Noninvasive Body Contouring by Low Frequency Ultrasound: A Clinical Study

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Abstract: Non-invasive transdermal focused ultrasound is an alternative method for body contouring, that is gaining interest both in patients and physicians. We report on a controlled clinical study assessing the safety and efficacy of a new therapeutic ultrasound device for non-invasive body contouring, named *Proslimelt* (PromoItalia Group S.p.A, Pozzuoli, Italy). A prospective study was conducted on 50 healthy patients (37 females and 13 males). The evaluation period lasted 8 consecutive weeks at the frequency of 1 session every 15 days for a mean total of 3,73 sessions. Results were assessed immediately after completion of the treatment protocol. Areas treated were the abdomen, the ankles, the arms, the buttocks and inner and outer thighs. Efficacy was determined by subjective and objective (plicometric and perimetric measurements, photographic and ultrasound evaluations) determinations. Safety was determined by clinical findings, assays of serum triglycerides, and hepatic transaminases. Finally, histopathological analyses were conducted in order to define morphological effects of the treatment. All patients showed significant reduction in subcutaneous fat thickness within the treated area, determined both by subjective an objective evaluations. Interestingly, weight was unchanged during the treatment and follow-up period and no adverse effects were observed. Histopathological analysis of the treated areas, showed cytoplasmic alteration of adipocytes. In conclusion the *Proslimet* device provides a safe and effective non-invasive technology for body contouring.

Keywords: Body contouring, ultrasound, cavitation.

INTRODUCTION

Body contouring by liposuction for the removal of excess weight is the most frequently performed cosmetic surgery in the Unites States [1]. Because of the numerous drawbacks of the surgical procedure (hospitalization, anaesthesia, clinical complications, long post-operative recovery), there is a greater demand in body aesthetic medicine for non-invasive procedures [2-4]. Non-invasive alternatives to liposuction to date include lifestyle changes in diet and exercise; alternatively mesotherapy, multiple injections of bile salt solutions, creams and lasers are currently used. Indeed, none of these procedures is approved by the U.S. Food and Drug Administration, with the exception of Cyanosure/DEKA laserlipolysis and mesotherapy [4,5].

Ultrasounds are elastic waves, not audible to the human ear (above 20000 Hz) artificially produced by the piezoelectric effect using a quartz or a ceramic material. Ultrasounds are propagated through a physical layer that may be gaseous, solid or liquid. Ultrasounds can be used in clinical practice as a diagnostic tool, when utilized for imaging, or as a therapeutic modality. In particular, novel applications using ultrasound without surgical intervention have been investigated to deliver an energy signature through the skin for the disruption of adipose tissue [6,7]. Ultrasound-assisted liposuction is becoming a popular alternative to liposuction for body contouring [8-11]. Indeed, an ideal non-invasive procedure of delivering energy to the fat would reduce peri-procedural morbidity such as infection, scarring, anaesthesia-related complications, and other risks associated with surgical procedures.

We describe here the pivotal clinical trial of a new non-invasive device for body contouring (*Proslimelt,* PromoItalia Group S.p.A., Pozzuoli, Italy) to reduce subcutaneous fat volume in areas that would normally be treated by liposuction. This device emits low frequency ultrasound waves ranging from 30 khz to 70 khz. The data produced show that the *Proslimelt* device provides a safe and effective non-invasive technology for body contouring.

MATERIALS AND METHODS

Apparatus

The apparatus used, *Proslimelt* (PromoItalia Grouop S.p.A, Naples, Italy), emits low frequency ultrasound pulsed waves ranging from 30 khz tp 70 khz through a transducer of 45 mm diameter at a power of 3 watts/cm^2 and with an emission time capacity ranging from 0'' to 99''. The duration of the impulses is 100 ms, while the period of the impulses is 300 ms. It is also equipped with two twin transducers, each with a surface of 16 cm^2, that allow the treatment to be carried out on two different areas or on two different patients simultaneously. The device allows to vary the following parameters: duration of the treatment, power

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and sweep time (time used to cover the range from 30 to khz). In order for the transducer to transfer the ultrasound waves, a conductive gel must be used.

