 ± 29.8	692.1 ± 4.7	102.7	17.4 %
Triceps_Male	3620.0 ± 98.7	4019.9 ± 76.8	399.9	11.1 %
Triceps_Female	1510.7 ± 37.6	1652.9 ± 22.2	142.3	9.4 %
Gastrocnemius_Male	3373.5 ± 79.4	3843.6 ± 85.1	470.1	13.9 %
Gastrocnemius_Female	2011.3 ± 67.4	2316.4 ± 85.2	305.1	15.2 %

FIGURE 3. Digital images of the female subject's biceps taken at baseline (left) and 1-month post-treatment (right). The red lines displayed at the baseline scans were duplicated into the 1-month scans to demonstrate the change.



Both subjects also showed a decrease in fat thickness, although the differences between the subjects were large.

The largest increase in the CSA was observed for the biceps brachii muscle as the average increase was 17.1%, while for triceps brachii it was 10.2%. The CSA of the gastrocnemius muscle was increased by 14.5% on average. Detailed results for each subject can be seen in Table 1. Examples of MRI images after the segmentation are shown in Figure 2.

The arm fat thickness for the male subject was decreased by 20.6% from 4.6 ± 2.3 mm to 3.7 ± 2.0 mm. The female subject lost 5.3% of her arm fat thickness as it decreased from 10.0 ± 3.8 mm to 9.5 ± 3.8 mm. The fat thickness on the calf was decreased by 11.9% for the male subject, from 4.6 ± 1.3 mm to 4.1 ± 1.2 mm. The female subject showed a reduction of 8.0%, from 12.3 ± 2.6 mm to 11.4 ± 2.5 mm.

Patients reported mild muscle fatigue after the treatments while no adverse events were reported. Digital photographs demonstrated aesthetic improvement in the treated area. The demonstration of the improvement in the biceps muscle observed for the female subject is shown in Figure 3.

CONCLUSIONS AND RECOMMENDATIONS

The MRI images showed an increase in muscle mass and a reduction in fat thickness after four HIFEM treatments, comparable with the results reported in previous studies.[10,11] Validation of observed results on a larger sample size is necessary.

The applicator placement appears to play a crucial role in the outcomes. It is interesting to note the anatomic individuality of each patient and the importance of proper applicator placement to achieve the largest muscle response, which differed subject to subject. Since HIFEM technology is based on stimulating motor neurons, the improper placement may not trigger contractions strong enough for the induction of a hypertrophic effect. It is thus important to pay special attention to the placement.

Based on the observed results, HIFEM technology appears to be feasible for arm and calf toning. Although it is necessary to collect data from a significantly larger sample size, the initial results provide a trace of what outcomes could be expected with a larger study population.

DISCLOSURES

The author has no conflict of interest to declare.

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JDD

DRUGS • DEVICES • METHODS

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC TECHNOLOGY (HIFEM) FOR NON-INVASIVE BUTTOCK LIFTING AND TONING OF GLUTEAL MUSCLES: A MULTI-CENTER EFFICACY SAFETY STUDY

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High Intensity Focused Electro-Magnetic Technology (HIFEM) for Non-Invasive Buttock Lifting and Toning of Gluteal Muscles: A Multi-Center Efficacy and Safety Study

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ABSTRACT

Objective: Surgical intervention has been the only method to improve the aesthetic appearance of buttocks apart from physical exercising. This study evaluates the efficacy of high intensity focused electro-magnetic (HIFEM) treatments as a non-invasive solution for improvement of buttocks through toning and lifting of gluteal muscles.

Materials and Methods: A total of 75 patients (aged 22-59) were treated using a device with HIFEM technology which stimulates gluteal muscles (EMSCULPT, BTL Industries, Boston, MA). The protocol included four 30-minute treatments. Patients' weight was monitored throughout the study. Standard photographs were taken at the baseline, after the 4th treatment, and at the 1-month follow-up. Two 7-point Likert scale questionnaires were used to evaluate patients' buttock and treatment satisfaction. Total score of buttock satisfaction was calculated as a sum of all individual questions to reflect the overall perception of patients' buttocks. The level of comfort during procedures was assessed on a visual analog scale (VAS).

Results: The overall buttock satisfaction score (range, 4-28) of all subjects improved from 13.1±5.7 at baseline to 18.4±5.2 after the treatment and 18.9±5.1 at follow-up. For subjects with initial buttock dissatisfaction the scores improved from 8.7±1.6 to 16.3±3.1 after the treatment and to 17.3±3.1 at follow-up. The average score of all treatment satisfaction questions (range, 1-7) was 5.2±1.2 immediately after the treatments and 5.1±1.3 at follow-up. In total, patients initially dissatisfied with the appearance of their buttocks reported a significant 85% improvement after the fourth treatment. Immediately after the fourth treatment, all the subjects reported that their buttocks felt more lifted and toned. Results were maintained at one-month follow-up. Weight of the patients didn't change significantly. Digital photographs showed aesthetic improvements of the buttocks for most of the patients. No adverse events were reported.

Conclusion: The results show that the investigated device safely and effectively improves the aesthetic appearance of buttocks non-invasively. The treatments not only resulted in a significant visual improvement but also increased patient confidence and satisfaction. The procedure is suitable for patients seeking improvement in tone, shape, lift, and tightness of the buttocks.

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INTRODUCTION

The popularity of surgical butt lifting, and augmenting procedures is rapidly growing. Since 2015, the number of performed procedures increased on average by 25% each year,[1] while the increase over the past two decades totals 342%,[2] with the total expenditures for these type of procedures reaching 120 million USD in 2016.[2] The most popular methods are represented by buttock augmentation using silicone implants, autologous fat grafting, and a traditional butt lift done by cutting out an ellipse of excess skin and suturing the remaining skin back together. In general, these procedures are associated with one to four weeks of downtime.[2]

Surgical procedures are associated with risk of complications. The rate of complications related to buttock augmentation using silicone implants were reported to be as high as 21.6%[3] and 38.1%,[4] while for autologous fat grafting complications were reported to occur in 9.9% of all cases.[3] The most common complications are wound dehiscence, seroma, and infection.[3] Further-

FIGURE 1. A photograph of a patient during an ongoing treatment.

more, all surgical procedures focus on artificially increasing the subcutaneous volume of buttocks, yet they do not target the underlying gluteal muscles, which play a crucial role in the buttock shape definition and overall aesthetic appearance of buttocks.

Magnetic stimulation has been widely and successfully used before, eg, in the treatment of incontinence by strengthening the pelvic muscles,[7] in cough restoration,[8] or in augmentation of resistance training.[9] This study investigates the efficacy and safety of a high-intensity focused electro-magnetic (HIFEM) technology (EMSCULPT, BTL Industries, Boston, MA) when used for non-invasive improvement of the appearance of buttocks. The device delivers magnetic impulses into the tissue where it stimulates the gluteal muscles (gluteus maximus, medius, and minimus) and induces supramaximal contractions of all these muscle groups simultaneously. The muscle tissue is forced to adapt to the supramaximal load, which then leads to muscle hypertrophy and hyperplasia.[5,6] As a result, the gluteal muscles responsible for the aesthetic appearance of buttocks increase in size and become firmer. This application has been shown to lead to an improvement of buttock shape.

MATERIALS AND METHODS

In total, 76 subjects (74 females and 2 males) participated in the study. The age of recruited subjects ranged between 22 and 59 years (average, 36.6±8.3) with average BMI 21.5±2.2 kg/m^2. The participants received bilateral treatments of buttocks with a novel device based on the HIFEM technology (EMSCULPT, BTL Industries, Boston MA). The therapy protocol consisted of 4 treatment sessions which were spaced by 2-3 days, each session including 30 minutes of application. During the treatment, subjects were placed in a prone position and the applicator of the device was placed over the buttocks to simultaneously affect all the gluteal muscles as seen in Figure 1. A fixation belt was used to avoid any movements of the applicator during the treatment. The output intensity was kept just below each patient's tolerance threshold in order to maintain the supramaximal contractions throughout the entire treatment.

Patients were evaluated at the baseline, after the last treatment, and at 1-month follow-up. Digital photographs of the treated area were taken, and patients' weight were measured as a control indicator. Two different non-standardized questionnaires based on 7-point Likert scales were used to assess the effects of the treatment. The buttock satisfaction questionnaire focused on measuring if the treatments can change the way patients perceive and/or think about the appearance of their buttock area. The total possible score ranged from 4 points (lowest possible satisfaction) to 28 points (highest possible satisfaction). See Table 1. The responses were compared between the baseline, post-treatments, and the follow-up. After the last treatment and at the follow-up, the second questionnaire was used to evaluate patients' satisfaction with the results of the treatments. See Table 2. Average scores were calculated, and a paired t-test was used for statistical analysis.

A visual analogue scale (0-10) was used to assess the level of comfort during the treatments. Any side effects or adverse events were monitored.

RESULTS

In total, 75 subjects (73 females and 2 males) completed the full treatment protocol; four subjects withdrew before the follow-up for reasons unrelated to the study. The results presented herein thus include data from 71 subjects.

FIGURE 2. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). Female, 31 years old.

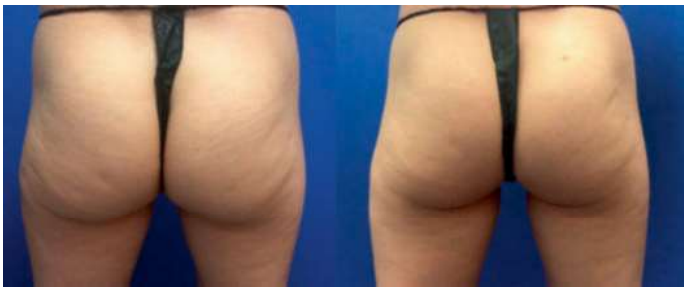

FIGURE 3. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). The demarcation line shows the improvement and lifting of the gluteal fold.

The average buttock satisfaction scores significantly improved (P<0.01) after the last treatment and at the one-month follow-up, both when measured as a total and individually for each question. The total average score increased by 40.5% from 13.1±5.7 at the baseline to 18.4±5.2 post-treatments, and further improved to 18.9±5.1 at the follow-up. The most significant improvement was seen in patients who were initially dissatisfied with the appearance of their buttocks prior to the treatments, with the average score increasing by 83% from 8.7±1.6 to 16.3±3.1 after the treatment, and on to 17.3±3.1 at the follow-up. See Table 1.

Statistical analysis of the results revealed that 69% of patients who initially reported buttock laxity improved to a higher degree of buttock tightness post-treatments and at the follow-up. In total, 85% of the patients initially dissatisfied with the appearance of their buttocks reported a significant improvement immediately after the fourth treatment, which was maintained over the course of one-month follow-up. Furthermore 80% of the patients initially dissatisfied with the shape of their buttocks reported a significant improvement immediately after the fourth treatment and during the follow-up. 79% of patients with low confidence while wearing the bikini at baseline felt significantly more confident after the fourth treatment and continued to feel confident during one-month follow-up.

In the patient satisfaction questionnaire, 76% of patients reported that the appearance of their buttock area has been improved after the treatments and during the one-month follow-up, while 80% of all the patients reported that their buttocks felt more lifted and toned right after the fourth treatment as well as at the follow-up. In total, 71% of all patients were satisfied with the treatment results immediately after the fourth treatment as well as during the one-month follow-up. The average scores can be seen in Table 2.

Patients found the treatments comfortable with an average VAS score of 2.01 (corresponding to none or very mild discomfort).

The analysis of weight did not show significant changes. No adverse events were observed during the treatments nor as a consequence of the treatments. Digital photographs showed improvements in aesthetic appearance of the buttocks. See Figures 2 and 3 for examples of patient images.

DISCUSSION

As of today, there are no standardized measurement tools that could be used for evaluation of a non-invasive improvement of buttocks. This can primarily be attributed to the fact that most currently used methods are surgical by nature. The study presented focused mainly on the evaluation of the subjective perception of the treated patients. This subjective satisfaction assessment was then further supported by visual improvement captured in digital images.

The results show a statistically significant positive trend in all of the measured criteria. This suggests that the treatments can have a positive effect on the way patients perceive the ap-

TABLE 1.

Buttock Satisfaction Questionnaire Results					
Question (Score range, 1-7)	Baseline	After	Change	1M FU	Change
Please rate your subjective perception of your buttock laxity/tightness[1]					
Total (n=75)	3.4±1.6	4.6±1.5	+1.2 (P<0.01)	4.8±1.3	+1.4 (P<0.01)
Baseline score <4 (n=42)	2.2±0.7	4.0±1.6	+1.8 (P<0.01)	4.5±1.4	+2.3 (P<0.01)
I am satisfied with the overall aesthetic appearance of my buttocks[2]					
Total (n=75)	3.2±1.5	4.8±1.3	+1.6 (P<0.01)	5.0±1.5	+1.8 (P<0.01)
Baseline score <4 (n=46)	2.2±0.7	4.4±1.5	+2.2 (P<0.01)	4.6±1.6	+2.4 (P<0.01)
I am satisfied with the shape of my buttocks[2]					
Total (n=75)	3.4±1.6	4.7±1.6	+1.3 (P<0.01)	4.9±1.4	+1.5 (P<0.01)
Baseline score <4 (n=45)	2.3±0.7	4.1±1.6	+1.8 (P<0.01)	4.5±1.5	+2.2 (P<0.01)
I feel confident about my buttock area when wearing the bikini[2]					
Total (n=74)	3.1±1.6	4.4±1.5	+1.3 (P<0.01)	4.3±1.6	+1.2 (P<0.01)
Baseline score <4 (n=48)	2.0±0.7	3.8±1.4	+1.8 (P<0.01)	3.7±1.6	+1.7 (P<0.01)
Total score	13.1±5.7	18.4±5.2	+5.3 (P<0.01)	18.9±5.1	+5.8 (P<0.01)
Total score (Baseline score < 4)	8.7±1.6	16.3±3.1	+7.6 (P<0.01)	17.3±3.1	+7.2 (P<0.01)

[1]1 – Very loose, 2 – Moderately loose, 3 – Slightly loose, 4 – Neither loose/tight, 5 – Slightly tight, 6 – Moderately tight, 7 – Very tight.
[2]1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

TABLE 2.

Treatment Satisfaction Questionnaire Results		
Question (range, 1-7)[1]	After	1-month FU
The appearance of my buttock area has been improved after the treatments	5.0±1.4	5.2±1.4
My buttocks feel more lifted and toned after the treatments	5.3±1.3	5.2±1.4
I am satisfied with the treatment results	5.2±1.3	5.1±1.4
I would recommend the treatment to a friend	5.1±1.5	4.9±1.5
AVERAGE SCORE	5.2±1.2	5.1±1.3

[1]1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

pearance of their buttocks, their level of confidence and overall satisfaction.

For the analysis of subjects' buttock satisfaction, the data was adjusted for patients who initially had a negative perception of their buttocks (score <4) as this would likely be the primary target group of the treatments. This group showed greater improvements than the total study population, which suggests that this sub-group of initially dissatisfied patients are the ideal profile that can most benefit from the treatments.

Visual inspection of digital photographs showed visible aesthetic improvement in most patients. The best results were seen in patients with lower BMI and in patients who reported a more active lifestyle. However, patient expectation management is crucial as the changes to the buttocks should not be compared to any surgical intervention. Rather than large volume augmentation, the patients in this study showed a lifting effect coupled with an improvement in their gluteal folds, as well as an increase in the overall buttock tightness. We thus suggest that the investigated device should not be considered a replacement for a surgical butt lift procedure yet brings a new alternative to patients seeking more toned and athletically appearing buttocks.

CONCLUSION

The EMSCULPT device proved to be effective and safe for non-invasive improvement of the aesthetic appearance of the buttocks. Future research should focus on bringing more evidence based investigational methods for the evaluation of non-invasive buttock treatments.

DISCLOSURE

Carolyn Jacob MD and Brian Kinney MD are medical advisors for BTL. Mariano Busso MD and Suneel Chilukuri MD are speakers for BTL. The other authors have no financial interest to declare in relation to any of the products or device mentioned in this article.

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Induction of Fat Apoptosis by a Non-Thermal Device: Mechanism of Action of Non-Invasive High-Intensity Electromagnetic Technology in a Porcine Model

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Objectives: While controlled thermal changes in subcutaneous tissue have been used to trigger apoptosis of fat cells and have been proven clinically efficacious, another mechanism of electromagnetic stress suggests that fat apoptosis could be achieved by a non-thermal manner as well. This animal model study investigates the use of a non-invasive high-intensity magnetic field device to induce apoptosis in fat cells.
Methods: Yorkshire pigs ($N = 2$) received one treatment (30 minutes) in the abdominal area using a High-Intensity Focused Electromagnetic (HIFEM) device. Punch biopsy samples of fat tissue and blood samples were collected at the baseline, 1 and 8 hours after the treatment. Biopsy samples were sectioned and evaluated for the levels of an apoptotic index (AI) by the TUNEL method. Statistical significance was examined using the rANOVA and Tukey's test (α 5%). Biopsy samples were also assessed for molecular biomarkers. Blood samples were evaluated to determine changes related to fat and muscle metabolism. Free fatty acids (FFA), triacylglycerol (TG), glycerol and glucose (Glu) were used as the main biomarkers of fat metabolism. Creatinine, creatinine kinase (CK), lactate dehydrogenase (LDH) and interleukin 6 (IL6) served as the main biomarkers to evaluate muscle metabolism.
Results: In treated pigs, a statistically significant increase in the apoptotic index (AI) ($P = 1.17E\text{-}4$) was observed. A significant difference was found between AI at baseline (AI = 18.75%) and 8-hours post-treatment (AI = 35.95%). Serum levels of fat and muscle metabolism indicated trends (FFA $-0.32\,mmol \cdot l^{-1}$, -28.1%; TG $-0.24\,mmol \cdot l^{-1}$, -51.8%; Glycerol $-5.68\,mg \cdot l^{-1}$, -54.8%; CK $+67.58\,\mu kat \cdot l^{-1}$, $+227.8\%$; LDH $+4.9\,\mu kat \cdot l^{-1}$,$+35.4\%$) suggesting that both adipose and muscle tissue were affected by HIFEM treatment. No adverse events were noted to skin and surrounding tissue.
Conclusions: Application of a high-intensity electromagnetic field in a porcine model results in adipocyte apoptosis. The analysis of serum levels suggests that HIFEM treatment influences fat and muscle metabolism. Lasers Surg. Med. © 2018 Wiley Periodicals, Inc.

Key words: apoptosis; fat disruption; HIFEM; magnetic technology; non-thermal

INTRODUCTION

High body dissatisfaction rates of up to 60.7% in males and 71.6% in females caused by sedentary lifestyle and unbalanced diet led to a rapid increase in demand for noninvasive fat reduction [1]. The most common non-invasive fat reduction procedures in aesthetic medicine are cryolipolysis, radiofrequency or thermal laser therapy [2] but none of these procedures deal with the underlying musculature, which highly contributes to the firm and toned body look.

A plausible muscle affecting technology appears to be electromagnetic muscle stimulation which has been previously used for muscle training [3–8]. This technology utilizes the concept of electromagnetic induction first described by Faraday in 1831. A wire coil generates an intense alternating magnetic field, which consequently induces a secondary electric current in the underlying tissue where it interacts with neurons. When the induced current in the tissue is of high magnitude, it can depolarize motor neurons and therefore trigger muscle contractions. Predominantly motor neurons are activated due to their large diameter and thus lower resistance in comparison to other types of neurons. Since the nociceptors are not activated, the application of magnetic stimulation is not painful [9].

The electromagnetic pulses are delivered in a high-frequency rate prohibiting muscle relaxation which results in a phenomenon referred to as supramaximal or tetanic contractions, not reproducible by voluntary muscle contraction. The study by Kent et al. [10] investigated the high intensity focused electromagnetic technology utilizing the principles of electromagnetic stimulation and found that

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: Robert Weiss is a medical advisor and speaker for BTL. Jan Bernardy has no conflicts to declare.

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therapy composed of four 30-minute sessions lead to a 16 % increase in abdominal muscle thickness and 19% reduction in the abdominal fat layer. As the treatment directly affects muscles, the continuity with reduced fat thickness is not clear.

We hypothesize that the induced supramaximal contractions may lead to an increased metabolic activity in the region of stimulation and subsequent breakdown of lipids into free fatty acids (FFA) and glycerol [8,11–13] as seen during intensive resistance training [14,15]. In the case of supramaximal contractions, the lipid breakdown could lead to overflow of free fatty acids (FFA) in the intracellular space. When the amount of FFAs exceeds a certain level in the intracellular space, this may lead to adipocyte dysfunction [16–19]. An increased intracellular concentration of FFA may also lead to the natural death of affected cells by a mechanism of the endoplasmic reticulum (ER) stress-induced apoptosis. The principle of ER stress and its contribution to apoptosis induction has been previously described by Hardy et al. [20] and Gunduz et al. [21], who studied the effect of FFA in treating cancerous cells. According to results published by Zhang et al. [22], it was confirmed that ER stress contributes to apoptosis induced by increased levels of FFAs. It may thus seem plausible to hypothesize that if high enough concentration of FFAs in adipose tissue is released through a metabolic reaction, incremental apoptotic processes could also be triggered in adipocytes *via* similar mechanisms.

Our study investigates a novel concept to induce cellular stress with increased FFAs leading to adipocyte apoptosis using High-Intensity Focused Electromagnetic (HIFEM) technology. The first step in investigating this phenomenon and the goal of this study is to examine whether a single High-Intensity Focused Electromagnetic treatment leads to apoptosis of adipocytes in a porcine model.

MATERIALS AND METHODS

The Institutional Animal Care and Use Committee (IACUC) and the committee for animal protection approved this study. Animal care complied with the convention for the protection of vertebrate animals used for experimental and other scientific purposes. The animals were treated under general anesthesia to minimize their discomfort. Animals were anesthetized under the supervision of a veterinarian who chose the anesthetic type and dosing. The study was conducted on three Yorkshire pigs (approx. 6 months old, 80 kg of live weight). Two pigs underwent the treatment; one pig served as a control subject.

The EMSCULP device (BTL Industries Inc., Marlborough, MA) was used to generate the high-intensity focused electromagnetic pulses for the treatment. The focused circular coil of the device generates electromagnetic pulses with the intensity of up to 1.8 Tesla. Areas on the *abdomen* in the region of the rectus abdominis in the porcine subjects were shaved and marked. Fat thickness was measured using ultrasonography (Mindray M5Vet) to ensure the treatment was applied to an area with sufficient fat deposits. The applicator was placed over the marked spot (diameter 15 cm) and secured using a Velcro belt. The time of procedure was set at 30 minutes with the intensity being 100% of the applicator output.

Punch biopsy samples of fat tissue together with blood samples were collected before treatment (baseline), 1 hour and 8 hours after the treatment. Biopsy samples were taken using a disposable biopsy punch (diameter 6 mm), and the incisions were sutured after the sample collection. Fat tissue samples for Apoptotic Index (AI) measurement was preserved in 4% neutral buffered formaldehyde, dehydrated, cleared, embedded with paraffin wax and sectioned to 5 μm thick slices. Tissue was stained for terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL). TUNEL is a standard method used for detecting DNA fragmentation that results from apoptotic signaling cascades. Apoptotic events in the specimens were quantified using AI which is a measure of the number of the apoptotic events expressed as a ratio or percentage of all cells counted.

Biopsy samples were also evaluated for molecular biochemistry apoptotic and antiapoptotic markers. Total RNA free of DNA contamination was obtained by isolation method using Tri RT Reagent (MRC, Cincinnati, USA) and was further purified using RNeasy Mini Kit columns (Qiagen, Darmstadt, Germany). M-MLV reverse transcriptase and oligo(dT) primer specific to mRNA were used to cDNA generation. Expression of 11 genes involved in apoptotic processes (TNF-α, IL-1β, IL-10, TIMP-1, TGF-β1, MMP 9, VEGFA, FGF-7, BAD, Bcl-2, TRX-2) was calculated according to the formula introduced by Zelnickova et al. [23] while HPRT1 gene was chosen as reference. QIAGEN QuantiTect SYBR Green PCR MasterMix was used for qPCR performed on a LightCycler 480 (Roche, Basel, Switzerland) under following conditions: denaturation at 95°C for 15 minutes and 45 amplification cycles at 95°C for 15 s, 58°C for 30 s and 72°C for 30 s. Gene-specific primers were designed using NCBI primer designing software Primer-Blast. Each sample was run in triplicate. The resulting melting curves were analyzed to test the product specificity using LightCycler 480 software 1.5.0.39. Non-template controls were included in each part of the gene expression assessment.

Additionally, to measure parameters related to safety as well as to fat/muscle metabolisms, blood samples were obtained. The safety parameters for liver and kidney function and lipid metabolism are mentioned in Table 2 and include: Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Cholesterol (Chol), Urea, Total protein (TP), Albumin (Alb), Calcium (Ca), Magnesium (Mg), Phosphorus (P) and Ferrum (Fe). Besides the safety parameters, the stability of the blood parameters involved in fat [24] or muscle metabolism [25–27] was observed including: Free fatty acids (FFA), Glucose (Glu), Triacylglycerol (TG), Glycerol, Creatinine (Crea), Creatinine kinase (CK), Lactate dehydrogenase (LDH) and Interleukin 6 (IL6). All data were evaluated using MINDRAY BS 200 Chemistry analyzer, except for the FFA, IL6, and GLY which were investigated using ELISA Test Kits (FFA Quantification Kit (Abcam),

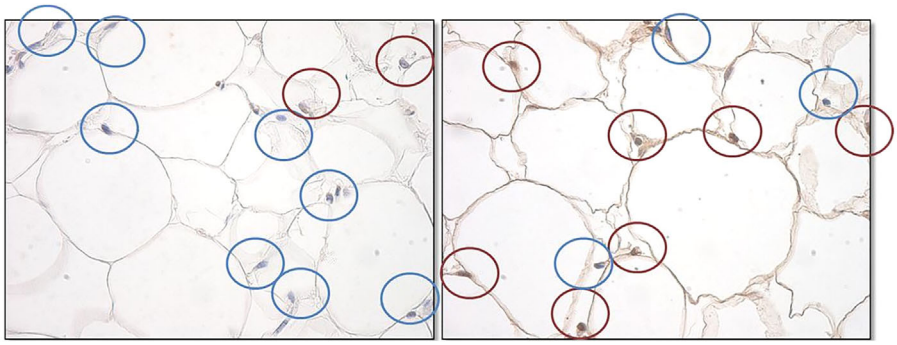

Fig. 1. Histological examination of apoptosis in pig fat tissue (TUNEL method). Apoptotic nuclei are marked brown, while the intact nuclei are marked blue. There was an increase in the number of apoptotic nuclei after the treatment.

Porcine IL-6 Quantikine ELISA Kit (Bio-techne R&D systems) and Glycerol Colorimetric Assay Kit (Cayman Chemical). Fluctuations of the studied parameters were evaluated concerning their reference ranges in pigs [28].

To investigate the statistical significance of changes in the apoptotic index on a total of 90 tissue samples we used a repeated measures ANOVA test (rANOVA). Tukey's test for equal sample sizes was used for post-hoc analysis, to identify significant changes. Significance level α was set in both as 5%. Blood parameters and RNA apoptotic markers were not statistically tested as only one sample was collected from each subject at a time.

RESULTS

Post-anesthesia the porcine subjects recovered well without any observable adverse effects. No erythema, change in skin texture, an increase in skin temperature, scarring or ruptures were seen. Analysis of the histology from treated pigs confirmed an increased number of apoptotic fat cells as predicted (Fig. 1). A statistically significant difference ($P = 1.17\text{E-}4$) was found between the baseline and 8-hour post-treatment measurements while the change in AI in the control pig was insignificant ($P = 0.15$).

An increase in the AI was observed in the two treated porcine subjects (Fig. 2). The highest average percentage of apoptotic cells in the total number of cells was measured at 1-hour after treatment in porcine subject #1 (43.10%). On average, apoptotic nuclei were observed to be at 18.75% at baseline, then 29.40% one hour after treatment and 35.95% 8 hours after treatment (Fig. 3). The control (untreated) animal did not show any significant increase in AI ($P > 0.05$).

Results of RNA apoptotic markers evaluation are summarized in Table 1. All the examined markers measured in treated pigs showed increased values 1 hour after treatment. Except for the IL-1β (which is also a mark of extreme muscular activity) their values decreased at 8 hours after the treatment. The highest relative increases were observed in the case of Pro-Apoptotic markers TNF-α (from 0.05 to 5.84) and MMP 9 (from 0.27 to 5.21). The Anti-apoptotic markers also changed considerably (especially the TIMP-1 and TRX-2 markers). The apoptotic markers of control pig showed only minimal fluctuations over the course of the study.

Biochemistry analysis of plasma samples demonstrated no severe abnormalities of safety parameters. Urea, TP, and Alb showed slight but negligible fluctuations over their reference ranges. In addition, data obtained from the control pig indicated stability of measured parameters. Results are summarized in Table 2.

In comparison to the control subject, the changes in parameters involved in fat metabolism were observed. The FFA and Glycerol showed an initial increase over the reference range 1-hour post-treatment, with a drop to almost half of their initial levels at 8 hours post-treatment. Similar

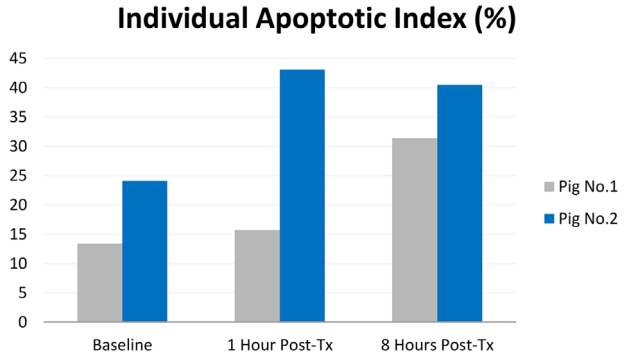

Fig. 2. Average AI (%) evaluated in each pig individually.

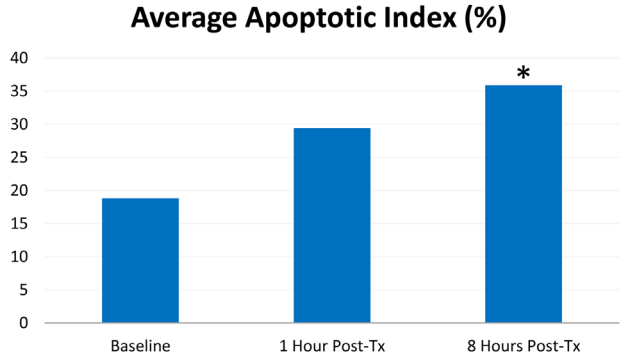

Fig. 3. Average AI (%). In treated subjects, there were on average 35.95% of apoptotic nuclei observed at 8 hours post-tx. An asterisk symbol (*) marks the statistically significant difference against the baseline.

findings were observed when evaluating the level of TG or GLU; nevertheless, the concentration of glucose remained within the reference range during the whole study.

Evaluation of parameters associated with muscle activity (specifically LDH and CK) showed an increase at 8 hours post-treatment in treated pigs. Both compounds exceeded reference ranges. LDH catalytic activity has increased by 35.40% from 13.84 $\mu kat \cdot l^{-1}$ to 18.74 $\mu kat \cdot l^{-1}$ while CK catalytic activity increased by 227.80% from 29.67 $\mu kat \cdot l^{-1}$ to 97.25 $\mu kat \cdot l^{-1}$. See Figures 4 and 5. The amount of IL6 has only barely changed and remained stable at zero (or close to zero) levels in all subjects. It's increase after 8 hours after the therapy was assessed as inappreciable, while the same tendency was also observed in the control pig. The creatinine level was stable, and despite slight fluctuations, it's level remained within the reference range in both control and treated groups.

DISCUSSION

This study was designed to investigate the clinical effect of HIFEM treatment in a porcine model. The primary finding was the statistically significant ($P < 1.17E\text{-}4$) increase in fat cell apoptotic activity. The high frequency oscillating magnetic field primarily affects the motor nerves in the treated area [29,30] causing supramaximal muscle contraction which then increases intracellular concentrations of FFA. This continuous release of FFA typically provokes a stress-induced apoptotic response [31,32].

The observed histological changes are comparable to previously published data evaluated on porcine models [33–35] and human volunteers [36], using thermal effect based devices. Based on previous findings it was also documented that adipocytes apoptosis cause a reduction of the fat layer. Nevertheless, due to the non-thermal nature of the magnetic field, no inflammatory responses were noted during our study.

Stability of safety parameters after treatment confirms the safety of the technology, although some of the parameters showed slight fluctuations above or below the reference ranges. However, these fluctuations were classified as irrelevant and related to the preparation of animals for the treatment procedure. The anesthesia most likely caused the slightly increased level of Urea 8 hours after treatment due to reduced water consumption. Total protein levels decreased as a response to starvation diet as a part of the preparation for anesthesia. Stability of cholesterol concentration follows findings from literature as general anesthesia or fasting before therapy did not affect cholesterol blood level [37].

Analysis of RNA markers involved in apoptotic processes revealed that tissue exposed to HIFEM treatment demonstrated a pro-apoptotic reaction. Several studies have documented the role of TNF-α in adipocyte apoptosis. It serves as the critical regulator of immune response, in part by inducing apoptosis during which its levels increases [38–40]. During apoptosis and pro-inflammatory processes, it influences the activity of other adipocytokines, such as tissue inhibitor of metalloproteinase (TIMP-1) [41] and matrix metalloproteinase 9 (MMP-9) [42]. The

TABLE 1. Results of RNA Apoptotic Markers Evaluation

		Control			Treated		
Parameter	Function	Before	1 hour Post-Tx	8 hours Post-Tx	Before	1 hour Post-Tx	8 Hours Post-Tx
TNF-α	P	0.11	0.08	0.12	0.05	5.84	0.16
IL-1β	P	0.14	0.11	0.14	0.09	0.14	0.20
IL-10	A	0.12	0.17	0.14	0.10	0.51	0.11
TIMP-1	A	1.86	1.11	2.09	0.71	7.54	1.93
TGF-β1	Both	0.72	0.74	0.81	0.51	1.30	0.30
MMP 9	P	0.23	0.25	0.27	0.19	5.21	0.17
VEGFA	A	1.13	1.56	0.81	1.36	2.28	0.59
FGF-7	A	0.33	0.86	1.47	0.57	3.97	2.79
BAD	P	0.57	0.55	0.64	0.47	1.20	0.73
BCL 2	A	1.32	1.27	1.47	3.23	3.86	1.59
TRX-2	A	11.93	18.13	13.39	11.77	73.98	16.63

The function of an evaluated marker can be Pro-Apoptotic (P), Anti-Apoptotic (A) or both (B). All values are expressed as a ratio to reference value.

TABLE 2. Summary of Plasma Blood Parameters of the Treated and Control Animals

		Control			Treated			
Parameter	Unit	Before	1 hour Post-Tx	8 hours Post-Tx	Before	1 hour Post-Tx	8 hours Post-Tx	Reference range (Min to Max)
ALT	$\mu kat \cdot l^{-1}$	0.66	0.61	0.65	0.79	0.80	0.84	0.50–1.00
AST	$\mu kat \cdot l^{-1}$	0.41	0.46	0.46	0.50	0.53	0.53	0.10–1.00
ALP	$\mu kat \cdot l^{-1}$	2.49	2.35	2.63	4.56	4.52	4.60	2.00–5.10
CK	$\mu kat \cdot l^{-1}$	29.99	26.08	31.71	29.67	28.83	97.25	0.00–35.00
LDH	$\mu kat \cdot l^{-1}$	10.94	11.04	10.29	13.84	13.74	18.74	3.90–11.50
Glu	$mmol \cdot l^{-1}$	5.46	4.19	4.70	5.11	5.84	5.04	3.80–6.40
Crea	$\mu mol \cdot l^{-1}$	114.85	109.62	138.78	130.36	125.47	129.27	88.00–145.00
Urea	$mmol \cdot l^{-1}$	2.00	3.00	4.00	4.88	4.88	6.06	3.00–6.00
TP	$g \cdot l^{-1}$	60.21	57.27	59.88	60.71	61.01	59.28	60.00–85.00
Alb	$g \cdot l^{-1}$	36.10	35.20	36.70	31.81	31.56	31.95	35.00–45.00
TG	$mmol \cdot l^{-1}$	0.14	0.10	0.12	0.56	0.52	0.27	0.00–0.50
Chol	$mmol \cdot l^{-1}$	2.32	2.41	2.67	2.40	2.37	2.29	2.00–3.30
Ca	$mmol \cdot l^{-1}$	2.46	2.35	2.38	2.44	2.47	2.36	2.30–3.10
Mg	$mmol \cdot l^{-1}$	0.74	0.69	0.76	0.82	0.82	0.82	0.50–1.20
P	$mmol \cdot l^{-1}$	2.46	2.42	2.61	2.61	2.38	2.60	2.10–3.30
Fe	$\mu mol \cdot l^{-1}$	19.80	21.30	20.80	21.65	22.25	18.65	18.00–35.00
FFA	$mmol \cdot l^{-1}$	0.70	0.42	0.60	1.14	1.50	0.82	0.00–1.00
IL6	$ng \cdot l^{-1}$	0.00	0.00	0.22	0.00	0.00	0.25	0.00–5.50
Glycerol	$mg \cdot l^{-1}$	3.06	3.83	4.79	10.36	11.03	4.68	0.00–10.00

increase of Thioredoxin-2 (TRX-2) mitochondrial protein that serves as a cell protector against oxidative stress induced apoptosis [43] may be explained either by its reaction to macrophage products or by the intensive muscle activity [44].

Bcl-2 belongs to a growing family of proteins which contain both anti- and pro-apoptotic members. During certain apoptosis pathways, it is dysregulated by pro-apoptotic protein BAD, which activity is related to TNF-α [45]. Anti-inflammatory cytokine IL-10 also upregulates during adipocyte apoptosis as a part of the signaling pathway between adipocytes and macrophages [40]. Changes were also observed in the TGF-β1 marker which plays a role in many cellular functions including cell proliferation, growth, differentiation, and it can provide signals for both cell survival and apoptosis. Results show that due to its increased numbers, HIFEM treatment may have an impact on TGF-β1 apoptotic regulations [46]. Only the IL-1β marker has maintained a growing tendency 8 hours after the treatment. Besides apoptosis, this marker is also related to extreme muscular activity [47]. This could explain its elevated levels at the time of the last measurement, which coheres with the observation of parameters related to intense muscle activity (CK and LDH). A similar mechanism may also explain the slightly increased levels of vascular endothelial growth factor A (VEGFA), angiogenesis inducing protein, of which intensive workout [48] might also upregulate expression in adipose tissue.

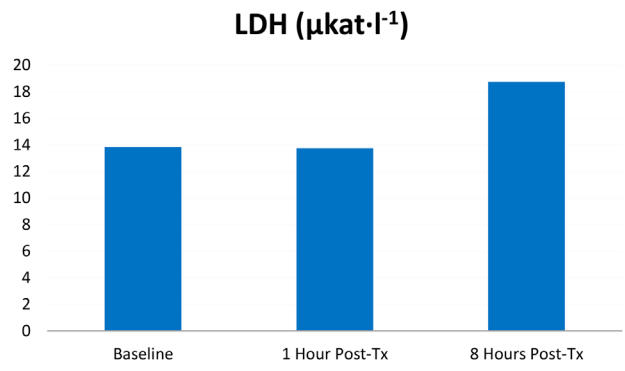

Fig. 4. Increase of LDH catalytic activity in porcine serum levels.

Increased levels of CK and LDH indicated extensive muscle activity. Elevation of these parameters after an intense muscle activity was also observed in other studies [25] on human subjects. CK is an enzyme that catalyzes the conversion of creatinine during muscle activity. Exercise increases the outflow of CK to the bloodstream with delayed onset [49]. The highest catalytic activity of CK in our study was measured 8-hours post-treatment ($97.25\,\mu kat \cdot l^{-1}$) and greatly exceeded the reference range. LDH is an enzyme which is also involved in muscle metabolism. It catalyzes the conversion of lactate to pyruvic acid and *vice versa*. This correlates with previous observations that LDH levels in blood serum increase considerably after intensive exercise in human subjects [25]. Similarly to CK, LDH levels in our study reached the highest values 8 hours after treatment (catalytic activity measured as $18.74\,\mu kat \cdot l^{-1}$).

Eight hours after the treatment, a drop was observed in the concentration of blood parameters associated with fat metabolism (TG −51.8%; FFA −28.1%; glycerol −54.8%).

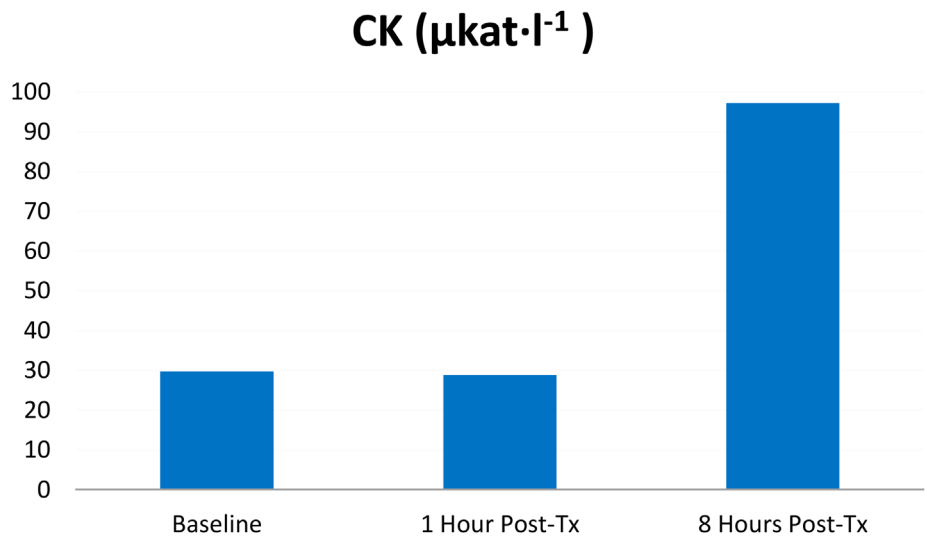

Fig. 5. Increase of CK catalytic activity in porcine serum levels.

This could have been caused by the body metabolism exceeding its basal level for a certain period after the actual muscle contractions. Also, the energy supplies in the form of FFA, TG, and glycerol are further metabolized. Similar trends were also noted by Ferguson et al. [50] who observed 26–36% reduction in TG 24 hours after the single exercise, depending on the caloric expenditure.

CONCLUSION

Application of a high-intensity electromagnetic field which induces non-voluntary, extensive muscle contractions results in apoptosis of adipocytes. The analysis of serum levels shows trends which suggest that HIFEM treatment directly influences fat and muscle metabolisms. Data to support these conclusions include histological TUNEL staining, RNA molecular analysis and serum levels of muscle metabolites. No adverse events were noted to skin and surrounding tissue.

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High Intensity Focused Electromagnetic Therapy Evaluated by Magnetic Resonance Imaging: Safety and Efficacy Study of a Dual Tissue Effect Based Non-Invasive Abdominal Body Shaping

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Objectives: This study introduces an initial evaluation of a novel High-Intensity Focused Electromagnetic (HI-FEM) technology. The primary goal is to quantify any effects the treatments may have on abdominal tissues, as well as to establish hypotheses for future research of this technology.
Methods: Twenty-two patients received four abdominal treatments using the EMSCULPT device (BTL Industries Inc., Boston, MA). Anthropometric evaluations were recorded and digital photographs were taken at baseline, at 2 months, and at 6 months post-treatments. The MRI without contrast determined by vertebras T12 and S1 (FIESTA and FSPRG sequences) was used to measure dimensions in coronal cross-sectional images of abdominal muscle and fatty tissues, in order to assess any anatomical changes induced by the application.
Results: Analysis of the same MRI slices verified by tissue artefacts showed a statistically significant (all $P < 0.0001$) average 18.6% reduction of adipose tissue thickness, 15.4% increase in rectus abdominis muscle thickness, and 10.4% reduction in rectus abdominus separation (diastasis recti) as measured from the medial border of the muscle 2 months post-treatment. More significant improvements were observed in patients with BMI 18.5–24.9 (classified as "normal"). MRI data from 6-month follow-up suggest the changes can be preserved in longer term. Tape measurements showed on average 3.8 cm subumbilical circumference reduction. The weight of the subjects did not change significantly (average -0.5 lb; $P > 0.05$). No adverse events were reported.
Conclusions: MRI, considered as a highly precise diagnostic method, revealed simultaneous muscle growth, fat reduction and reduced abdominal separation at 2 months and at 6 months post treatments, unrelated with dieting. Further research should investigate the exact physiological processes which stand behind the tissue changes observed in this study. Lasers Surg. Med. © 2018 The Authors. *Lasers in Surgery and Medicine* Published by Wiley Periodicals, Inc.

Key words: diastasis recti; fat reduction; HIFEM; magnetic technology; muscle growth

INTRODUCTION

The popularity of non-invasive body shaping procedures has been growing rapidly—the number of procedures performed in the US more than doubled between 2012 and 2016 [1]. Cryolipolysis, radiofrequency, low level laser therapy and focused ultrasound [2] are most widely used for treating patients' fat bulges, and their efficacy has been demonstrated in multiple previous studies. Similar to every aesthetic procedure, these technologies have also certain limitations. All current non-invasive fat removal treatments are based on thermal effects and as such, they may bring about various cold or heat related side effects. More importantly, all these modalities are designed to address only fat tissue.

Subcutaneous fat is an important factor affecting patient's body contours as it comprises approximately 25% [3] of human body composition. However, muscle tissue comprises even a larger portion of the human body composition (42% male/36% female [4]) and depending on individual characteristics, the condition of patient's muscle can play either an equal or even more important role in defining the overall aesthetic appearance. Still, physical workout is currently the only generally available method for natural strengthening of one's muscles.

The use of magnetic stimulation has a proven track record when treating various medical indications, ranging from neurology [5–7], psychiatry [8], physiotherapy [9–12], to treating urinary incontinence in women [13]. Furthermore, due to the non-thermal and non-ionizing nature of

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: Brian Kinney MD is a medical advisor to BTL. Paula Lozanova MD has no conflicts to declare.

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the technology, its application is considered relatively safe [8]. Even though the technology is highly effective, it is not as widely used as electrical stimulation [14].

This study brings an initial evaluation of a novel High-Intensity Focused Electro-Magnetic (HIFEM) technology applied to the abdominal area, in order to assess the physiological response in treated patients. The primary goal is to quantify any effects the treatments may have on abdominal tissues, as well as to establish hypotheses for future research of this technology. The outcomes of the study are expected to suggest if HIFEM can be potentially used as a new technology for non-invasive body shaping treatments.

MATERIALS AND METHODS

Study Population

Twenty-two subjects (10 females and 12 males) participated in this prospective, multi-center, non-randomized, pilot study. The average age of the participants was 39.4 ± 10.2 with a mean BMI prior to the treatments of $25.7 \pm 2.4\,kg/m^2$. The exclusion criteria included pregnancy, breastfeeding, any medical condition contraindicating the application of an electromagnetic field, heart disorders, unhealed wound in abdominal area, and any concomitant medication known to cause bloating or affect weight. See Table 1 for the baseline demographic profile. Patients were not financially incentivized for either participation or completion of the study; an informed consent was obtained from all of them. The study was conducted in compliance with applicable ethical standards and used an IRB approved protocol.

Study Design

Prior to the treatments, each subject was inquired about his/her physical activity habits and an approximate daily caloric intake was calculated in cooperation with a professional nutritionist. All patients were asked to maintain their routine diet and activity level without any modifications until study completion. Afterwards, patients received four treatments (spaced by 2–5 days) using a HIFEM technology device (EMSCULPT, BTL Industries, Boston, MA) as per the IRB-approved protocol.

TABLE 1. Baseline Demographic Profile of the Subjects

	Count	%
Age		
<30	6	27
30–40	4	18
40–50	7	32
>50	5	23
BMI		
<18.5 (Underweight)	0	0
18.5–24.9 (Normal)	8	36
25.0–29.9 (Overweight)	13	59
>30.0 (Obese)	1	5
Gender		
Female	10	45
Male	12	55
Ethnicity		
Caucasian	22	100
Deliveries (10 patients)	1.6[a]	

[a]Average nr. of childbirths.

EMSCULPT Procedure

During the application, patients did not receive any anesthesia and were lying in a supine position. All procedures were applied to the *abdomen* and each session included exactly 30 minutes of continuous application. One applicator (see Fig. 1) was placed on the skin at the umbilical level. The center of the magnetic coil was placed exactly above the navel. The applicator was affixed by a disinfected fixation belt to minimize movements during the procedure. The stimulation intensity started at 0% and within 60 seconds to the treatment it was slowly increased by the operator until reaching patient's tolerance threshold. The tolerance threshold was continuously challenged during the course of the treatments. A dual feedback principle was applied, with the operator visually checking the intensity and homogeneity of the muscle contractions across the *abdomen*, as well as regularly asking the patient about feedback regarding the level of comfort and the balance of contractions between different abdominal areas.

Evaluation Methodology

A complete evaluation of the patients was performed at baseline and 2 months after their last treatment, and included a brief medical history and examination, magnetic resonance imaging (MRI) scan, weight and waist circumference measurements, digital photography, and monitoring of any adverse events. Due to financial constraints, only four randomly selected patients were scheduled for a 6-month follow-up to gain an insight into the tendencies the result may have in the long term.

MRI scans were used to observe changes in abdominal fat and muscle tissues of the treated patients. The scanned body volume was defined by T12 and S1 vertebrae and the array coil system was set up in such a way to minimize any pressure on patient's torso. The images were acquired using the BH-Ax-T2-FIESTA and BH-Ax-T1-FSPGR sequences. For each patient, lateral subumbilical and

Fig. 1. Scheme of the EMSCULPT applicator.

epiumbilical slices of the same sequence and of the same bodily section were extracted in cooperation with a qualified radiologist (experienced in reading abdominal scans), and the thickness of subcutaneous adipose tissue as well as rectus abdominis were measured (InVesalius 3.1). The measurements were taken in multiple points which were laid out laterally in the range between patient's iliac crests. Direct umbilical area was excluded from evaluation due to absence of the muscle structure (linea alba) and adipose layer (the navel). Furthermore, the size of abdominal separation was measured from the same MRI slices.

Gulick II spring-loaded tape assisted measurements were taken 5 cm below umbilicus; patients had the most distinctive fat bulges in this region prior to the treatments. Frontal and lateral digital photography was taken; a positioning mat was used to ensure consistency.

All data collected prior to the treatments were compared with the follow-up data; all results were tested for significance with a two-sample paired *t*-test. Descriptive data were presented as the mean and SD.

RESULTS

The Procedures

All 22 subjects completed the entire study. On average, 12.6 ± 2.5 days and 57.1 ± 8.6 days elapsed between the baseline and the last procedure, and between the last procedure and the follow-up evaluation, respectively. Most patients tolerated stimulation intensities ranging between 90 and 100% already by the end of their first session or during their second session, depending on individual sensitivity. Minimum tolerable intensity was 74% (a patient with BMI 19.7), 17 out of 22 patients tolerated 100% intensity. Higher BMI patients tended to tolerate slightly higher intensity settings. No adverse events occurred. The only noticed side effect was mild muscle soreness 1 day after the first treatment reported by six patients; in all cases the soreness resolved itself within the next 24 hours. Overall the patients did not change their lifestyle or dietary intake significantly.

MRI Evaluation of Abdominal Tissues

The study average and individual patient changes in abdominal fat, abdominal muscle and diastasis are presented in Table 2 and Figure 2, respectively. On average a statistically significant improvement was observed in all three measurements when comparing the 2-month follow-up to the baseline—a reduction in adipose tissue thickness (−18.6%), an increase in rectus abdominis thickness (+15.4%) and a reduction in abdominal separation (−10.4%). In total 91 % ($n = 20$) of patients improved in all three facets simultaneously. The analysis did not show any non-responding patients who would not have any changes in the tissue at all. No other structural changes in the tissues were observed.

An increase in the abdominal muscle mass was observed in 95% ($n = 21$) of patients; one subject did not show any change. The muscle growth was relatively consistent, with majority of patients showing an increase in the range of 10–20% (see Fig. 3). The changes were calculated across both sides of the muscle; the difference in growth between the right and left rectus abdominis was insignificant. However, the distance (separation) between the left and right abdominal muscles decreased in 91% ($n = 20$) of patients; one patient did not show any change and for another patient the distance marginally increased (+0.26 mm or +2.4%). Contrary to our expectations, a subgroup of women who had previously been pregnant ($n = 9$) did not have higher values of abdominal separation before treatments (average 14.9 mm compared to 17.8 mm in other patients). They however did trend toward slightly greater proportional improvement (average reduction was 11.0% compared to 10.0% in the rest of the cohort). The percentage change in abdominal separation was independent of its severity (size) before treatments. Also, statistical analysis confirmed that the changes in muscle thickness and changes in abdominal separation were two highly independent effects ($P > 0.05$; correlation coefficient −0.31). MRI of subjects with major muscle growth thus did not necessarily reveal a major reduction in abdominal separation.

Measurements of the fat tissue revealed an opposite trend, with the average thickness decreasing in all patients. The reduction was slightly more variable than changes in the muscle (coefficient of var. 58.1%); this was primarily driven by two positive extremities. In total 82% ($n = 18$) of patients had the fat layer reduced by more than 10% at the follow-up. More significant absolute changes were observed in subumbilical MRI cuts opposed to epiumbilical cuts.

For both the reduction in fat and reduction in abdominal separation, slightly more significant improvements were seen in patients with BMI classified as "normal" (18.5–

TABLE 2. Average Changes in Abdominal Tissues in Treated Subjects

Measurement	Baseline	2-Month FU	Difference	*P*-value
Muscle thickness [mm]	11.1 ± 3.1	12.7 ± 3.3	1.6 ± 0.7	$P < 0.001$
Fat thickness [mm]	23.6 ± 8.2	19.3 ± 7.6	-4.3 ± 2.5	$P < 0.001$
Abdominal separation [mm]	16.6 ± 7.2	14.9 ± 6.7	-1.8 ± 1.5	$P < 0.001$
Waist circumference [cm]	95.3 ± 6.6	91.5 ± 7.4	-3.8 ± 2.1	$P < 0.001$
Weight [lb]	175.8 ± 24.8	175.2 ± 24.3	-0.5 ± 2.5	$P > 0.05$

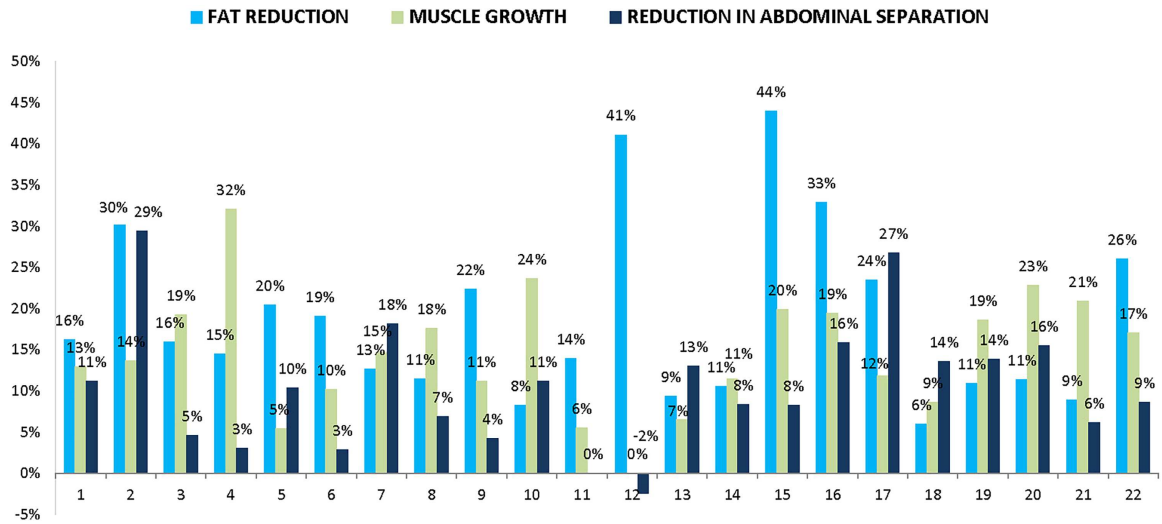

Fig. 2. Changes (%) in abdominal tissues in individual patients. Reduction in subcutaneous adipose tissue thickness (light blue), growth in rectus abdominis thickness (dark blue), and reduction in abdominal separation (gray) are presented.

24.9 kg/m^2). Their subcutaneous fat mass decreased on average by 20.6%, and the size of diastasis decreased by 11.7%. For "overweight" patients (25.0–29.9 kg/m^2) the same measurements averaged 18.1% and 10.0%, respectively.

6-Month Data

Based on MRI evaluation, the muscle thickness continued to grow and the abdominal separation continued to shorten in all four randomly selected patients when compared to the 2-month follow-up. The average thickness in these patients evolved from 9.67 mm (baseline), to 11.38 mm (17.7% increase at 2 months), and on to 11.65 mm (20.5% increase at 6 months). The abdominal separation further improved from average of 12.95 mm (2 months) to 11.18 mm (6 months). In the same patients, the average thickness of subcutaneous fat was on average 3.03 mm lower (22.69 mm) at 6 months compared to the baseline (25.72 mm), see Figure 4.

Other Evaluation

Compared to the baseline, the average subumbilical circumference of patients decreased by 3.8 ± 2.1 cm at the 2-month follow-up. The change was statistically independent of weight variations; the average weight remained stable. Digital photographs showed distinctive aesthetic

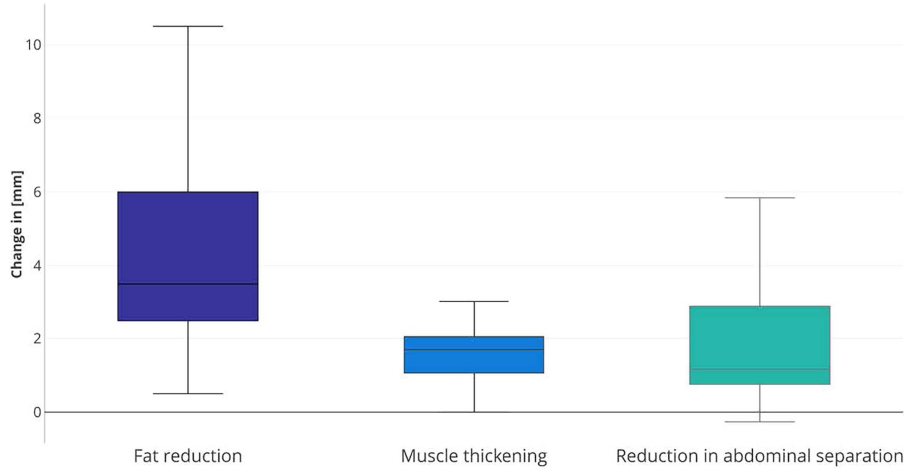

Fig. 3. Plots show the median value, quartile values, as well as the maximum and minimum sample value with regards to changes in abdominal tissues of treated patients calculated from MRI scans. The changes represent a comparison between the baseline and the 2-month follow-up.

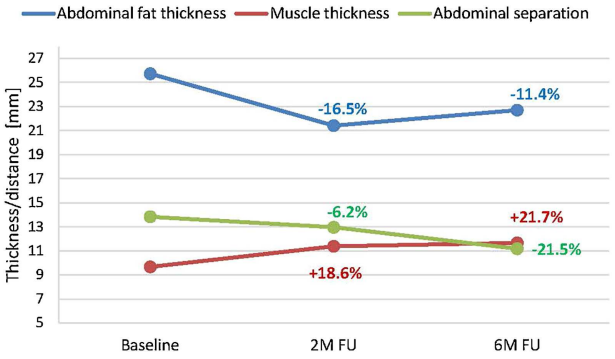

Fig. 4. Average results of MRI evaluation at 6 months post-treatments.

improvements in all patients except for one. Examples of digital photographs linked with corresponding MRI images are shown in Figures 5 and 6.

DISCUSSISON

The findings from MRI scans presented herein have shown that application of the HIFEM technology on the *abdomen* can cause three different simultaneous changes in abdominal tissues non-invasively. Visual improvement in patients' appearance observed 2 months after their last treatment very much resemble the effects of non-invasive heat or cold-based fat reduction treatments combined with an extremely intensive physical workout.

The majority of therapeutic approaches aim at reducing the subcutaneous fat layer (either surgically or non-invasively), yet none of the previous ones deal with strengthening of the muscular foundations. Currently, the only way to strengthen the core is a physical workout plan. The investigated device uses HIFEM technology to induce almost 20 thousand pulses in one 30-minute session. Such frequency of nerve stimuli leads to supra-maximal muscle contractions which are not achievable voluntarily. The muscle tissue is forced to adapt to this stress, resulting in muscle thickening. The principle of muscle hypertrophy and hyperplasia induced by intensive muscle contractions has already been proven in previous studies [15–19]. The 6 month data suggest that the muscles continue to improve in longer term, both in terms of their overall mass and lateral separation, yet further investigation is necessary to better understand the exact physiology.

Research on high intensity muscle training has shown that a lipolytic reaction takes plan in fat tissue adjacent to the contracting muscle [20]. The MRI scans presented herein show a reduction in adipose tissue not immediately after the treatments, but 2 months after the last procedure. A possible explanation for the lasting reduction in fat is that the lipolytic reaction is so intense, releasing large amount of free fatty acids (FFA) which intoxicate the adipocytes and trigger their death. This cell reaction has already been shown in multiple studies in other fields of medicine [21–24]. A recent histology study reported a significant increase in the apoptotic index of adipocytes after one HIFEM treatment on pigs (Weiss R, presented at ASLMS, Dallas TX, April 2018). Their observation was coupled with an increased presence of mRNA pro-apoptotic markers in molecular biochemistry results, as well as with an increased concentration of FFA in blood serum. In addition, an increase of 91.7% (from 18.8 to 35.9) in the apoptotic index was calculated from 120 histological

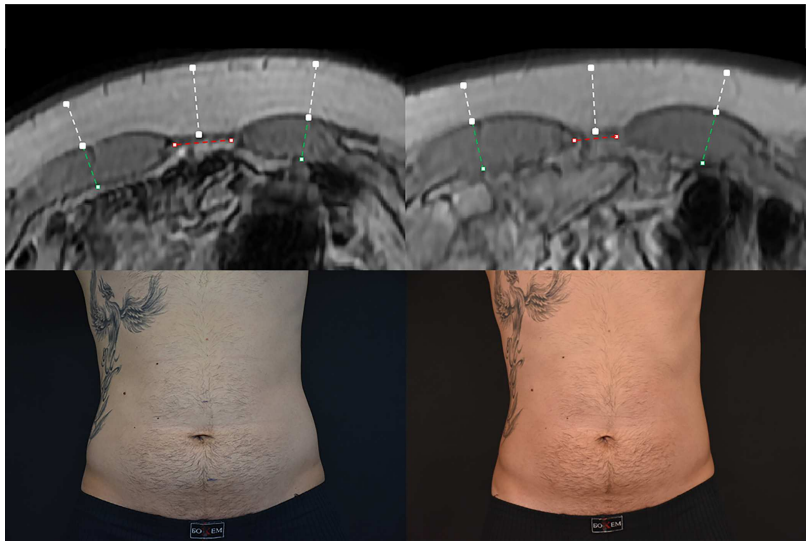

Fig. 5. Magnetic resonance and digital images of Subject ID2 before (left) and 2 months post-treatments (right). Male (30), BMI 24.8 kg/m^2 (before) and 24.5 kg/m^2 (2 months), weight −2.2 lb (−1.2 %), subcutaneous fat −30.3% (white markings), muscle thickness +13.7% (green markings), abdominal separation −24.9% (red markings), circumference −3 cm. Combination of the effects produced an overall visual improvement in patient's abdominal area.

