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Poly-L-Lactic Acid in Aesthetic Dermatology: Injection Techniques, Clinical Protocols, Skin Quality Outcomes, and Risk Management

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Abstract

Poly-L-lactic acid is a synthetic, biodegradable collagen biostimulator that has evolved over more than two decades from a corrective agent for human immunodeficiency virus-associated facial lipoatrophy into a widely used tool in regenerative aesthetic dermatology. Unlike hyaluronic acid fillers, which provide immediate volume by occupying space, it acts indirectly: its microparticles elicit a controlled subclinical foreign-body response that drives macrophage polarization, transforming growth factor-beta 1/Smad-mediated fibroblast activation, and progressive type I neocollagenesis. In this narrative review, PubMed/MEDLINE, Embase, and the Cochrane Library were searched through August 2026 for English-language, peer-reviewed studies, which were appraised narratively to summarize the evidence on injection techniques and reconstitution, clinical protocols and patient selection, clinical efficacy and skin quality outcomes, and the prevention and management of complications. Consensus statements and comparative studies associate higher reconstitution volumes, thorough suspension, subdermal placement, non-bolus delivery, and structured post-treatment care with fewer papules and nodules, although much of this guidance rests on expert opinion and observational data rather than head-to-head trials. A small number of randomized controlled trials report improvements in cheek wrinkle severity, skin elasticity, hydration, and dermal thickness compared with no treatment or saline, and indications are extending to the neck, décolletage, body, and patients with facial volume loss during glucagon-like peptide-1 receptor agonist therapy. However, the available trials are few, heterogeneous in protocols and outcome measures, and frequently at some or high risk of bias. Non-inflammatory nodules and inflammatory granulomas differ in mechanism and are managed along distinct pathways. Standardized protocols, a core outcome set for skin quality, and adequately powered comparative trials are needed before firm conclusions about the relative effectiveness of poly-L-lactic acid can be drawn.

Categories: Plastic Surgery, Therapeutics, Dermatology
Keywords: adverse events, aesthetic dermatology, collagen biostimulator, dermal filler, injection technique, neocollagenesis, poly-l-lactic acid, skin quality

Introduction And Background

Cutaneous aging is a multifactorial process in which the progressive loss and disorganization of dermal collagen and elastin, declining fibroblast activity, and redistribution of facial fat compartments together produce wrinkling, laxity, and loss of skin firmness and radiance. The number and diameter of collagen bundles fall with age while the ratio of type III to type I collagen rises, reducing the capacity of the dermis to resist and recover from mechanical stress [1,2]. Contemporary aesthetic medicine has consequently shifted from a purely corrective, volume-replacement paradigm toward regenerative strategies that aim to restore the biological architecture of the skin itself.

Collagen biostimulators sit at the center of this shift. Rather than occupying space in the way that hyaluronic acid (HA) gels do, biostimulators such as calcium hydroxylapatite, polycaprolactone, and poly-L-lactic acid (PLLA) recruit the host's own reparative machinery to generate new extracellular matrix [2,3]. This distinction has practical consequences: hyaluronic acid gels produce an immediate, largely mechanical correction whose duration depends on degradation of the gel, whereas the effect of a biostimulator develops gradually over months, depends on the host tissue response, and targets dermal quality as well as volume [2]. Among these, PLLA has the longest clinical track record. A synthetic polymer of the alpha-hydroxy-acid family, it was first approved in Europe in 1999 (New-Fill) and by the United States Food and Drug Administration in 2004 for the correction of human immunodeficiency virus (HIV)-associated facial lipoatrophy, with subsequent approval for aesthetic correction of nasolabial folds and other facial wrinkles; it is now marketed in more than 40 countries [4,5]. Over the past decade, its use has expanded well beyond volume restoration to encompass global improvement of skin quality and, increasingly, treatment of the neck, décolletage, and body [4,6].

Because the clinical effect of PLLA is biologically mediated and delayed, its outcomes depend heavily on operator-controlled variables: how the product is reconstituted, where it is placed, and how the patient is

selected and followed [7]. Consensus statements accordingly attribute most nodules and other late complications to technique, such as low dilution, superficial or intramuscular placement, and bolus delivery, rather than to the material itself [7]. Clinical interest has also shifted from volume replacement toward skin quality, meaning dermal thickness, elasticity, hydration, texture, and radiance, because these are the outcomes most directly linked to a collagen-stimulating mechanism [6]. The objectives of this narrative review are therefore to (1) summarize the physicochemical properties and mechanism of action that underpin rational protocol design; (2) synthesize current evidence and consensus guidance on reconstitution and injection technique; (3) outline clinical protocols and patient selection; (4) appraise the clinical evidence on efficacy and skin quality outcomes, distinguishing randomized from observational and consensus-based evidence; and (5) describe the prevention and management of complications before identifying methodological gaps for future research.

