Appendix

EVIDENCE LIBRARY

Detailed scientific and clinical data supporting TargetCool technology

Category : Aesthetic Outcome

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
TargetCool-based comparative study of transdermal PN/Rejuran delivery	A pilot split-face study in 4 adult subjects. The right side of the face received Rejuran cryogenic transdermal delivery using TargetCool after MTS, while the left side received manual intradermal injection using a 31G needle. After 3 treatment sessions at 2-week intervals, the study compared skin improvement, ultrasound-based dermal density, satisfaction, and pain.	The TargetCool-treated side showed skin improvement outcomes comparable to manual injection, and increased dermal density was observed in some subjects at 3 months. No statistically significant differences were found between sides in satisfaction or imaging indicators. No significant adverse reactions such as persistent erythema, infection, granuloma, or delayed hypersensitivity were observed.	Kim M et al., Supersonic Cryogenic Jet Delivery of Polynucleotides Compared With Manual Intradermal Injection, Plastic and Reconstructive Surgery Global Open, 2026.
Single-patient case of TargetCool-applied Skin Botox	A single-case analysis observing changes in skin texture, gloss, pores, and fine wrinkles based on before-and-after images taken after repeated Skin Botox procedures.	A trend toward improved surface gloss and skin texture was observed from approximately 2 weeks after the first treatment. Improvements in skin texture, gloss, and pores were most evident after the third treatment. At 4 weeks after the fifth treatment, improved skin texture and pore tightening appeared to be maintained.	Dr. Junhong Park, Owolui Achim Dermatology Clinic, Korea, 2025.
Controlled study of PDLLA-HA for skin quality improvement	A prospective controlled split-face study in 20 Korean women with melasma, hyperpigmentation, or dark spots. PDLLA-HA was applied to one side of the face using TargetCool Boosting Mode, while the same formulation was applied to the opposite side using a microneedle roller. The study compared skin tone, dermal density, pores, redness, satisfaction, and safety.	The TargetCool-treated side showed greater improvement than microneedling in melanin reduction (31.28% vs 23.40%), dermal density (30.07% vs 17.37%), pore volume (53.43% vs 33.61%), and pore density (57.80% vs 21.62%). Redness also significantly decreased on the TargetCool-treated side, and no adverse reactions were observed.	Seo SB et al., Targeted Precision Cryotherapy With a Poly-D,L-Lactic Acid–Hyaluronic Acid Hybrid Filler for Facial Skin Quality Enhancement: A Controlled Study, Dermatologic Therapy, 2026.