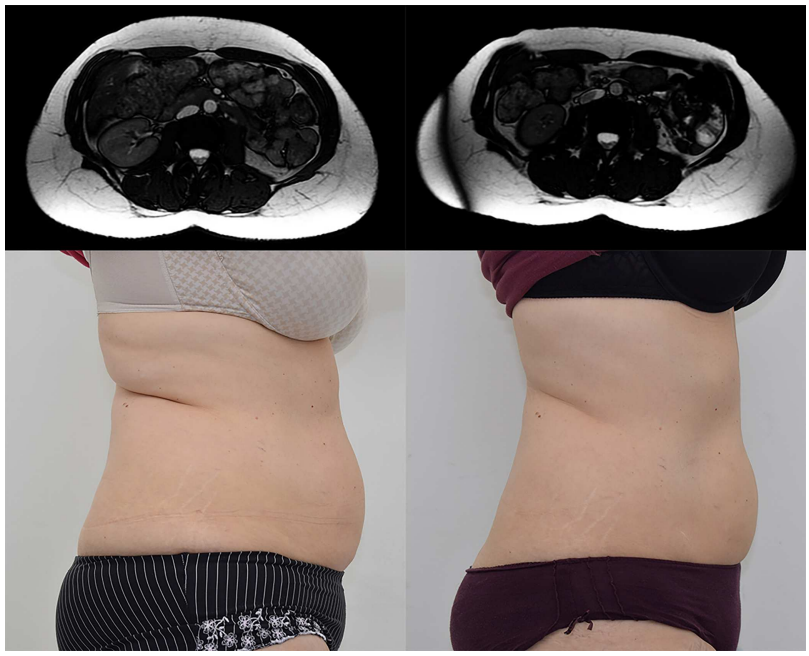

Fig. 6. Magnetic resonance and digital images of Subject ID16 before (left) and 2 months post-treatments (right). Female (52), BMI 25.1 kg/m^2 (before) and 24.4 kg/m^2 (2 months), weight −4.4 lb (−2.9%), subcutaneous fat −32.9%, muscle thickness +19.4 %, abdominal separation −15.9%, circumference −5.7 cm. Combination of the effects produced an overall visual improvement in patient's abdominal area.

samples. This again suggests a potential relationship between FFA released after the muscle contractions and fat apoptosis, however this hypothesis requires further research as its validation was not the purpose of our study.

The third major observation, a reduction in abdominal separation, was rather variable. An 84.8% coefficient of variation shows that the response in patients differed significantly, from very little change to more dramatic reduction in the muscle distance. At the baseline, only one patient suffered from actual diastasis recti as per the medical definition (i.e., gap >2.7 cm) [25]. Still 91% of subjects showed an improvement. This suggests that the application can not only help severely affected individuals, but is effective on most individuals regardless of their condition. This concept of reducing abdominal separation by using a magnetic field technology would deserve further investigation. In addition, there may be some role in prevention by intervention prior to reaching the medical definition of diastasis, although this would deserve further study as well.

Although the sample is not large enough for a detailed statistical analysis of fragmented sub-groups, the data indicate that neither gender nor age affect the outcomes of the treatments. The fact that slightly more significant changes in abdominal tissues were observed in thinner rather than overweight patients can most likely be attributed to the intensity of the magnetic field which decreases with an increasing distance from the actual magnetic coil. For higher BMI patients, the distance between the coil and the motor neurons responsive to the current will tend to be much larger due to the interspacing fat deposits. Such patients might not achieve as intensive muscle contractions compared to normal BMI individuals. Despite the fact that inductive effects of HIFEM taper with distance, they can be felt from a distance of more than 7 cm from the actual applicator. Data from our study suggest that ideal candidates might be patients with less than an inch (2.5 cm) of a pinchable subcutaneous fat. Our 6-month data suggest the tissue changes may last. However, due to the absence of any guidance in the literature on performing longer follow-up studies, 4 to 6 months seem to be a reasonable time window for re-invitation of patients to assess if any additional procedures may or may not be beneficial.

CONCLUSION

The aim of this study was not to establish conclusive evidence for the efficacy of the investigated device. To the best of our knowledge, no peer-reviewed study has investigated a potential use of the HIFEM technology for non-invasive body shaping. The data presented herein show an initial evaluation on 22 patients, and suggest possible physiological responses of the human body to the treatments. We may well conclude that the results have established a hypothesis of three simultaneous abdominal tissue effects induced as a direct result of the treatments, yet additional research is necessary to validate this in a larger controlled study, as well as in a histological study

that would help further cast light on the exact mechanism of action that would explain our observations. If confirmed, the technology would represent a completely new approach to non-invasive body shaping, bringing the additional muscle effects to the already established fat removal market.

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EMSCULPT® TECHNOLOGY FOR NON-THERMAL INDUCTION OF MUSCLE GROWTH AND FAT APOPTOSIS

MECHANISM OF ACTION

The role of fat and muscles in aesthetic appearance

The majority of human body composition comprises of fat (approx. 25%)[1] and muscle (42% male/36% female)[2] tissues. Many procedures address subcutaneous fat which correlates with the overall body shape, and its reduction can deliver a slimmer look. The underlying muscles are however equally important as an increased muscle tone better defines the body contour by reducing the localized prolapse/laxity and adds to a healthier aesthetic appearance.

HIFEM® technology

EMSCULPT is based on High-Intensity Focused Electro-Magnetic (HIFEM) field technology which has the ability to induce supramaximal muscle contractions. The rapidly changing magnetic field induces electric currents in the tissue where it depolarizes neural membranes and governs motor units in the target muscles, causing concentric contractions.[3,4] The effects are highly selective; due to its physiological characteristics only motor neurons are activated, while other neurons or tissues are not responsive to the current, and therefore stay unaffected.

Nerve depolarization for induction of supramaximal contractions

During normal voluntary muscle contractions, the muscle fibers relax between each nervous stimulus due to the central nervous system's inability to signal another impulse while the previous one is still in action. EMSCULPT generates impulses that are independent of brain function, and at such a rapid frequency that doesn't allow such a relaxation phase. Under normal conditions, the highest amount of tension that could be developed and held physiologically is called maximal voluntary contraction (MVC). Usually, it lasts only for a split second. Contractions with a tension higher than MVC are defined as supramaximal. EMSCULPT has the ability to generate supramaximal contractions and hold them for multiple seconds, which significantly increases the physiologic stress/workload needed to allow muscles to adapt.

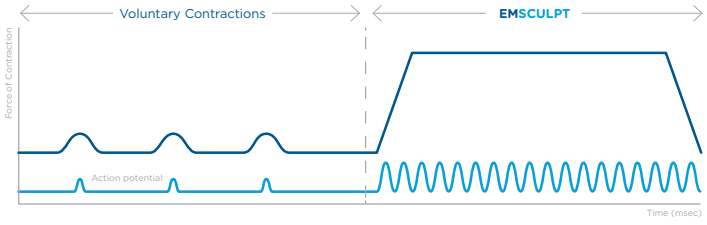

Figure 1: Muscle response to EMSCULPT treatment compared to common exercise.

The effects on muscle tissue

When exposed to supramaximal contractions, the muscle tissue is forced to adapt to such extreme conditions and responds with a deep remodeling of its inner structure, i.e., the growth of myofibrils (muscle hypertrophy) and creation of new protein strands and muscle fibers (muscle hyperplasia).[5–7] Increased muscle density and volume lead to a better definition and muscle tone.

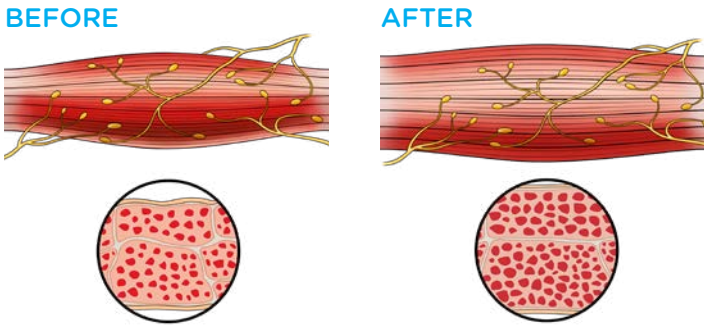

Figure 2: Illustration of muscle structure changes after exposure to extreme load.

The effects on fat tissue

During physical activity, muscles need energy to produce contractions. The energy is derived primarily from adenosine triphosphate (ATP) and secondarily from creatine phosphate and glycogen to fuel the muscles. When these are depleted, the body's catabolic processes take place in the form of lipolysis - i.e. the breakdown of lipids (triglycerides) into free fatty acids (FFA) and glycerol.[8–11] These

released molecules usually act as an energy source for the needed muscle activity and body metabolism.

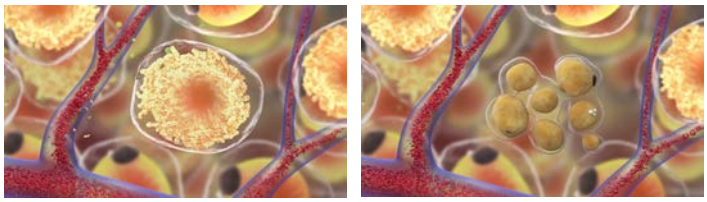

Figure 3: Illustration of induced FFA overflow and consequential apoptosis of fat cells.

During an EMSCULPT treatment, the muscles are contracted to supramaximal levels. Signals are sent to the brain that an extreme amount of energy is going to be needed to supply these contractions and the release of epinephrine is acutely increased. This results in an extreme catabolic reaction, and supramaximal lipolysis, which in turn brings about a dramatic release of FFA. When the amount of released FFA exceed normal levels, they start accumulating intracellularly in surrounding adipocytes (see Figure 3) and eventually lead to their dysfunction.[9, 12–14] This catabolic and supramaximal lipolysis effect occurs mostly in the area in close proximity to the actual contracting muscles, due to increased adipose tissue blood flow and paracrine substances released from the contracting muscles.[9] This principle of cell apoptosis induced by overflow of FFA has been previously observed and demonstrated in numerous research studies.[15–17]

The clinical effects

What a patient sees after a series of EMSCULPT treatments is a significant growth of their muscles and a reduction of fat. This combination effect on both tissue layers delivers unique aesthetic improvement.

Figure 4: An example of a female patient before and after four treatments with EMSCULPT. Courtesy of Paula Lozanova, M.D.

Figure 5: An MRI scan of a patient before and 2 months after 4 EMSCULPT treatments shows reduction in subcutaneous fat and growth in abdominal muscle.

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MAGNETIC RESONANCE IMAGING (MRI) STUDY: SIMULTANEOUS FAT AND MUSCLE EFFECT

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC THERAPY (HIFEM®) EVALUATED BY MAGNETIC RESONANCE IMAGING (MRI): SAFETY AND EFFICACY STUDY OF A DUAL TISSUE EFFECT BASED NON-INVASIVE ABDOMINAL BODY SHAPING.

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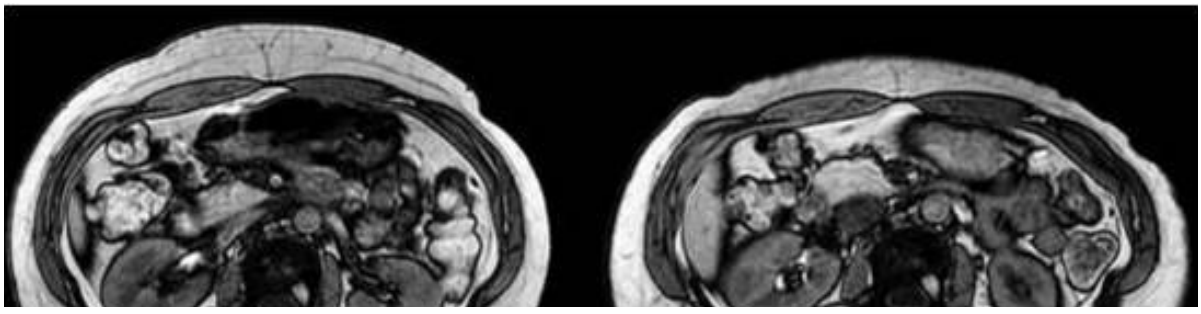
Published in Lasers in Surgery and Medicine Journal (LSM), October 2018, DOI: 10.1002/lsm.23024

HIGHLIGHTS

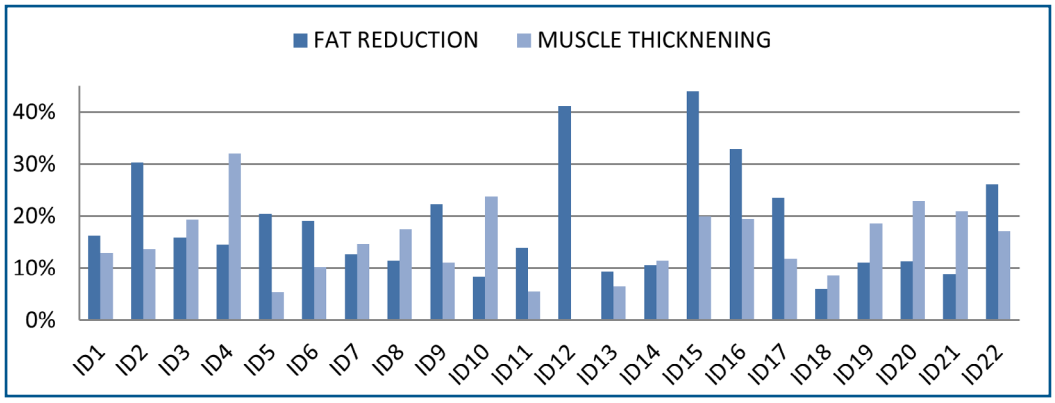
- **22 patients** were evaluated **2 months after four** 30-min **treatments**.
- Abdominal **fat thickness was reduced** on average **by 18.6 %** or 4.3 mm.
- Abdominal **muscle mass increased** on average **by 15.4 %**, coupled with a **10.4 %** average **reduction in diastasis recti**.
- Waist circumference decreased on average by **3.8 cm**.

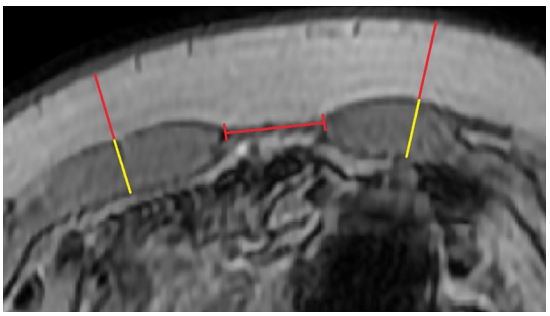


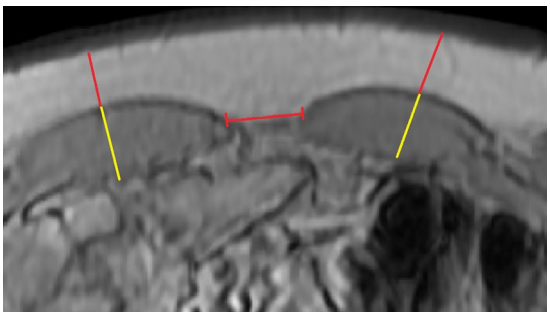
BASELINE 2 MONTH FU

RESULTS

- No adverse event. Several patients reported mild muscle fatigue which resolved within 12-48 hours.
- Simultaneous reduction in subcutaneous fat and strengthening of abdominal muscles in treated patients evaluated by MRI.







BASELINE

2 MONTH FU

Magnetic resonance and digital images of Subject ID2 before (left) and 2 months post-treatments (right). Male (30), BMI 24.8 kg/m2 (before) and 24.5 kg/m2 (2 months), weight -2.2 lb (- 1.2 %), subcutaneous fat -30.3% (white markings), muscle thickness +13.7% (green markings), abdominal separation -24.9% (red markings), circumference -3 cm. Combination of the effects produced an overall visual improvement in patient's abdominal area.

High Intensity Focused Electromagnetic Therapy Evaluated by Magnetic Resonance Imaging: Safety and Efficacy Study of a Dual Tissue Effect Based Non-Invasive Abdominal Body Shaping

Brian M. Kinney, MD, MSME, FACS[1]* and Paula Lozanova, MD[2]
[1]*USC School of Medicine, Hills Beverly, California*
[2]*Paula Fines Center, Sofia BG, Europe*

Objectives: This study introduces an initial evaluation of a novel High-Intensity Focused Electromagnetic (HI-FEM) technology. The primary goal is to quantify any effects the treatments may have on abdominal tissues, as well as to establish hypotheses for future research of this technology.
Methods: Twenty-two patients received four abdominal treatments using the EMSCULPT device (BTL Industries Inc., Boston, MA). Anthropometric evaluations were recorded and digital photographs were taken at baseline, at 2 months, and at 6 months post-treatments. The MRI without contrast determined by vertebras T12 and S1 (FIESTA and FSPRG sequences) was used to measure dimensions in coronal cross-sectional images of abdominal muscle and fatty tissues, in order to assess any anatomical changes induced by the application.
Results: Analysis of the same MRI slices verified by tissue artefacts showed a statistically significant (all $P < 0.0001$) average 18.6% reduction of adipose tissue thickness, 15.4% increase in rectus abdominis muscle thickness, and 10.4% reduction in rectus abdominus separation (diastasis recti) as measured from the medial border of the muscle 2 months post-treatment. More significant improvements were observed in patients with BMI 18.5–24.9 (classified as "normal"). MRI data from 6-month follow-up suggest the changes can be preserved in longer term. Tape measurements showed on average 3.8 cm subumbilical circumference reduction. The weight of the subjects did not change significantly (average -0.5 lb; $P > 0.05$). No adverse events were reported.
Conclusions: MRI, considered as a highly precise diagnostic method, revealed simultaneous muscle growth, fat reduction and reduced abdominal separation at 2 months and at 6 months post treatments, unrelated with dieting. Further research should investigate the exact physiological processes which stand behind the tissue changes observed in this study. Lasers Surg. Med. © 2018 The Authors. *Lasers in Surgery and Medicine* Published by Wiley Periodicals, Inc.

Key words: diastasis recti; fat reduction; HIFEM; magnetic technology; muscle growth

INTRODUCTION

The popularity of non-invasive body shaping procedures has been growing rapidly—the number of procedures performed in the US more than doubled between 2012 and 2016 [1]. Cryolipolysis, radiofrequency, low level laser therapy and focused ultrasound [2] are most widely used for treating patients' fat bulges, and their efficacy has been demonstrated in multiple previous studies. Similar to every aesthetic procedure, these technologies have also certain limitations. All current non-invasive fat removal treatments are based on thermal effects and as such, they may bring about various cold or heat related side effects. More importantly, all these modalities are designed to address only fat tissue.

Subcutaneous fat is an important factor affecting patient's body contours as it comprises approximately 25% [3] of human body composition. However, muscle tissue comprises even a larger portion of the human body composition (42% male/36% female [4]) and depending on individual characteristics, the condition of patient's muscle can play either an equal or even more important role in defining the overall aesthetic appearance. Still, physical workout is currently the only generally available method for natural strengthening of one's muscles.

The use of magnetic stimulation has a proven track record when treating various medical indications, ranging from neurology [5–7], psychiatry [8], physiotherapy [9–12], to treating urinary incontinence in women [13]. Furthermore, due to the non-thermal and non-ionizing nature of

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and have disclosed the following: Brian Kinney MD is a medical advisor to BTL. Paula Lozanova MD has no conflicts to declare.

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the technology, its application is considered relatively safe [8]. Even though the technology is highly effective, it is not as widely used as electrical stimulation [14].

This study brings an initial evaluation of a novel High-Intensity Focused Electro-Magnetic (HIFEM) technology applied to the abdominal area, in order to assess the physiological response in treated patients. The primary goal is to quantify any effects the treatments may have on abdominal tissues, as well as to establish hypotheses for future research of this technology. The outcomes of the study are expected to suggest if HIFEM can be potentially used as a new technology for non-invasive body shaping treatments.

MATERIALS AND METHODS

Study Population

Twenty-two subjects (10 females and 12 males) participated in this prospective, multi-center, non-randomized, pilot study. The average age of the participants was 39.4 ± 10.2 with a mean BMI prior to the treatments of $25.7 \pm 2.4\,kg/m^2$. The exclusion criteria included pregnancy, breastfeeding, any medical condition contraindicating the application of an electromagnetic field, heart disorders, unhealed wound in abdominal area, and any concomitant medication known to cause bloating or affect weight. See Table 1 for the baseline demographic profile. Patients were not financially incentivized for either participation or completion of the study; an informed consent was obtained from all of them. The study was conducted in compliance with applicable ethical standards and used an IRB approved protocol.

Study Design

Prior to the treatments, each subject was inquired about his/her physical activity habits and an approximate daily caloric intake was calculated in cooperation with a professional nutritionist. All patients were asked to maintain their routine diet and activity level without any modifications until study completion. Afterwards, patients received four treatments (spaced by 2–5 days) using a HIFEM technology device (EMSCULPT, BTL Industries, Boston, MA) as per the IRB-approved protocol.

TABLE 1. Baseline Demographic Profile of the Subjects

	Count	%
Age		
<30	6	27
30–40	4	18
40–50	7	32
>50	5	23
BMI		
<18.5 (Underweight)	0	0
18.5–24.9 (Normal)	8	36
25.0–29.9 (Overweight)	13	59
>30.0 (Obese)	1	5
Gender		
Female	10	45
Male	12	55
Ethnicity		
Caucasian	22	100
Deliveries (10 patients)	1.6[a]	

[a]Average nr. of childbirths.

EMSCULPT Procedure

During the application, patients did not receive any anesthesia and were lying in a supine position. All procedures were applied to the *abdomen* and each session included exactly 30 minutes of continuous application. One applicator (see Fig. 1) was placed on the skin at the umbilical level. The center of the magnetic coil was placed exactly above the navel. The applicator was affixed by a disinfected fixation belt to minimize movements during the procedure. The stimulation intensity started at 0% and within 60 seconds to the treatment it was slowly increased by the operator until reaching patient's tolerance threshold. The tolerance threshold was continuously challenged during the course of the treatments. A dual feedback principle was applied, with the operator visually checking the intensity and homogeneity of the muscle contractions across the *abdomen*, as well as regularly asking the patient about feedback regarding the level of comfort and the balance of contractions between different abdominal areas.

Evaluation Methodology

A complete evaluation of the patients was performed at baseline and 2 months after their last treatment, and included a brief medical history and examination, magnetic resonance imaging (MRI) scan, weight and waist circumference measurements, digital photography, and monitoring of any adverse events. Due to financial constraints, only four randomly selected patients were scheduled for a 6-month follow-up to gain an insight into the tendencies the result may have in the long term.

MRI scans were used to observe changes in abdominal fat and muscle tissues of the treated patients. The scanned body volume was defined by T12 and S1 vertebrae and the array coil system was set up in such a way to minimize any pressure on patient's torso. The images were acquired using the BH-Ax-T2-FIESTA and BH-Ax-T1-FSPGR sequences. For each patient, lateral subumbilical and

Fig. 1. Scheme of the EMSCULPT applicator.

epiumbilical slices of the same sequence and of the same bodily section were extracted in cooperation with a qualified radiologist (experienced in reading abdominal scans), and the thickness of subcutaneous adipose tissue as well as rectus abdominis were measured (InVesalius 3.1). The measurements were taken in multiple points which were laid out laterally in the range between patient's iliac crests. Direct umbilical area was excluded from evaluation due to absence of the muscle structure (linea alba) and adipose layer (the navel). Furthermore, the size of abdominal separation was measured from the same MRI slices.

Gulick II spring-loaded tape assisted measurements were taken 5 cm below umbilicus; patients had the most distinctive fat bulges in this region prior to the treatments. Frontal and lateral digital photography was taken; a positioning mat was used to ensure consistency.

All data collected prior to the treatments were compared with the follow-up data; all results were tested for significance with a two-sample paired *t*-test. Descriptive data were presented as the mean and SD.

RESULTS

The Procedures

All 22 subjects completed the entire study. On average, 12.6 ± 2.5 days and 57.1 ± 8.6 days elapsed between the baseline and the last procedure, and between the last procedure and the follow-up evaluation, respectively. Most patients tolerated stimulation intensities ranging between 90 and 100% already by the end of their first session or during their second session, depending on individual sensitivity. Minimum tolerable intensity was 74% (a patient with BMI 19.7), 17 out of 22 patients tolerated 100% intensity. Higher BMI patients tended to tolerate slightly higher intensity settings. No adverse events occurred. The only noticed side effect was mild muscle soreness 1 day after the first treatment reported by six patients; in all cases the soreness resolved itself within the next 24 hours. Overall the patients did not change their lifestyle or dietary intake significantly.

MRI Evaluation of Abdominal Tissues

The study average and individual patient changes in abdominal fat, abdominal muscle and diastasis are presented in Table 2 and Figure 2, respectively. On average a statistically significant improvement was observed in all three measurements when comparing the 2-month follow-up to the baseline—a reduction in adipose tissue thickness (−18.6%), an increase in rectus abdominis thickness (+15.4%) and a reduction in abdominal separation (−10.4%). In total 91 % ($n = 20$) of patients improved in all three facets simultaneously. The analysis did not show any non-responding patients who would not have any changes in the tissue at all. No other structural changes in the tissues were observed.

An increase in the abdominal muscle mass was observed in 95% ($n = 21$) of patients; one subject did not show any change. The muscle growth was relatively consistent, with majority of patients showing an increase in the range of 10–20% (see Fig. 3). The changes were calculated across both sides of the muscle; the difference in growth between the right and left rectus abdominis was insignificant. However, the distance (separation) between the left and right abdominal muscles decreased in 91% ($n = 20$) of patients; one patient did not show any change and for another patient the distance marginally increased (+0.26 mm or +2.4%). Contrary to our expectations, a subgroup of women who had previously been pregnant ($n = 9$) did not have higher values of abdominal separation before treatments (average 14.9 mm compared to 17.8 mm in other patients). They however did trend toward slightly greater proportional improvement (average reduction was 11.0% compared to 10.0% in the rest of the cohort). The percentage change in abdominal separation was independent of its severity (size) before treatments. Also, statistical analysis confirmed that the changes in muscle thickness and changes in abdominal separation were two highly independent effects ($P > 0.05$; correlation coefficient −0.31). MRI of subjects with major muscle growth thus did not necessarily reveal a major reduction in abdominal separation.

Measurements of the fat tissue revealed an opposite trend, with the average thickness decreasing in all patients. The reduction was slightly more variable than changes in the muscle (coefficient of var. 58.1%); this was primarily driven by two positive extremities. In total 82% ($n = 18$) of patients had the fat layer reduced by more than 10% at the follow-up. More significant absolute changes were observed in subumbilical MRI cuts opposed to epiumbilical cuts.

For both the reduction in fat and reduction in abdominal separation, slightly more significant improvements were seen in patients with BMI classified as "normal" (18.5–

TABLE 2. Average Changes in Abdominal Tissues in Treated Subjects

Measurement	Baseline	2-Month FU	Difference	*P*-value
Muscle thickness [mm]	11.1 ± 3.1	12.7 ± 3.3	1.6 ± 0.7	$P < 0.001$
Fat thickness [mm]	23.6 ± 8.2	19.3 ± 7.6	-4.3 ± 2.5	$P < 0.001$
Abdominal separation [mm]	16.6 ± 7.2	14.9 ± 6.7	-1.8 ± 1.5	$P < 0.001$
Waist circumference [cm]	95.3 ± 6.6	91.5 ± 7.4	-3.8 ± 2.1	$P < 0.001$
Weight [lb]	175.8 ± 24.8	175.2 ± 24.3	-0.5 ± 2.5	$P > 0.05$

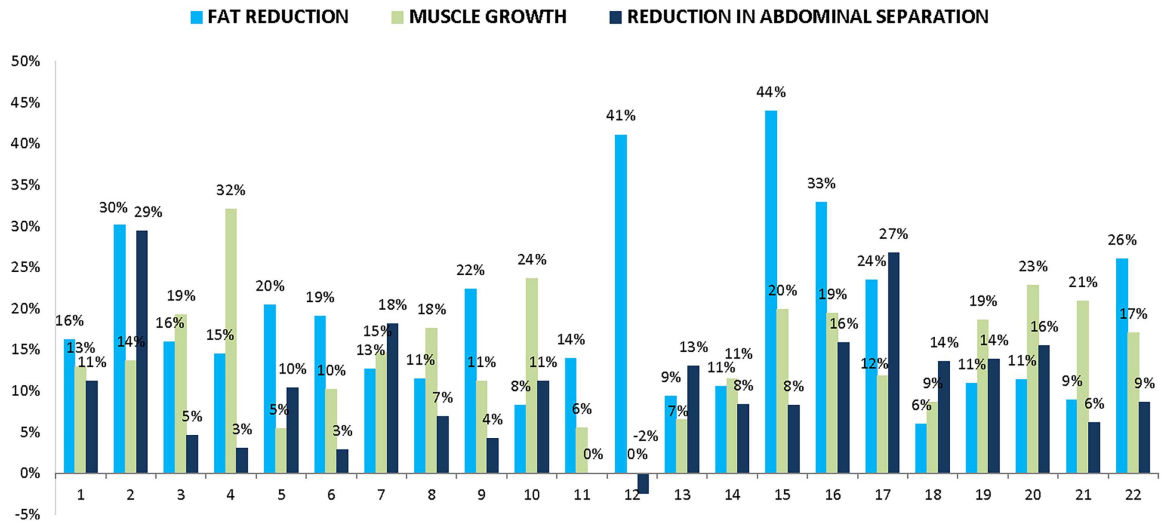

Fig. 2. Changes (%) in abdominal tissues in individual patients. Reduction in subcutaneous adipose tissue thickness (light blue), growth in rectus abdominis thickness (dark blue), and reduction in abdominal separation (gray) are presented.

24.9 kg/m^2). Their subcutaneous fat mass decreased on average by 20.6%, and the size of diastasis decreased by 11.7%. For "overweight" patients (25.0–29.9 kg/m^2) the same measurements averaged 18.1% and 10.0%, respectively.

6-Month Data

Based on MRI evaluation, the muscle thickness continued to grow and the abdominal separation continued to shorten in all four randomly selected patients when compared to the 2-month follow-up. The average thickness in these patients evolved from 9.67 mm (baseline), to 11.38 mm (17.7% increase at 2 months), and on to 11.65 mm (20.5% increase at 6 months). The abdominal separation further improved from average of 12.95 mm (2 months) to 11.18 mm (6 months). In the same patients, the average thickness of subcutaneous fat was on average 3.03 mm lower (22.69 mm) at 6 months compared to the baseline (25.72 mm), see Figure 4.

Other Evaluation

Compared to the baseline, the average subumbilical circumference of patients decreased by 3.8 ± 2.1 cm at the 2-month follow-up. The change was statistically independent of weight variations; the average weight remained stable. Digital photographs showed distinctive aesthetic

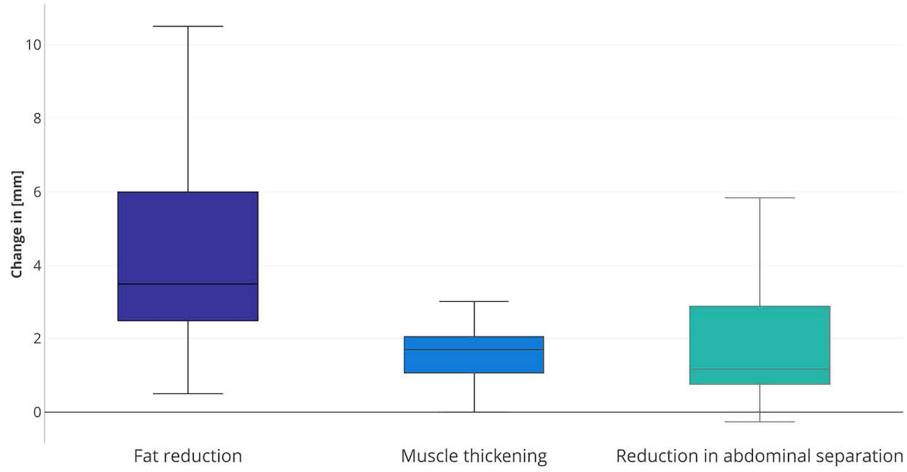

Fig. 3. Plots show the median value, quartile values, as well as the maximum and minimum sample value with regards to changes in abdominal tissues of treated patients calculated from MRI scans. The changes represent a comparison between the baseline and the 2-month follow-up.

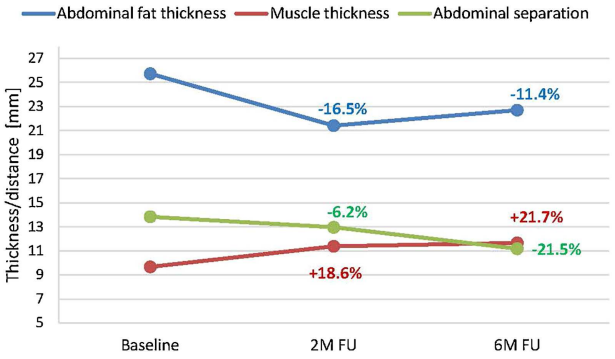

Fig. 4. Average results of MRI evaluation at 6 months post-treatments.

improvements in all patients except for one. Examples of digital photographs linked with corresponding MRI images are shown in Figures 5 and 6.

DISCUSSISON

The findings from MRI scans presented herein have shown that application of the HIFEM technology on the *abdomen* can cause three different simultaneous changes in abdominal tissues non-invasively. Visual improvement in patients' appearance observed 2 months after their last treatment very much resemble the effects of non-invasive heat or cold-based fat reduction treatments combined with an extremely intensive physical workout.

The majority of therapeutic approaches aim at reducing the subcutaneous fat layer (either surgically or non-invasively), yet none of the previous ones deal with strengthening of the muscular foundations. Currently, the only way to strengthen the core is a physical workout plan. The investigated device uses HIFEM technology to induce almost 20 thousand pulses in one 30-minute session. Such frequency of nerve stimuli leads to supra-maximal muscle contractions which are not achievable voluntarily. The muscle tissue is forced to adapt to this stress, resulting in muscle thickening. The principle of muscle hypertrophy and hyperplasia induced by intensive muscle contractions has already been proven in previous studies [15–19]. The 6 month data suggest that the muscles continue to improve in longer term, both in terms of their overall mass and lateral separation, yet further investigation is necessary to better understand the exact physiology.

Research on high intensity muscle training has shown that a lipolytic reaction takes plan in fat tissue adjacent to the contracting muscle [20]. The MRI scans presented herein show a reduction in adipose tissue not immediately after the treatments, but 2 months after the last procedure. A possible explanation for the lasting reduction in fat is that the lipolytic reaction is so intense, releasing large amount of free fatty acids (FFA) which intoxicate the adipocytes and trigger their death. This cell reaction has already been shown in multiple studies in other fields of medicine [21–24]. A recent histology study reported a significant increase in the apoptotic index of adipocytes after one HIFEM treatment on pigs (Weiss R, presented at ASLMS, Dallas TX, April 2018). Their observation was coupled with an increased presence of mRNA pro-apoptotic markers in molecular biochemistry results, as well as with an increased concentration of FFA in blood serum. In addition, an increase of 91.7% (from 18.8 to 35.9) in the apoptotic index was calculated from 120 histological

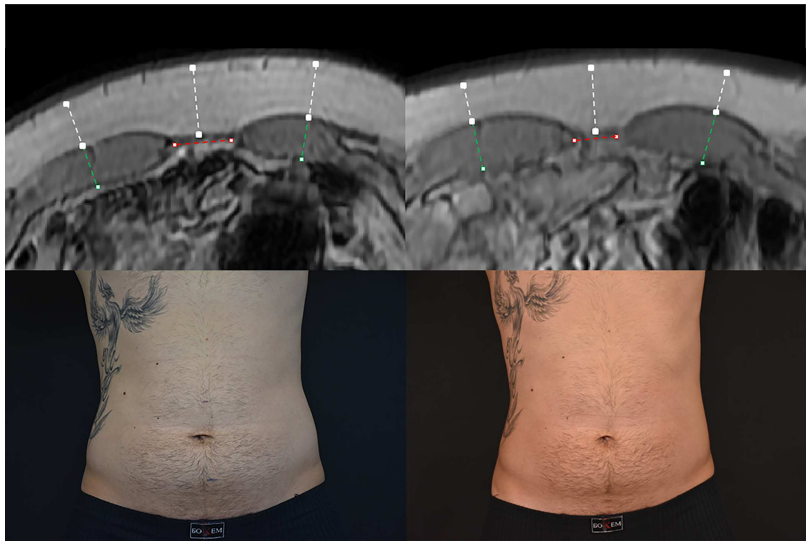

Fig. 5. Magnetic resonance and digital images of Subject ID2 before (left) and 2 months post-treatments (right). Male (30), BMI 24.8 kg/m^2 (before) and 24.5 kg/m^2 (2 months), weight −2.2 lb (−1.2 %), subcutaneous fat −30.3% (white markings), muscle thickness +13.7% (green markings), abdominal separation −24.9% (red markings), circumference −3 cm. Combination of the effects produced an overall visual improvement in patient's abdominal area.

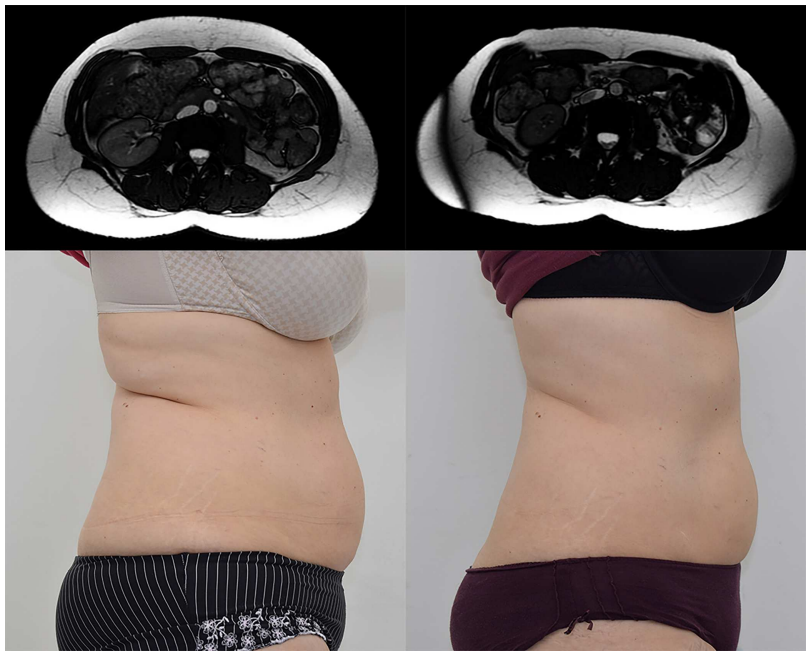

Fig. 6. Magnetic resonance and digital images of Subject ID16 before (left) and 2 months post-treatments (right). Female (52), BMI 25.1 kg/m^2 (before) and 24.4 kg/m^2 (2 months), weight −4.4 lb (−2.9%), subcutaneous fat −32.9%, muscle thickness +19.4 %, abdominal separation −15.9%, circumference −5.7 cm. Combination of the effects produced an overall visual improvement in patient's abdominal area.

samples. This again suggests a potential relationship between FFA released after the muscle contractions and fat apoptosis, however this hypothesis requires further research as its validation was not the purpose of our study.

The third major observation, a reduction in abdominal separation, was rather variable. An 84.8% coefficient of variation shows that the response in patients differed significantly, from very little change to more dramatic reduction in the muscle distance. At the baseline, only one patient suffered from actual diastasis recti as per the medical definition (i.e., gap >2.7 cm) [25]. Still 91% of subjects showed an improvement. This suggests that the application can not only help severely affected individuals, but is effective on most individuals regardless of their condition. This concept of reducing abdominal separation by using a magnetic field technology would deserve further investigation. In addition, there may be some role in prevention by intervention prior to reaching the medical definition of diastasis, although this would deserve further study as well.

Although the sample is not large enough for a detailed statistical analysis of fragmented sub-groups, the data indicate that neither gender nor age affect the outcomes of the treatments. The fact that slightly more significant changes in abdominal tissues were observed in thinner rather than overweight patients can most likely be attributed to the intensity of the magnetic field which decreases with an increasing distance from the actual magnetic coil. For higher BMI patients, the distance between the coil and the motor neurons responsive to the current will tend to be much larger due to the interspacing fat deposits. Such patients might not achieve as intensive muscle contractions compared to normal BMI individuals. Despite the fact that inductive effects of HIFEM taper with distance, they can be felt from a distance of more than 7 cm from the actual applicator. Data from our study suggest that ideal candidates might be patients with less than an inch (2.5 cm) of a pinchable subcutaneous fat. Our 6-month data suggest the tissue changes may last. However, due to the absence of any guidance in the literature on performing longer follow-up studies, 4 to 6 months seem to be a reasonable time window for re-invitation of patients to assess if any additional procedures may or may not be beneficial.

CONCLUSION

The aim of this study was not to establish conclusive evidence for the efficacy of the investigated device. To the best of our knowledge, no peer-reviewed study has investigated a potential use of the HIFEM technology for non-invasive body shaping. The data presented herein show an initial evaluation on 22 patients, and suggest possible physiological responses of the human body to the treatments. We may well conclude that the results have established a hypothesis of three simultaneous abdominal tissue effects induced as a direct result of the treatments, yet additional research is necessary to validate this in a larger controlled study, as well as in a histological study

that would help further cast light on the exact mechanism of action that would explain our observations. If confirmed, the technology would represent a completely new approach to non-invasive body shaping, bringing the additional muscle effects to the already established fat removal market.

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A LARGE-SCALE MULTICENTRIC STUDY: NON-INVASIVE **BUTT LIFTING EFFECTS**

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC TECHNOLOGY (HIFEM) FOR NON-INVASIVE BUTTOCKS LIFTING AND TONING OF GLUTEAL MUSCLES: A MULTI-CENTER EFFICACY AND SAFETY STUDY.

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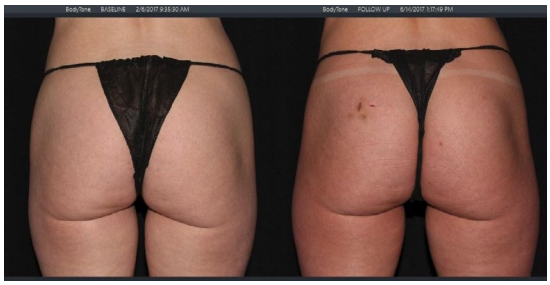
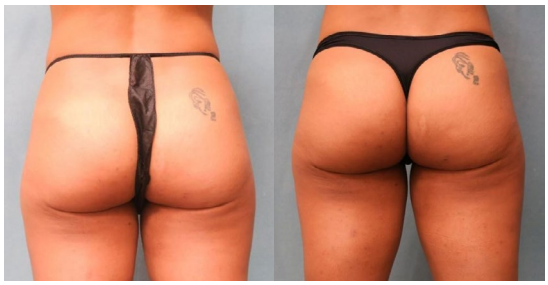
HIGHLIGHTS

- A total of **75 patients** received **4 bilateral treatments on** their **buttocks**, and were evaluated 1 month post-treatments.
- **85 %** of patients reported **significant improvement in appearance of their buttocks. 79 %** of patients reported improvement in their confidence.
- **80 %** of patients felt their buttock was **more lifted and toned** right after their last treatment. Patients reported improvement in **buttock laxity** and **tightness** post-treatment.
- Patient photography revealed **improvement in shape, tone** and **fullness of buttocks**.



BEFORE AFTER



BEFORE AFTER

IN VIVO MUSCLE HISTOLOGY STUDY

NONINVASIVE INDUCTION OF MUSCLE FIBER HYPERTROPHY AND HYPERPLASIA: EFFECTS OF HIGH-INTENSITY FOCUSED ELECTROMAGNETIC FIELD EVALUATED IN AN IN-VIVO PORCINE MODEL

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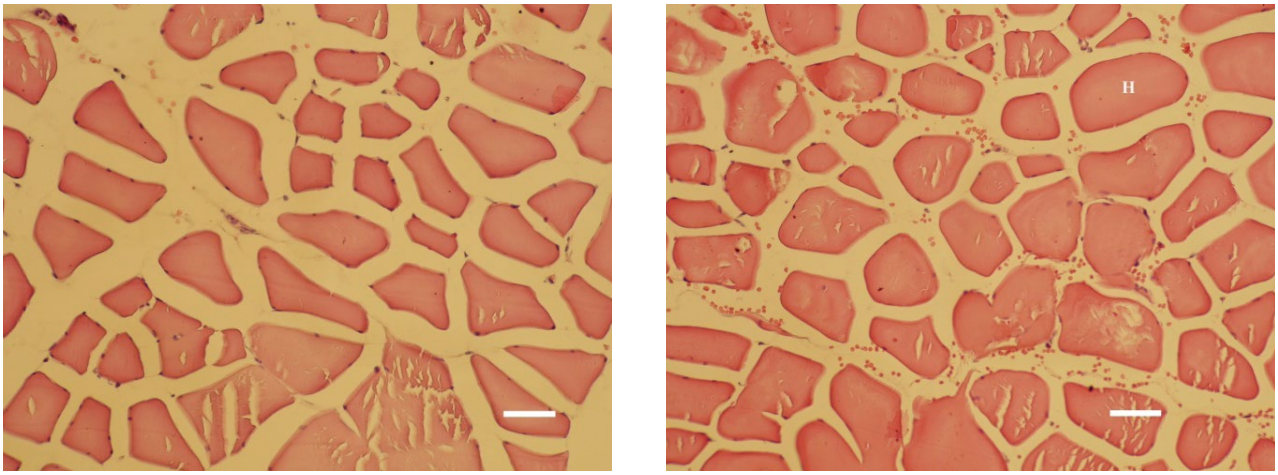
HIGHLIGHTS

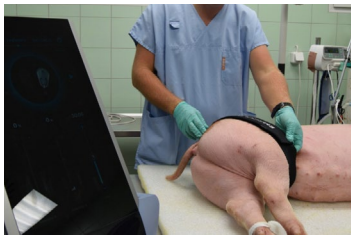
- In treated animals, the **muscle mass** in examined slices increased by **20.56%** (17053.4±5617.9 µm2) on average.
- The average **area per single muscle fiber** increased by **12.15%** (332.23±280.2 µm).
- The average **number of muscle fibers** increased by **8%**, and although not statistically significant, it **indicates** muscle fiber **hyperplasia**.
- Control animal did not show any significant changes in any of the measured parameters.



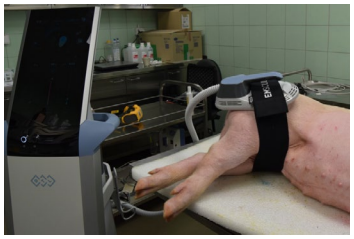
Histological evaluation showed strong muscle fiber hypertrophy and indicated fiber hyperplasia.

STUDY DESIGN

- **Three Yorkshire pigs** received **four 30-minute long treatments**. Fourth pig served as a control.

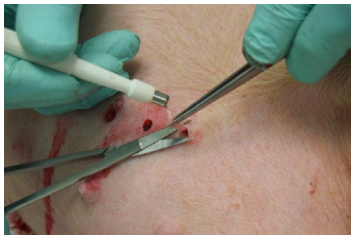


Animal care complied with the convention for the protection of vertebrate animals used for experimental and other scientific purposes.



The thigh was treated for 30 minutes using the HIFEM applicator secured by a fixation belt.

- Biopsy specimens of muscle tissue were taken **before the treatments** and during **2-week follow-up**. Collected tissue slices were evaluated for any structural changes by a certified histopathologist.

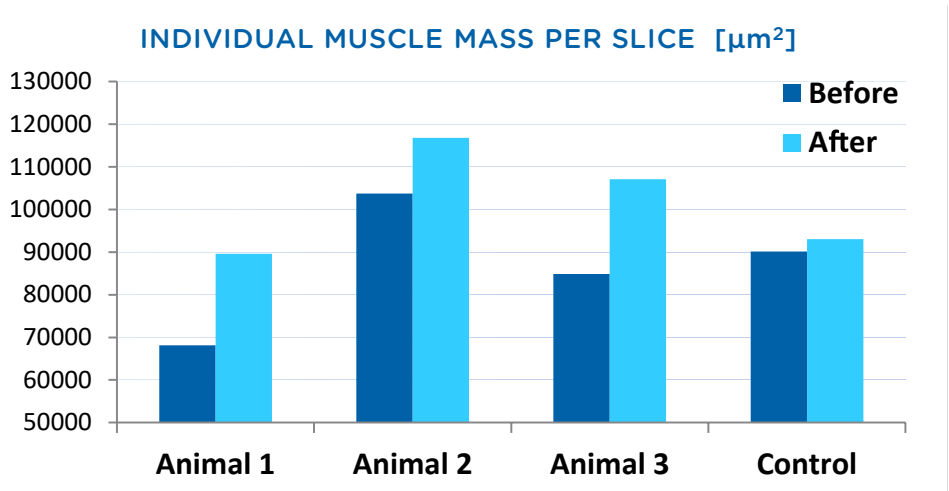


Punch biopsies of the muscle tissue were taken from the treated area and pulled out using tweezers.

The samples were fixed in 10% neutral buffered formalin and colored using hematoxylin. The samples were sliced and microscopically evaluated.

RESULTS

- The results confirmed **muscle hypertrophy** on the histological level, which correlates with previous CT and MRI studies.



The individual average muscle mass in a single slice for each animal.

MRI STUDY:
WOMEN AFTER CHILDBIRTH

ABDOMINAL REMODELING IN POST-PARTUM WOMEN BY HIFEM® PROCEDURE: MRI INVESTIGATIONAL STUDY

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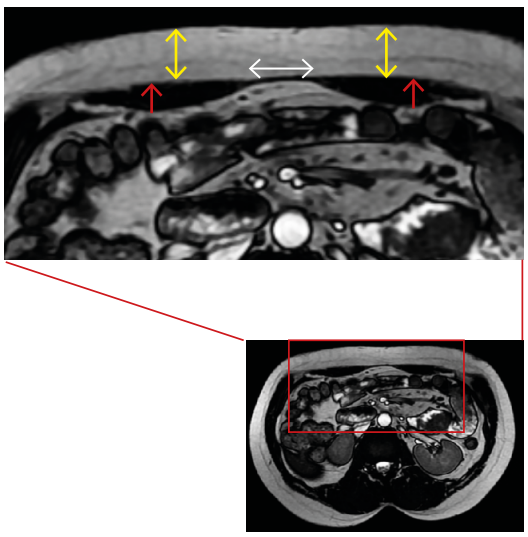
Journal of Clinical and Aesthetic Dermatology

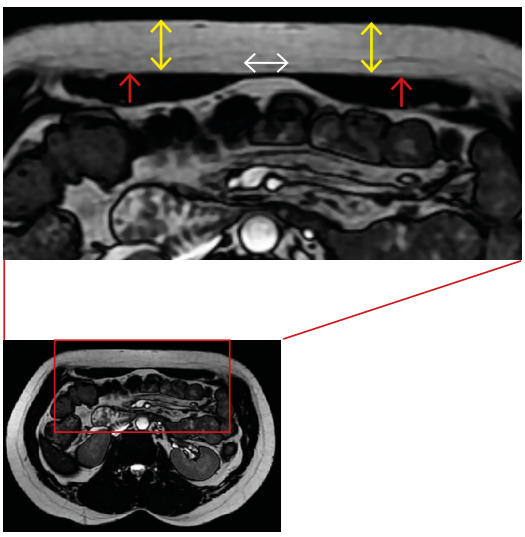
HIGHLIGHTS

- **10** enrolled patients: **women** 3-36 months **after the childbirth. 4 treatments** of the abdomen (30 minutes each). At least 3 days between treatments.
- **MRI** assessment was done at **baseline**, **1 month** and **3 months** after the last treatment.
- The **abdominal separation** was **reduced** by **22.65%** on average. This improvement measured in a group of **post-partum** women is **120% higher** than that seen in normal population*.
- It is **the only study** providing evidence of **non-invasive reduction in diastasis recti** on post-partum patients.

BASELINE



1 MONTH FU



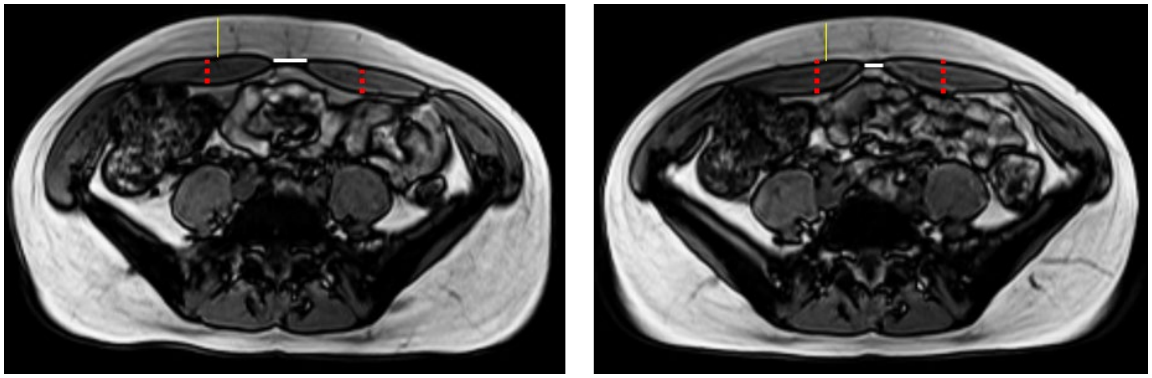
*Kinney BM, Lozanova P. High intensity focused electromagnetic therapy evaluated by magnetic resonance imaging: Safety and efficacy study of a dual tissue effect based non-invasive abdominal body shaping. Lasers Surg Med. 0(0). doi:10.1002/lsm.23024

RESULTS

- The **fat thickness** across the abdomen was **reduced** by **20.14%** on average.
- The **muscle thickness** was **increased** by **21.31%** on average.
- The **results** in fat and muscle **correlate** with previously published studies while the **effect on diastasis recti was significantly higher.**
- **Weight** change of 0.76 kg was **insignificant.**
- **88.2%** patients were **satisfied with** the treatment **results.**
- The study found the **HIFEM** procedure to be **highly effective** and **safe** for **mommy makeover** in post-partum women.

BASELINE

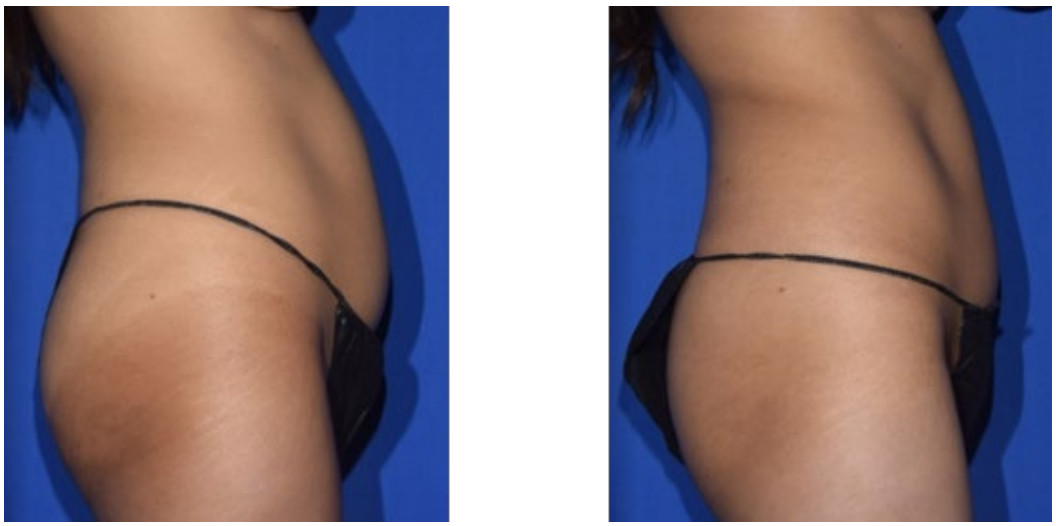
1 MONTH FU



Subject ID 6 (below umbilicus), age 38 years, separation of muscles -18.06%, reduction of fat layer by -12.04%, muscle thickness increase by +24.27%.

BASELINE

1 MONTH FU



Subject ID 10: Age 37, circumference reduction -2.5 cm, average reduction in abdominal separation 11.5%, average fat reduction 13.7%, average muscle thickening 19.0%.

OVERVIEW OF PRINCIPLES IN NEUROMUSCULAR STIMULATION BY ELECTROMAGNETIC FIELDS: CURRENT STATE ANALYSIS WITH EMPHASIS ON MAGNETIC SIMULATION TECHNOLOGY IN PHYSIOTHERAPY AND AESTHETICS

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ABSTRACT

The application of electric currents on human body has been intensively studied in the past and today, its neurostimulative effects are well understood. However, the utilization of induced currents by rapidly changing magnetic fields has recently raised an attention in the clinical practice as a complementary and possibly more advanced modality for muscle stimulation. The overall goal of this study is to review the essential technical parameters and principles of electromagnetic stimulation devices while focusing on the interaction of the electromagnetic fields with excitable biological tissues. The study discusses key differences between the electrical and magnetic stimulation and aims to summarize the current knowledge about magnetic stimulation of muscle tissue in physiotherapy and consequently its pioneering use in aesthetic.

1 INTRODUCTION

1.1 Anatomy of striated muscle

Striated skeletal muscle is one of three major muscle types in the body (besides the cardiac and smooth muscle) and it is under voluntary control by the somatic nervous system. The basic building units of all striated muscles are various types of muscle fibers, composed of cylindrical elongated cells that provide muscles with electrical and contractile properties. From the structural perspective, skeletal muscles are composed of type IIB (fast-twitch, fatigable), type IIA (fast-twitch, fatigue-resistant), and type I fibers (slow-twitch, resistant to fatigue). The actual representation of each fiber type in muscle tissue, as well as, the overall muscle fiber mix varies among different muscle groups due to genetic and phenotypic expression, physical conditioning and a number of other factors. Muscle fibers are activated by a stimulus in the form of action potential conducted by nerve fibers – motor neurons. Each motor neuron innervates a limited group of fibers together referred to as a motor unit. One motor unit may encompass as many as 1000 fibers. As the action potentials propagate along motor nerves to the muscles, the fibers become depolarized and contract. The greater the number of fibers is recruited, the greater the force is produced[1].

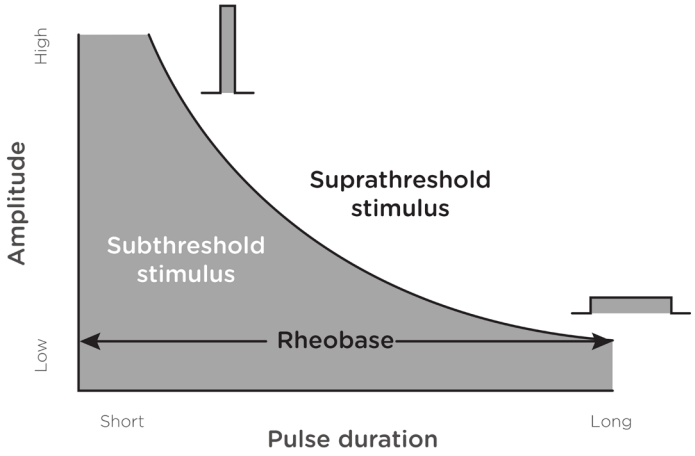

Figure 1. The strength-duration curve of excitable tissue. The area under the curve corresponds to the subthreshold stimulus. When the stimulus reaches sufficient pulse duration and amplitude, an action potential is induced[1].

1.2 External stimulation of neuromuscular tissue

Application of electric fields within the human body can induce action potentials in the nervous and muscle tissues. Such a stimulus is essentially indistinguishable from those evoked by the central nervous system

(CNS). Therefore there has been an increasing focus on non-invasive neuromuscular stimulation over these last decades, especially for rehabilitation[2], re-education[3], and strengthening[4]. Today, two popular modalities are used to elicit a response of excitable neural tissue, while bypassing the brain activity – electromyostimulation (EMS) and peripheral magnetic stimulation (MS). Historically, EMS was introduced for clinical applications much earlier than MS, resulting in its extensive usage and standardization of treatment protocols in rehabilitation. Contrarily the use of MS for peripheral stimulation is a relatively novel approach. It was first documented by Kolin et al. roughly half a century ago[5,6] in an animal model, and the first report of developing a magnetic stimulator for human patients was reported 1982[7].

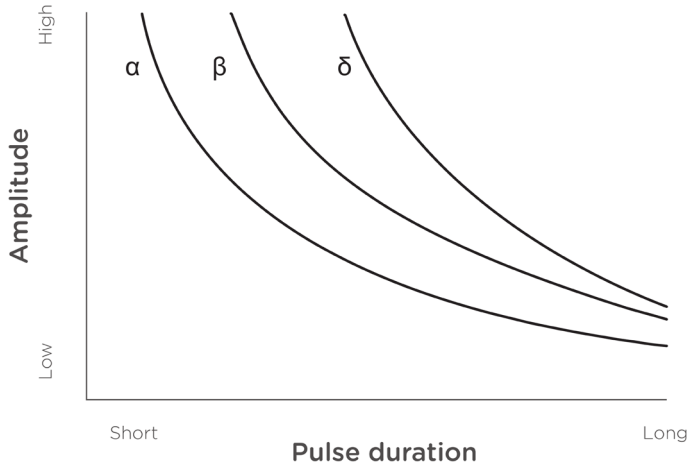

Figure 2. Strength duration curve for different types of peripheral nerve fibers (α = contraction, β = sensory, δ = pain receptors)[1].

The mechanism of stimulation at the neural level is essentially identical for both technologies. In general, the current passes across a nerve membrane into its axon and results in depolarization, which is required to trigger the opening of voltage-gated sodium and potassium ion channels. The action potential is initiated in response to a threshold and suprathreshold stimulus[1], and it is further propagated by the physiological mechanisms of nerve conduction, evoking a contraction of muscle fibers when reaching the neuromuscular junction[1,7].

The transmembrane stimulus must have sufficient amplitude (strength), as well as duration to overcome the resting membrane potential trigger depolarization and then evoke an action potential. The relation between the time and the strength of a stimulus is generally expressed by the strength-duration (S-D) curve. This curve shows that excitable tissue may be stimulated either by short but intense pulses or by longer pulses of at least minimum amplitude referred to as rheobase[1] (see Fig. 1).

The excitable neuromuscular tissues, including peripheral nerves and muscles, are stimulated during an application of sufficient stimulus. Peripheral nerves contain different fibers of various diameter and internal resistance. Fibers with the largest diameter and the lowest internal resistance are depolarized predominantly. This means that A_{α} motor neurons which are directly responsible for the initiation of muscle contractions tend to be activated first[1] (see Fig. 2).

1.3 EMS

EMS applies currents to the human body directly through attachable electrodes. The electric charge carried by electrons translates into an ion flow at the electrode-tissue surface. Unfortunately, only a fraction of these ions flow into axons of nerve fibers, and in order to reach satisfactory muscle contraction, the intensity of stimuli must often be enhanced.

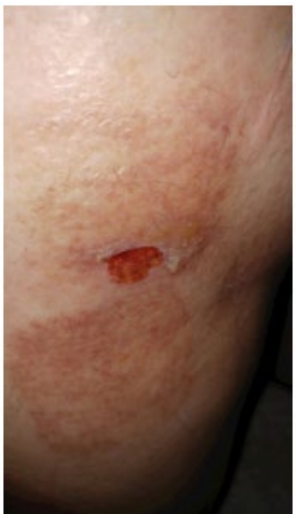

Figure 3. Example of an adverse event caused by the uncontrolled heating effects stemming from high current densities beneath the stimulation electrodes. The skin suffered severe burns in areas which were in direct contact with the electrodes.

