
is an Iceberg.
E-50 PrimaCure

PrimaCure was established in 2021 to meet the scientific interests of our advisory board committee for the latest developments in anti-aging and aesthetics.

Our advisory members from different countries provide anti-aging and aesthetic solutions curated for the specific needs of each region.

All of products are sourced and manufactured in Korea using the highest quality ingredients and stringent safety protocols.

Our products are optimized for maximum effectiveness by utilizing the latest technologies combined with the clinical expertise of our qualified advisory members.

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PrimaCure
OUR MISSION IS TO PROVIDE
THE LATEST ANTI-AGING SOLUTIONS IN AESTHETICS.
WE ARE CONSTANTLY STRIVING TO PUSH THE LIMITS OF NEW AND EXISTING TECHNOLOGIES
TO PROVIDE THE BEST ANTI-AGING AND AESTHETIC SOLUTIONS TO OUR CUSTOMERS.
PARTNERSHIP
INTEGRITY
INNOVATION

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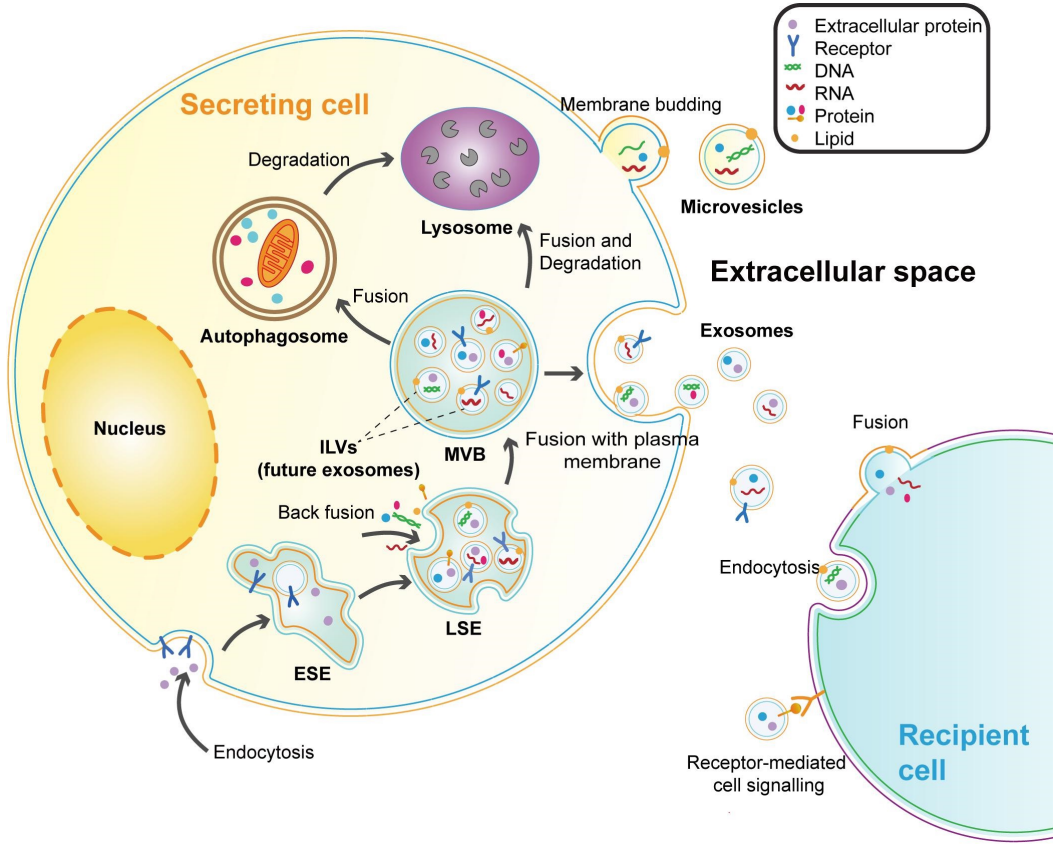
What are Exosomes?

Exosomes contain genetic material, proteins, and lipids

They act as small carriers or packages of information that can travel to other cells and deliver the information.

Exosomes possess a **phospholipid bilayer that enables seamless fusion with recipient cells**, facilitating the transfer of the packages of information.

This mechanism is a way for cells to communicate and influence each other's behavior and functions



Hofmann L, Ludwig S, Vahl JM, Brunner C, Hoffmann TK, Theodoraki M-N. The Emerging Role of Exosomes in Diagnosis, Prognosis, and Therapy in Head and Neck Cancer. *International Journal of Molecular Sciences*. 2020; 21(11):4072. https://doi.org/10.3390/ijms21114072

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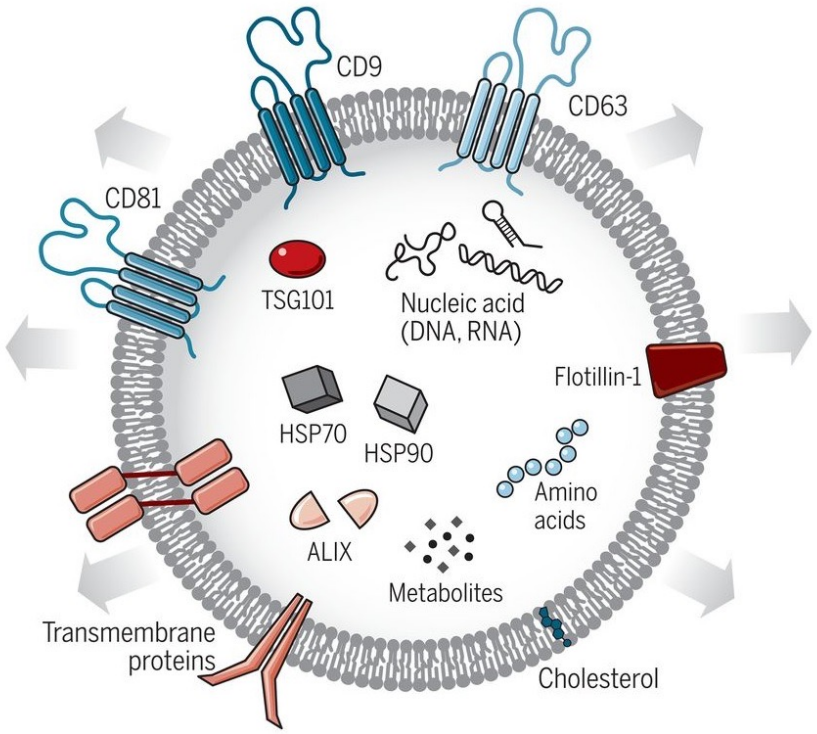
Exosomes: A Breakthrough in Regenerative Aesthetics



Basic structure of exosome

- nucleic acid: mRNA/miRNA/DNA
- lipid raft 30-150 nm

Cellular Therapy

Embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs). However, cell therapies have issues regarding immune rejection, tumorigenesis, and ethical concerns.

Growth Factors

Biggest challenge is their stability. Without a stability system, growth factors will fall apart.

Exosomes

The phospholipid membrane enables seamless fusion of the self-contained reprogramming factors with recipient cells

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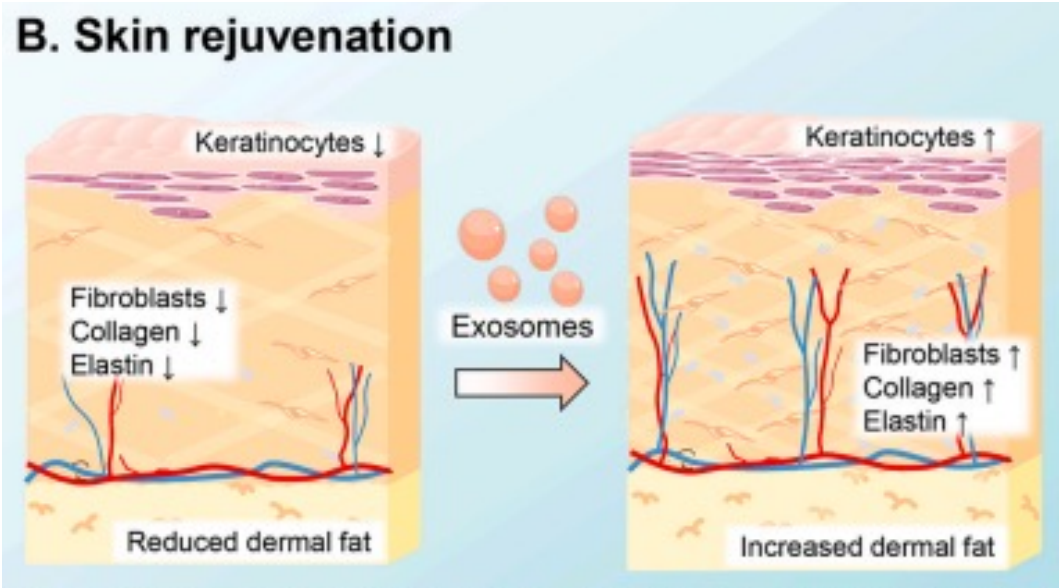
Action of Exosome on the Skin

The novel mechanisms and applications of exosomes

in dermatology and cutaneous medical aesthetics

Mingchen Xiong 1 , Qi Zhang 1 , Weijie Hu 1 , Chongru Zhao, Wenchang Lv, Yi Yi, Yichen Wang, Hongbo Tang * , Min Wu * , Yiping Wu * Department of Plastic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Avenue, Wuhan 430030, Hubei, China



(B) Exosomes improve keratinocytes and fibroblasts function, enhance collagen and elastin synthesis, and increase dermal fat, thus promoting the regenerative and restorative capacity for skin anti-aging.

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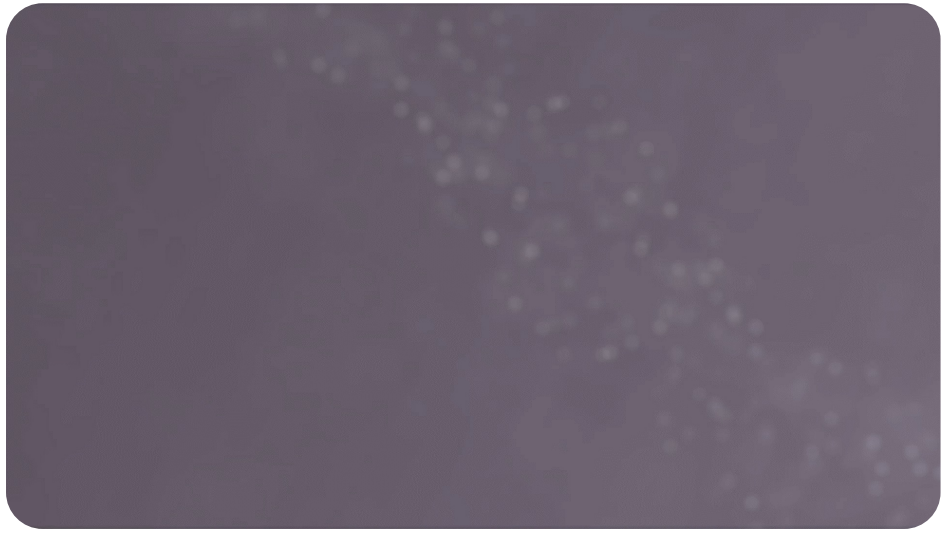
Choosing the Right Exosome

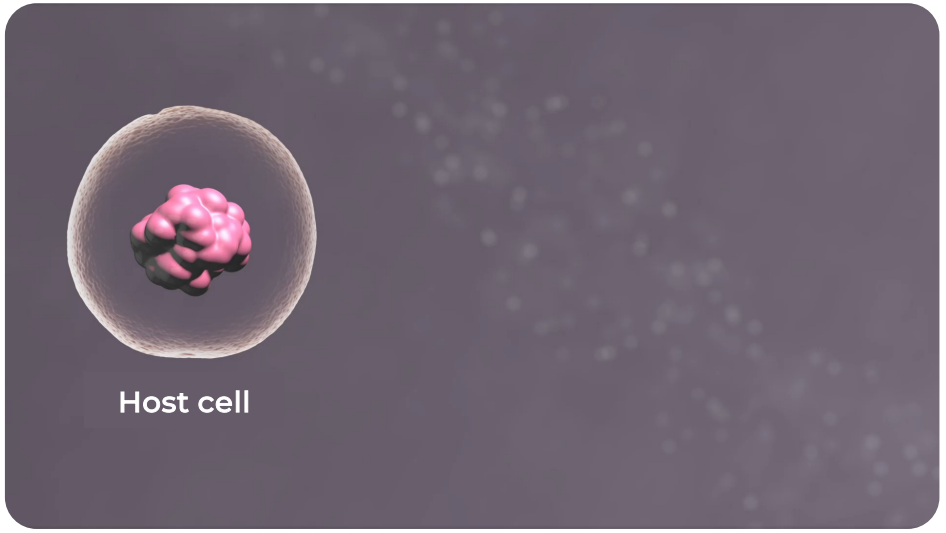
1. Naïve exosomes: Naturally secreted exosomes by cells. (Mesenchymal Stem Cells, Centella Asiatica).

2. Engineered exosomes: Exosomes loaded up with other material such as proteins, nucleic acids, or other biomolecules. (E-50).

3. Personalized engineered exosomes: Exosomes containing customized cargo for specific needs of the individual using mRNA technology. (Future of PrimaCure).



A-MSC Exosome Production



Reprogrammed Exosome Production

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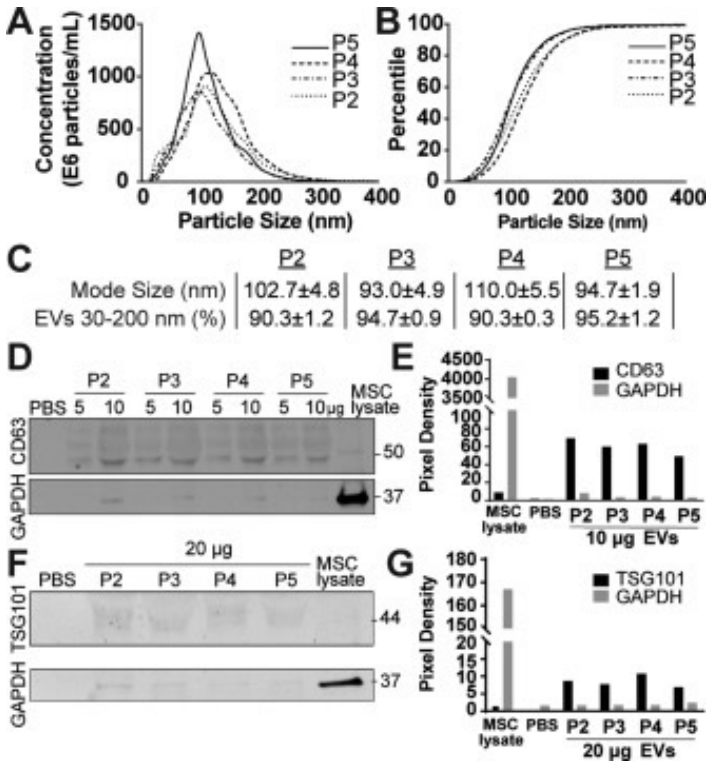
Naive Exosomes (MSCs and Plant Cell derived)



Patel DB, Gray KM, Santharam Y, Lamichhane TN, Stroka KM, Jay SM. Impact of cell culture parameters on production and vascularization bioactivity of mesenchymal stem cell-derived extracellular vesicles. Bioeng Transl Med. 2017 Jun 26;2(2):170-179. doi: 10.1002/btm2.10065. PMID: 28932818; PMCID: PMC5579732.

"The passage number can impact the cargo composition and functions of exosomes, as shown for MSCs. Within five serial passages, the level of the exosome "marker" CD63 was reduced, and the recovered exosome were less potent in stimulating migration of endothelial cells... Cells maintained in long-term cultures and undergoing numerous passages are likely to differ in exosome production."

Yuki Matsuki, Takayo Yanagawa, Hideaki Sumiyoshi, Jumpei Yasuda, Sachie Nakao, Mitsuaki Goto, Teiko Shibata-Seki, Toshihiro Akaike, Yutaka Inagaki,
Modification of exosomes with carbonate apatite and a glycan polymer improves transduction efficiency and target cell selectivity, Biochemical and Biophysical Research Communications, Volume 583, 2021, Pages 93-99, ISSN 0006-291X, https://doi.org/10.1016/j.bbrc.2021.10.063.

1. Host cell dependent
2. Extended time to collect the secreted exosomes
3. High variability of the final product from batch to batch

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E-50 Innovative Skin Booster for Advanced Skin Care

Formulated using the latest technology and the highest quality ingredients.

Customized exosomes that are optimized for skin rejuvenation and Regeneration

Pure exosomes without any impurities for maximum results and safety

Contains Safe and Verified contents.

