

# Lipolysis of Lipomas in Patients with Familial Multiple Lipomatosis: An Ultrasonography-Controlled Trial

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**Background:** Surgery of multiple lipomas, as in patients with familial multiple lipomatosis, is often limited by poor aesthetic outcome owing to extensive scarring.

For this reason, phosphatidylcholine (PDC) has been widely used to treat areas of localized fat accumulation. However, no reports of lipoma therapy with intralesional application of PDC, that is, injection lipolysis, have been published to date.

**Objective:** To investigate whether injection lipolysis with PDC is an effective therapeutic option for patients with multiple lipomas.

**Methods:** Thirty lipomas in 10 patients were sonographically measured prior to treatment. Four injections at intervals of 6 to 8 weeks were done. Sonographic measurements of lipoma size were repeated before each injection. Side effects, a pain score using a visual analogue scale, and patient satisfaction were noted. In one lipoma, histologic changes after lipolysis are described.

**Results:** After four injections, a significant reduction in size of 45.8% was achieved. No complete elimination was seen in any lipoma. Histology showed a mild granulomatous septal panniculitis. Hematoma occurred in eight cases (27%). Four patients described pain on pressure for 3 days after injection. No severe side effects or systemic reactions were observed.

**Conclusion:** Although surgery is the gold standard for lipoma therapy, injection lipolysis with PDC can also significantly reduce lipoma size. Complete elimination was not observed in any lipoma. Given that this was a short-term study, long-lasting therapeutic effects and possible recurrence of lipoma cannot be evaluated.

**Antécédents:** Le traitement chirurgical des lipomes multiples chez les patients souffrant par exemple de lipomatoses multiples familiales est souvent limité par les conséquences esthétiques découlant du nombre de cicatrices.

Pour cette raison, on a largement eu recours récemment à la phosphatidylcholine (PDC) pour traiter les zones d'accumulation de gras. Toutefois, aucun rapport n'a été publié jusqu'à ce jour au sujet du traitement des lipomes grâce à l'application intralésionnelle de PDC, c'est-à-dire lipolyse par injection.

**Objectif:** Examiner si la lipolyse par injection de PDC est une option thérapeutique efficace pour les patients présentant des lipomes multiples.

**Méthodes:** On a mesuré au moyen d'un ultrasonographe 30 lipomes chez 10 patients avant de commencer le traitement. Quatre injections à intervalle de 6 à 8 semaines étaient faites. Des mesures à l'ultrasonographe de la taille de chaque lipome étaient prises avant chaque injection. On a noté les effets secondaires, la cotation de la douleur au moyen de l'échelle visuelle analogue, et la satisfaction des patients. On décrit les changements histologiques postérieurs à la lipolyse dans un lipome.

**Résultats:** Après quatre injections, on a atteint une réduction de taille de l'ordre de 45.8%. Aucune élimination complète de lipome n'a été constatée. L'histologie a montré une panniculite septale granulomateuse secondaire. Huit cas (27%) on développé un hématome. Quatre patients ont mentionné, pendant 3 jours après les injections, sentir de la douleur lorsqu'une pression est exercée sur le site. Aucun effet secondaire grave et aucune réaction systémique n'ont été observés.

**Conclusion:** Bien que la chirurgie soit la norme dans le traitement des lipomes, la lipolyse par injection de PDC peut également réduire considérablement la taille des lipomes. Aucun lipome n'a été complètement éliminé. Toutefois, il ne s'agit que d'une étude de courte durée, où il est impossible d'évaluer les effets thérapeutiques à long terme et la récurrence possible des lipomes.

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**L**IPOMA is one of the most common mesenchymal tumors, occurring in about 1% of the population, mostly located between the skin and deep fascia on the trunk or the extremities.<sup>1</sup> Although lipomas are most often asymptomatic, therapeutic intervention may become necessary owing to discomfort or pain or for cosmetic reasons.

