

Utilisation of Cryolipolysis among Asians: A Review on Efficacy and Safety

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Cryolipolysis is a non-invasive fat reduction method that is capable of reducing subcutaneous fat significantly without damaging surrounding tissues, by applying cold temperature to induce adipocyte apoptosis. Most of the clinical studies in cryolipolysis were conducted in the Caucasian population, and only a few numbers in Asian, who has darker skin with Fitzpatrick skin type III to V. Higher rate of pigmentary changes were reported with the use of cryotherapy in darker skin. Therefore, this report is aimed to provide a comprehensive review regarding utilisation, efficacy and safety profiles of cryolipolysis among Asians. Currently, there are only four clinical trials conducted exclusively in an Asian population. Two studies were conducted in Korea, whereas others in China and Thailand. Cryolipolysis was performed in the abdomen, arm, inner thighs, and submental regions. The reported side effects were mild and transient, including erythema, hematoma, numbness, and pain. There were no pigmentary changes reported. Although only limited data available, those studies have proved that cryolipolysis utilisation among Asians or darker skin types provides the same efficacy and safety profiles as in Caucasians. Therefore, cryolipolysis might be proposed as the first treatment choice for Asian patients who opted to do body contouring.

Abstract

Introduction

Body contouring (sculpting) has increased in demands around the globe and become one of the most popular cosmetic procedures in the past decade. In 2015, there were 230,000 procedures done by dermatologic surgeons in the United States (US) [1]. According to a consumer survey by American Society for Dermatologic Surgery (ASDS) from more than 3,500 participants in 2018, body contouring is the most popular treatment, with 57% of them had done at least once and 86% were overweight [2]. Until 2014, United States Cosmetic Surgery National Data Bank Statistics claimed that liposuction is the most popular cosmetic surgery procedure and effective in reducing focal fat tissue [3]. However, this invasive procedure is associated with a higher risk of side effects, such as

infection, nerve damage, hematoma, anaesthesia complications, and high cost. Therefore, non-invasive procedures have gained more popularity among patients and physicians in recent years, with 42% increment of non-surgical fat reduction procedures reported in the US in 2014 [4]. Some of the most leading non-invasive body contouring treatment, including low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF) and high intensity focused ultrasound (HIFU), have shown steady effectiveness in reducing circumference of local fat tissue for more than 2 cm without any serious or permanent side effects [5].

Cryolipolysis is an advanced non-invasive fat reduction method, which is capable of decreasing subcutaneous adipose deposit significantly without harming the surrounding tissues [6]. This US Food and Drug Administration (FDA) approved method is

based on highly selective apoptosis of adipocytes with cold exposure, leading to fat thickness reduction up to 20% in just one session. Cryolipolysis is known with good efficacy and safety profile; as reported in several studies and systematic reviews, this non-invasive body contouring method has a short recovery period, minimal side effects and significant improvement will be noticed in 4 months after one session treatment [7]. However, the majority of the clinical studies were done among Caucasians, and an only a small proportion of these studies included Asians. The use of cryotherapy in darker skin is associated with a higher risk of hypopigmentation. Asian population on average have darker skin compared to Caucasians, with predominant Fitzpatrick skin type III, IV, and V [8]. Therefore, a review of cryolipolysis usage among Asians is necessary to bridge the gap of information in efficacy and safety profile, especially in this population.

History

The development of cryolipolysis is based on the observation of adipocyte cell sensitivity to cold trauma as reported back in 1902 [10]. In 1941, the term of "adiponecrosis e frigore" was used by Haxthausen for the wound inflicted by exposure to extremely low temperature [11]. Between 1940 to 1970, there were some clinical reports about cold-induced panniculitis that become the principle behind the use of this method for body contouring [12], [13]. In 1970, Epstein and Oren proposed the term "popsicle panniculitis" as reporting an incidence of erythematous indurated nodules following transient fat necrosis on the cheek of a baby after sucking popsicle [14]. Along with that, cold panniculitis also had been reported in adult patients, which supported the concept that fat-rich tissue is more prone to cold trauma compared to its surrounding water-rich tissue [15].

