Original Contribution

Cosmetic use of polylactic acid: report of 568 patients

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Summary

Background There are few methods for the correction of the reduction of subcutaneous volumes. Polylactic acid is a new material with which we can achieve interesting results.
Objective To review our case histories in the assessment of this material's safety and effectiveness, its best indications, and to outline our technique.
Materials and Method Polylactic acid was prepared and diluted with 5–8 mL depending on injection sites, which included patients' face, neck and hands volume restoration, as well as arm and thigh revitalization. A total of 568 patients were treated from January 1999 to December 2007.
Results The Definitive Graduated Score varied from 6.3 to 8.4 with an average score of 7.8. The principal side effect, collagen late nodules, appeared with a very low frequency (1%) and were the result of incorrect technique.
Conclusions The fibro-connective restoration of face contours and volumes is the winning strategy for a holistic, three-dimensional approach to the aged face, neck, and hands. Since the introduction of certified courses, side effects have become less common than in other methods, and can probably be further reduced to a minimum.

Keywords: poly-L-lactic acid, volume restoring, wrinkles, cosmetic procedures

Introduction

In every possible surgical or medical technique performed not only on the face, but also on the neck and hands, one of the enduring problems is the reduction of subcutaneous tissue (Fig. 1). Having been available for almost 10 years, today polylactic acid (PLA) is a familiar material[1–7] that can produce a substantial increase of subcutaneous tissue. Polylactic acid has been used in a wide range of medical and surgical procedures for many years.[8–11] The real use of PLA started in France in the 1990s, initially for the correction of face lipoatrophy[3,4,12,13] typical of HIV+ patients, but in the third millennium its use has gradually increased in the

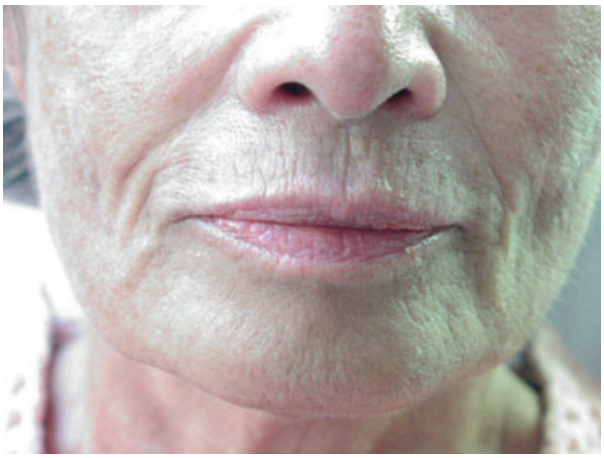

Figure 1 Reduction of volumes.

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cosmetic field. Today, PLA is used for cosmetic rejuvenation[5–7] of the face as well as in other interesting areas like the neck and hands.[14] Over the last 4 years in Italy, the availability of this material has been limited to trained doctors who have completed a certified training course; this strategy has notably decreased the incidence of side effects. The aim of this paper is to review our case histories based on the experience of two Italian medical doctors who used PLA from 1999 until December 2007.

Materials and methods

Patients

From January 1999 until December 2007 we treated 568 patients: 74 males (13.3%) and 494 females (86.9%). Female ages varied from 22 to 76 years (average age 48.0). Male ages varied from 27 to 77 years (average age 52.7). Total average age: 48.6 years. We began using PLA in 1999, treating 61 patients (10.7%) in that year alone. Currently, 20 of these patients continue to be seen in follow-up appointments more than 9 years later. 134 (23.5%) patients were ''lost'' when not seen again for longer than 2 years. 93 (16.3%) patients abandoned treatments: 12 because of side effects, 81 for personal reasons. A total of 2072 sessions were performed with an average of 3.6 sessions per patient. The number of sessions per patient varied from one session performed in 18 patients (3.1%), who were treated for small neck wrinkles and the inferior third of the face, to nine sessions performed in six patients (1%), who were treated for cheek lipoatrophy. The majority of patients (245, 43.1%) were treated in three sessions (Fig. 2). All patients have been treated for cosmetic problems. In 95% of sessions, pretreatment and post-treatment photographs were taken in frontal view, and at 45° and 90° angles from both sides. The photos were taken both pre- and postinjection and during every follow-up.

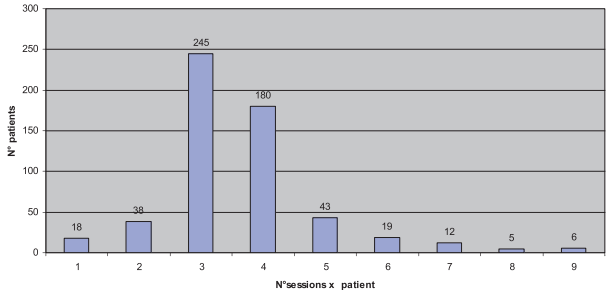

Figure 2 Number of sessions per patient: from 1 session in 18 patients to 9 sessions in 6 patients.

