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EXPERT OPINION

Consensus Recommendations for the Reconstitution and Aesthetic Use of Poly-D,L-Lactic Acid Microspheres

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Abstract: Poly-D,L-lactic acid (PDLLA) microspheres, marketed globally as Aesthefill® (Regen Biotech, Seoul, South Korea), are recognized for their biocompatible and biostimulatory properties, positioning them as a preferred option in aesthetic medicine. This article presents consensus recommendations from Brazilian experts on the reconstitution and clinical application of PDLLA for facial and non-facial treatments. Developed using a modified Delphi method with contributions from leading dermatologists and plastic surgeons, the consensus outlines protocols for reconstitution, injection techniques, and patient management. Key recommendations include reconstitution with 7–8 mL of sterile water for injection, the addition of lidocaine to improve patient comfort, and a preference for targeting the superficial subcutaneous layer. Dosing guidelines are specifically tailored to each treatment area and the desired degree of correction, underscoring the importance of personalized treatment plans. Maintenance treatments are advised at biennial intervals or at shorter intervals for patients exhibiting accelerated collagen degradation. The consensus also highlights the need for proper training and patient screening to minimize adverse effects, such as nodules and granulomas. This comprehensive guide aims to standardize the use of PDLLA, prioritizing patient safety and optimizing outcomes. While clinical trials evaluating PDLLA's aesthetic indications remain limited, these evidence-based guidelines bridge the gap by offering practical protocols grounded in clinical expertise. Further research is encouraged to validate these recommendations and explore new applications for PDLLA in aesthetic medicine.

Plain Language Summary: Poly-D, L-lactic acid (PDLLA) microspheres are small particles used in aesthetic medicine to improve skin appearance by stimulating collagen production. This summary outlines expert recommendations from experts on preparing and using PDLLA for facial and body treatments.

Why was the study done?
The study aimed to create standardized guidelines to help practitioners achieve the best results and ensure patient safety when using PDLLA for cosmetic purposes.

What did the researchers do and find?
They used a method called the Delphi approach to gather and refine recommendations on the reconstitution and injection of PDLLA. By consensus, the experts who participated in this study recommend using of sterile water for injection to prepare the PDLLA and adding lidocaine to reduce discomfort during injections. Specific techniques, such as linear retrograde and fanning methods, are advised for different areas of the face and body. The experts have also provided dosing guidelines and emphasize the need for individualized treatment plans.

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What do these results mean?
The recommendations help practitioners use PDLLA more effectively and safely, providing better aesthetic outcomes for patients. Regular maintenance treatments are suggested every two years, with more frequent sessions for those with faster collagen loss. Proper training and careful patient screening are essential to avoid complications such as nodules or granulomas.

Keywords: poly-D,L-lactic acid, polylactic acid, collagen stimulator, consensus, expert recommendations, filler

Introduction

Polylactic acid (PLA)-based fillers are composed of PLA microparticles and auxiliary components such as sodium carboxymethylcellulose and mannitol.[1] These fillers stimulate collagen production through a subclinical inflammatory response, ultimately increasing the content of type I collagen.[2,3] L-lactic acid and D-lactic acid are two enantiomers of lactic acid, sharing the same molecular formula but differing in their three-dimensional structures, which results in distinct pharmacological properties. The combination of these two compounds can yield four distinct substances: poly-D-lactic acid, poly-L-lactic acid (PLLA), poly-D,L-lactic acid (PDLLA), and meso-polylactic acid.[4]

Although PDLLA degrades more quickly than PLLA,[4] it demonstrates enhanced mechanical stability compared to both poly-L-lactic acid and poly-D-lactic acid, rendering it less brittle and more resistant to mechanical stress. This advantage is due to PDLLA's unique stereoisomeric composition, which results in an amorphous polymer structure, unlike the semi-crystalline, regular chain structure of PLLA. PDLLA has an irregular chain with a random distribution of L- and D-lactic acids, preventing the formation of large crystalline regions.[5]

The outer structure of PDLLA is spherical and foamy, which minimizes damage to surrounding tissue. The inner structure is characterized by a patented reticular and porous design, enhancing biocompatibility and biodegradability. This sponge-like structure increases surface area, providing a scaffold for neo-tissue formation, while maintaining volume even as the initial mechanical stretch dissipates, resulting in a more immediate and sustained effect. It also ensures slow decomposition "from the inside", preventing drastic changes in acidity around the particles.[5]

Following injection, PDLLA microspheres remain localized within the tissue, promoting the recruitment of myofibroblasts and adipose-derived stem cells (ASCs). Myofibroblasts are observed among the microspheres as early as 2 weeks post-injection, continuing to proliferate and eventually penetrating the porous PDLLA particles. By the fourth week, extracellular type I collagen is observed in the spaces between and on the outer surfaces of the microspheres. By the twentieth week, collagen synthesis is evident within individual particles.[2] Additionally, in models of cellular senescence, PDLLA has been observed to induce M2 macrophage polarization, which has been shown to increase NRF2 and IL-10 expression, enhancing ASC survival and supporting anti-inflammatory responses. PDLLA-conditioned media from macrophages has been demonstrated to reduce cellular senescence, increase TGF-β and FGF-2 expression, and when used on senescent ASCs, enhance collagen 1a1 and 3a1 expression while reducing NF-κB and MMP2/3/9, thereby favoring matrix stability.[6]

