

## Body Contouring

# Metabolic and Structural Effects of Phosphatidylcholine and Deoxycholate Injections on Subcutaneous Fat: A Randomized, Controlled Trial

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### Abstract

**Background:** Phosphatidylcholine and deoxycholate (PC-DC) injections are a popular nonsurgical method to eliminate unwanted fat. The safety and efficacy of this approach is uncertain.

**Objective:** The authors evaluate the effects of PC-DC treatments on body composition, adipocyte function, and mechanisms responsible for fat loss.

**Methods:** This randomized, open-label study enrolled 13 women with a body mass index (BMI)  $\leq 30$  kg/m<sup>2</sup> and lower abdominal subcutaneous fat suitable for small-volume liposuction. Patients were randomized by the final digit of their Social Security numbers and received between 2 and 4 PC-DC treatments, spaced 8 weeks apart. One side below the umbilicus was injected with PC-DC. The contralateral, control side received no treatment. Adipose tissue biopsies were performed on the treated side at baseline, 1 week after the first treatment, and 8 weeks after the final treatment. The primary outcome was change in adipose tissue thickness at baseline and 8 weeks after the final treatment.

**Results:** Seven women completed the study. Treatment with PC-DC significantly reduced the thickness of the anterior subcutaneous abdominal fat ( $P = .004$ ). Adipose tissue showed rapid increases in crown-like structures, macrophage infiltration, and reduced expression of leptin, hormone-sensitive lipase, adipose tissue triglyceride lipase, and CD36. Plasma C-reactive protein, lipid profile, and plasma glucose concentrations were unchanged.

**Conclusions:** PC-DC injections can effectively reduce abdominal fat volume and thickness by inducing adipocyte necrosis. These treatments do not appear to increase circulating markers of inflammation or affect glucose and lipid metabolism.

### Level of Evidence: 3

### Keywords

injection lipolysis, Lipodissolve, fat ablation, body contouring

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Liposuction to remove subcutaneous fat was first developed 35 years ago and is one of the most common aesthetic surgical procedures in the United States with 341144 procedures reported in 2011.<sup>1</sup> However, liposuction is costly, often requires general anesthesia, and has the potential for serious medical complications. Therefore, the use of less invasive, nonsurgical therapies to reduce localized fat deposits has gained interest. Subcutaneous injection of phosphatidylcholine (PC) solubilized in deoxycholate (DC) has been purported to eliminate body fat. These injections, marketed under a variety of names such as “Lipodissolve,” have become increasingly popular.<sup>2-4</sup>

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Subcutaneously injecting PC to eliminate unwanted local accumulations of fat was first proposed by Maggiori,<sup>5</sup> who treated xanthelasma by using tissue injections of PC. Several groups have now reported the use of this therapy to remove unwanted adipose tissue in other areas of the body, including the abdomen, thighs, buttocks, arms, and neck.<sup>6-9</sup>

Despite the widespread use of these therapies, the mechanism of action through which subcutaneous injection of PC and DC reduces fat deposits is unknown. Therefore, we conducted a clinical trial to examine the effect of PC solubilized by DC on subcutaneous lower abdominal adipose tissue mass, inflammation, and the potential mechanisms responsible for fat loss in healthy volunteers.

## METHODS

### Patients

This study was conducted in a private, outpatient cosmetic surgery center in St Louis, Missouri, and at the Clinical Research Unit (CRU) of Washington University School of Medicine, St Louis, Missouri. Thirteen women were recruited between July and November 2008 to participate. All patients had a medical evaluation, including a history and physical examination, and blood tests, including a lipid panel. To be participants, patients must have had a body mass index (BMI) < 30.0 kg/m<sup>2</sup> and presence of subcutaneous fat in the lower abdominal area suitable for small-volume liposuction. Exclusion criteria were (1) pregnancy or breastfeeding, (2) diabetes, (3) use of agents known to affect glucose and/or lipid metabolism, (4) tobacco use, (5) known sensitivity to components of the injection formulation, or (6) prior wound or infection in the treatment area. All patients provided their written informed consent before participating in this study, which was approved by the Human Studies Committee of Washington University School of Medicine and the Western Institutional Review Board. An investigational drug exemption was obtained from the US Food and Drug Administration for the use of PC-DC.

### Study Protocol

Patients were randomized to receive PC-DC subcutaneous injection therapy (Medisca, Inc, Plattsburgh, New York, and formulated by MasterPharm, Richmond Hill, New York) to either the right or left abdomen, below the umbilicus. The phosphatidylcholine was derived from soybean lecithins, half of which were composed of phospholipids. The sodium deoxycholate was a bile salt used to keep the PC soluble as it passed through the manufacturer's sterile filtration system and ensure that the PC remained in an injectable form without precipitating out of solution. This formulation was specifically chosen because it is the most commonly used commercially available formula in the United States. Each milliliter of the treatment formula

contained 50 mg PC, 42 mg DC, and 8 mg benzyl alcohol, which was added as a preservative. Patients were randomized according to the final digit of their Social Security numbers; those with an even-numbered final digit received treatment on the right side of the lower abdomen, and those with an odd final digit were treated on the left side. The contralateral side of the abdomen received no treatment and served as a control.