However, increasing the intensity of the electrical current may cause localized spots with high current densities under the electrodes resulting into undesirable side effects such as severe cutaneous erythema, burns (see Fig. 3), and activation of cutaneous nociceptors (sensation of pain) or sensory nerves, which makes it impossible to achieve maximal muscle activation[7–9].

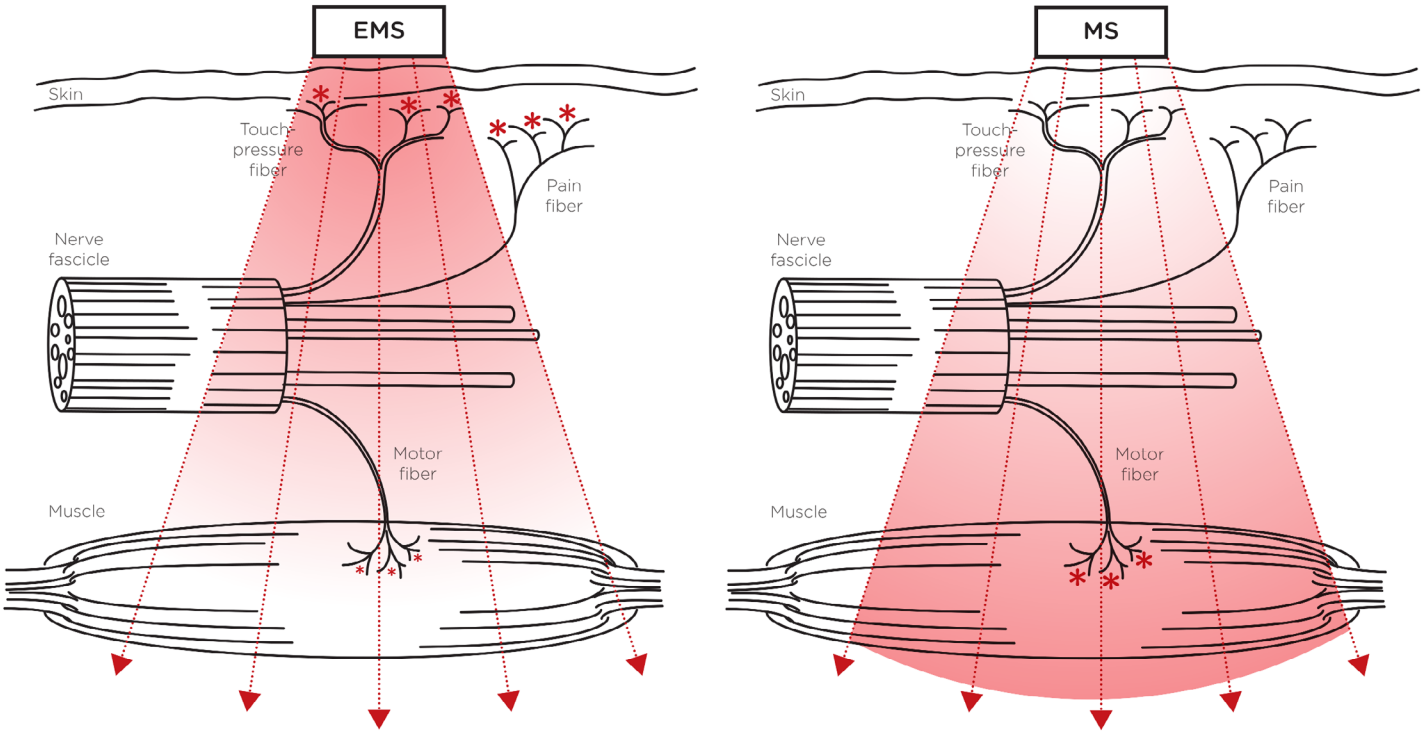

Figure 4. Differences in nervous tissue excitation (red asterisks) depending on the type of stimulator used. The pain and sensory fibers are located closer to the surface, which limits the use of EMS 1. The dotted lines schematically show the direction of electromagnetic field penetration, and red hatching depicts the intensity of EMS/MS generated fields. As shown, MS more selectively affects the excitable neuromuscular tissue and allows greater depth of stimulation.

1.4 Peripheral Magnetic Stimulation (MS)

MS achieves muscle stimulation differently. The muscles are stimulated using a pulsed magnetic field. A time-varying electric currents flow through a stimulation coil while generating a high intensity pulsed magnetic field[7]. As described by Faraday in 1832[10], pulsed magnetic fields induce electric currents in conductive volume (for instance biological tissues) depending on the electrical conductivity of that volume. Thus, as the pulses of a magnetic field pass through the body, the electrical current is predominantly generated in highly conductive tissues (nerves, muscles) and the effect is proportional to their conductivity levels. Due to this principle the magnetic field provides some fortunate advantages.

1.5 Differences between EMS and MS in neuromuscular tissue activation

The main differences between electric and magnetic stimulation are the selectivity of MS and its effective delivery of electromagnetic fields into targeted tissues. First, MS produces a stimulus at deeper levels, since the magnetic field can pass through biological tissues without attenuation of energy. Second, the strength of an induced electric field decreases much less rapidly with distance when compared to the fields produced by surface electrodes[7]. More importantly, there is minimal risk of a painful sensation since an insignificant portion of the currents flow through the skin surface, so activation of nociceptors, sensory nerves and the risk of cutaneous burns is avoided[8,9] (see Fig. 4). For these reasons, MS is currently recognized as the ideal solution in clinical use[8,11].

Recently many different names have emerged to promote magnetic stimulation technology such as HIFEM, rPMS, HIMMS, MMS, HI-EMT, and many others. While HIFEM is developed explicitly for use in aesthetics, many others are innovative or trade names for physiotherapy devices. Even though these technologies are based on the same basic principles of muscle stimulation they often claim to provide superior outcomes compared to competing devices. The true clinical efficiency of any magnetic stimulation technology depends on various parameters such as magnetic field strength, pulse pattern, frequency, the shape of the magnetic field, and the ability to sustain these parameters for a sufficient duration of time. These parameters depend on the level of technical sophistication of the technology.

2 PARAMETERS OF MAGNETIC STIMULATION

Although somewhat limited by the lack of data regarding the exact MS settings needed to stimulate muscle for different devices, we do understand that different parameters cause different preferential activation. When contraction is induced, its performance can be modulated by the proper configuration of various parameters including duty cycle, intensity of stimulus, total number of stimuli, frequency, time of therapy, pulse patterns and others.

2.1 Intensity

The recruitment of motor neurons and activation of muscle fibers is controlled by the intensity of electromagnetic fields. This intensity is defined by magnetic induction and magnetic flux, which are influenced by the characteristics of the current pulse applied to the coil. The distribution of the magnetic field also highly depends on the geometry of the stimulation coil itself.

2.1.1 Magnetic induction

MS intensity is often expressed in Tesla (T), the derived unit of magnetic induction. The absolute strength of the magnetic field alone does not indicate the efficacy of muscle stimulation. For instance, there are conventional MRI systems in use which generate homogenous magnetic fields of intensities 1.5 T and more (some experimental applications even achieved fields of up to 12 T[14–16]) while no stimulation of muscle is triggered. To induce action potential and thus initiate muscle contractions, it is essential to create a time-varying magnetic field which generates the current in a conductive volume according to the law of electromagnetic induction[10].

2.1.2 Stimulation pulse

To produce muscle contraction in an innervated muscle, the pulse duration should be optimally between 150-350 μs to stimulate the motor nerves[12]. Magnetic stimulators are inherently unable to produce monophasic pulses; therefore, the induced electric field is biphasic/sinusoidal and proportional to the rate of change of the magnetic field[7]. According to patient preferences, biphasic stimulation tends to be more comfortable[13].

2.1.3 Magnetic flux

The total amount of the magnetic field (T), which passes through a given area (m^2) is called the magnetic flux and is measured in Webers (Wb or T/m^2). Magnetic flux is a quantity which can directly explain the relationship between a magnetic and electric field, as the change of the magnetic flux over time generates electric currents. When a higher magnetic flux flows through the tissue or when it is changing more rapidly, a stronger electric field is generated. Therefore, it is not only the intensity of the magnetic field but also the length of the stimulation pulse passing through the coil that determines the magnitude of generated current and tissue response (e.g., the strength of muscle contraction).

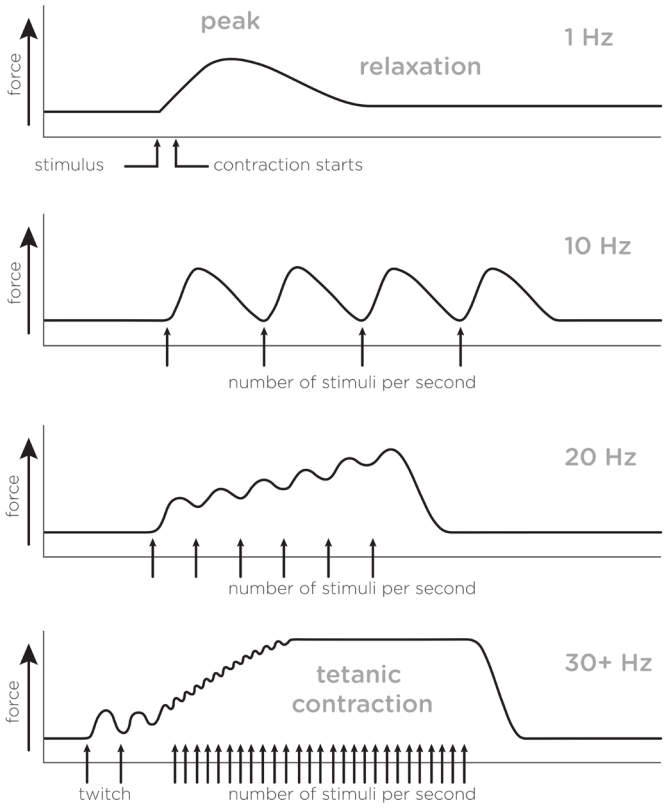

Figure 5: The muscle contractile response according to the frequency of the applied stimulus. A frequency of more than 30 Hz is needed to induce sustained, complete and rigid muscle contractions may be referred to as tetanic.

2.1.4 Coil design

The strength and shape of a magnetic field may also be influenced by the design of the electromagnetic coil while the induced electric field changes with its geometry[17,18]. The design of the coil and winding architecture plays an essential role in its ability to achieve sufficient flux of the magnetic field in the tissue, and ensuring the effective spot size is large enough to depolarize all the excitable structures in full. The shape of the coil logically influences the area

through which the magnetic flux is passing, and thus limits the extent of the induced electric field[30].

2.2 Frequency

Pulse repetition frequency is a major efficiency parameter of MS stimulation, as it determines the type of tissue response and directly affects the strength of muscle contractions. Each separate pulse may induce muscle contraction referred to as a twitch. As the frequency of muscle activation increases, the force produced by the muscle rises as well. With the increased frequency of pulses, the twitch-like contractions will occur closer together, eventually summating to produce a smooth complete and maximal contraction. Maximum fused rigid contractions are better indicators of muscle's contractile capabilities than twitch-like contractions often induced by nerves. To achieve a rigid contraction, rapid delivery of the stimuli is required – at least 30-40 stimuli per second (equivalent to a frequency of 30-40 Hz, see Figure 5). Further increase in frequency is not as beneficial for the muscle due to its rapid fatigue[1,12].

2.3 Pulse patterns

Individual pulses are merged into the waveforms referred to as trains. The waveforms differ in shape, and overall duration called duty cycle, which defines a rest-pause (On/Off) duration of stimulation. Both of these parameters - shape and duty cycle - significantly affect the performance of muscle contraction.

2.3.1 Shape of the pulse train

The train of stimuli may follow either the shape of a rectangle or a trapezoid with a gradual ramp up and ramp down time. During the trapezoidal pattern, the electrical current at the coil gradually builds up to the desired level, holds there for the programmed time and then slowly dissipates. The biggest advantage of a trapezoidal pulse train is that they mimic the natural course of muscle contraction by the gradual recruitment of particular motor units and then gradually returning back to the resting position[12,20,21]. This also makes the stimulation comfortable and much easier to tolerate. It also allows patients to achieve stronger muscular contractions (see Fig. 6). When rectangularly shaped pulse trains are applied, patients are not able to tolerate sudden high intensities of stimulation[22]. If depolarization and consequent muscle contraction follow a sudden excitation caused by rectangular pulses of high intensity, it can evoke an uncomfortable shock sensation. It has also been documented that stimulators which are capable of ramping the pulse train maximize the neuromuscular benefits of the therapy and reduce risks of stressing the tissue[12,21]. Overall, the perception of stimulation intensity might be misleading as slightly uncomfortable contractions may not be directly linked with higher therapeutic efficacy. Instead, it might be a sign of an aggressively set up train of pulses of rectangular shape. It is therefore recommended that when high levels of magnetic field flux are applied to tissue, such types of pulse trains should be avoided.

2.3.2 Length of the pulse train

The time of each pulse train may vary significantly. Shorter pulses can more likely be of subthreshold nature, i.e., they do not necessarily trigger muscle contractions, or the contractions are very short. Contrary to that, longer pulses of several seconds or more can mimic voluntary resistance training. Besides, longer pulses generally require more energy from the body.

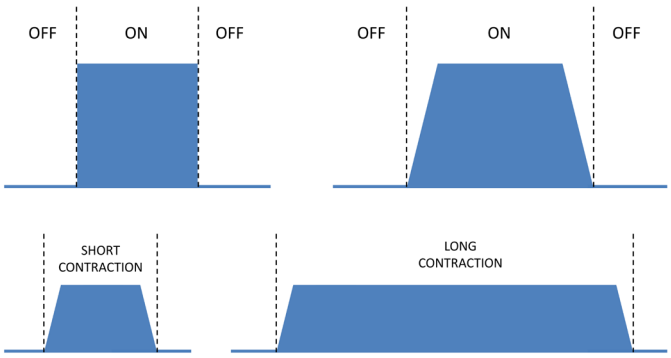

Figure 6: Example of the stimulation waveforms. The rectangular pulse train on the left, trapezoidal on the right. The endurance of contraction increases with the duration of the applied pulse train.

The generation of longer pulses may become challenging based on the apparatus used to induce electromagnetic fields. In general, former technologies are not able to continuously generate electromagnetic pulses of longer durations due to issues with cooling of the heated coil[7,17].

2.3.3 Duty cycle

Muscles must be allowed time to relax during the treatment, as the application of uninterrupted pulse trains would rapidly induce muscle fatigue. The optimal ratio of on and off periods for intermittent protocol differs according to the application of MS while ranging from 1:1 (50% duty cycle) to 1:10[11,19].

2.4 Total effective time

The overall duration of stimulation and the number of stimuli is highly variable across the literature and depends on the application of MS. Longer treatment procedures may have less effective time due to more extended pause period between individual trains of pulses. From the patient's perspective, the ideal technology should offer the right amount of stimulation (depending on the treated indication etc.) in the shortest possible treatment time. This again poses high requirements for the stimulation technology[11,23].

3 USE IN PHYSIOTHERAPY

3.1 Applications

MS of muscle tissue has been used intensively for a wide range of applications in physiotherapy and is recognized as a standard of physical therapy modality. It has been found that repetitive trains of stimuli can be used to improve motor functions and to reduce pain, which is affecting the neuromuscular system[11,24]. MS is also often used as a possible option for rehabilitation in conjunction with conventional muscle training or reconstructive surgical procedures to improve achieved results as it may speed up muscle healing[8,25]. Furthermore, MS might be used to reduce muscle degradation or to increase blood circulation locally[26].

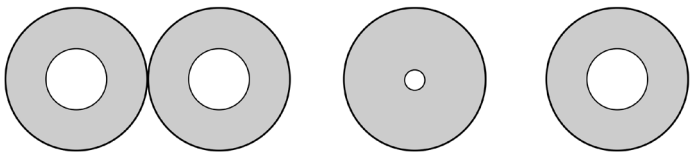

Figure 7: Schematic illustration of the stimulation coils. The Fof8 coil (primarily used for transcranial MS) on the left, round coil with a small-sized internal diameter generating concentrated field in the middle and round coil with big internal diameter for stimulation of large muscle areas on the right.

The applications of MS in physiotherapy usually require a highly selective stimulation, with electromagnetic coils that are specifically designed to concentrate magnetic energy to a small spot size. Predominantly round coils with small-sized internal diameters or occasionally figure-of-eight (Fof8) symmetrical coils are used for neuromuscular stimulation[11,30]. Due to its geometry, a magnetic field of Fof8 coil has the highest intensity right at the applicator's center. In case of a round coil, the maximal strength of magnetic field occurs around the edges of the inner circle. The bigger the internal diameter is, the broader is the distribution of the field (see Fig. 7).

3.2 Mechanism of action

It is assumed that the mechanism responsible for the restoration of muscle functions after MS might be the neuromodulation of cortical networks. Repeated magnetic stimulation of the muscle can directly activate type I and type II afferent nerve fibers by creating rhythmic contraction and relaxation-like vibration[27]. It is thought that properly administered physiotherapy can increase motor cortical excitability by facilitating and reorganization of CNS through the activation of the afferent sensory pathway and eventually improving the strength and performance of treated muscle[28]. In simple terms, this means that the effects of MS in physical therapy are primarily based on affecting the nervous system and improving or restoring its qualities and pathways. However, the functional impact of MS is hard to summarize, since it is often combined with other modalities, and treatment options and the outcomes are assessed under different parameters of stimulation.

3.3 Methodological limitations

Physiotherapy magnetic stimulators are designed with very specific functions in mind and face certain constraints which can limit their range of usage. First, there are limited standardized protocols for MS treatments, forcing therapists to adjust the settings of the stimulator according to their specific needs and hypotheses. From the literature[11], various applications and settings of MS therapy can be found, as an example, the applied penetration depth and intensities varied between deeper (muscle regeneration) and more superficial indications (anything in proximity to bones and spine)[24,29]. Modulation of intensity may also relate to the so-called movement threshold, meaning the lowest intensity of MS stimulus, which is able to induce a contraction. Depending on the type of therapeutic application, the applied stimulus is either sub-threshold or more frequently supra-threshold (Fig. 1) while the intensity of stimulation is defined as a percentage of the movement threshold[11]. Physical therapy with MS usually involves pulses delivered at lower repetition rate and intensities resulting in less than complete and rigid contractions[23,24].

3.4 Technical limitations

Besides the lack of methodological uniformity, certain technical disadvantages are also present when using physiotherapy devices at their technical limits. The thermal performance of the stimulation coil becomes a severe issue when higher

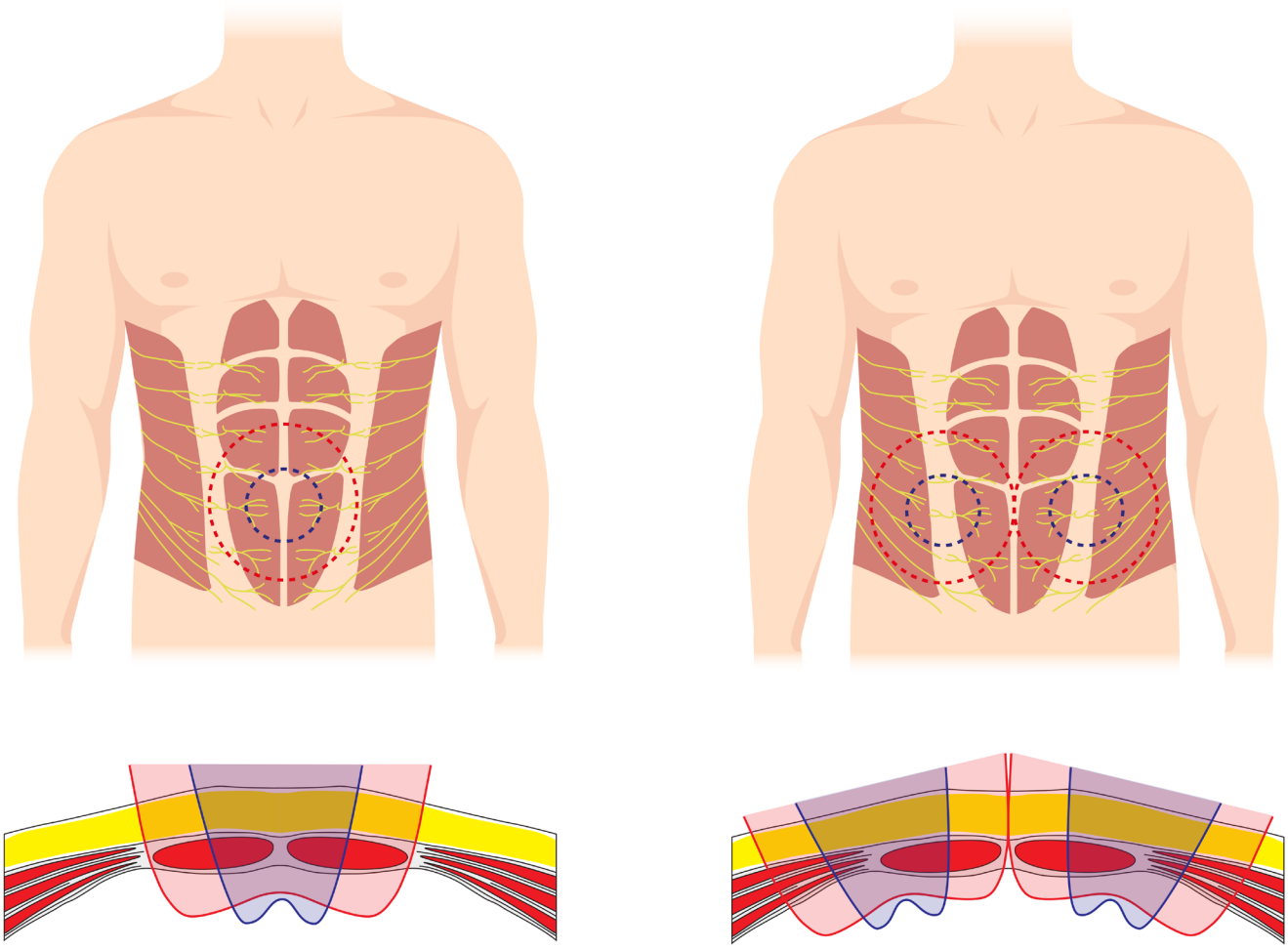

Figure 8. Illustration of a spot size covering rectus abdominis on the tighter and thicker patient when using a small spot size (blue line) and a more broadly distributed magnetic field (red line). Front view on the top, the cross-section view on the bottom. The hatching shows the hypothetical area of activated nervous/muscle tissue.

intensities and repetition rates of pulses are sustained for longer periods than intended. This especially holds true in cases where higher intensities of up to 1-1.5 T are used. It is known that a certain portion of the energy is not delivered to the patient, but creates heat within the coil itself. In order to comply with safety standards defining temperature limits of applied parts of a medical device that are in direct contact with patients (e.g. IEC 60601-1:2015+AMD1:2012), the time of therapy may be limited. Also, the number of pulses plays a role, and in that case, it is often reduced to only several tens or hundreds, which leads to suboptimal response by the muscle being treated.

In conclusion, to allow the sustained application of these higher intensities, compromises will be made in terms of the stimulator settings. Additional cooling may be necessary to prevent overheating of the active coils. The negative impact of adding such a cooling system is that the weight of the applicator may significantly increase. This may influence patient comfort during the therapy and can make the placement of the applicator difficult[7].

4 MAGNETIC STIMULATION FOR AESTHETICS

Until recently, the potential of muscle strengthening by MS had been omitted in aesthetic practice; this was primarily due to the absence of technology that would meet the criteria for application in aesthetics.

4.1 Required advancements of MS technology

Contrary to physiotherapy, which focuses on healing, mobilization, pain reduction, and other indications, in aesthetic medicine, it is essential to look at the application of MS from a total body approach. In aesthetics, it is ideal to involve larger muscle groups/volumes (for instance abdominal and gluteal muscles) to such an extent that the delivered load would induce muscle growth, which then projects into a visible change of body contours[31]. In addition, with respect to the natural pattern of muscle strengthening, the MS-induced contractions should be of maximum possible intensity since higher loads provide a greater stimulus for muscle hypertrophy[33]. To maximize the benefits of therapy, sections with the contraction frequency of more than 30 Hz must be achieved and maintained through the entire treatment time. Considering the great fluxes and intensities applied to the muscle tissue, the stimulation paradigm requires the utilization of trapezoidal shaped trains to ensure the patient's safety and comfort. The duty cycle plays an important role, as well. Finding specific pause duration and pause-stimulation times is essential for supporting the beneficial effect of the rest-pause approach, which avoids unnecessarily decreasing the muscle activity and minimizing muscle fatigue[44]. The ideally balanced pauses between contractions increase contraction volume and elicit greater mechanical stress on the muscle.

4.2 Spot size

The ability to target large muscle groups is strongly influenced by the specific design of the coil, and the coil geometry (see Fig. 7). Parameter considerations such as coil inner and outer diameter, its height/thickness, the winding architecture, as well as, the material used can all affect the shape of the resulting magnetic field. Even though magnetic fields don't have a clearly defined spot size similar to what is typical for lasers, the shape of the fields significantly define the area in which the high intensity of induced currents is achieved. Existing devices intended for physiotherapy often use single core coils which are purposely designed to stimulate only a smaller region (such as one specific joint or tender) and thus concentrate most of the intensity to a smaller spot size. The importance of spot size cannot be understated; it helps determine the number of nerve fibers which are effectively recruited (affected by the induced currents). The larger the spot, the more motor neurons are recruited. In some instances, the fields concentrated into smaller spots may suffice as long as they hit the superior motoric nerve and the action potential then spreads across all subordinate motor neurons. This is, however, usually not the case, since it would take a highly skilled technician with a thorough understanding of muscle anatomy. As an example, the rectus abdominis is the large vertically oriented muscle of the anterior abdominal wall, and it is innervated by multiple anterior rami of the spinal T6-T12 nerves. This means that all of the major branches and adjacent motor units should be activated to perform the most effective muscle contraction (see Fig. 8).

A highly concentrated field would inherently be able to activate only a smaller portion of the neuromuscular structure. With the use of a coil with larger diameter and thus greater field distribution, the total affected area would be substantially larger. This would allow targeting the entire large muscle group with the supra-threshold stimulus, thus recruiting a much higher number of muscle fibers. This results in a complex response of stimulated tissue and muscle enhancement[32].

4.3 Clinical evidence

Since the first muscle stimulator was introduced almost four decades ago, a lot of published evidence has become available that describes the efficacy of MS technologies for blood flow increase, pain management, fatigue recovery, bone healing, as well as many other indications. However, no study has been able to highlight any clinical results that would suggest potential use of MS in aesthetic medicine.

The first MS procedure with clinically proven results in aesthetics was HIFEM. It uses magnetic fields of very high intensities over a large area to induce strong muscle load referred to as supramaximal muscle contractions, and it is reported to be widely used for improving the aesthetic appearance of the abdomen[34–47] and buttocks[38,39]. As a result of the intensive stimulation, multiple studies have appeared that described an increased volume of striated muscles which was predominantly attributed to the hypertrophic effects as well as possible formation of new muscle fibers[35,37,38]. As a secondary effect, several studies also mentioned a significant reduction of the abdominal fat layer, which oscillates around the 20% bar depending on the source. In contrast with devices which affect fat by temperature stress[40], the mechanism of non-thermal fat reduction by HIFEM has been shown to have a hypermetabolic effect on the localized tissues in the body. Induced supramaximal contractions increase metabolic activity in the stimulated region to such an extent that the lipids (triglycerides) break into free fatty acids (FFA) and glycerol[41] and this lipid breakdown leads to an overflow of FFA in the intracellular space and consequently initiates adipocyte dysfunction by the mechanism of endoplasmic reticulum stress (ER-stress) apoptosis[42,43].

HIFEM procedure was specifically developed for use in aesthetics to combine several distinct characteristics of the magnetic technology. As such, it uses large-spot magnetic fields and also has much improved overall energetic balance, which allows it to maintain unique and very energy hungry treatment protocols.

4.4 HIFEM

HIFEM procedure uses unique and patented pulse configurations which offer high amplitudes, high intensities, and long durations. In order to do so, the procedure is based on uniquely designed treatment protocols with intense trapezoidal sequences intended to mimic an intensive muscle workout, interrupted with resting periods to prevent muscle fatigue (see Fig. 6). During the therapy, several thousands of stimuli are delivered to the muscle tissue at varying high frequencies and intensities to achieve tetanic contraction, and the procedure has a very high total effective stimulation time. The appropriate handling of these variables (duration of the pulse, pause-stimulation times, frequency and intensity) is crucial as overstimulation may lead to excessively long periods of complete tetanus and decrease in blood circulation, nutrient/waste exchange and insufficient outcomes. On the other hand, setting parameters too low may not be enough to induce desired effects[45,46].

The patented air-cooling system is one of the factors that enable to deliver full therapy even when the maximal possible settings are applied. Also, due to the double winding architecture of the coil the procedure allows to induce wide electromagnetic field which is more broadly distributed and covers much larger areas with high magnetic flux when compared to other technologies. In addition, the device is able to perform active bilateral treatment with two of its applicators simultaneously, which allows covering even larger body area at the same time.

5 CONCLUSION

Even though physiotherapy magnetic stimulators have been around for decades, there have been no reported studies highlighting the aesthetic benefits or an ability to affect fat. This can be easily explained by the fact that physiotherapy devices were not designed for such use in the first place and they are unable to mimic resistance training.

HIFEM seems to be the only MS-based procedure with peer-reviewed evidence suggesting hypertrophic effects of the treated muscle tissue that is accompanied with a localized reduction in subcutaneous fat. As such, HIFEM represents the logical evolution of electromagnetic technology that now can be used in the field of aesthetic medicine. Patient response, correlated with animal histological data, was observed clinically by MRI, CT and ultrasound, not only at the level of muscle tissue (hypertrophy), but also in subcutaneous fat (apoptosis of adipocytes). Therefore, the pioneering use of magnetic stimulation in aesthetics provides patients with a dual effect of both fat reduction and the enhancement of muscles which results in improved visual appearance. HIFEM is unique in that multiple studies demonstrate high patient satisfaction rates[34,36,37,39]. HIFEM represents a new class of MS technology that has been specifically designed for aesthetic procedures, and addresses specific previously unmet needs for muscle contouring. It offers a unique combination of technical features such as double winding architecture with high energy, high flux and large spot size, dual applicators, a trapezoidal ramp up for greater patient comfort and tolerability and safety in terms of remaining cool during the treatment cycles. This leads to superior patient outcomes and satisfaction. Multiple peer-reviewed studies have confirmed HIFEM technology results.

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AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

2018 LATE-BREAKING ABSTRACTS

BASIC SCIENCE & TRANSLATIONAL RESEARCH: *CLINICAL THERAPEUTICS*

ENHANCED TOPICAL DELIVERY OF INDOCYANINE GREEN WITH FRACTIONAL CO_2 LASER, FRACTIONAL Er:YAG LASER, MICRONEEDLING AND RADIOFREQUENCY

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Background: Different devices have been used to enhance topical drug delivery. However, comparative studies are rare. Indocyanine green (ICG) is currently not used topically due to insufficient bioavailability resulting from its large molecular structure. Aim of this study was to compare the efficacy of pretreatment with two fractional laser modalities, microneedling and fractional radiofrequency in the delivery of ICG in *ex vivo* human skin.

Study Design/Materials and Method: In six *ex vivo* human abdominal skin samples, test areas were allocated to pretreatment with fractional CO_2 laser, fractional Er:YAG laser (energy settings for both lasers matched 70 and 300 μm ablation channel depth, 5% density), microneedling (500 μm needle length), fractional radiofrequency and no pretreatment. ICG was applied to all areas. After 3 hours application time, fluorescence intensity of ICG was measured in arbitrary units at the skin surface and at 200 and 400 μm depth (after removing the superficial skin layer with a non-fractional CO_2 laser) using fluorescence photography.

Results: Significantly higher fluorescence intensities were found at 400 μm depth for fractional CO_2 300 μm channels (21.8; 19–26.4), fractional Er:YAG 300μm channels (30.6; 28.2–34.5), and microneedling (19.9; 18.5–23.5) as compared to no pretreatment (6.13.3–9.7). No significant increase was found for fractional radiofrequency (11.8; 3.1–14.7). Deeper laser channels (300 μm) gave significantly more fluorescence than superficial channels (70 μm) for both fractional CO_2 and Er:YAG laser. The fractional Er:YAG laser (300 μm channel) gave significantly higher fluorescence intensity at 400 μm than the fractional CO_2 laser (same channel depth), microneedling, and RF.

Conclusion: Pretreatment of the skin with fractional CO_2 laser, fractional Er:YAG laser and microneedling is effective for topical ICG delivery, while fractional radiofrequency is not. Higher energy levels result in improved drug delivery. In this study, Er:YAG laser pretreatment appears to be slightly more effective than CO_2 laser or microneedling, especially at higher energy settings. Further studies are required to examine these findings *in vivo*.

BASIC SCIENCE AND TRANSLATIONAL RESEARCH: *IMAGING AND SENSING*

ASSESSMENT OF SKIN STRUCTURE BY COMBINED PHOTOTHERMAL RADIOMETRY AND OPTICAL SPECTROSCOPY: COREGISTRATION WITH MULTI-PHOTON MICROSCOPY

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Background: We have recently introduced a methodology for non-invasive assessment of structure and composition of human skin *in vivo*, which combines diffuse reflectance spectroscopy (DRS), pulsed photothermal radiometry (PPTR), and analysis based on numerical modeling of light transport in human skin. In here we verify the assessed epidermal thickness values by coregistration with multi-photon microscopy (MPM) in vertical sectioning operation mode.

Study Design/Materials and Method: This pilot study involves one volunteer with healthy skin (Fitzpatrick type II, age 54). Two sites on the dorsal side of the forearm and upper arm, respectively, were characterized using our novel methodology, utilizing PPTR and DRS. PPTR measurements involved pulsed laser irradiation at 532 nm and recording of transient change in mid-infrared IR emission at 1000 frames per second. DRS spectra in visible spectral range (400–700 nm) were acquired using an integrating sphere and a compact optical spectrometer. Skin properties were assessed by fitting of experimental data with predictions from a dedicated numerical model of light transport in human skin (i.e., inverse Monte Carlo). The same test sites were subsequently coregistered with a MPM system, providing optical sectioning capability. By employing the contrast between two-photon fluorescence from biomolecules residing primarily in the epidermis and second-harmonic generation in dermal collagen, the epidermal-dermal junction can be easily identified in the acquired cross-sectional images.

Results: The MPM images indicate maximal epidermal thickness of 0.10 mm at both test sites. This is in very good agreement with the results of our PPTR-DRS analysis, indicating 0.10 mm and 0.11 mm for the two test sites, respectively.

Conclusion: The epidermal thickness values assessed by our approach combining PPTR and DRS techniques were confirmed by coregistration with MPM in two test spots *in vivo*.

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IMPROVING ORAL CANCER OUTCOMES IN REMOTE AND UNDERSERVED POPULATIONS

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Background: Long-term goal is to develop a simple low-cost, smartphone-based tool specifically designed for low- non-specialist use that will improve oral and oropharyngeal cancer (OC) outcomes through early detection and early specialist referral. Current non-specialist screening approaches typically have little or no effect on OC outcomes. Yet early diagnosis is the most important determinant of OC outcomes. Our objective is to improve OC outcomes by melding smartphone technology with artificial intelligence convolutional neural networks and deep learning (AI) to develop a smartphone application (App.) linked to a cloud-based AI-powered screening algorithm that provides triage and management guidance based on smartphone photos and individual risk factor analysis.

Study Design/Materials and Method: This was our first study to evaluate feasibility. Using 249 de-identified intraoral smartphone images containing 157 images of OPMLs/OC and 92 images of similar locations of healthy oral cavity, several convolutional neural networks were trained, including custom architectures with up to 8 hidden layers and models that were pre-trained on the ImageNet challenge data set and then refined on our data. We used regularization techniques such as dropout, early stopping, and heavy data augmentation during training.

Results: The best result was obtained using a six-fold cross-validation protocol was by the VGG16-based network with an average test accuracy of 82.8% and an AUC of 0.93, significantly above chance,

Conclusion: These first results show the considerable potential for using AI approaches to low-cost screening and surveillance.

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THE USE OF OPTICAL COHERENCE TOMOGRAPHY TO QUANTITATIVELY MEASURE HAIR REGROWTH IN ALOPECIA AREATA AFTER PLATELET-RICH PLASMA TREATMENT

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Background: Alopecia areata (AA) is an inflammatory, non-scarring condition causing hair loss. Current treatment modalities are limited due to side effects and recurrence after therapy cessation. Platelet-rich plasma (PRP) is a new treatment modality that has been used for multiple applications including skin rejuvenation, joint injection and hair growth. Thus far, results of PRP-induced hair regrowth have been controversial due to the inability to obtain accurate and reliable quantitative results. Optical coherence tomography (OCT) is a novel, non-invasive imaging system that can be used to measure hair follicle density and hair shaft diameter.

Study Design/Materials and Method: A 60-year-old female with a nine-year history of AA presents to the office for evaluation and treatment. Her last treatment with intralesional triamcinolone occurred in April 2017; since that time the patient has not used any hair regrowth therapies. The patient received intradermal injections of 9 mL PRP throughout the scalp. Using photographs, SALT scores and OCT, we accurately assess the patient's hair pre- and post-treatment. Six weeks after PRP treatment, the patient exhibit 9% improvement in SALT score (baseline 42.1, post-treatment 38.2), with a 28% increase in hair follicle count on the right side of the scalp and 14% on the left. Hair shaft diameter within the follicle increases threefold on the right side, however, no improvement is noted on the left.

Results: The use of PRP for the treatment of AA has been previously described, however, reports of treatment success are limited and controversial especially without the ability to reliably measure therapeutic efficacy. This represents the first case of quantitatively measured PRP treatment success in a patient with AA.

Conclusion: PRP is an effective treatment for AA with improvement in both hair follicle count and hair shaft diameter. OCT is a reliable and accurate method to quantitatively measure hair regrowth after PRP treatment.

THE UTILITY OF NON-INVASIVE *IN VIVO* IMAGING IN MONITORING HAIR LOSS DISORDERS: A PILOT STUDY

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Background: Hair loss disorders afflict people of all subtypes, are often difficult to treat, and extremely disruptive to the psychological well-being of patients. Unfortunately, clinicians are often limited in optimally addressing alopecia by imperfect diagnostic and monitoring methodologies, currently hinged on the gold standard of scalp biopsies and hair follicle histology. Researchers are currently investigating the potential and practicality of non-invasive imaging in order to enhance general alopecia care. The aim of this study was to evaluate the ability of non-invasive *in vivo* imaging to aid clinicians in diagnosing, characterizing, and monitoring various types of alopecia.

Study Design/Materials and Method: Optical coherence tomography (OCT) was used to capture quantitative scalp measurements including number of hair shafts, number and diameter of hair follicles, and epidermal thickness. These measurements were recorded for several separate 5×7 mm scalp locations commonly affected by alopecia on 20 subject scalps before and after respective treatment. Measurements were then compared across alopecia types.

Results: Twenty subjects participated in this observational study. Ten subjects have scarring and ten have non-scarring alopecia; fifteen underwent various scalp injections and five underwent other procedural treatments, such as localized fractional photothermolysis. Non-invasive imaging data for monitoring treatment course is consistent with clinician global assessments in over 80% of cases.

Conclusion: Findings of this study show that OCT has significant potential for clinical relevance in addressing alopecia. The process of image analysis elucidated the importance of developing systematic methods of characterizing

the sub-epidermal qualities of hair. This imaging modality potentiates the tracking of follicular units over an alopecia course that is unattainable by and safer than scalp biopsy.

BASIC SCIENCE AND TRANSLATIONAL RESEARCH: *IMAGING I—IMAGE BASED MONITORING*

FROM ORAL TO TOPICAL DELIVERY—AN *IN VIVO* STUDY OF SUSTAINED CUTANEOUS RELEASE OF VISMODEGIB USING ABLATIVE FRACTIONAL LASER AND MICRO-EMULSION VEHICLE

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Background: Altering drug administration from the oral to topical route can reduce the risk of adverse reactions, but may necessitate sustained drug delivery for efficient treatment. This *in vivo* study investigated biodistribution and pharmacokinetics of vismodegib, an oral hedgehog inhibitor targeting basal cell carcinoma, after topical delivery using ablative fractional laser (AFL) and micro-emulsion vehicle.

Study Design/Materials and Method: Dorsal skin of an anesthetized pig was exposed to fractional 10,600 nm CO_2 laser at 0 or 80 mJ/microbeam. Vismodegib (9.3 mmol/L) was formulated in a micro-emulsion consisting of soybean oil and Tween80 and applied to the skin for 4 hours. Vismodegib concentrations were measured after 4 hours, 2 days, 5 days and 9 days by liquid chromatography mass spectrometry in superficial (0-300μm), mid-dermal (600–900 μm) and deep (1200–1500 μm) skin compartments, displayed as medians and interquartile ranges.

Results: Vismodegib showed rapidly enhanced and sustained topical uptake at all skin depths with AFL delivery compared to intact skin, reaching peak concentrations at day 5 and 9. Uptake enhancement was thus 5.4–16.6-fold higher versus vimodegib-emulsion alone, with greatest impact in the deep skin layer. Drug concentrations reached clinically relevant levels. Thus, between 2d and 9d, mid-dermal vismodegib concentrations were 3.0–39.4-fold higher than steady-state plasma concentrations during oral vismodegib treatment, and corresponded well with earlier *in vitro* results for all skin depths (4 hours, $p = 0.035$–0.628). Importantly, minimal cutaneous toxicity from AFL-assisted vismodegib treatment was demonstrated in healthy skin in clinical images, by assessment of erythema and edema, and transepidermal water loss.

Conclusion: The combination of AFL and micro-emulsion vehicle provides sustained topical release of vismodegib at clinically relevant concentrations, supporting the potential for targeted topical administration.

THE EFFECT OF MELANIN ON *IN VIVO* OPTICAL IMAGING OF SKIN AND HAIR FOLLICLE MORPHOLOGY IN MULTIETHNIC COHORT

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Background: Non-invasive, real-time assessment of living tissue is quickly becoming invaluable for bolstering histologic and dermatoscopic diagnostic and prognostic measures of dermatologic conditions. While many skin researchers have explored the utility of non-invasive imaging in inflammatory and malignant skin conditions, there is yet to be a definitive and direct assessment of the effects of melanin on the quality of optical coherence tomography (OCT) and its accuracy in multiethnic patient populations. The aim of this study was to evaluate the effects of increased melanin on the quality of OCT imaging in regards to characterizing skin and hair follicle morphology.

Study Design/Materials and Method: Volunteers of various skin types were imaged in five locations of the body, including axilla and scalp. Cross-sectional data was compiled for image contrast, sharpness, tissue birefringence, epidermal thickness, and hair follicle morphological measurements of diameter and amount.

Results: Fifteen subjects were imaged, including at least two subjects of each Fitzgerald skin type. Contrast and tissue birefringence showed no variation between skin type, gender, or age. Morphological findings of skin and hair follicles varied based on personal history and subject demographics, except for skin type.

Conclusion: This study concludes that melanin does not have substantial effects on the quality or quantitative assessment capabilities of OCT images. Our findings support the use of OCT technology as a nondiscriminatory imaging tool that can obtain reliable data in different melanin skin types among multiethnic populations.

BASIC SCIENCE AND TRANSLATIONAL RESEARCH: *LIGHT-BIOFILM INTERACTIONS*

CONFOCAL AND IR ANALYSIS OF ANTI-MICROBIAL PHOTODYNAMIC THERAPY EFFECTS ON BIOFILM

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Background: Significant levels of antibiotic resistance are a major problem worldwide. Biofilms found in chronic infections consist of several different species of bacteria. Studies have demonstrated that once these organisms have established a presence they are difficult to eradicate. Found throughout the biofilm, resistant bacteria present a significant challenge to traditional anti-microbial treatment. Anti-microbial photodynamic therapy has been shown to be effective against bacterial biofilms. We studied the killing efficacy in and destruction of the exopolysaccharide matrix in defined multispecies biofilms.

Study Design/Materials and Method: Bacteria were grown for 48h to elicit biofilm growth on coverslip-modified polystyrene dishes. Treated biofilms were exposed to the photosensitizer at varying concentrations (25 μg/mL–50 μg/mL), and aPDT carried out at the appropriate wavelength. Light doses from 0.5–45 J/cm^2 were used. Biofilms were then exposed to Biofilm Viability Kit. Analysis of samples was performed using a LSM 510 Meta NLO Confocal Microscope with attached Axioimager Z1 and Axiovert 200 M for visual data collection, images were processed using a Digital Imaging software. Examination involved interrogation of 2×3 stacks to assess the effect on the biofilm matrix and cell kill. Data was compared to MAIR-IR and CFU results.

Results: These findings align with results, using MAIR-IR spectroscopy providing data demonstrating loss of exopolysaccharides and amides demonstrating matrix

fragmentation in treated biofilms and corresponding with colony forming unit assays. The demonstration of cell kill with biofilm destruction demonstrates that aPDT has the potential for use in the treatment of biofilm related infection.
Conclusion: These findings align with results, using MAIR-IR spectroscopy providing data demonstrating loss of exopolysaccharides and amides demonstrating matrix fragmentation in treated biofilms and corresponding with colony forming unit assays. The demonstration of cell kill with biofilm destruction demonstrates that aPDT has the potential for use in the treatment of biofilm related infection.

BASIC SCIENCE AND TRANSLATIONAL RESEARCH: *PHOTOBIOMODULATION*

EXPLOITING ENDOGENOUS PHOTORECEPTORS FOR TEMPORALLY PRECISE CONTROL OF MELANOCYTE LIGHT RESPONSE

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Background: Light-sensing *via* photoreceptors not only forms the basis of vision but also occurs in anatomical locations outside the eye. While previous studies demonstrate the existence of extraocular photoreceptors in a multitude of tissues including human skin, the function of these light-sensing proteins remains mostly unknown. Pigment production by human epidermal melanocytes occurs in response to ultraviolet (UV) light. In this study, we hypothesize that endogenous photoreceptors in human melanocytes play a critical role in UV responsiveness and, in turn, can be exploited as a novel molecular target for phototherapy.
Study Design/Materials and Method: In this study, we use live-cell imaging in combination with fluorescent calcium indicators to probe for UV light-evoked phototransduction in cultured primary human melanocytes.
Results: Our live-cell studies demonstrate the ability to exert temporally precise light-evoked control of human primary melanocytes, as evidenced by reliable, reversible intracellular calcium fluctuations over sub-second timescales in response to a single pulse of UV light. We further show that this calcium response requires the presence of a retinaldehyde chromophore and corresponds to the wavelength sensitivities of UV-specific photoreceptors found in human melanocytes, consistent with previous findings that suggest a phototransduction pathway mediates this response. In vivo studies to optimize photoresponse using various UV pulse frequency regimes with a murine model containing a genetically-encoded calcium sensor are ongoing.
Conclusion: Our findings unveil a previously underappreciated function of UV light in robustly activating single phototransduction events in human melanocytes, yielding an applicable approach for clinicians and scientists to both modulate and study melanocyte light response with greater temporal precision.

INFLUENCE OF INFRARED CONTINUOUS LASER EXPOSURE ON STRUCTURE OF EXPERIMENTAL ADENOCARCINOMA 755

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Background: In spite of well-known biostimulating features of low-intensity laser radiation (LILR), including its infrared (IR) range, influence of LILR on tumoral process is the least studied. It is determined that LILR has inhibiting effect on Ehrlich's carcinoma growth due to nuclear ultrastructure disturbances and "extrusion" of a chromatin from tumor cells nucleus, which leads to decreases of mitosis at cancer cells
Study Design/Materials and Method: By means of the adenocarcinoma 755 morphometry was done by light submicroscopy and radioautographics. 1st group was composed of 5 sessions of radiation, control group consisted irradiated tumors, 2nd group was composed of animals underwent 10 sessions of laser therapy
Results: Average mass of 1st group animals was 21.8 g and 15.6 g before and after radiation correspondingly. Average mass of tumor was 0.18 g. In control group: 20.8 g and 0.6 g. In the 2nd group the average mass of animals was 21.8 g and 22.2 g before and after radiation. The mass of tumor after 10 sessions of radiation was 1.15 g and 1.75 g without radiation. Thus, dynamics of tumors mass growth indicates a distinct decrease by LILR of range; in particular, after the 5 sessions of LILR tumor mass is more than three times less than control. After 10 days of radiation it decreased to 1/3 in nucleus, as well as increase of intercellular space, tumor cells become more polymorphic. It is essential that expressed increase of neuthrophyl number in a tumor stroma. The number of mitoses decreases significantly, as well as number of the nucleus including 3-H thymidine
Conclusion: LILR with IR range breaks adenocarcinoma 755 growth, which is presented by proliferation and mitosis activity decrease

PRELIMINARY STUDIES OF A NOVEL RED-EMITTING QUANTUM DOT LED SOURCE FOR PHOTOBIOMODULATION FOR *IN VITRO* MODEL OF THE WOUND HEALING

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Background: The ability to easily apply Photobiomodulation (PBM) paradigms experimentally and clinically is limited by the lack of stable, efficient light sources with low power consumption and heat dissipation. This study investigated using an ultrabright QLED source for PBM for *in vitro* model of wound healing ("scratch model").
Study Design/Materials and Method: HEp-2, L929 cells were cultured in 24 well trays in completed DMEM media without phenol red. When a confluent monolayer was formed it was scored with a sterile pipette tip to leave a scratch of approximately 0.4–0.5 mm in width. Photoradiation was performed using a 4 pixel (4×4 mm ea.) inverted QLED array emitting at 626 ± 23 nm (max output $\sim$20,000 nits @ 6V DC; $\approx$10 mW/cm^2) delivering 2.0 J/cm^2/5 min and 4.0 J/cm^2/10 min treatment @ 8 mW/cm^2 to the culture wells. Wound closure was monitored by collecting images at various time intervals after the scratch was performed until closure was either complete Images were analyzed using Image-J software to measure the width of the scratch at previously defined point.
Results: Closure rate ratio results at 24 hrs are presented below; LIGHT TREATMENT HEp-2 L929 NO TREATMENT 0.34 ± 0.018 0.089 ± 0.018 QLED 2.0J/cm^2 $0.471 \pm 0.031^{*}$ $0.208 \pm 0.030+$ QLED 5.0J/cm^2 $0.559 \pm 0.003^{**}$ $0.323 \pm 0.0570++$ LED 5.0J/cm^2

$0.651 \pm 0.022^{***}$ $0.424 \pm 0.057 +++$ (* $p = 0.020$ ** $p = 0.049$; $^{***}p = 0.003$: $+p = 0.025$; $++p = 0.017$; $+++p = 0.007$ *vs.* control)
Conclusion: This *in vitro* study is the first to demonstrate that PBM with a QLED device promotes cell migration (narrowing the scratch) in an *in vitro* model for wound healing. This result suggests that QLED devices may be useful in impaired wound healing treatments. Further studies to develop flexible QLED devices for PBM and their application in wound healing therapies are warranted.

BASIC SCIENCE AND TRANSLATIONAL RESEARCH: *PRECLINICAL THERAPEUTICS*

NON-INVASIVE OPTOACOUSTIC THERANOSTICS

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Background: Optoacoustic diagnostics is based on detection and analysis of optoacoustic waves induced in tissues. It can find a number of important clinical applications in large populations of patients such as diagnostics of cerebral hypoxia, circulatory shock, *etc.* Recently, we proposed nano-pulse laser therapy (NPLT) which utilizes short optical pulses to generate optoacoustic waves in tissues. It is well known that CW NIR light can be used for photobiomodulation (or low-level light therapy, LLLT). In the past few years, new works emerged on therapeutic effects of low-intensity ultrasound waves. The NPLT is based on irradiating tissue by low-level light and optoacoustic waves and combines merits of low-level light and ultrasound therapies.
Study Design/Materials and Method: In this work we combine optoacoustic diagnostics and NPLT to provide optoacoustic theranostics that can be used for diagnostics, therapy, and monitoring of therapeutic response as well as for follow-up after the therapy. We developed and built nanosecond, tunable, near infrared (680 nm–1064 nm), fiber-coupled systems for optoacoustic theranostics and tested them in rats with traumatic brain injury (TBI). Low energy pulses were used for optoacoustic monitoring of cerebral blood oxygenation, while pulses with higher energy were used for the NPLT.
Results: Our studies show that TBI results in cerebral hypoxia, while a 5-minute transcranial application of NPLT significantly reduces negative (both acute and chronic) effects of TBI. Microglia activation was assessed in brain sections by immunohistochemistry using specific antibodies against CD68 and Iba1 and quantified using ImageJ. Total volumes of the cortex and of the cortical lesion were also measured and quantified using ImageJ. Our results show that NPLT significantly decreased microglia activation in the thalamus, cortex and hippocampus dentate gyrus and also significantly reduced cortical volume loss after TBI.
Conclusion: The obtained results indicate that optoacoustic theranostics can be used for diagnostics and management of TBI and other disorders.

CLINICAL APPLICATIONS—CUTANEOUS: *ACNE*

CARBON DIOXIDE LASER EXCISION IN HIDRADENITIS SUPPURATIVA: DEMOGRAPHICS, COMORBIDITIES, HEALING TIME AND COMPLICATIONS

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Background: Hidradenitis suppurativa (HS) is often refractory to standard medical and surgical interventions. We characterized the efficacy and safety of carbon dioxide (CO_2) laser excision for the treatment of recalcitrant HS in an urban, academic dermatology center.
Study Design/Materials and Method: On initial data pull, 72 patients were identified. This number was reduced to 38 patients by including HS patients with all data points at Henry Ford Hospital who underwent CO_2 laser excision between August 2014 to May 2017. Data were obtained from medical charts including healing and recurrence rates, complications, smoking status, and history of diabetes mellitus.
Results: The average age at the time of the procedure was 37.5 years and mean BMI was 34.9. In total, 3 patients had recurrence at a mean of 6 months following the procedure. Post-operative complications included: infection ($n = 2$), contracture ($n = 2$), dehiscence ($n = 2$), nerve entrapment ($n = 1$). Patients with dehiscence were not smokers or diabetics. A total of 12 patients reported current cigarette use, 5 patients were former smokers, and 21 patients had never smoked. The mean healing time in both smokers and nonsmokers was 6 months. Nine patients had a history of diabetes mellitus, and 29 patients were not diabetic. The mean healing time was not significantly prolonged in diabetics when compared to non-diabetics and was 7.3 months and 5.4 months respectively.
Conclusion: Both smokers and non-smokers demonstrated similar wound healing time, recurrence rates, and post-operative complications. Patients with diabetes mellitus had a prolonged healing time when compared to those without diabetes mellitus. Our study identifies important characteristics that clinicians should consider when assessing HS patients for CO_2 laser excision.

CLINICAL APPLICATIONS—CUTANEOUS: *FAT REMOVAL*

CHANGES IN SUBCUTANEOUS ABDOMINAL FAT THICKNESS FOLLOWING HIGH-INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM) FIELD TREATMENTS: A MULTI CENTER ULTRASOUND STUDY

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Background: The fat deposits and underlying muscle structure together define the body contour, yet existing technologies focus only on treating adipocytes. HIFEM technology is FDA cleared for muscle toning, firming and strengthening. This ultrasound study aims to quantify the effect of HIFEM treatments on subcutaneous fat.
Study Design/Materials and Method: A group of 33 patients (mean age 41.7; BMI 22–28) with a 1–4 cm layer of subcutaneous fat had their *abdomen* treated with a HIFEM technology-based device. Each subject underwent four

treatments (per 30 minutes) administered 2–3 days apart. An ultrasound template was used to standardize the four data points to measure the subcutaneous fat layer thickness before procedures and at 1-month follow-up. Both 3D and 2D camera systems were used for photography. Weight measurements were documented. Patient satisfaction and comfort were assessed using questionnaires.
Results: Ultrasonography showed a significant reduction in the subcutaneous fat thickness at all measurement points, averaging 19.0%/4.4 ± 1.46 mm ($p < 0.01$) one-month post-treatments. The most significant reduction in subcutaneous fat was observed subumbilicaly (26.6%/6.5 ± 4.7 mm; $p < 0.05$) and epiumbilicaly (21.6%/5.1 ± 3.7 mm; $p < 0.05$), with lateral measurements showing a 17.0%/3.3 ± 4.5 mm reduction ($P > 0.05$). Weight changes were insignificant (+0.5 lbs). 3D and 2D digital photographs showed both a volumetric reduction and a visual aesthetic improvement in treated patients. Patients were satisfied with the results (30 out of 33) and found the treatments highly comfortable (1.2 out of 10). No adverse events reported.
Conclusion: The HIFEM application resulted in significant fat reduction at one-month post-treatments. Furthermore, patients reported a high level of satisfaction without any adverse events. The results show that HIFEM treatments are highly effective and safe for non-invasive fat reduction.

INDUCTION OF FAT APOPTOSIS BY NON-THERMAL DEVICE: SAFETY AND MECHANISM OF ACTION OF NON-INVASIVE HIFEM TECHNOLOGY EVALUATED IN A HISTOLOGICAL PORCINE MODEL

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Background: Controlled heating and cooling have been the only two mechanisms widely accepted as inducing apoptosis in fat cells in order to achieve changes in human body contours non-invasively. This study evaluates changes in the levels of programmed cell death of adipocytes in a porcine model *in vivo* following a High-Intensity Focused Electro-Magnetic (HIFEM) treatment. HIFEM is introduced as a non-thermal alternative for non-invasive fat reduction.
Study Design/Materials and Method: In this animal model, two Yorkshire pigs were treated on *abdomen* for 30 minutes using a novel HIFEM technology device which works with high intensity magnetic field to stimulate deep tissues through supramaximal muscle contractions. Third animal was not treated and served as a control subject. Punch biopsy specimens of fat together with blood samples were taken before, one hour after and eight hours post-treatment. TUNEL assay was used for detecting DNA fragmentation and changes in apoptotic index in the histologic samples. Biochemistry and hematology tests were performed to analyze safety as well as changes in fat and muscles metabolisms. Data was statistically analyzed using t-tests and repeated measures analysis of variance (rANOVA) with significance level set at 5%.
Results: TUNEL assay results from histological slices revealed an increase in the apoptotic levels on average from 18.75% (before) to 35.95% (8 hours post-treatment). Correlation with the therapy was highly significant ($p < 0.01$). Visual analysis of the slices further confirmed changes in the structure of adipose tissue after the treatment. The control subject didn't show any increase in apoptosis. Blood parameters involved in fat metabolism (primarily FFA, TGC, GLU and glycerol) changed significantly after HIFEM application, providing supporting evidence of changes in the subcutaneous fat tissue. Specific and non-specific serum markers confirmed intense muscle activity during the application, as well as a following metabolic reaction. None of the safety related parameters fluctuated significantly.
Conclusion: This study presents initial evaluation of a non-invasive induction of fat apoptosis using a non-thermal technology. Histology shows a significant increase in the levels of programmed fat cell death after HIFEM treatment in this porcine study. The data suggest a link between fat cells apoptosis and elevated levels of free fatty acids released during supramaximal muscle contractions. This mechanism deserves future investigation. We conclude that HIFEM is effective for non-invasive fat reduction bypassing side effects that may occur using thermal alternatives. HIFEM is a promising novel technology and is currently being investigated in clinical trials.

CLINICAL APPLICATIONS—CUTANEOUS: *REJUVENATION*

SAFETY AND EFFICACY OF A NOVEL REFRACTIVE LENS ARRAY USING A 1064 nm PICOSECOND LASER FOR LOW IMPACT TREATMENT OF SKIN TEXTURE AND FINE LINES

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Background: Rejuvenation procedures that are painless, quick and require no recovery are increasingly demanded by active patients. Consistent reproducible improvement is fundamentally important for positive, predictable patient satisfaction. Differences in fractional technology can impact the consistency of clinical outcomes. A short Rayleigh range of a fractional device has been correlated with treatment inconsistency due to large spot size variation over the normal treatment distance/angle variance. (LSM 48:555–561 2016) A novel micro-lens array was developed with a long Rayleigh range to mitigate clinical inconsistencies due to spot size variation. The aim of this study was to access the safety and efficacy of a novel refractive lens array with a long Rayleigh range using a 1064 nm picosecond laser.
Study Design/Materials and Method: Ten patients with Fitzpatrick skin type's I–IV were included. All patients received a series of three facial treatments at 4 week intervals. Each treatment consisted of approximately 3500 pulses with 0.85–1.7 milliJoules per 170 μm micro spot. A picosecond laser (Cutera) was used with 750 picosecond pulses at 10 Hz repetition rate.
Results: Significant improvements in fine rhytides, erythema-telangiectasia, dyspigmentation, and texture were observed in all subjects following three treatments at 1 and 3-month follow up intervals. Patients reported mild erythema which resolved within 1 to 2 hours and no other adverse events. Patient satisfaction was rated as high; subjects reported that the results were superior to prior non-ablative treatments they have received in the past, including intense pulsed light and fractional non-ablative resurfacing, and all subjects stated they would recommend the treatment to others.
Conclusion: Picosecond 1064 nm with refractive lens array yields appreciable improvements in rhytides and photoaging without significant side effects or recovery time. This novel modality may offer an alternative no downtime option to

fractional resurfacing. Further study is required to compare safety and efficacy to IPL and fractional resurfacing.

CLINICAL APPLICATIONS—CUTANEOUS: *SKIN CANCER*

BASAL CELL CARCINOMA TREATED WITH ABLATIVE FRACTIONAL LASER AND INGENOL MEBUTATE—AN EXPLORATORY STUDY MONITORED BY OPTICAL COHERENCE TOMOGRAPHY AND REFLECTANCE CONFOCAL MICROSCOPY

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Background: Ingenol mebutate (IM) has previously been applied to clear superficial BCC. Ablated fractional laser (AFXL) may improve efficacy of IM treatment by increasing drug uptake in the tumor. Using non-invasive optical coherence tomography (OCT) and reflectance confocal microscopy (RCM), our aim was to investigate tumor response and tolerability after combined AFXL-IM treatment of superficial and nodular BCC.
Study Design/Materials and Method: Fifteen patients with histologically verified superficial (n = 5) and nodular (n = 10) BCC were treated with combined AFXL (10,600 nm) and IM 0.015% or 0.05%. Treatment was repeated at day 29 depending on tumor response evaluated by OCT and RCM. Local skin reactions (LSR) were monitored using an LSR scale ranging from 0 to 24 (At day 1, 3 or 4, 8, 15, 29 and at 3 months). At 3 months, treatment efficacy was evaluated by OCT, RCM and histology.
Results: Interim analysis showed partial tumor response in fourteen of fifteen patients at day 29, and all patients received a second treatment. Tumor tissue was identified as dark tumor islands and tumor nests in OCT and RCM images. LSR were restricted to the treated area, and composite LSR score ranged from 2.5 (1.25–3.75) to 8 (8–11.5) peaking on day 3 to 4. Pain was tolerable and limited to maximum 24 hours after treatment. Complete data will be presented at ASLMS 2018.
Conclusion: One treatment of combined AFXL-IM resulted in partial tumor response at day 29 with tolerable LSR. OCT and RCM effectively detected tumor residuals, prompting further image-guided AFXL-IM-treatment.

