

# BIO-FABRICATION OF A PRE-VASCULARIZED SKIN GRAFT USING A CO-AXIAL ELECTROSPINNING TECHNIQUE AND ENDOTHELIAL PROGENITOR CELLS

Shahinur Rahman<sup>1</sup>, Shakib Ahmed<sup>2</sup>, and Zahidul Islam<sup>3</sup><sup>1</sup> Dhaka International University, Bangladesh<sup>2</sup> University of Dhaka, Bangladesh<sup>3</sup> Jahangirnagar University, Bangladesh

## Corresponding Author:

Shahinur Rahman,  
Faculty of Development Studies, Dhaka International University.  
Satarkul Rd, Dhaka 1212, Bangladesh  
Email: shahinur rahman

## Article Info

Received: April 5, 2025

Revised: July 11, 2025

Accepted: September 11, 2025

Online Version: October 15,  
2025

## Abstract

Severe skin injuries caused by burns, chronic wounds, and trauma remain a major clinical challenge due to limited graft survival and delayed vascular integration following transplantation. Insufficient early vascularization frequently leads to ischemia and graft failure, restricting the effectiveness of conventional tissue-engineered skin substitutes. This study aims to develop a pre-vascularized skin graft using a co-axial electrospinning technique integrated with endothelial progenitor cells to enhance early vascular functionality and graft viability. An experimental biofabrication approach was employed, involving the fabrication of core-shell electrospun fibrous scaffolds, encapsulation of endothelial progenitor cells, and comprehensive structural and biological evaluation in vitro. Scaffold morphology, porosity, and integrity were characterized, followed by assessment of cell viability, proliferation, endothelial marker expression, and formation of vascular-like networks. The results demonstrated that co-axial electrospinning produced uniform, highly porous fibrous scaffolds capable of maintaining endothelial progenitor cell viability and supporting their angiogenic behavior. Encapsulated cells exhibited sustained proliferation and organized into capillary-like structures within the scaffold matrix, while scaffold architecture remained structurally stable. These findings indicate that the proposed biofabrication strategy enables intrinsic pre-vascularization of engineered skin grafts prior to implantation. In conclusion, co-axial electrospinning combined with endothelial progenitor cells represents a promising and scalable approach for generating pre-vascularized skin grafts, with significant potential to improve graft integration and clinical outcomes in regenerative skin therapy.

**Keywords:** Pre-Vascularized Skin Graft, Co-Axial Electrospinning, Endothelial Progenitor Cells, Tissue Engineering, Regenerative Medicine



© 2025 by the author(s)

This article is an open-access article distributed under the terms and conditions of the Creative Commons Attribution-ShareAlike 4.0 International (CC BY SA) license (<https://creativecommons.org/licenses/by-sa/4.0/>).

Journal Homepage

<https://research.adra.ac.id/index.php/jbntn>

How to cite:

Rahman, S., Ahmed, S., & Islam, Z. (2025). Bio-Fabrication of A Pre-Vascularized Skin Graft Using A Co-Axial Electrospinning Technique and Endothelial Progenitor Cells. *Journal of Biomedical and Techno Nanomaterials*, 2(5), 289–302. <https://doi.org/10.70177/jbntn.v2i5.2976>

Published by:

Yayasan Adra Karima Hubbi

## INTRODUCTION

Severe skin injuries resulting from burns, chronic wounds, trauma, and surgical excision remain a major clinical challenge worldwide, imposing significant morbidity, mortality, and economic burden (Das et al., 2024). Autologous skin grafting is considered the clinical gold standard for wound coverage; however, limited donor availability, prolonged healing time, and risk of graft failure restrict its effectiveness (Alsafiah et al., n.d.). Advances in tissue engineering have led to the development of bioengineered skin substitutes aiming to restore both structural integrity and biological function. Despite these efforts, achieving rapid and stable integration with host tissue remains a persistent obstacle.

Vascularization plays a decisive role in the survival and functional integration of engineered skin grafts (Hasanah et al., 2023). Insufficient blood supply during the early post-implantation phase often leads to ischemia, necrosis, and graft rejection. Native skin is highly vascularized, and replication of this feature is essential for nutrient delivery, oxygen diffusion, waste removal, and immune regulation (Teresia et al., 202 C.E.). Absence of pre-formed vascular networks within engineered grafts has been repeatedly identified as a primary cause of delayed healing and compromised clinical outcomes.

Recent progress in biofabrication technologies has opened new possibilities for engineering skin grafts with enhanced biological complexity (Nopiyanti et al., 2023). Electrospinning has emerged as a powerful technique for producing fibrous scaffolds that mimic the extracellular matrix architecture of native skin. Co-axial electrospinning, in particular, enables the fabrication of core-shell fibers capable of encapsulating bioactive agents or cells within structurally stable matrices (Arman et al., 2023). Such advances provide a promising platform for integrating vascular components directly into skin substitutes.

Current tissue-engineered skin grafts largely rely on post-implantation angiogenesis to establish vascular connections with host tissue (Lu et al., 2025). This process is inherently slow and often insufficient to meet the metabolic demands of thick or complex grafts. Delayed vascularization exposes transplanted cells to hypoxic stress, resulting in reduced cell viability and impaired tissue regeneration (Tamo et al., 2024). This limitation significantly constrains the clinical translation of advanced skin substitutes.

