




Effective noninvasive body contouring by using a combination of cryolipolysis, injection lipolysis, and shock waves

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Abstract

Background: Cryolipolysis combined with shockwave therapy has been previously shown to have synergistic effects in body contouring results.

Objective: This open-label, prospective, multicenter, comparative study investigated the safety and efficacy of combined cryolipolysis, shockwave therapy with cryolipolysis, shockwave therapy, and injection polyenylphosphatidylcholine-based lipolysis.

Methods: Enrolled patients were treated in the abdominal or flank area with cryolipolysis, shockwave therapy and injection lipolysis (n = 10) or cryolipolysis and shockwave therapy (n = 4). All treatments were conducted the same day. Evaluations were conducted 3 months after treatment and included histological analysis, standardized photography, blinded-investigator efficacy, and safety ratings, as well as patient ratings of satisfaction and tolerance.

Results: Compared to baseline, the 3-month follow-up histological analysis revealed a more profound subcutaneous adipose tissue reaction with the triple combination therapy (cryolipolysis, injection lipolysis, radial shock wave) than with the double combination with regard to adipocyte damage and grade of inflammation. Waist circumference was significantly reduced in patients of both groups, but patients in the triple combination group were shown to have a significantly more pronounced reduction in subcutaneous fat. Factors that were shown to influence treatment outcome included baseline BMI and waist circumference. Age and gender had no effect. The abdominal area reacted better to the treatment compared to flanks. No significant side effects or adverse events were reported. The procedure was well-tolerated, and the majority of patients were satisfied with the treatment results.

Conclusions: Combination of cryolipolysis, radial shockwave, and injection lipolysis is a safe, well-tolerated treatment for reduction in subcutaneous fat.

KEYWORDS

apoptosis, cryolipolysis, injection lipolysis, noninvasive body contouring, shockwave

1 | INTRODUCTION

Over the last few years, cryolipolysis has proven to be a very effective treatment in noninvasive body contouring. Since its initial presentation by Dieter Manstein, apoptosis was suggested to be the mechanism of fat cell reduction, a hypothesis that was solidified by histological analysis that showed adipocyte damage and associated clearance after about 14 days.^{1,2} Aside from cryolipolysis, several other energy-based devices have emerged during the past few years offering noninvasive body contouring modalities, including cryolipolysis, radiofrequency (RF), low-level laser therapy (LLLT), and high-intensity focused ultrasound (HIFU), each procedure eliciting its effects through mechanisms of stimulating either adipose tissue apoptosis or necrosis.^{3,4} In addition to energy-based devices, injectable biologic agents that stimulate lipolysis have been developed over the years with the most advanced one being polyenylphosphatidylcholine (PPC)-based injection lipolysis.¹¹ The combined use of polyenylphosphatidylcholine and deoxycholate (PPC/DC) for injection lipolysis of fat started in 1995 when Patricia Rittes started to treat lower lip bulging due to prominent fat pads, and Adam Rotunda was focusing on the detergent effects of its solubilizer DC for localized fat dissolution.^{12,13}

While these modalities have clinical effects and high patient satisfaction as monotherapy, an emerging trend in aesthetic medicine is to combine different treatment methods in order to address several aesthetic concerns simultaneously and ultimately provide comprehensive and synergistic results.^{14,15} A previous study showed that the combination of shockwave treatment with cryolipolysis resulted in synergistic results in patients seeking body contouring.¹⁴ Results appeared quicker, and aside from fat reduction, improved laxity was simultaneously noted with the combination treatment regimen. In this study, the effect of a triple combination that included cryolipolysis, shockwave therapy, and injection PPC-based lipolysis was compared to cryolipolysis, shockwave therapy alone as a therapy for increased fat reduction.

2 | MATERIALS AND METHODS

2.1 | Study design

This was an open-label, retrospective, multisite, comparative study. Men and women between the ages of 21-60 were enrolled. The study was conducted in compliance with Good Clinical Practice, and the ethical guidelines outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants before study-related activities.