Review

Evidence acquisition

This is a narrative review; it was not designed or conducted as a systematic review, and no protocol was registered. PubMed/MEDLINE, Embase, and the Cochrane Library were searched from database inception to August 2026, which was the date of the last search in all three databases. A representative PubMed search string was: ("poly-L-lactic acid"[tiab] OR "polylactic acid"[tiab] OR PLLA[tiab] OR Sculptra[tiab]) AND (aesthetic*[tiab] OR filler*[tiab] OR "collagen biostimulator"[tiab] OR neocollagenesis[tiab] OR "skin quality" [tiab] OR reconstitution[tiab] OR "injection technique"[tiab] OR "adverse event*"[tiab] OR nodule*[tiab] OR granuloma*[tiab]); it was adapted to the syntax of Embase and the Cochrane Library.

Eligible sources were English-language, peer-reviewed publications on the aesthetic or dermatologic use of PLLA, including randomized controlled trials (RCTs), systematic reviews, prospective and retrospective clinical studies, expert consensus statements, and mechanistic in vitro and animal studies. Conference abstracts, preprints, and other non-peer-reviewed material were excluded, as were studies in which PLLA-specific findings could not be separated from those of other fillers. Studies of the closely related poly-D, L-lactic acid (PDLLA) were retained where they informed reconstitution, mechanism, or complication management, and they are identified as such in the text. Two authors independently screened titles and abstracts and then full texts; disagreements were resolved by discussion or by the senior author. Reference lists of included articles were hand-searched for additional sources. Priority was given to RCTs and to publications from the last five years, while seminal consensus documents were retained for historical and technical continuity.

Studies were appraised narratively for design, sample size, comparator, outcome measures, and potential sources of bias; no formal risk-of-bias tool was applied, but the risk-of-bias judgments of included systematic reviews are reported where available. Because study designs, protocols, and outcome measures were too heterogeneous for quantitative pooling, findings were synthesized narratively by domain, and the level of evidence (randomized trial, observational study, or expert consensus) is stated for key claims.

Material properties and biological mechanism of action

PLLA is supplied as a lyophilized powder of irregular or, in newer formulations, spherical microparticles typically 40-63 µm in diameter, combined with excipients such as sodium carboxymethylcellulose and non-pyrogenic mannitol that aid suspension and reconstitution [4,7]. It is immunologically inert and fully biodegradable; once implanted, the polymer undergoes gradual hydrolysis to lactic acid monomers, which are metabolized through normal cellular pathways to carbon dioxide and water [8].

The clinical effect of PLLA is not attributable to the volume of the injected suspension, most of which is water that resorbs within days, but to the tissue response the microparticles provoke. Placement of the particles initiates a controlled, subclinical foreign-body reaction: an early inflammatory phase in which monocytes and macrophages engage the particles, followed by a shift toward a pro-reparative M2 macrophage phenotype and the release of transforming growth factor-beta 1 (TGF-β1) [9]. TGF-β1 signaling through the Smad pathway activates fibroblasts and upregulates matrix genes, including COL1A1, fibronectin, and elastin, driving synthesis of predominantly type I collagen around the encapsulated particles [6,9,10]. In vitro work in human dermal fibroblasts confirms that PLLA directly increases collagen gene expression and synthesis via TGF-β/Smad signaling [10], and animal studies of PLLA and of the related PDLLA formulation demonstrate parallel increases in dermal collagen and angiogenesis in aged skin [9,11]. The biological cascade underlying PLLA-induced neocollagenesis is summarized in Figure *1*.