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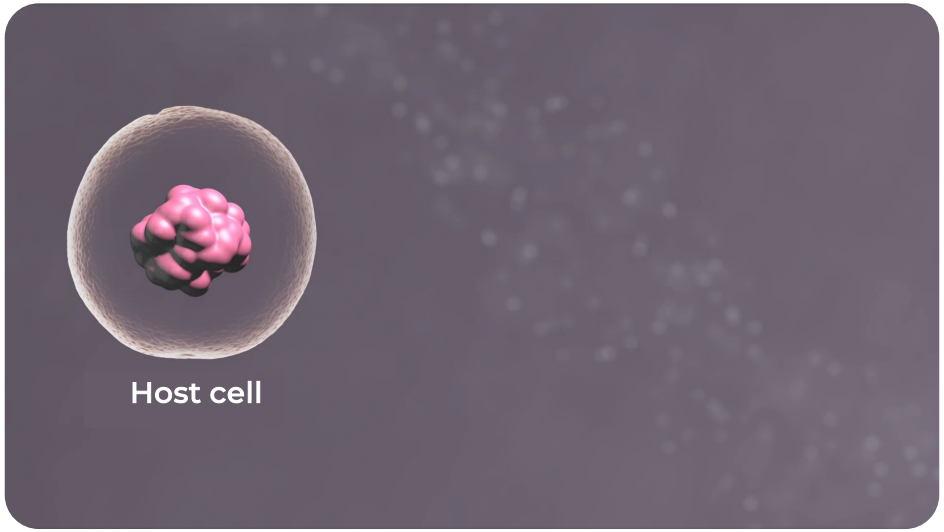
Customized Exosomes Using Patented Technology



Reprogrammed Exosome Production

Exosomes in E-50 are uniquely collected from salmon testes cells.

Salmon cells are safe and compatible in the human body. Salmon Spermatozoa contains highly purified DNA

Utilizing ultrasound and salmon testes cell media enriched with growth factors, cytokines, and peptides, E-50 Exosomes are tailored to specific indications while maintaining batch-to-batch homogeneity of the final product.

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Purity of the Final Product

↑Culture Time = ↓ Exosomal Purity

Exosomes in E-50 are induced from live cells and specific culture media in 12-48 hours.

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Length of Cell Culture Time vs. Purity of Final Product

↑Culture Time = ↓ Exosomal Purity due to Apoptotic bodies

Most cells can exhibit a biochemical pathway which mediates their own destruction…This phenomenon, which has been named apoptosis, accounts for most of the cell deaths that take place during the production of biopharmaceuticals

al-Rubeai M, Singh RP. Apoptosis in cell culture. Curr Opin Biotechnol. 1998 Apr;9(2):152-6. doi: 10.1016/s0958-1669(98)80108-0. PMID: 9588004.

Apoptosis removes many cells every single day, with adult human losses of approximately 50 billion cells on average per day

Raj, D., Brash, D. E. & Grossman, D. Keratinocyte apoptosis in epidermal development and disease. *J. Invest. Dermatol.* **126**, 243–257 (2006).

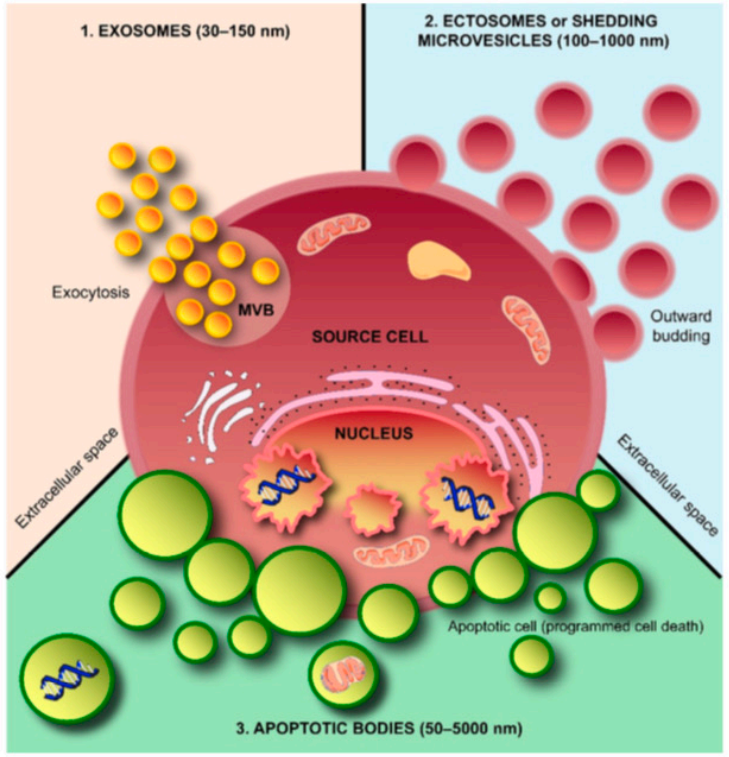

Figure 1. Schematic representation of subtypes of extracellular vesicles (EVs) released by a cell. Three subtypes of EVs, namely exosomes, shedding microvesicles or ectosomes and apoptotic bodies, are known to be secreted by a cell into the extracellular space. Exosomes are released by are known to be secreted by a cell into the extracellular space. Exosomes are released by exocytosis, exocytosis, whereas shedding microvesicles or ectosomes are secreted by outward budding of the plasma membrane. Apoptotic bodies are released by dying cells during the later stages of apoptosis so that cell debris can easily be eliminated by neighboring and immune system cells. MVB: multivesicular body.

Kalra H, Drummen GP, Mathivanan S. Focus on Extracellular Vesicles: Introducing the Next Small Big Thing. *Int J Mol Sci*. 2016;17(2):170. Published 2016 Feb 6. doi:10.3390/ijms17020170

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Apoptotic bodies are formed be during the execution phase of the apoptotic process, when the cell's cytoskeleton breaks up and causes the membrane to bulge outward. These bulges may separate from the cell, taking a portion of cytoplasm with them, to become apoptotic bodies.

Apoptotic bodies contain potentially toxic, enzymatically active or immunogenic components of dying cells into tissues.

Apoptotic Bodies contain proteins and genetic material associated with apoptosis, which can lead to **cytokine storm and inflammation**.

Summers,C.;Rankin,S.M.;Condliffe,A.M.;Singh,N.;Peters,A.M.;Chilvers,E.R.Neutrophilkineticsin health and disease. Trends Immunol. 2010, 31, 318–324.

Witko-Sarsat, V.; Pederzoli-Ribeil, M.; Hirsch, E.; Sozzani, S.; Cassatella, M.A. Regulating neutrophil apoptosis: New players enter the game. Trends Immunol. 2011, 32, 117–124.

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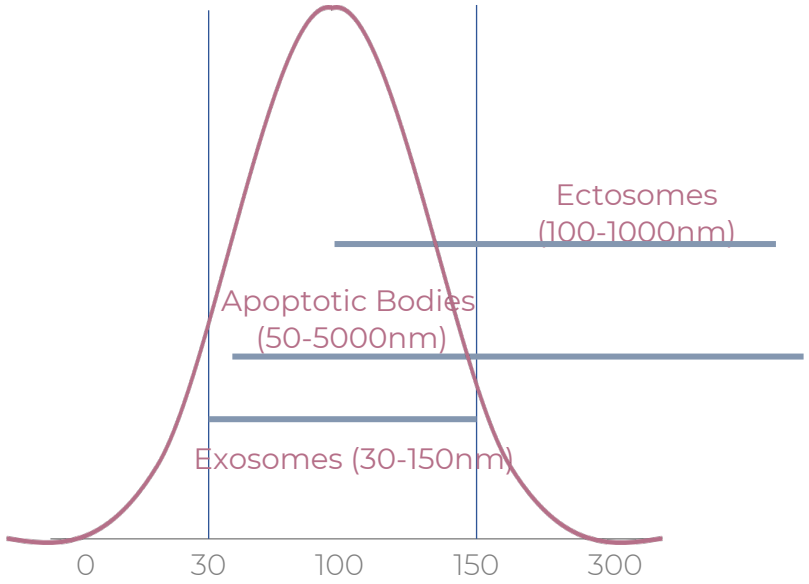
There are no commercially available isolation techniques to isolate only exosomes



"Most current isolation technologies cannot **completely separate** extracellular vesicles derived from non-endosomal pathways, resulting in low exosomal **purity**."

Ludwig N, Whiteside TL, Reichert TE. Challenges in Exosome Isolation and Analysis in Health and Disease. *Int J Mol Sci*. 2019;20(19):4684. Published 2019 Sep 21. doi:10.3390/ijms20194684

"Apart from exosomes, the "exosome samples" prepared via current technique also includes a great number of **non-exosome vesicles such as microvesicles, apoptotic bodies, and ectosomes.**"

Yang, D., Zhang, W., Zhang, H., Zhang, F., Chen, L., Ma, L., Larcher, L.M., Chen, S., Liu, N., Zhao, Q., Tran, P.H.L., Chen, C., Veedu, R.N., Wang, T. (2020). Progress, opportunity, and perspective on exosome isolation - efforts for efficient exosome-based theranostics. *Theranostics*, 10(8), 3684-3707. https://doi.org/10.7150/thno.41580.

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Commercially Available Isolation Methods

Ultracentrifugation

- The only commercially available filtration method to collect exosomes from cell media
- Collects particles via weight and density. Therefore the final collected product will contain ectosomes and apoptotic bodies.

Filtration

- Effective method for collecting only exosomes. However, not very time and cost effective.
- Collects particles via size and volume. And therefore, the final collected product will contain ectosomes and apoptotic bodies.
- May cause sheering to the membrane of the exosomes

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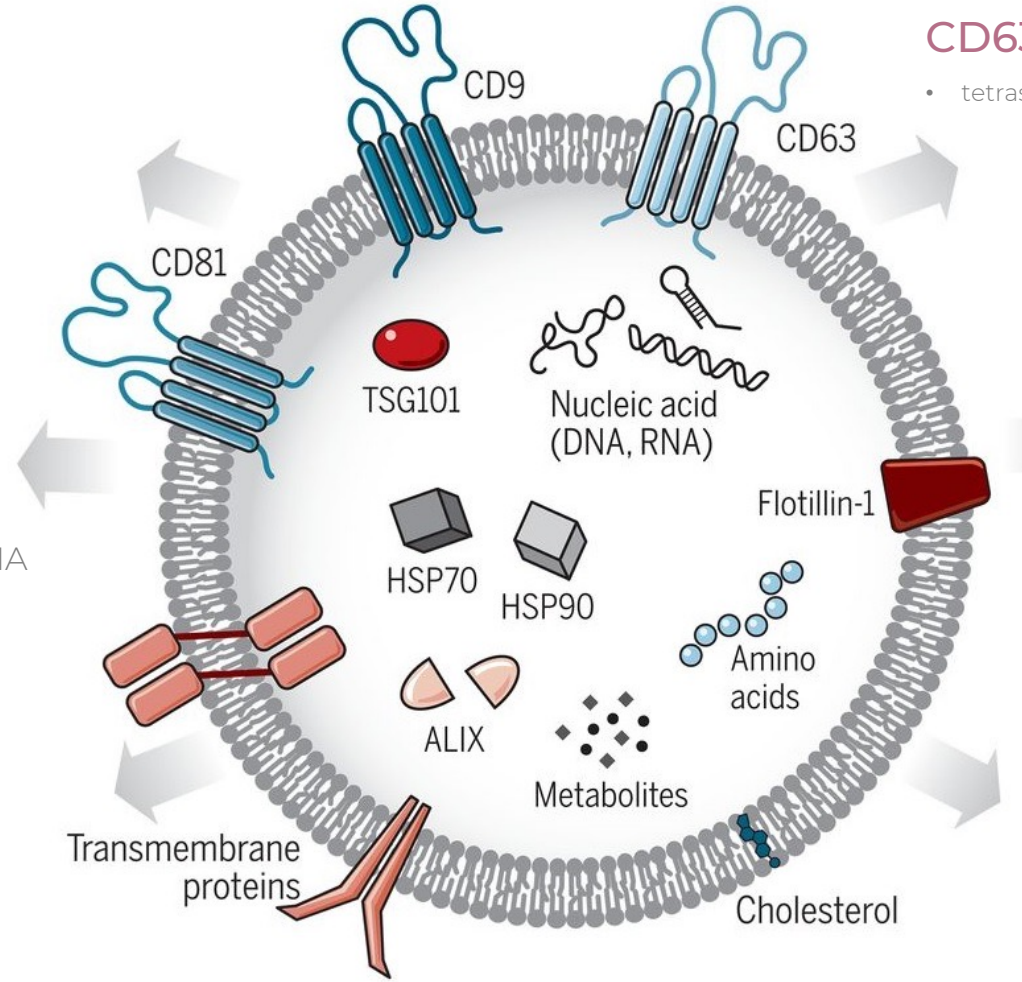
MARKERS FOR ANALYZING EXOSOMES

EXOSOME

Basic structure of exosome

- nucleic acid: mRNA/miRNA/DNA
- 30-150 nm diameter



CD63 Protein Stain

- tetraspanin: CD9/CD63/CD81

Lipid Stain

- Lipid Bi-layer

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SIDE/SIDE

COMPARING THE

Presence of Lipid Bi-layer Particles

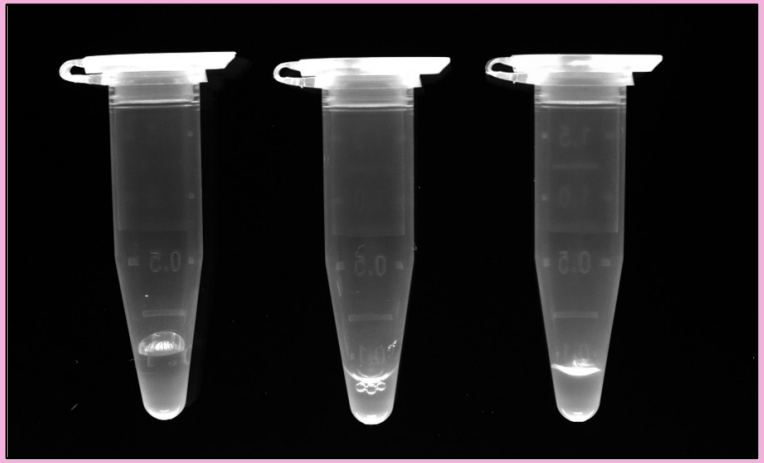
Method:

- Competitor's MSC derived Exosome (MSC-Exo) 1ml was dissolved in PBS, and $5x10^9$ E-50 Exosomes were added to PBS.
- ·After the lipid tracker stain for 30 min, the samples were washed with 15 ml of PBS. Then the exosomes were collected using a particle size-based filtration and added to 100ul of PBS for fluorescent testing

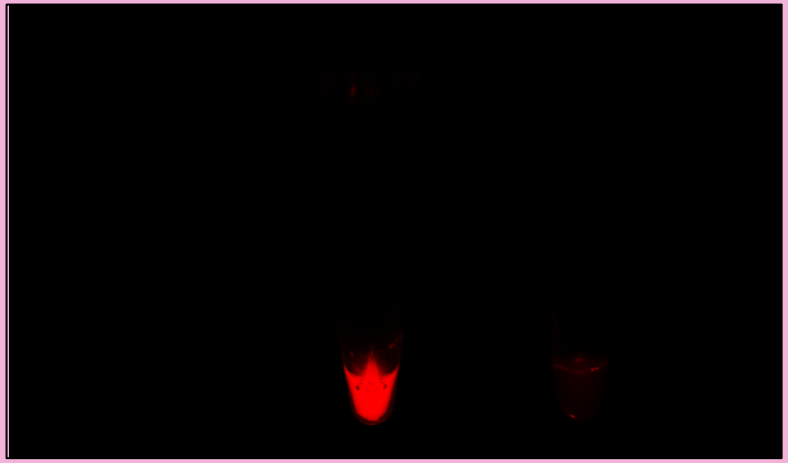
1 Control (PBS; No Exosome)

2 E-50 (approximately $5x10^9$ particles added)

3 Competitor's MSC derived Exosome 1 vial (Advertised to contain $5x10^9$ MSC Exosomes)



1 2 3



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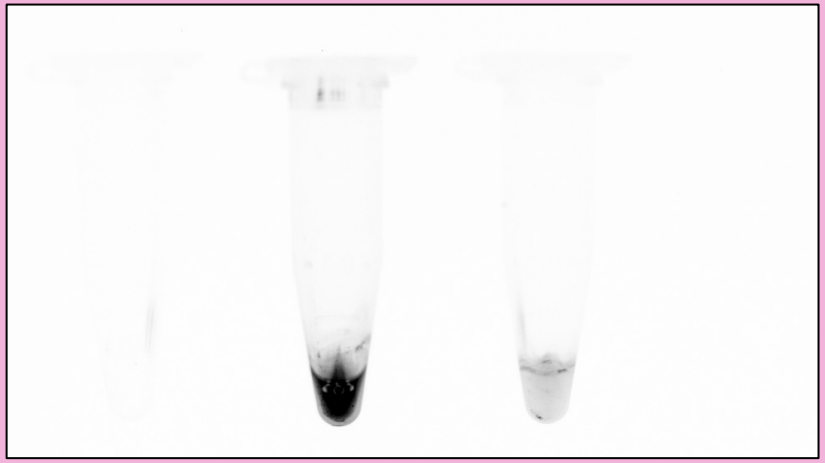

1 2 3

Pure Exosomes for Maximum Safety and Effectiveness

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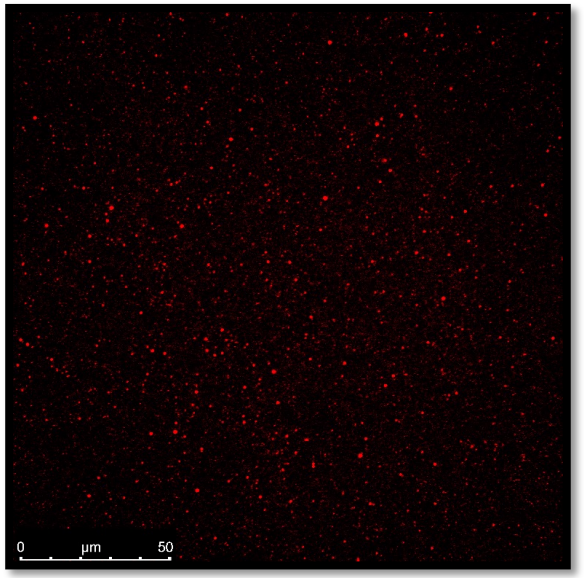
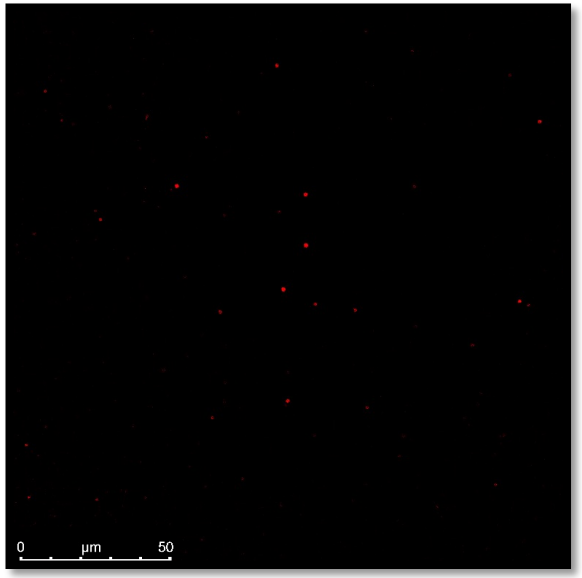
Testing for the presence of **“Real Exosomes”**, particles with CD 63 surface proteins.