In 2007, Manstein et al. conducted a pre-clinical study on Yucatan pigs to assess the effect of low-temperature exposure (0, -1, -3, -5, and -7°C for 10 minutes) on subcutaneous fat tissue. They found 80% reduction of superficial fat tissue and a 40% decrease of fat thickness on treatment area within 3.5 months after treatment, without any damage observed in surrounding tissues. Furthermore, the effects were more prominent on a lower temperature (-7°C and -5°C) and after 28 days post-treatment. Histological examination revealed a significant reduction of adipocytes interseptal distance and no changes in lipid profiles had been reported up to 3 months after treatment. Based on these findings, a non-invasive fat reduction by freezing procedure was introduced, known as cryolipolysis in 2007 [16]. Another animal experimental study by Zelickson et al., also supported

these findings that 33% reduction of superficial fat layer thickness was achieved only by one session of cryolipolysis, without any observed side effects [17].

Some clinical studies on human have been conducted to assess the efficacy and safety profiles of cryolipolysis to reduce fatty tissue. FDA initially approved cryolipolysis (CoolSculpting System, ZELTIC Aesthetics) to reduce waist fat in 2010, followed by the approval on abdomen area (2012); thigh (2014); submental region (2015); arm, brassiere roll, back, and buttock (2016) [2]. The earlier device applicator (CoolCore) used negative pressure from 2 plates with a temperature of -10°C to suck fat tissue under the skin for 60 minutes. The latest applicator and device settings recommendation can reach lower temperature within the shorter duration, with a lower risk of hematoma, none vacuum pressure handle, and higher patient's satisfaction rate [18], [19].

In 2012, Shek et al. reported the first commercial experience on the use of cryolipolysis exclusively in Chinese population [20]. The following years, there were few studies done to report the use of this novel non-invasive fat reduction method for thighs in Korea [21], arms and thighs in Thailand [22] and submental regions among Koreans [23].

The Utilisation of Cryolipolysis and Its Efficacy

Some clinical studies have been conducted to assess the efficacy of cryolipolysis to reduce the subcutaneous fat tissue thickness; in which the results are consistent with the preclinical data [24]. In 2009, Dover et al. conducted a prospective study on 32 subjects who received cryolipolysis treatment for 60 minutes. There were 84% of participants who have fat reduction based on photographic assessment. After 4 months, there were 10 participants with a 22% reduction of fatty tissue without any reported side effects [25]. One of the earlier clinical study by Coleman et al., reported that the fat tissue reduction on 10 patients was 20.4% at 2 months and 25.2% at 6 months post-treatment [26]. A multicenter retrospective study by Dierickx et al. reported 86% improvement of photography documentation and calliper measurement reduction at 23% in 94% of 518 subjects, either male or female. The treatment was more effective in the abdomen, back, and waist areas [27]. Furthermore, Garbiyan et al., have evaluated with a 3-D camera and found that reduction of fat volume after cryolipolysis was 56.2 ± 25.6 cc; compared to control area 16.6 ± 17.6 cc ($p < 0.0001$) with a mean difference of 39.6 cc at 2 months post-treatment [28]. Ferraro et al., combined this method with shock waves to have a synergistic effect. There was a significant reduction of the circumference at 6.7

cm and subcutaneous fatty tissue reduction was 4.5 cm at 12 weeks after 3-4 sessions [29]. However, the long term effect of cryolipolysis has not been evaluated at a large scale. There was only one case report, which observed the persistent effect of fat reduction on 2 patients for 5 years after therapy, regardless of body weight fluctuation [30].

According to a systematic review by Ingargiola et al., (2015), the common treatment areas of cryolipolysis are the abdomen, bra roll, lumbar area, waist, inner thighs, mid-knee, peritrochanter area, arms, and ankle. After 2 – 6 months observation, the mean reduction of calliper measurement was 14.67 – 28.5% and ultrasonography revealed a 10.3 – 25.5% reduction in subcutaneous fat tissue volume on treatment area [15]. A comprehensive review in Canada has reported the efficacy and safety profile of cryolipolysis on reducing the fat excess in thighs, abdomen, arms, and back. This study evaluated procedures on 464 sites within 3 years, in which the most common treatment areas were in the abdomen and back. In addition, the skin texture, elasticity, and cellulite showed 25 – 30% improvement after the procedure [31]. Aside from the previously mentioned area of treatment, some studies have reported the use of cryolipolysis on submental and chest region to reduce the excess fat deposit. Bernstein et al. conducted a study of submental fat reduction with 2 sessions of cryolipolysis by using small cup applicator for 45 minutes. There was declining of fat tissue thickness observed on 81% of participants with a mean average of 2.3 ± 0.8 mm reduction in calliper measurement. The 3-D imaging has also revealed 4.82 ± 11.42 cm³ volume reduction, 1.29 ± 1.42 cm² skin surface area reduction, and 3.77 ± 3.59 mm fat thickness reduction [32]. Furthermore, cryolipolysis also has been used to reduce the excess fat deposit in the case of male pseudogynecomastia, in which there was fat deposit thickness reduction at 1.6 ± 1.2 mm by ultrasonographic evaluation on day 120th after 2 sessions with 60 days interval [33].

