

RESEARCH ARTICLE OPEN ACCESS

Targeted Precision Cryotherapy With a Poly-D,L-Lactic Acid–Hyaluronic Acid Hybrid Filler for Facial Skin Quality Enhancement: A Controlled Study

Suk Bae Seo¹  | Gun-Ho Kim²  | Joon Hong Park³  | Kui Young Park⁴ 

¹Department of Dermatology, Seo Ah Song Dermatologic Clinic, Songpa, Seoul, South Korea | ²Department of Biomedical Engineering, Ulsan National Institute of Science and Technology, Ulsan, South Korea | ³Department of Dermatology, May Morning Dermatology Clinic, Jung, Seoul, South Korea | ⁴Department of Dermatology, Chung-ang University College of Medicine, Dongjak, Seoul, South Korea

Correspondence: Kui Young Park (kyky@cauhs.or.kr)

Received: 24 January 2026 | **Revised:** 18 March 2026 | **Accepted:** 7 April 2026

Academic Editor: Suraiya Saleem

Keywords: facial skin rejuvenation | melanin reduction and pore improvement | poly-D,L-lactic acid (PDLA) | targeted precision cryotherapy | transdermal delivery

ABSTRACT

Background: Targeted precision cryotherapy has emerged as a novel approach in aesthetic dermatology, offering enhanced precision and safety during procedures. This study evaluated the efficacy and safety of a poly-D,L-lactic acid–hyaluronic acid (PDLA–HA) hybrid filler administered using a TargetCool device to improve facial skin quality.

Materials and Methods: A prospective controlled study was conducted in 20 Korean women with melasma, hyperpigmentation, or dark spots. One hemiface was treated with PDLA–HA using a precision cryotherapy device, while the contralateral side received the same formulation via a microneedle roller. Skin parameters, including melanin content, dermal density, pore volume, pore density, pore count, and redness, were assessed at baseline, during treatment, and 1 month after the final session. Visual grading, patient-reported outcomes, and safety evaluations were also performed.

Results: Cryotherapy-assisted delivery demonstrated significantly greater improvements than microneedling in melanin reduction (31.28% vs. 23.40%), dermal density (30.07% vs. 17.37%), and pore-related parameters, including volume (53.43% vs. 33.61%) and density (57.80% vs. 21.62%). Redness was significantly reduced on the cryotherapy-treated side. Participant satisfaction was high, with consistent improvements in skin texture and overall appearance. No adverse events were observed.

Conclusion: Precision cryotherapy-assisted delivery of PDLA + HA provides superior efficacy and favorable safety compared with conventional application methods. This approach may enhance transdermal delivery while minimizing tissue trauma, representing a promising strategy for advanced aesthetic dermatologic treatments.

1 | Introduction

The desire for improved facial aesthetics has driven the development of advanced technologies and materials to address pigmentation, skin texture, and age-related changes. Poly-D,L-lactic acid (PDLA) is a biocompatible, biodegradable biostimulatory polymer that induces neocollagenesis and dermal

remodeling, while noncrosslinked hyaluronic acid (HA) provides immediate hydration and viscoelastic support. PDLA–HA hybrid formulations have therefore been used as “skin boosters” to improve overall skin quality (e.g., pigmentation, pores, fine lines, and dermal density) through a combination of early HA effects and gradual PDLA-driven biostimulation [1, 2]. Notably, PDLA (a racemic D/L polymer) is distinct from poly-L-lactic

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Copyright © 2026 Suk Bae Seo et al. *Dermatologic Therapy* published by John Wiley & Sons Ltd.

acid (PLLA); thus, evidence derived from PLLA-only products should not be directly extrapolated to PDLLA-based formulations.

Cryotherapy, particularly targeted precision cryotherapy, has emerged as a promising modality for aesthetic and medical dermatology. Devices such as the TargetCool system enable the controlled delivery of cryogenic cooling, providing benefits such as reduced inflammation, precise targeting, and minimized discomfort during procedures [3]. In recent years, cryotherapy has been increasingly applied to inflammatory and sebaceous gland-related skin disorders. Clinical and experimental studies have demonstrated its therapeutic potential in conditions such as hidradenitis suppurativa and acne by inducing selective cryolysis of sebaceous glands and modulating inflammatory pathways [4, 5]. Studies have demonstrated that cryotherapy-based treatments can effectively reduce pigmentation in benign pigmented lesions and hyperpigmented skin by modulating melanogenesis and enhancing skin rejuvenation [6, 7].

The combination of PDLLA-HA nano-complex with targeted precision cryotherapy represents a promising combination strategy, in which localized cooling enhances patient comfort and may enhance intradermal delivery and biological activity of PDLLA-HA. Although previous studies have established the effectiveness of PDLLA-HA in addressing pigmentation and dermal quality [1, 2], limited data are available regarding its delivery using targeted cryotherapy.

This study aimed to evaluate the efficacy and safety of the PDLLA-HA nano-complex administered using the TargetCool device for improving facial skin quality. The primary endpoints included improvements in melanin content, dermal density, pore characteristics, and redness as well as subjective satisfaction and safety outcomes.