Category : Drug Delivery

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
Ex vivo micropig skin permeability test	An ex vivo preliminary test using 3 kDa dextran in a micropig skin model to compare residual fluorescence signals after washing under topical application, derma roller, and cryo-device application conditions.	Residual fluorescence signals were observed on the skin surface after PBS washing under certain CryoVIVE application conditions, confirming the possibility of skin-surface retention depending on the application condition.	Prostemics, Skin Permeability Test Using Ex vivo Micropig Skin, 2021.
Ex vivo human skin Boosting Mode ampoule penetration evaluation	An ex vivo test evaluating the penetration intensity and depth of low-molecular-weight HA in Boosting Mode, compared with MTS alone and MTS combination conditions.	When combined with MTS, fluorescence intensity increased by 492.81% and penetration depth increased by 60.06%, showing the strongest penetration-enhancing effect.	Yi K-H et al., Efficacy of Cryogenic Particle Delivery in Enhancing Skin Penetration and Absorption, Aesthetic Plastic Surgery, 2025.
Ex vivo human cadaver skin filler combination penetration evaluation	A test comparing a filler-only group with a filler + TargetCool combination group in a human cadaver skin model to evaluate cumulative permeability, intradermal fluorescence intensity, and penetration depth.	At 24 hours, the filler + TargetCool combination group showed increasing trends versus the filler-only group in cumulative permeability (+133.75%), intradermal fluorescence intensity (+225.25%), and fluorescence penetration depth (+53.16%).	Korea Institute of Nonclinical Study, Human Skin Tissue Permeability Evaluation Test for TargetCool, 2023.
Pico laser + TargetCool ex vivo human-derived skin tissue permeability evaluation	A test using a female facial skin explant model to compare untreated, Pico laser-only, and TargetCool combination groups for the permeability-enhancing effect of HA-FITC.	The Pico laser + TargetCool combination group showed increasing trends versus the untreated group in fluorescence intensity (+208.51%) and fluorescence penetration depth (+45.01%). Compared with the Pico laser-only group, increases of 47.21% and 11.26%, respectively, were also observed. No significant structural changes were observed on H&E evaluation.	Korea Institute of Nonclinical Study, Permeability Evaluation Test of Pico Laser and TargetCool in an Ex vivo Human-Derived Skin Tissue Model, 2023.
Ex vivo study of TargetCool-enhanced skin permeability	A study comparing the skin-delivery efficiency of Acetyl Hexapeptide-8-FITC under TargetCool alone and microneedling combination conditions in an ex vivo human facial skin model.	TargetCool alone increased fluorescence intensity by +492% and penetration depth by +35.86%. Turtle pin + TargetCool showed the maximum increase in fluorescence intensity (+1,272%), while MTS + TargetCool showed the maximum penetration depth increase (+47.75%). No tissue damage was observed.	Yi KH et al., Ex Vivo Evaluation of Skin Permeability Enhancement Using TargetCool in Human-Derived Skin Tissue Models, Journal of Craniofacial Surgery, 2026.

Category : Drug Delivery

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
Ex vivo human-derived skin tissue Klardie permeability evaluation	A test comparing fluorescence intensity and fluorescence penetration depth after applying the Klardie product in an ex vivo human-derived skin tissue model under topical application, Turtle pin, MTS, TargetCool alone, and combination conditions.	Fluorescence intensity was highest in the Turtle pin 0.5 mm + TargetCool combination group at 1,272.00% versus control, and the MTS 1.5 mm + TargetCool combination group also showed a 1,000.00% increasing trend. Fluorescence penetration depth showed the highest increasing trend in the MTS 1.5 mm + TargetCool combination group at 47.75%. No significant structural changes were observed on H&E evaluation.	Korea Institute of Nonclinical Study, Permeability Evaluation Test of 'TargetCool' in an Ex vivo Human-Derived Skin Tissue Model, 2024.
Ex vivo human skin tissue absorption image evaluation of IN Mode test device	A test comparing the IN Mode application group with the hand-application group in ex vivo human skin tissue to evaluate absorption images and fluorescence absorption.	At 24 hours, the IN Mode test device group showed a significant 533.30% increase in epidermal fluorescence absorption compared with the topical application group ($p<0.05$), while dermal fluorescence absorption showed a 172.00% increasing trend.	Korea Biomedical Research Institute, Ex vivo Human Skin Tissue Absorption Image Evaluation Test for the 'IN Mode Test Device', 2024.
PIPD-based transdermal EV delivery study	A study proposing PIPD technology, which converts and accelerates liquid EVs into picoliter-scale ice particles using a supersonic cryogenic jet for skin delivery, and evaluates EV skin-delivery efficiency, physicochemical properties, and preservation of biological function.	In ex vivo porcine skin, an average delivery efficiency of 50% was observed. In in vivo mouse skin, EVs were distributed more uniformly across multiple skin layers compared with topical application and injection. The major characteristics, cellular uptake, anti-inflammatory and regenerative functions of EVs were maintained before and after PIPD, and improvement effects were confirmed in wound healing and atopic dermatitis animal models.	Son H et al., Picoliter Ice Particles by Supersonic Cryogenic Jets for Transdermal Drug Delivery: Extracellular Vesicle Application for Skin Diseases, Journal of Controlled Release, 2025.
CO_2 cryotherapy + EGF combined wound-healing evaluation	A preclinical study comparing AcuCool™-based CO_2 cryotherapy combined with EGF delivery with control and MTS+EGF groups in a Sprague Dawley rat full-thickness wound model, evaluating wound closure, inflammation regulation, and tissue regeneration-related indicators.	On Day 14, wound width in the Device+EGF group was 3,313 ± 279.0 μm, significantly reduced compared with the Control group (4,856 ± 233.3 μm) and MTS+EGF group (4,665 ± 358.6 μm). Decreases in inflammation/oxidative stress markers such as TNF-α, IL-1β, MCP-1, and NO, and increases in tissue regeneration/remodeling markers such as collagen deposition, TGF-β1, Collagen I, and Vimentin were also confirmed.	Jin Y et al., Synergistic CO_2 Cryotherapy and EGF Delivery for Accelerated Wound Healing Through Anti-Inflammatory and Regenerative Pathways, International Journal of Molecular Sciences, 2025.