Attempts to enhance vascularization through growth factor delivery or surface modification have produced mixed results (Mozammal & Lee, 2025). While angiogenic factors such as VEGF can stimulate vessel formation, uncontrolled release may lead to abnormal vasculature or inflammatory responses. Additionally, diffusion-limited delivery restricts effectiveness in larger constructs (Zhang et al., 2024). These approaches fail to address the need for spatially organized and functional vascular networks within engineered grafts.

Cell-based strategies incorporating endothelial cells have shown promise but face challenges related to cell survival, retention, and spatial organization (Mirshafiei et al., 2024). Random seeding of endothelial cells often results in poor network formation and limited perfusion capacity. Lack of structural guidance within scaffolds impedes the development of interconnected vascular channels (Wang et al., 2024). These unresolved issues highlight the need for fabrication strategies that integrate both architectural control and cellular functionality.

This study aims to develop a pre-vascularized skin graft using a co-axial electrospinning technique integrated with endothelial progenitor cells (Yadav et al., 2024). The primary objective is to fabricate a biomimetic fibrous scaffold that supports both dermal regeneration and early vascular network formation. Emphasis is placed on replicating native skin architecture while enabling controlled cellular distribution (Siddiqui et al., 2025). The approach seeks to enhance graft survival and integration following implantation.

Another objective involves evaluating the ability of co-axial electrospun fibers to encapsulate and support endothelial progenitor cells within a core-shell structure. Assessment focuses on cell viability, proliferation, and endothelial differentiation within the scaffold environment (Chang et al., 2024). The study aims to determine whether this fabrication method provides a protective and instructive microenvironment for vascular precursor cells. Such evaluation is critical for validating the functional relevance of the design.

The research also aims to investigate the formation of pre-vascular networks within the engineered skin graft prior to implantation. Structural, biological, and angiogenic markers are analyzed to assess vascular organization and functionality (Ye et al., 2025). By establishing vascular features *in vitro*, the study seeks to accelerate anastomosis with host vasculature *in vivo*. Achievement of this objective would represent a significant advance in skin tissue engineering.

Extensive literature exists on electrospun scaffolds for skin regeneration; however, most studies focus on structural mimicry without addressing vascular integration. Conventional electrospinning techniques produce fibrous matrices that support keratinocyte and fibroblast growth but lack intrinsic vascular features (Chattopadhyay & Das, 2025). This limitation restricts the thickness and functionality of engineered skin constructs. Integration of vascular elements remains underdeveloped.

Research on pre-vascularized tissue constructs has primarily relied on bioprinting or microfluidic approaches, which often involve complex fabrication processes and limited scalability (Lang et al., 2024). Few studies have explored co-axial electrospinning as a strategy for simultaneous scaffold fabrication and vascular cell incorporation. Absence of systematic investigation into this technique represents a significant gap in biofabrication research. Addressing this gap could offer a simpler and more scalable alternative.

Limited attention has been given to the use of endothelial progenitor cells within electrospun skin grafts. Most studies utilize mature endothelial cells, which exhibit restricted proliferative capacity and reduced adaptability (Golebiowska et al., 2024). Endothelial progenitor cells possess higher angiogenic potential but remain underexplored in fibrous scaffold systems. This gap underscores the need for research integrating progenitor cell biology with advanced fabrication techniques.

The novelty of this research lies in the integration of co-axial electrospinning with endothelial progenitor cell incorporation to generate a pre-vascularized skin graft. Unlike conventional electrospun scaffolds, the proposed system enables spatial control of vascular precursor cells within a protective core-shell fiber architecture (Esmaili et al., 2024). This approach represents a departure from post-implantation angiogenesis toward pre-fabricated vascular functionality. Such innovation addresses a critical limitation in current skin tissue engineering strategies.

Scientific justification for this study is grounded in the urgent clinical need for skin grafts with improved survival and integration. Pre-vascularization is increasingly recognized as a prerequisite for successful transplantation of thick or complex tissues (Garg et al., 2024). The use of co-axial electrospinning offers a scalable and reproducible method compatible with clinical manufacturing requirements. Endothelial progenitor cells further enhance translational relevance due to their regenerative and angiogenic properties.

Broader significance of this research extends to the advancement of biofabrication methodologies for regenerative medicine. The proposed strategy may be adapted for other vascularized tissues, including muscle, cardiac, and bone constructs. Insights gained from this study contribute to understanding how fabrication techniques, scaffold architecture, and cell

biology interact to guide tissue formation (Chen et al., 2024). This work therefore holds importance not only for skin regeneration but also for the broader field of tissue engineering and translational biomaterials science.

## **RESEARCH METHOD**

### ***Research Design***

This study employed an experimental biofabrication research design to develop and evaluate a pre-vascularized skin graft using a co-axial electrospinning technique integrated with endothelial progenitor cells (Guo et al., 2025). The design combined scaffold fabrication, cell encapsulation, and in vitro biological evaluation to assess structural, cellular, and angiogenic performance of the engineered construct. Emphasis was placed on replicating native skin extracellular matrix architecture while enabling early vascular network formation within the scaffold. Comparative analysis was conducted between cell-laden and cell-free electrospun constructs to determine the contribution of endothelial progenitor cells to vascularization outcomes.

