

**Sylvia R. Karasu M.D.**

The Gravity of Weight

# Frozen: What Do We Know about Cryolipolysis?

Let it go: Removing adipose tissue through controlled cooling.

Like 6

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"The Snow Queen," a fairy tale by Danish author Hans Christian Andersen, is the inspiration for the immensely popular Disney film "Frozen." Depicted by Elena Ringo, 1998, licensed under Creative Commons Attribution.

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Elsa, in the 2013 Walt Disney 3D-animated film, *Frozen*, loosely based on a Hans Christian Andersen fairy tale, *The Snow Queen*, possesses cryogenic magical powers: Everything she touches turns to ice. The story follows the trials and tribulations of the relationship between Elsa and her younger sister Anna as they encounter a deceitful prince intent on plotting to seize the throne in their kingdom of Arendelle. This extraordinarily successful film garnered two Academy Awards, including for its iconic song *Let It Go*, and is generating *Frozen-The Musical*, to be released on Broadway this coming Spring, and *Frozen 2*, the film's sequel, in 2019.

While we see gorgeous animation of ice-covered landscapes, villages, wildlife, and people completely encapsulated in ice, we, of course, hear nothing of the actual impact of ice on the tissues of the human body. The negative effects of extreme cold are well known: for example, physical evidence of frostbite, i.e., injury to tissues that can lead to gangrene and ultimate amputation of the affected extremities, was seen in a pre-Colombian mummy dating back 5000 years, and Napoleon's Surgeon-in-Chief wrote a definitive treatise on frostbite injuries seen in soldiers during the failed 1812-1813 winter invasion of Russia. (Handford et al, *Emergency Medicine Clinics of North America*, 2017)



"Mysterious Pearl," an ice sculpture, 2006 by G. Goodwin Jr. and Snark, Creative Commons Attribution.

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Less severe and often transient reactions to "an acute freezing reaction" when exposed to cold, though, had been reported in the literature by the early 20th century, and Haxthausen (*British Journal of Dermatology*, 1941) describes fat necrosis (with "firm infiltrations") due to prolonged, intense cold exposure in the "particularly conspicuous" cheeks which reminded him of a "Dutch cherub" of four children and one adolescent. He called this syndrome "adiponecrosis e frigore," and noted these infiltrations gradually "melt away" and present a clearly different clinical picture from frostbite; they are "extremely benign," with a tendency to spontaneous recovery. (Haxthausen, 1941) In the 1950s, there is mention that subcutaneous fat necrosis developed in infants during the use of general hypothermia in cardiac surgery. (Adams et al, *Surgical Forum*, 1955) Epstein and Oren labeled a transient syndrome "popsicle panniculitis" (i.e., inflammation of adipose tissue)

with erythematous nodules they had seen in the cheeks of several infants given popsicles. (*NEJM*, 1970) Further, Beacham et al described another similar reversible reaction "equestrian panniculitis" in the upper lateral thighs of young women, wearing non-insulated, tight-fitting pants, who rode horses for hours in very cold weather. (*Archives of Dermatology*, 1980.)

Are there therapeutic uses, though, for extreme cold on the body and, in particular, on adipose tissue? *Cryotherapy*, from the Greek for "frost" or "icy cold," has a history that dates back to the early part of the 20th century (*Oxford English Dictionary*: reference in *Lancet*, 1909, mentioned, but not defined, as one of the seven sections of treatment to be discussed at the 1910 International Congress of Physiotherapy.)

Throughout the years, as well, dermatologists have used "cold-based" therapies to destroy actinic keratoses and superficial skin tumors (Jalian and Avram, *Seminars in Cutaneous Medicine and Surgery*, 2013), but it was not until the mid-2000s that Manstein and his colleagues reported on a "novel" and noninvasive method, which they called "selective cryolipolysis," an intentional procedure that selectively damaged adipose tissue by "controlled cooling." (Manstein et al, *Lasers in Surgery and Medicine*, 2008) These researchers noted that all cell types are susceptible to damage by "conventional cryosurgery," with the extent of injury related to freezing rate, temperature used, duration of the exposure, and the thawing

time, but they noted that adipose tissue was “preferentially sensitive” to cold exposure. Their initial experiments were conducted on Yucatan pigs. (Manstein et al, 2008) Initially, there is an early inflammatory phase but after several months, there is a subsequent loss of fat tissue, without damage to the epidermis, dermis, or muscle—and without regeneration of the fat tissue or a rise in circulating lipid levels. Their speculation was that fat cells crystallize at temperatures well above the freezing point of water and “lipid ice” forms “at much higher temperatures than water ice.” (Manstein et al, 2008)



Lev Lagorio (1827-1905), "Transport of Ice," (1849) (Winter view on Basil Island in St. Petersburg), Irkutsk Regional Art Museum, Russia.