Material

Air-free bottles containing 150 mg of PLA were used in every session. The active principle was diluted with distilled water (from 4.5 to 8 mL, average dilution 6 mL in most cases) and 0.5 mL of mepivacaine cloridrate 3% without adrenaline (mepivacaine offers an immediate anesthetic result that lidocaine does not). Table 1 illustrates the dilutions, needles used, and timing of dilution, according to treated areas and required PLA strength. After the dilution, the preparation must be kept at room temperature. It is important to remember that we use a *dispersion*, not a solution. This is why immediately prior to patient injection, the active principle must be shaken. We shake the substance by hand, and never with laboratory vortex. A 2.5-cc syringe is used with needles from 25 to 27 G.

Technique used

An informed consent form is always signed, and patients are always examined and marked prior to treatment (Fig. 3).

In most cases, a linear retrograde technique (Fig. 4) was used. Only a few cases required the use of the ''fan technique'' (Fig. 5). The fan technique is a method of injection by which a long needle (from 25 mm to 42 mm 26 G needle) enters in one point, and by using an in-and-out movement, the solution spreads only in the subcutaneous layer.

The injections were made either in the deep dermis or in the subcutis layer,[5–7,28] according to different indications, and never superficially in the dermal layer: the finer the wrinkles, the more diluted the substance and the more superficial the injections.

Injection amounts vary according to the treated areas. In deep, easy areas, where the skin is thicker, the standard dose is 0.1 mL per injection. The only two points where we

Table 1 Comparison of minimal dilutions and needles used in treated zones

Treated areas	Dilution (water + mepivacaine 0.5), cc	Timing (h) before injections	Amount (mL) per injection	Needle used (G)
Nose labial folds	5–6	12–24	0.1	26
Cheeks	5–6	12–24	0.1	26
Chin	5.5	12–36	0.1	25
Zygomas	5.5	24	0.1	25
Neck and low neck	6–8	24–48	0.05	25–27
Hands	6–8	36–48	0.05	26–27

Figure 3 Before marks.

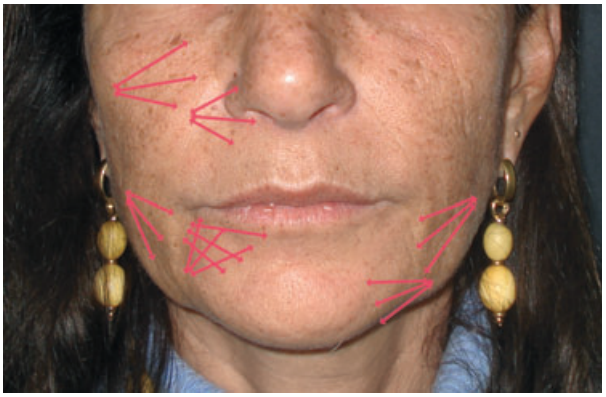

Figure 5 The fan technique.

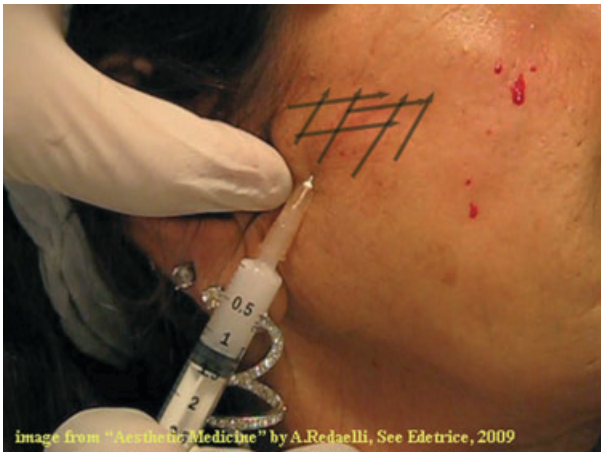

Figure 4 The linear retrograde technique.

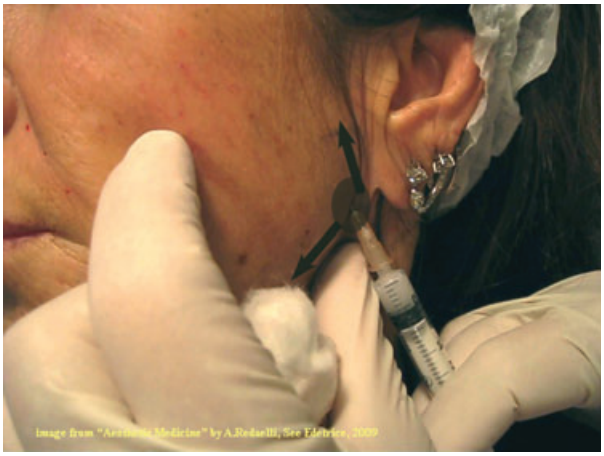

Figure 6 The retro-mandibular angle injections.

inject 0.2 mL are those immediately lateral to the base of the nose—where the nasolabial folds begin—and the retromandibular angle (Fig. 6). In difficult areas, where the skin is thinner, the amount infiltrated in each single injection point is always 0.05 mL.

