# Cryotherapy Induced Lipolysis: A Review by Dr Saad Sami Al Sogair **Abstract** Cold based therapies have been used on skin in the past due to their minimal damage of skin tissues. Cryolipolysis is a type of non-invasive body contouring technology that makes use of the ability of cold applications to create an inflammatory reaction within adipose tissues which may later on lead to apoptotic adipocyte cell death. Human and animal studies have revealed that cryolipolysis can significantly decrease subcutaneous fat and change body contour without causing damage to the overlying skin and surrounding structures or deleterious changes in blood lipids. Cryolipolysis has been described as a safe and effective procedure by previous studies. A thorough medical history and physical examination is done prior to the performance of this method to ensure its optimal efficacy. This method can either be used alone or in combination with other treatments such as shock wave treatment. More studies should be done to investigate further how cryolipolysis leads to adipocyte apoptosis so that new methods may be discovered that may enhance subcutaneous fat reduction. Dr Saad Sami Al Sogair is a Board certified Dermatologist and active speaking member of multiple international Aesthetic and Anti-Aging societies and academies including the Saudi Society of Dermatology and Dermatologic Surgery, the American Academy of Aesthetic Medicine and the American Academy of Anti-Aging Medicine. Dr Sogair has quickly established himself as an expert in Dermatology and Aesthetic Medicine and he is especially knowledgeable about Anti-Aging practices and Preventative Medicine. He takes pride in the quality of care provided in his clinic, Elite Derma Care, in Al Khobar, Saudi Arabia. 6 AJAM 2015 Official Journal of the American Academy of Aesthetic Medicine

### I. Introduction

Excess fat in the body has negative consequences. Not only does it affect physical appearance and self-esteem but it also makes a person prone to various life-threatening health problems such as hypertension, diabetes, atherosclerosis, heart disease and stroke. Excess fat can decrease a person's life span and can lower quality of life over the years. This is why numerous methods have been developed to manage fat in a non-invasive way and to contour the body.

Non-invasive body contouring technology is said to be the fastest growing segment of aesthetic medicine.<sup>1</sup> These technologies are in the form of suction or massage devices, thermal devices, radiofrequency energy devices, high-frequency focused ultrasound energy devices, low-level light laser therapy devices and cryolipolysis energy devices. Among these techniques, cryolipolysis is one of the most novel methods that uses cold exposure to reduce subcutaneous fat.

This review aims to discuss the origins of cryolipolysis as well as its safety and efficacy in subcutaneous fat reduction.

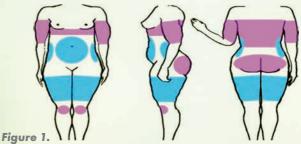
## II. History of Cryolipolysis

Cryolipolysis is a technique adapted from the older method cryotherapy, a method which has been used in dermatology since ancient times. Cold based therapies have been used on skin in the past due to their minimal damage of skin tissues. Cryotherapy has been employed in the destruction of superficial skin tumors, verrucae, actinic keratoses and other skin lesions. In 1902, Hoschinger reported on the sensitivity of adipose tissue to cold injury by observing an acute freezing reaction on firm nodules under the chin in young children. It was then in 1941 that Haxthausen published a case series of four young children and a teenager who had developed what he termed "adiponecrosis e frigore" or lesions that occur after exposure to cold. These lesions are created by cold induced panniculitis and appear as red indurated nodules with transient fat necrosis after exposure to cold. These findings have led experts to believe that fatty tissues are more susceptible to cold injury than other tissues. These results also conform to the fact that saturated fats are more solid at room temperature while less saturated fats are more liquid at room temperature. The colder it gets, the more solid saturated fats are.<sup>2</sup>

Thus the method of cryolipolysis became widely known afterwards. This method makes use of the ability of cold applications to create an inflammatory reaction within adipose tissues which may later on lead to apoptotic

adipocyte cell death. The cold stimulus applied is above the freezing point but below body temperature. Manstein et al have previously performed cryolipolysis experiments in pigs by using a copper plate that was cooled and regulated to -7 degrees Centigrade by an attached heat exchanger chamber. This plate was then applied to multiple sites in animals for about 5 to 21 minutes. The pigs were then observed after three and a half months. There were no significant skin changes observed; however there was selective fat absorption in the treatment sites as evidenced by contour indentations. There was also an observed 40% reduction in fat thickness and a reduction in distance between fat septae on histological examination. This study has led to human applications. The device was further developed into that consisting of a control console and an umbilical cable connecting the cooling applicator cup or paddles to the console. This device is to be applied on sites such as lower abdominal tissues or love handles so that mild suctioning can be done for about 30 to 60 minutes.1

