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REVIEW

The potential application of electrical stimulation in tendon repair: a review

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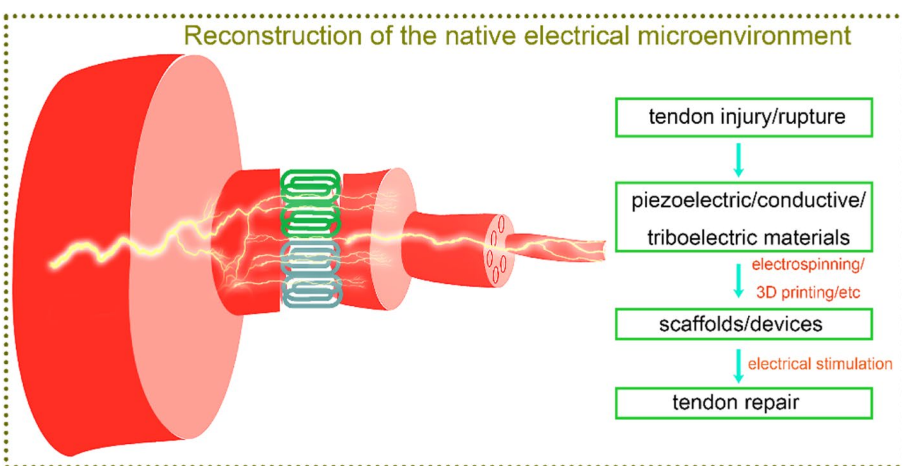
Abstract
Tendons are connective tissues with a regular three-dimensional structure containing collagen fibers, and the oriented collagen fibril gives tendons a piezoelectric effect. After tendon injury or rupture, the native electrical microenvironment in which it is located is disrupted, and the electrical signal pathway is blocked. Electrical stimulation (ES) can guide cell orientation, promote tissue differentiation, and enhance tendon repair. Therefore, bioactive materials that generate ES are ideal for repairing tendons by restoring the native electrical microenvironment. This review focuses on the application of piezoelectric materials, conductive materials, and triboelectric materials in tendon repair. They produce ES in different ways. Piezoelectric materials generate charges through deformation within the crystal under the action of force, which in turn causes the arranged dipole moments to deform, resulting in a net electric field. Conductive materials can generate a large number of freely moving charged particles under the action of an electric field and thus can conduct current. When two different triboelectric materials come into contact, opposite charges are formed on each surface, resulting in contact electrification. The materials are inextricably linked to each other, so the scaffold is developed that may be a single or multiple ES scaffold. For example, the mixed application of conductive material poly(3,4-ethylenedioxythiophene): poly(styrenesulfonate) (PEDOT: PSS) and piezoelectric material poly-L-lactic acid (PLLA), as well as the combined application of piezoelectric material polyvinylidene fluoride (PVDF) and triboelectric material nylon. More interestingly, PVDF is both a piezoelectric material and can generate charges under friction. Therefore, the development of high-performance cross-materials that can generate ES may be a better research direction in the future of tendon repair.

Graphical Abstract



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Highlights

- Tendon exhibits a piezoelectric effect due to the directional arrangement of the collagen fibril.
- Piezoelectric, conductive, and triboelectric biomaterials can generate electrical signals to repair tendon.
- Long-term self-powered, flexible, wearable devices that integrate therapeutic and monitoring functions will be needed for tendon repair.

Keywords Oriented collagen fibril · Native electrical microenvironment · Electrical stimulation · Tendon repair

Introduction

Tendons are connective tissues composed of collagen, elastin, water, and proteoglycans, efficiently transmitting muscle forces to bones to enable joint movements [1, 2]. Tendons have an oriented three-dimensional internal structure of collagen fibers, consisting mainly of longitudinally aligned fibers but also transversely and horizontally oriented fibers, which gives healthy natural tendons a fibro-elastic structure and high resistance to mechanical loading [1, 3].

Tendinopathy is a growing health problem that affects an estimated 100 million or more people worldwide each year [4]. The characteristics of tendinopathy include collagen fiber deformation, increased capillary and arterial proliferation, increased inflammatory mediators, dysregulation of extracellular matrix (ECM) homeostasis, changes in pain perception, and impaired tendon mechanical properties [5]. Injuries to tendons, tendon-bone junctions, and associated tissues can be caused by trauma, chronic overuse, and age-related degeneration [6, 7]. From a pathological and physiological perspective, various risk factors such as mechanical abuse, internal and external variables can lead to the onset of tendinopathy, which can still be repaired at this time; the accumulation and growth of risk factors lead to tendon injury and degeneration; finally, insufficient tendon function and load-bearing capacity can lead to tendon lesions, resulting in tendon tears or ruptures [8]. These injuries can be divided into two subcategories: acute injuries (traumatic injuries to previously healthy tissue) and chronic (degenerative) injuries [9]. It also can be categorized according to the structure affected: rotator cuff tendinopathy, lateral epicondylitis and medial epicondylitis, patellar tendinopathy, gluteal tendinopathy, hamstring tendinopathy, quadriceps tendinopathy, Achilles tendinopathy, iliotibial band syndrome [10, 11]. Tendon injury is a common debilitating musculoskeletal disease in sports medicine, which can lead to loss of function, comfort, and even mobility, and the treatment cost is relatively high [12, 13].

The diagnosis of tendinopathy is primarily based on clinical symptoms and examination of the patient's pain and stiffness after activity [14]. Tendon healing is a complex process that includes stages of inflammation, proliferation and remodeling [15]. Due to the slow, strain-dependent, and low cellular and vascular of the tendon repair, it leads to ECM disorder, making it difficult to treat after rupture [16, 17]. The natural healing ability of adult tendons is limited, and the current treatment methods mainly include conservative treatment with exercise, nonsteroidal anti-inflammatory drugs, and shock wave therapy in the early stage, as well as surgical treatment in the late stage [18, 19]. Currently, cell-free therapy in regenerative medicine is one of the main treatment methods for tendon injuries, with the most prominent source being the secretome of stem cell origin. The benefits of this therapy are multifaceted, including reducing immunogenic responses, maintaining post-storage activity, the ability to target characteristic tissues, and higher safety [20]. Chemical drugs are usually taken orally, while biological agents such as peptides, growth factors, or antibodies typically require parenteral administration [21]. Conservative treatments provide only temporary relief, and surgery can cause re-tearing and even harm that affects the patient's quality of life, these treatment options are limited and often lead to unsatisfactory clinical outcomes [19]. During the repair process, there may be complications such as tendon adhesions, local swelling and pain, wound infection, and limited movement [22, 23]. The structure and strength of the tendon are not fully restored after long-term repair, and patients rarely regain their pre-injury range of motion [24]. That is to say, the complete healthy repair of the tendon is a great challenge.

Currently, there are many strategies to enhance tendon repair through different technologies, interventions, and materials to create a variety of scaffolds (Fig. 1). They have been extensively studied in the field of tendon repair, either individually or in combination [25–28]. Biophysical cues present in biomaterials such as strain hardening, elasticity, porosity, cell adhesion ligands, mechanical loading, and fiber orientation are essential for adequate cell infiltration, cell differentiation, cell arrangement, matrix deposition, and cell migration [21]. Tu et al. [29] modified bioactive electrospinning fibers

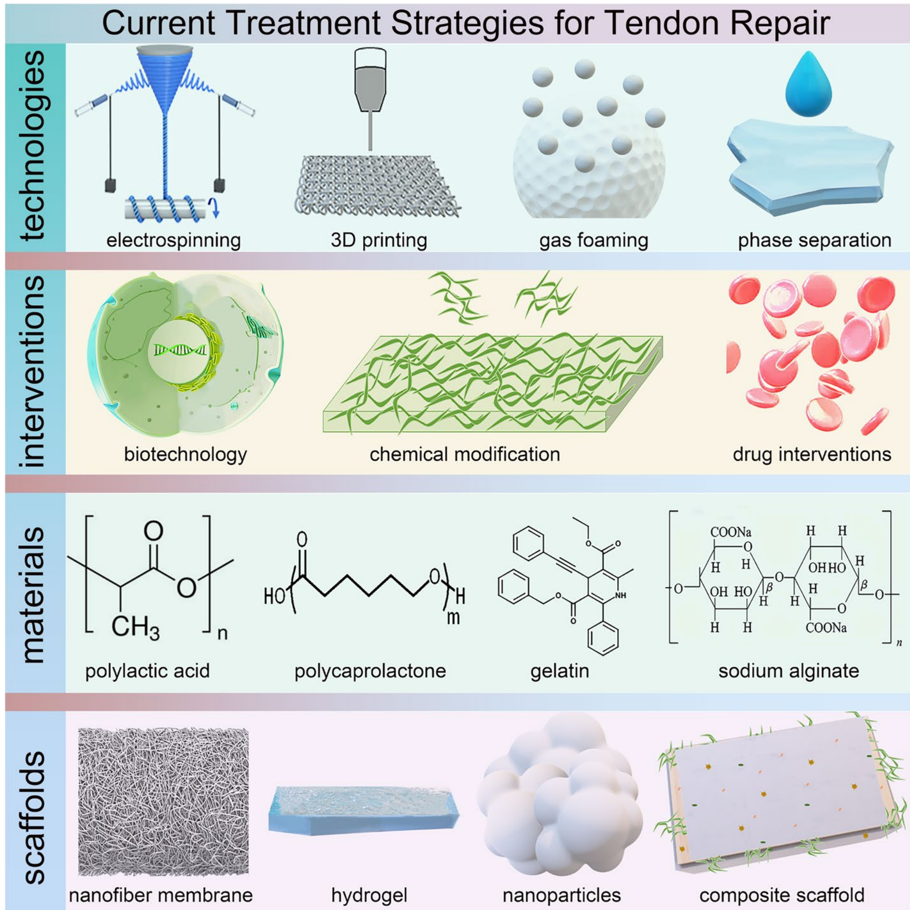

Fig. 1 Various scaffolds are made through different technologies, interventions, and materials and applied individually or in combination for tendon repair

with soluble tendon-derived ECM to promote mesenchymal tendon differentiation and rat Achilles tendon regeneration. Cai et al. [30] designed a self-healing hydrogel with macrophage regulatory and reactive gene silencing properties and found it to be highly effective in reducing inflammation and inhibiting tendon adhesion. Chae [31] proposed a gradient cell-loaded multi-tissue structural construct implant through three-dimensional cell printing technology, which promoted the effective recovery of shoulder motor function and accelerated the healing of the tendon-bone interface in vivo. The above methods are already very mature in the research of repairing tendons. Furthermore, tendon tissue engineering scaffolds that mimic the structure, composition, mechanical properties and induce tissue regeneration of tendons, which has shown great research value in this field.

