Journal of
# Regenerative Aesthetic Medicine

ISSUE 3
Aug 2025

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**Managing Scarring** with Polynucleotides

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JRAM Journal of Regenerative Aesthetic Medicine

# Welcome to the Journal of Regenerative Aesthetic Medicine

As we step into conference season over the Autumn months, we have to remind you to secure your ticket for the **Regenerative Aesthetic Medicine Conference and Exhibition (RAMCE)**, taking place on **November 8th**. If you haven't already booked your place, be sure to take advantage of **Early Bird Tickets before August 31st**. You can explore the full agenda on **page 11** - it's an inspiring lineup you won't want to miss.

In this issue, we also take a deep dive into the **evolution of artificial intelligence** and its implications for regenerative aesthetics. From advancing precision in treatments to enhancing patient outcomes, AI is transforming how we approach practice, research, and innovation. At the same time, it raises important questions about ethics, definitions, and the scope of our field.

This leads us to a question we'd love for you, our community, to weigh in on: **How should regenerative aesthetics be defined?** As our discipline grows and evolves, establishing clarity around this definition is crucial for progress, collaboration, and credibility. Please share your thoughts with us by completing our survey - details can be found on **page 67**.

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## The Team



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# Meet our Scientific Committee

## Steering the education of The RAM Institute

**Our Scientific Committee plays a crucial role in the success and credibility of The RAM Institute. Members oversee all JRAM content and curate the RAMCE programme to ensure everything we produce is cutting-edge and scientifically sound.**

### Professor Maurizio Cavallini

Professor Maurizio Cavallini is the Chief Medical Advisor at Monteverdi Tuscany in Italy. He graduated in medicine from the University of Milan, and holds postgraduate qualifications in plastic surgery, microsurgery and experimental surgery. A frequent writer and lecturer, Professor Cavallini has authored more than 130 pieces in notable national and international medical journals, as well as publishing books and speaking globally on plastic surgery and aesthetic medicine. He is also the President of the Italian Scientific Society of Aesthetic Medicine - Agora and adjunct professor in the University of Genova in Italy, along with being a fellow of many scientific societies in plastic surgery and aesthetic medicine.

### Mr George Christopoulos

Mr George Christopoulos is a plastic surgeon and Assistant Professor of Aesthetic Medicine at the College of Medicine & Dentistry at Ulster University. He has a Master's in Health Care Management and a PhD (Distinction) in the surgical treatment of cancer from the University of Athens. Since relocating to the UK in 2015, Mr Christopoulos has completed a second Master's in Reconstructive Microsurgery (Distinction), and held roles in burns and plastics throughout the UK.

### Dr Kate Goldie

With more than 15 years of global experience, Dr Kate Goldie is recognised as one of the leading figures in aesthetic medicine. Having trained more than 7,000 practitioners worldwide, her innovative approach and commitment to excellence have made her a sought-after educator and speaker. Beyond her extensive teaching, Dr Goldie is a respected thought leader, regularly sharing the stage with industry pioneers and contributing to groundbreaking research. Dr Goldie is deeply passionate about advancing the field of regenerative aesthetics and is at the forefront of new developments and innovations.

### Dr Lee Walker

Dr Lee Walker is Director and Clinical Lead at the award-winning BCity Clinics in Liverpool, with extensive experience in medical aesthetics since 2001. He chairs the Complications in Medical Aesthetics Collaborative (CMAC) UK and has published widely on blindness, vascular occlusion, facial ageing, anatomy and injection technique. A member of the Royal College of Surgeons in both Scotland and England, he also holds postgraduate qualifications in clinical education. Dr Walker is part of Teoxane's international faculty and serves as an educational consultant for Revance USA.

## Get in touch with the committee

Email **info@ram-institute.com** to discuss ideas and receive more information.

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# Contents

## In this issue...


*This one-day, high-impact event brings together the brightest minds and boldest innovations in regenerative aesthetic medicine.*

# RAMCE 2025

## The one event your future practice will thank you for

### Saturday 8th November 2025

**Pullman Hotel London**

In the ever-evolving world of aesthetic medicine, those who lead are the ones who look beyond the surface. Real progress in aesthetics now means understanding and working with the body's own regenerative potential.

RAMCE 2025 is your opportunity to step into that future with confidence.

This one-day, high-impact event brings together the brightest minds and boldest innovations in regenerative aesthetic

*Aesthetic patients today are asking for more than correction - they want restoration*

medicine. What you learn here could define how you work - and what you offer - for years to come.

## **Moving** beyond correction, towards regeneration

Aesthetic patients today are asking for more than correction - they want restoration. They seek natural, evidence-based outcomes that honour the integrity of their skin and physiology. RAMCE addresses this growing demand by putting regeneration at the centre of aesthetic care.

From polynucleotides and peptides to exosomes and biostimulatory fillers, the sessions weave together a clear, clinically relevant narrative: how to shift from surface enhancement to true dermal revitalisation. But this isn't science for science's sake - these are techniques and protocols you can start applying immediately.

Expect practical takeaways from globally respected experts. You'll gain clarity on topics like how to choose between biostimulatory options, integrate them with existing injectables, and navigate the growing territory with confidence and ethical clarity.

## **Real** cases, evidence and results

At RAMCE 2025, insight is grounded in what really happens in clinic. Across the programme, you'll hear from practitioners presenting real cases, not just theories - sharing their decision-making, techniques, and outcomes in detail. These are complemented by sessions led by researchers and experienced clinicians who bring clarity to the evidence base behind regenerative approaches.

Whether it's polynucleotides in complex skin presentations, hair regeneration techniques, or the evolving role of biostimulatory fillers, the focus is consistent: what's working, why it works, and how to apply it responsibly. It's this balance of data, practice and reflection



*Across the programme, you'll hear from practitioners presenting real cases, not just theories*

that makes RAMCE a uniquely valuable learning experience.

## **Protect** your practice, expand your impact

Innovation comes with responsibility, and RAMCE doesn't shy away from the hard questions. How do we educate patients on regenerative therapies? What's the ethical boundary with exosome use? What complications can arise - and how do we manage them?

With panels dedicated to these grey zones, the conference positions you not only as a better injector, but as a more informed, compliant, and trusted provider. In a competitive market, that matters.

## Trusted partnerships, valuable networking opportunities

The RAMCE exhibition has been intentionally curated - every partner, product, and platform has been selected for their alignment with regenerative principles, scientific credibility, and clinical value.

This isn't a hall of sales pitches. It's a focused environment where you can engage with innovators and suppliers who share your standards and are actively contributing to the evolution of aesthetic medicine.

You'll have the space to ask meaningful questions, trial tools, and build relationships with people who understand the realities of clinical practice.

And when the talks pause, the connections continue. With informal networking woven throughout the day and a relaxed evening reception to close, RAMCE offers time and space to connect with peers, mentors, and trusted industry voices.

*The RAMCE exhibition has been intentionally curated - every partner, product, and platform has been selected for their alignment with regenerative principles, scientific credibility, and clinical value*

**The regenerative shift** has already begun.
Are you in?

RAMCE is where future-focused clinicians gather to learn, connect, and lead. If your goal is to offer patients safer, smarter, more sustainable results - this is where you need to be.

Secure your place now and be part of the community redefining aesthetic medicine.

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# RAMCE 2025 Agenda

## Injectables

**Precision in Practice: Innovations & Techniques in Injectables**

***Moderator:*** *Professor Maurizio Cavallini*

**9:00 ↓ 9:30** **Setting the Stage: A New Era in Regenerative Aesthetic Medicine**
*RAMI Scientific Committee*

**9:30 ↓ 9:50** **Polynucleotides Update: Precision Techniques and Protocol Refinement**
*Professor Maurizio Cavallini*

**9:50 ↓ 10:00** **Healing in Action: A Case Study on Polynucleotides for Open Wound Repair**
*Dr Amy Law*

**10:00 ↓ 10:20** **Mastering Biostimulatory Fillers: Choosing Wisely, Injecting Strategically**
*Dr Kate Goldie*

**10:20 ↓ 10:40** **Next-Generation Autologous Therapies: Innovation in Self-Derived Healing**
*Dr Sophie Shotter*

**10:40 ↓ 11:00** **Panel Q&A**
*A dynamic panel discussion followed by an interactive Q&A*

**11:00 → 11:30** **REFRESHMENT BREAK**

## Topicals

**Skin Deep: Advances in Topical Regenerative Science & Application**

***Moderator:*** *Mr George Christopoulos*

**11:30 ↓ 11:50** **Skin Inflammation Decoded: When to Fuel It, When to Fight It**
*TBC*

**11:50 ↓ 12:10** **What Makes a Topical Regenerative? Science, Signals, and Skin Repair**
*Anna Baker*

**12:10 ↓ 12:30** **Exosomes: Current Evidence and Expert Perspectives**
*TBC*

**12:30 ↓ 12:40** **Case Study: Enhancing Skin Glow with Exosomes**
*Julie Scott*

**12:40 ↓ 12:50** **Panel Q&A**
*A dynamic panel discussion followed by an interactive Q&A*

**12:50 → 14:00** **LUNCH**

## Combination Approaches

**Synergy in Aesthetics: Integrating Modalities for Enhanced Results**

***Moderator:*** *Dr Kate Goldie*

**14:00 ↓ 14:20** **Regenerative Strategies for Photoageing: Integrating Injectables, EBDs, and Beyond**
*TBC*

**14:20 ↓ 14:40** **Cold Ablation in Modern Aesthetics (Ascelpion Lasers)**
*TBC*

**14:40 ↓ 15:00** **Slowing Down the Need for Surgery with Energy-Based Devices**
*Mr George Christopoulos*

**15:00 ↓ 15:20** **Targeting Pigmentation and Redness with Confidence: A Multimodal Approach**
*Dr John Quinn*

**15:20 ↓ 15:40** **Comprehensive Consultation and Combination Therapies in Hair Restoration**
*Caroline Hall*

**15:40 ↓ 15:50** **Panel Q&A**
*A dynamic panel discussion followed by an interactive Q&A*

**15:50 → 16:20** **REFRESHMENT BREAK**

## Longevity

**Beyond Beauty: Strategies for Healthspan and Ageing Well**

***Moderator:*** *Dr Lee Walker*

**16:20 ↓ 16:40** **How Mitochondria Works as a Skin Biomarker**
*Professor Mark Birch-Machin*

**16:40 ↓ 17:00** **Personalised by DNA: Guiding Regeneration with Genetic Insight**
*Gustavo Torres de Souza*

**17:00 ↓ 17:20** **Regeneration Through the Female Lens: Hormonal Health in Longevity Medicine**
*Dr Mayoni Gooneratne*

**17:20 ↓ 17:40** **The Dark Side of Repair: Identifying and Addressing Common Yet Challenging Complications**
*Dr Lee Walker*

**17:40 ↓ 18:10** **Panel Discussion: What's Next in Regenerative Aesthetics? Innovations Shaping the Decade Ahead**
*RAMI Scientific Committee*

**18:10 → 23:00** **NETWORKING AFTER PARTY**

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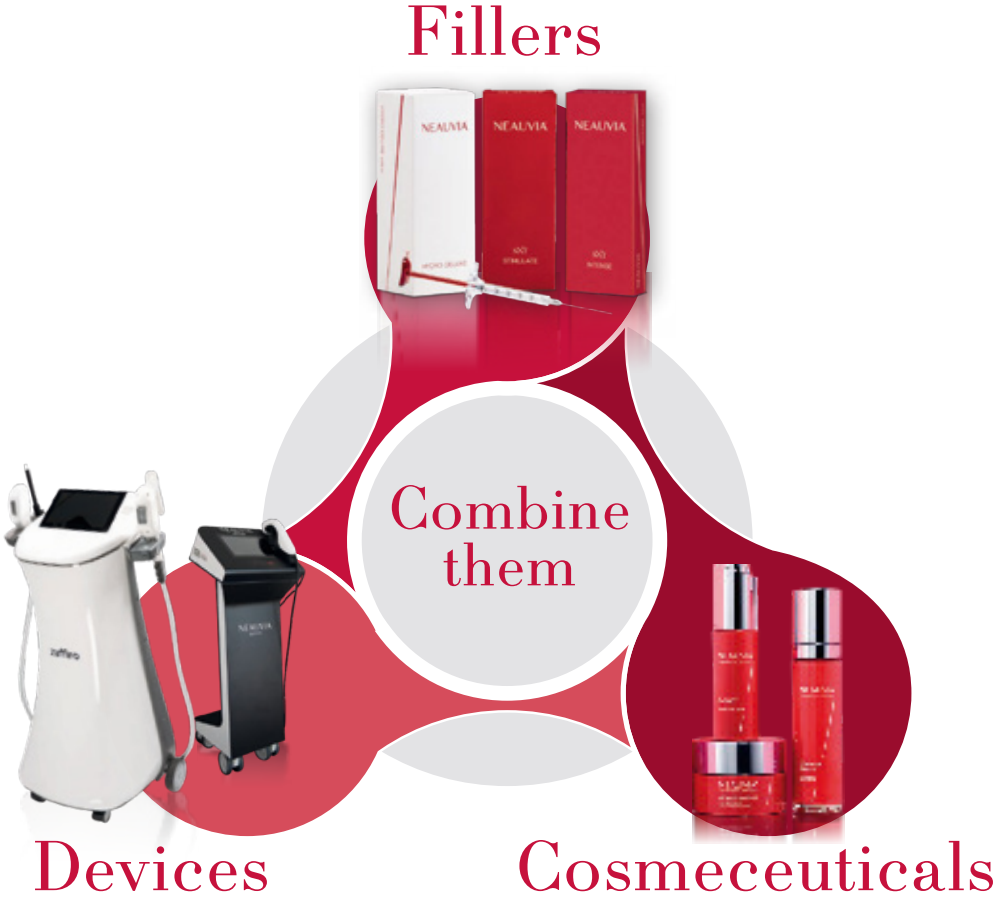


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1. Kubik, P.; Gallo, D.; Tanda, M.L.; Jankau, J.; Rauso, R.; Gruszczy ´nski, W.; Pawłowska, A.; Chrapczy ´nski, P.; Malinowski, M.; Grzanka, D.; et al. Evaluation of the Safety of Neauvia Stimulate Injectable Product in Patients with Autoimmune Thyroid Diseases Based on Histopathological Examinations and Retrospective Analysis of Medical Records. Gels 2023, 9, 440. https://doi.org/10.3390/gels9060440.
2. Zerbinati N, Capillo MC, Sommatis S, Maccario C, Alonci G, Rauso R, Galadari H, Guida S and Mocchi R. Rheological investigation as tool to assess physicochemical stability of a Hyaluronic Acid dermal filler cross-linked with Polyethylene Glycol Diglycidyl Ether and containing Calcium Hydroxyapatite, Glycine and L-Proline. Gels 2022, 8,264. https://doi.org/10.3390/gels8050264.
3. Paweł Kubik, Wojciech Gruszczyński, Heat Influence on Different Hyaluronic Acid Fillers, 25.10.2023. https://doi.org/10.56609/jac.v4i2.305.

# The JRAM News Brief

Essential reading on advancements in regenerative science and aesthetic practice

# Hair regeneration and follicle biology

**New Hair Loss Treatment Shows Promising Results in Early Human Trials**

A topical treatment for androgenetic alopecia, the most common form of hair loss, has shown encouraging early results in a Phase 2a clinical trial, according to biotechnology company Pelage Pharmaceuticals.

The investigational drug, PP405, is being evaluated in a randomised, double-blind, placebo-controlled study involving 78 adult participants with varying degrees of pattern hair loss. The study is designed to assess the safety, pharmacokinetics, and preliminary efficacy of the compound over several months.

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Unlike traditional therapies that aim to slow or stop hair loss, PP405 is intended to reactivate dormant hair follicle stem cells by inhibiting the mitochondrial pyruvate carrier (MPC) - a metabolic checkpoint that keeps these cells in a resting state. By disrupting MPC activity, the drug is believed to kick-start stem cell activation and hair regrowth.

According to preliminary data released by Pelage, approximately 31% of male participants treated with PP405 experienced at least a 20% increase in hair density at eight weeks, compared to 0% in the placebo group. Some individuals reportedly showed visible regrowth in areas of the scalp that were previously bald.

No serious or unexpected adverse events have been reported. The company also stated that systemic drug exposure was undetectable in blood samples, suggesting the topical formulation remains localised to the scalp.

The study includes a 28-day double-blind treatment period followed by a 3-month open-label extension, in which all participants receive PP405. Final data collection is expected by the end of 2025, and Pelage has indicated plans to begin Phase 3 studies in 2026.

---

**Study Shares Insights into Hair Regeneration Through the Immune System**

A recent study published in *Genes & Diseases* explores how the immune system - specifically dermal T cells - plays a critical role in hair follicle regeneration and in various forms of hair loss, including alopecia areata, androgenetic alopecia, and cicatricial alopecia.

Under normal conditions, hair follicles enjoy a form of 'immune privilege', protecting them from immune-mediated damage. When this protective state collapses, as seen in alopecia areata, cytotoxic CD8+ T cells, along with heightened Th1/Th17 inflammatory signaling, can damage follicles and halt normal hair growth. The study highlights key molecular pathways, such as Wnt/βcatenin signaling and epithelial-mesenchymal interactions, that govern stem cell activation and hair cycling. Regulatory T cells (Tregs) are identified as central players capable of reining in excessive immune responses, thereby potentially promoting follicle regeneration.

*Approximately 31% of male participants treated with PP405 experienced at least a 20% increase in hair density at eight weeks, compared to 0% in the placebo group*

Based on these findings, the authors propose that therapies aimed at modulating T cell activity, such as cytokine-targeting treatments and JAK inhibitors, could offer new, more targeted approaches to reversing immune-driven hair disorders.

Furthermore, by elucidating how immune cells regulate epithelial stem cells, the research may inform broader regenerative medicine strategies for skin repair and tissue engineering.

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**Collagen-Based Complex Stimulates Hair Follicle Regeneration**

Researchers have developed a novel formulation combining recombinant humanised collagens - types III, XVII, and XXI - with nicotinamide, showing promising effects on hair follicle regeneration in preclinical testing, according to a new study in *Frontiers in Bioengineering and Biotechnology*.

The team designed the therapy to target the extracellular matrix (ECM) niche surrounding hair follicles, which plays a critical role in supporting follicle stem cells and regulating hair cycling. In laboratory models, the complex stimulated the expression of key hair growth biomarkers, including those associated with stem cell activation and differentiation. It also increased the presence of basement membrane proteins important for anchoring and maintaining follicle structure.

When compared to 5% minoxidil, the current gold-standard topical treatment for androgenetic alopecia, the collagen-nicotinamide combination produced comparable improvements in regrowth. The researchers attribute the effect to synergistic actions: recombinant collagens help restore and stabilise the follicular ECM, while nicotinamide supports cellular metabolism and reduces oxidative stress, creating a favourable environment for regeneration.

The study's authors suggest that this ECM-targeted approach could represent a new therapeutic avenue for hair loss disorders, particularly those linked to follicle microenvironment deterioration. However, they stress that human clinical trials will be essential to confirm safety, determine optimal dosing, and evaluate long-term outcomes.

---

**Serine Restriction Shown to Shift Hair Follicle Stem Cells Toward Wound Repair**

A study from Rockefeller University, published in *Cell Metabolism*, has identified the amino acid serine as a key factor in determining whether hair follicle stem cells (HFSCs) maintain hair growth or participate in skin repair.

Using mouse models, the researchers found that limiting serine - either through diet or by disrupting its production -

triggered the integrated stress response (ISR) in HFSCs. This change redirected the cells away from hair production and toward re-epithelialising wounds, leading to faster closure but reduced hair regeneration. Pharmacological activation of the ISR produced similar effects, while higher serine levels partially reversed them.

The team also detected signs of ISR activation in human skin samples at the margins of healing wounds, suggesting that the mechanism may operate in people as well. The authors note that while these findings highlight a potential way to influence the balance between hair growth and skin repair, further research will be needed to understand the safety and feasibility of modulating serine metabolism in clinical settings.

# Skin regeneration, antiageing and cosmetic science

**SkinCeuticals Unveils Advanced RGN6 Cream**

Skincare brand SkinCeuticals, as part of L'Oreal, has introduced Advanced RGN6 - a regenerative cream inspired by laser-induced skin repair science.

Developed over nearly five years, RGN6 leverages insights from laser treatments, which create controlled microinjuries to trigger natural collagen production. SkinCeuticals says the new cream delivers laser-like rejuvenation benefits in a daily skincare product - ideal for both standalone use and postprocedural recovery.