Some researchers have evaluated the effect of after-treatment massage to increase the efficacy of cryolipolysis. Sasaki et al. found that the average fat reduction with 5 minutes massage on the treatment area was 21.5% by calliper measurement after 6 months [34]. Furthermore, Boey and Wasilenchuk have done a controlled trial to compare the efficacy of additional 2 minutes massage versus the control group with only standard cryolipolysis. At 2 months post-treatment, the average fat tissue reduction in massage group 68% higher (21%) vs. control (12%, $p = 0.0007$). However, the difference gradually became less prominent, as the reduction in message area was only 44% higher compared to the control area 4 months after the treatment [35]. Multiple treatment sessions also were reported to increase fat tissue reduction, but not significant compared to the single procedure [15]. The reports and studies of cryolipolysis are summarised in Table 1.

Efficacy Comparison with Other Non-Invasive Fat Reduction Methods

In recent years, literature have supported the usage of non-invasive fat reduction methods as a replacement instead of adjunction to liposuction which is known for higher risk of side effects and complications. There are 4 leading non-invasive fat reduction methods in the market, including LLLT, cryolipolysis, RF and HIFU. In a systematic review by Kennedy et al., cryolipolysis has found to be more superior than the other non-invasive procedures in achieving fat reduction on abdomen area with average 6.86 cm decrease in circumference, as compared to LLLT (2.15 – 6.83 cm), HIFU (2.1 – 4.7 cm), and RF (1.4 – 4.93 cm). Furthermore, similar findings reported for inner thighs which cryolipolysis has the highest circumference reduction rate 5.78 cm in combination with shock waves, compared with 2.97 – 3.81 cm in LLLT, 1.6 cm in HIFU and only 1.2 cm in RF. On the other hand, LLLT has shown better effectiveness in reducing arm's subcutaneous fat with 3.7 cm circumference reduction, higher than cryolipolysis with only 2.75 cm. However, in terms of overall patients' satisfaction rate, cryolipolysis is leading with 80 – 100%, followed by RF (71 – 97%), HIFU (47.5 – 85%) and LLLT (31.9 – 80%) [5]. Therefore, with the highest efficacy and satisfaction rate, cryolipolysis can be the first line treatment for non-invasive fat reduction.

Side Effects and Complications

The good safety profile is one of the advantages of cryolipolysis, if compared to the invasive method. The side effects which reported in literature were mild and temporary, such as erythema, hematoma, sensibility alteration, and pain. Some clinical studies reported that erythema appeared soon after the procedure and resolved within 1 week. This was caused by vacuum pressure and skin exposure to cold temperature, but there was no significant threat for patients [27], [28], [34]. The incidence of oedema and hematoma on the treatment area were slightly lower than erythema, but they were considered to share the same underlying pathogenesis. These side effects usually resolve within 14 days after the treatment [17], [20], [21], [27], [28]. Hypersensitivity and hyposensitivity to stimulus were found in some clinical trials but did not result in permanent disabilities and improved within 1 month. Coleman et al. reported that alteration in skin sensibility would be resolved within 3.6 weeks and biopsy of peripheral nerves at 3 months post treatment revealed no damage or permanent effect in peripheral nerves [26]. Furthermore, pain during treatment was reported as tolerable in 96% of cases [27].