Tendons can transmit electrical signals in the face of mechanical stress, distributing and controlling the force exerted by the muscle on the attaching tissues to produce movement [8]. However, once the tendon is ruptured, the electrical signal transmission pathway is blocked and the native microenvironment of the tendon is disrupted. During progressive wound healing, the rate of wound healing gradually slows down due to a decrease in bioelectricity released by the surrounding tissues [32]. It is equally important to be able to mimic the native microenvironment of tendons in future studies. Therefore, electroactive biomaterials have emerged as a new generation of smart biomaterials capable of directly applying ES to target cells or tissues [33]. The family of electroactive biomaterials consists mainly of piezoelectric biomaterials, conductive biomaterials, triboelectric biomaterials, and other biomaterials that generate electrical signals under specific stimuli (e.g., pH, light, temperature) [33]. In the latest research, the piezoelectricity of tendons can be used for tendon repair. However, there are few strategic studies summarizing the restoration of the tendon's native electrical microenvironment through ES materials to promote repair. Thus, this review will make a brief introduction to the piezoelectric source of tendon, the application of ES materials, and the future development in tendon repair.

Piezoelectricity of the tendons

Bioelectricity

Bioelectricity refers to electric fields that are naturally applied or generated in living systems [34]. Bioelectricity is an integral part of living systems, in which endogenous electric fields (EFs) play a crucial role in early embryonic development to tissue regeneration [35]. EFs are the basis of bioelectrical signal conduction and the priority signal of regeneration of damaged tissue [36]. At the cellular level, the difference in endogenous membrane potential within each cell leads to the generation of bioelectricity, which guides cell behavior including orientation, migration, adhesion, proliferation, and differentiation [37]. Physiological loads in asymmetric biological components such as skin, bones, dentin, tendons, muscles, hair, and many others can activate specific molecular cell signaling processes, triggering the generation of electrical potentials. This characteristic is called piezoelectricity [38, 39]. Due to the importance of bioelectricity, electrotherapy has evolved to accelerate wound healing, deep brain stimulation, tissue regeneration, improvement of musculoskeletal conditions, and fracture recovery [35].

The structure of the tendon determines its piezoelectric properties

In tendons, type I collagen (COL I) is the main structural protein, accounting for approximately 90% of the total collagen content and 60% of the tendon dry mass [40]. The fibrous tissue of tendons is regular: the tropo-collagen constitutes fibril, the fibril and primary resident cells, tenoblasts, and tenocytes constitute fiber, the fiber constitutes fascicle, and fascicle constitutes the tendon matrix [41, 42]. The hexagonal stacking of collagen molecules in cross-section is thought to be the origin of collagen piezoelectricity, where collagen generates an electrical charge under strain, and thus the oriented collagen fibril makes tendons piezoelectric [43, 44]. In other words, when the tendon is strained by force, the collagen fibril will keep the tendon in its native electrical microenvironment (Fig. 2).

Different piezoelectric domains on tens of nanometers to micrometers scale were observed in human tendons using piezoresponse force microscopy [45]. Moreover, at the nanoscale, it has been found that the longitudinal piezoelectric coefficient of a single collagen fibril is approximately one order of magnitude larger than the macroscopic measurement of tendons [46]. Studies have shown that collagen fibril exhibit unipolar axial polarization due to the redirection and magnitude changes of permanent dipoles of single charged and polar residues caused by mechanical stress, manifested as shear piezoelectric materials with a shear piezoelectric constant of $d_{15} \sim 1$ pm V^{-1} [47, 48]. Majid [49] showed that individual collagen fibril of the bovine Achilles tendon consist of piezoelectrically inhomogeneous gaps and overlapping regions, with the overlapping regions having significant piezoelectricity and the gaps regions having lesser piezoelectricity. This piezoelectric heterogeneity is essentially related to the structural heterogeneity of the region under subfibrillar. At the same time, it has also been found that the resistance of current passing through collagen fibril was minimal by the bovine Achilles tendon is connected in series with a control resistor in a direct current (DC) circuit. That is to say, when an electric current passes through, the inherent electrical characteristics of the tendon will cause the current to preferentially respond along the direction of collagen fibril [50].

Piezoelectric stimulation

Piezoelectric materials

Piezoelectric materials can convert mechanical energy into electrical energy and are considered smart materials [51]. This phenomenon is caused by the transient deformation of the atomic structure of the material under mechanical stress, where the material loses its center of symmetry and forms a net dipole moment [52]. In this case, the distance between the positive and negative charge centers changes

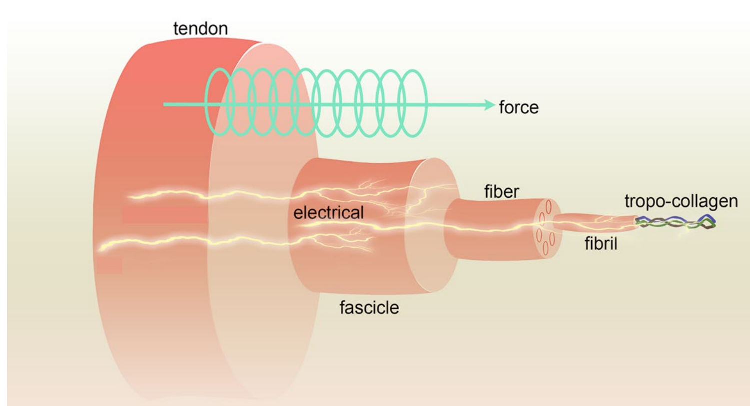

Fig. 2 The tendon composed of regular, oriented collagen fibril will strain under the action of force, which leads to the piezoelectric effect

and the surface free charge is partially released to generate piezoelectricity [53].

There are many applications of piezoelectric materials in tissue regeneration, including natural piezoelectric crystals, piezoelectric ceramics, piezoelectric polymers, and piezoelectric composite materials in bone, cartilage, nerve, skin, tendon, and cardiovascular tissue repair [54, 55]. Such as the scaffolds made from proteins, polysaccharides, PLLA, silk fibroin, etc. in tendon repair [56–58]. Due to their biocompatibility, biosafety and environmental sustainability, natural piezoelectric biomaterials are considered a promising candidate in this emerging field [59]. Meanwhile, piezoelectric polymers and their composite materials have become active scaffolds for tissue engineering applications due to their ability to enhance cellular function [60]. With the development of technology, piezoelectric composite materials will become mainstream, which retain the advantages and eliminate the disadvantages and has good flexibility, processability, high piezoelectric constant, and electromechanical coupling coefficient [61]. A wide range of piezoelectric nanomaterials has been explored by changing the material composition, crystallinity, nano to macroscale hierarchies, processing and post-processing conditions, which significantly affect their piezoelectric properties. The design of smart biomaterials capable of actively interacting with living systems by mimicking the properties of bio-piezoelectric structures is of great importance to the entire field of tissue engineering [62]. Scaffolds need to have excellent mechanical properties including stiffness, elasticity, and tensile strength to ensure functional integration and support physiological loads, which is particularly important in tissues subject to a dynamic mechanical environment [63]. Therefore, piezoelectric composite materials can provide high mechanical properties as well as continuously optimized piezoelectric properties to enhance the stability and functionality of tendon repair scaffolds in dynamic biological environments.

The electric fields exhibited by piezoelectric materials, whether strain-induced, temperature-induced, or spontaneously realized, have a dramatic effect on the electronic properties inside and outside the material [64]. Therefore, piezoelectric materials generate charges under physiological stress and body movement, and exhibit good effects in tissue regeneration and other aspects after implantation in the body [65]. As a tendon implant, it is very promising for tendon regeneration as it can use the body's kinetic energy to generate the electrical signals necessary for tendon growth and restore the native electrical microenvironment.

Application of piezoelectric materials

Tenocytes have high mechanical sensitivity. Their unique sensory mechanisms include mechanosensitive ion channels involved in repairing signaling pathways [66]. Mechanosensitive ion channels are a class of gated ion channels composed of membrane-integrated proteins that play an important role by converting mechanical forces into ionic currents across the cell membrane [67]. For example, PIEZO1 is a mechanically activated ion channel in tenocytes that promotes tendon function by inducing tendon-specific gene expression and structural changes, thereby enhancing motor function [68]. The piezoelectric-derived electric field generated during physiological movement may provide additional bioelectric signal clues to activate tendon-specific regeneration pathways [69]. Fernandez-Yague et al. [69] designed a self-powered piezoelectric-bioelectrical device to modulate tendon repair-related signaling pathways by modulating mechanosensitive ion channels to promote tendon-specific over non-tenogenic tissue repair processes. Ge et al. [70] developed a highly stretchable polyester-based piezoelectric elastomer with good biocompatibility, which promoted the regeneration of the Achilles tendon in a rat acute injury model, effectively improving its behavioral function and biomechanical properties.

Current research focuses on improving piezoelectricity by promoting dipole orientation such as blending with fillers [71]. Zhang [72] prepared Janus nanofiber scaffolds of PLLA/zinc oxide (PLLA/ZnO) and PLLA/barium titanate (PLLA/BTO) through electrospinning, and combined them with motion-driven ES and nano topological effects to promote tendon to bone healing (Fig. 3). Among them, PLLA is a common material used to make piezoelectric tissue engineering scaffolds, and the addition of both ZnO and BTO improved the piezoelectricity of the scaffolds, which stimulated the proliferation of tenocytes, induced tendon differentiation, and promoted the proliferation and differentiation of osteoblasts, thus promoting bone regeneration. It has been suggested that BTO naturally promotes tissue regeneration by using its piezoelectric properties to induce stable and repeatable electrical signals when subjected to mechanical stress. These electrical signals are transmitted simultaneously with mechanical forces to voltage-sensitive and mechanically-sensitive ion channels on the surface of the cell membrane, resulting in intracellular calcium ion inflow, which enhances cell regeneration [73]. Strontium (Sr) is the metal element with the highest content in tendon tissue. Tetragonal-$SrTiO_3$ (T-$SrTiO_3$) is particularly interesting, showing obvious piezoelectric properties at low temperatures and changing into ferroelectric properties under environmental conditions. The addition of T-SrTiO3 in the polymer can effectively create a favorable electrical microenvironment for tendon repair [74].