## *Sucralose, a widely used artificial sweetener, may support skin regeneration and protect against UVB-induced cell damage*

The formula combines six potent ingredients designed to enhance six dimensions of skin health: 10 % GlycoRepair™ (carobseed derivative) to encourage barrier repair, 1 % Eperuline to soothe irritation, 2 % Niacinamide to brighten and balance tone, 3 % Acetyl Tetrapeptide9 to support firmness, 0.2 % Ectoin to protect and hydrate, and 0.2 % Bioceramide 603 - an exclusive ingredient that reduces discoloration.

In a 12-week study, users reported dramatic results with daily use: a 69 % reduction in redness, 36 % fewer postacne marks, 26 % fewer dark spots, 18 % reduction in wrinkles, and 35 % improvements in both firmness and smoothness.

"Advanced RGN-6 is the result of nearly five years of research in regenerative skincare," said Qian Zheng, Senior Vice President of Advanced Research and Global Head of Regenerative Beauty at L'Oréal. "By decoding how the skin regenerates after procedures, we developed a targeted formula that strengthens, rejuvenates and augments visible skin health every day."

RGN6 is suitable for all skin types - including sensitive skin - and is formulated without fragrance, parabens, colorants, or alcohol.

---

**Sucralose Shows Potential for Skin Healing and UV Protection**

A new in vitro study published in the *Journal of Functional Foods* suggests that sucralose, a widely used artificial sweetener, may support skin regeneration and protect against UVB-induced cell damage. Researchers from Chulabhorn Royal Academy demonstrated that sucralose enhances keratinocyte proliferation, promotes wound closure, and reduces UV-induced cell death via the PKA/AMPK/SIRT-1/ERK signaling pathway.

In lab-grown skin cells, sucralose helped wounds heal faster, with stronger effects at higher doses. It also boosted cell growth and reduced damage from UVB light. These benefits disappeared when certain key cell signaling pathways were blocked, suggesting sucralose works through specific biological mechanisms.

The authors propose that sucralose may act via activation of the sweet taste receptor T1R3, which has been linked to tissue repair signaling cascades. However, they caution that findings are limited to cell models. The study lacks data from primary human keratinocytes, in vivo models, or clinical trials. Given sucralose's poor oral bioavailability, the authors recommend exploring topical delivery systems and evaluating safety in future preclinical studies.

While preliminary, this research opens the door to potential dermatological applications of a compound traditionally associated with food, though clinical relevance remains unproven.

---

**Study Explores Panthenol Citrate as a Potential UV-Protective Ingredient for Skin**

A recent study published in *ACS Applied Materials & Interfaces* has examined the potential of panthenol citrate - a compound derived from provitamin B5 and citric acid - as an ingredient that may help protect skin from ultraviolet (UV) radiation. The study evaluated the compound's antioxidant activity and ability to mitigate molecular damage in human skin models exposed to UV light.

In laboratory experiments, panthenol citrate showed several antioxidant properties, including free radical scavenging, iron chelation, and the inhibition of lipid peroxidation. When applied to human skin tissue models subjected to UV radiation, the compound was associated with lower levels of DNA damage, as measured by the marker 8OHdG, and a reduction in apoptosis, indicated by reduced caspase-3 expression. These results suggest that the compound may help reduce oxidative stress and cellular damage under UV exposure, though the study emphasises that these findings are limited to ex-vivo models.

The researchers also tested panthenol citrate in both water- and oil-based solutions - such as glycerol and coconut oil - and found that it retained stability and activity across these formulations. This suggests possible compatibility with different types of skincare products.

However, the authors caution that further studies are needed to determine the compound's effects in living human subjects. The next steps would likely involve clinical trials to assess safety, efficacy, and performance under real-world conditions. Dr Qing Zhang, a co-author, noted that while the compound may be a promising candidate for further development, conclusions about its commercial potential or effectiveness should be avoided at this stage.

Panthenol and citric acid are already widely used in skincare for their moisturising and pH-adjusting properties. The combination explored in this study represents a new approach to developing multifunctional skincare ingredients, though more research is required before practical applications can be confirmed.

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**Researchers Discover Antiageing Compounds from Human Blood Bacterium**

A study published in the *Journal of Natural Products* reports the discovery of six new indole-functionalised metabolites produced by Paracoccus sanguinis, a bacterium isolated from human blood. Some of these compounds have shown potential in reducing signs of skin ageing at the cellular level.

The research team, led by scientists from the University of California, Berkeley, and UCLA, used a combination of mass spectrometry, isotope labeling, and genome analysis to identify and characterise a total of 12 indole-based compounds. Six of them are newly reported.

Testing on human dermal fibroblasts showed that several of these metabolites reduced reactive oxygen species (ROS), inflammatory markers, and matrix metalloproteinase-1 (MMP-1), which is involved in collagen breakdown. These effects suggest possible applications in skin health.

"These data indicate that indole-functionalised natural products from P. sanguinis may serve as leads for the development of anti-skin-ageing agents," the authors write.

This study highlights blood-associated microbes as a potential source of bioactive small molecules, particularly those that might be relevant in dermatological or therapeutic contexts. However, further research is needed to evaluate their safety, efficacy, and mechanisms of action in more complex models.

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**Dermatologically Tested Apple-Derived Extracellular Vesicles Show Skin-Soothing and Antiageing Benefits**

A study in the *Journal of Cosmetic Dermatology* examines the safety and efficacy of a 2% apple-derived extracellular vesicle (ADV) formulation for topical skin application. The study rigorously tested the bioactive vesicles according to international safety standards.

The ADVs demonstrated an excellent safety profile, showing no genotoxic, cytotoxic, corrosive, or sensitisation effects in standard assays - including the Ames test and OECD-compliant skin and corneal models.

In functional assessments over 60 days, the formulation significantly reduced skin redness ($p < 0.05$) and improved wrinkle length, volume, and roughness - highlighting its soothing and antiageing potential.

For regenerative aesthetic medicine, these findings support the idea that plant-derived vesicles may offer a novel, biocompatible alternative to traditional bioactives. ADVs could be incorporated into post-procedural care to reduce inflammation and accelerate visible skin rejuvenation - without ethical or regulatory concerns tied to human or animal-derived ingredients.

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**OliX and L'Oréal Launch R&D Partnership to Advance Skin & Hair Health**

Biotechnology company OliX Pharmaceuticals has announced a strategic research and development partnership with global beauty giant L'Oréal, seeking to revolutionise skin and hair health through novel biotech innovations.

The collaboration is pioneering a fresh wave of scientific inquiry into biological systems related to dermatology and hair care. The primary aims include developing breakthrough molecules and delivery platforms tailored for skin and scalp health, and exploring biotech-driven cosmetic solutions that go beyond traditional topical treatments.

This strategic alliance leverages the respective strengths of each firm: OliX, known for its expertise in nextgeneration RNA-based therapeutics and targeted nanomedicines, and L'Oréal, with its long-standing knowledge in cosmetic science, formulation, and mass market distribution.

Together, they are aiming to transform both the therapeutic and cosmetic dimensions of skin and hair care, utilising advanced molecular technologies to create highly effective, science-backed products.

"We are very excited and look forward to working with L'Oréal, a leader in the global beauty industry, toward a common goal," said Lee Dongki, CEO of OliX. "By integrating our robust platform technology with L'Oréal's century long expertise in product development and their unwavering commitment to advancing the beauty sector, we aim to maximise the potential of both companies and achieve outstanding collaborative research outcomes."

# Wound healing and tissue repair

**Frequency-Specific Sound Shows Promise in Tissue Regeneration**

A recent systematic review by Armand *et al.*, published in the *International Wound Journal*, highlights growing evidence that low-frequency acoustic stimulation - both infrasound (1-20 Hz) and audible sound (20 Hz-20 kHz) - can enhance tissue regeneration processes in preclinical models.

The review analysed five studies, revealing that infrasound exposure in animal models improved fracture healing, bone mineral density, and expression of key markers such as CGRP and survivin. These effects may be mediated by neurogenic and osteogenic pathways.

Audible low-frequency sound, particularly around 100 Hz, was shown to increase fibroblast migration and metabolic activity in vitro. Directional application of sound waves influenced outcomes, with horizontal stimulation improving cell motility and vertical application producing inhibitory effects. In murine models, 20 kHz sound accelerated recovery of the skin barrier by enhancing keratinocyte activity and lamellar body secretion.

While results are promising, the review emphasises limitations in sample size, heterogeneity of methods, and lack of clinical data. Standardisation of acoustic parameters and further mechanistic studies are necessary before clinical translation.

The findings support the potential of non-invasive sound-based therapies as adjuncts in wound healing and bone regeneration, particularly for chronic or hard-to-heal injuries.

*It suggests that incorporating psychological screening and stress-reduction strategies - such as guided relaxation, cognitive-behavioural support, and patient education - could improve healing outcomes.*

**Psychological Stress Shown to Impair Wound Healing**

A recent review published in *Clinical, Cosmetic and Investigational Dermatology* has highlighted the significant impact psychological stress can have on wound healing. The review compiles evidence showing that stress alters normal physiological responses, potentially delaying the wound-healing process and affecting outcomes related to tissue repair and scarring.

Psychological stress activates the body's sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis, leading to elevated levels of hormones such as cortisol and catecholamines. These hormones are known to suppress immune function, impair circulation, and reduce collagen production - all of which are critical to efficient wound repair. According to several studies cited in the review, individuals experiencing psychological stress may exhibit slower inflammatory responses, delayed re-epithelialisation, and impaired tissue regeneration.

Meta-analyses and experimental studies support these findings. In one well-known study, caregivers of individuals with Alzheimer's disease experienced significantly delayed healing of small skin wounds compared to control participants, with healing times increased by up to 24 percent. Such findings suggest that psychological factors can have clinically relevant effects on healing timeframes, particularly in patients with chronic wounds or those undergoing surgical recovery.

The review also notes implications for healthcare professionals, particularly nurses and wound-care specialists. Stress not only affects patients but can also impair the clinical effectiveness of scar management techniques. Persistent stress appears to interfere with the body's ability to remodel scar tissue, which may reduce the efficacy of both pharmaceutical and physical interventions aimed at improving scar appearance.

Although most healthcare practitioners acknowledge that psychological wellbeing influences physical health, the review points out a gap in routine assessment and management of stress in clinical wound care settings. It suggests that incorporating psychological screening and stress-reduction strategies - such as guided relaxation, cognitive-behavioural support, and patient education - could improve healing outcomes.

The review concludes by calling for more interdisciplinary approaches to wound management, including collaboration between mental health professionals and wound care teams. Further research is recommended to better understand the mechanisms involved and to develop evidence-based interventions that can be integrated into standard care protocols.

**Bioengineered Scaffold Shows Promise for Accelerated Skin Wound Healing**

A newly developed bioengineered scaffold combining a peptide and a bioactive molecule has demonstrated improved skin wound healing in preclinical tests, according to a study published in *Advanced Healthcare Materials*.

The research, conducted by scientists at China Medical University, focused on creating an electrospun scaffold made from polycaprolactone and gelatin (PG), further enhanced with YIGSR peptide and heparin. The aim was to promote angiogenesis - the formation of new blood vessels - which plays a critical role in skin regeneration.

The resulting scaffold, referred to as PGHY, was tested in both in vitro (lab-based) and in vivo (animal) models. In cell-based studies, PGHY enhanced human endothelial cell proliferation, migration, and tube formation - key processes in blood vessel development. These effects were linked to the activation of the FAK/MAPK/ERK1/2 signaling pathway and increased expression of vascular endothelial growth factor (VEGF).

Among the variants tested, PGHY1.0 (with 1.0% YIGSR concentration) showed the most favorable results. It exhibited a stable release of the peptide and significantly improved vascular activity compared to control scaffolds without the modifications.

In a mouse model with full-thickness skin wounds, PGHY1.0 also led to faster wound closure and enhanced blood vessel formation compared to the unmodified scaffold. Histological analysis supported the observed improvements in tissue regeneration.

The study suggests that combining YIGSR and heparin within an electrospun scaffold can enhance both cellular responses and wound healing outcomes. While further research, including human trials, will be required to assess clinical applicability, the findings indicate potential for developing advanced wound care materials aimed at accelerating healing and promoting tissue regeneration.

**Multifunctional Conductive Gel Dressing Combines Electrical Stimulation and Antioxidant Therapy for Chronic Wound Repair**

A research team in China has developed a next-generation bioelectronic wound dressing that integrates electrical stimulation (ES) with targeted antioxidant therapy, offering a potent new approach to healing infected chronic wounds.

The study, published in *Acta Biomaterialia*, describes a supramolecular conductive gel - termed SPPCP - engineered from polyvinyl alcohol (PVA), the conductive polymer PEDOT:PSS, a citric acid-cyclodextrin network, and molybdenum-based cyclodextrin-polyoxometalates (CD-POM).

This composite design tackles two key obstacles in chronic wound care: persistent bacterial infection and oxidative stress. While conductive hydrogels can accelerate cell migration and angiogenesis through ES, they can also exacerbate reactive oxygen species (ROS) accumulation - slowing regeneration. The inclusion of CD-POM addresses this problem by catalytically scavenging ROS such as superoxide and hydroxyl radicals, creating a redox-balanced healing environment.

Laboratory testing showed that the dressing possessed strong adhesion, mechanical flexibility, and stable conductivity. In vitro, ES enhanced fibroblast proliferation and migration, disrupted bacterial biofilms, and improved antibacterial performance. In a rat model of Staphylococcus aureus-infected skin defects, the combined SPPCP + ES treatment accelerated wound closure, reduced inflammation, promoted angiogenesis, and increased collagen deposition.

The authors note that the dressing also induced macrophage polarisation toward an M2 anti-inflammatory phenotype, further supporting tissue repair. They propose that this dual-action strategy, merging electrotherapy with sustained ROS control, overcomes a major limitation of current bioelectronic dressings and could be adapted for a range of complex wound scenarios, including diabetic ulcers and post-surgical complications.

If validated in human trials, SPPCP could represent a new class of multifunctional smart dressings for regenerative medicine, particularly in cases where oxidative stress undermines standard healing.

*According to the authors, peptide-based wound therapies have the advantage of targeting multiple barriers to healing at once*

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**Brighton Scientists Pioneer Injectable Hydrogel for 'Deep Tunnel' Wound Healing**

A new EU-funded project, INJECTHeal, spearheaded by the University of Brighton's Centre for Regenerative Medicine and Devices, is developing a 4D injectable self-healing hydrogel designed to address chronic, difficult-to-reach "deep tunnel" wounds that affect millions globally, with healthcare costs accounting for 2-4% of European expenditure.

These wounds, such as diabetic foot ulcers and pressure sores, remain largely untreated by conventional dressings because of their depth and complexity. The INJECTHeal hydrogel aims to reach deep wound pockets, deliver medication directly, reduce infection and inflammation, and actively support tissue regeneration from within.

Launching in May 2025, the 3.5-year initiative has secured approximately €7.3 million in EU funding. At Brighton alone, more than €1.1 million will support preclinical testing of the hydrogel's antibacterial, anti-inflammatory, and angiogenic properties - critical functions for effective wound revascularisation and repair.

The project brings together 13 partners across eight European countries, including academic, clinical, and industry contributors, as well as patient advocates embedded from the outset to ensure real-world alignment.

Professor Matteo Santin, who leads the initiative, emphasises that advancing materials science for wound care must be rooted in patient needs: "INJECTHeal is about more than science. The hydrogel will be designed with, not just for, patients... restoring dignity to people who have waited too long for effective solutions."

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**Peptide-Based Strategies Offer Multi-Target Approach to Wound Healing**

A new review in Current Opinion in Solid State and Materials Science highlights how bioactive peptides are emerging as versatile, multi-functional tools in wound care - offering simultaneous antimicrobial, anti-inflammatory, and regenerative benefits.

The authors examine current literature on peptide-based dressings, gels, and scaffolds, outlining how these molecules can accelerate closure, promote angiogenesis, and improve collagen organisation in acute and chronic wounds.

Peptides discussed in the review are rarely extracted from human tissues. Instead, most are chemically synthesised in the laboratory using sequences inspired by human proteins such as collagen, growth factors, and antimicrobial peptides. This synthetic approach avoids donor-derived sourcing, supports large-scale manufacturing, and allows precise control over sequence and function. Other candidates originate from non-human sources, such as amphibian skin or marine organisms, but are modified to improve compatibility with human skin.

According to the authors, peptide-based wound therapies have the advantage of targeting multiple barriers to healing at once. By modulating inflammation, inhibiting bacterial growth, and stimulating fibroblast migration, they address the complex microenvironment of chronic wounds more effectively than many single-function dressings. The review notes promising preclinical data but acknowledges that issues such as peptide stability, delivery optimisation, and cost-effectiveness remain key hurdles before broad clinical adoption.

In regenerative aesthetics, such peptides hold potential not only for accelerating post-procedural healing but also for improving skin quality, reducing scarring, and supporting collagen remodelling after laser treatments, microneedling, or surgery.

*Science highlights how bioactive peptides are emerging as versatile, multi-functional tools in wound care*

# **Frontiers** in regenerative science and technologies

**University of Manchester Scientists Challenge Century Old View of Cell Division**

In a study published in *Science*, researchers at the University of Manchester have changed our understanding of how animal cells divide - an insight with implications for regenerative medicine.

For more than a century, biology textbooks have taught that animal cells must round up before dividing,

producing two identical daughter cells. The team discovered that many cells - including human endothelial cells - can divide while remaining elongated, generating two daughter cells that are unequal in size and potentially in fate.

The researchers call this newly characterised process 'isomorphic division'. Unlike classical division, where a cell becomes spherical and splits symmetrically, isomorphic division allows elongated cells to maintain their shape and split asymmetrically. This creates one larger and one smaller daughter cell, often with different internal contents and developmental roles.

According to the authors, "Distinct morphological changes switched cells to an 'isomorphic' mode... interphase morphology appeared to provide a geometric code defining mitotic symmetry, fate determinant partitioning, and daughter state."

The study involved live imaging of zebrafish embryos and experiments with human and mouse endothelial cells. One of the key findings was that this geometric code - based on a cell's shape prior to division - is read by specialised intracellular components, particularly Rab4-positive endosomes. These endosomes help distribute cellular materials unevenly, influencing what each daughter cell becomes.

This discovery carries significant relevance for regenerative medicine. If scientists can control the shape of a cell before it divides, they could potentially steer the identity of the resulting cells - an essential tool for tissue engineering and organ repair. Cells might be guided to divide in a way that produces a specialised type while also retaining a more primitive or supportive daughter, offering a precise method of building complex tissues.

Dr Shane Herbert, co-author of the study, explained the importance of this insight in an interview with Phys.org: "This means that manipulating cell shape could be used not just to predict cell behaviour, but to actively design it."

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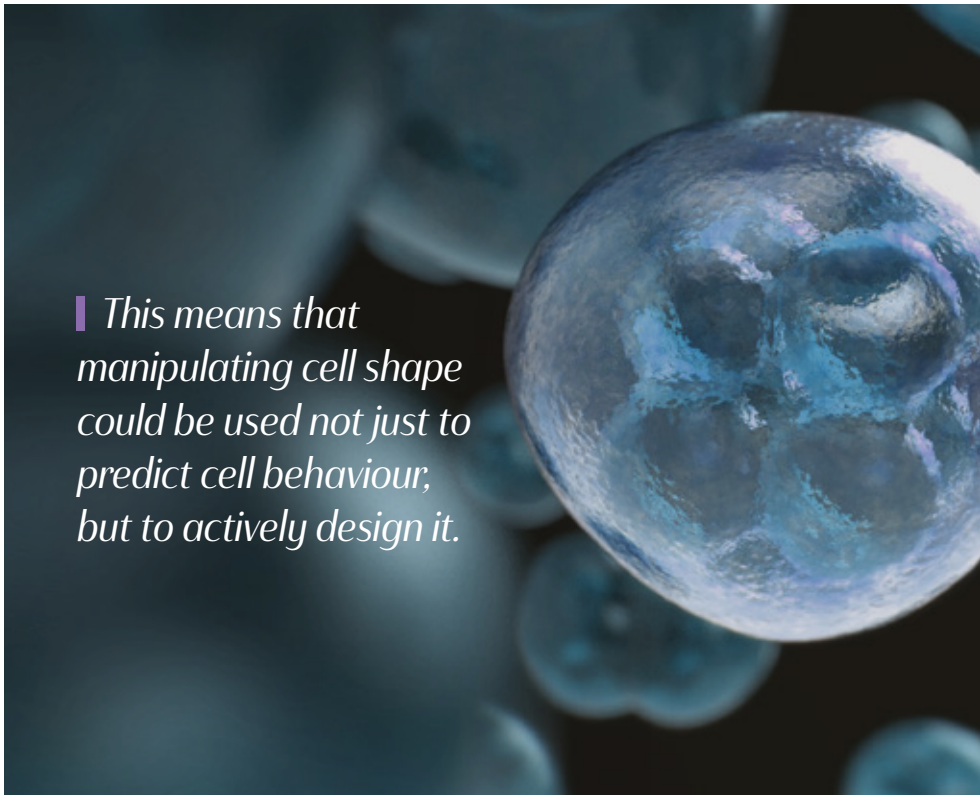
**Study Pinpoints Midlife Molecular Shift That Accelerates Ageing Across the Body**

A new study published in *Cell* has identified a midlife "inflection point" in human ageing, with molecular changes accelerating sharply between the ages of 45 and 55. Researchers from the Chinese Academy of Sciences conducted a proteomic analysis of 516 tissue samples from 13 organ systems, taken from 76 donors aged 14 to 68 who died of traumatic brain injury. They found that while some age-related shifts occur gradually, many disease-linked proteins show an abrupt increase in midlife, suggesting a coordinated, system-wide acceleration of ageing.