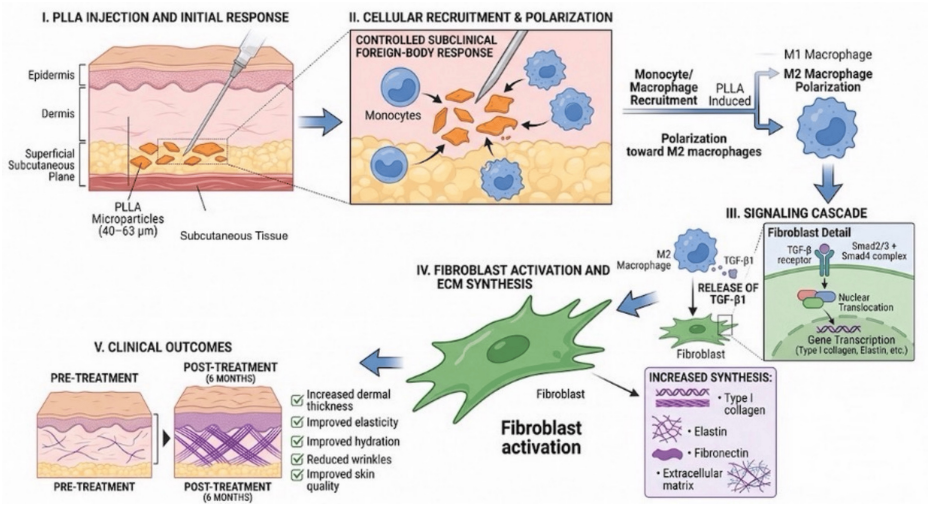


FIGURE 1: Mechanism of action of poly-L-lactic acid as a collagen biostimulator

Following subdermal injection, poly-L-lactic acid (PLLA) microparticles induce a controlled subclinical foreign-body response characterized by recruitment of monocytes and macrophages and polarization toward an M2 macrophage phenotype. Subsequent release of TGF-β1 activates the Smad signaling pathway, stimulating fibroblast activation and extracellular matrix synthesis, including type I collagen, elastin, and fibronectin. Progressive dermal remodeling results in increased dermal thickness, improved elasticity, enhanced skin quality, and gradual clinical rejuvenation [6,9,10].

ECM: extracellular matrix; PLLA: poly-L-lactic acid; TGF-β1: transforming growth factor-beta 1

Image credit: Original illustration created by the authors using Canva (Canva Pty Ltd, Sydney, Australia).

This biological cascade unfolds over a characteristic timeline that explains the clinical behavior of PLLA. An initial inflammatory and early matrix-deposition phase is followed by collagen maturation and reorganization from approximately weeks 6 to 16, and then a stabilization phase with ongoing extracellular matrix turnover that may extend to about 24 months [6]. Because correction accrues gradually as collagen matures rather than appearing immediately, treatment is intentionally staged across multiple sessions, and both clinician and patient must anticipate a delayed, progressive result. Emerging evidence also suggests PLLA may stimulate preadipocytes within dermal white adipose tissue, pointing to broader tissue remodeling beyond collagen alone [6]. The expected biological and clinical progression following PLLA injection is illustrated in Figure *2*.

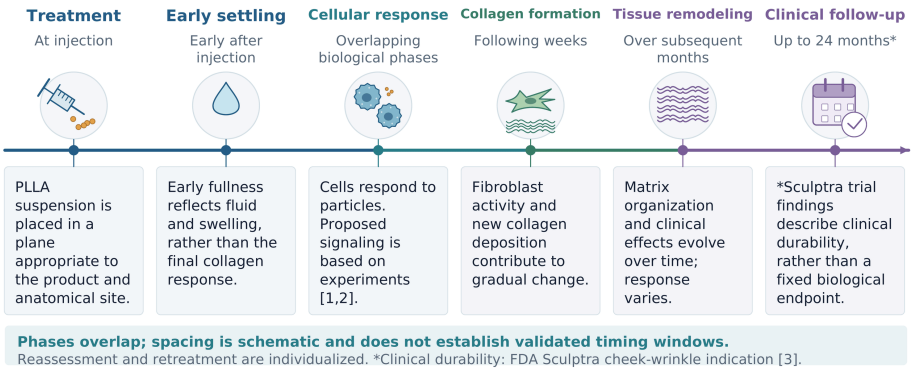


FIGURE 2: Biological and clinical timeline following poly-L-lactic acid injection

PLLA produces delayed clinical improvement because the injected suspension undergoes gradual biological remodeling rather than immediate volumization. Initial water resorption is followed by macrophage recruitment, fibroblast activation, neocollagenesis, extracellular matrix remodeling, and progressive improvements in dermal thickness, elasticity, hydration, and overall skin quality over approximately 24 months [6].

PLLA: poly-L-lactic acid; *Clinical durability: FDA Sculptra cheek-wrinkle indication [3]

Image credit: Original illustration created by the authors using Canva (Canva Pty Ltd, Sydney, Australia).

Injection techniques and reconstitution protocols

Reconstitution: Diluent, Volume, and Hydration

Reconstitution is the single most influential modifiable determinant of PLLA safety. The powder must be reconstituted with a liquid diluent to a homogeneous suspension, and inadequate dispersion, with residual carboxymethylcellulose aggregates, is a recognized driver of particle clumping and subsequent nodules, as emphasized in consensus recommendations developed for a related PDLLA formulation [7]. Practice has evolved decisively toward higher dilution volumes. Whereas early protocols used 3-5 mL, contemporary consensus favors reconstitution with sterile water for injection at volumes of 7-8 mL or more for the face, with the addition of approximately 1 mL of lidocaine for patient comfort [7,12,13]. A randomized study of 80 participants found that higher dilution volumes and immediate use after reconstitution were feasible without loss of efficacy [5,14], and expert consensus reports fewer nodules with an 8 mL than with a 5 mL reconstitution [13]. For body and off-face indications, still higher dilutions (commonly 16-20 mL per vial) are used to achieve broad, even dermal coverage [6]. Historically, prolonged hydration (hours to overnight) was advised to ensure complete particle wetting; more recent data supporting immediate use after adequate reconstitution have relaxed this requirement, though thorough suspension immediately before injection remains essential [14]. The evolution of these recommendations is summarized in Table *1*.