Patients

50 patients have been enrolled for this study (37 females and 13 males), aged between 21 and 62 years old, all with localized fat. For the study, the population of patients has been divided based on the areas treated: abdomen, ankles, arms, buttocks and inner and outer thighs. Prior to assessment and treatment, all patients received explanations about the procedure and read and signed an informed consent. All patients underwent a screening visit including physical examination and blood tests. Exclusion criteria for this study were: osteoporosis, phlebitis and thrombophlebitis, patients carrying metallic fragments, articular prosthesis, intrauterine devices or pace-maker, pregnant women, patients with a reduced nervous sensibility or with neurological pathologies, patients affected by obliterating arteriopathies and patients affected by important inflammatory processes or neoplastic diseases.

It is very important to assure that during the period of treatments the patients have assumed at least two litres of water a day, and have followed a moderated hyperproteic diet; moreover, none of the patients underwent other slimming or aesthetical procedures (endermologie, mesotherapy, radiofrequency, etc.) during the study.

Treatment and Evaluation Protocol

Each treatment has been carried out according to a default protocol and the duration set depending on the width of the area to treat, varied from a minimum of 15 minutes to a maximum time of 60 minutes. The treatment has been practised by placing one or two transducers on the skin that was previously covered with conduction gel. We have attended at least 15 days between a session and the following, in order to guarantee a total time of hepatic recovery, even in case of the eventual presence of pathologies in subclinical phases. Each target area was treated according to its size for a minimum of 15 minutes per session up to 45 minutes. The evaluation period lasted 8 consecutive weeks at the frequency of 1 session every 15 days for a mean total of 3,73 sessions. Prior to the start of the treatment program and at the end of the treatment, each subject's age, height and weight were recorded along with a perimetric measurement of the area to be treated and photos of the subject. In detail, for the perimetric measurements the conditions were: the patients with standing up feet apart at always the same distance; marking the height from the floor up to the area of concern; measuring just below the marking, making sure the measuring tape is parallel to the floor. The conditions for the photos (digital camera C5050 from Olympus) were: the subject standing up feet apart at always same distance; camera distance from subject always the same; camera height, angle and focal always the same; light always the same with 4 flash lights in slave mode (2 behind the subject and 2 on either side of the camera); 4 photos taken at each evaluation period (1 photo of front, I photo of back, 1 photo of right and left side). Ultrasound measurements of subcutaneous fat thickness were obtained before treatment and after completion of the treatment protocol.

Subjective Evaluations

An auto-evaluation questionnaire has been given to all patients, where a subjective evaluation concerning the skin's compactness, the volumetric reduction of fat, comfort, and satisfaction compared to the outcome of the treatment, was requested. For each point, a scale from 0 to 5 has been proposed. The final score was obtained making an arithmetical media of the scores registered for each parameter analyzed.

Instrumental Evaluations

Ultrasound survey's have been carried out before and after the treatment with the intent of evaluating the reduction of the hypodermic layer and the integrity of the surrounding structures.

Laboratory Evaluations

The haematic levels of cholesterol have been constantly verified with specific reference to the VLDL (fraction of cholesterol in which metabolization products of triglycerides contained in adypocites pass), in particular, the drawing has been performed 24 hours before the beginning of the first session, immediately after, after 96 hours and after7 days. An evaluation of the markers with hepatic functions (GOT, GPT, G-GT range) has been carried out, before the beginning of the treatment and 15 days after the last session.

Histology

A woman aged 51 had to have surgical abdominoplasty. After giving her informed consent, she agreed to have the skin at her abdomen treated with *Proslimelt* one time before surgery. The surgery was carried out 5 days after the treatment and under lumbar anesthesia and two representative full-thickness skin samples were taken at the same time, one at the site of the *Proslimelt* application and one at the contralateral, symmetric untreated side to be examined by means of histopathology. Excised tissue samples were transferred in 4% (m/v) paraformaldehyde solution and paraffin embedded. Sections of 5 microns were stained with haematoxylin-eosine, haematoxylin-van Gieson, and PAS-Alcian blue haematoxylin.