The most notable improvements are observed at the six-month mark. Although scores gradually decline over time, they remain elevated above baseline levels at the 24-month follow-up.[7,8] During this period, reported adverse events included arthralgia, gingival pain, musculoskeletal pain, urticaria, and gastrointestinal symptoms. These events were not associated with the poly-D,L-lactic acid filler injections and did not result in any severe adverse effects.[8]

The body's response to treatment is influenced not only by the composition of the substance but also by the unique characteristics of each commercial presentation. Consequently, each specific formulation of PLA-based implants necessitates tailored clinical management.[1] PDLLA is globally marketed as Aesthefill® (Regen Biotech, Seoul, South Korea), presented as a lyophilized powder in the form of round pellets that require reconstitution in sterile water for injection (SWFI) prior to use. The formulation consists of poly-D,L-lactic acid (154 mg) microporous spherical particles (average size: 27 μm) and carboxymethylcellulose (46 mg). It is approved for improving cutaneous atrophy through sustained collagen stimulation and for the correction of facial depressions resulting from such atrophy.[4,9]

Material and Methods

Consensus Group

The consensus group was composed of ten Brazilian physicians with specialized expertise in aesthetic treatments, selected based on their recognized experience in the clinical application of PDLLA as a collagen stimulator and their notorious contributions to professional education on its use. Participation was entirely voluntary, ensuring a comprehensive and credible representation of perspectives. The group included seven dermatologists, one plastic surgeon, and two aesthetic physicians.

Consensus Method

The study team conducted a descriptive research study employing a normative guideline/consensus formation approach, adapting principles from the Delphi methodology. The process involved multiple rounds of questionnaires administered via Google Forms (Google LLC., Mountain View, USA) to minimize participants' time commitment, and one face-to-face meeting for deliberation. Data collection was conducted anonymously, with no participant-identifying questions included. No patient interaction, data collection, or human subject research was involved; the study was exclusively based on existing literature and expert opinions. Consequently, ethics committee approval was not required, according to the guidelines of the Brazilian National Health Council (CNS Resolution No. 466/2012) and the Comissão Nacional de Ética em Pesquisa (CONEP), as well as international standards outlined by the ACCORD and ICH E6(R3) guidelines.[10–13]

Round 1: Initial Survey

Participants were invited to complete an anonymous questionnaire consisting of multiple-choice questions regarding their approach to the use of PDLLA as a collagen stimulator. They were also given the opportunity to provide additional comments. The responses were then collated and summarized to identify common viewpoints.

Round 2: Face-to-Face Meeting

The summarized data was reviewed in a face-to-face meeting to encourage reflection on group norms. This meeting aimed to establish common ground and refine the consensus recommendations. No queries were posed in the form of questions or in the format of a personal viewpoint.

Round 3: Refinement

A new questionnaire with refined recommendations was distributed. Responses were collected using a 4-point Likert scale, with participants selecting from the following options: "Totally Agree", "Partially Agree", "Partially Disagree", or "Totally Disagree". Participants were requested to provide written justifications in a free-text format if they did not "totally agree" with any of the proposed recommendations.

Round 4: Final Consensus

The final questionnaire included reviewed recommendations, rewritten to accommodate all opinions. Responses were again collected using the same 4-point Likert scale; however, participants were not offered the possibility to provide free-text justifications at this stage.

The recommendations were categorized based on the level of agreement achieved, with only those reaching significant consensus being adopted. Recommendations unanimously supported by participants (ie, 100% of respondents selecting "Totally Agree" or "Partially Agree") were classified as "Consensus Recommendations". Recommendations with 80–99% agreement were designated as "Strong Recommendations", while those with 51–79% agreement were categorized as "Partial Recommendations". Recommendations with less than 51% agreement were excluded from formal adoption but could be addressed in the article text for discussion.

Results

The group succeeded in reaching a consensus on a comprehensive set of recommendations pertaining to the reconstitution and application of poly-D,L-lactic acid as a collagen stimulator, with a particular focus on techniques and guidelines

that are specifically tailored to aesthetic indications. PDLLA was considered as both a standalone treatment and a component of combination therapies for male and female patients across various age groups. A detailed list of reconstitution, injection, and follow-up recommendations is presented in Table 1.

Reconstitution Techniques

The consensus group established specific guidelines for the reconstitution of poly-D,L-lactic acid microspheres. The group agreed that reconstitution can be efficiently performed in the original vial using an initial dilution volume of 7 to 8 mL of SWFI, as stated in the product insert.[9] An alternative technique, also judged valid and known as the vacuum-assisted "back-and-forth" method,[14,15] involves transferring PDLLA pellets into a 10- or 20-mL syringe, aspirating the vehicle using an 18-gauge needle, and repeatedly transferring the solution between syringes until a homogeneous mixture is achieved. Both methods aim a consistent and uniform suspension.

For the primary method, a hydration period of 10 to 30 minutes within the vial before agitation is recommended to ensure optimal consistency; however, the group agreed that immediate reconstitution before use is feasible, using the "back-and-forth" method.

Sterile water for injection emerged as the most recommended diluent. A 0.9% saline solution can also be utilized, but only with the back-and-forth technique. The initial reconstitution should employ 7 to 8 mL of diluent, although adjustments in volume may be necessary for specific situations.

The addition of 1 to 2 mL of 2% lidocaine immediately before injection is recommended to reduce patient discomfort, with most panelists preferring the use of 2 mL. This supplementation can be made directly into the vial or later, in the injection syringe, maintaining the same ratio of 8:1 or 8:2 for the mixture.