In 2010, a cryolipolytic device (CoolSculpting®; ZELTIQ Aesthetics, Inc., Pleasanton, CA, USA) was given FDA clearance for reduction of flank and abdominal fat. In 2014, it received clearance for the treatment of subcutaneous fat in the thighs. This particular device is made up of a cup-shaped applicator with two cooling panels that is applied to the treatment area. Under moderate vacuum, tissue is drawn into the hand piece and the temperature is regulated by thermoelectric elements and controlled by sensors that monitor the heat flux out of the tissue. The area should be treated for 45 minutes and massage should be done for two minutes after each therapy to maximize effects. The patient is then discharged after treatment. The number of treatment cycles depends on the area being treated. While flanks require only one treatment session, the back and the inner and outer thighs require more than two treatment cycles. Treatment cycles are spaced eight weeks apart from each other.3



Indications cleared by the US Food and Drug Administration (blue) and off-label indications (pink) for cryolipolysis as mentioned in peer-reviewed publications (Clinical, Cosmetic and Investigational Dermatology 2014:7).

### III. Mechanism of Action

The exact way by which cold stimuli removes fat in tissues is quite unknown; however, earlier studies have described that the responsible mechanism would be the development of a perivascular inflammatory infiltrate consisting of histiocytes and lymphocytes about 24 hours after cold exposure. The infiltrate results in a lobular panniculitis and leads to rupture of the adipocytes aggregation of the lipids and the formation of small cystic spaces. This gradually resolves over the next few weeks, leading to reduction of fat with no tissue damage or scarring.4

In animal studies there was observed inflammation, damage to fat cells with phagocytosis of the adipocytes. After treatment, there may be no fat damage observed; however adipocyte damage may be evident after two days until the next month. Adipocyte apoptosis is said to stimulate the inflammatory infiltrate consisting of neutrophils and mononuclear cells. This infiltrate later on becomes denser as panniculitis develops. Inflammation appears

within 14 days following treatment wherein adipocytes are surrounded by lymphocytes, neutrophils, histiocytes and other mononuclear cells. The macrophages envelope and take in adipocytes that have undergone apoptosis, making the adipocytes decrease in size, and widening the fibrous septae of the fat layer. All these occur within the next 90 days and further explain the mechanism behind cryolipolysis.<sup>4</sup> Apoptosis may be due to possible cold-induced reperfusion injury of temperature-sensitive adipocytes, resulting in free radical damage, oxidative stress, and subsequent cell death.<sup>5</sup>

Zelickson et al in 2009 determined whether cryolipolysis can selectively damage subcutaneous fat without causing damage to the overlying skin or rise in lipid levels. In their study, three Yucatan pigs underwent cryolipolysis at 22 sites: 20 at cooling intensity factor (CIF) index 24.5 (43.8mW/cm²), one at CIF 24.9 (44.7mW/cm²), and one at CIF 25.4 (45.6mW/cm²). Results revealed that there was a significant reduction in the superficial fat layer without damage to the overlying skin. An inflammatory response triggered



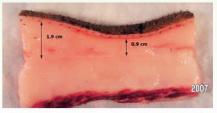


Figure 2.

Photographs of treatment areas from two animals in the Zelickson et al study showing skin surface contour changes three months after treatment (Dermatol Surg 2009;35:1462-1470).



Figure 3.
Gross pathology photograph showing an example of fat layer reduction responsible for the visible skin contour changes shown in Figure 2 (Dermatol Surg 2009;35:1462-1470).



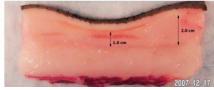


Figure 4.
Gross pathology sections showing reductions in superficial fat layer 90 days after treatment (Dermatol Surg 2009;35:1462-1470).

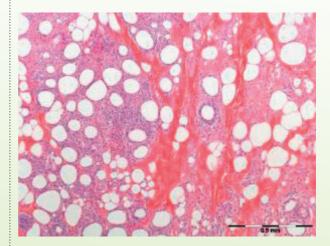


Figure 5.
The natural inflammatory response to cold exposure in one area treated (Dermatol Surg 2009;35:1462-1470).