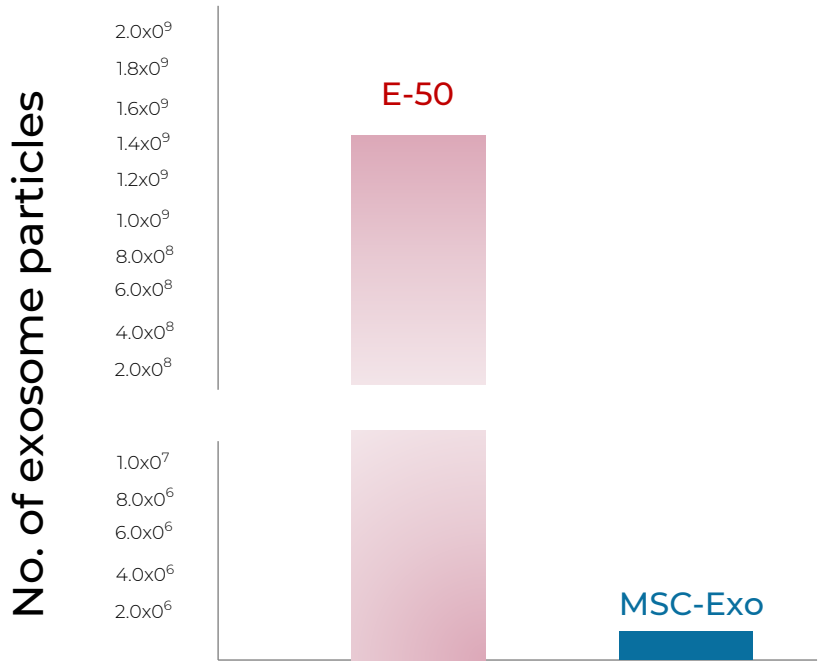
E-50



MSC-Exo



E-50 Contains 10,000+ times more exosomes than MSC-derived competitor



	E-50	MSC-Exo
Avg	$1.43x10^9$	$8.71x10^5$
Std Error	$\pm 3.17x10^8$	$\pm 6.31x10^4$

Testing the Number of Exosomes using ISEV 2018 Guidelines

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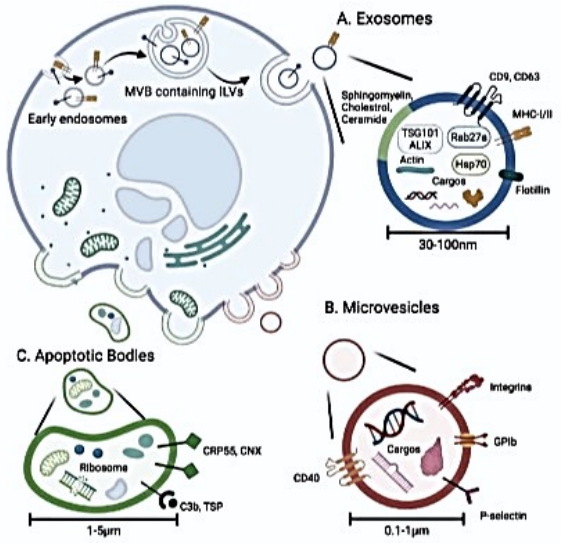

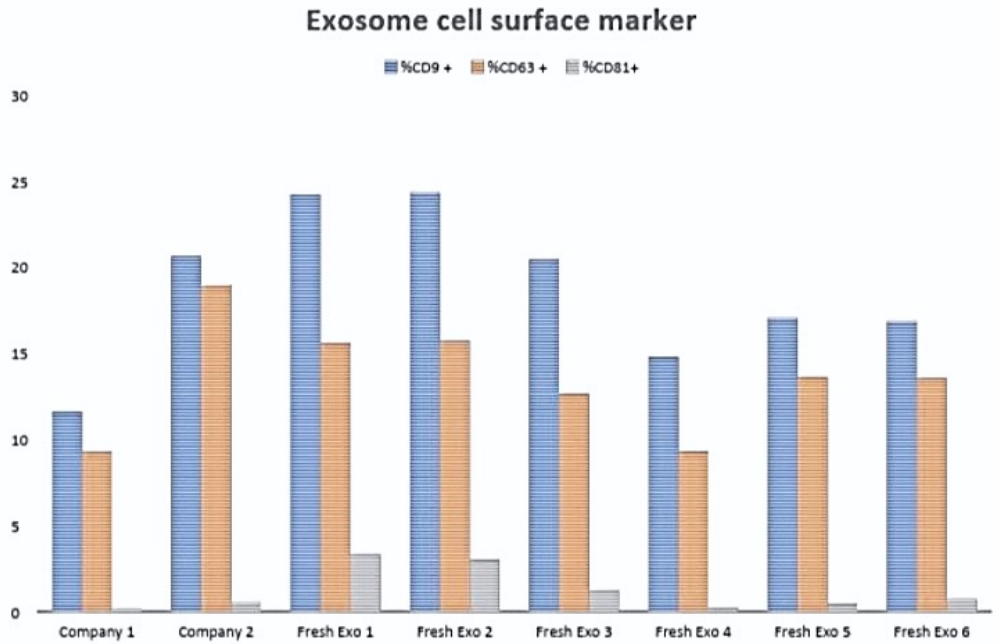

Independent Study conducted at Thammasat University Biochemistry Department in Bangkok, Thailand

Fresh Exo 1-6: Control group. Fresh Exo 1-3 derived from fat tissue sample preserved at -80 C for 7 days. Fresh Exo 4-6 derived from amniotic fluid preserved at -80C for 7 days.
Company 1: ASCE+
Company 2: E-50 Skin Booster

E-50 Skin Booster contains 2X number of real exosomes vs ASCE+

E-50 Pipeline

1. E-50 Skin Booster: Reprogrammed exosomes collected from Salmon Testes Cells for skin rejuvenation and anti-aging
2. E50-H for Hair: Reprogrammed exosomes collected from Salmon Testes Cells to promote increase in hair density and thickness
3. E50-W for Whitening: Reprogrammed exosomes collected from Salmon Testes Cells to promote skin brightening.

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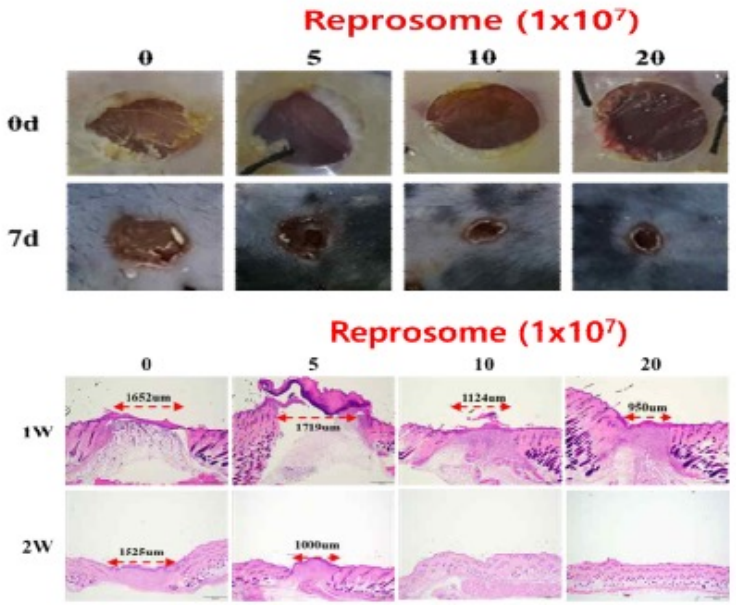
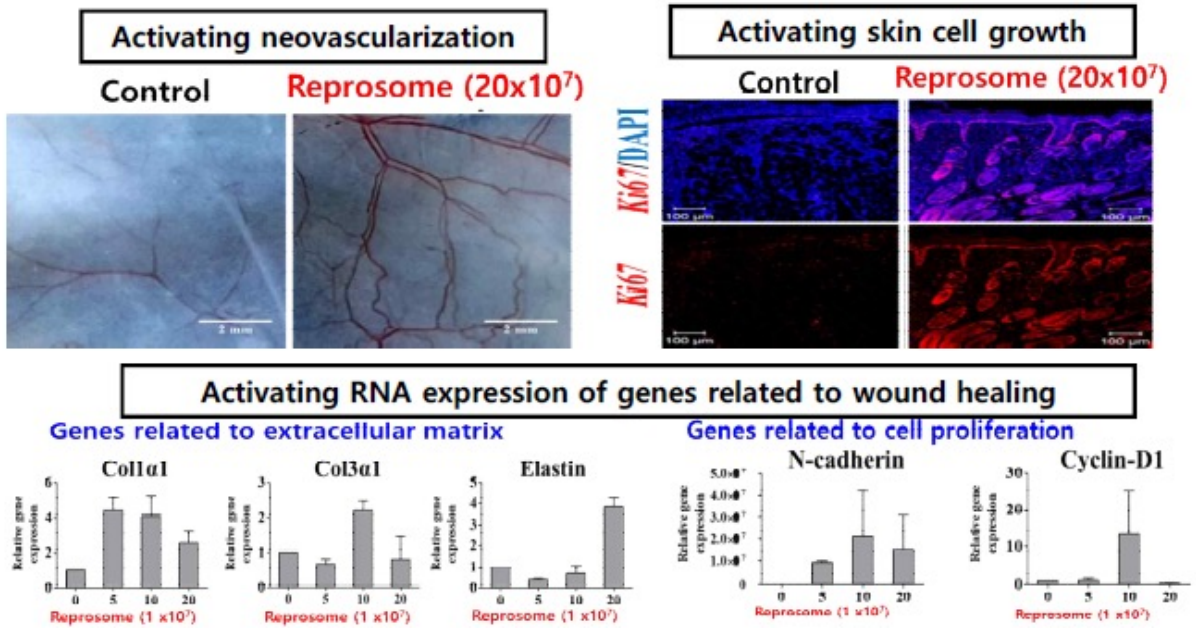
E-50 Wound Healing Study

Great effect on wound healing in C57 mice by spraying reprosomes on skin

Reprosomes promoting the recovery of injured skin tissue



Activation factors related to skin tissue regeneration



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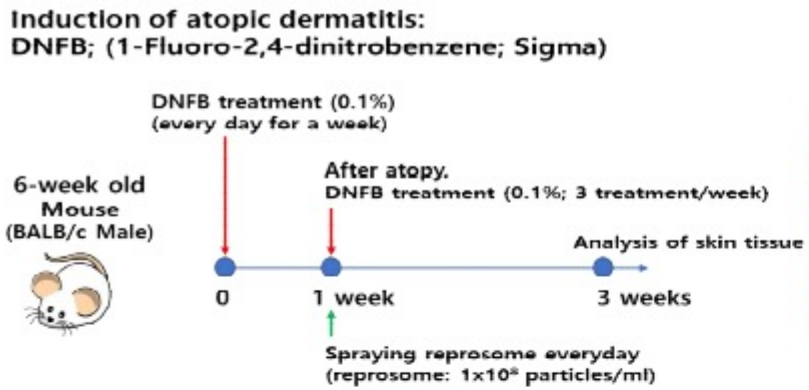
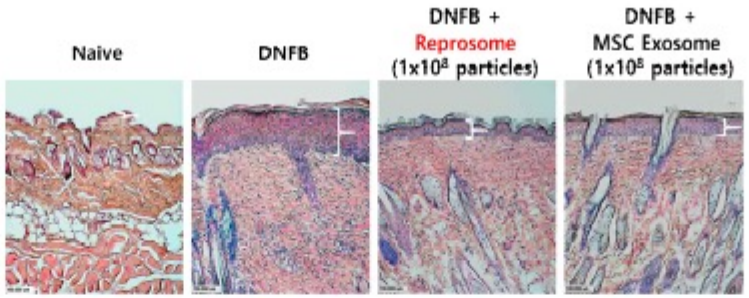
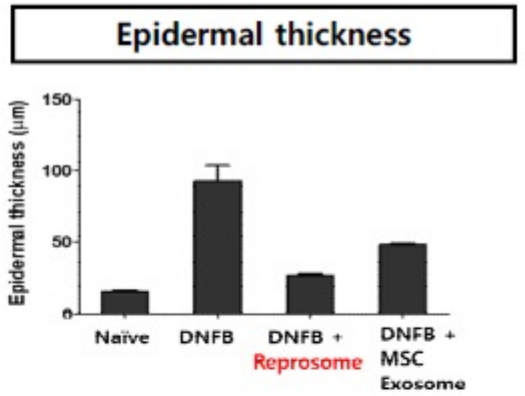
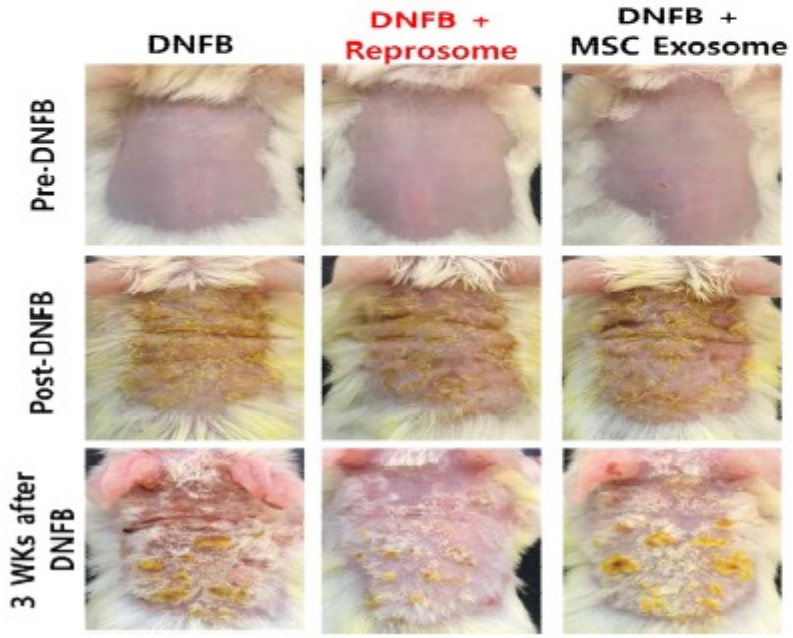
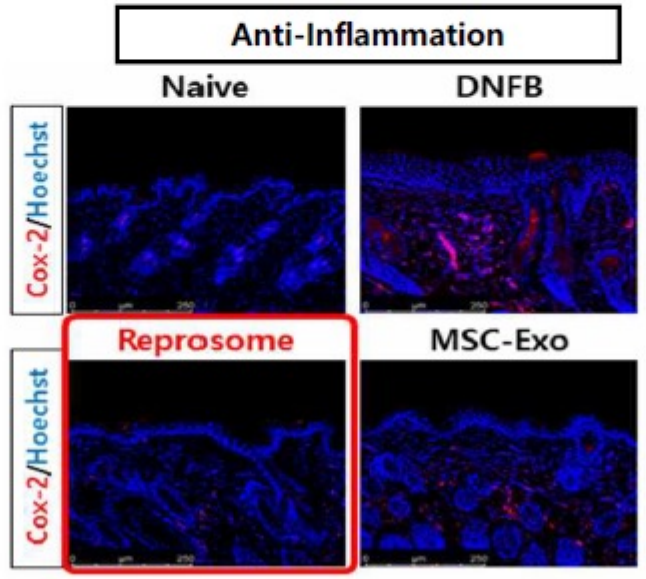
E-50 Effects on Atopic Dermatitis