Parameter	Early protocols	Current facial consensus	Body/off-face
Diluent	Sterile water ± lidocaine	Sterile water for injection + ~1 mL lidocaine	Sterile water for injection + lidocaine
Dilution volume	3-5 mL	7-8 mL or more	16-20 mL per vial (hyperdilution)
Hydration time	Hours to overnight	Immediate use acceptable after full suspension	Immediate use after full suspension
Primary rationale	Volumization	Even dispersion; lower nodule risk	Wide dermal coverage of thin-skinned zones
Delivery device	Needle	Needle or blunt cannula	Blunt-tipped cannula, fan retrograde

TABLE 1: Evolution of poly-L-lactic acid reconstitution and dilution recommendations

Values synthesized from consensus statements and randomized reconstitution studies [7,12-14]. Practitioners should follow the current approved product labeling for the specific device used.

Injection Planes, Instruments, and Regional Technique

The preferred plane for most PLLA indications is the superficial subcutaneous layer; the deep subcutaneous, sub-superficial musculoaponeurotic system (sub-SMAS), and supraperiosteal planes are used selectively for structural volumization [7]. Superficial dermal placement is avoided because it is a principal cause of visible papules, as is deposition within dynamic musculature, where repeated motion promotes product accumulation and nodule formation [7,15]. Both sharp needles and blunt-tipped microcannulas are used; cannulas are generally preferred for large or mobile areas and for reducing vascular and bruising risk. Delivery should consist of small aliquots distributed by linear retrograde threading, fanning, or cross-hatching, using multiple depots and syringes and avoiding single high-pressure boluses [13,15]. Ultrasound guidance can further reduce the risk of vascular injury in anatomically hazardous zones [15]. Representative injection patterns, together with common technical errors that should be avoided, are illustrated in Figure *3*.

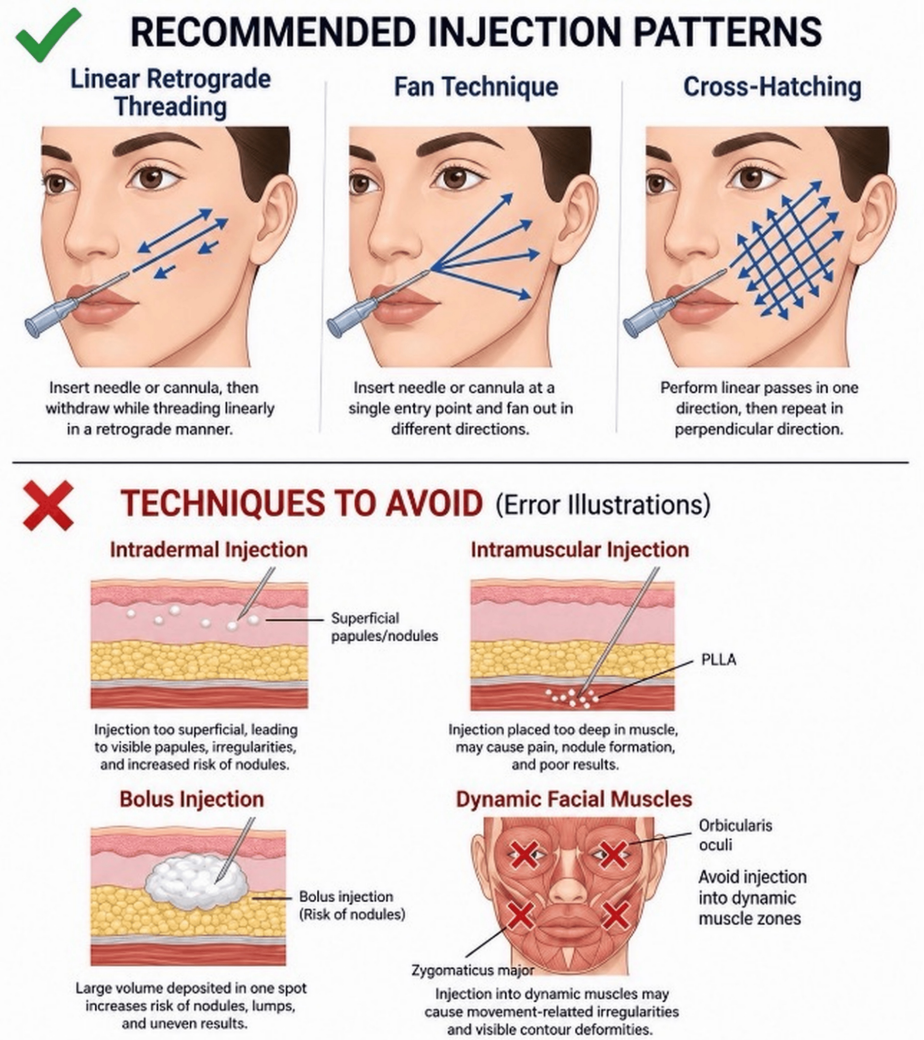


FIGURE 3: Recommended injection techniques and common technical errors during poly-L-lactic acid administration

Recommended delivery methods include linear retrograde threading, fan technique, and cross-hatching within the superficial subcutaneous plane using small aliquots distributed evenly throughout the treatment area. Incorrect techniques, including intradermal placement, intramuscular injection, bolus deposition, and injection into dynamic facial musculature, increase the risk of papules, nodules, contour irregularities, and other adverse outcomes [7,13,15].