Statistical Analysis

The differences were evaluated by Wilcoxon test for paired continuous variables. The software used for statistical analysis was SPSS (SPSS, Chicago 17.0). P value <0.05 was considered statistically significant.

RESULTS

Characteristics of the patients and measurement data are summarized in Table **1**. Fifty patients were enrolled and all completed the study. Areas treated included the abdomen (14 patients), the thighs (18 patients), the arms (8 patients), the buttocks (6 patients) and the ankles (4 patients). Except for the patients treated in the abdominal area, all the other patients had bilateral treatments at each session length. All patients were able to resume normal activities upon completion of the session. The median fat thickness reduction, measured by ultrasounds, at the end of the treatment was 6.2 cm for the abdomen, 6.3 cm for the thighs, 2.7 cm for the

Table 1. Characteristics of the Patients Enrolled in the Study

No.	Sex	Age	Weight (kg)	Height (cm)	Treatment Site	Perimetric Measurements (cm)	Subjective Evaluation	Cholesterol Levels (Before/After)
1	F	41	68	163	abdomen	92 /86 reduction 6	4	118/194
2	F	42	65	160	abdomen	84/79 reduction 5	5	199/200
3	F	48	70	168	abdomen	88/82 reduction 6	4	176/180
4	M	47	89	178	abdomen	106/98 reduction 8	5	180/181
5	F	51	58	155	abdomen	84/80 reduction 4	4	119/200
6	M	36	80	174	abdomen	96/89 reduction 7	5	186/190
7	M	44	84	180	abdomen	92/84 reduction 8	5	197/199
8	F	36	81	169	abdomen	94/89 reduction 5	4	167/168
9	M	21	76	177	abdomen	92/87 reduction 5	4	195/200
10	M	45	88	183	abdomen	108/98 reduction 10	5	185/184
11	M	45	67	166	abdomen	88/81 reduction 7	5	190/196
12	M	43	79	173	abdomen	100/92 reduction 8	5	176/180
13	M	43	72	166	abdomen	102/93 reduction 9	5	165/170
14	M	55	76	170	abdomen	99/91 reduction 8	5	197/199
15	F	62	65	156	tights	90/84 reduction 6	5	173/180
16	F	43	75	170	tights	90/83 reduction 7	5	198/201
17	F	40	74	167	tights	96/88 reduction 8	5	169/170
18	F	36	68	164	tights	94/88 reduction 6	5	186/188
19	F	42	74	180	tights	88/84 reduction 4	4	172/175
20	F	38	81	169	tights	102/96 reduction 6	5	187/188
21	F	47	77	171	tights	100/96 reduction 4	4	199/201
22	F	43	60	162	tights	92/86 reduction 6	5	187/189
23	F	35	75	172	tights	95/90 reduction 5	4	176/179
24	F	45	66	161	tights	95/88 reduction 7	5	189/198
25	F	39	74	165	tights	100/92 reduction 8	4	189/193
26	F	57	65	158	tights	99/90 reduction 9	5	200/202
27	F	34	54	160	tights	90/84 reduction 6	5	176/180
28	F	37	60	159	tights	91/84 reduction 7	5	196/199
29	F	45	64	159	arms	34/32 reduction 2	4	175/179
30	F	29	59	164	arms	36/33 reduction 3	5	192/196
31	F	37	70	162	arms	40/36 reduction 4	5	182/187
32	M	49	71	167	arms	37/34 reduction 3	5	197/199
33	M	44	70	172	arms	33/31 reduction 2	4	196/199
34	M	38	78	170	arms	36/33 reduction 3	4	182/189
35	F	50	55	154	arms	34/32 reduction 2	5	187/189
36	F	32	63	164	arms	36/33 reduction 3	5	198/200
37	F	37	70	162	buttocks	88/82 reduction 6	5	190/201
38	F	41	64	166	buttocks	90/85 reduction 5	4	190/198
39	F	38	69	163	buttocks	86/81 reduction 5	5	174/178
40	F	38	62	157	buttocks	83/79 reduction 4	4	188/200

(Table 1) Contd…..