In patients with multiple lipomas, surgical excision is often limited by extensive, unaesthetic scarring. Given that liposuction is considered preferable only for large lipomas, patients with multiple medium to small lipomas present a therapeutic predicament.<sup>2,3</sup>

For aesthetic purposes, topical fat dissolution with injectable phosphatidylcholine (PDC) formulation has become a popular and effective technique for the treatment of localized fat accumulation.<sup>4-6</sup> However, intralesional application of PDC in lipomas has not been investigated under sonographic control. The purpose of this study was therefore to investigate the efficacy of PDC injections in patients with familial multiple lipomatosis.

## Material and Methods

### Subjects

Ten subjects (median age 37.8 years; range 23–60 years; five males, five females) were enrolled in the study; all gave informed consent. All patients were clinically diagnosed with familial multiple lipomatosis. Thirty lipomas were treated. Seventeen lipomas were located on the upper extremities, five were on the lower extremities, five were on the back, and three were on the anterior abdominal wall. Exclusion criteria included a single lipoma, pregnancy, lactation, a history of malignancy, and soy allergy. Intramuscular lipomas and lipomas located near the tendons, bones, and larger nerves (eg, ulnar) were also excluded.

### Measurement

Lipomas were sonographically measured and documented using a 10 MHz linear transducer (SonoSite 180, SonoSite Inc., Bothell, WA). The width and length of the lipomas were measured at each study visit by long-axis and short-axis ultrasonography. Cross-sectional surfaces were then calculated in cubic millimeters. Measurements were done on the same points by defining the center of the lipoma and its distance from two characteristic anatomic landmarks with a measuring tape.

### Treatment

Each lipoma was treated with intralesional injections of 0.5 to 2.3 mL PDC (Lipostabil, Nattermann GmbH, Cologne, Germany) at four intervals of 6 to 8 weeks. Injection volume was calculated according to lipoma size. The largest diameter of the lipoma was divided by two, and the result was taken as injection volume in milliliters. Injections were performed by the same physician, who placed the needle into the center of the lipoma under sonographic control.

### Histology

One lipoma underwent histologic examination 3 weeks after the final injection. Biopsy was evaluated by a board-certified histologist.

### Side Effects and Patient Satisfaction

Side effects (eg, bleeding, hematoma, paresthesia, scarring) were registered.

To compare postoperative pain, patients were monitored by a visual analogue scale for pain intensity at days 1 and 3, with 0 representing no pain and 10 representing maximum pain. In addition, patient satisfaction was evaluated using an analogue scale from 1 to 4 (1 = complete satisfaction, 2 = satisfied, 3 = not completely satisfied, 4 = not satisfied at all).

### Statistics

Explorative data analysis was performed using SPSS, version 11, for Microsoft Windows XP (Microsoft Corp., Redmond, CA). All dimensions of measured cross sections were expressed as mean  $\pm$  SD. Analysis of distribution was performed by the Kolmogorov-Smirnov test. Comparison between the lipoma cross sections was performed using the two-tailed *t*-test for paired samples. Differences were considered significant when  $p < .01$ .

## Results

After four intervals, PDC injections resulted in a significant decrease in the horizontally measured cross section, from  $278.23 \pm 132.47 \text{ mm}^2$  to  $154.63 \pm 92.21 \text{ mm}^2$  (difference between means:  $123.6 \text{ mm}^2$ ;  $p < .01$ ; 95% confidence interval 100.8–146.4), corresponding to a reduction of 44.4%.

The vertically measured cross section was reduced from  $281.57 \pm 134.66 \text{ mm}^2$  to  $148.55 \pm 88 \text{ mm}^2$  (difference

between means:  $133.02 \text{ mm}^2$ ;  $p < .01$ ; 95% confidence interval 108.89–157.16), corresponding to a reduction of 47.2% (Figure 1). The overall reduction was 45.8%. No lipoma was completely dissolved after four injections. On clinical inspection, 22 lipomas (73%) showed palpable consolidation after therapy.

