Cosmetic use of poly-L-Lactic acid for skin rejuvenation: new indications

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SUMMARY

Background: Bio-reconstructive materials have enjoyed a notable increase over the recent years, thanks to their effectiveness and lack of side effects.

Objective: To provide updated information on injectable Poly-L-lactic acid to doctors who wish to use it, highlighting the varied indications and describing the correct techniques for use.

Materials and methods: Poly-L-lactic acid has been diluted and prepared according to the current models. It has been diluted with quantities from 4 ml to 8 ml of water per injectable dose, including 0.5 cc of 3% mepivacaine without adrenaline, depending on indications. In addition to the traditional indications in the lower third of the face, it has been used for the rejuvenation of the neck, décolleté, and hands as well as for the revitalization of the arms and the medial part of the thighs. Prior tests for allergies are not necessary.

Results: Excellent results are confirmed in the lower third of the face, the jawline and the mid-jawline. The preliminary results for the other, more difficult to treat areas other than the face are positive but need to be confirmed with further studies conducted over time. For the most part, the results were extremely well-received by the patients. The immediate side effects were edemas, hematomas and redness - all of which disappeared in a matter of days. Instances of nodules and hypercorrections were extremely rare.

Conclusions: The possibility of modifying the dilution both in terms of timing, amount of injectable material employed, as well as quantity of water used, renders Poly-L-lactic acid an extremely versatile substance, which lends itself to new indications that will be discussed in the article. Poly-L-lactic acid allows for a natural-looking and long-lasting correction that may last for years.

KEY WORDS: Poly-L-lactic acid, Fibro-connective reconstruction, Volume

INTRODUCTION

Several techniques of aesthetic medicine have been developed since the Seventies, some disappeared within a few years due to their substantial lack of usefulness, others becoming essential mainstays in the sector. The age of collagen in the Seventies was followed by the appearance of the hyaluronic acid, which has changed aesthetic treatment dramatically. It is a very safe material and provides immediate results, without any need for allergy tests. It is the most widespread material to date.

In the meantime, the use of non-resorbable materials has gradually decreased due to their inborn risks over time. Then the botulinum toxin spread, for the purpose of treatment of a crucial part of aesthetic medicine, the one related to movement. Yet aesthetic physicians know that the reduction of excessive mimics is a cornerstone in the struggle against aging. Even the other specialists and the media have put aside their initial preconceived hostility. Meanwhile several peeling, laser and other non-invasive techniques were developed for skin treatment purposes.

In the Nineties, however, especially in France, experts already noticed that the subcutaneous
volumes, when thinning out, give a highly older complexion, almost that of an ill person! Just think of the HIV positive patients, treated with antiretroviral medications, who develop the classic lipodystrophy of the malar area. Such patients were targeted when the French National Centre of Research came up with the PolyLactic-L Acid (PLLA) in the early Nineties. The results were very interesting from the very beginning, but some side effects, in particular the collagen nodules, clouded up its innovative character during a few years. The transition to the purely cosmetic treatment – in women requiring major subcutaneous restructuring – was very rapid. Over time it appeared that the dilution was too reduced; PLLA should be injected more deeply and not dermally, not in large quantities for each injection, and should be massaged carefully to allow for homogeneous spread. Furthermore, in 2004 the distributing company opted for compulsory training of the doctors using PLLA. That was the turning point for elimination of side effects, in particular the subcutaneous nodules. In fact, most of these problems turned out to be technique errors. There are not many techniques available for volume restitution:

- Classic Lipofilling is a surgical approach, often without long-lasting results;
- Lipofilling according to Coleman, with good results, is still an invasive approach: only few patients accept the surgical treatment;
- Resorbable fillers are safe but not long-lasting;
- Non-resorbable fillers are inherently more dangerous and hardly used today;
- PLLA is the only material allowing the proper subcutaneous volumes to be restored in an aging face without filling it, but rather through a fibro-connective restructuring of subcutaneous soft tissues.

The present article lays the foundations of the technique employed by the Author both in classic and emergent indications.

**Materials**

PolyLactic-L Acid

PLLA is a biosynthetic material studied by the French National Centre of Research in the Sixties for plasma implants, vectors and substitutes. Figure 1 shows its structural formula.

