Cryolipolysis

for the Removal of Fat

A Review and Clinical Update

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The removal of unwanted fat is one of the most talked about procedures in cosmetic and aesthetic surgical circles. Many different modalities have come into play as researchers and clinicians try to find the Holy Grail to successfully remove fat from our patients in a comfortable and non-invasive manner. The Zeltiq CoolSculpting device may be the closest modality yet developed to achieve non-invasive fat removal for those seeking treatment for unwanted areas of localized fat. This device, to be summarized in this review, does have US FDA approval for the non-invasive removal of fat.

Liposuction and abdominoplasty are the two main surgical modalities to remove fat. Liposuction and abdominoplasty are a true invasive procedure and comes with it all of the associated surgical complications including the potential for excessive scarring, something many patients receiving abdominoplasty are not wanting to encounter in the post-operative period. (1) Liposuction, also a truly invasive procedure, has become safer and more acceptable in recent years with the advent of tumescent anesthesia and smaller and less traumatic cannulas to remove the excess fat. (2)

As well, laser lipolysis has gained favor amongst many, although this procedure is also limited, as is liposuction, to those truly skilled in both laser use and liposuction use. The potential for adverse events, including infection, perforation, non-uniform fat removal, sepisis, and death, remain important considerations for those performing and those receiving liposuction, either alone or in combination with lasers. (3, 4)

The trend in aesthetic and cosmetic surgery has been towards less invasive procedures with numerous modalities being used for the treatment of cellulite and for body contouring which have entered into the aesthetic “space” in recent years. Whether they are based on massage rollers, low level laser energy incorporated into the massage effects, pulsed light, or even radiofrequency, many of these have direct impact on the fat cells themselves. These devices are acceptable for the temporary improvement in the appearance of cellulite or for the circumferential reduction of certain body areas or for tissue tightening – all from a dermal point of view, again not impacting directly on the fat cells themselves. Several focused ultrasound devices, using large transducers to target deeper layers including the fat, have been introduced outside of the United States, and have shown some promise in removing unwanted areas of fat in clinical studies; however, experience with these devices in the US is lacking, as the two current available machines are not yet cleared by the US FDA.

The use of cold is not a new concept in dermatology. Many of us are very aware, or perhaps not that aware, of how often we use “cold” in our everyday practice of dermatology. Cold air cooling has become a common part of most lasers and pulsed light or radiofrequency procedures. This cold air is not used for any therapeutic effect but for the comfort of our patients during these procedures. Liquid nitrogen is a mainstay of dermatology, and is used for a treatment for many of the common dermatologic entities we see on a daily basis in our practices, whether it be for the treatment of actinic keratoses or for the treatment of verrucae. Irreversible cell damage by the liquid nitrogen is the mechanism of action in which by liquid nitrogen works. However, this does not affect cells lower than the dermis, and thereby has no direct impact on fat.

Manstein et al (5) proposed that fat cells may be preferentially sensitive to cold injury. Using their knowledge of fat necrosis in infants, known as popcorn panniculitis, and the concept of equestrian panniculitis, and the concept of equestrian panniculitis in which there is selective injury to fat cells in response to exposure to cold, they were able to design an elaborate preclinical animal study looking at the use of cold in the selective destruction of fat cells. (6, 7) The term “cryolipolysis” has been introduced as the mechanism of localized fat destruction via the use of cold. The concept is to cause a localized panniculitis within the skin using controlled fat cooling, or energy extraction, which will result in fat reduction. In doing this controlled fat cooling concept and through modulating the cold exposure, the goal is to “melt” fat without damaging the overlying epidermis and dermis. If successful, a non-invasive localized treatment for excessive areas of fat could be achieved.

The first animal studies performed with this concept involved experiments on four Yucatan pigs. Manstein et al (5) described three different clinical approaches in their first report on cryolipolysis. This included their initial exploratory study, a dosimetry study, and a study on serum lipid levels. The initial exploratory study used a cold copper applicator device which was chilled with a circulating anti-freeze solution. This solution was maintained at a constant temperature of -7 degrees Celsius, and was applied to the skin of the pigs for various time ranges, varying from 5 to 21 minutes. In the buttock regions of the pigs, it was found that 80% of the superficial fat layer was able to be removed which was equivalent to 40% of the total fat layer. This effect was noted at 3 and one half months after the application of the treatment. An example of this is shown in Figure 1.
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A prototype “real world” device was then developed by Zeltiq Aesthetics, Pleasanton, CA. This device contained a thermo-electric cooling element and allowed the use of plates which could maintain the temperature via temperature sensors located within these plates. The treated areas of the skin would be placed within two plates and the skin, and associated fat would be exposed to cold in the range of 20 degrees Celsius to -7 degrees Celsius for 10 minutes. Manstein et al (5) found that those subjects with the more degrees Celsius to -7 degrees Celsius exposed to cold in the range of 20 adipose layer following the therapy. that those subjects with the more adipose layer following the therapy. This is shown in Figure 2. Upon pathologic examination, a 50% reduction in the fat layer was observed. No serious adverse events were noted in their experiment and serum lipid levels were also found to be constant during this preclinical animal assessment.

