RESEARCH PAPER

Mechanical Cell Harvesting and Delivery Technologies for Stable Vitiligo: Beyond Conventional Non-Cultured Epidermal Cell Suspension

Samar Salman[1*], **Tarek El-Sayed Amin**[1], **Mohammed Attia**[2], **Lamia H. Elgarhy**[1], **Ghada Fawzy Rezk Hassan**[1]

[1]Department of Dermatology and Venereology, Faculty of Medicine, Tanta University, Tanta, Egypt

[2]Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author, Samar Salman, *samarsalman26@gmail.com*, *https://orcid.org/0000-0001-8278-7684

Received 26 July 2026, Revised 28 July 2026, Accepted 10 August 2026, Available Online 20 August 2026

Abstract

Vitiligo is a chronic acquired pigmentary disorder in which surgical intervention remains the treatment of choice for stable lesions unresponsive to medical therapy. Conventional non-cultured epidermal cell suspension (NCES) has long been considered the reference cellular transplantation technique because of its favorable efficacy and ability to treat relatively large areas in a single session. However, the requirement for enzymatic digestion, specialized equipment, and laboratory processing has stimulated the development of alternative mechanical harvesting approaches. Recent advances in mechanical tissue dissociation, skin micrograft technologies, and automated harvesting systems, while preserving encouraging clinical outcomes. In parallel, innovations in cell delivery including biological carriers, biomaterial scaffolds, laser-assisted delivery, microneedling, and injectable cell suspensions are expanding the therapeutic potential of cellular transplantation. Beyond simple melanocyte replacement, emerging evidence suggests that mechanical harvesting may preserve extracellular matrix components, stromal cells, and regenerative signals that contribute to restoration of the cutaneous microenvironment. This narrative review summarizes the evolution of cellular therapies for vitiligo, critically discusses current mechanical harvesting and delivery technologies, reviews available clinical evidence, and highlights future directions toward standardized, regenerative, and minimally manipulated cell-based therapies.

Keywords: Vitiligo; Cellular therapy, Regenerative niche, Dermal stem cells, Adipose derived stromal cells, Regenerative medicine.

How to cite this article: Samar Salman1* Tarek El-Sayed Amin1 Mohammed Attia2 Lamia H. Elgarhy1 Ghada Fawzy Rezk Hassan1. Mechanical Cell Harvesting and Delivery Technologies for Stable Vitiligo: Beyond Conventional Non-Cultured Epidermal Cell Suspension. Int J Drug Deliv Technol. 2026;16(77s):1282-1287. DOI: 10.25258/ijddt.16.77s.149

1. Introduction

Vitiligo is a chronic acquired pigmentary disorder characterized by the selective destruction of functional melanocytes, resulting in well-demarcated depigmented macules and patches.[1] It affects approximately 0.5–2% of the global population irrespective of age, sex, or ethnicity, often leading to profound psychosocial distress and impaired quality of life.[2] Although considerable advances have been made in understanding the complex pathogenesis of vitiligo, which involves autoimmune mechanisms, oxidative stress, genetic susceptibility, neural factors, and melanocyte detachment, achieving complete and durable repigmentation remains a significant therapeutic challenge.[3]

Conventional medical therapies, including topical corticosteroids, calcineurin inhibitors, systemic immunomodulators, phototherapy, and more recently Janus kinase inhibitors, primarily aim to suppress disease activity and stimulate residual melanocytes. [4]However, these approaches often produce incomplete repigmentation in long-standing stable lesions where melanocytes have been depleted.[5]

Surgical intervention has therefore become an important therapeutic option for stable vitiligo. Over the past three decades, treatment has evolved from tissue grafting techniques to

sophisticated cellular transplantation procedures.[6] Among these, [7–9] epidermal cell suspension (NCES) has become the benchmark because of its efficacy, simplicity, and ability to treat large areas in a single session.

Despite its success, NCES has limitations including enzymatic digestion, laboratory processing, procedural time, and regulatory concerns. [10]Consequently, mechanical cell harvesting technologies have emerged as simplified alternatives that reduce manipulation while preserving cell viability. Recent innovations suggest that these approaches may preserve extracellular matrix fragments and regenerative signals in addition to melanocytes.[11,12]

This review summarizes the evolution of cellular therapies for vitiligo with particular emphasis on mechanical cell harvesting and delivery technologies, discusses the biological rationale, critically appraises current evidence, and highlights future directions toward regenerative cellular therapies.