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The interest in noninvasive controlled cooling for “body-contouring” grew out of the “significant risks” and complications, such as pain, infection, scarring, edema, prolonged recovery time, and even more serious deep vein thrombosis and pulmonary embolism associated with liposuction. (Kennedy et al, *Journal of the European Academy of Dermatology and Venereology*, 2015)

The procedure of “body sculpting” or “body contouring” (Ho and Jagdeo *Journal of Drugs in Dermatology*, 2017) is considered one of those “lunchtime procedures.” (Krueger et al, *Clinical, Cosmetic, and Investigational Dermatology*, 2014)

It is done by a special machine without any

anesthetic or even mild analgesics. Cooling panels with gel are applied to the area to be treated, and vacuum suction is used to draw the adipose tissue slightly away from the body. Depending on the area, the suction may be more uncomfortable than the cooling intensity. The treatments vary according to the examiner and can range from 30 to 120 minutes each; multiple sites can be treated simultaneously without any effect on serum lipid levels. (Derrick et al, *Aesthetic Surgery Journal*, 2015; Klein et al, *Lasers in Surgery and Medicine*, 2017) Most sites require more than one treatment, often spaced from two weeks to two months apart, again depending on the clinician’s own protocol. After each treatment, there is a recommendation to do two minutes of manual massage (though no study delineated the science behind that specific two-minute time recommendation), and some researchers question whether post-treatment manual massage and repeat treatments increase the procedure’s efficacy. (Ingargiola et al, *Plastic and Reconstructive Surgery*, 2015) Transient reactions include erythema, bruising, edema, numbness, and mild pain after the procedure. There is speculation that a “more-pronounced inflammatory response” may lead to a more-pronounced treatment response. (Dierickx et al, *Dermatologic Surgery*, 2013)

The most common complication, although rare, is a temporary decreased sensation in the treatment area that can last several weeks. The most troublesome, but very rare complication, is the development of paradoxical hyperplasia (incidence of one in 4,000 cases), possibly (although the etiology is not known)

caused by a reactive fibrosis secondary to the damaged fat cells, that occurs three to nine months after the treatment. There may be a higher predisposition in men and a possible genetic susceptibility (in one study, all four cases were Hispanic men) (Kelly et al, *Plastic and Reconstructive Surgery*, 2016) as well as more likely seen with large applicators. (Ho and Jagdeo, 2017)



German painter Caspar David Friedrich (1744-1840): "Wreck in the Sea of Ice/Ship in the Polar Sea," 1798. Kunsthalle Hamburg.

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results in only a modest reduction of subcutaneous (and not visceral) adipose tissue in selected areas. Its results cannot be seen for months, and it is not as effective as liposuction. (Jalian and Avram, 2013) Further, certain areas of the body are apparently more amenable (e.g. abdominal area and “love handles” of the flank) than others, (e.g. inner thighs and knees), even with multiple treatments.(Stevens et al, 2013; Dierickx et al, 2013)

Clinicians have evaluated cool sculpting in several ways, including measurement by calipers, photographic comparisons, evaluation of before and after photos by investigators who are blind to the procedures, and patient satisfaction surveys. Some use objective measurement by ultrasound. (Derrick et al, 2015) On average, patients lost about 23 percent of the fat in the treated area. In one study of 513 patients (73 percent female), 73 percent reported being “extremely satisfied” or “satisfied,” and 82 percent said they would recommend the procedure to a friend. (Dierickx et al, 2013) Sometimes, those dissatisfied had gained a “significant” amount of weight at six months of follow-up. (Wanitphakdeedech et al *Lasers in Medicine and Surgery*, 2015)

Patient selection and patient counseling, though, are crucial. Controlled cooling is not a treatment for obesity nor a substitute for weight control through diet and exercise. Potential patients must have “realistic expectations” (Stevens et al, *Aesthetic Surgery Journal*, 2013) and appreciate this is a “fine-tuning” cosmetic treatment that

Despite heavy marketing targeted to professionals as well as patients (e.g. television and magazine advertisements), there are many unanswered questions about cryolipolysis. For one, adipose



The technique of cryolipolysis on the lower abdomen. Note the cooling pad (with gel) and the vacuum machine. Patients require no anesthesia and can even work on their computers during the procedure. Discomfort from the cooling and the suction is mild, and there is no recovery time. Credit: Tuty.