REAL TIME, NON-INVASIVE, *IN VIVO* SKIN CANCER DIAGNOSTICS BASED ON LASER SPECTROSCOPY AND MACHINE LEARNING ALGORITHMS USING AESTHETIC LASERS

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Background: There have been several *in vivo* skin cancer detection devices based on different types of optical techniques, such as multi-spectral imaging and Raman spectroscopy. However, they implement high-cost lasers or imaging sources and have insufficient diagnostic accuracies for clinical use with sensitivity of 87 ~ 98% and specificity of 9 ~ 38%. This study shows the effectiveness of a real time, non-invasive, *in vivo* skin cancer diagnostic device based on molecular laser induced breakdown spectroscopy and machine learning algorithms utilizing pre-existing short pulsed aesthetic lasers as its excitation sources.
Study Design/Materials and Method: A single-site study was designed to evaluate the effectiveness and safety of the device. The device consists of the light collection module attached to a handpiece and the analysis module mounted on any kind of short pulsed (ps ~ ns) laser system. A Q-switched (QS) 1064 nm laser (Lumenis, Ltd., Yokneam, Israel) was used to induce the micro plasma from the suspicious skin lesion. The analysis module of the device analyzes the plasma light spectrally to extract the elemental and molecular information from the skin lesion. More than total 1000 emission spectra from non-melanoma skin cancer (NMSC), melanoma and benign lesions from patients have been acquired and analyzed.
Results: The spectral analysis algorithm analyzes the acquired spectra and then determines the similarity to the embedded spectral database, implying the probability of malignancy. We validated the algorithms using ten-fold cross-validation with two-class disease partition based on the spectral data labelled with biopsy results. The deep neural network (DNN) algorithm in this study achieved up to sensitivity of 92% and specificity of 86% for the detection of skin malignancy.
Conclusion: A novel skin cancer diagnostic device based on laser spectroscopy and machine learning algorithms demonstrated to be a promising, low-cost tool for the detection of skin cancers with superior diagnostic accuracy compared to other optics-based diagnostic techniques.

CLINICAL APPLICATIONS—CUTANEOUS: *SKIN TIGHTENING*

SAFETY AND EFFICACY OF A NOVEL MICRO-EXCISIONAL DEVICE FOR FACIAL REJUVENATION

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Background: Traditional approaches for facial rejuvenation include ablative and non-ablative lasers and RF devices based on thermal energy effects. A novel micro-excisional device has been designed to perform facial rejuvenation without the use of thermal energy.
Study Design/Materials and Method: This study was designed to treat subjects bi-laterally in the mid to lower face with a 22G coring needle and 5% and 7.5% densities in up to 2 treatments, after administration of local aesthetic. Side effects and adverse events were to be recorded up to 180 days. Biopsies were to be taken pre- and post-treatment at 60 or 90 days. Efficacy would be assessed based on Lemperle (per PI and 3 independent reviewers), GAIS (per PI and subject) and Subject Satisfaction Scales at 90 days.
Results: Twenty three subjects with average age of 64 years (53 to 76 years) and Fitzpatrick skin types II and III were enrolled in the study. No unanticipated adverse events or serious adverse events were recorded. Histology from 3 subjects shows no scarring and excellent healing profile. Average pain during treatment was 0.36 (0–10 scale) and average downtime was 3.8 days and included erythema and swelling. Interim 90 days efficacy data of 15 subjects shows that 87% of 30 cheek areas had 1, 2 or 3 levels of improvement in moderate to severe cheek wrinkles, per Lemperle Scale, based on PI assessment. Both

investigators and subjects scored "improved to very much improved" in 93% of subjects, based on GAIS. 80% of subjects were "satisfied to extremely satisfied", with their aesthetic results.
Conclusion: Clinical data establishes this novel micro-excisional device as an effective treatment for facial rejuvenation without the use of thermal energy and without scarring.

CLINICAL APPLICATIONS—CUTANEOUS: *VASCULAR*

THE TOXIC EDGE—A NOVEL TREATMENT FOR REFRACTORY ERYTHEMA AND FLUSHING OF ROSACEA

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Background: Rosacea is a common, chronic facial skin disease. Facial erythema is a frequent and often distressing complaint of patients with rosacea. Treatment of facial erythema with botulinum toxin has previously been proposed and reported. However, the current literature has mixed results. This study evaluated the safety and efficacy of thermal decomposition of the stratum corneum using a novel non-laser thermal resurfacing system to increase skin permeability for botulinum toxin A in the treatment of facial flushing of rosacea.
Study Design/Materials and Method: The device is a thermal resurfacing system which can generate ablative as well as non-ablative micropores opening the skin for transdermal delivery of compounds with no associated pain, bleeding or downtime. 12 patients were enrolled in the study. Affected facial areas were treated by a thermo mechanical system operated at 400 °C for 6 ms–10 ms. Immediately after skin treatment, 40 units of abobotulinum toxin-A were applied over the treatment area and blocked with occlusion for 30 minutes. After 30 minutes the block was removed, and the patient discharged home. All patients received 3 consecutive treatment 1 month apart. Instrumental evaluation included erythema-directed digital photography and X10 dermoscopy. Two non-involved evaluators assessed the facial erythema of rosacea using a standardized grading system (0 = absent, 1 = mild erythema, 2 = moderate erythema, and 3 = severe erythema) to evaluate digital photographs at baseline, 1, 2, and 3 months after last treatment. Statistical analysis of erythema grade included one-way repeated-measures analysis of variance and pairwise comparisons. Patients completed *via* the FACE-Q validated patient-reported outcome instrument.
Results: There was a significant mean improvement of pre- and post-treatment independent assessment and FACE-Q scores ($p = 0.001$ for both). 9 subjects (75%) reported moderate-to-high satisfaction. No adverse effects were noted.
Conclusion: Thermal decomposition of the stratum corneum using the novel mechanothermal system increases skin permeability for botulinum toxin A in the treatment of facial flushing of rosacea seems both effective and safe.

CLINICAL APPLICATIONS—GYNECOLOGIC/WOMEN'S HEALTH: *CO_2 LASER FOR VAGINAL APPLICATIONS*

THE EFFECT OF PIXELATED CO_2 LASER ON THE VAGINAL EPITHELIUM IS NOT THE SAME AS THAT OF LOCAL ESTROGEN: CYTOLOGIC EVIDENCE

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Background: Genitourinary syndrome of menopause (GSM) includes many symptoms that negatively impact the lives of countless women. Vaginal estrogen has been the mainstay of therapy for vaginal symptoms associated with GSM. Previous studies have demonstrated that laser therapy can have similar effects on GSM symptoms. There is predictable cytologic effect of estrogen on the vaginal mucosa as measured by maturation index values.
Study Design/Materials and Method: Patients with symptomatic vaginal atrophy completed pre-treatment evaluations. Subjects underwent three pixelated CO_2 laser treatments over 2 months. Use of other treatments during the study period were prohibited. In addition to completing subjective questionnaires and physical assessments by physicians, a vaginal cytologic maturation value was performed at 9 months after the first laser treatment. Subjects underwent vaginal biopsies before and after treatment as well. A p-value of less than 0.05 was considered statistically significant for comparison of pre- and post-treatment results.
Results: Fifteen patients were enrolled with an average age of 58.3 years (range 43–70 years). Vaginal maturation scores pre-treatment were, predictably, in the postmenopausal range. However, after three treatments with the pixelated CO_2 laser, despite having significant improvement in both subjective and objective symptoms of vaginal atrophy, the maturation index was not significantly improved over pre-treatment scores (mean difference −0.55, CI 95% −16.03 to 14.94, $p = 0.734$). In addition, representative vaginal biopsies were obtained from three subjects >6 months after treatment. Histologically, the surface epithelium ranged from within normal limits to mild squamous atrophy. There was mild submucosal vascular congestion in all specimens, with neovascularization noted in two. One biopsy had mild submucosal fibrosis with scattered reactive stromal fibroblasts.
Conclusion: Clinically significant improvement in all assessed vaginal atrophy symptoms was noted following pixelated CO_2 laser therapy. However, there was no improvement on vaginal cytologic maturation index scores. Histologic changes were consistent with mild submucosal neovascularization rather than epithelial squamous maturation, which coincides with the maturation index findings.

CLINICAL APPLICATIONS—GYNECOLOGIC/WOMEN'S HEALTH: *COMBINED Nd: AND Er:YAG LASER FOR VAGINAL APPLICATIONS*

LABIAPLASTY

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Background: Nowadays aesthetics is increasingly important and women are more concerned with the appearance of intimate areas. The labiaplasty allows the lips of the female genitals to intervene in order to satisfy the needs of the patients. There are several surgical techniques of labiaplasty, depending on the alteration to be treated. In the case of the labia minora, the most common is the reduction of those segments protruding from the labia majora. As for the labia majora, the most frequent is to correct the appearance of aging, by increasing the volume.

Study Design/Materials and Method: The patient is asked to come previously shaved in the genital region to avoid the discomfort caused by the hair when performing the sutures. The patient lies in a gynecological position. For the reduction of the labia minora, a drawing is made marking the internal and external or posterior area where the incisions are to be made, seeking the greatest possible symmetry. Subsequently asepsis and antisepsis of the region with providone-iodine and local anesthetic infiltration with a mixture of 20 ml + ½ amp xylocaine adrenaline + 30 ml of physiological solution is carried out.
Results: If it is also necessary to correct the labia majora, it is done by means of the lipotransference of autologous fat, previously obtained from the crotch zone, under aseptic and antisepsis techniques and local anesthetic infiltration. Additionally, we perform Erbium + CO_2 laser, in order to reduce hyperpigmentation of the genital area, obtaining better aesthetic results.
Conclusion: Analgesic and antibiotic treatment is indicated during the first week and relative rest is recommended during the first 48 hours. During the first month it is indicated not to wear tight clothes, to carry out sports or activities that imply local friction and continuous contact with water, as well as to abstain from having sexual relations. This procedure is performed on an outpatient basis and patients usually reincorporate their regular activities within the first week.

CLINICAL APPLICATIONS—GYNECOLOGIC/WOMEN'S HEALTH: *HIFEM TECHNOLOGY FOR URINARY APPLICATIONS*

SAFETY AND EFFICACY OF HYBRID FRACTIONAL LASER (1470 nm AND 2940 nm) FOR SYMPTOMS OF GENITOURINARY SYNDROME OF MENOPAUSE: PROSPECTIVE MULTI-CENTER STUDY: INTERIM ANALYSIS

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Background: Genitourinary syndrome of menopause (GSM) is a new term describing menopausal symptoms including genital, sexual, and urinary. Recent surveys demonstrate 45–63% of post-menopausal women experience symptoms of GSM. Energy-based therapies, including fractional lasers and radiofrequency have demonstrated promise at alleviating symptoms of GSM. A novel hybrid fractional laser (1470 nm diode and 2940 nm Er: YAG laser, Sciton Inc., Palo Alto, CA) has recently been developed that may offer advantages over prior technology. The objective is to evaluate safety and efficacy of hybrid fractional laser for treatment GSM symptoms.
Study Design/Materials and Method: Prospective, multi-center (5), 50 patient study enrolling peri- and post-menopausal females (40–70). Selection criteria based on at least 2 self-reported symptoms of GSM. Baseline demographics, quality-of life, and exam data recorded including: pelvic exam, vaginal maturation index (VMI), vaginal health index scale (VHIS), female sexual function index questionnaire (FSFI), Day-to-day Impact of Vaginal Aging questionnaire (DIVA) and histology (2/site). Subjects received three treatments at four week intervals (settings: 1470 nm–200–600 um [density 6–15%], 2940 nm–200–300 um [density 7–14%]). Follow-up visits conducted at 1, 3, 6 and 12 month intervals from third treatment. Data points repeated and adverse events recorded at all visits.
Results: Interim analysis included 35 subjects at 1 ($n = 35$) and 3 ($n = 20$) month follow-up. Mean age 58 ± 7 years. FSFI scores demonstrated significant improvement in all domains and overall at 1 and 3 months ($p < 0.05$). DIVA scores demonstrated significant improvement in all domains at 1 and 3 months ($p < 0.05$) with exception of daily activities at 1 month ($p = 0.17$). Maturation index improved at 3 months compared to baseline with marked increase in percent of superficial cells and decrease in parabasal cells. VHIS improved in all domains (elasticity, epithelial integrity, lubrication) changing from poor to good at 1 and 3 months. Significant histological changes were observed with 88.2% increase in epithelial thickness at 3 months. No adverse events reported.
Conclusion: Hybrid fractional laser appears to be safe and efficacious for treatment of GSM. Prospective data collection are ongoing.

THE SYNERGISTIC EFFECTS OF MULTIMODAL THERAPY RESULTING IN BETTER OUTCOMES FOR VAGINAL REJUVENATION AND THE TREATMENT OF STRESS URINARY INCONTINENCE

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Background: Sexual dysfunction related to vaginal laxity and stress urinary incontinence are common difficulties women experience after childbirth. In the past, options for treatment were limited to pelvic floor exercises and more invasive surgical options. Over the past few years, energy-based devices, particularly lasers (Er:YAG dual wavelength and CO_2) have been adopted and marketed as a non-surgical option for treating women's health issues. Results with lasers have been favorable for many women, but there is still room for improvement. Most recently, cryogen-cooled monopolar radiofrequency (CMRF) energy administration to the vaginal canal has also been shown to provide benefit to women for sexual dysfunction and incontinence. The modes of energy administration have different mechanisms of action and depth of penetration so there may be synergy with combination treatment. The objective of this pilot clinical study was to demonstrate that combining a single CMRF treatment (Viveve) with just one CO_2 laser (Aguirre Specialty Care) treatment would provide superior results to the laser 3-treatment protocol alone or a single CMRF treatment alone and would reduce treatment time to one session instead of the three-treatment protocol over 2–3 months. In addition, this study would support the addition of the single CMRF treatment procedure to other vaginal laser procedures for optimum benefit to the patients.
Study Design/Materials and Method: This pilot study was conducted in women seeking improvement in sexual function and incontinence symptoms ($n = 15$). Women were included in one of three groups: 5 patients: One a single CMRF treatment; 5 patients: One single CMRF treatment combined with one CO_2 laser treatment; 5 patients: 3 single CO_2 laser treatments at 0,1 and 2 months. Outcome measures included the validated patient-reported Female Sexual Function Index Questionnaire (FSFI), Urogenital Distress Inventory (UDI-6), Incontinence Impact Questionnaire (IIQ-7), ICIQ-UI-SF and Patient Satisfaction Questionnaire. Time points of assessment included 1, 3 and 6 months post-treatment completion.
Results: Data analysis for the study is currently underway. The summary will include patient demographics and tabulated

results of all questionnaires for each group, along with appropriate comparison between groups and for sexual function and incontinence.
Conclusion: Based upon the mechanism of action and available data for the single CMRF treatment, a potential synergy in combination treatment with laser, resulting in increased benefit to women is expected. With this benefit, the treatment time could also be reduced as the number of laser treatments could possibly be decreased. Even though this is a pilot study, the preliminary data suggest a tremendous advance to women's health and worthy of consideration for the approach chosen in treating sexual dysfunction and SUI. The study represents the first direct comparison for these treatment options.

CLINICAL APPLICATIONS—GYNECOLOGIC/WOMEN'S HEALTH: *PDT/PHOTOBIOMODULATION*

EFFECT OF LOW LEVEL LASER ACUPUNCTURE ON HOT FLASHES AND QUALITY OF LIFE IN POST-MENOPAUSAL WOMEN

Eitedal M. Daoud, Gasser El-Beshry, Doaa Ismail, Maha Saber
Medical Division National Research Centre, Giza, Egypt; Ain Shams University, Cairo, Egypt

Background: Hot flashes are a common and potentially disabling symptom during the menopause that affect greatly on their quality of life. While hormonal replacement therapy is an effective treatment, it isn't accepted by all women either due to potentially serious adverse events or due to relative contraindications. Low Level Laser Therapy (LLLT) is an effective, safe, and non-invasive, non-hormonal treatments for vasomotor symptoms (hot flashes).
Study Design/Materials and Method: The aim of the study is to evaluate LLLT as a safe, and non-invasive modality for treating menopausal hot flashes and its impact on their quality of life. Forty cases of pre- and post-menopausal women who presented to outpatient clinic of the Maternity Hospital of Ain Shams University and Centre of Excellence, National Research Centre Egypt were recruited. For all women included in the study, their menopausal symptoms were assessed according to Modified Kupperman Index. They were randomly divided into 2 groups: Group A (Study group) = Laser acupuncture active group: included 20 women who was subjected to low level laser acupuncture at standard acupoints (Spleen 6, Large Intestine 4, Lung 7, Liver 3, Cardiovascular 4, Heart 6, Kidney 6, Kidney 7) and ear points (Shen Men, sympathetic and endocrine) was exchanged every week. Group B (Control group) = Placebo group: included 20 women, was subjected to low level laser acupuncture on the same acupoints but Laser was off. Each woman received 2 sessions per week for 6 weeks. After 6 sessions and at the end of the study, again all menopausal symptoms were assessed according to Modified Kupperman Index. Follow-up: Six months after end of laser acupuncture sessions, menopausal symptoms were assessed again in each case using Modified Kupperman Index.
Results: After 12 sessions among intervention group compared to controls, there is significant improvement in both frequency and severity of hot flashes. In the same time there were significant improvement in paresthesia, nervousness, headache and sexual complaints. Also, there were highly significant improvement in melancholia, insomnia, vertigo, fatigue, formication, palpitation and UTI symptoms. Followed up after treatment for six months gave us the same positive effects of laser acupuncture.
Conclusion: In this study, there was significant improvement in menopausal symptoms without side effects. So, laser acupuncture can be used as an alternative to hormone replacement therapy which doesn't suit all women either because of concerns over potentially adverse events or because of relative contra-indications.

CLINICAL APPLICATIONS—MULTI-SPECIALTY: *PHOTOBIOMODULATION*

A CASE REPORT: AN EFFECTIVE TREATMENT STRATEGY FOR DRY AGE-RELATED MACULAR DEGENERATION WITH COMBINATION OF ACUPUNCTURE AND PHOTOBIOMODULATION

Steve Liu, Hui Liu, Michael Hamblin
HanLing Acupuncture Healing Center, Tucson, AZ; University of Massachusetts, Boston, MA; Massachusetts General Hospital, Wellman Center for Photomedicine, Boston, MA

Background: Age macular degeneration (AMD) is a leading cause of vision loss in Americans older than 60. While treatment progress of wet-type AMD has been made over the past 20 years, currently there is no standard treatment for dry-type AMD, which accounts for 90% of the disease. However, strategies for using either acupuncture or photobiomodulation (PBM) have shown clinical efficacy in dry AMD as alternative methods. Here we report for the first time a combined strategy of using acupuncture and PBM to treat dry AMD with an immediate and long-lasting result.
Study Design/Materials and Method: We used Scandinavian acupuncture points in the palms and soles of feet in conjunction with LED PBM therapy to treat the patients. The retina was evaluated by an ophthalmologist with the standard procedure. The acupuncture treatments are rendered twice a day with a one-hour break in between; the LED PBM therapy then is given during the break and after the second acupuncture treatment for 4 minutes in each eye. This protocol takes place every day for five days straight in the first week. It is repeated for another five days in the following week.
Results: The patient's vision reported improvement immediately after the first six treatments with no visual distortion and better acuity. Her follow-up clinical exams by her ophthalmologists showed right eye distance acuity improved to 20/40 (1/29/2015) from 20/60 (10/20/2014) and left eye to 20/30 (1/29/2015) from 20/200 (10/20/2014) after the total of 20 treatments. The better vision has been maintained up to date (phone conversation with the patient on 2/2/2018) since the last treatment (1/16/2015).
Conclusion: We reported a clinical case of successfully treating dry AMD with a combined therapy of acupuncture with LED PMB with no known side effects, which may have a potential impact on dry AMD with systematic fundamental scientific research and controlled studies.

CHANGES IN CLINICAL AND OXIDATIVE STRESS PARAMETERS IN PERIODONTAL POCKETS TREATED WITH LASER THERAPY: A PRELIMINARY SPLIT-MOUTH STUDY

Katia Rupel, Giulia Ottaviani
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Background: Periodontal disease is a pathological process which involves complex interactions between microorganisms in the oral cavity and host immune system, which cause the

formation of gingival pockets, and eventually loss of teeth. There is growing evidence about the efficacy of laser therapy for the treatment of periodontitis, but little is known about the possible effects on oxidative stress parameters in periodontal pockets.
Study Design/Materials and Method: The study was conducted according to the declaration of Helsinki and was approved by the local ethical committee. 4 patients meeting inclusion and exclusion criteria with chronic periodontal disease assessed by periodontal chart were included in the study and treated in split-mouth, where half mouth was treated with scaling root planing (SRP), while the other half was treated with SRP + laser therapy including two protocols: an antimicrobial phase with 445 nm wavelength, peak power 0.5 W, frequency 20 Hz and fluence 13 mJ/cm^2, and a biostimulating phase with 970 nm wavelength, peak power 0.1 W, and fluence 6 J/cm^2. Gingival crevicular fluid (GCF) samples from 26 pockets (13 SRP, 13 SRP + laser) with probing depth $\geq$4 mm were obtained using Periopaper at following time points: T0 (before treatment), T1 (24 hours after treatment), T2 (7 days after treatment), T3 (14 days after treatment) and T4 (45 days after the treatment). A blinded rater recorded clinical parameters repeating the periodontal chart 45 days after the treatment. GCF samples were processed performing tests for the determination of both oxidative stress and antioxidant capacity: TOS (Total Oxidant Status), AOPP (Advanced Oxidation Protein Products) and FRAS (Ferric Reducing Ability of Saliva). A $p < 0.05$ was assessed for the rejection of the null hypothesis.
Results: Clinical parameters significantly improved in both groups. Among the selected pockets, the probing depth decreased significantly in both groups. The number of SRP + laser (−56.16%) treated pockets that reduced probing depth to <4 mm was higher than the SRP (−42.36%) group, but the difference wasn't statistically significant. Oxidative stress increased significantly at T1 in SRP group, while in the SRP + LT it remained at baseline. In addition, both TOS and AOPP increases at T1 were able to identify the pockets that responded less to both therapies.
Conclusion: The addition of laser therapy to conventional periodontal therapy reduced oxidative stress during healing time. Oxidative stress markers TOS and AOPP seem to be able to identify early the response to the treatment.

EARLY CAREER: *BASIC SCIENCE*

THERMAL PHOTODYNAMIC THERAPY INCREASES APOPTOSIS AND REACTIVE OXYGEN SPECIES GENERATION IN SQUAMOUS CELL CARCINOMA CELLS

Evan Austin, Eugene Koo, Christopher Wong, Daniel Fischer, Jared R. Jagdeo
University of California at Davis, Sacramento, CA; Dermatology Service, Sacramento VA Medical Center, Mather, CA; SUNY Downstate Medical Center, Brooklyn, NY

Background: In the United States, it is estimated that greater than 700,000 new cases and 8,000 deaths each year are attributable to cutaneous squamous cell carcinoma (SCC). Thermal photodynamic therapy (thermal PDT) is a two-step process that includes heating of tissues or cells during the application of a photosensitizer and is followed by light activation of the photosensitizer. This approach is designed to optimize PDT outcomes. Traditional PDT is typically used for pre-cancerous actinic keratosis, but we believe thermal PDT may be applicable for the treatment of SCC. We have previously demonstrated that thermal incubation of 5-ALA at temperatures between 33 °C and 42 °C for 30 minutes increases apoptosis and reactive oxygen species (ROS) generation in dermal cells. We hypothesized that thermal incubation of 5-ALA for 30 minutes followed by blue light would increase apoptosis and ROS generation in cutaneous SCC cells. Herein, we incubated SCC cell lines with 5-ALA for 30 minutes at temperatures between 21 °C and 42 °C and then irradiated the cells with 1000 seconds of blue light, which has many parallels to the clinical therapeutic protocol.
Study Design/Materials and Method: We measured changes in apoptosis and ROS generation using flow cytometry with annexin-V/7-aminoactinomycin D and dihydroethidium, respectively. Statistical testing was performed using ANOVA and t-test with significance of $p < 0.05$. SCCs responded to 5-ALA with a dose-dependent increase in apoptosis and free radical ROS generation after a 30-minute incubation at 36 °C. Thermal PDT increased apoptosis and free radical ROS in a temperature-dependent manner.
Results: Our results indicate that thermal PDT may be a potential treatment for SCC as cellular apoptosis and ROS generation increased following thermal PDT.
Conclusion: Future clinical trials are required to determine specific treatment parameters and to compare thermal PDT efficacy to standard of care treatments. The study was funded by a grant awarded to the VA non-profit foundation.

EARLY CAREER: *CLINICAL APPLICATIONS OF LASER & LIGHT*

A COMPARISON OF THREE DIFFERENT LASER MODALITIES FOR THE TREATMENT OF HYPERPIGMENTED SCARS IN A SKIN TYPE VI AFRICAN AMERICAN MAN

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University of Alberta, Edmonton, Alberta, Canada; Cosmetic Laser Dermatology, San Diego, CA

Background: The development of hyperpigmented scars due to persistent post-inflammatory hyperpigmentation is a common problem amongst patients with darker skin types. Treatment of these lesions is challenging due to the propensity for further hyperpigmentation following any attempted therapy. Bleaching creams can have some benefit, but are often insufficient to achieve complete resolution. In this study, a fractionated 1927 nm diode laser, a fractionated 1927 nm thulium fiber laser, and a fractionated 1064 nm picosecond laser were used to treat multiple hyperpigmented scars to the right shin of an African American man.
Study Design/Materials and Method: A 36-year-old African American man presented with a 10 year history of persistent hyperpigmented scars due to injuries suffered while performing a variety of physical activities. Previous use of topical hydroquinone as well as superficial chemical peels had been ineffective. A total of 10 discrete geometric oval to rectangular hyperpigmented flat scars were present to the right anterior shin. After obtaining informed consent, five were treated with a fractionated 1927 nm diode laser (1927-D) at 9 mJ pulse energy and 10% density; three were treated with a fractionated 1927 nm thulium fiber (1927-TF) laser at 5 mJ pulse energy and 20% density; and two were treated with a fractionated 1064 nm picosecond laser (1064-PS) at 2.1 J, 6 × 6 mm spot size, 450 picosecond pulse duration, and 70 pulses.

Results: At the 6 month follow up time point, all treated scars demonstrated significant improvement. The scars treated with 1064-PS were 90–100% resolved; with 1927-TF, 90% resolved; and with 1927-D, 80–90% resolved. There was no evidence of post-inflammatory hyperpigmentation and the post-laser recovery period was unremarkable.
Conclusion: In this study, we demonstrate the safety and efficacy of three different laser systems for treating pigmented scars in dark-skinned individuals. We highlight the requirement for low fluences and low densities, as well as the novel use of fractionated picosecond laser for this purpose.

FRACTIONAL CO_2 LASER TREATMENT OF MICROSTOMIA IN SYSTEMIC SCLERODERMA

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Washington Hospital Center/Georgetown University Hospital Dermatology, Washington, DC

Background: Orofacial disease is one prominent regional pattern of disease expression in systemic scleroderma (SSc). Microstomia and limited mouth opening are primary factors implicated by patients with orofacial disability. We report the use of fractional CO_2 laser to treat microstomia and limited mouth opening in SSc.
Study Design/Materials and Method: At our initial visit, we referred the patient to physical therapy where a jaw home exercise program was prescribed. Two-months after, the patient's orofacial pathology had progressed and we proceeded with a fractionated CO_2 laser (Lumenis, Santa Clara, CA) of the bilateral oral commissures; settings: 600 Hertz, 10 ms timed exposure, and 20 mJ fluence. Two passes of single pulse treatments were performed at different angles. Ultimately, we performed 6 treatments of the oral commissures at 1–2 month intervals, with increasing fluences up to 50 mJ. Additionally, we performed 5 treatments circumferentially of the cutaneous lips.
Results: Consistently, immediately post-operatively, the patient reported the ability to open her mouth wider than preoperatively and immediate softening of the scarred tissue was apparent. Immediate post-laser erythema was noted, however no complications occurred. During the weeks following the initial treatment, she felt increased skin laxity around her mouth leading to increased oral aperture. Previously, most tension was lateral to the lips near the commissures, but post-therapy more tension was above and below her mouth likely due to relief at previously more limiting sites. With the addition of circumferential laser application, the patient reported a uniform decrease in tension.
Conclusion: Although further trials are necessary to investigate this therapy, fractional ablative CO_2 laser treatments proved successful to improve symptoms in our patient. We propose this therapy be considered in the therapeutic armamentarium for SSc-associated orofacial disease. To date, neither non-fractionated or fractionated ablative CO_2 lasers have been reported to cause complications in the treatment of orofacial disease manifestations in SSc patients.

INTRAOPERATIVE RESURFACING WITH FRACTIONATED Er:YAG TO MINIMIZE SCARRING: RESULTS OF A SPLIT SCAR PILOT STUDY

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Beaumont Health Dermatology Residency Program, Bloomfield Hills, MI: Legacy Dermatology Group, Bloomfield Hills, MI

Background: Laser resurfacing to minimize the appearance of surgical scars has proven beneficial. New research has shown that the earlier we can treat scars with laser ablation, the better. Therefore, why not treat the skin intra-operatively before the scar has a chance to form? Multiple studies have proven that intraoperative fractional CO_2 laser ablation improves the appearance and texture of surgical scars. All current intraoperative studies on the body have used fractionated CO_2 ablation, while fractionated Er:YAG ablation can more effectively target water in the upper dermis. After the deep sutures are in place, the laser can target the dermo-epidermal junction and epidermis to minimize fibrosis during the earliest phases of wound healing. Fractional Er:YAG also has fewer side effects than ablative or fractionated CO_2.
Study Design/Materials and Method: Five patients being treated for non-melanoma skin cancer on the trunk or extremities, *via* surgical excision were selected for the study. All patients had a surgical wound length greater than four centimeters. The scar was split in half and two passes using a fractionated Er:YAG laser were performed on the treatment side. The patients returned for follow-up at two weeks and three months. Photos were taken at the three-month visit, and the patient rated their scar using the patient and observer scar assessment scale (POSAS). A blinded, board certified dermatologist also rated all scars using the POSAS.
Results: Patient and physician POSAS scores favored the treated half of the surgical wound. One patient developed two suture abscesses in the control side of the wound, but there were no adverse outcomes in the wound halves treated with Er:YAG ablation.
Conclusion: This small pilot study shows that there is a measurable cosmetic benefit to using a fractionated Er:YAG laser to treat surgical sites other than the head and neck prior to superficial suture placement. Larger studies will be useful to further validate the statistical significance of this procedure.

LASER ASSISTED MICROFOLLICULAR UNIT TRANSPLANTATION FOR FRONTAL HAIRLINE RESTORATION IN FEMALES: STEPS TOWARDS PERFECTION

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Background: Hair transplantation has been a highly effective technique in reducing wide foreheads and recontouring the hairline in both females and males. Creating a natural hairline is one of the most important and challenging factors for a successful hair transplant (Sirinturk et al, 2017). The mini- and micro-grafting method has been the most current treatment methods for male pattern baldness and female androgenic alopecia. The preparation of the recipient area with 16G needle has been reported in the literature. However, during the insertion of grafts, the neighboring grafts tend to 'pop out' (Zor et al, 2011). A new technique; LASER Assisted MicroFollicular Unit Transplantation (LAMFUT) using a recently developed scanner of Fractional carbon dioxide Laser (FxCR) has been recently in hair restoration of Secondary Cicatricial Alopecia (SCA) with great success. We hypothesized that our (LAMFUT) technique would produce a natural appearing distribution of hairline by minimizing 'pop out' and increasing the hair density at the recipient area in an acceptable time frame.
Study Design/Materials and Method: Forty-six female patients diagnosed with Androgenetic Alopecia or originally high Frontal Hairline were included in our study for a single session of hair restoration. Follicular Unit Extraction (FUE) by a regular handheld micropunch (0.9 mm diameter) was done. Grafts preparation, by highly trained surgical assistants, was done simultaneously to shorten the whole procedure time. The

grafts were rapidly and finely cut, counted into groups (single, double, triple and quadri) then kept in special containers filled with Platelets Rich Plasma (PRP) prepared from the patient earlier upon starting the FUE step. Immediately after finishing FUE step, we used LAMFUT LASER scanner of FxCR before the implantation step. Variable parameters were applied to determine the density plan and prepare holes for follicular units' insertion in the recipient area. Trichoscopy Evaluation using hair counter of a new Trichoscopy for hair density was done immediately after LAMFUT Scanner and 9 months after surgery for comparison. Digital photographic evaluation was made for comparison of pictures before and after 9 months. The pictures for the results after 9 months were mixed with pictures for other unoperated patients in a ratio of 1:3 and presented to two blind assessors for testing the natural hairline design. The two blind assessors and the patient were asked to grade the results on scale from zero to ten.

Results: Using the scanner of LAMFUT, we were able to prepare hole densities ranging from 72 to 108 holes per cm^2 according to Trichoscopy software. There was minimal popping up of implanted hair follicles and the intraoperative bleeding was notably decreased; thus, higher density in such cases was possible. After 9 months, hair regrowth was more than 90% of implanted grafts. The hairline density ranged from 88 to 122 hairs per cm^2 according to Trichoscopy software. In the thirty-nine patients who completed the follow up visits after 9 months, the blind assessors were only successful to correctly identify eight operated patients (20.5%). A score of 8.8 out of 10 was the result on calculating the average score for both blind assessors' and the patient's evaluations.

Conclusion: The new scanner of LAMFUT is a new promising tool for optimizing results of frontal hairline restoration in females. Further studies should be done for males' frontal hairline.

NURSING/ALLIED HEALTH

NURSING CONSIDERATIONS FOR INTRAOCULAR SHIELD USE

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Introduction/Overview: Non-invasive periorbital and eyelid procedures are increasingly being used in dermatology as an alternative to invasive surgeries for skin tightening and periorbital fine lines.

Analysis: Our practice has developed detailed patient management protocols based on the high volume of periorbital procedures performed in our office. This review will detail our nursing pre-operative, intra-operative and post-operative protocols for intraocular shield use.

Discussion: We present a review of nursing considerations for safe and effective intraocular shield use within our practice. These guidelines include primary indications and contraindications, safe sterilization and maintenance of shields, appropriate intra-operative directions, and post-operative patient management. In addition, we review common complications seen such as corneal abrasions and blepharitis. While complications are rare, they can occur and require immediate recognition and management to reduce related adverse reactions.

Conclusion: Nursing considerations are reviewed to optimize patient outcomes while using intraocular shields for safe and optimal outcomes.

Patient Feedback: There is a need for standard nursing protocols and education to ensure safe and effective use of intraocular shields during these procedures.

HISTOLOGICAL IN VIVO STUDY: THE MECHANISM OF ACTION

INDUCTION OF FAT APOPTOSIS BY A NON-THERMAL DEVICE: SAFETY AND MECHANISM OF ACTION OF NON-INVASIVE HIFEM® TECHNOLOGY EVALUATED IN A HISTOLOGICAL PORCINE MODEL.

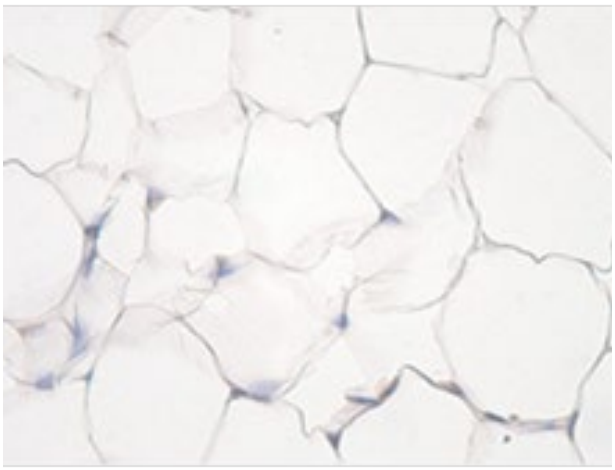
Robert Weiss M.D.[1], MVDr. Jan Bernardy[2]

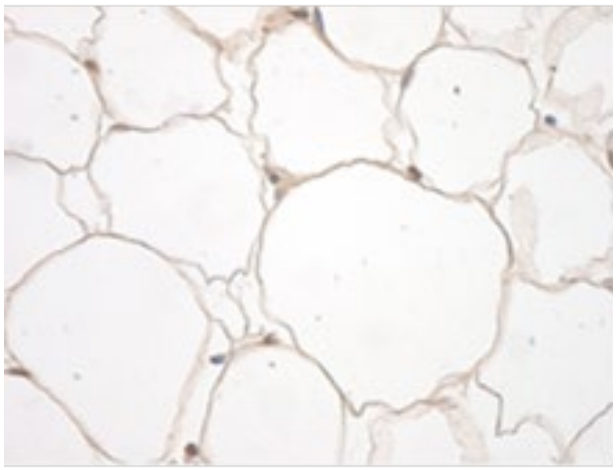
1. Maryland Laser Skin, & Vein Institute, Hunt Valley, MD; 2. Veterinary Research Institute, Brno, CZ

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

- **92 % increase in average apoptotic levels** in fat cells from 18.75 % at baseline to 35.95 % 8 hours post 1 treatment (levels in the control subject remained stable).
- The results show link between **fat cells apoptosis** and elevated levels of free fatty acids released during **supramaximal muscle contractions** induced by the treatment.
- Blood analysis confirmed a rapid metabolic reaction after the treatment as supporting evidence of changes in the subcutaneous fat tissue. **No safety risks were identified**.



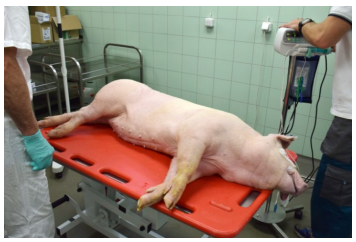


Microscopic analysis of the fat tissue confirmed that the amount of apoptotic cells increased significantly after the treatments (right) compared to the baseline (left).

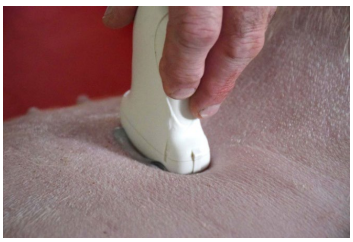
STUDY DESIGN

- Evaluation of changes in the levels of **programmed cell death of adipocytes** in a porcine model in vivo **following a single** EMSCULPT® **treatment**.

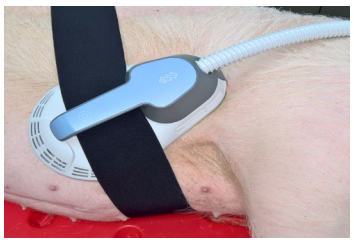
- Two Yorkshire pigs were treated for 30 minutes. One pig was recruited as a control subject.



Animal care was in compliance with the convention for the protection of vertebrate animals used for experimental and other scientific purposes.



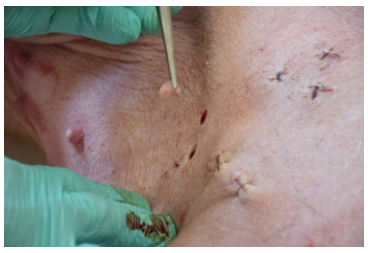
The fat thickness was checked before the experiment using the linear probe of a diagnostic ultrasound device (Mindray M5Vet).



The abdomen was treated for 30 minutes using the EMSCULPT applicator secured by a fixation belt.

- **Punch biopsy** specimens of fat tissue together with **blood samples** were taken before the treatment, after 1 hour and 8 hours post-treatment.

- **TUNEL assay** was applied on **histological samples** and the blood samples were tested for biochemical and hematological parameters.



An image of a biopsy sample being taken 8 hours post-treatment.

RESULTS

- The apoptotic index was calculated from **120 histological samples**. Data were statistically analyzed using rANOVA.

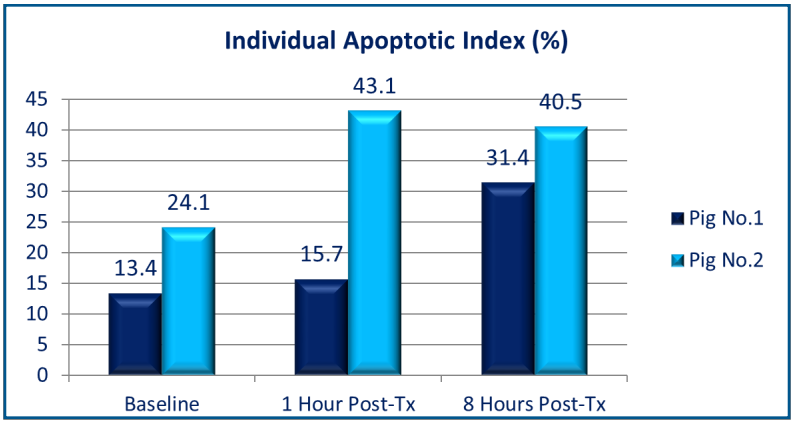


Figure 1: Average apoptotic index (%) evaluated in each pig individually.

ULTRASONOGRAPHY STUDY: SUBCUTANEOUS FAT REDUCTION

CHANGES IN SUBCUTANEOUS ABDOMINAL FAT THICKNESS FOLLOWING HIGH-INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM®) FIELD TREATMENTS: A MULTI CENTER ULTRASOUND STUDY.

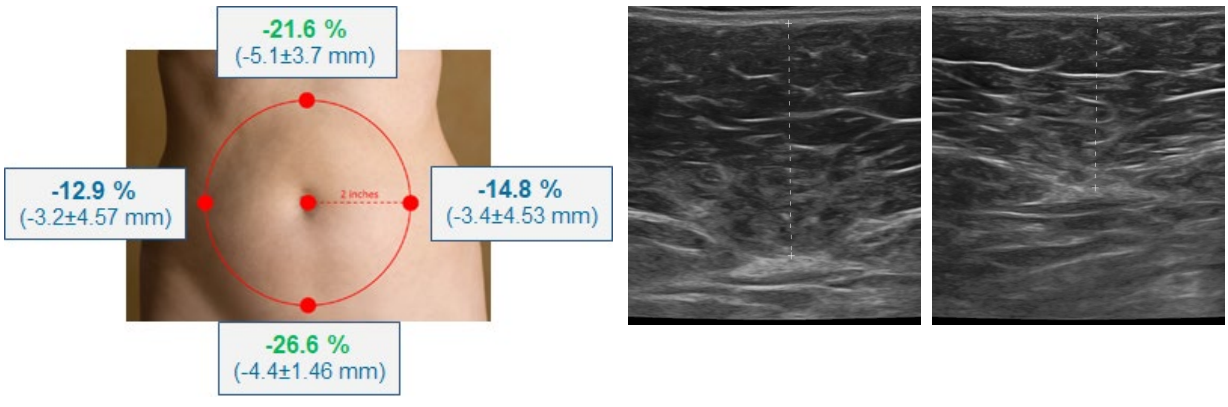
Bruce Katz M.D.[1], Robert Bard M.D.[2], Richard Goldfarb M.D.[3], Aaron Shiloh M.D.[4], Dilyana Kenolova M.D.[5]

1. Juva Skin and Laser Center, Manhattan NY, USA; 2 Bard Cancer Diagnostics, Manhattan, NY, USA; 3. Center for SmartLipo & Plastic Surgery, Langhorne PA, USA; 4. Shiloh Vein and Aesthetic Institute, Philadelphia PA, USA; 5. Dermasense Dermatology Clinic, Burgas, Bulgaria.

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

- **33 patients** received four 30-minute treatments and were evaluated 1 month post application.
- **Ultrasonography** calculated fat thickness in multiple mesurement points **covering the whole abdomen**.
- On average **19.0 % (4.4 mm) reduction of fat** was observed. The most significant **reduction in fat (26.6 %)** was observed **subumbilicaly**.
- **High consistency** with **0 non-responders**; 21 out of 33 patients had greater than 15 % fat reduction.
- **91 % satisfaction** with treatment results.

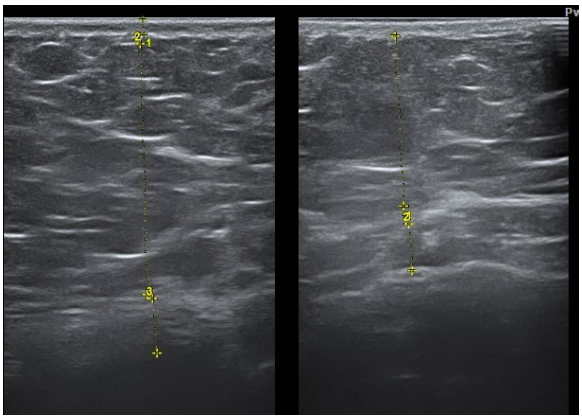


Ultrasound measurements revelated that fat was reduced significantly ($p<0.05$) in all abdominal areas, with the highest change seen in epi- and sub-umbilical regions.

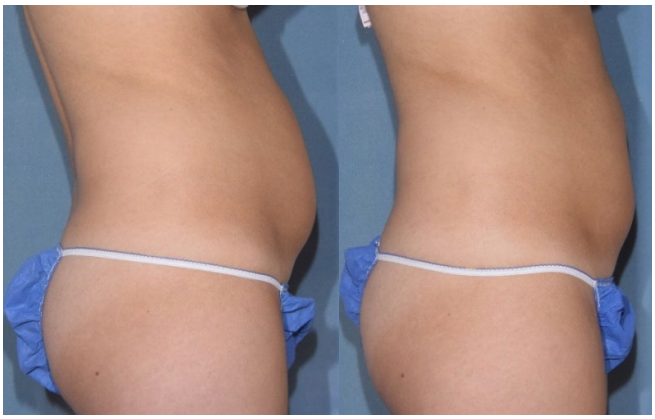
RESULTS

Patient 3: 24 years old female

BASELINE 1 MONTH FU

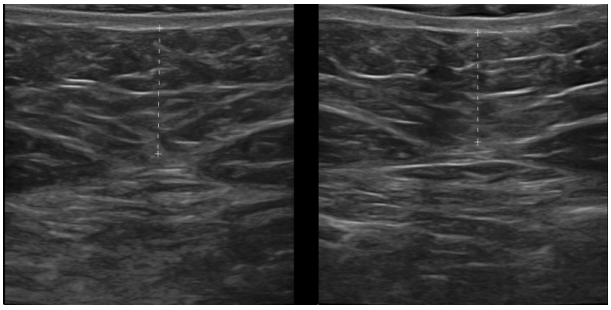


BASELINE 1 MONTH FU

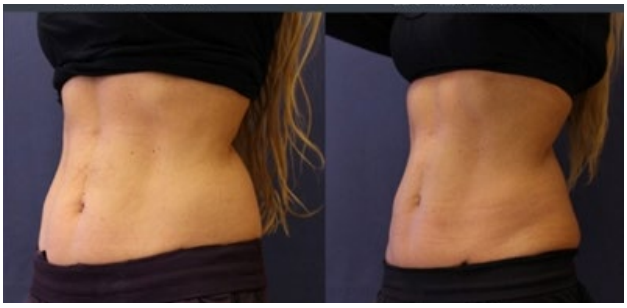


Patient 15: 47 years old female

BASELINE 1 MONTH FU



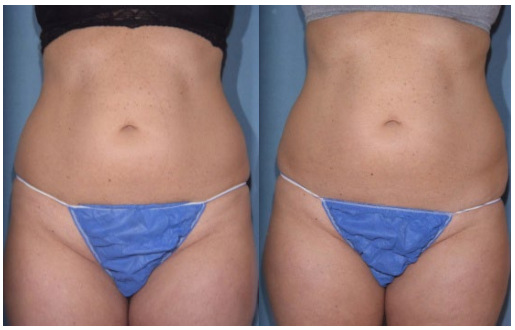
BASELINE 1 MONTH FU



Patient 6: 44 years old female

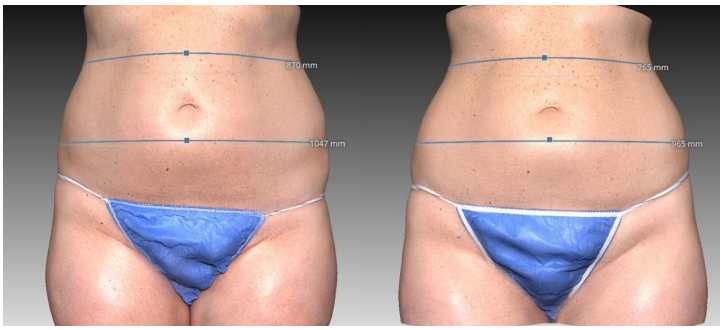
2D Photography

BASELINE 1 MONTH FU



3D Photography

BASELINE 1 MONTH FU



AMERICAN SOCIETY FOR LASER MEDICINE AND SURGERY

2018 ELECTRONIC POSTERS (ePOSTERS) TOWN HALL AND ePOSTERS

ePOSTER TOWN HALL: *BODY CONTOURING*

A NOVEL NON-INVASIVE TECHNOLOGY BASED ON SIMULTANEOUS INDUCTION OF CHANGES IN ADIPOSE AND MUSCLE TISSUES: SAFETY AND EFFICACY OF A HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM) FIELD DEVICE USED FOR ABDOMINAL BODY SHAPING

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Background: Current approaches to non-surgical abdominal contouring are represented by fat reduction technologies inducing thermal effects (radiofrequency, cryolipolysis, laser). These are ideal for patients with fat bulges/overall abundance. Our study investigates effects of a novel approach which affects both the subcutaneous adipocytes and the underlying muscle structure in a non-thermal manner, as a new way of treating lower-to-medium BMI patients.

Study Design/Materials and Method: 22 patients (avg. BMI 23.8 $kg \cdot m^2$) received four 30-min treatments using a non-invasive High Intensity Focused Electro-Magnetic (HIFEM) field device. The therapy was applied on abdomen, inducing supramaximal contractions of musculus rectus abdominis, obliquus externus and obliquus internus. No anesthesia was applied. Weight and waist measurements as well as photographs were taken at the baseline and at 3-month follow-up. Patient satisfaction was evaluated using questionnaires. Photographs were given to blinded evaluators for recognition. All data was tested by t-tests.

Results: 19 patients completed the study. The average waist size was reduced by 4.37 ± 2.63 cm ($p < 0.01$) at 3 months. In 89.47% of cases the evaluators successfully recognized the before image from the 3-month image. Patients reported their abdominal appearance has improved (91%), that they're satisfied with treatment results (96%), and that they'd recommend the treatment to a friend (92%). No adverse events occurred.

Conclusion: We focused on significantly lower-BMI patients (avg. 23.8 $kg \cdot m^2$) than most studies published on other body shaping devices. With this consideration, the average waist reduction represents a highly competitive result. Subjects showed a combination of reduction in fat and muscles remodeling. The additional muscle strengthening effect was critical in achieving improvement in patients with less subcutaneous fat. The device represents a new modality for body contouring with primary application on lower and medium BMI patients. It's a new extension to current devices only targeting adipose tissue.

CARBOXYTHERAPY FOR SUBCUTANEOUS ABDOMINAL FAT REDUCTION: A RANDOMIZED CONTROLLED TRIAL

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Background: There are now many available treatments for subcutaneous fat reduction. Non-invasive fat removal treatments are appealing to patients because of the ease of recovery and less adverse events compared to invasive methods. Carboxytherapy is the insufflation of carbon dioxide gas into the skin layers, and one potential non-invasive treatment for fat reduction. The efficacy of carboxytherapy for the reduction of subcutaneous fat in the *abdomen* area will be evaluated in this study.

Study Design/Materials and Method: This was a randomized, sham-controlled, double-blind, split-body study. Adult participants who met inclusion and exclusion criteria were enrolled. One side of the body was randomized to receive infusions of 1000 cc of CO_2 every week for 5 weeks in the flank region, while the contralateral side received sham treatments. Outcomes measured were fat layer thickness using a diagnostic ultrasound, total circumference, and body weight.

Results: 16 participants completed the study. There was a significant difference in fat thickness one week after the last treatment ($p = 0.011$) with the carboxytherapy side working better, but this difference was not maintained at 28 weeks as measured by diagnostic ultrasound. Total circumference decreased nominally but not significant. Body weights did not significantly change throughout the study.

Conclusion: Carboxytherapy may provide a small but transient decrease in subcutaneous fat. Unfortunately, this effect did not last for a meaningful period of time after the treatment was stopped.

CLINICAL STUDY TO ASSESS A 1060 nm HYPERTHERMIC DIODE LASER FOR THE TREATMENT OF CONTOUR DEFORMITIES POST LIPOSUCTION

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Background: Liposuction has become increasingly popular in the past decade due to advances in technique and technology. Although successful for the most part, there is a population of patients who have contour deformities post-surgery. The 1060 nm non-invasive diode laser has been approved for the removal of unwanted fat, so it was theorized that it could be used to even out these areas of deformities.

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Study Design/Materials and Method: This study was designed to retrospectively study the clinical changes induced by a 1060 nm diode system on contour deformities in tissue post liposuction. 15 patients with contour deformities post liposuction (minimally 6 months post-surgery) were treated in the area of the deformity with the noninvasive hyperthermic 1060 nm diode. Each patient received 2 treatments at a 6-week interval in the anatomical area of their contour deformity.
Results: Although this is technically a retrospective study based on treatment schedules, some patients are still in follow up. At the time of submission, 10 of 15 patients had completed 2 treatments and the necessary follow up to be included in these results. Two blinded evaluators could correctly identify the pretreatment image compared to the post treatment image in an average of 85% of subjects. 100% of the patients were graded to be at least "Improved" with an average of 50% of subjects being "Much Improved" and an average of 40% of subjects being "Very Much Improved". Patient satisfaction was "High" in all subjects who have completed the treatment protocol. There were no unanticipated adverse events or complications.
Conclusion: The noninvasive hyperthermic 1060 nm diode system is safe and highly effective in the treatment of contour deformities post liposuction.

COMPUTED TOMOGRAPHY (CT) BASED EVIDENCE OF SIMULTANEOUS CHANGES IN HUMAN ADIPOSE AND MUSCLE TISSUES FOLLOWING A HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC FIELD (HIFEM) APPLICATION: A NEW METHOD FOR NON-INVASIVE BODY SCULPTING

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Background: We investigated the effects of a novel non-invasive device utilizing non-thermal technology for induction of changes in patient's subcutaneous adipose tissue (SAT) and abdominal wall muscle. Morphologic changes in SAT and rectus abdominis muscles were evaluated by computed tomography (CT) following a series of treatments with this novel non-thermal technology.
Study Design/Materials and Method: We treated 16 male and female subjects (aged 34 to 64, mean BMI 23.4kg · m-2) using a High Intensity Focused Electro-Magnetic (HIFEM) field device. Subjects underwent CT scanning at baseline and 1 month after five to eight 30-minute abdominal treatments administered bi-weekly. Changes in subcutaneous fat and abdominal muscle thickness were calculated from the same subumbilical and epiumbilical CT cuts, respectively, using midsternal and lateral measurement points. Data collected included standardized photographs, and circumference measurements taken throughout the study. Patients were instructed to maintain their routine diet and activity level without any modifications. All patients completed a standardized questionnaire regarding their treatments
Results: Comparing patient baseline to follow-up measurements, CT data showed on average $19.2 \pm 9.7\%$ reduction in subcutaneous fat and simultaneous $15.8 \pm 10.1\%$ thickening of rectus abdominis, and patients lost on average 1.64 ± 1.35 inch off their waist. Most of the waist reduction effect was achieved already after 4th treatment. All results proved highly significant ($p < 0.01$) while weight change was insignificant. Digital photographs showed aesthetic improvement in most patients. The treatments were painless and without adverse events.
Conclusion: Results suggest that the investigated device is effective for abdominal body sculpting. CT scans documented improvement in both SAT and rectus abdominis muscle. This method delivers improvement in two tissues (fat and muscles), thus allows practices to treat a wide range of patient profiles. It has very low risk profile stemming from its non-thermal technology. Data suggest 4 treatments as the ideal protocol.

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC THERAPY (HIFEM) EVALUATED BY MAGNETIC RESONANCE IMAGING (MRI): SAFETY AND EFFICACY STUDY OF A DUAL TISSUE EFFECT BASED NON-INVASIVE ABDOMINAL BODY SHAPING

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Background: Physicians are facing increasing demand for body contouring, creating pressure for emergence of innovative methods to deliver aesthetic improvement non-invasively to a wide range of patients. This study evaluates the efficacy of a High Intensity Focused Electro-Magnetic (HIFEM) technology for abdominal body shaping as a new way of treating patients in aesthetic practices.
Study Design/Materials and Method: In total 13 patients (5 female, 8 male, average age 36.0, BMI 24.8 kg/m^2) received 4 treatments over umbilicus, 30 minutes each, separated by 2–3 days. Anthropometric evaluations were recorded and digital photographs were taken. The MRI without contrast determined by vertertebras T12 and S1 (FIESTA and FSPRG sequences) was used to measure fat and abdominal muscle thickness before the treatments and 2 months ($\pm$10 days) after the last procedure, in order to assess anatomical changes in abdominal tissues as a consequence of the application.
Results: All patients tolerated the treatments well with no adverse events. Two patients reported mild muscle fatigue one day after the treatment. Analysis of the same MRI slices verified by tissue artefacts showed a statistically significant average $18.1 \pm 9.1\%$ reduction of adipocyte tissue and $14.4 \pm 7.9\%$ increase in muscle mass ($p < 0.001$), coupled with measurable circumferential reduction. Fat changes were visible in all patients; one patient didn't have any muscle growth reaction. The weight of the subjects didn't change significantly.
Conclusion: MRI considered as a highly precise diagnostic method revealed significant simultaneous muscle growth and fat reduction 2 months post treatments, unrelated with dieting. This suggests the therapy as a unique solution for patients whose aesthetic problem isn't driven by fat mass only, but also by the underlying muscle structure. This positions the treatment next to existing technologies, and opens physicians' access to a completely new segment of patients who aren't ideal candidates for stamping or suction based fat removal treatments.

LIMITED RELEASE TISSUE STABILIZED-GUIDED SUBCISION FOR THE TREATMENT OF MILD-TO-MODERATE CELLULITE OF THE BUTTOCKS AND THIGHS

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Background: Tissue stabilized-guided subcision (TS-GS) has been shown to be effective for improving the appearance of moderate-to-severe cellulite in the buttocks and posterolateral

thighs. Mild-to-moderate cellulite, however, is characterized by shallower dimples and interconnected ripples. Herein we describe the use of smaller focal or limited tissue releases to effectively treat mild-to-moderate dimples on the posterolateral thighs and buttocks.
Study Design/Materials and Method: A retrospective chart review was conducted of all patients in our practice who had undergone TS-GS. Two independent blinded raters, not affiliated with the study, analyzed before and after photos and rated cellulite improvement after treatment on a quartile scale (0 = 0%, 1 = 1–25%, 2 = 26–50%, 3 = 51–75%, and 4 = 76–100%). The buttocks and thighs were assigned separate improvement scores, and a global score was assigned to the overall appearance of the cellulite after treatment.
Results: All patients (23) were female and exhibited cellulite of mild to moderate severity. All subscisions were performed at a fixed depth of 6 mm below the surface of the skin, with a minimum of 3-mm between each dimple/fold. The treating physician administered smaller, focal tissue releases for smaller dimples and folds on the buttocks and thighs. The blinded raters correctly and independently identified which photos represented pre- and post-treatment states in 22 out of 23 patients (95.6%). Among those correctly identified, the raters' combined average cellulite improvement scores were 2.9, 2.8, and 3.1 for the buttocks, thighs, and global appearance, respectively. Overall, the procedure was well tolerated, with no unexpected adverse events reported.
Conclusion: Our study demonstrates significant improvement in the buttocks, posterolateral thighs, and overall appearance of mild-to-moderate cellulite in 95% of patients treated with limited release TS-GS. This technique of uniform treatment of all targeted dimples and folds at a depth of 6 mm, separating each treated area by at least 3 mm, and administering focal, limited tissue releases to smaller dimples/folds is safe and effective in the treatment of mild-to-moderate cellulite of the buttocks and posterolateral thighs.

ePOSTER TOWN HALL: *DEVICE DEVELOPMENT*

BIOLOGICAL EFFECT OF A SHORT-PULSED LASER ON THE INFLAMMATORY RESPONSE AND EXPRESSION OF HEAT SHOCK PROTEINS

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Background: Short pulse lasers have significant advantages for therapeutic applications due to their ability to precisely deliver the desired energy dose with minimal heat spread to surrounding healthy tissues. Heat shock proteins (HSPs) are highly conserved chaperone families that are expressed in response to various biological stresses. Induction of HSP47 can indicate healing of damaged tissues by collagen synthesis. HSP70 is a tissue-damaging indicator and has a protective function for thermotolerance. In this study, the inflammatory response and expression of HSP70 and 47 induced by short-pulsed laser as well as effect of different laser parameter on the expression of these proteins is investigated on the human embryonic kidney cells 293 (HEK 293T) and human cervical cancer cells (HeLa). Also, the expression of HSP70 and 47 will be studied *in vivo* using rat tissues.
Study Design/Materials and Method: HEK 293T and HeLa cells were exposed to the short-pulsed laser irradiation with varying exposure parameter (different power, frequency, and irradiation time) to study the expression of HSP 70 and 47. The extent of thermal damage and healing process on cells were visualized with western blot and immunohistochemical localization over time 2, 6, 8, 12, and 18 hours following irradiation. Expression of TNF-α was used as a marker to study the inflammatory response.
Results: It is expected that expression of TNF-α and HSPs increase initially with time as a result of laser damage and then decrease systematically as the healing process starts. Also the level expression is expected to increase systematically with increasing laser power.
Conclusion: In order to understand the impact of laser irradiation on tissue damage and healing, HSPs are used as a marker. Studying effects of different laser parameters on HSP expression at different times will be beneficial in optimizing the short pulse laser parameters for therapeutic applications.

MULTI-PHASE STUDY FOR THE VALIDATION AND USABILITY OF A NOVEL RADIOFREQUENCY DEVICE

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Background: Radiofrequency (RF) technology is commonly used in surgery, non-invasive treatments and aesthetic applications. Inconsistencies in energy profile, as well as issues with patient comfort have traditionally been negative factors associated with this type of technology. In this multi-phase study we perform a system validation for a novel RF device which incorporates precise temperature sensing and monitoring capabilities, an opto-mechanical tip contacting the patent to ensure safety and comfort due to contact, and a counter giving precise time-at-temperature readings throughout the treatment.
Study Design/Materials and Method: Phase 1- Animal tissue was used to perform a comparison of the thermally affected zones (TAZ) between the novel RF device and the predicate RF device at different power settings. Phase 2- two subjects were treated, and temperature readings from both the device and a thermal camera were compared to ensure accurate temperature sensing capabilities. 10 subjects were treated with the two different devices and the adverse event profile was compared. All treated subjects were used to observe the usability of the system.
Results: Across the three types of animal tissue, the affected tissue was considered substantially equivalent for both devices and it was observed that the TAZ overlapped in each of the tissue areas with at least 2 of the 3 power settings. Across eighteen treatments performed on two subjects, the average temperature difference between the device and the thermal camera was within ± 1.5°C. Adverse events in the 10 subjects assessed were minimal and included erythema and edema lasting an hour on average.
Conclusion: This novel RF device for heating tissue has been shown to be equivalent to a previously approved electrosurgical device in terms of affected tissue. It was proven to be capable of reporting accurate tissue temperature readings providing safety and comfort during treatment.

ePOSTER TOWN HALL: *FACE AND NECK CONTOURING*

3D PHOTOGRAPHY OF SUBMENTAL FAT FOLLOWING TREATMENT WITH 1060 nm NON-INVASIVE DIODE LASER

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Laser and Skin Surgery Center of New York, New York, NY

Background: Several studies have utilized two-dimensional (2D) photography as a method of evaluating efficacy of fat

reduction. In this study, we employ three-dimensional (3D) photography to demonstrate fat reduction in the submental area after treatment with a 1060 nm diode laser.
Study Design/Materials and Method: A total of 21 subjects were enrolled to evaluate efficacy of the 1060 nm diode laser in reduction of submental fat. Subjects received up to two treatments with the diode laser, and a 3D photography system was used to capture patient images pre-treatment and at 12 weeks post final treatment. To ensure consistency and accuracy in 3D photography, specific landmarks were used for each subject's images. All images were reviewed and analyzed, and contour maps outlining reduction in 3D volume were created through analysis of the 3D data. All subjects also underwent 2D photography and 3D ultrasound measurement of adipose tissue thickness before treatment and at 12 weeks after final treatment.
Results: A clear reduction of fat in the submental area was seen in over 90% of the subjects' 3D photos as demonstrated through volume change in 3D data analysis. These results were comparable to the outcomes from blinded analyses of 2D images performed by board-certified dermatologists. The results also correlated with the subjects' 3D ultrasound measurements of the submental area.
Conclusion: Three-dimensional imaging is a helpful tool for demonstrating fat reduction in the submental area. The analyses of 3D images in this study further validated the efficacy of a 1060 nm diode laser in reducing submental fat.

