Title

Fat Removal Using a French Cryolipolysis Device: Retrospective Study of 418 Treatments

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• Figures: 5 Figures

• Pictures: 6 Pictures

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Abstract

Introduction: Cryolipolysis is a technique that induce selective apoptosis of the adipocytes using controlled exposure to intense cold. The aim of our work was to study the tolerance and efficacy of a new device.

Method: Retrospective observational post-commercial study in patients treated with a cryolipolysis device designed and manufactured in France. The assessment was done after a single session, in patients who paid for their treatment, by evaluating tolerance, measuring the perimeter of the treated area, and measuring physician and patient satisfaction.

Results: A total of 418 areas were treated. The treatment was carried out without any significant side effect in 92.5% of cases. Mean loss of circumference was 2.8 cm. The maximum circumference differential was 10 cm. A loss of at least 1 cm was reported in 89.4% of cases. A total of 75.4% of patients were satisfied or very satisfied. Out of all patients, 80.6% wanted to carry out a second session.

Discussion: Most side effects had already been reported in the literature and no serious complications were reported. This safety of use is important when faced with an influx of devices sold in Europe and serious side effects are reported for some of them. We also show a high level efficacy of the French cryolipolysis device based on objective and subjective evaluation in patients who paid for their treatments. It was not possible to define the predictive factors for treatment response.

Conclusion: Cristal™ cryolipolysis is a safe and effective device for fat removal.
Introduction

Requests for dermatological aesthetic treatments are constantly increasing. Patients want less invasive procedures with a minimum amount of sequelae and side effects. This explains why the demand for surgical techniques is stagnating, while the demand for non-invasive medical techniques is booming. Out of the most common requests, changing the body’s silhouette is the most difficult to carry out. This generic term covers different problems: sagging skin ( laxity), cellulite (orange peel effect), and excess fat. There are several different techniques used for fat removal [1]: radio frequency and soft laser, whose effects are relatively limited; high intensity focused ultrasound, that is cumbersome and/or a painful procedure; and more recently cryolipolysis. The most important aspect of non-invasive aesthetic treatments is selectivity. As with any treatment, selectivity helps act on the target area with minimal impact on surrounding tissue: selective destruction of vessels, hair, or pigment using lasers, selective treatment of a facial muscle with botulinum toxin, etc. The selective effect of cold on hypodermis is a long-known medical phenomenon that can cause cold panniculitis when it reaches its peak, as described in horsewomen [2] or children who eat popsicles [3]. Several authors have shown that it is possible to induce selective apoptosis in the adipocytes of animals using controlled exposure to cold [4][5]. This selective fat destruction technique using cold was named cryolipolysis [6] and was then applied to humans using a device that can suck out fat pad into a hollow handpiece and then chill it with two electrodes, cooled by the Pelletier effect. The first device’s safety and efficacy of use has been reported in many studies [7][8][9][10][11][12][13]. This is a technique whose efficacy is particularly noteworthy on localized fat pad. Many cryolipolysis devices have appeared on the market, especially in Europe, and operate in the same way. Their reliability was recently challenged by an article on cold burns that occurred after using some devices imported from Asia [14]. The goal of our study was to evaluate the safety and efficacy of use of a new cryolipolysis device manufactured in France, and to try to determine the predictive factors for treatment response.
Method

This retrospective observational monocentric post-commercial study was carried out in patients treated at the Nogent sur Marne Laser Center in France for a period of one year. Inclusions were carried out consecutively. All patients paid for their treatment. A single session was evaluated.

The inclusion criterion was: an adult patient treated for one or several localized fat pad that could be pinched between the inch and index fingers.

Exclusion criteria included: a medical history of cold disorders (cryoglobulin, Raynaud’s disease, etc.), visceral hernias, pregnancy, a recent Caesarean section (<6 months).

Treatment Procedure

The device used was the Cristal™ cryolipolysis (Deleo, Saint Raphael, France). It was designed and built in France and benefits from medical CE marking. It has two slightly curved handpieces that can be used simultaneously, and that exist in three different sizes. The device has been sold and used in France for over a year for fat removal.

The largest sized handpiece was chosen based on the size of the area to be treated. A thick protective epidermal membrane was laid over the treatment area after marking it with a dermographic pencil. The markings were also used to measure circumference by noting the vertical distance between an anatomical area (most often the umbilicus) and the area to be treated. The membrane was then soaked with a cold-resistant gel in order to maximize the drop in temperature on the treatment area. The treatment probe was placed on the area, then the suction was set between 3 and 4 according to the thickness of the fat pad (the larger the bulge, the stronger the suction). The cooling temperature was between -6°C and -10°C. In case of pain during the suction phase, suction was kept at 1 with a gradual increase made possible by progressive anesthesia by the cold. Treatment duration was 60 minutes per area. A 5-minute energetic massage was carried out immediately after the probe was removed. Cicabio Arnica+ (Bioderma, Lyon, France) was prescribed and it was to be applied once daily for one week after treatment.
Evaluation Criteria

Evaluation of Tolerance

Immediate tolerance was evaluated by examining the patient during the session and 15 minutes after it. Patients were contacted, by telephone, the day after the session in order to screen out and take care of any precocious complications. If needed, they were brought back in and treated until symptoms were alleviated.

