Can Second Treatment Enhance Clinical Results in Cryolipolysis?

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There is a large and increasing demand for body contouring and fat-reduction treatments. The gold standard continues to be surgical procedures such as liposuction. While clearly very effective, many patients do not want to assume the risks or the recovery time necessary with the invasive therapies, which have added to this pursuit for effective noninvasive body contouring procedures. Cryolipolysis, cold-induced apoptotic fat cell death, is emerging as a new noninvasive treatment for the reduction of localized subcutaneous fat pockets. The Cryolipolysis procedure is cleared by the US Food and Drug Administration, Health Canada, and the European Union for use as a noninvasive fat layer reduction procedure.

Historically, studies have shown that under certain conditions, exposure to cold can cause localized inflammation of the subcutaneous fat layer, known as cold panniculitis.[1,2] Manstein et al[3] expanded on this idea and conducted animal studies to determine if controlled, localized exposure of skin to cold could result in selective destruction of subcutaneous fat cells. In 3 separate studies on porcine tissue, Manstein et al[3] demonstrated that it was possible via cold exposure to induce apoptosis of adipocytes without any damage to the overlying skin or surrounding structures.

Additional porcine studies led by Zelickson et al[4] supported the theory that Cryolipolysis could selectively reduce adipocytes without injury to surrounding tissues. In this study, a subcutaneous fat layer reduction of 1 cm was confirmed in tissues corresponding to the treatment sites after a single application of cold exposure. These results were documented by ultrasound, photography, and pathology. The histologic analysis showed that the primary mechanism of fat cell death is cold-induced apoptosis. Within 3 days of treatment, there was evidence of an inflammatory cascade induction that became more evident by days 7 to 14.[4] The adipocytes begin a process of shrinking and changing shape and upon death are engulfed and digested by macrophages. Serial serum samples demonstrated slight variations. However, all remained within defined normal limits suggesting the lipids remain trapped within the subcutaneous tissue until they are digested and cleared by a natural inflammatory process. This resorption takes place over more than 90 days, resulting in a very gradual displacement of the lipids.[5]

Cryolipolysis is based on a thermal extraction rate defined as cooling intensity factor (CIF), a proprietary numerical value in milliwatts per centimeter squared (mW/cm^2). The goal is to reduce tissue temperature under controlled parameters. A pad saturated with coupling gel is placed on the skin surface to ensure consistent coupling between the epidermis and the applicator during treatment. The applicator of the cooling device is then applied to the treatment area with a moderate vacuum that draws a bulge of fat into the applicator. The applicator contains 2 opposing cooling panels that perform a precise energy extraction (cold) that is optimized

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to injure only adipocytes. The applicator remains on each treatment site for a preset amount of time ranging from 45 to 60 minutes.

Multicenter, prospective, nonrandomized human studies have further examined the results of the initial porcine studies at reducing localized pockets of fat.[6] Thirty-two human participants (male and female) were given initial treatments on love handles at CIF 33 (−64 mW/cm^2) for 60 minutes. Participants were deemed appropriate for treatment if they demonstrated discrete bulges of fat in the love handle or back fat areas. The study excluded obese participants or participants who had general or amorphous fat. Contralateral untreated areas (eg, the opposite flank or portion of the back) were maintained as controls. Interim results on a subset of 10 participants showed all participants demonstrated a fat layer reduction, with an average reduction of 22.4% measured by ultrasound, at 4 months posttreatment. Thirty of 32 participants (94%) indicated they had either no discomfort during the procedure or felt a level of discomfort no greater than what they had expected.

Coleman et al[7] subsequently completed an additional study on the safety and efficacy of Cryolipolysis. Nine participants were treated with a prototype cooling device and participants were evaluated at baseline and 2 and 6 months postprocedure. Treatment resulted in a normalized fat layer reduction of 20.4% at 2 months and 25.5% at 6 months after treatment. Transient reduction in sensation occurred in 6 of 9 participants 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 participants evaluated.

