



Efficacy of Cryogenic Particle Delivery in Enhancing Skin Penetration and Absorption

Kyu-Ho Yi^{1,2} · Jin-Hyun Kim² · Jong Keun Song³ · Michael James Kim⁴ · Chan Yeong Heo⁵ · Suk Bae Seo⁶ · Gun Ho Kim⁷



Received: 7 February 2025 / Accepted: 6 August 2025

© Springer Science+Business Media, LLC, part of Springer Nature and International Society of Aesthetic Plastic Surgery 2025

Abstract

Background Cryogenic particle delivery is a novel cryotherapy-based transdermal delivery system that converts liquid drugs into micro-ice-crystallised needles, which are propelled into the skin using a cryogenic CO₂ jet. This study evaluates its efficacy in enhancing skin penetration and absorption, alone and in combination with the Microneedle Therapy System (MTS).

Objective To assess fluorescence intensity, penetration depth, and structural integrity in ex vivo human skin tissues treated with cryogenic particle delivery, MTS, or a combination of both.

Methods Ex vivo human skin tissues were divided into four groups: untreated (Control), MTS alone (Control 1), MTS combined with cryogenic particle delivery (Control 2), and Picolitre ice particle delivery alone (Test Group). Fluorescence-labelled hyaluronic acid (HA-FITC) was applied, and fluorescence intensity and penetration depth were evaluated using confocal microscopy. Structural

integrity was assessed through haematoxylin and eosin (H&E) staining. Statistical analysis was performed using paired t tests ($p < 0.05$).

Results Fluorescence intensity increased significantly in all treated groups compared to the untreated control: by 279.06 (MTS alone), 492.81 (MTS + cryogenic particle delivery), and 251.88% (cryogenic particle delivery alone) ($p < 0.05$). Penetration depth also increased significantly: by 52.00 (MTS alone), 60.06 (MTS + cryogenic particle delivery), and 36.99% (Cryogenic particle delivery alone). H&E staining confirmed no structural damage in any group.

Conclusion Cryogenic particle delivery significantly enhances skin penetration and absorption, particularly when combined with MTS, demonstrating a synergistic effect. Its ability to deliver compounds safely and effectively highlights its potential as a transformative tool for therapeutic and cosmetic transdermal applications. Future

✉ Kyu-Ho Yi
kyuho90@daum.net

✉ Gun Ho Kim
gunhokim@unist.ac.kr

Jin-Hyun Kim
gina1kim@naver.com

Jong Keun Song
syss77@hanmail.net

Michael James Kim
jihyomike@gmail.com

Chan Yeong Heo
lionheo@snu.ac.kr

Suk Bae Seo
kddm7@naver.com

¹ BK21 FOUR Project, Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, Yonsei University College of Dentistry, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea

² You and I Clinic, Seoul, Korea

³ Pixelab plastic surgery clinic, Seoul, Korea

⁴ Aeon Medical and Aesthetic Centre, Singapore, Singapore

⁵ Department of Plastic Surgery, Seoul National University Bundang Hospital, Seongnam-si, South Korea

⁶ SeoAhSong Dermatologic Clinic, Seoul, Republic of Korea

⁷ Department of Biomedical Engineering, Ulsan National Institute of Science and Technology, Ulsan, South Korea

in vivo studies are warranted to validate these findings and optimise its clinical applications.

Level of Evidence V This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Cryogenic particle · Microneedle Therapy System (MTS) · Skin Penetration · Ex Vivo Skin Models · Cryotherapy

Introduction

The stratum corneum, the outermost layer of the skin, presents a significant barrier to the transdermal delivery of therapeutic and cosmetic agents [1, 2]. Traditional methods, including topical applications and microneedling, often face limitations such as poor penetration, discomfort, and variability in absorption. The development of minimally invasive techniques that enhance transdermal delivery while reducing side effects has been a critical focus of research in dermatology [3–5].

Cryogenic particle delivery is a novel transdermal delivery method that utilises cryotherapy to convert liquid drugs into micro-ice-crystallised needles. These needles are propelled into the skin at high-velocity cryogenic jet propulsion using a cryogenic CO₂ jet, allowing for precise penetration through the stratum corneum into the dermal layer. This technique achieves effective drug delivery with minimal pain, reduced inflammation, and enhanced absorption efficiency. By combining cryotherapy with precision delivery, cryogenic particle delivery addresses key limitations of conventional methods, offering a potentially transformative approach to transdermal drug administration.