In addition, piezoelectric materials have other functions, such as inhibiting bacterial growth and colonization by inducing changes in charge distribution under stress. For example, ZnO can produce reactive oxygen species (ROS)

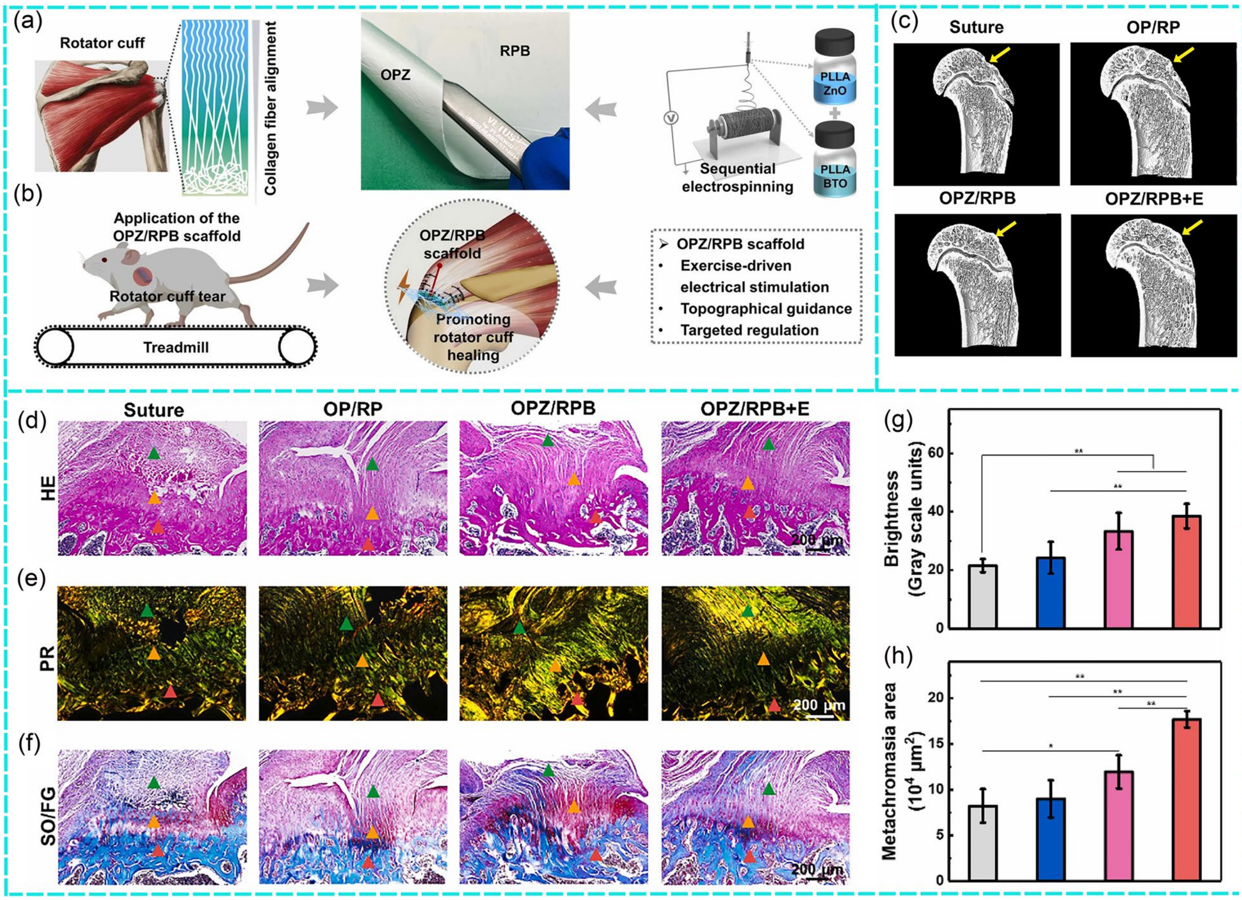

Fig. 3 Schematic illustration of the fabrication of the Janus nanofibrous scaffolds (**a**). The possible synchronous healing mechanism of the tendon-bone interface stimulated by exercise-driven ES and topographical guidance (**b**). The representative micro-CT images (the yellow arrows pointed to the insertion site of the greater tuberosity) (**c**). Representative images of the reconstructed tissues at 4 weeks after surgery (red triangle: bone; orange triangular: cartilage; green triangular: tendon), Hematoxylin and eosin (H&E) staining (**d**), Picrosirius red (PR) staining (yellow: Col I; greed: Col III) (**e**), and Safranin-O/Fast green (SO/FG) staining (**f**). Analysis of the collagen birefringence based on PR staining (**g**). Comparative analysis of total metachromasia area based on SO/FG staining (**h**). Reproduced with permission from [72]. Copyright © 2024 Elsevier Ltd

to effectively eliminate bacteria, demonstrating strong antibacterial activity [75]. Furthermore, the effective interfacial charge transfer caused by the piezoelectric effect makes the piezoelectric materials have good redox catalytic activity [76]. In addition, piezoelectric materials can mimic natural electrical currents in human cells [77]. For example, when piezoelectric devices are implanted in the body, they can collect the body's movement to self-power, thus avoiding the use of medical implants with toxic batteries [78].

Piezoelectric devices

The piezoelectric phenomenon has been observed in many biological tissues and macromolecules, which has promoted the development of bio-intelligent devices. Piezoelectric devices usually refer to a type of electronic or optoelectronic device based on the piezoelectric effect, and their most basic regulating unit is usually called a piezoelectric transistor. According to their structure and working mechanism, they can be broadly divided into two categories, namely field-effect transistors and piezoelectric transistors [79]. With the in-depth research in the field of piezoelectricity, many piezoelectric materials have been used to make piezoelectric crystal devices, such as aluminum nitride, lead zirconate titanate, ZnO, gallium nitride, barium titanate, PVDF-co-hexafluoropropylene [80, 81]. Piezoelectric devices have many advantages such as high electromechanical coupling effect, high power density, fast response time, compact structure, and so on, which make them used in the biomedical field [82].

Biological piezoelectricity has great potential for in vivo sensing, drug delivery, and tissue reconstruction, especially in biomaterials and systems where piezoelectric responses caused by strong supramolecular dipoles can be modulated through molecular chemistry and packaging [83]. Furthermore, many electric devices are powered by batteries, and power supply for a long period cannot be guaranteed because of the loss of ordinary batteries, while piezoelectric materials can be realized to be self-powered in the body to meet practical needs. At the same time, computer modeling makes it possible to insert various requirements such as shape, size, thickness, type, energy supply, and load-bearing capacity. Moreover, the degradation rate and piezoelectric effect of the material can be precisely adjusted through computer-aided design and simulation technology, thus preventing the material from degrading too fast or too slow to ensure the stability of piezoelectricity [84]. The personalized customization of the piezoelectric biosensor is realized by optimizing the structure of the piezoelectric scaffold. Thus, in the new field of body computing in personalized healthcare, biosensors can extract physical and physiological signals in real-time and parse them into actionable health information using big data analytics and artificial intelligence to determine interventions and treatments based on sensor output [85]. It has led to substantial results in the research and development of piezoelectric and sensor devices made of functional piezoelectric materials, such as piezoelectric nanogenerators that convert mechanical energy into environmentally friendly, sustainable electrical energy via nanoscale piezoelectric materials [86]. Wearable sensors provide continuous, noninvasive monitoring of physiological signals, enabling real-time health tracking for early detection of disease and improved management practices [87]. Implantable medical electronic devices that can improve people's quality of life, such as cochlear implants, cardioverter defibrillators, artificial retinas, etc. [88]. These wearable or implantable piezoelectric devices facilitate the development of self-powered medical devices. Li [89] reported an amino acid-based piezoelectric bio-crystalline film with tissue-compatible all-round stretchability and non-destructive piezoelectricity, which is a key step towards tissue-compatible biomedical devices. Shu [90] proposed a wearable and stretchable bioelectronic patch for detecting tendon activity. It was composed of functional piezoelectric thin films containing PVDF, metal conductors, and dielectric materials, and had been systematically optimized in terms of structure and mechanics. In addition, by integrating the patch with the microcontroller unit, a real-time monitoring and healthcare system for tendons was established, which could process the collected data and provide feedback for motion assessment. Specifically, the patch on the ankle could be used to measure the maximum force exerted on the Achilles tendon during jumping. This work not only provided a simple strategy for monitoring changes in the Achilles tendon throughout the body, but also contributed to a deeper understanding of human activities (Fig. 4).

Currently, in the development of viable bio-piezoelectric materials and the realization of applications such as biosensors, electric motors, and energy harvesters, the biggest challenges are constrained modes, directional control, and polarization direction. To overcome these obstacles, researchers have recently experimented with bio-piezoelectric element recognition, screen printing, cloud computing, and electromagnetic field-induced configuration techniques [91]. Some defective devices may cause immune reactions when piezoelectric devices are implanted into the body. Therefore, a strict device safety evaluation system is required for biocompatibility assessment, toxicity assessment, degradation cycle research, and long-term monitoring [92]. Based on this, the demand for piezoelectric devices with high performance, small size, low power consumption, and flexibility is growing [93]. However, the large-scale synthesis and manufacturing of piezoelectric biological devices are still difficult to achieve practical applications at present. Many studies are still at the basic stage of research. Combining wearable piezoelectric collectors with high power density and wireless charging technology is a developmental driver for future implantable medical devices to increase their lifespan [94]. Piezoelectric materials are expected to be the next generation of tissue engineering scaffolds, so computational models of piezoelectric scaffolds will have significant potential in supporting structural design that promotes tendon repair.

Direct electrical stimulation

Common types and application

Extracorporeal shock waves, low-intensity pulsed ultrasound, mechanical stress, direct ES, combined magnetic fields and exercise therapy have been shown to have a beneficial effect on tendon healing [95]. It can be noted that direct ES can guide the development and regeneration of many tissues [96]. Direct ES may be a potential regulator that promotes cell proliferation, differentiation, and ultimately ECM synthesis in vitro [97]. Carla [98] found that micro-current stimulation could promote hyaline cartilage repair in immature male rats. Casagrande [99] found that low-frequency ES could increase collagen synthesis and promote the healing of rat Achilles tendon. Labanca et al. [100] proposed that ES was effective in improving the strength and function of the patient's hamstring tendon graft after reconstruction of the anterior cruciate ligament (ACL).

