Application of Electrospun Nanofiber Scaffolds in Tissue Engineering

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Abstract:

Electrospun nanofiber scaffolds play a pivotal role in tissue repair due to their biomimetic three-dimensional structure that mimics the natural extracellular matrix (ECM), tunable mechanical properties, and excellent biocompatibility. This article first reviews the application mechanisms of nanofiber scaffolds fabricated by this technology in bone, cardiac, vascular, and neural tissue engineering. Subsequently, in the field of personalized precision medicine, an innovative three-dimensional pathway strategy is proposed, integrating CT/MRI imaging modeling, AI algorithm optimization, and smart responsive materials to achieve anatomical compatibility and dynamic regulation of personalized scaffolds. Finally, future advancements of this technology may involve the integration of microfluidic chips, 4D printing deformation response, and multi-material collaborative manufacturing techniques to construct biomimetic scaffolds with gradient interfaces and dynamic adaptability. Although this type of scaffold shows good prospects in tissue repair, it still faces challenges in large-scale production, biocompatibility stability and long-term efficacy in clinical transformation. In the future, with the integration of smart materials and personalized medical technology, electrospun nanofiber scaffolds are expected to be more widely used in the field of regenerative medicine.

Keywords: Electrospinning, Nanofiber scaffolds, tissue engineering, tissue repair

1. Introduction

In daily life, human tissues often suffer varying degrees of damage due to various causes. With the emergence of novel biomaterials and their integration with diverse technological approaches, regenerative therapies have been developed for various tissue injuries. As a critical branch of regenerative med-

icine, tissue engineering facilitates the repair and functional reconstruction of damaged tissues through the interaction between biomimetic scaffold materials and cells. A key challenge in tissue repair lies in constructing biomimetic scaffolds that functionally match the native extracellular matrix (ECM).

Electrospinning technology utilizes a high-voltage electric field to stretch polymer solutions or melts

into continuous fibers with diameters ranging from 50 to 1000 nm. The resulting nanofiber scaffolds exhibit high specific surface area (porosity up to 95%), tunable fiber alignment (random or oriented), and mechanical anisotropy, which can mimic the topological structure and biochemical signaling functions of native ECM. This provides an ideal microenvironment for cell adhesion, proliferation, and differentiation.

In recent years, nanofiber scaffolds fabricated via electrospinning technology have demonstrated broad application prospects in tissue engineering fields such as cardiac, bone, neural, and vascular regeneration. Due to their unique advantages, electrospinning has become a core method for producing nanofiber scaffolds. For instance, in cardiac repair, poly (lactic acid) (PLA) electrospun tubular scaffolds achieved a tensile toughness of (15.2 ± 1.3) MPa by adjusting the weaving density and poly(glycerol sebacate) (PGS) coating, closely matching the mechanical properties of native myocardial tissue while significantly promoting the aligned arrangement of human mesenchymal stem cells (hMSCs) [1]. In bone regeneration, silk fibroin/hydroxyapatite composite scaffolds functionalized with bone morphogenetic protein-2 (BMP-2) peptides enhanced osteogenic gene expression by threefold and increased mineralized area by 60% in a rat calvarial defect model [2]. These advancements indicate that the functional design of electrospun scaffolds has evolved from simple structural biomimicry to a precision medicine regulation stage characterized by "structural-biochemical signal coupling."

This review aims to explore the application progress of electrospun nanofiber scaffolds in various tissue engineering fields, with a primary focus on cardiac and bone tissue engineering. It highlights the advantages of fabrication strategies and the influence of functionalized designs on cellular behavior. Furthermore, by analyzing scaffold applications in different tissues (e.g., bone, heart, blood vessels, nerves), this review discusses the pivotal roles scaffolds play in these contexts.

The anticipated outcomes and potential contributions of this study lie in reviewing the aforementioned research content, proposing optimized strategies for the fabrication technology of electrospun nanofiber scaffolds, and predicting their future application directions and pathways in the field of precision personalized medicine.