Category : Hair & Scalp

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
Mouse study evaluating minoxidil drug efficacy	A nonclinical study in a C57BL/6 mouse model with dexamethasone-induced hair-growth suppression. Minoxidil was applied with either MTS or a cryogenic/supersonic transdermal drug-delivery system, and hair-growth area at Days 0, 7, 10, and 14, as well as skin thickness and follicle count on Day 14, were compared.	On Day 14, the hair-growth area was higher in the cryogenic/supersonic system + minoxidil group (95.54%) than in the MTS + minoxidil group (66.14%). Histological evaluation on Day 14 also showed higher values in the test group for skin thickness (881.00 μm) and follicle count (24.33 N) compared with the MTS group (674.00 μm and 19.78 N).	Korea Institute of Nonclinical Study, KINS / KSRC, Efficacy Evaluation Test of a 'Cryogenic/Supersonic Transdermal Drug Delivery System' Using a C57BL/6 Mouse Model, 2024.
Evaluation of hair-growth mechanism based on cold stimulation	A study evaluating the effect of TargetCool-controlled cold shock on anagen induction and hair-growth-related molecular markers in C57BL/6 mice, and confirming biological responses to cold stimulation in ORSC and ex vivo human hair follicle models.	Cold stimulation at 5°C for 30/60 seconds and 0°C for 30 seconds significantly induced anagen phase in mouse dorsal skin. In the 5°C 60-second condition, increases in CD31, VEGF, CIRP, and RBM3 mRNA were confirmed. In ORSC, CIRP, RBM3, and VEGF increased after 32°C cold shock, while IL-1β and CXCL1 decreased. In ex vivo human hair follicles, hair shaft elongation and increased Ki-67-positive cells were confirmed.	Lee S et al., Cold Shock Therapy Promotes Hair Growth in Association with Upregulation of Cold-Inducible RNA-Binding Protein and Vascular Endothelial Growth Factor, Journal of Dermatological Science, 2024.
Comparative clinical study of cryotherapy for alopecia areata	An intrasubject split-lesion pilot study comparing negative control, 10-second cryotherapy, 20-second cryotherapy, and intralesional triamcinolone acetonide injection in four sections of a single alopecia lesion in patients with alopecia areata. Treatment effects by cooling duration were evaluated at 0°C using TargetCool™.	The final evaluation included 15 subjects. Hair-regrowth rate versus baseline was assessed after a total of 6 treatments at 2-week intervals. The 20-second cryotherapy × 2 cycles group showed a median hair-regrowth rate of 55%, a significant improvement versus the negative control group (32.5%, p=0.048), and results comparable to the TA injection group (50%, p=0.038). The 10-second cryotherapy group did not show significant improvement (p=0.97).	Lee HJ et al., Comparative Analysis of Temperature-Controlled Cryotherapy versus Intralesional Triamcinolone Acetonide Injection for Alopecia Areata: An Intrasubject Split-Lesion Pilot Study, Journal of the European Academy of Dermatology and Venereology, 2024.
Investigator-initiated clinical study of itch improvement in scalp seborrheic dermatitis	A single-arm prospective clinical trial in patients with moderate scalp seborrheic dermatitis. Precision cryotherapy was applied 3 times at 2-week intervals, and itch VAS, PGA, clinical severity score, erythema index, TEWL, and subjective symptoms were evaluated at Week 6 and Week 8.	At Week 8, itch VAS decreased by 50.4%, from 6.77 ± 2.29 to 3.36 ± 2.46. PGA score improved from 2.86 ± 0.62 to 1.66 ± 0.61, and clinical severity score improved from 4.55 ± 1.30 to 2.45 ± 1.37. Erythema index decreased by 19.6%, and no serious adverse event was reported.	Choi YG et al., Efficacy and Safety of Precision Cryotherapy to Treat Seborrheic Dermatitis of the Scalp, Dermatologic Surgery, 2023.