Currently, common ES devices include direct coupled (DCP) stimulation, capacitive coupled (CCP) stimulation, inductive coupled (ICP) stimulation, or a combination thereof. DCP requires placing a cathode at the site of injury and a complementary anode in the surrounding soft

Fig. 4 Applications and an exploded view of the patch (**a**). The operating procedures of the system and demonstration of applying the patch for recoding the arm's bending (**b**). An optical image of the patch's fixation, using the bioelectronic system for gait analysis, and APP displays on a cellphone (**c**). Reproduced with permission from [90]. Copyright © 2021 Sheng Shu et al.

tissue to exert its effect [101]. Common applications of DC stimulation include transcranial DC stimulation, which is a non-invasive technique consisting primarily of a battery-powered current generator and a cathode and anode on the scalp [102]. Transcranial DC stimulation can establish a causal relationship between a limited area of the brain and its potential perception, cognition, and motor functions. It has been tested to treat various mental and neurological disorders, including depression, stroke, and changes in consciousness [103]. In addition, DC stimulation can promote the secretion of prostaglandins, morphological factors, and growth factors by cells, thereby affecting them

[79]. DC electric fields can enhance the migration ability of anterior cruciate ligament fibroblasts and promote the expression of COL I, which can be used to promote ligament healing and repair [92].

CCP stimulation typically involves placing two skin electrodes on opposite sides of the target tissue. By applying low-frequency alternating current, the electric field can be generated at the defects [101]. The U.S. Food and Drug Administration has approved non-invasive bone growth stimulators that function through two methods: CCP and ICP [104]. It has also been shown that CCP electric fields are a non-invasive and cost-effective treatment modality that can potentially restore internal homeostasis in articular cartilage [105]. Lee et al. [106] constructed a wireless, chipless, immune-tolerant in vivo strain sensing suture system around an inductor connected to a capacitive fiber optic strain sensor, which could continuously monitor the mechanical stiffness changes of reconstructed Achilles tendon throughout the healing process.

ICP stimulation is applied through an electromagnetic coil. A pulsed magnetic field is generated by a wire coil that circulates current, and the pulsed magnetic field induces a secondary electric field that varies over time within the exposed tissue [107]. Pulsed current has many functional effects, such as attaching surface electrodes to painful areas and applying low-frequency pulse current (1–100 Hz) to suppress excessive pain [108]. In addition, because most portable or battery-powered stimulators can only provide pulsed current, it is more widely used in sports training and rehabilitation [109]. Pulsed electromagnetic fields regulate cellular processes by emitting pulsed, variable intensity and frequency electromagnetic fields [110]. Girolamo et al. [111] found that 1.5 mT- pulsed electromagnetic fields treatment was the most effective in terms of cell proliferation, up-regulation of tendon-specific gene expression, and release of anti-inflammatory cytokines and growth factors in healthy human tenocyte cultures in vitro. In a rat model of acute bilateral supraspinatus tear repair, a non-invasive pulsed electromagnetic field might promote early postoperative tendon-to-bone healing, improve biomechanical properties and COL I expression [112].

Direct ES plays multiple important roles in promoting tendon repair. In a recent study, it was noted that neuromuscular ES can induce the development of tissues such as bone, cartilage, and tendons, which are important components of motor organs and basic mechanisms of repair after injury [113]. Dohnert et al. [114] found that continuous high-frequency transcutaneous electrical nerve stimulation significantly reduced pain intensity and significantly improved knee mobility, muscle strength, and medication uptake after ACL reconstruction. A similar study found that neuromuscular ES of the adductor humerus muscle in patients with rotator cuff tears improves shoulder-humerus distance and the ability to rotate the shoulder blades upward during arm lifts [115]. It has been shown that low-frequency ES promotes mitochondrial bioactivation [116]. Further studies have shown that electrical signals can affect the polarization of macrophages by improving mitochondrial function and promoting adenosine triphosphate synthesis [75]. This was similarly validated by Tu et al. [117], who suggested that ES of the sympathetic nerves can lead to a decrease in the concentration of the inflammation-related factors IL-6 and IL-1β and inhibit the inflammatory response around the tendon. In addition, ES also has the function of promoting vascular dilation, enhancing vascular permeability, and increasing local tissue blood flow [118].

Conductive materials

Research showed that direct ES could modulate cellular components, such as ion channels and cytoskeletons, to regulate cell behavior and function [119]. The inherent conductivity of conductive scaffolds in tissue regeneration provides local ES at the implantation site, allowing for the transmission of ion signals based on cells during cellular processes, guiding cells to align in specific directions, and promoting their differentiation in various tissues, achieving the effect of repairing damaged target tissues [101]. Common conductive materials include platinum-gold alloy, magnesium alloy, polypyrrole, polyaniline, PEDOT, carbon nanotubes, graphene and other two-dimensional (2D) nanomaterials [120, 121].

PEDOT: PSS with high conductivity and water dispersibility is a favorite combination in bioelectronics [122]. An anisotropic, high strength, toughness, and conductivity hydrogel made from poly (vinyl alcohol), cellulose nanofiber, PEDOT: PSS as a tendon substitute has restored the motor function and contributed to the treatment and rehabilitation of dysfunctional tissues in SD rats [123]. PEDOT: PSS nanoparticles were coated on electrospun nanofibers of poly (ε- caprolactone), which reduced the gap area between muscle fibers under the ES and enhanced muscle regeneration after rotator cuff repair [124]. The researchers further found that PEDOT: PSS matrix could inhibit fat accumulation and fibrosis, improve tendon morphology and tensile properties [125]. Yang [126] reported a bondable, stretchable, biocompatible, and gel-free TPP electrode based on tannic acid, PEDOT: PSS, and polyvinyl alcohol, and then a metal-polymer electrode array patch (MEAP) composed of liquid metal circuitry and TPP electrodes, which could continuously monitor tendon displacements and control tendon stretching within a safe range, thus reducing the risk of muscle or tendon injury (Fig. 5).

Carbon-based conductive materials can be used as load-bearing materials and are also capable of adsorbing proteins, and can be used to stimulate tissue growth by forming conductive microcircuits through exogenous ES [127, 128]. Carbon nanomaterials have good conductivity and can be used for electrophysiological signal transmission in muscle and nerve tissues, as well as for controlling cell fate [129]. Thus, various structures of carbon-based materials can be designed to mimic the spatial structure and surface morphology of tendon fibers, and epigenetic cues provided by the morphology and topography of the cellular microenvironment synergize with those derived from ECM stiffness to enhance overall regeneration [130]. Pan [131] made an electro-tendon by Nephila pilipes spider dragline silk, single-walled carbon nanotube, and PEDOT: PSS. This electro-tendon could be bent and stretched over 40,000 times without changing conductivity. When attached to a pressure sensor and mounted on the fingers of a humanoid robot, the robotic hand could grasp a variety of objects, such as balloons, needles, and aerosols, without crushing and damaging the objects (Fig. 6). Wang [132] designed hierarchical helical carbon nanotube fibers as a substitute for the bone-integrated anterior cruciate ligament. Due to the multi-scale channels of the fibers and carbon-driven osteogenesis, the rabbit and sheep models were able to run and jump normally after 13 weeks of implantation. Yu et al. [133] designed a carbon fiber-mediated electrospinning scaffold, which was almost filled with collagen fibers in a rabbit Achilles tendon defect repair model. The transcriptome sequencing results showed that the expression of fibronectin and tenomodulin was upregulated, and their related proteoglycans and glycosaminoglycan binding protein pathways were enhanced, which could regulate the TGF-β signaling pathway, optimize ECM assembly, and promote tendon repair.

Compared with traditional materials, 2D materials such as the graphene family are widely used in tissue regeneration, such as tendon regeneration, due to their excellent mechanical properties, large surface area, good biocompatibility, optical transparency, biological function, and controllable electronic and electrochemical properties [134]. The gel of graphene oxide and platelet-rich plasma developed by Bao et al. [135] had good biocompatibility and could promote the proliferation of bone marrow mesenchymal stem cells and the differentiation of osteogenesis and cartilage. The structure of newly formed tendons was similar to natural tendons and had good biomechanical properties, which could effectively improve tendon-bone healing. In addition to graphene, other 2D nanomaterials such as transition metal dichalcogenides (TMDs), antimonene (AM), black phosphorus (BP), metal-organic frameworks (MOFs), 2D metal carbides and nitrides (MXenes) have emerged successively in biomedical applications [136]. Compared to one-dimensional or three-dimensional (3D) nanomaterials, 2D nanomaterials have the highest specific surface area, resulting in a greater number of surface atoms compared to volume atoms. The presence of a large number of surface atoms provides high surface energy and can provide a large number of surface anchoring points. This unique characteristic enhances the interaction between 2D nanomaterials and biological components, including cells, cellular components, and biomolecules [137]. Chen et al. [138] designed a NO-loaded MOFs encapsulated in polycaprolactone/gelatin aligned coaxial scaffold, it could promote tendon regeneration in a shorter healing period with better biomechanical properties by angiogenesis. Garg et al. [139] proposed wearable MXene high-density surface electromyography arrays. In the context of biomechanical research and rehabilitation of joint and tendon pathology, this array could be used to identify and study pathological muscle activation patterns, provide precise rehabilitation treatment, and contribute to overall quality of life. These emerging materials are currently not widely used in tendon repair and are in the development stage. In the future, their potential for tendon regeneration can be further studied.

Triboelectric stimulation

Currently, there are also triboelectric nanogenerator (TENG) mechanisms that can access human signals. The TENG is a device that uses the coupled effects of electrostatic induction and triboelectrification to convert mechanical energy in the surrounding environment into electrical energy [140]. In general, when two materials come into contact with each other, chemical bonds are formed between certain parts of the surface, and frictional charges are generated due to the transfer of charges from one surface to the other to balance the electrochemical potential [141]. When the frictional layer of TENG circulates between contact and separation caused by biomechanical motion, an alternating current is generated between the two electrodes, which can be used for biomedical applications [142]. Thus, the TENG itself can be used as a highly sensitive sensor or electrical simulator to enable self-powered biomedical technologies for human diagnosis and therapy [143]. TENG can work as a self-powered device, which is conducive to reducing the size and cost of the entire integrated system, thus improving portability and longevity. At the same time, it has significant features and performance such as flexibility, lightweight, high electrical output, and fast response to mechanical stimuli [144]. At present, many materials have been used as triboelectric materials to fabricate high-performance TENG due to their excellent charge transfer and capture ability during friction. For example, polytetrafluoroethylene (PTFE), fluorinated ethylene propylene (FEP), and PVDF have been used as the electron-withdrawing part of the TENG. In turn, polymer materials containing electron-donating groups, such as nylon, silk and wool, are often used as electrophobic parts of the TENG [145].