2.2 | Patients

The study enrolled 14 patients (12 women and 2 men) with localized fat in the flanks or the abdominal area (Table 1). Patients carrying metallic fragments, pregnant women, patients with nervous system disorders or other serious medical conditions were

excluded. Enrolled patients were not allowed to undergo other fat reduction procedures for the duration of the study (liposuction, mesotherapy, endermology, and RF). Possible seasonal fluctuations in fat distribution and body weight were controlled by Tanita monitor/scaling.

2.3 | Treatment

All treatments were completed on the same day. Cryolipolysis was first performed (Z Lipo; Zimmer MedizinSysteme, Neu-Ulm, Germany) on the designated area according to manufacturer guidelines, followed by radial shockwave therapy used with a conductive gel applied at 16 Hz and 120 mJ (Z Wave pro; Zimmer MedizinSysteme Company). Injection lipolysis was performed last in the appropriate patient group (compound PPC-based solution 50% NLW1/50% NLW2; 10-20 mL; NETWORK-Lipolysis, Drensteinfurt, Germany). The amount of injected solution was dependent on the size of the treatment area.

2.4 | Histological staining and immunohistochemistry

Skin biopsies were obtained by lipectomy from the treated region at baseline and at the 3-month follow-up. Tissues fixed in formalin and paraffin-embedded were sectioned, stained with hematoxylin-eosin, and observed using light microscopy (Olympus BX41, Tokyo, Japan).

2.5 | Standardized photography

Standardized photographs were taken at baseline and at the 3-month follow-up using the Visia[®] CR system (Canfield Imaging Systems, Fairfield). Four photographs were taken with the subject standing up, feet apart at the same distance: 1 of the front, 1 of the back, and 1 of each side view. Photographs were taken in a private room with standardized photography equipment including anatomical alignment, illumination, and background.

2.6 | Assessment and outcomes

Histology specimens were evaluated by two independent histopathologists that measured damage to adipocytes and its clearance, grade of inflammation, and phagocytic activity (O to +++). Measurement of body mass index and abdomen circumference was

TABLE 1 Histological results. Comparison of the two treatment regimens on the 3-mo follow-up in regard to adipocyte damage, grade of inflammation, and phagocytic activity rated by two independent pathologists

	n	Adipocyte damage	Grade of inflammation	Phagocytic activity
Cryolipolysis + RS	4	+(+)	+	++
Cryolipolysis + RS +IL	10	+++	++	+++

done at baseline and at the 3-month follow-up. Investigator evaluations were conducted by two physicians blinded to the treatment and included grading of digital images at baseline using questionnaires with a scale of 0-5 that addressed skin's compactness and volumetric fat reduction. Patient satisfaction was rated on a scale 1-6 (1 = not satisfied at all to 6 = very satisfied) while patient tolerance was evaluated using a pain scale from 1 to 10 (1 = no pain to 10 = extremely painful).

2.7 | Statistical analysis

Quantitative variables were presented by mean value and standard deviation. In order to compare the mean values of two groups, a two-sample *t* test or a *t* test according to Satterthwaite was performed, as appropriate. Pearson correlation coefficients were calculated in order to assess the strength of association between two quantitative variables. Multiple linear regression analysis was conducted in order to test the influence of several parameters on the quantitative outcome "waist circumference reduction" simultaneously. In univariable analyses, test results with a *P* value of less than 0.05 were

considered as statistically significant. In the multiple regression analyses, the "selection = forward" option was used with a significance level of 0.10. All statistical calculations were performed with SAS, release 9.4 (SAS Institute Inc., Cary, NC, USA).

3 | RESULTS

3.1 | Histological analysis

Histological analysis of the biopsies by two independent pathologists at baseline and the 3-month follow-up revealed that the combination of cryolipolysis, shockwave treatments, and injectable lipolysis led to greater adipocyte damage, a greater grade of inflammation, and increased phagocytic activity compared to the combination of cryolipolysis and shockwave treatment (Figure 1, Table 1).