No.	Sex	Age	Weight (kg)	Height (cm)	Treatment Site	Perimetric Measurements (cm)	Subjective Evaluation	Cholesterol Levels (Before/After)
41	F	52	68	161	buttocks	88/81 reduction 7	5	198/202
42	F	36	60	156	buttocks	82/79 reduction 3	4	140/143
43	F	33	60	160	ankles	28/27 reduction 1	4	178/186
44	F	27	58	154	ankles	27/25 reduction 2	5	148/152
45	M	47	82	179	ankles	30/26 reduction 4	5	174/178
46	F	31	65	161	ankles	29/27 reduction 2	4	194/200
47	F	33	70	166	tights	58/55 reduction 3	4	180/177
48	F	44	63	159	tights	56/53 reduction 3	5	201/209
49	F	51	67	160	tights	58/54 reduction 4	5	145/145
50	F	46	71	160	tights	62/57 reduction 5	5	152/156

arms, 5 cm for the buttocks and 2.2 cm for the ankles. Final reduction of fat thickness was significant when compared to the measurement prior to the treatment ($Z=-5.384$, $P<0.0001$). The greatest reductions were observed in the thighs and in the abdomen, while the ankles showed the lowest reduction. There was no statistical difference in fat thickness reduction between men and women. Interestingly, patient weight remained constant over the treatment in all patients, strongly suggesting that the fat thickness reduction was due to the treatment. Improvements in body contour were visibly appreciable in all patients at the end of the treatment, as supported also by the data from the subjective evaluations, that showed always a clear satisfaction in all the patients treated with a score of 4 or 5. In Fig. (**1**) an example of body contouring is depicted, while in Fig. (**2**) a representative ultrasound image pair, showing fat thickness before and after treatment of the abdomen is shown. Cholesterol levels were mildly increased after the treatments, but remained within normal limits, as depicted in Table **1**. Consistently, evaluation of the markers with hepatic functions (GOT, GPT, GT range) demonstrated no alterations in the hepatic functions (data not shown). Finally, no severe adverse events were reported during and after the completion of the procedures; in particular no paresthesias, haematomas, ecchymoses, or oedema were noted or reported. Nevertheless, mild adverse events, such as edema and redness, itching, bruising and tenderness were noted.

To further characterize the nature of the injury to the subcutaneous layer of ultrasonically treated skin, histopathological analysis of an area of the abdomen of a patients treated with ultrasounds was performed and compared to another untreated area of the abdomen of the same patient. Biopsies were taken 5 days after completion of the treatment, as specified in the method section. The histological analysis, indeed, showed adipocyte lysis with loss of membranes of adjacent cells creating holes in the treated skin specimen. Connective tissue, blood vessels and nerves had no observable damage by haematoxylin and eosin and Van Gieson trichromic staining techniques. To note, no signs of tissue repair were visible, such signs of a response to an injury would be tissue-necrosis, extravasation of erythrocytes, the infiltration of neutrophils lymphocytes and macrophages and