The final volume for facial treatments should be between 9 to 10 mL per vial, while for non-facial areas, the recommended volume ranges from 10 to 20 mL to facilitate distribution over larger treatment areas. The most frequently suggested volumes for each non-facial area were: 10 to 12 mL for the hands; 12 to 16 mL for the neck and chest; and 16 to 20 mL for other areas, such as buttocks and thighs.

Table 1 General Recommendations for PDLLA Reconstitution and Injection

Segment	Consensus recommendations
Reconstitution techniques	Use 7–8 mL of sterile water for injection. Standing time in the vial of 10–30 minutes. Agitate manually before injection. Immediate utilization and/or dilution with saline solution might be viable options using the "back-and-forth" method. Add 1–2 mL of lidocaine to reduce patient discomfort.
Injection Techniques	The overall volume of the final solution should be: 9–10 mL for the facial areas; 10–20 mL for non-facial areas. For further details, please refer to Table 2. Luer-lock syringes are advocated: 1–3 mL for the face and up to 10 mL for non-facial areas, in accordance with the skill levels of the injector. Needles ranging from 26 to 30-gauge or cannulas of 22 to 25-gauge diameter. Prefer retrograde injections, in linear or fanning patterns. Bolus in deeper layers, for specific cases. Superficial subcutaneous layer injection is preferred; sub-SMAS and juxtaperiosteal layers in specific indications. Periocular and perilabial injections are feasible, but risk/benefit ratio should be considered.
Follow up and Special Considerations	Post-treatment massage is not essential, but is recommended twice daily, for 3–5 days after treatment. Pain control medication is usually not necessary, but it may be recommended as needed. Upkeep treatments are typically needed every 24 months, but annual top-ups may be required for patients with accelerated collagen degradation or advanced facial aging. Treatment outcomes should be evaluated 2 to 6 months after the final session, although some effects may be noticeable within the first few weeks.

Injection Techniques and Special Considerations

The use of luer-lock syringes is recommended, with the syringe volume selected to match the injection time for each specific area and the skill level of the injector. This ensures that the product does not remain in the syringe for an extended period, preventing unintended sedimentation. For facial injections, the use of syringes with volumes of 1 to 3 mL is advised, while for neck treatments, syringes of 1 to 5 mL are recommended. For other body areas, syringes with volumes ranging from 1 to 10 mL are suggested.

Injections should be administered using needles ranging from 26 to 30 gauge or cannulas of 22-to-25-gauge diameter. The recommended injection techniques include linear retrograde and fanning patterns, although bolus injections in deeper planes can be utilized in specific cases. Some panelists also utilize subcutaneous bolus injections in certain situations.

The preferred injection layer for PDLLA microspheres is the superficial subcutaneous layer, although sub-SMAS and juxtaperiosteal layers may be used for specific indications. The consensus group acknowledges the use of PDLLA in periocular regions in small quantities, with techniques that prioritize even distribution. Similarly, small quantities of PDLLA may be used in the perilabial region, excluding the vermilion, with careful spreading techniques. However, further studies are needed to establish the risk/benefit ratio for these areas.

While post-treatment massage is not essential, it is recommended for the first 3 to 5 days following the procedure to ensure even allocation of the product, thus reducing the risk of nodule formation and optimizing results.

Indications and Recommended Amounts per Area

Poly-D,L-lactic acid is indicated for the treatment of aging and sagging skin, subcutaneous tissue restructuring, and hypotrophic scars. It is also utilized to prevent sagging and aging, as well as for subcutaneous or deep replacement of facial folds. Non-facial indications extend to areas such as the neck, collarbone, arms, thighs, abdomen, buttocks, hands, knees, and the genital/peri-genital region.

The panelists detailed recommendations on the number of vials required per session for different treatment areas. Typically, for facial treatments, 1 to 2 vials per treatment session are adequate (Figure 1), with the possibility of extending the treatment to parts of the neck when using two vials. Figure 2 illustrates the outcome observed at the 4-month follow-up visit of a patient who received 2 vials of PDLLA, one per hemiface. Each vial was reconstituted with 7 mL of sterile water for injection and 1 mL of 2% lidocaine solution. Figure 3 depicts the volumes injected into each facial region.

To treat the neck in a targeted manner, 1 vial would be ideal for each session. For the decolletage (upper chest), 1 to 2 vials are advised. Treating the arms typically requires 1 vial per side, and for the dorsum of the hands, 0.5 to 1 vial per side. For the abdomen, the recommended quantity per session ranges from 1 to 4 vials. For the gluteal region, the proposed dosage for addressing issues such as cellulite or skin quality ranged between 1 to 5 vials per side, with the precise number of vials dependent on the size of the area to be treated and the number of sub-regions selected for treatment (roughly 0.5 to 1.5 vials per quadrant). The advised dosage for the treatment of the thighs is between 1 to 4 vials, to be determined by the specific area(s) to be treated, whether medial, lateral, posterior, and/or anterior facets. A comprehensive list of the suggested amounts of product per area can be found in Table 2.

Treatment Frequency and Scheduling

The consensus group outlines treatment frequencies based on the severity of the condition. For mild and preventive cases, one session may suffice, while moderate cases may require 2 to 3 sessions. Severe cases may necessitate three or more sessions, potentially in combination with other treatment modalities. The minimum interval between sessions should be 30 days, with the last session scheduled at least 90 days after the penultimate session to ensure that the final results of the previous injection can be evaluated to plan the next intervention.