The aorta exhibited the most dramatic changes, highlighting the potential role of the vascular system as a driver and indicator of overall physiological decline. The adrenal glands began showing alterations as early as age 30, pointing to hormonal pathways that may set the stage for later systemic effects. Among the 48 proteins most strongly linked to cardiovascular and liver disease, many spiked during the identified midlife window, creating a potential set of molecular targets for preventive or regenerative interventions.

For regenerative medicine and aesthetic practice, the findings suggest a critical window for intervention before structural and functional decline becomes entrenched. The vascular shifts identified may help explain midlife changes in skin tone, elasticity, and healing capacity, while the proteomic signatures could inform personalised approaches to slowing tissue ageing. The authors note that the work has limitations, including the modest sample size and the absence of data from the brain, kidneys, and reproductive tissues.



Nonetheless, by defining a clear molecular turning point, the study opens the door to earlier and more targeted strategies for maintaining tissue health and slowing visible signs of ageing.

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**New Label-Free Technique Uses Electric Fields to Identify Ageing Cells**

A team of researchers at Tokyo Metropolitan University has developed a new method for identifying ageing human cells - without using any chemical labels. The technique, which relies on the application of alternating electric fields, promises to streamline ageing research and accelerate progress in the study of age-related diseases.

Known as frequency-modulated dielectrophoresis (FM-DEP), the process enables scientists to distinguish senescent (ageing) cells from healthy ones by analysing how they respond to electric fields. Unlike conventional methods that require chemical stains or fluorescent tags, FM-DEP detects differences in the cells' physical and electrical properties.

The team demonstrated the technique using human dermal fibroblasts - cells commonly found in connective tissue. According to the research team, senescent cells exhibit a significantly lower "cutoff frequency" compared to non-senescent cells when exposed to varying frequencies of electric fields. This difference is caused by changes in the composition of the cell membrane - particularly the lipids - which affect how the cells polarise in response to the field.

The new method offers several key advantages. Because it does not require chemical labeling, it preserves the cells' natural state, avoids introducing artifacts, and reduces processing time.

Senescent cells are implicated in many age-related diseases, including neurodegeneration, cardiovascular disease, and certain types of cancer. Efficiently identifying these cells without chemical interference could improve research into the biological mechanisms of ageing and help in the development of targeted treatments.

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**Canadian Researchers Launch $24M Mitochondrial Transplantation Programme to Advance Regenerative Therapies**

A consortium of Canadian researchers has launched MitoRevolution, a $24 million translational research initiative aimed at developing mitochondrial transplantation as a therapeutic tool for organ repair and treatment of chronic disease.

Mitochondrial dysfunction is a key driver of cellular energy failure in a range of conditions, including ischemia-reperfusion injury, neurodegeneration, and organ failure. The MitoRevolution team is working to refine the isolation, preservation, and delivery of viable mitochondria, and to understand their integration and function post-transplantation.

Preclinical studies have demonstrated that introducing exogenous mitochondria into damaged tissues - such as cardiac or neural tissue - can restore bioenergetics, reduce cell death, and improve functional recovery. The consortium aims to scale these efforts toward clinical translation.

Research priorities include optimising mitochondrial delivery vehicles and injection strategies, enhancing survival and biointegration of transplanted mitochondria, and establishing biomarkers to track mitochondrial viability and therapeutic response.

Funded by the New Frontiers in Research Fund, this national effort brings together specialists in cell biology, imaging, regenerative medicine, and bioengineering from leading Canadian institutions.

The project holds promise for future therapies targeting myocardial infarction, stroke, solid organ transplantation, and metabolic disorders with a mitochondrial component. While clinical applications remain in development, mitochondrial transplantation is emerging as a novel platform for cellular-level energy repair in regenerative medicine.

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**Micropatterned Culture Dish Enhances Therapeutic Potential of Mesenchymal Stem Cells**

A collaborative team of researchers from Hiroshima University, Keio University, Tokyo Women's Medical University, and the University of Utah has developed a novel culture method that significantly enhances the functional properties of mesenchymal stem cells (MSCs).

Their findings, published in *Materials Today*, suggest that physical alignment of MSCs on micropatterned culture dishes improves their therapeutic efficacy in regenerative applications.

The team utilised temperature-responsive culture dishes etched with microgroove patterns to promote the formation of aligned MSC sheets. This configuration facilitated improved cell-to-cell interactions and better preservation of extracellular matrix components. Upon cooling, the intact sheets could be detached from the culture surface without enzymatic treatment, maintaining their structure and bioactivity.

*The team utilised temperature-responsive culture dishes etched with microgroove patterns to promote the formation of aligned MSC sheets*

Aligned MSC sheets showed significantly increased secretion of key paracrine factors, including vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), and transforming growth factor beta (TGF-β). These cytokines play critical roles in angiogenesis, tissue regeneration, and immunomodulation, making the enhanced MSC sheets more promising for clinical use.

Importantly, the alignment process did not compromise the cells' multipotency. The MSCs retained their capacity to differentiate into osteogenic, adipogenic, and chondrogenic lineages, ensuring their continued relevance for diverse therapeutic applications.

The researchers also noted that delivering MSCs in sheet form - rather than as single-cell suspensions -offers practical advantages in vivo, such as improved cell retention at the implantation site and enhanced survival rates post-transplantation.

This study highlights a scalable, non-invasive technique to increase the functional performance of MSCs for regenerative therapies. Further preclinical studies are expected to evaluate the therapeutic outcomes of aligned MSC sheets in specific models of tissue injury and degenerative disease.

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**Scientists Use DNA 'Origami' to Help Promote Angiogenesis**

Researchers have engineered tiny DNA-based structures to deliver a healing protein that helps grow new blood vessels - a critical step in tissue repair and recovery.

The study, published in the *International Journal of Biological Macromolecules*, showcases how scientists used DNA origami - nanoscale shapes made by folding DNA – to transport a peptide called QKCMP, which is known to stimulate angiogenesis, the process by which new blood vessels form.

"Think of these DNA structures as microscopic delivery drones," explained the researchers. "They carry the peptide safely through the body and release it slowly, exactly where it's needed."

Angiogenesis plays a central role in healing damaged tissues, especially in wounds, heart conditions, and diseases where blood flow is reduced. But delivering pro-angiogenic factors like QKCMP effectively has long been a challenge - they degrade quickly and don't always reach the target site.

To solve this, the team built triangular DNA origami carriers that protected the QKCMP peptide, helped it survive longer, and ensured a steady release. In laboratory tests, the peptide-loaded nanostructures significantly improved biological activity, promoting better blood vessel growth compared to the peptide alone.

The approach could pave the way for next-generation treatments in regenerative medicine where controlled blood vessel growth is essential for restoring tissue health.

"This method gives us more control," the authors noted. "We're not just delivering the healing signal - we're guiding when and where it works best."

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**AI-Driven Monitoring Could Transform Stem Cell Manufacturing Quality Control**

A new review in *Biotechnology Journal* outlines how artificial intelligence (AI) could overhaul the way stem cell cultures are monitored and controlled, paving the way for more consistent, scalable, and clinically compliant regenerative therapies.

Current quality control for stem cells relies heavily on periodic, labour-intensive endpoint assays such as microscopy, flow cytometry, and immunostaining - methods that are destructive and offer limited real-time insight.

The review describes AI-powered alternatives that integrate high-resolution imaging, environmental sensors, and multi-omics data to continuously track critical quality attributes (CQAs) including morphology, proliferation, differentiation potential, genetic stability, and contamination risk.

Key approaches include convolutional neural networks for non-invasive morphology assessment, predictive modelling to forecast optimal subculture timing, reinforcement learning for dynamic environmental adjustments, and multi-omics fusion for detecting early genetic drift. According to the research, these systems can detect anomalies hours to days earlier than traditional methods and adapt culture conditions in real time, potentially reducing batch failures and improving therapeutic reproducibility.

The authors also highlight emerging capabilities with potential to address longstanding challenges. Generative adversarial networks (GANs) can generate realistic synthetic images to train models for rare events, improving classification accuracy while reducing dependence on

*Think of these DNA structures as microscopic delivery drones. They carry the peptide safely through the body and release it slowly, exactly where it's needed*

*According to the research, these systems can detect anomalies hours to days earlier than traditional methods and adapt culture conditions in real time, potentially reducing batch failures and improving therapeutic reproducibility.*

scarce annotated data. Digital twin bioreactor models - virtual simulations continuously updated with live sensor and imaging data - could predict culture trajectories and suggest interventions before quality is compromised. Federated learning frameworks offer a way to train robust, multisite AI models without sharing raw patient- or donor-derived data, enhancing privacy and regulatory compliance.

For the medical aesthetics and regenerative medicine sectors, the potential is clear: real-time, automated culture optimisation could speed the delivery of stem cell-derived products for applications ranging from tissue repair to hair follicle regeneration, while strengthening compliance with good manufacturing practice (GMP) standards.

According to the review, "By integrating heterogeneous data streams - including high-resolution imaging, environmental sensor data, and multi-omics profiles - AI systems can dynamically track critical quality attributes (CQAs), forecast culture trajectories, and proactively guide process interventions."

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**Porcine-Derived Vaginal Matrix Shows Promise for Regenerating Atrophic Tissue**

Researchers have developed a tissue-specific extracellular matrix (ECM) scaffold from porcine vaginal tissue that could one day support the regeneration of atrophic vaginal tissue – a common issue in postmenopausal women and some cancer survivors.

The study, published in *Advanced Materials*, describes how the decellularised porcine vaginal ECM (vECM) retained native structural proteins and biochemical cues that promoted cell proliferation, angiogenesis, and collagen remodelling in preclinical models.

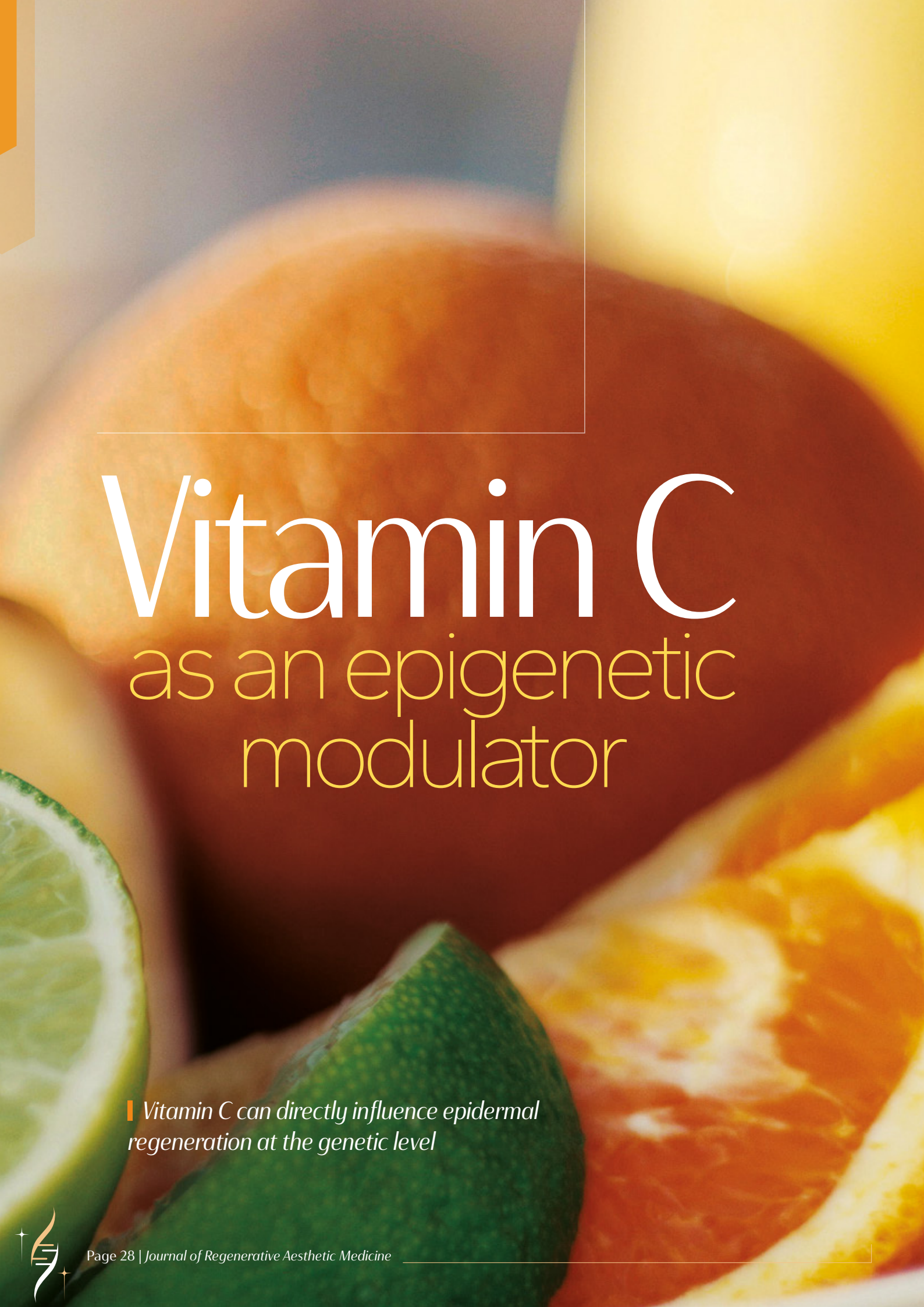
The team used a decellularisation process to strip away all living pig cells, leaving behind a structural and biochemical framework. This material, rich in collagen, glycosaminoglycans, and growth factor-binding sites, was then fabricated into a porous, biocompatible scaffold. In animal testing, implantation of the vECM supported tissue regeneration and improved local vascularisation compared to non-tissue-specific scaffolds.

Porcine-derived biomaterials are already used in certain approved human implants, such as heart valves, dermal substitutes, and hernia meshes. However, translating this vaginal ECM to human use raises additional considerations. Ethical and cultural objections to porcine products may limit acceptance in some populations, and sourcing from animal tissue requires rigorous screening for pathogens and manufacturing under clinical-grade conditions.

The authors emphasise that this research is still at an early, preclinical stage. Before any human application, the vECM would need extensive safety and efficacy testing, regulatory review, and possibly the development of alternative sources, such as human donor tissue or synthetic ECM analogues, for patients who cannot or do not wish to receive porcine-derived implants.

While far from clinical availability, the study highlights the potential of organ- and tissue-specific ECM scaffolds to provide more tailored regenerative cues than generic biomaterials, potentially offering new options in the treatment of vaginal atrophy.

*The team used a decellularisation process to strip away all living pig cells, leaving behind a structural and biochemical framework*



# Vitamin C as an epigenetic modulator

*Vitamin C can directly influence epidermal regeneration at the genetic level*

# An exploration of the new research that reveals vitamin C's potential role in reactivating regenerative pathways in the skin

Vitamin C (ascorbic acid) has long been heralded in aesthetic dermatology for its collagen-stimulating, antioxidant, photoprotective, and tyrosinase-inhibiting properties.[1,2,3] Topically, it's employed to enhance dermal collagen synthesis, reduce photoageing, brighten pigmentation, and protect against reactive oxygen species generated by UV exposure. Intradermal or systemic administration has also been explored to support wound healing, scar maturation, and tissue repair. [4,5] Yet, despite its widespread use, limited mechanistic understanding exists regarding its direct influence on epidermal cell biology - beyond its role in extracellular matrix modulation. Recent findings now offer new insight into this gap in understanding, with evidence suggesting that vitamin C can directly influence epidermal regeneration at the genetic level.[6]

## **Study goals** and methods

This emerging role is the focus of a new study by Sato *et al.*, published in the *Journal of Investigative Dermatology* earlier this year which investigates how vitamin C regulates epidermal proliferation through epigenetic DNA demethylation in a 3D human epidermal equivalent model.

*Vitamin C uptake led to a marked increase in epidermal thickness, as confirmed by histological analysis*

The study aimed to determine whether vitamin C could actively enhance epidermal thickness and drive keratinocyte proliferation. To explore this, researchers used a reconstructed human epidermis model, applying intracellular vitamin C and observing morphological changes alongside molecular markers of cell growth. Importantly, the team examined global levels of 5-hydroxymethylcytosine, a key epigenetic marker linked to active DNA demethylation, to assess whether vitamin C influenced the epigenetic landscape.

To test the specificity of this mechanism, a TET enzyme inhibitor was introduced. TET enzymes facilitate the conversion of 5-methylcytosine to 5-hydroxymethylcytosine - an essential step in gene reactivation.[7] Inhibiting this process provided clear evidence that vitamin C's effects were indeed TET-dependent.

Beyond broad epigenetic changes, the researchers conducted high-resolution genomic analyses, combining DNA microarray and whole-genome bisulfite sequencing. This allowed them to identify a specific set of genes involved in proliferation that were epigenetically reactivated by vitamin C exposure, offering a mechanistic link between treatment and observed cellular outcomes.

## **Key** findings

The study identifies a series of mechanistic insights that support vitamin C's emerging role in regenerative aesthetics - demonstrating not only its influence on skin structure, but its capacity to modulate epidermal renewal at the genetic level.

### Epidermal thickness and proliferation

Vitamin C uptake led to a marked increase in epidermal thickness, as confirmed by histological analysis. In treated models, epidermal thickness increased by approximately 35% compared to controls ($p < 0.01$). This thickening was accompanied by elevated expression of proliferation markers such as Ki-67, indicating active keratinocyte division. These effects paralleled a global rise in 5-hydroxymethylcytosine (5hmC), suggesting enhanced epigenetic activity through DNA demethylation.

### Essential role of TET enzymes

To confirm the epigenetic mechanism, the researchers introduced a TET enzyme inhibitor alongside vitamin C treatment. This intervention nearly abolished the rise in 5hmC and significantly blunted the increase in epidermal thickness and proliferation, clearly indicating that the regenerative effect of vitamin C is TET-dependent. Quantitative measures showed that 5hmC levels returned close to baseline in the presence of the inhibitor.

### Epigenetic reactivation of proliferation genes

Using whole-genome bisulfite sequencing and microarray analysis, the study identified 12 key genes involved in cell cycle regulation and keratinocyte maintenance that were both hypomethylated and upregulated following vitamin C treatment. The changes in DNA methylation were highly localised to promoter and enhancer regions, with a strong correlation to gene expression levels ($p < 0.001$), supporting a direct role in transcriptional reactivation.

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*This study offers important mechanistic insight into how vitamin C may influence epidermal regeneration*

## Discussion

These findings go beyond reinforcing vitamin C's topical benefits - they uncover a previously unappreciated mechanism of action, positioning vitamin C as a biologically active agent in epidermal regeneration through epigenetic modulation.

### Mechanistic insight

Vitamin C functions intracellularly as a TET cofactor that facilitates conversion of 5-methylcytosine to 5-hydroxymethylcytosine, reactivating genes silenced by hypermethylation. This epigenetic reprogramming enhances keratinocyte proliferation and thickens the epidermis - not by altering extracellular collagen, but via intracellular gene regulation. In other words, by reactivating these genes, vitamin C encourages skin cells to multiply and thicken the outer skin layer, working from within the cell rather than by boosting collagen outside it.

### Relevance to skin ageing

The study offers a compelling mechanism for vitamin C's traditional role in antiageing, especially in counteracting epidermal thinning. With thinning epidermis characteristic of aged or photoaged skin and chronic dermatoses, vitamin C could be a non-invasive agent to restore epidermal integrity. It also suggests potential for vitamin C to support regeneration in wound healing, scar remodelling, and barrier restoration.