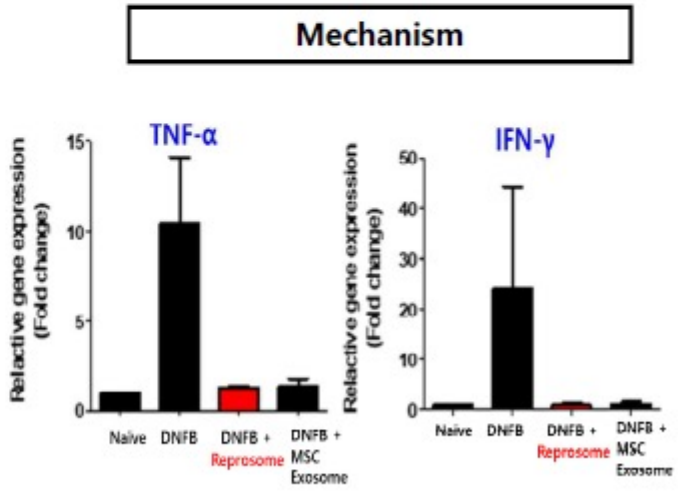








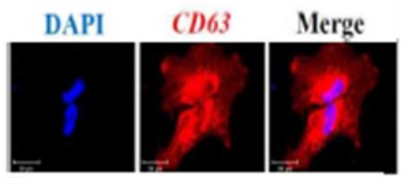


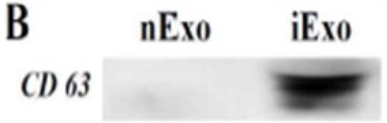


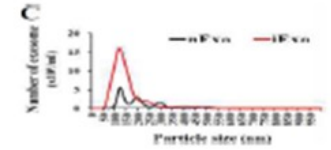
E50-H for Hair

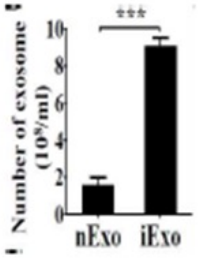
Massive induction of reprosomes containing reprogramming factors for hair follicles

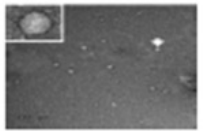
Hair follicle differentiation media-based treatment induced massive production of exosome

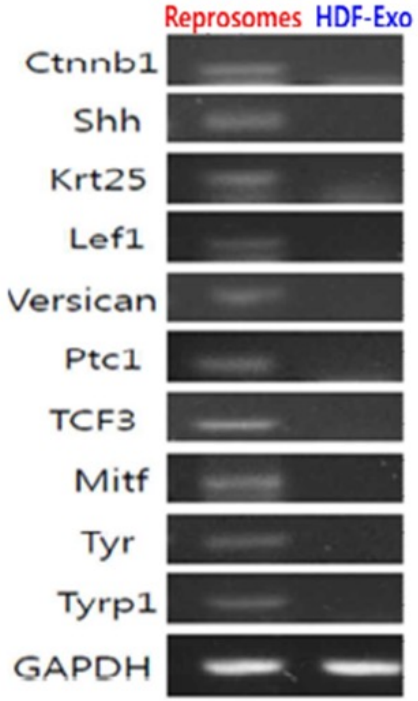




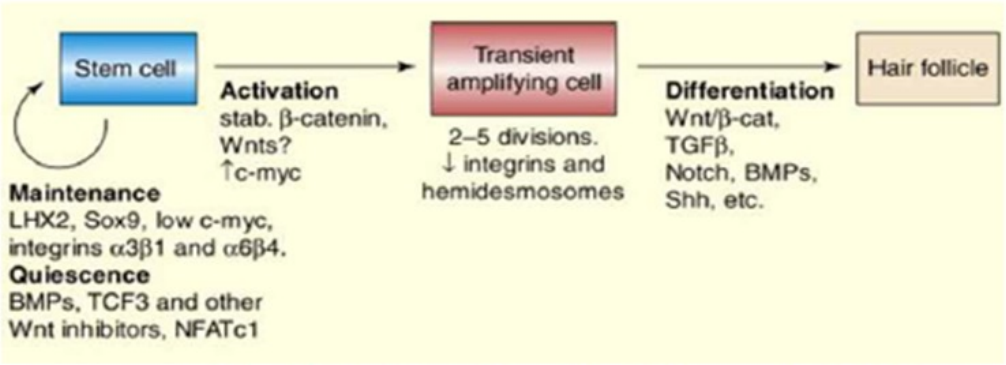


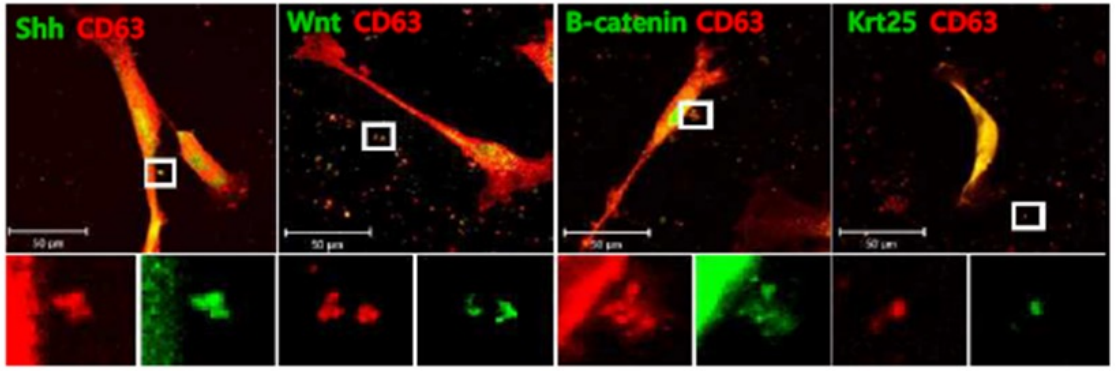






Reprosomes containing various reprogramming factors for hair follicles

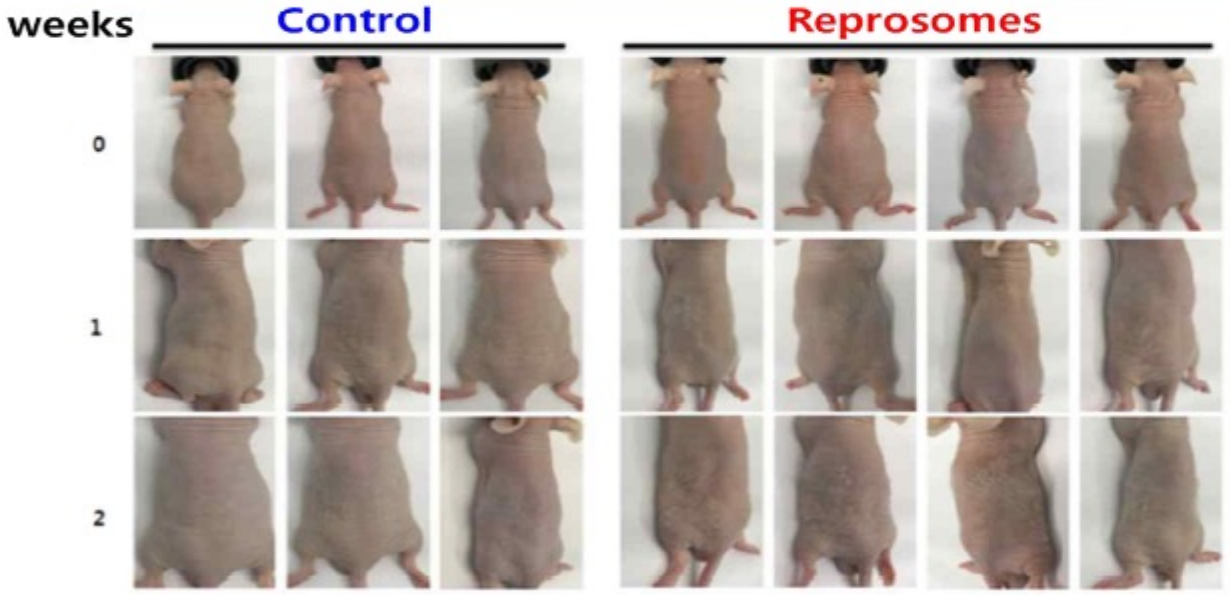




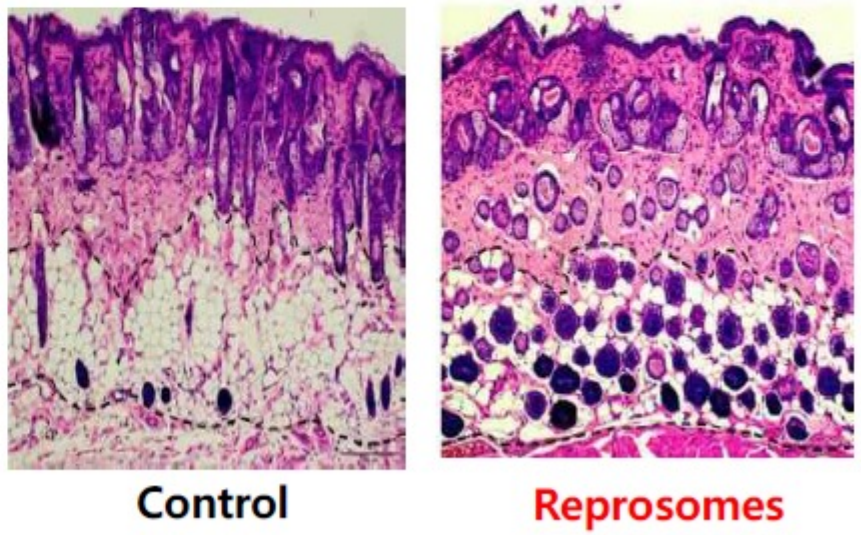
E50-H for Hair Animal Study

Great effect of hair regeneration by reprosomes

Hair growth-promoting activity by spraying reprosomes on skin



Activating hair follicle regeneration by reprosomes



Control Reprosomes

The first success case of hair growth using a nude mouse

E-50 Safety inspection (determined as non-toxic)

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Test items	Company	Test result
Single dose toxicity test (rat-dermal)	Biotoxtech	No abnormality
13-week repeated dose toxicity test (rat-dermal)	Biotoxtech	No abnormality
Skin sensitization test (LLNA-alternative test method)	Biotoxtech	No abnormality
In vitro 3T3 NRU phototoxicity test (alternative test method)	Biotoxtech	No abnormality
Photosensitization test	Biotoxtech	No abnormality
Return mutation test	Biotoxtech	No abnormality
Chromosomal abnormality test	Biotoxtech	No abnormality
Micronucleus test	Biotoxtech	No abnormality
Skin irritation test (alternative test method)	Biotoxtech	No abnormality
Eye irritation test (alternative test method)	Biotoxtech	No abnormality
Human patch test	KDRI	Hypoallergenic det ermination
COA	**Company**	**Test result**
Mycoplasma residual test	BIOPS	No abnormality
Sterility (fungal, bacterial) test	BIOPS	No abnormality
Virus residual test (in vitro)	BIOPS	No abnormality
Virus residual test (in vivo)	KNOTUS	No abnormality

* KDRI (Korea Dermatology Research institute)

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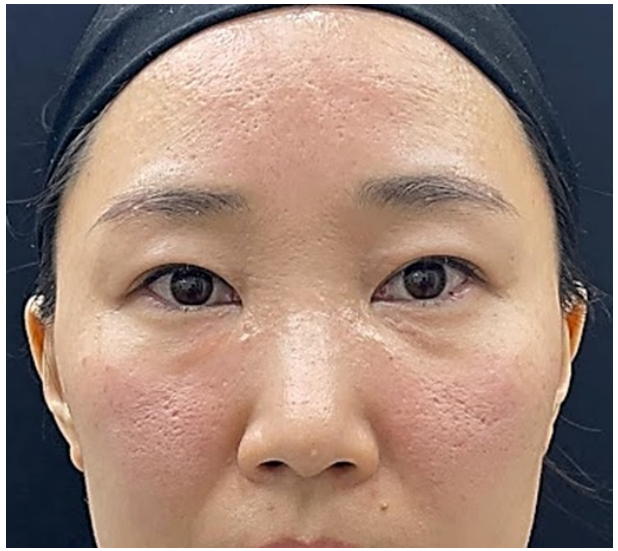
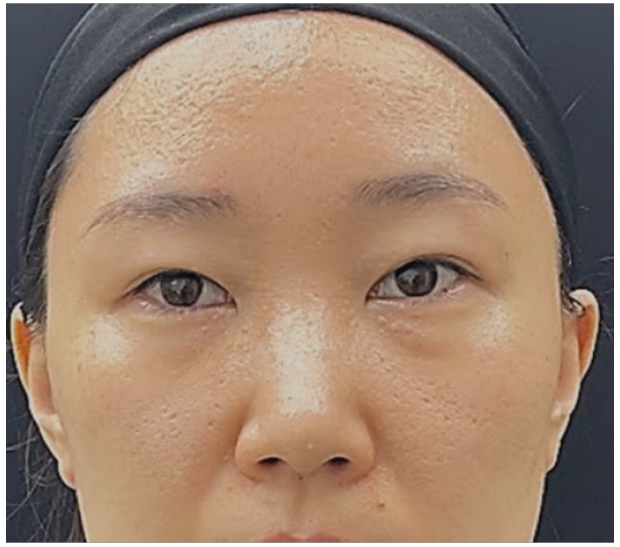
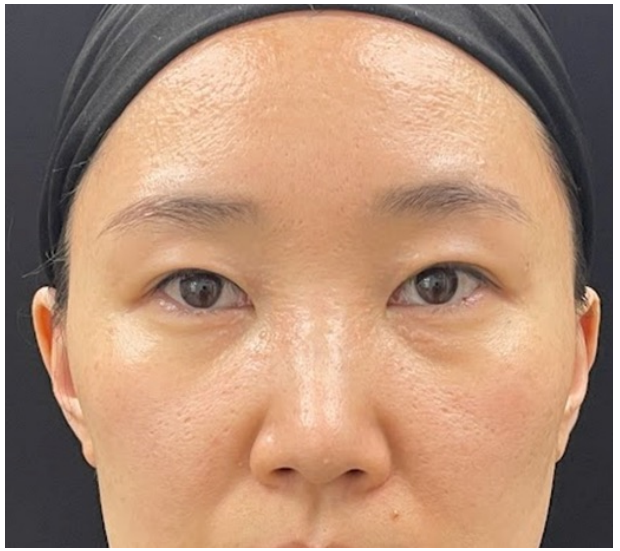
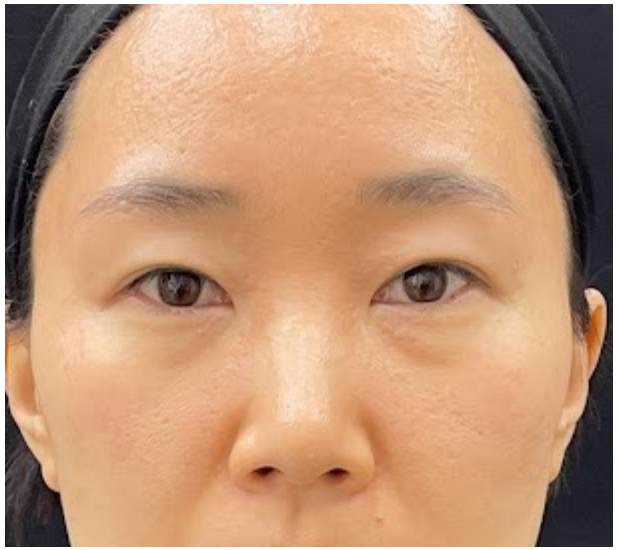
CLINICAL CASES

E-50 improves keratinocytes and fibroblasts function, enhances collagen and elastin synthesis, and increase dermal fat, thus promoting the skin’s regenerative and restorative capacity.