Follow-Up

Upkeep treatments are recommended every 24 months. However, for patients exhibiting accelerated collagen degradation or more advanced signs of facial aging, top-ups may be needed annually. While some results are already noticeable within the first few weeks (unlike other collagen stimulators), the best timing for final evaluation is 2 to 6 months after the last treatment.

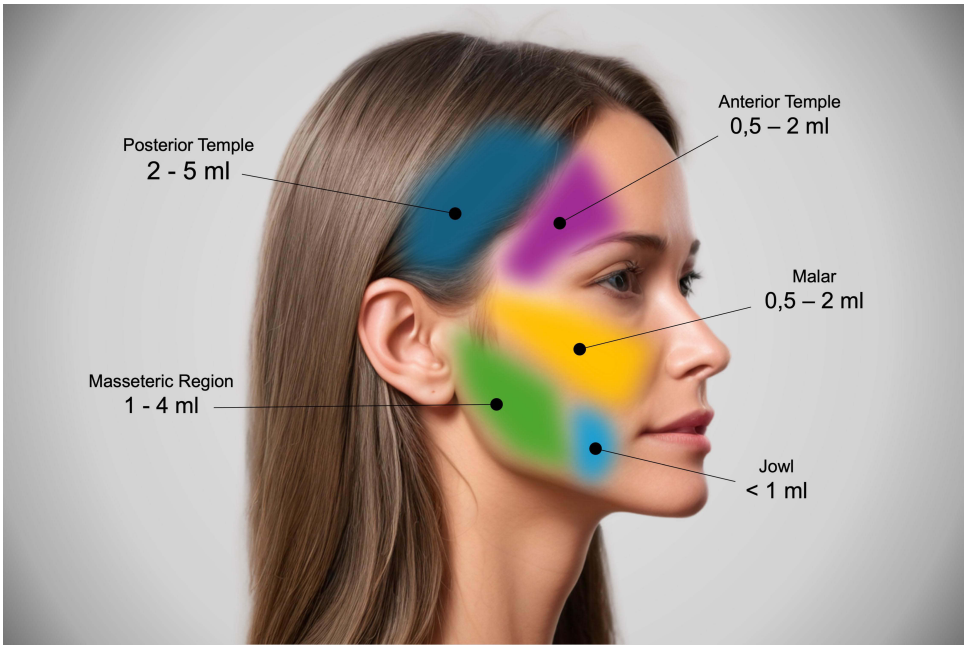

Figure 1 Recommended injection volumes for different facial areas.

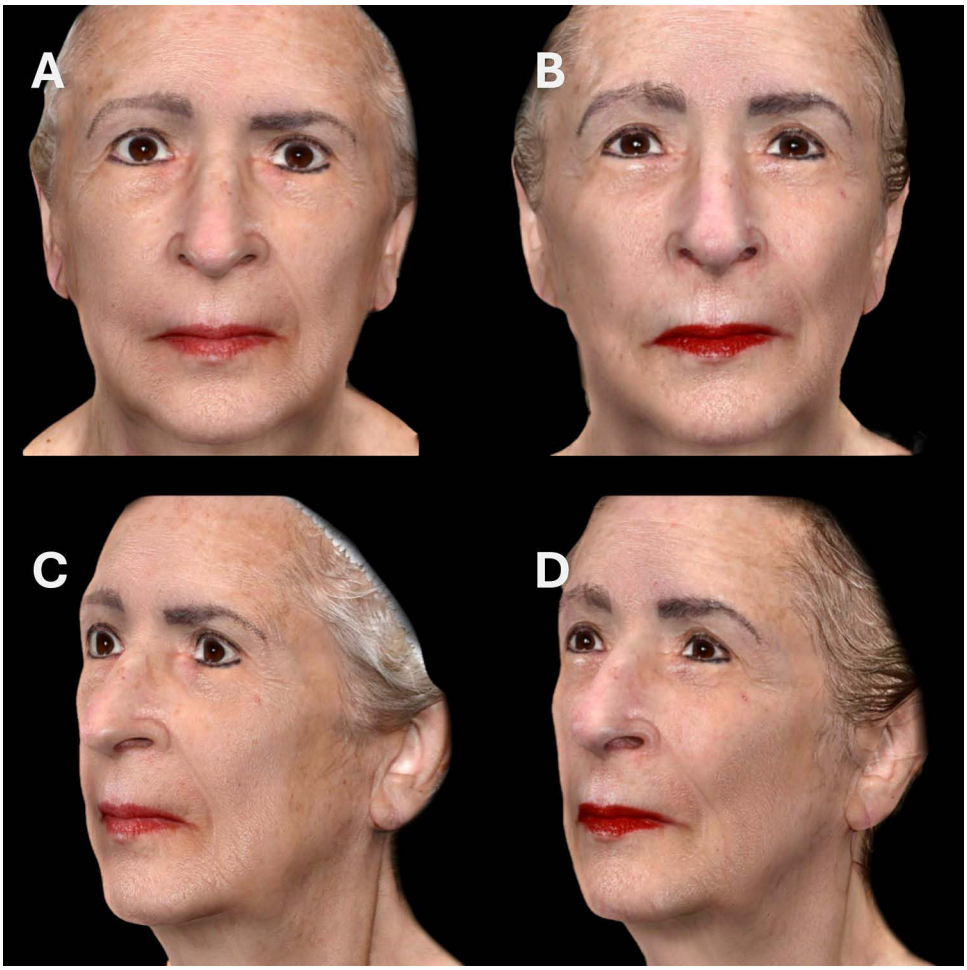

Figure 2 A 69-year-old woman is depicted in frontal view, before (**A**), and 4 months after treatment (**B**), and in oblique view, before (**C**), and 4 months after treatment (**D**). The treatment involved two vials of PDLLA collagen stimulator injected into the anterior temporal, malar, jowl, and masseteric regions. Images were captured using a three-dimensional LifeViz digital imaging system (QuantifiCare S.A., Valbonne, France).