At the end of the session, it is fundamental to massage the treated area thoroughly: the subdermal and dermal filling derives from neocollagen thickness. It will be homogeneous only if the dispersion of PLA particles is uniform. We can never emphasize enough the importance of a long massage to obtain uniform results.

Indications and treated areas

Treated areas are shown in Figure 7.

As in all previous surveys, the most commonly treated area has been the inferior third of the face;[6,7,14,28] we treated the cheeks, the nose-labial and puppet (labio-

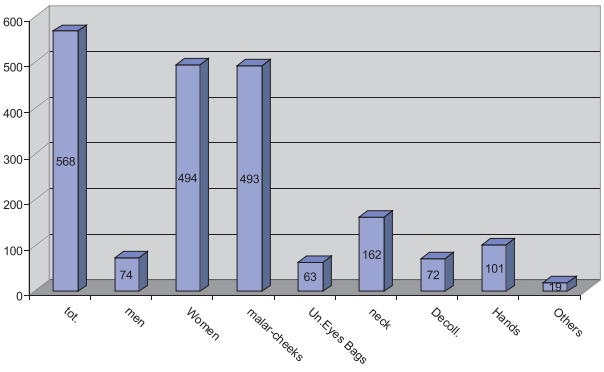

Figure 7 Number of patients treated in each zone.

Figure 8 Lifting of the mandibolar edge.

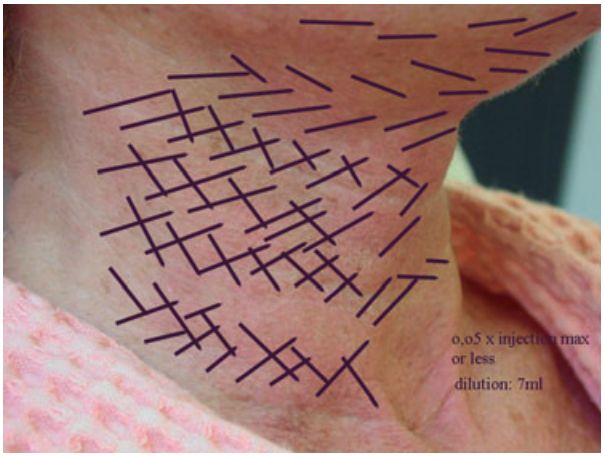

Figure 9 Neck injections.

mental) folds in 493 patients (86.8%). Treating the lower jaw profile is also very important, particularly at the retromandibular angle (Fig. 6), in order to lift the entire mandibular edge (Fig. 8).

The tear troughs have also been treated in 63 patients (12%). The injections in this area were made only on the bone, leaving 0.1 mL of solution diluted with 6 mL in the area near the nose, the continuation of eye sockets. This area is quite difficult to treat; if overcorrected, nodules are likely to develop.[15]

Polylactic acid's most recent and innovative indication is the restoration of volume in areas like neck, décolleté and hands.[14]

The neck was treated in 162 patients (28.5%) with the intermandibular area, an essential part of the neck, always being treated *after* the face. To avoid nodule formation due to the thinness of the skin in this region, very small amounts of the substance (0.05 mL each) were used, and injections were never confined to the horizontal folds (Fig. 9). In one case, due to this technical error, we experienced a hypercorrection of the folds, without resulting in nodules. The average quantity of active principle used in a typical session was 1.5 mL.

The décolleté region was treated in 72 patients (12.6%). The dilution was slightly increased (7–8 mL of water), and the amount injected was never more than 0.05 mL per injection. Here again, the average quantity injected was 1.5 mL.