PrimaCure

LARGE SKIN PORES

Before and After

1st Treatment	2nd Treatment	No Treatment	
			
Before	After 3 wks	After 6 wks	After 6 Mo

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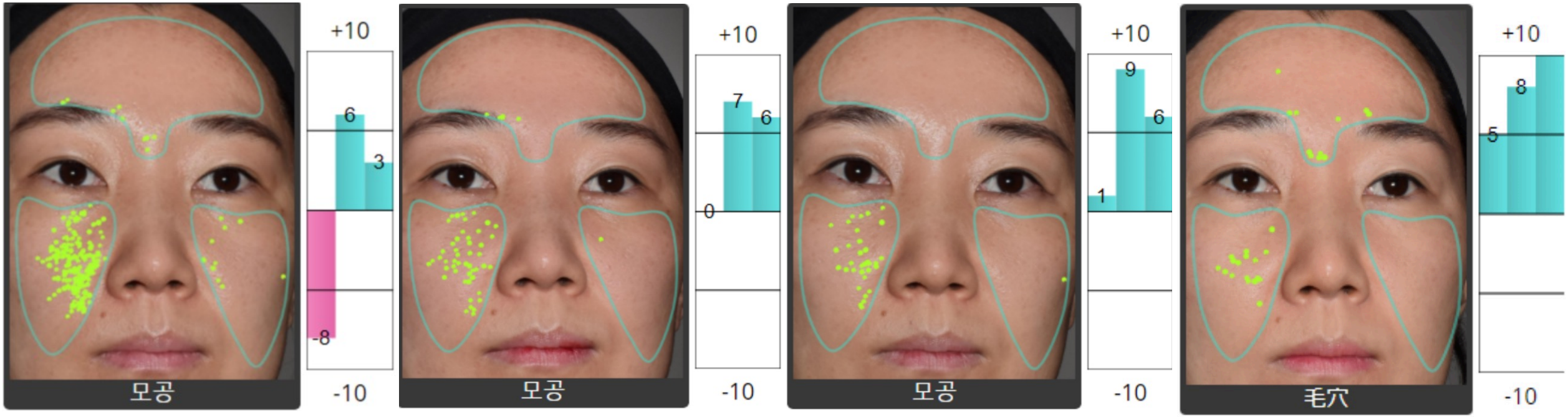
QuantifiCare Skin Pore Analysis

Before and After



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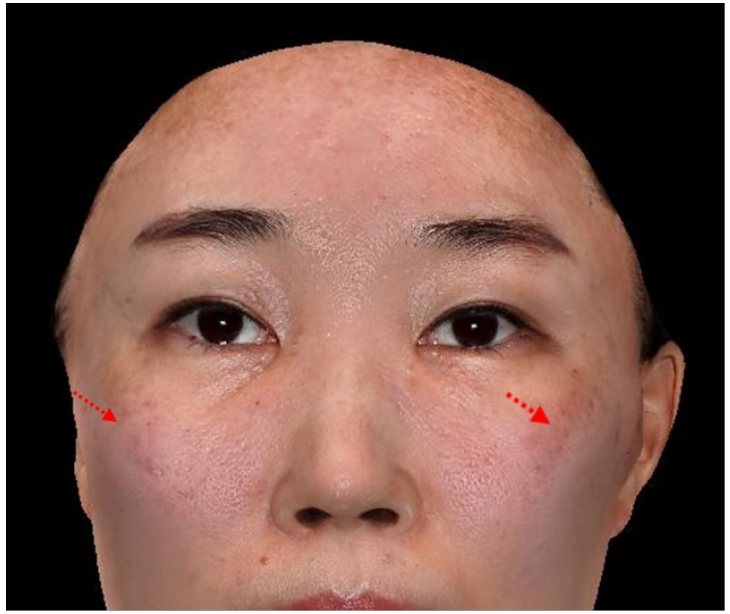
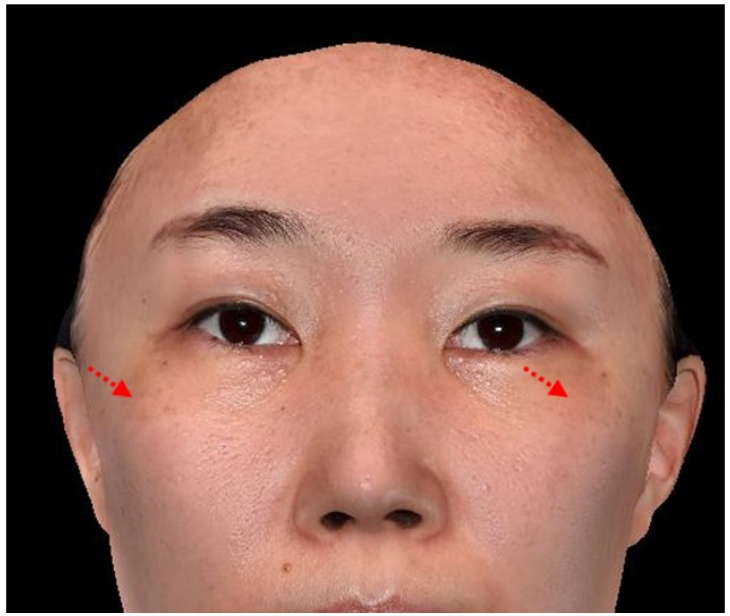
QuantifiCare Dark Spot Analysis

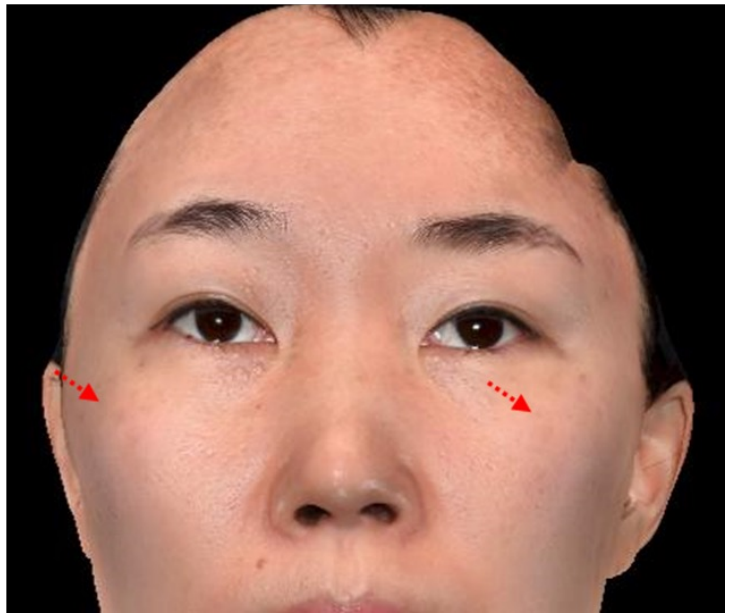
Before and After



Before



After 6 wks



After 6 Mo

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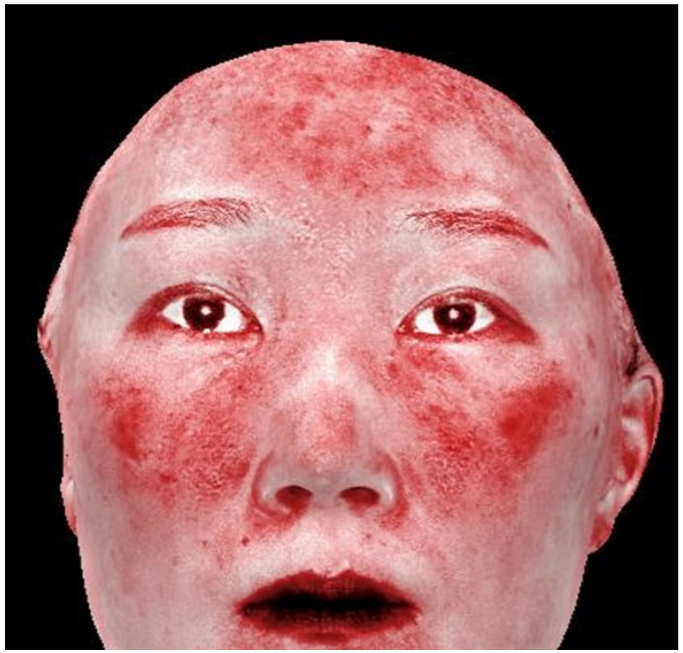
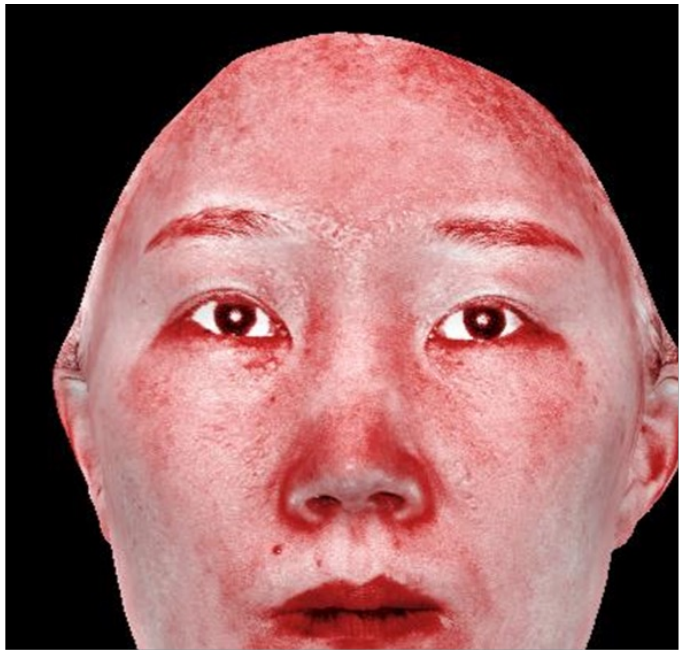
QuantifiCare Skin Flushing Analysis

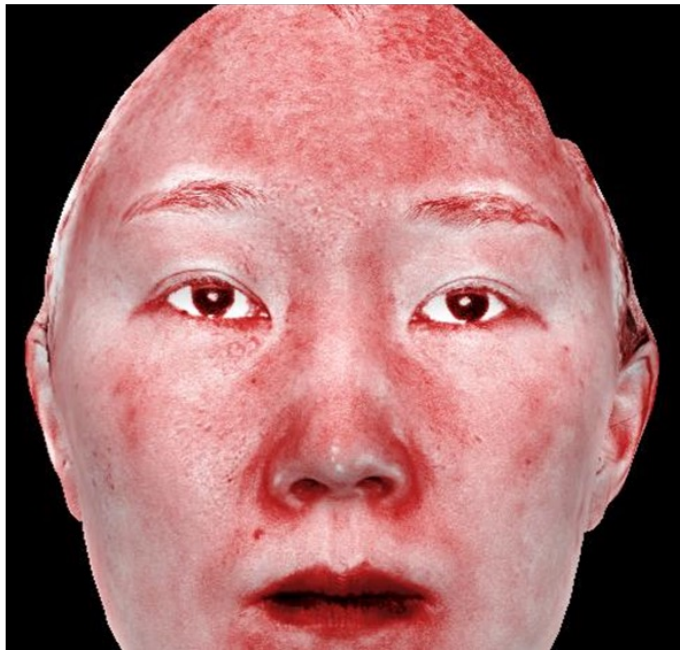
Before and After



Before



After 6 wks



After 6 Mo

Rosecea

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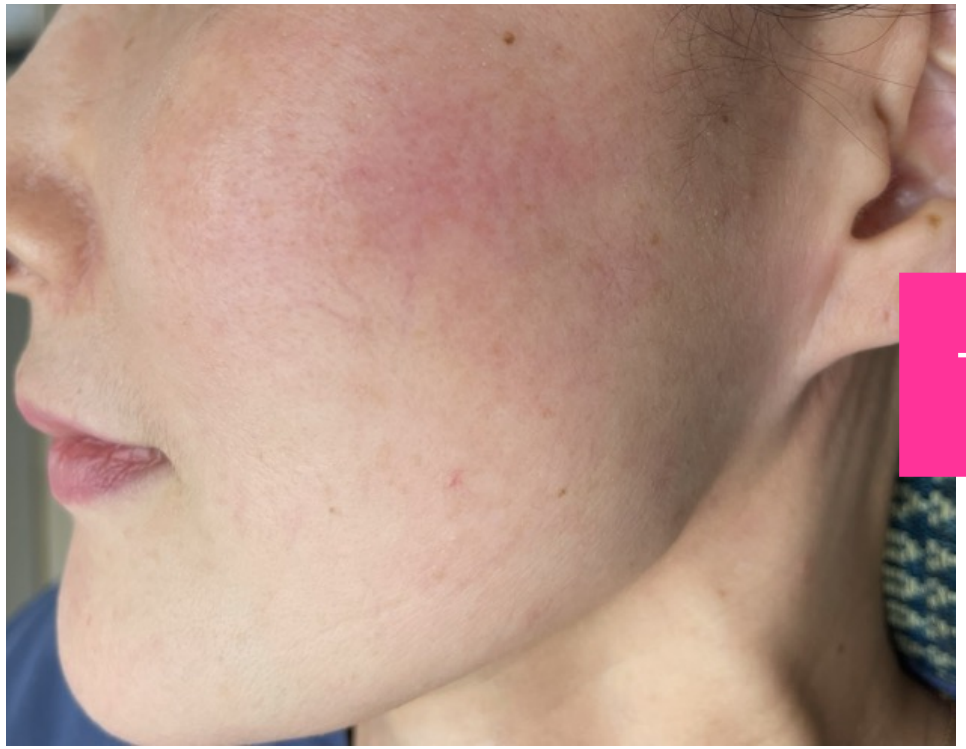
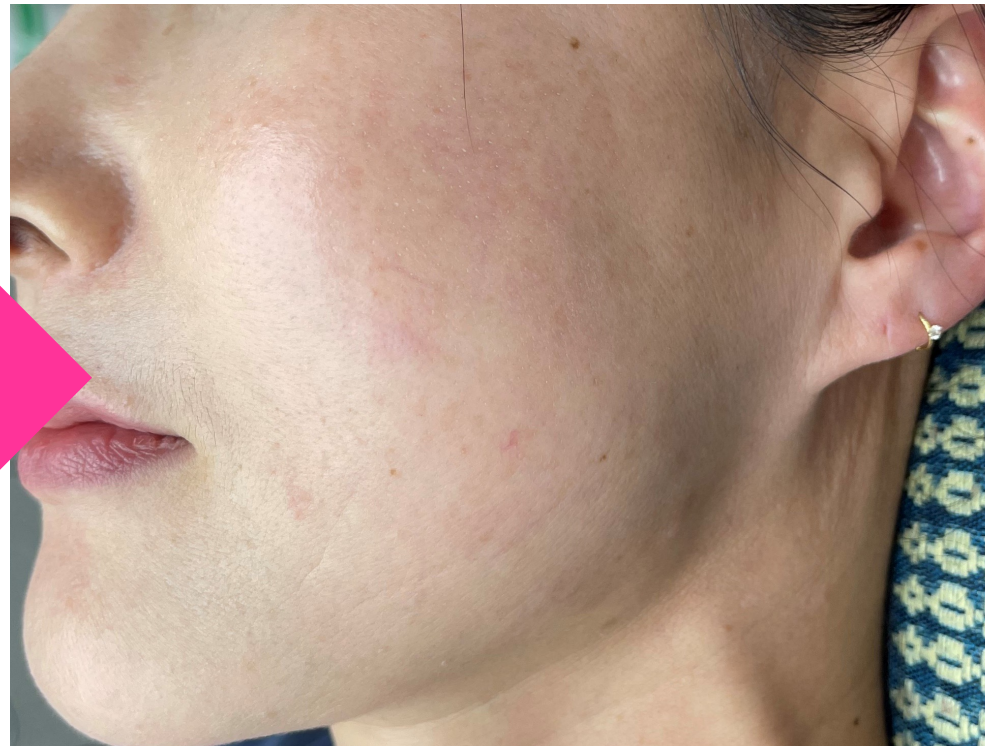
Before and After



1 Month



26.Nov.22

27.Dec.22

Telangiectasia

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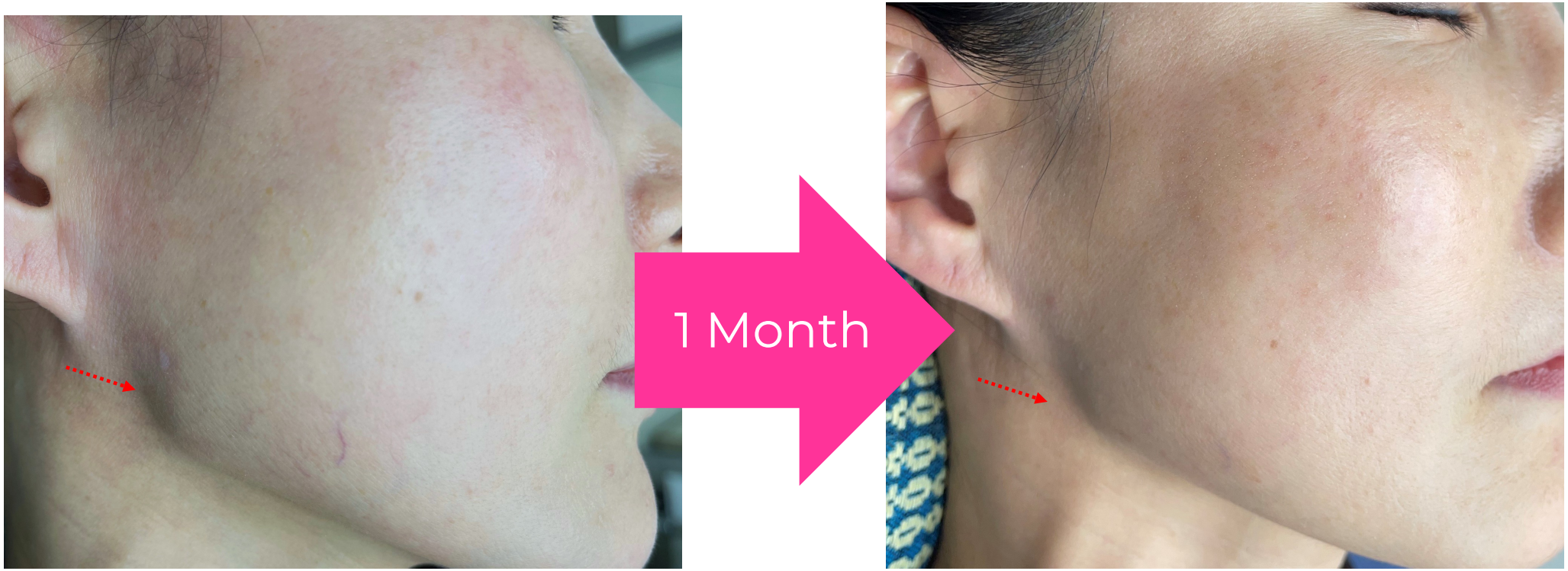
Before and After