PLLA: poly-L-lactic acid

Image credit: Original illustration created by the authors using Canva (Canva Pty Ltd, Sydney, Australia).

Regional technique varies with anatomy. In the midface and temples, PLLA restores structural support and dermal density; the jawline and pre-auricular region benefit from supportive subdermal placement; and the

nasolabial folds, where randomized comparative data exist, respond well to conservative layered correction [16]. Off-face zones (neck, décolletage, upper arms, abdomen, thighs, buttocks, and knees) present thin dermis, mobility, and variable fat, and are best treated with hyperdilution, blunt cannulas, and fan-shaped retrograde threading to spread product widely at low concentration [4,6,17,18]. Historically cautious areas such as the periorbital region and perioral vermilion should be approached, if at all, only in small quantities with even-distribution techniques, as the risk/benefit ratio there is not well established [7]. An anatomical overview of commonly treated facial regions, recommended injection vectors, and areas requiring caution is presented in Figure *4*.

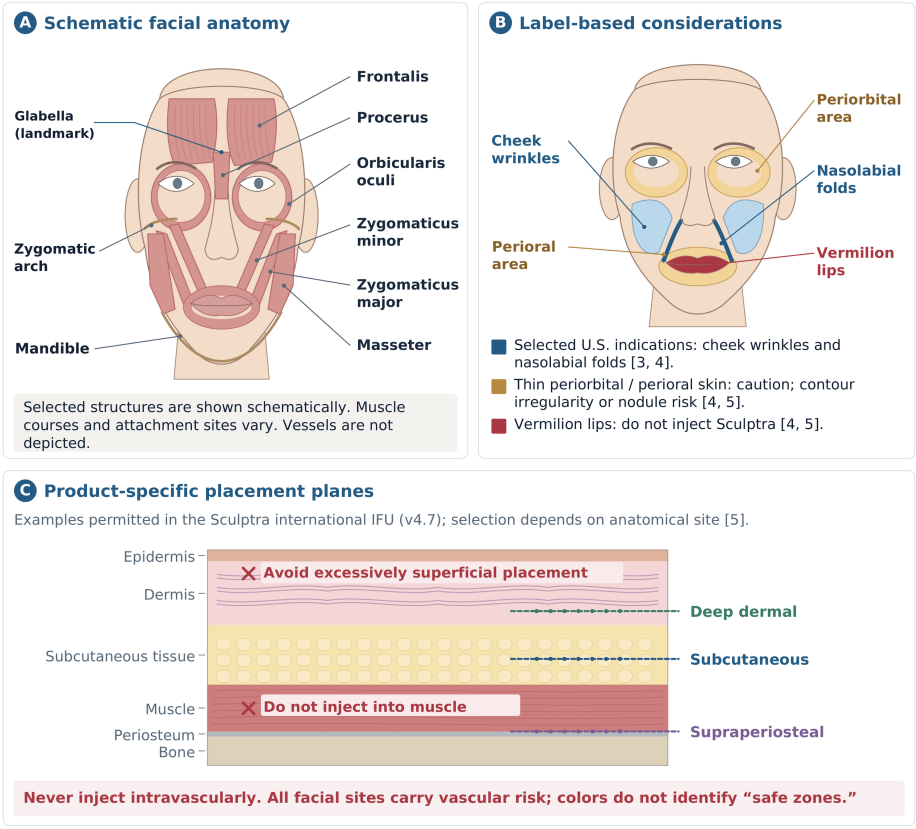


FIGURE 4: Anatomical treatment map for facial poly-L-lactic acid injection

Recommended treatment zones include the temples, cheeks, preauricular region, and jawline. The nasolabial folds should be approached conservatively, whereas the periorbital region, glabella, lips, and superficial dermis require avoidance or particular caution because of increased risks of visible nodules, contour irregularities, and vascular complications. The inset illustrates correct placement of PLLA within the superficial subcutaneous plane [7].

Sculptra-specific schematics. U.S. indications [3,4] and international placement guidance [5] are identified separately.

PLLA: poly-L-lactic acid

Image credit: Original illustration created by the authors using Canva (Canva Pty Ltd, Sydney, Australia).

