

Understanding Zeltiq

Practical considerations for integrating lasers and energy based devices in a dermatology practice.

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The Claim: *Fat reduction is a component of a multibillion dollar industry, and liposuction remains the most common surgical cosmetic procedure performed in the US.¹ While liposuction is an effective therapeutic option for the removal of fat, it remains an invasive procedure. There is, therefore, a great demand for an effective, selective, and non-invasive treatment option for excess adipose tissue. Cryolipolysis is based on clinical observations that controlled cold exposure, under the proper circumstances, can result in localized fat cell apoptosis, which leads to the removal of the affected adipose tissue.^{2,4} By controlling the cold exposure, cryolipolysis selectively damages adipocytes, while avoiding damage to the overlying epidermis and dermis.² This results in an effective, localized, and non-invasive treatment for excess adipose tissue.*

THE TECHNOLOGY

The CoolSculpting System was developed by scientists at Harvard University and Massachusetts General Hospital and commercialized by ZELTIQ Aesthetics, Inc. The device is placed upon the skin as heat is extracted at a specific Cooling Intensity Factor (CIF). CIF, is an index value representing the rate of heat flux (mW/cm²) into, or out of, tissue opposite the cooling device. Upon completion of treatment the system automatically stops the cold exposure and the clinician releases the vacuum. The Zeltiq treatment device is cleared by the FDA for cold-assisted lipolysis of the flank, or “love handles,” in individuals with a Body Mass Index (BMI) of 30 or less. It can also be used off label for the treatment of central abdominal fat and back fat in the bra area.

THE MOA

The exact pathogenesis by which cold results in adipose tissue removal is unknown. In animal models, cold exposure has been shown to result in inflammation, damage to the fat cells, and ultimately phagocytosis of the adipocytes.² Initial fat damage from histological evidence appears at day 2, and increases throughout the next month. It is believed that adipocyte apoptosis stimulates the initial inflammatory infiltrate, though the exact mechanism is not fully characterized; pig adipocytes in culture have been shown to undergo apoptosis and necrosis following exposure to cool temperatures.³ Inflammation appears to peak at approximately 14 days, and between days 14-30 the inflammatory infiltrate becomes more monocytic, consistent with a phagocytic process.

Macrophages begin to envelop and digest the apoptotic adipocytes, thereby facilitating their gradual elimination from the body over the course of 90 days, which clinically corresponds to a decrease in the thickness of the subcutaneous fat layer.^{4,5}

THE EVIDENCE

Human Clinical Studies. A multi-center, prospective, non-randomized clinical study evaluating the use of cryolipolysis for fat layer reduction of the flanks and back was conducted at 12 sites.⁴ Patients underwent cryolipolysis treatment to one area, while a contralateral area was left untreated to serve as a control. At four months post-treatment the majority of patients had a clinical improvement with a visible contour change, as assessed by physician observation and digital photography. A subset of 10 patients underwent pre- and post-treatment ultrasound imaging. Of these 10 patients, all had a decrease in the thickness of their fat layer, with an average reduction in thickness of 22.4 percent at four months.

Kaminer, et al.⁵ demonstrated that cryolipolysis results in a visible cosmetic improvement in the flank/love handle region. A blinded comparison of pre-procedure and six month post-procedure photographs was performed on 50 subjects. The physicians were able to accurately differentiate between the pre and post-photographs in 89 percent of cases.

Results from several other studies are consistent with these findings. Riopelle, et al.⁶ measured the flanks of five male subjects via ultrasound and reported an average 18.2 percent fat layer reduction six months post-procedure. Similarly, Coleman, et al.⁷ treated the flanks of nine subjects and reported a 20.4 percent fat layer reduction at two months and 25.5 percent reduction at six months post-procedure. Shek, et al.⁸ determined efficacy results from 21 subjects to be statistically significant after only one treatment and found that 86 percent of subjects would recommend the treatment to friends/family.

Safety Profile. In the previous clinical studies, treatment is well tolerated by the subjects. Patients typically develop erythema in the treatment area, lasting up to a few hours following cryolipolysis. Patients may also develop bruising of the treatment area from the vacuum application which may last approximately one week. The treated skin also becomes cold and firm following cryolipolysis. In all clinical studies to date, no ulceration or scarring has been reported.

