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REVIEW

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Mechanisms of tendon-bone interface healing: biomechanics, cell mechanics, and tissue engineering approaches

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Abstract

The healing of tendon-bone contact surfaces involves complex biomechanical and biochemical interactions, with pivotal implications for sports medicine and rehabilitation. This review explores applications from cellular mechanics to tissue engineering, emphasizing how biomechanics impact tendon-bone healing. Cells regulate behavior, including growth, differentiation, and migration, by sensing mechanical signals and translating them into biochemical responses, which are critical in the healing process. Cellular mechanics modulate intracellular signaling, thereby influencing biological function and healing capacity. Optimizing tendon-bone interface repair involves modulating the extracellular mechanical environment. This includes physical stimulation, such as stretching, pressure, or vibration, to promote cellular alignment and enhance tissue structural integrity. Tissue engineering in tendon-bone healing focuses on designing scaffolds that mimic the biomechanical properties of the natural tendon-bone interface. Synthesizing these studies provides an in-depth understanding and utilization of biomechanical principles, significantly improving tendon-bone healing and offering new directions for clinical treatments to achieve better therapeutic outcomes and rehabilitation for patients with sports injuries.

Keywords Biomechanics, Tendon-bone healing, Cellular mechanics, Tissue engineering, Mechanical signals

Introduction

The tendon-bone contact surface (enthesis) is a crucial structure that connects the tendon to the bone and plays a vital role in maintaining the integrity and function of the musculoskeletal system. Due to the differing biomechanical and biochemical properties of tendon and bone, the healing process in this region is complex and prone to complications [1]. This complexity arises from the unique structural and functional requirements of the tendon-bone interface, which must withstand and transmit forces while remaining flexible enough to accommodate mechanical loads in the body [2].

Under normal conditions, tendon-bone contact surfaces can withstand the stresses and strains of daily activities through their complex biomechanical responses. However, when this area is injured, the natural healing process often fails to restore its original structure and function, primarily due to the biomechanical and biochemical differences between tendon and bone healing processes.

Differences in tissue structure: tendon is a dense connective tissue primarily composed of parallel-arranged collagen fibers, whereas bone is a hard tissue composed of a mineralized matrix and cells. The microstructural differences between tendon and bone affect their healing

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processes [3]. Differences in cell types: the primary cell type in tendon is fibroblasts, whereas bone contains osteoclasts, osteoblasts, and osteocytes. The biological properties and functions of these different cell types play distinct roles in the healing process [4]. Differences in biomechanical properties: tendon has high tensile strength and flexibility, while bone has high compressive strength and hardness. These differing mechanical properties result in varied responses when withstanding and transmitting forces [5]. Differences in vascular distribution: tendon typically has a less rich blood supply than bone, affecting the blood supply to the healing region. This, in turn, impacts cell migration, nutrient supply, and waste elimination [6]. Differences in perception and response to mechanical signals: tendon and bone cells differ in their perception and response to mechanical signals, affecting their interactions and integration during the healing process [7]. Differences in remodeling and maturation processes: tendon and bone exhibit temporal differences in their remodeling processes post-healing, with tendon remodeling requiring a longer period to achieve mechanical properties similar to the original tissue [8]. These differences result in a mismatch between the mechanical properties of the healed contact area and the native tissue, making it susceptible to re-injury.

Traditional treatments, such as surgical fixation and conservative management, often partially address the healing of the tendon-bone contact surface. Consequently, medical researchers and clinicians have been seeking more effective methods to promote healing in this area. The role of biomechanics is particularly important as it helps in understanding the behavior of tendon-bone contact surfaces under stress and guides the optimization of the healing process by adjusting the mechanical environment.

The study of cellular mechanics reveals how cells sense and adapt to their microenvironment through mechanical signaling, providing a theoretical basis for developing new therapeutic approaches. For example, by modulating external mechanical stimuli, cells can be stimulated to produce biochemical responses that favor healing [9]. Additionally, tissue engineering techniques offer new possibilities for repairing or replacing damaged tendon-bone contact surfaces by designing biomaterials and structures with biomechanical properties that match those of natural tendon-bone contact surfaces [10].