2. Evolution of Cellular Therapies for Vitiligo

Vitiligo surgery has progressively evolved from replacing depigmented skin with intact pigmented tissue to delivering isolated regenerative cellular components. [6,13]Early techniques included punch grafting, suction blister grafting, split-thickness skin grafting, and follicular unit transplantation. Although effective, these procedures were associated with donor-site morbidity, color mismatch, limited expansion ratios, and technical difficulties.[14–18]

The introduction of cellular transplantation represented a major advance. Cultured melanocyte transplantation enabled treatment of large areas but required specialized laboratories, prolonged preparation, and high costs. [19]The subsequent development of NCES revolutionized vitiligo surgery by allowing same day preparation and transplantation of melanocyte rich epidermal cell suspensions.[20]

Enzyme-free epidermal cell harvesting techniques have emerged as promising alternatives to conventional enzymatic methods for the surgical treatment of stable vitiligo. Elgarhy et al. (2020) introduced a novel non-cultured melanocyte–keratinocyte cell suspension in which epidermal tissue harvested by dermabrasion was homogenized in autologous plasma gel before transplantation, followed by narrowband ultraviolet B (NB-UVB) phototherapy. After six months of follow-up, 65% of patients achieved >75% uniform repigmentation, with overall improvement ranging from 23.3% to 100%, including lesions at traditionally resistant anatomical sites. The authors attributed these favorable outcomes to the dual role of plasma gel as a biological scaffold that enhanced cell retention and viability, together with the synergistic effect of NB-UVB in stimulating melanocyte proliferation and melanogenesis. Control lesions treated with NB-UVB alone demonstrated significantly inferior repigmentation, underscoring the therapeutic contribution of the transplanted cell suspension.[10]

Similarly, the Jodhpur Technique, described by Sonthalia and Kachhawa (2019), is a simple office-based, non-cultured, non-trypsinized cell harvesting technique that avoids enzymatic digestion and specialized laboratory processing. In this method, epidermal cells are obtained by scraping a split-thickness skin graft and transferred to the recipient site, followed by psoralen plus ultraviolet A (PUVA) phototherapy. Evaluated over a 12-month follow-up period, the technique achieved favorable repigmentation while maintaining a simple and cost-effective protocol. Collectively, these studies demonstrate that non-trypsinized cell harvesting techniques can achieve clinical outcomes comparable to conventional enzymatic NCES while simplifying tissue processing, reducing costs, and improving accessibility, particularly in resource-limited settings.[21]

More recently, interest has expanded beyond epidermal cell suspensions to mechanically processed suspensions containing epidermal, dermal, and even subcutaneous tissue components. Unlike conventional epidermal suspensions, these preparations may preserve extracellular matrix fragments, fibroblasts, stromal cells, and other regenerative elements that support melanocyte survival and tissue repair. This broader cellular composition has shifted the focus from simple melanocyte replacement toward restoration of a regenerative cutaneous microenvironment, representing an important direction in the evolution of non-trypsinized mechanical cell harvesting technologies. [22]More recently, mechanical harvesting technologies including smashed skin grafts, automated tissue dissociation, and skin micrograft techniques have simplified tissue processing while maintaining encouraging clinical outcomes.[11,12]

3. Conventional Non-Cultured Epidermal Cell Suspension (NCES): Principles and Limitations

NCES is widely regarded as the cornerstone of cellular transplantation for stable vitiligo. A thin split-thickness skin graft is harvested, enzymatically digested with trypsin, and processed to produce a suspension enriched with melanocytes and keratinocytes for transplantation onto a prepared recipient site.[23]

Keratinocytes play a crucial supportive role by promoting melanocyte survival, adhesion, and melanogenesis. Numerous studies have demonstrated excellent repigmentation rates, particularly for facial and truncal lesions.[24]

Nevertheless, NCES has several limitations. Enzymatic digestion increases procedural complexity and operative time, while specialized equipment and trained personnel are required. Variability in digestion protocols, cell yield, and melanocyte viability may influence outcomes. Furthermore, conventional NCES primarily provides epidermal cells with limited preservation of stromal and extracellular matrix components.[25]