2 | Materials and Methods

This study was conducted in accordance with the Declaration of Helsinki. The study protocol, informed consent forms, and all relevant study documents were reviewed and approved by the Institutional Review Board of the Human Clinical Research Center (IRB No. HM-IRB-P24-0362). Written informed consent for participation and publication of identifiable images and clinical information was obtained from all participants prior to study enrolment.

We recruited 20 healthy adult women seeking cosmetic improvements in facial melasma, hyperpigmentation, dark spots, or dark skin tones. The exclusion criteria were pregnancy, breast-feeding, or planning to conceive during the study. Patients with psychiatric disorders, infectious skin diseases, or skin hypersensitivity were excluded from the study. Participants currently using topical steroids for more than 1 month to treat dermatological conditions or who had skin abnormalities at the test site, such as moles, acne, erythema, or telangiectasia, were excluded. Individuals who had used cosmetics or pharmaceuticals with similar claims on the test site within the past 3 months or had undergone dermatological treatments or cosmetic procedures, such as liposuction, laser therapy, ultrasound fat reduction, or other skincare treatments, on the test site within the past 6 months were also excluded. Employees of the sponsoring

company and those deemed unsuitable by the principal investigator for any other reason were excluded.

2.1 | Treatment Protocols

In this study, each participant's face was divided longitudinally into two hemifaces. One side was assigned to the experimental group, in which 1 mL of a PDLLA-HA formulation containing PDLLA 42.5 mg and HA 7.5 mg (Juvelook Shine, VAIM Global, Korea) was administered using the boosting mode of the TargetCool device for 1 min. Juvelook Shine represents a PDLLA-HA-based skin biostimulator protocol aimed at improving skin tone, elasticity, and texture rather than structural volumization. The Boosting mode of the TargetCool device converts the liquid PDLLA-HA liquid formulation into micro-sized ice particles and delivers the agent into the superficial dermis (approximately 0.3 mm in depth) via a high-velocity supersonic CO₂ jet, thereby facilitating transdermal penetration and uniform diffusion into the surrounding tissue [8]. The velocity of the cryogenic jet produced by TargetCool ranged from Mach 1 to 5, varying with the CO₂ phase (i.e., gas or dry ice). The jet temperature was regulated to maintain the target surface at approximately 5°C. The contralateral hemiface served as the control side, where an equal volume (1 mL) of the same PDLLA-HA formulation was administered using a manual microneedle roller (needle length: 0.5 mm). To ensure procedural standardization, microneedling was performed by a single trained operator using consistent application pressure and multiple passes in horizontal, vertical, and diagonal directions until uniform coverage of the treatment area was achieved. For both sides, the PDLLA-HA formulation was reconstituted in 10 mL of normal saline and vortexed for 2 h prior to administration and prepared under controlled conditions using a standardized protocol to ensure consistency in formulation and administration across all treatment sessions. Five treatment sessions were performed at 2-week intervals (Weeks 0, 2, 4, 6, and 8), with a final follow-up evaluation conducted at Week 12 (1 month after the fifth session). A biweekly (every 2-week) interval was selected to allow resolution of procedure-related erythema/edema and to align with prior PDLLA microjet skin-quality protocols that were administered twice monthly for a total of five sessions [9]. Five sessions were chosen to maximize cumulative remodeling effects within a pragmatic clinic-based protocol and to remain consistent with the broader literature on PDLLA-based skin quality/acne-scar treatments that use repeated treatments over several months [9, 10].

2.2 | Assessment

All follow-up measurements (after the first session; before the second, third, fourth, and fifth sessions; and 1 month after the fifth session) were statistically compared with baseline values. The DUB SkinScanner (tpm taberna pro medicum GmbH, Germany) was used to measure and compare skin density in the cheek region. Additionally, the Antera 3D (Miravex Ltd., Ireland) system was employed to analyze the following parameters in the same area: total pore volume (mm³), mean pore area (mm²), pore density (pores/cm²), pore count, maximum pore depth (mm), and average redness (redness index). Facial images were captured using the DermaVision (Opto Biomed Co. Ltd., Republic of Korea). The cross-polarization imaging mode was used to obtain

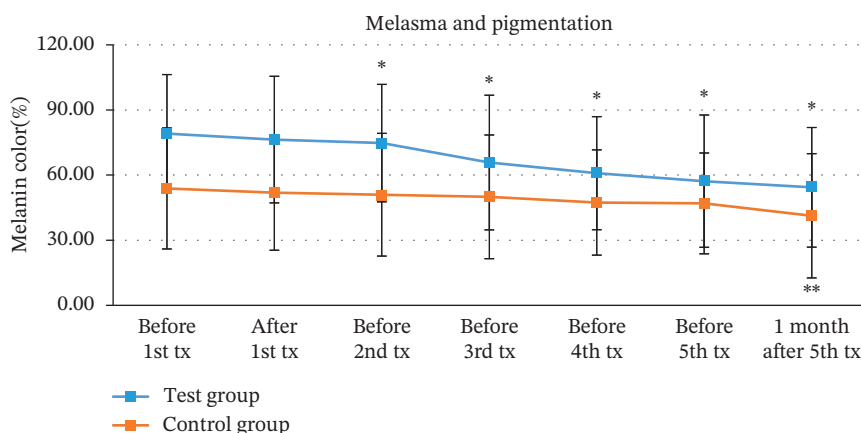


FIGURE 1 | Changes in melanin index over time. Melanin index (%) was measured at baseline, before each treatment session (Weeks 2, 4, 6, and 8), and 1 month after the fifth session (Week 12) in the experimental and control hemifaces. * $p < 0.0083$, ** $p < 0.05$ vs. baseline.

frontal facial images, and specialized software was employed to analyze the melanin content (%) in the cheek region.