It is resorbable, biocompatible and totally biodegradable. It has been extensively employed for resorbable sutures, intraosseous implantation and soft tissues implants. Recently it has also been used for the silhouette sutures of mini-invasive face lifts.

It is an aliphatic polyester: a polymer of the lactic acid. It has been chemically synthesized and has a molecular weight of 170,000 Daltons. All aliphatic polyesters, and in particular the lactic acid, are biodegradable, totally resorbable and immunologically inert.

Injectable PLLA for cosmetic use (Sculptra®) consists of microparticles (approximately 40 micron of diameter) suspended in a gel of sodium carboxy-methyl cellulose, a well-known material with a very high safety profile. Packages of 150 mg are marketed in Italy. PLLA has no animal origin, but it is a synthetic product and therefore does not require preventive allergy tests. Allergy testing is not required by law nor by the manufacturer, and the Author himself has never dealt with established cases of allergy to the product. PLLA has a very high safety profile in the treatment of both HIV positive subjects and any other patient. PLLA has received FDA approval for correction of lipoatrophy in HIV positive patients.

**Mechanism of action**

The mechanism of action has not been completely clarified, although Gogolewski et al. have greatly contributed to its understanding.

Its resorption takes place by hydration, break of covalent bonds, loss of molecular weight, solubilization, degradation and final elimination as CO₂. PLLA is therefore totally resorbable.

The increase in volumes is caused by a light reaction to PLLA with formation of fibrotic collagen. This reaction is generally cold. The mechanism of action and the rationale of use therefore suggest a cautious and gradual approach to patients.

![Figure 1. Formula of PolyLactic-L Acid (PLLA).](image)
Methods

Personal technique

The dilution of the active principle (150 mg) is a major feature of the technique with a view to adjusting the implant to the various indications. PLLA is a highly versatile material, which can be used in several regions of the body. The response of the treated area is directly linked to three technical aspects:

Greater or lower dilution

The Sculptra® packaging includes 150 mg of PLLA, which can be diluted with greater or lower amounts of water.

The Author generally employs 5.5 ml of water for injectable preparations and 0.5 ml of mepivacaine chlorohydrate at 3% without adrenaline. The Author does not use lidocaine due to its greater inborn dangerousness and the slow onset of its anaesthetic effect.

If a lower quantity of water is used, the subcutaneous answer is more important. If the dilution is greater, the amount of active principle injected is lower as is the answer of the recipient tissue.

Greater or lower dilution time

If the dispersion (it should be recalled that it is a dispersion rather than a solution) is prepared shortly in advance, from three to five hours before, the response of the tissue will be greater.

The higher the time passing between preparation of the suspension and injection, the higher the hydration of the hydrolep and the lower the response of the recipient tissue.

Quantity of active principle injected with each injection

It is essential that the amount of active principle diluted with each injection be not excessive, otherwise the collagen might accumulate in that site. According to the Author, the right amount is 0.1 ml in the lower third of the face and 0.05 ml in other difficult areas (neck, décolleté). More expert specialists might inject 0.2 ml per injection. The Author, however, believes that two 0.1-ml injections are better than a single 0.2-ml injection. Such an approach is more cautious, especially when the patient is not familiar to the doctor nor are their responsibilities.

PLLA is therefore diluted 24 hours before injection.

After dilution, the material should be kept at room temperature. The preparation should be accurately mixed before injection by means of an electric mixer or by manual shaking (the latter being the method preferred by some users).

It is equally important to shake the syringe during its use in order to preserve a homogeneous solution, the risk lying in the injection of a poorly concentrated solution in one site and a highly concentrated one in another.

Dilution depends on the regions to be treated and the treatment session (Table 1). PLLA is indicated in facial lines and wrinkles (cheeks and chin), especially in depressed scars, but its main and innovative indication refers to volume restitution: cheek bones, cheeks and neck. The Author combines the treatment of the jawline and the entire mid-jawline in almost 100% of cases.

The results of PLLA injection should be adequately explained to patients before starting treatment: there is an initial filling, which is temporary and disappears within two to three days, due to the injected water volume.

That is not the result expected. Only during the following sessions will the late filling appear: the final result will be achieved at least 3–4 months after the last session, as a consequence of the stimulated neocollagenesis.