Source: istockphoto/used with permission

tissue is “not just a fat storage depot” (Henry et al, *The International Journal of Biochemistry & Cell Biology*, 2012) but rather is a fascinating and complex endocrine organ that secretes many compounds called “adipokines” (e.g. leptin, adiponectin) and occurs in depots throughout the body. There are differences among these depots, with the notion that these adipose depots exist as individual “mini-organs.” (Cleal et al, *Adipocyte*, 2017) To what extent selective destruction of even a few grams of subcutaneous adipose tissue in different areas of the body does over the long-term is not completely known. It is not even known what determines a person’s total number of adipocytes or total adipose volume. (Henry et al, 2012) Nor is

it known “how the local microenvironment determines adipose tissue function and its impact on systemic metabolism.” (Vegiopoulos et al, *The EMBO Journal*, 2017) Further, adipose tissue can be white, beige, or brown, and I could not find any reference to what effect controlled cooling has on brown fat (brown fat is “stimulated” by cold temperatures) (Hansen et al, *Experimental Cell Research*, 2017), nor could I find any reference to whether the timing of adipose tissue removal makes any difference. Adipocytes, like all cells in the body, are affected by circadian rhythms, and circadian clocks within these fat cells may be sensitive to environmental stimuli at different times of the day. (van der Spek et al, *Progress in Brain Research*, 2012)



German painter Caspar David Friedrich (1774-1840), "The Sea of Ice," aka "Polar Sea," also known as "The Wreck of Hope," (1823-24), Kunsthalle Hamburg.

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To date, there is only one long-term follow-up of more than a few months (Bernstein, *Journal of Cosmetic Dermatology*, 2016) in two male patients followed for from 6 to 9 years without a recurrence of adipose tissue. As a result, the long-term duration of the procedure’s effects has yet to be established, though it is not likely that the fat removed will regenerate in that area. (Krueger et al, 2014) In an editorial in *Aesthetic Surgery Journal* (2015), Nahai wonders why some physicians and surgeons are “so willing to jump on the bandwagon of new, relatively unproven innovations,” especially when there is a “lack of high-level evidence.”

For a thorough review of the noninvasive devices (e.g. those using radiofrequency, ultrasound, low-level light laser, mechanical suction, or cryolipolysis) for selective adipose tissue removal, see comprehensive articles by Nassab, *Aesthetic Surgery Journal*, 2015; Kennedy et al, 2015; or Alizadeh et al, *International Journal of Endocrinology and Metabolism*, 2016). Nassab emphasizes that there are currently no randomized controlled or comparative trials of cryolipolysis devices to prove their effectiveness and notes many of the studies have been industry-sponsored or have failed to consider patient variables such as weight loss over time that are due to changes in diet or exercise that may impact results. In published studies, average fat reduction ranges from 14 to 25.5 percent, depending on the area involved (i.e., on average, about one to two cm.)



Adam van Breen, (circa 1585-circa 1645), "Skating on the Frozen Amstel River," 1611, National Gallery of Art, London.

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**Bottom line:** Cryolipolysis is one of several treatments currently available for selective destruction of small, localized deposits of unwanted adipose tissue. It has now been FDA-approved for many areas of the body, (earliest FDA approval in 2010) including the abdomen, knees, back, flank, chin, and inner thighs, though there are no randomized controlled trials or long-term follow-up. Most studies are retrospective and observational. (Naouri, *Journal of the European Academy of Dermatology and Venereology*, 2017) It is a purely cosmetic procedure with modest effects for those with a normal or slightly overweight BMI and clearly not a treatment for obesity. Though not

as effective as liposuction in removing quantities of adipose tissue, cryolipolysis is noninvasive, well-tolerated, with mild discomfort during the procedure, no recovery time, few transient side effects, and almost no adverse effects. Further, patient satisfaction, at least according to short-term follow-up in many of the studies, is high.

## About the Author



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**In Print:** *The Gravity of Weight: A Clinical Guide to Weight Loss and Maintenance*

**Online:** my own website