26.Nov.22

27.Dec.22

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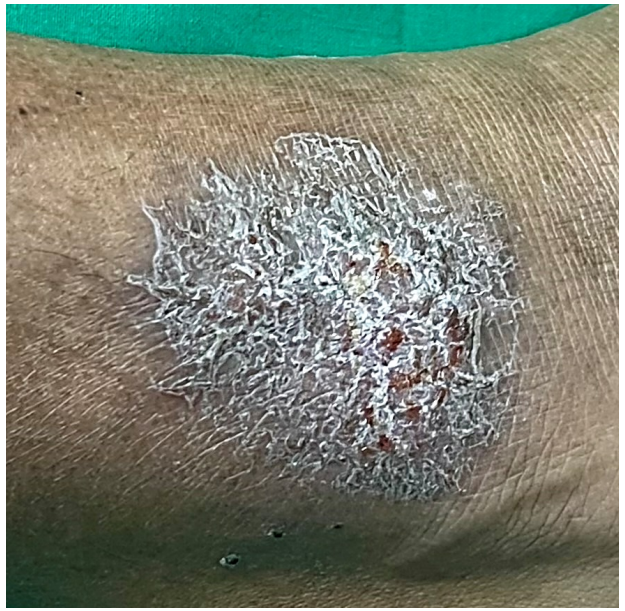
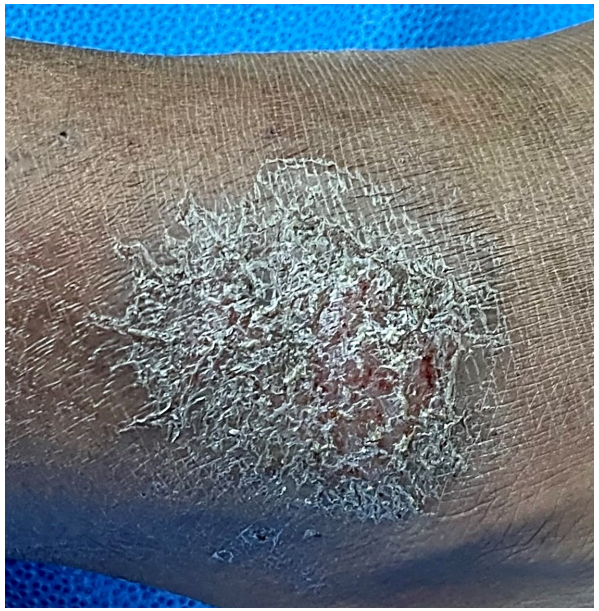
Chronic Eczema treatment

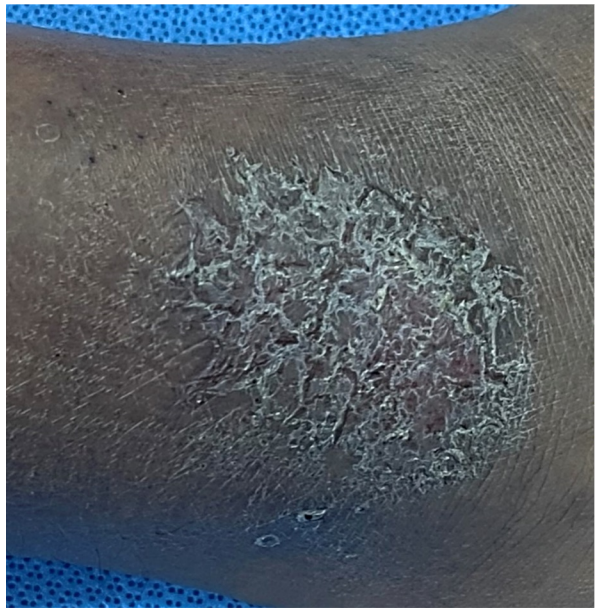
Before and After 1day. 2days 3rd days: 7days Only 2 times treatment



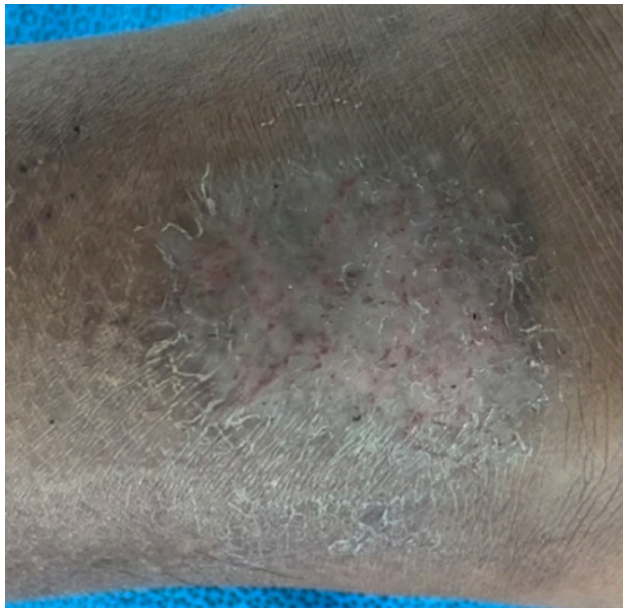
Before



After 1 day



After 2 days



After 2 Mo

Comedogenic Acne

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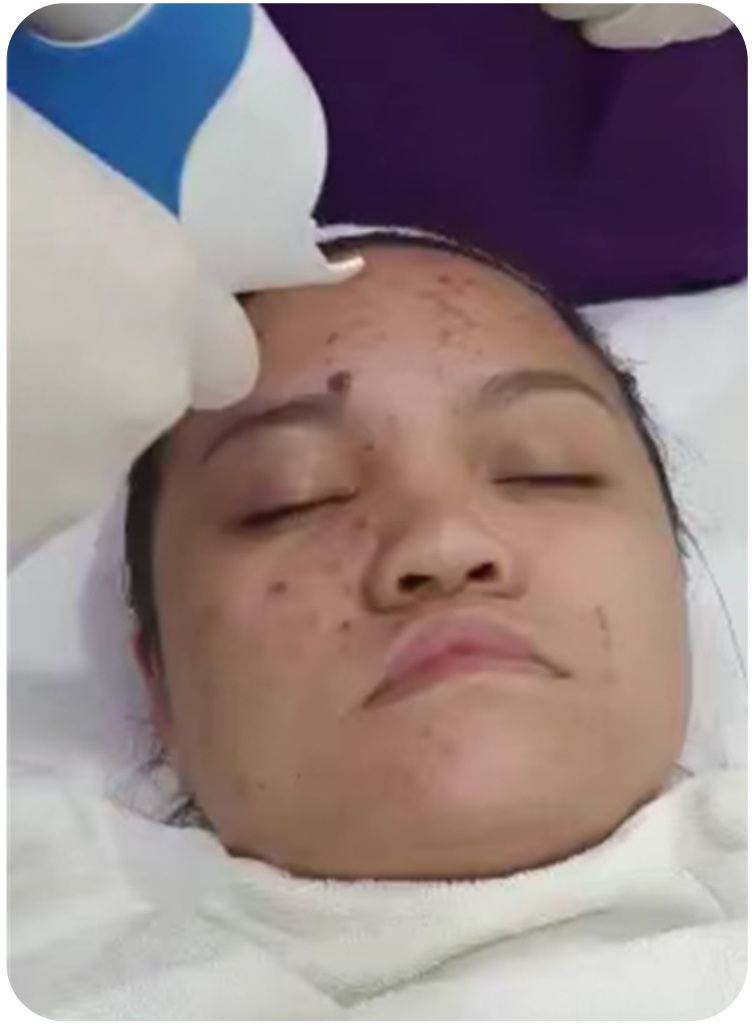

Auto MTS + E-50

(Microneedle Therapy System)

.toey
ttroublettaker

I mean it's depend on patient behavior and cause of acne; like if her cause of acne from irritant to some cosmatics, if she stop it'll be better in a 1-2 weeks. But if the cause mainly from hormonal issue, it probably take times.

because there's a new acne eruption if she doesn't continue using topical therapy

but at the clinic for 1 time treatment acne like this; I always do extraction + injection + vbeam + LED (red) 20 min + prescribe topical treatment.

Mostly I always make 1-2 weeks follow-up, and see better results around 2 weeks with proper combination therapy, in case that there's is no new active acne eruption.

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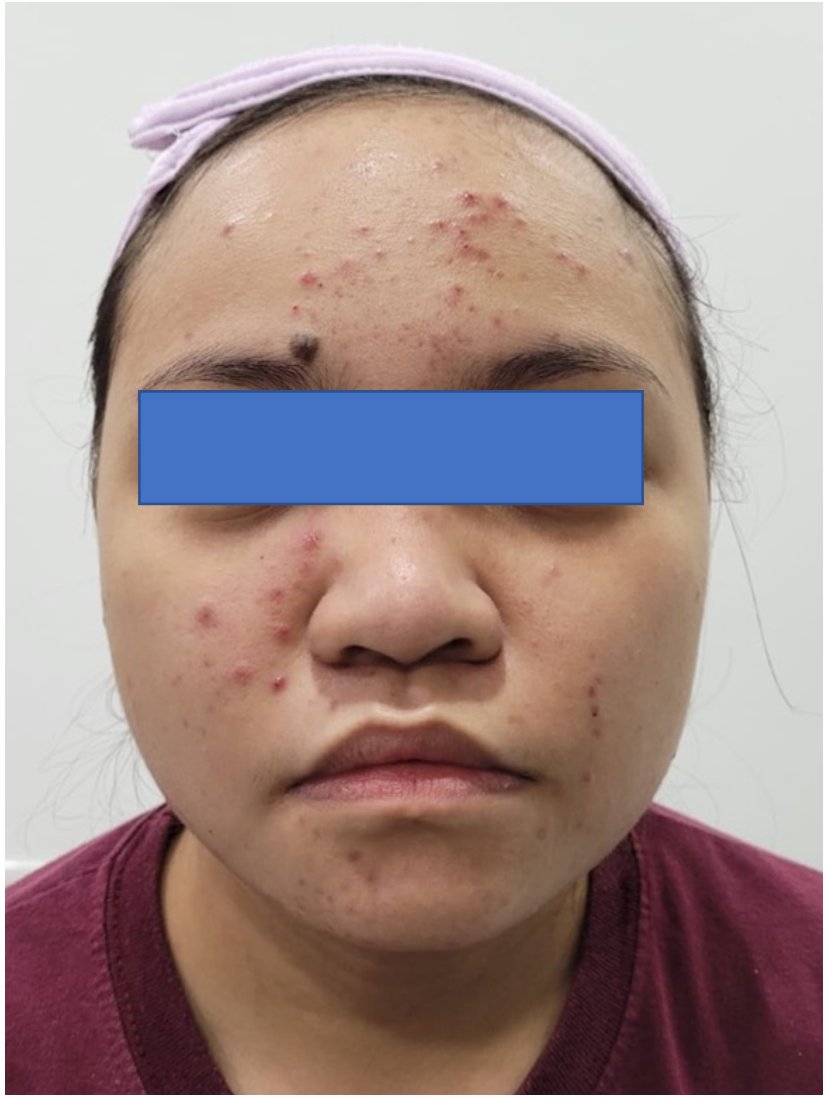
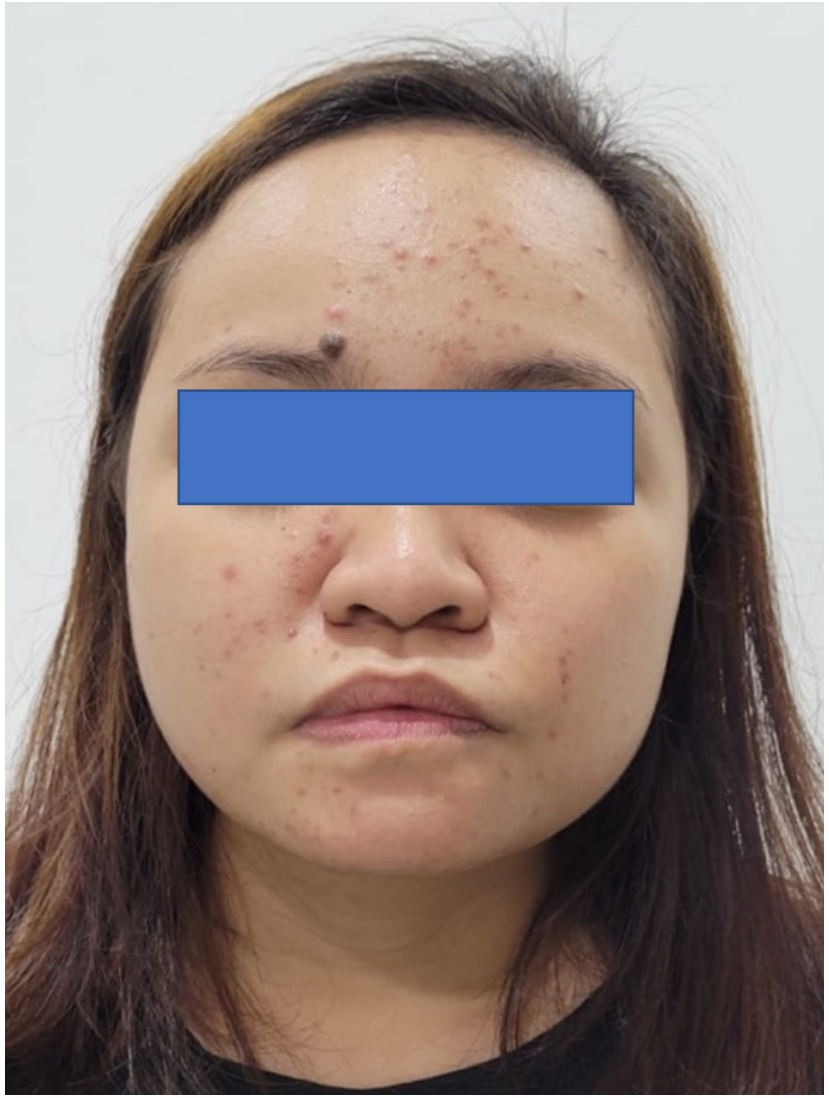