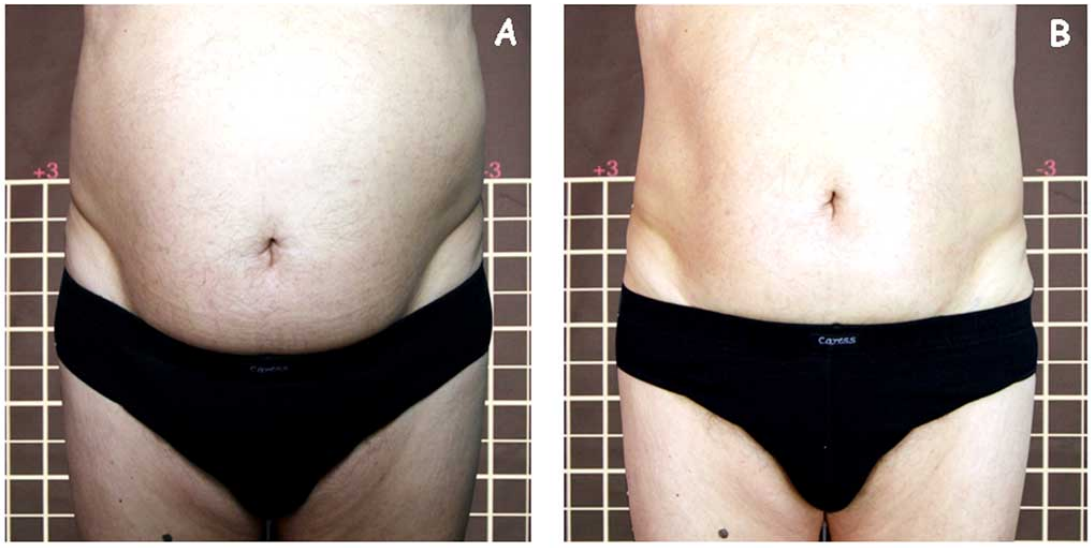

Fig. (1). Abdomen (**A**) before treatment and (**B**) after treatment.

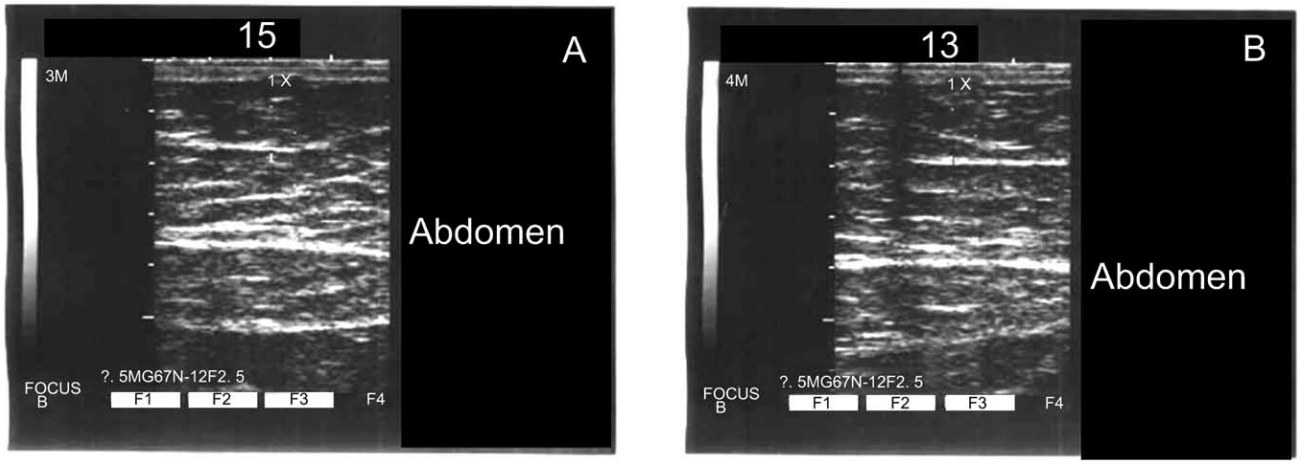

Fig. (2). Fat thickness assessment by ultrasound before (**A**) treatment and after (**B**) treatment, shows thinning of the subcutaneous fat layer from 15 mm to 13 mm (reduction of 2 mm). This patient was treated on the abdomen.

the subsequent scar-formation. Logically, in the untreated skin specimen, all tissue components remained intact. In Fig. (**3**) the histological pattern of treated and untreated skins is depicted.