For visual assessment of efficacy, the whitening grades of both cheeks were assessed and compared at baseline using a 10-point visual grading scale ranging from 0 (very bright and clear) to 9 (very dark and dull). The pore grades for both cheeks were assessed based on a previously described grading system [11]. The redness grades for both cheeks were observed and scored using the Clinician Erythema Assessment (CEA) scale [12].

The participants subjectively evaluated the survey items provided by the client. The evaluation was conducted using a six-point scale (1 = strongly disagree, 2 = disagree, 3 = somewhat disagree, 4 = somewhat agree, 5 = agree, and 6 = strongly agree), with responses in the 4–6 range considered positive. During the test period, the physician monitored the patient for adverse skin reactions and use of concomitant medications that could affect the test results.

2.3 | Statistical Analysis

Statistical analyses were performed using SPSS Statistics 26 (IBM Corp., Armonk, NY, USA). Continuous outcomes are presented as mean $\pm$ SD. Normality was assessed using the Shapiro–Wilk test. For repeated-measures outcomes, a linear mixed-effects model (LMM; random intercept for participant; fixed effects for treatment side, visit, and their interaction) was used as the primary analytic approach to account for within-subject correlation and to allow unbiased estimation under missing-at-random assumptions. When model assumptions were not met, nonparametric repeated-measures tests (Friedman) were used as sensitivity analyses. Post hoc pairwise comparisons were adjusted for multiple testing using the Bonferroni method. All within-group comparisons were made versus baseline, and between-group comparisons were made between hemifaces at the same visit. A two-sided p value < 0.05 was considered statistically significant. Because minimal clinically important difference (MCID) thresholds were not prospectively defined, clinical interpretability was contextualized using distribution-based effect size interpretation supported by literature on instrumental endpoint validity.

3 | Results

All 20 enrolled Korean women with an average age of 50.25 years (± 8.49) successfully completed the entire study protocol and attended all follow-up visits. The distribution of skin types among the participants was as follows: 15 had dry skin, four had normal skin, and one had combination skin. All within-group comparisons were performed versus baseline, and between-group comparisons were conducted between hemifaces at identical time points. Detailed repeated-measures mean $\pm$ SD values for all instrumental parameters are provided in Supporting Table S1.

3.1 | Assessment of Melanin Content Using Imaging System

In the experimental group, melanin color (%) significantly decreased before the third ($p = 0.027$), fourth ($p = 0.038$), and fifth sessions ($p = 0.030$), and 1 month after the fifth session ($p = 0.017$). The improvement rates were 16.86% before the third session, 27.68% before the fifth session, and 31.28% 1 month after the fifth session. In the control group, a significant reduction in melanin color (%) was observed only 1 month after the fifth session ($p < 0.001$), with an improvement rate of 23.40%. Between-group comparisons revealed no significant differences after the first session or before the second session. However, significant differences were observed before the third ($p = 0.027$), fourth ($p = 0.038$), and fifth sessions ($p = 0.030$), and 1 month after the fifth session ($p = 0.017$), favoring the experimental group (Figure 1).

3.2 | Assessment of Dermal Density Using Imaging System

In the experimental group, skin density revealed no significant change after the first treatment ($p = 0.062$), but significantly increased before the second ($p < 0.001$), third ($p < 0.001$), fourth ($p < 0.001$), and fifth treatments ($p < 0.001$), and 1 month after the fifth treatment ($p < 0.001$). The improvement rates in skin density relative to baseline were 13.42% before the second treatment, 18.53% before the fourth treatment, and 30.07% 1 month after the fifth treatment. In the control group, the skin density significantly improved after the first treatment ($p = 0.006$) and at all subsequent time points ($p < 0.001$). However, the improvement rates were consistently lower than

