

[워크샵]

포스파티딜콜린을 사용한 지방분해

윤 세 진

다남재활의학과

PPC (Phosphatidylcholine) → PC



Table 1. Injectable Phosphatidylcholine Formula

Phosphatidylcholine	5% (w/v)
Sodium deoxycholate	4.75%
Benzyl alcohol	0.9%
Water	100 mL

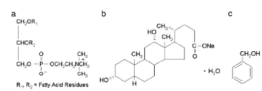


Figure 1. Molecular structure of (A) phosphatidylcholine, (B) sodium deoxycholate, and (C) benzyl alcohol.

cf) Deoxycholic acid

→ PC를 soluble하게 만들어 주는 필수적 성분

cf) Benzyl alcohol

→ Preservative in injectable solution

PC

- Bile component
- Deit의 lipid를 emulsification
- Soybean lecithin 혹은 egg yolk로부터 추출
- Cholesterol 과 TG의 systemic level 감소
- Cell membrane에서 insulin 의 감수성을 증가
- 냉장보관, light에 노출 시 역가 감소

History

- 1st reports of cardiological use :
→ Lipostabil 70's
- 1st cosmetic use :
→ Italy, Sergio Maggiori in 1998'
Brazil, 1990'
- : The drug was administered orally and parenterally,
mainly by Italian and Russian physicians.
- Injectable PC
Lipostabil (Aventis, fat embolism)
Essentiale (Rhône-Poulenc Rorer, liver dis.,
Riboflavin 함유)
Lipo-bean (진양제약, liver dis.)

Fat dissolution 이외의 다른 적응증

- Cardiac ischemia
- Lipid atheroma, hypercholesterolemia
- Fat embolism, fatty deposits or plaque
- Mental disturbance
(Alzheimers dis., Bipolar disorders etc.)
- Chronic liver disease et al.

Potential Mechanism(s) of Action

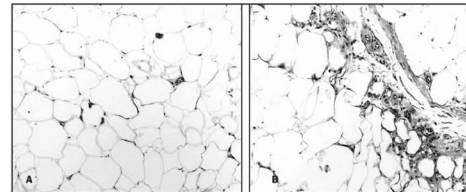
1. PC penetrates the adipocytes through the double layers: acting as an emulsifying/tensioactive agent. → altered stored lipid → soluble lipid
 2. the capacity of PC to stimulate lipase release, which might result in breakdown of TG to FA that are then transported as lipoproteins. (histamine release a/w lipase activity → itching & erythema)
- cf: The capacity of phosphatidylcholine to reduce blood cholesterol as well as high and low lipoprotein levels was reported

Summary: mechanism of action

1. Cell-wall disruption
2. Enzymatic and lipoprotein transport of TG and FA out of the adipocyte → smaller adipocyte
3. Inflammation → tissue retraction
4. New collagen formation in the subdermal plane, causing skin retraction and a denser, firmer skin character.

Histological changes

- Kopera etc. 2006'
- Focal fibrosis
inflammatory reaction with granulomatous features
pseudomembranous degeneration of fat cells
- "Inflammatory-mediated necrosis & resorption"



Cell-wall disruption, focal inflammation, and strands of collagen deposition aligned with a palisade of fat cells with marked reduction in diameter

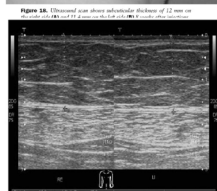
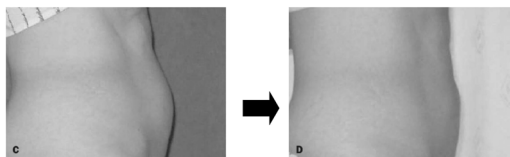


Figure 2. Ultrasound scan shows subcutaneous thickness of 12 mm on the right side, 20 mm on the left side, and normal redundancy of subcutaneous fatty tissue.