CASE REPORT

While most previous published studies have been based on one application of Cryolipolysis, we look to assess degree of efficacy examined in the clinical study by Rosales-Berber and Diliz-Perez[8] looking at theoretical enhanced efficacy with more than one treatment in the same anatomic area. A 32-year-old male participant presented to our clinic after having lost 100 pounds through diet and exercise over the course of 2 years. He had persistent localized fat deposits on his flanks that were not able to be reduced with diet and exercise. The participant did not want to undergo an invasive surgical procedure and sought another solution to complement the results he had achieved in losing a substantial amount of weight.

After a complete physical exam to determine candidacy for treatment, it was determined that best clinical results are most likely to be achieved by undergoing Cryolipolysis (CoolSculpting by ZELTIQ, Pleasanton, CA) treatment in 2 different locations on each flank, for a total of 4 treatment locations. The 2 treatment sites on each flank were directly above one another placed in a horizontal fashion. The treatment parameter for each site was a CIF of 42 (−72.9 mW/cm^2) for 60 minutes. Due to the degree of subcutaneous fat present in this participant's flanks, using prior study data as an example, we theorized a greater result could be achieved through repeat treatments at the same sites. Therefore, this participant did undergo a second course of treatments at the same sites on the flanks at 2 months postbaseline treatment with the same treatment parameters.

At baseline, the participant weighed 202 pounds and his circumferential abdominal/flank measurement was 97.0 cm, taken approximately 3 cm below the umbilicus to include the center of the treated flank area. The second treatment was conducted 10 weeks later, and his circumferential abdominal/flank measurement at that time was 96.4 cm. Five months after the second and final treatment, the participant's measurement was 94.6 cm and his weight was 204 pounds. Overall, this participant manifested a 2.4-cm reduction in the circumference measurement as a result of treating only 2 areas along the circumference (Figures 1 and 2).

All measurements were taken using 3-dimensional (3-D) imaging system (Vectra, Canfield Scientific Inc, Fairfield, NJ). This program includes taking a 3-D photograph at baseline, which is then compared via overlay with follow-up images with system analysis to calculate degree of change in measurements and volume. It has been demonstrated that this method of measurement carries greater validity than circumferential tape measure.[9]

Of note, at baseline the participant had mild skin laxity and 5 months after the second treatment there was no change as the same degree of skin laxity was present.

COMMENT

This case with 2 courses of treatment demonstrated a successful reduction of subcutaneous fat in the participant's flanks. The original trials were completed with one treatment, with cell apoptosis lasting up to 4 months, at which time final results could be seen. Prior histological studies have demonstrated trailing off of the incited inflammatory process around days 30 to 60. Thus it was hypothesized that if a second treatment was conducted before the apoptosis of cells had completed, perhaps an even greater inflammatory response would be generated, resulting in greater reduction of fat over the long term.

Aside from the hypothesized synergistic effects of more than one treatment application, there are a