### Clinical translation considerations

**Form and delivery:** For vitamin C to have an effect on gene activity inside skin cells, it needs to be delivered in a way that ensures it actually enters those cells. This might require advanced delivery methods such as lipid-based formulations, electrical stimulation (like iontophoresis), or specially modified vitamin C compounds that can cross cell membranes more easily.

- **Concentration thresholds:** The effective doses used in laboratory experiments may not directly translate to safe or practical concentrations for clinical use. More studies are needed to determine how much vitamin C is needed in real-world applications to achieve similar regenerative effects without irritation or toxicity.
- **Target populations:** These findings are particularly promising for patients with thinning or fragile skin, such as older adults, individuals undergoing aesthetic procedures, or those with delayed wound healing. Vitamin C may offer a targeted, non-invasive way to support skin regeneration in these groups.

## **Limitations** and areas for future research

While the findings open up exciting possibilities, the study authors acknowledge several limitations to their findings and propose areas for future investigation to confirm and extend their results, before translating this approach into routine clinical practice:

- **In vitro setting:** The 3D skin model used mimics the structure of human epidermis but doesn't fully replicate the complex interactions of living skin. Follow-up studies in animals and humans will be essential to confirm these effects under real-life physiological conditions.
- **Gene specificity:** Although 12 proliferation-related genes were identified, it remains unclear how each one individually contributes to skin regeneration. Further research is needed to map their exact roles and functional interactions.
- **Inhibitor specificity:** The TET enzyme inhibitor used in the study may have had off-target effects, influencing other cellular processes. More precise techniques, such as genetic knockdown or CRISPR editing, would provide stronger validation of the pathway.
- **Safety profile:** Stimulating gene activity to enhance skin growth introduces potential risks, including uncontrolled cell proliferation. Long-term safety studies will be critical to ensure that these interventions do not raise the risk of adverse outcomes such as tumour formation.

## **Future directions** in regenerative aesthetic medicine

This study offers important mechanistic insight into how vitamin C may influence

*By reactivating these genes, vitamin C encourages skin cells to multiply and thicken the outer skin layer*

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epidermal regeneration - not through its traditional roles in antioxidant defense or collagen production, but by reactivating gene expression via TET-mediated DNA demethylation.

The findings suggest potential applications for vitamin C in addressing conditions such as epidermal thinning, impaired barrier function, and post-procedural recovery. However, further research is needed to determine optimal delivery systems, safe and effective dosing, and long-term safety, particularly when targeting epigenetic pathways.

As interest in regenerative strategies continues to grow within aesthetic medicine, this work contributes meaningfully to an evolving understanding of how established compounds like vitamin C might be re-evaluated through a more molecular lens.

## Clinical comment

Vitamin C (ascorbic acid) has long been a cornerstone in dermatology and aesthetic medicine due to its well-documented roles in collagen synthesis, antioxidant protection, and modulation of pigmentation. The recent study by Sato et al. (2025) in the Journal of Investigative Dermatology expands this paradigm, uncovering a novel epigenetic mechanism through which vitamin C directly enhances epidermal regeneration. This work positions vitamin C not merely as a supportive antioxidant but as an active regulator of gene expression in keratinocytes.

### Study significance

The investigators used a reconstructed 3D human epidermal equivalent model to examine how intracellular vitamin C affects keratinocyte proliferation and epidermal thickness. Their central hypothesis - that vitamin C acts as a cofactor for TET enzymes to promote DNA demethylation - was supported by robust molecular and histological findings. A 35% increase in epidermal thickness and upregulation of proliferation markers (e.g., Ki-67) strongly suggest a direct proliferative effect mediated by epigenetic reactivation. The reversal of these changes by TET inhibition provides mechanistic clarity.

### Epigenetic insights

The identification of 12 hypomethylated, upregulated genes associated with cell cycle regulation provides a compelling mechanistic link between vitamin C exposure and enhanced keratinocyte activity. This represents a conceptual leap in understanding vitamin C's action - from extracellular collagen modulation to intracellular epigenetic reprogramming. Such findings highlight vitamin C as a biologically active molecule capable of re-establishing regenerative pathways suppressed by age or environmental stressors.

### Clinical relevance

Epidermal thinning is a hallmark of intrinsic and extrinsic ageing, impairing barrier integrity and resilience. The demonstration that vitamin C can restore epidermal thickness through gene regulation suggests therapeutic potential in several domains: prevention of photoageing, support in chronic dermatoses with barrier compromise, and optimisation of post-procedural recovery. Importantly, this mechanism also reinforces vitamin C's role in wound healing and scar modulation.

### Translation challenges

Despite its promise, clinical application requires caution. Effective intracellular delivery of vitamin C remains a challenge due to its instability and poor dermal penetration. Advanced delivery vehicles - liposomal carriers, iontophoresis, or stable vitamin C derivatives - will be essential. Moreover, the effective concentrations used in vitro may not be achievable or safe in vivo, necessitating dose-finding studies. Equally, any therapy that stimulates proliferation through epigenetic modulation raises theoretical concerns regarding oncogenic risk, requiring rigorous long-term safety evaluation.

### Final thoughts

This study reframes vitamin C as more than an antioxidant or collagen stimulant: it is a potential epigenetic modulator of skin renewal.

While further translational research is critical, the findings introduce an exciting avenue for regenerative aesthetic medicine.

**Dr Lee Walker**
RAMI Scientific Committee member

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# Regenerating Compromised Skin

Dr Hannah Chapman presents a case study demonstrating successful management of facial dermatitis and acne using exosomes and LED therapy

Facial dermatitis and acne are common yet challenging conditions in aesthetic practice, especially when co-existing. These conditions often create a vicious cycle of inflammation, barrier dysfunction, and microbial imbalance, leading to both physical discomfort and psychological distress[1-4]

Here we explore the synergistic benefits of combining microneedling with exosome therapy and LED light treatment in a patient with persistent dermatitis and acne.

## Patient profile and diagnosis

In 2024, a female patient presented with a 12-month history of persistent red, irritated, and flaking skin across the face, including the periocular area and eyelids. In addition, she was experiencing regular breakouts of pustular acne.

The symptoms caused significant discomfort and distress - particularly the itching and irritation, which disrupted her sleep and led to noticeable declines in confidence and social engagement. Over-the-counter skincare solutions had proven ineffective.

Upon detailed consultation and assessment, a dual diagnosis of facial dermatitis and acne was made.

## Treatment approach

The agreed treatment protocol consisted of the following:

- SkinPen microneedling at a depth of 0.25mm, performed every four weeks for a total of three sessions.
- Each microneedling session was combined with E-50 exosome serum, selected for its regenerative, anti-inflammatory, and barrier-repairing properties.
- In between microneedling sessions, the patient underwent six sessions of Dermalux Flex LED therapy (30 minutes per session, twice weekly) using a combination of red, near-infrared (NIR), and blue wavelengths to address inflammation, acne bacteria, and dermal healing.
- At-home skincare routine using the Biojuve system. These products specifically aim to support and repair the microbiome. Active topical agents that would normally treat acne (such as retinoids and salicylic acid) were contraindicated due to the patient's dermatitis, while any emollients that treat dermatitis would have potentially been comedogenic.

## Rationale

This patient presented with a complex combination of chronic facial dermatitis and pustular acne, significantly affecting both her physical comfort and mental wellbeing. Traditional interventions, such as corticosteroids or topical acne treatments, often come with limitations - particularly around the delicate periocular area - and can exacerbate irritation or lead to rebound symptom.[5-6] Given her sensitive skin, history of treatment failure, and psychosocial impact, a regenerative, non-pharmaceutical strategy was deemed most appropriate.

## Microneedling with exosomes: calming from within

Microneedling using the SkinPen® at a shallow depth (0.25mm) was selected to gently stimulate dermal regeneration without provoking excessive inflammation. This technique initiates controlled micro-injuries that activate the skin's natural repair processes, promoting the production of collagen and elastin - both crucial for restoring skin integrity.[7,8]

To maximise healing while avoiding irritation, the microneedling was combined with E50 exosome serum. E-50 exosomes are derived from salmon fibroblast cells using proprietary ENTR® technology, delivering a concentrated dose of bioactive molecules including growth factors, peptides, and anti-inflammatory signals. These exosomes are specifically formulated to enhance barrier repair, reduce inflammation, and support cellular renewal - qualities essential for managing both dermatitis and acne-prone skin.[9]

For this patient, exosome therapy offered a steroid-free, targeted regenerative solution that addressed the underlying inflammation while accelerating recovery. By improving cell-to-cell communication and calming overactive immune responses, the E-50 exosomes helped break the cycle of chronic irritation without the risk of sensitisation or barrier disruption.

## LED phototherapy: supporting anti-inflammatory and anti-microbial action

To complement the regenerative effects of microneedling and exosomes, Dermalux Flex MD LED phototherapy was incorporated into the treatment regimen. The patient underwent six sessions utilising a tri-wave protocol comprising red (633nm), near-infrared (830nm), and blue (415nm) light. Each wavelength serves a distinct therapeutic purpose:[10]

- **Blue Light (415nm):** Targets and eliminates acne-causing bacteria, aiding in the reduction of breakouts.
- **Red Light (633nm):** Stimulates fibroblast activity, promoting collagen and elastin production, which are essential for skin repair and reducing inflammation.
- **Near-Infrared Light (830nm):** Penetrates deeper skin layers to modulate inflammation and enhance circulation, facilitating tissue repair.

This combination offers a non-invasive, non-thermal adjunct therapy that soothes the skin while addressing the underlying causes of the patient's symptoms. Importantly, LED therapy is associated with no downtime, minimal risk of irritation, and is safe for use on all facial zones, including the sensitive periocular area.[11]

Given the patient's need for a gentle yet effective protocol to restore barrier function, reduce acne lesions, and improve skin clarity, this combination was well- suited. The visible and progressive improvement in her skin also provided psychological reassurance, helping to restore her confidence and sense of control.


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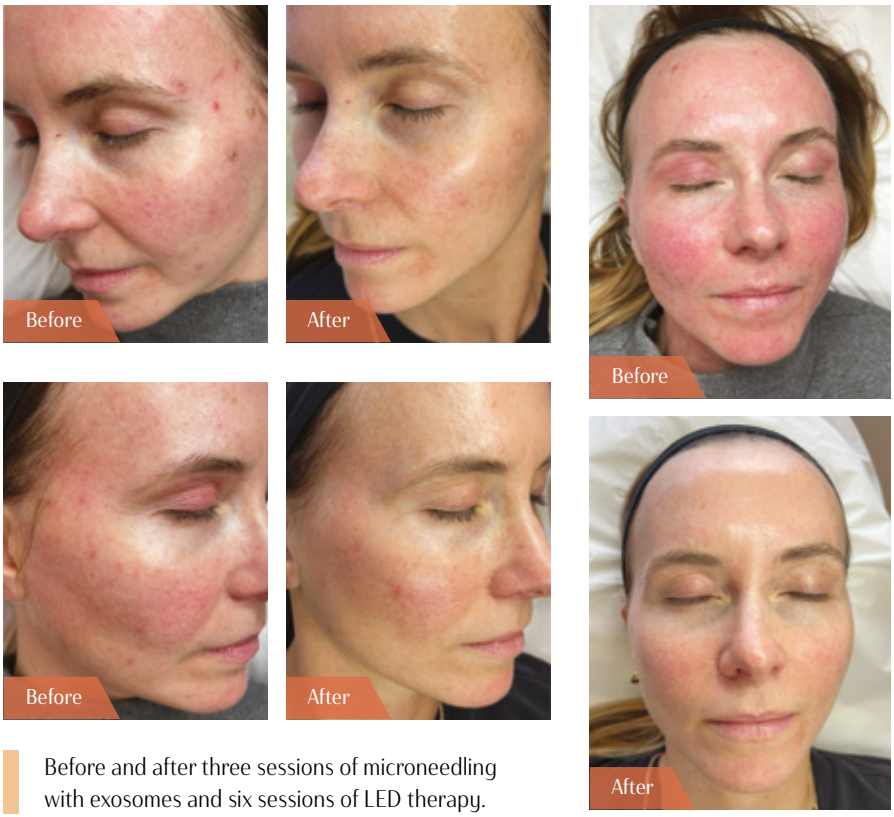
## Clinical outcome




Before and after three sessions of microneedling with exosomes and six sessions of LED therapy.

Visible improvement in skin condition was noted within four weeks of initiating treatment. Redness and flaking diminished significantly, with concurrent reductions in pustular acne and periocular irritation. By the conclusion of the initial treatment cycle, the patient reported improved sleep quality, reduced itching, and a marked uplift in confidence and mood.

At follow-up, the patient's skin remained clear and stable. She has continued with maintenance exosome microneedling sessions every six months, with no recurrence of dermatitis or acne. This sustained result underscores the long-term benefits of regenerative therapy for chronic inflammatory skin conditions.

## Summary

This case illustrates the efficacy of exosome-enhanced microneedling combined with LED light therapy in addressing coexisting facial dermatitis and acne. The regenerative, non-steroidal nature of the treatment made it particularly suitable for sensitive areas such as the eyelids and periocular region. The patient's rapid and sustained improvement highlights the potential for exosomes and phototherapy to restore skin health, reduce inflammation, and improve overall wellbeing without pharmaceutical intervention.

## Patient reflection

After the first exosome treatment my skin was red for a couple of days, but once that had calmed the change overnight was remarkable, and it continued to improve as the skin plan was implemented. I haven't had any further acne breakouts and the eczema is totally gone - my skin has never looked or felt so healthy. I am so grateful to Dr Hannah and these amazing treatments!

*Visible improvement in skin condition was noted within four weeks*

Dr Hannah Chapman BMBS BMedSci (Hons) RCGP(2011), DFSRH, DRCOG is a GP and aesthetic doctor based in Bristol. Through her medical training and 19 years of NHS practice she has gained extensive experience in anatomy, pharmacology, dermatology and surgery (including maxillofacial surgery). Dr Chapman has a particular interest in regenerative aesthetics and was one of the first doctors in Bristol to introduce polynucleotides to her practice. She believes that multifaceted concerns need a multimodal approach and specialises in combining regenerative techniques such as Morpheus8 with polynucleotides for outstanding results.

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# Where Aesthetics Meets Longevity: The Evolution of Esteem Life Medical Group

What happens when an aesthetics clinic expands its vision from surface-level results to regenerative, longevity-driven care? Dr Cemal Kavasogullari, private GP and founder of Glasgow's Esteem Life Medical Group, walks us through how he established a new model of care - from rethinking protocols to reshaping patient relationships - and shares lessons for peers considering a similar path.

## **Time** for change

The aesthetic industry is at a crossroads. As science evolves and patients become more educated, the demand for integrative, longevity-focused care is reshaping what it means to 'look and feel well'. Leading this transformation is Dr Cemal Kavasogullari, a private GP with a deep-rooted passion for holistic health. Esteem Life Medical Group was established with a forward-thinking vision: to unite aesthetic medicine, regenerative science and longevity care into a singular patient-focused experience.

At Esteem Life, aesthetic interventions are seen as a vital part of whole-person longevity. "How we look is a social signal of how we're functioning internally," explains Dr Kavasogullari. "It affects how we see ourselves and how we're seen by others. That's not vanity - it's human biology." This philosophy is rooted in biological, psychological and social health - the foundation of every patient pathway he designs.

In this conversation, Dr Kavasogullari opens up about what inspired his business, the challenges of building a new kind of medical aesthetics practice, and what he believes is next for a sector increasingly driven by science, substance and a deeper kind of self-care.

## **Making** the move

### What inspired you to shift from traditional aesthetics to regenerative aesthetics?

As a GP with a deep interest in holistic health, I've always believed that true wellbeing is biological, psychological and social. Appearance is not vanity - it's a visible reflection of internal health and, from an evolutionary perspective, plays a major role in how we're perceived and how we feel about ourselves. Patients weren't just asking to look good - they wanted to feel good, perform at their best, and keep their bodies at optimum level. Regenerative aesthetics perfectly aligns with this. It allows us to improve skin, tissue and cellular function - enhancing visible beauty while also supporting healthy ageing.

From a practitioner perspective, I saw that traditional aesthetics treated symptoms, not causes. Regenerative techniques allow us to change that - to actually improve skin architecture and biological function.

*As a GP with a deep interest in holistic health, I've always believed that true wellbeing is biological, psychological and social*

### Was there a specific patient need or market trend that drove this transition?

Definitely. We serve mainly professionals - CEOs, high performers, barristers - who live fast-paced, high-stress lives. They don't have the luxury of taking weeks off to recover. They need effective solutions that respect their time. From a female perspective, the awareness of accelerated collagen loss during menopause drove demand for regenerative solutions that maintain skin integrity naturally.


## **A new** identity

### How would you define your clinic's mission?

Esteem Life was founded on a new mission entirely: to create an advanced clinical environment focused on optimising function at every age. Our aim is to help patients gift something to their

*Longevity isn't just about living longer – it's about performing at your best at every age.*

future selves. We focus on identifying individual goals and aligning treatments that support long-term resilience, regeneration, and performance. It's longevity from the inside out - with aesthetics as one visible measure of success.

Really, our mission is simple: empower you to look well, feel well and stay well.

### How did you decide the clinic's name, visual identity and service model?

As a newly formed medical group, Esteem Life was designed from the ground up with its own visual identity, philosophy and clinical framework. The name reflects our core values - esteem, empowerment, and life lived well. The brand aesthetic promotes natural elegance and trust, while our service model emphasises ongoing clinical relationships rather than single interventions.

### What were the biggest considerations during the branding process?

The biggest consideration was designing a fully integrated clinical model that united aesthetic, regenerative, and longevity disciplines under one patient experience. Treatments had to complement each other, staff had to be trained to speak the same language, and our internal systems needed to track measurable health and skin outcomes across time. The metamorphosis was complete - we just had to break the cocoon and show our new colours.

### What kind of training or certifications did you and your staff pursue?

We invested heavily in upskilling: regenerative medicine, women's health, herbal medicine, holistic health coaching. Internal workshops helped the team see patient care from multiple perspectives - biological, psychological and social.

### Which regenerative treatments have become your flagship services?

Personalised IV protocols such as NAD+ and Methylene Blue are among our most in-demand services, especially from high-functioning professionals looking to sustain energy, clarity, and resilience. Alma Hybrid laser and EBD protocols combined with collagen stimulators like PDLLA (Lenisna®) and CaHA (Novuma®) deliver natural but refined rejuvenation. We've also strengthened our women's health offering with a specialist GP, holistic coach and medical herbalist. Focus is on long-term outcomes, not temporary fixes.

## **Communicating** the change

### How did you communicate the shift to your existing patient base?

As a new clinic, our focus was on articulating a clear identity from day one. While some patients had worked with me in previous contexts, we approached the launch of Esteem Life as a completely fresh proposition - rooted in education, trust, and vision. Our social channels, internal communication systems and patient materials were aligned with this philosophy from the outset.

### How do you ensure patient education around regenerative treatments?

First, we do our own research - every treatment is backed by literature and clinical evidence. We distil this into blogs, social posts and in-depth consultations. We also speak at conferences, publish insights and keep patients informed through clear, digestible content.

## **A shift** in culture, not standards

### How has the new approach affected business performance?

As a newly launched clinic, we've been fortunate to attract a highly engaged patient base that values longevity, performance and integrity. Retention is high, referrals are frequent, and many of our patients engage across multiple treatment pathways - from aesthetics to IV therapy to preventative health.

### Are your target demographics the same or have they shifted?

Our demographic is broader but more refined. Less transactional - more committed. Our patients want to be part of the longevity culture we're cultivating. We are expanding our tribe.

### Any unexpected reactions?

The response has been overwhelmingly positive. Staff were energised and new team members integrated quickly.

*Your skin is the only part of you everyone sees – so let it tell the right story*

Patients were supportive - some were cautious at first but became enthusiastic once they saw real results and trusted data.

## **Lessons** looking back

### What were the biggest challenges?

Launching Esteem Life Medical Group was both exciting and demanding. One of the key challenges was developing a unified clinical model that genuinely merged aesthetics, longevity medicine, and wellness - not just as menu items, but as an integrated philosophy. That meant retraining our team, rewriting protocols, and creating new frameworks for outcome tracking that could capture both visible and invisible transformations.

Operationally, the clinic buildout required careful coordination of infrastructure, brand development, technology integration and supplier relationships, all while staying true to our patient-centred values. Clinically, the biggest hurdle was educating patients about regenerative medicine in a market still saturated with quick fixes and aesthetic commodification.