These limitations have stimulated the development of mechanical harvesting technologies that minimize enzymatic manipulation, simplify workflow, and may preserve a broader regenerative cell population, representing the next evolution in vitiligo cellular therapy.[12]

5. Mechanical Harvesting Technologies

The introduction of mechanical cell harvesting represents one of the most important advances in vitiligo surgery over the past decade. [12]Conventional NCES relies on enzymatic digestion using trypsin to separate epidermal cells before transplantation. Although highly effective, enzymatic processing requires controlled laboratory conditions, prolongs operative time, and introduces variability related to enzyme concentration and incubation. Mechanical harvesting techniques were developed to simplify this workflow while preserving cell viability and minimizing tissue manipulation.

Mechanical dissociation uses physical disruption of donor tissue to generate a suspension of viable cells and microtissue fragments. In contrast to enzymatic digestion, these techniques may preserve extracellular matrix, dermal stromal cells, fibroblasts, vascular-associated cells, and endogenous growth factors. Consequently, their therapeutic effect may extend beyond melanocyte replacement to include regeneration of the cutaneous microenvironment.[11,12]

Several mechanical approaches have been described. Smash skin grafting involves finely mincing a thin split-thickness graft into microscopic fragments that are spread over a prepared recipient site. [11]Hair follicle-derived mechanical suspensions exploit melanocyte stem cells in the outer root sheath and may be advantageous for leukotrichia.[18] Although encouraging outcomes have been reported, standardized protocols and large comparative trials are still required before these technologies can replace conventional NCES.

6. Cell Delivery Technologies

Successful cellular transplantation depends not only on harvesting viable cells but also on effective delivery to the recipient site. Dermabrasion remains the standard method for recipient-site preparation because it creates a vascularized wound bed that supports cell attachment. [10]Carbon dioxide, microneedling, and erbium:YAG lasers provide precise epidermal removal, while microneedling has emerged as a minimally invasive alternative.[26–29]

After harvesting, cells may be applied directly or combined with biological carriers. Platelet-rich plasma functions as both a carrier and a source of regenerative growth factors. [10]In addition, umbilical cord-derived mesenchymal stem cells (UC-MSCs) have emerged as a promising regenerative adjunct in vitiligo because of their immunomodulatory, anti-inflammatory, and trophic properties. Through paracrine signaling and secretion of bioactive factors, UC-MSCs may promote melanocyte survival, migration, and repigmentation while modulating the autoimmune microenvironment. Although early preclinical and clinical studies are encouraging, further well-designed clinical trials are required to establish their role in routine vitiligo cell-based therapy.[30]

Injectable cell suspensions represent an emerging strategy that may simplify vitiligo surgery by delivering mechanically processed cells directly into the dermis. [31] Future delivery technologies are expected to integrate biomaterials, regenerative scaffolds, and standardized application systems to maximize cell viability, improve engraftment, and enhance long-term repigmentation. [32]

7. Clinical Evidence

Clinical evidence demonstrates that cellular transplantation is an effective treatment for stable vitiligo, with conventional NCES remaining the reference standard and consistently achieving high repigmentation rates, particularly on the face, neck, and trunk.[33,34] Emerging simplified

harvesting techniques, including mechanically dissociated epidermal suspensions, smashed skin grafts[11], skin micrografts[12], and hair follicle-derived cell suspensions[35], have shown encouraging results comparable to conventional NCES in selected patients while reducing procedural complexity. Combination approaches incorporating epidermal, follicular, or dermal regenerative cells may further enhance therapeutic outcomes.[36,37] Overall, these techniques demonstrate favorable safety profiles with predominantly mild, transient adverse effects. However, heterogeneity in study design, patient selection, outcome measures, and follow-up limits direct comparison between methods, highlighting the need for standardized protocols and adequately powered randomized controlled trials to define the comparative effectiveness of emerging cell-harvesting technologies.