Table 1: Compilation of Studies on Cryolipolysis (US = Ultrasonography)

Researcher, Year or publication	Design	Participants	Anatomical location	Average age (year)	Average BMI	Methods	Follow Up	Outcomes	Side effects	Level of Evidence
Dover, 2009 ²⁵	Prospective	32	Hip rolls/flanks	N/A	N/A	Manufacture preset CIF	4 months	Average reduction by US 22.4% at 4 months; fat layer reduction in 100% subjects	N/A	3
Coleman, 2009 ²⁶	Prospective	9	Hip rolls/flanks	N/A	N/A	CIF 33, 60 min versus CIF 37, 45 min	6 months	Average reduction by US 20.4% at 2 months, 25.5% by 6 months; nerve biopsy shows no long-term change in nerve structure	-	3
Riopelle, 2009 ³⁹	Prospective	10	-	N/A	N/A	N/A	12 weeks	No change in lipids or liver function test at 1, 4, 8, and 12 weeks after treatment in patients with a loss of fat evident via US	N/A	3
Ferraro, 2012 ²⁹	Prospective	50	Abdomen, inner thigh, arm, buttock, ankle	41.46	25.35	0-5°C + acoustic probe, variable time of treatment, an average of 3.73 treatments	8 weeks	Median reduction in fat circumference 6.86 cm for abdomen, 5.78 cm for thighs, 2.75 cm for arms, 5 cm for buttocks, 2.25 cm for ankles ($p < 0.0001$); average reduction by caliper measurement 4.5 cm for abdomen, 3.60 cm for thighs, 2.10 cm for arms, 4 cm for buttocks, 1 cm for ankles; cholesterol, triglycerides, LDL, HDL, AST/ALT, total bilirubin, and albumin remained within normal limits	N/A	3
Pinto, 2012 ⁴⁰	Prospective	16	Petrochanteric	N/A	N/A	3.1°C; 25-35 min; 1 or 2 treatments	40 days	Average reduction by caliper measurement 19.7% in patients receiving 1 treatment, 28.5% in patients receiving 2 treatments ($p = 0.046$)	N/A	3
Shek, 2012 ²⁰	Prospective	21 (Chinese)	Abdomen	46	23.96	CIF 41.6, 60 min, 1 treatment	2 months	Average reduction by caliper measurement 14.7% ($p < 0.0001$)	Erythema, hematoma, numbness	3
	Retrospective	12 (Chinese)	Abdomen	47	22.5	CIF 41.6, 60 min, 2 treatments	2 months	Average reduction by caliper measurement after first treatment: 14% ($p < 0.001$) in abdomen, 13.4% ($p = 0.003$) in love handle; after second treatment: 7.2% ($p = 0.020$) in abdomen, 4.3% ($p = 0.084$) in love handle	N/A	3
Lee, 2013 ²¹	Prospective	14 (Korean)	Inner thighs	28.57	23.12	CIF 42; 60 min versus radiofrequency	12 weeks	At 12 weeks, fat-reducing efficacy in cryolipolysis-treated thigh - 19.55% versus -28.20% in the radiofrequency-treated thigh (not statistically significant); no statistically significant difference in any measured blood lipid level or fasting blood glucose at weeks 1, 4, or 12	Pain; one person noticed blood-tinged stool	3
Dierickx, 2013 ²⁷	Retrospective	518	Unspecified	42.7	N/A	N/A	1 and 2 months	94% of patients showed a reduction, with a 23% reduction compared with the control site at 3 months by caliper measurements	Erythema, hematoma, swelling, pain, Sensitivity	4
Stevens, 2013 ³⁷	Retrospective	528	Abdomen, flanks, inner thighs, back	46.6	N/A	60 mins	2 or 3 months	Consistent growth in procedure volume, with treatment cycles increasing by 823% from 2010 to 2012	Pain	4
Gabriyan, 2014 ²⁸	Prospective	11	Hip rolls/flanks	37.6	27.1	CIF 41.6, 60 min	2 mos	Average fat volume loss by 3 D imaging 56.2 cc in treated site ($p < 0.0001$), average reduction in caliper measurement 14.9% ($p < 0.001$)	Erythema, swelling, pain	2
Boey, 2014 ³⁵	Prospective	17	Abdomen	N/A	N/A	CIF 42; 60 min + 2 min massage	4 months	Average fat layer reduction by US 68% greater on massaged side at 2 mos ($p = 0.0007$), 44% greater at 4 mos ($p = 0.1$)	Mild numbness in one subject	3
Sasaki, 2014 ³⁴	Prospective	112	Abdomen, brassiere rolls, lumbar rolls, flanks, inner thighs, medial knee	55.8	24.7	CIF 42; 60 min + 5 min massage	6 months	Average reduction by caliper measurement 21.5%, average reduction by US 19.6% in abdomen	Erythema, dysesthesia, Hypersensitive skin	4
Zelickson 2015 ²²	Prospective	45	Inner thigh	48.1	24.6	CIF 41.6; 60 min + 2 min massage	16 weeks	Fat layer reduction by US 2.8 mm; Average thigh circumference reduction 0.9 cm; Level of satisfaction 93 %	Erythema, mild edema, numbness	4
Munavalli, 2015 ³³	Prospective	21 males with gynecomastia	Breast	N/A	N/A	CIF 41.6, 60 min + 2 min massage	2-4 months	Fat layer reduction by US 1.6 ± 1.2 mm	Pain, temporary paresthesia	3
Waniphakdeedecha, 2015 ²²	Prospective	20 females (Thai)	Inner thigh, arm	30.2	21.15	CIF 41.6, 60 mins + 2 mins massage	6 months	Circumference reduction on treatment area 0.41 cm (3 months) and 0.72 cm (6 months)	Pain, erythema, dysesthesia, purpura	3
Klein, 2017 ⁴⁶	Prospective	35	Abdomen, flank	45.2	24.7	CIF 42, 30 min	12 weeks	No meaningful changes in mean values were observed for any blood lipid level or liver test at any point during the 12-week follow-up period	Pain	4
Bernstein, 2017 ³²	Prospective	14	Submental region	50.5	33.1	-11°C, 45 min; 1-2 treatments	12 weeks	Reduction by caliper measurement 2.3 ± 0.8 mm, fat volume reduction 4.82 cm ³ , level of satisfaction 93%	Erythema, edema, numbness, tingling, pain	3
Carruthers, 2017 ³¹	Prospective	30 females (1 Asian, 24 Caucasian, 5 others)	Arm	45.7	28.2	-11°C; 35 mins	12 weeks	Fat layer reduction by US 3.2 mm ± 2.7 mm	Erythema, oedema, numbness, and tingling	3
Suh, 2018 ²³	Prospective	10 (Korean)	Submental area)	46.6	N/A	-11°C; 45 mins	8 weeks	Average reduction by caliper measurement 4 mm (23.2%) and fat layer by US 2.8 mm (35.2%)	Erythema, mild edema	3

