

Safety and Efficacy of a Noninvasive 1,060-nm Diode Laser for Fat Reduction of the Flanks

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BACKGROUND Preliminary reports indicate a hyperthermic diode laser treatment could be a safe and effective method for noninvasive fat reduction using the 1,060-nm wavelength. This wavelength penetrates the skin to heat subcutaneous adipocytes causing cellular disruption, leaving extracellular lipids, and cellular debris to be evacuated naturally by the body.

OBJECTIVE To evaluate the safety and effectiveness of this modality for noninvasive fat reduction of the flanks.

MATERIALS AND METHODS Forty-nine subjects received single laser treatment to 1 flank. Ultrasound images were taken at baseline, follow-up at 6 and 12 weeks after treatment. High-resolution photographs were taken at baseline and 12 weeks after treatment and then evaluated by independent reviewers. Adverse events recorded at all visits. Subjects completed a satisfaction questionnaire at the conclusion of the trial.

RESULTS Ultrasound images showed statistically significant ($p < .001$) average fat reduction of 2.6 ± 1.1 mm. Reviewers correctly ordered photographs 90.3% of the time. Ninety-six percentage of subjects rated that they were satisfied. Noted side effects were transient mild to moderate tenderness which subsided within 1 to 3 weeks; no serious adverse events were reported.

CONCLUSION The hyperthermic 1,060-nm diode laser treatment used in this study was safe and effective for noninvasive fat reduction of the flank.

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The achievement of a more aesthetically pleasing silhouette has been a desire of men and women throughout the ages, so as technology has evolved, demand for body contouring procedures has evolved with it.¹ For individuals with localized areas of unwanted fat such as the thighs, flanks, or abdomen, liposuction has been the standard,² and thus is the most commonly performed body contouring procedure.³

Although dramatic clinical improvement can be achieved with surgery, there is considerable associated postoperative recovery and monetary expense.⁴ Noninvasive or minimally invasive procedures with quick postoperative recovery and a low side-effect

profile are considered ideal by many patients if the quality of the outcome is visible. Alternative modalities for localized fat destruction⁵ include lasers,⁶ high-intensity-focused ultrasound (HIFU),⁷⁻⁹ radio-frequency (RF) devices,¹⁰ and selective cryolysis.¹¹⁻¹³

Decreases in fat layer thickness with these technologies occur gradually over the 3 months following treatment and is most pronounced in patients with limited, discrete fat bulges.¹⁴ Histological findings from both human and animal studies show that the reduction of fat tissue occurs gradually. With selective cryolysis, precise application of cold temperatures triggers apoptosis, inducing an inflammatory response resulting in mobilization of macrophages^{10,15} which engulf and

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digest disrupted adipocytes.^{11,16–19} Reduction in subcutaneous fat is accomplished without injury to adjacent tissues. Animal and human data indicate that cryolipolysis has no effect on serum lipid profiles or liver tests.^{19–25}

The 1,060-nm wavelength is highly efficient in delivering laser energy through the skin to the subcutaneous target. Its low affinity for melanin also makes it safe to treat dark skin as demonstrated in this study. High-penetration depth in fat as compared with other wavelengths in the visible to infrared wavelengths creates heat over a larger volume without creating hot spots. The skin is further protected by contact cooling at 15°C during treatment.

Hyperthermia is known to cause catastrophic adipocyte damage, and previous investigation has also shown that hyperthermic temperature can be achieved and maintained in subcutaneous adipose tissue by a 1,060-nm laser in conjunction with surface cooling.^{26,27} Elevation of tissue temperature to within the range of 42 to 47°C is proposed to result in adipocyte injury and eliciting an inflammatory response.¹⁰ The amount of tissue damage can be quantified by the relationship between exposure time and tissue temperature, calculated using the Arrhenius equation.²⁸ With even a moderate increase in temperature (5–10°C above normal), the structural integrity of the lipid bilayer is compromised, given adequate exposure time; damage to cell membranes is evident after only 5 minutes at 45°C.^{10,29,30} At temperatures greater than 43°C, cell death due to hyperthermia is significantly increased, especially when combined with radiation and various cytostatic drugs by sensitization.^{31,32} Earlier studies have also demonstrated the deleterious effect of mild hyperthermia on adipocytes. Moussa and colleagues³⁰ demonstrated the loss of structural integrity of the lipid bilayer of cell membranes by elevating temperatures 6°C above normal (i.e., 43°C). Work by Gaylor²⁹ evidenced that damage to cell membranes occurs when heated to 45°C for more than 5 minutes. Hyperthermically disrupted adipocytes and other cellular debris are removed through the body's natural mechanisms, beginning with induction of inflammation stimulating macrophage mobilization to remove cellular debris.^{10,27}