CLINICAL STUDY TO ASSESS THE SAFETY AND EFFICACY OF A 1060 nm DIODE LASER FOR TREATING THE SUBMENTAL AREA

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Background: Non-invasive fat reduction can occur with temperature alterations as minimal as a 6°C increase above normal body temperature. Lipid bilayer components of the adipocyte cell membranes held together only by forces of hydration, are the most vulnerable to temperature variation. The 1060 nm wavelength has been used for laser lipolysis. The treated adipocytes are generally removed by the human body through the inflammatory clearing process which takes weeks to months. This laser already had approval for non-invasive lipolysis of the abdomen, flanks, back, inner and outer thighs.
Study Design/Materials and Method: Eight subjects were recruited from a pool of healthy male or female volunteers between 20 and 65 years old presenting with significant submental fat and a BMI of $\leq$45. Subjects received 2 treatments (25 minute treatment time for each) and had 12 week follow ups for physician grading based on a 5 point scale. 2D and 3D digital images were taken. A subject satisfaction question was also answered based on a 6 point scale.
Results: The physician assessment of photographs indicated an average score of 4 (much improved) for all eight subjects. No subject scored under a 3. Subject assessments indicated an average score of 2.5 (between extremely satisfied and satisfied). A subset of 3 subjects had digital 2D and 3D image analysis which demonstrated an average improvement of: −21.5% in Lift, −3.0% in Skin Tightening, −5.3% Minor Strain Median measurements and an average reduction of 5.6 cc in volume.
Conclusion: Reduction in submental fat improvement of cosmetic contouring occurred in all subjects. Skin lifting/tightening was quantified in the subject subset which had 3D analysis.

MULTI-CENTER STUDY FOR THE SAFETY AND EFFICACY OF FACIAL PROCEDURES USING A RADIOFREQUENCY DEVICE WITH TEMPERATURE REGULATION

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Background: Radiofrequency (RF) is a commonly accepted treatment modality targeting early signs of skin aging. In this study we examine the safety and efficacy of an RF device, with integrated temperature monitoring, recently FDA cleared as a non-ablative treatment option for mild to moderate facial wrinkles and rhytides.
Study Design/Materials and Method: 25 subjects (Fitzpatrick skin type II–IV) with facial laxity and rhytides were enrolled and received 3–5 full face treatments 2 or 4 weeks apart. Individual zones were treated (forehead, periocular, upper cheek, lower cheek) using either a 20 mm, 15 mm or 10 mm hand piece. The initial target temperature was set to 39°C and increased throughout the treatment. High resolution 2D photographs were taken prior to each treatment and 30, 60 and 90 days post last treatment. Parameters recorded were; energy dosage, temperature, pain, and time. Subjects were assessed for adverse events immediately post-treatment and 1 week post-treatment.
Results: Treatment time ranged from 30–40 minutes. The target temperature of 43°C was achieved by incrementally increasing temperature, aiding subject tolerability. Average pain score was 2.0/1 across all treatment zones. Erythema lasting less than an hour was reported and less than 10% of subjects reported swelling lasting a few hours. All subjects were satisfied with their treatments. Subject noted their skin felt smooth, soft and firm. No additional side effects were noticed in subjects that had 2 week treatment intervals as compared to 4 week intervals.
Conclusion: This new RF device with temperature regulation and an integrated thermistor tip visually improved laxity and rhytides determined through photographic analysis and subject evaluation by achieving and maintaining target temperature for neocollagenesis (42–43°C) with high patient tolerability and minimal downtime in both 2 and 4 week interval patients.

SAFETY AND EFFICACY OF A 1060 nm DIODE LASER FOR THE REMOVAL OF SUBMENTAL FAT

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Background: Non-invasive fat reduction is an efficacious option for body contouring in the flanks, abdomen, thighs and back. In this study we examine a non-invasive laser treatment for fat reduction in the submental area.
Study Design/Materials and Method: Fifty-seven subjects enrolled at 3 study centers and received up to two treatments with a 1060 nm laser on the submental area. High resolution 2D photography was taken before treatment and 12 weeks post final treatment. Subject satisfaction was recorded at the end of the study. Weight was recorded at each subject visit. Adverse events were assessed at all subject visits in addition to phone calls as necessary. All subjects were requested to maintain their standard diet and exercise routine throughout the course of the study. Three blinded evaluators were asked to choose the post-treatment photo from randomized pre- and post-treatment sets.

Results: Of the 57 subjects treated, 55 returned for the 12 week post final treatment follow up. Post treatment photos were correctly identified 93% of the time across all subjects. All subjects were satisfied with their results. A majority of events were mild (75.2%) in nature and transient. The most common events were swelling and tenderness which lasted less than 11 days on average. Subjects reported an average treatment comfort level of 3.3/10.
Conclusion: The use of a non-invasive 1060 nm diode laser is an effective and safe method for fat reduction in the submental area.

SUCCESSFUL TREATMENT OF RHINOPHYMA USING COMBINATION ERBIUM AND CO_2 LASER

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Background: Rhinophyma is a manifestation of longstanding rosacea where the sebaceous glands and connective tissue of the nose become hypertrophied, notably on the distal nose. This causes bulbous swelling and hyperemic large masses of the nasal tip and nostrils. Advanced stage rhinophyma can commonly be seen in men over the age of 40. Although generally benign, the disfigurement can be cosmetically undesirable. Histologic findings include hugely dilated follicles with inflamed sebaceous apparatus and keratin plugging. We report 20 patients with rhinophyma successfully cosmetically treated with combination erbium and CO_2 laser.
Study Design/Materials and Method: Nineteen male patients and one female patient, Skin Types I–III, presented with rhinophyma. The lesions appeared on primarily distal nose. The patients underwent treatment with a CO_2 laser at 30–40 watts, 3 mm collimated spot for debulking to desired shape. A combination CO_2/ Erbium laser was then used with a defocused 0.2 mm spot size at 0.3–0.5 J/cm^2, 50% density of CO_2 with 6 watts of CO_2, in a focused and defocused application. Four blinded observers graded pre- and post-high resolution photographs for therapeutic response.
Results: All four observers correctly chose pre- and post-photographs. There was an average of 92.5% global improvement, 90.9% improvement in bulking, 84.7% texture improvement, and 53.75% improvement in erythema after one treatment session. Adverse effects were erythema and mild edema at the site of treatment, which resolved in 1–5 days. No additional pigmentary changes or scarring were caused by the treatment.
Conclusion: Rhinophyma is a rare complication of advanced rosacea that can be cosmetically distressful to patients, with limited surgery options and variable results. The combination of CO_2 laser provides debulking and fine detail shaping, while Erbium ablates without char, allowing accurate design and clean healing. We report excellent cosmesis of rhinophyma treatment using combination Erbium and CO_2 laser.

SUCCESSFUL TREATMENT OF RHINOPHYMA WITH CO_2 LASER

Muhammad Javed, Max Murison
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Background: Rhinophyma is characterized by soft tissue hypertrophy of nose which leads to functional, cosmetic and psychosocial concerns. The use of CO_2 laser has been well described for the treatment of this disease. We report our experience of treating rhinophyma patients with CO_2 laser at our regional plastic surgery center.
Study Design/Materials and Method: A retrospective study was conducted at the Welsh Centre for Burns and Plastic Surgery, Morriston hospital, Swansea. Clinical data, subjective assessment by senior author and complications of all the patients undergoing CO_2 laser treatment for rhinophyma from 2012–2016 was recorded.
Results: Twenty patients (exclusively male) underwent treatment of rhinophyma. Mean age was 61.7 years and 70% had history of rosacea. 55% had moderate to severe disease at presentation. 70% had cosmetic concerns and 20% had symptoms related to infection. 85% had single CO_2 laser treatment for rhinophyma. Minimal complications were noted. On subjective assessment all patients had good/excellent results following the treatment. Photographic evidence is presented.
Conclusion: CO_2 laser treatment successfully restores the nasal shape and contour. The complications associated with this treatment are minimal.

ePOSTER TOWN HALL: *OPTICAL IMAGING*

A NOVEL STEREOSCOPIC OPTICAL SYSTEM FOR OBJECTIVELY MEASURING ABOVE SURFACE SCAR VOLUME—FIRST TIME QUANTIFICATION OF RESPONSES TO VARIOUS TREATMENT MODALITIES

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Background: Current approaches use subjective semi-quantitative or cumbersome objective methodologies to assess physical characteristics of hypertrophic and keloid scars.
Study Design/Materials and Method: This pilot study aimed to evaluate the accuracy and feasibility of a new stereoscopic optical and high-resolution three-dimensional (3D) imaging system, for objectively measuring changes in above surface scar volume following various interventions. Feasibility of the system was assessed by monitoring the above surface scar volume of five scars in two patients for five successive months. Above surface scar volume and Vancouver Scar Scale (VSS) scores and the investigator and patient volume improvement assessment scores were assessed before and twelve weeks after last intervention.
Results: Scar volume measured by the imaging system correlated significantly with the gold standard (actual weight). The greatest volume reduction followed a combination of cryotherapy and intralesional triamcinolone acetonide and 5-fluorouracil injections in Patient 1, and a combination of pulse dye laser and intralesional triamcinolone acetonide injections in Patient 2.
Conclusion: The new stereoscopic optical system is a valid, accurate and practical objective method for assessing scar volume and for monitoring treatment response. It is more sensitive and accurate than semi-quantitative objective scales. Further studies with a higher number of patients and scars are required to increase the measurement validity of the system.

EVALUATION OF OPTICAL IMAGES FOR SKIN DISEASES *IN VIVO*

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Background: Optical coherence tomography (OCT) is a non-invasive imaging technique that can be applied to diagnose

various skin diseases. In order to accurately diagnose skin diseases, it is essential to develop OCT device that can obtain high quality images. We have evaluated the performance of the developed system and *in vivo* clinical data of skin diseases.
Study Design/Materials and Method: The purpose of our research is to develop a high definition OCT device with high resolution and deep penetration depth for diagnosis of various skin diseases and to increase accuracy in clinical prescription. The developed device was used to compare the depth of skin and epidermis using OCT images and microscopic skin biopsies.
Results: For precise identification of skin tissue, a high-speed line scan camera with 76 kHz axial scan rate was used to improve image acquisition speed. It can acquire image 3.5 times faster than commercial OCT device, and can obtain more real-time images. OCT images were measured using the developed device, and skin biopsies was compared and analyzed to obtain a confidence level of 95% or more.
Conclusion: The results presented in this study considered non-invasive diagnosis of skin diseases as compared to skin biopsies. There are various kinds of skin diseases, and causes are also diverse. Therefore, treatment methods are also diverse. However, before therapy, accurate diagnosis will be can increase the effectiveness of treatment using an imaging device such as OCT.

ePOSTER TOWN HALL: *OTHER RESEARCH TOPICS*

A RETROSPECTIVE CHART REVIEW EXAMINING SCALP MALIGNANCIES AFTER THE INITIATION OF PHOTOBIOMODULATION FOR ALOPECIA

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Background: Photobiomodulation (PBM) uses low-level laser light (approximately 650 nm–678 nm) or light emitting diodes in red or near-infrared wavelengths to induce photochemical reactions at the cellular level. PBM devices were Food and Drug Administration cleared in 2007 for androgenetic alopecia (AGA). Clinical trials have demonstrated efficacy; however, long-term safety outcomes remain to be elucidated. We aimed to examine whether PBM use in alopecia increases the risk of developing cutaneous malignancies within the area treated.
Study Design/Materials and Method: A retrospective chart review using a repository containing electronic medical record data from the University of Minnesota was performed. Records from 2007 to current with an alopecia diagnosis and search terms associated with PBM were identified. Estimated treatment number, skin cancer type and location, immunosuppression, and ultraviolet phototherapy were recorded.
Results: Three hundred twenty-one patients met search criteria (247F, 47M, ages 16–78 years). Of these, 133 began PBM and returned to clinic at least once. Alopecia diagnoses were as follows: 56 AGA, 8 alopecia areata, 14 telogen effluvium, 9 frontal fibrosing alopecia, 13 lichen planopilaris, 14 non-scarring alopecia, 2 central centrifugal scarring alopecia, and 13 with combination alopecia. Months of treatment ranged from 0–89 (average = 21.4). Two cutaneous malignancies developed on/near the scalp: one forehead unknown type of non-melanoma skin cancer (latency of 12.5 months); one scalp basal cell carcinoma (latency of 60 months). Both skin cancers occurred in patients with a prior history of non-melanoma skin cancer. Only laser diode containing devices were identified.
Conclusion: We found a very low rate of skin cancer occurrence in our population with alopecia using PBM. This preliminary data does not suggest that PBM results in an increased rate of skin cancer over the time-period examined. Cutaneous malignancies may take many years to develop, so longer term studies with a control group comprising patients with alopecia will be needed to fully elucidate the risk.

IMPROVING THE PATIENT EXPERIENCE THROUGH THE DEVELOPMENT OF PATIENT-CENTERED LASER CARE PLANS

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Background: Laser treatments have safety risks that may be avoided with the implementation of standardized laser safety procedures. While preliminary laser safety processes are often in place at large academic centers, there are often no means of evaluating staff compliance. The aim of this project was to implement standardized laser safety protocols within a large academic multisite dermatology clinic and achieve a staff compliance of at least 95% within six months, without a significant change in clinic efficiency.
Study Design/Materials and Method: Standardized safety protocols were created for five different lasers, including rooming checklists, timeout, goggle identification, room signs, and device preparation and maintenance. Staff training, onboarding, pre-laser eye checks, and competency checklists were also developed. Baseline laser clinic processes, compliance, and the time spent in room with the physician (measured using an automated patient tracking system) were mapped and reassessed 90 days after the above interventions.
Results: A total of 34 patient times were recorded. Of these, 31 laser procedure audits were performed (23 in clinic #1, and 8 in clinic #2). Staff compliance exceeded 98% for all laser protocols, with no significant difference between either clinic ($p = 0.23$). Mean patient times with the physician were reduced to 13.8 ± 7.8 minutes from the baseline of 14.5 ± 10.8 minutes ($n = 74$), though this difference was not statistically significant ($p = 0.372$).
Conclusion: Following implementation and standardization of new safety protocols, both the compliance rate and patient times with the physician exceeded initial goals. Despite additional laser clinic protocols and processes, an increase in patient times with the physician was not seen. The high compliance rate demonstrates that laser safety process changes can be readily adapted in large academic Dermatology clinics in an efficient manner.

ePOSTER TOWN HALL: *PIGMENTED LESIONS AND ANOMALIES*

AN AUTOMATED MOLE RANKING SYSTEM (MOLELIST) FOR SKIN CANCER SCREENING

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Background: Recent work has demonstrated that the specificity of clinical visual skin examination for skin cancer screening is substantially improved when the dermatologist conducts an intra-patient assessment, i.e., considers the

appearance of a mole relative to the patient's other moles. However, dermatologists have to conduct clinical visual skin examinations very quickly given the practical constraints on the time available per patient visit. This limits the dermatologist's ability to conduct an intra-patient assessment and find 'ugly duckling' lesions which are different from other lesions on the patient and typically at higher risk for malignancy. Thus, we propose an automated mole ranking system (MoleList) that provides the dermatologist with a visual list of the patient's moles, sorted from most to least actionable, to assist in skin cancer screening. Mole A is more "actionable" than Mole B if an action other than routine monitoring is more likely to be taken for Mole A than for Mole B.

Study Design/Materials and Method: A proof-of-concept demonstration was performed on a small set patients ($n = 11$), for which dermoscopic images of at least 5 of their moles were available in their medical record. We extracted features from each mole image and used a linear regression model with leave-one-participant-out cross-validation to predict the actionability ranking.

Results: The actionability ranking predicted by the MoleList system compared favorably to the actionability ranking produced by an experienced dermatologist, both by visual assessment of the images and quantitatively in terms of a weighted correlation measure that accounts for the fact that it is more important to correctly rank the actionability of the most actionable moles than the least actionable moles.

Conclusion: This study shows initial promise of an automated mole ranking system that could improve the efficiency and specificity of clinical visual skin examination for skin cancer screening.

COMBINATION LASER THERAPY AND TOPICAL HYDROQUINONE DRUG DELIVERY IN THE TREATMENT OF MELASMA

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Background: Melasma is a common dermatologic discoloration of brown to gray-brown patches that appear primarily on the cheeks, bridge of the nose, forehead, chin, and upper lip of adults, particularly in women. It results from the production of excess pigmentation due to homeostatic dysregulation. Topical treatments such as hydroquinone and corticosteroids may be used alone, but laser therapies are preferred for persistent cases due to the condition's recurrent and refractory nature.

Study Design/Materials and Method: In order to further understand the safety and efficacy of laser therapy and hydroquinone drug delivery, the medical records at a dermatology practice were reviewed for all melasma patients who underwent this combination procedure. Two blinded reviewers assessed the improvement in pigmentation and skin texture as mild, moderate, good, or excellent, and significant trends were identified using regression analyses in StataMP version 14.

Results: A total of 43 patients who underwent an initial laser therapy with adjuvant hydroquinone or triluma were followed for an average of 3.5 months. Of these patients, the majority ($n = 41$) were females, and identified as either Asian ($n = 17$), Hispanic ($n = 17$), or White ($n = 9$), averaging 45 years of age. For all measures, reviewers agreed within one degree of assessment. Overall, patients demonstrated moderate improvements in both pigmentation and skin texture. Asians experienced slightly poorer outcomes overall as compared to Hispanic or White patients, whereas older patients experienced significantly better outcomes ($p < 0.05$). There were no complications.

Conclusion: This data suggests that laser therapy combined with a topical bleaching agent is useful in the treatment of melasma in terms of producing improvements in pigmentation and skin texture, but that results are more likely to be promising in non-Asian and older patients. The combination of laser therapy and topical hydroquinone drug delivery in the treatment of melasma is safe and effective in this group of patients.

EVALUATION OF A NOVEL DERMAL CRYOTHERAPY SYSTEM FOR THE TREATMENT OF BENIGN PIGMENTED LESIONS IN ASIAN PATIENTS

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Background: Photoaging in Chinese often presents with benign pigmentary lesions. Various light based devices have been used for the management of benign pigmentary lesions, such as long pulsed Nd:YAG laser, Q-switched laser and picosecond laser. All of these light-based devices have risk of post-inflammatory hyperpigmentation. The objective of this study is to assess the efficacy of a dermal cooling system to reduce pigmentation in benign pigmentary lesions in Asian patients.

Study Design/Materials and Method: Up to 100 Asian male and female subjects above 18 years of age with good past health are recruited. They have at least one benign pigmentary lesions on their face. Standardized photography is taken at baseline, one month post treatment and 2, 6, 12 months after final treatment. Up to 3 treatments at one month interval is given. The treatment area and parameter is determined by the physician after assessment. The end point is *via* patient real time feedback in terms of a change in sensation. Any adverse effect is recorded. Standardized photographs are assessed by two independent physicians. Subjective assessments are recorded at follow up visits.

Results: The study is ongoing with 25 subjects undergoing treatments. 36% has lentigines only, 36% has freckles only and 28% has both lentigines and freckles. A total of 267 treatment sites have been carried out. 20 subjects have reached one month follow up; 57.5% has improvement objectively by GAIS score and 90% reported improvement subjectively. No adverse effects were recorded.

Conclusion: The novel cryotherapy device is promising for the treatment of benign pigmentary lesions in Asians.

ePOSTER TOWN HALL: *TOPICAL DRUG AND DEVICE DELIVERY*

COMPARATIVE EFFECTIVENESS OF TWO TOPICAL LIDOCAINE MIXTURES TO REDUCE PAIN DURING A NON-ABLATIVE LASER PROCEDURE: A RANDOMIZED CONTROLLED TRIAL

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Background: Topical anesthesia is used to reduce pain and increase comfort associated with minor procedures, including laser treatment. Both lidocaine-tetracaine (LTTA) and lidocaine-prilocaine (LPTA) are topical lidocaine mixtures used commonly

before laser dermatology procedures. Unfortunately, data is lacking regarding comparative effectiveness of the topical lidocaine mixtures during common non-ablative laser procedures.
Study Design/Materials and Method: This is a cross-sectional, split-face and -body, parallel-group randomized control trial. The purpose of this study was to compare the clinical effectiveness of topical LTTA versus LPTA for pain relief prior to non-ablative laser treatment. Healthy, adult females with Fitzpatrick phototype I–III and moderate lentigines or photodamage were enrolled. Participants were randomized to 30 min pre-treatment with LPTA, 7%-7% LTTA, or a placebo vehicle (PV) to six areas prior to Q-switched laser treatment. The pre-treated areas were the right and left foreheads, cheeks, and inner arms. The primary outcome was pain with laser treatment measured by visual analog scale.
Results: 24 participants completed the study. Reported side effects were redness and swelling that resolved within one week of treatment. Pain scores for the three pre-treatments were significantly different on the forehead ($p = 0.0051$), cheek ($p < 0.0001$), and arm ($p = 0.05$). Pairwise analysis revealed significantly lower pain scores with LTTA compared to placebo at all three anatomical sites, while LPTA had only significantly lower pain scores compared to placebo on the cheek. There were no significant differences in reported pain between LPTA and LTTA.
Conclusion: Pre-treatment with LPTA and LTTA were both effective at reducing pain associated with non-ablative laser treatment. LTTA was more effective at reducing pain on many areas of the body with a 30 min incubation time compared to placebo. LPTA was only effective at reducing pain after 30 min incubation on the cheek, which is lower than the 60 min incubation time recommended by the manufacturer.

FRACTIONAL LASER-ASSISTED PERCUTANEOUS DRUG DELIVERY *VIA* TEMPERATURE-RESPONSIVE LIPOSOMES

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Background: Liposomes are used for transdermal delivery of drugs and vaccines. Our objective was to develop temperature-responsive (TR) liposomes to achieve temperature-dependent, controlled release of an encapsulated drug, and use fractional laser irradiation to enhance transdermal permeability of these liposomes. Effect of temperature on liposome size and drug release rate was estimated at two temperatures. Transdermal permeation through hairless mouse skin, with and without CO_2 fractional laser irradiation, and penetration into Yucatan micro-pig skin were investigated using Franz cell and fluorescence microscopy.
Study Design/Materials and Method: Dynamic light scattering showed that mean liposome diameter nearly doubled from 190 nm to 325 nm between 37 and 50 °C. The rate and amount of OVA-FITC released from TR-liposomes were higher at 45 °C that those at 37 °C. Transdermal permeation of OVA-FITC across non-irradiated skin from both TR- and unmodified liposomes was minimal at 37 °C, but increased at 45 °C. Laser irradiation significantly increased transdermal permeation of both liposome groups at both temperatures.
Results: Fluorescence microscopy of frozen biopsy specimens showed deeper penetration of FITC from unmodified liposomes compared to that from polymer-modified liposomes. Rhodamine accumulation was not observed with polymer-modified liposomes at either temperature. Temperature-dependent controlled release of an encapsulated drug was achieved using the TR-liposomes. However, TR-liposomes showed lower skin permeability despite higher hydrophobicity.
Conclusion: Fractional laser irradiation significantly increased the transdermal permeation. Additional studies are required to control liposome size and optimize transdermal permeation properties.

SAFETY OF PERFLUORODECALIN-INFUSED SILICONE PATCH IN PICOSECOND LASER-ASSISTED TATTOO REMOVAL

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Background: Use of a perfluorodecalin (PFD)-infused silicone patch has been shown to enable multiple laser passes in a single treatment session safely and effectively during laser-assisted tattoo removal with a 755 nm QS alexandrite laser. Quantitative analyses have shown that exposure of PFD patch samples to additional QS and picosecond lasers does not alter the optical transmission or chemical stability. The purpose of this retrospective chart review was to assess the safety of treating tattoos with picosecond lasers using multiple passes with PFD patch.
Study Design/Materials and Method: Retrospective study of consecutive patients treated using picosecond lasers in combination with the PFD patch. Information extracted from the medical records included patient demographics, treatment location, tattoo characteristics, laser treatment parameters, and adverse events.
Results: Forty-five patients (16 males, 29 females) included in the study had a mean age of 35.5 years. Patients with Fitzpatrick skin types I–V were represented. The distribution of tattoos included 2 on the neck, 15 on trunk, 20 on upper extremities, and 8 on lower extremities. The mean number of passes per treatment session was 2.6 (range of 1–4 passes). Twenty-nine (64.4%) patients had black tattoos, and the remaining patients had multicolor tattoos with mixtures of black, blue, green, red, and yellow ink. Twenty-eight (62.2%) patients had at least two picosecond laser treatment sessions with PFD patch. Laser tattoo treatments with multiple passes using the PFD patch were well tolerated and effective. No dyspigmentation, scarring, textural changes, or unanticipated adverse events directly related to the treatment were observed.
Conclusion: Multiple passes with 755 nm and 532 nm picosecond lasers may be safely used in combination with PFD patch to treat unwanted black or multicolor tattoos on different body sites in patients of diverse Fitzpatrick skin types. Notably, there were no unexpected treatment-related adverse events, including post-treatment dyspigmentation.

ePOSTER TOWN HALL: *TREATMENT OF SUPERFICIAL CUTANEOUS LESIONS*

EVALUATION AND COMPARISON OF VARIOUS LASER MODALITIES FOR THE TREATMENT OF SEBORRHEIC KERATOSES

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Background: Seborrheic keratoses are benign growths on the skin that are a common cosmetic concern for patients. Standard therapies for these lesions include cryotherapy, shave excision

and electrosurgery, which are effective, but can cause scarring, pain, and dyschromia. Laser therapy offers a promising treatment option for seborrheic keratoses. Our study compares seven distinct lasers for the treatment of seborrheic keratoses on the back with cryotherapy as a "control" to determine which treatment options are safe and efficacious.
Study Design/Materials and Method: This was a case study of one patient, Fitzpatrick skin type II, who had symmetric seborrheic keratoses on the entire back. A 2 by 4 grid was drawn on the patients back to produce 8 squares, each with a minimum of 8 seborrheic keratoses. Seven different laser devices were used to treat all of the seborrheic keratoses in each square in a single treatment, and one square was treated with cryotherapy for control.
Results: Preliminary results 30 days post-treatment show the most improvement in seborrheic keratoses with the fractional CO_2 laser (70%), Er:YAG 2940 nm laser (70%) and 1927 nm thulium fiber laser (50%) as assessed by two blinded investigators. There was less improvement with the 1064 nm picosecond laser (40%) and Q-switched 755 nm alexandrite laser (30%). Both the 755 nm picosecond and cryotherapy had 20% resolution of seborrheic keratoses. No major adverse events were reported with any of the treatment modalities.
Conclusion: Long term follow-up will be presented.

PHOS-ISTOS CLINICAL TRIAL: A NEW SOLUTION FOR PHOTODYNAMIC TREATMENT OF ACTINIC KERATOSIS WITHOUT PAIN

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Background: Actinic keratosis (AK) are common precancerous skin lesions which mainly affect the elderly population. The lesions are usually present on the scalp of the patients and thus are easily reachable by light, making PDT one of the first line treatment. The planar shape of current light sources used for photodynamic therapy (PDT) of actinic keratosis lead to inhomogeneous light distribution on lesions located on curved parts, such as the scalp. Moreover, PDT is known to be very painful.
Study Design/Materials and Method: Resulting from a European project, PHOSISTOS, based on light emitting fabrics (LEF) was developed to overcome those drawbacks. This helmet consists of a 3D printed frame and a patented flexible structure composed of knitted optical fibers. Besides its original design, the project aims to demonstrate that an illumination performed 30 minutes after 5-ALA application, with a low irradiance (1.33 mW/cm^2) during 2h30, and a reduced fluence (12 J/cm^2) is as efficient as the conventional protocol and less painful: illumination 3 hours after 5-ALA application, 75 mW/cm^2, 37/cm^2. PHOSISTOS device was assessed in a comparative (split face intra-individual comparison), randomized, phase II study that takes place in France and in Germany. The main objective was to show the non-inferiority of PHOSISTOS device compared to the conventional PDT. One of the secondary objectives was also to show a significant pain reduction on the PHOSISTOS side. 42 patients with at least 10 actinic keratosis of the scalp and forehead were included.
Results: Preliminary results had shown that PHOSISTOS is effective in the treatment of AK of the scalp with pain scores much lower than the conventional protocol (0.7/10 vs. 7.3/10). Final results of the European project study will be presented.
Conclusion: PHOSISTOS could offer an effective and well tolerated alternative to LEDs for the treatment of AK by PDT. An ambulatory version of the PHOSISTOS device can be easily developed.

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3D ULTRASOUND IMAGING OF PELVIC PROLAPSE

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Background: Pelvic organ prolapse (POP) is commonly associated with postpartum levator sling tears which are difficult to image on MRI.
Study Design/Materials and Method: 23 females over a 5 year period were imaged with translabial volumetric 3D imaging. Scans were performed with and without Valsalva maneuvers to measure degree of bladder descent and presence of tear in the attachment of the levator muscle to the pelvic sidewall. Study was performed by one investigator with 14 years experience.
Results: Pelvic partial or complete disruptions in the levator sling were noted in 4/23 patients. Associated prolapse of bladder, cervix or anal structures were documented contemporaneously.
Conclusion: 3D translabial sonogram imaging is a cost effective and non invasive diagnostic modality to document levator muscle tears.

A CASE OF INCREASED COLLAGEN VII EXPRESSION AFTER FRACTIONAL ABLATIVE LASER TREATMENT IN RECESSIVE DYSTROPHIC EPIDERMOLYSIS BULLOSA

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Background: Recessive dystrophic epidermolysis bullosa (RDEB) is a genetic skin disorder resulting in severe skin fragility, frequent blisters, scarring, increased risk of squamous cell carcinomas and decreased life expectancy. RDEB results from autosomal recessive mutations in type VII collagen, which is a critical component of the basement membrane. Skin fragility can predispose patients to great morbidity and effective methods to prevent and treat these lesions are limited.
Study Design/Materials and Method: We report the case of a 27-year-old woman with a mosaic phenotype of RDEB who presented for management of large non-healing chronic erosions on her upper back and posterior neck. These areas were treated with deep fractional carbon dioxide (CO_2) laser, which has been shown to help with collagen remodeling in other clinical scenarios. Immediately after treatment, topical poly-L-lactic acid (PLLA) was placed on the skin surface to act synergistically with the laser. Additionally, punch biopsies were performed to compare the collagen distribution in treated and untreated skin.
Results: After seven treatments, she has had great clinical improvement with decreased bleeding during the procedure and decreased frequency of blistering. On hematoxylin and eosin staining, the untreated skin had abnormal collagen organization whereas the treated skin demonstrated a collagen distribution akin to normal skin. Furthermore, a

Herovici stain was performed to differentiate mature (type I) versus immature (type III) collagen, with a notable shift in expression patterns between the treated and untreated samples. Samples were also evaluated for direct immunofluorescence for type VII collagen, which confirmed that the treated samples had increased type VII collagen compared to the untreated sample.
Conclusion: This case illustrates the potential for fractional CO_2 laser in combination with PLLA to aid in the normalization of collagen and the potential for a "mechanical" treatment to increase activity of collagen VII in select patients with RDEB.

A PILOT STUDY ON THE COMBINED USE OF NON-ABLATIVE UNIPOLAR RF AND ABLATIVE FRACTIONAL CARBON DIOXIDE LASER 1064 nm ON UPPER LID PTOSIS AND PERIORBITAL WRINKLES IN ASIAN PATIENTS

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Background: In most Asians the aging eye area always presents with wrinkling of the skin and upper lid ptosis. Upper lid ptosis refers to drooping of the upper eyelid of one or both eyes. The droop may be barely noticeable, or the lid can descend over the entire pupil. Ptosis can affect both children and adults, but usually occurs because of aging, this prompts patients to seek doctors consult. Each year approximately 100,000 people choose to have cosmetic surgery of the eyelids, the gold standard of treatment is surgical Upper Blepharoplasty, this surgical technique may have complications such as overcorrection, undercorrection, exposed sutures, suture abscess and scarring. Because of this problems, clinicians are actively exploring and combining non-invasive alternatives. In this study we combined non ablative unipolar radiofrequency with ablative fractional carbon dioxide 10,600 nm laser in attempting to address upper lid ptosis and periorbital wrinkles.
Study Design/Materials and Method: Randomized control trial of 20 patients (male and female) was selected, aged 30–50 years old. All subjects had 1 session of non-ablative unipolar RF using eye tip, 450 shots, followed immediately by Fractional CO_2 10,600 nm at 15 mJ with 5% density. Photos and measurement of the Margin reflex distance and Margin crease distance before and 3 months after the procedure was recorded. Data collected tallied, interpreted and statistically analyzed.
Results: A single combined treatment of non-ablative unipolar RF using eye tip and Fractional Carbon dioxide laser around the eye area yielded an average increase in Marginal reflex distance of 0.99 mm mean difference for the right eye and 1.09 mm mean difference in the left eye after 3 months. Marginal Crease Difference mean average for the right eye is 0.99 mm increase and 0.98 mm increase on the left after 3 months. All patients manifested both increase in MDR1 and MCD. All patients observed significant degrees of skin tightening, texture improvement and wrinkle reduction in the eye area. Statistical data analysis using paired T-test collected was significant
Conclusion: This study proved that combined treatment of non-ablative unipolar RF using eye tip and fractional carbon dioxide laser around the eye area showed a statistically significant improvement in upper lid ptosis based on marginal reflex distance and marginal crease distance. Skin tightening, texture improvement and wrinkle reduction was observed by all patients.

BLINDED COMPARISON TRIAL OF LIDOCAINE 4% AND BENZOCAINE 20% IN A NOVEL TRANSDERMAL DELIVERY SYSTEM VERSUS COMPOUNDED LIDOCAINE/TETRACAINE (23%/7%) FOR PAIN MITIGATION DURING MICROFOCUSED ULTRASOUND WITH VISUALIZATION TREATMENT

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Background: The efficacy of various pre-medication strategies for comfort management during microfocused ultrasound with visualization (MFU-V) treatment has not been studied. Here the objective was to compare lidocaine 4% and benzocaine 20% products formulated with a novel transdermal delivery system versus compounded lidocaine 23%/tetracaine 7% (23/7) to mitigate discomfort during MFU-V treatment.
Study Design/Materials and Method: This was a randomized, double-blinded, split-face study. Subjects (n = 14) received 50 mg IM meperidine/25 mg IM promethazine/5 mg oral diazepam 1 hour before treatment. Fifteen minutes before treatment, 1 side of the face was treated with 1 application of 4% lidocaine, followed by 1 application of 20% benzocaine; the contralateral side was treated with 2 applications of 23/7 (to maintain blinding). A blinded clinician assessed numbness (scale from 1 = completely numb to 4 = not numb) before treatment and collected subject pain scores (scale from 0 = no pain to 10 = worst pain) following MFU-V treatment. Adverse events and subjective clinician measures were also assessed.
Results: Fourteen females (mean age 51.7 years) were treated. Mean subject pain scores for 23/7 and lidocaine 4%/benzocaine 20% were 5.6 and 5.7, respectively. Mean numbness scores were similar for 23/7 (2.5) and lidocaine 4%/benzocaine 20% (3.0). All clinicians rated both products as "very easy" to apply. For lidocaine 4%/benzocaine 20% 7.1% of subjects required no pauses during treatment, versus 14.3% of subjects for 23/7. However, more subjects required 4+ pauses with 23/7 (21.4% vs. 7.1%). lidocaine 4%/ Benzocaine 20% was preferred by 78.5% of subjects overall; 35.7% of subjects rated benzocaine 20%/ lidocaine 4% as "Very Effective" versus 7.1% for 23/7. No adverse events were reported.
Conclusion: Lidocaine 4% and Benzocaine 20% formulations utilizing a novel transdermal delivery system perform similarly to a compounded lidocaine 23%/tetracaine 7% product for discomfort mitigation during MFU-V treatment. More subjects reported a preference for lidocaine 4%/benzocaine 20% and rated this novel topical product as "very effective" versus the compounded product.

CASE SERIES: FRACTIONAL ABLATIVE LASER-ASSISTED TOPICAL STEROID DELIVERY IN COMBINATION WITH PDL FOR TREATMENT OF HYPERTROPHIC SCARS

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Background: Hypertrophic scars often cause functional and psychological burden on affected patients. Pulsed dye lasers (PDL) produce selective photothermolysis of the microvasculature of hypertrophic scars. As a result, PDL can

improve erythema and texture of hypertrophic scars especially in their early phase. Fractional CO_2 laser emits beams which absorb water and results in microthermal destruction zones through the stratum corneum, epidermis, and dermis which stimulate scar remodeling and facilitate drug delivery to the dermis.
Study Design/Materials and Method: We report treatment of four patients ages 3–44 with skin Fitzpatrick types I–V suffering from hypertrophic scars on face, trunk, and extremities occurred following burn, acne, toxic epidermal necrosis, and thyroidectomy. Follow up period ranged from 1–5 years. Patients were treated with PDL 595 nm prior to or in conjunction with fractional CO_2 10,600 nm laser. Each fractional CO_2 laser treatment was followed by immediate application of topical triamcinolone acetonide suspension at a concentration of 40 mg/ml. Fractional CO_2 laser settings used were power of 60 watts, pulse width of 200 ms, using a 7 mm × 7 mm hand piece and 4 laser passes over affected areas. Fractional CO_2 treatments were spaced at 3–12 month intervals and were repeated 1–4 times in our patients.
Results: All patients showed significant improvement in scar appearance, erythema, texture, and symptoms following treatments. No significant adverse effects were observed.
Conclusion: PDL can improve erythema and texture of early hypertrophic scar, however results are not optimal. Fractional ablative laser-assisted delivery of topical steroid can offer a safe and effective treatment option for management of hypertrophic scars. Combination of fractional ablative laser and topical steroid therapy optimizes dispersion of steroid molecules with minimal discomfort. Data are limited and more studies are needed to determine safety, optimal treatment parameters, treatment frequency, and steroid dosing.

CLINICAL EVALUATION OF DIAMONDPOLAR APPLICATOR TREATMENT FOLLOWED BY AC DUAL APPLICATOR TREATMENT USING 2 INTENSE PULSED LIGHT WAVELENGTH BANDS FOR FACIAL ACNE VULGARIS

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Background: Acne affects almost 100% of the population, from ages 8 to 80, and is a source of great distress particularly in the adolescent/young adult age group. The clinical presentation ranges from comedonal disease, to red papules and large cysts. The cause is essentially unknown. Several energy-based devices have been tested to treat acne, from laser-light to radiofrequency. Blue/red light with dual bacterioside/anti-inflammatory action has been hypothesized to be effective in reducing acne manifestations. Moreover radiofrequency devices have demonstrated effectiveness in reducing inflammation and preventing scarring. In this study, the efficacy of blue/red light compared to the combination of blue/red light together with radiofrequency to treat acne was examined.
Study Design/Materials and Method: 40 subjects (ages 18–55 years) were enrolled in this multi-center, prospective, open label study. Each subject received 4 full treatments at 1 week intervals. Follow-up took place 6 weeks after the last treatment. Half of the subjects were treated with either blue/red light or blue/red light together with multipolar radiofrequency with pulsed electromagnetic field. The objectives were to evaluate the individual efficacy of facial acne vulgaris treatment with the single or combination treatment, and the subject's assessment of improvement, comfort & satisfaction with the treatments.
Results: Overall all inflammatory lesions responded to both single and combination treatments. Inflammatory lesions responded better to combination therapy compared to blue/red light alone (40% vs. 30%). Both open and closed comedones responded better with the combination therapy. There were no differences in reduction of nodules/cysts between the two groups. Patient self-assessments revealed that single therapy group were more satisfied with their overall appearance and acne appearance compared with the combination group. There were no serious adverse effects, but combination therapy resulted in increased erythema and irritation compared to the blue/red light group alone.
Conclusion: Blue/red light and multipolar radiofrequency with pulsed electromagnetic field treatments are effective and safe for reduction of acne lesions and improvement of patient appearance. Patient satisfaction is increased with blue/red light alone compared to combination therapy.

CLINICAL STUDY OF INTENSE FOCUSED ULTRASOUND THERAPY TO DEEP DERMAL FACIAL SKIN AND SUBCUTANEOUS TISSUES

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Background: Non-ablative skin tightening technologies offer the prospect of reduction of wrinkles and skin sagging with minimal downtime, discomfort, and risk of adverse events. The excellent safety profile is mitigated by the limited efficacy of such procedures. The objective of this study is to evaluate the clinical safety of intense ultrasound in the treatment of the dermis and subcutaneous tissues of the face in terms of skin inflammation, pain and adverse events.
Study Design/Materials and Method: In an open-label study, patients scheduled to undergo a tightening facial treatment. Intense ultrasound treatments were performed as a series of several linear exposures delivered 1.5 to 2.0 mm apart with the use of 1 of 3 available handpieces with different focal depths. Subject pain ratings and standardized digital photographs were obtained at uniform points.
Results: One hundred and twenty subjects were enrolled. Most patient exposures were associated with transient superficial skin erythema and slight to mild discomfort on a standardized pain scale. No other adverse effects were noted. Epidermis was spared in all cases. Primary outcome measure was detection of improvement in paired comparison of pretreatment and posttreatment (day 90) photographs.
Conclusion: In this clinical study of intense ultrasound therapy to facial tissues the treatment appears to be a safe and effective modality for facial skin tightening.

CLINICAL STUDY WITH A PICOSECOND ALEXANDRITE LASER AND A DIFFRACTIVE OPTIC FOR PHOTO-REJUVENATION AND PIGMENT REDUCTION IN SKIN TYPES II–IV DURING THE SUMMER MONTHS IN A SUN RICH ENVIRONMENT

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Background: Photo rejuvenation with pigment reduction has been a popular procedure using devices. Patients and providers

have wanted a device that can safely treat darker skin patients and they have wanted to able treat during the summer months. In this study we evaluated patients (skin type II to IV) treated for unwanted pigmentation as well as skin tone and texture during the summer months in California. All patients were treated with a diffractive lens array optic on the picosecond 755 nm alexandrite laser. This optic creates an area of laser induced optical breakdown in the epidermis which is responsible for epidermal and dermal remodeling and pigment reduction.

Study Design/Materials and Method: 18 patients were treated prospectively with the picosecond 755 nm alexandrite system employing a diffractive optic. Lighter skinned patients were treated with the 6 mm optic at 0.71 J/cm^2 and darker skinned patients were treated with the 8 mm optic at 0.40 J/cm^2. Patients received topical anesthesia 30 min prior to treatment.

Results: 2 blinded evaluators were able to determine the pre-treatment image as compared to the post treatment image an average of 74% of the time. In grading, an average of 78.5% of the patients had noticeable improvement with 31% of them being much improved to very improved. There were no adverse reactions or unanticipated complications.

Conclusion: The picosecond 755 nm alexandrite with this fractional optic is safe and effective photo rejuvenation and pigment reduction in light and dark skin types during the summer months in a sunny climate.

COMPARISON OF A NOVEL WOUND DRESSING VERSUS CURRENT CLINICAL PRACTICE AFTER LASER RESURFACING

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Background: A variety of wound dressings have been used for post-ablative laser resurfacing. Historically, silicone-based gels have only been used for fully healed wounds. This study evaluated the comparative healing response after full field erbium laser resurfacing to either the commonly used petroleum jelly ointment versus a novel new-silicone based gel that is intended to be used on open wounds.

Study Design/Materials and Method: A randomized, open label, split-face study was performed. Twenty subjects (Skin types I–III) underwent Er:YAG laser resurfacing at fluences ranging from 12.5 J–50 J/cm^2—depending on the anatomic facial area that was to be treated. Following the procedure either petroleum jelly (Aquaphor, Beiersdorf) or a silicone-based gel (Stratpharma, Basel Switzerland) were applied to the right or left sides of the face. Subjects applied the products twice a day and were evaluated at 60 days. Using 3D Skin Analysis, pictures were taken pre-procedure, immediately post-procedure, and at day 7, 30, and 60. Blinded evaluation of photographs were performed. In addition subjects reported on the overall general aesthetic outcome, perceived pain, itch, and tightness *via* questionnaires.

Results: All subjects healed without complications. By 60 days, there was no difference in healing between the 2 different dressing approaches. However, patients treated with the silicone gel had less post-treatment erythema and post-inflammatory hyperpigmentation. All subjects preferred the simplicity of a topically applied silicone gel as compared to petroleum jelly.

Conclusion: A novel new silicone-based gel represents an exciting alternative approach to post laser resurfacing wound dressings.

DERMATOLOGICAL DEVICE REGULATION WITHIN THE FOOD AND DRUG ADMINISTRATION'S 510(K) PATHWAY

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Background: Device development in the field of dermatology is increasing. Applications for new devices identified as "substantially equivalent" to predicate devices by the U.S. Food and Drug Administration (FDA) may be exempt from Premarket Approval. These devices undergo clearance *via* the 510(k) process with less clinical data requirements. The objective of this study is to investigate characteristics of dermatological devices approved by the 510(k) process.

Study Design/Materials and Method: A retrospective review of the publicly available FDA 510(k) and device recall databases was performed with records from January 1st, 1993 to December 31st, 2016. Records were included if devices were intended for cutaneous use or application within the dermatology outpatient setting. Devices were categorized into laser/thermal, light-based, non-thermal surgical, wound, ultrasound, or cooling/cryogenic per database nomenclature. Data was collected on device characteristics, approval pathways, FDA decisions, recalls, and geographic location of device applicant. Statistical analyses were performed using uni-variate tests and linear regression with $p < 0.05$ considered significant.

Results: 1,986 records were identified from 551 unique applicants. The laser/thermal category was the largest group, representing 77.0% (1,530/1,986) of total dermatological devices approved by the 510(k) process. Application decisions for light-based and wound devices increased significantly during the study period, while laser/thermal slightly decreased, $p < 0.01$. Total recalls amounted to 9.3% (185/1,986) with the majority being class 2. All class 1 ($n = 2$) recalls originated from the laser/thermal group. Applicants were most commonly located in California and Massachusetts.

Conclusion: Few serious adverse events were identified from dermatological devices approved *via* the 510(k) process. Clinicians should be aware of criteria for FDA device approval and associated patient safety data.

DOPPLER IMAGING OF URINARY INCONTINENCE

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Background: Stress urinary incontinence (SUI) is a common clinical problem that may be caused by urthritis or non-inflammatory urethral pathologies. Doppler histogram imaging documents and quantifies inflammatory neovascularity non-invasively.

Study Design/Materials and Method: 21 patients with chronic symptoms over a 2 year period were scanned with 3D Volumetric Doppler Ultrasound for SUI. External probe covers allowed non-invasive imaging of the bladder and urethra.

Results: 2 patients has urethral diverticula. 5 patients had periurethral hyperemia resolving after therapy. 9 patients had pelvic organ prolapse. 5 patients demonstrated no pathology on imaging. no bladder calculi were noted.

Conclusion: Doppler ultrasound may identify periurethral inflammation and monitor treatment results.

EARLY LASER INTERVENTION TO REDUCE SCAR FORMATION: A SYSTEMATIC REVIEW OF CLINICAL TRIALS

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Background: The ability of laser treatment to affect wound healing and subsequently minimize scar formation has been investigated in recent years, but no systematic review links these clinical trials. The aim of this study is to systematically review and evaluate clinical evidence for early laser intervention introduced in inflammation, proliferation or remodeling phases of wound healing with first treatment performed <3 months after wounding.

Study Design/Materials and Method: We searched PubMed using relevant key words in June 2017. Titles, abstracts and articles were sorted according to inclusion and exclusion criteria. Methodological quality was evaluated according to Cochrane Collaborations risk-of-bias assessment guideline by two independent authors.

Results: Twenty-five articles met the inclusion criteria. The following laser devices have been investigated; pulsed dye (PDL) laser, potassium-titanyl-phosphate (KTP) laser, fractional Er:Glass 1540 nm/1550 nm, fractional/full-ablation erbium-doped-yttrium-aluminum-garnet (Er:YAG) laser, or fractional CO_2 laser. Eighteen studies applied laser treatments 2–4 times with 2–8 weeks intervals, while 7 studies applied only one laser treatment. Follow-up time ranged from 1–12 months with 18 studies using a follow-up time $\leq$3 months. In general, laser treated wounds and scars showed benefit from laser intervention, though not always reaching significance. Significant scar improvement were found in: 3 of 4 studies using laser treatment in inflammation phase, in 6 of 16 studies with laser initiated in the proliferation phase and in 2 of 5 studies in the remodeling phase. Methodological quality included high risk-of- bias in terms of randomization and allocation concealment, but low risk-of-bias with regard to blinding of outcome assessment and lost to follow-up.

Conclusion: Laser intervention, when introduced in inflammation, proliferation or remodeling phase has the potential to reduce cutaneous scar formation. Further high quality studies are needed before standard protocols can be implemented in clinical practice.

EFFECT OF LOW-LEVEL LASER THERAPY ON MASSETER AND ANTERIOR TEMPORAL MUSCLES PRIOR TO INDUCTION OF FATIGUE: A RANDOMIZED, SHAM-CONTROLLED, BLIND, CLINICAL TRIAL

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Background: The aim of the present study was to evaluate the effect of low-level laser therapy on bite force, mandibular range of motion, sensitivity to palpation and fatigue in the masseter and anterior temporal muscles of young patients when administered prior to the induction of fatigue.

Study Design/Materials and Method: Fifty-two healthy volunteers aged 18 to 23 years were randomly allocated to a laser group and sham group. Both groups were submitted to a clinical evaluation to record mandibular range of motion, bite force, muscle sensitivity to palpation and muscle fatigue. The laser group was then submitted to low-level laser therapy (780 nm, 25 J/cm^2, 50 mW, 20 seconds per point) on three points of the masseter and one point of the anterior temporal muscle on each side. The sham group was submitted to the same procedure, but with the device switched off. The volunteers were then instructed to chew two pieces of gum (one on each side) for six minutes, with the pace set by a metronome calibrated to 80 bpm, followed by the reevaluation of all variables. The results were submitted to analysis of variance and then to Tukey's multiple comparisons method. For intra-group comparison the Wilcoxon and Mann–Whitney test were applied.

Results: No statistically significant inter-group or intra-group differences were found for the variables analyzed.

Conclusion: With the proposed protocol, low-level laser therapy administered prior to the induction of fatigue did not lead to any changes in bite force and mandibular range of motion, indicating that further studies are needed with different low-level laser dosimetric parameters.

EFFECTIVENESS OF PHOTOBIOMODULATION IN SLEEP BRUXISM CHILDREN WITH HEADACHE ASSOCIATED BY STRESS

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Background: Sleep bruxism (SB) is mandibular movements, as clenching and grinding teeth during the night. Headache may be another additional sign, which appears during the day, after an intense muscle effort during the night. Stress has been investigated in SB cases. Salivary cortisol levels have been measured to verify physiologically potential stress situations. SB treatments in children are controversial yet. Gold standard, occlusal splints therapy, needs a great patient cooperation, however it is not enough in some cases. Photobiomodulation has been used in other muscles treatment, could be an alternative for this case, especially for good properties as analgesia for biostimulation, increased local blood by vasodilation, anti-inflammatory effects. Thus, this study aimed to investigate the use of laser therapy in SB treatment in children with headache associated by stress.

Study Design/Materials and Method: SB was diagnosed according to ICDS-4 guideline: guardian's report and presence of wear facets in permanent teeth. Total sample was composed by 76 children, 6–12 years old, divided in 4 groups: G1- With SB, Laser therapy treated in acupuncture points ($\lambda = 94$ nm, 5 J/cm^2, 1.675 mW/cm^2, 0.070W, 20 s/point); G2–With SB, Occlusal Splint treated, G3–With SB, Placebo treated; and G4–Without SB, Control group. The presence or absence of headache was reported by guardians in anamnesis. The saliva was collected during the morning, freeze and processed by ELISA (Salimetrics, State College, PA). Statistical analysis was performed with the aid of the SPSS 20.0 program with a 5% significance level ($p \leq 0.05$), using Kolmogorov–Smirnov, Shapiro–Wilk and ANOVA tests.

Results: When observed intra-groups, there was a statistically significant difference between the frequency of children with headache before and after treatment in the G1 ($p = 0.005$) and G2 ($p = 0.0001$). However, in an inter-groups analysis, there was no difference between these two groups (G1 and G2). In salivary cortisol levels analysis between groups after treatment, G3 had statistically significant higher levels from the others.
Conclusion: Thus, results showed Laser therapy group (G1) performing as well as occlusal splints therapy (G2), considered gold standard treatment currently, confirming the accuracy of laser effects in muscle tissues. The increase of a salivary cortisol levels in placebo (G3) may suggest a propensity to anxiety for the technique applied by the patient, and the necessity to demystify the use and benefits of these therapy.

EFFICACY OF HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM) FIELD THERAPY WHEN USED FOR NON-INVASIVE BUTTOCKS AUGMENTATION AND LIFTING: A CLINICAL STUDY

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Background: Despite practitioners facing increasing demand for aesthetic improvement of buttocks, there is currently no non-surgical alternative to buttock augmentation based on fat grafting or silicone implants. The investigated device utilizes non-invasive magnetic technology that induces supramaximal deep muscle contractions, which cause gluteus muscles growth and remodeling. The goal was to identify the effects of the therapy and satisfaction of patients when applied to buttocks, and to determine if this may be a completely new approach to non-invasive buttock improvement.
Study Design/Materials and Method: 21 women (32.9 average age) were treated with a High Intensity Focused Electro-Magnetic (HIFEM) field device. The protocol encompassed 4 sessions (30 minutes each) within two weeks. Supramaximal contractions of gluteus maximus, minimus and medius were induced during the treatments. Subjects were evaluated at baseline, after the last treatment, and at 1-month follow-up; evaluation included weight measurement, patient photographs, and level of treatment comfort and satisfaction with results using a visual analogue scale (VAS) questionnaire.
Results: Weight change was insignificant. After the last session and 1 month post treatments, respectively, patients consistently reported high levels of satisfaction with treatment results (average score 7.2 ± 1.77 and 7.4 ± 1.73) and found the treatments very comfortable (8.3 ± 1.9 after last session) on a 0–10 VAS. None of the subjects reported discomfort or dissatisfaction with results (score <5). Digital photographs showed aesthetic improvement in most patients through improved shape and volume of the treated area, overall buttocks lifting and reduction in muscle laxity).
Conclusion: The treatments caused significant changes to gluteus muscles which translated into overall aesthetic improvement of the treated area. Patients reported high levels of satisfaction while primarily appreciating the lifting effect of the treatments. All subjects responded to the treatment. We suggest the device can be used as a unique non-invasive way to augment and improve the buttock area in patients, as an alternative to surgical procedures.

EVALUATION OF THE EFFECT OF PHOTOBIOMODULATION COMBINED WITH FIG EXTRACT TO MINIMIZE THE UVA RADIATION DAMAGE TO KERATINOCYTES

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Background: In Brazil and worldwide there is a trend in the use of plant extracts in cosmetic products of all kinds. These extracts present antioxidant activity, mainly due to the presence of polyphenols. For this reason, these compounds are used to stimulate cell renewal or inhibit deleterious processes induced by ultraviolet radiation (UV) in the skin. On the other hand, photobiomodulation has been shown to be an efficient tool to induce cell renewal. The combination of antioxidant therapy with extracts and photobiomodulation seems to be an interesting possibility to reduce the harmful effects of UV radiation. The objective of this work is to evaluate the therapeutic effect of fig extract in human keratinocytes in culture combined with red LED, to minimize the effects of UV-A radiation.
Study Design/Materials and Method: Human normal keratinocytes (HaCaT–CLS CM1) were seeded in 48 well plates (60,000 cells/well). The cells were exposed to UV-A (366 ± 10 nm, 2.5 mW/cm^2, 90 minutes), then treated with fig extract (0.3% in 1% FBS DMEM, for 24 hours). At the end of this treatment, cells were washed and received photobiomodulation (640nm $\pm$ 12.5 nm, 2.6 mW/cm^2, 7 minutes). Untreated controls were also performed. At the end of the treatments, cells were washed with PBS and 10% FBS DMEM was added, keeping the cells in the incubator for 48 hours. Finally, the MTT colorimetric assay was performed.
Results: It was observed that 13.5 J/cm^2 of UV-A causes damage in keratinocytes, reducing the amount of living cells to 80%. However, the use of photobiomodulation (2.6 mW/cm^2) after UV-A damage promoted recovery (to approx. 92%), but did not reach the baseline levels. The application of LED without previous damages has no effect on the keratinocytes, as well as the application of fig extract. On the other hand, treatment of keratinocytes with fig extract after UV-A damage caused a 28% reduction in cell amount. Also in this case, the photobiomodulation promoted recovery (to approx. 85%) without reaching basal levels.
Conclusion: After oxidative damage caused by UV-A radiation, keratinocytes were sensitive to fig extract, which presented toxicity. On the other hand, photobiomodulation could recover cells after UV-A damage, as well as after the exposure to fig extract. Further studies are necessary to understand clearly this effect, since MTT evaluates living cells in terms of mitochondrial activity and the observed effect can be related to increase in mitochondrial activity.

EVALUATION OF THE SAFETY AND EFFICACY OF THE PICOSECOND ALEXANDRITE LASER WITH SPECIALIZED FOCUS LENS ARRAY FOR TREATMENT OF THE MELASMA IN ASIAN PATIENTS

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Background: Melasma is caused by not only over production of melanin but hyperactivity of melanocytes. The objective of this study was to evaluate the efficacy and safety of picosecond 755 nm alexandrite laser plus focus lens array which can cause laser induced optical breakdown (LIOB) for melasma treatment.
Study Design/Materials and Method: Twenty melasma patients were recruited. All of them undergone two sessions of picosecond 755 nm alexandrite laser (Cynosure, MA) with 4–6 weeks interval. The parameters were 8 mm spot size, 750 ps pulse duration, 2-treatment passes, connected with focus lens array which carried the energy fluence of 0.4 J/cm^2. Melasma Area and Severity Index (MASI) and multi-lighting analyzed imaging system (Canfield Scientific, Inc., NJ) were used to assess and evaluate at the 4-week visit after completion of the second session. Clinical improvement and side effects were assessed by physician and patient.
Results: All 20 patients finished 2-session treatment were female with Fitzpatrick skin type IV. The average age was 43.75 (SD = 8.15) years old. Nine (45%) patients scored 50%–75% improvement, while 5 (25%) scored 25%–50% improvement. In physician's evaluation, 8 (40%) patients showed 50%–75% improvement, and 8 (40%) patients showed 25%–50% improvement. The mean MASI score showed significant improvement from 9.0 ± 4.8 to 6.5 ± 3.7 ($p < 0.001$). The MASI score at baseline had high correlation with MASI improvement ($r = 0.73$, $p < 0.001$). VISIA analysis of frontal face presented improvement in spots, wrinkles, texture, pores, UV spots, brown spots and porphyrins, although only significant for spots ($p = 0.007$) and porphyria ($p = 0.032$). Some patients experienced erythema (25%), pruritus (20%) and scaling (20%), which subsided after few days of usage of emollients and sunscreen. Only one patient (5%) had mild PIH, which regressed by three weeks.
Conclusion: Picosecond 755 nm alexandrite laser with focus lens array objectively demonstrated great efficacy for melasma treatment in just two sessions without obvious side effects.

EXOGENOUS ANDROGEN INDUCED TELANGIECTASIAS TREATED WITH IPL AND PULSED DYE LASER

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Background: A 48-year-old male with a history of intramuscular testosterone administration (depo-testosterone cypionate) for idiopathic hypogonadism presented with a three year history of worsening redness over the chest, shoulders, neck and back. He complained of flushing and warmth of his upper trunk and face while on depo-testosterone cypionate. A biopsy of the trunk showed telangiectasias. Extensive workup and clinical history revealed no underlying etiology for his telangiectasias. Cessation of Depo-testosterone and transition to topical testosterone (Abbvie) coincided with stabilization of the telangiectasias. He was diligent about sun protection and had no other risk factors for these findings. His testosterone level was 309 ng/dL (240–950) at presentation to dermatology.
Study Design/Materials and Method: The patient was treated with intense pulsed light (Lumenis) using the 515 nm filter, 18 J/cm^2, double pulse of 3.5 ms with a 15 msec rest. After his first IPL treatment, he had one pulsed dye laser (Candela) treatment using a 10 mm spot size, 10 ms pulse duration and fluency of 6 J/cm^2.
Results: Over 15 months, the patient had 5 IPL treatments and one pulsed dye laser treatment with a satisfactory response. His testosterone level remained within the reference range on topical testosterone and he did not subjectively appreciate any worsening of his condition.
Conclusion: Depo-testosterone cypionate is a common treatment for hypogonadism in males. Men presenting with new onset or worsening telangiectasias should be queried about their use of exogenous testosterone. Exogenous-androgen induced telangiectasias can be successfully treated with IPL and PDL.

EXPERIMENTAL MODEL OF TRAM FLAP IN RATS TO STUDY PHOTOBIOMODULATION

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Background: Myocutaneous flaps are widely used in order to facilitate the reconstruction of an injured area. This type of flap keeps their own vascularization and fill the wound. The TRAM flap is a very known flap used in breast reconstruction. Skin necrosis is a possible complication. The experimental model of TRAM flaps in rats has been used by our research group to study pharmacological and not pharmacological agents to prevent skin necrosis. The present study intends to present the experimental TRAM Flap in rats as a standardized model to study different photobiomodulation protocols.
Study Design/Materials and Method: The TRAM flap is marked in Rats Rattus norvegicus Albinus Wistar, 250–280 g. The surgery can include the use of micro clamps to study ischemia and reperfusion, if applicable. The clinical diagnosis of skin necrosis occurs at the 7th day post op. Photobiomodulation can be tested with different parameters, sessions, can be applied pre-op, intra-op and or post-op to simulate the clinical uses. The results are evaluated by calculating and comparing the area of necrosis the animals presented at seven days post op. Blood and tissue samples can be obtained.
Results: This study presents the design and results of three previous projects to demonstrate the importance of this model to study photobiomodulation effects. The first study: LOW LEVEL LASER THERAPY ON TRAM FLAPS IN RATS SUBMITTED TO NICOTINE APPLICATION. The second: PHOTOBIOMODULATION EFFECT ON MYOCUTANEOUS FLAPS: DIFFERENT DOSE EVALUATION IN NICOTINE RATS. The third: PHOTOBIOMODULATION IN EXPERIMENTAL MODEL OF ISCHEMIA AND REPERFUSION IN TRAM FLAP IN RATS
Conclusion: The TRAM Flap is a standardized experimental model in rats that can be used to compare different protocols of photobiomodulation.

HIGH INTENSITY Nd:YAG LASER TREATMENT FOR CHRONIC WOUNDS HEALING

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Background: Chronic wounds that are difficult to heal represent a serious problem, the lesions severely affect the quality of life of individuals, decrease the mobility and cause the loss of productivity. In this paper we are reporting about results of high intensity pulsed Nd:YAG laser treatment of chronic wounds and are giving the assessment of efficacy and safety of this laser therapy.
Study Design/Materials and Method: This is a case series study performed in a single medical center: Skin Rachel Clinic, Bandar Lampung, Indonesia. Patients having chronic wounds

which were not healing for longer than a year were treated with Nd:YAG 1064 nm laser. Treatment protocol consisted of two phases, in the first 20 ms long pulses were used while in the second we used shorter, 1.6 ms pulses. In both phases 4 mm spot, 35 J/cm^2 and 6 Hz were used. The wounds were manually scanned with laser beam in horizontal and vertical directions with two full passes. Patients received one to four sessions with one week intervals. At each visit the size of the wound and reduction of the pain were assessed

Results: 8 patients having various chronic wounds and one patient with acute necrotic wound were treated in period from January to August 2017. Four patients had chronic leg ulcers, three had anal fistulas, one chronic dermatitis and one palmar post injury necrosis. In all patients the wound healing was accelerated already after the first session and in all but one wound closure was achieved after two sessions. All patients tolerated the treatment well and no one was reporting any adverse effects.