Indication a/w local fat

Table 2. Areas of treatment in the Lipodissolve study

Facial	Infraorbital fat pads, jowls, immediate submandibular jawline, chin, bulging reconstructive facial flaps, and submental fat deposits
Upper torso	Preaxillary fat pads, male gynecomastia, upper back rolls, axillary bra rolls, upper volar arms, overhanging skin and fat deposits at waistline, epigastrium, "six pack" area definition (in bodybuilders), male and female abdomen, male and female flanks, buffalo hump secondary to prednisone use
Lower torso	Medial buttock cellulite, lower lateral buttock, infragluteal banana roll, posterolateral thigh cellulite, outer thigh/saddlebags, inner thigh, anterior thigh, medial and suprapatellar knees, and upper calves

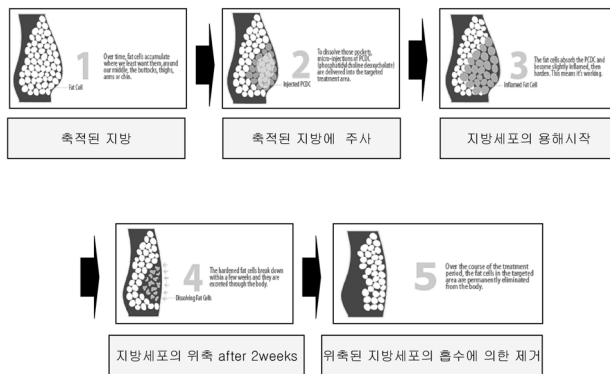
Best indication : thin skin, soft fat, appropriate skin laxity

The best areas to treat (% of good results)

1. Abdomen: 78.7%
2. Flanks: 42.7% (female > male)
3. Submental chin: 37.3%
4. Back and "bra rolls"
5. Outer thigh: frequently fibrous in nature.
6. Inner thigh: generally 3 treatments for optimal results.
7. Jowls
8. Upper arms: variable due to skin laxity.
The best candidates –younger patients without a large amount of excess skin.
9. Neck: submandibular jawline : an advanced learning curve.
10. Knees: strongly technique dependent.
11. Gluteal fold

Worst Areas to Treat

1. Below the knee as there is a high risk of skin loss and /or ulceration
2. Flat fat deposits
3. Firm, fibrous fat
4. A large amount of skin laxity
5. Obesity
6. estrogen–dominant women with hypoactive thyroid function.



Injection method 1

- 27G needle, 메조렐
 - Subcutaneous injection
 - PC 1) alone : lipoma
2) mix it with lidocaine (injection pain)
and/or Pentoxifylline, Buflomedil (circulation)
aminophylline, multi-vitamine
and/or Normal saline (dilution)
and/or Hyaluronidase (edema) etc.
- ex) 1) PC 1 ample (5ml) + N/S 4ml + 2% or 1% Lidocaine 1ml = 10ml
→ total 100ml (10 vials of PC)
(0.5ml/site, 1~1.5cm apart, 6~15mm depth, > 2 weeks interval)

Injection method 2

- Deep → fascia 나 muscle에 injury 가능
- If more skin retraction is desired → a 1.0cm interval & 6~8mm depth
- If fat loss is the primary goal, the first injection is done at the 10- or 13-mm level, followed by a 6mm injection level for the second treatment.
- Soft fat & Thinner skin → more responsive

Dispersion: 0.4ml

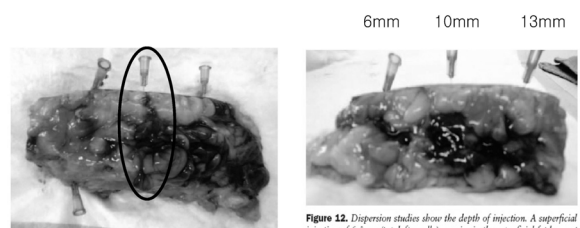


Figure 11. Dispersion studies show the effect of spacing of injections. The top left needle indicates a 1.5-cm spacing with no coalescence of formula. The central needle shows the effect of a 1.0-cm spacing, with good coalescence. The far right needle shows the effect of a 0.75-cm spacing, with dense coalescence and upward migration.

