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# Research Progress of Nanofibrous Scaffolds in Long Bone Treatment

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**Abstract:**
Currently, through electrospinning and solution blow molding techniques, new material bone scaffold nanofiber scaffolds have been developed for bone repair applications. The research background is rooted in the urgent need for bone injury treatment worldwide and the significant limitations of traditional metal-ceramic scaffolds, which have high infection and wear rates. This paper explores the methods and technical advantages and disadvantages of the two spinning techniques as well as their effects on fiber properties. Additionally, it discovers that the physical structural advantages of the nanofibers in the scaffolds can meet the simulated microenvironment of natural bone. Due to their unique fiber properties, they can significantly enhance the biocompatibility and wear resistance of the scaffolds. With the global digital development, nanofiber scaffolds can evolve towards an intelligent and personalized direction. By utilizing artificial intelligence and biosensing technologies, a more natural structural scaffold closer to the patient's own bone tissue can be created, thereby further improving the biocompatibility of the scaffolds and the regeneration effect of bone tissue.

**Keywords:** Electrospinning; nanofiber scaffolds; solution blow molding.

## 1. Introduction

Nanofibrous scaffolds are artificial extracellular matrices that mimic the native bone micro environment. Due to their unique properties such as high surface area, these scaffolds can profile, differentiate and promote cell adsorption more efficiently [1], demonstrating great potential in biotextile and tissue engineering. Currently, the main options for surgical treatment of these injuries are using some material including Synthetic substitutes composed of metals, ceramics and polymers. However, these materials are used as substitutes for damaged tissues or organs, rather than as platforms for repairing and regenerating tissue defects. They usually cause infection in the surrounding tissues or fail to integrate properly [2].

Nanofibrous scaffolds are a major area of interest within the field of treatment of long bone. Every year, there are over 2.2 million bone graft surgeries worldwide, which has greatly stimulated research on bone regeneration. The clinical need is particularly acute in China.

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According to the „White Paper on Osteoporosis in China“, the number of osteoporosis patients in China currently is close to 70 million. Additionally, there are over 80 million patients with various severe joint diseases, approximately 750,000 limb-disabled patients, and about 3 million new bone injury patients each year. As for artificial bone materials for bone tissue repair, there is a huge potential market [3].

This article presents the development and research of nanofibrous materials, their application in long bone repair, and offers a perspective for the future.

# 2. Technique

## 2.1 Electrospinning technique

Electrospinning is a technique that utilizes high-voltage electrostatic forces to draw polymer solutions or melts into nano-scale fibers. From the Figure 1A, the core components of the electrospinning device include the syringe (Syringe), syringe pump (Syringe pump), spinneret (Spinning head), high-voltage power supply (High-voltage power supply), and collector (Collector). During the process, electrospinning involves an electro-hydrodynamic process: the electric field force is utilized to overcome the surface tension of the polymer solution, forming a Taylor cone, and ultimately spraying the ultra-fine fibers onto the collector. Figure 1B shows the morphological changes during the initial stage of the jet. This illustrates the process where the jet becomes thinner and longer due to the continuous stretching caused by the electrostatic force under the influence of the electric field. Figure 1C records the dynamic process of the Taylor cone and the formation of the jet in a time sequence (-28 ms to + 32 ms). The Taylor cone gradually becomes sharper, and the jet continues to stretch. Figure 1D magnifies the detailed structure of the Taylor cone, clearly showing the initial shape of the jet at the tip of the cone [4]