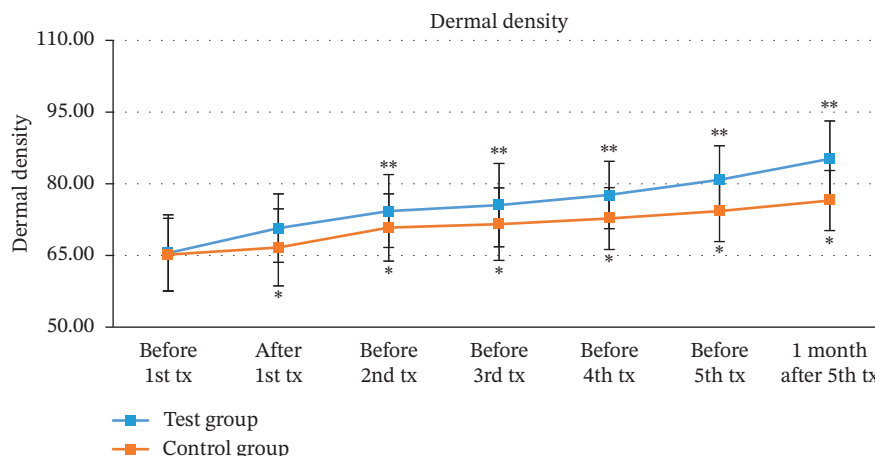


FIGURE 2 | Changes in dermal density over time. Dermal density was assessed at baseline, before each treatment session (Weeks 2, 4, 6, and 8), and 1 month after the fifth session (Week 12) in the experimental and control hemifaces. * $p < 0.0083$, ** $p < 0.05$ vs. baseline.

those in the experimental group, reaching only 17.37% 1 month after the fifth treatment. Between-group comparisons revealed statistically significant differences in skin density at all time points ($p < 0.001$), with the experimental group showing more improvements, particularly at the later stages (Figure 2).

3.3 | Assessment of Pore Changes (Volume and Density) Using Imaging System

In the experimental group, both the total pore volume (mm^3) and pore density (ea/cm^2) significantly decreased at all time points, including after the first session ($p < 0.001$ for volume, $p = 0.001$ for density), before the second, third, fourth, and fifth sessions, and 1 month after the fifth session ($p < 0.05$, for all). The improvement rates in pore volume were 42.07% before the fifth session and 53.43% 1 month after the fifth session, whereas the improvement rates in pore density peaked at 57.80% 1 month after the fifth session. In the control group, reductions in pore volume were significant at all time points ($p < 0.001$), with a maximum improvement of 33.61% 1 month after the fifth session. However, reductions in pore density were significant only from the third session onward ($p < 0.05$), with an improvement rate of 21.62% 1 month after the fifth session. Between-group comparisons revealed no significant differences in the pore volume or density before the second or third session. However, significant differences were observed after the first session ($p < 0.001$, for both), before the fourth and fifth sessions ($p < 0.05$), and 1 month after the fifth session ($p < 0.05$), consistently favoring the experimental group (Figures 3(a), 3(b)).

3.4 | Assessment of Redness Using Imaging System

In the experimental group, the average redness significantly decreased after the first session ($p = 0.028$), before the second ($p = 0.002$), third ($p = 0.030$), fourth ($p = 0.002$), and fifth sessions ($p = 0.002$), and 1 month after the fifth session ($p = 0.002$). The improvement rates were 6.02%, 7.32%, and 10.85% after the first, before the third, and before the fifth sessions, respectively. In the control group, no significant reduction in average redness was observed, except before the fourth session ($p = 0.049$), with minimal improvement rates of 6.34%. Between-group comparisons revealed significant differences in the average redness after

the first session ($p = 0.003$) and at all subsequent time points ($p < 0.05$), favoring the experimental group (Figure 4).

In addition to mean changes, an individual-level responder analysis was performed using prespecified MCID thresholds (melanin reduction $\geq 15\%$ and total pore volume reduction $\geq 30\%$ from baseline). The proportion of participants achieving MCID at each endpoint and visit is summarized in Supporting Table S2.

3.5 | Visual Assessment (Whitening, Pores, and Redness Grades)

Representative clinical photographs demonstrating overall skin quality improvement are presented in Figure 5.

3.5.1 | Whitening Grade

The experimental group demonstrated significant improvements in whitening grade from the second session onward ($p < 0.001$ at all time points), with an improvement rate of 39.58% 1 month after the fifth session. The control group also showed a significant improvement ($p < 0.001$) but with a lower peak improvement rate of 22.92%. Between-group comparisons revealed significant differences from the third session onward ($p < 0.05$), favoring the experimental group (Figure 6).

3.5.2 | Pore Grade

No significant changes in pore grade were observed in the experimental or control groups at any time point ($p > 0.05$). However, significant differences were observed between the groups before the second and third sessions ($p < 0.05$), with the experimental group demonstrating superior outcomes.

3.5.3 | Redness Grade

No significant changes in redness grade were observed within the groups across all time points ($p > 0.05$). Similarly, no significant differences were observed between groups throughout the study ($p > 0.05$). Figure 5 presents representative images of a study participant demonstrating skin quality enhancements before and after treatment. The treated areas exhibit visible improvements,