Figure 12. Dispersion studies show the depth of injection. A superficial injection of 6-mm (top left needle) remains in the superficial fat layer at 1 hour. The central needle shows a 10-mm injection depth in which the formula disperses at the level of Scarpa's fascia. The deeper 13-mm injection level (needle, far right) shows deep migration. Unless the fat pad is very thick, deep injections should be avoided.

1cm 간격이 제일 적당

주사목적과 Target으로 하는 지방층의 깊이에 따라 주사 깊이도 조절

Maximum safety dosage

- 2000 to 2500mg/treatment session

After Care

Drink enough / Exercise (15min/day)
 Compression: to reduce edema
 Analgesics : Acetaminophene 24-48hrs
 Antihistamine and 시네크 캄셀
 Lymphatic drainage: to help edema & fat absorption within 2 days
 US : cavitation증가로 fat necrosis 증가, skin retraction 증가 효과
 Avoidance of aspirin & NSAIDs:
 stops adipocytes from bursting open

Adverse effects

- Buring sensation (15min)
- Edema (peak : 6hr- 7hrs, moderate to severe)
- Eye : impaired vision, atrophy, swelling
- Local erythema
- Localized heat
- Discomfort & pain Nodule
- Itching at the application points Dermatology 2008;
- Encapsulated fat necrosis in calf (Dermatology 2008)
- Possible A/Ex: Infection, allergic reaction, necrosis, irregularity

Complications

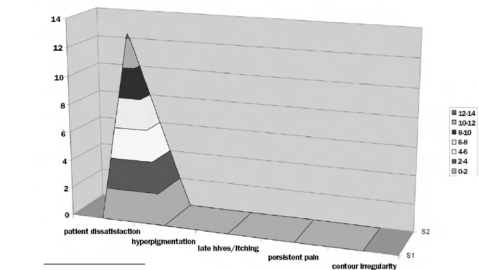


Figure 5. Complications following injection lipolysis.

Pain after injection

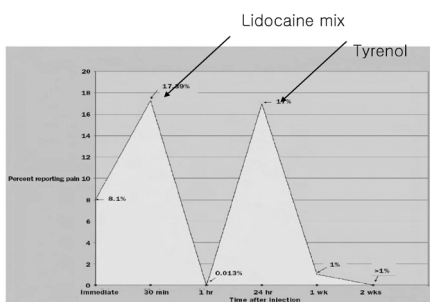


Figure 3. Pain incidence following injection lipolysis.

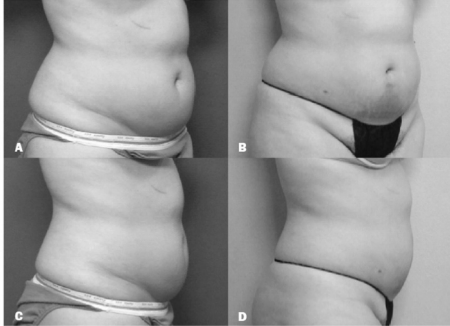


Arnica Montana



시네크 캄셀

Hyperpigmentation



PC or DC ?

ADAM M. ROTUNDA: Dermatol Surg 30:7:July 2004

Detergent Effects of Sodium Deoxycholate (DC) Are a Major Feature of an Injectable phosphatidylcholine Formulation Used for Localized Fat Dissolution

DC as a detergent causing nonspecific lysis of cell membranes.

Sodium deoxycholate is the major active component responsible for cell lysis. Detergent substances may have a role in eliminating unwanted adipose tissue.

It is advised that physicians use caution until adequate safety data are available.