3.2 | Investigator assessments

Patient characteristics at baseline and following treatment at 3 months are summarized in Table 2. According to investigator grading of digital

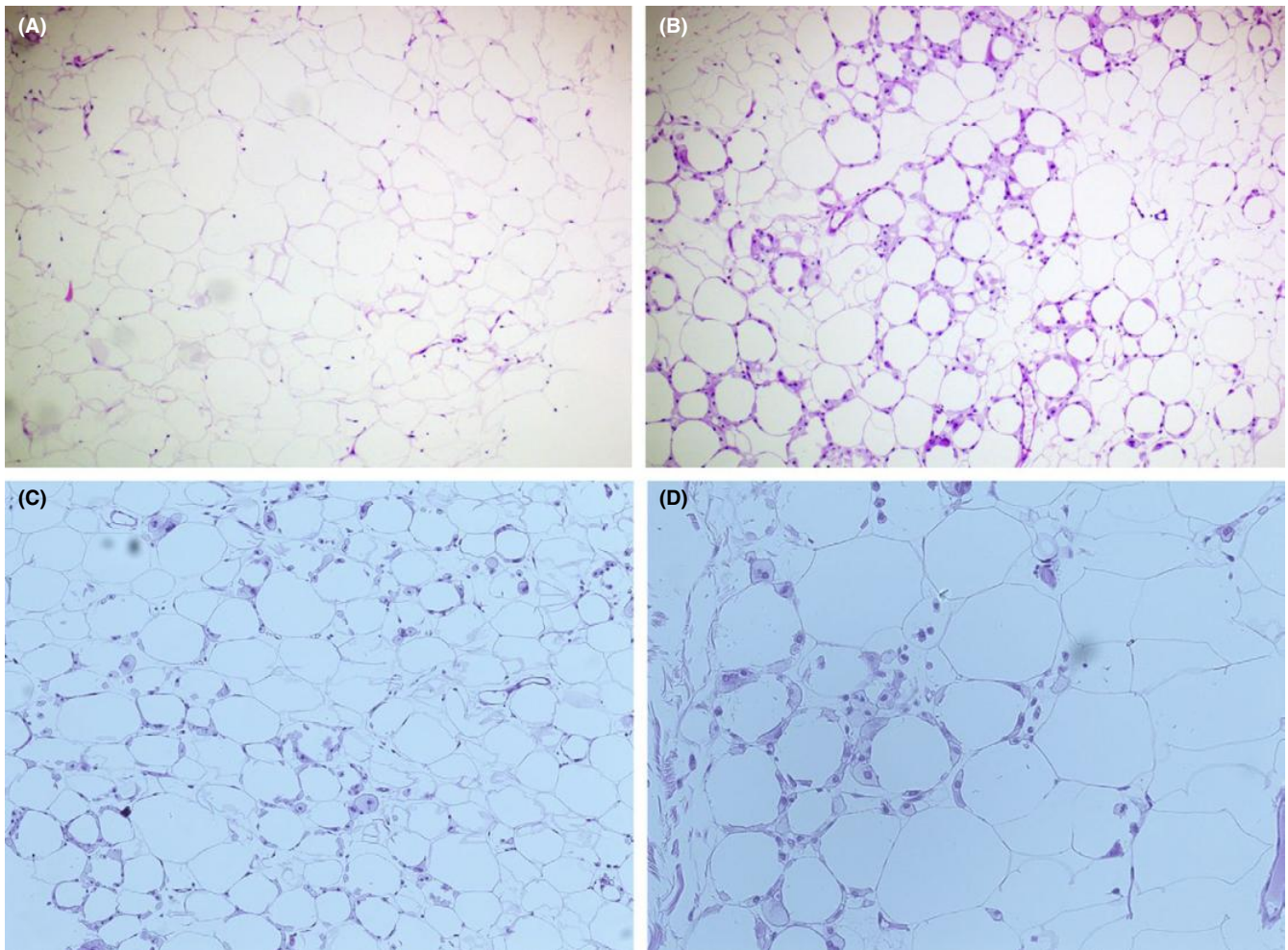


FIGURE 1 Histology in two subjects before (A) and after (B) applying cryolipolysis (Z Lipo, Zimmer MedizinSysteme) and radial shock wave distribution (Z Wave Pro, Zimmer MedizinSysteme). Histology in two subjects before (C) and after (D) applying cryolipolysis (Z Lipo, Zimmer MedizinSysteme), radial shock wave distribution (Z Wave Pro, Zimmer MedizinSysteme), and injection lipolysis