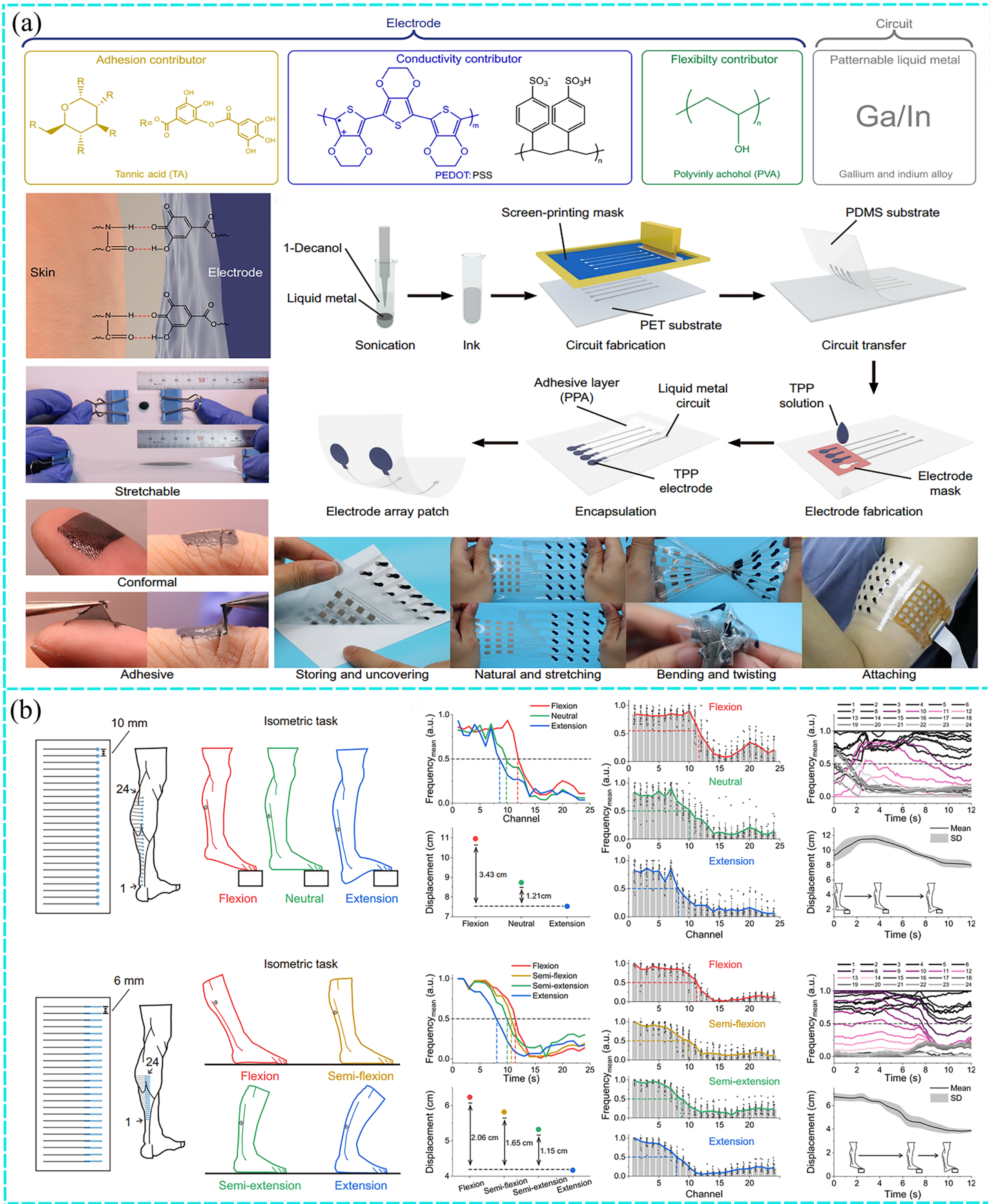

Fig. 5 Schematic diagram of the composition and fabrication of MEAP (**a**). Schematic diagrams of MEAPs on the gastrocnemius and Achilles tendon, and normalised mean frequencies of the electromyography signals tests (**b**). Reproduced with permission from [126]. Copyright © 2023, The Author(s)

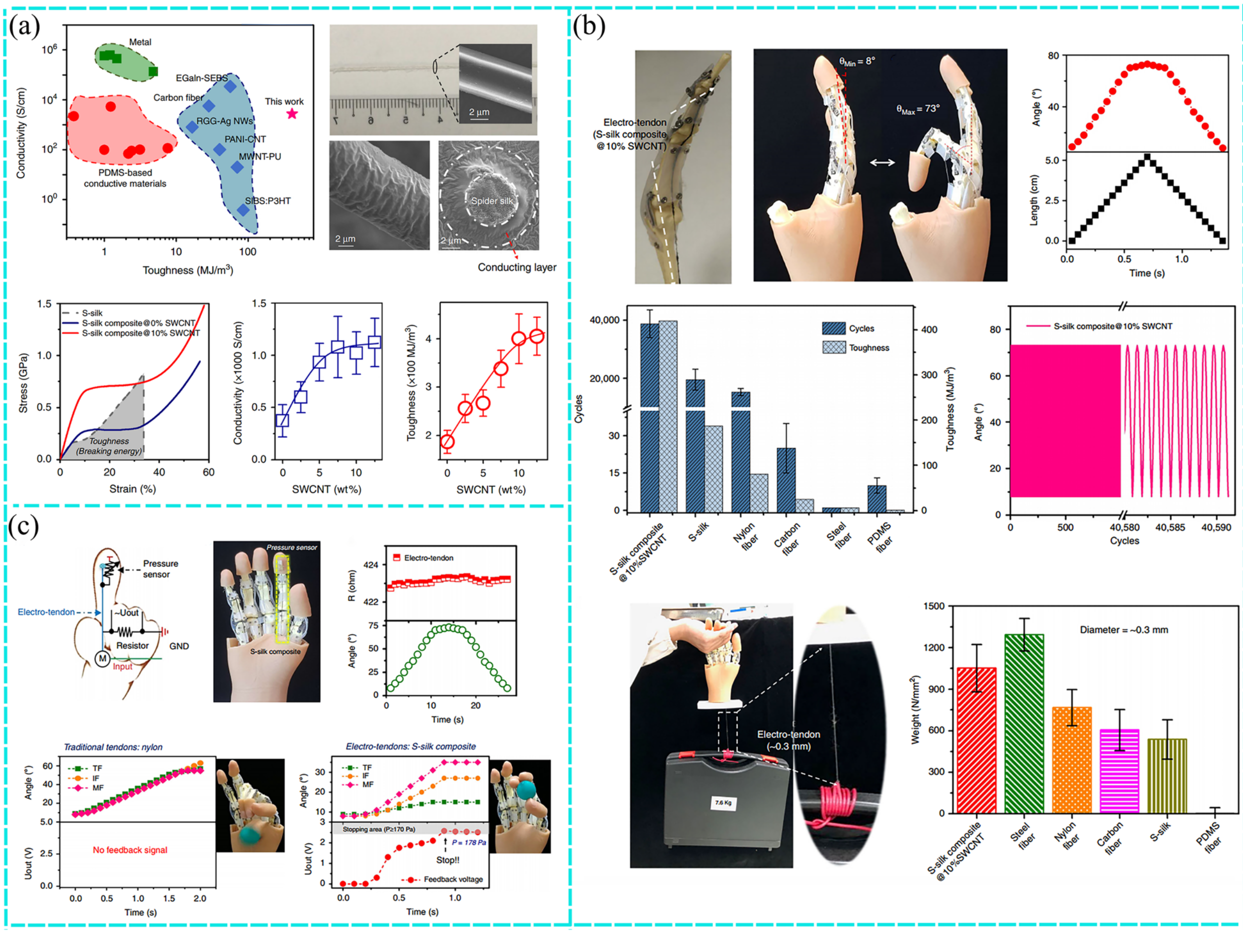

Fig. 6 Toughness and conductivity of spider silk composites (**a**). Performance of humanoid robotic hands assembled with S-silk composite as electro-tendon (**b**). Feedback processes of the humanoid robotic hand when grasping objects (**c**). Reproduced with permission from [131]. Copyright © 2020, The Author(s)

The ability of living cells to generate electrical signals and respond to electrical stimuli is a key feature in the regulation of cell behavior and cell-microenvironment interactions [146]. Therefore, TENG can be applied to living organisms to collect energy and output electrical stimulation to act on cells and change their activities. Thus, it regulates cell function and interferes with cell fate, which is further developed into a new method for health care and disease intervention [147]. Hu et al. [148] designed a rotatory disc-shaped TENG (RD-TENG). The RD-TENG consists of a print circuit board (PCB) deposited with radial Cu as the rotator and another PCB-coated interdigital Cu electrodes and adhered with a PTFE film as the stator, providing a variable alternating signal in a wide range of voltages and currents. The test found that RD-TENG could promote fibroblast proliferation and migration through triboelectric stimulation. At the same time, other studies have found that triboelectric stimulation could restore the vitality of aging bone marrow mesenchymal stem cells [149]. These studies showed that triboelectric stimulation could play a positive role in cell regulation. Wang et al. [150] developed a diode-amplified TENG that could amplify the triboelectric output, thereby effectively stimulating the muscle directly. Sharma [151] indicated that ES induced by piezoelectric-driven TENG and electroactive hydrogel composites accelerates the repair of diabetic foot ulcers. Wu et al. [152] prepared polyvinylidene fluoride-trifluoroethylene (PVDF-TrFE) films with high porosity. It was combined with polyamide (nylon 6, PA6) to form a flexible, high-performance TENG. Based on this, a self-powered wearable ES patch with an integrated TENG was proposed for tendinopathy treatment. The bionically designed ES patch is attached directly to the affected tendon. It underwent deformation and friction during movement and generated a pulsed electrical output, which was then converted into an electric field to treat the tendon lesion. The ES patch could significantly improve motor function, promote collagen regeneration, and reduce the degree of tissue inflammatory infiltration and recovery time in rats with tendinopathy (Fig. 7).