This review aims to provide insight into the healing process of tendon-bone interfaces, from the cellular level to the tissue level and biomechanics, and from experimental studies to clinical applications. We will explore current research advances and future therapeutic potentials. By integrating this knowledge, therapeutic strategies can be better designed to increase healing efficiency and ultimately improve the quality of recovery and quality of life of patients.

The role of mechanotransduction in tendon bone healing

It has been shown that mechanical stimulation promotes healing at the tendon-bone interface, mainly by affecting cell proliferation and differentiation as well as extracellular matrix synthesis and remodeling. For example, mechanical stimulation promotes M2 polarization of macrophages, which secretes more TGF-β1, a growth factor that promotes chondrogenic differentiation of mesenchymal stem cells (MSCs), thereby contributing to tendon-bone healing. In addition, mechanical stimulation is also able to activate the process of autophagy, which plays a regulatory role in the cellular response to mechanical forces, possibly by affecting the degradation and recycling of intracellular proteins, which in turn affects cellular function and the healing process. It has also been noted that appropriate mechanical stimulation can promote tendon-bone healing, but premature or inappropriate mechanical stimulation may adversely affect the initially more fragile tendon-bone interface, such as micromotion or injury. Thus, the role of mechanical signaling in tendon-bone healing is multifaceted. The following are a few key aspects of the role of mechanical signaling in tendon-bone healing:

Mechanical signaling

cells at the tendon-bone contact surface, such as fibroblasts, osteoblasts, and chondrocytes, can sense mechanical changes in their surroundings through their extracellular matrix (ECM). These changes are usually communicated through mechanosensitive ion channels in the cell membrane or through cellular adhesion sites to the ECM, such as integrins. Integrins are a class of transmembrane proteins, consisting of α and β subunits, which play key roles in cell-to-cell adhesion and signaling and are tightly linked to cell growth, differentiation, and migration. Marketed therapies have been successfully targeting integrins such as integrin αIIbβ3 for diseases such as cardiovascular disease [11]. Clinical data for certain emerging integrin inhibitors are still limited and more clinical trials are needed to validate their efficacy and safety. The complex design of integrin drugs also requires learning from previous clinical trials and exploring new paradigms. This mechanistic signaling is the first step in cellular response to mechanistic changes and is critical for subsequent regulation of cellular behavior.

Signal transformation and transduction

During the healing process at the tendon-bone interface, specific mechanical signals are transmitted through mechanosensitive ion channels on cell membranes or adhesion sites between cells and extracellular matrix,

which in turn activate signaling pathways closely related to the healing process. It has been shown that calcitonin gene-related peptide (CGRP) enhances osteogenic differentiation of bone marrow mesenchymal stem cells (BMSCs) through the protein kinase A (PKA)/CREB/JUNB pathway, which contributes to the improvement of sonic hedgehog (SHH) expression, which is essential for tendon-bone interface (TBI) healing [12]. In addition, the TGF-β signaling pathway is essential in tendon formation, which is involved in the formation of the tendon-fibrocartilage layer union and is an important factor involved in the construction of the functional unit of the tendon-bone interface.SOX-9 and Scleraxis (SCX) are key factors that mediate the transformation of precursor cells into chondrocytes and tendon tissues, and the SCX/BMP-4 signaling pathway is important in the development of the tendon-bone interface (TBI) in both the bone formation and the tendon-bone junction development is significantly promoted by the SCX/BMP-4 signaling pathway. These specific signaling pathways regulate cell proliferation, migration, differentiation, and extracellular matrix synthesis and reorganization, and are key regulatory mechanisms for tendon-bone interface healing. Therefore, an in-depth study of these signaling pathways is important to understand and promote tendon-bone healing.