Most users, including the Author, envisage successive sessions. The first ones take place after 30–40 days, but in some patients a single session might be sufficient.

A written informed consent is adequately discussed and signed.

Patients are photographed and accurately studied; sketches are made on their skin before treatment to establish exactly the place and quantity of the implant. A prudent and gradual approach is advisable in this case too.

<table>
<thead>
<tr>
<th>Treated area</th>
<th>Initial dilution</th>
<th>Final dilution</th>
<th>Needle used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasolabial folds</td>
<td>5-6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Cheeks</td>
<td>5-6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Chin and jawline</td>
<td>5-6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Cheek bones</td>
<td>4-6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Neck and décolleté</td>
<td>6-7 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Mid-jawline</td>
<td>5-6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Hands</td>
<td>6 cc</td>
<td>1:1</td>
<td>26 G</td>
</tr>
<tr>
<td>Rivilatization</td>
<td>6 cc</td>
<td>1:4</td>
<td>27 G</td>
</tr>
</tbody>
</table>

Table 1. Dilutions and needles.
Injections should always be deep, but the actual depth can only be determined according to the area to be treated: the larger the volumes to be corrected, the deeper the injection, with lower dilution. Upper and middle dermis must never be injected. The deep dermis should be injected only after considerable experience.

The Author generally recommends that no more than 0.1 ml per injection be applied and the highest possible number of injections be performed in order to obtain the desired filling effect.

In more difficult areas, and when the doctor is not very experienced, even lower amounts (0.05 ml) should be injected.

A long massage - at least 5 to 7 minutes - at the end of the session is absolutely necessary and should not be entrusted with inadequately trained staff.

In the following days patients too should be trained to perform a 5-minute massage twice a day in the areas treated.

New indications

Jawline and mid-jawline

PLLA is optimally indicated to reduce the ptotic descent of the cheek along the jawline. The Author, however, has gradually extended the area treated to include the mid-jawline too.

This area has a tendency to ptosis over time, causing often the so-called “double chin” defect as a result of sagging problems rather than fat accumulation. PLLA is certainly indicated in these cases.

The standard dilution is 6 ml, with 0.1-ml injections.

The linear retrograde approach is adopted and carried out along the main traction vector, thus supplying the typical lifting effect (Figure 2).

Neck and décolleté

The neck should not be treated if there is little subcutaneous tissue, thin skin and excessive mimics.

On the contrary, the patients with thick skin, abundant subcutaneous layer and deep neck wrinkles are favourite targets. Hypertrophic platsymatic striae are not indicated.

The vectors should always be followed when intervening in the neck, although some injection might be intersected.

Furthermore, as a rule the entire region should be treated rather than the individual wrinkles. The décolleté is always treated with injections into the subcutaneous layer, which has to be quite thick.

Injections only into vertical wrinkles should be avoided. The entire region should be treated.

The standard 6 ml dilution is used. Sometimes, if the skin is not very thick, a greater dilution (8 ml) is possible. The amount of fluid to be injected with each injection, on the contrary, should be conservative and should not exceed 0.05 ml. The dilution is generally carried out at least 24 hours before in order to allow for better hydration of the active principle.

Hands

According to the Author, PLLA can be used for the hands too. Until now, few techniques were available for the treatment of this region:

1. Lipofilling according to Coleman is a very effective technique, which however requires a surgical approach and is out of league for most aesthetic physicians;
2. Resorbable fillers have a high degree of reticulation but are not long-lasting. Moreover, when injected into thick layers, they often appear through the skin and give a very unaesthetic bluish discoloration;
3. PLLA is probably the only alternative, with long-term results and highly natural appearance.

The initial dilution is always 6 ml and injections should include a maximum amount of liquid of 0.05 ml.

The Author constantly applies the linear retro-
Avoiding retrograde tunneling, but a serial-point injection technique with long smoothing massage is also possible.

**Rivalization**

By definition PLLA induces restoration rather than rivalization. However, in some large areas which over time tend to sag and become ptotic (medial arm or thigh), this new technique has been successful. The dilution pattern is peculiar: 3 ml of water for injectable preparations are added to 1 ml of the normal dilution (made with 6 ml). Eventually we have a total of 4 ml with 1 ml of active principle. This suspension at lower concentration is used to apply the implants into the regions to be rivalized. A technique with 1 cm grid mesh is used with linear retrograde approach in a given orientation at first, followed by orthogonal orientation. This technique has turned out particularly useful in the prevention of ptosis due to the action of the fibrotic collagen which is formed, and provides a very useful support over time.