2. Electrospinning Technology and Nanofiber Scaffolds

2.1 Electrospinning Process and Preparation Strategies

Electrospinning, as an efficient technique for fabricating nanofibers, has emerged as a core technology for preparing ECM-mimicking scaffolds due to its precise control over fiber diameter (ranging from nanometers to micrometers), high porosity, and three-dimensional interconnected structure [3]. The fundamental principle relies on the stretching effect of electric field forces on polymer solutions or melts. Under a high-voltage electric field, charged polymer droplets overcome surface tension to form jets, which subsequently solidify through solvent evaporation or melt cooling, ultimately depositing as nanoscale fibers on the collector. This process involves multiple critical processing parameters, including solution concentration (affecting viscosity and surface tension), voltage (determining electric field strength), spinneret type (single-axis, coaxial, or multi-axial), and collection device (static or dynamic), all of which significantly regulate fiber morphology and performance [4].

In terms of fabrication strategies, uniaxial, coaxial, and multi-axial electrospinning techniques provide diverse approaches for fiber structure modulation. Uniaxial electrospinning is suitable for homogeneous fiber fabrication, whereas coaxial/multi-axial techniques enable the generation of core-shell structures or functionally graded fibers, such as composite fibers with drug-loaded cores and biodegradable shells. From a material compatibility perspective, solution electrospinning is widely employed for natural polymers (e.g., collagen, chitosan) and synthetic polymers [e.g., poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL)], while melt electrospinning is more applicable to thermally unstable materials (e.g., polyethylene). Regarding alignment control, dynamic collectors (e.g., rotating drums) can induce fiber orientation, mimicking the topological structure of the ECM, thereby significantly promoting directional cell migration and differentiation [3,4].

2.2 Advantages of Electrospinning Technology

Compared to traditional material fabrication methods such as phase separation and self-assembly, electrospinning technology demonstrates significant advantages, as shown in Table 1. First, the fiber diameter can be precisely controlled over a wide range (50 nm to several micrometers), and the fibrous structure within this scale closely resembles the ECM, enabling accurate simulation of ECM structures in different tissues, which facilitates cell adhesion and growth [4]. Second, electrospinning can produce highly porous (>80%) and three-dimensionally interconnected structures, which promote nutrient transport and cell infiltration, whereas phase separation techniques often suffer from uneven pore sizes that limit cellular penetration [5]. Additionally, this technique exhibits excellent material compatibility, accommodating natural and synthetic polymers, ceramics, and metal nanoparticles for composite fabrication, such as PLGA/hydroxyapatite composite scaffolds for bone repair [6,7]. More importantly, the surface functionalization of electrospun nanofiber scaffolds is highly flexible and easily achievable. BioacISSN 2959-409X

tive surface functionalization can be enhanced through blending, post-modification (e.g., plasma treatment), or in situ loading (e.g., growth factors, antibiotics) [8].

Table 1. Analysis of Core Advantages of Electrospinning Technology

Core Advantages	Function and Role	References
The fiber diameter can be widely regulated (ranging from 50 nm to several micrometers).	The fibrous structure at this scale closely resembles the ECM, accurately mimicking the ECM structure of various tissues, which facilitates cell adhesion and growth.	[4]
Capable of forming a highly porous (>80%) and three-dimensionally interconnected structure	The three-dimensional interconnected structural network facilitates	[5]
Excellent material compatibility	Both natural and synthetic polymers, as well as ceramic and metal nanoparticles, can be incorporated into composites.	[6,7]
Surface functionalization is flexible and easily achievable.	Biofunctionalization and activity enhancement of surfaces can be achieved through blending, post-modification (e.g., plasma treatment), or in situ loading (e.g., growth factors, antibiotics).	

2.3 Characteristics and Functions of Electrospun Nanofiber Scaffolds

2.3.1 Structural Characteristics

The structural properties of nanofiber scaffolds significantly influence cellular behaviors. Studies have demonstrated that fiber diameter and alignment can markedly regulate cell adhesion, proliferation, and differentiation. Finer nanofibers are more conducive to cell spreading and migration, while aligned fibers can guide directional cell growth along the fiber orientation. For instance, fibers with diameters ranging from 200 to 500 nanometers are optimal for osteoblast adhesion, whereas aligned fibers facilitate the directional growth of neural cells, offering novel strategies for nerve regeneration [3].

Moreover, the porosity and pore size of the scaffold directly influence the efficiency of nutrient transport and the infiltration depth of cells. For instance, pores larger than 100 μ m facilitate effective infiltration of vascular endothelial cells, while micropores smaller than 10 μ m are suitable for sustained drug release [3]. Therefore, rational design of the pore structure is a critical factor in promoting tissue regeneration.