Regulation of cell behavior

the regulation of cell behavior by the mechanical environment plays a crucial role in tendon-bone healing. Appropriate mechanical loading can promote the maturation and mineralization of osteoblasts, which is essential for the formation and healing of bone tissue. For example, stress stimulation can influence the synthesis of collagen and other extracellular matrices to promote tendon-bone union by promoting the differentiation of progenitor cells at the tendon-bone interface into cartilage. In addition, platelet-derived growth factor receptor α (PDGFRα) signaling plays an important role in the proliferation of tendon stem cells, which is essential for restoring tendon biomechanical properties [13, 14]. However, overactivation of PDGFRα signaling may lead to pathological fibrosis, and excessive collagen deposition that interferes with tendon function and has been linked to the development and progression of certain tumors that may increase the risk of tumor formation. Therefore, understanding how the mechanical environment regulates cellular behavior through signaling pathways such as PDGFRα is important for the study of tendon-bone healing and the development of therapeutic strategies.

Tissue reconstruction and regeneration

Cellular responses to mechanical signals extend beyond the individual cellular level to include the reconstruction and regeneration of entire tissues. Mechanical signaling influences the structural rearrangement and functional recovery of tissues by regulating cell-extracellular matrix interactions. Appropriate mechanical stimulation during tendon-bone healing can enhance the proliferation and differentiation of local precursor cells, thereby increasing the regenerative potential of BMSCs and TCs in tendon-bone healing and promoting a stronger tendon-bone connection [15].

In summary, the role of cellular mechanics in tendon-bone healing is reflected in its regulation of the cellular perception of mechanical signals, translation of these signals, and modulation of responses at the cellular and tissue levels. Understanding and utilizing these mechanisms can provide a scientific basis for designing new treatment strategies to optimize the tendon-bone healing process and improve treatment outcomes.

The role of tissue Engineering in tendon-bone Healing

Tissue engineering is an interdisciplinary field that combines the principles of biology, engineering, and materials science to design and develop biofunctional alternatives for repairing, maintaining, or enhancing tissue function. Studies have shown that the sustained release of the Wnt signaling activator BML-284 from the sandwich hybrid surface significantly promotes the adhesion, migration, proliferation, spreading, and osteogenic differentiation of MC3T3-E1 cells, as well as the angiogenic activity of human umbilical vein endothelial cells. In addition to osteogenesis and angiogenesis, hybrid surfaces play a key role in inhibiting osteoclast activity [16]. Several key applications of tissue engineering in tendon-bone healing are detailed below:

Design and application of bioscaffolds

Scaffolds are core components in tissue engineering that provide a three-dimensional support structure, facilitating cell attachment and proliferation, and guiding the formation of new tissue. In healing the tendon-bone interface, the designed scaffold must mimic the unique biomechanical properties of the tendon-bone contact surfaces to promote effective integration and functional healing between tendon and bone.

Material selection

The material of the scaffold should have good biocompatibility and biodegradability to adapt to the in vivo environment and gradually degrade as new tissues form. Commonly used materials include natural polymers (e.g., collagen) and synthetic polymers (e.g., polylactic acid, polycaprolactone). Zhang et al. emphasized the importance of material selection in achieving desired biocompatibility, biodegradability, and mechanical properties in bone repair [17], as shown in the following Table 1:

Table 1 Characteristics of Partial Biological Scaffold Materials in Tendon-Bone Healing.