Hands were treated in 101 cases (17.7%) and we treated thinner metacarpal spaces with a 7-mL water dilution. We injected 0.05 mL per injection with parallel vectors to the metacarpal bone, taking care to leave the active principle under the veins. We did not experience

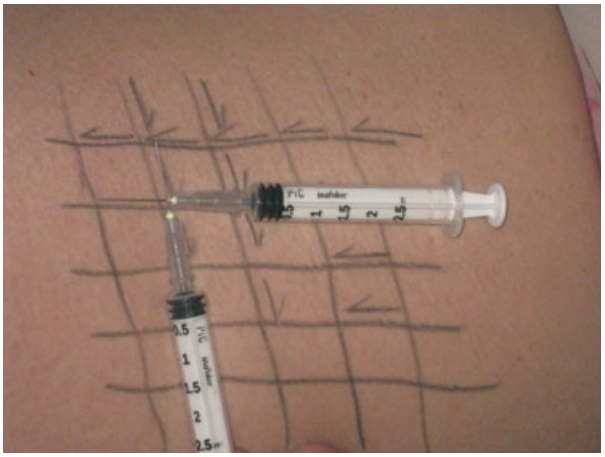

Figure 10 Linear retrograde netting technique.

any incidence of hypercorrections, but in five cases the end result proved to be minimal. Hands were always treated in conjunction with the principal area, the face. In these cases, the average quantity of material used was 2 mL (1 mL for each hand)

In 19 cases (0.42%), we treated other areas: in one case the inferior part of the breast for a local augmentation, and in another a thoracic axillary fold, just above the lateral part of the breast to improve the subcutaneous tissue and fold. Seventeen cases were treated for arm and medial thigh revitalization. This is another emerging area with promising results, although further studies are required.

In these instances, we used the following dilution: to 1 mL of standard dilution (6 mL), 3 mL of distilled water was added. The active principle was injected using a linear retrograde netting technique (Fig. 10).

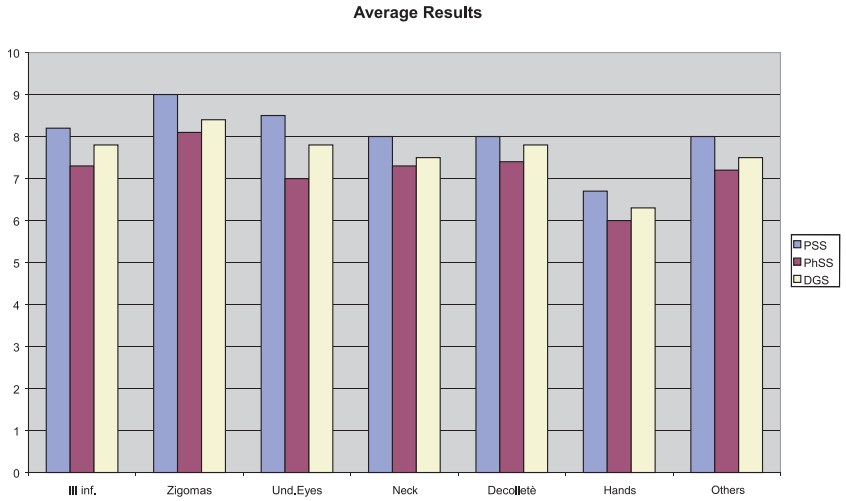

Figure 11 Results – range 1:10. PSS, Patient's Satisfaction Score; DSS, Physician Satisfaction Score; DGS, Definitive Graduated Score.

Results

Patient satisfaction is illustrated in Figure 11. To evaluate results we have recorded a physician (PhSS) and patient (PSS) satisfaction score in each case, on a scale of 1–10.

After the third session, if conducted, patients were evaluated every 3 months for the first year. In most cases, a Definitive Graduated Score (DGS) was calculated by the physician (1–10) by using the photographic results and the average PhSS and PSS.[5]

The best DGSs (8.4) were achieved from treatments to the cheekbones and malar areas.

Good results can also be achieved in difficult and delicate regions, those which are often treated with surgery, like the tear troughs. Of the 63 treated patients, all have shown an above-8 PSS. However, the PhSS in these cases was higher than 8 in two cases. This was probably due to the patient's inability to objectively evaluate the photographic findings.

Very good results were also achieved on the inferior third of the face (average DGS 7.8). The jawline is a crucial part of the inferior third of the face and is almost always treated in conjunction with this area.

Patients were quite pleased by their results (PSS 8.2) on this part of the face, where the skin visibly improves and becomes more compact. The lifting effect in this area was significant and very noticeable in some patients, with definite skin tightening, by the improved retromandibular volume (Figs. 12–14).

Treating the neck continues to gain in popularity, with an overall DGS of 7.5. Results were good (Fig. 15), except in the case of one patient who was treated in the initial period of our survey, and whose result was exaggerated.

The vertical decolleté wrinkles pose a special problem for many patients; other than PLA injections, there is little else that can be done. We did not have any significant side effects and the average DGS was 7.8.