Before each treatment session, standardized photos of the abdomen were obtained using a high-resolution digital camera with a 50-mm lens as patients stood in the right lateral, left lateral, and anterior-posterior positions. Each patient had a minimum of 2 and a maximum of 4 PC-DC treatment sessions, spaced 8 weeks apart. The maximum dose of PC given at any treatment session was limited to 2500 mg, which is the highest dosage recommended for minimizing potential side effects such as nausea or diarrhea while maximizing the therapeutic response.<sup>10</sup> Prior to injection, a grid was drawn on the abdominal treatment area and marked into 1.5-cm squares as symmetrically as possible. Each 1.5-cm square site received 0.5 mL of the PC-DC solution injected into the center of each grid square. To increase the reproducibility of grid placement at future treatment sessions, the distance from the inferior border of the grid to the floor was measured and recorded so it could be duplicated later. All injections were delivered with a standard 27-gauge, 13-mm needle attached to a 10-mL syringe. Patients were counseled to maintain their normal lifestyle and body weight for the duration of the study.

Body composition was assessed at baseline and 8 weeks after the final treatment session. Total body fat and fat-free mass were determined by using dual-energy x-ray absorptiometry (DXA; QDR 4500; Hologic, Waltham, Massachusetts). Abdominal subcutaneous and intra-abdominal adipose tissue masses were evaluated by using magnetic resonance imaging (3-T magnet; Siemens, Erlangen, Germany). Three cross-sectional images were obtained: at the L3 to L4 intervertebral space, above the L3 to L4 intervertebral space, and below the L3 to L4 intervertebral space. Consistent slice localization was accomplished by using a rigid landmark (ie, the iliac crest) to position the patient in the machine and by using coronal scouting images to identify the site for image acquisition. Intra-abdominal and abdominal subcutaneous adipose tissue volume (cm<sup>3</sup>) was determined by using Analyze software (Mayo Clinic, Rochester, Minnesota).

Abdominal subcutaneous adipose tissue biopsies were obtained 3 times during the study: (1) approximately 1 week before the first PC-DC injection from the control side of the abdomen, (2) 1 week after the first treatment session from the treatment area, and (3) 8 weeks after the final treatment session from both the treated and control sides. Adipose tissue was obtained by needle aspiration. The biopsy site was anesthetized with 1% lidocaine, and adipose tissue was aspirated with a 10-mL syringe and a 14-gauge needle. Tissue samples were vigorously irrigated with iced saline; 1 sample was flash frozen in liquid nitrogen, and a second sample was placed in formalin for subsequent histological analysis. Quantification of the number of crown-like structures and macrophage dispersal were performed as previously

reported.<sup>11</sup> Blood samples were obtained during fasting conditions at baseline, 1 week after the first PC-DC treatment, and 8 weeks after the final treatment session to measure plasma lipids and the plasma concentrations of insulin, glucose, leptin, adiponectin, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and interleukin-6 (IL-6).

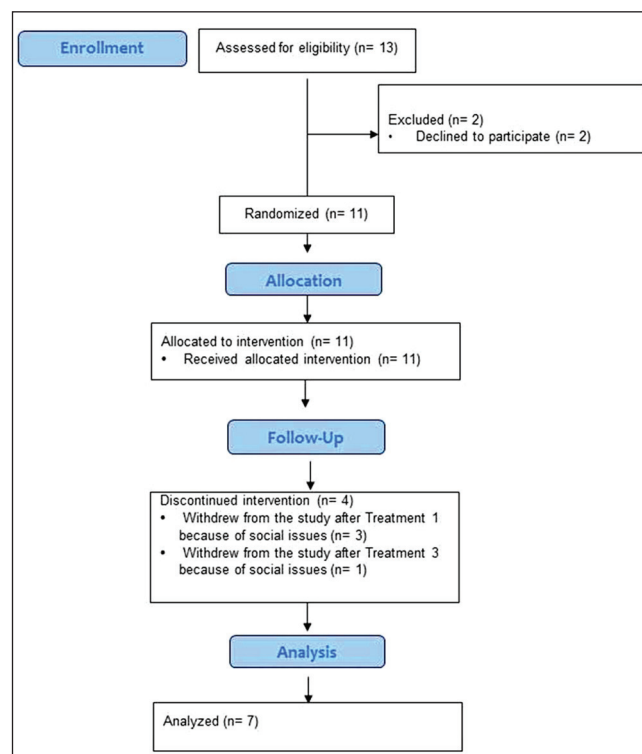
## Safety Assessments

Patients received a diary that listed common side effects and were asked to record which (if any) of these side effects they experienced during the first week after treatment. Patients were seen 1 week after each treatment session for follow-up. Study patients had a final visit at 24 weeks after the last study treatment session. At the final follow-up visit, body weight, abdominal circumference, and skin fold thickness measurements were obtained. Both the patient and surgeon completed questionnaires to assess body contour and degree of improvement in localized fat deposits, baseline and final photographs, and patient satisfaction.

## Analyses of Samples

Plasma lipids were measured with commercially available kits. Plasma insulin was measured by enzyme-linked immunosorbent assay (ELISA) (Immulite; Diagnostic Products Corp, Los Angeles, California). Plasma IL-6, C-reactive protein (CRP), and leptin were measured by ELISA (Quantikine Immunoassay kits; R&D Systems, Minneapolis, Minnesota).