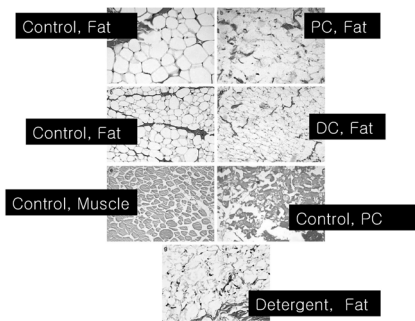


Figure 5. Light microscopy of porcine skin biopsies revealing (A) control lipocytes and (B) lipocytes after phosphatidylcholine formula injection (hematoxylin and eosin, original magnification, 20). (C) Control lipocytes and (D) lipocytes after sodium deoxycholate injection (hematoxylin and eosin, original magnification, 10). (E) Control muscle and (F) muscle after phosphatidylcholine formula injection (hematoxylin and eosin, original magnification, 10). (G) Fat after injection with Emipigen detergent (hematoxylin and eosin, original magnification, 20).

- Rotunda 2005', J Am Acad Dermatol:
6 patients, 12 lipomas
Low concentration deoxycholate maybe a relatively safe and effective treatment for small correction of fat (lipoma)
- Disadvantage
 1. Intense pain and persistent numbness
 2. The injections remained in the in vitro porcine specimen for only 1 to 4 hours. A human in vivo biopsy with a longer duration of action would be necessary to better understand the compound's effect on subcutaneous fat over a 1-month time period. *By Diane Irvine Duncan*

- Deoxycholate → non-specific cell lysis가능
- 하지만 주사 후 PC, DC 모두 Cell mb의 disruption을 일으키지만 일단 주사 후에는 PC가 8-10주간 작용한다.
- 단 조직내 PC의 critical concentration
> 250mmol - adipocyte cell disruption
< - effusion of cytoplasmic contents
- 결론 : PC or DC 모두 fat reduction에 관여하지만 보다 장기적 지방 분해 효과는 PC의 역할이 클 가능성이 있다.

Advantage of PC

- No reduction of skin laxity without "surgical look"
- No surgical or anesthetic risk
- Rapid office procedure; "lunch-time lipo"
- No skin scars
- A 4-cm waistline reduction (Franz Hasengschwandtner)
A 2.7-cm circumference reduction (Heinrich)

Factors of treatment failure

- Incorrect antisepsis
- Medication of dubious origin
- Excessive total dose & volume at each points
- Inappropriately small distance between the points
- Superficial injection less than 1cm below the epidermal surface.

A less-than-expected response

Unrealistic expectations
 Poor patient selection
 Low dose injection in a large area
 Obesity
 Severe hypothyroidism
 Area of firm, fibrous fat

FACE

1. Lower lid bulging

- Rittes
 30 patients, 2 years follow up
 no recurrence
 adv: no scar tissue
- Medication : PC(250mg/5ml) 0.4cc
- Depth : 0.5 cm
- Position : Seated position
- Needle : 0.5 inch, 30 gauge
- 3 direction (central, medial, and lateral)
- Post injection : Ice compression after injection(10min)
 Upright position for 4 hours
- Contraindication: prominent malar folds
 lax lower eyelid skin

► Prominent lower eyelid fat pads (71-year-old woman)

Pretreatment Posttreatment (+ 6 weeks)

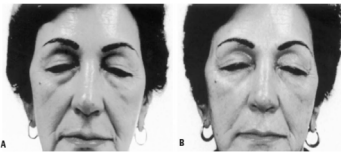


Figure 3. A, A 71-year-old woman with prominent lower eyelid fat pads. B, Patient following 3 Lipostabil injections. (Photos courtesy of Dr. Patricia Gaudin-Berthel)

- Using : 0.4ml of PC(250mg/5ml), 3 injections at 15-days intervals

Reference : V.Leroy Young MD, Lipostabil : The effect of Phosphatidylcholine on Subcutaneous Fat, Aesthetic surgery Journal, p413-417, 2003

► Prominent lower eyelid fat pads (55-year-old woman)