Category : Itch / Inflammation

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
LPA-induced pruritus mouse model evaluation	A preclinical/preprint study applying a temperature- and time-adjustable precision cryotherapy device in an LPA-induced pruritus mouse model and evaluating changes in mRNA and protein expression of itch-related biomarkers under different cooling conditions.	Under conditions of 5°C for 10/20 seconds and 0°C for 5/10/20 seconds, gene expression of pruritus- and inflammation-related markers, including TRPA1, TRPV1, TRPM8, PAR2, IL-4, IL-10, IL-13, IL-31, and IFN-γ, generally decreased. Protein expression also tended to decrease under key cooling conditions.	Kwack MH et al., Effect of a Precision Cryotherapy Device With Temperature-Adjustability on Mice With Lysophosphatidic Acid-Induced Pruritus, Research Square, 2021.
Investigator-initiated clinical study of local itch improvement in atopic dermatitis	A 2-month split-body clinical trial in 28 patients with mild-to-moderate atopic dermatitis, comparing cryotherapy device-treated areas with untreated control areas. The device was applied once weekly for 8 weeks at -5°C for 5 seconds, and itch VAS, patient satisfaction, and adverse reactions were evaluated.	On the treatment day, itch VAS in the cryotherapy-treated area decreased from baseline 5.86 ± 1.80 to 2.89 ± 2.25 at 10 minutes, 2.86 ± 2.31 at 30 minutes, and 3.18 ± 2.53 at 60 minutes, and was significantly lower than control. At the 8-week follow-up, itch VAS reduction versus baseline was observed, and no serious adverse event was reported.	Lee EH et al., Effect of a New Cryotherapy Device on an Itchy Sensation in Patients With Mild Atopic Dermatitis, Journal of Cosmetic Dermatology, 2021.
Investigator-initiated clinical study of acne lesion improvement	A pilot clinical trial in 20 patients with acne vulgaris evaluating lesion count, IGA, erythema index, satisfaction, and safety after TargetCool-based precision cryotherapy application.	At Week 4, acne lesion count decreased by 90.25%, and IGA score and erythema index also significantly improved. Satisfaction was 6.75 ± 0.79, and no adverse reactions, pain, or discomfort were reported.	Hong JY et al., Targeted Precision Cryotherapy for Acne Vulgaris, Skin Research and Technology, 2024.