Parameter	Cryolipolysis + SW (n = 4)	Cryolipolysis + IL +SW (n = 10)	P value
Age (y)	33.8 ± 4.8	40.4 ± 15.6	0.2481
Gender (male/female)	0/4	2/8	1.0000
Height (cm)	164.0 ± 5.2	168.8 ± 11.4	0.4417
Weight (kg)	61.0 ± 9.9	69.0 ± 14.9	0.3497
BMI	22.6 ± 2.8	24.1 ± 4.3	0.5209
Location (abdomen/love handles)	3/1	5/5	0.5804
Waist circumference pretreatment (cm)	88.5 ± 8.2	97.5 ± 11.5	0.1858
Waist circumference after treatment (cm)	86.0 ± 8.2	93.1 ± 10.1	0.2411
Waist circumference difference (cm)	2.5 ± 0.6	4.4 ± 2.2	0.0288*

* $P < 0.05$.

TABLE 2 Summary of patient characteristics at baseline and 3-mo follow-up. Clinical data are summarized as mean ± SD

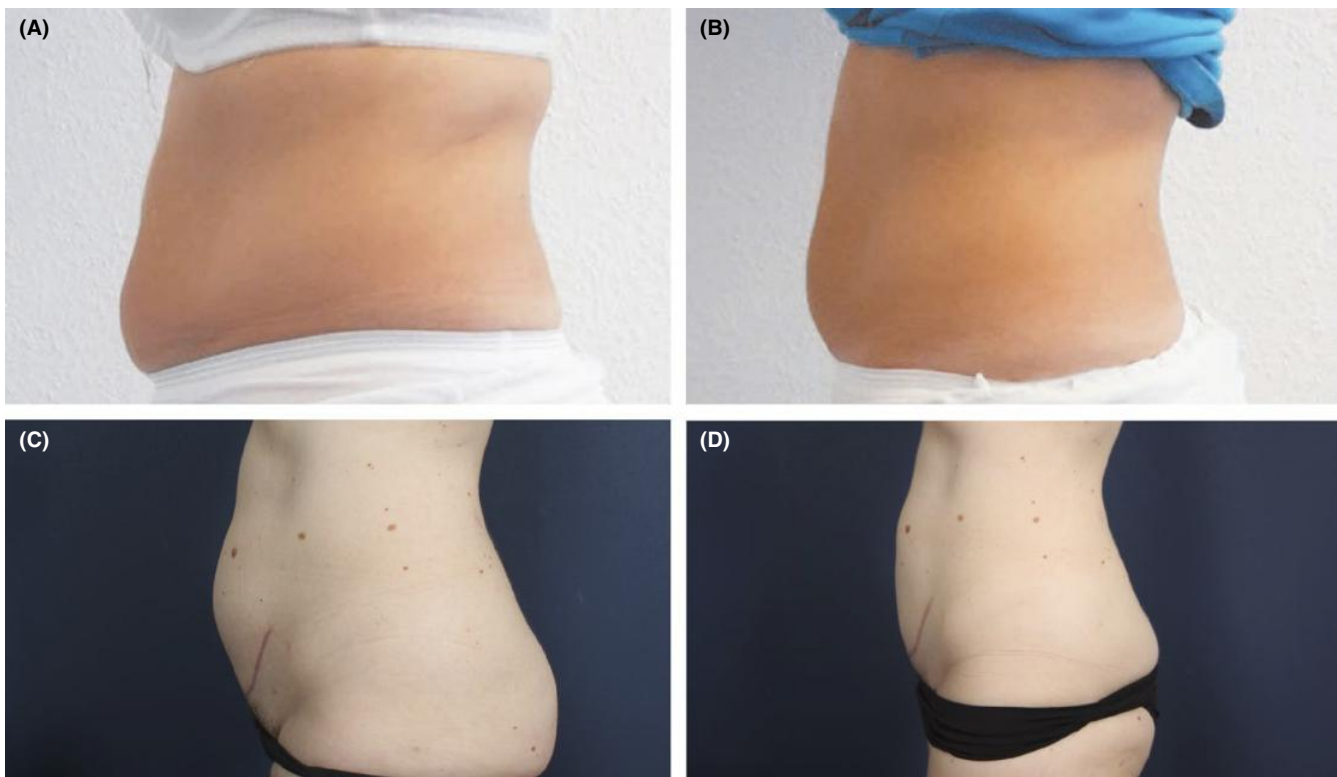


FIGURE 2 Female patient before (A) and after one month of combination of cryolipolysis with shockwave (B). Female patient before (C) and after one month of combination of cryolipolysis with shockwave and injection lipolysis (D)