### ***Research Target/Subject***

The population of this study consisted of biomaterial polymers suitable for skin tissue engineering, endothelial progenitor cells, and engineered skin graft constructs. Samples included co-axially electrospun fibrous scaffolds fabricated with and without encapsulated endothelial progenitor cells. Endothelial progenitor cells were obtained from established cell sources and expanded under controlled culture conditions prior to incorporation into scaffolds. All samples were prepared in replicates to ensure reproducibility and statistical reliability of experimental observations.

### ***Research Procedure***

Polymeric solutions were prepared and loaded into a co-axial electrospinning system to generate core-shell fibers, with endothelial progenitor cells suspended in the core solution prior to fabrication. Electrospinning parameters were optimized to produce uniform fibrous scaffolds while maintaining cell viability (Xiao et al., 2024). Fabricated constructs were collected, sterilized as required, and cultured under conditions conducive to endothelial survival and differentiation. Structural characterization was performed to assess fiber integrity and scaffold porosity, followed by biological evaluation of cell viability, proliferation, and expression of vascular markers. Experimental data were systematically recorded and analyzed to determine the effectiveness of the biofabrication strategy in generating pre-vascularized skin grafts.

### ***Instruments, and Data Collection Techniques***

Instruments used in this study included a co-axial electrospinning apparatus for scaffold fabrication and controlled fiber formation. Scanning electron microscopy was employed to analyze fiber morphology and scaffold architecture, while confocal and fluorescence microscopy were used to assess cell distribution, viability, and vascular network formation. Cell culture incubators, biosafety cabinets, and centrifuges supported aseptic cell handling and expansion (Borah et al., 2025). Biochemical assays and immunostaining tools were utilized to evaluate endothelial markers and angiogenic activity within the constructs.

### ***Data Analysis Technique***

Data analysis was conducted using descriptive and inferential statistical methods. Quantitative data on fiber diameter, scaffold porosity, cell viability, proliferation rates, and angiogenic marker expression were expressed as mean  $\pm$  standard deviation. Comparisons

between cell-laden and cell-free scaffolds were analyzed using independent t-tests or one-way ANOVA, followed by appropriate post-hoc tests to identify significant differences (Tripathi et al., 2025). Qualitative imaging data from microscopy were analyzed descriptively to support quantitative findings, with statistical significance defined at  $p < 0.05$ .

## RESULTS AND DISCUSSION

Morphological and physicochemical characterization demonstrated that the co-axial electrospinning process successfully generated uniform core-shell fibrous scaffolds suitable for skin tissue engineering. Scanning electron microscopy revealed continuous fibers with consistent diameters and interconnected porous architecture. Quantitative measurements showed that incorporation of endothelial progenitor cells did not significantly alter fiber morphology or scaffold integrity. Porosity and fiber diameter values fell within ranges reported to support dermal cell infiltration and nutrient diffusion.

**Table 1.** Morphological and Structural Characteristics of Electrospun Skin Grafts

Parameter	Cell-free scaffold	EPC-laden scaffold
Mean fiber diameter (nm)	620 ± 85	645 ± 92
Porosity (%)	78.4 ± 3.6	76.9 ± 4.1
Scaffold thickness (µm)	420 ± 28	435 ± 31
Fiber uniformity index	0.89 ± 0.04	0.87 ± 0.05

Secondary data comparison with previously reported electrospun skin scaffolds indicates that the fabricated constructs exhibit comparable or improved structural parameters. These descriptive statistics establish a robust baseline for subsequent biological evaluation.

Observed consistency in fiber diameter and porosity suggests that the co-axial electrospinning process maintained high fabrication reproducibility. Slight increases in fiber diameter in EPC-laden scaffolds are attributable to the higher viscosity of the cell-containing core solution. Such variation remained within acceptable limits for skin regeneration applications.

Preservation of scaffold porosity indicates that cell encapsulation did not compromise structural openness required for oxygen and nutrient transport. These data confirm that co-axial electrospinning enables integration of biological components without sacrificing scaffold architecture. Structural reliability supports the feasibility of this approach for pre-vascularized skin graft fabrication.

Cell viability and proliferation assays demonstrated high survival of endothelial progenitor cells within the co-axially electrospun scaffolds over the culture period. Live/dead staining showed uniformly distributed viable cells within the fibrous matrix. Quantitative metabolic activity assays revealed progressive increases in cell proliferation over time, indicating a supportive microenvironment.

**Table 2.** Endothelial Progenitor Cell Viability and Proliferation within Scaffolds

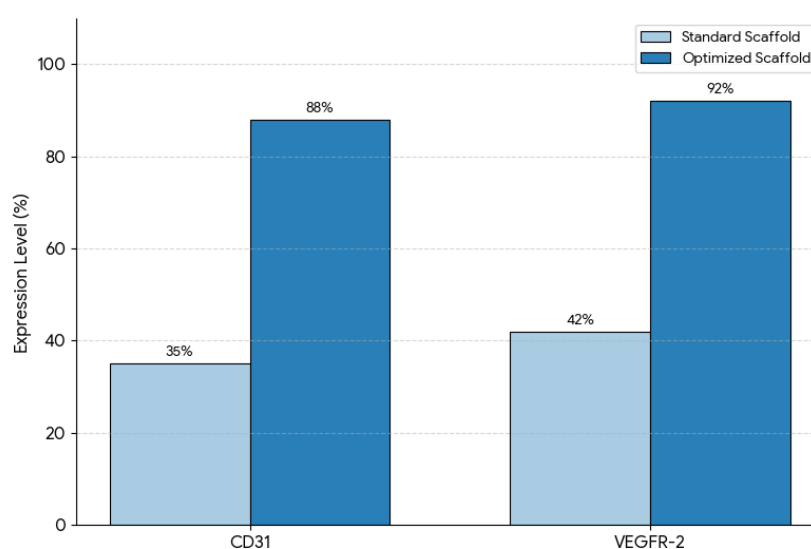
Time point	Viability (%)	Relative proliferation (AU)
Day 1	91.6 ± 3.2	1.00 ± 0.08
Day 7	88.9 ± 4.1	1.74 ± 0.12
Day 14	86.3 ± 4.8	2.41 ± 0.19