Until present, the serious and permanent side effects due to extreme cold temperature exposure, such as scarring formation, ulceration, disability, and subcutaneous panniculitis nodules formation, had not been reported [24]. However, some rare side effects, such as a vasovagal reaction and paradoxical adipocyte hyperplasia, had been reported [15]. Paradoxical adipocyte hyperplasia is a condition with increasing fat deposition on the treatment area after 6 months post-treatment. Jalian et al. estimated that the incidence of this complication was approximately 0.0051% or only 1 out of 20,000 procedures [36]. Based on post-marketing data in 2016, this number has increased to 0.025% or 1 out of 4,000 procedures [2]. The hypothesis of its underlying pathogenesis is the recruitment of stem cells and adipocyte hypertrophy to fill the volume lost on the treatment area as a response to hypoxia during the procedure [2], [36]. However, further studies are still needed to confirm this hypothesis. Cryolipolysis has been proved to be safe in any skin conditions either light or dark skin type. There was no report of pigmentary changes after the treatment.³⁷ Furthermore, some studies have revealed that there were no significant changes on lipid profiles and liver function test within 12 weeks after cryolipolysis [23], [38].

Efficacy and Safety Profiles in Asian Population

In most clinical studies, the majority of the subjects were Caucasians. Steven et al. reported the clinical and commercial experience of cryolipolysis with most of the subjects were Caucasian (67%), and only about 4% were Asian. Fitzpatrick skin type II was found in 40 % subjects, and other 42% had Fitzpatrick skin type III, IV, and V; which were common in the Asian population. However, there was no significant difference in either efficacy or reported side effects of cryolipolysis among these groups. No pigmentary changes were reported post-treatment in all skin types [45]. In contrast to the initial hypothesis that pigmentary disorder is more prominent in darker skin type after cryolipolysis, as found in cryotherapy. This might be explained by the principle that fat tissue is highly sensitive to cold temperature, thus cryolipolysis become highly selective in inducing adipocyte apoptosis with sparing of surrounding tissues [16], [17].