Studies by Decorato and colleagues have showed that a hyperthermic treatment on adipose tissue raises the tissue temperature to 42 to 47°C over tens of minutes can induce adipocyte injury. In that study, a series of histology were taken up to 6 months after treatment and demonstrated the sequence of tissue response to the injury. Inflammatory changes in adipose tissue were evident within 1 week. The inflammation continued to intensify through 1 month with evidence of phagocytosis. The clearing process last 3 to 6 months after treatment and the volume of fat in treated areas therefore decreased over time.²⁷

This 1,060-nm diode laser device was FDA approved for hyperthermic noninvasive fat layer reduction under the tradename SculpSure (Cynosure, Inc., Westford, MA) in January 2015. Up to 4 treatment heads may be used at 1 time with the current device.

The purpose of this prospective, controlled study was to evaluate the safety and efficacy of the hyperthermic 1,060-nm diode laser therapy for noninvasive fat reduction of the flanks.

Patients and Methods

This 2-center study was approved by an independent Institutional Review Board (New England IRB, Newton Centre, MA) and informed consent was obtained from all subjects. The inclusion criteria for the patient population consisted of healthy male and female volunteers of any Fitzpatrick skin Type (I–VI) aged between 20 and 65 years, presenting a body mass index (BMI) ≤ 30 with unwanted localized fat deposits in the flanks.

Exclusion criteria included photosensitivity or the use of photosensitizing medication; presence of a neuropathic disorder, impaired skin sensation, or diabetic neuropathy; active or localized systemic infection; presence of coagulation disorder or use of anticoagulant medication; previous treatment with parenteral gold therapy (gold sodium thiomalate); previous liposuction/liposculpture or similar procedure in the treatment area; history of keloids or evidence of compromised wound healing; history of squamous cell carcinoma or melanoma; immunosuppression/

immune deficiency disorders (including HIV infection or AIDS) or use of immunosuppressive medications; use or anticipated use of antiplatelet, anticoagulant, thrombolytic, or anti-inflammatory medications within 2 weeks before treatment; and the presence of any condition or situation which, in the opinion of the investigator, may represent significant risk to patient health, confound study results, or interfere with patient participation. Subjects were also excluded due to enrolment in an investigational drug or device trial, or use of an investigational drug/treatment with an investigational device, within 3 months before or concurrent with the study period, recent pregnancy (concurrent or within the past 3 months), and breastfeeding or planned pregnancy during the study period. Subjects were expected to refrain from tanning or any other activity which would result in excessive exposure to sunlight during the study.

In addition to standard health assessment and medical history, investigators determined the treatment area at baseline by assessing each patient's localized contouring needs. The exact area to be treated was delineated with a surgical marker using a template. Photographs and ultrasound images were taken of the study areas and each subject's weight was recorded.

The 1,060-nm diode laser device used in the study employs 4 applicator heads joined to create a rectangular zone of thermal radiation of approximately 140 or 35 cm² per applicator. Each applicator contains a water-cooled sapphire window which directly contacts the skin, keeping the skin cool at 15°C throughout the treatment. Treatment time is set at 25 minutes for all patients.

Subjects received a single treatment with the study device on 1 randomized flank. The opposite flank was left untreated as a control. Power density of the laser was 0.9–1.4 W/cm². Contact cooling was administered continuously during treatment. Initial power setting was 1.1 W/cm² and adjusted between 0.9 and 1.4 W/cm² based on subject comfort. The number of applicator heads (1–6) were adjusted to patient comfort and determined by the clinician based on the size and shape of the treatment target. Treatment comfort was recorded at all treatment visits using a 10-point

scale (0 = none to 10 = worst). Adverse events were assessed at each treatment and follow-up visit.

After treatment, aftercare instructions were reviewed with the subject. Patients were instructed to maintain their current weight and to not change their diet or exercise routine, clean the area daily with mild soap and water and pat dry, and not to rub or scratch the area. If a subject experienced any discomfort, the use of ice packs or acetaminophen was permitted, along with gentle massage of the treated area for 5 to 10 minutes daily to increase healing.