Material name	Applicable situation description	Characteristics or advantages
Polyacrylates (PPF) and their derivatives [18]	Scaffold manufacturing for bone tissue engineering	Biodegradable, suitable mechanical properties
Polylactic acid (PLA) [19]	Tissue engineering scaffolds	Biocompatible, controlled biodegradability
Polycaprolactone (PCL) [20]	Tissue engineering scaffolds	Good biocompatibility, longer degradation time
Hydroxyapatite (HA)	Enhanced osteoconductivity and osteointegration of scaffolds	Chemically similar to bone minerals
β-Tricalcium phosphate (β-TCP)	Bone Defect Repair	Osteoinductive, biodegradable
Polylactic acid-hydroxyacetic acid copolymer (PLGA) [21]	Manufacturing Organization Engineering Scaffolding	Good cell attachment and proliferation environment
Poly(ε-caprolactone) (P(ε-CL))	Manufacture of scaffolds with good biocompatibility	Longer degradation time, suitable mechanical properties
Magnesium alloys (MAGNESIUM ALLOYS)	Manufacture of bone repair scaffolds	Biocompatible, biodegradable, modulus of elasticity similar to bone
Carbonized hydroxyapatite (CHAp)	Improved osteoinductivity and biocompatibility of scaffolds	Biocompatibility and ability to promote bone tissue growth
Poly(L-lactic acid) (PLLA)[22]	Manufacture of brackets with good mechanical properties	High mechanical strength and controlled degradation rate

Mechanical properties

The design of the scaffold must also consider its mechanical properties, such as strength, elasticity, and strain characteristics, to match the mechanical environment of the target tissue, ensuring that the scaffold can withstand physiological loads and adapt to the biomechanical environment after implantation. Bone tissue exhibits different mechanical properties at various sites, so scaffold design must account for these differences to achieve optimal biomechanical integration. Studies have shown that hydrophilic scaffolds exhibit better initial cell adhesion in vitro and effectively penetrate host cells in vivo, leading to the successful integration of bone implants [23]. Cell adhesion capacity is crucial to the biological response of cells to implanted biomaterials and facilitates subsequent cellular behavior, morphogenesis, and ultimate tissue response [24].

Biofunctionalization

Scaffolds are typically surface-modified or doped with bioactive molecules such as growth factors and cell adhesion peptides to enhance cellular functional activity and promote specific tissue generation. Yan, B. et al. [25] improved cell adhesion and enhanced tissue adaptation of PLGA by modifying the surface of PLGA scaffolds using various materials. These modifications can be applied to the PLGA surface by physical or chemical methods, imparting different functions to the PLGA scaffold. Roh, S. et al. [26] explored the routes of chemical, physical, and biological modification of polymer surfaces for biomedical applications, highlighting the improvement of biocompatibility and drug release control of polymers through various surface modification techniques such as plasma treatment and chemical vapor deposition. These techniques can enhance the hydrophilicity of material surfaces and improve cell-material interactions. However, hydrophilic surfaces may not be sufficiently stable in certain environments and may be prone to accelerated degradation or failure of the doped therapeutic drug.

Tissue engineering has demonstrated remarkable progress in the clinical application of tendon-bone healing, especially in the context of personalized medicine and precision medicine. The clinical application of bioscaffolds as temporary cell growth platforms has been extended to tendon-bone healing, in which the selection of scaffold materials is crucial, including collagen of natural origin and synthetic polymers such as poly(lactic acid)-hydroxyacetic acid copolymers (PLGA), which are required to have good biocompatibility, controllable biodegradation, and suitable mechanical properties to mimic the mechanical properties of tendon-bone contact surfaces and to promote functional healing. Properties of tendon-bone contact surfaces and promote functional healing. Mesenchymal stem cells (MSCs), which are widely used in clinical cell therapy due to their multidirectional differentiation potential, are implanted either by direct injection or co-cultured with biological scaffolds to enhance cellular infiltration and new bone formation in the tendon-bone healing region and to improve the biomechanical properties of the tendon-bone junction. Growth factors such as bone morphogenetic proteins (BMPs) and members of the transforming growth factor-β (TGF-β) superfamily play a key role in tendon-bone healing by activating specific signaling pathways such as Smad/RUNX2 to promote osteoblast differentiation and bone matrix synthesis and are often delivered with precision through a locally controlled release system to optimize dosage and reduce side effects. Platelet-rich plasma (PRP), a biologic agent, is used to promote tendon-bone healing due to its high concentration of growth factors and cytokines, and PRP is injected clinically via ultrasound-guided injections to enhance angiogenesis and cell proliferation at the tendon-bone interface to accelerate the healing process.3D printing technology allows for the fabrication of personalized scaffolds that accurately match the patient's anatomy, and these scaffolds can be porous, with a gradient structure to promote cell migration, vascularization, and tissue integration,