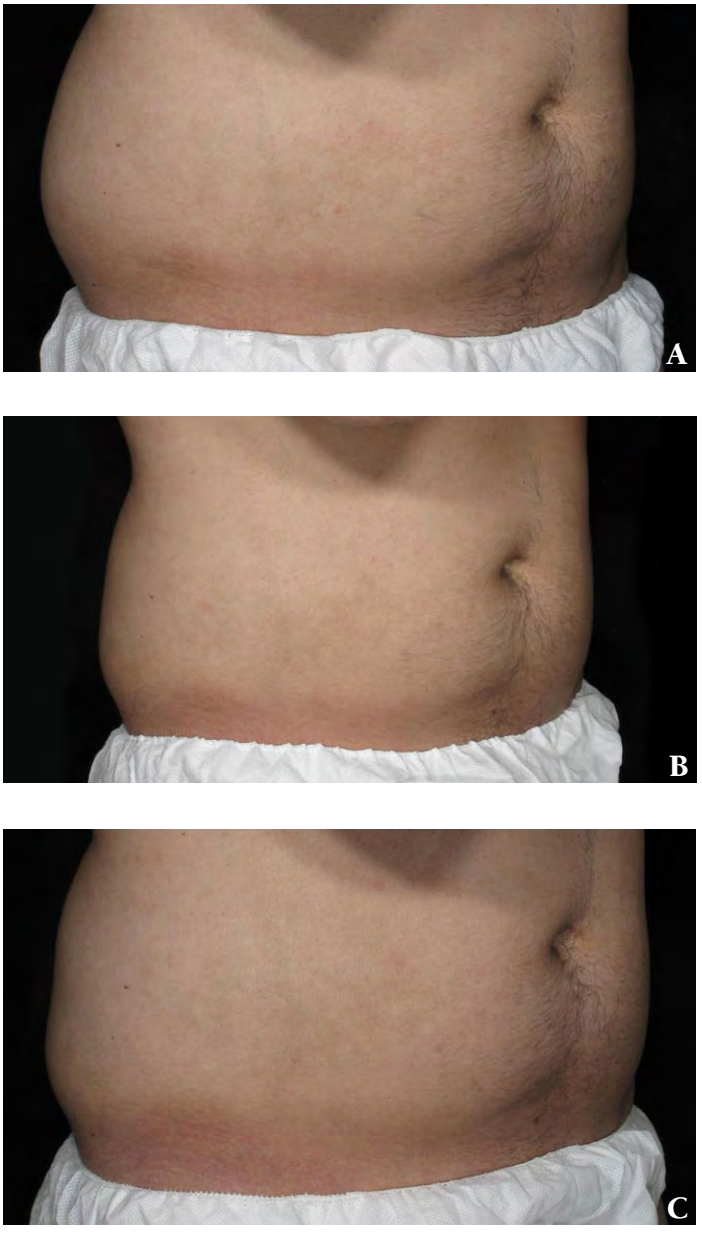

Figure 1. Two applications of each flank. Baseline (A), after one treatment (B), and a 2.4 cm circumference reduction is shown after 2 treatments (C).

number of other factors that can contribute to the degree of efficacy including appropriate participant selection, reasonable expectations, and technique. As demonstrated by prior studies, appropriate candidates are those that are generally fit with localized, persistent pockets of fat that cannot be diminished through careful diet and exercise.[5,6,8] This procedure is not appropriate for people looking for large volume reduction or who only have visceral fat.

It also is extremely important to create appropriate participant expectations. Because Cryolipolysis is not an invasive procedure and there is a degree of variability in results, it is important that candidates understand this procedure does not produce the same more dramatic changes possible with surgery. Historically, treatment with this procedure has shown 4 months posttreatment an average of 20% reduction of fat in the treatment areas. This smaller volume reduction has not been shown to create greater laxity in treatment areas, likely due to natural skin retraction over time.

The final element to degree of efficacy is a thorough physical examination. One should thoroughly assess the participant for the exact appropriate location, the body site with the greatest degree of localized subcutaneous fat.

Although this case report using 2 courses of treatment shows greater than average fat reduction, this technology is still in its infancy. Further prospective controlled

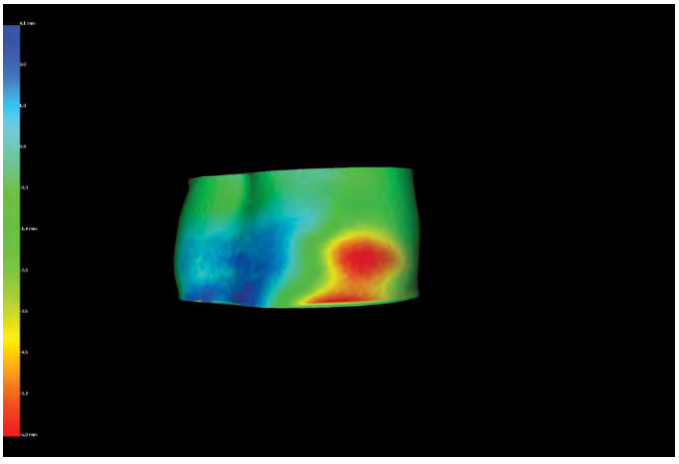

Figure 2. Three-dimensional image, baseline compared to 5 months postsecond treatment. Red reflects area of greatest degree of change; noted to be in exact treatment location. Circumference reduction of 2.4 cm.

studies need to be conducted to define the most efficacious treatment parameters.

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