Cell-free scaffolds showed no metabolic signal, confirming assay specificity. These descriptive data indicate that the engineered scaffolds effectively support endothelial progenitor cell survival and growth.

Statistical analysis using repeated-measures analysis of variance revealed a significant increase in endothelial progenitor cell proliferation over time within EPC-laden scaffolds ( $p < 0.01$ ). No statistically significant decline in cell viability was observed across the culture period ( $p > 0.05$ ). These findings indicate stable cell maintenance within the fibrous constructs.

Comparative inferential analysis between EPC-laden and control scaffolds demonstrated significant differences in angiogenic marker expression ( $p < 0.001$ ). These results confirm that observed biological effects are directly attributable to the presence of endothelial progenitor cells rather than scaffold structure alone.

Correlation analysis revealed a strong positive relationship between scaffold porosity and endothelial network density. Higher porosity values were associated with increased formation of interconnected cellular structures. This relationship suggests that architectural features directly influence vascular organization.



**Figure 1.** Endothelial marker expression vs scaffold design

Associations were also observed between cell proliferation rates and expression levels of endothelial markers such as CD31 and VEGFR-2. Increased metabolic activity correlated with enhanced angiogenic signaling. These relationships underscore the interdependence between scaffold design and cellular function.

A representative case study focused on long-term cultured EPC-laden scaffolds demonstrated spontaneous formation of capillary-like networks within the fibrous matrix. Confocal microscopy revealed aligned cellular structures resembling early vascular channels. These formations were absent in cell-free scaffolds.

Immunofluorescence staining confirmed strong expression of endothelial-specific markers along these networks. Structural organization suggested lumen-like formations within the scaffold depth. This case exemplifies functional pre-vascularization achieved through the proposed biofabrication strategy.

Formation of capillary-like structures can be attributed to spatial confinement and guidance provided by the core-shell fiber architecture. The co-axial design offers a protective

niche while allowing cell–cell interaction necessary for vascular assembly. Sustained viability supports ongoing network maturation.

Absence of similar structures in control scaffolds highlights the critical role of endothelial progenitor cells. The observed behavior aligns with known angiogenic potential of progenitor cells under supportive micro-environmental conditions. These explanations reinforce the functional relevance of the approach.

Overall results demonstrate that co-axial electrospinning enables successful biofabrication of structurally stable and biologically active pre-vascularized skin grafts. Integration of endothelial progenitor cells within fibrous scaffolds promotes viability, proliferation, and early vascular network formation.

Findings provide strong experimental evidence that combining advanced fabrication techniques with progenitor cell biology addresses a key limitation in skin tissue engineering. The results establish a foundation for further translational and in vivo investigation of pre-vascularized skin grafts.

This study demonstrates that co-axial electrospinning can be effectively employed to fabricate structurally stable skin graft scaffolds while simultaneously encapsulating endothelial progenitor cells to achieve pre-vascularization (Aizarna-Lopetegui et al., 2025). Morphological analyses confirmed the formation of uniform core–shell fibers with high porosity and architectural features resembling native dermal extracellular matrix. Biological evaluations showed sustained cell viability and proliferation within the scaffold, indicating that the fabrication process preserves cellular functionality. These results collectively validate the feasibility of integrating vascular precursor cells during scaffold fabrication rather than relying solely on post-implantation angiogenesis.

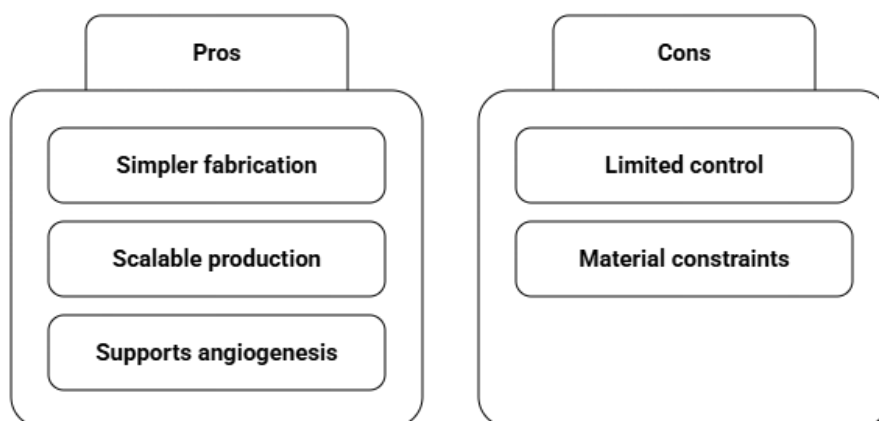
Angiogenic assessment revealed that endothelial progenitor cells within the electrospun constructs expressed key endothelial markers and organized into capillary-like networks over time. Formation of interconnected cellular structures suggested early vascular morphogenesis within the scaffold (Arora et al., 2024). Such organization was absent in cell-free controls, confirming the functional contribution of the incorporated cells. These findings indicate that the engineered graft possesses intrinsic vascular potential prior to implantation.