2.3.2 Mechanical Compatibility

In tissue engineering applications, the mechanical properties of scaffolds must match those of the target tissue. By adjusting parameters such as material composition and fiber diameter, the mechanical properties of nanofiber scaffolds can be effectively modulated. For instance, in bone tissue engineering, scaffolds with high strength and stiffness are required to support nascent bone tissue. PLGA/collagen composite scaffolds exhibit a tensile strength of 15–20 MPa, closely resembling the mechanical properties of cancellous bone [6]. In contrast, soft tissue repair emphasizes scaffold flexibility and elasticity. For example,

polyurethane microfiber scaffolds, fabricated via electrospinning, form an elastomeric network with small fiber diameters and interconnected pores. Their hydrolytic and enzymatic degradation properties make them suitable for soft tissue engineering, such as muscle or vascular repair [3]. Cardiac patches require flexibility (elastic modulus ≈1 MPa), and conductive nanofibers (e.g., polyaniline composites) can simultaneously transmit electrical signals [9].

2.3.3 Biofunctionalization Strategy

Biofunctionalization of nanofiber scaffolds is a crucial approach to enhance their tissue repair efficacy. Surface modification can alter the hydrophilicity/hydrophobicity and charge properties of scaffold surfaces through physical or chemical methods, thereby improving cell adhesion performance. For instance, plasma treatment can introduce amino groups to enhance the adsorption of cell adhesion proteins such as fibronectin [8].

The loading of bioactive molecules can regulate cellular biological behaviors and promote tissue regeneration. In terms of classification, molecules that enhance cell adhesion (e.g., RGD peptide sequences) can improve the interaction between cells and scaffolds. For instance, RGD peptide-modified PCL fibers increase fibroblast adhesion rates by 40% [10]. Molecules used for immune regulation (e.g., anti-inflammatory cytokines) can modulate the local immune microenvironment and mitigate inflammatory responses. For example, chitosan fibers loaded with interleukin IL-10 inhibit macrophage M1 polarization and reduce inflammation [11]. Additionally, molecules that guide differentiation (e.g., bone morphogenetic proteins) can induce stem cells to differentiate into specific tissue cells. For instance, BMP-2 sustained-release PLGA scaffolds significantly promote osteogenic differentiation of mesenchymal stem cells [12].

Moreover, the integration of conductive or magnetic func-

tionalities demonstrates unique advantages in cardiac and neural tissue engineering. For instance, in cardiac tissue engineering, magnetic iron oxide (Fe3O4) nanoparticles embedded within fibers can guide cardiomyocyte alignment under an external magnetic field [9]. In neural tissue engineering, magnetoelectric nanoparticles incorporated into fibers generate electrical signals through magnetostrictive and piezoelectric effects under an external magnetic field, activating voltage-gated calcium channels (VGCCs) in neural cells, thereby promoting nerve regeneration during spinal cord injury repair [13].

3. Applications of Electrospun Nanofiber Scaffolds in Various Tissue Repairs

3.1 Applications in Bone Tissue Engineering

3.1.1 Cartilage Repair

Cartilage tissue has limited self-repair capacity due to the absence of blood vessels and nerves. Electrospun nanofiber scaffolds have emerged as ideal materials for cartilage repair owing to their excellent biocompatibility and tunable mechanical properties. Studies have demonstrated that hyaluronic acid/PLA composite fiber scaffolds provide a cartilage ECM-mimicking microenvironment. When combined with sustained release of transforming growth factor (TGF- β 3), these scaffolds promote chondrocyte proliferation and type II collagen secretion, thereby facilitating cartilage tissue regeneration [7,14], as shown in Table 2.