The cryogenic particle delivery process creates micro-needle-like effects without mechanical damage to the skin [6]. The method allows for the targeted delivery of various substances, including hyaluronic acid, polydeoxyribonucleotide (PDRN), and exosomes, which are commonly used in cosmetic and therapeutic applications. In addition to improving the penetration of active compounds, cryogenic particle delivery is designed to minimise product wastage and provide a uniform distribution of substances, making it an appealing option for both patients and practitioners.

Previous studies on microneedling and related transdermal delivery systems have demonstrated their potential to enhance skin permeability and absorption [7–9]. However, the combined use of cryogenic delivery systems, such as cryogenic particle delivery, and existing techniques like the Microneedle Therapy System (MTS), remains

underexplored. Understanding how cryogenic particle delivery compares to or synergises with MTS could provide valuable insights into its efficacy and potential applications [10, 11].

This study aims to evaluate the efficacy of cryogenic particle delivery in enhancing skin penetration and absorption using ex vivo human skin tissue models. Specifically, the study investigates the fluorescence intensity, penetration depth, and structural integrity of skin tissues treated with cryogenic particle delivery, either alone or in combination with MTS. By examining these parameters, this research seeks to establish cryogenic particle delivery as a viable and innovative tool for transdermal drug delivery in both dermatological and aesthetic practices.

Material and Method

Ex Vivo Human Skin Tissue Model

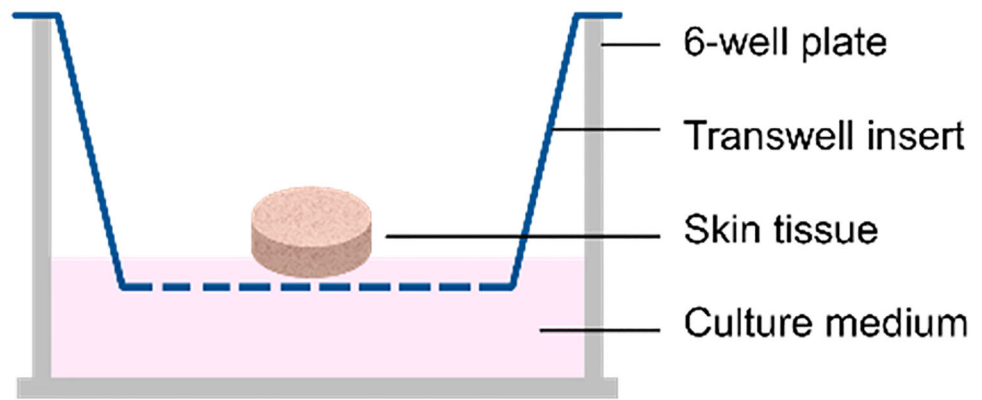
Human skin tissues were sourced from discarded facial skin samples of Korean women aged 50 years or older during surgeries, with ethical approval obtained from the Institutional Review Board (IRB) of the KSRC Korea Skin Research Center. The tissues were thoroughly washed with phosphate-buffered saline (PBS) to remove impurities and contaminants. They were then trimmed into uniform sections measuring 2 cm × 2 cm and mounted onto six-well plates with Transwell inserts (Corning, USA). The inserts were filled with Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% foetal bovine serum (FBS) and 1% penicillin–streptomycin (P/S) to maintain tissue viability during the experiments (Fig. 1).

Experimental Design

The skin tissues were divided into four experimental groups to evaluate the efficacy of cryogenic particle delivery and its combination with the Microneedle Therapy System (MTS):

1. Untreated Control (Control Group): Skin tissues received no treatment and served as a baseline reference for comparison.
2. MTS Alone (Control 1): The Microneedle Therapy System (MTS) was applied to create microchannels on the skin surface, followed by the topical application of 500 µL fluorescence-labelled hyaluronic acid (HA-FITC; Haworths, USA).
3. MTS + cryogenic particle delivery (Control 2): Skin tissues were first treated with MTS, and cryogenic

Fig. 1 Schematic diagram of the experimental setup for ex vivo skin tissue culture. Skin tissues were mounted onto Transwell inserts and placed in six-well plates containing DMEM supplemented with 10% foetal bovine serum (FBS) and 1% penicillin–streptomycin (P/S)



particle delivery was then used to deliver 500 μ L HA-FITC into the dermis.