Fat tissue RNA was extracted from frozen adipose tissue using the RNeasy total RNA kit (Qiagen, Valencia, California). The first-strand cDNA was generated by reverse transcription using total RNA. Real-time reverse transcription-polymerase chain reaction (RT-PCR) was performed using the ABI PRISM 7700 Sequence Detection System and the TaqMan kit (Applied Biosystems, Foster City, California). Gene expression of multiple target genes for adipocyte inflammation (IL-6, TNF-, monocyte chemoattractant protein-1 [MCP-1]),<sup>12,13</sup> adipocyte production (leptin, adiponectin),<sup>14</sup> adipocyte function (adipose triglyceride lipase [ATGL], cluster of differentiation 36 [CD36], fatty acid synthase [FAS], and hormone-sensitive lipase [HSL]),<sup>15,16</sup> macrophage infiltration and vascularization (EGF-like module-containing mucin-like hormone receptor-like 1 [EMR1], integrin alpha M [ITGAM], and vascular endothelial growth factor [VEGF]),<sup>17</sup> and fibrosis (collagen type IV, alpha 1 [COL4A1]; collagen type VI, alpha 1 [COL6A1]; collagen type VI, alpha 3 [COL6A3])<sup>18,19</sup> were measured by using quantitative real-time RT-PCR, using gene-specific primers. Gene expression of several different apoptosis markers (an initiator caspase, Casp8; an effector caspase, Casp3; the Fas receptor-ligand complex, CD95/Fas) and GRP78, a marker of endoplasmic reticulum (ER) stress,<sup>20,21</sup> were also analyzed by RT-PCR using gene-specific primers.



**Figure 1.** Patient selection and participation flowchart. Eleven patients were randomized into the study, and 7 patients completed the study.

## Statistical Analyses

The primary outcome was change in adipose tissue thickness between the treated and untreated sides. Secondary outcomes were changes in plasma lipids, markers of inflammation (IL-6, TNF- $\alpha$ ), and adipose tissue mRNA expression. Primary and secondary outcomes were tested by using repeated measurements of analysis of variance (ANOVA) with post hoc testing, when appropriate, using a Bonferroni correction for multiple comparisons. A paired *t* test was performed to compare the differences in measures between the untreated and treated sides at the 8-week posttreatment time point. A related-samples Wilcoxon signed ranks test was conducted to determine differences in the count of dispersed macrophages and crown-like structures. We also examined changes in body weight, abdominal circumference, skin fold measurements, patient diaries, aesthetic evaluations, and patient satisfaction. *P* values of  $\leq .05$  were considered statistically significant.

## RESULTS

### Participant Selection

A participant selection flowchart is shown in Figure 1. Patients were recruited starting in July 2008, and the study was completed in December 2009. After obtaining informed

consent, 13 women received a physical examination, medical interview, routine blood tests, and a lipid panel at the CRU of Washington University School of Medicine. Two patients withdrew from the trial after the evaluation at the IRU: 1 because her husband did not want her to participate and the other because she did not want to participate. Neither progressed to treatment. The 11 remaining patients had an average age of 43.6 years at the time of enrollment. After the first treatment, 3 patients withdrew from the study: 1 because of the treatment's disruption to daily activities, 1 because of a job change, and 1 because of family issues. Another patient withdrew after the third treatment following a family health emergency. Thus, 7 women completed all study visits in the experimental portion of the study and the final evaluation at the IRU. Six of the 7 chose to have the same treatments on the control side because of abdominal asymmetry. The seventh patient decided that liposuction would be quicker and better for her. The average number of injections on 1 side of the abdomen per treatment was 71 (range, 27-124 injections), for an average PC-DC dose of 888 mg (range, 337.5-1550 mg).

### Patient Characteristics

Average BMI ( $26.5 \pm 1.2$  vs  $26.2 \pm 1.0$  kg/m<sup>2</sup>) and age ( $44 \pm 2$  vs  $44 \pm 2$  years) were not different between the 11 randomized patients and 7 completed patients. In this article, we report the data for the 7 patients who completed the study. There were no changes in body weight, plasma lipid profile, glucose and insulin concentrations, leptin, liver enzymes, circulating markers of inflammation (IL-6, CRP), or white blood cell count during the study (Table 1). Hematocrit significantly decreased ( $P < .021$ ) between baseline and the first posttreatment visit, possibly due to repeated blood sampling. This difference was not observed at the final study visit.

### Body Composition and Fat Distribution

As expected, there were no changes in total body adiposity (Table 2). The thickness of the anterior ( $32.8 \pm 4.0$  vs  $28.7 \pm 3.4$  cm,  $P = .004$ ) and lateral ( $24.0 \pm 4.1$  vs  $21.7 \pm 4.0$  cm,  $P < .001$ ) abdominal subcutaneous fat was greater before than after treatment. Although there was no change in patients' measured abdominal circumference over time, there was a significant difference of 9.1 mm in subcutaneous fat measured by skin fold thickness between treated and control sides at the end of the experimental study ( $P = .032$ ). Representative photographs and magnetic resonance images are shown in Figures 2 and 3, respectively.