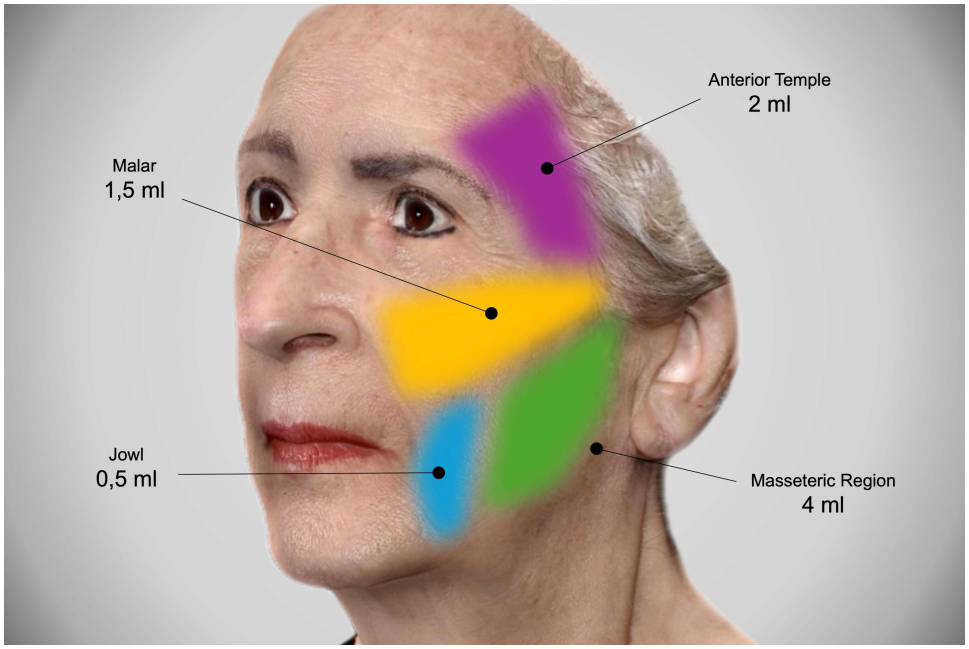

Figure 3 Regions and volumes of poly-D,L-lactic acid (PDLLA) that were injected for the treatment of the patient depicted in Figures 2 and 4.

Adverse Effects and Contraindications

In the panelists' clinical experience, the most common adverse effects are minor, including bruising, mild tenderness, and edema. Severe adverse effects are rare. The group outlines formal contraindications for PDLLA use, including active inflammatory or infectious processes at the application site, active collagen disorders, the presence of permanent fillers in the same location and plane, ongoing pregnancy, and active herpes infections. Relative contraindications should include other active inflammatory processes, autoimmune diseases (including collagen disorders in remission), blood dyscrasias and anticoagulation, liver dysfunction, different types of permanent fillers in other locations or planes, lactation, the use of anti-inflammatory or immunosuppressive drugs, recent surgical interventions at the treatment site (within the last two months), and other significant disruptions in homeostasis. These contraindications, as recognized by the group, are listed in Table 3.

Table 2 Recommended Dosage (per Treatment Session)

Area	Dosage
Face	1–2 vials (refer to Figure 1)
Face + Submandibular Neck	2 vials
Neck	1 vial
Decolletage	1–2 vials
Arm	1 vial (per side)
Dorsum of the hand	0,5–1 vial (per hand)
Abdomen • Supraumbilical: 1 vial • Infraumbilical: 1 via • Flanks: 2 vials	1–4 vials
Gluteal Area	1–5 vials*
Thighs	1–4 vials**

Notes: *Estimated between 0.5 to 1.5 vials per quadrant. **Approximately 1 vial per facet.

Table 3 Contraindications for PDLLA Treatment

Contraindication	Relevant Medical Conditions
Absolute	Active inflammatory or infectious processes at the application site Active collagen disorders Presence of permanent fillers in the same location and plane Ongoing pregnancy Active herpes infections near the treatment area
Relative	Other active inflammatory processes Autoimmune diseases (including collagen disorders in remission) Blood dyscrasias and anticoagulation Liver dysfunctions Different types of permanent fillers in other locations or planes Lactation The use of anti-inflammatory or immunosuppressive drugs Recent surgical interventions at the treatment site (within the last two months) Other significant disruptions in homeostasis

Summary

The initial step in treatment with collagen biostimulators involves thorough patient assessment and selection, considering factors such as medical history, age, and lifestyle habits. To help assess potential risks, patients' medical history should include current skin condition, prior treatments, and any systemic diseases. Additionally, the desired timing of results—whether immediate or gradual—should be discussed to ensure appropriate expectations.[16]

Safety is a paramount concern in aesthetic treatments, and PDLLA has demonstrated a favorable safety profile.[8] While common adverse effects are generally mild and transient, there are rare instances of more significant issues, such as nodules or granulomas. Granulomas occur due to an exaggerated inflammatory response, whereas nodules are mainly caused by improper injection techniques leading to abnormal accumulation of the product, often in dynamic facial muscles.[17] To minimize these risks, it is crucial for practitioners to receive proper training in injection techniques and to conduct thorough patient screenings. Additionally, adhering to appropriate reconstitution methods and recommended injection protocols is essential.