Conclusion: High intensity long pulse Nd:YAG laser had shown good results in chronic wounds healing and seems to be a promising alternative to existing therapies. Larger series and longer follow ups are needed to allow us to draw the firm conclusions.

HIGH SENSITIVITY SPATIAL AND TEMPORAL QUANTIFICATION OF SKIN GLOSS EFFECT OF COSMETIC COMPOSITIONS

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Background: We demonstrate a low-cost, non-contact optical method with improved sensitivity for assessing skin attributes such as skin gloss. The presently used methods for skin gloss measurements are based on the ratio of specular to diffuse intensity. This method is more sensitive for measurements of high-gloss surfaces such as ceramics, than low-gloss surfaces like skin. Apart from that, skin gloss measurements require high sensitivity to detect small incremental gloss values changes that occur in the low gloss regime. The proposed methods open new possibilities in the fields of cosmetology and dermatopharmacology for measuring absorption kinetics and the pharmacodynamics of various external agents applied on the skin.

Study Design/Materials and Method: We developed an optical prototype comprising a low-cost camera and ring illumination. The skin is illuminated with multiple unpolarized white light sources (Lumileds LXZ1-4070) at an angle of incidence of approximately 22°. Gloss value is calculated from the camera image based on the slope of the intensity gradient in the transition between specular and diffuse reflection and on the sum over the intensities of pixels above threshold [1]. Using the prototype, we measured the absorption kinetics of common cream bases: unguentum emulsificans aquosum, uecrin cum aqua, vaseline white, paraffinum perliquidum. The creams (0.5 g per 65.5 cm^2) were applied on the forearm of a clinically healthy female volunteer (26 years). The measurements were taken immediately after application, 1 min, 10 min, 20 min and 30 min after application of the creams. The experimental results obtained with the prototype were compared with professional skin gloss measurement devices such as SAMBA (Bossa Nova) and skin gloss meter (Courage & Khazaka).

Results: The measurements showed different absorption kinetics for different creams. The fastest changes were detected for unguentum emulsificans aquosum, than paraffin perliquidun, than eucerin cum aqua, than vaseline. Detected kinetics was in line with the anticipated nature of interaction of applied creams with skin. The performance and linearity of the method compared with different conventional professional gloss measurement devices showed improved sensitivity for quantifying the temporal evolution of skin gloss as an indicator of absorption kinetics.

Conclusion: We report low-cost highly sensitive non-contact optical method for quantitative assessment of the skin gloss in the low gloss regime. The proposed method has potential applications in the fields of fundamental as well as applied research in cosmetology and dermatopharmacology for measuring absorption kinetics and also for testing the acceptance of various cosmetic and pharmaceutical products that are used for influencing the skin gloss conditions.

LASER MODALITIES FOR THE TREATMENT OF ARGYRIA: REVIEW OF THE LITERATURE

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Background: Argyria, or argyrois, is an acquired condition characterized by systemic or localized skin discoloration to purple and grey due to excessive exposure to the element silver. Treatment options for argyria are poorly documented and have not been standardized.

Study Design/Materials and Method: The present review seeks to discuss the utilization of the picosecond 755 nm Q-switched alexandrite laser and Q-switched 1064 nm Nd:YAG laser in the treatment of argyria. Systemic review of the literature demonstrated 12 patients with argyria that underwent novel laser treatment.

Results: The results demonstrated that both the picosecond 755 nm Q-switched alexandrite laser and Q-switched 1064 nm Nd:YAG laser were both 100% effective in immediate clearance of the dyspigmentation caused by elemental silver. Both laser techniques had sustained clearance up to one-year post-treatment. Transient negative side effects were present in all cases and included pain during the procedure as well as post-procedural erythema, edema, and scaling without crusting or blistering.

Conclusion: Laser therapy is a novel and successful treatment modality in the treatment of this rare but disfiguring disorder. Given the rarity of this disorder, this review of available case studies serves to comprehensively describe clinical presentation and novel laser treatment approaches to argyria.

MOLLUSCUM CONTAGIOSUM INFECTION FOLLOWING 1927 nm NON-ABLATIVE FRACTIONAL LASER TREATMENT

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Background: The potential for infectious complications after laser procedures is well known, especially with fully ablative lasers. Currently, herpes simplex virus (HSV) reactivation remains one of the more notorious infectious events, for which prophylaxis is commonly given. This case describes infection with molluscum contagiosum (MC) following non-ablative fractional laser treatment.

Study Design/Materials and Method: A 45-year-old Caucasian female presented for photorejuvenation of her upper back and arms. Two 1927 nm non-ablative fractional laser

treatments were performed to her upper back, spaced 8 weeks apart. Over a similar period, she underwent three treatments to her bilateral arms, spaced 4–6 weeks apart. The laser settings were as follows: energy of 10 mJ, treatment level 4, and 4–6 passes. A slightly pruritic, papular rash appeared on the patient's arms 7 to 10 days following the last arm treatment. The pink papules and pseudovesicles spread to the patient's back, most without apparent central umbilication.
Results: The differential diagnosis included folliculitis, candidiasis, and polymorphous light eruption, among others. A punch biopsy was performed and confirmed the diagnosis of MC. The lesions resolved with cryotherapy and topical imiquimod. The patient did later admit to brief exposure to children infected with MC. MC is a poxvirus, and infections can be exacerbated by disruptions in the epidermal barrier function, such as in children with atopic eczema. Non-ablative fractional lasers cause focal areas of epidermal and dermal injury. Theoretically, this leads to a breakdown of the protective epidermal barrier, allowing for enhanced local spread of the poxvirus. The timing and distribution of the patient's lesions supports the contributing role of the laser in this infection.
Conclusion: Practitioners must be aware of all potential infectious post-laser complications, usually resulting from an impaired epidermal barrier. Viral culprits can go beyond the commonly discussed HSV to include MC, especially when there is known exposure.

NEW ENERGY DEVICES FOR NECK REJUVENATION: A LITERATURE REVIEW ON MODALITIES AND EFFICACY

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Background: During the aging process, the neck develops skin dyspigmentation, rhytides, loss of mandibular contour, accumulation of submental fat, and prominence of platysmal bands. Assorted energy producing modalities are used to target distinct factors of the aging process
Study Design/Materials and Method: Novel publications from 2014–2016 regarding neck rejuvenation technologies were reviewed. This revealed a surge of new technologies including lasers, radiofrequency devices, photodynamic therapy, and combination therapies.
Results: One prospective study of non-ablative fractionated laser resurfacing in 18 women found immediate improvement in skin dyschromia, laxity, and wrinkles; re-evaluation at 3-months only showed sustained improvement in dyschromia and wrinkles. Another study evaluated long-term efficacy of fractional CO_2 laser utilizing independent blinded reviewers. Participants had significant improvement in skin laxity, jowls, fat deposition, and horizontal neck lines both one-month and one-year post-treatment. No persistent complication was identified at one-year follow-up making this a safe option with proven long-term efficacy. In regards to photodynamic treatment of the neck, a comparison study evaluated intense pulse light (IPL) and red light energy with and without photodynamic therapy (PDT) using 5-ALA. The neck was divided into four equal sections and treated with a different single or combination therapy. The IPL-PDT and red light-PDT groups had better efficacy than IPL or red light alone.
Conclusion: With regards to photodamage and dyschromia, it is the author's opinion that non-ablative fractionated lasers proved efficacious clinically compared to photodynamic therapies. In regards to skin laxity and submental fullness, the studies support superior outcome for CO_2 lasers but with more downtime and need for expert clinicians. Using lasers in combination with secondary treatment modalities have the best cosmetic outcomes. This is an exciting new era for neck rejuvenation. As physicians continue to mix and match treatment modalities to meet each patients' individual needs, more research on combination therapies can be expected.

NON-SURGICAL FAT REDUCTION: A SOCIAL MEDIA ANALYSIS

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Background: Social media has become a mainstream method of allowing patients to report and rate their satisfaction with cosmetic procedures and providers. These outlets may provide a more transparent view of patient satisfaction and with the recent growth of non-surgical fat reduction treatments, we sought to perform a social media analysis.
Study Design/Materials and Method: Data was collected from 2006–2017 examining trends in satisfaction of all non-surgical fat reduction treatments from the RealSelf website. Additionally, google trends data was analyzed over this period, comparing the relative interest between non-surgical fat reduction search terms.
Results: Consumers visited RealSelf over 7 million times in the past year to research non-surgical fat reduction, a 1% decrease compared to the prior year. Consumers spend the most time viewing Photo 56% (38% user photos, 18% provider photos), followed by reviews 25%, questions 16%, discussions 1% and guides 1%. The overall satisfaction rating of all non-surgical fat reduction treatments was 78%. Based on all ratings since 2006, CoolSculpting was the most popular treatment with 2056 ratings and an overall satisfaction of 77%, followed by Kybella (235 ratings, 79% satisfaction), SculpSure (230 ratings, 69% satisfaction), Vanquish (165 ratings, 71% satisfaction), and Ultrashape/Ultrashape power (139 ratings, 85.5% satisfaction). The overall surgical fat reduction satisfaction rating was 88%. Top questions asked by consumers related to cost, long-term results, efficacy, and modality comparisons. Google trends data revealed CoolSulpting as the most popular trending non-surgical fat reduction search term which peaked popularity in January 2016. As of October 2017, relative google trend interests were; 49/100 CoolSculpting, 16/100 Kybella, 6/100 SculpSure, 1/100 Ultrashape.
Conclusion: Social media can provide transparent insight into how procedures are evaluated and perceived. Non-surgical fat reduction has lower overall satisfaction compared to surgical fat reduction. Before and after photography continues to play a critical role in informing aesthetic consumers.

OPTIMIZATION OF Er:FIBER LASER FOR NON-ABLATIVE FRACTIONAL TREATMENT OF SKIN AND ORAL TISSUES

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Background: Non-ablative fractional laser treatment of skin has met with considerable success when used for various indications in dermatology. At the same time, effects of fractional treatment on oral soft tissues are much less studied. Evolution of dermatological fractional systems and expansion of the application ability of fractional technologies in other fields such as dentistry requires good understanding of interaction between soft tissues and laser light in fractional regime.

Study Design/Materials and Method: In this work, we used Er:fiber laser with wavelength of 1550 nm, peak power of 25 W, operated in pulsed mode. *Ex vivo* experiments were conducted on porcine skin and porcine soft oral tissues. Effects of laser beam diameter variation from 25 to 400 um (through scanning beam waist along z-axis) and pulse energy in the range from 10 to 150 mJ on coagulative columns' shape were investigated in detail. NBTC staining was used to assess depth and diameter of the columns. Laser parameters for human clinical study were determined based on the results of *ex vivo* experiments. Clinically, biopsies of keratinized gum and alveolar mucosa were collected for subsequent histological analysis using H&E staining. The results were compared with *ex vivo* data.

Results: Ex vivo data revealed that under optimal conditions columns up to 800 μm in depth could be reliably produced in the keratinized gum and alveolar mucosa with 130 mJ pulses, and in the skin with 70 mJ pulses. Non-monotonic dependence of the column's depth on position of the beam waist (and, hence, beam diameter) has been found for both types of tissues *ex vivo*. Generally, good agreement between *ex vivo* and *in vivo* datasets was observed.

Conclusion: Ex vivo data offer reliable and valuable information for optimal design of tissue-specific Er:fiber laser-based fractional devices.

PARADOXICAL INCREASE IN TELANGIECTASIA FOLLOWING PULSED DYE LASER TREATMENT OF RADIATION-INDUCED TELANGIECTASIA

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Background: Radiation-induced telangiectasia are a common sequela to radiation therapy. Several studies have demonstrated the efficacy of 585 nm and 595 nm pulsed dye laser (PDL) in the treatment of radiation induced telangiectasia. Though paradoxical hypertrichosis following laser epilation has been reported, paradoxical increase in telangiectasia following PDL has not been described. We report a case of paradoxical increase in telangiectasia following treatment with 585 nm PDL.

Study Design/Materials and Method: A 34-year-old female with history of subglottic adenosquamous carcinoma status post radiation treatment with 7000 Gy in 35 fractions presented 25 months following her final radiation treatment. Telangiectasia were noted on the anterior neck. A 585 nm PDL (Syneron Candela), 7 mm spot size, 10 ms pulse duration, and fluence of 13 J/cm^2 was used for treatment of her telangiectasia. A total of 39 pulses were delivered with 30/20 cryogen cooling. The patient tolerated the procedure well with expected post-treatment purpura, no burns noted.

Results: Telangiectasia initially regressed, but within 2 weeks new telangiectasia were noted both inside and outside the treatment field. Twelve months following initial PDL treatment the patient was treated with 585 nm PDL with 7 mm spot size, 10 ms pulse width, and fluence of 11.5 J/cm^2. A total of 140 pulses were delivered with cryogen set at 30/20. Again, the patient tolerated the procedure well with expected post-treatment purpura. At 2 weeks following second treatment a decrease in telangiectasia was achieved.

Conclusion: Laser therapy and subsequent thermal injury has been shown to induce several inflammatory mediators and angiogenic factors. Many authors suggest that paradoxical hypertrichosis may in part be explained by increased vascularization of hair follicles. It is possible that similar mediators may cause a paradoxical increase in telangiectasia following PDL treatment.

PILOT EVALUATION OF A NOVEL 1927 nm LASER SYSTEM, WITH MAGNETIC ROLLER-ASSISTEDTRACKING, FOR THE TREATMENT of FACIAL PHOTOAGING

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Background: Since its introduction more than a decade ago, non-ablative fractional laser wavelengths have become widely popularized for using in facial rejuvenation. In this IRB-approved pilot study evaluated an investigational device, fractional 1927 nm fiber laser (Lutronic, Goyang, S Korea), indicated for non-ablative skin resurfacing and the treatment of pigmented lesions (lentigines), dyschromia; or cutaneous lesions such as, but not limited to: actinic keratosis, melasma, wrinkles; or improving skin tone/skin texture.

Study Design/Materials and Method: 43 subjects with mild to severe photoaging were enrolled at 5 US sites, and received 1–4 treatments. The majority of subjects received 3 treatments (n = 26, 60%). 18 subjects completed ≥1 follow-up visit at 2–3 weeks (n = 3, 6%), 1 month (n = 11 26%), and/or 3 months (n = 4, 9%). Facial treatments encompassed a majority of treatments—face (n = 114, 97%). Other treatment variables: Mean treatment passes = 14.8 ± 2.8, treatment time = 11.4 ± 7.7 minutes, mean pain score = 2.9 ± 2.0

Results: Transient effects post-treatment were noted, included erythema, bronzing, edema, and post-treatment discomfort. No serious adverse events were reported, thus demonstrating device safety. Follow-up assessment demonstrated that 75% of the subjects had a greater than 1 grade improvement, by physician assessment, using a VAS scale (at 1 month post last treatment) in one or more following treatment areas: peri-orbital and peri-oral wrinkles, fine lines, pigmented lesions, skin tone, and enlarged pores.

Conclusion: Results of a series of treatment in this study population showed safety and efficacy in the application of a novel 1927 nm laser system for the treatment of facial photoaging.

RESTROSPECTIVE ANALYSIS OF THE EFFICACY AND SAFETY OF COMBINATION TREATMENT WITH Q-SWITCHED 755 nm ALEXANDRITE AND 1927 nm THULIUM FIBER LASER FOR HYPERPIGMENTATION

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Background: Hyperpigmentation is a common concern among patients and is caused by several factors such as photodamage,

aging, and melasma, and laser therapy can be an effective treatment option. The Q-switched 755 nm alexandrite and 1927 nm thulium fiber laser are frequently used to treat hyperpigmentation, but there have been no reports in the literature of using them as a combination treatment. Our goal is to describe the efficacy and safety of this combination treatment to improve hyperpigmentation both on and off the face.
Study Design/Materials and Method: We performed a retrospective chart review of 39 patients from January 1, 2014 to September 25, 2017 who had one treatment with Q-switched alexandrite laser combined with the 1927 nm thulium fiber laser for hyperpigmentation on the face, neck, chest, and arms (institutional review board approval not required). Blinded assessments of clinical improvement based on a modified grading scale (adapted from Alexiades–Armnenakas) and a global aesthetic improvement scale were performed by two clinicians 2–4 weeks and 1–4 months post treatment.
Results: Preliminary statistical analysis showed an improvement in pigmentation at assessment at both 2–4 weeks (2.22 +/− 0.62 to 1.51 +/− 0.71) and 1–3 months (2.15 +/− 0.75 to 1.24 (+/−1) on a 0 to 4 scale that was statistically significant ($p < 0.05$). Fine lines and skin texture showed statistically significant improvement ($p < 0.001$) at 1–4 months post-treatment on a 0–4 scale as well. Overall global aesthetic was improved to very much improved in 55% of patients at 2–4 weeks and 69% at 1–4 months. No major adverse events were reported.
Conclusion: Combination treatment of Q-switched 755 nm alexandrite and 1927 nm thulium fiber laser for hyperpigmentation on the face and upper body show statistically significant improvement in pigmentation, fine lines, and skin texture. Further analysis of this retrospective study will be presented.

RETROSPECTIVE STUDY OF SAFETY AND EFFICACY OF PICOSECOND ALEXANDRITE 755 nm LASER FOR THE TREATMENT OF MELASMA IN CHINESE

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Background: Melasma is a very common pigmentary skin condition in Asian women. Q-switched Nd:YAG 1064 nm laser with larger spot size and low fluence has been widely used to treat Melasma in Asia. However, it has been reported that some patients didn't respond to the treatment and may result in PIH. Since the introduction of picosecond alexandrite 755 nm laser, promising clinical results for pigmentation removal have been reported. In this study, we aimed to evaluate the efficacy and safety of picosecond alexandrite laser for Melasma in Chinese.
Study Design/Materials and Method: 35 patients diagnosed with Melasma and received picosecond 755 nm laser during January 2016 to December 2016 were included in this study. The patients received laser 3 treatment sessions with one-month interval. All patients' demographics were recorded. Photography were taken at baseline, prior to each treatment session and one month following the last treatment. Images were evaluated independently by two trained dermatologists. Melasma Area and Severity Index (MASI) was used for the evaluation of treatment efficacy: Excellent (>90%), very good (50–89%), Fair (10–49%), poor (<10%). Adverse events and patient satisfaction were monitored until 6-months follow up.
Results: The average age of 35 patients was 39 years-old and all females with Fitzpatrick skin type III to IV. The averaged MASI for baseline and the last follow up are 7.98 ± 5.86 and 4.89 ± 3.93, respectively, which shows statistical improvement ($p < 0.01$). The overall response rate is 80% (excellent: 5%; very good: 29%; fair: 46%), and poor: 20%. Some of the patients experienced a transient PIH after the treatment, all of the PIHs were resolved in 2 weeks to 1 month. The average patient satisfaction rate is 62%. 2 patients with rebound hyperpigmentation 6 months after the treatment, while most of the patients can experience further improvement in their skin condition after 6 months.
Conclusion: The overall response rate of using picosecond alexandrite 755 nm laser for Melasma in Chinese is high, and with low rebound rate. No sever PIH was observed which demonstrated a high safety profile. However, the satisfaction rate should be further improved.

SAFETY AND EFFICACY OF REGIONAL SKIN CRYOTHERAPY TO TREAT AXILLARY HYPERHIDROSIS

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Background: Primary hyperhidrosis (PHY) of the axillae remains difficult to treat if botulinum toxins, anticholinergics or surgery are not applicable. Energy-based treatment modalities comprise lasers, microwaves, radiofrequency or iontophoresis. They are effective but painful. Recently cryotherapy, a well-established concept in medicine, with pain killing qualities has been implemented to treat PHY.
Study Design/Materials and Method: A prospective, single-center, proof of principle study was designed to evaluate safety, efficacy, and tolerability of an integrated cold-hot therapy system in PHY after two treatments within 4 weeks at follow-up 1 and 6 month post interventions. Subjective assessments (HDSS), clinical photographs, pain score (VAS), and minors starch test were chosen for evaluation. Study subjects ($n = 5$) were asked 48 hours prior to treatment to stop shaving of both axilla and not to use of deodorants or antiperspirants. In stationary mode cold and heat was applied following the protocol: cooling down to $-5^{\circ}C$ within 10 min followed by re-heating up to $+30^{\circ}C$ 1 min. The primary endpoint was set to a decrease in sweating defined as a reduction of 1 HDSS level compared to baseline at 1 and 6 month follow-up.
Results: The new integrated cold-hot therapy system was found to be highly tolerable, less painful and showed no down- or healing times in 5 study subjects (3 females, two males). Pain levels were reported as below 1 in all subjects. HDSS at baseline was measured as 3.8, at one month follow-up 1.9 and at 6 month follow-up 1.8. Minors starch test reveal in some axillae a less intense staining at the treatment area.
Conclusion: The new integrated cold-hot therapy system was found to be highly tolerable, less painful and showed no down- or healing times in 5 study subjects (3 females, two males). Pain levels were reported as below 1 in all subjects. HDSS at baseline was measured as 3.8, at one month follow-up 1.9 and at 6 month follow-up 1.8. Minors starch test reveal in some axillae a less in intense staining at the treatment area.

SINGLE-CENTER, RANDOMIZED, SPLIT-FACE TRIAL, COMPARING DOWNTIME POST-HYBRID NON-ABLATIVE AND ABLATIVE FRACTIONAL SKIN RESURFACING OF THE FACE WITH REGENERATIVE SKIN NECTAR

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Background: A proprietary combination of tripeptides and hexapeptides clears the ECM, stimulates collagen and elastin production, and decreases inflammation leading to an accelerated epidermal healing process. A regenerating skin nectar (RSN) containing tripeptides has been shown to decrease healing time following energy-based device procedures. We hypothesize that the antioxidant RSN will shorten downtime following hybrid non-ablative and ablative laser resurfacing to the face.
Study Design/Materials and Method: We performed a split-face, single-blind, randomized study comparing healing time of hybrid non-ablative and ablative laser resurfacing of the face with application of RSN. Five subjects were randomized to apply the RSN to half of the face two weeks pre- and 1 week post-laser procedure. Standardized clinical photography, physician assessment, and subject self-assessments were performed on days 0, 1, 3, 4, and 7.
Results: Based on physician post-treatment assessments, redness was significantly reduced as early as day 1 on the RSN-treated side compared to control, while decreased roughness was seen on day 3 and 4. On day 7, all five subjects had recovered fully from the hybrid laser resurfacing with no appreciable redness, swelling or roughness on either side of the face. All but 1 patient preferred the RSN and felt their complexion looked better on the subject self-assessment.
Conclusion: For patients concerned with downtime, pre and post-procedure treatment with RSN with tripeptides can decrease healing time associated with facial hybrid laser resurfacing, most notably in erythema and roughness.

SONOGRAPHY OF GLAUCOMA

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Background: Early treatment of glaucoma reduces visual loss. Sonography at 15–22 MHz can show disruption of the cribriform plate of the retina which may lead to clinical disease.
Study Design/Materials and Method: 36 patients with glaucoma were scanned with 3D ultrasound over a one year period. The integrity of the cribriform plate was studied in 3 planes by one observer with 35 years of experience with ophthalmic sonograms.
Results: 34/36 patients had interruptions of the plate structural architecture. There was no correlation with disease severity in this study.
Conclusion: 3D sonogram imaging of the retina including the cribriform plate is well tolerated and may allow for early treatment of glaucoma.

SUCCESSFUL TREATMENT OF ACQUIRED NEVI AND SOLAR LENTIGINES WITH 755 nm LONG-PULSED ALEXANDRITE LASER

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Background: Two common melanocytic skin lesions are acquired nevi and solar lentigines, both of which may be cosmetically undesirable for patients. Acquired Nevi are benign lesions that occur on any body site. They may be flat or elevated and vary in color and size. Solar lentigines are light brown macules that arise in sun-exposed areas of patients with lighter skin types. Acquired nevi are often left untreated, with few reports showing efficacy with long-pulsed 755 alexandrite lasers in patients with Asian skin. Solar lentigines are treated with various lasers and pulsed light, but the results are not always satisfactory. We present two patients with acquired nevi and solar lentigines in skin type III–IV treated with long-pulsed 755 alexandrite laser with complete cosmetic resolution and no scarring.
Study Design/Materials and Method: A 63-year-old woman with skin type III and 29-year-old man with skin type IV, both with acquired nevi and solar lentigos were treated with long-pulsed 755 nm alexandrite laser using a 6 mm spot size at 70 J/cm^2, 1.5 ms pulse with dynamic cooling device of 20/10/30 to visibly vaporize each individual nevi or lentigo.
Results: Immediate vaporization was observed of all targeted nevi or lentigos. After one month, complete cosmetic clearance was noted on both patients, without evidence of scarring or hypopigmentation. Healing time may vary from a few weeks to 3 months.
Conclusion: Acquired nevi and solar lentigines can be cosmetically undesirable for patients. With assurance of no suspicious features deeming a necessary biopsy, 755 nm long-pulsed alexandrite laser offers removal without scarring and hyper or hypopigmentation for skin types III and IV. We report two cases of successful cosmetic clearance of solar lentigines and acquired nevi using 755 nm long-pulsed alexandrite laser.

SUCCESSFUL TREATMENT OF MULTIPLE MILIARY OSTEOMA CUTIS USING ERBIUM LASER

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Background: Osteoma Cutis (OC) is a rare condition of bone formation in the skin. OC can occur as a single entity or multiple nodules scattered throughout, also known as multiple military. The formation of the bone metaplasia can be idiopathic or secondary to a condition of chronic inflammation, such as acne, trauma, venous stasis, or genetic disorders such as Albright hereditary dystrophy. Cosmetically concerning, OC papules can be difficult to treat due without risk of scarring or pigmentation, as topical and systemic therapies are ineffective. We report a case of multiple miliary osteomas of the face successfully vaporized and therapeutically treated with Er:YAG laser.
Study Design/Materials and Method: A 64-year-old woman with histologically-proven multiple miliary osteomas of the face were treated with Er:YAG laser using a 0.2 mm spot size at 50 J/cm^2, 10 Hz, 300 microsecond short pulse in a focused and defocused mode to visibly vaporize each individual osteoma.
Results: Immediate vaporization was observed of all osteoma cutis papules, as Er:YAG laser targets the water chromophore present in bone and can vaporize overlying skin with much precision and little thermal conduction. After one month of therapy, the patient healed well by secondary intention. Adverse effects may include textural change and erythema, pending depth of ablation with Er:YAG. Healing time may vary from a few weeks to 3 months.
Conclusion: Osteoma cutis is a rare benign condition that can be cosmetically distressful to patients, with limited surgery options without risk of scarring, pigmentation or complete removal. We report successful therapeutic treatment of osteoma cutis utilizing Er:YAG laser to target the water chromophore in bone.

SUCCESSFUL TREATMENT OF RECALCITRANT HAILEY-HAILEY WITH CO_2 LASER

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Background: Hailey-Hailey disease (HHD) is a rare, autosomal dominant disease, due to loss of function mutation in ATP2C1. This causes abnormal cytoplasmic calcium levels and subsequent acantholysis. It presents with macerated, eroded plaques in the body folds. Given associated malodor, pain, and disfigurement with HHD, patients often experience a significant amount of psychosocial distress secondary to this disease.
Study Design/Materials and Method: A 76-year-old female with HHD for 35 years in the axilla and groin presented for evaluation after failing therapy with topical corticosteroids and acitretin. Diagnosis of HHD was confirmed with histopathology and she was treated with oral glycopyrrolate and magnesium, as well as topical ciclopirox gel and tacrolimus ointment. Patient had minimal improvement and thus CO_2 laser treatment was considered.
Results: Patient was treated with a fractionated carbon dioxide (CO_2) laser (Lumenis) at 150 mJ with 15 watts to the left groin and left axilla, with nearly complete clearance of her disease after 2 treatments.
Conclusion: Hailey–Hailey disease is a rare, painful, malodorous, and disfiguring, acantholytic disease. While topical and oral steroids and retinoids are often considered first line, the addition of CO_2 laser can offer prolonged or permanent remission, with little adverse effects, and high patient satisfaction.

SUCCESSFUL USE OF A FRACTIONAL 2940 nm LASER IN TREATING CHRONIC, SEVERE EROSIVE PUSTULAR DERMATOSIS OF THE SCALP

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Background: Erosive pustular dermatosis of the scalp (EPDS) is a rare inflammatory condition that causes chronic, sterile pustular, crusting lesions which often leave patients with scarring alopecia. Historically, treatments include local and systemic antibiotics and potent steroids which are associated with multiple side effects and prove to be minimally effective. This report details the successful treatment of EPDS using a fractional ablative laser on a patient with long-standing EPDS that was unresponsive to traditional therapies.
Study Design/Materials and Method: A 73-year-old Caucasian female presented with a history of EPDS for eleven years unsuccessfully treated with therapies such as debridement, skin grafts, oral and topical steroids as well as dapsone, azathioprine, methotrexate and mycophenolate mofetil. She underwent 19 treatments with a fractional 2940 nm Er:YAG. Each session included one *pass.* Depth of treatment ranged from 175–250 microns with a density of 11% or 22%. Combination 8% lidocaine and 8% tetracaine cream was used as anesthetic.
Results: Improvements were seen after the first few treatments. At the start of treatment approximately 80% of our patient's scalp and forehead were affected by EPDS. After 19 treatments, only 5% of her scalp remained affected. Fractional ablative laser therapy proved successful in treating severe recalcitrant EPDS.
Conclusion: Fractional Er:YAG may be a promising option for difficult to treat cases of EPDS. Our patient had significant improvement over traditional therapies. Fractionated Er:YAG poses fewer side effects or risks than chronic immunosuppressant medications, and may be an excellent alternative to these therapies in EPDS of any severity. Although more studies are needed, physicians should consider this as a reasonable treatment option for patients with recalcitrant EPDS.

THE APPLICATION OF SUBSURFACE FRACTIONAL ABLATIVE RESURFACING FOR PERIAREOLAR SCAR USING 1064 nm PICOSECOND LASER WITH FRACTIONAL MODE (MLA)

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Background: The main purpose of picosecond laser was more effective treatment of pigmented lesion including tattoo at first. But, In 2014, the FDA approved 755 nm picosecond Alexandrite laser not only for the treatment of pigmented lesions and tattoos but for the treatment of scarring and wrinkles. We studied the use of a 1064 nm picosecond Nd:YAG laser with fractional mode (MLA) in the treatment of Periareolar operative scar.
Study Design/Materials and Method: 15 patients had scar on periareolar area due to breast surgery. When the wounds were completely healed and at least 6 months had passed, the resulting scars each received multiple treatments with a picosecond Nd:YAG laser device (WONTECH, Daejeon, Korea). Treatments were spaced about 1 month apart. Topical anesthetic cream (eutectic mixture of 2.5% lidocaine hydrochloric acid and 2.5% prilocaine; EMLA cream, AstraZeneca AB, Södertälje, Sweden) applied 1 hour before treatment to reduce patient discomfort during the procedure. The laser treatment was performed with a pulse duration of 750 picoseconds and a spot size of 7 mm. To make complete epithelization, a moisturizer and antibiotics ointment were applied for 1 week. Patient satisfaction degrees were compared using Vancouver scar scale(VSS), and adverse events using a Wilcoxon signed-rank test with SPSS version 17.0 (SPSS Inc., Chicago, IL). Differences were considered statistically significant when $p < 0.05$
Results: Mean VSS scores for the treated scars were 7.5 (standard deviation [SD] 1.70) before treatment, 2.7 (SD 0.57) six months after treatment. The mean improvement of VSS score was 4.8, which was evaluated by 2 experienced physicians ($P < 0.05$). The patient's overall satisfaction using a grading scale was also significantly high with their treated scar. Three of the 9 patients (60%) were excellent, 6 (40%) were good with the results. The average of time to reepithelization of epithelial cell was 7 days. After laser treatment, minor complications, such as pain, erythema, scaling have remained for 3 days up to 2 weeks. Any serious adverse effects, such as wound disruption, post inflammatory hyperpigmentation, or dyspigmentation, were not shown in this study.
Conclusion: We got an excellent result from subsurface fractional ablative Resurfacing for periareolar scar using 1064 nm picosecond laser with fractional mode (MLA).

THE EFFICACY OF A DUAL WAVELENGTH PICOSECOND LASER FOR FACIAL TREATMENT OF MELASMA AND SKIN REJUVENATION

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Background: Photoaging in Chinese often presents with benign pigmentary lesions. Q-switched laser for pigmented lesions in Asians reported a 25% post inflammatory hyperpigmentation risk whilst long pulsed Nd:YAG was

reported to have a lower PIH risk. Picosecond lasers of various wavelengths were introduced. The objective of this study is to assess the efficacy of a picosecond laser for the treatment of melasma and skin rejuvenation.
Study Design/Materials and Method: 10 subjects with melasma and 10 subjects with photoaging were recruited. Each subject receives up to 9 facial treatments. Each session they will receive 4 passes of picosecond laser at 1064 nm wavelength with an endpoint of mild erythema. Standardized photographs were taken at baseline, each treatment visit as well as 6 weeks and 12 weeks after the last treatment. These photographs were assessed by two independent physicians. The physician offering treatment rated the MASI score for subjects with melasma and global assessment for subjects for skin rejuvenation. Any adverse effects were recorded. At follow up visits, subjects will assess improvement and satisfaction.
Results: The study is ongoing with 5 subjects being treated for melasma and 7 subjects having skin rejuvenation. Overall, 59 treatment sessions were carried out. For skin rejuvenation, 57% had slight improvement. There was reduction in MASI score but was not statistically significant. No adverse effects were recorded.
Conclusion: The 1064 nm picosecond laser demonstrated some improvement for skin rejuvenation and melasma.

THE INFLUENCE OF PERIODONTAL TREATMENT ASSOCIATED WITH PHOTODYNAMIC THERAPY IN EXPERIMENTAL MODEL OF ASTHMA

Ellen Perim Rosa, Felipe M. da Silva, Larissa C. Candeo, Adriana Lino dos Santos Franco, Kristianne P. Fernandes, Ana Paula Ligeiro-Oliveira, Anna Carolina R. Horliana
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Background: Asthma and periodontal disease (PD) present high relevance economic and social. Evidence suggests that PD can exert systemic immunomodulatory effects. Conventional periodontal treatment (PD) has been associated with photodynamic therapy (PDT). To evaluate the influence of TP associated with PDT on the modulation of pulmonary inflammation in experimental model of asthma.
Study Design/Materials and Method: After approval by the CEP-Uninove (CEUA 020/2015), forty-five Balb/c male mice were divided into 5 groups ($n = 9$): 1. Basal, 2. Asthma (A), 3. A + PD, 4. A + PD + TP, 5. A + PD + TP + PDT. Periodontitis was induced by ligation technique (15 days) and the asthma by administration of ovalbumin (OVA) subcutaneously (days 0 and 7) and nebulization (3 x/week, for 2 weeks). TP was performed with curettes, PDT with methylene blue (0.005%) and irradiated red diode laser = 660 nm, energy density 6,369 J/cm^2, with 9 J per point, delivered in 90s, 2 points. Euthanasia was performed for morphological analysis of the lung and mandible. Cytokines IL-4, IL-5, IL-10, IFN-γ, TNF-α, IL-1β and IL-6 were evaluated. Total and differential counts of inflammatory cells were performed in the Broncho Alveolar Lavage (BAL). To statistical analysis was used one-way ANOVA followed by the Student-Newman–Keuls test.
Results: Group 2 presented an increase in the total number of cells 31,25 (±5,41) in BAL ($p < 0.05$), corresponding to ± 8% of total leukocytes. In group 3, the presence of PD in asthmatic mice decreased 81 (±41) ($p < 0.001$) the release of IL-5 when compared to the control group. Group 2 had reduced IFN-γ values 230.5 (±67,17) 250 pg/ml ($p < 0.05$). There was an increase in mucus production in groups 2, 342.99 (±79) and 5, 295.22 (±65,44) ($p < 0.001$).
Conclusion: PD can influence lung inflammation in experimental model. However, group 3 presented an improvement in pulmonary inflammation after PD associated with PDT.

TOLERANCE OF A LOW-LEVEL BLUE AND RED LIGHT THERAPY ACNE MASK IN ACNE PATIENTS WITH SENSITIVE SKIN

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Background: Acne and sensitive skin are often associated, due to the involvement of an impaired skin barrier in both conditions, which can be further aggravated by certain topical acne treatments. Often, treatment-induced signs and symptoms of irritation can lead to poor patient compliance and dissatisfaction with treatment outcomes. Therefore, a non-topical, chemical-free treatment that is well-tolerated by patients with acne and self-perceived sensitive skin is highly desirable. The benefits of red and blue light therapy in the treatment of mild to moderate acne are well known, with blue light reported to target acne-causing bacteria and red light demonstrating anti-inflammatory activity. Recently, clinical evidence reported on the ability of new low-level red and blue light therapy technology to effectively reduce both inflammatory and non-inflammatory lesions.
Study Design/Materials and Method: A 4-week, open-label clinical study was conducted to evaluate the tolerance of a new low-level blue and red light therapy technology (acne mask) in males and females (12–40 years of age) with mild to moderate acne and self-perceived sensitive skin. The acne mask provided simultaneous low-level blue and red exposure to the face in a single-step, and was performed at home. Objective cutaneous tolerance attributes were evaluated by the Investigator and sensory irritation was self-assessed by the patients.
Results: The acne mask was well-tolerated over the 4-week study, with no treatment-related adverse events. In addition, the patients agreed that the acne mask was comfortable and gentle to their sensitive skin, including those subjects who had experienced irritation to topical acne treatments in the past.
Conclusion: This clinical study confirms that a new low-level blue and red light therapy acne mask provides a chemical and UV-free treatment option for mild-to-moderate acne patients with sensitive skin, including those who have experienced sensitivity to topical acne treatments.

TREATMENT ALGORITHM FOR EXTRA-MAMMARY PAGET'S DISEASE USING THE CARBON DIOXIDE LASER—A PILOT STUDY

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UT Health Sciences Center at Houston, Houston, TX; MD Anderson Cancer Center, Houston, TX

Background: Extra-mammary Paget's disease of the vulva is a rare intraepithelial non-squamous adenocarcinoma of the skin that accounts for about 1% of all vulvar cancers. Most commonly pursued treatment alternatives include surgical modalities such as Mohs micrographic surgery or radical vulvectomy with or without lymphadenectomy. Unfortunately, it is frequent for patients to experience recurrences, as clear margins are difficult to achieve given this disease is often multi-focal. Reported local recurrence rates following surgery range from 34% to 56%. Additional treatment options that have been reported in the scientific literature include topical imiquimod

cream, topical 5-fluorouracil, radiation therapy, ALA and photodynamic therapy, systemic chemotherapy and carbon dioxide laser ablation.
Study Design/Materials and Method: This is a pilot study with a single patient where we present a treatment algorithm for the use of fractionated carbon dioxide laser and topical imiquimod in a case of unresectable Extra-mammary Paget's disease.
Results: Given the extent of the patient's disease, multi-focality and history of multiple failed excisions, Mohs micrographic surgery was not recommended. The patient was treated with a combination of fractionated carbon dioxide laser at fluences of 100 mJ, 125 mJ and 150 mJ and topical imiquimod 5% cream.
Conclusion: This study provides a viable alternative for treatment for Extramammary Paget's disease that is surgically unresectable.

TREATMENT OF FOLLICULITIS DECALVANS WITH CONVENTIONAL AND DAYLIGHT PHOTODYNAMIC THERAPY

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Hôpital Huriez, Lille University Hospital, Lille, France

Background: A 41-year-old Caucasian male was diagnosed with folliculitis decalvans at 29. This condition has been treated with cyclin, isotretinoine, topical cortoid, amoxicillin and rifampicine, high posology of zinc, disulone, topical tacrolimus and corticotherapy *in situ* without any success. Scarring alopecia progressed and frequency of the outbreaks of follicular pustules increased.
Study Design/Materials and Method: In 2016, we observed some patches of scarring alopecia at the expanding margins of which are follicular pustules. DLQI was poor and the patient was highly embarrassed by the social discomfort and his painful scalp. We proposed a treatment by photodynamic therapy, based on its anti-inflammatory effects. The patient gave his informed consent. We performed 3 sessions 1-month apart using topical methylaminolevulinate (Galderma) and red light-illumination (Galderma) at 37 J/cm2 after 180 minutes of incubation at obscurity. The procedure induced a severe and diffuse pain (EVA = 8). After the procedure, we observed erythema, oedema at the margins and the patient reported minor pain over the treated area. These side effects were resolved within 3 days. At one month after the first session, the patient describes a significant improvement of his quality of life and he decided to stop disulone.
Results: After 3 sessions at one-month interval, we observed a total clearance of the pustules, DLQI was radically increased. Since the first session, alopecia area didn't expand. 3 months later, the patient describes a recurrence of hitching and a few follicular pustules were observed. We performed 3 sessions at 1-month apart using methylaminolevulinate and daylight illumination during 150 minutes (Daylight PDT). Procedure was painless (EVA = 0) and side effects were similar but shorter (24 hours). The same benefits were observed at 1 and 3 months. According this patient, PDT is the only effective treatment.
Conclusion: We reported one case of folliculitis decalvans treated by conventional then daylight PDT with satisfactory results.

TREATMENT OF TRICHOEPITHELIOMAS WITH Er:YAG CUTANEOUS LASER RESURFACING IN A FEMALE WITH BROOKE-SPIEGLER SYNDROME

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Howard University Hospital, Washington, DC; Washington DC VA Medical Center, Washington, DC

Background: Brooke-Spiegler Syndrome is a genodermatosis caused by mutations in the CYLD gene and is characterized by the development of adnexal tumors such as spiradenomas, trichoepitheliomas, and cylindromas. Surgical excision serves as the mainstay treatment of these tumors. However, laser resurfacing technology may provide an effective less invasive treatment modality.
Study Design/Materials and Method: This case study was performed at the Veterans Affairs Medical Center in Washington, DC.
Results: This is a case of a 55-year-old Caucasian female with no remarkable past medical history who presented to dermatology clinic with, golf ball sized, skin-colored subcutaneous nodules on the scalp and numerous asymptomatic, firm, shiny papules on the face. She stated that the lesions began developing in her 30s and were now leading to visual and nasal airway passage obstruction. In the past, she had approximately 20 lesions surgically excised and also attempted a course of topical imiquimod therapy without resolution. Of note, she had a remarkable family history of similar lesions in her mother, maternal grandfather, maternal uncles and aunts, maternal cousins, two brothers, and one sister. The patient was referred to Plastic Surgery for excision of a larger, symptomatic scalp lesions which were consistent with cylindromas. Histopathology of multiple facial lesions was consistent with trichoepithelioma. Genetic testing confirmed CLYD mutation consistent with Brooke-Spiegler Syndrome. We attempted treatment of her refractory facial trichoepitheliomas with a 2940 nm Er:YAG laser, which proved successful.
Conclusion: This case study highlights the efficacy of Er:YAG lasers in the treatment of trichoepitheliomas in a patient with Brooke-Spiegler Syndrome. Ablative laser resurfacing may provide a non-surgical approach compared to conventional excision for the treatment of persistent facial trichoepitheliomas.

USE OF LOW FLUENCE Q-SWITCHED Nd:YAG FOR CLEARANCE OF HYPERPIGMENTATION: SEQUELAE OF SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: Subacute cutaneous lupus erythematosus (SCLE) is an autoimmune condition in which a lymphohistiocytic interface dermatitis occurs, often resulting in pigmentary dropout. Although SCLE is a non-scarring condition, melanin accumulates in the macrophages in the papillary dermis and post-inflammatory hyperpigmentation (PIH) ensues as a common disfiguring hallmark. As topical preparations are ineffective, specific laser-tissue interaction is necessary to disrupt deep pigment and enhance phagocytosis.
Study Design/Materials and Method: A forty-year-old woman (Fitzpatrick II) presented with asymptomatic ill-defined tan patches on her chest, upper extremities, and back. She had been successfully treated for terbinafine-induced SCLE one year earlier with prednisone and then methotrexate. The resultant hyperpigmentation had not responded to azeleic acid or hydroquinone. Multiple laser test sites were performed to ensure safety; lasers tested included pulsed dye laser with compressed lens, intense pulsed light, QS Nd:YAG, and non-ablative thulium laser.

Results: None of the laser tests produced any blistering, textural change, or unintended pigmentary alteration. However, the low fluence QS Nd:YAG parameters (5 mm, 2.25 J/cm^2, 5 Hz) showed significant clinical improvement and was well-tolerated during and post-procedure. Two full treatments of the affected areas were then performed one month apart. Follow-up one year later confirmed persistent clinical improvement and two additional treatments were performed. There were no side effects experienced during the two years of observation.
Conclusion: The 1064 nm wavelength of the QS Nd:YAG enables penetration, while minimally affecting uninvolved melanin at the dermal-epidermal junction. The thermal relaxation time of melanin-containing structures coupled with a nanosecond pulse duration allows photoacoustic fragmentation of melanin-containing particles. This enables phagocytosis of melanin which in turn results in clinical clearance of dark patches. For a clinically-stable patient with PIH from SCLE; low fluence QS Nd:YAG appears to be a safe, comfortable, and efficacious laser treatment with long-lasting results.

USE OF OPTICAL COHERENCE TOMOGRAPHY IN HYBRID LASER RESURFACING

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Cleveland Clinic Florida, Boca Raton, FL; Vanderbilt Volunteer Clinic, Lincoln Memorial University, Harrogate, TN

Background: Optical coherence tomography (OCT) provides real-time *in vivo* imaging of skin structures including blood vessels and capillaries and providing precise measurements of their depth and density. This allows us to treat these blood vessels with parameters tailored to the size and depth of the vessels.
Study Design/Materials and Method: 25 patients being treated with the fractional hybrid laser (Sciton) were scanned with OCT device (Michelson Diagnostics Ltd) prior to treatment. OCT was used to determine the depth and position of blood vessels that were targeted. OCT images were then used intra-operatively to determine optimal settings.
Results: Under OCT guidance the settings used differed from prior settings routinely used and resulted in considerable clearing and improved aesthetic result. OCT immediate and late post scans confirmed vessel destruction.
Conclusion: OCT is a very useful technology to help determine optimal laser settings for vascular treatment with a hybrid fractional laser.

VASCULAR MONITORING OF PROSTATE CANCER TREATMENT

Robert L. Bard
Bard Cancer Center, New York City, NY

Background: Prostate cancer of low grade may be followed clinically but PSA is not accurate in many cases. 3D vessel histogram analysis is available to quantify changes in tumor vessel density non-invasively avoiding biopsies.
Study Design/Materials and Method: From 1990–2010 over 50,000 3D Doppler sonograms were performed on men with low grade prostate cancer. Vessel histogram analysis was performed on a 6 month routine.
Results: Patients with low grade cancer demonstrated no increase in tumor neovascularity in 95% of this study and continued routine follow up. 5% of patients developed higher grade tumors and were biopsied and received definitive therapy.
Conclusion: Non-invasive vascular imaging by 3D Doppler is highly predictive of tumor aggression. This is important since dying cancers can develop cystic internal necrosis that enlarges the lesion simulating tumor progression.

MAGNETIC RESONANCE IMAGING (MRI) STUDY: SIMULTANEOUS FAT AND MUSCLE EFFECT

HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC THERAPY (HIFEM®) EVALUATED BY MAGNETIC RESONANCE IMAGING (MRI): SAFETY AND EFFICACY STUDY OF A DUAL TISSUE EFFECT BASED NON-INVASIVE ABDOMINAL BODY SHAPING.

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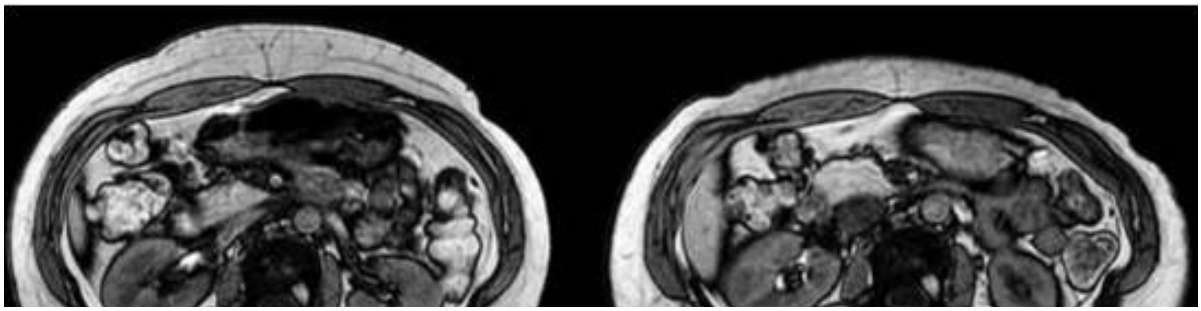
1. Plastic Surgery Excellence, Beverly Hills CA, USA; 2 Paula Fines Center, Sofia BG, Europe

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

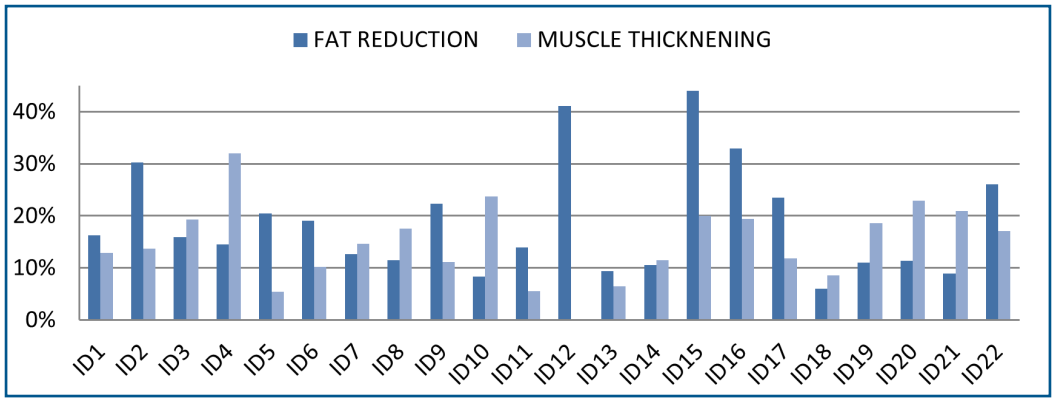
- **22 patients** were evaluated **2 months after four** 30-min **treatments**.
- Abdominal **fat thickness was reduced** on average **by 18.6 %** or 4.3 mm.
- Abdominal **muscle mass increased** on average **by 15.4 %**, coupled with a **10.4 %** average **reduction in diastasis recti**.
- Waist circumference decreased on average by **1.4 inch**.

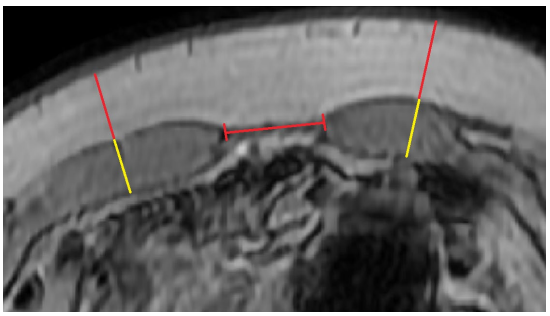


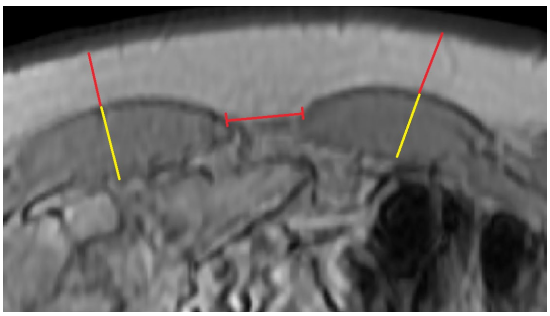
BASELINE 2 MONTH FU

RESULTS

- No adverse event. Several patients reported mild muscle fatigue which resolved within 12-48 hours.
- Simultaneous reduction in subcutaneous fat and strengthening of abdominal muscles in treated patients evaluated by MRI.







BASELINE

2 MONTH FU

Tissue changes 2-months post-treatment (right) versus baseline (left) captured by magnified MRI cuts. The patient showed 30.2% reduction in subcutaneous fat thickness (upper red lines) and 14% thickening of rectus abdominis (yellow lines) compared to baseline. This tissue re-composition was coupled with a 24.9% reduction in the lateral sinister/dexter distance (middle red line segment). Subject ID2, aged 30, weight change -2.2 lbs (-1.2%).

COMPUTED TOMOGRAPHY STUDY: SIMULTANEOUS FAT AND MUSCLE EFFECT

COMPUTED TOMOGRAPHY (CT) BASED EVIDENCE OF SIMULTANEOUS CHANGES IN HUMAN ADIPOSE AND MUSCLE TISSUES FOLLOWING A HIGH INTENSITY FOCUSED ELELCTRO-MAGNETIC FIELD (HIFEM®) APPLICATION: A NEW METHOD FOR NON-INVASIVE BODY SCULPTING.

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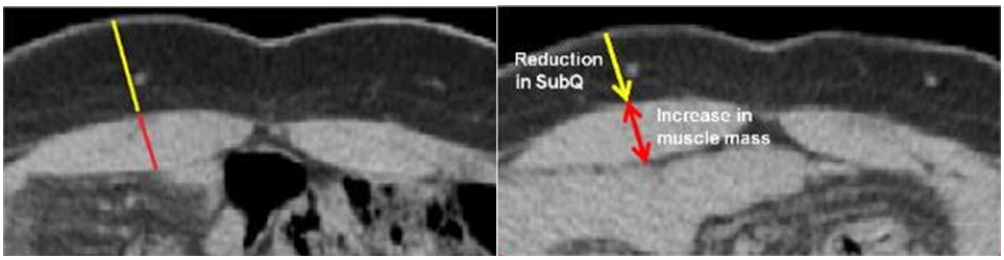
1. Dermatologic Surgery Specialists, Macon GA, USA; 2. Chicago Cosmetic Surgery and Dermatology, Chicago IL, USA

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

- 16 patients received 5-8 treatments to evaluate effects of an extended protocol. Subject were evaluated 1 month post-treatments.
- Abdominal **fat thickness** was **reduced** on average **by 19.2 %** or 3.4 mm.
- Simultaneously a **15.8 % increase in abdominal muscle thickness** was observed, coupled with a 10.8 % reduction in diastatis recti.
- **Waist circumference decreased on average by 1.2 inch** (after 4th Tx) and 1.6 inch (after the last Tx).
- Data suggest **4 treatments as the ideal protocol**.

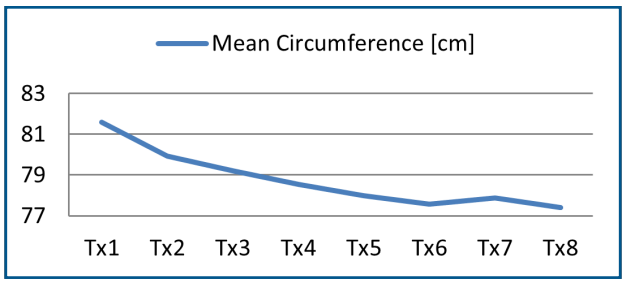


BASELINE 1 MONTH FU

RESULTS

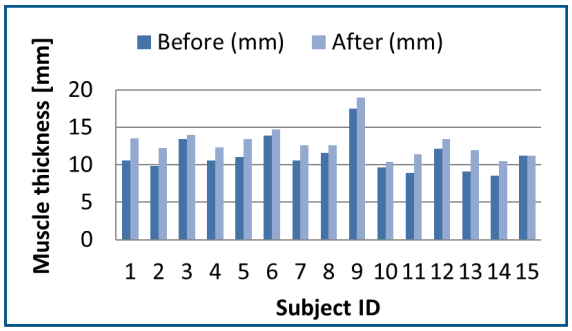
UMBILICAL CIRCUMFERENCE

- The average circumference decreased by 3.04 cm and 4.17 cm after 4th and last (5th to 8th) treatment, respectively ($p<0.003$)

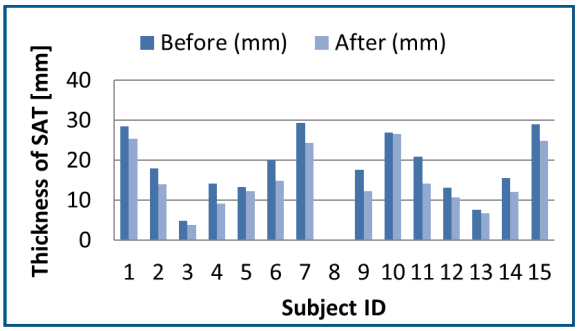


CT MEASUREMENTS

CT calculated thickness of rectus abdominis at baseline and 1 month post treatments.

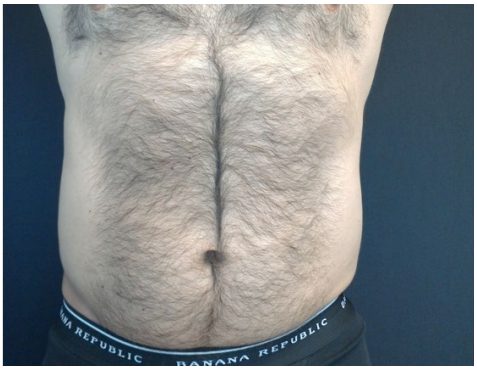


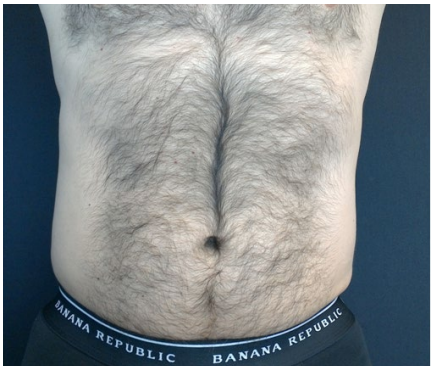
Subcutaneous fat thickness at baseline and 1-month post treatments. Patient ID8 fat measurements could not be objectively made due to close-to-zero baseline fat thickness.



BASELINE

1 MONTH FU





CT scans of patient ID9 at baseline (left) and 1-month post treatments (right). The scan shows reduction of subcutaneous fat (-30.3%) and thickening of rectus abdominis muscle (+8.4%).

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ORIGINAL CONTRIBUTION

WILEY JCD Journal of Cosmetic Dermatology

Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping

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Abstract

Background: Thermal fat reduction technologies are leading the market for nonsurgical abdominal contouring. However, they are ideal principally for patients with fat bulges.

Objectives: Our study investigates the effects of a novel nonthermal technology affecting the abdominal musculature and subcutaneous adipose tissue.

Materials and Methods: A total of 22 patients (avg. BMI 23.8 kg m^{-2}) underwent 4 treatments on abdomen with high-intensity focused electromagnetic (HIFEM) field device. Treatments took 30 minutes and were spaced apart by 2-3 days. Photographs, weight, and waist measurements were taken at the baseline, after the last treatment, and at month 3 follow-up. Patient satisfaction was noted. Photographs were evaluated by blinded evaluators.

Results: The study protocol was completed by 19 patients. At month 3, the average waist size reduction was 4.37 ± 2.63 cm ($P < 0.01$). The evaluators identified the before image from the 3-month image 89.47% of the time. About 91% of patients reported their abdominal appearance improved, and 92% stated they are satisfied with treatment results at month 3. No adverse events occurred.

Conclusion: Observed waist size reduction and aesthetic improvement appear to be a combination of fat reduction and increased muscle definition of abdominal wall. In lower BMI patients, the increased abdominal muscle definition was largely responsible for the improvement. This novel energy device provides an additional tool for body contouring with primary application for lower and medium BMI patients.

KEYWORDS
body, contouring, electromagnetic, HIFEM, muscle, toning

1 | INTRODUCTION

The media-driven images of thin and muscular bodies lead to a high dissatisfaction rate of nonideal body type patients which may result in chronic depression.[1] Currently, up to 60.7% of men and 71.6% of women in US population are dissatisfied with their body size.[2] The desire for an easy solution to reduce fat and to improve the appearance of the abdomen is driving the market for body shaping procedures.

In 2017, liposuction was the most common surgical cosmetic procedure, after breast augmentation, with over 300 000 conducted procedures that year.[3] Due to the risk of complications (eg, infection, scarring or hematoma[4]), related downtime and substantial financial

cost associated with surgical procedures, there has been a rapid increase in the demand for noninvasive solutions. Since 2012, noninvasive procedures have grown by 217.3%.[3] The leading technologies in the noninvasive body shaping are low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF), and high-intensity focused ultrasound (HIFU).[5]

Surgical as well as noninvasive body shaping procedures are effective for fat disruption but require patients with well-defined bulges for successful and safe treatment. Many patients, especially those with lower BMI, who desire body shaping procedure, are not suitable candidates. Furthermore, none of the procedures focus on the underlying musculature, which is highly responsible for toned and aesthetically pleasing abdominal appearance.

Besides physical exercise, electric and electromagnetic stimulation has been used for muscle training.[6–8] Electromagnetic stimulation appears to dominate over the electrical stimulation as it induces double the peak torque,[9] penetrates deeper into the tissue[10] and is not associated with any pain[9] or risks of burns.[11,12] As electromagnetic stimulation has been shown to strengthen the muscles,[9,13,14] and an intensive muscle training was shown to induce lipolysis,[15,16] we hypothesize that the concept of electromagnetic stimulation can be applied for body shaping. Utilization of this technology would open possibilities for the patients not suitable for other procedures since the penetration of the magnetic field is not restricted by fat deposits.

Recently, there has been an introduction of a novel device (EMSCULPT, BTL Industries, Boston, MA) utilizing a high-intensity focused electromagnetic (HIFEM) field with frequencies inducing tonic muscle contractions. The study aims to examine the effect of the HIFEM technology on patients' waist circumference, the effect on abdominal appearance, the treatment satisfaction, and the safety of the procedure and to investigate the suitability of the treatment for lower BMI patients.

2 | MATERIALS AND METHODS

A total of 22 patients (avg. BMI 23.8 ± 3.3 kg m^{-2}) desiring aesthetic improvement of the abdomen voluntarily participated in this study. The patients' age ranged from 20 to 47 years with an average of 32 ± 7.1 years. Exclusion criteria included pregnancy, cardiac pacemakers, implanted electronic devices, metal implants, heart disorders, and any medical conditions contraindicating the use of the electromagnetic field. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Boards (IRB).

The patients underwent treatment of the abdomen by a device utilizing high-intensity focused electromagnetic field (EMSCULPT, BTL Industries, Boston, MA). The entire procedure consisted of 4 sessions distributed across two weeks (twice weekly, separated by 2-3 days). Each session lasted for 30 minutes during which the operator monitored the patients. Prior to treatment, informed consent was obtained from each patient.

The treatment was applied in a supine position with the device applicator positioned over the umbilicus. The targeted muscles were the rectus abdominis, external and internal obliques. The applicator position was being adjusted at the beginning of the treatment to ensure homogenously distributed contractions. The applicator was secured by a fixation belt to avoid any movement of the applicator during the treatment. The initial stimulation intensity was set according to patients' tolerance threshold and was further increased during the treatment once the patients got used to the muscle contractions. Over the course of a single session, most patients were able to reach an intensity of 90%-100%. No anesthesia was required.

To evaluate the treatment, weight, and waist circumference measurements, as well as frontal and lateral digital photographs, were taken before treatment, after the last treatment, and during a 3-month follow-up. Randomized digital photographs taken at baseline and during 3-month follow-up were given to three blinded evaluators for recognition. Furthermore, patient satisfaction with the treatment results was assessed using a 5-Likert scale questionnaire after the last treatment and during a 3-month follow-up. All data were tested by *t* test.

3 | RESULTS

The full study protocol was completed by 19 subjects (3 men, 16 women); 3 subjects opted out for reasons unrelated to the study. The results presented herein therefore comprise data from 19 patients.