Before



After 3 days

Wound Healing After LASER

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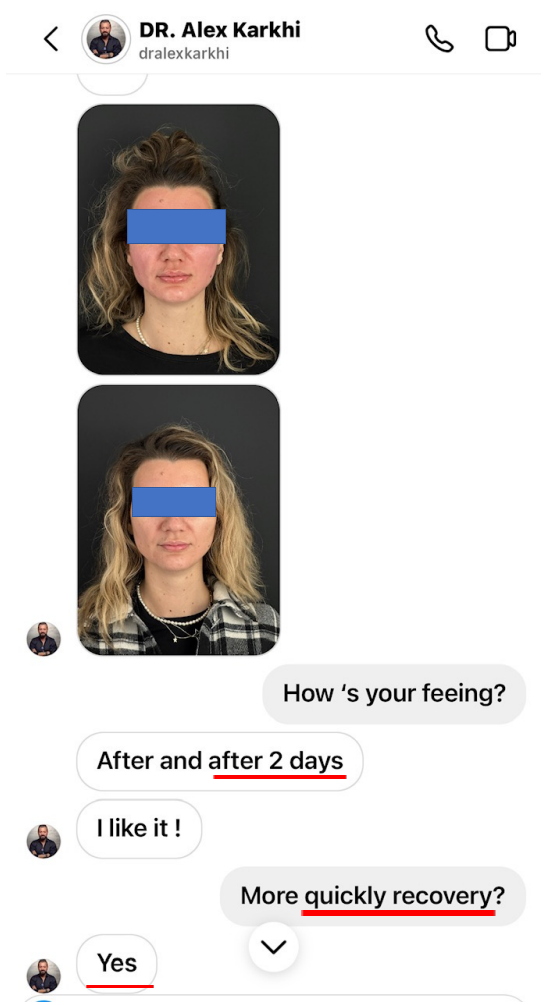
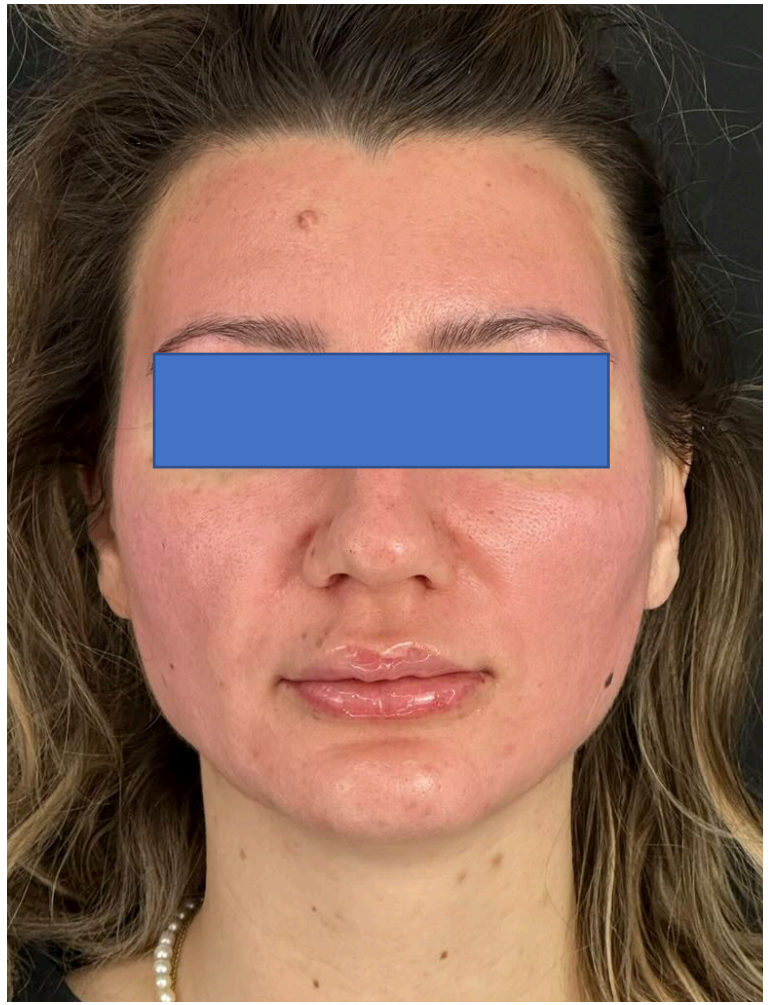
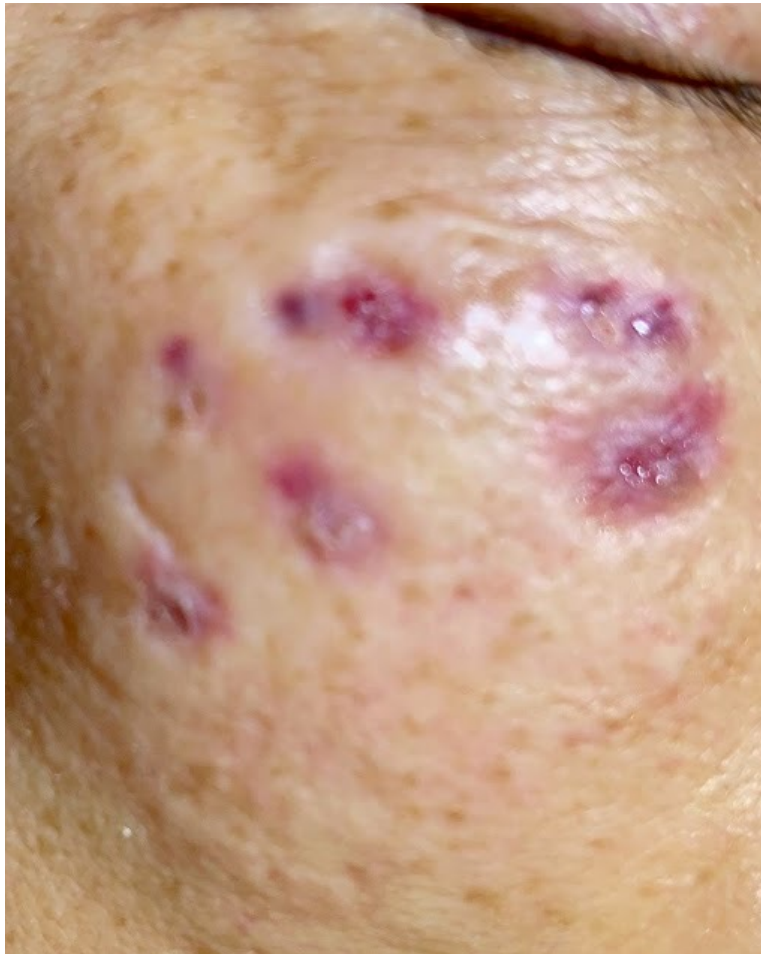


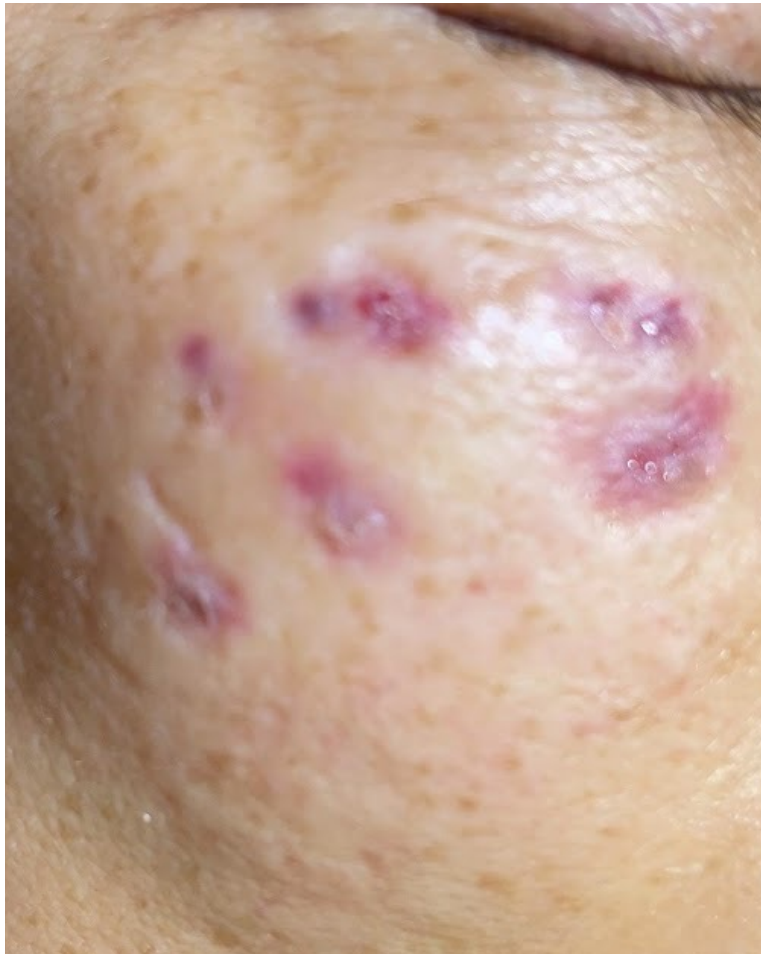


Skin

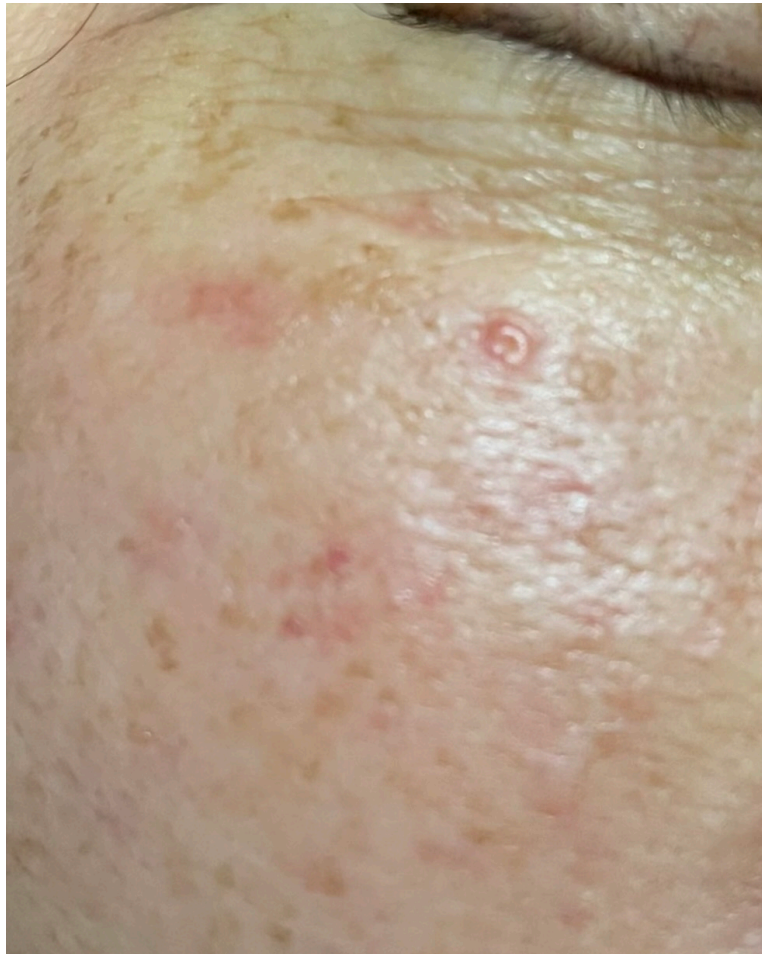
Wound Healing After Cauterization of Warts