8. Future Perspectives

The future of vitiligo surgery is expected to extend beyond simple melanocyte replacement toward comprehensive regenerative cellular therapy. Mechanical harvesting technologies provide an attractive platform for this transition because they enable rapid tissue processing while potentially preserving extracellular matrix components, stromal cells, and endogenous regenerative signals. Further optimization of these systems may improve cell viability, reproducibility, and clinical outcomes while reducing procedural complexity.[32,38]

Future research should prioritize multicenter randomized studies directly comparing enzymatic and mechanical harvesting techniques using standardized protocols and clinically meaningful endpoints. Cost-effectiveness analyses, regulatory considerations, and quality-control standards for cell processing will be equally important to facilitate wider clinical adoption.

Conclusion

Mechanical cell harvesting represents a significant step in the evolution of cellular therapy for stable vitiligo.[11,12] Avoiding the need for enzymatic digestion and simplifying tissue processing, these technologies have the potential to improve accessibility, reproducibility, and procedural efficiency while maintaining clinical efficacy comparable to conventional NCES.[39] Furthermore, preservation of extracellular matrix fragments, stromal cells, and regenerative mediators may provide biological advantages beyond melanocyte replacement, supporting the concept of regenerative skin restoration.[12,37] Advances in cell delivery systems, including biomaterial carriers and minimally invasive delivery techniques, are expected to further enhance cell survival and engraftment. Despite these promising developments, current evidence remains limited by heterogeneity in study design, outcome assessment, and follow-up duration. Well-designed multicenter randomized trials, standardized processing protocols, and long-term comparative studies are required to define the optimal harvesting and delivery strategies. As regenerative medicine, biomaterials, and precision technologies continue to evolve,[30,32] mechanical cell harvesting is likely to become a cornerstone of next-generation cellular therapy for vitiligo.

References

[1] Bergqvist C, Ezzedine K. Vitiligo: A Review. Dermatology 2020;236:571–92. https://doi.org/10.1159/000506103.

[2] Speeckaert R, van Geel N. Vitiligo: An Update on Pathophysiology and Treatment Options. Am J Clin Dermatol 2017;18:733–44. https://doi.org/10.1007/s40257-017-0298-5.

[3] Felsten LM, Alikhan A, Petronic-Rosic V. Vitiligo: A comprehensive overview: Part II: Treatment options and approach to treatment. J Am Acad Dermatol 2011;65:493–514. https://doi.org/10.1016/J.JAAD.2010.10.043.

[4] Ezzedine K, Whitton M, Pinart M. Interventions for vitiligo. JAMA - Journal of the American Medical Association 2016;316:1708–9. https://doi.org/10.1001/JAMA.2016.12399.

[5] Daniel BS, Wittal R. Vitiligo treatment update. Australasian Journal of Dermatology 2015;56:85–92. https://doi.org/10.1111/ajd.12256.

[6] Ghia DH, Mulekar S. Vitiligo surgeries-modifications to simplify the technique. Pigment Cell Melanoma Res 2014;27:986. https://doi.org/10.1111/pcmr.12292.

[7] Sritanyarat T, Wongpraparut C, Jansuwan N, Yothachai P, Nuntawisuttiwong N, Silpa-archa N. Outcomes of autologous non-cultured melanocyte keratinocyte transplantation in vitiligo and nevus depigmentosus. Journal of Dermatological Treatment 2020:1–6. https://doi.org/10.1080/09546634.2020.1793885.

[8] Valecha N, Artemi P. Non-cultured melanocyte transplantation for treatment of stable leucoderma: Experiences of an Australian centre. Australasian Journal of Dermatology 2017;58:97. https://doi.org/10.1111/ajd.12652.

[9] Malhotra SK, Puri KJPS, Singh S. Non-cultured epidermal cell suspension-a simpler solution for a complex disease vitiligo. Pigment Cell Melanoma Res 2010;23:462.