Internally, managing rapid innovation alongside compliance, safety protocols, and medical oversight was another layer of complexity - especially as we built a hybrid team that spans aesthetic, functional and lifestyle domains.
But ultimately, the most rewarding challenge has been creating a culture - not just a clinic - that patients want to belong to, and that staff feel proud to co-create.

*Start with your mission and vision - this will define everything you do*

### What would you do differently?

I'd run deeper market research into our area's unique demographics and kick off with a clearer, bolder social campaign that drills our values home from day one.

### What advice would you give to other clinic owners?

Start with your mission and vision - this will define everything you do, from service design to marketing. Be clear about your value proposition. Patients are more informed than ever - they'll follow you if you lead with integrity and real expertise.

## **The** next chapter

### What's next for the clinic?

We're currently exploring a number of advanced modalities that align with our focus on performance, prevention, and cognitive optimisation. These include epigenetic profiling, genetic testing, hypoxia-based training protocols, hyperbaric oxygen therapy, and electro-stimulation of the vagus nerve and central nervous system - all aimed at enhancing mental resilience, recovery, and cognitive longevity.

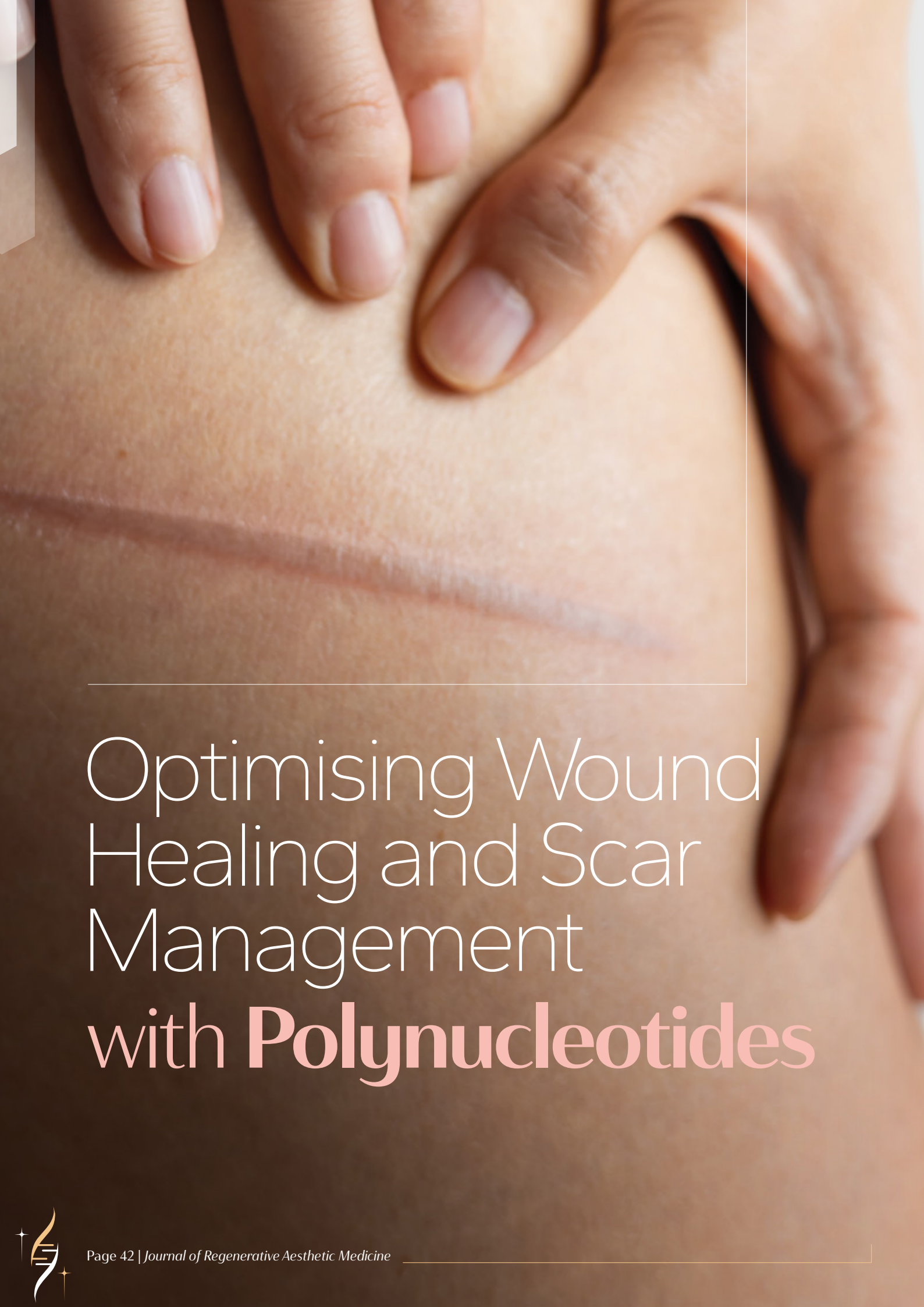
On the clinical side, we're expanding our multidisciplinary team to include specialties such as plastic surgery, dermatology, ENT, and psychology, ensuring that patients receive fully integrated care across aesthetic, functional, and emotional dimensions. These additions will allow us to support our patients through every phase of their ageing journey - from aesthetic optimisation to surgical interventions, sensory health, and psychological wellbeing.

## **A new era** of aesthetic practice

Dr Cemal Kavasogullari's story is a clear example of how regenerative aesthetics isn't just a trend - it's a strategic and clinical evolution. By aligning internal health with visible outcomes, he's built a model that respects patients' time, biology, and long-term wellbeing. For clinicians considering a similar shift, his advice is grounded but galvanising: start with purpose, lead with science, and never underestimate how informed today's patient truly is.

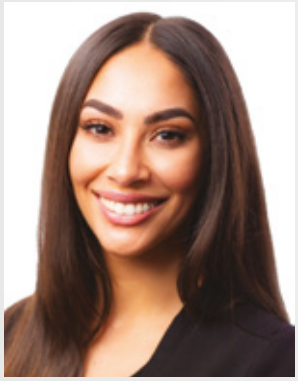
As the boundaries between aesthetics, medicine and performance continue to blur, practices like Esteem Life Medical Group are setting the pace - not just for how we age, but how we live.

*Our mission is simple: empower you to look well, feel well and stay well*



# Optimising Wound Healing and Scar Management with **Polynucleotides**

# Dr Amy Law reports on the role of early polynucleotide therapy in a young self-harm patient



Scarring represents the abnormal repair of skin following dermal injury, often characterised by excess or disorganised collagen deposition. Timely intervention can dramatically alter scar trajectory, especially with novel regenerative treatments such as polynucleotides.

This case details the outcomes of polynucleotides treatment on extensive self-inflicted wounds in a young female patient, highlighting the importance of early management, realistic expectations, and ethical considerations.

## Patient profile

- **Age:** 20-year-old female
- **Skin type:** Caucasian
- **Medical History:** Recurrent self-harm behaviour; under active psychological care; resident in a sheltered home environment.
- **Lifestyle Factors:** Non-smoker, doesn't drink alcohol engaged in ongoing mental health therapy.

## Initial presentation

The patient presented with several complex wounds:

- **Leg:** A large, chronic wound open for 2.5 months, repeatedly infected, failing to close naturally.
- **Arm:** A recent wound (2-3 days old) that hospital services chose not to suture, opting instead for bandaging.
- **Neck:** A newer wound, treated early post-injury. When compared to the wounds on her arm and leg, the skin viability was better.

The quality of her skin was notably compromised, attributed to chronic self-harm, leading to poor perfusion, delayed healing, and increased risk of infection.

## Pathophysiology of scar formation

Scar tissue results from the body's attempt to quickly restore dermal integrity following injury. When the dermis is disrupted, a complex cascade of inflammatory, proliferative, and remodeling phases is triggered to re-establish the skin barrier.

Injuries penetrating the dermis stimulate fibroblast activation and collagen deposition. In abnormal healing, collagen types I and III are produced excessively or in a disorganised fashion, leading to poor-quality scar tissue.[1,2]

## Scar types:

- **Normotrophic Scars:** These are flat, pale scars that form when wound healing proceeds in a balanced and orderly fashion. They are typically well-aligned with the surrounding skin and represent optimal scar outcomes.[3]
- **Hypertrophic scars:** Raised scars that remain confined to the boundaries of the original wound, often associated with excessive but organised collagen deposition.[3]
- **Atrophic scars:** Depressed scars caused by insufficient collagen deposition or excessive tissue loss.[4]
- **Keloid cars:** Overgrown scars that extend beyond the original wound margins, characterised by persistent fibroblast activity, increased collagen synthesis, and heightened inflammatory response.[5]

Several factors impair normal wound healing and predispose to abnormal scar formation, including poor vascularisation, infection, repeated trauma, and patient-related factors such as smoking and nutritional deficiencies.[6,7]

In this patient's case, the risk of developing hypertrophic or atrophic scars was significant due to the chronicity of her wounds, repeated trauma from self-harming behaviour, and the poor baseline quality of her dermal tissue. The large size of the leg wound, the extended period during which it remained open and infected, and the compromised blood supply all increased the likelihood of an abnormal scarring response. Although keloid formation was a potential risk, particularly if inflammation remained uncontrolled, her clinical presentation - including her lighter skin type and lack of previous keloid scarring - suggested a greater likelihood of hypertrophic scarring confined to the original wound area.

Early intervention with polynucleotides

*Timely intervention can dramatically alter scar trajectory, especially with novel regenerative treatments such as polynucleotides*

aimed to modulate this risk by promoting more organised collagen deposition and supporting more functional, less fibrotic tissue repair.

## Treatment approach

Given the extensive tissue damage and impaired healing environment, Plinest® (a highly-purified polynucleotide-based injectable consisting of 20mg/ml) was chosen to promote tissue regeneration. The primary aim was to enhance tissue repair, promote revascularisation, and modulate collagen production to improve both healing outcomes and scar quality - effects that have been clinically demonstrated with Plinest®.

The treatment involved direct subdermal injections administered with a fine needle, rather than a cannula, to achieve precise product placement. Approximately one syringe was used per wound site. Injections were initiated from the periphery of each wound, with the needle bevelled towards the wound bed to facilitate delivery into both the central and surrounding tissues, while minimising patient discomfort. Injecting into the inflamed, fragile centre of the wounds was avoided whenever possible to reduce pain and the risk of additional trauma. In addition to polynucleotides therapy, the patient maintained regular wound care practices. Dressings were changed frequently, and topical iodine was applied to prevent infection and support a clean healing environment.

Treatment sessions were scheduled based on the severity and chronicity of each wound. The large leg wound required four sessions spaced over four months, while the arm and neck injuries underwent three sessions over three months.

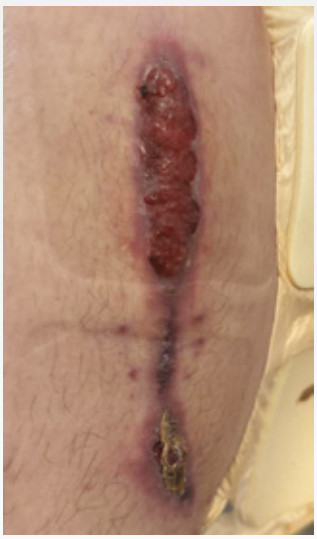
Throughout treatment, close attention was given to infection control, wound hygiene, and patient education on lifestyle factors that could influence healing outcomes.

*The primary aim was to enhance tissue repair, promote revascularisation, and modulate collagen production*

## Results

Following the administration of polynucleotide therapy, the patient demonstrated significant improvements in wound healing and scar quality across the three injury sites.

The chronic wound on the leg, which had been open and infected for over two and a half months, showed dramatic progress. Within four weeks of the initial treatment session, the wound exhibited substantial closure, with marked reduction in inflammation and infection risk (Figure 1). After four sessions, the wound had fully closed, and the resulting scar tissue appeared paler and flatter, indicating a favorable remodeling phase (Figure 2).



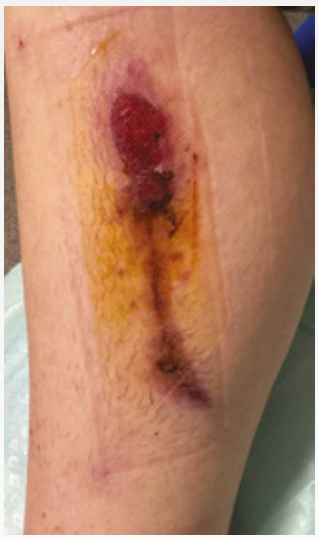
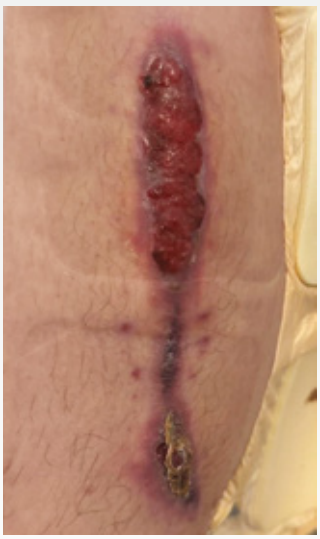


**Figure 1:** Before and four weeks after one session of Plinest®



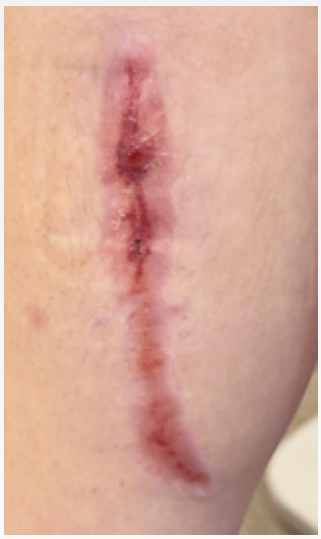


**Figure 2:** Before and after four sessions of Plinest®

The more recent wounds on the arm and neck, which were treated early, within days of injury, responded even more rapidly. The arm wound achieved closure within three weeks after a single session (Figure 3), and the neck wound showed significant reduction in redness and visibility in some parts (Figure 4).

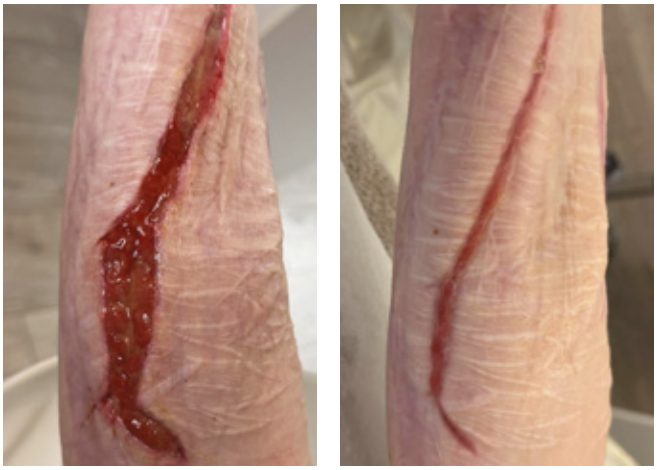


**Figure 3:** Before and after one session of Plinest®

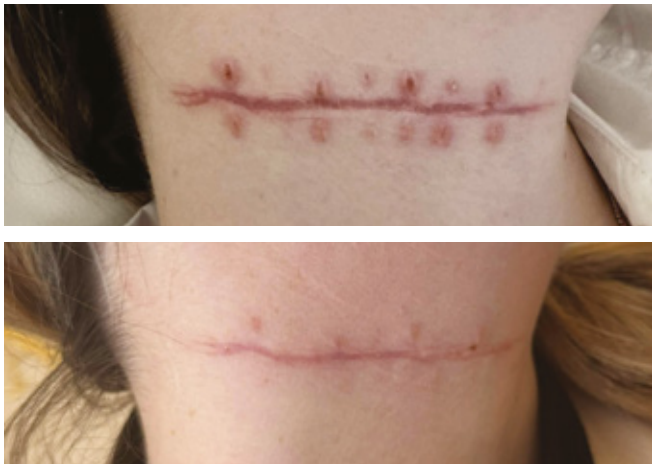


**Figure 4:** Before and after one session of Plinest®

***Throughout the treatment course, no adverse reactions were reported.***

## Ethical considerations

The management of this case required careful ethical judgment alongside clinical decision-making. Initially, treatment was provided for wounds on the patient's leg with the intention of supporting healing and improving aesthetic outcomes, given the significant psychosocial impact her scarring had on her wellbeing. However, following this intervention, the patient engaged in further self-harming behaviour, presenting with new injuries to both her neck and arm.

This development raised important ethical concerns. While my primary goal was to assist the patient in achieving better healing outcomes, it became apparent that continued cosmetic intervention risked inadvertently reinforcing maladaptive behaviours. There is a potential danger that the availability of effective aesthetic treatments could lessen the perceived consequences of self-harm, unintentionally encouraging repetition.

While the initial decision to proceed with treatment was made in good faith, giving the patient the benefit of the doubt, after careful reflection, treatment was discontinued following the second incident. Although the desire to help was strong - particularly in light of the clear emotional distress the patient experienced regarding her scarring - the ethical priority was to avoid enabling ongoing self-injury. The patient's broader psychological support remained the focus, emphasising the need for multidisciplinary care in such complex cases.

## Key learnings

This case underscores the pivotal role of early regenerative intervention in wound healing and scar modulation. The administration of polynucleotide-based therapies shortly after injury accelerated wound closure, improved tissue quality, and helped avoid the development of hypertrophic and hyperpigmented scars.

While the primary focus of treatment was on acute wounds, I did also treat one of the patient's older scars, which only experienced subtle improvement. This reinforces that earlier intervention during the active wound healing stages may yield the greatest benefit.

Ethical considerations were central to managing this case. Although the desire to assist the patient was strong, the emergence of further self-inflicted injuries after initial treatment raised concerns about inadvertently reinforcing harmful behaviour. It was ultimately necessary to discontinue cosmetic interventions, prioritising the patient's broader psychological care over aesthetic outcomes.

Overall, this case underscores the value of early regenerative therapy, and the importance of ethical, patient-centered decision-making in complex wound management.

**Disclaimer:** Dr Law is a DermaFocus faculty member.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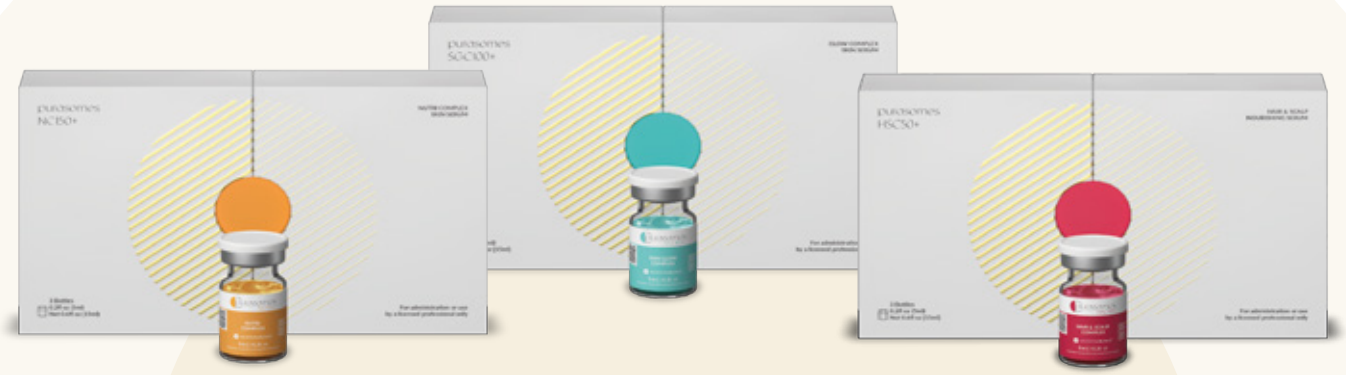

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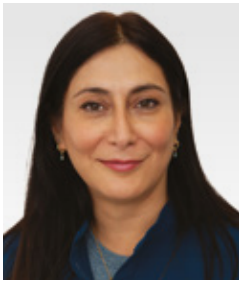
# Advancing Intimate Health through **regenerative treatments**



Dr Uzma Qureshi examines vulvovaginal ageing and the growing role of regenerative treatments in restoring intimate health

Women's intimate health, particularly as it pertains to vulvovaginal ageing, is an often-overlooked aspect of medical care. Physiological changes associated with ageing, hormonal shifts, and childbirth can significantly affect the structure and function of the vulva and vagina, leading to symptoms that impact quality of life.