Before administration, the powdered form of poly-D,L-lactic acid (PDLLA) microspheres must be reconstituted with a liquid diluent to achieve a homogeneous suspension. PDLLA microspheres tend to separate and disperse within the solution, making it essential to thoroughly dissolve all carboxymethylcellulose particles during reconstitution to prevent aggregation. The consensus group endorsed the reconstitution method outlined in the product's package insert, which specifies using sterile water for injection (SWFI) followed by a standing period of 10 to 30 minutes prior to manual agitation. However, the group noted that this process may be unnecessarily prolonged. Additionally, we observed that sterile 0.9% sodium chloride solution (normal saline), which is readily available in most medical offices, is anecdotally reported to cause less discomfort upon injection compared to SWFI. It was therefore recognized that an alternative method, the "back-and-forth" methods,[14,15,18] were viable options. These methods generate greater shear forces by transferring the solution back and forth between syringes, which have been demonstrated to overcome the ionic strength of normal saline and accelerate the dilution process.[18]

The proposals also suggest the use of 1 to 2 mL of 2% lidocaine to minimize discomfort. Injection techniques include linear retrograde and fanning patterns, with a preference for luer-lock syringes as well as cannulas and needles ranging from 26 to 30 gauge. The solution volumes for each vial vary by treatment area to facilitate even distribution. It is prudent to select an appropriately sized syringe to prevent sedimentation, considering the anticipated time required to inject the contents of each syringe. Therapeutic indications include the treatment of aged skin and subcutaneous restructuring, with session frequencies and upkeep protocols based on the severity of the patient's condition. Special consideration must be given to bolus injections and to procedures involving the periocular and perilabial regions, where caution is strongly advised. Maintenance treatments are recommended every 24 months, with annual upkeep for cases exhibiting a greater degree of severity.

Although both the consensus recommendations and the package insert[9] advise against the use of PDLLA in patients with active infections, collagen disorders, or during pregnancy, the package insert provides a more comprehensive list of contraindications, including specific conditions such as hypersensitivity, oncological diseases, and a range of systemic conditions such as renal failure and blood disorders. This broader approach in the package insert may reflect a more cautious stance, aiming to cover a wider range of potential risks and ensure the safety of a wider patient demographic.

The proposals presented here also prompt thoughtful comparison to existing guidelines on the use of poly-L-lactic acid (PLLA), underscoring the distinctions between poly-L-lactic acid (PLLA) and poly-D,L-lactic acid (PDLLA), particularly in their composition and microparticle morphology. PLLA is composed exclusively of the L-isomer of lactic acid, forming a semi-crystalline polymer with solid, irregular microparticles. In contrast, PDLLA is a racemic mixture of the D- and L-isomers of lactic acid, resulting in an amorphous polymer with sponge-like, porous microparticles.[4] These differences significantly impact reconstitution and injection processes, with PDLLA's structure allowing faster reconstitution and more uniform distribution.[19]

Consequently, the consensus group suggests using smaller-diameter needles and cannulas for PDLLA and does not contraindicate periocular or perilabial treatments, in contrast to standard PLLA guidelines.[16,20–22] Furthermore, differences in particle dispersion and morphology may contribute to the earlier onset of perceived aesthetic effects.[23] This feature is evident in the previously presented patient at the 15-day follow-up, as illustrated in Figure 4.