https://doi.org/10.1111/j.1755-148x.2010.00707.x.
[10] Elgarhy LH, Nofal OE, El-shorbagy SH, Abdel-Latif AM. Autologous noncultured, nontrypsinized melanocyte-keratinocyte graft homogenized in plasma gel followed by narrow-band ultraviolet B therapy for stable vitiligo: A novel technique. Dermatol Ther 2020;33. https://doi.org/10.1111/DTH.14362.
[11] Rao KMS, Koti VR, Gaikwad S. Comparison of Smash Skin Grafting and Autologous Non-cultured Epidermal Cell Suspension in Re-pigmentation of Stable Vitiligo. J Cutan Aesthet Surg 2022;15:288. https://doi.org/10.4103/JCAS.JCAS_122_21.
[12] Menchini G, Astarita C. Effects of autologous micrografts on stable bilateral vitiligo: A focus on hand lesions. Journal of Dermatology 2020;47:1417–23. https://doi.org/10.1111/1346-8138.15564;CTYPE:STRING:JOURNAL.
[13] Falabella R. Surgical Approaches for Stable Vitiligo. Dermatologic Surgery 2006;31:1277–84. https://doi.org/10.1111/J.1524-4725.2005.31203.
[14] Chandrashekar B, Madura C, Varsha D. Autologous Mini Punch Grafting: An Experience of Using Motorized Power Punch in 10 Patients. J Cutan Aesthet Surg 2014;7:42. https://doi.org/10.4103/0974-2077.129977.
[15] Lahiri K. Evolution and evaluation of autologous mini punch grafting in vitiligo. Indian J Dermatol 2009;54:159–67. https://doi.org/10.4103/0019-5154.53195.
[16] Raboobee N, Raboobee M. Epidermal cell suspension prepared inside suction blisters for transplantation in vitiligo. Pigment Cell Melanoma Res 2017;30:e18. https://doi.org/10.1111/pcmr.12548.
[17] Chopra A, Lekshmipriya K. A comparative study of efficacy of split-thickness skin grafting versus autologous melanocyte transfer in the management of stable vitiligo. Med J Armed Forces India 2022;78:S42–8. https://doi.org/10.1016/j.mjafi.2020.06.007.
[18] Muhammed RT, Kumar R, Rani S, Kumaran SM, Tanwar S, Parsad D. Combination of Follicular and Epidermal Cell Suspension as a Novel Surgical Approach in Difficult-to-Treat Vitiligo: A Randomized Clinical Trial. JAMA Dermatol 2018;154:301–8. https://doi.org/10.1001/JAMADERMATOL.2017.5795.
[19] Zokaei S, Farhud DD, Keykhaei M, Zarif Yeganeh M, Rahimi H, Moravvej H. Cultured epidermal melanocyte transplantation in vitiligo: A review article. Iran J Public Health 2019;48:388–99. https://doi.org/10.18502/ijph.v48i3.881.
[20] Verma R, Grewal RS, Chatterjee M, Pragasam V, Vasudevan B, Mitra D. A comparative study of efficacy of cultured versus non cultured melanocyte transfer in the management of stable vitiligo. Med J Armed Forces India 2014;70:26–31. https://doi.org/10.1016/j.mjafi.2013.09.004.
[21] Sonthalia S, Kachhawa D. Jodhpur Technique. StatPearls 2019.
[22] Thakur V, Kumar S, Kumaran MS, Kaushik H, Srivastava N, Parsad D. Efficacy of Transplantation of Combination of Noncultured Dermal and Epidermal Cell Suspension vs Epidermal Cell Suspension Alone in Vitiligo: A Randomized Clinical Trial. JAMA Dermatol 2019;155:204–10. https://doi.org/10.1001/jamadermatol.2018.4919.
[23] Pascal M, Maillard H, Ghasemi M, Ghasemi R, Ezzedine K. Innovative autologous non-cultured epidermal cellular graft for segmental and non-segmental vitiligo. Pigment Cell Melanoma Res 2014;27:989–90. https://doi.org/10.1111/pcmr.12292.
[24] El-Zawahry BM, Zaki NS, Bassiouny DA, Sobhi RM, Zaghloul A, Khorshied MM, et al. Autologous melanocyte-keratinocyte suspension in the treatment of vitiligo. Journal of the European Academy of Dermatology and Venereology 2011;25:215–20. https://doi.org/10.1111/j.1468-3083.2010.03759.x.
[25] Ghia D, Nayak C. To trypsinise, or not to trypsinise, that is the question. Pigment Cell Melanoma Res 2011;24:796. https://doi.org/10.1111/j.1755-148X.2011.00885.x.
[26] Post NF, Ezekwe N, Narayan VS, Bekkenk MW, Van Geel N, Hamzavi I, et al. The use of lasers in vitiligo, an overview. Journal of the European Academy of Dermatology and Venereology 2022;36:779. https://doi.org/10.1111/JDV.18005.
[27] Al-Hadidi N, Griffith JL, Al-Jamal MS, Hamzavi I. Role of Recipient-site Preparation Techniques and Post-operative Wound Dressing in the Surgical Management of Vitiligo. J Cutan Aesthet Surg 2015;8:79. https://doi.org/10.4103/0974-2077.158439.
[28] Benzekri L, Gauthier Y. The first transepidermal transplantation of non-cultured epidermal suspension using a dermarolling system in vitiligo: A sequential histological and clinical study. Pigment Cell Melanoma Res