Dosing, Treatment Intervals, and Post-treatment Care

Because collagen accrues over months, PLLA is delivered as a course rather than a single treatment. A typical facial program comprises two to four sessions spaced roughly four to six weeks apart, with the number of vials titrated to the degree of correction and the treatment area [12,16]. Maintenance is generally advised at intervals of approximately two years, or sooner in patients with accelerated collagen loss [13]. Post-treatment massage, traditionally summarized by the "rule of fives" (several minutes, several times daily, for several days), is recommended to promote even distribution, although evidence indicates that massage cannot compensate for inadequate dilution or faulty placement and is not by itself sufficient for nodule prevention [19]. Patients should be counseled on the delayed, gradual nature of the result to align

expectations with the biology.

Clinical protocols and patient selection

Rational patient selection begins with matching the mechanism to the indication. PLLA is best suited to diffuse dermal atrophy, skin laxity and crepiness, and generalized volume and quality loss, rather than to the precise correction of a discrete line or contour, for which an HA gel may be more appropriate. Realistic expectations regarding the delayed onset and staged delivery are essential to satisfaction [12].

Screening should identify relative and absolute contraindications. Active infection or inflammation at the treatment site, a history of hypertrophic scarring or keloids, and known hypersensitivity to any component are contraindications; a history of granulomatous or autoimmune disease warrants particular caution given the immune-mediated mechanism of action. Injecting into or immediately adjacent to areas of prior permanent filler, and treating patients who are unable to comply with post-procedure care, both increase risk. Anatomical judgment, avoiding superficial, dynamic, and vascular-dense regions, is itself part of patient selection [7,20].

PLLA is frequently integrated into combination regimens. It is commonly layered with HA, where the hygroscopic gel provides immediate hydration and surface smoothing while PLLA drives longer-term dermal remodeling, and with neuromodulators, energy-based devices, and suspension threads as part of a global rejuvenation plan [18,21]. A rapidly growing indication is the population experiencing facial and body volume loss during glucagon-like peptide-1 receptor agonist (GLP-1 RA) therapy; the accelerated depletion of facial fat and skin firmness in these patients aligns well with a regenerative, collagen-restoring approach, and combined PLLA-plus-HA regimens have been reported to improve facial harmony and skin quality in this group [6,22].

Clinical efficacy and skin quality outcomes

Evidence that PLLA improves skin quality, as distinct from restoring volume, comes from a small number of RCTs supplemented by observational studies; key study characteristics are summarized in Table *2*. In a randomized, double-blind, saline-controlled, multicenter trial, 40 women aged 30-60 years received 3 sessions of PLLA or an equal volume of saline at 4-week intervals [23]. At 12 months, skin elasticity (cutometry) and hydration (corneometry) had increased significantly in the PLLA group, and blinded photographic evaluation showed significant improvement in radiance and smoothness and reductions in pigmentation, erythema, and pore size [5,23]. Transepidermal water loss decreased in both arms, so this change cannot be attributed to treatment [23]. Patient-reported improvements in skin quality have also been described with combined PLLA and hyaluronic acid regimens [21].

Study (design)	Population (n)	Intervention vs. comparator	Follow-up	Primary/key outcomes and results	Limitations
Bohnert 2019 [23] (multicenter, double-blind RCT)	Healthy women aged 30-60 years, Fitzpatrick I-IV (n = 40)	PLLA, 3 sessions every 4 weeks vs. equal-volume saline	12 months	Elasticity and hydration increased significantly with PLLA; radiance and smoothness improved and pigmentation, erythema, and pore size decreased on blinded photographic review; TEWL decreased in both arms. Effect sizes/CIs: NR	Small sample; instrument-based surrogate outcomes
Fabi 2024 [24] (multicenter, evaluator-blinded RCT, 2:1)	Adults with moderate/severe cheek wrinkles; mean age 60.7 years; 96.6% women (n = 149: 97 vs. 52)	PLLA, 8 mL SWFI + 1 mL lidocaine per vial, up to 4 monthly sessions vs. no treatment	12 months	≥1-grade GCWS improvement (both cheeks): 66.2% vs. 38.6% (M7, p = 0.0043); 70.6% vs. 31.1% (M9, p < 0.0001); 71.6% vs. 26.1% (M12, p < 0.0001). 95% CIs: NR	Untreated (not sham) control; industry-sponsored; high risk of bias (D2) per [5]
Signori 2024 [5] (systematic review of RCTs)	11 RCTs (HIV-associated lipoatrophy and immunocompetent populations)	PLLA vs. human collagen, polyacrylamide hydrogel, saline, no/delayed treatment, or another PLLA protocol	Up to ≥25 months	Increased dermal thickness; improved lipoatrophy and aesthetic scores; superior to human collagen in 2 trials; no meta-analysis	RoB 2: 0 low, 6 some concerns, 5 high risk; overall low-quality evidence
Zubair 2024 [25] (double-blind, split-body RCT)	Women with hip dell deficits (n = 15)	PLLA 150 mg per side, 3 monthly sessions vs. contralateral saline	9 months	Ultrasound: dermis +26.1% and adipose layer +27% from baseline on PLLA side; saline side unchanged; improved collagen and elastic fibers on histology. p-values/variability: NR	Very small sample; single center
Joseph 2026 [26] (open-label RCT, 1:1)	Women with moderate/severe décolletage wrinkles (n = 30)	PLLA in 8 mL vs. 17 mL SWFI (+1 mL lidocaine), up to 4 monthly sessions	9 months	≥1-grade GDS improvement at M9: 93.8% vs. 78.6%; GAIS improvement >90% in both arms; 1 treatment-related AE, none serious. Between-group test: NR	Unblinded investigator assessment; no untreated control