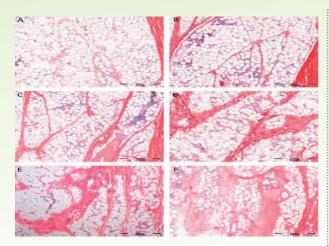


Figure 6. Progression of inflammatory response to cold exposure in tissue taken from pig D: (A) 3 days, (B) 7 days, (C) 14 days, (D) 30 days, (E) 60 days, (F) 90 days (Dermatol Surg 2009;35:1462-1470).

by cold-induced apoptosis of adipocytes preceded the reduction in the fat layer. Evaluation of lipids over a 3-month period following treatment demonstrated that cholesterol and triglyceride values remained normal. Thus it was noted by the researchers that cryolipolysis can significantly decrease subcutaneous fat and change body contour without causing damage to the overlying skin and surrounding structures or deleterious changes in blood lipids.6

Avram et al has described in detail the changes in the subcutaneous fat and in the adipocytes after cryolipolysis. They noted that immediately after treatment, there are no discernible changes in the subcutaneous fat without the presence of inflammatory cells and with intact cell membranes. Within three days after treatment, the inflammatory process brought about by apoptosis of adipocyte begins and peaks at about 14 days after treatment, during which the adipocytes are surrounded by histiocytes, neutrophils, lymphocytes, and other mononuclear cells. Within 14 to 30 days, there is phagocytosis of fat as macrophages and other phagocytes surround, envelope and digest the contents of dead adipocytes as a natural response of the body to injury. After 30 days, there may be a decrease in the inflammatory response with remarkable thickening of the interlobar septae and a decrease in fat cell volume. This decrease in inflammation further continues up to 90 days when the resorption of digested adipocytes takes place with displacement of lipids. There is also a clear reduction in fat layer thickness. Further studies are needed to ascertain the cause of the apoptotic injury of adipocytes.<sup>7</sup>

### IV. Pre-Clinical and Clinical Studies

One pilot pre-clinical study sought to determine the effects of cryolipolysis on fat using a single Yucatan pig exposed to a copper plate cooled to 7°C with circulating antifreeze solution. Firm pressure was used to ensure contact as well as to decrease perfusion, facilitating a more rapid rate of cooling. After three months, all ten sites demonstrated visible indentation with a measurable decrease in superficial fat layer thickness. The conclusions were further confirmed by a subsequent study with three swine which revealed a 30% reduction in the thickness of the superficial fat layer in the treatment area, as measured by ultrasonography. There was limited incidence of transient hyperpigmentation in these two studies that resolved within one week and there were no ulcerations or hypopigmentations noted nor significant changes in serum lipids or liver function.<sup>2</sup>

There were also in vitro studies on adipocyte cell cultures which have shown that cold-induced adipocyte apoptosis was responsible for cryolipolysis effects. Some studies have also implicated reperfusion injury of cryosensitized adipocytes, leading to inflammation, generation of reactive oxygen species, and cell death.<sup>2</sup>

	Posttreatment Day							
Lipid	7	28	59	89				
Cholesterol	Cholesterol							
Α	11.6	16.3	20.9	16.3				
В	- <i>7.7</i>	-23.1	0	-9.9				
С	5.6	5.6	0	7.4				
Low-density lipoprotein cholesterol								
A	16. <i>7</i>	72.2	50.0	50.0				
В	25.8	-51.6	0	16.1				
С	41.2	17.6	0	11.8				
High-density lipoprotein cholesterol								
A	40.0	-30.0	-5.0	-5.0				
В	-2.9	-20.0	0	-2.9				
С	7.7	-7.7	0	30.8				
Triglycerides								
A	-22.2	-14.8	3.7	-33.3				
В	-55.9	5.5	0	-52.8				
С	-53.7	16.7	0	-51.8				

Days for evaluation in Pig C were 8, 29, 59, and 90.

Table 1. Posttreatment changes in lipids from baseline in Pigs A to C (Dermatol Surg 2009;35:1462-1470).