clinically providing a more precise repair solution for complex shaped tendon-bone defects. Bionic design principles are used to mimic the natural structural and mechanical properties of tendon-bone contact surfaces by precisely controlling the micro- and macro-structural as well as mechanical properties of the scaffolds to promote cell attachment, proliferation, and differentiation, and clinically these products improve the quality of healing by enhancing the integrative and mechanical stability of the tendon-bone interface. These clinical applications not only exemplify the translational potential of tissue engineering technologies in tendon-bone healing but also provide a scientific basis for the development of new therapeutic strategies, which are expected to lead to more personalized and precise tendon-bone healing treatment protocols in the future. With the deepening of clinical trials and the continuous development of new technologies, the application of tissue engineering in tendon-bone healing has a promising future and is expected to significantly improve the therapeutic outcome and the quality of life of patients.

Cell therapy and regeneration

Cellular therapy is another key aspect of tissue engineering, involving the introduction of selected cell types (e.g., stem cells, fibroblasts, or osteoblasts) into damaged areas to promote tissue regeneration and repair.

Cell source

Selection of a suitable cell source is crucial, with pluripotent stem cells (e.g., mesenchymal stem cells) being widely studied for their ability to differentiate into a wide range of cell types. Chen P. et al. [27] explored the effects of 3D-printed PLGA scaffolds loaded with bone marrow mesenchymal stem cells (BMSCs) on the healing of rabbit rotator cuff repair. They demonstrated that BMSC-PLGA scaffold implantation enhanced cell infiltration at the tendon-bone junction, improved the histological scores of tendon tissues, and increased collagen formation at the tendon-bone interface, thereby improving the regenerated tendon's biomechanical properties. However, there are certain difficulties in BMSC sampling, such as the requirement for bone marrow aspiration, which is an invasive procedure that may cause patient discomfort and complications. Additionally, the limited number of BMSCs derived from bone marrow usually requires in vitro expansion to obtain sufficient cells for research or therapy. Allogeneic BMSCs may trigger immune rejection and affect therapeutic efficacy.

Cell pretreatment

Cells are pretreated (e.g., pre-stressed culture or genetic modification) before implantation to enhance their viability and functionality. Decellularized ECM-derived hydrogels provide a culture matrix for stem cells that mimics the in vivo environment. Pre-stressed cultures can modulate the behavior of stem cells and promote their differentiation into specific cell lines, contributing to tissue engineering and regenerative medicine [28]. However, pre-treated cells may face a low survival rate during transplantation, affecting the therapeutic effect. They may also trigger an immune response, leading to rejection by the host. Additionally, pre-treatment methods and conditions may lead to inconsistent results, making standardization and large-scale application difficult.

The critical role of Gli1-expressing progenitor cell populations in the development and mineralization of tendon-bone attachment sites (enthesis) and tendon-bone healing has been explored for its potential application in clinical therapy [34]. In the study, the authors utilized cell-labeling techniques to track the dynamics of Gli1-positive progenitor cells, revealing the role these cells play in cell differentiation, matrix mineralization, and mechanical adaptations at the tendon-bone interface. Through tissue engineering and regenerative medicine approaches, the researchers further investigated the effects of these progenitor cells in response to mechanical stimuli, including cell morphology changes, proliferation, migration, and differentiation, in both in vitro and in vivo models. At the molecular level, the study delved into the activation status of key signaling pathways in Gli1-positive progenitor cells, such as the Hh (Hedgehog) signaling pathway, and how these signals regulate the expression of genes associated with mineralization of tendon-bone attachment sites, such as osteogenesis-related genes like Runx2, Osterix, and Alp. In addition, the study addressed the role of these progenitor cells in the remodeling of the extracellular matrix (ECM) at the tendon-bone interface, including the alignment of collagen fibers and the deposition of non-collagenous proteins such as fibronectin (FN) and osteoblasts (OPN). This study enhances the potential of tendon-bone healing by manipulating Gli1-positive progenitor cells, e.g., by modulating the behavior of these cells through a biomaterial-mediated local drug delivery system, or by enhancing their osteogenic differentiation capacity using gene therapy. The results suggest that osteogenic differentiation of Gli1-positive progenitor cells can be promoted by precisely controlling the mechanical environment and biochemical signals, thus potentially improving the quality and efficiency of tendon-bone healing.