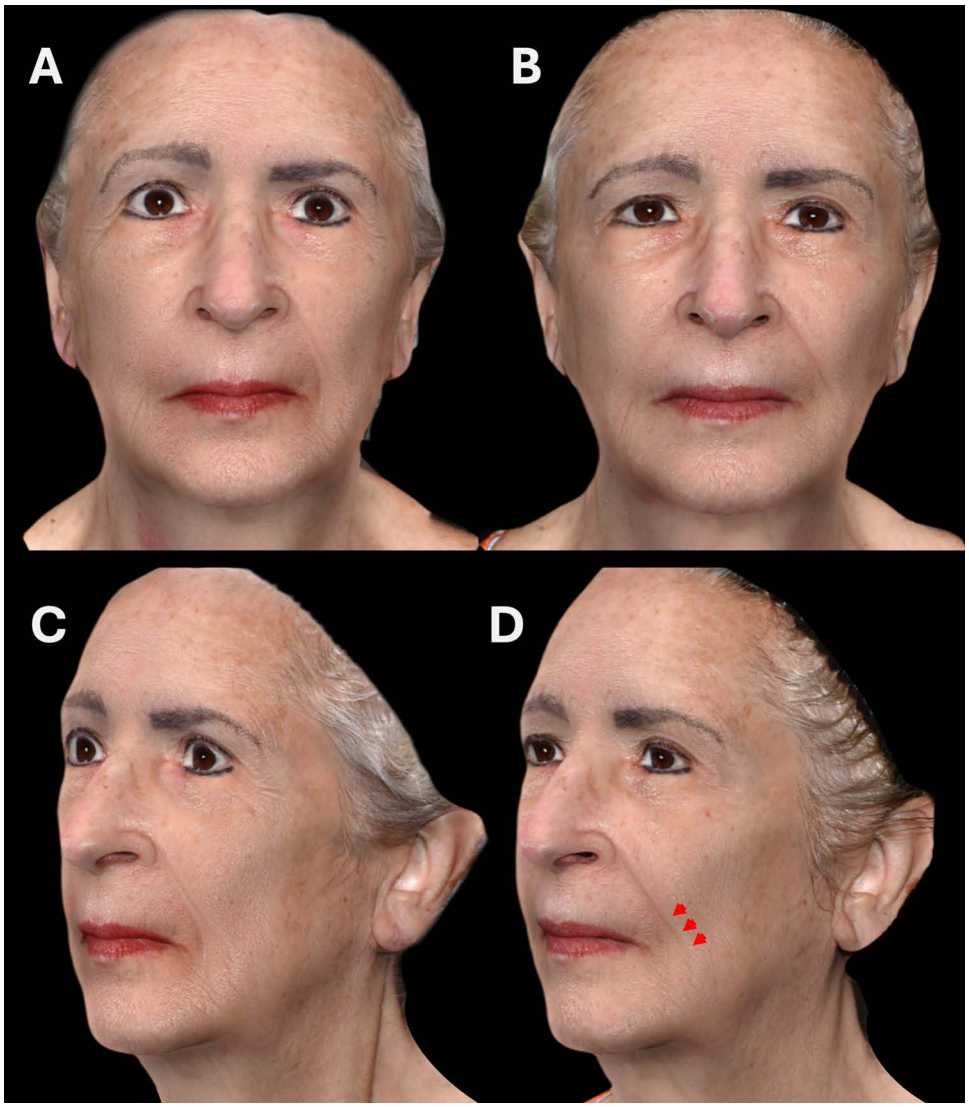

Figure 4 The previously shown patient (Figures 2 and 3) is depicted before (**A**), and 15 days post-treatment (**B**), in frontal view, and before (**C**), and 15 days post-treatment (**D**), in oblique view. The red arrows indicate rectification of the nasolabial fold, which was evident as early as 15 days post-treatment. The images were obtained using the LifeViz imaging system (QuantifiCare S.A., Valbonne, France).

As aesthetic medicine continues to evolve, further research is needed to validate these recommendations through larger, multicenter studies and to explore additional indications and techniques for poly-D,L-lactic acid use. Future studies should focus on refining injection techniques, exploring use in combination with other aesthetic treatments, and investigating new applications. Clinical studies are essential to confirm the recommendations outlined in this article. Continued innovation and research will enhance understanding of how best to utilize these materials to achieve optimal aesthetic outcomes while ensuring patient safety.

Conclusion

Although clinical trials specifically evaluating aesthetic outcomes with poly-D-L-lactic acid collagen stimulators remain limited, the consensus recommendations presented herein aim to bridge this gap by providing evidence-based instructions grounded in empirical data and clinical expertise. These guidelines integrate local insights with international standards in aesthetic medicine, aligning with best practices while addressing the unique demands of the current aesthetic landscape.

While developed within the Brazilian context and potentially reflecting some region-specific aesthetic preferences, they offer valuable insights that may guide international practice, with appropriate consideration for local variations. Additionally, as with many consensus-based guidelines, they require further validation through experimental studies or controlled clinical trials.

The recommendations emphasize detailed protocols for reconstitution, selection of appropriate diluents, and precise treatment techniques, aiming to support practitioners in achieving optimal outcomes. Given the limited available scientific data, future research should focus on substantiating and refining these recommendations to enhance patient safety and improve treatment efficacy.

Ethical and Photo Consent Statement

The patient whose case details and photographs are presented in this manuscript has provided written informed consent for the publication of their details and images and has had the opportunity to review the contents of the article. No institutional approval was required for this publication. The author confirms that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

Dr F.N. Magacho-Vieira is a medical director for Derma Dream Corporation Brazil and was a regular speaker for Galderma, until May, 2024. A. Soares Jr, H.C.L. Alvarenga, I.R.A. Oliveira Jr. J.A.C. Daher, J.V.M.P. Napoli, J.P.A. Serra, and S.C. Provázio are speakers for Derma Dream Corporation Brazil. A. Soares Jr is also a speaker for Medsystem Brazil and Evopharma Brazil. Abrahao Vieira reports being a Speaker for Dermadream Corporation Brazil. João Napoli reports non-financial support from Derma Dream Corporation Brazil, during the conduct of the study; non-financial support from Dream Corporation Brazil, outside the submitted work. The authors report no other conflicts of interest in this work.