3.1.2 Cortical bone repair

In the field of hard bone repair, nanofiber scaffolds must possess high mechanical strength and osteoinductive activity. Hydroxyapatite (HA) and polymer composite nanofiber scaffolds are widely used in bone defect repair due to their excellent biomineralization properties [2]. In osteogenic repair, silk fibroin/hydroxyapatite composite scaffolds increase the mineralization area by 60% through BMP-2 peptide segments [2]. Another study demonstrated that HA/PLGA composite scaffolds fabricated via electrospinning not only provide mechanical support for new bone growth but also promote the mineralization process of bone tissue by releasing calcium ions. Additionally, porous PLGA/hydroxyapatite scaffolds loaded with dexamethasone exhibit sustained release over 21 days, resulting in a threefold increase in the expression of osteogenic genes (Runx2, Osteocalcin) [6,12], thereby facilitating bone formation and achieving the goal of hard bone repair, as shown in Table 2.

3.2 Applications in Cardiac Tissue Engineering

Cardiac tissue repair requires addressing the dual challenges of electrical conduction and mechanical matching.

Conductive nanofiber scaffolds, such as polypyrrole (PPy), have been widely used in cardiac tissue engineering due to their high conductivity and biocompatibility. Studies have shown that conductive scaffolds fabricated from PPy and polyurethane/silk fibroin (PU/SIS) composites can mimic the electrical signal conduction properties of cardiomyocytes and promote synchronized contraction. These materials also exhibit tensile strength and conductivity similar to those of native cardiac tissue, supporting functional cardiac recovery [15].

In addition, adjusting the mechanical properties of the scaffold to match those of cardiac tissue can effectively improve cardiac function. Studies have shown that nanocomposites (such as carbon nanotube-reinforced PLGA) achieve a balance between mechanical strength and flexibility by modulating fiber structure and porosity, thereby supporting cardiomyocyte adhesion, proliferation, and synchronized contraction [16]. This promotes functional cardiac recovery, as summarized in Table 2.

3.3 Applications in Vascular Tissue Engineering

The key to vascular tissue engineering lies in constructing vascular scaffolds with excellent biocompatibility and mechanical properties. The alignment of electrospun nanofibers can guide the orientation of smooth muscle cells (SMCs) and endothelial cells (ECs) along the fiber direction, mimicking the layered structure of the vascular wall. By adjusting fiber thickness, alignment, and pore size, cell infiltration and tissue growth can be promoted, thereby enhancing the scaffold's mechanical properties and biological functions [17], such as the aforementioned electrospun polyurethane microfiber scaffold [3]. Additionally, studies have shown that PCL/gelatin/MgO (magnesium oxide) composite scaffolds, through sustained Mg2+ release, upregulate vascular remodeling-related factors (e.g., vascular endothelial growth factor) and induce neovascularization within one week of subcutaneous implantation in rats, promoting vascular repair. Another vermiculite nanosheet composite scaffold enhances neovascularization in diabetic wounds by activating the HIF-1α signaling pathway, facilitating re-epithelialization and collagen deposition, thereby repairing blood vessels [18], as shown in Table 2.

3.4 Applications in Neural Tissue Engineering

In neural tissue engineering, nanofiber scaffolds primarily serve to guide axonal growth and promote neural regeneration. Highly aligned nanofiber scaffolds can directly direct the migration and growth of neural cells along the fiber orientation through surface topological cues. Studies have demonstrated that in electrospun polycaprolactone (PCL)/silk fibroin (SF) composite scaffolds, aligned fibers significantly enhance the elongation of neural cells along the fiber direction and promote directional extension through cytoskeletal reorganization [19,20], thereby achieving the goal of neural repair, as shown in Table 2.

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Table 2. Representative research examples of electrospun nanofiber scaffolds in different tissue engineering applications

Tissue engineering	Scaffold Material	Function	References
Bone(cartilage,-cortical bone)	1.Cartilage: Hyaluronic Acid/PLA 2.Bone: Hydroxyapatite/ PLGA	Cartilage: Provides an ECM-like environment to promote cartilage tissue regeneration Cortical bone: Provides structural support for new bone formation, promotes bone mineralization and osteogenic gene expression.	[2,6,7,12,14]
Heart	PPy and polyurethane/ silk fibroin (PU/SIS) Nanocomposites (such as carbon nanotube-rein- forced PLGA)	1:Capable of simulating the electrophysiological signal conduction properties of cardiomyocytes and promoting synchronized contraction of myocardial cells, thereby facilitating cardiac recovery. 2: By adjusting the fiber structure and porosity, a balance between mechanical strength and flexibility was achieved, supporting the adhesion, proliferation, and synchronous contraction of cardiomyocytes.	[15,16]
Blood Vessels	bers 2.PCL/gelatin/MgO (magnesium oxide) composite scaffold	 The formation of an elastomeric network via electrospinning enhances the mechanical properties and biological functionality of scaffolds, thereby promoting the regeneration of soft tissues such as blood vessels. By promoting the release of vascular-related remodeling factors, thereby repairing blood vessels. Promoting angiogenesis by activating relevant signaling pathways. 	
Nervous System		The surface topological structure directly guides the migration and growth of nerve cells along the fiber direction, thereby promoting nerve regeneration.	