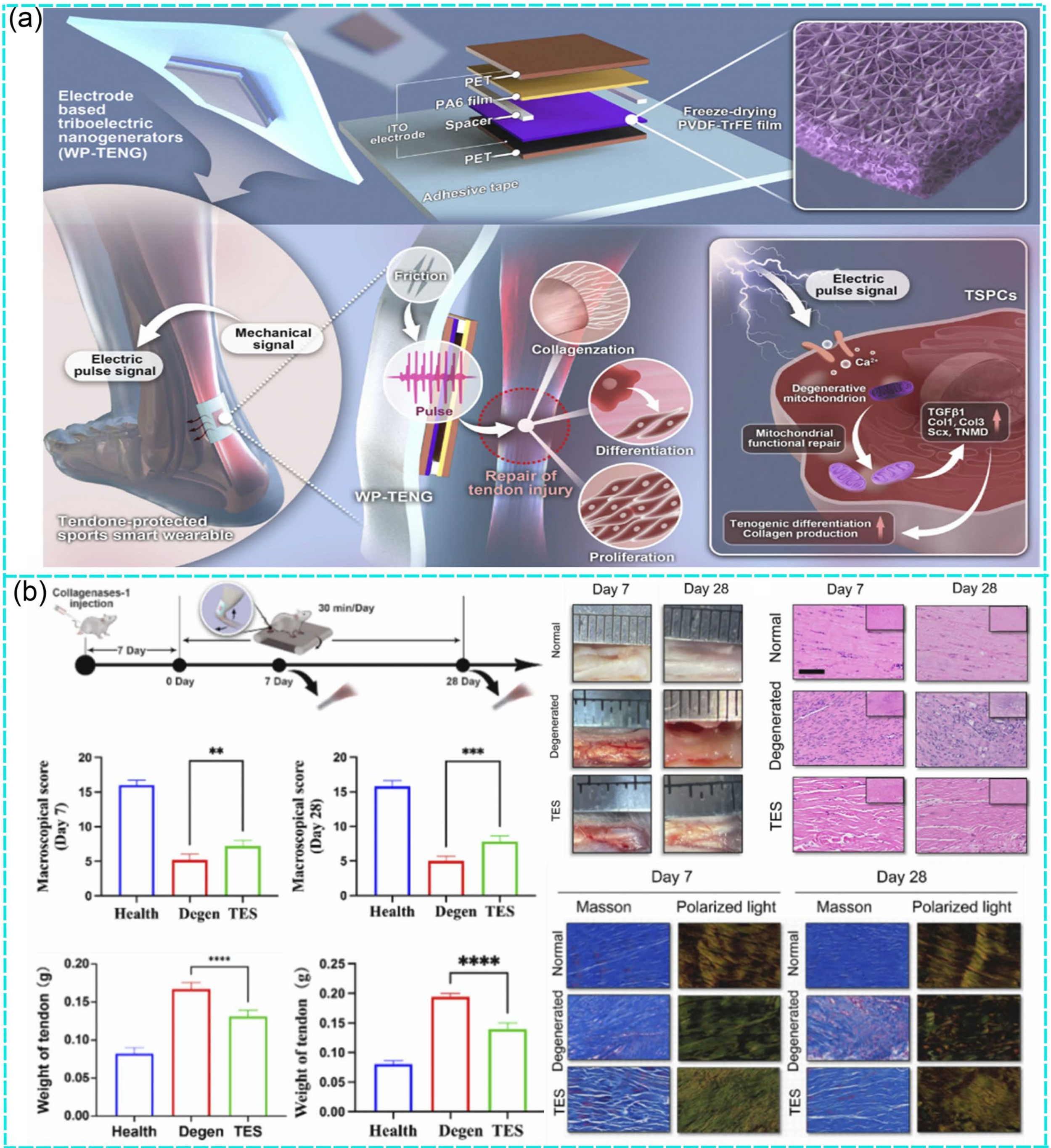

Fig. 7 Schematic illustration of the wearable TENG and TES patch-mediated treatment of tendinopathy (**a**). In vivo tendinopathy treated using a collagenase 1 model using a self-powered TES patch (**b**). Reproduced with permission from [152]. Copyright © 2023 Elsevier Ltd

In addition, the TENG still has some critical issues that need to be addressed. For example, the output stability of TENG is threatened by a variety of external environmental conditions, including the temperature and humidity of the human body. TENG may be affected by corrosion, internal compression, or oxidation caused by humidity in body fluids [143]. Therefore, the criteria for selecting TENG materials for higher efficiency and performance are generally: biocompatibility, mechanical properties, surface potential properties, flexibility, chemical stability, additional features consistent with the applications [153].

Discussion and future outlook

Tendons are an important part of the musculoskeletal system, which holds muscle ends firmly to the bone and stores and transfers energy during movement. When tendon ruptures, it can cause pain, affect movement, and reduce quality of life. Minor tendon injuries will recover gradually with bed rest assisted by medication and functional exercises. For severe injuries that involve surgery, the subsequent repair time becomes longer, and there may be complications such as re-rupture and tendon adhesions during this process. Repairing a ruptured tendon, therefore, is not a matter to be taken lightly. Most of the artificial, non-biodegradable materials such as Gore-Tex polytetrafluoroethylene, polycarbonate, and polypropylene that are now commonly used in clinical have not been satisfactory over time [154, 155]. Currently, more and more researchers have developed a series of biodegradable scaffolds that mimic the structure and function of tendons to replace defective tendons. Such as 3D printing scaffolds, electrospinning scaffolds, hydrogels, microspheres, etc. It is worth noting that all living organisms have an intricate network of bioelectric signals. In the human body, endogenous bioelectric signals carried by ions and electrons mediate the regulation of patterns and behaviors at the cellular, tissue, and organ levels [156]. Bioelectricity plays an important role in physiological and pathological processes such as cell arrangement, adhesion, proliferation, differentiation, migration, and tissue regeneration. The biophysical clues provided by suitable biomaterials can simulate the function of tendons, affect cell expression, and affect the speed of tendon repair. Among them, electroactive biomaterials can help ruptured tendons restore their native electrical microenvironment, assist surrounding tissues in releasing bioelectricity, and accelerate wound healing. Therefore, the emergence of low-cost ES materials can be used to create scaffolds or devices that can reconstruct the tendon's electrical microenvironment for use in tendon surgery.

Materials exhibiting piezoelectric effects typically have asymmetric crystal structures, allowing ions within the material to rearrange during mechanical deformation, thereby generating charges on the two opposing surfaces of the material. When the material is subjected to an external electric field, the arrangement of these ions is further adjusted, causing the overall polarization of the material and enhancing its piezoelectric response [157]. The ability of tendons to maintain their homeostasis after dynamic loading and return to their original state after injury depends in part on the restoration of primitive multiscale strain transfer mechanisms. When forces are applied through the ECM, cellular deformation through the actin cytoskeleton induces nuclear strain, which in turn affects transcription and a range of cellular responses [158]. Further, piezoelectric materials simulate the natural internal environment to regulate local immunity, promote cell proliferation and differentiation, and enhance ECM synthesis, thereby achieving the goal of tissue repair [157]. In the design of the scaffolds, it is necessary to fully consider their electrical characteristics to maintain stability under mechanical load. Therefore, in order to adapt to the deformation, flexible and scalable scaffolds were developed, which gave the scaffolds basic wavy structure and hierarchical buckling structures to bear better mechanical properties [159]. The design of percolated networks has also been used in conductive materials, which can form a continuous network and adapt to mechanical strain through hinging/sliding, such as carbon nanotubes, silver nanowires, and copper nanowires [160]. Metal-based biomaterials are commonly used as reinforcement materials, and the conductivity and mechanical strength of tissue engineering scaffolds can be improved through surface modification and mixed filling, such as gold nanomaterials [161].

However, the application of piezoelectric materials in biomedical fields also faces several problems: the fragility of some materials, low efficiency, toxicity, and environmental impact [162–164]. As a result, green and biodegradable piezoelectric materials such as organic biodegradable amino acids, peptides, proteins, polysaccharides, and synthetic polymers are increasingly being pursued [165]. These natural or synthetic materials can either be broken down into basic molecules such as water and carbon dioxide or reabsorbed under biologically benign or physiological conditions [166]. In the long-term repair of tendons, the above adverse conditions can be avoided and the healthy repair of tendons can be promoted. For example: chitosan is a linear polysaccharide consisting of two different β(1–4) structural units randomly bonded together, which is recognized as a piezoelectric material. It is biocompatible, biodegradable, non-toxic, and easy to form a film, so it has a wide range of applications in the field of medicine and other fields [167]. PLLA is a transparent and very flexible plant-derived piezoelectric polymer material suitable for use in mobile devices. In addition, the piezoelectric constant of PLLA films can be designed and improved by increasing the crystallinity and molecular orientation, giving it many applications in future biosensors [168]. PVDF is a semi-crystalline piezoelectric polymer with five different crystal phases, among which the β phase is the most important, with high polarizability and high high-voltage sensitivity [169]. Kim [170] proposed a tendon-inspired piezoelectric sensor based on PVDF. The sensor can resist tensile loads and slides, and has the advantages of being flexible, lightweight, and compatible.

Smart repair scaffolds are endowed with mechanical, and electrical responses, etc., so the healing process can be optimized through dynamic response to the physiological environment [63]. For example, piezoelectric materials under mechanical response, conductive materials under electrical response, and TENG under electrostatic and frictional coupling response. Our somatosensory system relies on receptors to convert stimuli into action potentials and transmit signals through neurons that are ultimately received and analyzed by the brain in order to make timely decisions. So the ideal sensors made from smart repair materials should be endowed with intelligent feedback and real-time monitoring capabilities [171]. For instance, carbon-based nanomaterials, MXenes, and other materials have been made into flexible sensors. Interestingly, the electromechanical properties of piezoelectric materials make it possible to convert the strain generated by biological movements (such as muscle contractions, body movements, blood circulation, breathing, heartbeat, etc.) into electrical energy [172]. It can easily record affinity interactions without the need for any special reagents, and the required loading sensitivity can typically be in the microgram range [173]. Therefore, piezoelectricity is highly suitable for manufacturing physical sensors and biosensors. Especially in the development of intelligent repair scaffolds and biosensors related to tendons, the cellular level electrical stimulation has a regulatory effect on the response of mechanical signals, which can manipulate ion channel activity to promote tenocytes differentiation [174]. Furthermore, it can not only be used as an implantable medical device to achieve a long-term stable energy supply, but also as a real-time sensing device to monitor a variety of vital signs such as heart rate, breathing, and blood pressure [53]. The use of the electrical release characteristics of piezoelectric materials to achieve accurate, controllable, and minimally invasive catalytic treatment may bring breakthroughs for future precision medicine or smart therapy [76]. In this way, biosensing scaffolds (electrospinning fiber membrane, hydrogel, 3D printing scaffolds, etc.) made from piezoelectric materials in various ways can not only restore the electrical microenvironment of tendon loss, but also monitor the status of tendon repair in real-time and make timely adjustments according to the actual situation. This not only saves time and costs, but also accelerates the tendon repair process, which is beneficial for the repair of ruptured tendon defects in patients.