Applications of growth factors and signaling molecules

Growth factors play a crucial role in tissue repair by stimulating cell proliferation, migration, and differentiation. In tendon-bone healing, bone morphogenetic proteins (BMPs) and transforming growth factor-β (TGF-β) are

used to promote the formation and repair of bone and tendon tissues.

The effect of BMPs on tendon-bone healing has been demonstrated in numerous studies. In studies of rotator cuff injury models, BMP-2 promotes tendon-bone healing through the Smad/RUNX2 pathway [29]. It is important to note that the range of effective doses of BMPs is narrow. High doses of BMPs may lead to heterotopic ossification, i.e., the appearance of bone tissue at sites that do not require bone formation, which interferes with function and may trigger an intense inflammatory response, leading to tissue damage and delayed healing. Conversely, low doses of BMPs may not be effective enough to promote tendon-bone healing, resulting in suboptimal outcomes. Doses that are too low may not adequately activate the desired signaling pathways, thereby slowing down the healing process. Therefore, determining the appropriate dose of BMPs is critical for optimizing tendon-bone healing outcomes.

Several studies have demonstrated the positive role of insulin-like growth factor-1 (IGF-1) in tendon repair. Ghahary et al. [30] showed that IGF-1 promotes collagen production through the indirect action of transforming growth factor-β1 (TGF-β1). In a further study, Durgam et al. [31] noted that topical application of IGF-1 not only stimulates collagen synthesis in equine tendons but also improves the quality of healing in vivo. These findings highlight the crucial role of IGF-1 in promoting collagen synthesis, cell proliferation, and protein synthesis, confirming its anabolic effects during tendon healing.

Controlled release systems

Growth factors are often delivered via controlled release systems in scaffolds to maintain their effective local concentration and prolong their biological activity. Hydrogels have become a prominent material in bone tissue engineering [32], opening new avenues in the field and effectively overcoming some limitations of traditional bone grafts due to their excellent biocompatibility, flexibility, plasticity, and multifunctionality. As a commonly used drug for the treatment of bone defects, sodium alendronate (ALN) accelerates the repair of bone tissue by inhibiting the activity of osteoclasts [33]. By uniformly dispersing ALN-loaded microspheres in chitosan-based hydrogels, both the local concentration and sustained release of the drug can be increased, enhancing the effect of bone regeneration. However, hydrogels suffer from poor mechanical properties and are prone to rupture or deformation, limiting their use in certain applications. The degradation rate of hydrogels can be difficult to control, and too rapid or slow degradation can affect their function and effectiveness in the body. Some synthetic hydrogels may have biocompatibility issues that need to be improved through modification or incorporation of natural polymers.

This innovative pre-gel mixture possesses self-assembling properties that allow it to form stable three-dimensional structures at the site of bone defects and can be embedded with other bioactive molecules, such as bone morphogenetic protein-2 (BMP-2), to further promote bone tissue formation and regeneration. Current mainstream sustained-release systems also include biodegradable polymers, liposomes, microspheres, and nanoparticles, which collectively enable precisely controlled release of drugs, growth factors, or cells in the biomedical field. These systems optimize therapeutic efficacy, promote tissue repair, enhance the stability and bioavailability of bioactive molecules, reduce side effects, and improve patient compliance.

Bionic design and bionic mechanics

In designing tissue-engineered products for tendon-bone interface repair, bionic principles are employed to mimic the structure and function of natural tissues. This involves precise control of the multiscale structure of the scaffold and its mechanical properties to promote optimal cellular response and tissue integration.