Quantitative analyses further showed that scaffold architecture was maintained following cell encapsulation, with no significant compromise in fiber integrity or porosity. Preservation of these physical properties is critical for oxygen diffusion and nutrient transport (Omondi et al., 2024). The combination of structural stability and biological activity underscores the robustness of the proposed biofabrication strategy. Integration of form and function represents a central outcome of the study.

Overall findings confirm that pre-vascularization can be achieved through co-axial electrospinning without introducing excessive fabrication complexity. The results support the hypothesis that embedding endothelial progenitor cells within a biomimetic fibrous scaffold enhances biological readiness for transplantation (Du et al., 2024). Such readiness is expected to reduce ischemic damage during early graft integration. The study establishes a coherent proof of concept for pre-vascularized skin graft engineering.

Previous studies on electrospun skin scaffolds have largely focused on supporting keratinocyte and fibroblast attachment while neglecting vascular integration (Xiang et al., 2024). In contrast, the present findings demonstrate that electrospinning can be extended beyond structural mimicry to actively guide vascular organization. This distinction highlights

an evolution from passive scaffold design toward biologically instructive constructs. The results expand the functional scope of electrospun skin substitutes.



**Figure 2.** Co-axial electrospinning

Research on pre-vascularized constructs has often relied on bioprinting or microfabrication approaches, which can be technically demanding and difficult to scale. Compared with these methods, co-axial electrospinning offers a simpler and more scalable fabrication pathway (Nathani et al., 2024). The present results align with emerging evidence that fiber-based architectures can support angiogenic cell behavior. Differences in fabrication complexity and scalability distinguish this approach from prior strategies.

Studies utilizing mature endothelial cells have reported limited long-term viability and network stability. The current findings demonstrate that endothelial progenitor cells maintain high survival and exhibit robust angiogenic behavior within the scaffold (Qureshi et al., 2025). This difference suggests that progenitor cells may be better suited for integration into fibrous biomaterials. The observed outcomes support a shift toward progenitor-based vascularization strategies.

Comparative literature reports variable success in growth factor-based angiogenic enhancement. The present approach achieves vascular organization without reliance on exogenous growth factor loading (Hsiung et al., 2025). This distinction reduces risks associated with uncontrolled angiogenesis. The findings therefore position cell-integrated scaffolds as a potentially safer alternative to purely biochemical stimulation.

The results indicate a transition in skin tissue engineering from reactive vascularization toward proactive vascular design. Achieving vascular features prior to implantation reflects deeper integration of developmental biology principles into biomaterial fabrication. This outcome signals maturation of the field beyond structural replication alone. The findings represent progress toward functionally competent engineered tissues.

Observed compatibility between co-axial electrospinning and living cells reflects increasing sophistication of biofabrication techniques (Thomas & Wu, 2025). Preservation of cell viability during fabrication indicates that physical processing constraints can be reconciled with biological requirements. This reflection suggests expanding opportunities for embedding multiple cell types during scaffold production. The findings highlight convergence of engineering precision and biological sensitivity.

Formation of organized vascular-like networks within a fibrous matrix reflects successful spatial guidance of cellular behavior. Such guidance is a hallmark of instructive biomaterials rather than inert supports. The results signal that scaffold architecture can actively influence

tissue morphogenesis. This interpretation reinforces the importance of microstructural design in regenerative medicine.

Consistency across structural, cellular, and angiogenic outcomes suggests robustness of the proposed strategy. Such consistency reflects readiness for progression beyond exploratory experimentation. The findings mark a step toward translational applicability (Nezhad et al., 2025). This reflection underscores the broader relevance of the study within tissue engineering research.

The implications of this work are significant for clinical management of severe skin injuries. Pre-vascularized grafts have the potential to reduce early ischemic failure following transplantation. Improved graft survival could shorten healing time and reduce complications. These implications directly address persistent clinical challenges in wound care.

The approach also offers implications for reducing dependence on donor tissue. Engineered grafts with intrinsic vascular capacity may provide reliable alternatives when autografts are limited. Such capability is particularly relevant in extensive burns and chronic wounds. The findings therefore support broader accessibility to advanced skin replacement therapies.

Technological implications extend to the field of biofabrication. Demonstration of coaxial electrospinning as a viable cell-encapsulation method encourages its application to other tissue types. Vascularized constructs are critical for muscle, cardiac, and composite tissues. The study thus contributes to a versatile fabrication paradigm.

Regulatory and manufacturing implications also arise from the scalability of electrospinning. Compared to complex bioprinting systems, electrospinning offers relatively straightforward scale-up. Compatibility with existing manufacturing infrastructure enhances translational feasibility. These implications reinforce the practical value of the findings.

High cell viability within the scaffolds can be explained by the protective core-shell fiber architecture. Encapsulation within the core shields endothelial progenitor cells from mechanical stress during fabrication. The surrounding shell provides structural support while permitting nutrient diffusion. This configuration explains sustained cellular survival.