Manstein et al was the first to perform initial exploratory studies of cryolipolysis in Yucatan pigs. In their article, they described the results of 3 different studies: an initial exploratory study, a dosimetry study, and a study of treatment effect on serum lipid levels. The initial exploratory study used a cold copper applicator, chilled by circulating antifreeze solution. The cooling device was maintained at a constant temperature of 7°C, and was applied to the Yucatan pig for times ranging from 5 to 21 minutes. The highest degree of clinical effect was noted in a treatment area on the buttock; 3.5 months after the single treatment, 80% of the superficial fat layer was removed (40% of total fat layer).<sup>4</sup>

A follow-up animal study was then performed by Zelickson et al. In this study, four pigs were treated with the cryolipolysis device. About 25%-30% of the total body surface of each animal was treated. Ultrasound assessments demonstrated a 33% reduction in the thickness of the superficial fat layer following cryolipolysis. Pathologic specimens revealed an approximate reduction of 50% in the thickness of the superficial fat layer. Erythema lasting approximately 30 minutes developed in treatment areas. The skin became cool, though not frozen, after treatment. There was no edema, bruising, purpura, or scarring observed in the trial. There were no significant variations in the lipid profiles of the animals throughout the study. In the above animal studies, the cryolipolysis treatments were well tolerated by the animals.<sup>4</sup> Clinical studies have also confirmed the efficacy of cryolipolysis for improvement in localized adiposity according to Jalian et al in 2013. These clinical studies have also demonstrated improvement in adiposity of the flanks, so-called "love handles," in 32 subjects. There was both subjective and objective improvement in adiposities. Ten subjects who underwent ultrasonography examination demonstrated a 22.4% average reduction of fat-layer thickness. A subsequent larger prospective study of 50 subjects confirmed this subjective improvement. All these data were made the basis by the Food and Drug Administration (FDA) clearance for cryolipolysis to be applied on non-invasive fat removal in the flanks. Later in 2012, cryolipolysis gained FDA clearance for use on the abdomen.<sup>2</sup>

Stevens et al in 2013 made a retrospective chart review on 528 consecutive patients who underwent cryolipolysis treatment (performed by L.K.P.) from January 2010 to December 2012. Over the study period, 1785 anatomic sites were treated with 2729 cycles (multiple cycles were often delivered to the same treatment site). Treatments were delivered primarily to the lower abdomen (28%, n = 490), upper abdomen (11%, n = 189), left flank (19%, n = 333), right flank (19%, n = 333), inner thigh (6%, n = 111), outer thigh (5%, n = 87), and back (6%, n = 99). The commercially available applicators used in the study period were the

CoolCurve (eZ App 6.2), CoolCore (eZ App 6.3), and CoolMax (eZ App 8.0). The review found that the typical side effects of cryolipolysis procedures reported in clinical studies include erythema, edema, bruising, and transient neuralgia. These were typically reported to resolve spontaneously within two weeks posttreatment.8

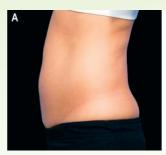




Figure 7.

(A) This 27-year-old woman was active and healthy before treatment but was concerned about fat in her lower abdomen. (B) Three months after cryolipolysis of the lower abdomen, the patient is shown with a weight change of +1 lb. over baseline (Aesthetic Surgery Journal 2013;33:835).





Figure 8.

(A) This 58-year-old woman was unhappy about her "bra rolls." (B) Three months after cryolipolysis treatment to the upper back, the patient is shown with no weight change since baseline (Aesthetic Surgery Journal 2013;33:835).

#### V. Candidates

Patient selection is important in any procedure. This is why a thorough medical history and physical examination is done prior to any procedure. Areas with focal adiposity should be lifted from the underlying musculature and examined. There should be a sufficient fat layer, otherwise the device may not attach correctly with the vacuum applicator. Patients with hernias should be excluded, as there may be a potential for hernia incarceration with the vacuum suctioning in these patients. Contraindications for this procedure include cold-sensitive disorders, including Raynaud's phenomenon,

cold urticaria, cryoglobulinemia, and paroxysmal nocturnal hemoglobinuria. Caution should also be exercised in those with known neurologic disease (e.g. multiple sclerosis) since there are temporary neurologic effects.<sup>2</sup>

Good candidates for cryolipolysis are those within their ideal weight range and those who engage in regular exercise, eat a healthy diet, have noticeable fat bulges on the trunk, are realistic in their expectations, and are willing to maintain the results of cryolipolysis with a healthy, active lifestyle.<sup>3</sup>

# VI. Safety and Adverse Effects

Immediately after treatment, there may be edema and erythema which may persist for up to 72 hours. There may also be ecchymosis secondary to the vacuum applicator especially in those who are on anticoagulation medications. There may also be a decreased cutaneous sensation, which is common yet transient, as well as dysthesia which may be transient, only lasting

for a week. However, in very few patients, this decrease in sensation may continue up to two months. There were no reports of permanent sensory alteration after cryolipolysis treatment. There were also no reports of significant changes

Figure 9.