Pretreatment Posttreatment (+ 8 weeks)

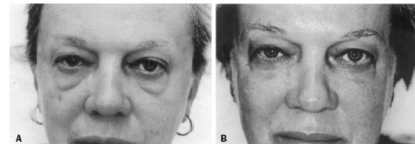


Figure 3. A, A 55-year-old woman with prominent lower eyelid fat pads and what appears to be excess skin in that area. B, Patient following 4 Lipostabil injections. (Photos courtesy of Dr. Patricia Gaudin-Berthel)

- Using : 0.4ml of PC(250mg/5ml), 4 injections at 15-days intervals

Reference : V.Leroy Young MD, Lipostabil : The effect of Phosphatidylcholine on Subcutaneous Fat, Aesthetic surgery Journal, p413-417, 2003

Pretreatment



Posttreatment



One treatment session, results after 8 weeks, no weight loss.

Other localized fat

Localized fat

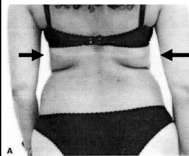
- Doris Hexsel 2003
213 patients : thigh, hip, abdomen, flanks, and/or face

1-5 treatment sessions
Interval : 15 days (>10days)
Pure or diluted in saline solution (0.9%)
Depth : 1-2cm
volume: 0.2ml at each point
distance between the points :2cm
< 2 vials /session
< total 5 sessions of treatment

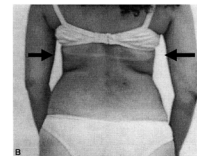
: effective

► Local fat deposit (29-year-old woman)

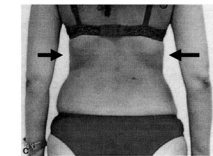
Pretreatment



Posttreatment (+ 15 days)



Posttreatment (+ 30 days)

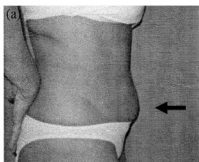


- Using : 30G 1/2 insulin needle to inject 5ml(250mg PC)/80cm²

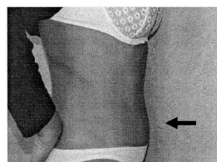
Reference : Patricia Guedes Rittes, M.D., The use of Phosphatidylcholine for Correction of Localized Fat Deposits, Aesthetic Plastic Surgery 27, p315-318, 2003

► Lower belly

Pretreatment



Posttreatment (+6 months)



- 2 treatment sessions, no weight loss, reduction of lower belly of 9cm

Reference : Franz Hasengschwandtner, Phosphatidylcholine treatment to induce lipolysis, Journal of Cosmetic Dermatology 4, p308-313, 2005

► Skin laxity in the epigastric region (51-year-old woman)

Pretreatment



Posttreatment (+2 weeks)



Posttreatment (+4 weeks)



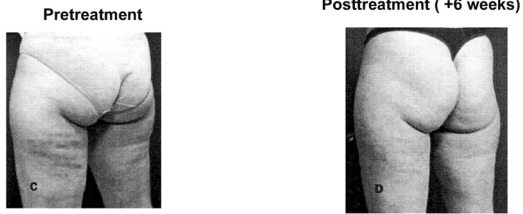
- 2 treatment session (4 to 8 weeks interval)

- Using : 0.4ml(250mg PC)/apart

* She received a more superficial injection technique resulting in a much more dramatic improvement in skin retraction.

Reference : Diane Irvine Ducan, M.D., Lipodissolve for Subcutaneous Fat Reduction and Skin Retraction, Aesthetic Surgery Journal 25, p530-543, 2005

▶ Cellulite and Saddlebags (32-year-old woman)

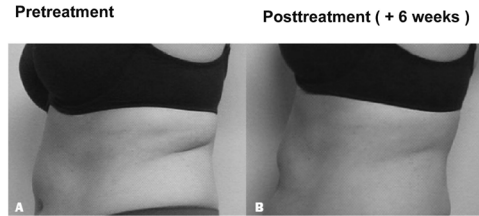


- 3 treatment session (4 to 8 weeks interval)
- Using : 0.4ml(250mg PC)/apart

※ Significant improvement was noted in both areas.