2017;30:493–7. https://doi.org/10.1111/PCMR.12600.
[29] Lagrange S, Montaudié H, Fontas E, Bahadoran P, Lacour JP, Passeron T. Comparison of microneedling and full surface erbium laser dermabrasion for autologous cell suspension grafting in nonsegmental vitiligo: a randomized controlled trial. Br J Dermatol 2019;180:1539–40. https://doi.org/10.1111/BJD.17464.
[30] Yang RL, Zhao DZ, Yang YB, Wei HX, Yang K, Zhao YJ, et al. The immunological pathogenesis of vitiligo and the potential role of mesenchymal stromal/stem cells in its treatment. J Transl Med 2025;23:707. https://doi.org/10.1186/S12967-025-06627-8.
[31] Kumar S, Mehta T, Pandey SS. Intraepidermal injection of autologous non-cultured epidermal cell suspension in lesions of stable vitiligo: A novel method of repigmenting vitiligo. J Dermatol Nurses Assoc 2020;12.
[32] Jafarzadeh A, Mohammad AP, Goodarzi A. A Systematic Review of Case Series and Clinical Trials Investigating Regenerative Medicine for the Treatment of Vitiligo. J Cosmet Dermatol 2024;24:e16660. https://doi.org/10.1111/JOCD.16660.
[33] Sritanyarat T, Wongpraparut C, Jansuwan N, Yothachai P, Nuntawisuttiwong N, Silpa-archa N. Outcomes of autologous non-cultured melanocyte keratinocyte transplantation in vitiligo and nevus depigmentosus. Journal of Dermatological Treatment 2020:1–6. https://doi.org/10.1080/09546634.2020.1793885.
[34] Ramos MG, Ramos DG, Gontijo G, Ramos CG, Rocha TN, Rocha RH. Non-cultured melanocyte/keratinocyte transplantation for the treatment of stable vitiligo on the face: Report of two cases. An Bras Dermatol 2013;88:811–3. https://doi.org/10.1590/abd1806-4841.20132054.
[35] Shah AN, Marfatia RK, Saikia SS. A Study of Noncultured Extracted Hair Follicle Outer Root Sheath Cell Suspension for Transplantation in Vitiligo. Int J Trichology 2016;8:67–72. https://doi.org/10.4103/0974-7753.188042.
[36] Gunaabalaji DR, Pangti R, Challa A, Chauhan S, Sahni K, Arava SK, et al. Comparison of efficacy of noncultured hair follicle cell suspension and noncultured epidermal cell suspension in repigmentation of leukotrichia and skin patch in vitiligo: a randomized trial. Int J Dermatol 2020;59:1393–400. https://doi.org/10.1111/IJD.15188.
[37] Thakur V, Kumar S, Kumaran MS, Kaushik H, Srivastava N, Parsad D. Efficacy of Transplantation of Combination of Noncultured Dermal and Epidermal Cell Suspension vs Epidermal Cell Suspension Alone in Vitiligo: A Randomized Clinical Trial. JAMA Dermatol 2019;155:204. https://doi.org/10.1001/JAMADERMATOL.2018.4919.
[38] Nimitha P, Sharma VK. Can suspending non-cultured epidermal cell suspension in platelet rich plasma improve surgical repigmentation in stable vitiligo: A double blinded randomized control trial. J Dermatol Nurses Assoc 2020;12.
[39] Van Geel N, Ongenae K, Naeyaert J-M. Surgical techniques for vitiligo: A review. Dermatology 2001;202:162–6. https://doi.org/10.1159/000051626.