TABLE 2: Characteristics and principal findings of key studies on poly-L-lactic acid and skin quality

AE: adverse event; CI: confidence interval; D2: risk-of-bias domain 2 (deviations from intended interventions); GAIS: Global Aesthetic Improvement Scale; GCWS: Galderma Cheek Wrinkle Scale; GDS: Galderma Décolletage Scale; M: month; NR: not reported; PLLA: poly-L-lactic acid; RCT: randomized controlled trial; RoB 2: Cochrane Risk-of-Bias tool, version 2; SWFI: sterile water for injection; TEWL: transepidermal water loss

The largest skin-quality RCT randomized 149 adults (mean age 60.7 years; 96.6% women) with moderate or severe cheek wrinkles in a 2:1 ratio to PLLA (n = 97; up to four monthly sessions; 8 mL sterile water plus 1 mL lidocaine per vial) or no treatment (n = 52) [5,24]. On blinded live evaluation, the proportion achieving at least a 1-grade improvement on the Galderma Cheek Wrinkle Scale on both cheeks was 66.2% versus 38.6% at month 7 (p = 0.0043), 70.6% versus 31.1% at month 9 (p < 0.0001), and 71.6% versus 26.1% at month 12 (p < 0.0001) [24]. Treatment-related adverse events were mostly mild, and none was serious [24]. The use of an untreated rather than a sham control should be considered when interpreting these results, and a subsequent systematic review rated this trial at high risk of bias for deviations from the intended intervention [5].

That systematic review included 11 RCTs of facial PLLA (searched to February 2024) and found increased dermal thickness and improvements in lipoatrophy severity and aesthetic scores, with effects lasting at least 25 months in four trials and superiority over injectable human collagen in two [5]. Quantitative pooling was not feasible; using the Cochrane Risk-of-Bias 2 tool, no trial was judged at low risk of bias, six raised some concerns, and five were at high risk, and the authors rated the overall evidence as low quality [5].

Evidence for body indications is more limited. In a double-blind, split-body RCT, 15 women received 3 monthly treatments with 150 mg of PLLA to one lateral gluteal depression (hip dell) and bacteriostatic saline to the other [25]. At 9 months, ultrasound showed increases from baseline of 26.1% in dermal thickness and 27% in adipose-layer thickness on the PLLA side, with no change on the saline side, and histology showed

improved collagen and elastic-fiber quality relative to saline [25]; the small, single-center sample limits the precision of these estimates.

An open-label RCT in 30 women with moderate or severe décolletage wrinkles compared reconstitution in 8 mL versus 17 mL of sterile water (each plus 1 mL lidocaine) over up to 4 monthly sessions; at month 9, 93.8% and 78.6% of participants, respectively, achieved at least a 1-grade improvement on the Galderma Décolletage Scale on investigator assessment, with one treatment-related adverse event and no serious events [26]. Because assessment was unblinded, this trial supports the feasibility and tolerability of both volumes rather than the superiority of either. Use in the face and neck has been reviewed elsewhere [15], and a prospective observational study and a recent narrative appraisal report improved texture, firmness, and contour with high patient satisfaction [27,28]; these uncontrolled data should be regarded as hypothesis-generating. Overall, randomized evidence for skin quality outcomes rests on a few small-to-moderate trials with heterogeneous endpoints, and statistically significant changes in instrumental measures do not necessarily translate into clinically meaningful improvement for patients.

Safety profile, complications, and their management

The adverse-event profile of PLLA is best understood in two temporal categories. Early events are largely injection-related and self-limiting: transient erythema, edema, bruising, and tenderness. Late events are the biologically important ones and comprise subcutaneous papules and non-inflammatory nodules, delayed inflammatory nodules and granulomas, and, rarely, vascular compromise or infection and biofilm formation [13,20]. Reported nodule rates vary widely with formulation, dilution, technique, and length of follow-up; among RCTs included in a systematic review, they ranged from isolated cases to 41% in an early trial in HIV-associated lipoatrophy [5], and expert consensus indicates that rates fall with higher reconstitution volumes and correct technique [13].