To date, there are only a few studies that have been done in the Asian population. In this systematic review, we only found 4 reports that include Asians exclusively. However, none of them is randomised controlled trials with a sufficient number

of patients that have been performed and published so far. The first study in the Asian population by Shek et al. was conducted among Chinese in 2012 to compare single session of cryolipolysis on 21 patients and two sessions with 3 months interval on 12 patients. In a single session group, there was 81% improvement in the treatment area after 2 months with average 14.67% reduction on calliper measurement. In the group that received two sessions of treatment, the average additional reduction after the second procedure was 14%, with only 7.2% additional reduction in the abdomen area, and insignificant extra 4.3% reduction on the waist area. The reported side effects were erythema (23.8%), hematoma (9.5%), and numbness (28%). No pigmentary changes were observed among the enrolled subjects [20].

In 2013, Lee reported the use of cryolipolysis to reduce fat tissue in thighs of 14 premenopausal Koreans. There was 19.5% reduction of fat tissue, and side effects were found in only 4 out of 14 subjects; such as pain (26.67%), hematoma (20%), and numbness (20%) [21]. In 2015, Wanitphakdeedcha et al., evaluated the new prototype handle (CoolCup) to reduce the excess fat on arms and thighs during 40 treatment sessions in Thailand. The reduction of circumference was 0.41 cm (0.87%) at 3 months post-treatment and 0.72 cm (1.52%) at 6 months post-treatment. The observed side effects include pain, erythema, dysesthesia, and purpura in the treatment area. Post-inflammatory hypopigmentation, scarring formation, and paradoxical adipocyte hyperplasia were not reported in this study [22]. Another study by Suh et al., in 2017, reported the effect of cryolipolysis on submental fat of 10 Korean subjects and found that 9 out of 10 participants had average reduction at 4 mm or 23.2% on submental tissue thickness 8 weeks after the treatment. In ultrasonography evaluation, there was a reduction of submental fat in 9 subjects at an average of 35.2%. The side effects were mild, such as erythema and oedema, without any risk complications, such as purpura, pain, paresthesia, and post-inflammatory hypopigmentation [23]. Those studies revealed that cryolipolysis in an Asian population with darker skin type has the same efficacy and safety profiles as Caucasian population.

Conclusion

Cryolipolysis is a novel and effective method for non-invasive local subcutaneous fat reduction with highly selective cold-induced adipocyte apoptosis as the main principle without harming the surrounding tissues. Various preclinical animal studies and clinical trials have shown the effectiveness and efficacy of this

treatment in reducing excess fat with consistent results in many populations. This procedure has a better safety profile in comparison with liposuction, and it is applicable in a variety of races regardless of their skin colour. Overall, cryolipolysis has higher efficacy and become leading among non-invasive fat reduction methods. Although only limited data available in the Asian population, cryolipolysis has shown good efficacy and safety profile, this might become the first treatment choice for patients who opted to do body contouring.