### Adipose Tissue Histology

There were no changes in adipocyte diameter, volume, or lipid content after PC-DC injections (Table 3). At 1 week after the first treatment, there were significantly more dispersed macrophages ( $P = .015$ ) (Table 4) and a trend toward increased crown-like structures compared with baseline

**Table 1.** Body Weight and Plasma Concentrations Measured During the Study

	Baseline	Visit 1	Final Visit
Patients, n	7	7	7
Body weight, kg	71.0 $\pm$ 3.7	71.6 $\pm$ 3.6	71.9 $\pm$ 3.8
Glucose, mg/dL	86.1 $\pm$ 1.4	85.7 $\pm$ 1.6	88.4 $\pm$ 4.0
Insulin, $\mu$ U/mL	6.0 $\pm$ 1.5	9.11 $\pm$ 3.1	9.6 $\pm$ 3.0
HOMA-IR value	23.2 $\pm$ 6.2	34.7 $\pm$ 11.8	39.8 $\pm$ 13
FFA, mM	0.74 $\pm$ 0.08	0.71 $\pm$ 0.13	0.57 $\pm$ 0.06
IL-6, pg/mL	2.44 $\pm$ 0.2	2.52 $\pm$ 0.4	2.18 $\pm$ 0.1
Leptin, ng/mL	16.8 $\pm$ 5.8	19.3 $\pm$ 6.5	19.5 $\pm$ 4.5
CRP, mg/L	3.40 $\pm$ 1.7	1.44 $\pm$ 0.3	1.89 $\pm$ 0.6
AST, IU/L	19.7 $\pm$ 1.6	24.4 $\pm$ 3.6	21.2 $\pm$ 1.9
ALT, IU/L	17.1 $\pm$ 2.5	22.1 $\pm$ 5.5	21.2 $\pm$ 2.6
Amylase, U/L	64.7 $\pm$ 9.5	63.1 $\pm$ 10	72.4 $\pm$ 9.6
WBC, $\times 10^3$ cells/ $\mu$ L	6.11 $\pm$ 0.5	6.48 $\pm$ 0.4	5.71 $\pm$ 0.4
HCT, %	40.2 $\pm$ 0.7	38.5 $\pm$ 0.7 <sup>a</sup>	40.8 $\pm$ 0.6
Triglyceride, mg/dL	94.8 $\pm$ 21	114 $\pm$ 29	121 $\pm$ 31
HDL-C, mg/dL	57.8 $\pm$ 4.9	56.7 $\pm$ 4.4	61.8 $\pm$ 7.7
LDL-C, mg/dL	109 $\pm$ 7.5	98.4 $\pm$ 8.4	112 $\pm$ 5.9

Values are means  $\pm$  SEM. ALT, alanine transaminase; AST, aspartate aminotransferase; CRP, C-reactive protein; FFA, free fatty acids; HCT, hematocrit; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment-estimated insulin resistance; IL-6, interleukin-6; LDL-C, low-density lipoprotein cholesterol; WBC, white blood cell.

<sup>a</sup> $P < .021$  between baseline and visit 1.

( $P = .083$ ) (data not shown). However, by 8 weeks after the final treatment, there was no difference in these measures between the treated and untreated sides.

### Adipocyte Gene Expression

Monocyte chemoattractant protein-1 expression was greater at 1 week after the first treatment ( $P = .04$ ) and 8 weeks after the final treatment ( $P = .049$ ) than at baseline (Table 5). Adipocyte VEGF was lower at 1 week ( $P = .004$ ) after treatment but was no longer different from baseline or from the untreated side 8 weeks after the final treatment. The expression of macrophage marker ITGAM did not change during the study.

### Adipocyte Metabolic and Hormonal Gene Expression (Table 5)

Leptin expression was almost 80% lower at 1 week after the first treatment than at baseline ( $P = .02$ ) and tended to remain lower at 8 weeks after the final treatment than at baseline ( $P = .1$ ). At 8 weeks after the final treatment, leptin

**Table 2.** Body Composition and Fat Distribution Measured at Baseline and 8 Weeks After the Final Treatment

	Baseline	Final Visit
Body fat, %	29.3 ± 4.8	34.1 ± 2.3
Total body fat, kg	23.8 ± 2.6	24.5 ± 2.7
Anterior abdominal subcutaneous fat thickness, cm, control side	33.2 ± 4.2	31.7 ± 3.0
Anterior abdominal subcutaneous fat thickness, cm, treated side	32.8 ± 4.0	28.7 ± 3.4 <sup>a</sup>
Lateral abdominal subcutaneous fat thickness, cm, control side	23.0 ± 3.9	23.5 ± 3.7
Lateral abdominal subcutaneous fat thickness, cm, treated side	24.0 ± 4.1	21.7 ± 4.0 <sup>b</sup>
Abdominal circumference, cm	100.4 ± 2.6	98.8 ± 3.8
Skinfold thickness, mm, control side	36.9 ± 1.7	33.3 ± 1.3 <sup>c</sup>
Skinfold thickness, mm, treated side	34.4 ± 1.7	24.2 ± 1.6

Values are means ± SEM.

<sup>a</sup> $P = .004$ .

<sup>b</sup> $P < .001$ .