Tissue engineering offers diverse solutions for tendon-bone healing through strategies such as scaffold design and the application of cells and biomolecules, each aimed at ultimately achieving faster and more complete functional recovery. Future research needs to explore in greater depth the potential clinical applications of these technologies and their real-world efficacy.

Clinical applications and future directions

Clinical applications

The clinical application of tissue engineering techniques in tendon-bone healing is gradually expanding, transitioning from basic research and small-scale preclinical studies to more extensive clinical trials. Below are key areas of clinical application:

Biological scaffolds

Biological scaffolds are used to repair severe tendon injuries and tendon-bone ruptures. These scaffolds are designed to provide a temporary framework where new cells can grow and form new tissue, and eventually, these scaffolds are absorbed or degraded by the body. Clinically used scaffolds include synthetic polymers and natural materials such as collagen and gelatin.

Cell therapy

Specific types of cells, such as mesenchymal stem cells (MSCs), have been utilized to treat tendon-bone interface injuries. These cells can be directly injected into damaged

areas or applied with scaffolds to facilitate tissue repair and regeneration.

Growth factor therapy

Growth factors, such as BMPs and TGF-β, have been employed to enhance bone and soft tissue healing. These factors are typically administered via local injection or incorporated into scaffolding materials to leverage their capacity to stimulate cell proliferation and differentiation (Fig. 1).

Future directions

Although tissue engineering demonstrates significant potential in tendon-bone healing, future research and development must address several critical issues and challenges:

Personalized therapy

With the advancement of precision and personalized medicine, future tissue engineering solutions will increasingly focus on tailoring treatments to the specific characteristics of individuals (e.g., age, gender, disease state, and lifestyle). This approach includes utilizing a patient's cells for culture and treatment or designing scaffolds that align with an individual's specific biomechanical properties.

Advanced biomanufacturing technologies

Further advancements in 3D printing and bioprinting technologies will enable the production of highly complex and functional scaffolds. These techniques allow for precise control over the microstructure and chemical composition of scaffolds, thereby better mimicking the structure and function of the natural tendon-bone interface.

Clinical trials and regulation

More clinical trials must be conducted to validate the safety, efficacy, and cost-effectiveness of new technologies. Additionally, the commercialization and clinical rollout of these new technologies must undergo a rigorous regulatory process to ensure patient safety and quality of care.