4. Cryogenic particle delivery Alone (Test Group): Cryogenic particle delivery was used directly to deliver 500 μ L HA-FITC without prior MTS treatment.

For cryogenic particle delivery, a Boosting Container (Haworks, USA) was positioned 10–20 mm above the skin surface. This device converted the HA-FITC solution into cryogenic particles generated from rapid freezing and delivered via high-velocity jet propulsion into the skin using a cryogenic CO jet.

Experimental Procedure

1. Treated tissues were incubated for 24 hours at 37°C in a humidified atmosphere with 5% CO₂.
2. After incubation, tissues were fixed with 10% formaldehyde and sectioned into thin slices for analysis.
3. Tissue samples were stained with haematoxylin and eosin (H&E) to assess structural integrity. DAPI staining was performed to visualise nuclei, and fluorescence microscopy was used to observe HA-FITC distribution.

Evaluation Parameters

1. Fluorescence Intensity

Confocal fluorescence microscopy (Zeiss Axio Observer 7, Zeiss, Germany) was used to measure fluorescence intensity in arbitrary units (AU). Defined regions of interest (ROIs) were analysed with Image J software to quantify the fluorescence signal across groups (Fig. 2).

2. Penetration Depth

Fluorescence penetration depth was determined by measuring the vertical distance from the skin surface to the deepest visible fluorescence using calibrated scale bars (in μ m). Eight measurements were taken per image, with three images analysed per donor (Fig. 3).

3. Structural Integrity

H&E-stained sections were examined for structural disruption in both the epidermal and dermal layers (Fig. 4).

To ensure experimental consistency, 500 μ L of HA-FITC solution was applied to all groups, including the untreated control group, immediately following treatment or mock treatment. All skin tissue samples were then

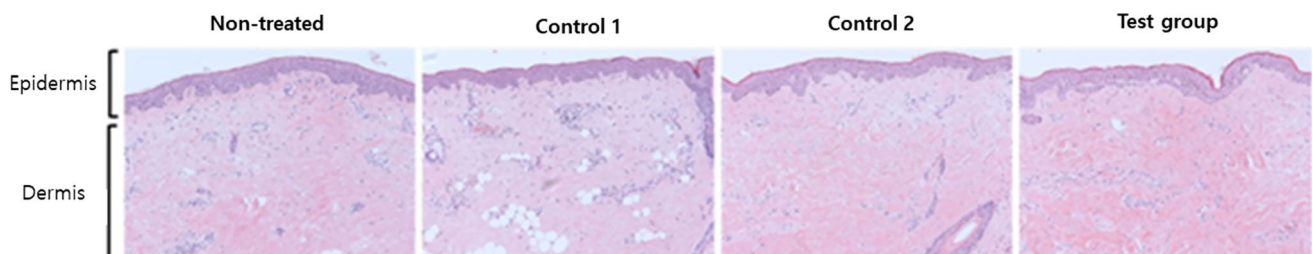


Fig. 2 Representative haematoxylin and eosin (H&E)-stained sections of skin tissues from all experimental groups

Fig. 3 Representative fluorescence images of human-derived skin tissue cross sections