Patients were told to call in the case of unusual side effects, especially paradoxical adipose hyperplasia on the treatment area within 3 months after cryolipolysis.

Evaluation of Efficacy

Efficacy was evaluated in patients at least 2 months after their session.

An objective evaluation was carried out by measuring the perimeter of the treated area before and 2 months after treatment according to anatomic markings with a deep breath. Three measurements were taken for each evaluation and the mean of the three measurements was used as a reference if the difference between them did not exceed 10%. Otherwise, three new measurements were taken.

A subjective evaluation was carried out by measuring physician and patient satisfaction (1: dissatisfaction, 2: minimal satisfaction, 3: high satisfaction, 4: very high satisfaction). We also noted patients who wanted to redo a cryolipolysis session.

Statistical analysis

All statistical analyses were performed using Minitab version 17 software with statistical significant set at p<0.05. For quantitative variables, descriptive statistics were presented as mean ± standard deviation, minimum, maximum and median. For qualitative variables, results were presented as a percentage.

Differences in quantitative outcomes were assessed using paired Student test (T-test). Pearson’s correlation tests were performed when applicable.
Results

A total of 418 areas were treated on 147 patients. The treated areas were: the abdomen (144), the love handles (156), the inner thighs (48), the back (26), the underside of buttocks (26), the inner knees (12), and the breasts (6).

Tolerance (Table 1)

Out of all patients, 92.5% did not have any side effects except for minimal regressive ecchymosis.

Two treatments could not be carried out. The first one was supposed to be on the inner knees. The female patient had a large lipedema. Suction while placing the probe led to high pain that was expected with her condition [15]. This caused her to stop treatment. The second one was interrupted because a female patient had a vasovagal attack with loss of consciousness 20 minutes after the probe was placed. The patient fell off the examination table while she was alone. In spite of this incident, she wanted to start the session again, but the physician refused. Two other vasovagal attacks without loss of consciousness occurred. One at the beginning of the session and the other happened when the probe was taken out. These were rapidly controlled after the patients were put in decubitus and treatment could be continued.

Eight patients had unusual sequelae:

- painful induration after the session: 4 patients
- skin anesthesia in the treatment area: 1 patient
- large ecchymosis: 2 patients
- erythema and phlyctena: 1 patient. The protective membrane slipped off the patient during treatment.

No serious or irreversible complication was reported.

Efficacy

A total of 57 patients were reviewed for the efficacy evaluation (Table 2, Table 3, Figure 1 and Figure 2).
A mean statistically significant loss of circumference of 2.8 cm was observed after treatment including the placement of 1-3 probes (Table 2). A loss of circumference of at least 1 cm was observed in 89.4% of patients. The maximum loss observed was 10 cm. For the population studied, cryolipolysis induced a significant loss of perimeter of the treated area that averaged between 2.218 and 3.361 cm; with a confidence interval of 95% [CI at 95% (2.218; 3.361)] (Table 2).

The mean loss according to localization and the number of areas treated appear in Table 3. The loss of circumference was statistically higher after treating the abdomen and love handles (3 probes) than when treating the abdomen only (1 probe) (Table 3 and Figure 2). On the other hand, the difference between the loss of circumference between treating the abdomen (1 probe) and the love handles (2 probes) was not statistically significant.

Mean patient and physician satisfaction was 3/4 (Figure 3). A total of 75.4% of patients and 75.4% of physicians were satisfied or very satisfied.

**Correlation Analyses**

No correlation could be made between patient age or initial perimeter and the relative or absolute loss of circumference (Table 4).

There was a positive correlation between the physician's and patients’ subjective evaluation (Table 4) and the objective decrease in circumference as well as between the physician's and patients’ evaluation (Figure 4 and Figure 5). The physician’s score was more precise and objective because it helped better differentiate the mean level of loss.
Discussion

Our study showed the safety and efficacy of use for a new cryolipolysis device that was designed and manufactured in France.