<sup>c</sup> $P < .05$  vs pretreatment.

expression was lower in the treated than in the untreated side ( $P = .05$ ). Changes in expression of several genes related to lipid uptake and metabolism by adipocytes were noted. Expression of HSL decreased by ~75% from baseline ( $P = .004$ ) 1 week after the first treatment and was lower 8 weeks after the final treatment than measurements for baseline ( $P = .03$ ) and the untreated side ( $P = .05$ ). Adipose triglyceride lipase was lower at 1 week after the first treatment ( $P = .03$ ) and 8 weeks after the final treatment ( $P = .02$ ) and was markedly lower than the untreated side ( $P = .03$ ). CD36 expression was not significantly different 1 week after the first treatment ( $P = .16$ ) but was significantly lower at 1 week after the first treatment as compared with 8 weeks after the final treatment ( $P = .05$ ).

### Fibrosis

No changes in expression of COL4A1 and COL6A1 genes (Table 6) were found. Expression of the COL6A3 gene tended to be greater at 1 week after the first treatment than at baseline ( $P = .08$ ) but was not different from baseline values 8 weeks after the final treatment.

### Apoptosis

Caspase 8 expression was greater at 1 week after the first treatment than at baseline ( $P = .02$ ) and was slightly greater than the untreated side 8 weeks after the final treatment ( $P = .05$ ). Caspase 3, CD95/fas, and GPR78 expression were unchanged during the study (Table 7).

### Patient Satisfaction

Patient satisfaction with the treatment protocol was high. All participants reported they were glad that they had the

treatments. Six of 7 participants reported seeing a visible difference in the treated side, preferred the treatment side and thought the amount of fat seemed less, elected to receive a similar treatment on the control side, and would recommend the treatment to others. Two of 7 participants said that they wished they could have had liposuction instead of the injection protocol.

No serious adverse events (SAE) were reported during the trial. Typical side effects reported in the treatment area were those expected based on reports in the literature: edema, erythema, pain, stinging or burning sensation, tenderness to touch, bruising, and temporary nodules or lumps. Less frequent side effects were itching and brief episodes of facial flushing, nausea, diarrhea, hyperpigmentation, and contour irregularity. Most of these tended to resolve within 1 week, with swelling and tenderness sometimes lasting into the second week following treatment. Pain following treatment was generally limited to a few days and was usually treated by over-the-counter medications, but narcotics were also made available and sometimes used.