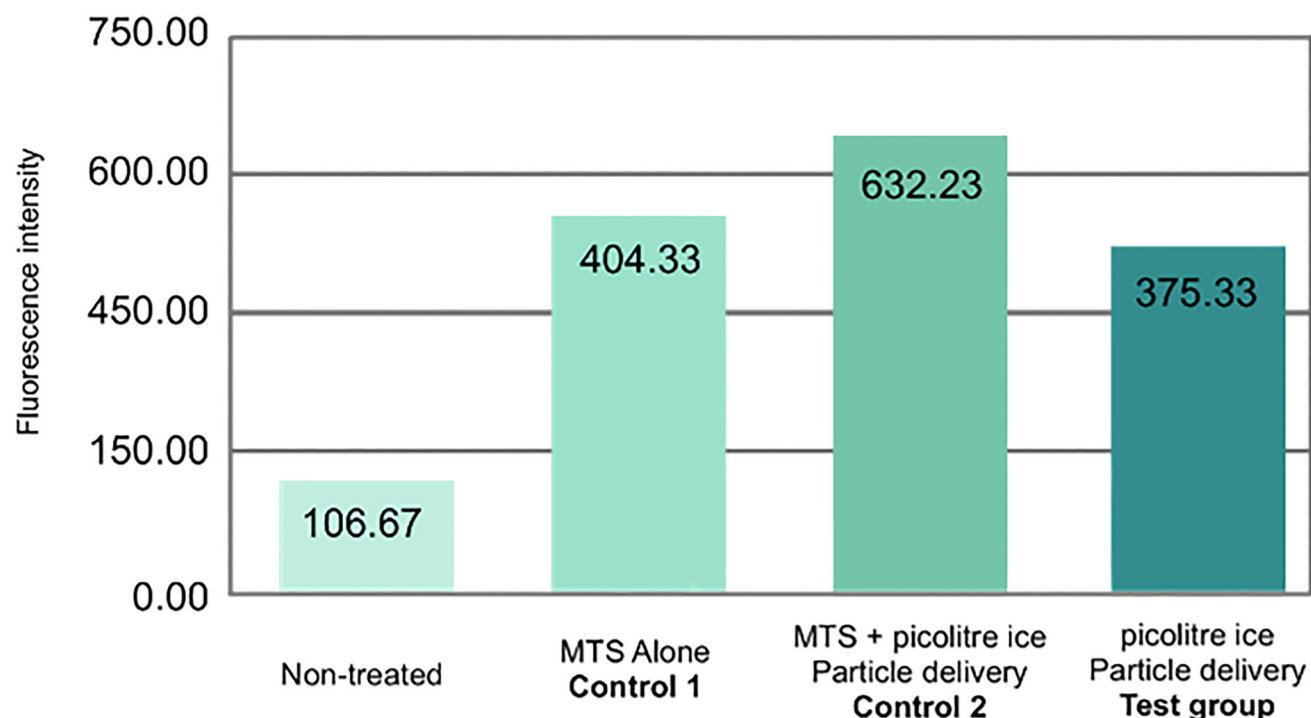
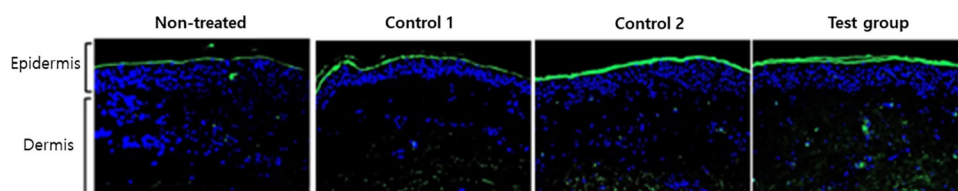


Fig. 4 Bar graph comparing fluorescence intensity across experimental groups

incubated under identical conditions—at 37°C in a humidified atmosphere with 5% CO₂ for 24 hours—prior to fixation and analysis. This uniform handling allowed for direct comparison of fluorescence intensity and penetration depth across groups while minimising potential confounding variables related to incubation time or reagent exposure.

Statistical Analysis

All experiments were performed using skin tissues from three donors, and results were expressed as mean ± standard error of the mean (SEM). Data were analysed using paired t tests to compare differences between groups, with statistical significance set at $p < 0.05$. The percentage changes in fluorescence intensity and penetration depth relative to the untreated control group were calculated using the following formulas:

- *Fluorescence Intensity Change Rate (%)*

$$\text{Change Rate} = \left(\frac{\text{Experimental Group Mean} - \text{Control Mean}}{\text{Control Mean}} \right) \times 100$$

- *Fluorescence Penetration Depth Change Rate (%)*

$$\text{Change Rate} = \left(\frac{\text{Experimental Group Mean} - \text{Control Mean}}{\text{Control Mean}} \right) \times 100$$