At 6 weeks after treatment, subjects were required to return for a follow-up visit at which ultrasound images were taken and adverse events were assessed, and a 12-week follow-up visit at which ultrasound images and photographs were taken, and adverse events assessed again; subjects also completed a satisfaction questionnaire at final follow-up. All subjects were invited to attend an optional 1-week follow-up visit to assess adverse events as well. Subject weight was measured and recorded before treatment and a 6- and 12-week follow-up.

The primary end point was photographic evaluation with correct identification of randomized pre-treatment images when compared with images taken at 12 weeks, performed by 3 independent, blinded, board-certified dermatologist reviewers. These expert evaluators each had relevant clinical experience (i.e., performed studies using other noninvasive fat reduction technologies) and attended a training session before assessment. Change from baseline in adipose layer thickness between device and control based on ultrasound measurements at baseline, 6 and 12 weeks was the secondary end point. Ultrasound imaging was performed using the Sonosite MicroMaxx (Sonosite, Bothell, WA) system (transducer HFL38/13-6MHz) on both treated and nontreated (control) flank at baseline and at the 6- and 12-week follow-up visits. The same technician performed the ultrasound recording on all patients using a standardized, validated technique to assure the consistent image capture. Change in thickness of the fatty layer at the 6- and at 12-week time points was calculated as compared with baseline. Normalized fat reduction was based on

TABLE 1. Demographics						
	All (N = 49)		Site 1 (N = 33)		Site 2 (N = 15)	
Age						
Average, yrs	46.1 ± 9.6*		45.0 ± 10.1		48.3 ± 8.3	
Range	25–61		25–61		34–59	
BMI						
Average	26.4 ± 3.05		26.59 ± 3.30		26.00 ± 2.50	
Range	21.6–35.0		21.6–35.0		22.1–30.9	
	All (N = 49)		Site 1 (N = 33)		Site 2 (N = 15)	
	No.	%	No.	%	No.	%
Sex						
Male	7	14	6	18	1	6
Female	42	86	27	82	15	94
Racial demographics						
Caucasian	29	59.2	16	48.5	13	81.3
African American	8	16.3	8	24.2	0	0
Hispanic	8	16.3	5	15.2	3	18.8
Indian	2	4.1	2	6.1	0	0
Asian	2	4.1	2	6.1	0	0
Fitzpatrick skin type						
I	4	8.1	2	6.1	2	13
II	9	18.3	5	15.2	4	25
III	19	39.0	10	30.3	9	56
IV	8	16.3	7	21.2	1	6
V	8	16.3	8	24.2	0	0
VI	1	2.0	1	3.0	0	0

*Average ± SD.
BMI, body mass index.

subtraction of the control value from the treated value. The tertiary end point was a Subject Satisfaction Survey taken at final follow-up (12 weeks), where subjects

rated satisfaction using a 6 point Likert scale (1 = extremely satisfied, 2 = satisfied, 3 = slightly satisfied, 4 = slightly dissatisfied, 5 = dissatisfied, and 6 =

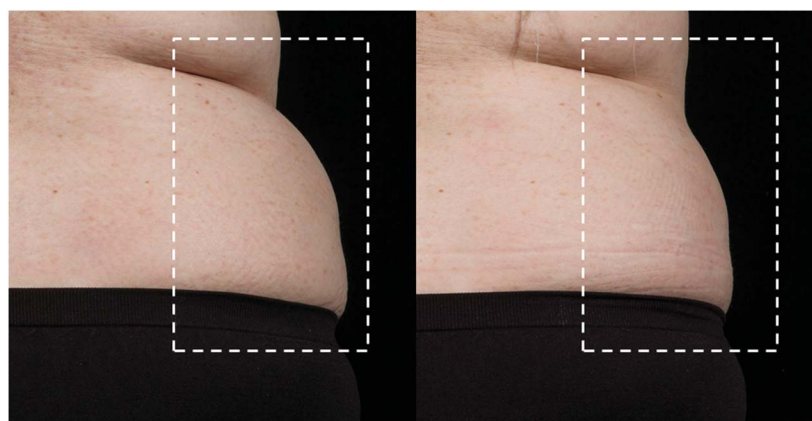


Figure 1. Right flank before and after treatment.