Reference : Diane Irvine Duncan, M.D., Lipodissolve for Subcutaneous Fat Reduction and Skin Retraction, Aesthetic Surgery Journal 25, p530-543, 2005

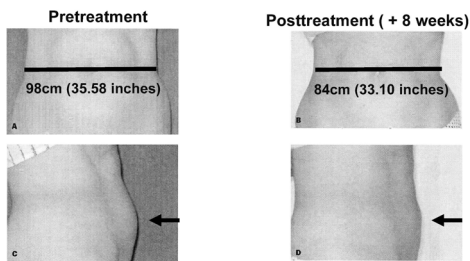
▶ Back roll (52-year-old woman)



- 1 treatment session

Reference : Diane Irvine Duncan, M.D., Clinical Safety Data and Standards of Practice for Injection Lipolysis : A Retrospective Study, Aesthetic Surgery Journal 26, p575-585, 2006)

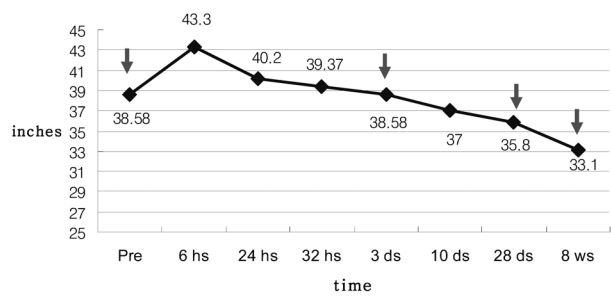
▶ Upper & Lower abdominal (54-year-old woman) 1



- Using mixture : PC(250mg/5ml) + NaCl 0.9%(50%) + Buflomedil(5%) + Vitamin B
- Using needles of 27-gauge thickness and 12-mm length, Depth was 12mm

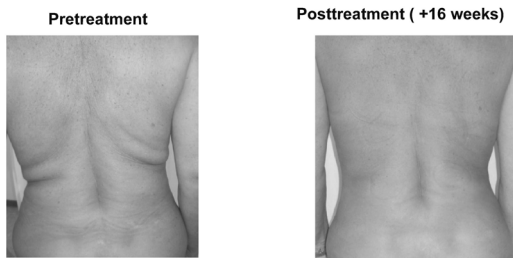
Reference : Franz Hasengschwandtner, M.D., Detailed Documentation of one Lipolysis Treatment : Blood Values, Histology, and Ultrasound Findings, Aesthetic Surgery Journal 27, p204-211, 2007

Lower abdominal (54-year-old woman) 5



Reference : Franz Hasengschwandtner, M.D., Detailed Documentation of one Lipolysis Treatment : Blood Values, Histology, and Ultrasound Findings, Aesthetic Surgery Journal 27, p204-211, 2007

▶ Dorsal fat and Skin laxity (57-year-old woman)



- 1 treatment session
- Mixture : PC(250mg/ml) + NaCl(50%) + Buflomedil(5%) + B-vitamin

Reference : Franz Hasengschwandtner, M.D., Injection Lipolysis for Effective Reduction of Localized Fat in place of Minor Surgical Lipoplasty, Aesthetic Surgery Journal 26, p125-130, 2006

Lipoma

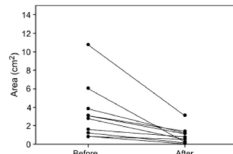


Fig 1. Lipoma area before and after subcutaneous deoxycholate injections.