Post-treatment erythema of the abdomen immediately after cryolipolysis treatment. Erythema is confined to the treatment area and is visible immediately after removal of the device applicator (Semin Cutan Med Surg 31:121-125).

Analyte			Ti	me					
(units) [reference range]	Baseline	1 day	1 week	4 weeks	8 weeks	12 weeks	P-value		
Cholester	Cholesterol (mg/dl) [125–200]								
Mean	173.3	171.2	174.4	172.1	175.2	177.1	0.6286		
Std dev.	23.1	27.3	23.8	25.7	25.9	26.5			
Ν	39	30	28	39	38	38			
Tryglyceri	ides (mg/	dl) [<150	]						
Mean	82.1	84.7	93.4	90.8	92.6	93.2	0.2218		
Std dev.	30.3	45.9	37.2	44.8	47.5	40.0			
Ν	39	30	28	39	38	38			
HDL chole	sterol (m	g/dl) [≥4	6]						
Mean	67.0	64.4	63.3	64.0	66.3	66.7	0.0296*		
Std dev.	11.4	10.6	12.0	11.9	12.4	11.6			
Ν	39	30	28	39	38	38			
LDL chole	sterol (ca	lc) (mg/d	l) [<130]						
Mean	89.8	89.8	92.4	89.9	90.4	91.8	0.9903		
Std dev.	18.9	21.6	20.8	20.4	21.6	23.7			
Ν	39	30	28	39	38	38			
VLDL cholesterol (mg/dl) [5–35]									
Mean	16.5	1 <i>7</i> .1	18.6	18.2	18.5	18.6	0.2987		
Std dev.	6.0	9.2	7.6	9.0	9.5	8.1			
Ν	39	30	27	39	38	37			

<sup>\*</sup>A P-value < 0.05 is considered statistically significant.

**Table 2:**Mean serum lipid values (Lasers in Surgery and Medicine 2009;41:785-790).

in triglyceride levels or liver function tests in humans after treatment. Rarely, there may be severe pain after treatments which may be shooting and stabbing in character and may last for about a week. This may be controlled by oral or topical analgesics and may resolve spontaneously within one to four weeks.<sup>2</sup>

Coleman et al in 2009 studied the clinical efficacy of non-invasive cryolipolysis and its effects on peripheral nerves. In their study, ten subjects were treated with a prototype cooling device. Cryolipolysis resulted in a normalized fat layer reduction of 20.4% at two months and 25.5% at six months after treatment. Transient reduction in sensation occurred in six of nine subjects assessed by neurologic evaluation. However, all sensation returned by a mean of 3.6 weeks after treatment. Biopsies showed no long-term change in nerve fiber structure. There were no lasting sensory alterations or observations of skin damage in any of the subjects evaluated. These side effects were all modest reversible short-term changes in the function of peripheral sensory nerves. 9

Analyte	Time							
(units) [reference range]	Baseline	1 day	1 week	4 weeks	8 weeks	12 weeks	P-value	
AST-SGOT (U/L) [10-30]								
Mean	19.2	18.1	20.2	20.1	19.4	19.6	0.8101	
Std dev.	5.5	5.3	12.3	8.6	6.6	6.6		
N	39	28	28	39	39	38		
ALT-SGPT	ALT-SGPT (U/L) [6-40]							
Mean	1 <i>7</i> .1	15.4	15.9	16.1	16.2	15.9	0.9368	
Std dev.	6.6	5.2	6.1	5.9	6.9	6.4		
Ν	39	28	28	39	39	38		
Alkaline F	Phosphate	ase (U/L)	[33-115]					
Mean	56.0	55.3	57.5	55.6	55.3	57.1	0.5264	
Std dev.	15.3	18.7	15.1	17.0	14.9	17.0		
Ν	39	28	28	39	39	38		
<b>Total Bilir</b>	ubin (mg/	/dl) [0.2-1	.2]					
Mean	0.7	0.6	0.6	0.6	0.7	0.7	0.4119	
Std dev.	0.2	0.2	0.2	0.2	0.3	0.3		
Ν	39	28	28	39	39	38		
Albumin (g/dl) [3.6-5.1]								
Mean	4.5	4.4	4.4	4.4	4.5	4.4	0.4792	
Std dev.	0.3	0.2	0.2	0.3	0.2	0.2		
Ν	39	28	28	39	39	38		