4. Implementation Pathways of Electrospun Nanofiber Scaffolds in Precision Personalized Medicine

4.1 Image-Guided Stent Modeling

Three-dimensional modeling techniques based on medical imaging data such as computed tomography (CT) and magnetic resonance imaging (MRI) provide precise anatomical information for the design of personalized stents. By converting the patient's tissue morphology and structural information into a three-dimensional model and integrating it with 3D printing technology, highly specific nanofiber stents that closely match the patient's lesion site can be fabricated. For instance, in cranial repair, porous stents printed based on the patient's cranial CT model exhibit a morphological error of less than 5% compared to the defect site [21]. This imaging-guided stent modeling approach significantly enhances the fit between the stent and the tissue, reduces surgical complications, and improves therapeutic outcomes, as shown in Table 3.

4.2 AI Algorithm-Assisted Fiber Parameter

Regulation

Artificial intelligence algorithms play a crucial role in the fabrication of nanofiber scaffolds. Machine learning analyzes the relationship between material parameters (e.g., solution viscosity, voltage) and scaffold properties (e.g., porosity, mechanical strength) to optimize electrospinning process conditions. By establishing mathematical models linking material characteristics, fabrication parameters, and scaffold performance, AI algorithms can dynamically optimize fiber parameters in real-time, achieving precise control over scaffold properties, while incorporating patient-specific variations and therapeutic feedback. For instance, in neural tissue engineering, AI-based neural network models predict PCL fiber diameter with an error margin of less than 8% [22]. This intelligent fabrication approach not only enhances scaffold personalization but also significantly reduces the development cycle, as shown in Table 3.

4.3 Case Studies of Intelligent Scaffolds Interacting with Biological Signals

Smart nanofiber scaffolds can dynamically regulate their functions in response to physiological signals such as temperature and pH within the biological environment. Thermosensitive nanofiber scaffolds undergo phase transitions at body temperature, altering their pore structures to facilitate drug release. For instance, in cardiac therapy, thermosensitive gelatin/poly(N-isopropylacrylamide) (PNIPAM) scaffolds exhibit a contraction rate exceeding 50% at 37°C, conforming to the dynamic deformation of the heart while enabling sustained anti-inflammatory

drug release [23]. In wound management, pH-sensitive scaffolds release corresponding therapeutic agents in the acidic microenvironment of infected wounds. For example, chitosan/polyacrylic acid fibers swell in acidic wound environments, accelerating antibiotic release [11]. These intelligent scaffolds offer novel technological approaches for precision and personalized medicine, as summarized in Table 3.

Table 3. Implementation pathways of electrospun nanofiber scaffolds in precision personalized medicine

Technical Name	Implementation method	Technical advantages	Application Scenarios and Case Studies	Refer- ences
Image-Guided Stent Modeling	Three-dimensional CT/ MRI modeling com- bined with 3D printing technology	Providing precise anatomical information for the design of personalized scaffolds can significantly enhance scaffold specificity and tissue conformity, reduce surgical complications, and improve therapeutic outcomes.	In cranial repair, the porous scaffold printed based on the patient's cranial CT model exhibits a morphological error of less than 5% at the defect site.	[21]
	Machine learning establishes material-property mathematical models	By integrating individual patient differences and therapeutic feedback, AI algorithms can dynamically optimize fiber parameters to achieve precise regulation of scaffold performance, thereby effectively shortening the development cycle.	In neural tissues, the error in predicting PCL fiber diameter using AI-based neural network models is less than 8%.	[22]
Thermosensitive intelligent scaffold		Synchronized drug release and deformation adaptation for functionalized dynamic regulation	In cardiac therapy, thermosensitive gelatin/poly(N-isopropylacrylamide) (PNIPAM) scaffolds exhibit a contraction rate exceeding 50% at 37°C, conforming to dynamic cardiac deformation while enabling sustained release of anti-inflammatory drugs.	[23]
pH-sensitive scaffold		Environmentally responsive drug re- lease enables functionalized dynamic regulation	In wound treatment, pH-sensitive scaffolds can release corresponding drugs in the wound microenvironment to assist therapy. For example, chitosan/polyacrylic acid fibers swell in the acidic environment of infected wounds, accelerating antibiotic release.	[11]