Increasing awareness, alongside advancements in regenerative medicine, has led to novel therapeutic strategies aimed at restoring tissue health and function. This article explores the pathophysiology of vulvovaginal ageing and discusses the evolving role of regenerative modalities such as platelet-rich plasma (PRP), polynucleotides, laser therapies, radiofrequency, and cellular therapies in clinical management.

## **Understanding** women's concerns

Many women experience intimate health symptoms that affect their comfort, confidence, and quality of life but often remain undiscussed due to embarrassment or stigma. Common concerns include vaginal dryness, itching, irritation, burning, reduced elasticity, and pain during intercourse.[1,2] Others report decreased sexual satisfaction, increased susceptibility to infections, or a sense of laxity following childbirth or menopause.[1,3] These symptoms can significantly impact physical and emotional wellbeing, yet many women are unaware that safe and effective treatments are available.

Recent studies show up to 84% of postmenopausal women experience symptoms consistent with genitourinary syndrome of menopause (GSM) - including dryness, dyspareunia, and irritation.[4] Yet only about 25-50% discuss these symptoms with a healthcare provider,[5] and fewer than 30% receive appropriate treatment.[5] These figures reflect a significant gap in care and indicate a need for greater awareness, clinical inquiry, and access to effective therapies.

Research further reveals that GSM symptoms significantly impair emotional wellbeing, self-perception, sexual function,

daily activities, and body image.[4,5] In one multicentre study, women reported reduced self-confidence, feelings of shame, and strained relationships as a direct consequence of untreated GSM symptoms.[4]

It should be noted that while GSM is a recognised clinical syndrome defined by oestrogen deficiency and urogenital symptoms, vulvovaginal ageing encompasses a broader spectrum of structural and functional changes that may occur independently or alongside hormonal decline.

In recent years, regenerative medicine has emerged as a promising solution for GSM and vulvovaginal ageing concerns, offering new hope to women seeking non-hormonal, minimally invasive therapies that not only alleviate symptoms but also aim to restore tissue structure and function. This article reviews the underlying changes in vulvovaginal ageing and highlights the clinical applications and evidence behind regenerative treatments in intimate health.

## **The science** of vulvovaginal ageing

The structural integrity and function of vulvovaginal tissues are heavily influenced by oestrogen. Due to the abundance of oestrogen receptors in the urogenital tract, the hypo-eostrogenic state, triggers a cascade of tissue changes that define GSM. These include thinning of the vaginal epithelium, loss of rugae, diminished glycogen content, and a corresponding shift in the vaginal microbiome.[3]

Reduced oestrogen also leads to decreased collagen production, loss of elastin, and reduced vascularity, contributing to tissue dryness, fragility, and reduced responsiveness to sexual stimulation.[3] Common findings include thinning or loss of pubic hair, reduced labial fat leading to labial thinning, and possible resorption or fusion of the labia minora and majora. The vulvar skin appears pale and thin, and the clitoral hood may retract or fuse, potentially causing pain with stimulation. The vagina becomes dry, smooth, shiny, and pale, with loss of rugae, reduced elasticity, and possible shortening or stricturing. Inflammation, petechiae, and introital narrowing may lead to discomfort.[6]

Microscopically, these changes reflect reduced fibroblast activity, extracellular matrix degradation, and altered immune response.[3] The cumulative result is a significant decline in both form and function, often accompanied by inflammation, irritation, and susceptibility to trauma.[3]

Understanding this pathophysiological basis is essential in tailoring effective interventions. While hormone replacement therapy (HRT) and local oestrogen remain mainstays of traditional treatment, the growing interest in regenerative strategies focuses on restoring tissue structure, hydration, and resilience through stimulation of collagen, angiogenesis, and cellular repair.[3]

## **Valuable roles** of regenerative therapies

Regenerative medicine offers an innovative approach to managing vulvovaginal ageing by targeting the underlying tissue degeneration rather than simply alleviating symptoms. While some treatments are well established in aesthetic and dermatological practice, awareness of their gynaecological application is still growing. Below, we explore key modalities currently available or under investigation:

### Platelet-Rich Plasma (PRP)

PRP is an autologous concentration of platelets suspended in plasma, containing high levels of growth factors including platelet-derived growth factor (PDGF), transforming growth factor-beta (TGF-β), and vascular endothelial growth factor (VEGF). These factors stimulate cell proliferation, angiogenesis, and collagen production. When injected into the vaginal walls and clitoral area, PRP has been shown to improve vaginal lubrication, reduce pain, and enhance sexual satisfaction. It is particularly valuable for women who do not want to use hormone-based therapies or simply cannot due to contraindications.

PRP has progressed from anecdotal reports to a growing body of clinical evidence. Randomised trials and prospective studies have demonstrated improvements in vaginal health scores, lubrication, and sexual function, with some suggesting safety outcomes comparable to local oestrogen.[7,8,9] A 2023 randomised controlled trial showed PRP to be as effective as oestriol in improving GSM symptoms,[10] while ongoing trials are expected to further validate these findings. While long-term data are still forthcoming, the current literature supports PRP as a viable, low-risk intervention in the management of vulvovaginal ageing.

### Laser therapy

Laser therapy is a regenerative technique that harnesses thermal energy to stimulate collagen remodelling, mucosal regeneration, and angiogenesis in the vaginal epithelium. Devices deliver controlled micro-injuries to the mucosa, stimulating a wound-healing response that promotes neocollagenesis, epithelial thickening, and angiogenesis. These effects can lead to improved tissue hydration, elasticity, and overall vaginal health.[11]

Multiple studies - including randomised trials and long-term observational data - have demonstrated significant improvements in GSM symptoms, including vaginal dryness, dyspareunia, and itching. Improvements are often measurable using the Vaginal

Health Index (VHI) and Female Sexual Function Index (FSFI), with symptom relief commonly reported after two to three sessions and lasting up to a year. Both fractional $CO_2$ and erbium: YAG lasers are now well-supported by clinical data, making them important tools in the management of postmenopausal vulvovaginal atrophy.[11-14]

## Radiofrequency

Radiofrequency (RF) is increasingly recognised as a regenerative therapy due to its ability to remodel collagen and stimulate tissue renewal without ablative damage. RF treatment uses low-frequency electrical currents to generate controlled heat within the deeper layers of vaginal tissue, stimulating collagen remodeling and elastin fibre production. Unlike lasers, RF does not ablate tissue, making it a gentler option for women with thin, atrophic epithelium or those unsuitable for hormonal treatments.[15,16]

Multiple clinical studies and real-world reports have demonstrated improvements in vaginal laxity, lubrication, mucosal integrity, and symptoms of GSM - including dryness, itching, and mild urinary incontinence. Patients often report enhanced comfort and sexual satisfaction after a series of non-invasive, well-tolerated RF sessions. While long-term data are still evolving, RF has hown a consistently favorable safety profile and remains a viable option in the regenerative toolkit for intimate health.[15-18]

## Microneedling

Microneedling - especially when combined with RF - is gaining traction as a regenerative, minimally invasive therapy for women's genitourinary health. Instead of ablating tissue, microneedling creates micro-injuries in the vulvovaginal mucosa, triggering a healing cascade: collagen remodeling, elastin fibre regeneration, angiogenesis, and improved hydration and thickness of the superficial mucosa.

In one prospective series of 20 women with genitourinary syndrome of menopause (GSM) and concomitant stress or mixed urinary incontinence (SUI/MUI), a fractional bipolar RF device delivered RF energy via 24 microneedles inserted into the vaginal canal at 1-3mm depths. This single session was well tolerated and associated with significant improvements in both urinary symptoms (measured by UDI-6, MESA-SI/UI, iQoL) and vaginal health (Vaginal Health Index Score, FSFI), sustained through six months. Biopsies at three months confirmed increased elastic fiber density without submucosal scarring.[19]

A randomised pilot study (n = 30) compared microneedling using a dermaroller against fractional RF in postmenopausal women with external genital laxity. Both groups demonstrated significant improvements in Vaginal Laxity Questionnaire (VLQ) scores at 60 days, and histological analysis of labia majora biopsies revealed elevated type III collagen and vimentin expression in both modalities, suggesting effective collagen remodeling and tissue tightening.[20]

Another retrospective case series specifically focused on vulvar lichen sclerosus (LS), where patients unresponsive to steroid therapy received three sessions of bipolar RF combined with microneedling (depths of 1-3mm) over four to eight weeks. According to patient questionnaires, 86% reported significant or complete symptom resolution - including itching, tearing, and dryness - with 91% noting improvement in pruritus. Benefits lasted at least six months in 87%, and for 39% persisted 12 months or more.[21,22]

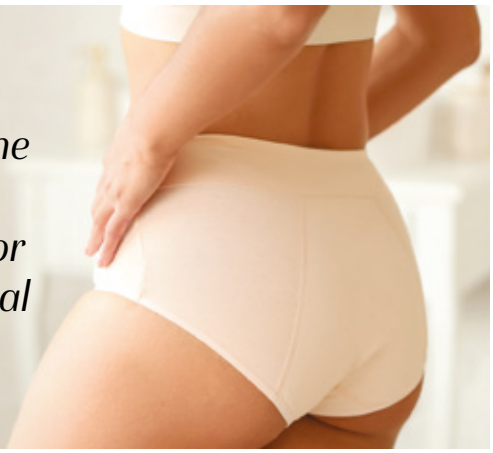
Taken together, microneedling, with or without RF augmentation, is emerging as a compelling option to address vaginal laxity, GSM, urinary symptoms, and vulvar dermatoses. It combines structural collagen remodeling (type III collagen, elastin) with minimal downtime and a favourable safety profile, making it particularly suitable for women with atrophic conditions or contraindications to hormonal treatments.

## Polynucleotides

Polynucleotides are naturally derived biopolymers that stimulate tissue repair by enhancing fibroblast proliferation, promoting hydration, modulating inflammation, and improving extracellular matrix function. Their regenerative mechanism involves free radical scavenging and activation of cellular pathways that restore mucosal integrity and elasticity.[23,24]

Although relatively new to gynaecology, early clinical studies and growing real-world experience suggest meaningful improvements in vaginal tone, hydration, elasticity, and comfort - particularly for patients with mild to moderate GSM symptoms or those recovering from energy-based treatments. In a 2021 prospective trial, polynucleotide gel applied intravaginally over 12 weeks led

*In recent years, regenerative medicine has emerged as a promising solution for GSM and vulvovaginal ageing concerns*



to significant improvements in Vaginal Health Index scores and patient-reported symptoms, with excellent tolerability.[25] Other small-scale investigations have demonstrated improvements in atrophic vulvitis and lichen sclerosis symptoms using injectable PDRN.[26]

Additional observational data support use as monotherapy or in combination with energy-based devices - particularly in patients seeking non-hormonal options or post-treatment recovery.[18] Further large-scale trials are warranted, but polynucleotides are increasingly viewed as a valuable addition to the regenerative toolkit in intimate health.

### Stem cells and biologic therapies

Stem cell-based therapies offer promising implications for vulvovaginal ageing. Most current research has focused on adipose-derived mesenchymal stem cells (ADSCs) due to their accessibility, safety profile, and regenerative potential. These cells release growth factors and cytokines that promote angiogenesis, fibroblast activation, extracellular matrix restoration, and immune modulation - critical pathways for repairing atrophic or traumatised mucosa.[27]

Preclinical and early clinical studies have demonstrated encouraging results. In a 2014 feasibility study, postmenopausal women were treated with ADSCs injected into the vaginal wall. Results showed significant improvement in symptoms of vaginal atrophy, enhanced epithelial thickness, and improved vascularity with no major adverse events. Histological evaluation confirmed mucosal regeneration and collagen remodeling.[27]

More recently, animal studies and clinical reviews have investigated combination protocols, such as ADSCs delivered within protein scaffolds or alongside platelet-rich plasma to enhance cellular survival and regenerative signaling in intimate tissues. A 2020 rat model demonstrated that ADSC-scaffold complexes outperformed standalone ADSCs in regenerating the vaginal epithelium and restoring tissue architecture.[28] In a nonhuman primate model, MSC injections significantly improved collagen, elastin, microvascular density, and tensile strength of the vaginal wall.[29] A 2023 systematic review further reports synergistic benefits of combined PRP + ADSC therapy in genital lichen sclerosis - suggesting combined biologic regimens may enhance mucosal repair in atrophic conditions.[30]

In addition to cell-based therapies, amniotic fluid and extracellular vesicles (EVs) are under investigation for their potential to deliver anti-inflammatory and pro-regenerative signals without the complexities of live cell implantation. While current research does not explicitly focus on GSM, the underlying mechanisms - such as epithelial repair, immune modulation, and angiogenesis - are highly relevant. Though early-stage, these acellular biologics may eventually broaden the toolkit for non-hormonal mucosal rejuvenation.[31,32]

It should be highlighted that in the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) regulates any substance administered with a therapeutic intent, including exosomes. Injectable exosomes (whether from plant, human, or animal origin) would likely be considered a biologic medicine or an Advanced Therapy Medicinal Product (ATMP) and as such not currently authorised for injections into humans.[33]

## **Clinical** integration

As awareness of intimate health grows, so too does the need for evidence-based, patient-centred approaches to vulvovaginal ageing. While hormone-based treatments remain effective, not all women are candidates for or comfortable with them. Regenerative therapies, such as the ones discussed in this article, offer a diverse toolkit for restoring mucosal health, alleviating symptoms, and improving quality of life.

*Polynucleotides are increasingly viewed as a valuable addition to the regenerative toolkit in intimate health*

Integrating these therapies requires a nuanced understanding of both the underlying pathophysiology and the specific mechanism of each modality. Patient selection, informed consent, and realistic outcome setting are essential. Practitioners should remain guided by current evidence while contributing to ongoing research and data collection, particularly for emerging biologics and cell-based options.

Ultimately, regenerative strategies are not only reshaping how we manage GSM and intimate ageing - they are broadening the scope of personalised care. With continued innovation and clinical rigour, these treatments have the potential to address a long-overlooked dimension of women's health with safety, dignity, and efficacy.

## Case Study

### **Restoring Function and Comfort** with Polynucleotides

A woman in her early 60s presented with longstanding symptoms of vulvar discomfort secondary to biopsy-proven lichen sclerosus, affecting the labia majora and minora, as well as lichen planus at introitus. She was already under the care of both dermatology and gynaecology teams and had been receiving regular topical corticosteroids and emollient therapy. Due to the refractory nature of her symptoms, biologic immunosuppressive treatment was being considered.

Her condition was severely impacting her quality of life. As a self-employed professional who frequently travelled, she struggled with activities of daily living - reporting significant discomfort when wearing clothing on the lower half of her body, and complete avoidance of activities such as cycling. She described persistent irritation, soreness, and pain in the vulvar area, including the vestibule and perineum.

After discussing her goals and available options, the patient sought a non-hormonal, minimally invasive treatment with low downtime. Given her need for a gentle, regenerative approach, she underwent a course of polynucleotide injections using NewGyn® (Mastelli) to improve vulval LS symptoms. She also received a course of vaginal radiofrequency to help improve vaginal atrophy and LP symptoms affecting the introitus.

NewGyn® is a CE-certified injectable combining PN-HPT® polynucleotides, hyaluronic acid, and mannitol. It is designed specifically for intradermal use in vulvovaginal tissues, where it enhances fibroblast activity, neocollagenesis, and hydration, while mannitol stabilises oxidative stress and prolongs the action of hyaluronic acid.

She received three sessions spaced two weeks apart, following the recommended protocol using a full 2 ml syringe per session. Product was injected into the labia majora, labia minora, vestibular area, and perineal zone. Micro-wheal injection techniques were used, followed by gentle massage to promote dispersion.

Following treatment, the patient reported significant improvements:

- She was able to comfortably wear trousers and jeans - something she had previously avoided due to significant discomfort.
- She resumed cycling, an activity she had long abandoned.
- Her reliance on topical steroids reduced substantially. Flare-ups were less frequent, and when they did occur, they responded within days rather than requiring weeks of treatment.
- She described the experience as life changing, noting a marked improvement in daily comfort and the ability to enjoy holidays and travel without limitations.

This case highlights the potential of polynucleotide-based regenerative therapy to provide symptom relief and restore function in chronic intimate conditions where conventional treatment is inadequate or poorly tolerated.

Dr Uzma Qureshi is a UK-trained General Practitioner with over 17 years of clinical experience and a strong background in gynaecology and surgery. She holds MRCGP, MRCS, DRCOG, and DFSRH qualifications, with extensive NHS experience in managing a wide range of women's health issues. In her CQC-registered private clinic, Dr Qureshi offers a comprehensive range of intimate health treatments, including energy-based devices, regenerative injectables, and dermal fillers. She combines medical expertise with innovative techniques to provide personalised, evidence-based care for women at all stages of life.

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# Integrating *AI* into practice

An examination of the clinical utility, current evidence and future horizons for the use of AI in regenerative aesthetics.

**Clinically reviewed by Dr Sach Mohan**

The application of artificial intelligence (AI) in aesthetic medicine is gaining traction, particularly in regenerative aesthetics where biologically-driven treatments intersect with precision-based interventions.

As the field evolves, AI promises to redefine clinical paradigms through advanced diagnostics, personalised treatment design, and predictive analytics. With recent advances accelerating across medical domains, including dermatology, plastic surgery, and cellular therapeutics, it is imperative to critically examine the utility of AI in regenerative aesthetics.

The review highlights emerging capabilities, ongoing limitations, and ethical imperatives that must be addressed for the safe and effective integration of AI technologies in aesthetic practice.

## Core applications of AI in aesthetic medicine

AI technologies in aesthetic medicine can be broadly categorised into four domains: diagnostics, treatment planning, procedural optimisation, and post-treatment assessment.

### Diagnostics

In diagnostics, AI-powered imaging tools analyse skin topography, pigmentation patterns, and structural ageing markers with high resolution and consistency.[1,2] These tools have the potential to outperform traditional assessments in identifying early changes in skin quality and symmetry.

### Treatment planning

In treatment planning, machine learning algorithms utilise patient-specific data - such as age, skin type, genetic predisposition, and lifestyle factors - to recommend individualised treatment protocols, including optimal dosages for PRP or specific energy-based therapies.[3,4]

### Procedural optimisation

During procedures, AI-enhanced devices use real-time feedback to adjust parameters dynamically, optimising outcomes in regenerative modalities like RF microneedling or autologous fat transfer. Procedural automation and robotic precision further minimise human error.[5,6]

### Post-treatment assessment

Post-treatment, AI systems track healing trajectories and treatment response using image-based analytics and patient-reported outcomes, allowing for early intervention if suboptimal results or complications arise. These tools enhance both the precision and safety of regenerative aesthetic practice.[7]

## Adjunct AI technologies

While regenerative aesthetics traditionally centres around biologically active materials and autologous therapies, a growing body of evidence supports the complementary role of adjacent AI-enabled technologies.

Robotic systems, particularly those designed for precision follicular unit extraction and implantation, are increasingly being adapted to deliver autologous grafts or tissue micrografts with enhanced accuracy and reduced trauma. This principle may extend to AI-guided delivery of cell-based therapies or scaffold placement in future regenerative procedures.[5]

Real-time facial analysis tools, originally

developed for symmetry evaluation and cosmetic planning, are being incorporated into regenerative workflows to assess volume deficits, skin laxity, and dermal quality. These assessments can be used to quantify treatment baselines and track tissue remodeling over time.[1]

Augmented reality (AR)-based planning interfaces allow practitioners to overlay predictive models of facial change or tissue restoration onto the patient's anatomy, supporting both consultation and procedural precision. When paired with regenerative modalities such as PRP, stem cells, or polynucleotides, these systems enable a multi-dimensional understanding of projected outcomes and tissue behaviour.[5]

Together, these technologies represent an emerging infrastructure that supports more precise, personalised, and measurable regenerative aesthetic interventions.

## **Emerging evidence** and practical integration

Recent studies are beginning to validate AI's role in regenerative aesthetics across diagnostic, predictive, and therapeutic domains. A seminal paper by Alvino et al. (2025) highlighted AI's transformative potential in dermatology and aesthetic medicine.

Leveraging convolutional neural networks (CNNs) trained on clinical image datasets, their study demonstrated diagnostic accuracy on par with experienced dermatologists in detecting actinic damage, melasma, and early photoageing - conditions frequently encountered in regenerative practice. [1]

Notably, the authors explored predictive modeling for biologic interventions such as platelet-rich plasma (PRP) and exosome therapy. By integrating data from patient biomarkers, genomic profiles, and treatment histories, they showed how AI models could forecast regenerative outcomes and suggest pre-emptive adjustments - potentially reducing trial-and-error in clinical planning and improving patient satisfaction.[1]

Alvino et al. also underscored the utility of AI in post-treatment monitoring, particularly when paired with imaging modalities like dermoscopy and reflectance confocal microscopy. These tools enabled granular, longitudinal tracking of tissue remodeling - an essential step in refining treatment intervals and gauging long-term efficacy.