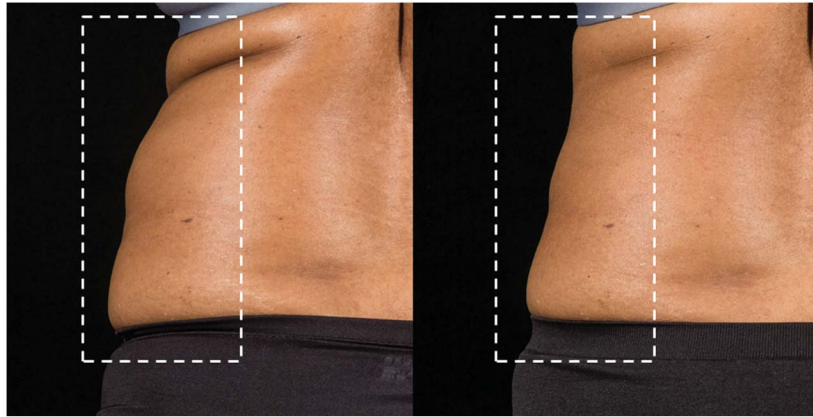


Figure 2. Left flank before and after treatment.

extremely dissatisfied) as detailed in Table 1; thus, a score ≥ 3 indicated subject satisfaction with treatment. Statistical significance was measured (when appropriate) using the standard paired *t*-test with the traditional cutoff of $p < .05$.

The 2 study centers enrolled a total of 49 subjects with an average BMI of 26.4, most of which were Caucasian (59.2%) and female (86%) (Table 1). Approximately 65% of subjects were Fitzpatrick skin Type I–III with the remainder classified as skin Type IV–VI (Table 1). At the 12-week time point, 43/49 (88%) returned for the final (Week 12) follow-up visit and were considered completed subjects. No subjects were withdrawn from the study due to an adverse event. At final (12 weeks) follow-up, 6 subjects had been withdrawn from the study; 4 were lost to follow-up, 2 were unable to attend the remaining scheduled visit, and 1 was excluded from the efficacy analysis due to substantial weight gain (37 lbs). As such, the efficacy analysis included 42 of 49 subjects. All 49 treated subjects were included in the safety analysis. None withdrew from the study or were discontinued due to an adverse event. A total of 15 subjects consented to

the optional 1 week adverse events follow-up visit, and these data were included in additional safety analysis. Before treatment, subjects had an average weight of 158.1 lbs (range 122–225 lbs). At the 12-week follow-up, the average weight was 155.3 lbs (121–238 lbs). Average change of weight from the baseline to the 12-week follow-up was 0.8 lbs (range –7 lbs to +13 lbs).

Results

Three blinded expert reviewers evaluating randomized baseline photographs and those taken at Week 12 were able to correctly order the post-treatment photographs 90% (114/126) of the time on average. Before and after photographs of selected patients are shown in Figures 1–3, each displaying improvement in contour regardless of weight changes at 12 weeks. Calculations based on ultrasound images showed average fat reduction (approximately $9\% \pm 5\%$) at 6 weeks after treatment ($n = 45$); average reduction on the control side was $1\% \pm 5\%$; and average normalized fat reduction was approximately 8%. At 12 weeks ($n = 42$), average fat reduction increased to $13\% \pm 6\%$; average reduction on the control side was $1\% \pm$

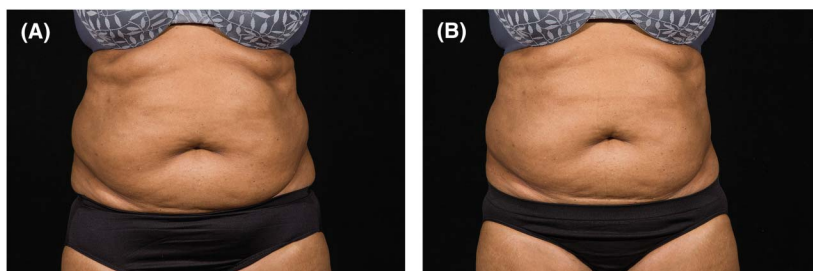


Figure 3. (A) Before left flank treated. (B) After left flank treated.

5%; and normalized fat reduction averaged approximately 13% from baseline (Table 2). Results were statistically significant ($p < .001$). Subjects were also broken into groups by age (Table 3), BMI (Table 4), and sex (Table 5). Results between the different age groups and the different BMI groups were found to not be statistically significant ($p > .05$). At the 12-week follow-up visit, 96% (41/43) of the subjects rated that they were satisfied (slightly satisfied, satisfied, or extremely satisfied) with their treatment on the Likert Satisfaction Scale (Table 6).

During the study, the number of applicator heads (1–6) and the power density of the laser (0.9–1.4 W/cm²) were variable. The number of applicator heads used ranged from 2 to 6, with 25 of 49 patients (51%) being treated with 5 applicator heads. Power density during the sustain phase ranged from 0.9 to 1.4 W/cm², with an average of 1.2 (± 0.1) W/cm².