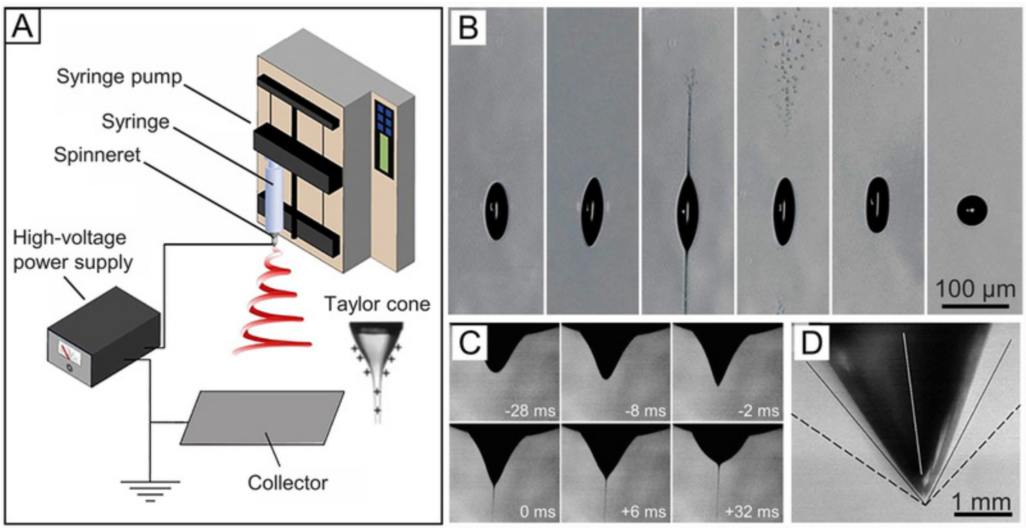


**Fig. 1 [A] The basic equipment for electrospinning [B] A levitated droplet of ethylene glycol charged to the Rayleigh limit for the ejection of two jets [C] The evolution of a pendant drop of PEO in water from a spherical to a conical shape, followed by the ejection of a jet [D]the droplet at the critical point [4].**

The resulting fibers exhibit high surface area (>10 $m^2/g$), tunable porosity (70-90%), and biomimetic structures, closely mimicking the natural extracellular matrix (ECM) to provide an optimal microenvironment for cells [4]. According to its formation principle, the fiber morphology, diameter and properties of electrospinning technology are influenced by multiple factors. Including electric field voltage, receiving distance, solution concentration, and so on.

Common materials for electrospinning include Natural polymers (Collagen, gelatin), which have excellent biocompatibility but limited mechanical strength, Synthetic polymers (PVA, PLA) offering controllable degradation rates and mechanical properties, and composite materials (graphene) combining bioactivity with enhanced mechanical performance [5].

**Table 1. The influence of various factors on the performance of electrospinning technology.**

| Parameter | Range | Relationship |
|---|---|---|
| Voltage | 5 - 30 kV | As voltage increases, fiber diameter decreases (but if it is too high, fiber will break [6]. |
| Collection Distance | 0.1 - 2 mL/h | As the distance increases, the fibers become drier, but may be unevenly dispersed [6]. |
| Solution Flow Rate | 5 - 20% w/v | As the concentration increases, fiber continuity increases, but the diameter also increases [6]. |
| Polymer Concentration | 30 - 60% RH | As the humidity increases, fiber porosity increases [6][7]. |

Table 1 summarizes the key parameters in the electrospinning process and their influences. The voltage range is 5-30 kV. An increase in voltage usually leads to a reduction in fiber diameter, as a stronger electric field force can more effectively stretch the polymer jet. However, excessively high voltage may cause jet instability and even fiber breakage. The receiving distance is 0.1-2 mL/h. An increase in distance allows the fibers to have a longer flight time for solvent evaporation, making them drier. But an overly large distance may lead to jet dispersion and uneven fiber deposition. The solution flow rate is 5-20% w/v. An increase in concentration enhances the solution viscosity, improving fiber continuity, but it also results in a larger fiber diameter due to the solution being more difficult to stretch. The environmental humidity is within the range of 30-60% RH. An increase in humidity slows down the solvent evaporation rate and promotes the phase separation process, thereby increasing the fiber porosity. In actual process optimization, these parameters often need to be adjusted in coordination to achieve the desired fiber morphology and performance.

### 2.2 Solution Blow Spinning

Solution Blow Spinning (abbreviated as SBS) is a new method for preparing nanofibers that combines traditional spinning technology with air-assisted processing.

The polymer is dissolved in a suitable solvent to form a spinning solution with a certain viscosity. When the polymer solution (such as PCL/chloroform) is extruded through the nozzle, it is sheared and atomized by the high-speed airflow around the nozzle into fine droplets. At the same time, the traction force of the airflow causes the droplets to be stretched and solidified to form fibers. The solidified fibers are finally deposited on a rotating drum or a static substrate [8].