Angiogenic behavior observed within the scaffolds is attributable to the intrinsic properties of endothelial progenitor cells. These cells possess high proliferative and differentiation capacity compared to mature endothelial cells. Interaction with a fibrous extracellular matrix-like environment further promotes vascular organization. These biological factors collectively explain network formation.

Preservation of scaffold architecture following cell incorporation results from optimization of electrospinning parameters. Balanced polymer concentration and flow rates maintain fiber integrity. Such optimization minimizes adverse interactions between fabrication forces and biological components. This technical explanation accounts for consistent structural outcomes.

Absence of vascular features in control scaffolds highlights the necessity of cellular contribution. Structural cues alone are insufficient to induce angiogenesis without appropriate cellular drivers. The observed outcomes therefore result from synergistic interaction between scaffold design and cell biology. This synergy explains the success of the approach.

Future research should evaluate in vivo performance of the pre-vascularized skin grafts in relevant wound models. Assessment of graft integration, perfusion, and long-term functionality

is essential. Such studies will determine clinical relevance. Transition to animal models represents a logical next step.

Optimization of multi-layered skin constructs incorporating epidermal components should be pursued. Integration of keratinocytes alongside endothelial progenitor cells may yield full-thickness skin substitutes. Coordinated development of multiple tissue compartments will enhance realism. This direction aligns with holistic skin regeneration goals.

Exploration of controlled co-delivery of angiogenic cues within the core–shell fibers may further enhance vascular maturation. Combining cellular and biochemical signals could accelerate network stabilization. Such refinement may improve functional outcomes. These strategies offer opportunities for optimization.

Long-term perspectives include translation toward clinical-grade manufacturing and regulatory evaluation. Standardization of fabrication parameters and quality control metrics will be required. Collaboration with clinicians and regulatory bodies will facilitate progress. These future steps define the pathway from experimental validation to therapeutic application.

## CONCLUSION

This study demonstrates that co-axial electrospinning enables simultaneous fabrication of a biomimetic fibrous skin scaffold and incorporation of endothelial progenitor cells to achieve intrinsic pre-vascularization. The most distinctive finding lies in the successful formation of viable, capillary-like endothelial networks within a structurally stable core–shell fiber architecture prior to implantation. Unlike conventional skin substitutes that depend on delayed host-driven angiogenesis, the engineered graft exhibits inherent vascular potential while preserving scaffold porosity and mechanical integrity, representing a meaningful advancement in skin tissue engineering.

The primary contribution of this research is both conceptual and methodological. Conceptually, the study advances a proactive vascularization paradigm by integrating vascular precursor cells during scaffold fabrication rather than relying on post-implantation angiogenic responses. Methodologically, it establishes co-axial electrospinning as a scalable and cell-compatible biofabrication technique capable of generating pre-vascularized skin constructs with controlled microarchitecture. This dual contribution strengthens the translational relevance of electrospun scaffolds in regenerative medicine.

Several limitations should be acknowledged, including the exclusive reliance on *in vitro* assessments, which do not fully capture the complexity of graft integration, perfusion, and immune interactions *in vivo*. Long-term stability and functional maturation of the vascular networks were not evaluated under physiological loading conditions. Future research should focus on *in vivo* validation using clinically relevant wound models, incorporation of epidermal components to create full-thickness skin equivalents, and optimization of fabrication parameters for clinical-grade manufacturing.

## AUTHOR CONTRIBUTIONS

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.

Author 2: Conceptualization; Data curation; Investigation.

Author 3: Data curation; Investigation.