5. Future Trends and Technological Optimization of Electrospun Nanofiber Scaffolds

5.1 Integration of Various Cutting-Edge Technologies with Electrospun Nanofiber Scaffolds

The integration of microfluidic chip technology and electrospinning offers a novel approach for the precise fabrication and functionalization of nanofibers. Through the precise fluid control enabled by microfluidic chips, high-throughput production and multicomponent composite nanofibers can be achieved, further enhancing scaffold performance. For instance, microfluidic chips regulate fiber composition gradients to construct biomimetic bone-cartilage interfaces and enable multi-material co-electrospinning, facilitating the one-step fabrication of vascular network-mimicking scaffolds [3,24].4D printing technology allows nanofiber scaffolds to undergo shape transformations under specific conditions, providing new possibilities for tissue repair. These 4D-printed nanofi-

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ber scaffolds can dynamically adjust their morphology post-implantation according to tissue growth requirements, better adapting to the tissue regeneration process [23]. For example, shape-memory polymers (e.g., PLA/thermoplastic polyurethane elastomers) respond to temperature or pH changes, dynamically conforming to tissue defect morphology. Multi-material synergistic electrospinning enables the fabrication of nanofiber scaffolds with multi-layered structures, where each layer can be endowed with distinct functional properties. For instance, layer-by-layer electrospinning constructs "soft-hard" gradient scaffolds that mimic the bone-cartilage interface [7,14]. Such multilayered scaffolds more accurately replicate the complex architecture of native tissues, demonstrating broad potential in tissue engineering and regenerative medicine.

5.2 Future Directions for Optimization and Improvement of Preparation Techniques

In the future, the optimization of electrospinning technology should primarily focus on improving preparation efficiency, reducing costs, enhancing environmental sustainability, and optimizing scaffold performance. By developing novel electrospinning equipment and processes, such as near-field electrospinning and multi-nozzle electrospinning, high-precision fabrication and large-scale production of nanofibers can be achieved. For instance, near-field electrospinning can increase production efficiency to 20 g/h, while current needleless electrospinning technology enhances the yield to 1 g/h, meeting clinical demands [4]. However, challenges such as batch-to-batch consistency (coefficient of variation in fiber diameter <10%) and scalable manufacturing still need to be addressed. Concurrently, in-depth research and development of material systems are essential. For example, replacing conventional solvents with greener alternatives and developing water-based electrospinning systems can minimize toxic residues. In summary, these advancements will further expand the application scope of nanofiber scaffolds in the biomedical field.

6. Conclusion

This study further analyzes the application directions and examples of nanofiber scaffolds fabricated via electrospinning. It reveals that such scaffolds exhibit remarkable advantages and immense potential in tissue repair, including bone, cardiac, vascular, and neural tissues, owing to their ultrahigh specific surface area, biomimetic structure, functionalization, and intelligent responsiveness. Through multifunctional design, these scaffolds can be tailored to meet diverse tissue repair requirements and significantly enhance therapeutic outcomes when combined with personalized medical technologies. However, challenges remain in achieving consistency in large-scale production. Current research primarily consists of experimental

findings, with limited clinical application cases, making it difficult to fully demonstrate their efficacy and value in real-world medical settings. Additionally, there is insufficient investigation into long-term effects, particularly regarding the long-term biocompatibility and stability of nanofiber scaffolds, which hinders their widespread adoption in regenerative medicine. Therefore, it is imperative to deepen the integration of multidisciplinary technologies, promote green manufacturing processes, accelerate clinical translation, and conduct long-term studies. In the future, with the deep integration of smart materials and imaging technologies, electrospun nanofiber scaffolds are expected to unlock broader application prospects in regenerative medicine.

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