Direct ES provides a precise, non-pharmacological means to regulate and control biological processes. This method has the potential to restore or enhance physiological functions damaged by disease or injury by integrating complex electrical signals, device interfaces, and designs targeting specific biological mechanisms [175]. According to previous research reports, DC stimulation, alternating current stimulation, and low-frequency pulsed electromagnetic fields could promote the healing of tissues such as bone, cartilage, nerves, and tendons [176]. Meanwhile, many biomaterials have attracted attention due to their conductivity properties, such as carbon-based conductive materials, metal-based conductive materials, ion-based conductive materials, conductive polymers, and conductive composite materials [177]. Traditional direct ES devices require additional external power sources, making them less portable and comfortable. In addition, the potential for clinical use of ES therapy has not been fully realized due to spasticity, muscle pain, skin irritation, and inconvenience to the patient. Although some preclinical studies have reported the use of ES in tendons, these have not been translated into clinical research. Therefore, the potential strategic mechanism of conductive materials as tendon-tissue engineering scaffolds remains to be explored to a large extent. Therefore, the development of self-powered, flexible ES devices and the implementation of integrated treatment scaffolds or equipment are of great significance [178]. This requires high sensitivity, self-healing ability, and good biocompatibility to be taken into account in material design and manufacturing [179]. The materials that can generate ES are often diverse in dynamic environments, such as piezoelectric PVDF can also produce triboelectricity under friction. Therefore, there are intricate relationships between piezoelectric materials, conductive materials, and triboelectric materials. Further, the scaffolds and devices that can generate ES through electrospinning, 3D printing, etc. are also diverse. Therefore, the cross-application of materials that generate ES to maximize its functionality may have great potential for the development of tendon repair.

However, these materials still face many challenges that need to be solved, and efforts to break through the bottlenecks to hope for early clinical applications, the main points are as follows:

1) The surface morphology and structure of generated ES can affect cell behavior and tissue repair time. At present, there is a great need for intelligent biomaterials that can simulate tendon orientation structures, transmit physiological signals, and restore the native electrical microenvironment.
2) In addition, the degradation of the material can affect ES effectiveness. Therefore, the key challenge is to determine the balance between the degradation rate of scaffolds and the kinetics of tissue repair. That is to say, materials with different degradation rates should be selected based on the duration of tissue repair, and in vivo degradation should be simulated in vitro to repeatedly verify whether the degraded materials at different time points can still generate ES. For tendon, sufficient voltage and lifespan during degradation to ensure continuous current output and play a long-term role in the body to be suitable for the repair of various major tendon diseases.
3) Furthermore, some materials can cause excessive immune responses after implantation and affect the

repair process, so various scaffolds need to have biocompatibility and non-toxic degradation. For example, some conductive materials can be toxic in excess, and some electrodes can precipitate toxic products due to excessive heat. Then the scaffolds should be treated reasonably well in advance of fabrication to ensure that they are not harmful to organisms while not affecting their performance.

4) Computer modeling can help optimize the structure of the scaffold to achieve personalized customization, and it is also important to be able to monitor the connection between the scaffold and the surrounding tissue after implantation. At the same time, it should be possible to monitor the recovery of electrical pathways in the damaged tissue. The scaffold is further endowed with the function of monitoring the recovery of key pathways related to tendon diseases, so as to improve the rehabilitation plan in real time.
5) Finally, the comfort of the scaffolds in vivo also needs to be taken into account. The search for non-foreign body sensing and the long-term function of scaffolds is not only needed for tendon tissue repair but also for other tissue regeneration. With the increasing demand for wearable and implantable electronics, matching energy conversion devices and storage devices have become a popular research topic. Tendon, as an important connector that transmits muscle power to the bone, is an indispensable part of energy conversion. It is also important to develop a wearable and implantable electronic device to replace the missing tendon and achieve energy transfer.

Conclusions

Tendons have a piezoelectric effect due to their special tissue structure, i.e. the directional arrangement of collagen fibril. The reconstruction of the destroyed native electrical microenvironment after the tendon injury is crucial. Currently, the scaffolds made of piezoelectric biomaterials, conductive biomaterials, triboelectric biomaterials, and other biomaterials that generate ES are a key means to reconstruct the native electrical microenvironment of tendons. However, ES scaffolds are currently limited in development or clinical translation. In the future, the development of long-term self-powered, flexible, and therapeutically integrated scaffolds or ES devices would be a major advancement in the field of tendon repair.

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Declarations

Ethics approval and consent to participate Not applicable.

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References

1. Rinoldi C, Costantini M, Kijenska-Gawronska E, Testa S, Fornetti E, Heljak M, Cwiklinska M, Buda R, Baldi J, Cannata S, Guzowski J, Gargioli C, Khademhosseini A, Swieszkowski W. Tendon Tissue Engineering: Effects of Mechanical and Biochemical Stimulation on Stem Cell Alignment on Cell-Laden Hydrogel Yarns. Adv Healthc Mater. 2019;8(7): e1801218.
2. Juneja SC, Veillette C. Defects in Tendon, Ligament, and Enthesis in Response to Genetic Alterations in Key Proteoglycans and Glycoproteins: A Review. Arthritis. 2013;2013(1): 154812.
3. Brennan DA, Conte AA, Kanski G, Turkula S, Hu X, Kleiner MT, Beachley V. Mechanical Considerations for Electrospun Nanofibers in Tendon and Ligament Repair. Adv Healthcare Mater. 2018;7(12):1701277.
4. Beldjilali-Labro M, Garcia Garcia A, Farhat F, Bedoui F, Grosset JF, Dufresne M, Legallais C. Biomaterials in Tendon and