Immediately after the last treatment, the waist circumference was significantly ($P < 0.01$) reduced on average by 3.29 ± 1.9 cm. This further improved three months after the last treatment, with the average reduction reaching 4.37 ± 2.63 cm compared to baseline. The total average circumference can be seen in Figure 1.

Circumferential reduction in 16 out of 19 subjects (84%) exceeded 2.5 cm at month 3 post-treatment. These results were independent of weight changes ($P > 0.05$). A significant portion of the reduction (75%) was measured after the last treatment, further improving at month 3. The waist circumference of 1 patient increased immediately post-treatment number 4, and 2 patients (10.5%) did not have any waist size change at the follow-up. The waist reduction was found to be independent of the baseline BMI ($P < 0.05$). The individual results can be seen in Figure 2. Patients' weight did not change significantly ($P > 0.05$) throughout the measurements.

On average, the evaluators successfully recognized the before images from the 3-month images in 89.47% of cases. In 15 patients (79%), the images were uniformly recognized by all 3 evaluators. The successful recognition rate was positively correlated with the amount of circumference reduction ($P < 0.01$). Example of patient photographs can be seen in Figures 3 and 4.

Analysis of the patient questionnaire revealed that 89% of patients were satisfied with the treatment results immediately after the last treatment. During the 3-month follow-up visit, the satisfaction increased as all patients reported a certain degree of satisfaction. The patient satisfaction was independent of the amount of waist size reduction. After the last treatment, 95% of the patients

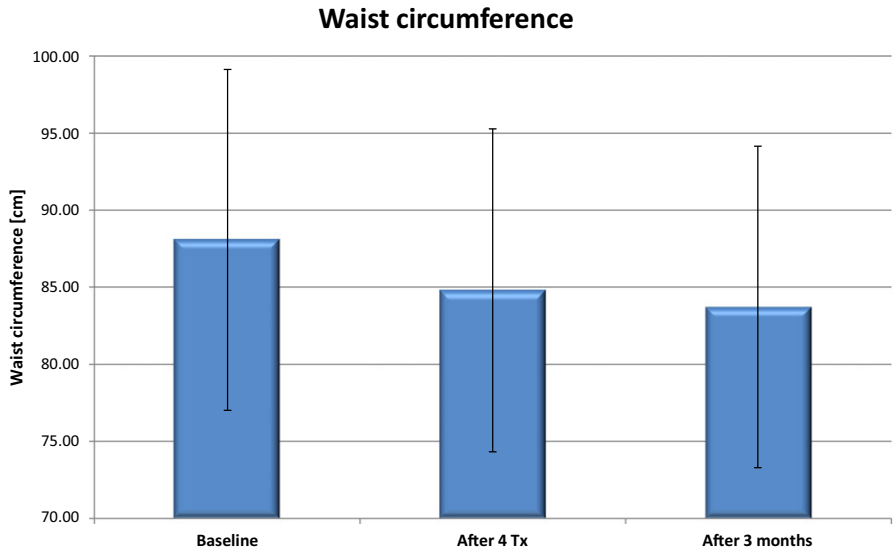

FIGURE 1 Average waist circumference at baseline, after fourth treatment and 3 months after last treatment

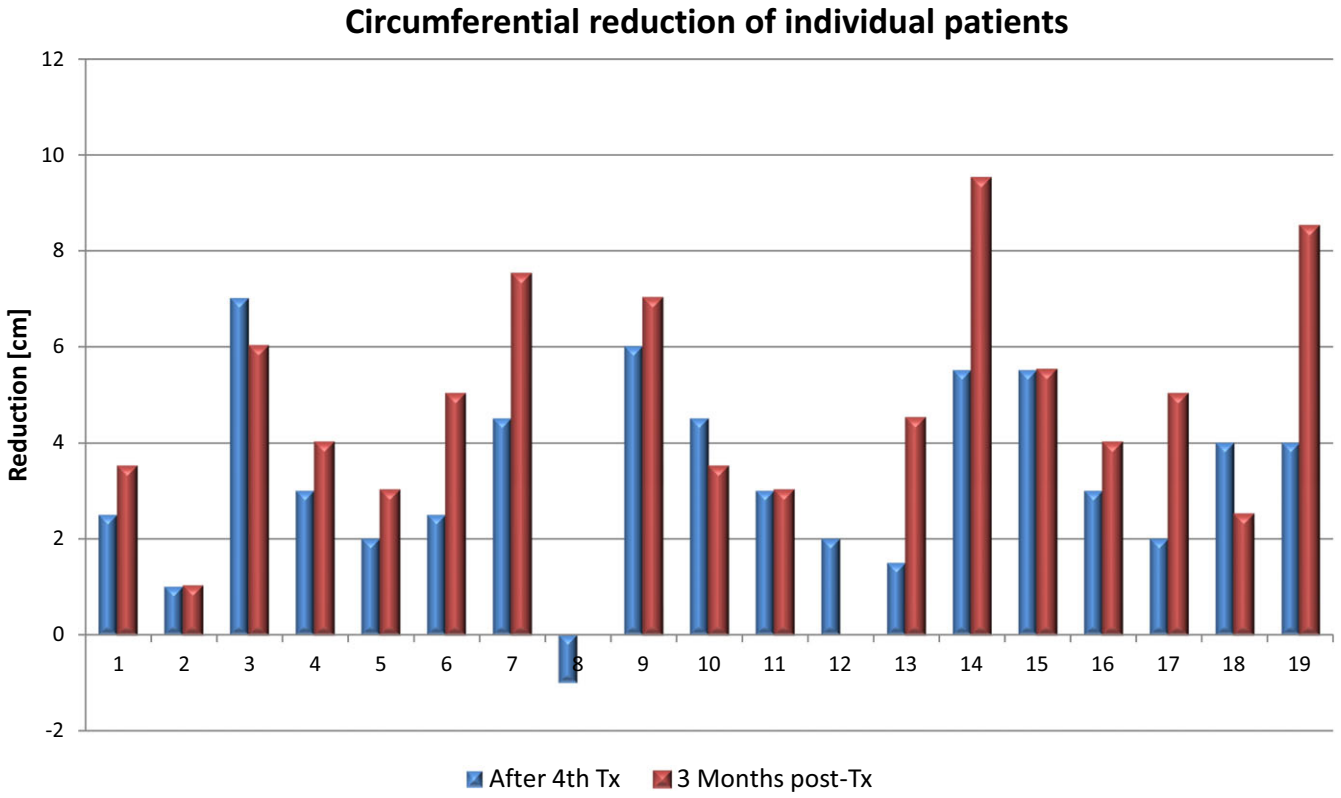

FIGURE 2 The individual waist circumference reduction measured immediately after the last treatment and during the 3-month follow-up

reported that they would recommend the treatment to a friend, while this decreased to 90% during the 3-month follow-up. Also, 89% of patients reported that their abdominal appearance improved immediately after the last treatment and this self-report further increased to 95% at month 3 follow-up. In general, the patient satisfaction improved at month 3 compared to evaluation after their last treatment, showing a similar trend as the measured waist reduction.

Muscle fatigue was a relatively frequent side effect that resolved within 12-48 hours. No adverse events were observed.

4 | DISCUSSION

Fifteen out of the 19 subjects had a BMI lower than 25, and the total average BMI was 23.8 ± 3.3 kg m^{-2}. Many of the subjects

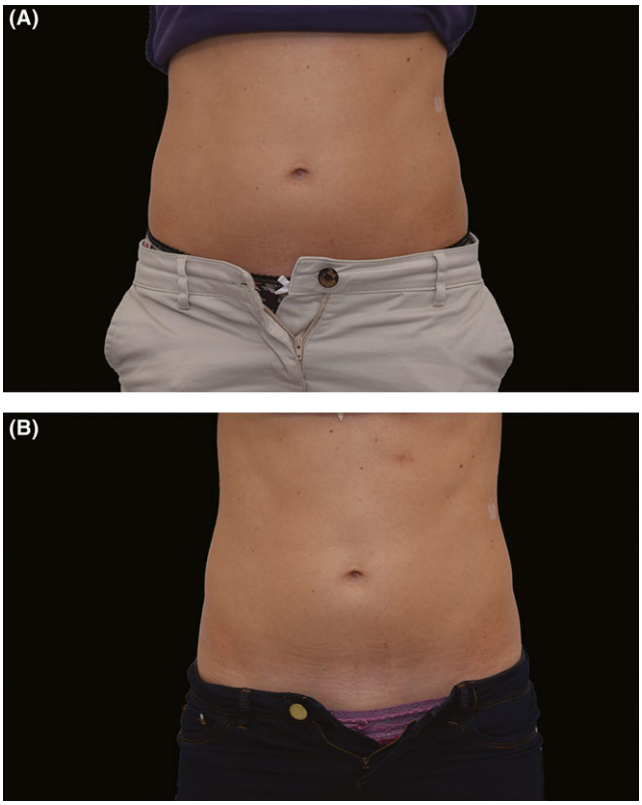

FIGURE 3 Digital images before (A) and 3 months after last procedure (B). Subject 13, age 30, BMI 18.9, waist circumference −3 cm (−4.0%), weight unchanged

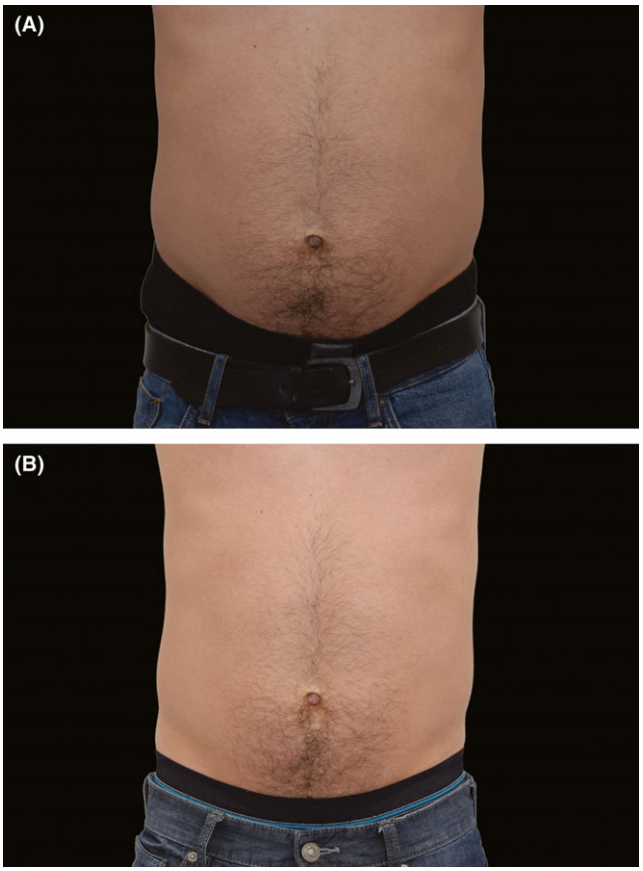

FIGURE 4 Digital images before (A) and 3 months after last procedure (B). Subject 11, age 33, BMI 25.2, waist circumference −7 cm (−7.7%), weight change −1.8 kg (−2.2%)

would not be suitable candidates for fat debulking treatments, such as suction based or stamping fat reduction devices. The primary goal was to understand if HIFEM can be used for lower BMI patients who are not ideal candidates for other available technologies.

The presented results showed that the treatment of the abdomen utilizing the HIFEM technology was effective in reducing the patients' waist circumference and in improving the aesthetic appearance of the abdomen. This was accompanied with high patient satisfaction. The waist size reduction was present already after the fourth treatment and continued to further reduce over the course of 3 months in most patients. The fact that the amount of waist size reduction was not correlated with the baseline BMI, suggests that the treatment was effective at the same level for the study patients' BMI range (18.8-33.3). The patients were satisfied with the results, and the treatment was generally perceived as comfortable.

The visual aesthetic improvement was confirmed by a high rate of successful photograph recognition done by blinded independent evaluators. The rate of successful recognition was correlated with the amount of waist size reduction, indicating that the higher the waist size reduction, the more the aesthetic improvement of the subject.

The study found that a significant weight loss did not accompany the waist size reduction. The device delivers pulses in a frequency that produces supramaximal contractions not achievable voluntarily. The muscle does not have time to relax between the 2 consecutive stimuli and is exposed to the extreme condition, which triggers a stress response in the tissue. Energy for supplying the contractions is taken from the fat cells presumably through lipolysis. The same effect, when muscles begin to use lipolysis as an energy supply, has already been seen during intense acute resistance exercise.[15,16] Further, when regularly exposed to these conditions, the muscle needs to adapt to them, which leads to a volumetric growth of muscle (hypertrophy)[17,18] and possibly hyperplasia.[19] The waist circumference reduction can therefore result from both fat reduction and strengthening and tightening of the abdominal wall. The lack of weight loss after the treatment thus appears to be logical effect since the weight of lost fat tissue is compensated by the weight of gained muscle volume.

In comparison to other technologies for noninvasive body shaping, the HIFEM showed competitive results regarding the waist circumference reduction. A study by Ferraro et al[20] on cryolipolysis reported circumference reduction of 6.86 cm, an LLLT study by Savoia et al[21] reported waist reduction as much as 6.83 cm, and RF study by Fajkosova et al[22] showed 4.93 cm. Studies on HIFU[23–25] showed a reduction of 4.1-4.7 cm. Looking at these results, the average waist reduction of 4.37 cm observed in the present study is highly competitive. However, the reduction presented in the mentioned studies is attributed to the fat loss, while the reduction in the present study appears to be a combined effect of a fat loss and strengthening of the abdominal wall muscles.

5 | CONCLUSION

The overall results are competitive in the noninvasive field of abdominal aesthetic improvement. The waist size reduction and improvement seen in photographs were driven by a combination of reduced fat and strengthened abdominal muscles. HIFEM treatments are effective for body shaping in both lower and medium BMI patients due to its effect on 2 tissues, showing high levels of patient satisfaction coupled with visible aesthetic improvement. We conclude the technology is ideal for treating patients who might not be candidates for other exiting technologies or whose problem is driven by a combination of fat deposits and underlying muscle laxity.

DISCLOSURE

Carolyn I. Jacob MD is medical advisor for BTL. Katya Paskova MD has no financial interest to declare in relation to any of the products or device mentioned in this article.

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WAIST CIRCUMFERENCE **REDUCTION** TESTED IN A MULTICENTRIC STUDY

A NOVEL NON-INVASIVE TECHNOLOGY BASED ON SIMULTANEOUS INDUCTION OF CHANGES IN ADIPOSE AND MUSCLE TISSUES: SAFETY AND EFFICACY OF A HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC FIELD DEVICE USED FOR ABDOMINAL BODY SHAPING

Carolyn I. Jacob M.D.[1], Katya Paskova M.D.[2]

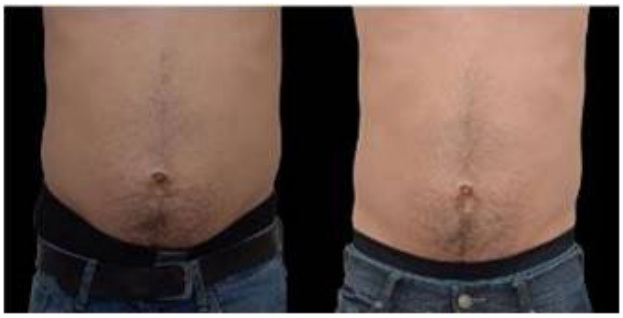
1. Chicago Cosmetic Surgery and Dermatology, Chicago IL; 2. Derma Vita Clinic, Sofia, BG.

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

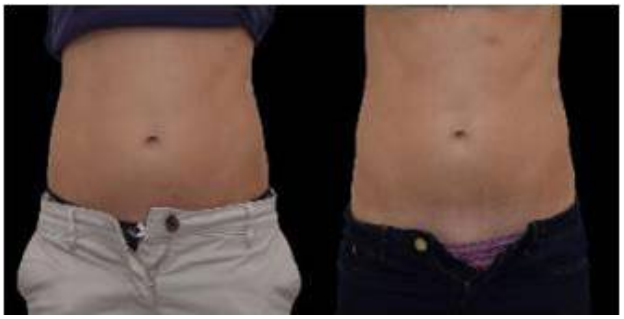
- **22 patients** (lower BMI profile - average 23.8kg/m2) were treated in 4 sessions within 2 weeks.
- Patient **waist** size **was reduced** on average **by 4.37 cm** at **3 month post-treatments**.
- Patient photography captured a combination of **muscle toning and fat reduction.**
- **96 % patients** were **satisfied with** treatment **results**.

Higher-BMI patient



BASELINE 1 MONTH FU

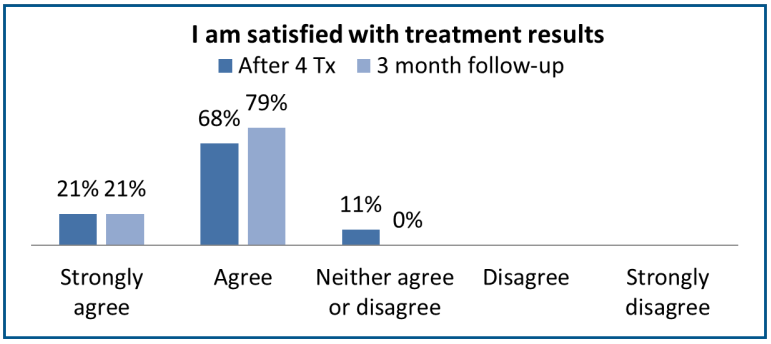
Lower-BMI patient



BASELINE 1 MONTH FU

DETAILED RESULTS

- 19 patients completed the study; no adverse events.
- **16 out of 19 subjects** (84%) showed >**2.5 cm circumferential reduction** 3-months post-treatment (independent of weight changes).
- A significant portion of the **reduction** (75%) was measured **already after the last treatment**, further improving at 3-months.
- Two patients (11%) didn't have any waist size change, but their aesthetic appearance improved in digital photographs.
- The **overall recognition** rate of digital photographs (before and 3-months post) averaged **89.47%**. Images of 15 subjects were uniformly recognized by all 3 reviewers.
- At 3-months all patients expressed some level of satisfaction with treatment results, there were **no dissatisfied patients**.



BASELINE 1 MONTH FU

Digital images before (left) and 3-months after last procedure (right). Subject 04, age 36, BMI 20.4, waist circumference -4 cm (-5.3%), weight change +1.1 lbs (+0.7%).

AN INITIAL STUDY INVESTIGATED THE **EFFECTS ON BUTTOCKS**

EFFICACY OF HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC FIELD THERAPY WHEN USED FOR NON-INVASIVE BUTTOCKS AUGMENTATION AND LIFTING: A CLINICAL STUDY.

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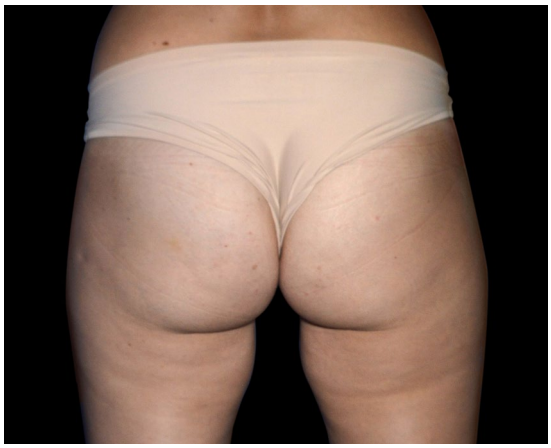
1. Aesthetic Dermatology, Coconut Grove FL, USA; 2. Aesthe Clinic Beauty, Sofia, BG

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX.

HIGHLIGHTS

- **22 women** received **4 bilateral treatments on** their **buttocks**.
- The treatments caused **significant changes** to gluteus muscles which translated into **overall aesthetic improvement**.
- Digital photographs showed **overall buttock lifting** and **reduction in muscle laxity**.
- **High levels of satisfaction** with treatment results **(7.3/10)**.
- The **results triggered a** following **large-scale multicentric study** to bring further evidence.



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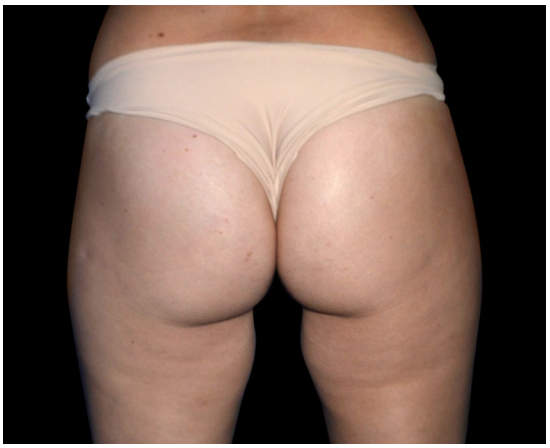


AFTER

DESIGN AND METHODOLOGY

- Evaluation at baseline, after last treatment, 1-month post, and 3-month post:
  - Weight measurement, standardized digital photography.
  - Patient comfort and satisfaction with results.

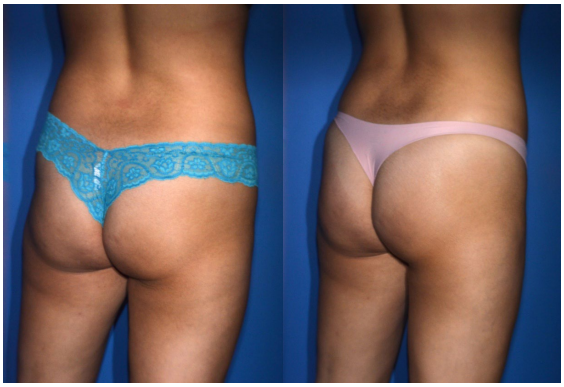
RESULTS

Satisfaction with results (0-10)	After treatment	1 month follow-up	3 month follow-up
Average (n=22)	7.2±1.8	7.4±1.8	7.8±2.0

Chronologic evaluation of patient satisfaction with the treatment results using a VAS scale (10 = Complete satisfaction, 0 = Complete dissatisfaction). Average satisfaction was high and increased over time.

Treatment comfort (0-10)	1st session	4th session
Average (n=22)	7.0±2.3	8.3±1.9

VAS scale patient comfort during the treatment (10 = Complete comfort, 0 = complete discomfort).



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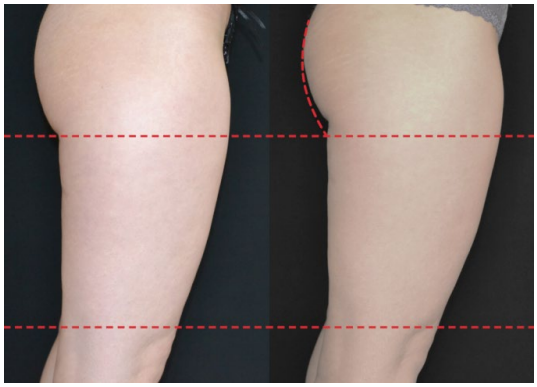


BEFORE AFTER

Digital images of two patients showing overall lifting of their buttock coupled with elevation of the gluteal fold and a tighter and more sporty look after HIFEM® treatment (4x30min).

A LARGE-SCALE MULTICENTRIC STUDY: NON-INVASIVE **BUTT LIFTING EFFECTS**

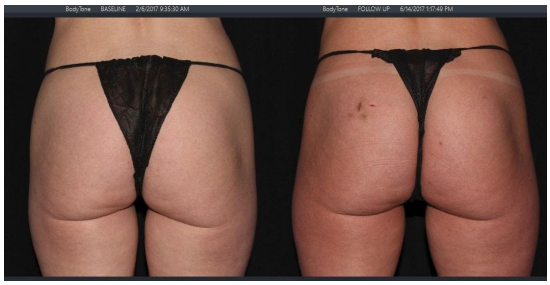
HIGH INTENSITY FOCUSED ELECTRO-MAGNETIC TECHNOLOGY (HIFEM) FOR NON-INVASIVE BUTTOCKS LIFTING AND TONING OF GLUTEAL MUSCLES: A MULTI-CENTER EFFICACY AND SAFETY STUDY.

C. Jacob M.D.[1], B. Kinney M.D.[2], M. Busso M.D.[3], S. Chilukuri M.D.[4], JD McCoy N M.D.[5], C. Bailey[6], R. Denkova M.D.[7]

1. Chicago Cosmetic Surgery and Dermatology, Chicago IL; 2. Plastic Surgery Excellence, Beverly Hills CA; 3. Aesthetic Dermatology, Coconut Grove FL; 4. Refresh Dermatology, Huston TX; 5. Contour Medical, Gilbert AZ; 6. Ovation Med Spa, Houston TX; 7. Aesthe Clinic Beauty, Sofia BG.

HIGHLIGHTS

- A total of **75 patients** received **4 bilateral treatments on** their **buttocks**, and were evaluated 1 month post-treatments.
- **85 %** of patients reported **significant improvement in appearance of their buttocks. 79 %** of patients reported improvement in their confidence.
- **80 %** of patients felt their buttock was **more lifted and toned** right after their last treatment. Patients reported improvement in **buttock laxity** and **tightness** post-treatment.
- Patient photography revealed **improvement in shape, tone** and **fullness of buttocks**.



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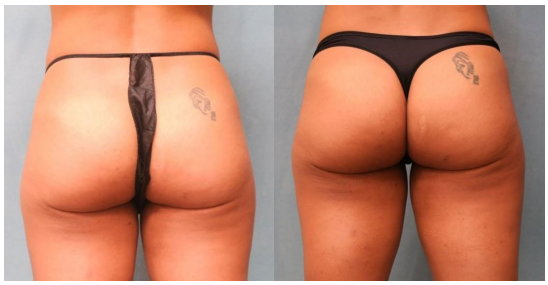

BEFORE AFTER

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MRI AND CT EVALUATION STUDY: 1-YEAR FOLLOW-UP

LONG-TERM FOLLOW-UP ON PATIENTS WITH HIFEM-INDUCED ABDOMINAL TISSUE CHANGES: MRI AND CT ASSISTED QUANTIFICATION OF MUSCLE GROWTH AND FAT REDUCTION.

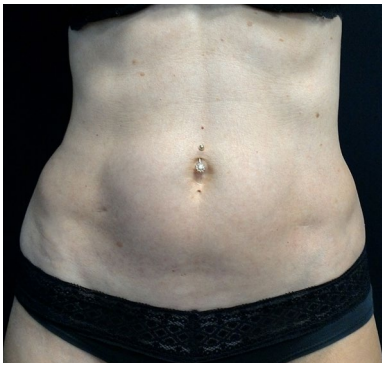
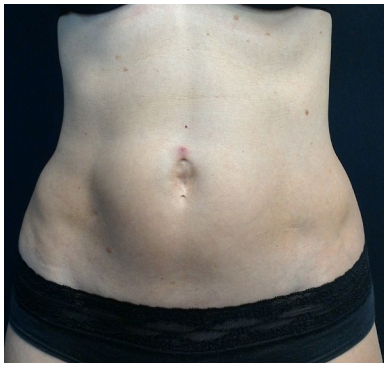
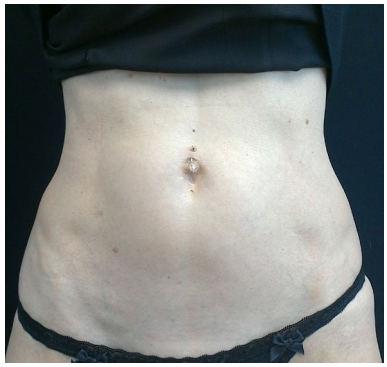
Brian Kinney M.D.[1], David E Kent M.D.[2]

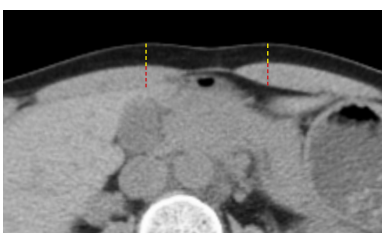
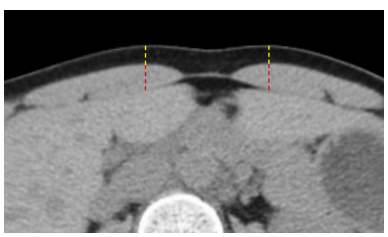
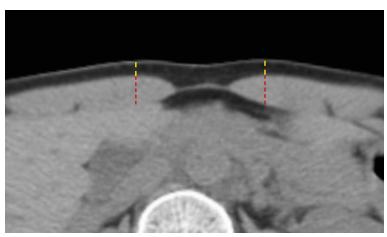
1. Clinical Associate Professor of Plastic Surgery, USC School of Medicine, Beverly Hills CA, USA
2. Skin Care Physicians of Georgia, Macon GA, USA

HIGHLIGHTS

- **21 subjects** were recalled **1 year** after **4-8 abdominal treatments** for long-term evaluation.
- The patients showed an **average fat reduction** of **14.63%** 1 year post-treatment.
- In comparison to baseline, the muscle thickness was **increased** by **19.05%**, and abdominal separation was **reduced** by **10.46%** 1 year post-treatment.
- Treatment results were **preserved on average 1 year** after the last session.

BASELINE | 6-WEEK FU | 1-YEAR FU

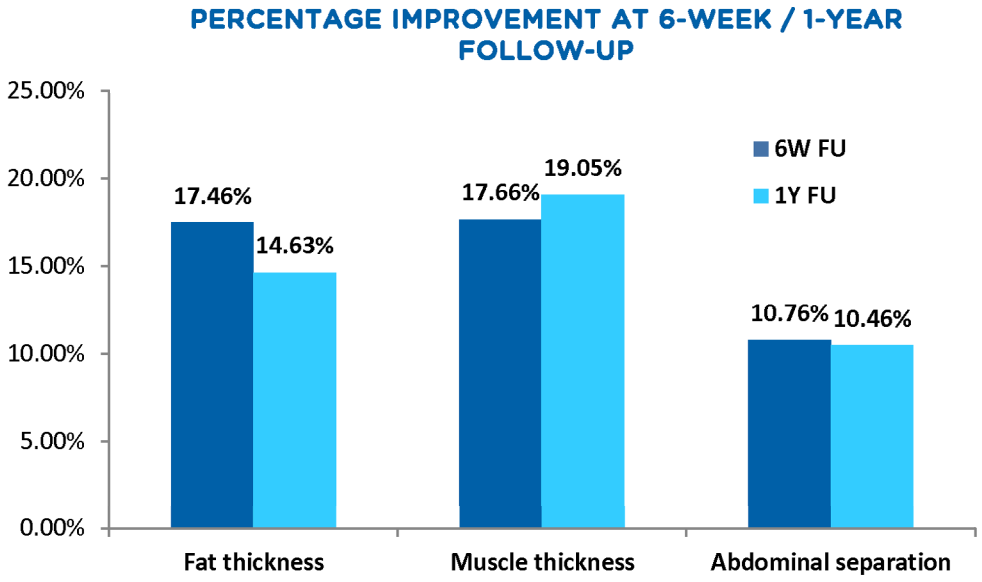




DESIGN AND METHODOLOGY

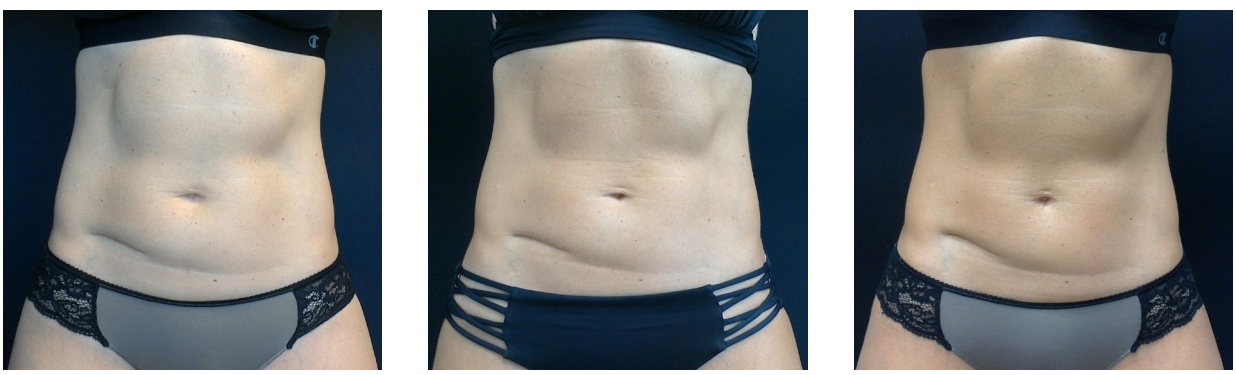
- The initial **evaluation** was performed at the **baseline** and **6-week** follow-up.
- The average time of the follow-up visit was **333±88.5** days after the last treatment.
- No additional treatments were delivered.

RESULTS

- **HIFEM** is effective for inducing long-lasting changes.
- **Results** were **independent** of the number of treatments and the time of the follow-up.
- **No adverse events** were observed during the 1-year follow-up.



BASELINE | 6-WEEK FU | 1-YEAR FU



Digital images of patient ID14 at the baseline (left), after 6 weeks (in the middle) and 1 year (right) after the last treatment. The fat reduction measured at 6 weeks was preserved during 1Y FU.

LITERATURE REVIEW: HIFEM® AND THERMAL PROCEDURES

THERMAL VS. NON-THERMAL TECHNOLOGIES IN NON-INVASIVE BODY CONTOURING.

Dr. Rita Rakus MBBS FBCAM[1]

1. Dr. Rita Rakus Clinic, London, UK

Presented at the World Congress of the International Master Course on Aging Science, 2019 Paris, FR

HIGHLIGHTS

- Results based on **42** identified studies using quantitative evaluation of outcomes.
- **HIFEM** is the **most effective** technology for **reduction in waist circumference.**
- **HIFEM** technology combines **fat reduction (18.6%)** and **muscle thickening (15.4%)**.
- **Thermal technologies show risks** of AE due to tissue hyper/hypothermia such as erythema, swelling, pain, burns, numbness, bruising, etc. **No adverse events** related to the **HIFEM** treatments were **reported**.

RESULTS

MODALITY	FAT THICKNESS	MUSCLE THICKNESS	WAIST CIRCUMFERENCE
LLT	0.0%	0.0%	-3.03 cm
HIFU	0.0%	0.0%	-2.76 cm
RF	-29.0%	0.0%	-3.44 cm
CRYOLIPOLYSIS	-21.2%	0.0%	-3.88 cm
HIFEM	-18.6%	+15.4%	-4.09 cm

Efficiency comparison of different body contouring methods.

MECHANISM OF ACTION: EFFECT OF HIFEM® ON FAT

BIOCHEMICAL PERSPECTIVE OF FAT PHYSIOLOGY AFTER APPLICATION OF HIFEM FIELD TECHNOLOGY: ADDITIONAL INVESTIGATION OF FAT DISRUPTION EFFECTS IN A PORCINE STUDY.

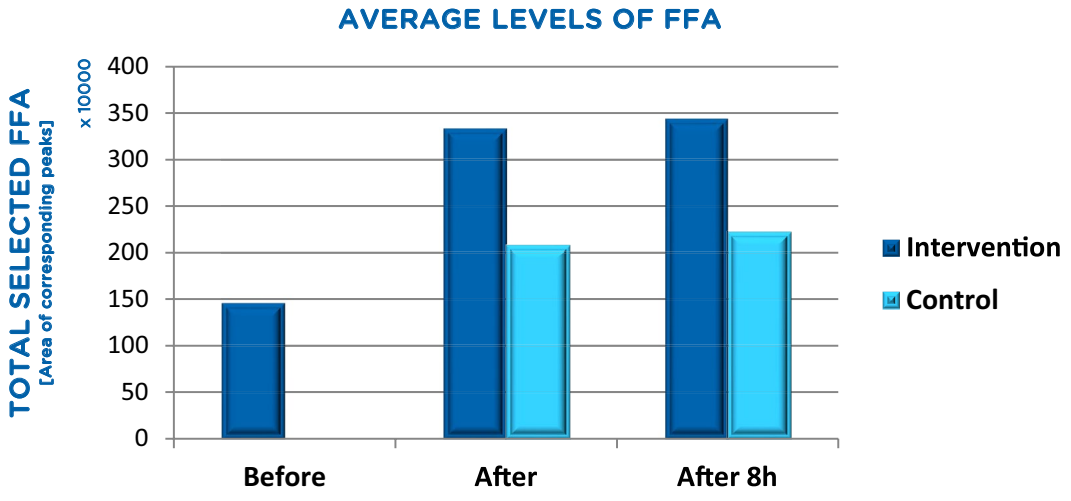
Yael Halaas M.D.[1], MVDr. Jan Bernardy[2]

1. Facial Plastic and Reconstructive Surgery, New York NY, USA
2. University of Life Sciences - Department of Veterinary Sciences, Prague, CZ

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2019 Denver, CO

HIGHLIGHTS

- **The levels of FFA** (free fatty acids) in the treated area **increased by 127.1%** immediately post-treatment and **by 134.1%** 8h post-treatment. High levels of FFA indicate **strong metabolic response** in the fat tissue.
- The levels of four out of five analyzed DNA **pro-apoptotic markers increased significantly** after application, providing evidence of **enhanced apoptosis in the subcutaneous adipose tissue**.
- The average fat **pH decreased from 7.30±0.12 to 6.60±0.07** immediately post-treatment and to **7.19±0.12** 8h post-treatment.

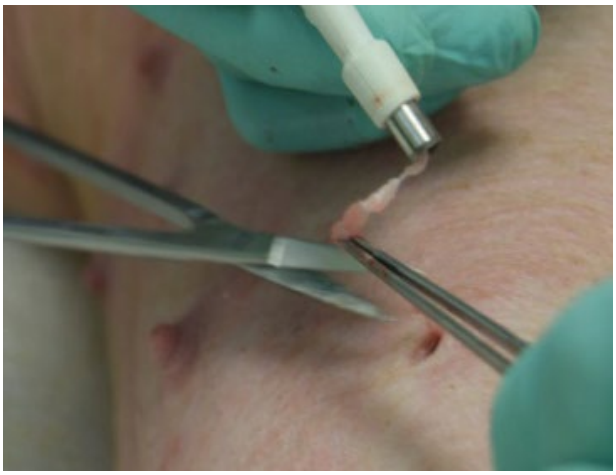


Metabolic reaction leading to the breakdown of fat into FFA and glycerol was superior in the treated area, where it could possibly lead to saturation and initiation of apoptosis.

STUDY DESIGN

- The aim was to investigate the mechanism of apoptosis induced through saturation of FFA in the fat cells.
- Two Large White pigs received a **single 30-minute** long treatment of thigh.
- **Punch biopsies** were collected **before, immediately after and 8 hours after treatment**. Control samples were obtained from the abdomen at the baseline and 8 hours post-treatment.

Measurements of pH were performed immediately after the punch biopsy directly in the fat tissue.



Collection of control punch biopsies of the fat tissue from the abdomen. The bioptate was pulled out by tweezers.

CONCLUSIONS

- **Levels of pro-apoptotic markers** in histological samples were **increased post-treatment**, indicating enhanced **apoptosis** in the tissue.
- **FFA concentrations increased and pH decreased significantly post-treatment**, suggesting that HIFEM induces a strong metabolic response in the fat tissue which leads to **the breakdown of fat**. High levels of FFA may saturate the fat cell and trigger fat cell apoptosis.
- Results of this study **correlate with previous research** reporting elevated apoptotic levels post HIFEM treatments as well as with fat reduction observed in human studies.
- **The results support the proposed MOA** stating that HIFEM contractions evoke a strong metabolic reaction and trigger cascade effect leading to FFA saturation, the stress of endoplasmic reticulum and fat cell apoptosis.

IN VIVO MUSCLE HISTOLOGY STUDY

NON-INVASIVE INDUCTION OF MUSCLE FIBER HYPERTROPHY AND HYPERPLASIA: EFFECTS OF HIGH-INTENSITY FOCUSED ELECTROMAGNETIC (HIFEM) FIELD EVALUATED IN AN IN-VIVO PORCINE MODEL.

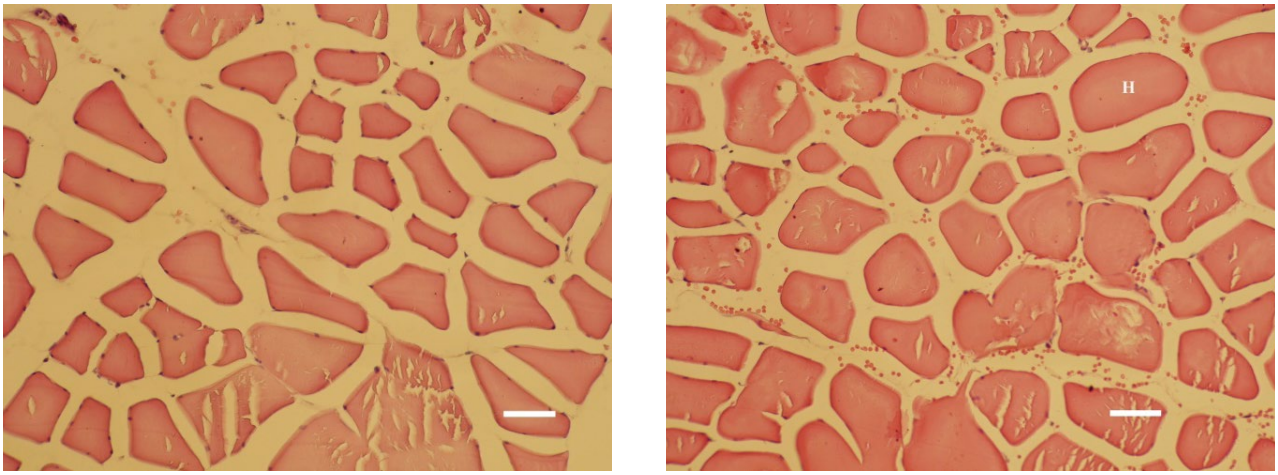
Diane I. Duncan M.D.[1], Prof. Dr. Ivan Dinev[2]

1. Plastic Surgery Associates, Fort Collins CO, USA
2. General and Clinical Pathology, Faculty of Veterinary Medicine, Trakia University, Stara Zagora, Bulgaria

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2018 Dallas, TX

HIGHLIGHTS

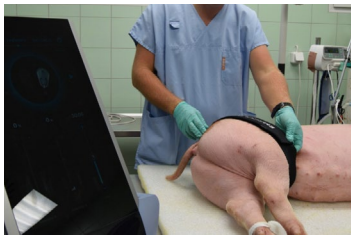
- In treated animals, the **muscle mass** in examined slices increased by 23.44% (18934.0±5089.5 µm2) on average.
- The average **area per single muscle fiber** increased by **16.4%** (469.48 ±371.95 µm).
- The average **number of muscle fibers** increased by 7%, and although not statistically significant, it **indicates** muscle fiber **hyperplasia**.
- Control animal did not show any significant changes in any of the measured parameters.



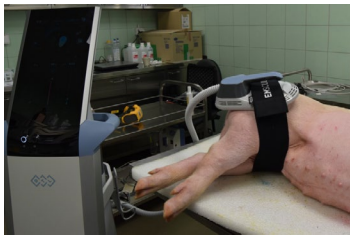
Histological evaluation showed strong muscle fiber hypertrophy and indicated fiber hyperplasia.

STUDY DESIGN

- **Three Yorkshire pigs** received **four 30-minute long treatments**. Fourth pig served as a control.

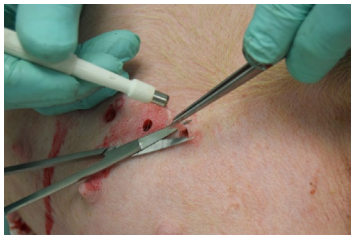


Animal care complied with the convention for the protection of vertebrate animals used for experimental and other scientific purposes.



The thigh was treated for 30 minutes using the HIFEM applicator secured by a fixation belt.

- Biopsy specimens of muscle tissue were taken **before the treatments** and during **2-week follow-up**. Collected tissue slices were evaluated for any structural changes by a certified histopathologist.

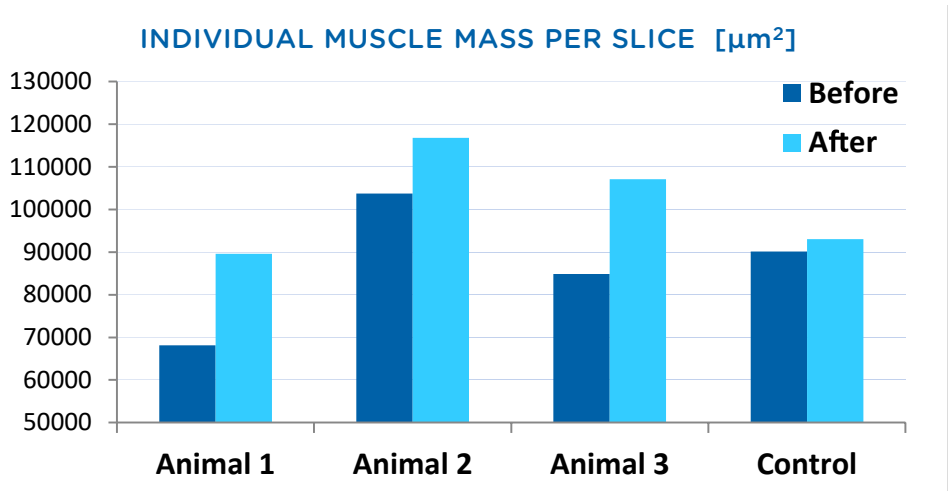


Punch biopsies of the muscle tissue were taken from the treated area and pulled out using tweezers.

The samples were fixed in 10% neutral buffered formalin and colored using hematoxylin. The samples were sliced and microscopically evaluated.

RESULTS

- The results confirmed **muscle hypertrophy** on the histological level, which correlates with previous CT and MRI studies.



The individual average muscle mass in a single slice for each animal.

QUANTIFICATION OF HIFEM® EFFECTS ON BUTTOCKS

MRI EVALUATION OF CHANGES IN GLUTEAL MUSCLES FOLLOWING TREATMENTS WITH THE HIGH-INTENSITY FOCUSED ELECTROMAGNETIC (HIFEM) TECHNOLOGY.

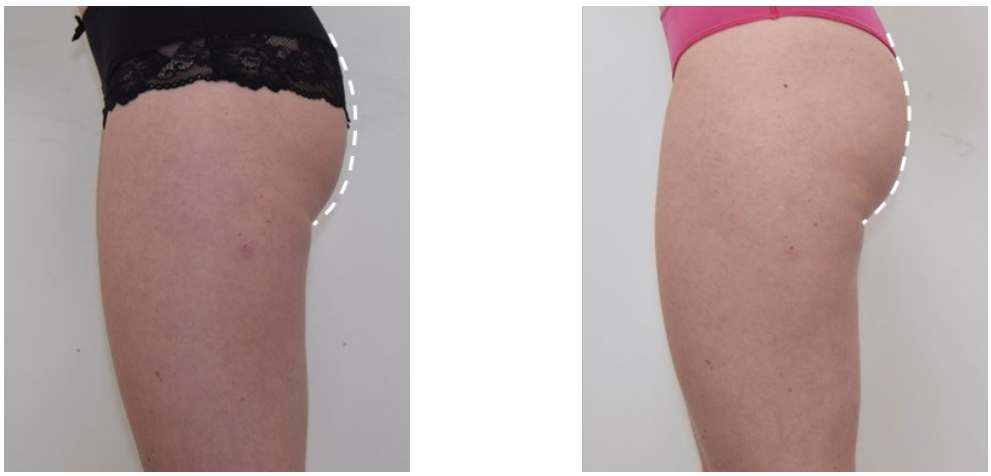
Melanie Palm M.D.[1], Paula Lozanova M.D.[2]

1. Art of Skin MD, Solana Beach CA, USA 2. Paula Fines Center, Sofia, Bulgaria

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2019 Denver, CO

HIGHLIGHTS

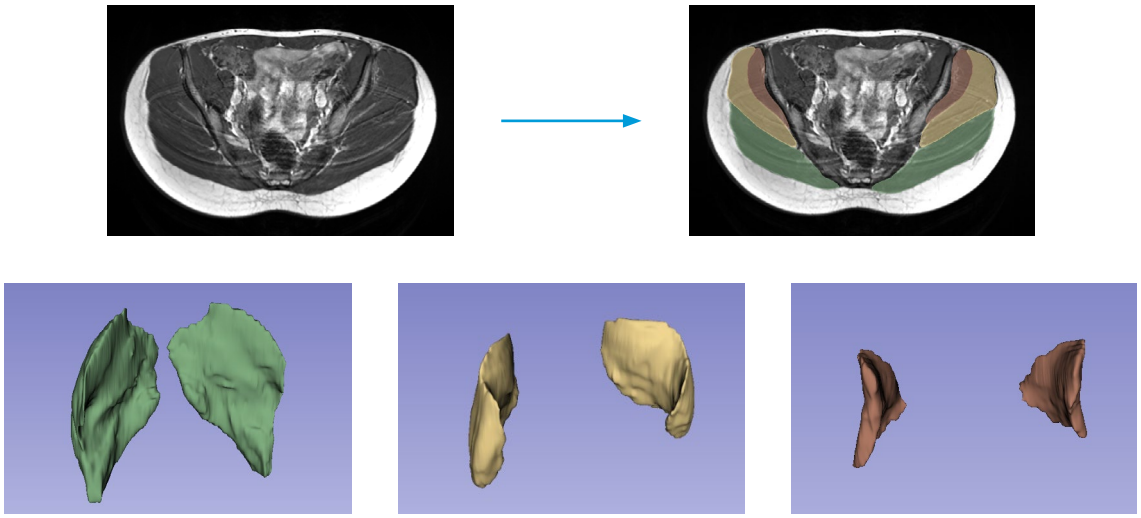
- Patient group of **25 subjects** who received four **30-minute HIFEM treatments** underwent MRI screening at the baseline and 1-month follow-up.
- MRI analysis of **gluteal muscles** (musculus gluteus maximus, medius and minimus) revealed an average **volumetric increase in muscle mass** after four HIFEM treatments.
- **The most substantial increment** was observed in the **gluteus maximus** (10.59+3.37%*), the muscle enhancement showed to be **uniform across all three evaluated muscles**.
- **The most profound** hypertrophic effect was observed in **the upper buttock region**, where it translated into a **visible buttock lifting**.



Standardized photography of a patient at baseline (left) and 1-month follow-up (right), left view. The dotted line indicates visible enhancement of muscle tissue and buttock lifting.

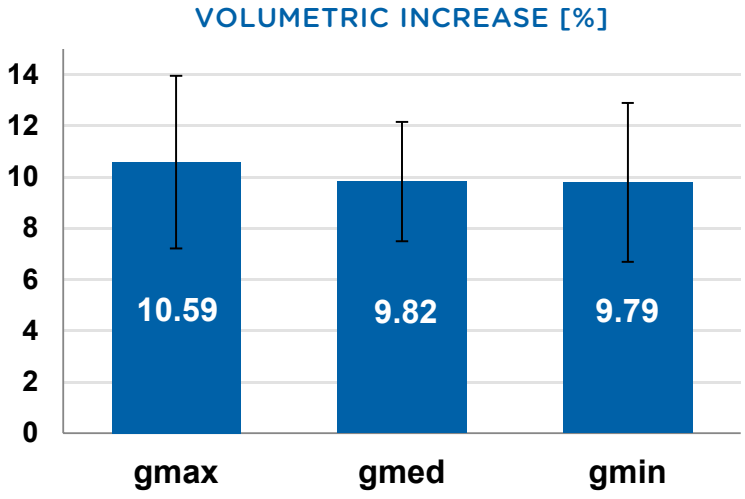
STUDY DESIGN

- **MRI scans** of the **pelvic region** along with standardized photographs were collected.
- MRI scans were **manually segmented** to reconstruct **3D volumes** of m. gluteus maximus (gmax), m. gluteus medius (gmed) and m. gluteus minimus (gmin). Volumetric changes were calculated and statistically analyzed using a paired t-test.



Example of gluteal muscle segmentation and 3D reconstruction. The gluteus maximus (green), medius (yellow) and minimus (red) were identified and manually segmented slice by slice.

RESULTS



Average muscle enhancement of individual muscles increase at the 1-month follow-up. All of the results were statistically significant.*

*Based on the evaluation of 18 out of 25 patients.

ULTRASOUND IMAGING STUDY: 6-MONTH FOLLOW-UP

CHANGES IN SUBCUTANEOUS ABDOMINAL FAT THICKNESS FOLLOWING HIGH-INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM) FIELD TREATMENTS SIX MONTHS POST-TREATMENT: A MULTICENTER ULTRASOUND STUDY.

Bruce Katz M.D.[1], Robert Bard M.D.[2],

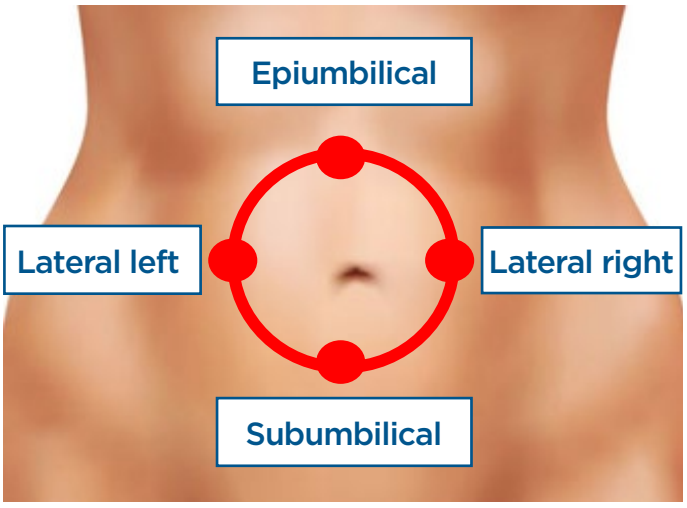
Richard Goldfarb M.D.[3], Aaron Shiloh M.D.[4]

1. Juva Skin and Laser Center, Manhattan NY, USA, 2. Bard Cancer Diagnostics, Manhattan NY, USA
3. Center for SmartLipo & Plastic Surgery, Langhorne PA, USA, 4. Shiloh Vein and Aesthetic Institute, Philadelphia PA, USA

Presented at the Annual Meeting of the American Society for Laser Medicine and Surgery, 2019 Denver, CO

HIGHLIGHTS

- **18 patients** were recalled 6 months after four 30-minute treatments for ultrasound assessment of abdominal fat thickness.
- **Ultrasound measurements** were performed at **four predefined locations**, and the outcomes were compared with baseline and 1-month results.
- Average reduction across abdomen was **7.73±5.68 mm at 6M FU**.*
- **High consistency**: Each subject showed a reduction, 11 out of 18 patients had a total reduction greater than 20%.



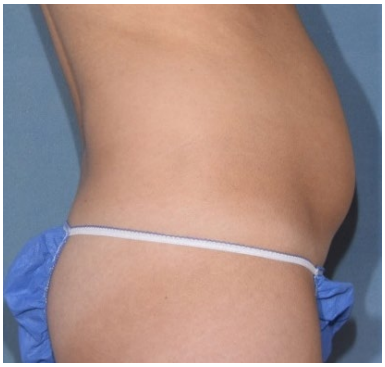
Visualization of predefined locations for ultrasound measurements. Four different points at a distance of 2 inches from the umbilicus were used.

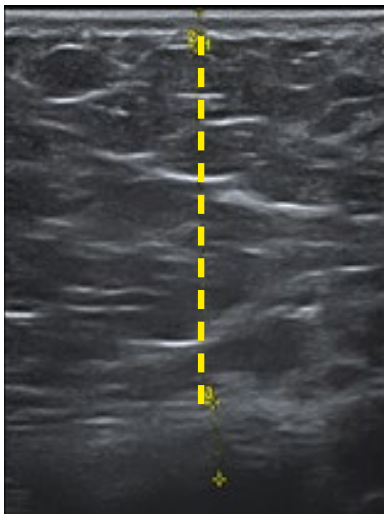
*Weight changes were insignificant.

RESULTS

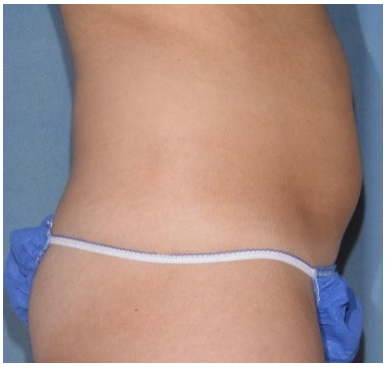
PATIENT 3: 23 years old female

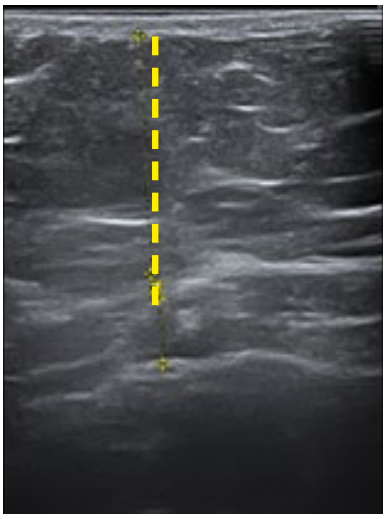
BASELINE



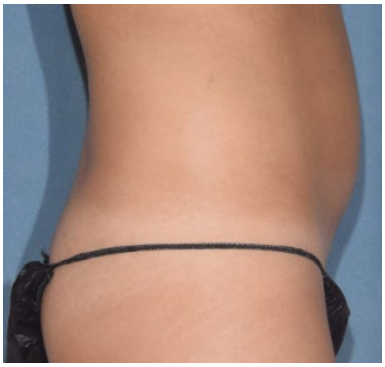


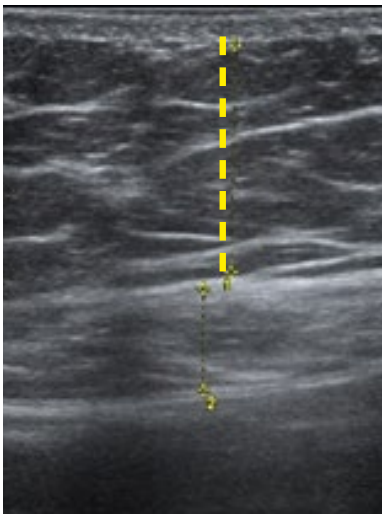
1-MONTH FU





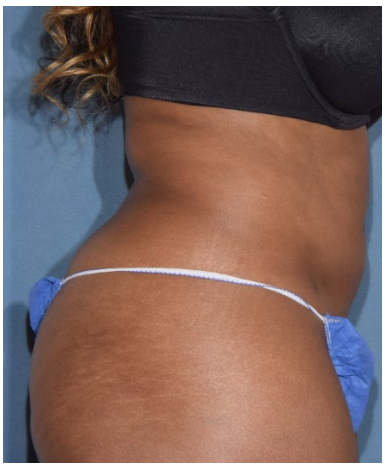
6-MONTH FU



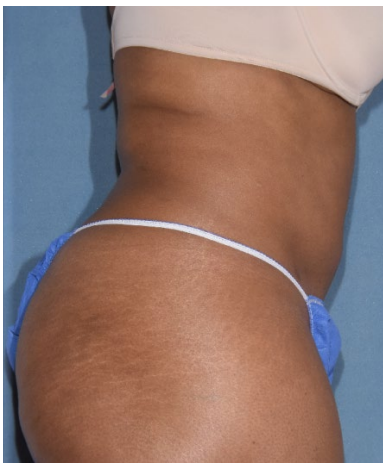


PATIENT 4: 32 years old female

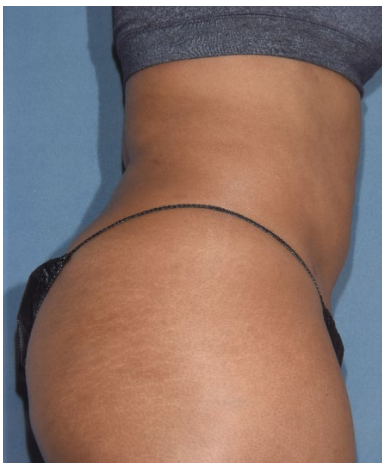
BASELINE



1-MONTH FU



6-MONTH FU



MRI STUDY:
WOMEN AFTER CHILDBIRTH

EFFICACY OF TREATMENT WITH HIFEM PROCEDURE IN WOMEN AFTER CHILDBIRTH.

Carolyn I. Jacob MD FAAD[1], Paula Lozanova MD[2]

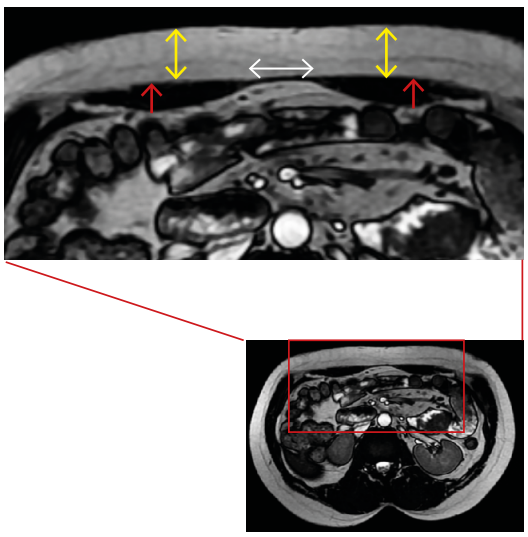
1. Chicago Cosmetic Surgery and Dermatology, Chicago, IL, USA
2. Paula Fines Center, Sofia, Bulgaria

Presented at the Vegas Cosmetic Surgery and Aesthetic Dermatology Conference, 2019 Las Vegas, USA

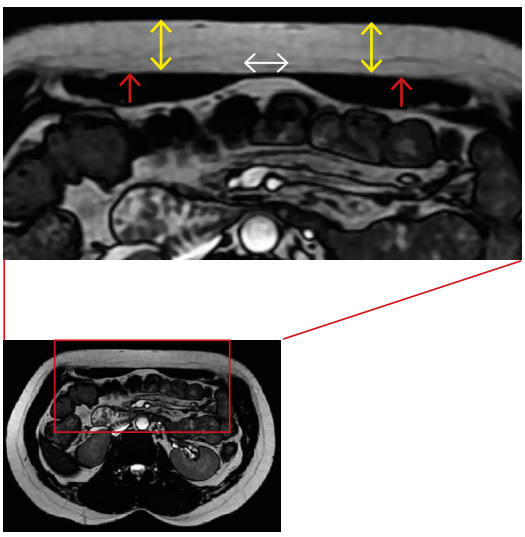
HIGHLIGHTS

- **16** enrolled patients: **women** 3-36 months **after the childbirth.** **4 treatments** of the abdomen (30 minutes each). At least 3 days between treatments.
- **MRI** assessment was done at **baseline** and **1 month** after the last treatment.
- The **abdominal separation** was **reduced** by **16.6% (2.42 mm)** on average. This improvement measured in a group of **post-partum** women is **60% higher** than that seen in normal population*.
- It is **the only study** providing evidence of **non-invasive reduction in diastasis recti.**

BASELINE



1 MONTH FU



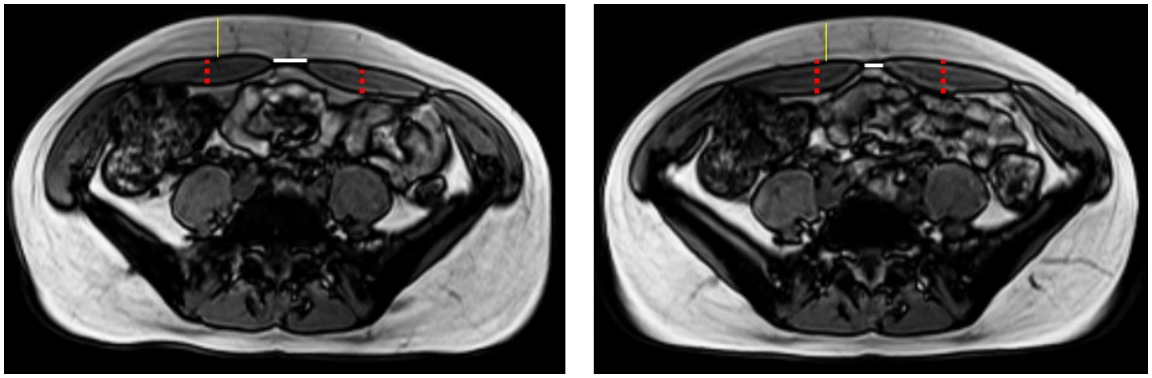
*Kinney BM, Lozanova P. High intensity focused electromagnetic therapy evaluated by magnetic resonance imaging: Safety and efficacy study of a dual tissue effect based non-invasive abdominal body shaping. Lasers Surg Med. 0(0). doi:10.1002/lsm.23024

RESULTS

- The **fat thickness** across the abdomen was **reduced** by **17.7% (2.99 mm)** on average.
- The **muscle thickness** was **increased** by **17.85% (1.73 mm)** on average.
- The **results** in fat and muscle **correlate** with previously published studies while the **effect on diastasis recti was significantly higher.**
- **Weight** change of 0.76 kg was **insignificant.**
- **88.2%** (15/17) patients were **satisfied with** the treatment **results.**
- The study found the **HIFEM** procedure to be **highly effective** and **safe** for **mommy makeover** in post-partum women.