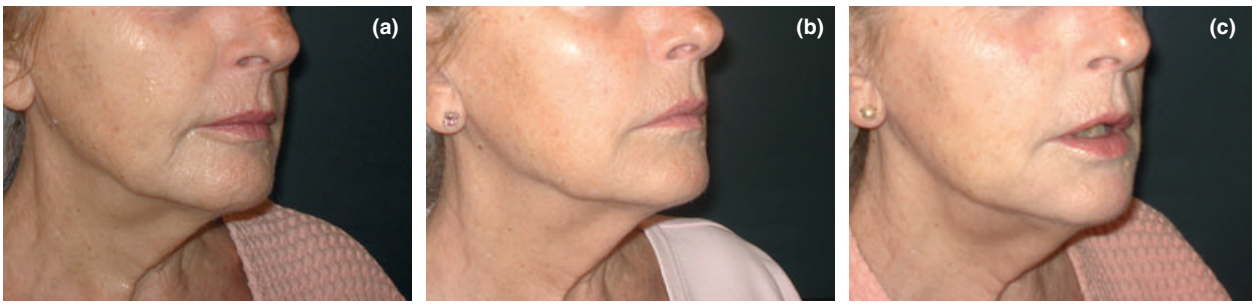

Figure 12 Patient B: before treatment (a); after 5 months, four sessions (b); after 14 months, five sessions (c).

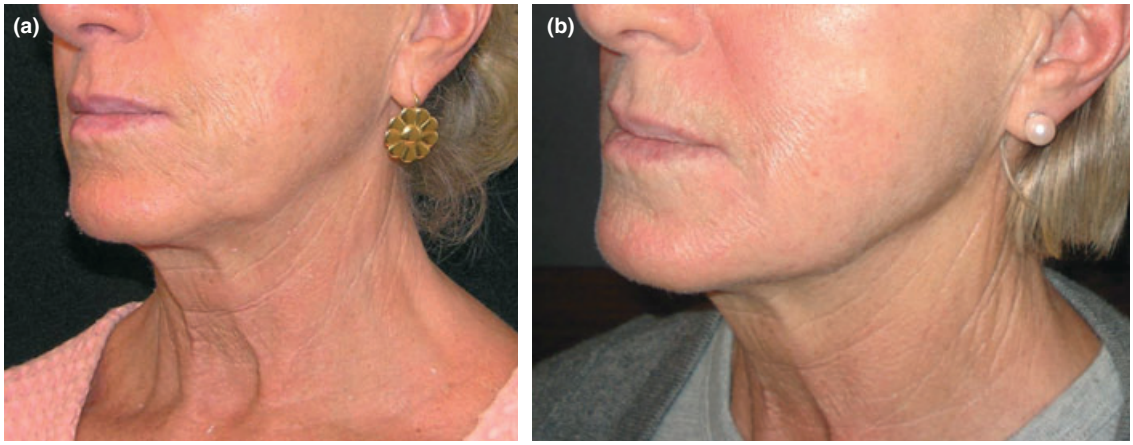

Figure 13 Patient C: before treatment (a); after 14 months, five sessions (b).

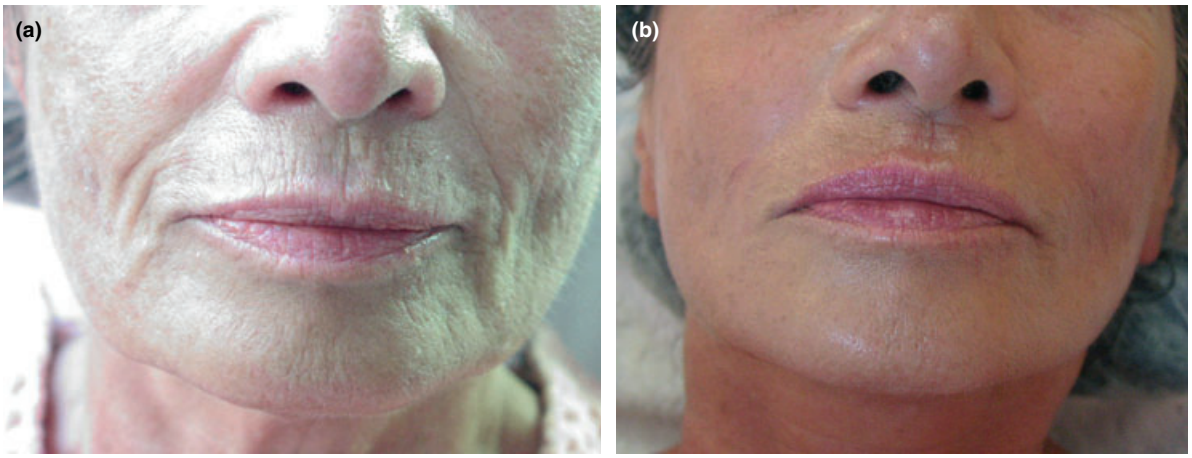

Figure 14 Patient E: before treatment (a); after 12 months, four sessions (b).