However, the authors warned that without large, standardised datasets tailored to regenerative outcomes (e.g., neocollagenesis, elastin remodeling, volumetric response), AI systems risk limited clinical relevance.[1] They also raised ethical flags regarding over-reliance on AI-generated protocols without adequate human oversight.

Complementing this, Khurana et al. (2024) focused on simulating patient-specific cellular responses to regenerative agents using AI.[3] Their models - trained on molecular, histological, and clinical data - predict tissue response to agents such as polynucleotides, PRP, and exosomes, allowing for tailored protocol design and optimised dosing.

In aesthetic plastic surgery, Nogueira et al. (2024) reviewed applications of deep learning (DL) and machine learning (ML), particularly in preoperative planning and outcome simulation. These approaches are increasingly relevant in regenerative workflows, especially where AI can model volumetric restoration from fat grafting or stem cell-based interventions.[5]

From a diagnostic standpoint, Shaikh et al. (2024) reported that AI algorithms achieved AUROC scores exceeding 90% in common dermatoses.[2] However, their study flagged significant limitations in accuracy across diverse skin types, particularly darker tones - an issue that directly affects regenerative protocol design, where phenotype impacts both product selection and safety.

Together, these studies point to an increasingly evidence-backed integration of AI in regenerative aesthetics. Yet they also reinforce key challenges: data diversity, biologic specificity, and the need for aesthetic-tailored validation frameworks. Bridging the gap between AI's theoretical capability and real-world clinical utility will depend on collaborative development of fit-for-purpose tools trained on regenerative-specific, longitudinal datasets.

## **Cross-sector** innovations shaping regenerative aesthetics

As regenerative aesthetics continues to integrate AI, innovation from adjacent sectors is shaping the tools and paradigms that may soon become standard practice. These cross-disciplinary advances expand the scope of what's possible - not only through technical capabilities, but also through infrastructure, ethics, and patient engagement.

Telehealth and AI-enabled accessibility are gaining traction across healthcare. Singh (2024) explored how virtual platforms and automated diagnostics are helping bridge gaps in care, particularly in under-served populations.[4] In aesthetic medicine, similar technologies can streamline patient onboarding, remote consultations, and post-treatment monitoring - making regenerative procedures more accessible and consistent across varied settings.

Data quality remains a critical enabler. Wiens and Spector-Bagdady (2024) emphasise the need for high-fidelity, longitudinal data to support AI in precision medicine.[7] For regenerative aesthetics, this includes not only imaging and biomarker data, but also patient-reported outcomes, procedural nuances, and delayed biological responses such as neocollagenesis. Without such datasets, AI applications risk misclassification or oversimplification of treatment efficacy.

In biopharmaceutical research, Huang et al. (2024) demonstrate how AI-driven drug discovery is accelerating the identification of novel peptides and bioactive compounds.[8] These

## *AI in regenerative aesthetics remains in its early stages*

breakthroughs are directly relevant to regenerative aesthetics, where next-generation injectables and topicals - designed to stimulate fibroblast activity or modulate inflammation - can be personalised through AI based on an individual's skin biology.

Meanwhile, the rise of generative AI in clinical documentation, as analysed by Dwivedi et al. (2023), raises ethical considerations around consent, authorship, and communication clarity.[9] In aesthetic medicine, where informed consent and expectation-setting are paramount, reliance on AI-generated materials must be tempered with clinician oversight to ensure transparency, trust, and medico-legal integrity.

These innovations collectively signal a converging ecosystem in which regenerative aesthetics stands to benefit from broader shifts in AI-enabled healthcare. However, translating these gains will require purposeful adaptation - including aesthetic-specific data standards, regulatory engagement, and tools designed with both biological and experiential nuance in mind.

## **Considerations** for clinical and ethical integration

The expanding role of AI in regenerative aesthetics brings not only technical promise but also complex clinical, ethical, and infrastructural considerations. As innovation continues, integration must be grounded in real-world outcomes, inclusive design, and transparent oversight.

A critical shift already underway is toward patient-centred metrics. While regenerative procedures are biologically driven, their success is ultimately measured by patient satisfaction, perceived aesthetic improvement, and quality of life. AI tools that incorporate patient-reported outcome measures (PROMs), satisfaction indices, and feedback loops will help align interventions with both biological and personal goals - a balance essential to ethical, effective practice.

From a validation standpoint, general standards such as TRIPOD-AI (for transparent reporting), DECIDE-AI (for early-phase evaluation), and CONSORT-AI (for clinical trial reporting) are important benchmarks. Yet, there remains no aesthetic-specific framework for evaluating AI performance, especially in contexts where biologic interventions intersect with device-based systems. Without such standards, it is difficult to ensure safety and efficacy across diverse patient groups and practice settings.

Regulatory bodies including the FDA, EMA, and MHRA are beginning to address AI in medical devices, but the pace of alignment is variable.[10,11] In regenerative aesthetics, where interventions may include autologous materials, bioactive injectables, and AI-guided treatment planning, a hybrid regulatory model may be necessary - one that bridges biologic, digital, and procedural domains.

Moreover, the creation of interoperable, multimodal datasets is an urgent priority. These should capture imaging, genomics, histological findings, procedural details, and subjective outcomes across varied skin types, ages, and aesthetic concerns. Such datasets will not only enable more robust AI training but also help reduce algorithmic bias, which remains a significant barrier to equitable care.

Finally, ethical integration demands algorithmic transparency. Clinicians must be able to understand, explain, and, when necessary, override AI-generated recommendations. In regenerative aesthetics, where treatment decisions are deeply personal and outcomes unfold over time, human judgment remains irreplaceable.

## **Limitations** and future directions

Despite accelerating progress, the use of AI in regenerative aesthetics remains in its early stages - limited by both technical constraints and systemic gaps.

Most current algorithms are adapted from general dermatology or surgical applications, rather than being purpose-built for regenerative contexts. As a result, they often fail to capture biologically specific endpoints like neocollagenesis, elastin remodeling, or long-term volumetric restoration - markers critical to gauging success in regenerative care.

A second limitation is the lack of diverse, high-resolution datasets. Underrepresentation of darker skin tones, older age groups, and complex aesthetic presentations hampers the generalisability of AI tools. Without broad and inclusive training data, there is a risk of uneven performance, particularly in protocols that rely on image analysis or phenotype-driven planning.

Ethical and regulatory frameworks tailored to aesthetic medicine are also underdeveloped. Questions surrounding data ownership, informed consent for AI-derived recommendations, and the medico-legal status of algorithmic outputs remain unresolved - particularly when biologics and software-as-a-medical-device (SaMD) tools converge. Looking ahead, the field must prioritise:

- **Development of aesthetic-specific AI tools,** trained on regenerative datasets with validated clinical endpoints
- **Prospective, real-world validation studies,** including diverse patient cohorts
- **Interdisciplinary collaboration** between data scientists, clinicians, and regulators to shape evidence-based, ethical implementation
- **Explainable AI (XAI) frameworks** that allow clinicians to interrogate and contextualise AI outputs
- **Tele-aesthetic integration** enabling accessible, remote-supported regenerative care

As these advances unfold, AI will increasingly act not as a replacement for human judgment but as a precision enhancer; refining diagnostics,

personalising protocols, and enabling more consistent, patient-aligned outcomes.

## Key Takeaways

AI is emerging as a transformative force in regenerative aesthetics, with growing potential to enhance diagnostic accuracy, personalise biologic treatment protocols, and optimise procedural outcomes. Early evidence confirms AI's utility across imaging, predictive modeling, and longitudinal tracking, while highlighting the need for aesthetic-specific datasets and safeguards.

However, realising this potential will require more than adapting general-purpose tools. Purpose-built AI frameworks, trained on high-quality, diverse datasets that reflect the unique biological and experiential nuances of regenerative aesthetics, are essential. The tools must go beyond static predictions to enable dynamic, explainable, and patient-aligned decision support.

Interdisciplinary collaboration is equally critical. Data scientists, clinicians, ethicists, and regulators must co-design systems that are not only technically robust but clinically relevant, equitable, and transparent. Current gaps in data diversity, regulatory oversight, and algorithm explainability must be addressed to ensure safe and ethical deployment in real-world settings.

Moreover, the shift toward patient-centred outcomes - encompassing not only biological markers but also satisfaction, quality of life, and aesthetic goals - will define the next frontier of AI integration. Systems that incorporate PROMs, enable remote follow-up, and align with evolving consent standards will elevate both care quality and trust.

Ultimately, AI will not replace aesthetic judgment. Instead, it will amplify clinical expertise, helping practitioners deliver regenerative treatments that are more precise, personalised, and predictably effective. The future of aesthetic medicine belongs to those who can thoughtfully combine technological innovation with human insight, shaping outcomes that are as meaningful as they are measurable.

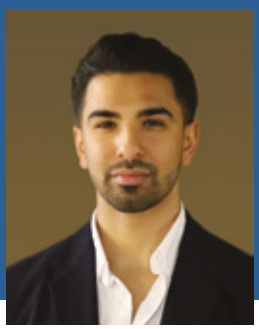
Artificial intelligence is rapidly moving from theoretical promise to practical reality in regenerative aesthetics. In my own clinical work, I've seen first-hand how AI-powered imaging, predictive modelling, and longitudinal tracking can enhance precision and patient engagement. For example, high-resolution AI skin analytics can detect subclinical changes long before they become visible - enabling earlier, more targeted interventions with PRP, polynucleotides, or energy-based devices.

Where AI truly shines is in personalisation. By integrating patient-specific factors - age, skin phenotype, genetic markers, and lifestyle data - algorithms can help design regenerative protocols that are both biologically sound and outcome-aligned. Yet these outputs are only as strong as the inputs. A thorough, human-led consultation is essential to capture the nuance of a patient's goals, context, and lived experience - a principle I embed in my Consultation Catalyst® training. This ensures AI recommendations are grounded in complete, human-informed insight, making them more relevant and actionable.

However, the challenges outlined in this article are pressing. Current tools are often adapted from dermatology or surgical datasets and may not capture regenerative-specific endpoints such as neocollagenesis or elastin remodelling. Without inclusive, high-fidelity datasets - spanning varied skin tones, ages, and biologic responses - AI risks perpetuating bias rather than reducing it.

From an ethical standpoint, both clinically and in consultation, AI should act as an intelligent co-pilot, not an autopilot. Clinicians must understand and contextualise recommendations, ensuring that technology amplifies, rather than replaces, human judgment.

Looking ahead, the fusion of regenerative biologics with AI-driven precision planning will define the next era of aesthetics. The winners will be those who embrace AI as an integrated, validated, and patient-centred tool - one that enhances both the science and the art of regenerative medicine. In that future, technology and human expertise will work together to deliver outcomes that are as meaningful as they are measurable."



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# A Strategic Approach to *Skin Triage*

Dr Ahmed El-Houisseny offers guidance on inflammation control, barrier integrity, and cutaneous stability to optimise outcomes from regenerative treatments

In regenerative aesthetics, treatment outcomes rely heavily on the biological state of the skin at the time of intervention. Initiating therapy without evaluating skin readiness can lead to inflammation, suboptimal responses, or complications. This article outlines a clinically structured approach to skin triage, highlighting key biomarkers of skin stability and strategies for pre-treatment optimisation to support improved outcomes and patient safety.

## The biological basis for treatment readiness

Regenerative aesthetic procedures function by initiating and modulating wound healing pathways, stimulating fibroblast activity, enhancing angiogenesis, and improving extracellular matrix (ECM) architecture.[1] However, these responses are highly dependent on the skin's baseline condition - particularly inflammation levels, barrier integrity, and dermal cellular function.

An impaired stratum corneum, elevated inflammatory cytokines (e.g., IL-1α, TNF-α), or dysregulated melanocyte activity can compromise healing and provoke pigmentary or fibrotic complications.[2,3] Therefore, proceeding with regenerative treatment in unstable skin may amplify subclinical inflammation and reduce therapeutic efficacy.

## Clinical indicators of skin instability

A clinically unstable skin barrier may not always be visibly compromised. Subtle signs, often overlooked during consultation, can significantly increase the risk of inflammation, pigmentary change, or delayed healing following regenerative treatment. Below are key indicators and their clinical significance:

- Persistent erythema or flushing post-cleansing may indicate underlying neurovascular instability, such as early rosacea or subclinical inflammation. This can increase the likelihood of exaggerated inflammatory responses to regenerative stimuli.[7,8]
- Post-inflammatory hyperpigmentation (PIH) triggered by minor trauma suggests unstable melanocyte activity, common in Fitzpatrick skin types IV-VI. These patients are more prone to pigmentary complications after procedures involving thermal or mechanical stimulation.[9,10]
- Patient-reported reactivity to neutral skincare products (e.g., stinging or burning sensations) reflects impaired barrier integrity and cutaneous nerve hypersensitivity. These symptoms are often seen in sensitive skin syndromes and signal a lower threshold for inflammatory flare-ups.[11,12]
- History of frequent exfoliation, chemical peels, or unprotected UV exposure is associated with stratum corneum thinning, lipid depletion, and impaired antioxidant defences. Such skin is less resilient to dermal intervention and more prone to oxidative stress and inflammation.[13,14]
- Tight, hot, or stinging sensations following mild product use can reflect neurosensory dysfunction. These patients may report symptoms of burning without visible erythema, indicating cutaneous nerve hyperresponsiveness - a known contraindication for aggressive treatment.[15,16]
- Signs of microbiome dysbiosis or elevated skin pH (above 5.5) point to acid mantle disruption and altered cutaneous flora. This can increase trans-epidermal water loss (TEWL), reduce enzymatic barrier function, and raise susceptibility to inflammatory dermatoses.[17,18]

Identifying these indicators allows practitioners to delay intervention in favour of a targeted skin preparation phase, ultimately enhancing safety and efficacy.

## Characteristics of treatment-ready skin

Skin that is biologically primed for regenerative therapies demonstrates the following:

- **Calm inflammatory state:** minimal erythema, no active lesions, and low patient-perceived sensitivity. A low-inflammatory environment supports better control of healing and reduces risk of post-procedural flare-ups.[4]
- **Hydration competence:** functional stratum corneum with adequate TEWL values. Proper hydration ensures better percutaneous absorption and cellular responsiveness.[13]
- **Barrier integrity:** intact lipid lamellae, low incidence of stinging/burning with neutral products. Barrier repair correlates with improved tolerance of regenerative agents and reduced sensitivity.[12]
- **No recent exacerbations:** no history of flares, allergic reactions, or topical irritant exposure within 2-4 weeks. Skin stability increases the predictability of treatment response.[7]
- **UV protection behaviours:** routine broad-spectrum sunscreen use and absence of recent sunburn or tanning. Photodamage impairs collagen production and inflammatory regulation, negatively affecting regenerative treatment efficacy.[14]

This does not imply perfection but indicates a biologically receptive environment capable of modulated response to regenerative stimuli.

## The skin preparation phase

Deferring regenerative intervention is often a necessary clinical step to optimise cutaneous conditions and ensure favorable biological outcomes. When the skin barrier is disrupted, or active inflammation is present, regenerative therapies may elicit dysregulated responses, hinder cellular signaling, or lead to poor tissue integration.[4] A well-structured preparation phase allows for the restoration of epidermal integrity, modulation of inflammatory pathways, and priming of the extracellular matrix for subsequent regenerative stimulation. Although patients may anticipate immediate intervention, particularly when treatment timelines are pre-planned, it is essential to communicate that this preparatory phase is not a delay, but a critical component of regenerative care. These therapies rely on coordinated biological processes that require a stable microenvironment, functional cellular machinery, and time to achieve meaningful repair. Positioning skin preparation as a strategy to maximise therapeutic efficacy, reduce complications, and improve long-term outcomes reinforces clinical credibility and enhances patient trust. Preparation approaches may include:

- **Topical agents** with barrier-repairing lipids, ceramides, or anti-inflammatory compounds (e.g., niacinamide, panthenol)[4]
- **Polynucleotide preconditioning:** Although polynucleotides are classified as regenerative agents, they may be selectively introduced during the preparatory phase due to their unique bio-modulatory profile. At low concentrations, polynucleotides have been shown to enhance fibroblast viability and ECM repair without provoking significant inflammatory activity, making them appropriate for gentle priming of compromised skin.[5]
- **Photobiomodulation therapy** (e.g., low-level LED) to stimulate cytochrome c oxidase, reduce reactive oxygen species, and promote cellular energy metabolism[6]
- **Cessation of exfoliating agents** (e.g., alpha hydroxy acids, retinoids) to reduce barrier disruption[13]
- **Temporary withdrawal of perfumed or allergenic cosmetics** which are common irritants and allergens that can trigger inflammatory reactions, particularly in already sensitised or barrier-compromised skin[11]

Clinical improvement is often observable within 2-4 weeks, and can be monitored through re-evaluation of TEWL, erythema index, or patient-reported outcomes.

## Building better outcomes

Regenerative aesthetic medicine requires more than technical accuracy; it depends on careful alignment with the skin's biological state. Optimal outcomes rely on precise timing, guided by structured triage and a clear assessment of tissue readiness. Integrating these steps into clinical protocols enhances therapeutic efficacy, reduces the risk of complications, and elevates the practitioner's role as a biologically informed clinician.

By respecting the skin's regenerative processes and intervening at the most appropriate phase, we move toward a standard of care that is both scientifically sound and ethically responsible.

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# Restoring *Skin Quality* Through Hydration-Driven Regeneration

Dr Linea Strachan and Dr Cemal Kavasogullari share case studies on correcting age-related atrophy and long-standing acne scarring with non-volumising hyaluronic acid

Hydration plays a pivotal role in regenerative aesthetic strategies, influencing fibroblast activity, extracellular matrix integrity, and collagen synthesis. As skin ages or undergoes scarring, its ability to retain water and maintain structural cohesion diminishes, leading to visible textural and functional decline.

These two case studies explore a hydration-led regenerative protocol using a non-volumising, hyaluronic acid-based injectable to restore dermal quality in cases of age-related atrophy and long-standing atrophic acne scarring.

Outcomes demonstrate the value of targeted dermal rehydration in improving tissue resilience, softening static lines, and enhancing skin tone and elasticity - while offering a low-risk, well-tolerated alternative to more invasive modalities.

## **The role** of hydration in skin ageing and acne scarring

Hydrated skin is a fundamental prerequisite for maintaining the structural and functional integrity of the dermis. As the skin ages, there is a progressive decline in natural moisturising factors, glycosaminoglycans (notably hyaluronic acid), and epidermal lipids, which together reduce the skin's ability to retain water. This leads to transepidermal water loss (TEWL), thinning of the dermis, reduced turgor, and impaired fibroblast activity - all of which contribute to the formation of static rhytides, laxity, and dermal fragility.[1]

The regenerative potential of the skin becomes increasingly compromised in this dehydrated state, with key repair mechanisms - including collagen and elastin synthesis - downregulated in the absence of adequate hydration. In this context, therapeutic rehydration using non-volumising hyaluronic acid-based injectables offers a biologically aligned method of restoring dermal density, improving extracellular matrix cohesion, and supporting fibroblast function.[2] When targeted appropriately, hydration-based therapies can soften the appearance of fine and deep wrinkles, improve elasticity,

*Hydrated skin is a fundamental prerequisite for maintaining the structural and functional integrity of the dermis*

and enhance the skin's responsiveness to subsequent regenerative treatments.

In acne-scarred skin, hydration plays an equally critical role but through a slightly different mechanism. Atrophic acne scars are associated with abnormal collagen remodelling and dermal tethering, often within a background of chronic inflammation and disrupted barrier function.[3] Dehydrated scarred skin typically exhibits reduced elasticity, impaired wound healing, and greater susceptibility to erythema and pigmentation - particularly in higher Fitzpatrick skin types. Restoring dermal hydration in this context improves pliability, reduces scar rigidity, and promotes a more favourable environment for fibroblast-led tissue repair. Hydrating injectables may also attenuate residual vascularity and support skin tone homogeneity by stabilising the extracellular matrix and enhancing microcirculation.[4]

Therefore, across both ageing and post-acne skin, hydration should be considered not only a supportive adjunct but a primary driver of regenerative outcomes. By re-establishing water balance within the dermis, practitioners can create a biological foundation that enhances both the efficacy and longevity of skin repair interventions.