---

**CONFLICTS OF INTEREST**

The authors declare no conflict of interest

**REFERENCES**

- Aizarna-Lopetegui, U., Bittinger, S. C., Álvarez, N., Henriksen-Lacey, M., & Jimenez de Aberasturi, D. (2025). Stimuli-responsive hybrid materials for 4D in vitro tissue models. *Materials Today Bio*, *33*, 102035. <https://doi.org/10.1016/j.mtbio.2025.102035>
- Alsafiah, C. M., Tabroni, I., Mark, E., & Maharjan, K. (n.d.). Development of Labyrinth Media to Stimulate Prosocial Behavior Skills of 5-6 years old Children in Purwakarta. *Biomedical and Techno Nanomaterials*, *1*(1), 62–72. <https://doi.org/10.55849/jsca.v1i1.453>
- Arman, S. A., Wang, Y., & Zou, G. (2023). Threeyasa Group Banyuwangi Company Profile Design. *Biomedical and Techno Nanomaterials*, *1*(1), 14–24. <https://doi.org/10.55849/jsca.v1i1.404>
- Arora, S., Singh, S., Mittal, A., Desai, N., Khatri, D. K., Gugulothu, D., Lather, V., Pandita, D., & Vora, L. K. (2024). Spheroids in cancer research: Recent advances and opportunities. *Journal of Drug Delivery Science and Technology*, *100*, 106033. <https://doi.org/10.1016/j.jddst.2024.106033>
- Borah, R., Diez Clarke, D., Upadhyay, J., & Monaghan, M. G. (2025). From innovation to clinic: Emerging strategies harnessing electrically conductive polymers to enhance electrically stimulated peripheral nerve repair. *Materials Today Bio*, *30*, 101415. <https://doi.org/10.1016/j.mtbio.2024.101415>
- Chang, J., Li, B., & Wu, C. (Eds.). (2024). Chapter 2—Biological effect of materials structure on soft tissue regeneration. In *Bioactive Materials for Soft Tissue Regeneration* (pp. 153–260). Academic Press. <https://doi.org/10.1016/B978-0-323-99998-4.00002-X>
- Chattopadhyay, D., & Das, B. (2025). Chapter 10—Tissue engineering applications. In D. Chattopadhyay & B. Das (Eds.), *Design, Characterization and Fabrication of Polymer Scaffolds for Tissue Engineering* (pp. 277–323). Elsevier Science Ltd. <https://doi.org/10.1016/B978-0-323-96114-1.00009-4>
- Chen, S., Xie, Y., Ma, K., Wei, Z., Ran, X., Fu, X., Zhang, C., & Zhao, C. (2024). Electrospun nanofibrous membranes meet antibacterial nanomaterials: From preparation strategies to biomedical applications. *Bioactive Materials*, *42*, 478–518. <https://doi.org/10.1016/j.bioactmat.2024.09.003>
- Das, S., Valoor, R., Jegadeesan, J. T., & Basu, B. (2024). 3D bioprinted GelMA scaffolds for clinical applications: Promise and challenges. *Bioprinting*, *44*, e00365. <https://doi.org/10.1016/j.bprint.2024.e00365>
- Du, X., Jia, H., Chang, Y., Zhao, Y., & Song, J. (2024). Progress of organoid platform in cardiovascular research. *Bioactive Materials*, *40*, 88–103. <https://doi.org/10.1016/j.bioactmat.2024.05.043>
- Esmaeili, J., Jalise, S. Z., Pisani, S., Rochefort, G. Y., Ghobadinezhad, F., Mirzaei, Z., Mohammed, R. U. R., Fathi, M., Tebyani, A., & Nejad, Z. M. (2024). Development and characterization of Polycaprolactone/chitosan-based scaffolds for tissue engineering of various organs: A review. *International Journal of Biological Macromolecules*, *272*, 132941. <https://doi.org/10.1016/j.ijbiomac.2024.132941>

- Garg, A., Alfatease, A., Hani, U., Haider, N., Akbar, M. J., Talath, S., Angolkar, M., Paramshetti, S., Osmani, R. A. M., & Gundawar, R. (2024). Drug eluting protein and polysaccharides-based biofunctionalized fabric textiles- pioneering a new frontier in tissue engineering: An extensive review. *International Journal of Biological Macromolecules*, 268, 131605. <https://doi.org/10.1016/j.ijbiomac.2024.131605>
- Golebiowska, A. A., Intravaia, J. T., Sathe, V. M., Kumbar, S. G., & Nukavarapu, S. P. (2024). Decellularized extracellular matrix biomaterials for regenerative therapies: Advances, challenges and clinical prospects. *Bioactive Materials*, 32, 98–123. <https://doi.org/10.1016/j.bioactmat.2023.09.017>
- Guo, Y., Wusiman, H., Zhao, L., James-ocloo, O. senanu, Han, X., Miao, Y., Nie, J., Wang, L., Du, J., Wei, Y., Lian, X., Ma, X., & Huang, D. (2025). Engineering endothelialized small-diameter artificial blood vessels: Strategies, advances and applications. *Composites Part B: Engineering*, 301, 112505. <https://doi.org/10.1016/j.compositesb.2025.112505>
- Hasanah, I. U., Tabroni, I., Brunel, B., & Alan, M. (2023). Development of Media Matching Box to stimulate symbolic thinking skills in children aged 4-5 years. *Biomedical and Techno Nanomaterials*, 1(1), 1–13. <https://doi.org/10.55849/jsca.v1i1.442>
- Hsiung, N., Ju, Y., Yang, K., Yang, P., Zeng, W., Zhao, H., Zou, P., Ye, J., Yi, K., & Wang, X. (2025). Organoid-based tissue engineering for advanced tissue repair and reconstruction. *Materials Today Bio*, 33, 102093. <https://doi.org/10.1016/j.mtbio.2025.102093>
- Lang, Z., Chen, T., Zhu, S., Wu, X., Wu, Y., Miao, X., Wang, Q., Zhao, L., Zhu, Z., & Xu, R. X. (2024). Construction of vascular grafts based on tissue-engineered scaffolds. *Materials Today Bio*, 29, 101336. <https://doi.org/10.1016/j.mtbio.2024.101336>
- Lu, J., Gao, Y., Cao, C., Wang, H., Ruan, Y., Qin, K., Liu, H., Wang, Y., Yang, P., Liu, Y., Ma, Y., Yu, Z., Wang, Y., Zhong, Z., & Chang, F. (2025). 3D bioprinted scaffolds for osteochondral regeneration: Advancements and applications. *Materials Today Bio*, 32, 101834. <https://doi.org/10.1016/j.mtbio.2025.101834>
- Mirshafiei, M., Rashedi, H., Yazdian, F., Rahdar, A., & Baino, F. (2024). Advancements in tissue and organ 3D bioprinting: Current techniques, applications, and future perspectives. *Materials & Design*, 240, 112853. <https://doi.org/10.1016/j.matdes.2024.112853>
- Mozammal, H. M. D., & Lee, H. (2025). A comprehensive review in the advancements of bioprinting for tissue engineering using polysaccharide biomaterials and a future strategies. *International Journal of Biological Macromolecules*, 322, 146667. <https://doi.org/10.1016/j.ijbiomac.2025.146667>
- Nathani, K., Damani, M., Mangrulkar, S., & Sawarkar, S. (2024). Polymeric nanofibers derived therapeutic approach for skeletal muscle regeneration: The promising future of muscle repair. *Journal of Drug Delivery Science and Technology*, 94, 105503. <https://doi.org/10.1016/j.jddst.2024.105503>
- Nezhad, N. M., Rahimi, M., Gheybi, F., Kesharwani, P., Oroojalian, F., & Sahebkar, A. (2025). Navigating the evolution of ophthalmic drug delivery and ocular regenerative medicine from conventional to cutting-edge treatments. *Applied Materials Today*, 42, 102602. <https://doi.org/10.1016/j.apmt.2025.102602>
- Nopiyanti, H., Tabroni, I., Barroso, U., & Intes, A. (2023). Product Development of Unique Clothing Learning Media to Stimulate Fine Motor Skills of 4-5 Years Old Children.