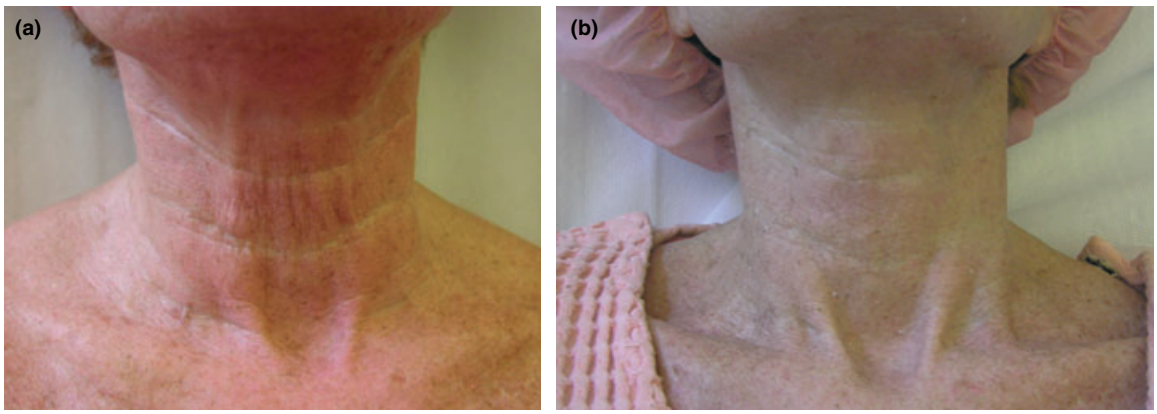

Figure 15 Patient D: before treatment (a); after 18 months, six sessions (b).

The lower average DGS for hands (6.3) was probably due to the number of sessions required and the relatively high level of dilution needed to treat this area. Nevertheless, it is very important not to ''inflate'' the hands, as it would make them appear ill and swollen. It is better to obtain a too-subtle result than an exaggerated one, which would be difficult to correct.[14]

With a DGS = 9, the results in the breast area were very positive. The procedure was performed in eight sessions, with deep injections and a 4-mL dilution. Unfortunately this case remained singular and was carried out in the initial period of our survey.[5]

The definitive score in arm and medial thigh revitalization was promising (DGS = 7.5) and will surely increase with further experience in this particular region. It is important to note that there was no one dominant side effect, probably on account of the substantial dilution.

In general, with regards to all treated areas, the PhSS was less than the PSS and the definitive graduated score (DGS) varied from 6.3 to 8.4 with an average of 7.6.

Side effects

As in other injection techniques, there are a few temporary side effects:[6,16,17] bruising (201 cases – 35%), edema (87 cases – 15.3%), and pain are perfectly normal and patients must be informed about this. We also had seven intolerant reactions (1.2%): a slight edema, or itch, appeared along with a bit of redness; not a real allergic situation, but enough to stop the treatment.

No one case of real allergic reaction was experienced. The principal side effect was the formation of collagen nodules, which has also been reported by many colleagues.[6,7,15–17] In our case survey, there were six instances (1%) of nodule formation: cold nodules in four of these cases, and warm nodules in the remaining two cases. However, they were always noninfectious.

Discussion

After our experience there are three main topics that we want underline in the discussion section.

First: the preparation of PLA

The concentration and timing of dilution is a way of modifying—either increasing or decreasing—the potency of PLA. This is one of the characteristics that makes it an extremely safe, versatile, and appropriate substance for a variety of indications and areas.

The *first method* depends on the amount of water used to dilute the vial of PLA: the less the active principle is diluted, the more concentrated the final dispersion will be (4/5 mL of water for injectable preparations), and hence, the stronger the response. With increased dilution of the active principle, the dispersion consequently becomes less concentrated (6–8 mL), and the response will be less evident.

Based on our clinical experience, we underline a *second method* used to modify the active principle's potency: the timing of dilution. Diluting the substance well in advance (from 24 h up to 72 h beforehand) results in a lighter reaction, which will become increasingly evident when less time passes between the dilution and the procedure. The softer, less visible results are due to the fact that over time, the covalent links break down and the substance becomes more hydrated as PLA polymers are degraded into monomers;[10,26,27] it is the author's opinion that monomers are less effective than polymers. This can be a very useful strategy for all cosmetic procedures where the indications are subtle and less volume is needed. Employing a longer dilution time allows for a very precise technique and results in a lighter, more natural reaction.

For this very reason, the product is sold lyophilized and not ready for immediate use.

The *third important method* used to calibrate the PLA's response is the amount of water injected in each single point (normally 0.1 mL or less).

This is what makes PLA appropriate for use in the treatment of HIV patients as well as for cosmetic purposes.