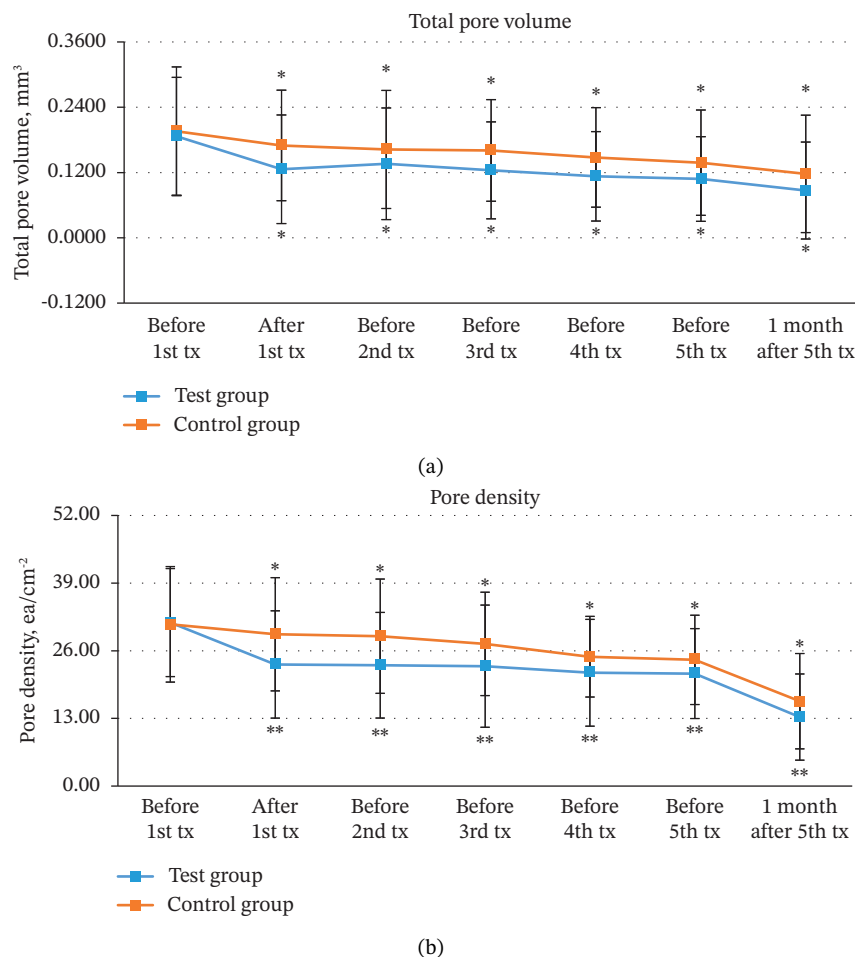


FIGURE 3 | Changes in pore volume and pore density over time. Total pore volume (mm³) and pore density (ea/cm²) were measured using an imaging analysis system at baseline, before each treatment session (Weeks 2, 4, 6, and 8), and 1 month after the fifth session (Week 12) in the experimental and control hemifaces. * $p < 0.0083$, ** $p < 0.05$ vs. baseline. (a) Total pore volume and (b) pore density.

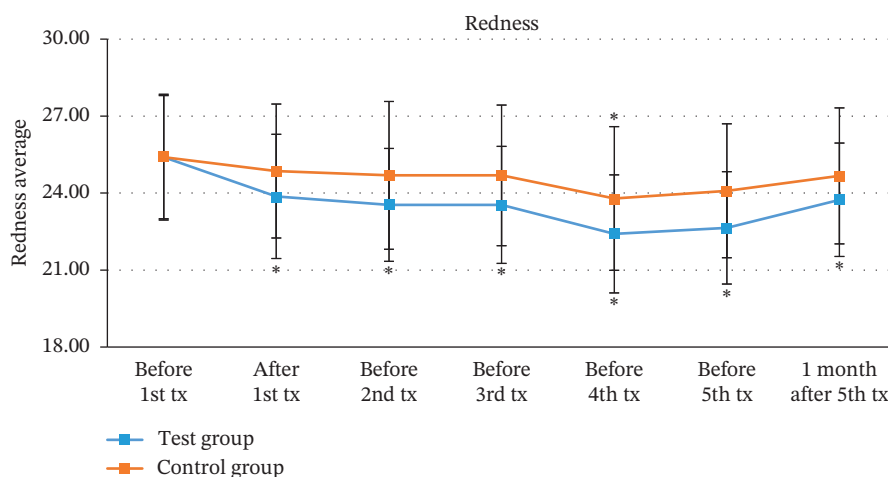


FIGURE 4 | Changes in skin redness over time. Average redness was assessed using an imaging analysis system at baseline, before each treatment session (Weeks 2, 4, 6, and 8), and 1 month after the fifth session (Week 12) in the experimental and control hemifaces. * $p < 0.0083$, ** $p < 0.05$ vs. baseline.

TABLE 1 | Participants' survey results on the effects of the test product.

Survey items	Positive responses (%)
1. Melasma and pigmentation on the left facial area seem to have improved.	100.00
2. The skin texture of the left facial area seem to have improved.	95.00
3. The pores (volume, area, density, number, depth) on the left facial area seem to have improved.	100.00
4. Redness of the left facial area seem to have improved.	90.00
5. There was no pain or discomfort during the procedure on the left facial area.	90.00
6. There was no pain or discomfort after the procedure on the left facial area.	90.00
7. The skin elasticity of the left facial area seems to have improved.	100.00
8. Overall, I am highly satisfied with the left facial area.	95.00
9. Melasma and pigmentation on the right facial area seems to have improved.	95.00
10. Skin texture of the right facial area seems to have improved.	100.00
11. Pores (volume, area, density, number, depth) of the right facial area seem to have improved.	100.00
12. Redness of the right facial area seems to have improved.	95.00
13. There was no pain or discomfort during the procedure on the right facial area.	90.00
14. There was no pain or discomfort after the procedure on the right facial area.	95.00
15. The skin elasticity of the right facial area seems to have improved.	100.00
16. Overall, I am highly satisfied with the right facial area.	95.00
17. I am willing to recommend cryotherapy treatment to others.	95.00

Note: Positive response were defined as scores of 4 (somewhat agree), 5 (agree), or 6 (strongly agree).