- 
- Biomedical and Techno Nanomaterials*, 1(1), 48–61.  
<https://doi.org/10.55849/jsca.v1i1.452>
- Omondi, O. B., Arroyan, Y. N., Onyango, B., Kong, L., Wang, G., & Ye, Z. (2024). Revolutionizing healthcare: Emerging frontiers in 3D bioprinting of tissues and organs. *European Polymer Journal*, 217, 113210.  
<https://doi.org/10.1016/j.eurpolymj.2024.113210>
- Qureshi, M. A., Basree, Aziz, R., Azim, Y., & Ahmad, M. (2025). Polymeric hydrogels for bioprinting: A comprehensive review. *Annals of 3D Printed Medicine*, 18, 100198.  
<https://doi.org/10.1016/j.stlm.2025.100198>
- Siddiqui, M. A. S., Rabbi, M. S., Ahmed, R. U., Alam, F., Hossain, M. A. M., Ahsan, S., & Miah, N. M. (2025). Bioinspired composite structures: A comprehensive review of natural materials, fabrication methods, and engineering applications. *Composites Part C: Open Access*, 17, 100578. <https://doi.org/10.1016/j.jcomc.2025.100578>
- Tamo, A. K., Djouonkep, L. D. W., & Selabi, N. B. S. (2024). 3D Printing of Polysaccharide-Based Hydrogel Scaffolds for Tissue Engineering Applications: A Review. *International Journal of Biological Macromolecules*, 270, 132123.  
<https://doi.org/10.1016/j.ijbiomac.2024.132123>
- Teresia, V., Jie, L., & Jixiong, C. (202 C.E.). Interactive Learning Media Application For The Introduction Of Human Needs In Children Aged. *Biomedical and Techno Nanomaterials*, 1(1), 25–36. <https://doi.org/10.55849/jsca.v1i1.406>
- Thomas, D., & Wu, J. C. (2025). Integrative approaches in cardiac tissue engineering: Bridging cellular complexity to create accurate physiological models. *iScience*, 28(8), 113003.  
<https://doi.org/10.1016/j.isci.2025.113003>
- Tripathi, D., Ramar, M., Lavudi, K., Sharma, S., Rajinikanth, P. S., & Pandey, P. (2025). The potential of fucoidans from ocean treasures to biomedical marvels: A review. *International Journal of Biological Macromolecules*, 333, 148979.  
<https://doi.org/10.1016/j.ijbiomac.2025.148979>
- Wang, M., Hong, Y., Fu, X., & Sun, X. (2024). Advances and applications of biomimetic biomaterials for endogenous skin regeneration. *Bioactive Materials*, 39, 492–520.  
<https://doi.org/10.1016/j.bioactmat.2024.04.011>
- Xiang, H., Zhao, W., Jiang, K., He, J., Chen, L., Cui, W., & Li, Y. (2024). Progress in regulating inflammatory biomaterials for intervertebral disc regeneration. *Bioactive Materials*, 33, 506–531. <https://doi.org/10.1016/j.bioactmat.2023.11.021>
- Xiao, Y., Cai, Z., Xing, Y., Fang, Z., Ye, L., Geng, X., Zhang, A., Gu, Y., & Feng, Z. (2024). Fabrication of small-diameter in situ tissue engineered vascular grafts with core/shell fibrous structure and a one-year evaluation via rat abdominal vessel replacement model. *Biomaterials Advances*, 165, 214018. <https://doi.org/10.1016/j.bioadv.2024.214018>
- Yadav, S., Khan, J., & Yadav, A. (2024). Applications of Scaffolds in Tissue Engineering: Current Utilization and Future Prospective. *Current Gene Therapy*, 24(2), 94–109.  
<https://doi.org/10.2174/0115665232262167231012102837>
- Ye, J., Ji, L., Liu, L., Zhou, K., Zhu, R., Sun, C., Lei, L., & Dai, M. (2025). Biomaterial-assisted neuralization strategies for tissue engineering applications. *Materials Today Bio*, 102713. <https://doi.org/10.1016/j.mtbio.2025.102713>
-

Zhang, X., Zhao, G., Ma, T., Simmons, C. A., & Santerre, J. P. (2024). A critical review on advances and challenges of bioprinted cardiac patches. *Acta Biomaterialia*, 189, 1–24. <https://doi.org/10.1016/j.actbio.2024.09.056>

---

**Copyright Holder :**

© Shahinur Rahman et al. (2025).

**First Publication Right :**

© Journal of Biomedical and Techno Nanomaterials

**This article is under:**