Because this was a device with aesthetic purposes used on healthy people, safety of use was the most important factor. Most cryolipolysis devices operate according to the same principle, but may differ based on how reliable their manufacturing and treatment protocols are. The objective retrospective survey of all treatments carried out consecutively helped us objectively evaluate treatment safety on a very large number of treated areas. To our knowledge, it is the largest series of safety studies on cryolipolysis done after Diericx’s [7]. Our study showed that the device’s tolerance was excellent without side effects or serious and/or irreversible complications in over 90% of cases. Most complications described were already reported at higher frequencies with other cryolipolysis devices. We had one case of cold burning. It was a superficial second-degree burn: erythema and phlyctena, and healed rapidly without sequelae. It was due to the membrane slipping and not to the device malfunctioning. This helped us to show the importance of epidermic protection with a suitable membrane. Be as it may, the frequency of this complication was much lower than for other energy-based devices commonly used for aesthetic purposes, such as hair removal lasers or radio frequency [14]. On the other hand, there were no cases of paradoxical adipose hyperplasia reported. This is a much more serious condition because it is irreversible and is the opposite result of the treatment goal [11][13]. We deliberately used strong sucking pressure in order to improve fat pad penetration in the probe and to increase the cold effect by diminishing the treated area’s vascularization. Cicabio Arnica+ was consistently prescribed in order to limit and treat secondary ecchymosis caused by suction from the cryolipolysis probe. To our knowledge, vasovagal attacks have never been mentioned in the literature with this type of technique. However, they are a common complication. This is why we always stayed in the treatment room at the beginning and end of each session. In spite of this, we reported the occurrence of a vasovagal attack after 20 minutes of treatment that could have led to traumatic and/or neurological complications. After this incident, we put in place and recommend the consistent use of alarms, as well as checking up on the patient every 15 minutes.
To our knowledge, this is the largest series of efficacy studies on cryolipolysis. Perimeter of the area treated was the objective evaluation criterion of the efficacy that we chose for the clinical practice of cryolipolysis. We tried to make it as objective as possible by using anatomical markings and taking multiple measurements. In our experience, measuring perimeter is more easily reproducible that measuring fat fold and it is especially matches with what the patient feels. So we believe it is the most pertinent way to evaluate them.

Loss of circumference was around 3 cm with 1-3 probes. To evaluate the effect of the number of probes, we focused on studying the abdominal area (abdomen +/- love handles) which was where most treatments occurred. Even though we showed that treating these three areas is significantly more efficacious than treating one area; it is interesting to note that the loss of circumference was not significantly different between treating one (abdomen) and two areas (love handles). Treating the two love handles was slightly less efficacious than only treating the abdomen. This shows the meshing of different parameters in the loss of circumference: the number of treatment areas but also the quantity of fatty tissue in the area and ease of suction. These two aspects were less important on the love handles than in the abdominal area and may explain their lower response in spite of placing two probes there.

Patients’ objective response to treatment was very different from one patient to another. Some patients were able to lose 10 cm of waist circumference after one session and others responded less well to cryolipolysis. This is common with treatments using energy-based devices. In a previous study on CO2 fractional lasers, we showed that young patients with thin skin were the best responders [16][17]. In this study, we tried to determine the predictive response criteria to cryolipolysis. Unfortunately, none of the criteria tested (initial perimeter and patient age) were statistically correlated to treatment success. There are probably individual susceptibilities of hypodermis to cold that cannot currently be predicted by clinical exam or history taking.

In spite of this response variability, the level of patient satisfaction to the technique was very important. According to some authors, the satisfaction criterion is the single most important consideration in the choice of an energy-based device treatment [18]. Since all treated patients paid for their treatment, there
was no gratitude bias [19]. The fact that over 80% of patients were ready to pay for a new session also showed how objective this high satisfaction is. This goes along with the 80% of patients who were ready to recommend this treatment to a friend in Dierix’s study [7]. This last statistic encouraged us to suggest several sessions to the patient during the preliminary consultation, even though we showed efficacy and very high satisfaction after a single session. It has been shown that a second session could help improve results [19]. We showed that patient satisfaction is more subjective than doctor satisfaction, which is more correlated with the objective measurement of the perimeter. This impelled us to provide better information to the patients on the reality of this technique in order to avoid excessive or unrealistic expectations.

Our study showed that the Cristal™ cryolipolysis is a safe and effective device for fat removal with a high level of patient satisfaction.
### Tables

**Table 1: Tolerance**

<table>
<thead>
<tr>
<th>Condition</th>
<th>N total (patients)</th>
<th>Percentages (%)</th>
<th>N total (number of areas treated)</th>
<th>Percentages (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasovagal Attack</td>
<td>147</td>
<td>1.36</td>
<td>418</td>
<td>0.48</td>
</tr>
<tr>
<td>Painful Induration After the Session</td>
<td>147</td>
<td>2.72</td>
<td>418</td>
<td>0.96</td>
</tr>
<tr>
<td>Skin Anesthesia in the Treatment Area</td>
<td>147</td>
<td>0.68</td>
<td>418</td>
<td>0.24</td>
</tr>
<tr>
<td>Large Ecchymosis</td>
<td>147</td>
<td>1.36</td>
<td>418</td>
<td>0.48</td>
</tr>
<tr>
<td>Erythema and Phlyctena</td>
<td>147</td>
<td>0.68</td>
<td>418</td>
<td>0.24</td>
</tr>
<tr>
<td>Total</td>
<td>147</td>
<td>6.80</td>
<td>418</td>
<td>2.39</td>
</tr>
</tbody>
</table>
### Table 2: Efficacy