Significant improvements in dermal density were observed in this study, consistent with the biostimulatory effects reported for PDLLA-based skin boosters and the supportive viscoelastic properties of noncrosslinked HA [1, 2]. The integration of TargetCool, a transdermal delivery platform, may further enhance these effects by converting the formulation into micro-IceNeedles that facilitate penetration and dispersion at controlled superficial dermal depths. This localized cooling may also reduce procedure-related inflammation, creating a favorable microenvironment for collagen remodeling [3–5]. Collectively, these mechanisms may explain the greater improvements in dermal density and overall skin texture compared with the microneedle roller control.

Recent advances in transdermal delivery systems have highlighted the role of physical enhancement techniques in improving penetration efficiency of bioactive compounds [13]. Emerging strategies, including cryogenic-assisted delivery and hybrid biomaterial platforms, have demonstrated the potential to facilitate controlled penetration and sustained release within the dermis. Recent studies have also emphasized the advantages of hybrid biomaterials, particularly HA-based microneedle systems, in promoting skin regeneration through combined structural and biochemical signaling effects [14]. These findings support the plausibility of synergistic interactions between cryotherapy-based delivery and PDLLA–HA biostimulatory mechanisms.

Prior experimental investigations of cryogenic particle delivery systems have demonstrated that rapid cryogenic propulsion can generate micro-ice crystallized structures capable of penetrating the stratum corneum and reaching the superficial dermis. Ex vivo human skin studies using fluorescence-labelled compounds and

histologic staining have confirmed enhanced penetration depth and dermal distribution without structural tissue disruption, supporting the proposed transdermal delivery mechanism of cryo-jet platforms [15].

Although direct histologic confirmation of micro-IceNeedle deposition was not performed in this clinical study, prior transdermal cryo-jet delivery investigations suggest that rapid cryogenic propulsion can facilitate superficial dermal penetration. Future mechanistic studies incorporating histologic or imaging analyses will be valuable to quantify penetration depth and tissue distribution. Such characterization would allow comparison with conventional solid microneedle systems, which have reported dermal penetration depths in the range of approximately 572–650 μm [14].

A potential mechanistic explanation is a sequential, bi-phasic effect of the hybrid formulation: noncrosslinked HA may provide an immediate hydration and viscoelastic “pulse,” whereas PDLLA particles degrade more slowly and may support sustained fibroblast activity and extracellular matrix remodeling [1, 2]. This framework is conceptually analogous to recently described bi-phasic microneedle designs, in which an initial rapidly dissolving component enables early payload release while a secondary compartment supports prolonged delivery [16].

Improvements in pore parameters, including volume and density, further emphasize the efficacy of combining cryotherapy with PDLLA–HA. Although cryotherapy alone has been shown to modulate sebaceous gland activity and reduce pore size [3–5], the addition of PDLLA–HA appears to amplify structural changes in the dermis, contributing to reduced pore volume and improved skin smoothness [16, 17].

Although the experimental group demonstrated a significant reduction in redness, the control group exhibited minimal change. This finding suggests that the anti-inflammatory properties of cryotherapy play a key role in reducing erythema [18]. Previous studies have highlighted the benefits of cryotherapy in managing redness and inflammation in various dermatological conditions [19].

Clinical relevance of instrumental improvements also warrants consideration. Although prespecified MCID thresholds were not prospectively defined in this exploratory split-face trial, post-hoc contextual interpretation suggests meaningful effect sizes. The melanin index decreased by approximately 31%, representing a change exceeding 0.5 standard deviations from baseline, a commonly applied distribution-based MCID surrogate. Objective melanin metrics have been validated for pigmentation assessment and are widely used as endpoints in depigmentation studies [20]. Similarly, total pore volume decreased by more than 50%, and pore volume has been shown to correlate strongly with visual pore assessment, supporting clinical interpretability beyond statistical significance [11]. These contextual interpretations are summarized in Supporting Table S2.

The safety profile observed in this study further supports the use of targeted precision cryotherapy. No adverse skin reactions, including redness, swelling, or discomfort, were reported. This is in line with the well-described analgesic and anti-inflammatory effects of local cryotherapy, which can reduce pain and inflammatory responses in treated tissues [19]. Compared with other advanced delivery systems, such as automated micro-needling pens and laser-assisted drug delivery, cryotherapy-assisted microjet delivery offers distinct advantages, including minimal mechanical disruption, reduced procedural pain, and simultaneous anti-inflammatory effects [3, 21, 22]. While microneedling devices rely on physical channel formation and laser-assisted systems depend on thermal ablation, cryogenic jet delivery may enable more uniform dispersion with reduced tissue trauma [21, 22]. These characteristics suggest that cryotherapy-assisted delivery may represent a complementary or alternative strategy within the spectrum of transdermal enhancement technologies.