BASELINE

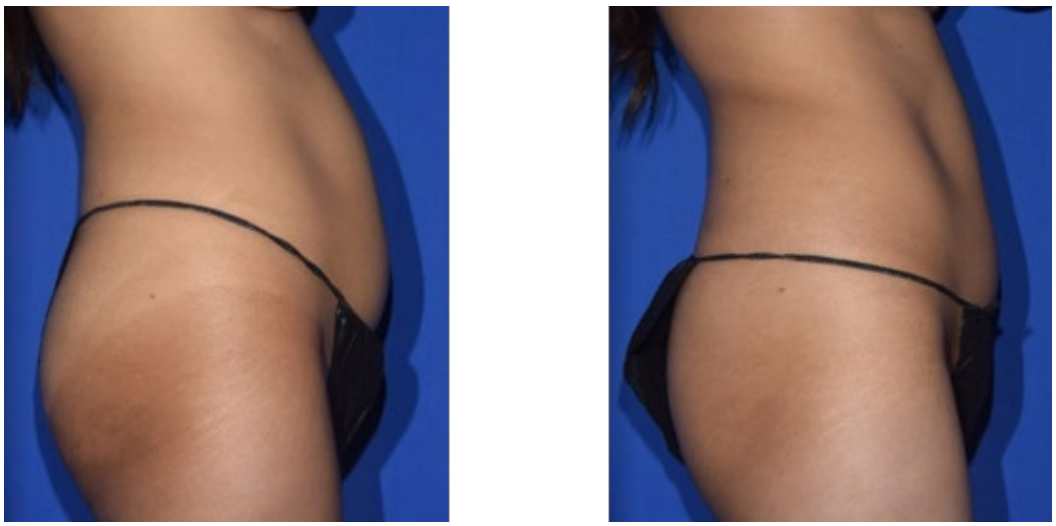
1 MONTH FU



Subject ID 6 (below umbilicus), age 38 years, separation of muscles -18.06%, reduction of fat layer by -12.04%, muscle thickness increase by +24.27%.

BASELINE

1 MONTH FU



Subject ID 10: Age 37, circumference reduction -2.5 cm, average reduction in abdominal separation 11.5%, average fat reduction 13.7%, average muscle thickening 19.0%.

LITERATURE REVIEW: HIFEM® AND THERMAL PROCEDURES

THERMAL VS. NON-THERMAL TECHNOLOGIES IN NON-INVASIVE BODY CONTOURING.

Dr. Rita Rakus MBBS FBCAM[1]

1. Dr. Rita Rakus Clinic, London, UK

Presented at the World Congress of the International Master Course on Aging Science, 2019 Paris, FR

HIGHLIGHTS

- Results based on **42** identified studies using quantitative evaluation of outcomes.
- **HIFEM** is the **most effective** technology for **reduction in waist circumference.**
- **HIFEM** technology combines **fat reduction (18.6%)** and **muscle thickening (15.4%)**.
- **Thermal technologies show risks** of AE due to tissue hyper/hypothermia such as erythema, swelling, pain, burns, numbness, bruising, etc. **No adverse events** related to the **HIFEM** treatments were **reported**.

RESULTS

MODALITY	FAT THICKNESS	MUSCLE THICKNESS	WAIST CIRCUMFERENCE
LLT	0.0%	0.0%	-3.03 cm
HIFU	0.0%	0.0%	-2.76 cm
RF	-29.0%	0.0%	-3.44 cm
CRYOLIPOLYSIS	-21.2%	0.0%	-3.88 cm
HIFEM	-18.6%	+15.4%	-4.09 cm

Efficiency comparison of different body contouring methods.

ULTRASOUND IMAGING STUDY: 6-MONTH FOLLOW-UP

CHANGES IN SUBCUTANEOUS ABDOMINAL FAT THICKNESS FOLLOWING HIGH-INTENSITY FOCUSED ELECTRO-MAGNETIC (HIFEM) FIELD TREATMENTS SIX MONTHS POST-TREATMENT: A MULTICENTER ULTRASOUND STUDY.

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HIGHLIGHTS

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- **Ultrasound measurements** were performed at **four predefined locations**, and the outcomes were compared with baseline and 1-month results.
- Average reduction across abdomen was **7.73±5.68 mm at 6M FU**.*
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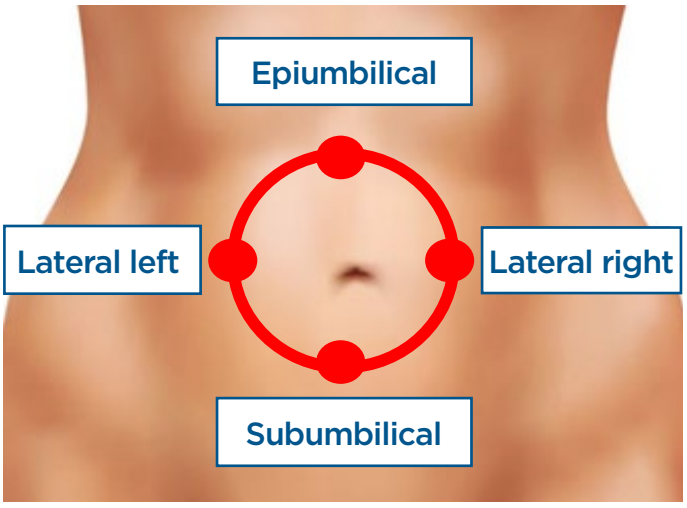


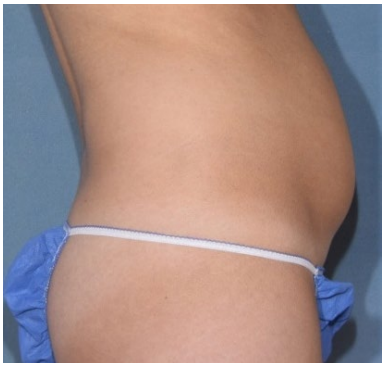
Visualization of predefined locations for ultrasound measurements. Four different points at a distance of 2 inches from the umbilicus were used.

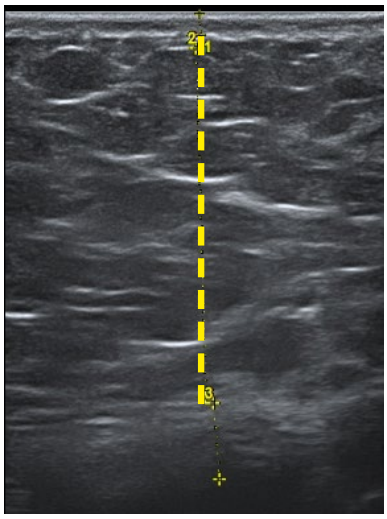
*Weight changes were insignificant.

RESULTS

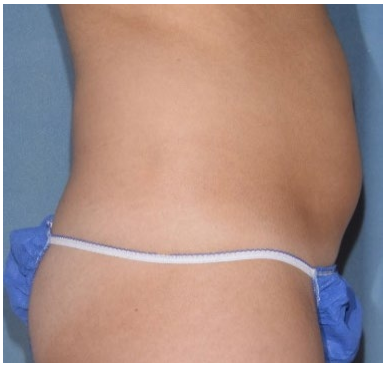
PATIENT 3: 23 years old female

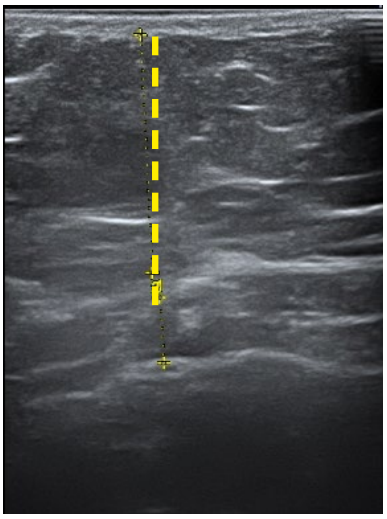
BASELINE



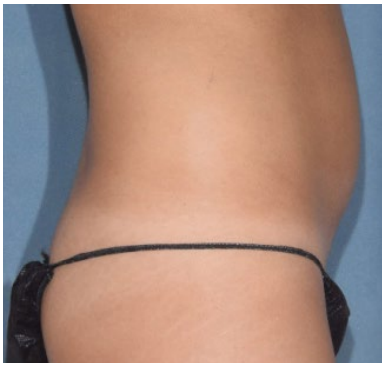


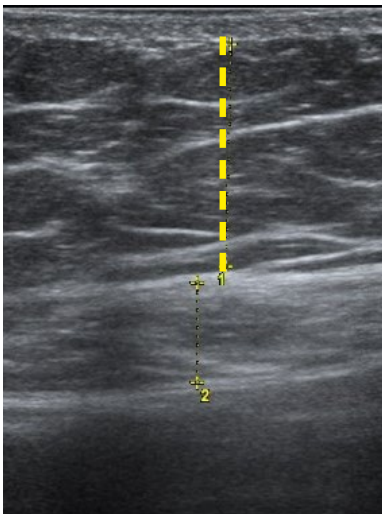
1-MONTH FU





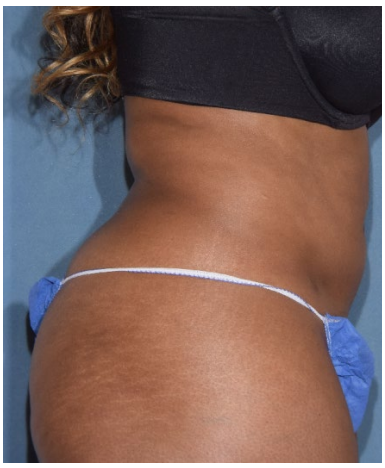
6-MONTH FU



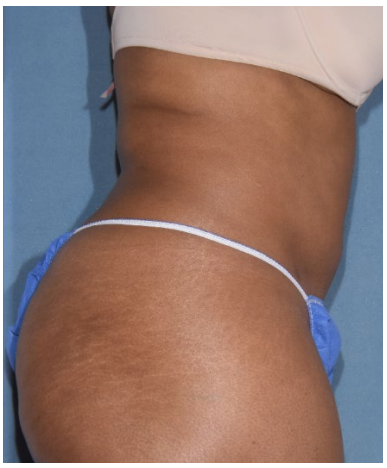


PATIENT 4: 32 years old female

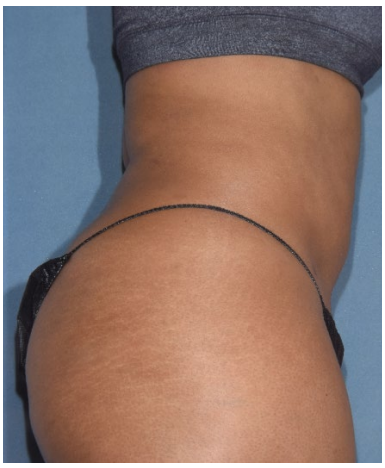
BASELINE



1-MONTH FU



6-MONTH FU



COMPUTED TOMOGRAPHY SCAN STUDY: EFFECTS OF HIFEM® ON VISCERAL FAT

THE EFFECT OF THE HIFEM PROCEDURE ON ABDOMINAL VISCERAL FAT: A RETROSPECTIVE CT ASSESSMENT.

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HIGHLIGHTS

- CT scans of **22 Patients (19 females and 3 males)**, average BMI 23.5±3.5 kg/m² **were evaluated retrospectively** for the levels of visceral fat.
- The average **visceral fat reduction** across the abdomen was **14.3%**.
- **17 out of 22** patients showed **reduction higher than 10%**.
- The results are first indications of HIFEM's ability to positively affect visceral fat.

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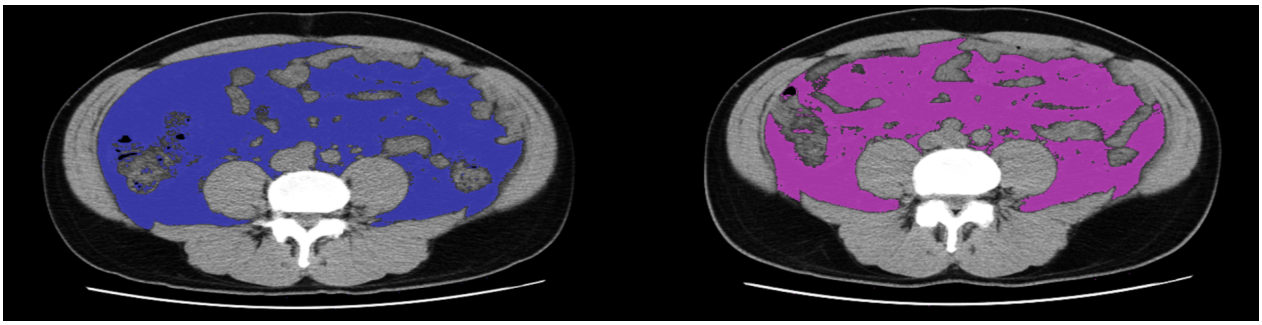

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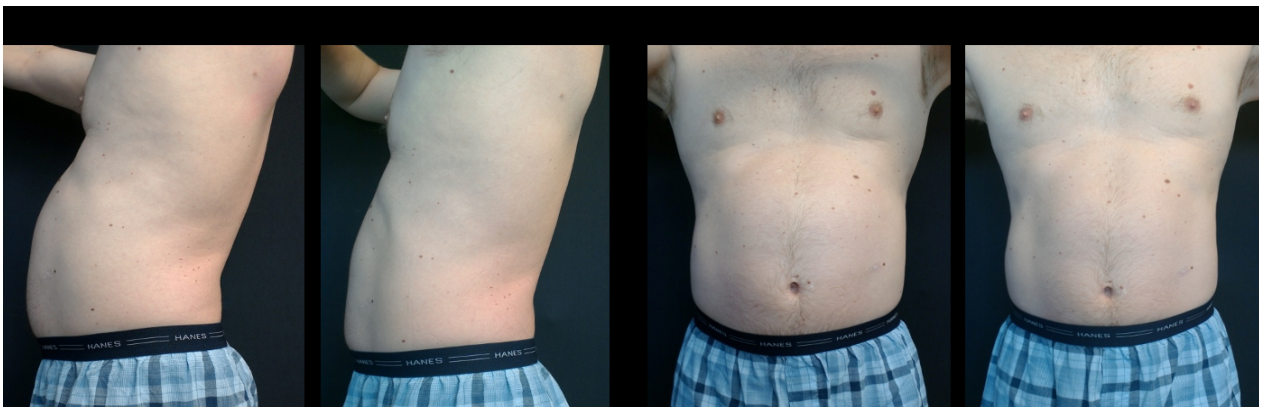


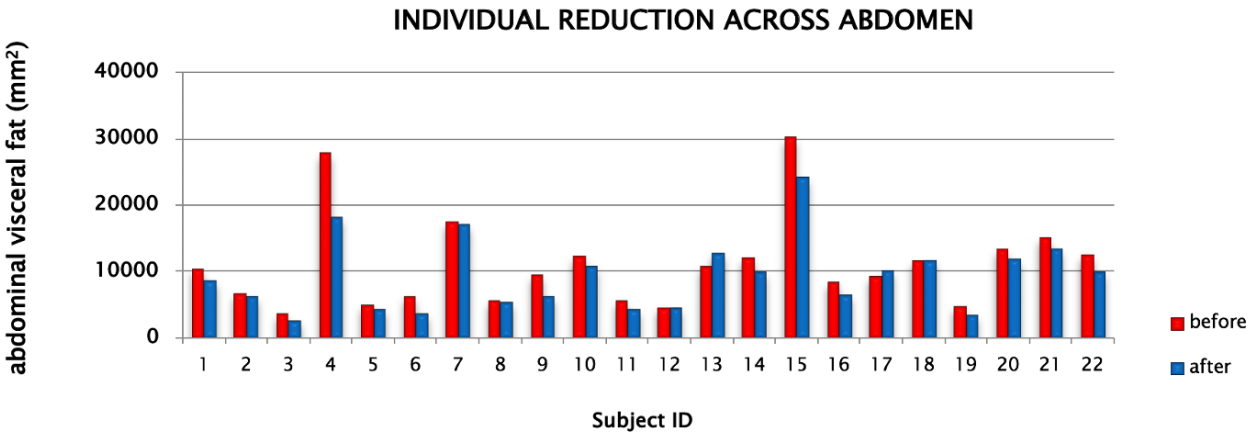
SUBJECT ID 15: Sub-umbilical slice, 48 years old male, average BMI of 31.8 kg/m², average VF reduction of 19.9%.

STUDY DESIGN

- CT scans of 22 patients, who initially received 8 HIFEM treatments of the abdomen (2 per week) were retrospectively evaluated for the levels of visceral fat.
- The CT scans obtained before and 1-month after the last treatment were evaluated.
- Cross-sectional umbilical, sub-umbilical and epi-umbilical slices were used for analysis.
- The levels of visceral fat were calculated through segmentation, as an area within the slice occupied by fat tissue.

RESULTS

- The retrospective analysis of the cross-sectional CT slices showed an average reduction in the visceral fat of 14.3% (-1667.2±2380 mm^2) across the abdominal area.
- 17 out of 22 patients showed a reduction higher than 10%, while three patients did not have any change in visceral fat.
- Majority of the visceral fat reduction was seen in the sub-umbilical area (17.1%). The average visceral fat loss epi-umbilically was 15.15% and at umbilicus, the patients lost 10.7% on average.
- The outcomes suggest that HIFEM procedure may have a positive effect on visceral fat.



Graphical representation of individual results on visceral fat reduction at baseline and 1- month FU

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ORIGINAL CONTRIBUTION

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Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping

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Abstract

Background: Thermal fat reduction technologies are leading the market for nonsurgical abdominal contouring. However, they are ideal principally for patients with fat bulges.

Objectives: Our study investigates the effects of a novel nonthermal technology affecting the abdominal musculature and subcutaneous adipose tissue.

Materials and Methods: A total of 22 patients (avg. BMI 23.8 kg m^{-2}) underwent 4 treatments on abdomen with high-intensity focused electromagnetic (HIFEM) field device. Treatments took 30 minutes and were spaced apart by 2-3 days. Photographs, weight, and waist measurements were taken at the baseline, after the last treatment, and at month 3 follow-up. Patient satisfaction was noted. Photographs were evaluated by blinded evaluators.

Results: The study protocol was completed by 19 patients. At month 3, the average waist size reduction was 4.37 ± 2.63 cm ($P < 0.01$). The evaluators identified the before image from the 3-month image 89.47% of the time. About 91% of patients reported their abdominal appearance improved, and 92% stated they are satisfied with treatment results at month 3. No adverse events occurred.

Conclusion: Observed waist size reduction and aesthetic improvement appear to be a combination of fat reduction and increased muscle definition of abdominal wall. In lower BMI patients, the increased abdominal muscle definition was largely responsible for the improvement. This novel energy device provides an additional tool for body contouring with primary application for lower and medium BMI patients.

KEYWORDS
body, contouring, electromagnetic, HIFEM, muscle, toning

1 | INTRODUCTION

The media-driven images of thin and muscular bodies lead to a high dissatisfaction rate of nonideal body type patients which may result in chronic depression.[1] Currently, up to 60.7% of men and 71.6% of women in US population are dissatisfied with their body size.[2] The desire for an easy solution to reduce fat and to improve the appearance of the abdomen is driving the market for body shaping procedures.

In 2017, liposuction was the most common surgical cosmetic procedure, after breast augmentation, with over 300 000 conducted procedures that year.[3] Due to the risk of complications (eg, infection, scarring or hematoma[4]), related downtime and substantial financial

cost associated with surgical procedures, there has been a rapid increase in the demand for noninvasive solutions. Since 2012, noninvasive procedures have grown by 217.3%.[3] The leading technologies in the noninvasive body shaping are low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF), and high-intensity focused ultrasound (HIFU).[5]

Surgical as well as noninvasive body shaping procedures are effective for fat disruption but require patients with well-defined bulges for successful and safe treatment. Many patients, especially those with lower BMI, who desire body shaping procedure, are not suitable candidates. Furthermore, none of the procedures focus on the underlying musculature, which is highly responsible for toned and aesthetically pleasing abdominal appearance.

Besides physical exercise, electric and electromagnetic stimulation has been used for muscle training.[6–8] Electromagnetic stimulation appears to dominate over the electrical stimulation as it induces double the peak torque,[9] penetrates deeper into the tissue[10] and is not associated with any pain[9] or risks of burns.[11,12] As electromagnetic stimulation has been shown to strengthen the muscles,[9,13,14] and an intensive muscle training was shown to induce lipolysis,[15,16] we hypothesize that the concept of electromagnetic stimulation can be applied for body shaping. Utilization of this technology would open possibilities for the patients not suitable for other procedures since the penetration of the magnetic field is not restricted by fat deposits.

Recently, there has been an introduction of a novel device (EMSCULPT, BTL Industries, Boston, MA) utilizing a high-intensity focused electromagnetic (HIFEM) field with frequencies inducing tonic muscle contractions. The study aims to examine the effect of the HIFEM technology on patients' waist circumference, the effect on abdominal appearance, the treatment satisfaction, and the safety of the procedure and to investigate the suitability of the treatment for lower BMI patients.

2 | MATERIALS AND METHODS

A total of 22 patients (avg. BMI 23.8 ± 3.3 kg m^{-2}) desiring aesthetic improvement of the abdomen voluntarily participated in this study. The patients' age ranged from 20 to 47 years with an average of 32 ± 7.1 years. Exclusion criteria included pregnancy, cardiac pacemakers, implanted electronic devices, metal implants, heart disorders, and any medical conditions contraindicating the use of the electromagnetic field. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Boards (IRB).

The patients underwent treatment of the abdomen by a device utilizing high-intensity focused electromagnetic field (EMSCULPT, BTL Industries, Boston, MA). The entire procedure consisted of 4 sessions distributed across two weeks (twice weekly, separated by 2-3 days). Each session lasted for 30 minutes during which the operator monitored the patients. Prior to treatment, informed consent was obtained from each patient.

The treatment was applied in a supine position with the device applicator positioned over the umbilicus. The targeted muscles were the rectus abdominis, external and internal obliques. The applicator position was being adjusted at the beginning of the treatment to ensure homogenously distributed contractions. The applicator was secured by a fixation belt to avoid any movement of the applicator during the treatment. The initial stimulation intensity was set according to patients' tolerance threshold and was further increased during the treatment once the patients got used to the muscle contractions. Over the course of a single session, most patients were able to reach an intensity of 90%-100%. No anesthesia was required.

To evaluate the treatment, weight, and waist circumference measurements, as well as frontal and lateral digital photographs, were taken before treatment, after the last treatment, and during a 3-month follow-up. Randomized digital photographs taken at baseline and during 3-month follow-up were given to three blinded evaluators for recognition. Furthermore, patient satisfaction with the treatment results was assessed using a 5-Likert scale questionnaire after the last treatment and during a 3-month follow-up. All data were tested by *t* test.

3 | RESULTS

The full study protocol was completed by 19 subjects (3 men, 16 women); 3 subjects opted out for reasons unrelated to the study. The results presented herein therefore comprise data from 19 patients.

Immediately after the last treatment, the waist circumference was significantly ($P < 0.01$) reduced on average by 3.29 ± 1.9 cm. This further improved three months after the last treatment, with the average reduction reaching 4.37 ± 2.63 cm compared to baseline. The total average circumference can be seen in Figure 1.

Circumferential reduction in 16 out of 19 subjects (84%) exceeded 2.5 cm at month 3 post-treatment. These results were independent of weight changes ($P > 0.05$). A significant portion of the reduction (75%) was measured after the last treatment, further improving at month 3. The waist circumference of 1 patient increased immediately post-treatment number 4, and 2 patients (10.5%) did not have any waist size change at the follow-up. The waist reduction was found to be independent of the baseline BMI ($P < 0.05$). The individual results can be seen in Figure 2. Patients' weight did not change significantly ($P > 0.05$) throughout the measurements.

On average, the evaluators successfully recognized the before images from the 3-month images in 89.47% of cases. In 15 patients (79%), the images were uniformly recognized by all 3 evaluators. The successful recognition rate was positively correlated with the amount of circumference reduction ($P < 0.01$). Example of patient photographs can be seen in Figures 3 and 4.

Analysis of the patient questionnaire revealed that 89% of patients were satisfied with the treatment results immediately after the last treatment. During the 3-month follow-up visit, the satisfaction increased as all patients reported a certain degree of satisfaction. The patient satisfaction was independent of the amount of waist size reduction. After the last treatment, 95% of the patients

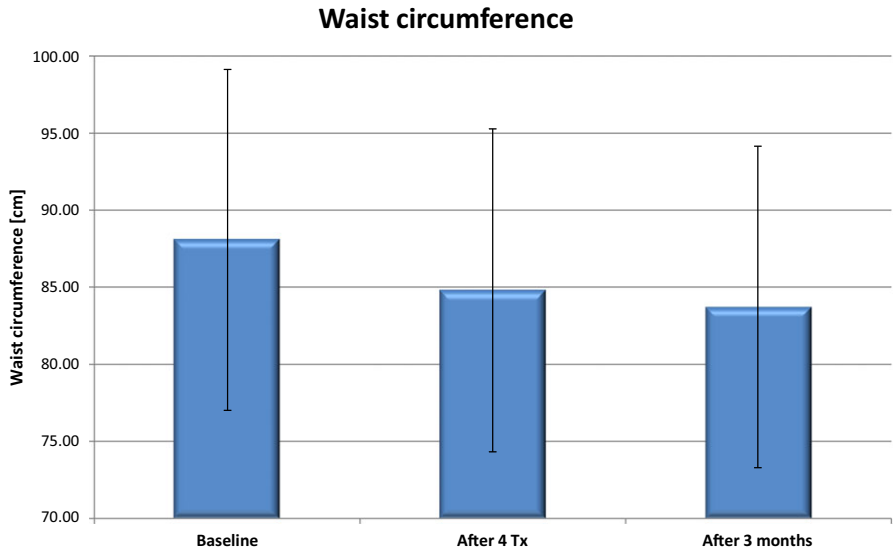

FIGURE 1 Average waist circumference at baseline, after fourth treatment and 3 months after last treatment

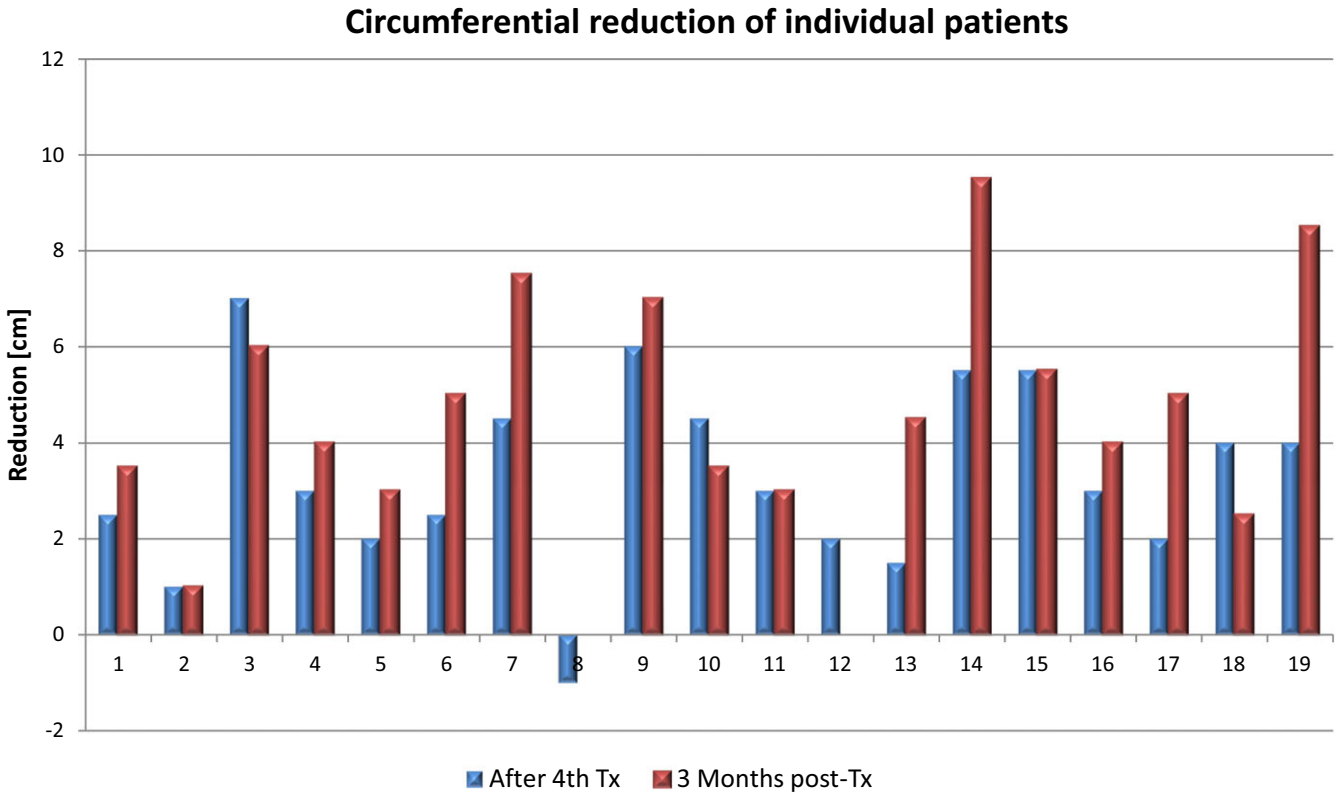

FIGURE 2 The individual waist circumference reduction measured immediately after the last treatment and during the 3-month follow-up

reported that they would recommend the treatment to a friend, while this decreased to 90% during the 3-month follow-up. Also, 89% of patients reported that their abdominal appearance improved immediately after the last treatment and this self-report further increased to 95% at month 3 follow-up. In general, the patient satisfaction improved at month 3 compared to evaluation after their last treatment, showing a similar trend as the measured waist reduction.

Muscle fatigue was a relatively frequent side effect that resolved within 12-48 hours. No adverse events were observed.

4 | DISCUSSION

Fifteen out of the 19 subjects had a BMI lower than 25, and the total average BMI was 23.8 ± 3.3 kg m^{-2}. Many of the subjects

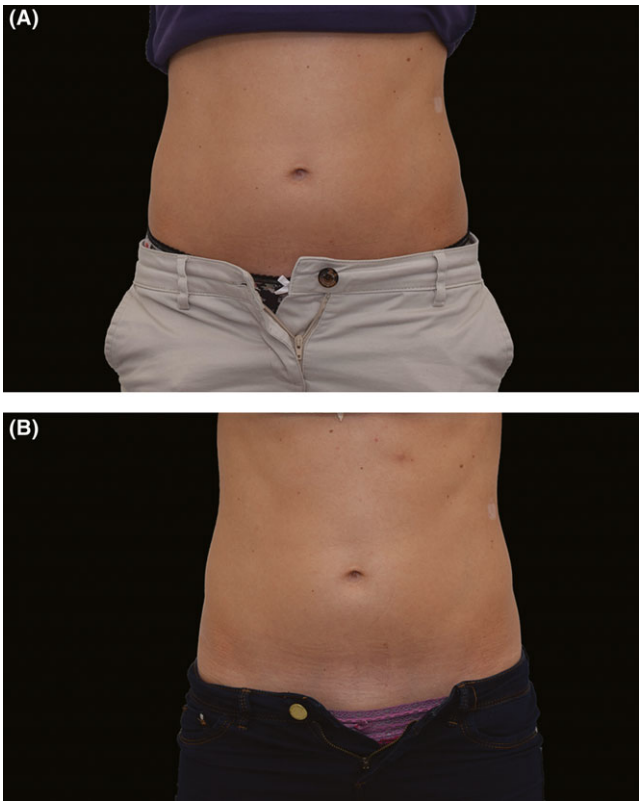

FIGURE 3 Digital images before (A) and 3 months after last procedure (B). Subject 13, age 30, BMI 18.9, waist circumference −3 cm (−4.0%), weight unchanged

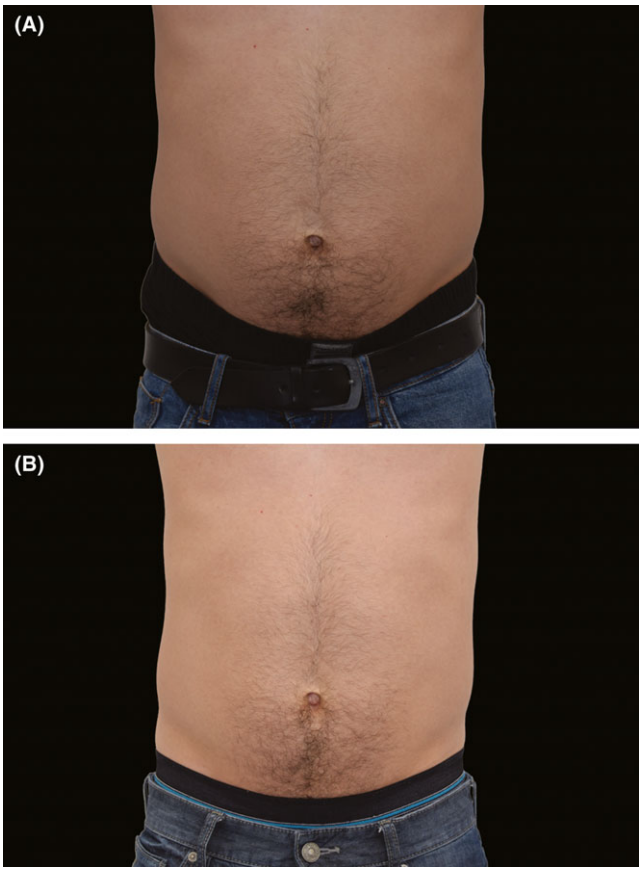

FIGURE 4 Digital images before (A) and 3 months after last procedure (B). Subject 11, age 33, BMI 25.2, waist circumference −7 cm (−7.7%), weight change −1.8 kg (−2.2%)

would not be suitable candidates for fat debulking treatments, such as suction based or stamping fat reduction devices. The primary goal was to understand if HIFEM can be used for lower BMI patients who are not ideal candidates for other available technologies.

The presented results showed that the treatment of the abdomen utilizing the HIFEM technology was effective in reducing the patients' waist circumference and in improving the aesthetic appearance of the abdomen. This was accompanied with high patient satisfaction. The waist size reduction was present already after the fourth treatment and continued to further reduce over the course of 3 months in most patients. The fact that the amount of waist size reduction was not correlated with the baseline BMI, suggests that the treatment was effective at the same level for the study patients' BMI range (18.8-33.3). The patients were satisfied with the results, and the treatment was generally perceived as comfortable.

The visual aesthetic improvement was confirmed by a high rate of successful photograph recognition done by blinded independent evaluators. The rate of successful recognition was correlated with the amount of waist size reduction, indicating that the higher the waist size reduction, the more the aesthetic improvement of the subject.

The study found that a significant weight loss did not accompany the waist size reduction. The device delivers pulses in a frequency that produces supramaximal contractions not achievable voluntarily. The muscle does not have time to relax between the 2 consecutive stimuli and is exposed to the extreme condition, which triggers a stress response in the tissue. Energy for supplying the contractions is taken from the fat cells presumably through lipolysis. The same effect, when muscles begin to use lipolysis as an energy supply, has already been seen during intense acute resistance exercise.[15,16] Further, when regularly exposed to these conditions, the muscle needs to adapt to them, which leads to a volumetric growth of muscle (hypertrophy)[17,18] and possibly hyperplasia.[19] The waist circumference reduction can therefore result from both fat reduction and strengthening and tightening of the abdominal wall. The lack of weight loss after the treatment thus appears to be logical effect since the weight of lost fat tissue is compensated by the weight of gained muscle volume.

In comparison to other technologies for noninvasive body shaping, the HIFEM showed competitive results regarding the waist circumference reduction. A study by Ferraro et al[20] on cryolipolysis reported circumference reduction of 6.86 cm, an LLLT study by Savoia et al[21] reported waist reduction as much as 6.83 cm, and RF study by Fajkosova et al[22] showed 4.93 cm. Studies on HIFU[23–25] showed a reduction of 4.1-4.7 cm. Looking at these results, the average waist reduction of 4.37 cm observed in the present study is highly competitive. However, the reduction presented in the mentioned studies is attributed to the fat loss, while the reduction in the present study appears to be a combined effect of a fat loss and strengthening of the abdominal wall muscles.

5 | CONCLUSION

The overall results are competitive in the noninvasive field of abdominal aesthetic improvement. The waist size reduction and improvement seen in photographs were driven by a combination of reduced fat and strengthened abdominal muscles. HIFEM treatments are effective for body shaping in both lower and medium BMI patients due to its effect on 2 tissues, showing high levels of patient satisfaction coupled with visible aesthetic improvement. We conclude the technology is ideal for treating patients who might not be candidates for other exiting technologies or whose problem is driven by a combination of fat deposits and underlying muscle laxity.

DISCLOSURE

Carolyn I. Jacob MD is medical advisor for BTL. Katya Paskova MD has no financial interest to declare in relation to any of the products or device mentioned in this article.

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Supramaximal deep muscle remodeling and ER stress-induced fat disruption using the Emsculpt High Intensity Focused Electro-magnetic field device

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Abstract

Emsculpt is a high intensity focused electromagnetic-magnetic field device, causing a unique combination of non-invasive subcutaneous fat reduction and deep muscle remodeling that can achieve strong aesthetic improvement of the treated area. The device induces supramaximal muscle contractions via its High Intensity Focused Electro-Magnetic (HIFEM) field. This results in cell membrane porosity changes, electroporation and an outflow of free fatty acids (FFAs) from adipocytes. The fat cells cannot process such amount of FFAs released during the contractions, and they thus induce apoptosis via a chemical reaction called Endoplasmatic Reticulum stress ('ER stress'). At the same time, the muscle is forced to adapt to the supramaximal muscle contractions which results in a highly effective deep muscle remodeling through muscle hypertrophy and muscle fiber hyperplasia. The introduced mechanisms lead to bulking and firm toning of the treated area.

Keywords: apoptosis; deep muscle stimulation; HIFEM; ER stress; supramaximal contractions; hypertrophy, hyperplasia

1. Introduction

1.1. Induction of muscle contractions via nerve pathways

The unit induces supramaximal muscle contractions by generating a High Intensity Focused Electro-Magnetic field (HIFEM). This field has an ability to selectively interact with peripheral motor neurons.[1–4] The interaction between the HIFEM fields and excitable nerve tissue creates electric currents in the neurons. Electric currents depolarize neural membranes in order to initiate action potentials spreading down the peripheral nerve, and governing motor units in the target muscles. Contractions mediated through the nerve allow the impulse to activate the whole muscle, encompassing the deep and the superficial parts. The muscle tension is sufficient to overcome the static load, and the muscle shortens as it contracts. This mechanism is referred to as concentric muscle contractions.[5,6]

Due to its physiological characteristics, other tissue is less responsive to the current, and therefore stays relatively unaffected. Emsculpt's field has the ability to penetrate deep into the tissue. This allows for fully effective activation of all motor nerves in the treated area in a wide range of patient profiles with different physiological characteristics.

1.2. Unique focused technology

The magnetic field is targeting directly the fibers of peripheral motoric nerves[7] in the stimulated area, thus leads to a contraction of the whole muscle group innervated by the specific nerve or nerve plexus. Also, motor nerve cells respond much more selectively to the HIFEM. Importantly, it selectively activates larger fibers, more than the smaller fibers that mediate pain. This occurs because the induced electric field forms only after it has passed through the cutaneous pain receptors. When applied over mixed motor and sensory nerves, only the motoric fibers are activated due to their size, without any sensoric reaction. Moreover, the magnetic field doesn't produce radial current which is

responsible for pain mediation in the skin.[7,8] This makes the application largely painless.

1.3. Principle of supramaximal contractions

During a voluntary muscle action, the muscle fibers relax between each nervous stimulus. This is due to the central nervous system's inability to signal another impulse whilst the previous one is still in action. The mechanism of action potential activation has a well-known temporal cycle that includes a short refractory phase as cells re-polarize their membranes in preparation for another cycle. Contrary to that, Emsculpt generates impulses of a frequency that does not allow the muscle to relax between the stimuli (see figure 1). These selective impulses are independent of brain function. This phenomenon leads to supramaximal contractions which cannot normally be achieved by voluntary muscle action, and therefore results in intensive lipolysis and extremely effective muscle structure changes.

The greatest amount of tension that could be developed and held physiologically is called maximal voluntary contraction (MVC). Usually it lasts only for a split second. Contractions with a tension higher than MVC are defined as supramaximal. Emsculpt with its HIFEM is able to generate supramaximal contractions and hold them for multiple seconds, which significantly increases the difficulty of the conditions that muscle adapts to.

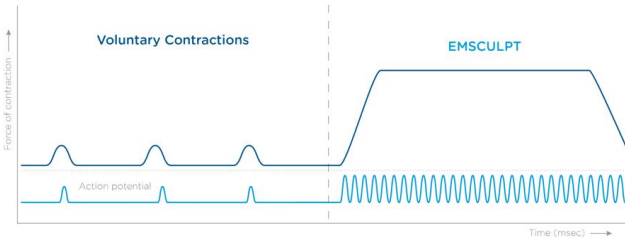

Fig. 1. Muscle action frequency and intensity of Emsculpt compared to regular exercise.

2. Fat disruption

HIFEM-induced supramaximal muscle contractions of a certain frequency and amplitude lead to an intensive supramaximal lipolysis - breakdown of lipids (triglycerides) into free fatty acids (FFA) and glycerol.[1,9–11]

Adipose tissue lipolytic activity is regulated by the balance between hormones that stimulate (primarily catecholamine) and those that inhibit hormone-sensitive lipase (primarily insulin), which hydrolyzes triacylglycerol to fatty acids and glycerol. The release of epinephrine is acutely increased by the muscle activity.

Lipolysis is mediated by an intracellular cascade reaction, which is activated by a catecholamine epinephrine (adrenaline). It includes the cAMP activity as a second messenger and activator of protein kinase, which catalyzes the phosphorylation of the enzyme hormone sensitive lipase (HSL). HSL then hydrolyze FFAs from stored triglycerides.[12,13]

Released molecules normally act as the primary energy source for the muscle and body metabolism. However, when the amount of released FFAs exceeds certain level, they start accumulating intracellularly in adipocytes, and eventually cause their dysfunction.[14–17] The lipolysis starts primarily in the area around the muscles undergoing contractions. It is due to an increased adipose tissue blood flow (ATBF) and paracrine substances released from contracting muscles, which diffuse to the adipose tissue stimulating blood flow and adipose tissue lipolysis.[9]

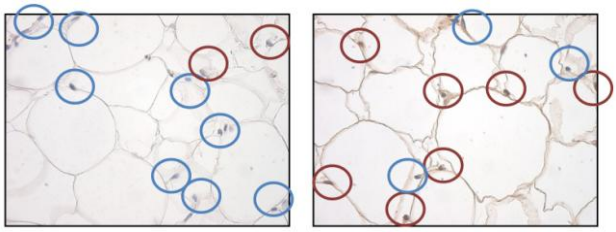

Fig. 2. The amount of apoptotic cells increased significantly after an Emsculpt treatment. The apoptotic index was increased by 91.7%. Illustration was adopted from Weiss et al.[18]

During the HIFEM therapy, the mechanism that leads to adipocyte cells death is ER-stress-induced apoptosis.[14–17] The fat cell apoptosis following an Emsculpt treatment was proven in a veterinary study, where the apoptotic index increased by 91.7 %.[18] This reaction is triggered by an increased intracellular concentration of FFA. The ER is central for protein folding, secretions, calcium homeostasis, and lipid synthesis. With regards to adipocytes, the ER is directly involved in LD (lipid droplets - reservoir for the cholesterol and triglycerides) formations and maintenance of lipid homeostasis, meaning if the homeostasis is disrupted, ER signals to the cell through the unfolded protein response (UPR). This is a stress reaction which accelerates the production of proteins needed for protein folding, while decreasing the transcription and increasing the degradation of other nonessential proteins. If the UPR is unable to return the ER to a homeostatic condition due to continuous release of FFA, it will then trigger an ER-stress-induced apoptosis response.[19,20]

The cell reacts to the dysfunction with initiation of an ER stress response to restore homeostasis. However, one of the additional cell responses to the ER stress is

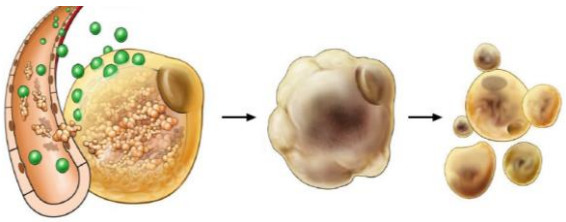

Fig. 3. EMSCULPT induced apoptosis mediated by accumulation of FFA intracellularly.

lipolysis itself. By applying this high intensity magnet field to the body, we enable a dual lipolysis effect at the cellular level, creating both a continuous flow of FFA through lipolysis caused by the supramaximal muscle contractions, and lipolysis triggered by the ER stress.[21–23]

Hardy et al. successfully treated MDA-MB-231 breast cancer cells by FFA induced apoptosis. Their results established that high intracellular levels of un-metabolized FFA decrease the mitochondrial membrane potential and cause cytochrome c release, which is involved in initiation of apoptosis. They successfully proved an increase in apoptosis by measuring Caspase-3 activity and concluded that FFA may be used as a treatment method for degradation of cancerous cells.[24]

The cell degradation is a consequence of the excess FFA accumulating in vesicles that displace the cytoplasm in cells. This cell overflow with FFA was proven by fluorescence microscopy and microfluometry by Gunduz et al[25] when treating HCV cells. Filter sterilized mixture of FFA was added to the cell culture medium, and the cells were co-cultured with different concentrations of FFA.

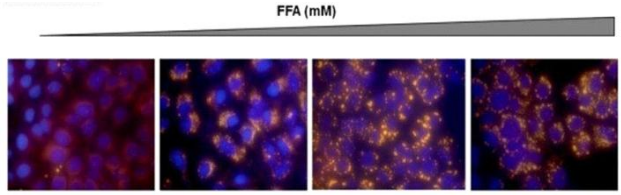

Fig. 4. Fluorescence microscopy showing cell overflow with FFA. Image adopted from Gunduz et al.[25]

In another study, hepatoma cells were cultured in vitro and consequently treated by a prepared solution containing certain types of FFA which had been previously studied as apoptotic triggers in pre-adipocytes culture by the same mechanism.[26] The apoptotic response to the fatty acid treatments was confirmed by measurement of cytoplasmic histone-associated DNA fragments. The results confirmed that the ER stress contributes to apoptosis induced by increased intracellular levels of FFA.[27]

Apoptosis is defined as programmed cell death[28] and as such, induction of increase in apoptotic index is accepted to be causing permanent changes in adipose tissues.[29] Best aesthetic improvement after non-invasive fat reduction treatments has been widely claimed to appear between 1 to 3 months after the actual treatment[30,31] when the body fully processes and cleans the cell debris and other metabolic waste.

3. Deep muscle remodeling

Powerful muscle contractions have a very strong effect on deep muscle remodeling and firm toning, due to their supramaximal nature.

The muscle structure is directly modified through the specific conditions to which the muscles have to adapt (supramaximal intensity and high frequency of impulses). These changes include a highly efficient growth of myofibrils - muscle fiber hypertrophy, creation of new protein strands and muscle fibers - muscle fiber hyperplasia[32–34] (see figure 5).

The device works with a unique combination of various field intensities, frequencies and contraction lengths to induce optimum changes in muscle tissue. Shorter intervals lead to muscle hyperplasia and sarcoplasmic muscle hypertrophy - increased volume of the sarcoplasm in the muscle cell, which is typically seen in bodybuilders. It is accompanied with growth of sarcoplasm itself and non-contractile proteins. The result is a total enlargement of the muscle mass and improvement of the muscle shape. Longer stimulation intervals induce both muscle hyperplasia and muscle hypertrophy, but these sequences are inducing mainly myofibrillar muscle hypertrophy, characterized by the creation of new myofibrils, actin and myosin filaments and thus enlargement of muscle fibers, leading to substantial increase of muscle strength.

In accordance with previous research, the best results of muscle structural improvements can be seen 14 days after the last systematic muscle contractions, when the tissue growth, thickening, and regeneration have fully completed.[1]

Various investigators have also studied the longevity of muscle changes after strenuous exercise[35–44]. Their findings vary, mainly depending on studied muscle group, age and gender of investigated subjects, however clear tendencies in the persistence of induced muscle changes can be concluded. The muscle changes were largely or fully maintained after 2 months since the last performance.[37,41] Modest impairments were seen after 3 months[36,38,43] and in most cases the exercise induced muscle changes were still maintained after 6 months, even though already showing decreasing tendencies.[35,38,39]

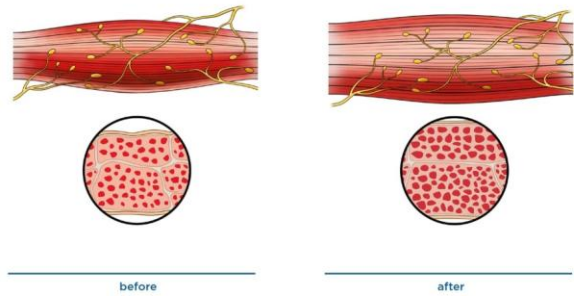

Fig. 5. Changes in the muscle structure: Muscle fibre hypertrophy and hyperplasia

Increased muscle density and enhanced volume lead to an increase in the muscle tone, i.e. muscle tonisation.

Muscle form and volume are crucial factors for creating symmetric contours with a potential resultant improvement in the appearance of a firmer and slimmer body. This laid basis for a total aesthetic improvement of the body shape.

By all these mechanisms, Emsculpt delivers a unique combination of subcutaneous fat reduction, deep muscle remodeling and toning; all while being completely safe and essentially pain-free due to the selective nature of the magnetic field. Best results can be seen between 2 to 4 weeks after the last treatment.

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High Intensity Focused Electro-Magnetic (HIFEM) technology for non-invasive buttocks lifting and toning of gluteal muscles: preliminary data

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***Abstract*— Surgical intervention has been the only method to improve the aesthetic appearance of buttocks apart from physical exercising. This study evaluates the efficacy of High Intensity Focused Electro-Magnetic (HIFEM) treatments as a non-invasive solution for improvement of buttocks through toning and lifting of gluteal muscles. A total of 75 patients underwent four 30-minute treatments of buttocks. Evaluation was done at baseline, after the 4th treatment and during a 1 month follow-up. The evaluation included weight measurements, digital photographs, and two patient's satisfaction questionnaires. The overall score (range 4-28) reflecting patient's perception of their buttocks improved from 13.1±5.7 at baseline to 18.4±5.2 after the treatments and 18.9±5.1 at follow-up. The average score of all treatment satisfaction questions (range 1-7) was 5.2±1.2 immediately after the treatments and 5.1±1.3 at follow-up. The results show that the investigated device safely and effectively improves the aesthetic appearance of the buttocks non-invasively. The treatments not only resulted in a significant visual improvement but also increased patient confidence and satisfaction. The procedure is suitable for patients seeking improvement in tone, shape, lift and tightness of the buttocks.**

***Index Terms*— deep muscle stimulation, HIFEM, Emsculpt, supramaximal contraction, magnetic stimulation, non-invasive, butt lift, body shaping, muscle toning**

I. Introduction

THE popularity of surgical butt lifting, and augmenting procedures is rapidly growing. Since 2015 the number of performed procedures increased on average by 25 % each year[1], while the increase over the past two decades totals 342 %[2], with the total expenditures for these type of procedures reaching 120 million USD in 2016[2]. The most popular methods are represented by buttock augmentation using silicone implants, autologous fat grafting, and a traditional butt lift done by cutting out an ellipse of excess skin and suturing the remaining skin back together. In general, these procedures are associated with one to four weeks of downtime[2]. Furthermore, all surgical procedures focus on artificially increasing the subcutaneous volume of buttocks, yet they do not target the underlying gluteal muscles which play a crucial role in the buttock shape definition and overall aesthetic appearance of buttocks.

Magnetic stimulation has been widely and successfully used before e.g. in the treatment of incontinence by strengthening the pelvic muscles[3], in cough restoration[4] or in augmentation of resistance training[5]. This study investigates the efficacy and safety of a High-Intensity Focused Electro-Magnetic (HIFEM) technology (Emsculpt, BTL Industries, Boston MA) when used for non-invasive improvement of the appearance of buttocks. The device delivers magnetic impulses into the tissue where it stimulates the gluteal muscles (gluteus maximus, medius, and minimus) and induces supramaximal contractions of all these muscle groups simultaneously.

II. Materials and Methods

In total 75 subjects (73 females and 2 males) participated in the study. The age of recruited subjects ranged between 22 and

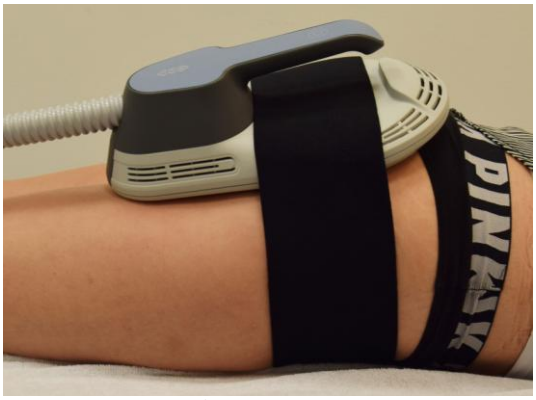

Fig. 1. A photograph of a patient during an ongoing treatment

Carolyn Jacob MD and Brian Kinney MD are medical advisors for BTL. Mariano Busso MD and Suneel Chilukuri MD are speakers for BTL. The other authors have no financial interest to declare in relation to any of the products or device mentioned in this article.

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TABLE 1
BUTTOCK EVALUATION QUESTIONNAIRE RESULTS

Question (Score range 1-7)	Baseline	After	Change	1M FU	Change
Please rate your subjective perception of your buttock laxity/tightness[1]					
Total (n=75)	3.4±1.6	4.6±1.5	+1.2 (p<0.01)	4.8±1.3	+1.4 (p<0.01)
Baseline score <4 (n=42)	2.2±0.7	4.0±1.6	+1.8 (p<0.01)	4.5±1.4	+2.3 (p<0.01)
I am satisfied with the overall aesthetic appearance of my buttocks[2]					
Total (n=75)	3.2±1.5	4.8±1.3	+1.6 (p<0.01)	5.0±1.5	+1.8 (p<0.01)
Baseline score <4 (n=46)	2.2±0.7	4.4±1.5	+2.2 (p<0.01)	4.6±1.6	+2.4 (p<0.01)
I am satisfied with the shape of my buttocks[2]					
Total (n=75)	3.4±1.6	4.7±1.6	+1.3 (p<0.01)	4.9±1.4	+1.5 (p<0.01)
Baseline score <4 (n=45)	2.3±0.7	4.1±1.6	+1.8 (p<0.01)	4.5±1.5	+2.2 (p<0.01)
I feel confident about my buttock area when wearing the bikini[2]					
Total (n=74)					
Baseline score <4 (n=48)	3.1±1.6	4.4±1.5	+1.3 (p<0.01)	4.3±1.6	+1.2 (p<0.01)
	2.0±0.7	3.8±1.4	+1.8 (p<0.01)	3.7±1.6	+1.7 (p<0.01)
Total score	13.1±5.7	18.4±5.2	+5.3 (p<0.01)	18.9±5.1	+5.8 (p<0.01)
Total score (Baseline score < 4)	8.7±1.6	16.3±3.1	+7.6 (p<0.01)	17.3±3.1	+7.2 (p<0.01)

[1] 1 – Very loose, 2 – Moderately loose, 3 – Slightly loose, 4 – Neither loose/tight, 5 – Slightly tight, 6 – Moderately tight, 7 – Very tight.
[2] 1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

59 years (average 36.6±8.3) with average BMI 21.5±2.2 kg/m^2. The participants received bilateral treatments of buttocks with a novel device based on the HIFEM technology (Emsculpt, BTL Industries, Boston MA). The therapy protocol consisted of 4 treatment sessions which were spaced by 2-3 days, each session including 30 minutes of application. During the treatment subjects were placed in a prone position and the applicator of the device was placed over the buttocks to simultaneously affect all the gluteal muscles as seen in **Figure 1**. A fixation belt was used to avoid any movements of the applicator during the treatment. The output intensity was kept just below each patient's tolerance threshold in order to maintain the supramaximal contractions throughout the entire treatment.

Patients were evaluated at the baseline, after the last treatment, and at 1-month follow-up. Digital photographs of the treated area were taken and patients' weight was measured as a control indicator. Two different non-standardized questionnaires based on 7-point Likert scales were used to assess the effects of the treatment. The buttocks evaluation questionnaire focused on measuring if the treatments can change the way patients perceive and/or think about the appearance of their buttock area. The total possible score ranged from 4 points (lowest possible satisfaction) to 28 points (highest possible satisfaction). See **Table 1**. The responses were compared between the baseline, post-treatments and the follow-up. After the last treatment and at the follow-up, the second questionnaire was used to evaluate patients' satisfaction with the results of the treatments. See **Table 2**. Average scores were calculated and a paired t-test was used for statistical analysis.

A visual analogue scale (0-10) was used to assess the level of comfort during the treatments. Any side effects or adverse events were monitored.

III. Results

In total 75 subjects (73 females and 2 males) completed the full treatment protocol; four subjects withdrew before the follow-up for reasons unrelated to the study. The results presented herein thus include data from 71 subjects.

The average scores reflecting patients' satisfaction with their buttocks significantly improved (p<0.01) after the last treatment and at the one month follow-up, both when measured as a total and individually for each question. The total average score increased by 40.5 % from 13.1±5.7 at the baseline to 18.4±5.2 post-treatments, and further improved to 18.9±5.1 at the follow-up. The most significant improvement was seen in patients who were initially dissatisfied with the appearance of their buttocks prior to the treatments, with the average score increasing by 83 % from 8.7±1.6 to 16.3±3.1 after the treatment, and on to 17.3±3.1 at the follow-up. See **Table 1**.

TABLE 2
TREATMENT SATISFACTION QUESTIONNAIRE RESULTS

Question (range 1-7)[1]	After	1-month FU
The appearance of my buttock area has been improved after the treatments	5.0±1.4	5.2±1.4
My buttocks feel more lifted and toned after the treatments	5.3±1.3	5.2±1.4
I am satisfied with the treatment results	5.2±1.3	5.1±1.4
I would recommend the treatment to a friend	5.1±1.5	4.9±1.5
AVERAGE SCORE	5.2±1.2	5.1±1.3

[1] 1 – Strongly disagree, 2 – Disagree, 3 – Slightly disagree, 4 – Neither agree/disagree, 5 – Slightly agree, 6 – Agree, 7 – Strongly agree.

Statistical analysis of the results revealed that 69 % of patients who initially reported buttocks laxity improved to a higher degree of buttock tightness post-treatments and at the follow-up. In total, 85 % of the patients initially dissatisfied with the

appearance of their buttocks reported a significant improvement immediately after the fourth treatment which was maintained over the course of one-month follow-up. Furthermore 80 % of the patients initially dissatisfied with the shape of their buttocks reported a significant improvement immediately after the fourth treatment and during the follow-up. 79 % of patients with low confidence while wearing the bikini at baseline felt significantly more confident after the fourth treatment and continued to feel confident during one-month follow-up.

In the patient satisfaction questionnaire 76% of patients reported that the appearance of their buttock area has been improved after the treatments and during the one-month follow-up, while 80% of all the patients reported that their buttocks felt more lifted and toned right after the fourth treatment as well as at the follow-up. In total 71% of all patients were satisfied with the treatment results immediately after the fourth treatment as well as during the one-month follow-up. The average scores can be seen in **Table 2**.

Patients found the treatments comfortable with an average VAS score of 2.01 (corresponding to none or very mild discomfort).

The analysis of weight didn't show any significant changes. No adverse events were observed during the treatments nor as a consequence of the treatments. Digital photographs showed improvements in aesthetic appearance of the buttocks. See **Figures 2 and 3** for examples of patient images.

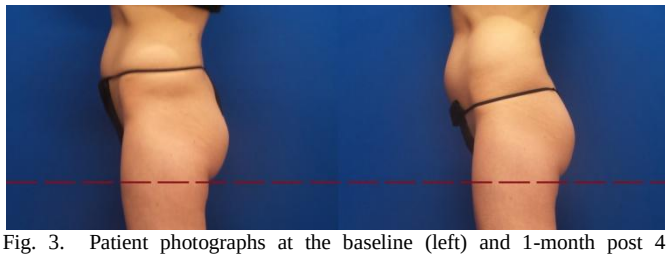

Fig. 3. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). The demarcation line shows the improvement and lifting of the gluteal fold.

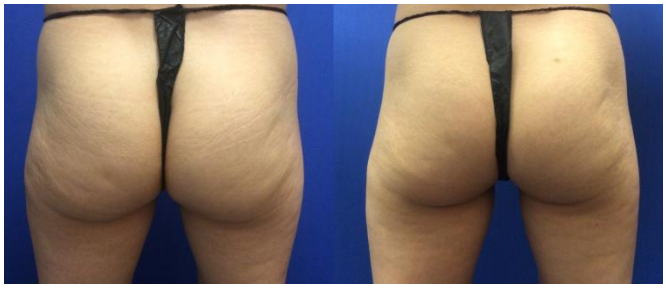

Fig. 2. Patient photographs at the baseline (left) and 1-month post 4 treatments (right). Female, 31 years old.

IV. Discussion

The results show a statistically significant positive trend in all of the measured criteria. This suggests that the treatments can have a positive effect on the way patients perceive the appearance of their buttocks, their level of confidence and overall satisfaction.

For the analysis of subjects' satisfaction with their buttocks, the data was adjusted for patients who initially had a negative perception of their buttocks (score < 4) as this would likely be the primary target group of the treatments. This group showed greater improvements than the total study population, which suggests that this sub-group of initially dissatisfied patients are the ideal profile that can most benefit from the treatments.

Visual inspection of digital photographs showed visible aesthetic improvement in most patients. The best results were seen in patients with lower BMI and in patients who reported a more active lifestyle. The patients in this study showed a lifting effect coupled with an improvement in their gluteal folds, as well as an increase in the overall buttock tightness. We thus suggest that the investigated device brings a new alternative to patients seeking more toned and athletically appearing buttocks.

V. Conclusion

The Emsculpt device proved to be effective and safe for non-invasive improvement of the aesthetic appearance of buttocks. Future research should focus on bringing more evidence based investigational methods for the evaluation of non-invasive buttock treatments.

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