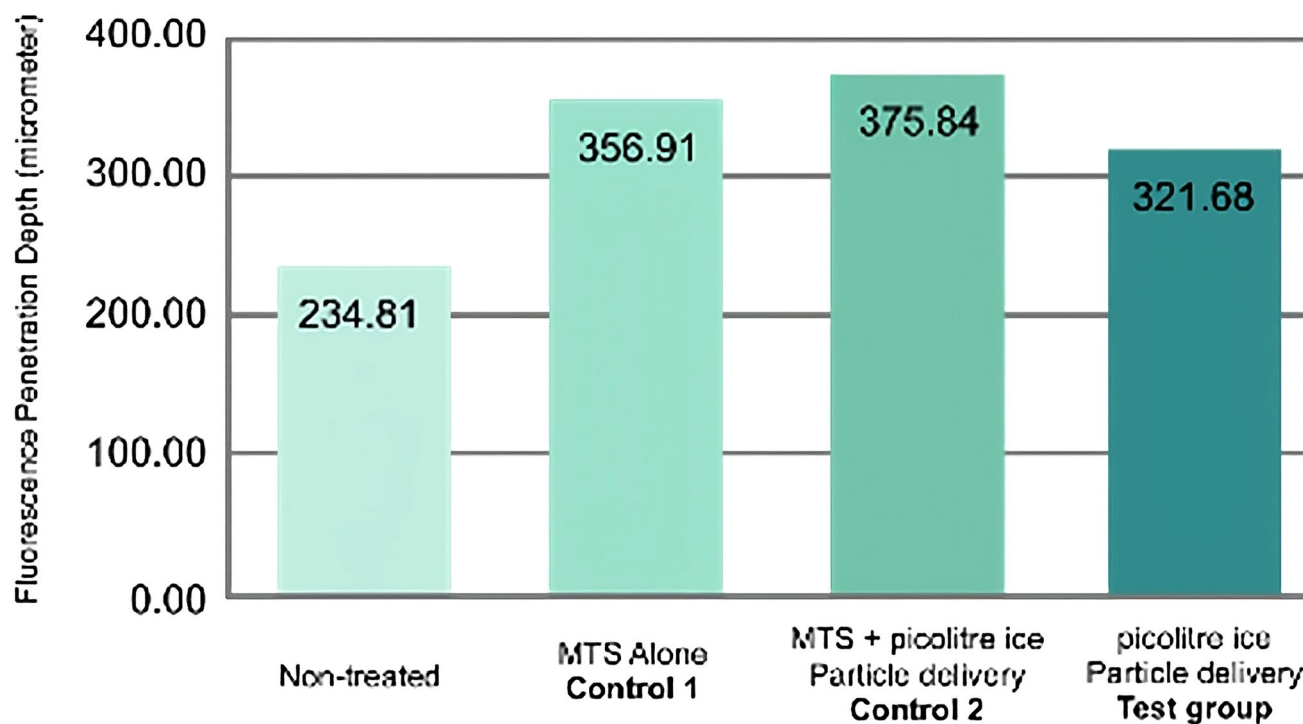
Results

Fluorescence Intensity

Fluorescence microscopy revealed significant increases in fluorescence intensity across all treated groups compared to the untreated control (Table 1, Fig. 5). The MTS + cryogenic particle delivery group (Control 2) achieved the highest fluorescence intensity, followed by MTS alone (Control 1) and Picolitre ice particle delivery alone (Test Group). The percentage increases relative to the untreated control were:

Table 1 Fluorescence intensity across delivery conditions

Group	Treatment	Mean fluorescence	SEM	SD	<i>p</i> value	Change versus Control (%)
Control	–	106.67	15.45	26.76	–	–
Exp 1	MTS	404.33	54.04	93.60	0.044*	279.06▲
Exp 2	MTS + Ice Needling	632.33	21.94	38.00	0.005**	492.81▲
Exp 3	Ice Needling	375.33	45.06	78.04	0.038*	251.88▲

**Fig. 5** Bar graph comparing fluorescence penetration depth across experimental groups**Table 2** Penetration depth of HA-FITC across delivery conditions

Group	Treatment	Fluorescence penetration Depth (μm)	SEM	SD	<i>p</i> value	Change versus Control (%)
Control	–	234.81	30.40	52.65	–	–
Exp 1	MTS	356.91	9.09	15.75	0.030*	52.00▲
Exp 2	MTS + Ice Needling	375.84	8.90	15.42	0.029*	60.06▲
Exp 3	Ice Needling	321.68	35.72	61.87	0.041*	36.99▲

- 279.06% for MTS Alone (Control 1) ($p = 0.044$)
- 492.81% for MTS + cryogenic particle delivery (Control 2) ($p = 0.005$)
- 251.88% for cryogenic particle delivery Alone (Test Group) ($p = 0.038$)

Penetration Depth

The penetration depth of HA-FITC was significantly increased in all treated groups compared to the untreated control (Table 2, Fig. 2). The MTS + cryogenic particle

delivery group (Control 2) achieved the deepest penetration, followed by MTS alone (Control 1) and cryogenic particle delivery alone (Test Group). The percentage increases relative to the untreated control were:

- 52.00% for MTS Alone (Control 1) ($p = 0.030$)
- 60.06% for MTS + cryogenic particle delivery (Control 2) ($p = 0.029$)
- 36.99% for cryogenic particle delivery Alone (Test Group) ($p = 0.041$)

Structural Integrity

Histological analysis of H&E-stained sections confirmed the absence of structural damage in the epidermal and dermal layers across all groups (Fig. 4). Representative fluorescence microscopy images further showed uniform distribution of HA-FITC within the dermis in treated groups, with deeper penetration observed in the MTS + cryogenic particle delivery group compared to the other groups (Fig. 3).

Fluorescence microscopy revealed distinct patterns of HA-FITC distribution across treatment groups. In the MTS + cryogenic particle delivery group, fluorescence signals were not only more intense but also penetrated more uniformly and deeply into the dermal layer compared to other groups. The increased penetration depth—averaging 60.06% greater than the untreated control—suggests that the combined mechanical disruption from microneedling and the propulsive force of cryogenic delivery facilitates compound entry beyond superficial layers. In contrast, the cryogenic particle delivery alone group exhibited a slightly shallower but still significantly enhanced depth of delivery, indicating that even in the absence of pre-formed microchannels, the ice-crystallised particles possess sufficient momentum for effective dermal targeting. These observations support the potential of this dual-modality approach to overcome the stratum corneum barrier and achieve consistent transdermal penetration.

Although the difference in penetration depth between the MTS alone group and the MTS combined with cryogenic particle delivery group was 8.06%, this increase was statistically significant ($p = 0.029$). This finding suggests that the addition of cryogenic particle propulsion provides a measurable enhancement in transdermal delivery, even when used in conjunction with established microneedling techniques. The statistical significance of this modest increase highlights the potential synergistic effect of combining mechanical microchanneling with high-velocity cryogenic delivery to optimise penetration efficiency.

Discussion

The findings of this study demonstrate the efficacy of cryogenic particle delivery (TargetCool, Recens Medical, Seoul, Republic of Korea) as a novel cryotherapy-based transdermal delivery technique that significantly enhances skin penetration and absorption of active compounds. Compared to the untreated control, fluorescence intensity and penetration depth increased significantly in all treated groups, with the combination of MTS and cryogenic particle delivery (Control 2) showing the most pronounced effects. This highlights the synergistic potential of combining cryogenic particle delivery with conventional microneedling techniques, such as MTS, for transdermal drug delivery.

The significant increase in fluorescence intensity observed in the MTS + cryogenic particle delivery group (492.81%) compared to MTS alone (279.06%) or cryogenic particle delivery alone (251.88%) suggests that MTS creates microchannels that facilitate deeper and more uniform penetration of HA-FITC propelled by cryogenic particle delivery. The cryogenic particles generated from rapid freezing and delivered into the skin via high-velocity cryogenic jet propulsion generated by cryogenic CO₂ enhances the distribution of active compounds beyond the microchannels created by MTS, resulting in improved delivery efficiency. This combination addresses a critical limitation of traditional transdermal techniques, which often face challenges in achieving uniform absorption and penetration.

The observed penetration depths further validate this synergistic effect. The MTS + cryogenic particle delivery group achieved a 60.06% increase in penetration depth compared to the untreated control, outperforming MTS alone (52.00%) and cryogenic particle delivery alone (36.99%). This indicates that cryogenic particle delivery not only complements but also amplifies the penetration achieved by MTS, making it a valuable addition to existing microneedling protocols.

The safety profile of cryogenic particle delivery was confirmed by histological analysis. H&E-stained sections revealed no structural damage to the epidermis or dermis in any of the treated groups. This finding is significant, as traditional invasive techniques, such as needle injections or ablative procedures, often carry risks of scarring, inflammation, or disruption of skin integrity. Cryogenic particle delivery minimises these risks by combining cryotherapy with precision delivery, making it suitable for repeated applications and sensitive skin areas.

From a clinical perspective, the ability of cryogenic particle delivery to enhance transdermal delivery has important implications for both therapeutic and cosmetic

applications. Substances such as hyaluronic acid, PDRN, exosomes, and other biologically active compounds can benefit from this technique, particularly in treatments aimed at skin rejuvenation, scar revision, or pigmentation management [4]. The reduced pain and inflammation associated with cryogenic particle delivery are likely to improve patient compliance and satisfaction, making it an attractive option for aesthetic practitioners.