## **Product selection** in hydration-led regenerative treatments

Injectable treatments that target dermal hydration have become an integral part of regenerative aesthetic practice, offering a non-volumising approach to restoring skin health, elasticity, and resilience. These formulations typically rely on hyaluronic acid (HA) as the core active component due to its high water-binding capacity, biocompatibility, and role in extracellular matrix support. However, variations in HA concentration, cross-linking, molecular weight, and the presence of adjunctive agents can significantly influence product behaviour and clinical outcomes.[1,5]

Hydrating injectables can be broadly grouped into two categories:

### Lightly cross-linked or non-cross-linked HA injectables

These products are designed to integrate into the superficial to mid-dermis, improving skin texture, hydration, and fine lines through biophysical rather than volumising effects. Their low viscosity makes them suitable for delivery via microinjection or linear threading, and they are commonly used in protocols aimed at enhancing skin glow, elasticity, and barrier function.[5,6]

### Hybrid HA-based injectables with biostimulatory components

A newer class of injectables combines HA with other bioactive agents such as antioxidants, amino acids, peptides, or osmoprotectants. These additions aim to not only hydrate but also stimulate collagen synthesis, protect HA from

degradation, and modulate oxidative stress - making them particularly valuable in treating aged or structurally compromised skin. Their slightly higher viscosity often enables deeper dermal integration and a longer duration of action, making them suitable for regenerative protocols requiring both hydration and tissue support.[7,8]

## Our product choice

In both case studies, Stylage® Hydromax was selected for its ability to deliver deep dermal hydration without volumisation. Comprising 12.5 mg/ml hyaluronic acid and 0.9% sorbitol, the product supports hydration-driven regeneration - particularly in patients prioritising skin quality over contour enhancement.[9]

Three main factors informed its use:

**1. Hydration without volume**

Its soft rheology enables smooth diffusion through the dermis without projection, making it ideal for aged or scar-prone skin and for patients cautious about volume change.[9]

**2. Antioxidant support**

Sorbitol acts as an antioxidant and osmoprotectant, helping stabilise HA, reduce inflammation, and extend hydration - especially beneficial in skin affected by oxidative stress or impaired healing.[1,10]

**3. Regenerative mechanisms**

Evidence shows this formulation enhances Aquaporin-3 expression, stimulates fibroblast activity, and improves dermal-epidermal cohesion, supporting improvements in texture, elasticity, and hydration retention.[2,10,11]

By using Hydromax, we were able to apply a hydration-first regenerative approach, yielding functional improvements in skin quality with minimal invasiveness and high patient satisfaction.

*Stylage® Hydromax was selected for its ability to deliver deep dermal hydration without volumisation*

Dr Linea Strachan

## Case 1:

### Hydration-led remodelling in age-related dermal atrophy

#### Patient profile

A 65-year-old female presented with visible skin laxity, volume loss, deep wrinkles and generalised dermal thinning. She was highly apprehensive about volumising treatments such as dermal fillers, and her primary concerns focused on the deep lines around the periorbital and perioral regions.

#### Clinical observations

Assessment revealed hallmark signs of intrinsic ageing: volume loss, dermal atrophy, and static lines across the upper cheeks, crow's feet, and upper white lip. The patient's skin appeared thin and fragile, with reduced hydration and elasticity.

#### Treatment plan

Given the patient's hesitation around volumisation, a non-volumising injectable treatment was proposed to address dermal quality through hydration and regeneration. The focus was to improve skin texture, reduce rhytides, and build dermal resilience gradually.

The patient underwent a series of three monthly treatments, each using 2 ml of Stylage® Hydromax, administered via a 25G, 50 mm cannula using linear threading.

Key areas treated included:

- Upper cheek and crow's feet
- Upper white lip
- Accordion lines
- Oral commissures

#### Patient management and aftercare

Topical anaesthesia (EMLA) was applied prior to each session to maximise comfort. The patient received both written and verbal aftercare instructions, including

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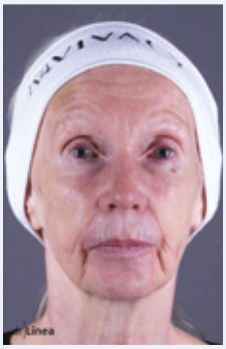
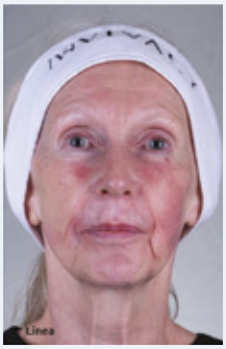
|  |  |  |

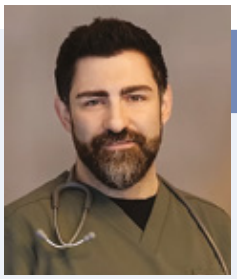

guidance on avoiding heat exposure, strenuous exercise, and alcohol post-treatment. Medical-grade skincare was also recommended to enhance and maintain outcomes.

### Results

The patient reported visible improvements in skin texture, elasticity, and fine line reduction. Clinically, the dermis showed signs of increased hydration, improved tone, and a softening of deep rhytides. A subtle lifting effect was noted, likely resulting from enhanced dermal thickness and matrix support.The patient expressed high satisfaction and reported a boost in self-confidence following treatment.

### Next steps

To maintain results, maintenance sessions are recommended every 6-9 months. Should the patient become more comfortable with aesthetic treatments, further dermal support could be considered using structural fillers in a phased, regenerative approach.



Dr Cemal Kavasogullari

## Case 2:

## **Subcision and hydration** atrophic acne scarring

### Patient profile

A 66-year-old female presented with long-standing acne scarring affecting both cheeks. Her concerns included visible rolling and boxcar scars, persistent post-inflammatory erythema, and overall poor skin quality. The patient reported psychological impacts related to appearance, especially in professional settings.

### Clinical observations

On examination, the patient exhibited mixed atrophic scars with tethering, dermal thinning, and textural irregularity. Fitzpatrick Skin Type IV was noted, prompting caution around aggressive resurfacing due to risk of post-inflammatory hyperpigmentation.

*The patient expressed high satisfaction and reported a boost in self-confidence following treatment*

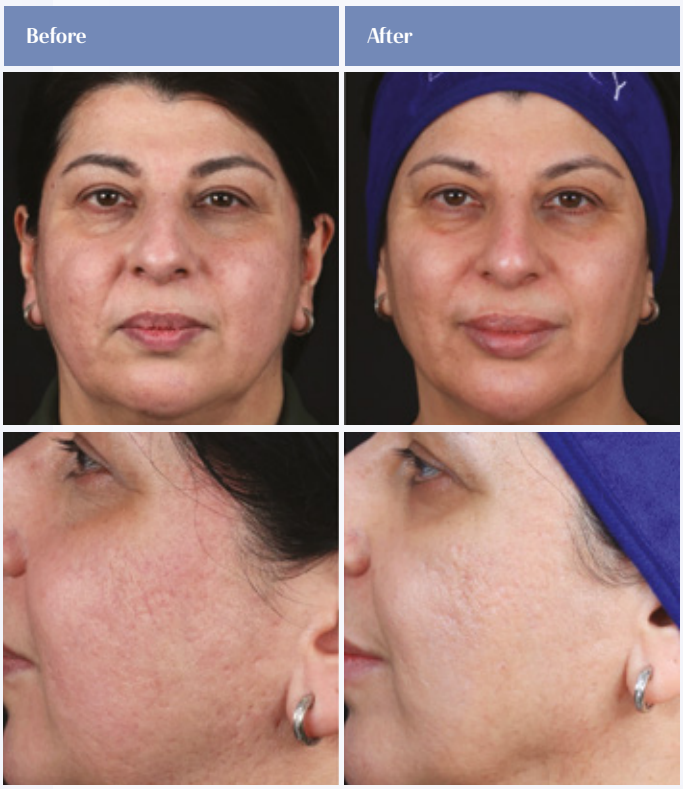
### Treatment plan

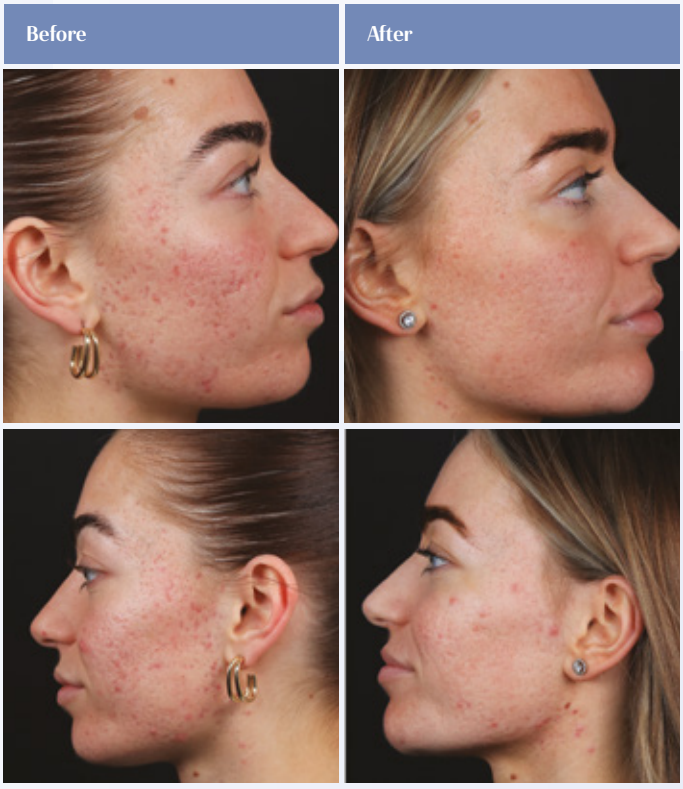
Given the patient's scar morphology and skin type, a regenerative approach was selected combining mechanical subcision with hydrating injectable therapy. This aimed to release fibrotic bands, restore hydration, and improve dermal texture without triggering pigmentary complications.

Using a 25G, 40-50 mm cannula, subcision was performed at the deep dermis-subcutaneous interface. Approximately 1 ml of Stylage® Hydromax per side was administered via retro-tracing and fanning techniques to:

- Mechanically release tethered scars
- Rehydrate the dermis
- Stimulate fibroblast activity and collagen support

Entry points were positioned in lateral cheek safety zones, allowing for even product dispersion across the areas of greatest textural deficit.




*Hydration-driven regeneration offers a biologically harmonious alternative to volumising or ablative procedures*

## Patient management and aftercare

The procedure was well tolerated without anaesthesia. The patient was advised to avoid strenuous activity, maintain hydration, and apply a post-treatment balm. Daily gentle massage was recommended to encourage product distribution and reduce fibrosis risk. Mineral makeup was suggested to camouflage bruising during the healing phase.

## Results

Improvements were consistent with a reduction in Goodman & Baron scar grade from 4 (severe, tethered scarring) to grade 3 (moderate, shallower scarring). Visual improvements were also noted in erythema, relief, and tone, corresponding with observer-assessed POSAS domains. These changes suggest functional tissue regeneration in both vascular and collagenic dimensions, achieved with minimal downtime. The patient reported a marked improvement in confidence and reduced reliance on cosmetic camouflage.

## Next steps

The patient will commence a tailored home skincare protocol including topical retinoids to support epidermal turnover. A staged plan involving non-ablative energy-based therapies is under consideration to further enhance skin texture while respecting her pigmentation risk.

## **Hydration** as a foundational strategy in regenerative aesthetics

### Key clinical takeaways:

- Non-volumising, HA-based injectables can significantly improve skin texture and elasticity in both age-related and acne-scarred skin.
- In atrophic scars, hydration appears to enhance pliability, reduce tethering, and improve the skin's regenerative microenvironment.
- Combining subcision with HA-hydration offers a safe, pigment-conscious option in higher Fitzpatrick types.

These case studies underscore the regenerative value of targeting dermal hydration in patients with both age-related atrophy and longstanding acne scarring. By selecting a non-volumising hyaluronic acid-based injectable with antioxidant properties, the practitioners were able to improve skin texture,

elasticity, and tone with minimal invasiveness and high patient tolerability.

Hydration-driven regeneration offers a biologically harmonious alternative to volumising or ablative procedures - particularly for patients seeking natural results or presenting with skin fragility, scar tissue, or pigmentary risk factors. This approach not only supports dermal architecture but enhances the skin's responsiveness to other regenerative modalities, such as microneedling, subcision, or light-based treatments.

### Dr Cemal Kavasogullari

Dr Cemal Kavasogullari (MRCGP, PGCert, AFMLM), Director of Esteem Life Medical Group, is a Glasgow-based medical doctor with expertise in general practice, aesthetic medicine, digital health, and healthcare leadership. He is an international trainer and key opinion leader for several leading aesthetic brands, including L'Oréal and Alma Lasers. His clinical interests include regenerative aesthetics, health optimisation, and longevity-based care. Dr Kavasogullari regularly lectures at international conferences such as IMCAS and CCR, and contributes to the advancement of evidence-based, patient-centred aesthetic practice.

### Dr Linea Strachan

Dr Linea Strachan (DMD) is a highly experienced practitioner, who has specialised in aesthetics since 2007. She has developed a strong reputation for delivering safe, natural-looking results in non-surgical facial rejuvenation. Dr Strachan is the founder and clinical lead at Dr Linea Medical, a CQC-registered clinic with locations in Suffolk and Norfolk. Her advanced anatomical knowledge, combined with extensive experience in aesthetic treatments, underpins a patient-focused approach that prioritises precision, safety, and subtle enhancement. She regularly trains other medical professionals in cannula technique and is a multi-award-winning practitioner recognised for full-face aesthetic transformations. Dr Strachan remains committed to clinical excellence and ongoing professional development through international training and evidence-based practice.

**Disclaimer:** Dr Strachan and Dr Kavasogullari are Vivacy faculty members.

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# Beyond the Knife: Regenerative Solutions for Post-Facelift Scarring

Nurse prescriber Caroline Hall explores the use of non-ablative fractional laser and polynucleotide injectables to successfully treat visible scarring following surgery


## Abstract

Scarring following rhytidectomy (facelift) can be distressing for patients and presents a therapeutic challenge for clinicians. This case study outlines the successful treatment of prominent post-surgical scars using a combination of non-ablative fractional laser therapy (Lumenis Stellar M22 ResurFX) and polynucleotide injections (Plinest®), resulting in marked clinical and patient-reported improvements. The case underscores the potential use of regenerative approaches in scar management.


## Introduction

Facelift surgery is commonly performed to rejuvenate the lower face and neck, with generally favourable outcomes. However, post-operative complications such as hypertrophic scarring or poor wound healing can significantly affect patient satisfaction and psychological wellbeing. While surgical scar revision is a conventional recourse, it is not always feasible due to skin laxity limitations, timing, or patient preference. Increasingly, regenerative therapies - such as polynucleotide-based injectables and energy-based devices - offer minimally invasive alternatives for scar remodeling and aesthetic restoration.

Polynucleotides such as Plinest® have demonstrated biostimulatory, anti-inflammatory, and tissue remodeling effects through fibroblast activation and hydration of the extracellular matrix.[1,2] Non-ablative fractional lasers, such as the ResurFX system, are effective in improving the appearance of scars by inducing controlled dermal remodeling while sparing the epidermis.[3] The synergy between these modalities has not been widely documented in scar-specific literature, making this case valuable for clinical practice.

## Case presentation

A 68-year-old female presented with significant dissatisfaction following a facelift performed 12 weeks prior. She expressed emotional distress due to visible scarring that she described as more cosmetically concerning than her pre-operative condition. On examination, the scars appeared hypertrophic and erythematous but without evidence of infection or dehiscence.

After consultation with a plastic surgery colleague, a full revision was considered; however, the skin's residual tension and lack of laxity rendered this approach suboptimal at this stage of healing. As an alternative, we proposed a regenerative approach combining non-ablative fractional laser treatment with polynucleotide injections, with the goal of improving scar texture, colour, and overall integration with surrounding skin.

## Treatment protocol

### Pre-treatment preparation

- Patient stopped using topical retinoids, alpha-hydroxy acids (AHAs), and beta-hydroxy acids (BHAs) five days prior to each treatment session.
- The same protocol was followed post-treatment to minimise the risk of irritation and optimise healing.

### Laser therapy

- **Device:** Lumenis Stellar M22 ResurFX
- **Mode:** Non-ablative fractional laser, 1565 nm wavelength
- **Protocol:** Single pass over the scarred areas
- **Frequency:** 3 sessions spaced 3-4 weeks apart

Non-ablative fractional laser treatment stimulates neocollagenesis and dermal remodeling through controlled thermal injury.[3] Care was taken to individualise fluence and density settings to patient tolerance and scar characteristics.

### Polynucleotide injections

- **Product:** Plinest® (20 mg/ml), derived from high-purity trout DNA

- **Dosage:** 2ml per session
- **Technique:** Micro-bolus injections along the full length of the scars immediately post-laser

Plinest® polynucleotides act via hydration, scavenging of free radicals, and stimulation of fibroblast activity, contributing to collagen production and tissue repair.[1,2]

### Adjunctive skincare

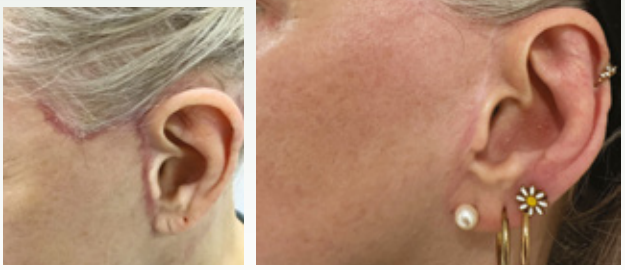
- **Product:** ALLSKIN MED Regenerating Ampoules - contain SCA® Growth Factors clinically proven to stimulate the production of collagen and elastin
- Used daily throughout the treatment period to support epidermal recovery and enhance cellular communication.

## Outcome

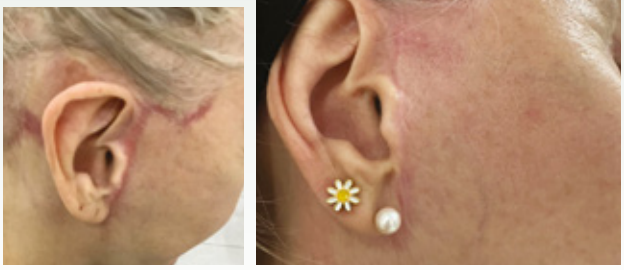
After three combined sessions of laser and polynucleotide therapy, the patient reported high satisfaction with the aesthetic improvement. Clinically, the scars appeared significantly flatter, with improved pigmentation and texture. There were no adverse events reported during or after treatment. The patient has since elected to continue polynucleotide treatments for general skin rejuvenation but has not required further intervention on the original scar sites.

The patient said, "The improvement was remarkable. The scars began to soften and become paler and, at some point, they faded to the extent that they are not noticeable, unless you are really looking for them. I don't know exactly when this happened because I simply forgot about them, which is the best outcome I could've hoped for."

Left side before and after



Right side before and after



## Considerations

This case illustrates a successful non-surgical approach to post-facelift scarring using regenerative methods. The combination of non-ablative fractional laser with polynucleotides appears synergistic in stimulating collagen remodeling and improving scar aesthetics. Timing of intervention - neither too early to risk disrupting healing nor too late to limit remodeling potential - was a critical consideration.

Possible side effects of laser treatment include transient erythema, oedema, and rarely post-inflammatory hyperpigmentation (PIH), particularly in Fitzpatrick skin types IV-VI.[3,4] With polynucleotide injections, common reactions include transient swelling or erythema at the injection site; serious adverse events are rare.[2]

Patient selection, pre-treatment counseling, and careful protocol adherence are key to achieving optimal outcomes and minimising complications.

## Conclusion

Regenerative therapies are increasingly valuable in the management of post-surgical complications in aesthetic medicine. This case demonstrates that a combination of non-ablative fractional laser and polynucleotide injections can offer a safe, effective, and non-invasive solution for scar refinement in post-facelift patients. Further controlled studies are warranted to validate long-term efficacy and define optimal protocols.

Caroline is an Independent Nurse Prescriber and Midwife with over 18 years of experience in Emergency Medicine and Midwifery. In 2016 she launched her aesthetics career, creating R&R Aesthetics where she leads a team providing skin, injectable and laser treatments. Caroline is also a faculty member of AesthetiCare and DermaFocus, as well as a trainer for Acquisition Aesthetics, priding herself on creating a safe, professional clinic which focuses on natural results for patients. Caroline is particularly interested in regenerative medicine and gut health, and loves to share this passion with her patients.

**Disclaimer:** Caroline Hall is a DermaFocus faculty member.

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