Average overall discomfort during treatments was rated a 4 of 10 possible points (0 = none to 10 = high). The most common adverse event recorded among the 49 subjects in the safety analysis was treatment discomfort. Overall, most reported events (83%) were mild, and 17% of adverse events were reported as moderate. All adverse events were among those typical for laser treatments including transient edema, blistering, and erythema (resolving within 4–6 days); pain and bruising (resolving within 9–11 days); and subcutaneous nodules or hardness (resolving within 32–78 days) not interfering with daily activities or requiring surgical intervention. There were no reports of pinpoint bleeding, crusting, scabbing, itching, pustules, skin burns, scarring, infection, allergic reactions, hypopigmentation, and hyperpigmentation. No severe

TABLE 2. Fat Reduction Measurements for All Subjects

	Treated Side	Control Side	Normalized Reduction
Min	3%	–14%	–3%
Max	32%	6%	30%
Average	13%	–1%	13%
SD	6%	5%	6%

TABLE 3. Fat Reduction Among Age Groups

Age	N	% Fat Reduction
18 ≤ 39	10	12.1 ± 4.53
40 ≤ 49	11	11.4 ± 5.50
50 ≤ 55	10	14.3 ± 7.66
56 ≤ 65	11	15.8 ± 7.23

Fat reduction between age groups was not statistically significant (p -value $>.05$).

adverse events were reported. Safety results are summarized in Table 7.

Discussion

This study expands on the findings from a previous study by Decorato and colleagues²⁷ that established the ability of the hyperthermic laser device to (1) cause therapeutic adipocyte disruption safely and (2) effectively provide clinically relevant noninvasive fat reduction in vivo. The Decorato study also convincingly established by histology the mechanism by which outcomes were achieved (hyperthermia causing adipocyte disruption, with the resulting detritus cleared by the body’s natural waste removal processes over time) and demonstrated equivalency (albeit on a smaller scale) to a popular and effective noninvasive alternative (cryolipolysis). In that case, the treatment was well tolerated with neither evident skin damage nor significant changes in blood lipid or liver chemistry after treatment. Treatment time between 20 and 25 minutes was found to be optimal. At treatment times longer than 30 minutes, there was a reported risk of developing palpable nodules in subcutaneous fat. Laser treatment with time less than 20 minutes

TABLE 4. Fat Reduction Among BMI Groups

BMI	N	% Fat Reduction
21.0 ≤ 23.9	12	13.3 ± 5.34
24.0 ≤ 26.9	15	13.6 ± 6.76
27.0 ≤ 29.9	10	12.6 ± 7.57
30.0 ≤ 35.0	5	16.0 ± 6.96

Fat reduction between BMI groups was not statistically significant (p -value $>.05$).
BMI, body mass index.

TABLE 5. Results by Sex

	<i>Male</i>	<i>Female</i>
Subject satisfaction	100%	95%
Normalized fat reduction	7.7 ± 7.7%	14.2 ± 5.9%
Photographic evaluation	87%	91%

had minimal effect. The results of the current study seem to confirm previous results by Decorato.

A separate pilot clinical study demonstrated that hyperthermic lipolysis compared favorably with cryolipolysis in average fat reduction at 3 and 6 months after treatment.²⁷ Treatment was tolerable without analgesia or anesthesia. In addition to confirming the results of previous histology studies of hyperthermic adipocyte disruption, the device was demonstrated equivalent to cryolipolysis at both 3- and 6-month follow-up visits. Histology revealed no obvious signs of damage immediately after treatment, but inflammatory response was noted at 5 to 7 days after treatment, with manifestation of damage beginning at approximately 14 days with further evidence at 1 month. Macrophage activity with increased fibrosis was noted within 2 to 3 months and to a greater degree at the 6 months time point. No signs of skin damage were present at any time, and extensive testing of lipid and liver chemistry revealed no appreciable changes. Lack of reported numbness indicated that local nerves were undamaged as well.