When compared to other transdermal delivery systems, such as electroporation or iontophoresis, cryogenic particle delivery offers unique advantages. Unlike iontophoresis, which requires specific electrical properties for drug delivery, cryogenic particle delivery is independent of the physicochemical characteristics of the delivered compound. Similarly, while electroporation relies on electrical pulses to disrupt the lipid bilayer, Picolitre ice particle delivery uses mechanical penetration through cryogenic particles generated from rapid freezing and delivered into the skin via high-velocity cryogenic jet propulsion, minimising cellular disruption.

In addition, cryogenic particle delivery addresses some of the limitations of MTS, such as variability in microchannel depth and uneven distribution of active compounds. By delivering substances directly into the dermis in a controlled manner, cryogenic particle delivery ensures more consistent outcomes, especially when used in combination with MTS. The study of Son et al. introduces a cryogenic particle delivery system that uses controlled supersonic cryogenic jets to atomize liquid drug into micro-droplets, flash-freeze them into sub-picoliter ice particles, and propel them across the skin barrier in ~ 300 μ s. On ex vivo porcine skin, this approach achieved an average 50% delivery efficiency, while in vivo mouse experiments showed dermal deposition comparable to conventional needle injections. By delivering in solid phase at picoliter unit doses, cryogenic particle delivery enhances penetration and distribution, reduces patient discomfort, and avoids heat/UV-related degradation seen with some microneedles. Importantly, stem cell-derived extracellular vesicles retained anti-inflammatory and regenerative activity after delivery, producing significant therapeutic benefits in wound healing and atopic dermatitis models [12].

While the results are promising, this study has several limitations that should be addressed in future research. The experiments were conducted using ex vivo human skin tissue, which, although biologically relevant, may not fully replicate in vivo conditions. Factors such as vascularisation, immune response, and patient variability could influence the effectiveness of cryogenic particle delivery in clinical settings. Future studies should include in vivo trials to validate the findings and assess the long-term safety and efficacy of the technique.

While our findings provide compelling ex vivo evidence for the efficacy and safety of cryogenic particle delivery, further research is needed to validate its clinical applicability. To enhance the reliability of our results, ex vivo experiments were conducted using skin tissues obtained from three independent donors. This approach helped mitigate inter-individual variability and ensured that observed outcomes were not limited to a single specimen. However, we acknowledge that broader validation is necessary to establish the reproducibility and generalizability of the technique. Future studies should incorporate a larger and more diverse donor pool, accounting for variables such as age, skin thickness, anatomical location, and phototype, to comprehensively evaluate the consistency of cryogenic particle delivery across different skin types and clinical contexts. One limitation of this study is the use of fluorescence-labelled hyaluronic acid (HA-FITC) as the sole model compound. While suitable for proof of concept, future studies should assess the delivery of a broader range of therapeutic and cosmetic agents—such as growth factors, peptides, and stem cell-derived exosomes—across different molecular weights and physicochemical properties. Although preliminary observations suggest that this delivery system may function independently of compound characteristics, additional studies are needed to determine how factors such as particle size, viscosity, and formulation influence delivery efficiency. Additionally, optimisation of key parameters, including ice-crystal size, jet pressure, and delivery depth, may enhance delivery efficiency and broaden the clinical scope of this technology. In vivo studies are also required to evaluate pharmacokinetics, immune response, and patient outcomes in dynamic physiological environments. The cost-effectiveness and scalability of this method should be further explored to determine its feasibility for widespread use. Comparative evaluations with other transdermal delivery technologies will help clarify the unique advantages and limitations of cryogenic particle delivery and guide its integration into clinical practice.

Conclusion

This study demonstrates that Picolitre ice particle delivery significantly enhances skin penetration and absorption in ex vivo human skin models. When combined with the MTS, it produces the greatest increases in fluorescence intensity and penetration depth, highlighting its synergistic potential. Picolitre ice particle delivery offers unique advantages, including deeper penetration with minimal pain and no structural damage, making it a safe and effective alternative to existing techniques like microneedling and iontophoresis. Future in vivo research should

validate these findings, optimise the technique, and explore its broader applications, establishing Picolitre ice particle delivery as a valuable tool in dermatology and aesthetic medicine.