Skeletal Muscle Tissue Engineering: Current Trends and Challenges. Materials (Basel). 2018;11(7):1116.
5. Najafi Z, Rahmanian-Devin P, Baradaran Rahimi V, Nokhodchi A, Askari VR. Challenges and opportunities of medicines for treating tendon inflammation and fibrosis: A comprehensive and mechanistic review. Fundament Clin Pharmacol. 2024;e12999.
6. Titan AL, Foster DS, Chang J, Longaker MT. Flexor Tendon: Development, Healing, Adhesion Formation, and Contributing Growth Factors. Plast Reconstr Surg. 2019;144(4):639e–47e.
7. Lambrianides Y, Epro G, Arampatzis A, Karamanidis K. Evidence of different sensitivity of muscle and tendon to mechano-metabolic stimuli. Scand J Med Sci Sports. 2024;34(5): e14638.
8. Liang W, Zhou C, Deng Y, Fu L, Zhao J, Long H, Ming W, Shang J, Zeng B. The current status of various preclinical therapeutic approaches for tendon repair. Ann Med. 2024;56(1):2337871.
9. Snedeker JG, Foolen J. Tendon injury and repair - A perspective on the basic mechanisms of tendon disease and future clinical therapy. Acta Biomater. 2017;63:18–36.
10. Zhang X, Wang D, Wang Z, Ling SK-K, Yung PS-H, Tuan RS, Ker DFE. Clinical perspectives for repairing rotator cuff injuries with multi-tissue regenerative approaches. J Orthop Translat. 2022;36:91–108.
11. Canosa-Carro L, Bravo-Aguilar M, Abuín-Porras V, Almazán-Polo J, García-Pérez-de-Sevilla G, Rodríguez-Costa I, López-López D, Navarro-Flores E, Romero-Morales C. Current understanding of the diagnosis and management of the tendinopathy: An update from the lab to the clinical practice. Dis Mon. 2022;68(10): 101314.
12. Vaquette C, Kahn C, Frochot C, Nouvel C, Six JL, De Isla N, Luo LH, Cooper-White J, Rahouadj R, Wang X. Aligned poly(L-lactic-co-e-caprolactone) electrospun microfibers and knitted structure: a novel composite scaffold for ligament tissue engineering. J Biomed Mater Res A. 2010;94(4):1270–82.
13. Cai J, Liu J, Xu J, Li Y, Zheng T, Zhang T, Han K, Chen S, Jiang J, Wu S, Zhao J. Constructing high-strength nano-micro fibrous woven scaffolds with native-like anisotropic structure and immunoregulatory function for tendon repair and regeneration. Biofabrication. 2023;15(2): 025002.
14. Bizzoca D, Brunetti G, Moretti L, Piazzolla A, Vicenti G, Moretti FL, Solarino G, Moretti B. Polydeoxyribonucleotide in the Treatment of Tendon Disorders, from Basic Science to Clinical Practice: A Systematic Review. Int J Mol Sci. 2023;24(5):4582.
15. DeFoor MT, Cognetti DJ, Yuan TT, Sheean AJ. Treatment of Tendon Injuries in the Servicemember Population across the Spectrum of Pathology: From Exosomes to Bioinductive Scaffolds. Bioengineering. 2024;11(2):158.
16. No YJ, Castilho M, Ramaswamy Y, Zreiqat H. Role of Biomaterials and Controlled Architecture on Tendon/Ligament Repair and Regeneration. Adv Mater. 2020;32(18): e1904511.
17. Yu X, Cui J, Shen Y, Guo W, Cai P, Chen Y, Yuan Z, Liu M, El-Newehy M, El-Hamshary H, Morsi Y, Sun B, Shafiq M, Mo X. Current Advancements and Strategies of Biomaterials for Tendon Repair: A Review. Front Biosci (Landmark Ed). 2023;28(4):66.
18. Citro V, Clerici M, Boccaccini AR, Della Porta G, Maffulli N, Forsyth NR. Tendon tissue engineering: An overview of biologics to promote tendon healing and repair. Journal of Tissue Engineering. 2023;14:20417314231196276.
19. Xia X, Fang Z, Qian Y, Zhou Y, Huang H, Xu F, Luo Z, Wang Q. Role of oxidative stress in the concurrent development of osteoporosis and tendinopathy: Emerging challenges and prospects for treatment modalities. J Cell Mol Med. 2024;28(13): e18508.
20. Lyu K, Liu T, Chen Y, Lu J, Jiang L, Liu X, Liu X, Li Y, Li S. A "cell-free treatment" for tendon injuries: adipose stem cell-derived exosomes. Eur J Med Res. 2022;27(1):75.
21. Freedman BR, Mooney DJ, Weber E. Advances toward transformative therapies for tendon diseases. Sci Translat Med. 2022;14(661):eabl8814.
22. Baumgartner W, Wolint P, Hofmann S, Nüesch C, Calcagni M, Brunelli M, Buschmann J. Impact of Electrospun Piezoelectric Core-Shell PVDFhfp/PDMS Mesh on Tenogenic and Inflammatory Gene Expression in Human Adipose-Derived Stem Cells: Comparison of Static Cultivation with Uniaxial Cyclic Tensile Stretching. Bioengineering. 2022;9(1):21.
23. Zhang XL, Wang CY, Pan LL, Li YJ. Effects of evidence-based nursing care interventions on wound pain and wound complications following surgery for finger tendon injury. Int Wound J. 2024;21(3): e14818.
24. Katoh M, Kishimoto Y, Ohkawara B, Sakai T, Ito M, Masuda A, Ishiguro N, Shukunami C, Docheva D, Ohno K. Wnt/β-catenin signaling suppresses expressions of Scx, Mkx, and Tnmd in tendon-derived cells. PLoS ONE. 2017;12(7): e0182051.
25. Dong L, Li L, Song Y, Fang Y, Liu J, Chen P, Wang S, Wang C, Xia T, Liu W, Yang L. MSC-derived immunomodulatory extracellular matrix functionalized electrospun fibers for mitigating foreign-body reaction and tendon adhesion. Acta Biomater. 2021;133:280–96.
26. Chen Y, Dong X, Shafiq M, Myles G, Radacsi N, Mo X. Recent Advancements on Three-Dimensional Electrospun Nanofiber Scaffolds for Tissue Engineering. Advanced Fiber Materials. 2022;4(5):959–86.
27. Fu G, Lu L, Pan Z, Fan A, Yin F. Adipose-derived stem cell exosomes facilitate rotator cuff repair by mediating tendon-derived stem cells. Regen Med. 2021;16(4):359–72.
28. Wang Z, Xiang L, Lin F, Tang Y, Deng L, Cui W. A Biomaterial-Based Hedging Immune Strategy for Scarless Tendon Healing. Adv Mater. 2022;34(19): e2200789.
29. Tu T, Shen Y, Wang X, Zhang W, Zhou G, Zhang Y, Wang W, Liu W. Tendon ECM modified bioactive electrospun fibers promote MSC tenogenic differentiation and tendon regeneration. Appl Mater Today. 2020;18: 100495.
30. Cai C, Zhang X, Li Y, Liu X, Wang S, Lu M, Yan X, Deng L, Liu S, Wang F, Fan C. Self-Healing Hydrogel Embodied with Macrophage-Regulation and Responsive-Gene-Silencing Properties for Synergistic Prevention of Peritendinous Adhesion. Adv Mater. 2022;34(5): e2106564.
31. Chae S, Yong U, Park W, Choi YM, Jeon IH, Kang H, Jang J, Choi HS, Cho DW. 3D cell-printing of gradient multi-tissue interfaces for rotator cuff regeneration. Bioact Mater. 2023;19:611–25.
32. Du Y, Du W, Lin D, Ai M, Li S, Zhang L. Recent Progress on Hydrogel-Based Piezoelectric Devices for Biomedical Applications. Micromachines. 2023;14(1):167.
33. Zhang X, Wang T, Zhang Z, Liu H, Li L, Wang A, Ouyang J, Xie T, Zhang L, Xue J, Tao W. Electrical stimulation system based on electroactive biomaterials for bone tissue engineering. Mater Today. 2023;68:177–203.
34. Nain A, Chakraborty S, Barman SR, Gavit P, Indrakumar S, Agrawal A, Lin Z-H, Chatterjee K. Progress in the development of piezoelectric biomaterials for tissue remodeling. Biomaterials. 2024;307: 122528.
35. Kapat K, Shubhra QTH, Zhou M, Leeuwenburgh S. Piezoelectric Nano-Biomaterials for Biomedicine and Tissue Regeneration. Adv Func Mater. 2020;30(44):1909045.
36. Wang J, Lin J, Chen L, Deng L, Cui W. Endogenous Electric-Field-Coupled Electrospun Short Fiber via Collecting Wound Exudation. Adv Mater. 2022;34(9): e2108325.
37. Goonoo N, Bhaw-Luximon A. Piezoelectric polymeric scaffold materials as biomechanical cellular stimuli to enhance tissue regeneration. Materials Today Communications. 2022;31: 103491.

38. Das B, Mohanty S. A comprehensive review on piezoelectric inks: From concept to application. Sens Actuators, A. 2024;366: 114939.
39. Ghosh S, Qiao W, Yang Z, Orrego S, Neelakantan P. Engineering Dental Tissues Using Biomaterials with Piezoelectric Effect: Current Progress and Future Perspectives. Journal of Functional Biomaterials. 2022;14(1):8.
40. Kim SE, Kim JG, Park K. Biomaterials for the Treatment of Tendon Injury. Tissue Eng Regen Med. 2019;16(5):467–77.
41. Vasiliadis AV, Katakalos K. The Role of Scaffolds in Tendon Tissue Engineering. J Funct Biomater. 2020;11(4):78.
42. Lim WL, Liau LL, Ng MH, Chowdhury SR, Law JX. Current Progress in Tendon and Ligament Tissue Engineering. Tissue Eng Regen Med. 2019;16(6):549–71.
43. Kim D, Han SA, Kim JH, Lee JH, Kim SW, Lee SW. Biomolecular Piezoelectric Materials: From Amino Acids to Living Tissues. Adv Mater. 2020;32(14): e1906989.
44. Denning D, Abu-Rub MT, Zeugolis DI, Habelitz S, Pandit A, Fertala A, Rodriguez BJ. Electromechanical properties of dried tendon and isoelectrically focused collagen hydrogels. Acta Biomater. 2012;8(8):3073–9.
45. Brown CP, Boyd JL, Palmer AJ, Phillips M, Couture CA, Rivard M, Hulley PA, Price AJ, Ruediger A, Légaré F, Carr AJ. Modulation of Mechanical Interactions by Local Piezoelectric Effects. Adv Func Mater. 2016;26(42):7662–7.
46. Denning D, Kilpatrick JI, Fukada E, Zhang N, Habelitz S, Fertala A, Gilchrist MD, Zhang Y, Tofail SAM, Rodriguez BJ. Piezoelectric Tensor of Collagen Fibrils Determined at the Nanoscale. ACS Biomater Sci Eng. 2017;3(6):929–35.
47. Minary-Jolandan M, Yu M-F. Nanoscale characterization of isolated individual type I collagen fibrils: polarization and piezoelectricity. Nanotechnology. 2009;20(8): 085706.
48. Zhou Z, Qian D, Minary-Jolandan M. Molecular Mechanism of Polarization and Piezoelectric Effect in Super-Twisted Collagen. ACS Biomater Sci Eng. 2016;2(6):929–36.
49. Majid Minary-Jolandan M-FY. Uncovering nanoscale electromechanical heterogeneity in the subfibrillar structure of collagen fibrils responsible for the piezoelectricity of bone. ACS Nano. 2009;3(7):1859–63.
50. West CR, Bowden AE. Using Tendon Inherent Electric Properties to Consistently Track Induced Mechanical Strain. Ann Biomed Eng. 2012;40(7):1568–74.
51. Peidavosi N, Azami M, Beheshtizadeh N, Ramazani SA. Piezoelectric conductive electrospun nanocomposite PCL/Polyaniline/Barium Titanate scaffold for tissue engineering applications. Sci Rep. 2022;12(1):20828.
52. Liu P, Wang K, Li L, Zhang R, Xu ZP. Lead-free piezoelectric materials for musculoskeletal tissue engineering. Materials Today Sustainability. 2023;22: 100393.
53. Xu Q, Gao X, Zhao S, Liu YN, Zhang D, Zhou K, Khanbareh H, Chen W, Zhang Y, Bowen C. Construction of Bio-Piezoelectric Platforms: From Structures and Synthesis to Applications. Adv Mater. 2021;33(27):2008452.
54. Rajabi AH, Jaffe M, Arinzeh TL. Piezoelectric materials for tissue regeneration: A review. Acta Biomater. 2015;24:12–23.
55. Shlapakova LE, Surmeneva MA, Kholkin AL, Surmenev RA. Revealing an important role of piezoelectric polymers in nervous-tissue regeneration: A review. Materials Today Bio. 2024;25: 100950.
56. Sensini A, Gualandi C, Zucchelli A, Boyle LA, Kao AP, Reilly GC, Tozzi G, Cristofolini L, Focarete ML. Tendon Fascicle-Inspired Nanofibrous Scaffold of Polylactic acid/Collagen with Enhanced 3D-Structure and Biomechanical Properties. Sci Rep. 2018;8(1):17167.
57. Chen P, Li L, Dong L, Wang S, Huang Z, Qian Y, Wang C, Liu W, Yang L. Gradient Biomineralized Silk Fibroin Nanofibrous Scaffold with Osteochondral Inductivity for Integration of Tendon to Bone. ACS Biomater Sci Eng. 2021;7(3):841–51.
58. Ali M, Bathaei MJ, Istif E, Karimi SNH, Beker L. Biodegradable Piezoelectric Polymers: Recent Advancements in Materials and Applications. Adv Healthcare Mater. 2023;12(23):2300318.
59. Wang R, Sui J, Wang X. Natural Piezoelectric Biomaterials: A Biocompatible and Sustainable Building Block for Biomedical Devices. ACS Nano. 2022;16(11):17708–28.
60. Donnelly H, Sprott MR, Poudel A, Campsie P, Childs P, Reid S, Salmerón-Sánchez M, Biggs M, Dalby MJ. Surface-Modified Piezoelectric Copolymer Poly(vinylidene fluoride–trifluoroethylene) Supporting Physiological Extracellular Matrixes to Enhance Mesenchymal Stem Cell Adhesion for Nanoscale Mechanical Stimulation. ACS Appl Mater Interfaces. 2023;15(44):50652–62.
61. Ren G, