

Histological Evaluation of Dual-depth Poly-L-Lactic Acid and Hyaluronic Acid Injections

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Summary: This single-case histological study evaluated the safety and tissue effects of dual-depth injections of poly-L-lactic acid (PLLA) and hyaluronic acid (HA)-based skin booster administered into the same anatomical region. A 77-year-old woman received PLLA in the subcutaneous fat layer and HA in the deep dermis/subdermal layer of the right jowl. The untreated left side served as a control. Histological analysis revealed that PLLA induced a localized foreign-body reaction with increased fibroblast activity, dense collagen, and elastic fiber formation in the subcutaneous layer, indicative of extracellular matrix remodeling. HA-treated dermal layers showed mild matrix compaction and low-grade inflammation, consistent with the hydration effects. There was no histological evidence of filler overlap or adverse interaction. Three-dimensional imaging further supported volumetric enhancement and tissue elevation on the treated side. The results demonstrate that when spatially separated by depth, PLLA and HA can exert independent, synergistic effects without compromising safety. This dual-layer approach may offer a novel strategy for targeted skin rejuvenation in clinical practice. In this single-patient case, layer-separated PLLA and HA elicited independent, compartment-specific tissue responses without observed interaction. Findings are descriptive and anecdotal and should not be generalized without larger, controlled studies incorporating quantitative volumetry and histomorphometry. (*Plast Reconstr Surg Glob Open* 2026;14:e7402; doi: 10.1097/GOX.0000000000007402; Published online 28 January 2026.)

Improving skin quality—specifically hydration, texture, elasticity, and volume loss—is a key goal in aesthetic dermatology. Among injectable fillers, poly-L-lactic acid (PLLA) and hyaluronic acid (HA)-based skin boosters are frequently

used. PLLA stimulates collagen production in deeper facial compartments, such as the malar area and prejowl sulcus.^{1,2} This effect is mediated by the host tissue response and direct stimulation of collagen production in fibroblasts.³⁻⁵ HA-based skin boosters enhance hydration and skin texture through water-binding and extracellular matrix stimulation.^{3,4}

Although each filler is effective independently, clinical guidelines recommend against injecting PLLA and HA into the same anatomical region due to the risk of excessive foreign-body reaction. Typically, they are applied in separate sessions or planes.⁶ However, as soft tissue continuity may still allow for overlap, this study explored whether both products can be safely administered into the same anatomical site when clearly separated by depth: PLLA into the subcutaneous layer and HA into the deep dermis/subdermal layer. This study aimed to confirm histologically that this dual-depth technique maintains layer-specific responses without adverse outcomes and to assess whether combining PLLA's volumizing effect with HA's hydrating properties produces synergistic rejuvenation.

METHODS

This report describes a single patient treated in routine clinical practice and analyzed retrospectively. The patient provided written informed consent for treatment, bilateral

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Disclosure statements are at the end of this article, following the correspondence information.

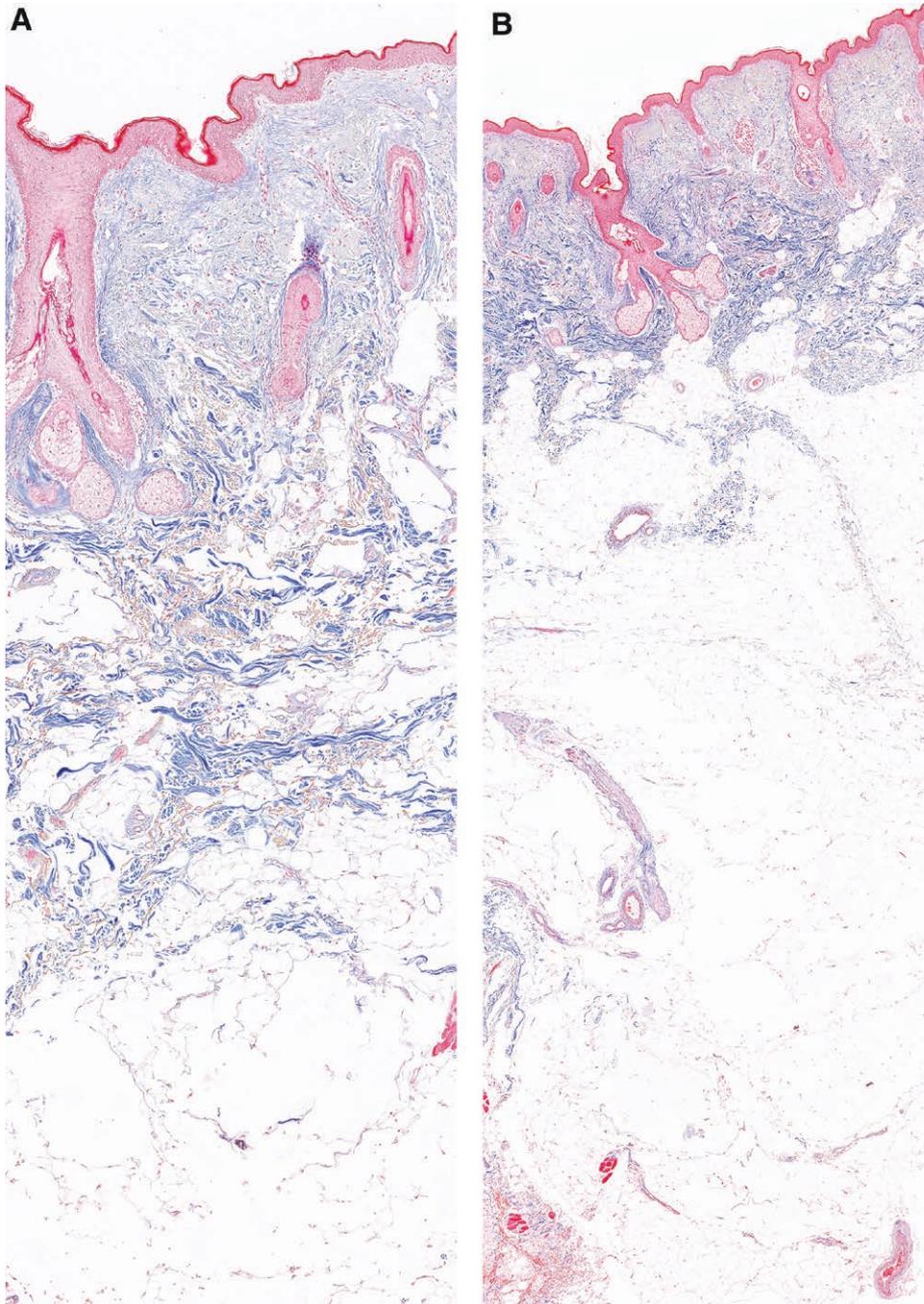


Fig. 1. Jowl histology. A, A treated sample with PLLA in the subcutaneous layer and HA in the deep dermis. B, An untreated control. Masson trichrome staining was used to visualize collagen and tissue structure at 40 \times magnification.

tissue excision performed as part of indicated clinical care, histological examination of surgical discard tissue, clinical photography, and the publication of de-identified images and data, consistent with the Declaration of Helsinki.

This single-patient in vivo study adhered to ethical guidelines, with informed consent obtained. A 77-year-old woman with prior cosmetic procedures received dual-layer injections in the right jowl: PLLA (Sculptra) into the subcutaneous fat and HA (Restylane Vital Light) into the deep dermis/

subdermal layer. Injections were performed 8 and 4 weeks before excision. PLLA was reconstituted with 8 mL of sterile water (in 2 stages) and 1 mL of 2% lidocaine, yielding a total of 9 mL, delivered via a 23G, 50-mm cannula. HA was injected afterward using a 33G, 4-mm nanoneedle, avoiding overlap. Full-thickness excisions were performed bilaterally, with the untreated left side serving as the control. Tissues underwent hematoxylin and eosin staining and were assessed by blinded dermatopathologists. Three-dimensional facial imaging was

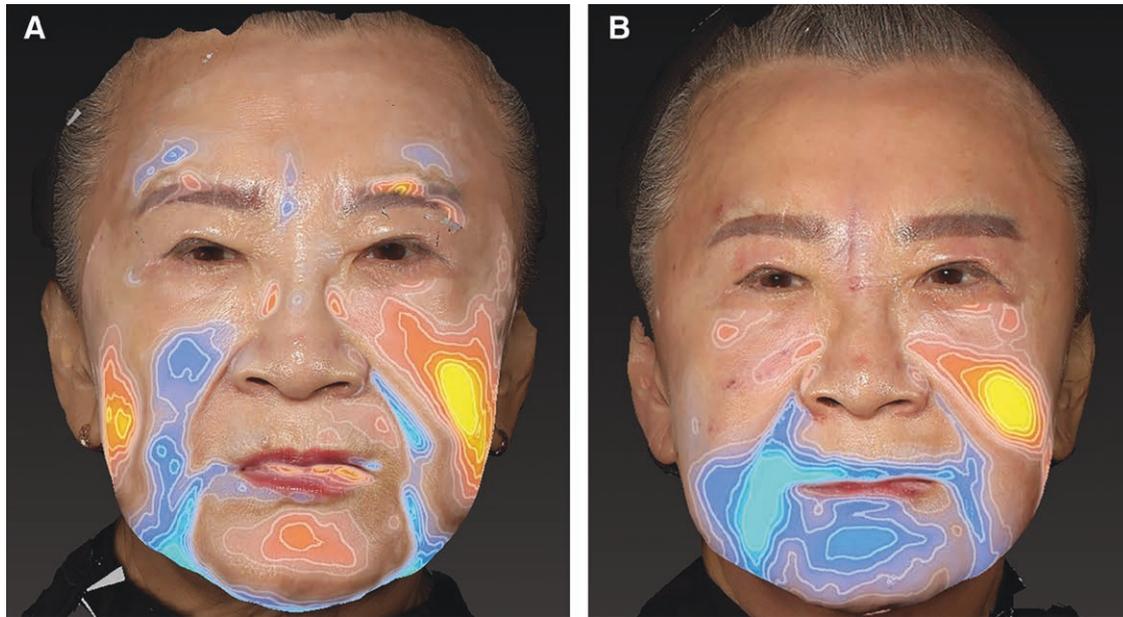


Fig. 2. Pre- and posttreatment 3-dimensional topographic analysis. A, Pretreatment analysis reveals symmetrical topography and vector displacement in the prejowl areas. B, Posttreatment, the right marionette area shows a warmer, denser vector pattern, indicating localized volume increase following dual filler injection.

used pre- and posttreatment to evaluate volume changes, with longer arrows and warmer colors indicating greater displacement. Slides were reviewed qualitatively by 2 blinded dermatopathologists.

RESULTS

Histology of the treated right side revealed layer-specific responses. Subcutaneous PLLA was surrounded by giant cells, showing foreign-body reaction, increased collagen, and fibrosis, indicating active remodeling. In the HA-treated dermal/subdermal layer, no filler remained, but mild fibroblast proliferation and matrix compaction were noted, consistent with hydration-induced changes. No overlap or adverse interaction was observed between the 2 planes. The untreated left side showed mild fibrosis and residual foreign material, likely from prior treatments. Three-dimensional imaging confirmed greater volume in the right prejowl and marionette regions posttreatment, with warmer color mapping and outward vector displacement indicating localized enhancement (Figs. 1–2). The subcutaneous PLLA plane exhibited an expected host granulomatous foreign-body response with multinucleated giant cells and extracellular matrix remodeling, as reported for PLLA microspheres, and was not indicative of an adverse reaction. Because both sides had remote prior filler, the contralateral side does not constitute a true control; comparisons are interpreted descriptively.

DISCUSSION

This study demonstrated that PLLA and HA, when injected into separate tissue layers, induce independent histological responses with no overlap. In this study, collagen fibers in the PLLA-treated region appeared denser and more widely distributed than in the untreated side,

indicating broader and more organized tissue remodeling. These findings align with previous *in vivo* and *in vitro* findings that attribute collagen synthesis to fibroblast and macrophage activation.^{3,7,8}

The HA-injected dermal regions exhibited mild extracellular matrix changes and minimal inflammation, reflecting HA's hydrating effects and consistent with prior literature.³ There was no histological evidence of interaction between the 2 fillers, supporting the effectiveness of dual-depth delivery in preserving the independent actions of each agent.

Notably, this technique allowed PLLA to provide deep structural support through collagen induction, whereas HA improved surface hydration and elasticity. This layered rejuvenation approach may offer synergistic benefits within a single treatment zone.

Prior remote fillers on both sides limit contralateral comparisons; the untreated side cannot be considered a true control. Three-dimensional vector maps were qualitative; no objective volumetric quantification (mm^3) was performed and should be incorporated in future studies. This report was based on a single patient and was descriptive; no quantitative histomorphometry was performed. These observations were hypothesis-generating; conclusions regarding safety and effectiveness require prospective studies with appropriate controls and quantitative outcomes.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

PATIENT CONSENT

The patient provided written consent for the use of her image.

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