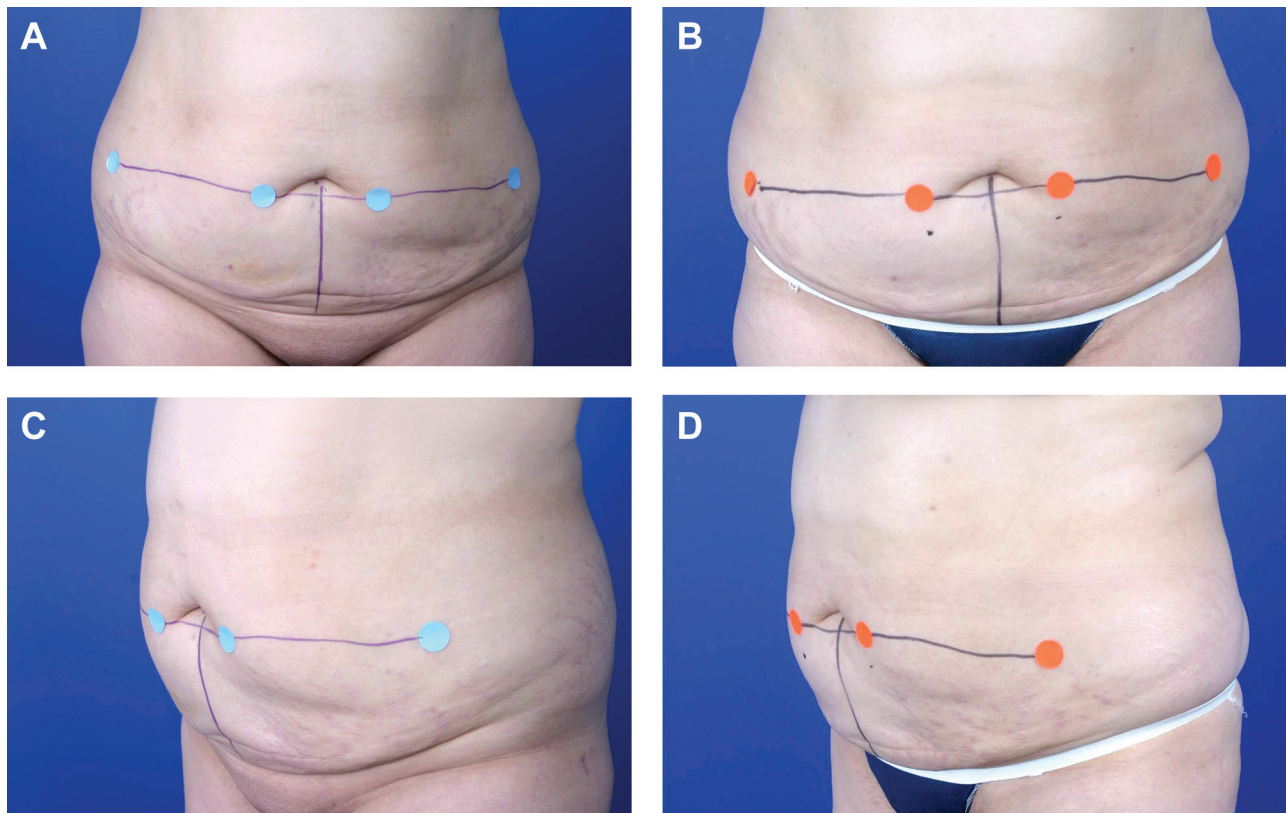
## DISCUSSION

The purpose of the present study was to carefully evaluate the effect of PC-DC treatment on glucose and lipid metabolism and plasma markers of inflammation. Furthermore, we wished to examine the effect of treatment on adipose tissue histology and gene expression in addition to aesthetic measures of efficacy. Treatment with PC-DC subjectively and objectively reduced abdominal adipose tissue and was well tolerated. Seven days after treatment with PC-DC, there was increased local gene expression of MCP-1 and increased macrophage dispersal and crown-like structures. In addition to causing a transient local inflammatory infiltrate, PC-DC treatment reduced markers of lipid uptake (CD36), triglyceride metabolism (HSL, ATGL), and adipose-tissue associated hormones (leptin). These data suggest that PC-DC treatment effectively reduced local adipose tissue deposits, increased tissue inflammation, and reduced fat mass by adipocyte necrosis. The treatment had no effects on glucose and lipid metabolism or circulating inflammatory markers.

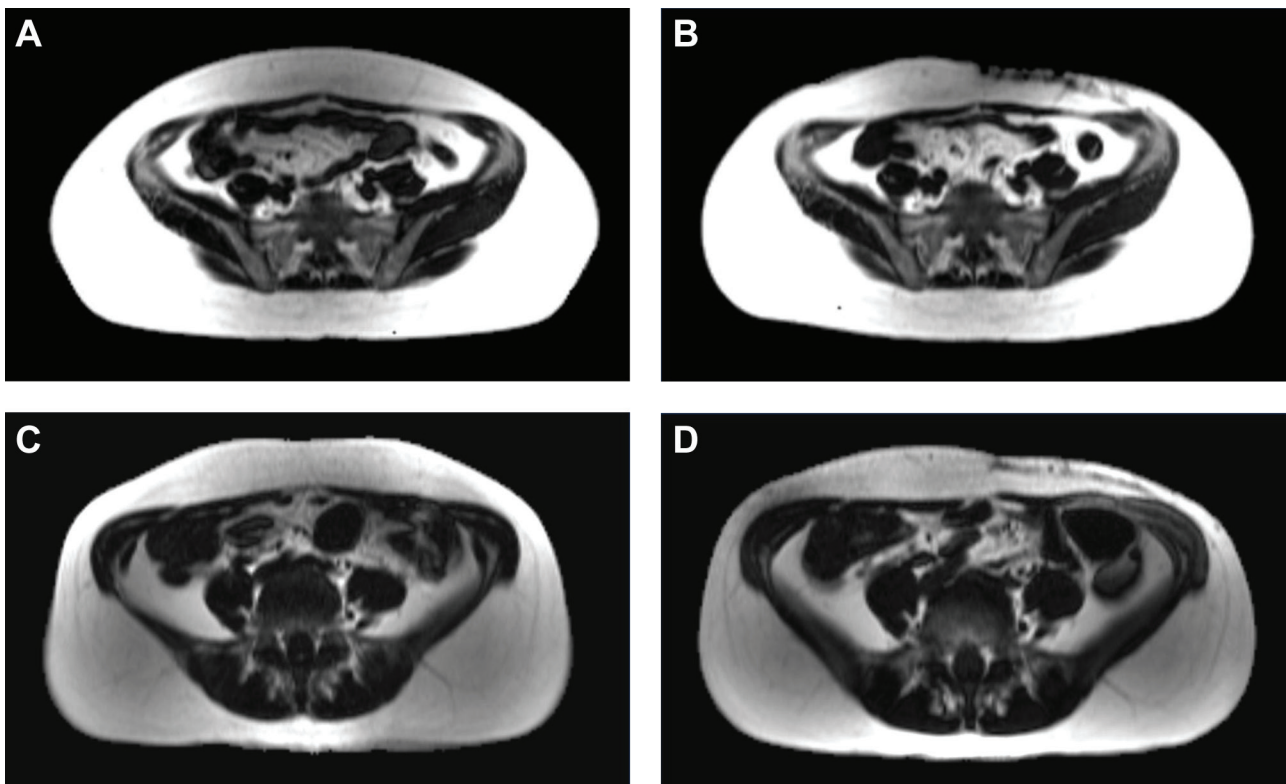
To our knowledge, this is the first study to sequentially evaluate the effects of PC-DC injection on adipose tissue histology and gene expression in a cohort of human subjects.

We found that PC-DC reduced abdominal adipose tissue volume in the treated areas. These findings are in agreement with most, but not all, prior studies using PC-DC injections.<sup>9,22,23</sup> The majority of the patients in the published literature saw improvements with treatment, but in all series, there were some patients who were non-responders to the treatment. Tawfik et al<sup>24</sup> failed to see any improvement in lower eyelid appearance after multiple injections of PC-DC in a randomized, double-blind, placebo-controlled study in 45 healthy adults.

It is likely that DC is predominantly responsible for the reduction in adipose tissue mass in subjects treated with



**Figure 2.** (A, C) This 52-year-old woman with a BMI of 29.3 wanted to decrease her abdominal subcutaneous fat. (B) Six weeks after the last phosphatidylcholine and deoxycholate treatment. (D) Eight months after the patient's first treatment.