pictures and questionnaires, the reduction in fat and compactness of skin was significantly more enhanced with the addition of injection lipolysis ($P = 0.04$), (Figure 2, Table 2). Factors that were found to significantly influence the degree of fat reduction included the baseline BMI ($P = 0.02$) and waist circumference ($P = 0.006$). Moreover, the patients that were treated in the abdomen experienced significantly increased reduction in waist circumference reduction compared to those treated in love handles group ($P = 0.04$) (Table 3).

3.3 | Patient assessments

In both groups, patient satisfaction was high. In the cryolipolysis combined with shockwave group, 50% of patients gave the highest rating for patient satisfaction while in the triple combination group 60% of the patients gave the highest rating for the treatment. The majority of patients in both groups would recommend the treatment to friends (Figure 2C,D).

TABLE 3 Subgroup analysis of different regimens effects depending on location

Group	Location	n	Waist circumference reduction (\pm SD)
Cryolipolysis + SW	Abdomen	3	2.7 \pm 0.6
	Love handles	1	2.0 \pm 0.0
Cryolipolysis + SW +IL	Abdomen	5	6.0 \pm 1.9
	Love handles	5	2.8 \pm 1.1

3.4 | Safety

No significant side effects were observed in patients compared to monotherapy, just temporary knots that were moderately painful on palpitation and temporary hyperpigmentation that resolved within 3 months.

4 | DISCUSSION

Today, the popularity of noninvasive techniques such as cryolipolysis, RF, LLLT, HIFU, and injection lipolysis has skyrocketed due to their positive results on body contouring, without surgery, downtime, or side effects.⁶ Combination treatments have also been the latest trend as they can provide more comprehensive, synergistic results than monotherapy alone. There is however notable paucity of studies that investigate reasonable combination therapies to improve the outcome and patient satisfaction.^{15,17}

In our study, we showed that a triple combination of cryolipolysis, shockwave treatment, and injection lipolysis had statistically significant greater effects in reducing unwanted fat than the combination of cryolipolysis with shockwave treatment alone. Results were supported by independent investigator assessments of questionnaires together with digital photography and corroborated by histological analysis of biopsies that were obtained at baseline and three months after treatment. Patient satisfaction was high in both groups, but increased satisfaction was noted in the patient group that received injection lipolysis in addition to the other treatments.

Clinical studies that evaluate and validate treatment regimens combining different fat reduction technologies are very important for the physicians as they can obtain additional treatment protocols that increase patient success and improve clinical outcomes. This particular regimen is particularly advantageous as by applying injection lipolysis in the cryoanaesthetized area immediately after the cryolipolysis, the patient experiences less pain. Moreover, data revealed that the abdominal area responds more positively to the triple combination protocol than the flanks, and baseline BMI/waist circumference can negatively influence the strength of the results. This observation makes sense as in the flanks the fat tissue is a structural fat as opposed to the metabolic fat found in the abdomen. Together, the influence of these factors is informative for the physician as they can better tailor clinical strategies for their patients and advise what

kind of treatment will work better depending on the location and the patient profile.

As our present study was designed with a single treatment end point, the long-term outcome, effect of repetitive sessions, or recurrence of subcutaneous fat must be evaluated in further studies. Another limitation of our results is related to the small subject number and retrospective design of the study. Thus, the results have to be confirmed in a prospective study at a larger scale.

In summary, the combination of cryolipolysis, injection lipolysis, and radial shock wave is a very effective method of noninvasive body contouring. It improves the outcome and patient satisfaction compared to the treatment with cryolipolysis and radial shockwave alone. This optimized combination for noninvasive body contouring may improve the effectiveness of single treatments and patient satisfaction in nonsurgical body contouring.

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