**Deep scars and abscess sequelae**

Several patients ask for treatment of scars. This is generally an excellent indication, even in the face. An equally positive response is given by hollow abscess sequelae of the gluteus. The classic 6 ml dilution is used, with very high quantities of the active principle to be injected. The Author almost always uses up all the 150 mg of product.

It is very important to apply a long massage at the end of the session to make the implant homogeneous.

Patients are always required to perform a 5-minute massage twice a day for approximately ten days. Solar exposure is not recommended for at least 15 days.

**Results and discussion**

Patients’ appreciation has always been very high during approximately ten years of experience in the use of PLLA, both thanks to the excellent results obtained over time and because patients have been accurately selected, avoiding those who favour short-term results. Furthermore, PLLA results improve substantially over time: we often visit again a patient several months after the last session detecting further clear improvements. The dermis too tends to get compact over time and skin tends to get stretched.

The best results are achieved in the lower third of the face: cheek bones, cheeks and “marionette” wrinkles always give excellent results. As regards the correction of cheek bones and the malar area, the results are definitely better than those obtained with other materials, such as hyaluronic acid macroparticles or non-resorbable materials, which do not provide fine integration into the host tissue.

The implants remain visible and unnatural especially during movements (for example the cheek bone when smiling).

PLLA implants, on the contrary, are always absolutely natural and closely integrated into the surrounding tissues.

This is the reason why such material is well accepted by men too, who generally accept only highly natural corrections.

Unexpectedly good results are also achieved with naso-labial folds (Figures 3 and 4).

Optimal indication is for a young woman, very thin, who wishes to appear slightly fatter, especially in her face, but without succeeding. In this case too, the results are very natural (Figures 5 and 6) and attainable with a very limited number of sessions.

There are still some risks for expression lines or in areas with poor subcutaneous tissue, like the forehead and temporal or lateral canthal areas, although some major users suggest such indication too. Their experience, however, is far higher compared with their average colleagues. It is better to avoid risks. In these areas with little subcutaneous tissue and thin skin, a minimal excess of dosage might be particularly visible.

Very good results are obtained on the jawline, especially in association with the mid-jawline. Evident normalization of the jawline is constantly observed, together with apparent elevation (Figure 4).

It is of utmost importance that accurate and standardized pictures of the patients be taken. The Author generally takes 5 pictures: anteroposterior, 45° left and right, left and right profile. Moreover, the Frankfort plane is always used in the lateral projections, whereby the same inclinations are preserved and the pictures are comparable over time (Figure 7). It would be very difficult to evaluate the results...
over time and to discuss them with patients without truthful pictures. As regards the new indications, further experiences are required as well as more accurate scientific and statistical studies with a view to assessing results and side effects. No major or dangerous side effects have been identified so far according to the Author’s experience. In particular, no nodules have been detected in the last few years. This is certainly related to the decision adopted by the distributing company about the sale of the product exclusively to the physicians who had attended a dedicated training course. As a consequence, the rate of technique errors have dropped to almost zero.

Conclusions

The reduction of volumes and the loss of dermal texture and tonicity have become major aspects of aesthetic correction in the last few years. Furthermore, after the initial period in which some colleagues favoured somewhat excessive and unnatural corrections, today more natural and absolutely invisible corrections tend to prevail. The best results are certainly obtained through integration of the vari-
ous techniques; in this respect, reconstruction by PLLA should be well mastered by any aesthetic physician wishing to be a good all-round professional. The Author believes that PLLA is a highly versatile material, with unique features: of particular interest is the possible diversification of its preparation according to the indications. The results in the lower third of the face have proved excellent and highly natural.

The results in emergent indications require confirmation by scientific studies, although the preliminary results are definitely encouraging. Equally significant is the reduction of major side effects – like nodules – which were certainly caused by technique errors, especially in the early use of PLLA. Compulsory training for all user physicians throughout the world was the right choice for a material of such great aesthetic impact.

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