**Figure 3.** These representative magnetic resonance images, taken approximately 4 cm below the umbilicus, illustrate changes over time in abdominal subcutaneous fat following treatment. (A, B) A 48-year-old woman is shown prior to treatment and 8 weeks following final treatment. (C, D) A 42-year-old woman is shown prior to treatment and 8 weeks following final treatment.

**Table 3.** Adipocyte Parameters at Baseline, 1 Week After the First Treatment, and 8 Weeks After the Final Treatment

	Baseline	1 Week	8 Weeks After the Final Treatment	
			Treated Side	Control Side
Adipocyte diameter	104 ± 7	104 ± 7	104 ± 7	108 ± 10
Adipocyte volume, ×10 <sup>5</sup>	7.45 ± 1.77	7.26 ± 1.57	7.91 ± 2.51	9.09 ± 3.00
Lipid content	0.69 ± 0.16	0.67 ± 0.14	0.83 ± 0.27	0.72 ± 0.23

Data are means ± SEM.

**Table 4.** Macrophage Dispersal in Adipose Tissue at Baseline, 1 Week After the First Treatment, and 8 Weeks After the Final Treatment

Patient	Baseline	1 Week	8 Weeks After the Final Treatment	
			Control Side	Treated Side
Y-01	1	2	1	3
Y-02	0	2	1	2
Y-04	0	1	0	1
Y-07	0	2	1	0
Y-08	0	2	1	0
Y-11	1	2	2	2
Y-13	1	2	1	1

Data scored by blinded observer. 0 = no dispersed macrophages; 1 = minimal dispersal; 2 = moderate dispersal; 3 = heavy dispersal.

PC-DC. Salti et al<sup>25</sup> compared the effects of injections of PC-DC or DC into subcutaneous fat on the outer thigh in 40 women. Injections of PC-DC were administered on 4 occasions over an 8-week period to 1 outer thigh, and a comparable dose of DC was placed in the opposite thigh. After 8 weeks of treatment, an overall reduction in fat was seen in 91.9% of patients. There was no difference in fat loss between the sides, suggesting that DC was the active component. Similarly, others have reported no difference in efficacy in submental fat between patients treated with PC-DC or DC alone after a 4-week intervention.<sup>26</sup>

The mechanisms through which PC-DC reduces adipose tissue mass are unclear; both adipocyte apoptosis and increased lipolysis have been proposed. We found that injection of PC-DC rapidly caused an increase in crown-like structures, expression of caspase-8, and macrophage chemotactic factors. These changes were accompanied by a reduction in genes associated with the metabolic and hormonal activity of adipocytes (ie, leptin, ATGL, HSL). These results suggest, in agreement with the literature, that PC-DC induces adipocyte dysfunction, necrosis, and macrophage infiltration, causing fat loss. These findings

**Table 5.** Adipocyte Gene Expression and Macrophage Markers at Baseline, 1 Week After the First Treatment, and 8 Weeks After the Final Treatment

	Baseline	1 Week	8 Weeks After the Final Treatment	
			Control Side	Treated Side
CD36	2.36 ± 0.37	1.23 ± 0.16	2.93 ± 0.43	2.14 ± 0.23 <sup>a</sup>
HSL	4.84 ± 0.70	1.08 ± 0.18 <sup>b</sup>	4.46 ± 0.89	2.14 ± 0.29 <sup>b,c</sup>
ATGL	1.07 ± 0.19	0.34 ± 0.14 <sup>b</sup>	1.31 ± 0.38	0.18 ± 0.07 <sup>b,c</sup>
FAS	1.72 ± 0.27	0.80 ± 0.44	1.48 ± 0.26	1.29 ± 0.15
Leptin	0.58 ± 0.13	0.11 ± 0.03 <sup>b</sup>	0.53 ± 0.11	0.22 ± 0.06 <sup>c</sup>
Adiponectin	5.56 ± 0.84	2.43 ± 0.75	5.08 ± 1.01	1.89 ± 0.35
TNF $\alpha$ , ×10 <sup>-3</sup>	0.61 ± 0.14	0.83 ± 0.21	0.66 ± 0.13	0.89 ± 0.19
IL-6	1.42 ± 0.21	2.41 ± 0.49	1.41 ± 0.53	0.95 ± 0.29
MCP-1, ×10 <sup>-2</sup>	2.54 ± 0.44	6.35 ± 0.78 <sup>b</sup>	3.10 ± 0.98	4.12 ± 0.68 <sup>b</sup>
EMR1, ×10 <sup>-4</sup>	8.53 ± 4.40	8.45 ± 1.16	6.26 ± 3.84	5.38 ± 1.60
ITGAM, ×10 <sup>-3</sup>	7.45 ± 1.95	14.02 ± 2.39	10.66 ± 2.29	5.85 ± 1.45
VEGF	0.20 ± 0.04	0.09 ± 0.03 <sup>b</sup>	0.16 ± 0.29	0.10 ± 0.01

Values are means ± SEM. ATGL, adipose triglyceride lipase; CD36, cluster of differentiation 36; EMR1, EGF-like module-containing mucin-like hormone receptor-like 1; FAS, fatty acid synthase; HSL, hormone-sensitive lipase; IL-6, interleukin-6; ITGAM, integrin alpha M; MCP-1, monocyte chemoattractant protein-1; TNF- $\alpha$ , tumor necrosis factor- $\alpha$ ; VEGF, vascular endothelial growth factor.