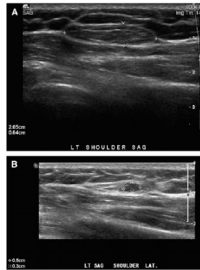


Fig 2. A, Ultrasound of lipoma 7 located on the shoulder measuring 2.65 × 0.64 cm before treatment. B, Same lipoma measuring 0.5 × 0.3 cm 4 months after second and last injection.

Table II. Clinical response and duration of reaction based on clinician and patient observations after injections

Reaction	Duration	Comments
Burning	30 min-24 h	None-very mild (1% deoxycholate) or severe (2.5% and 5.0% deoxycholate)
Erythema	24 h-5 days	Mild-moderate in all patients; longer duration more common with 2.5% and 5.0% deoxycholate
Tenderness	Several days-weeks	Very mild-moderate in all patients; longer duration and higher intensity related to increasing concentrations
Echymoses	10 and 14 days	Occurred in two patients using 1% and 5% deoxycholate who experienced bleeding at the injection site
Cutaneous anesthesia (no pinprick, soft touch)	4 and 6 wk	Occurred in two patients with forearm lipomas injected with 5% deoxycholate; resolved without intervention in both cases

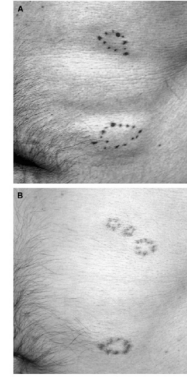
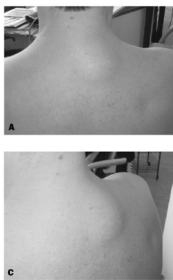


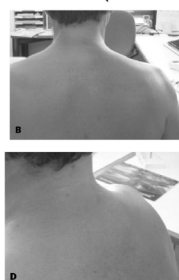
Fig 3. Lipomas 2 and 3 before (A) and after (B) treatment. Lipoma 2 fragmented into 3 divided lesions 4 months after third and last injection.

► Lipoma (47-year-old man)

Pretreatment



Posttreatment (+8 weeks)



Reference : Franz Hasenschwandtner, M.D., Injection Lipolysis for Effective Reduction of Localized Fat in place of Minor Surgical Lipoplasty, Aesthetic Surgery Journal 26, p125-130, 2006

► Efficacy & Safety

● Efficacy

Reported	No.	%
Total patients	20	100.00
Reduction in the deposits of localized fat on the face after PC treatment	18	90.00
- Marked reduction	9	50.00
- Moderate reduction	6	33.30
- Discreet reduction	3	16.00
The improvement persisted up to 3 years after the treatment sessions	16	80.00

● Safety

Reported	Show	No.	%
Pain, Itching, Erythema	1 or 2 days	20	100.00
Edema	Max. 10 days		
Bruising	Immediately		
No systemic side effect was reported by these patients			
Although these side effects disappeared in a shot time			

* Patients may cause more discomfort in facial areas than in body areas, where they can be hidden by clothing.

Reference : Doris Maria Hexel, M.D., Cosmetic use of injectable phosphatidylcholine on the face
Otolaryngologic Clinics of North America (SCI) 38, p1119-1129, 2005

► Analysis 1. (Number of treatment sessions)

치료부위	시술횟수								합계
	1회		2회		3회		4회		
	환자수	%	환자수	%	환자수	%	환자수	%	
상복부 / 하복부	17	13.93	88	72.13	15	12.30	2	1.64	122
문대퇴의 비만증	8	7.21	81	72.97	15	13.51	7	6.31	111
러브handles / 장골능선	17	26.56	44	68.75	3	4.69	0	0.00	64
넓다리 안	15	51.72	9	31.03	5	17.24	0	0.00	29
이중턱 / 얼굴	6	30.00	14	70.00	0	0.00	0	0.00	20
무릎관절 안	0	0.00	18	90.00	2	10.00	0	0.00	20
영덩이	0	0.00	20	100.00	0	0.00	0	0.00	20
지방종	2	16.67	9	75.00	1	8.33	0	0.00	12
기타(볼,목,가슴,상완,장딴지)	3	6.98	36	83.72	2	4.65	2	4.65	43
합계	68	15.42	319	72.34	43	9.75	11	2.49	441