Second: the results

The most interesting results of PLA have been the increase in dermal thickness and its ability to produce a continual and gradual improvement of the skin surface for months after the last injection.[2,5–7] While this increase is visible in photographs, we would like to state that all patients were very pleased by their volumes and appearance after the procedure's end.

Even after a period of months, and in some cases years, it is possible to verify the second important result of PLA injections: a very definite lifting effect, which may be evaluated with pre- and postphotographs.

In the author's opinion, the previously mentioned lifting effect is due to the increase of volume in the superior and lateral part of the face (malar zone and retromandibular angle), as well as resulting from the retraction of collagen fibers as normally found in fibrotic collagen. This result can best be seen on the cheek areas

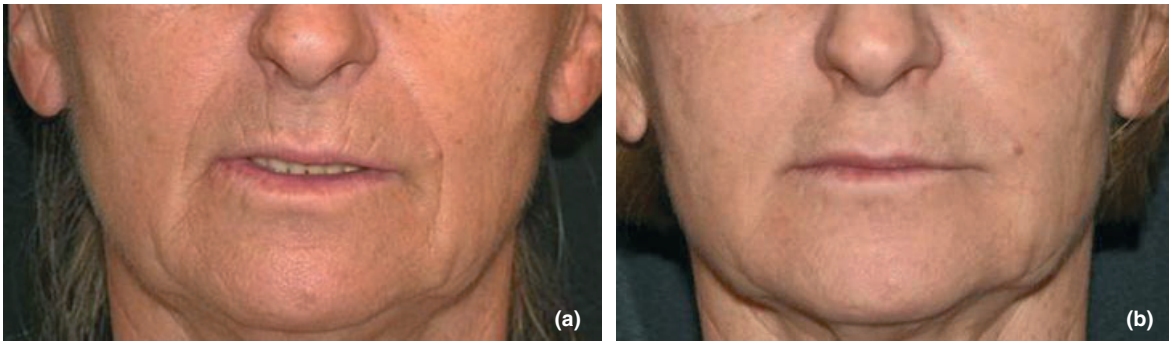

Figure 16 Patient A: before treatment (a); after 12 months, four sessions (b).

and jaw line, where photographs are very effective and clear. This lifting effect is also the result of localized skin tightening due to increased thickness and the subsequent smoothing of the skin (see Fig. 16).

It is very important to offer patients a viable option for particularly challenging areas, like the neck and hands, which may otherwise be left untreated. Up until now, there have been very few alternatives for the aging of these regions, which we have always advised patients to treat in conjunction with the face; we have found that they are increasingly receptive to the idea. Unsatisfactory results in these areas are due to excessively prudent dilutions and the injection of reduced quantities; despite this, results are often very good and last longer then treatments with hyaluronic acid. The best results in these difficult areas can be obtained by remaining prudent but increasing the number of sessions and integrating other techniques like peelings and revitalizations, particularly those with amino acids.

Emerging treatments like arm and medial thigh revitalization need more cases to assess results, but the absence of side effects is an incentive to search for improved technique.

Third: the side effects

Improved appearance with an absence of side effects is probably one of the most important topics to keep in mind.[7]

After the Gogolewski studies[21] it is evident that a slight foreign body reaction—the formation of macrophages, lymphocytes, mast cells, and foreign body cells— always occurs, and tends to remain for 3–4 months after treatment. After this initial period, the connective tissue gradually improves as the PLA microparticles slowly decrease in size and are gradually eliminated. This is not a side effect, but a normal, expected reaction to the injection of the material. Biopsies taken by Vleggaar confirmed this mechanism: the filling effect is not the result of *physical* filling with PLA, but rather of the production of fibrous tissue over an extended period of time.[7] This leads to an overall increase of thickness in the dermal layer, with the distension of wrinkles, the filling of depressions, an increased mechanical resistance, and greater turgidity (lifting effect).

The appearance of nodules in the latest surveys[16,17] confirms that all problems arise due to technical mistakes, for example:

- In certain areas (i.e., the periorbital and perioral area, the forehead) the injections were made at an incorrect depth.
- An insufficient ratio of dilution (less then 5 mL) and the addition of lidocaine at the moment of injections, instead of at the moment of dilution.
- The use of inappropriate anesthetic solutions for the dilution: i.e., using lidocaine instead of mepivacaine. This difference in anesthetic solutions can provoke a different dispersion of the active principle in the vial.
- The treatment of particular patients. Patients with certain diseases (i.e., rheumatoid arthritis or any collagen-related problems) must never be treated. It is also critical not to treat patients who have undergone injections of nonresorbable fillers, particularly silicone.
- The use of saline solution instead of distilled water.

It must be emphasized, however, that we never experienced bacterial infections with this procedure. Furthermore, there were never variations in responses according to injection site.[17] If PLA is injected deeply and in the appropriate area, reactions will occur only in a very small percentage of cases.