Subjects typically report temporary dulling of sensation and

numbness in treated areas. To explore this further, Coleman, et al. had subjects from his aforementioned study undergo neurologic assessment by a board-certified neurologist at baseline and weekly thereafter until resolution.⁷ One subject underwent skin biopsy for histological analysis of nerve fibers. Patients reported numbness in 96 percent of treated sites, which had largely resolved by one week following treatment. Transient reductions in sensation were reported in 67 percent of subjects but spontaneously resolved by two months post-procedure. Baseline and three month post-treatment histology results from the biopsied subject showed no differences and confirmed regrowth of the epidermal nerves fibers. These results indicate that cryolipolysis treatment results in a decrease in sensation of treated areas but that altered sensation is transient and appears to resolve without any further intervention.

Several animal and clinical studies have analyzed blood serum lipids and liver function analytes following cryolipolysis.^{6,9,10} Klein, et al. obtained lipid values, including triglycerides, total cholesterol, and VLDL, LDL and HDL cholesterol, for 40 human subjects who received cryolipolysis treatment on both flanks.¹⁰ Additionally, liver-related blood tests including: AST, ALT, alkaline phosphatase, total bilirubin and albumin were obtained prior to treatment. Follow-up values were determined at weeks 1, 4, 8, and 12 after treatment. Triglyceride values were noted to increase slightly following cryolipolysis, though the increase was not statistically significant ($p=0.22$). There was, however, a significant decrease in HDL cholesterol in the first few weeks, which returned to baseline values by 12 weeks. No statistically significant changes from baseline for any of the liver function tests were observed following cryolipolysis.

These initial safety reports support that a cryolipolysis treatment results in a significant reduction in fat layer thickness without significant adverse events. During the informed consent process prior to cryolipolysis treatment, it is important to emphasize known risks including erythema, bruising, and temporary altered sensation. It remains to be determined whether patients with rare, cold induced dermatologic conditions, such as cryoglobulinemia, cold urticaria, or paroxysmal cold hemoglobinuria can be safely treated with cryolipolysis. Patients with a known history of cold-induced disease should not be treated with the cryolipolysis device until further data are available.

REMAINING QUESTIONS

Further studies are needed to fully characterize the full clinical potential of cryolipolysis and its mechanisms of action. Additional investigations regarding means of enhancing efficacy, such as optimal retreatment intervals and effect of increased treatment duration or decreased treatment temperature, have yet to be completed. In addition, other areas such as the inner and outer thighs, submental area, and arms are also potential areas where controlled cryolipolysis may offer benefits.

PRACTICAL CONSIDERATIONS & PRACTICE GROWTH

Both authors have been performing cryolipolysis for over two years and to date have performed a total of over 1,500 treatment cycles in about 350 patients. In more than two years, there have been no significant adverse effects. All skin types have been treated with safety and efficacy. The patient satisfaction rate is exceptionally high; for this to occur key patient selection is necessary. The Coolsculpting patient is also a captive patient for other aesthetic procedures and in the practices of both authors, Coolsculpting has introduced the otherwise aesthetically naive patient to other procedures. In addition, both practices have noted an increase in male patients who ordinarily may not be a typical patient of the practice. The procedure is particularly popular in men, as they do not want downtime and recovery and are less receptive to aesthetic procedures. A practical consideration is room use and revenue. Different strategies can address these items. In a smaller office with limited space, the procedure can be performed during less busy times, such as the noon hour and at the end of the day. A dedicated room is desirable as it can expand the practice of CoolSculpting.

THE BOTTOM LINE

Cryolipolysis is a novel procedure that utilizes controlled cold energy extraction to produce non-invasive, effective, and selective damage to adipocytes. In animal and human clinical studies, cryolipolysis has been shown to result in significant improvement in the clinical appearance of fat. Clinical studies have shown potential efficacy in the treatment of excess flank fat and abdominal fat. In clinical studies, cryolipolysis treatments have been well tolerated by patients with limited, mild adverse events, such as erythema and bruising. No clinically meaningful alterations in blood lipid profiles or liver function tests have been observed following cryolipolysis.

Because Cryolipolysis is a non-invasive procedure, there is a degree of variability in results. In the human clinical studies, results were most visible in patients with discrete, localized fat bulges. Cryolipolysis does not appear to be as effective in obese patients or patients with excess skin laxity. Additionally, the improvement following cryolipolysis is not immediate, but rather occurs slowly over the course of two to three months via natural processes. Cryolipolysis is a selective, effective, and non-invasive treatment option for excess adipose tissue. ■

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