Author Contributions Kyu-Ho Yi, Jin-Hyun Kim; Michael James Kim; Heo Chan Yeong, Suk Bae Seo, Gun Ho Kim contributed to *conceptualisation*. Kyu-Ho Yi and Jong-Keun Song were involved in *writing—original draft preparation*. Kyu-Ho Yi, Heo Chan Yeong, Suk Bae Seo, and Gun Ho Kim contributed to *writing—review and editing*. Kyu-Ho Yi was involved in *visualisation*. Kyu-Ho Yi and Gun Ho Kim contributed to *supervision*. All authors have reviewed and approved the article for submission.

Funding The authors received no financial support for the research, authorship, and publication of this article. The products utilised in this study were donated by the injectors for the purposes of this study.

Declarations

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article. This study was conducted in compliance with the principles set forth in the Declaration of Helsinki.

References

1. Alkilani AZ, McCrudden MT, Donnelly RF. Transdermal drug delivery: innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. *Pharmaceutics*. 2015;7(4):438–70. <https://doi.org/10.3390/pharmaceutics7040438>.
2. Gorzelanny C, Mess C, Schneider SW, Huck V, Brandner JM. Skin barriers in dermal drug delivery: which barriers have to be overcome and how can we measure them? *Pharmaceutics*. 2020. <https://doi.org/10.3390/pharmaceutics12070684>.
3. Waghule T, Singhvi G, Dubey SK, et al. Microneedles: A smart approach and increasing potential for transdermal drug delivery system. *Biomed Pharmacother*. 2019;109:1249–58. <https://doi.org/10.1016/j.biopha.2018.10.078>.
4. Nguyen HX, Nguyen CN. Microneedle-mediated transdermal delivery of biopharmaceuticals. *Pharmaceutics*. 2023. <https://doi.org/10.3390/pharmaceutics15010277>.
5. Guillot AJ, Cordeiro AS, Donnelly RF, Montesinos MC, Garrigues TM, Melero A. Microneedle-based delivery: an overview of current applications and trends. *Pharmaceutics*. 2020. <https://doi.org/10.3390/pharmaceutics12060569>.
6. Zhang X, Fu X, Chen G, Wang Y, Zhao Y. Versatile ice microneedles for transdermal delivery of diverse actives. *Adv Sci (Weinh)*. 2021;8(17):e2101210. <https://doi.org/10.1002/advs.202101210>.
7. Jung JH, Jin SG. Microneedle for transdermal drug delivery: current trends and fabrication. *J Pharm Investig*. 2021;51(5):503–17. <https://doi.org/10.1007/s40005-021-00512-4>.
8. Ramadan D, McCrudden MTC, Courtenay AJ, Donnelly RF. Enhancement strategies for transdermal drug delivery systems: current trends and applications. *Drug Deliv Transl Res*. 2022;12(4):758–91. <https://doi.org/10.1007/s13346-021-00909-6>.
9. Ahmed Saeed Al-Japairai K, Mahmood S, Hamed Almurisi S, et al. Current trends in polymer microneedle for transdermal drug delivery. *Int J Pharm*. 2020;587:119673. <https://doi.org/10.1016/j.ijpharm.2020.119673>.
10. Wan J, Seo SB, Yoon SE, Yi KH. The efficacy of combined microneedling and topical poly-D,L-lactic acid (Juvelook) application for facial pore reduction and skin texture improvement. *Plast Reconstr Surg Glob Open*. 2025;13(6):e6838. <https://doi.org/10.1097/GOX.00000000000006838>.
11. Wan J, Yoon SE, Pamela R, Kai Jie Wong I, Vitale M, Cartier H, Garson S, Yi KH. Lactobacillus-derived exosome therapy for active acne vulgaris, post-inflammatory hyperpigmentation, and atrophic scarring. *J Craniofac Surg*. 2025. <https://doi.org/10.1097/SCS.00000000000011408>.
12. Son H, Kim S, Lim KM, Kim D, Song K, Song M, Lee Y, Yu S, Kim D, Cho SG, Kim GH. Picoliter ice particles by supersonic cryogenic jets for transdermal drug delivery: extracellular vesicle application for skin diseases. *J Control Release*. 2025;387:114184. <https://doi.org/10.1016/j.jconrel.2025.114184>.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.