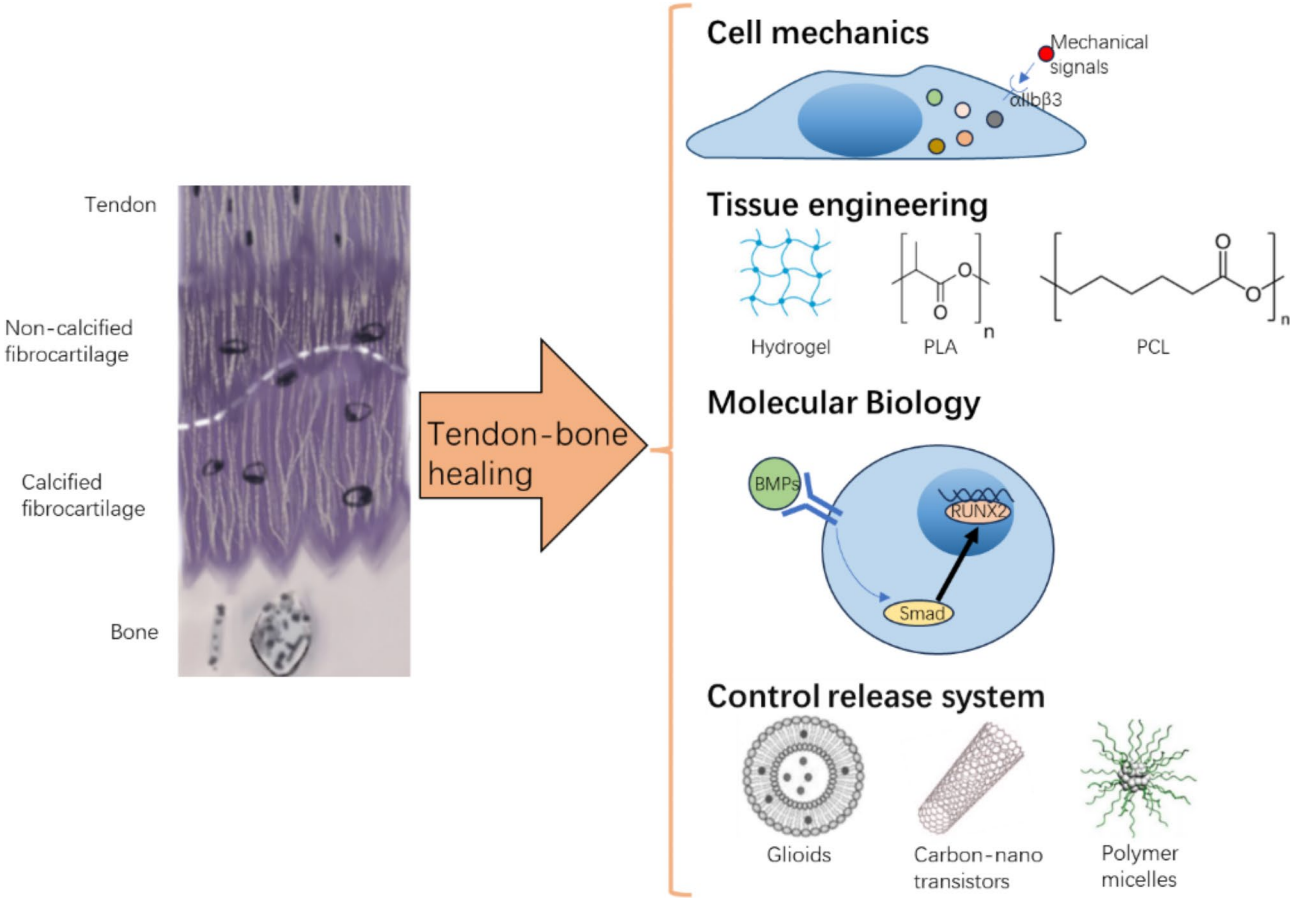

Fig. 1 Strategies for promoting tendon bone healing in various fields.

Interdisciplinary collaboration

Future progress depends on close collaboration among biologists, engineers, clinicians, and materials scientists. This interdisciplinary collaboration facilitates the integration of the latest advances across different fields to develop more effective treatment strategies.

In conclusion, the application of tissue engineering in tendon-bone healing demonstrates significant potential and is anticipated to substantially enhance the therapeutic outcomes of tendon-bone injuries and the quality of life for patients through ongoing technological innovation and clinical research.

Conclusion

The application of biomechanics to tendon-bone healing demonstrates a wide range of influences, from cellular mechanics to tissue engineering. By gaining a deeper understanding of how mechanical signals affect responses at the cellular and tissue levels, combined with advanced tissue engineering techniques, the healing of tendon-bone contact surfaces can be more effectively promoted. Future research must further explore the specific roles of these mechanisms and how this knowledge can be applied clinically to improve treatment strategies and patient recovery.

Author contributions

Zhixiong Xu: responsible for the overall design and implementation of the study, including the development and execution of the experimental protocol; led the data analysis and interpretation, and wrote the main part of the paper Tao Zhang: participated in the design and experiments of the study, especially the execution of experiments related to cell mechanics and data collection; assisted in data analysis, and revised and improved the first draft. Luo Long: responsible for literature search and organization, assisted in writing and revising some chapters, and analyzed and discussed the research results. Wensheng Xu (corresponding author): guided the whole research process, provided suggestions on key theoretical frameworks and methods, supervised the data analysis and paper writing, and ensured the quality of the research and the overall quality of the paper.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethical approval

Not applicable.

Informed consent

Not applicable.

Competing interests

The authors declare no competing interests.

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