This study has several limitations. The sample size was modest and the follow-up period was relatively short. Larger, randomized controlled studies with extended follow-up are warranted to confirm the durability of treatment effects and long-term safety. Second, this study relied on noninvasive imaging to assess treatment outcomes and did not include direct histological evaluation of micro-IceNeedle penetration depth or tissue distribution. Future studies incorporating ex vivo skin models or optional research biopsies are warranted to provide mechanistic validation and further characterize intradermal delivery. Third, the microneedle roller was selected as an accessible, broadly used mechanical comparator; however, comparisons with automated microneedling pens and/or other energy-based delivery platforms would be informative. Finally, patient-centered outcomes and responder analyses based on prespecified MCID thresholds should be incorporated into future trials.

The combination of targeted precision cryotherapy with PDLLA-HA is a safe and effective method for improving facial skin quality, particularly the pigmentation, dermal density, pore parameters, and redness. This innovative approach demonstrates

significant advantages over conventional PDLLA-HA application methods and represents a promising advancement in the field of aesthetic dermatology.

Author Contributions

Suk Bae Seo: conception and design of the study, drafting the manuscript, and critical revision of the manuscript for important intellectual content.

Gun-Ho Kim: data acquisition and coordination of the clinical aspects of the study, assisting in manuscript preparation and revision.

Joon Hong Park: patient recruitment and clinical procedures, contribution to data collection and interpretation, and review of the manuscript.

Kui Young Park: oversight of the entire project, final approval of the manuscript, and contributions to the conception and design of the study, as well as critical revision of the manuscript.

Acknowledgments

This work was supported by the Technology Innovation Program (or Industrial Strategic Technology Development Program-Material and Component Technology Development Project [Heterogeneous Technology Convergence Type] [20024946, Development of Tissue Regenerative Biosurgery Convergence Medical Products Using High-Functional Implantable Biomaterials]) funded by the Ministry of Trade, Industry and Energy (MOTIE, Korea).

The authors used AI-assisted language editing tools (e.g., ChatGPT, OpenAI) to improve the grammar, clarity, and readability of the manuscript.

Funding

This study was supported by the RecensMedical Inc. and VAIM Global.

Disclosure

All scientific content, study design, data analysis, and interpretation were independently developed and verified by the authors.

Conflicts of Interest

Suk Bae Seo serves as an advisor to VAIM Global and RecensMedical Inc.

Gun-Ho Kim is the CEO of RecensMedical Inc.

The remaining authors declare no conflicts of interest.

Data Availability Statement

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

References

1. K. W. A. Lee, L. K. W. Chan, A. W. K. Lee, C. H. Lee, S. T. H. Wong, and K. H. Yi, "Poly-D,L-Lactic Acid (PDLLA) Application in Dermatology: A Literature Review," *Polymers* 16, no. 18 (2024): 2583, <https://doi.org/10.3390/polym16182583>.
2. A. S. Ghatge and S. B. Ghatge, "The Effectiveness of Injectable Hyaluronic Acid in the Improvement of the Facial Skin Quality: A Systematic Review," *Clinical, Cosmetic and Investigational Dermatology* 16 (2023): 891–899, <https://doi.org/10.2147/ccid.s404248>.
3. N. K. Rho, "Revisiting the Role of Local Cryotherapy for Acne Treatment: A Review and Update," *Journal of Clinical Medicine* 12, no. 1 (2022): 26, <https://doi.org/10.3390/jcm12010026>.
4. M. Dell'Antonia, J. Anedda, A. Tatti, et al., "Non-Surgical Treatment of Hidradenitis Suppurativa: The Role of Cryotherapy," *Frontiers of Medicine* 10 (2023): 1141691, <https://doi.org/10.3389/fmed.2023.1141691>.