<sup>b</sup>P < .05 vs corresponding value before treatment.

<sup>c</sup>P < .05 vs corresponding value on untreated side at 8 weeks.

<sup>a</sup>P < .05 vs corresponding value at 1 week.

**Table 6.** Caspase and GRP78 Expression at Baseline, 1 Week After the First Treatment, and 8 Weeks After the Final Treatment

	Baseline	1 Week	8 Weeks After the Final Treatment	
			Control Side	Treated Side
COL4A1	1.37 ± 0.13	1.27 ± 0.20	1.30 ± 0.23	0.87 ± 0.11
COL6A1	1.20 ± 0.13	1.57 ± 0.15	1.36 ± 0.13	1.12 ± 0.08
COL6A3	0.41 ± 0.06	0.61 ± 0.07	0.53 ± 0.08	0.47 ± 0.04

Values are means ± SEM. COL4A1, collagen type IV, alpha 1; COL6A1, collagen type VI, alpha 1; COL6A3, collagen type VI, alpha 3.

are in agreement with several prior studies that have examined the cellular effects of local treatment with PC-DC.<sup>27</sup> Klein et al<sup>28</sup> examined the in vitro effects of PC-DC on lipolysis and cell viability in 3T3-L1 adipocytes. Deoxycholate alone and PC-DC both produced dose-dependent cell death in 3T3-L1 adipocytes, whereas PC alone had no effect. Neither PC alone nor the PC-DC combination induced lipolysis. Gupta et al<sup>29</sup> found similar

**Table 7.** Collagen Markers at Baseline, 1 Week After the First Treatment, and 8 Weeks After the Final Treatment

	Baseline	1 Week	8 Weeks After the Final Treatment	
			Control Side	Treated Side
Caspase 3	1.73 ± 0.30	1.36 ± 0.16	1.10 ± 0.13	1.18 ± 0.25
Caspase 8	2.69 ± 0.36	3.37 ± 0.46 <sup>a</sup>	2.64 ± 0.22	3.16 ± 0.33 <sup>b</sup>
CD95/fas	7.50 ± 0.47	9.82 ± 1.28	7.48 ± 0.43	12.00 ± 1.25
GRP78	0.46 ± 0.06	0.48 ± 0.05	0.45 ± 0.06	0.45 ± 0.05

Data are means ± SEM. CD95/fas, cluster of differentiation 95/Fas receptor; GRP78, 78-kDa glucose-regulated protein.

<sup>a</sup>*P* < .05 vs corresponding condition before treatment.

<sup>b</sup>*P* < .05 vs control side 8 weeks after the final treatment.

effects in treated 3T3-L1 adipocytes, fibroblasts, neonatal human dermal microvascular endothelial cells, and fetal human skeletal muscle cells.

Inflammation has been closely associated with impaired insulin sensitivity and adverse effects on plasma lipids. We systematically examined the effects of treatment on glucose and lipid metabolism and on markers of inflammation. Fortunately, despite robust increases in inflammation in the treated adipose tissue, there were no changes in plasma glucose or cholesterol. Furthermore, we saw no change in the plasma concentration of CRP, suggesting that total-body inflammation was not dramatically affected by the intervention.

Overall, PC-DC treatments were well tolerated and produced highly significant improvements in adipose tissue mass in the treated areas. As expected, some discomfort and bruising occurred following treatment, but there were no major SAE. Several authors have reported case series for PC-DC treatment to multiple anatomical areas. In 2006, Hasengschwandtner<sup>8</sup> reported the results of the 2004 Network Lipolysis group, which included 400 physicians from 29 countries. At that time, the Network Lipolysis database had data on 5000 patients and side effects experienced by a total of 753 treated patients, including pain at the injection site, bruising, itching, burning, redness, swelling, sensitivity to touch, dents, nodules, and cysts. Results of over 10 000 PC treatments administered during a 13-month period from a network of 39 UK doctors specially trained to administer the injections revealed that 73.8% of patients reported either being “very satisfied” or “satisfied” with the treatments.<sup>30</sup> Local side effects in these patients included swelling, erythema, burning/stinging, pain, tenderness, and bruising, which were described as very mild or mild by most patients. Systemic side effects were reported in 3% of cases and included diarrhea, nausea, dizziness/light headedness, and intermenstrual bleeding. These data suggest that PC-DC injections have minimal risk when administered by trained physicians. However, this study must be interpreted in view of

its limitations, which include that it was a small phase I clinical trial directed mainly at determining safety, with efficacy as a secondary end point. Also, photographic results are not very impressive, indicating that these injections could be used only to treat minimal excesses of fat. Larger, multicenter trials would be necessary to better define safety and determine the best parameters for use.

## CONCLUSIONS

In summary, we have shown in this small study that injections of PC-DC can effectively reduce abdominal fat volume and thickness, with no serious adverse effects in healthy adult women. We believe that the ideal candidate for injection lipolysis desires treatment of small areas of excess fat or localized deposits, such as the correction of postlipoplasty contour irregularities or asymmetry. Injection lipolysis is a tool for those patients who wish to have less invasive procedures and/or are afraid of anesthesia. However, patients need to be aware that achieving desired results may take several months.

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