**Table 3:**Mean serum liver test values (Lasers in Surgery and Medicine 2009;41:785-790).

Klein et al in 2009 studied whether cryolipolysis affects serum lipid levels or liver function tests. Forty subjects with fat bulges on their flanks ("love handles") were treated bilaterally with a non-invasive device (Zeltiq Aesthetics, Pleasanton, CA) that precisely cools tissue to achieve a reduction in the fat layer. Serum lipid levels and liver tests were measured prior to treatment, and at day one and one, four, eight and twelve weeks post-treatment. There were no meaningful changes in mean values for any blood lipid level or liver test at any point over the 12-week follow-up period.<sup>10</sup>

Brightman et al hypothesized that a second treatment given before completion of apoptosis of cells could lead to greater inflammatory response and a greater reduction in fat over the long term. Greater reduction in fat is also dependent on other factors such as appropriate patient selection, reasonable expectations and technique. Appropriate candidates for this technique are those who are generally fit with localized and persistent fat pockets which cannot be reduced by diet and exercise. This procedure is not suitable for people who want to reduce large volumes of fat and individuals who have

Cryolipolysis has been described as a safe and effective procedure by previous studies. Animal models were able to prove a reduction of up to 1cm or 40% of the total fat layer thickness after a single exposure without harming the overlying skin. A study by Manstein et al has demonstrated changes such as lipid-laden mononuclear inflammatory cells and local thickening of fibrous septae at two weeks post-procedure. In another study in 2009 described by Nils et al, ten subjects reported a 20.4% and 25.5% reduction in the fat layer two months and six months after treatment, respectively. One retrospective multicenter study has reported that 86% of 518 subjects showed improvement after cryolipolysis. The body sites at which cryolipolysis were most effective were the abdomen, back, and flank. Patients completed a satisfaction questionnaire, with 73% reporting being satisfied and 82% being prepared to

recommend cryolipolysis to a friend. The majority described minimal to tolerable discomfort during the procedure. Another study by Garibyan et al used a three-dimensional camera to evaluate the amount of fat loss after cryolipolysis. Mean fat loss between baseline and the 2-month follow-up visit was  $56.2\pm25.6$ cc on the treated side and  $16.6\pm17.6$ cc on the control side. Two months post-treatment, the mean difference in fat loss between the treated and untreated sides was 39.6cc. In another study by Ferraro et al, cryolipolysis was combined with acoustic waves to achieve possible synergistic effects. These authors reported significant reductions of up to 6.7cm in circumference and up to 4.5cm in thickness of the fat layer 12 weeks after 3-4 treatments.

Nils et al also noted that several publications including two systematic literature reviews have failed to identify any significant adverse events that could be attributed to cryolipolysis, including scarring, ulceration, or disfigurement. Although cold temperatures are known to induce subcutaneous panniculitis, no cases of nodule formation have been reported.<sup>3</sup>

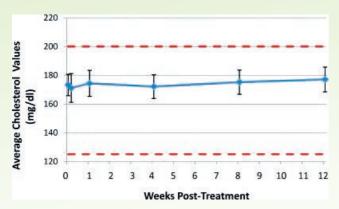


Figure 10.

Plot of mean cholesterol values reveals no significant change over time. Mean values their 95% confidence interval (denoted by the error bars) remain within the reference range (shown as dashed lines) (Lasers in Surgery and Medicine 2009;41:785-790).

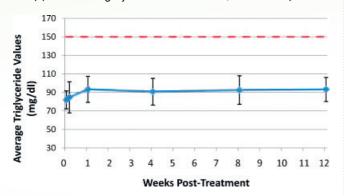


Figure 11.

Plot of mean triglyceride values reveals no significant change over time. Mean values their 95% confidence interval (denoted by the error bars) remain well below the upper limit of the reference range (shown as a dashed line) (Lasers in Surgery and Medicine 2009;41:785-790).

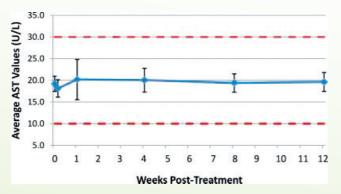


Figure 12.
Plot of mean AST values reveals no significant change over time.
Mean values their 95% confidence interval (denoted by the error bars) remain well within the reference range (shown as dashed lines).