DISCUSSION

Our clinical study shows that *Proslimelt* ultrasound system is safe a defective in body contouring. Ultrasound is applied externally and transmitted through the skin to the subcutaneous fat, where it is adsorbed. In particular, this procedure reduced significantly the circumference in the treated areas. This reduction was caused by a reduction in fat thickness, as assessed by ultrasound measurement. Interestingly, the reduction in fat thickness could not be ascribed to weight loss, since no statistically significant weight reduction was observed in any of the patients treated. Concerning to the fat released from the treated adipocytes, it is important to underline the fact that no clinically significant modifications were registered at the endo of the treatment protocol in any of the known metabolic pathways of fat metabolism monitored in this study. Indeed, it is well known that the body is able to move water-insoluble fat. Future studies are undergoing in order to characterize at the biochemical level this phenomenon. Nevertheless, it would be interesting to assess the direct effect of the diet on distribution of the fat. To this end, a new treatment protocol has been designed, in which circumferences will be determined also an un-treated areas of the body. One of the most important aspects that distinguishes ultrasound-assisted liposuction from other methods of liposuction is the much less numerous drawbacks respect to the surgical procedures. Indeed, the procedure described was well tolerated. The great majority of the patients treated reported that they experienced minimal or no discomfort during or after the procedure. Physical examination and laboratory assessment throughout the study period showed no clinically significant changes. In particular, no paresthesias, haematomas, ecchymoses, or oedema were noted, neither hyper-pigmentation or hypo-pigmentation was reported. Moreover, cholesterol levels were mildly increased after the treatments, but remained within normal limits and assessment of hepatic function revealed no changes in markers of liver functions (GOT, GPT, G-GT range), thus suggesting that fat released from treated areas was cleared by the natural fat metabolism pathways. Histopathological analysis of treated areas confirmed that with ultrasound-assisted liposuction there is a better preservation of the anatomical

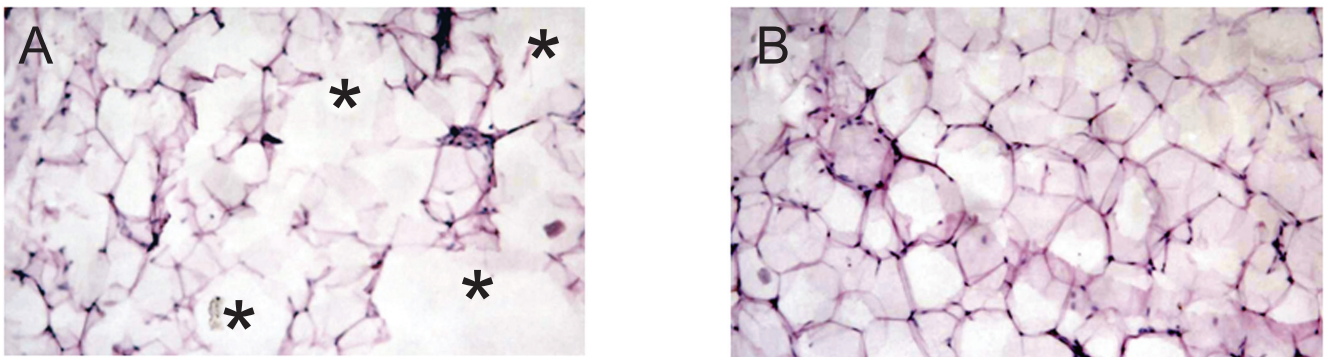

Fig. (3). Histopathology of skin and of subcutaneous fat tissue, taken five days after the ultrasound treatment. One characteristic and representative slide taken from the central part of the skin-sample (**A**) and a corresponding slide (control) of the not treated skin-sample (**B**) are depicted. While intact fat cells are observed in the untreated control, fat damage is detected in the ultrasound-treated samples, where selective adipocytes disruption (indicated by asterisks) is observed (Haematoxylin and Eosin staining, original magnification X20).

structures. In fact, connective tissue, blood vessels and nerves had no observable damage by haematoxylin and eosin and Van Gieson trichromic staining techniques. On the other hand, a cell-type selectivity was noted concerning the effects of the ultrasounds, with damages clearly visible only at level of adipocyte, that displayed loss of membranes of adjacent cells with creation of holes.

We conclude that ultrasound-assisted liposuction using the *Proslimelt* apparatus is a safe, effective, and well-tolerated non-invasive procedure for body contouring. In particular, we believe that this could be an ideal non-invasive alternative to conventional liposuction for patients who would require only small or moderate amounts of adipose tissue removal or are not suitable for surgical approaches to body contouring. Further studies are required to assess whether serial treatments would produce incremental fat reduction and whether greater fat reduction could be achieved through various treatment combinations, in conjunction with weight loss strategies or other aesthetic technologies to treat obesity related fat depots.

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