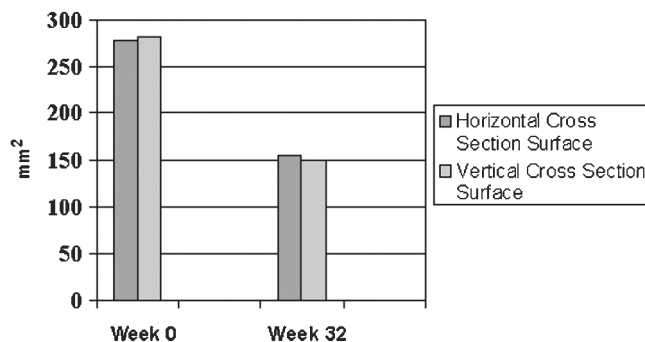
### Histology

The lipoma is surrounded by a pronounced connective tissue capsule with broadened septa within (Figure 2A). In the broadened septa, only a few inflammatory cells (lymphocytes) and no inflammatory infiltration of the vessel walls are visible. The lipocytes adjoining the broadened septa are smaller than the normal fat cells in normal subcutaneous tissue and in other parts of the lipoma. In these areas, large histiocytes with foamy cytoplasm can be observed (Figure 2B). Altogether, a mild granulomatous septal panniculitis with reduced size and number of lipocytes is present.

### Side Effects and Patient Satisfaction

No severe complications or systemic reactions occurred. Minor complications were hematoma in eight lipomas (27%). Hematomas were limited to the region of injection and required no specific treatment.

Pain limited to pressure on the treated sites was observed in four patients (40%) and persisted for approximately 3 days. Five patients (50%) described constant pain after injection. These five patients were included in the pain score. Mean visual analogue scale scores were 3.2 at day 1 after injection. Visual analogue scale scores fell to zero by day 3. All patients described a burning sensation.



**Figure 1.** Significant decrease in lipoma size after injection with phosphatidylcholine. Overall reduction of 45.8% after 32 weeks (four injection intervals).

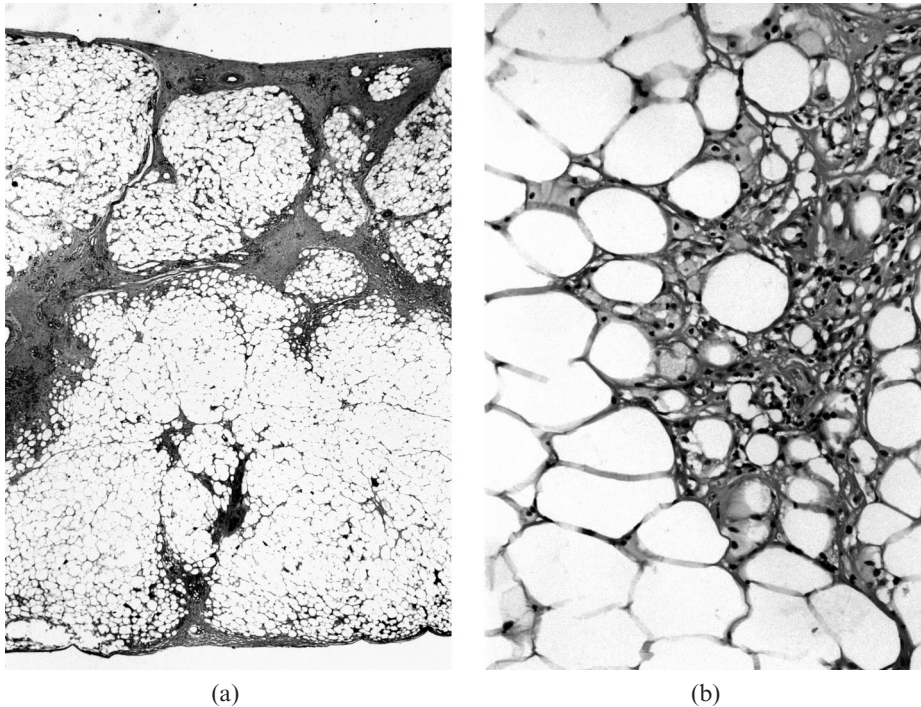
Nine patients were completely satisfied or satisfied (three were completely satisfied and six were satisfied). Only one patient was not satisfied (3 on the visual analogue scale).