5. J. H. Ray, J. Tam, L. N. Vuong, et al., "Selective Cryolysis of Sebaceous Glands," *Journal of Investigative Dermatology* 135, no. 9 (2015): 2173–2180, <https://doi.org/10.1038/jid.2015.148>.
6. C. S. M. Wong, M. W. M. Chan, S. Y. N. Shek, C. K. Yeung, and H. H. L. Chan, "Evaluation of a Novel Dermal Cooling System for the Treatment of Benign Pigmented Lesions in Asians," *Lasers in Surgery and Medicine* 56, no. 6 (2024): 541–550, <https://doi.org/10.1002/lsm.23809>.
7. M. H. Kwack, S. Lee, E. H. Lee, G. U. Ha, G. H. Kim, and W. J. Lee, "Effect of a Precision Cryotherapy Device With Temperature Adjustability on Pigmentation," *Indian Journal of Dermatology* 67, no. 2 (2022): 204, https://doi.org/10.4103/ijd.ijd_755_21.
8. H. Son, S. Kim, K. M. Lim, et al., "Picoliter Ice Particles by Supersonic Cryogenic Jets for Transdermal Drug Delivery: Extracellular Vesicle Application for Skin Diseases," *Journal of Controlled Release* 387 (2025): 114184, <https://doi.org/10.1016/j.jconrel.2025.114184>.
9. S. B. Seo, J. Wan, L. K. W. Chan, K. W. A. Lee, S.-B. Kim, and K.-H. Yi, "Poly-D,L-Lactic Acid-Enhanced Atrophic Scar Treatment via Transdermal Microjet Drug Delivery in Asians," *Skin Research and Technology* 30, no. 6 (2024): e13762, <https://doi.org/10.1111/srt.13762>.
10. J. H. Hyeong, J. W. Jung, S. B. Seo, H. S. Kim, and K. H. Kim, "Intradermal Injection of Poly-D,L-Lactic Acid Using Microneedle Fractional Radiofrequency for Acne Scars: An Open-Label Prospective Trial," *Dermatologic Surgery* 48, no. 12 (2022): 1306–1311, <https://doi.org/10.1097/dss.0000000000003627>.
11. S. J. Kim, M. K. Shin, J. H. Back, and J. S. Koh, "Pore Volume is Most Highly Correlated With the Visual Assessment of Skin Pores," *Skin Research and Technology* 20, no. 4 (2014): 429–434, <https://doi.org/10.1111/srt.12135>.
12. J. Tan, H. Liu, J. J. Leyden, and M. J. Leoni, "Reliability of Clinician Erythema Assessment Grading Scale," *Journal of the American Academy of Dermatology* 71, no. 4 (2014): 760–763, <https://doi.org/10.1016/j.jaad.2014.05.044>.
13. Z. Zhang, J. Ke, Y. Dai, et al., "Tumor Cells Targetable Graphene Oxide Doped Microneedle for Synergistic Photothermal-Chemotherapy Treatment of Melanoma," *Journal of Pharmaceutical Analysis* 15, no. 10 (2025): 101270, <https://doi.org/10.1016/j.jpha.2025.101270>.
14. Z. Zhang, C. Fang, J. Ke, et al., "Microneedle Drug Delivery System Based on Hyaluronic Acid for Improving Therapeutic Efficiency of Hypertrophic Scars," *International Journal of Biological Macromolecules* 297 (2025): 139790, <https://doi.org/10.1016/j.ijbiomac.2025.139790>.
15. K. H. Yi, J. H. Kim, J. K. Song, et al., "Efficacy of Cryogenic Particle Delivery in Enhancing Skin Penetration and Absorption," *Aesthetic Plastic Surgery* 50, no. 3 (2026): 1269–1276, <https://doi.org/10.1007/s00266-025-05228-6>.
16. S. Oh, S. B. Seo, G. Kim, S. Batsukh, K. H. Son, and K. Byun, "Poly-D,L-Lactic Acid Stimulates Angiogenesis and Collagen Synthesis in Aged Animal Skin," *International Journal of Molecular Sciences* 24, no. 9 (2023): 7986, <https://doi.org/10.3390/ijms24097986>.
17. Y. Gao, Y. Sun, H. Yang, et al., "A Low Molecular Weight Hyaluronic Acid Derivative Accelerates Excisional Wound Healing by Modulating Pro-Inflammation, Promoting Epithelialization and Neovascularization, and Remodeling Collagen," *International Journal of Molecular Sciences* 20, no. 15 (2019): 3722, <https://doi.org/10.3390/ijms20153722>.
18. A. Dzidek and A. Piotrowska, "The Use of Cryotherapy in Cosmetology and the Influence of Cryogenic Temperatures on Selected Skin Parameters—A Review of the Literature," *Cosmetics* 9, no. 5 (2022): 100, <https://doi.org/10.3390/cosmetics9050100>.
19. J. E. Hocutt, "Cryotherapy," *American Family Physician* 23, no. 3 (1981): 141–144.
20. A. R. Matias, M. Ferreira, P. Costa, and P. Neto, "Skin Colour, Skin Redness and Melanin Biometric Measurements: Comparison Study

Between Antera 3D, Mexameter and Colorimeter," *Skin Research and Technology* 21, no. 3 (2015): 346–362, <https://doi.org/10.1111/srt.12199>.

21. T. S. Alster and P. M. Graham, "Microneedling: A Review and Practical Guide," *Dermatologic Surgery* 44, no. 3 (2018): 397–404, <https://doi.org/10.1097/dss.0000000000001248>.

22. L. R. Sklar, C. T. Burnett, J. S. Waibel, R. L. Moy, and D. M. Ozog, "Laser Assisted Drug Delivery: A Review of an Evolving Technology," *Lasers in Surgery and Medicine* 46, no. 4 (2014): 249–262, <https://doi.org/10.1002/lsm.22227>.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Supporting Information.** Supporting Table S1. Repeated-measures mean $\pm$ standard deviation values for instrumental skin parameters (melanin index, dermal density, total pore volume, and redness index) at each study visit, including baseline, post-first session, before each subsequent session (second–fifth), and 1 month after the fifth session, analyzed separately for experimental and control hemifaces. Supporting Table S2. Distribution-based interpretation of clinical relevance for key outcome parameters, including percentage changes from baseline and contextualization with previously published literature on instrumental skin measurements, supports interpretation of effect size and clinical meaningfulness.