From the initial animal studies described above, the next assessment was to study the device in humans. For this purpose, a multi-center US clinical trial was begun at 12 clinical sites looking at fat layer reduction in either the flanks, or love-handles, or on the back, i.e., fat pads in the back. (9) All in the patients that were enrolled into this clinical trial, one area was chosen as the treatment site and the contralateral areas served as the control site. Interim data from this clinical study has been presented and shows results from 32 of the patients who had their flanks, or love handles, treated with the Zeltiq system. From the results that were reported, “visible contour changes” were seen in the majority of the patients. Ten of the subjects had ultrasound measurements performed which showed that all of the subjects had a fat layer reduction with an average reduction noted to be 22.4% at four months following their Zeltiq treatment. It was also determined that those subjects with the more “modest” fat bulges had the best cosmetic results. They also noted that there were no device-related adverse events in this treatment group. A clinical example from the original multi-center study is shown in Figure 3.

Other clinical trials have shown further positive results with the Zeltiq system. Kaminer et al (10) evaluated 50 subjects in a blinded comparison of pre-procedure and six month post-procedure photographs who were treated in the flanks with the device. Three skilled, independent physicians evaluated the photographs in a blinded review process. This review showed that these physicians were accurate in assessing pre- and post-treatment assessments in 89% of the patients treated, which improved to 92% when they limited their evaluation to those who maintained their weight close to their baseline throughout the study. Rispelle et al (11) evaluated lipid and liver function tests in 10 subjects who were treated with the Zeltiq system. They obtained lipid profiles and liver function tests at baseline, 1, 4, 8, and 12 weeks post-treatment and found no significant changes in laboratory assessments during this time. Ultrasound skin assessments showed that objective fat layer reduction was noted in eight of the ten subjects during their six-month trial evaluation time period. Klein et al (12) expanded on this lipid profile report when they reported on 40 subjects who received treatment with the Zeltiq system and had their lipid profiles and liver function tests measured throughout a 12 week period of time. In the 40 patients evaluated, no significant laboratory values were noted. Coleman et al (13) also was interested in the safety profile of the therapy and their group treated 10 patients with the device. In 9 of the 10 patients, fat reduction was assessed via ultrasound. Ultrasound measurements showed that there was fat layer reduction of 20.4% at 2 months and 25.5% at six months following treatment in the flank areas. To assess sensory function following treatment, neurologic evaluation was performed in nine of the subjects and a nerve biopsy was performed in one. A transient reduction in nerve sensation was noted in 6 of the 9 subjects evaluated, which lasted up to 3.6 weeks in mean time duration. All sensation did return in all of the subjects. The nerve biopsy analysis showed no long term change in the structure of the nerve fiber. They also noted no lasting sensory alterations or observations of skin changes as a result of the therapy. Rosales-Berber and Dilia-Perez (14) have also reported on preliminary results with the Zeltiq system in treating abdominal fat. Utilizing 42 patients with symmetrical abdominal fat bulges, all received one treatment with a sub-group receiving a second treatment with the device. The interim data, which has been presented, showed that 79% of the subjects reported a clinical improvement within the first 2-4 months following the treatment. Further assessments will be forthcoming. An example from the abdominal study is shown in Figure 4.

Figure 2: Ultrasound analysis: baseline ultrasound image (a) and 4 post-procedural ultrasound image (b). Photos courtesy of Zeltiq Aesthetics.

Figure 4: Clinical results of single CoolSculpting procedure of “love handles”; pre-procedure (a) and four months post-procedure (b). Photos courtesy of Zeltiq Aesthetics.

Figure 5: Zeltiq CoolSculpting System (Zeltiq Aesthetics, Pleasanton, CA). Photos courtesy of Zeltiq Aesthetics.
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It consists of a control console with a cable connecting the console to a cooling applicator cup with an associated vacuum apparatus which is then applied to the desired treatment area after a gel application sheet is applied to the treatment site. The gel sheeting is a 23cm x 23cm thin cotton sheet soaked with thermal coupling solution which ensures efficient thermal coupling with the device. It is shown in Figure 6. There is also an EZ Card which fits into the applicator treatment head and controls the number of cycles for the treatment. The EZ Card is where the cycles are kept and are pre-programmed with the CoolSculpting procedure profiles which have been developed over time and are kept and are pre-programmed with evaluation and investigation.

Several different applicator heads are now available from Zeltiq (Figure 8) with several more sizes currently under demonstration in the Zeltiq CoolSculpting System in use is demonstrated in Figure 7.

As one can see from the clinical evidence presented and from this review of the CoolSculpting procedure profiles, we now have a true modality for the non-invasive removal of unwanted fat. This can definitely make a difference for your patients.

References:

Figure 6: The Zeltiq CoolSculpting System single cycle use gelpad (Zeltiq Aesthetics, Pleasanton, CA). Photos courtesy of Zeltiq Aesthetics.

Figure 7: The Zeltiq System Applicator Attaches to Patient and Self Monitors (Zeltiq Aesthetics, Pleasanton, CA). Photos courtesy of Zeltiq Aesthetics.

Figure 8: Zeltiq CoolSculpting System applicator heads. (Zeltiq Aesthetics, Pleasanton, CA). eZ App for petite or trim athletic frames. Photos courtesy of Michael H. Gold, M.D., Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, TN.

Figure 9: Clinical example of “abdominal fat”, pre-procedure (a) and eleven weeks post single procedure (b). Photos courtesy of Michael H. Gold, M.D., Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, TN.

Figure 10: Clinical example of “love handles”, pre-procedure (a) and sixteen days post single procedure (b). Photos courtesy of Michael H. Gold, M.D., Gold Skin Care Center, Tennessee Clinical Research Center, Nashville, TN.