### Discussion

Injections with PDC have been reported to successfully treat localized fat accumulation.<sup>7–9</sup> In 2001, Rittes published a report about the use of PDC for correction of lower lid bulging owing to prominent fat pads.<sup>5</sup> “Buffalo hump” lipodystrophy and fat accumulations on the waist and the hip have also been reported as possible indications for dissolution with PDC.<sup>6,10</sup> As lipolysis of lipomas has not been described, the aim of this study was to investigate whether injections with PDC could be an effective therapy in patients with multiple lipomas. Especially in patients with familial multiple lipomatosis, surgery potentially causes problems from extensive scarring. Alternative methods, such as liposuction, have been described as a therapy option for medium and large solitary lipomas.<sup>11,12</sup> However, multiple small lipomas are not ideal for liposuction,<sup>2</sup> and conventional surgery (alternative: extraction through small incisions) remains the first line of therapy.<sup>13</sup>

The results of our study show a significant reduction of lipoma size after four injections at intervals of 6 to 8 weeks. However, no complete dissolution was observed in any lipoma. Given that therapy was terminated after the fourth cycle, it remains unclear whether more injections would have had any positive effect on reducing lipoma size. Further investigations with more injection cycles, including a larger injection volume, are necessary. From our patients’ point of view, the reduction in lipoma size was sufficient and graded as satisfactory. This could be explained by the improved cosmetic result. Patients were generally satisfied by the fact that lipomas were no longer evident as bumps on their body surface.

Despite these results, several points should be critically evaluated. In our opinion, a single lipoma should not be seen as an indication for lipolysis because a single scar can be tolerated, and, although rare, the possibility of cutaneous liposarcoma should not be ignored. Because liposarcomas are most often located on the legs, tissue diagnosis is strongly recommended for tumors on the lower extremities.<sup>14</sup> That the working mechanism of PDC-containing formulas has not been completely elucidated should also be noted. In mesotherapeutic concepts, PDC is thought to be the active ingredient in injectable formulations used for dissolving fat. Rotunda and colleagues



**Figure 2.** A, Histopathology of lipoma 3 weeks after injection with phosphatidylcholine. Thickened capsula and broadened septa (hematoxylin-eosin stain;  $\times 10$  original magnification). B, Higher magnification of the same lipoma 3 weeks after injection of phosphatidylcholine. Small lipocytes with large foam cells and a few lymphocytes between (hematoxylin-eosin stain;  $\times 25$  original magnification).

recently reported that the detergent sodium deoxycholate, a component of injectable PDC formulation, causes nonspecific lysis of cell membranes and therefore may be the active ingredient for lipolysis.<sup>15</sup> The possible synergistic effects of PDC and detergents cannot be evaluated at the moment and deserve further investigation. Based on Rotunda and colleagues' *in vitro* observations that PDC formulas are not specifically dissolving fat cells but also muscle tissue, the use of these formulas for treating lipomas located near tendons, muscles, or nerves could be dangerous.

Rose and Morgan described histologic changes after injection lipolysis with PDC.<sup>16</sup> They proposed that a reduction in subcutaneous fat is likely due to a panniculitis, with consequent inflammation-mediated necrosis and resorption of fat cells. These results correspond to our histologic observations showing a mild granulomatous septal panniculitis with smaller adipocytes. Fat cells seem to be dissolved owing to the subcutaneous inflammation. Moreover, a thickening of subcutaneous septa and the lipoma capsula was visible in our patient, whose lipoma underwent histologic examination. This supports the clinical observation of consolidated lipomas after injection lipolysis. The panniculitis appears to induce a fibrotic process in subcutaneous connective tissue, which may be seen as a possible risk factor for subcutaneous scarring with an unaesthetic clinical outcome, although this observation has not been reported. A positive aspect of

the broadened capsula was reported by the surgeons who extirpated the lipomas. They noted a simplified preparation owing to the clear demarcation of lipoma and surrounding subcutaneous tissue. Owing to the reduced size, a shorter incision with a better aesthetic outcome was possible.

This study shows that patients who refuse surgery for an extensive number of lipomas might benefit from a new alternative therapy that potentially improves appearance by reducing lipoma volume. However, the effects of long-term therapy and possible recurrence of lipoma cannot be assessed as long-term data are unavailable. To summarize, to date, injection lipolysis with PDC is an experimental therapy. Its ultimate value should be evaluated in further studies.

### Acknowledgment

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