### 2.3 Comparison and Complementary Nature of Solution Blow Spinning and Electrospinning

Solution blow spinning and electrostatic spinning each have their own advantages and disadvantages. In terms of the specific application and operation of the equipment, Due to the production method of solution blow spinning, it does not require a high-voltage power supply, the operation is simple, and the range of materials that can be used is wide. It can use non-conductive polymers. Therefore, the production efficiency is high, it can be mass-produced, and is suitable for industrial applications. In contrast, the electrospinning equipment consists of a high-voltage power supply, a spinning nozzle, a receiving device, and a solution supply system, and precise control of the electric field parameters is required [8].

In terms of fiber properties, the problem is that the fibers produced by solution blow spinning have a larger diameter and cannot be used to produce nanofibers [9], and cannot be used for more precise applications. Because the stability of the airflow has a significant impact on the fiber morphology, the fiber uniformity is poor. In the field of bone tissue engineering, solution blow-film spinning is often combined with electrospinning: first, the main structure of the scaffold is constructed through blow-film spinning, and then, electrospinning is used to deposit a nanofiber coating on the surface to achieve the synergistic optimization of mechanical strength and cell affinity.

## 3. Structural Biomimetic Design

### 3.1 Osteogenic mechanism and Immune regulation

In the process of long bone repair, the nano scaffolds simulate the physical microenvironment of natural bone (nano-scale fibers, appropriate pores) and reconstruct the chemical signal network (ion release, growth factors), thereby creating a „promoting adhesion - promoting differentiation - inhibiting inflammation“ osteogenic micro-ecology. Eventually, this enables the functional repair of long bone defects [10]. The key to this mechanism lies in the precise control at the nano scale, making the scaffolds a „bioactive template“ guiding bone regeneration rather than a mere physical filling material. Furthermore, surface modification of the materials is an important means for achieving immune regulation. By coating the surface of the nanofiber scaffolds with bioactive substances such as hyaluronic acid, inflammation can be reduced, creating a

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favorable immune microenvironment for bone tissue regeneration [11].

### 3.2 Multi-level Hole-structured Design

The multi-level hole-structure is one of the core elements in the design of bone tissue engineering scaffolds. Natural bone tissue exhibits a complex and exquisite multi-level pore structure, which provides a habitat for cells, greatly facilitating the exchange of nutrients and metabolic wastes, and also reserves sufficient space for the growth of blood vessels [12]. Inspired by this, researchers are dedicated to constructing nanofiber scaffolds with multi-level pore structures, aiming to simulate the structure and function of natural bone.

The porosity of the scaffold usually ranges from 50% to 80% [11]. An appropriate porosity is beneficial for cell migration, the transportation of nutrients, and the ingrowth of blood vessels. Pores of different sizes play distinct roles and work together during the bone regeneration process. The large pores can facilitate the rapid growth of blood vessels, providing the necessary oxygen and nutrients for the regeneration of bone tissue. The medium-sized pores and micro-pores can increase the specific surface area of the scaffold, enhance the interaction with cells, and thereby promote the differentiation and mineralization of osteoblasts [13].

### 3.3 Biocompatibility

Apart from the multi-level void structure, the biocompatibility of the nanofiber scaffold mainly depends on the selection of the material and its surface properties. From the perspective of material selection, there are significant differences in the biological properties of different materials. Currently, the two materials, PCL and PLGA, are widely used. They have controllable degradation properties and excellent mechanical characteristics, thus being able to sustain the mechanical strength of the scaffold over a long period of time and are suitable for bone repair with load-bearing capacity [14]. However, their hydrophobicity is relatively poor, which may lead to a decrease in cell adhesion rate. In contrast, natural polymer materials such as collagen have excellent cell affinity, and the cell proliferation rate can be significantly increased [15], but their mechanical properties are relatively poor.

The surface properties of the material are also a significant factor in the biocompatibility of the nanofibers. Studies have shown that when the fiber diameter is controlled within the range of about 600, it is most conducive to the spreading and migration of cells [16] This size range can simulate the fiber structure of natural extracellular matrix (ECM), providing appropriate topological cues for cells.

Surface roughness is another important parameter. When the surface roughness (Ra) is controlled below 50 nm, it can significantly reduce the conformational changes of proteins and maintain their biological activity [17]. Because cell migration requires a suitable surface structure for attachment and force generation, rough surfaces may provide more attachment points and guidance directions. Therefore, rough surfaces can promote the interaction between cells and scaffolds, stimulate relevant signaling pathways within cells, and thereby promote cell proliferation.