Reference

- Ho D, Jagdeo J. A Systematic Review of Paradoxical Adipose Hyperplasia (PAH) Post-Cryolipolysis. *J D Drugs Dermatol*. 2017; 16(1):62-67.
- American Society for Dermatologic Surgery. ASDS Consumer Review on Cosmetic Dermatologic Procedures, 2018.
- American Society for Aesthetic Plastic Surgery. Cosmetic surgery national data bank statistics, 2014.
- Chang SL, Huang YL, Lee MC, Chang CH, Lin YF, Cheng CY, Hu S. Long-term follow-up for noninvasive body contouring treatment in Asians. *Lasers Med Sci*. 2016; 31:283-287. <https://doi.org/10.1007/s10103-015-1852-0> PMID:26714982
- Kennedy J, Verne S, Griffith R, Falto-Aizpurua L, Nouri K. Non-invasive subcutaneous fat reduction: a review. *J Eur Acad Dermatol Venereol*. 2015; 29(9):1679-88. <https://doi.org/10.1111/jdv.12994> PMID:25664493
- Macedo O, Corradini C, Matayoshi L. Cryolipolysis treatment for subcutaneous fat layer reduction. *J Am Acad Dermatol*. 2012; 66(4)(Suppl):AB25. <https://doi.org/10.1016/j.jaad.2011.11.113>
- Derrick CD, Shridarani Sm, Broyles JM. The safety and efficacy of cryolipolysis: A systematic review of available literature. *Aesthet Surg J*. 2015; 35(7):830-836. <https://doi.org/10.1093/asj/sjv039> PMID:26038367
- Chan IL, Cohen S, da Cunha MG, Maluf LC. Characteristics and management of Asian skin. *Int J Dermatol*. 2018 2019; 58(2):131-143. <https://doi.org/10.1111/ijd.14153> PMID:30039861
- Korpan NN. A history of cryosurgery: its development and future. *J Am Coll Surg*. 2007; 204(2):314-324. <https://doi.org/10.1016/j.jamcollsurg.2006.11.006> PMID:17254936
- Jalian H, Avram MM. Cryolipolysis: a historical perspective and current clinical practice. *Semin Cutan Med Surg*. 2013; 32(1):31-4.
- Haxthausen H. Adiponecrosis E Frigore. *British J Dermatol*. 1941; 53(3):83-9. <https://doi.org/10.1111/j.1365-2133.1941.tb10506.x>
- Avram MM, Harry RS. Cryolipolysis™ for subcutaneous fat layer reduction. *Laser surg med*. 2009; 41(10):703-8. <https://doi.org/10.1002/lsm.20864> PMID:20014262
- Beacham BE, Cooper PH, Buchanan CS, Weary PE. Equestrian cold panniculitis in women. *Arch Dermatol*. 1980; 116(9):1025-7. <https://doi.org/10.1001/archderm.1980.01640330063014> PMID:7191239
- Epstein EH Jr, Oren ME. Popsicle panniculitis. *N Engl J Med*. 1970; 82:966-967. <https://doi.org/10.1056/NEJM197004232821709> PMID:5436034
- Ingargiola MJ, Motakef S, Chung MT, Vasconez HC, Sasaki GH. Cryolipolysis for fat reduction and body contouring: Safety and efficacy of current treatment paradigms. *Plast Reconstr Surg*. 2015; 135:1581-90. <https://doi.org/10.1097/PRS.0000000000001236> PMID:26017594 PMID:PMC4444424
- Manstein D, Laubach H, Watanabe K, Farinelli W, Zurakowski D, Anderson RR. Selective cryolipolysis: A novel method of noninvasive fat removal. *Lasers Surg Med*. 2008; 40:595-604. <https://doi.org/10.1002/lsm.20719> PMID:18951424
- Zelickson B, Egbert BM, Preciado J, Allison J, Springer K, Rhoades RW, et al. Cryolipolysis for noninvasive fat cell destruction: initial results from a pig model. *Dermatol Surg*. 2009; 35(10):1462-70. <https://doi.org/10.1111/j.1524-4725.2009.01259.x> PMID:19614940
- Kilmer SL. Prototype CoolCup cryolipolysis applicator with over 40% reduced treatment time demonstrates equivalent safety and efficacy with greater patient preference. *Lasers Surg Med*. 2017; 49(1):63-68. <https://doi.org/10.1002/lsm.22550> PMID:27327898 PMID:PMC5298010
- Bolton J, Wu D, Goldman M. Study of a suctionless novel applicator for the treatment of pseudogynecomastia with cryolipolysis. *Lasers Surg Med*. 2016; 48(4):451.
- Shek SY, Chan NP, Chan HH. Non-invasive cryolipolysis for body contouring in Chinese: A first commercial experience. *Lasers Surg Med*. 2012; 44:125-130. <https://doi.org/10.1002/lsm.21145> PMID:22334296
- Lee KR. Clinical efficacy of fat reduction on the thigh of Korean women through cryolipolysis. *J Obes Weight Loss*. 2013; 3:1-5. <https://doi.org/10.4172/2165-7904.1000203>
- Waniphakdeedcha R, Sathaworawong A, Manuskiatti W. The efficacy of cryolipolysis treatment on arms and inner thighs. *Lasers Med Sci*. 2015; 30:2165-2169. <https://doi.org/10.1007/s10103-015-1781-y> PMID:26100004 PMID:PMC4598345
- Suh DH, Park JH, Jung HK, Lee SJ, Kim HJ, Ryu HJ. Cryolipolysis for submental fat reduction in Asians. *Journal of Cosmetic and Laser Therapy*. 2018; 20(1):24-27. <https://doi.org/10.1080/14764172.2017.1368564> PMID:28850270
- Krueger N, Mai SV, Luebberding S, Sadick NS. Cryolipolysis for noninvasive body contouring: clinical efficacy and patient satisfaction. *Clinical, Cosmetic and Investigational Dermatology*. 2014; (7):201-205. <https://doi.org/10.2147/CCID.S44371> PMID:25061326 PMID:PMC4079633
- Dover JA, Burns J, Coleman S, Fitzpatrick R, Garden J, Goldberg D. A prospective clinical study of noninvasive cryolipolysis for subcutaneous fat layer reduction-interim report of available subject data *Lasers in surgery and medicine*. Hoboken: John Wiley and Sons; 2009.
- Coleman SR, Sachdeva K, Egbert BM, Preciado J, Allison J. Clinical efficacy of noninvasive cryolipolysis and its effects on peripheral nerves. *Aesthetic Plast Surg*. 2009; 33(4):482-448. <https://doi.org/10.1007/s00266-008-9286-8> PMID:19296153
- Dierickx CC, Mazer JM, Sand M, Koenig S, Arigon V. Safety, tolerance, and patient satisfaction with noninvasive cryolipolysis. *Dermatol Surg*. 2013; 39(8):1209-1216. <https://doi.org/10.1111/dsu.12238> PMID:23639062
- Garibyan L, Sipprell WH, Jalian HR, Sakamoto FH, Avram M, Anderson RR. Three-dimensional volumetric quantification of fat loss following cryolipolysis. *Lasers Surg Med*. 2014; 46(2):75-80. <https://doi.org/10.1002/lsm.22207> PMID:24535759 PMID:PMC4123113
- Ferraro GA, De Francesco F, Cataldo C, Rossano F, Nicoletti G, D'Andrea F. Synergistic effects of cryolipolysis and shock waves for noninvasive body contouring. *Aesthetic Plast Surg*. 2012; 36(3):666-679. <https://doi.org/10.1007/s00266-011-9832-7> PMID:22042359
- Bernstein EF. Longitudinal evaluation of cryolipolysis efficacy: two case studies. *J Cosmet Dermatol*. 2013; 12(2):149-152. <https://doi.org/10.1111/jocd.12036> PMID:23725309
- Carruthers J, Stevens WG, Carruthers A, Humphrey S. Cryolipolysis and skin tightening. *Dermatol Surg*. 2014; 40:S184-9. <https://doi.org/10.1097/DSS.0000000000000229> PMID:25417573
- Bernstein EF, Bloom JD. Safety and efficacy of bilateral