Category : Pain Control

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
Investigator-initiated clinical study of pain reduction during intralesional steroid injection for acne lesions	A two-stage, non-randomized clinical trial evaluating the pain-reduction effect and safety of CryoVIVE® cold anesthesia during intralesional triamcinolone acetonide injection for nodulocystic acne lesions. In Stage 2, 60 acne lesions in 30 patients were compared between cold anesthesia-treated lesions and non-anesthetized lesions.	In Stage 2, the pain VAS score in the cold anesthesia group was 3.667 ± 2.23, significantly lower than the non-anesthesia group at 5.933 ± 2.03. Patient satisfaction was higher in the cold anesthesia group (3.867) than in the non-anesthesia group (2.5), and no adverse reactions such as pigmentation changes or scarring were observed.	Park SJ et al., Cold Anesthesia for Pain Reduction During Intralesional Steroid Injection for Nodulocystic Acne, Journal of Cosmetic Dermatology, 2023.
Evaluation of pain reduction during laser tattoo removal	A prospective split-body study in 12 subjects comparing the pain-reduction effect of TargetCool cooling application with 9.6% lidocaine topical anesthetic cream during laser tattoo removal.	The pain VAS score in the TargetCool-treated group was 4.33 ± 1.55, significantly lower than the topical anesthetic cream group at 7.58 ± 1.16. Seventy-five percent of subjects indicated willingness to use cryotherapy instead of topical anesthetic cream in the future. No serious adverse event was reported, and mild tingling sensation was reported in 2 subjects.	Jung S et al., Efficacy of a New Cryotherapy Device on Pain Relief During the Laser Tattoo Removal, Medical Lasers, 2022.
Comparison of pain relief during scalp PRP injection	A split study comparing the pain-relief effect, preference, and safety of TargetCool and the conventional Zimmer cooler during PRP scalp injection.	Nine of 10 subjects preferred TargetCool over the conventional Zimmer cooler, while 1 subject responded that both devices were equally effective. No adverse effects were reported for either device, and physician usability was assessed as equivalent.	Avram MR., Cryogen Cooling Device for Anesthesia, Platelet-Rich Plasma Therapy, and Hair Loss, Dermatologic Surgery, 2024.
Pain reduction during injections for keloids and hypertrophic scars	A single-center prospective study in 20 subjects evaluating the pain-reduction effect and safety of precision cryotherapy during intralesional triamcinolone ± 5-FU injection for keloid lesions, comparing cryotherapy-treated areas with untreated control areas.	The pain score in the precision cryotherapy-treated group was 2.4 ± 1.9, a 59% reduction versus the untreated control group at 5.9 ± 2.4 ($p < .001$). Among subjects completing the 1-week follow-up survey, 94% indicated willingness to reuse the treatment in the future. Adverse reactions were mild and transient, and no pigmentation changes, blisters, or persistent irritation were reported.	Eskibozkurt GE et al., Efficacy of Precision Cryotherapy in Reducing Pain During Intralesional Injections for Keloids, Dermatologic Surgery, 2025.

Category : Pigmentation

Appendix
Evidence Library

Evidence	Summary	Key Data	Reference
UVB-induced pigmentation mouse model evaluation	An animal study applying a temperature- and time-adjustable precision cryotherapy device in a mouse model with UVB 200 mJ-induced pigmentation-related responses, and evaluating mRNA and protein expression changes of pigmentation-related biomarkers.	After cryotherapy application, gene expression of pigmentation-related biomarkers such as TYR, MITF, MC1R, and c-kit generally decreased, with some exceptions, and protein expression also tended to decrease. Under the study conditions, 0°C for 10 seconds was proposed as the most appropriate condition.	Kwack MH et al., Effect of a Precision Cryotherapy Device with Temperature Adjustability on Pigmentation, Indian Journal of Dermatology, 2022.
Laser combination treatment for pigmented lesions	A split-face short report in 5 subjects with Fitzpatrick skin types III–IV and benign facial pigmented lesions, comparing 785-nm picosecond Nd:YAG laser alone with laser + precision cryotherapy combination treatment.	Four weeks after completion of 5–6 treatment sessions, all 5 subjects were rated as having a higher clinical improvement grade on the laser + cryotherapy combination side than on the laser-only side, and patient satisfaction was higher or equal on the combination side. No adverse reactions were reported during the study period.	Park JW et al., Split-Face Comparative Trial of 785-nm Picosecond Neodymium:Yttrium-Aluminum-Garnet Laser and Precision Cryotherapy Combination Treatment for Facial Benign Pigmented Lesions, Dermatologic Therapy, 2021.