The mechanisms of the two principal late lesions differ and dictate different management. Non-inflammatory nodules arise chiefly from technique (inadequate dilution, superficial or intramuscular placement, bolus delivery, and product accumulation in mobile areas), producing a localized aggregation of particles and collagen. Inflammatory granulomas, in contrast, reflect an exaggerated, often delayed, immune response and may be precipitated by systemic immune triggers [7,20]. This distinction is why consensus guidance repeatedly identifies prevention as the most important safeguard: appropriate dilution, correct reconstitution, adequate injection depth, and non-bolus delivery are the strongest modifiable protective factors, and massage alone cannot substitute for them [19].

When lesions do occur, management follows a stepwise pathway derived mainly from expert consensus, guidelines, and case series rather than comparative trials, including a recent guideline developed for PDLLA nodules [19,20]. Small, non-visible, non-inflammatory nodules may simply be observed with reassurance and massage. Palpable non-inflammatory nodules respond to intralesional normal saline, with or without lidocaine, which disperses the aggregate; reported series describe substantial improvement (on the order of 80%) after 2 to 3 sessions [13,19]. Inflammatory nodules and granulomas are treated with intralesional corticosteroid (triamcinolone), often combined with 5-fluorouracil to limit fibrosis, with antibiotics added when biofilm or infection is suspected and surgical excision reserved for refractory lesions [20]. High-frequency ultrasound and, where needed, cross-sectional imaging assist in characterizing and localizing deep or persistent lesions [19]. Vascular occlusion, though rare with a biostimulator, is a medical emergency requiring immediate recognition and standard filler-emergency protocols. The classification, prevention, and management of adverse events are summarized in Table *3*.

Event	Principal mechanism	Prevention	Management
Early erythema/edema/bruising	Needle/cannula trauma	Cannula in mobile zones; gentle technique	Reassurance; cold compress; self-limiting
Papules/non-inflammatory nodules	Technique: low dilution, superficial or intramuscular/bolus placement, accumulation	High dilution; subdermal plane; small aliquots; no bolus; avoid dynamic sites	Observation + massage; intralesional saline ± lidocaine (~80% improvement over 2-3 sessions)
Inflammatory nodules/granulomas	Exaggerated/delayed immune response ± systemic trigger	Screening; avoid overcorrection; caution in granulomatous/autoimmune history	Intralesional triamcinolone ± 5-fluorouracil; antibiotics if biofilm; excision if refractory
Vascular occlusion (rare)	Intravascular/compressive compromise	Anatomical knowledge; aspiration/cannula; ultrasound guidance	Emergency filler protocol; urgent referral

TABLE 3: Classification, prevention, and evidence-mapped management of poly-L-lactic acid adverse events

Synthesized from consensus statements, a guideline on nodule management, and complication reviews [7,13,19,20]. Management should be individualized and consistent with local regulatory guidance.

Methodological limitations and future directions

This review has its own limitations: as a narrative review, it is susceptible to selection bias; it was restricted to English-language peer-reviewed publications, and risk of bias in individual studies was appraised narratively rather than with a formal tool. Despite an expanding and increasingly favorable evidence base, the PLLA literature carries important methodological limitations that temper the strength of its conclusions. Protocols for reconstitution volume, hydration time, injection plane, dosing, and session spacing vary widely between studies and practices, which complicates cross-study comparison and pooled analysis. Outcome measurement is similarly heterogeneous: studies mix validated wrinkle and global-improvement scales, instrumental measures of elasticity and hydration, histology, and patient satisfaction, often without a common core outcome set, so that apparently concordant "improvement" is not always measuring the same construct. Much of the body and off-face evidence still rests on case series, single-arm studies, and expert consensus rather than adequately powered RCTs, and comparative effectiveness data against other biostimulators remain limited [3,27].

These are, at their core, methodological problems, and they define the research agenda of the field. Priorities include standardization of reconstitution and injection protocols; development and adoption of a validated core outcome set for skin quality that integrates instrumental, histological, and patient-reported measures; adequately powered randomized and comparative trials, particularly for body indications and the growing GLP-1 RA population; and prospective registries to capture the true incidence and determinants of delayed nodules. Consistent, transparent reporting of technique and outcomes would do more than any single new agent to consolidate the evidence base for PLLA.

Conclusions

Poly-L-lactic acid has evolved from a corrective filler for lipoatrophy into a regenerative biostimulator with a well-characterized collagen-stimulating mechanism and an expanding range of facial and body indications. Randomized trials, although few and heterogeneous, suggest improvements in wrinkle severity, skin elasticity, hydration, and dermal thickness compared with no treatment or saline, while observational and consensus-based evidence indicates that careful technique, including adequate dilution, subdermal non-bolus placement, appropriate patient selection, and structured follow-up, is associated with fewer papules and nodules. Technique alone cannot guarantee reproducible outcomes, however, because patient factors, product formulation, and study design also influence results, and existing trials differ substantially in protocols, comparators, and endpoints. Adequately powered comparative trials against other biostimulators and fillers, standardized reconstitution and injection protocols, and a validated core outcome set for skin quality are needed to define the true magnitude, durability, and safety of benefit.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the

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