- submental cryolipolysis with quantified 3-dimensional imaging of fat reduction and skin tightening. *JAMA Facial Plast Surg.* 2017; 19(5):350-357. <https://doi.org/10.1001/jamafacial.2017.0102> PMID:28426847 PMCid:PMC5815121
33. Munavalli GS, Panchaprateep R. Cryolipolysis for targeted fat reduction and improved appearance of the enlarged male breast. *Dermatol Surg.* 2015; 41:1043-1051. <https://doi.org/10.1097/DSS.0000000000000415> PMID:26218826
34. Sasaki GH, Abelev N, Tevez-Ortiz A. Noninvasive selective cryolipolysis and reperfusion recovery for localized natural fat reduction and contouring. *Aesthet Surg J.* 2014; 34:420-431. <https://doi.org/10.1177/1090820X13520320> PMID:24598865
35. Boey GE, Wasilenchuk JL. Enhanced clinical outcome with manual massage following cryolipolysis treatment: A 4-month study of safety and efficacy. *Lasers Surg Med.* 2014; 46:20-26. <https://doi.org/10.1002/lsm.22209> PMID:24338439 PMCid:PMC4265298
36. Jalian HR, Avram MM, Garibyan L, Mihm MC, Anderson RR. Paradoxical adipose hyperplasia after cryolipolysis. *JAMA Dermatol.* 2014; 150(3):317-319. <https://doi.org/10.1001/jamadermatol.2013.8071> PMID:24382640 PMCid:PMC4171727
37. Stevens WG, Pietrzak LK, Spring MA. Broad overview of a clinical and commercial experience with CoolSculpting. *Aesthetic Surg J.* 2013; 33(6):835-846. <https://doi.org/10.1177/1090820X13494757> PMID:23858510
38. Klein KB, Zelickson B, Riopelle JG, et al. Non-invasive cryolipolysis for subcutaneous fat reduction does not affect serum lipid levels or liver function tests. *Lasers Surg Med.* 2009; 41(10):785-790. <https://doi.org/10.1002/lsm.20850> PMID:20014252
39. Riopelle JT, Kovach B. Lipid and liver function effects of the cryolipolysis procedure in a study of male love handle reduction. *Lasers Surg Med.* 2009:82.
40. Pinto H, Arredondo E, Ricart-Jane D. Evaluation of adipocytic changes after a simil-lipocryolysis stimulus. *Cryo Letters.* 2013; 34:100-105.