Before



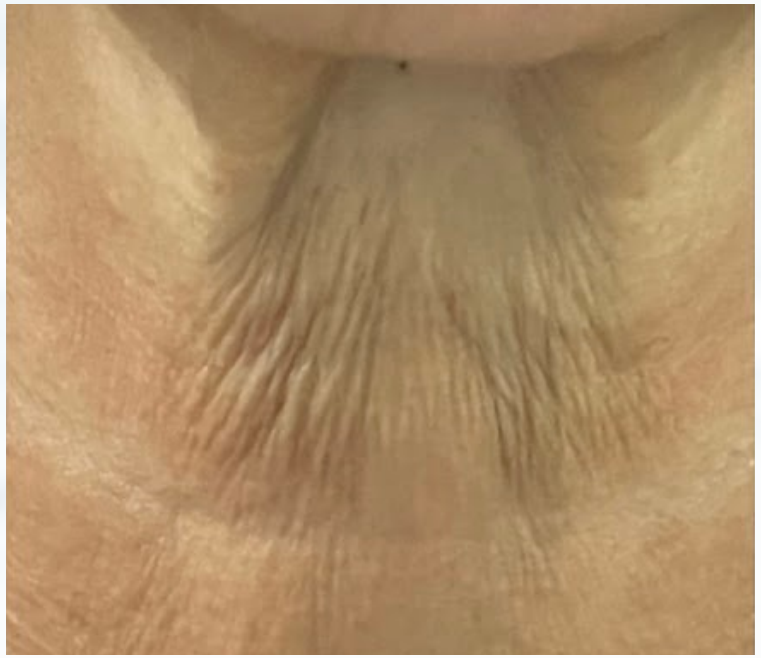
After 1 days later



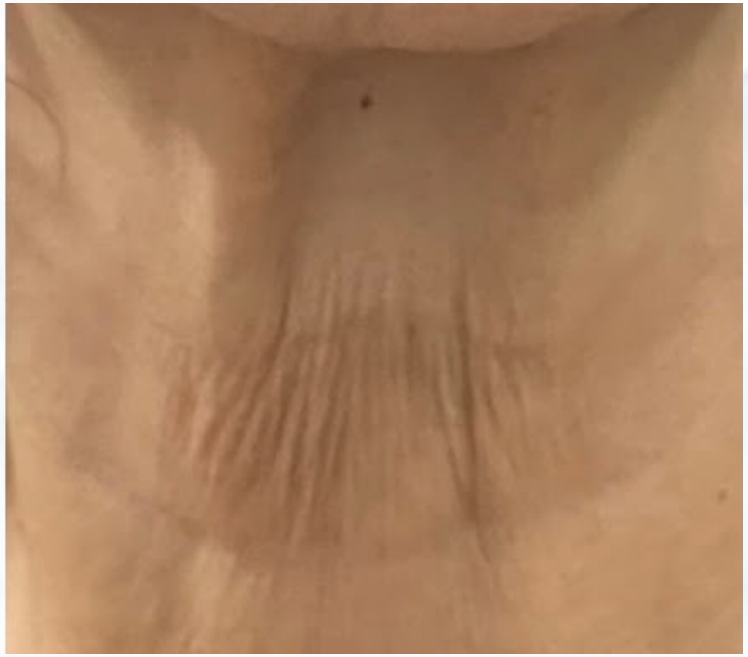
After 2 wks later

Antiaging - Only E-50

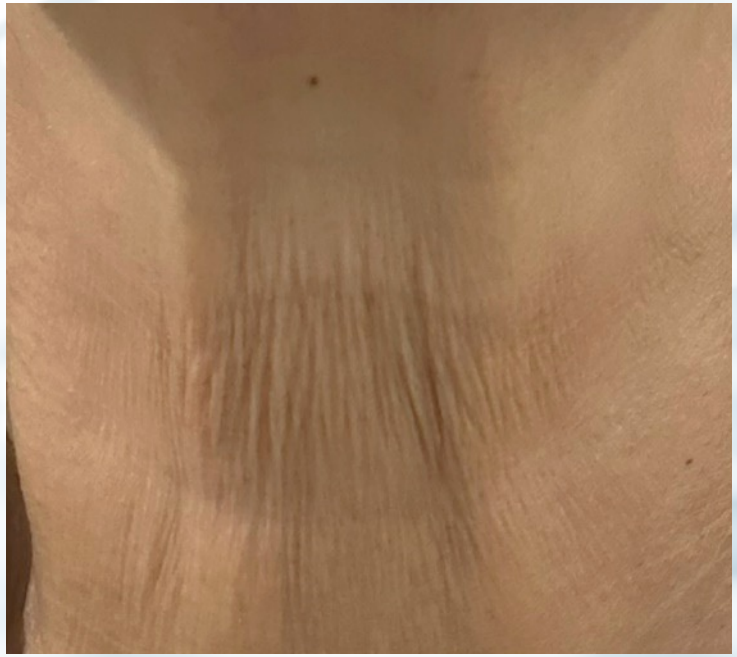
Only one time treatment



Before

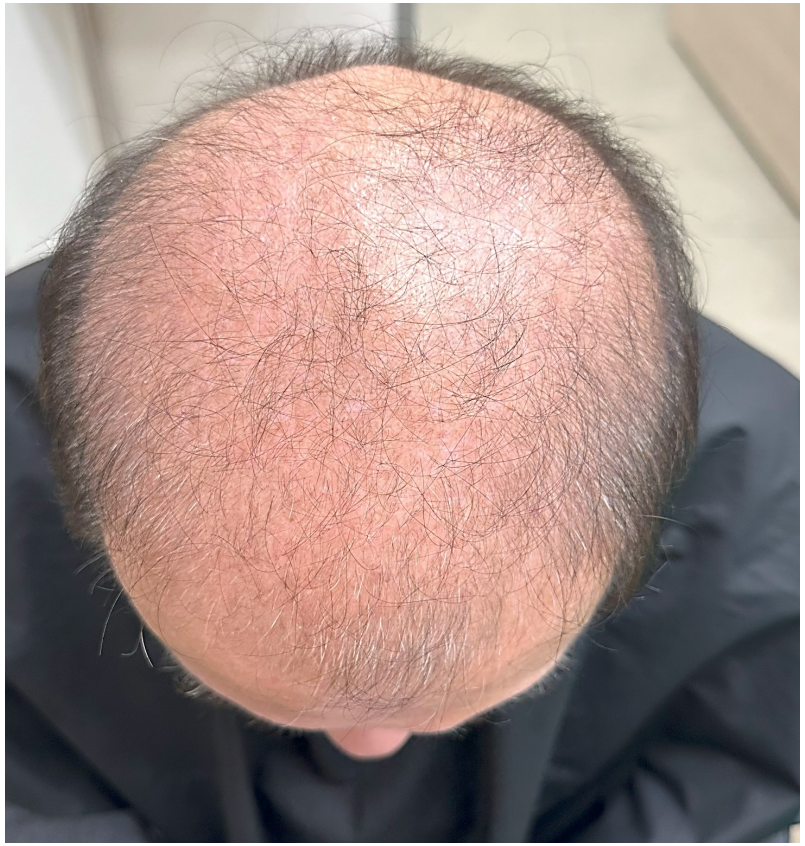


After 2Ms

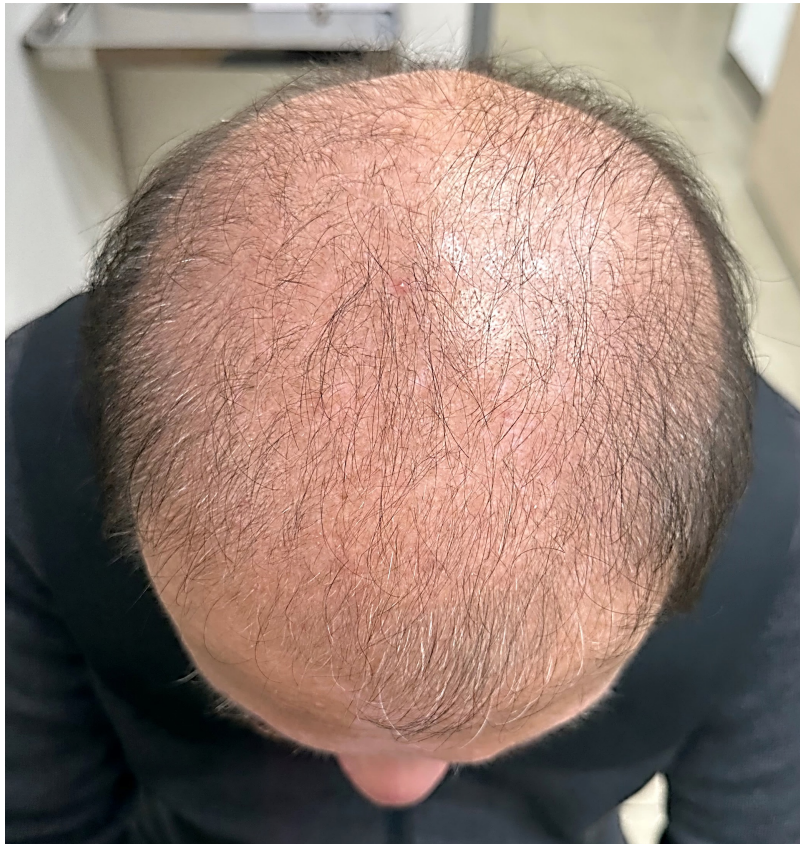


After 4Ms

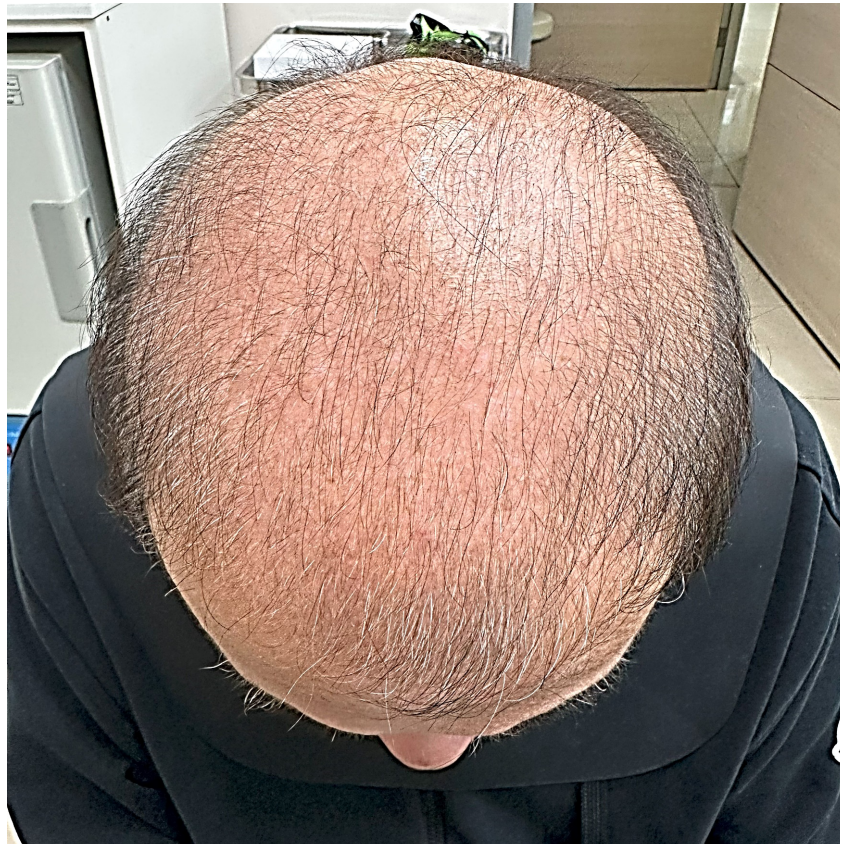
Alopecia- E50-H for Hair



Before

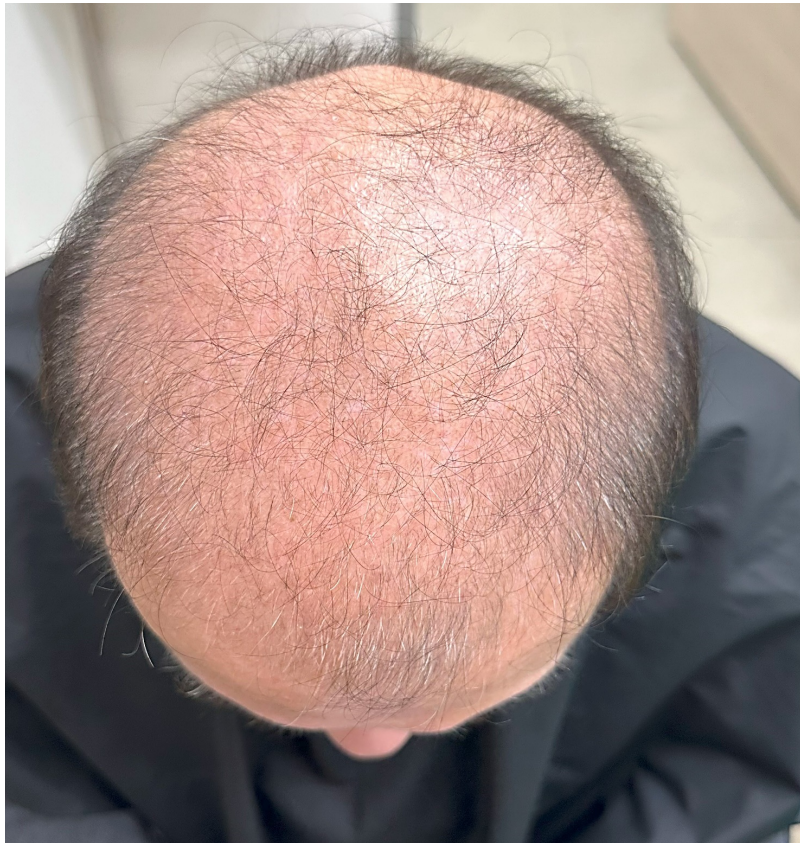


After 7days

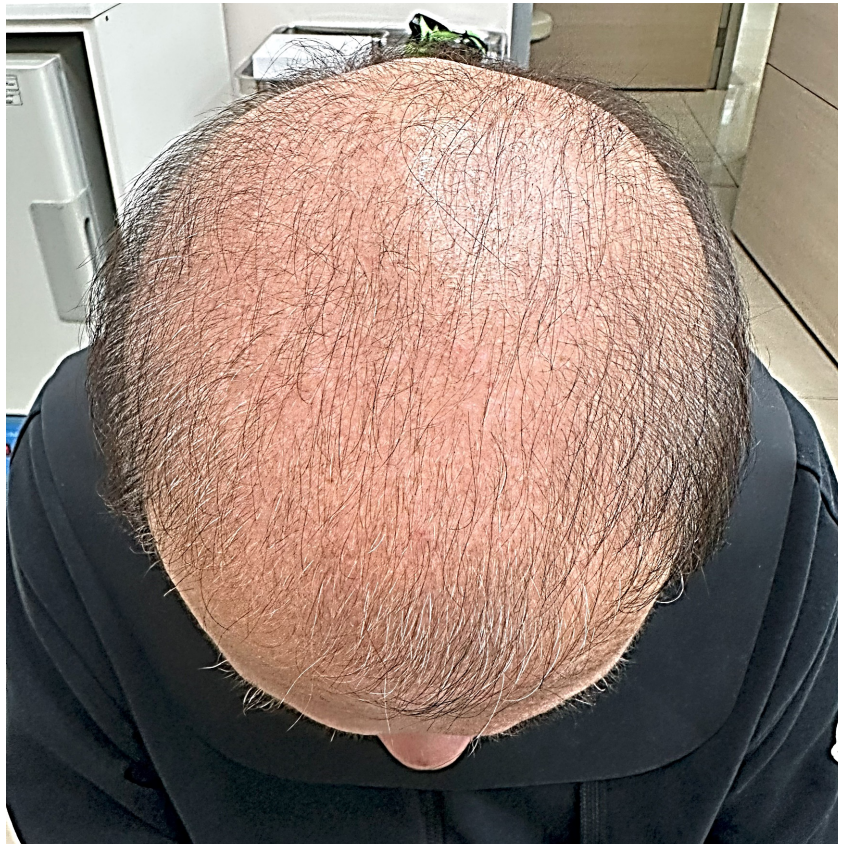


After 14days

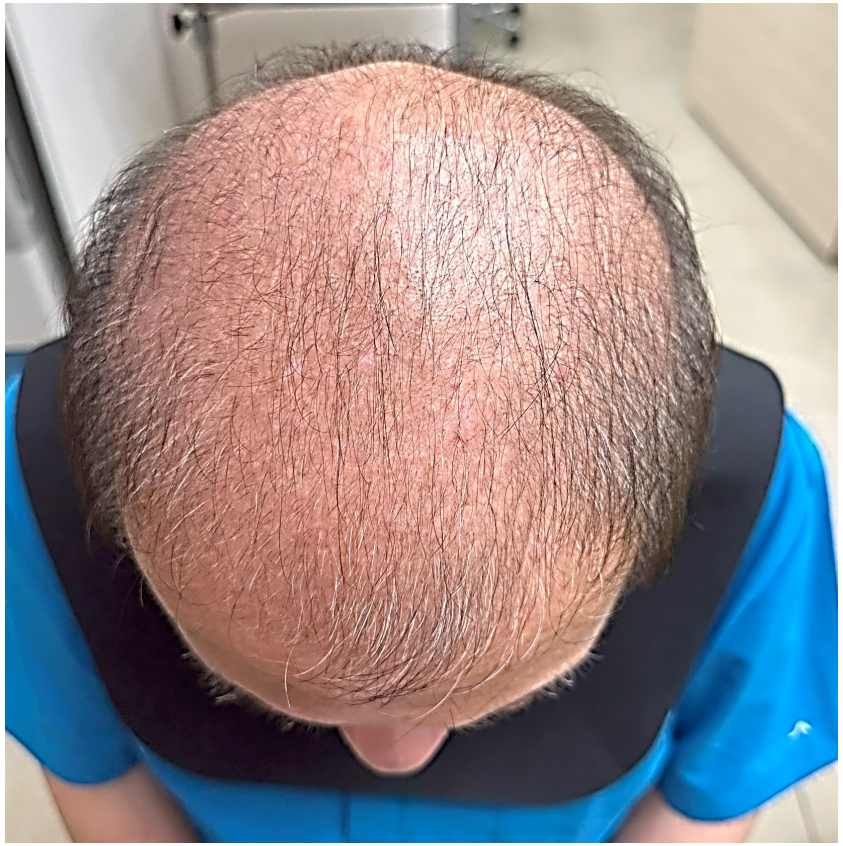
Alopecia- E50-H for Hair



Before

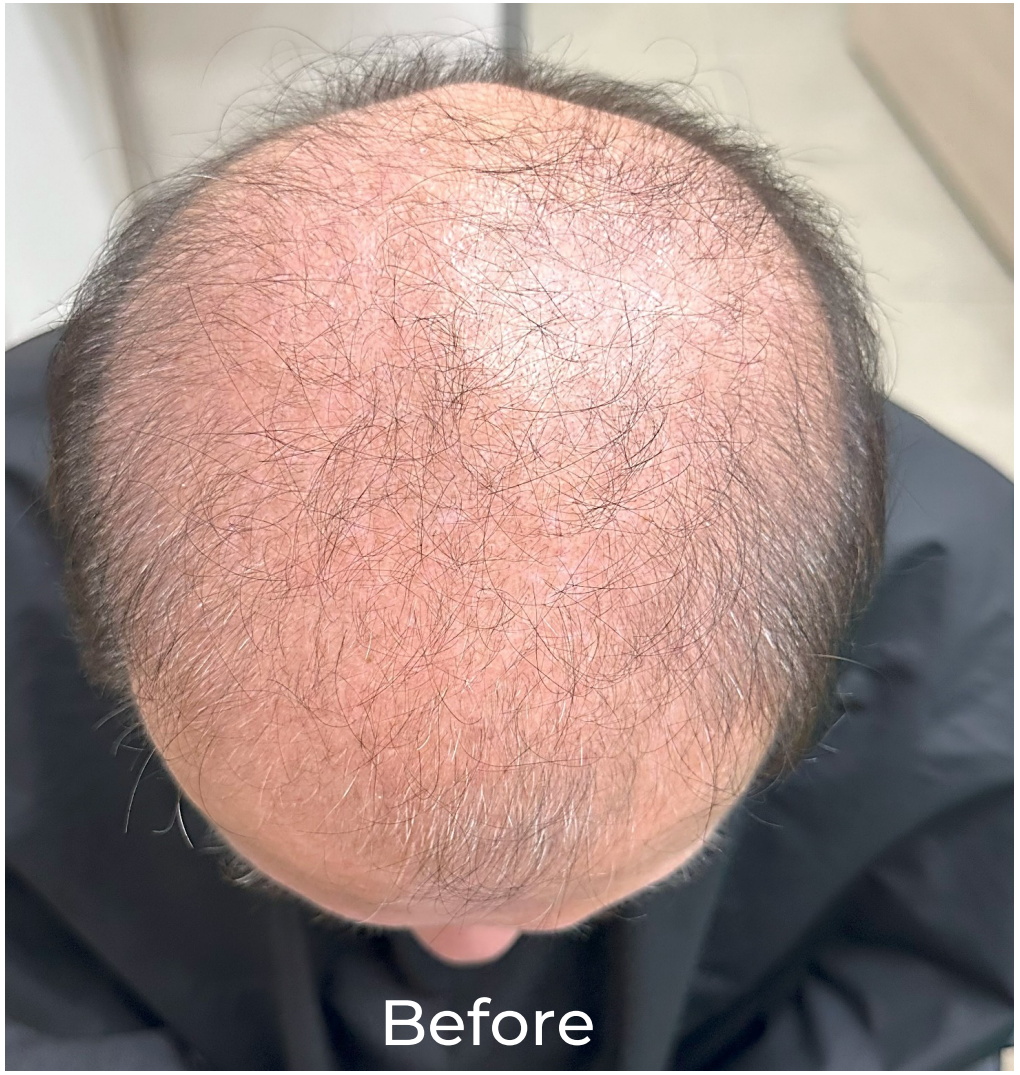


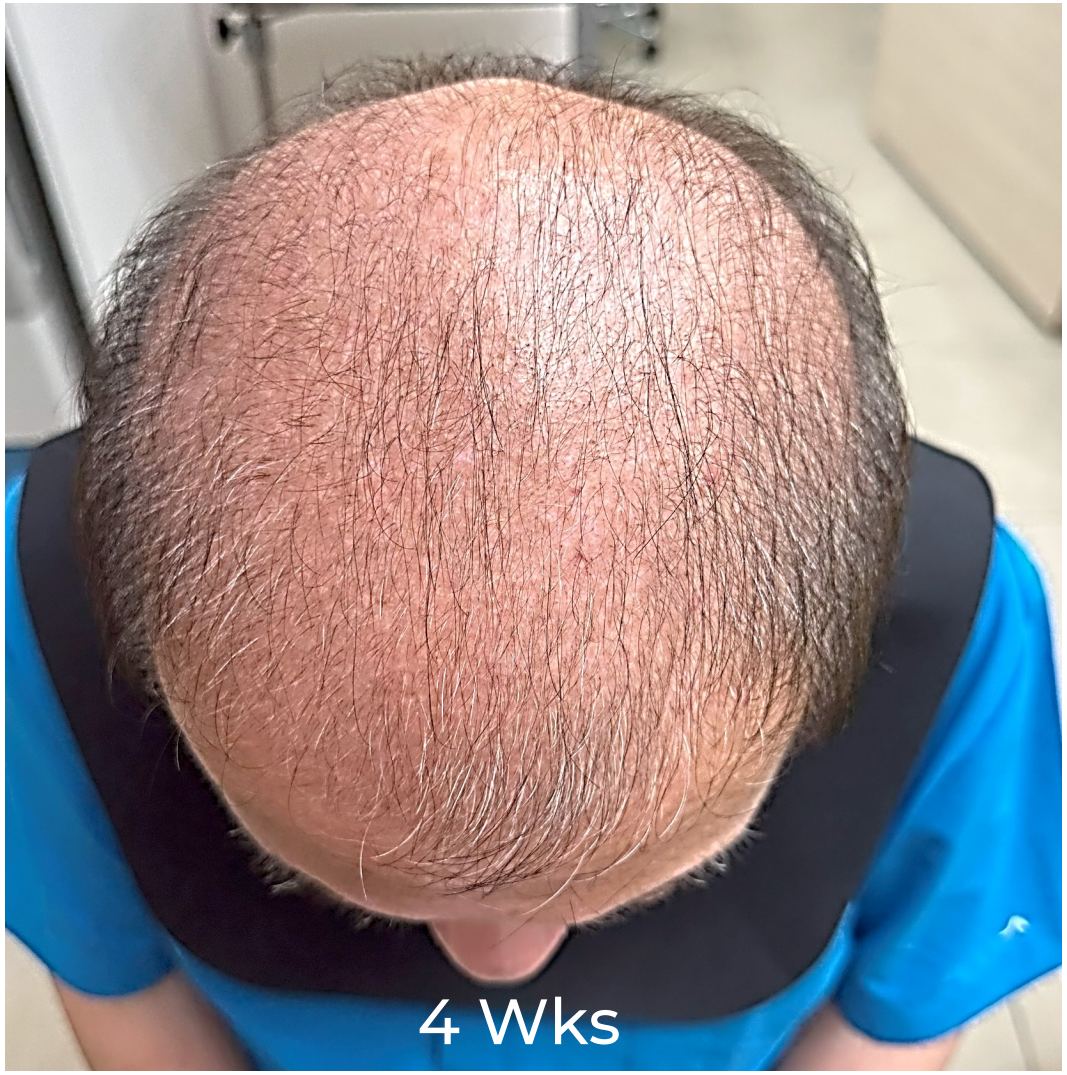
After 7days



After 4 wks

Alopecia- E50-H for Hair





PrimaCure

OUR SERVICES

TRAINING

Continuously Training Doctors in your region and providing updates regarding new protocols and indications

Advisory Board Members

Collaborating with our global advisory members to continue research to develop new indications and collect clinical data

Q&A

Immediately answer any users questions via Email or video conference