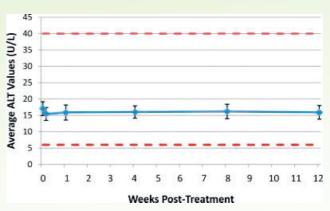


Figure 13.

Plot of mean ALT values reveals no significant change over time.

Mean values their 95% confidence interval (denoted by the error bars) remain well within the reference range (shown as dashed lines) (Lasers in Surgery and Medicine 2009;41:785-790).

Nelson et al remarked in 2009 that, in previous clinical studies, the device has been well tolerated by the subjects. In all clinical studies to date, no ulceration or scarring has been reported. In all human studies to date, no clinically significant alterations in lipid profiles or liver function tests have been observed. Klein et al reported on 40 patients with bilateral fat bulges on their flanks (i.e. love handles) treated with cryolipolysis. The patients were treated on one or two sites on each flank, depending on the size of the fat bulge, to a maximum of four treatment applications. No statistically significant changes from baseline for any of the cholesterol and triglyceride tests as well as the liver function tests were observed following cryolipolysis.<sup>4</sup>

A study by Dierickx et al in 2013 investigated the clinical outcomes of cryolipolysis in European subjects. This was a retrospective study performed at clinical sites in Belgium and France and evaluated safety, tolerance, and patient satisfaction. A total of 518 patients were studied. No significant side effects or adverse events were reported. The procedure was well-tolerated, with 89% of respondents reporting a positive perception of treatment duration and 96% reporting minimal to tolerable discomfort. Survey results demonstrated 73% patient satisfaction and that 82% of patients would recommend the cryolipolysis procedure to a friend. Caliper measurements demonstrated 23% reduction in fat layer thickness at three months. Abdomen, back, and flank treatment sites were most effective, with 86% of subjects showing improvement per investigator assessment. The authors concluded that cryolipolysis is a safe, well-tolerated, and effective treatment method for reduction of subcutaneous fat.<sup>12</sup>

#### VII. Concomitant Treatments

Ferraro et al in 2012 studied the effects of a combination of acoustic wave treatment and cryolipolysis in subcutaneous fat



Figure 14. Patient satisfaction surveys revealed that most patients were satisfied (n = 243) (Dermatol Surg 2013;1-8).

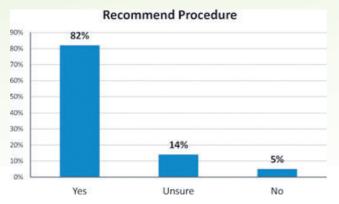


Figure 15. Eighty-two percent of patients would recommend the procedure to others (Dermatol Surg 2013; 1-8).

reduction. This method is known as ice-shock lipolysis and is a new noninvasive procedure for reducing subcutaneous fat volume and fibrous cellulite in areas that normally would be treated by liposuction. Shock waves have been previously used in the treatment of renal calculi and musculoskeletal disorders and are focused on the collagen structure of cellulite-afflicted skin. The combination of the two procedures causes the programmed death and slow resorption of destroyed adipocytes. In this study, 50 patients with localized fat and cellulite were treated with a selective protocol for the simultaneous use of two transducers: a Freezing Probe for localized fatty tissue and a Shock Probe for fibrous cellulite. The procedure significantly reduced the circumference in the treated areas, significantly diminishing fat thickness. The mean reduction in fat thickness after treatments was 3.02cm. Circumference was reduced by a mean of 4.45cm. Weight was unchanged during the treatment, and no adverse effects were observed. Histologic and immunohistochemical analysis confirmed a gradual reduction of fat tissue by programmed cell death. Moreover, the reduction in fat thickness was accompanied by a significant improvement

in microcirculation, and thus, the cellulite. The safety of the method has also been highlighted because it is accompanied by no significant increase in serum liver enzymes or serum lipids.<sup>13</sup>

### VIII. Conclusion

Cryolipolysis, a method which makes use of the ability of cold applications to create an inflammatory reaction within adipose tissues which later on leads to apoptotic adipocyte cell death, is a safe and effective procedure for the reduction of subcutaneous fat. Proper patient selection is needed for it to be more effective. This method can either be used alone or in combination with other treatments such as shock wave treatment. More studies should be done to investigate how cryolipolysis leads to adipocyte apoptosis so that new methods may be discovered that may enhance subcutaneous fat reduction.

#### References

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