References

1. Azarkevich PN, Gorskaya AA. Physicochemical Characteristics and Hydrolytic Degradation of Polylactic Acid Dermal Fillers: a Comparative Study. *Cosmetics*. 2023;10(4):110. doi:10.3390/cosmetics10040110
2. Lin CY, Lin JY, Yang DY, Lee SH, Kim JY, Kang M. Efficacy and safety of poly-D,L-lactic acid microspheres as subdermal fillers in animals. *Plast Aesthet Res*. 2019;6:16. doi:10.20517/2347-9264.2019.23
3. Haddad S, Galadari H, Patil A, Goldust M, Al Salam S, Guida S. Evaluation of the biostimulatory effects and the level of neocollagenesis of dermal fillers: a review. *Int. J Dermatol*. 2022;61(10):1284–1288. doi:10.1111/ijd.16229
4. Doe J, Smith A. Compositions of Injectable Poly-D,L-lactic Acid and Injectable Poly-L-lactic Acid. *Aesthetic Surg J*. 2024;44(3):199–207. doi:10.1093/asj/sjab023
5. Lee KWA, Chan LKW, Lee AWK, Lee CH, Wong STH, Yi KH. Poly-d,l-lactic Acid (PDLLA) Application in Dermatology: a Literature Review. *Polymers*. 2024;16(18):2583. doi:10.3390/polym16182583
6. Oh S, Seo SB, Kim G, et al. Poly-D,L-Lactic Acid Filler Increases Extracellular Matrix by Modulating Macrophages and Adipose-Derived Stem Cells in Aged Animal Skin. *Antioxidants. Basel*. 2023;12(6):1204. doi:10.3390/antiox12061204
7. Lin JY, Lin CY. Injectable Poly-D, L-lactic Acid in Facial Rejuvenation: Three Case Reports. *Cosmetol J*. 2020;4(1):000120.
8. No YA, Seok J, Hyun MY, et al. Long-Term (24-Month) Safety Evaluation of Poly-DL-Lactic Acid Filler Injection for the Nasolabial Fold: a Multicenter, Open, Randomized, Evaluator-Blind, Active-Controlled Design. *Plast Reconstr Surg*. 2015;135(6):1074e–1075e. doi:10.1097/PRS.0000000000001247
9. *Regen Biotech, Inc. Aesthefill® [Package Insert]*. Daejeon, South Korea: Daedeok-gu; 2024.
10. Conselho Nacional de Saúde. Resolução. de dezembro de 2012. Conselho Nacional de Saúde. Availabe from: http://conselho.saude.gov.br/resolucoes/2012/Reso466.pdf. Accessed October 26, 2024.
11. Comissão Nacional de Ética em Pesquisa (CONEP). Manual Operacional para Comitês de Ética em Pesquisa. Brasília, Brazil: Ministério da Saúde; 2006. Availabe from: https://pesquisa.bvsalud.org/portal/resource/pt/biblio-926003. Accessed November 27, 2024.
12. van Zuuren K, Goldman P, Logullo P, et al. ACCORD guideline for reporting consensus-based methods in biomedical research and clinical practice. *Res Integr Peer Rev*. 2022;7(3):1–10. doi:10.1186/s41073-022-00122-0
13. International Council for Harmonisation. ICH E6(R3) Guideline on Good Clinical Practice (GCP). ICH; 2023. Availabe from: https://database.ich.org/sites/default/files/ICH_E6%28R3%29_DraftGuideline_2023_0519.pdf. Accessed October 26, 2024
14. Brown T, White H. Reconstitution of Injectable Poly-D,L-lactic Acid: Efficacy of Different Diluents and a New Accelerating Method. *Dermatol Surg*. 2024;50(6):678–685. doi:10.1097/DSS.0000000000003410
15. Johnson K, Lee S. Vacuum-assisted Hydration before the Back-and-forth: a Novel Accelerating Method for Reconstituting Injectable Poly-D, L-lactic Acid. *J Cosmet Dermatol*. 2024;23(2):144–150. doi:10.1111/jocd.15032
16. Avelar, Luiz, Ong, Amanda, Ong, David et al. Consensus Recommendations on the Use of Injectable Poly-L-lactic Acid in Asian Patients. *Dermatol Ther*. 2024;37(1). doi:10.1111/dth.14878
17. Perez Willis KM, Ramirez Galvez R. Granuloma after the Injection of Poly-D,L-Lactic Acid (PDLLA) Treated with Triamcinolone. *Case Rep Dermatol Med*. 2024;2024:6544506. doi:10.1155/2024/6544506
18. Chen SY, Chen ST, Lin JY, Lin CY. Reconstitution of Injectable Poly-D-L-lactic Acid: efficacy of Different Diluents and a New Accelerating Method. *Plast Reconstr Surg Glob Open*. 2020;8(5):e2829. doi:10.1097/GOX.0000000000002829
19. Smith R, Garcia M. Efficacy and Safety of Poly-D,L-lactic Acid Microspheres as Subdermal Fillers in Animals. *Plast Aesthet Res*. 2019;6:16. doi:10.20517/2347-9264.2019.23
20. Müller P, Schmidt H. European Expert Recommendations on the Use of Injectable Poly-L-lactic Acid for Facial Rejuvenation. *Aesthetic Med*. 2024;5(2):76–85. doi:10.1093/aestmed/amz022
21. Green S, Evans T. Consensus Recommendations on the Use of Injectable Poly-L-lactic Acid for Facial and Nonfacial Rejuvenation. *Plast Reconstr Surg*. 2024;145(5):1051–1062. doi:10.1097/PRS.0000000000006510
22. Harris D, Brown M. Recommendations on the Use of Injectable Poly-L-lactic Acid for Skin Laxity in Off-Face Areas. *J Clin Aesthet Dermatol*. 2024;17(3):45–52. doi:10.1249/JCD.0000000000000634
23. Chen SY, Chen ST, Lin JY, Lin CY. Early-stage volume effect difference between injectable poly-L-lactic acid and injectable poly-D, L-lactic acid. *J Cosmet Dermatol*. 2022;21(5):1702–1703. doi:10.1111/jocd.15595