## 4. Challenges and Future prospective

### 4.1 Preparation Technology Challenges

The preparation technology of nanofiber scaffolds faces multiple challenges, mainly in aspects such as large-scale production and precise structural control. As mentioned in the previous text, in the electrospinning technique, the high-voltage electric field causes the jet to become unstable, thereby affecting the unevenness of the fibers produced that affect the performance of the support structure [18].

The solution blow spinning process also leads to uneven fiber diameters due to the instability of the airflow. However, the interaction between the airflow and the solution is complex, making it difficult to effectively control the fiber orientation. As a result, the fibers often exhibit disordered arrangement [19]. This limitation restricts the application of this technology in some scenarios where specific fiber orientation is required (such as in tissue engineering scaffolds with directional structures).

### 4.2 Applicability of Sterilization Process

The sterilization process has a crucial impact on the material properties of bone tissue engineering scaffolds. It not only affects the safety of the scaffolds in clinical applications, but also directly determines whether the physical and chemical properties as well as the biological characteristics of the materials can meet the requirements for bone tissue repair.

Ethylene oxide sterilization is one of the commonly used sterilization methods for bone tissue engineering scaffolds. However, this sterilization method has potential risks. Ethylene oxide has certain chemical reactivity and may react chemically with the scaffold materials, causing changes in the chemical structure of the materials. For degradable polymer scaffolds such as polylactic acid - glycolic acid copolymer (PLGA), after ethylene oxide sterilization, the degradation behavior of the materials may be abnormal

[20] This is because the alkylation effect of ethylene oxide disrupts the stability of the PLGA molecular chain, making it more susceptible to degradation by enzymes and water molecules in the body. Moreover, if ethylene oxide remains in the scaffold materials, it may slowly release after being implanted into the body, triggering local inflammatory reactions and affecting the activity of cells and the repair process of tissues [21].

Low-temperature plasma sterilization, as an emerging sterilization technology, has advantages such as lower temperature and shorter action time compared to traditional sterilization methods [22]. Theoretically, it has less impact on material properties. However, there are still challenges in practical applications. For bone tissue engineering scaffolds containing natural polymers, the active particles in the low-temperature plasma may damage the biological active groups of the natural polymers [23], thereby affecting their interaction with cells.

### 4.3 Clinical Translation Difficulty

The clinical application of bone tissue engineering scaffolds faces multiple challenges. From the perspective of production costs, the prices of raw materials such as PCL (poly(lactic-co-glycolic acid)) are high. The maintenance of equipment like electrospinning machines also requires a significant amount of funds, which results in expensive scaffolds and makes them unaffordable for a large number of people. Therefore, they cannot be widely popularized. Meanwhile, as a new type of scaffold, the nanofiber scaffold lacks relevant understanding among patients, which inevitably leads to concerns and confusion. There is a shortage of technical personnel, and it requires a significant amount of effort to train relevant personnel. Moreover, it is impossible to achieve rapid popularization.

## 5. Conclusion

This article mainly explores the preparation of nanofiber scaffolds through electrospinning and solution blow molding techniques, and compares the feasibility of large-scale production and the final stability of the nanofiber morphology. In the research on structural biomimetic design, the immunoregulatory effect of the nanofiber scaffold was deeply analyzed. In terms of biocompatibility, the effects of different material selections and surface characteristics on scaffolds and bone repair were compared.

This study addresses the urgent need for global bone injury treatment and the limitations of traditional metal-ceramic scaffolds, such as high infection rates and severe wear. It proposes a novel solution in the form of nanofiber scaffolds for bone repair. Through biomimetic structure and material properties, it provides a more optimized microenvironment for bone tissue regeneration, breaking through the limitation of traditional materials as merely physical fillers and promoting the transformation of bone repair from “replacement therapy” to “regenerative therapy”.

In the future, nanofiber scaffolds will rely on artificial intelligence and biosensing technologies to develop towards an intelligent and personalized direction, constructing natural structure scaffolds that are closer to the patient’s own bone tissue. This will further enhance biocompatibility and bone tissue regeneration effects. Achieving interdisciplinary integration is the key to breaking through existing preparation technologies, sterilization processes, and clinical transformation challenges. Through collaborative efforts in multiple fields, the industrial application of nanofiber scaffolds will be promoted, providing more efficient solutions for long bone injury repair.

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