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Year</td>
<td>57</td>
<td>49.40</td>
<td>14.69</td>
<td>23</td>
<td>66</td>
<td>52</td>
</tr>
<tr>
<td>Perimeter Before Cryolipolysis, cm</td>
<td>57</td>
<td>89.58*</td>
<td>17.28</td>
<td>38</td>
<td>116</td>
<td>95</td>
</tr>
<tr>
<td>Perimeter After Cryolipolysis, cm</td>
<td>57</td>
<td>86.79*</td>
<td>16.97</td>
<td>34</td>
<td>115</td>
<td>92</td>
</tr>
<tr>
<td>Loss of Perimeter, cm</td>
<td>57</td>
<td>2.79</td>
<td>2.15</td>
<td>0</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Wanted a Second Session</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* CI at 95 % for the difference in means: (2.218; 3.361)

T test of the difference in means = 0 (and ≠ 0): T-value = 9.78; p-value = 0.000
Table 3: Loss of Perimeter Based on the Location and Number of Probes Placed

<table>
<thead>
<tr>
<th>Location</th>
<th>N (patients)</th>
<th>Number of Probes Placed</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of Perimeter, cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdomen</td>
<td>24</td>
<td>1</td>
<td>2.38*</td>
<td>1.69</td>
<td>0</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Thighs</td>
<td>3</td>
<td>1</td>
<td>1.33</td>
<td>0.58</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Knees</td>
<td>3</td>
<td>1</td>
<td>2.00</td>
<td>1.73</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>2 Love Handles</td>
<td>8</td>
<td>2</td>
<td>2.13**</td>
<td>2.36</td>
<td>0</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Under the Breasts</td>
<td>2</td>
<td>2</td>
<td>3.00</td>
<td>1.41</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Buttocks</td>
<td>2</td>
<td>2</td>
<td>4.50</td>
<td>4.95</td>
<td>1</td>
<td>8</td>
<td>4.5</td>
</tr>
<tr>
<td>2 Love Handles + Abdomen</td>
<td>15</td>
<td>3</td>
<td>4.00*</td>
<td>2.36</td>
<td>2</td>
<td>10</td>
<td>3</td>
</tr>
</tbody>
</table>

*: CI at 95% for the difference in means: (0.173; 3.077)
T test of the difference in means = 0 (and ≠): T-value = 2.32; p-value = 0.030; DL = 22

**: CI at 95% for the difference in means: (-0.34; 4.09)
T test of the difference in means = 0 (and ≠): T-value = 1.82; p-value = 0.091; DL = 14
Table 4: Pearson’s Correlation Test

<table>
<thead>
<tr>
<th>Pearson’s Correlation Test</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pearson’s Correlation of Loss (cm) and Initial Perimeter (cm) = 0.206</td>
<td>p-value = 0.124</td>
</tr>
<tr>
<td>Pearson’s Correlation of Relative Loss (%) and Initial Perimeter (cm) = -0.114</td>
<td>p-value = 0.396</td>
</tr>
<tr>
<td>Pearson’s Correlation of Perimeter Loss (cm) and Age (year) = 0.036</td>
<td>p-value = 0.791</td>
</tr>
<tr>
<td>Pearson’s Correlation of Relative Loss (%) and Age (year) = -0.040</td>
<td>p-value = 0.768</td>
</tr>
<tr>
<td>Pearson’s Correlation of the Physician Satisfaction and Patient Satisfaction = 0.684</td>
<td>p-value = 0.000</td>
</tr>
</tbody>
</table>
Figures

Figure 1: Diagram of Individual Values (Before – After)

Figure 2: Diagram of Individual Values of Perimeter Loss Based on Location
Figure 3: Histogram of Physician (up) and Patient (down) Satisfaction
Figure 4: Loss of Perimeter (cm) Based on Physician Satisfaction

Figure 5: Loss of Perimeter (cm) Based on Patient Satisfaction
Pictures

Picture 1: red bump: appearance withdrawal of the probe, disappear in a few minutes during the massage

Picture 2: phlyctena and erythema where the membrane slipped (to be noted, the absence of lesion on the protected underlying pinkish skin)
Picture 3: Oedema and indurated appearance

Picture 4: Abdomen (Before/After)
Picture 5: Side (love handle) – Before/After

Picture 6: Abdomen + Love Handles (Before/After)
References