So, at the end, the variation in the frequency of nodules in different surveys is most likely due to imprecise technical methods.

Cold nodules were result of poor technique or treatment of an inappropriate area, like that of the periorbital area, the forehead, or the ''barcode'' wrinkles, the

vertical wrinkles around the lips.[2,12] Cold nodules always appeared in the inferior third of the face, especially in the cheek area.

While difficult to correct and often long-lasting, cold nodules almost always eventually disappear. Two years after treatment, the nodules have disappeared in three out of our four cases. In the last case, they are already significantly diminished and will soon vanish completely.

Cold nodules are those that appear early on, normally between 3 and 6 months, due to an excessive amount of product in one point, and an incorrect technique. They typically have no signs of inflammation, which are present in the warm nodules.

It is important to state that PLA always causes a slight foreign-body reaction; this must be considered normal and patients must be aware of this. It is this foreign-body reaction that leads to the desired neocollagenesis.[7,21]

Normally macrophages, lymphocytes, and foreign body cells can be detected in first 3–4 months, after which time they decrease while collagen fibers and connective tissue begin to increase.[21] It is common, however, to find scientific articles in which this outcome is explained as a side effect.[22–24]

A foreign-body granuloma reaction can also occur, but it is a side effect that becomes increasingly common due to imprecise technique on the doctor's behalf: this is the reason that in some case surveys, the incidence of nodules is higher than in others.[15]

In some cases, after the initial sessions—when the tissue was not yet completely filled—it was possible to feel small nodules in the subcutaneous layer, which remained invisible to patients. Patients never returned for this problem because they were advised in advance, something that we consider absolutely mandatory. This must not be considered a side effect but rather the normal outcome of a not entirely precise technique. With increased practitioners' experience, improved technique, and a greater number of sessions, this problem decreases until it completely disappears. It is mentioned on the informed consent form.

Cold nodules can be treated with cortisone cream or, in more severe cases, a local injection with distilled water can reduce reabsorption time. Some authors use diluted triamcinolone acetonide (1:20 mL with water) but in the author's opinion, it has not been proven effective for cold nodules and it could possibly be dangerous; simply waiting is much safer and just as effective. The nodules in our case survey were corrected only with distilled water injections and time.

Monopolar radiofrequency has recently been used to successfully destroy the nodules with very interesting results; in our experience one treatment can result in 80% reabsorption of nodules in just 3 weeks.

In the two cases of warm nodules, one was most likely the result of hormone levels: a 36-year-old woman began to show many small nodules, distributed all over her face, during the early stages of pregnancy. We would like to emphasize that she received the third and final treatment 1 year before getting pregnant. Nodules disappeared 4 months after birth.

Evidence of hypercorrection without nodules was seen in one case on the neck but, predictably, was concentrated exclusively on the horizontal wrinkles.

Other cases of increased subdermal consistency were most evident on the cheeks. Upon touching the treated area, physicians were able to feel (while patients were not) an increased consistency, which is considered normal in all treated patients. As this increased consistency was never excessive, it was noticed only by the physician and not by the patients and therefore we did not consider it a side effect. We do not have a precise number of these occurrences; they occurred during the first part of our survey and probably do not exceed 5% of patients treated. But we repeat, no patients ever complained about this problem.

As is the case with all other fillers and injections,[25,26,27] there is always a possibility of infection, although none occurred in our survey. Preparing the patient thoroughly and accurately was most likely the key step in avoiding this potential problem.

Conclusion

The fibro-connective restoration of face contours and volumes is one of the most important strategies for a holistic, three-dimensional approach to the aged face. All aesthetic medical doctors wishing to conduct a complete practice must familiarize themselves with this material and its technique of injection.

The PLA technique is an effective (and perhaps the only) medical method of restoring volume in the aged face, while maintaining a very natural appearance.

Other medical methods are not as consistent or natural-looking; a contrived appearance can often be perceived with facial movement, and patients will have the undesired appearance of having had ''something done'' to them.

Surgical methods do have an effective outcome but these procedures are invasive and not always appealing to patients.

Furthermore, PLA is indicated for use in many areas of the face and body: in HIV patients, it can be used to rejuvenate both the face as well as the arms, and it is

suitable for cosmetic purposes in the face, neck, and other areas of the body. Its preparation can be varied in many different ways, making the substance uniquely versatile. The results of our survey (and especially the high level of patient satisfaction) make it a very encouraging alternative to or in conjunction with surgical methods of face ritidolisis.

The incidence of side effects, after all modifications to the initial technique (i.e., timing, concentration of dilution and quantities injected) confirms the importance of proper training for new practitioners and we sustain that the company's current policy regarding this is correct and prudent.

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