The 1,060-nm wavelength does not have a specific chromophore in the skin and, therefore, generates nonspecific heating and penetrates subcutaneously to

cause photomechanical and photothermal effects with very limited downtime.³³ Properly harnessed, the 1,060-nm wavelength heats the fat layer in a controlled manner and distributes the heating more evenly over a broad zone than higher wavelengths with good small vessel coagulation.^{26,34} Previous investigation has also shown that hyperthermic temperature can be achieved and maintained in subcutaneous adipose tissue by a 1,060-nm laser in conjunction with surface cooling²⁶ as was shown in studies of hyperthermia-induced tissue damage studies and ex vivo temperature measurements.^{10,29,30}

Other treatments that depend on heat destruction of adipose tissue include ultrasound³¹ and RF.¹⁰ With HIFU, the temperature quickly reaches 56°C and has been reported to rapidly raise tissue temperature above 70°C,^{35,36} which is effective in coagulative necrosis of the adipocytes and subsequent reduction of the fat layer, suggesting the potential to cause nonselective instantaneous cell necrosis at the designated target.^{7,36} The high temperature required in HIFU modality can cause pain and often requires analgesia. The moderate temperature rise in the 1,060-nm design makes the treatments much tolerable with pain score of 4 of 10 as demonstrated in this study.

Radiofrequency technology utilizes the resistance (impedance) of the tissue itself to generate heat rather than directly transferring heat energy through light waves. Because adipocytes have high-tissue resistance and low-heat transfer coefficients, they generate significant heat when RF energy is passed through the

TABLE 6. Satisfaction

		<i>Subject Satisfaction</i>					
		<i>All</i>		<i>Site 1</i>		<i>Site 2</i>	
	<i>Score</i>	<i>N = 42</i>	<i>%</i>	<i>N = 27</i>	<i>%</i>	<i>N = 15</i>	<i>%</i>
Extremely satisfied	1	14	32.6	7	26	6	40.0
Satisfied	2	23	53.5	17	63	6	40.0
Slightly satisfied	3	4	9.3	3	11	1	6.7
Slightly dissatisfied	4	1	2.3	0	0	1	6.7
Dissatisfied	5	0	0.0	0	0	0	0.0
Extremely dissatisfied	6	1	2.3	0	0	1	6.7

TABLE 7. Adverse Events at 2 Study Centers

Adverse Events at 2 Study Centers: N = 49 Subjects								
Event	Total # of Subjects	Occurrence %	# Subjects			Duration, d		
			Mild	Moderate	Severe	Average	Min	Max
Edema	4	8	4	0	0	6.0	2	9
Bruising	1	2	1	0	0	11.0	—	—
Discomfort	36	71	28	8	0	9.0	1	31
Blistering	1	2	1	0	0	4.0	—	—
Nodule	6	12	6		0	78.0	38	138
Hardness	3	6	3	0	0	32.0*	4	77
Erythema	2	4	2	0	0	1.5	1	2
			85%	15%	0%			

*One instance of hardness at Dr. Katz is reported as ongoing.

tissue while limiting the diffusion of heat to surrounding tissue structures.³⁷

Based on the susceptibility of lipid-rich adipocytes to cold injury when compared with surrounding water-rich cells, cryolipolysis employs transcutaneous cooling of the target tissue to very low temperatures to induce a slow lysis of adipocytes. This phenomenon was established in a study on pigs which showed damage to subcutaneous fat without damage to the overlying skin.^{11,18,19} The treatment has applicators designed to extract energy (cooling) from the underlying fat tissue. The applicator cup uses vacuum pressure to draw the tissue between the cooling panels. During the procedure, the applicator delivers precisely controlled cooling conditions that have been proven to target and eliminate fat cells in specific areas of the body. Fat cells are crystallized during this process, and they trigger a process of natural removal that gradually reduces the thickness of the fat layer.¹⁹

The results of this study suggest that this 1,060-nm laser system is useful for subcutaneous fat reduction. Laser technology can be easily adapted to different sized and shaped treatment heads with relatively little effort. The benefits of this 1,060-nm laser system include the hands-free flexible applicator system which allows treatment of up to 4 anatomical areas at 1 time and the relatively short treatment time of

25 minutes. There were also no significant adverse events and no downtime. A limitation of this device is the small amount of fat removed at each session. This is true of most of the noninvasive fat reduction technologies and patients should have realistic expectations of the limited amount of fat they can expect to have removed. A second treatment with the 1,060-nm laser 6 weeks later may produce better results. The efficacy of this device depends on laser energy being safely transmitted through the skin into the subcutaneous tissues. Therefore, the water-cooled sapphire windows have to be in contact with the skin surface at all times. Fortunately, there is a safety feature that stops the laser from firing if contact with the skin is lost. This reduces the risk of burns.

Conclusion

The results of this prospective controlled trial indicate that the 1,060-nm hyperthermic laser treatment is safe and effective for noninvasive fat reduction of the flank.

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