Reference : Franz Hasenschwandtner, M.D., Injection Lipolysis for Effective Reduction of Localized Fat in place of Minor Surgical Lipoplasty, Aesthetic Surgery Journal 26, p125-130, 2006

► Analysis 2. (Patient satisfaction)

치료부위	높음		보통		낮음		합계
	환자수	%	환자수	%	환자수	%	
상복부 / 하복부	110	90.16	11	9.02	1	0.82	122
문대퇴의 비만증	94	84.68	15	13.51	2	1.80	111
러브handles / 장골능선	57	89.06	6	9.38	1	1.56	64
넓다리 안	25	86.21	4	13.79	0	0.00	29
이중턱 / 얼굴	19	95.00	1	5.00	0	0.00	20
무릎관절 안	14	70.00	5	25.00	1	5.00	20
영덩이	19	95.00	1	5.00	0	0.00	20
지방종	7	58.33	4	33.33	1	8.33	12
기타(볼,목,가슴,상완,장딴지)	35	81.40	8	18.60	0	0.00	43
합계	380	86.17	55	12.47	6	1.36	441

Reference : Franz Hasenschwandtner, M.D., Injection Lipolysis for Effective Reduction of Localized Fat in place of Minor Surgical Lipoplasty, Aesthetic Surgery Journal 26, p125-130, 2006

Network-Lipolysis Therapy standard

- 50ml PC(2500mg) + 50ml
- Mix = 100ml compound /session
- Bigger region & different tx. area
- Distance of inj. 1.5cm & 0.5ml/single shot
- 8weeks interval between tx. Sessions
- 1-4 treatment session

Network-Compound

- PC 50ml (10 vials)
 - NaCl 0.9% (for dilution: 50ml)
 - 2.5ml of
Vasodilator(pentoxifylline 2.5ml, 1/2 vial)
Vitamine B complex (1/2 vial)
- Total 102.5ml /person/session ("maximum")

Why compound?

- Improvement of compatibility

less pain
less swelling,
less local reaction
greater safety
more effects

Contraindications

Pregnant or nursing women
Minors or children
Allergy or sensitivity to soy products
Infections
Diabetes, vasculitis, or circulatory disturbances
Hepatic carcinoma or altered hepatic function
Regional cancer in the area treated such as breast or skin cancer
Any use in the female breast
Autoimmune diseases such as pemphigus, SLE, dermatomyositis
Obesity
Extreme skin laxity
Severe renal disease etc.

Clinical Safety Data and Standards of Practice for Injection Lipolysis: A Retrospective Study

Diane Irvine Duncan, MD; and Roman Chubaty, MD
Dr. Duncan is in private practice in Ft. Collins, CO. Dr. Chubaty is in private practice in Scottsdale, AZ.

- 75 physicians from 17 countries
- 17,376 patients – 56,320 injection sessions
- Safety records is excellent
- No death or hospitalization
- 0.0021% transient hyperpigmentation
- 0.015% persistent pain beyond 2 weeks posttreatment
- 0.0003% a late allergic reaction
- 0.00006% a contour irregularity
- Disappointment at a less than expected aesthetic result : 12.34%

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Summary

- 0.5ml /site, 1-1.5cm apart, 6-15mm depth, > 2 weeks interval
- Dosage exception
face including N-L fold
0.2ml/shot , 1.5cm apart, 4-6 mm depth
- Lipoma : pure PC as the only exception
- Maximal dosage : 2500mg/session
- 1st result → after 14 days
- Main melting period from week 4 to 8
- Edema, pain, itching & bruises : nearly 100%

- *It will not replace traditional lipoplasty techniques, but is an excellent adjunct or alternative for those patients seeking minimally invasive treatment.*
- *Thank you for your attention!*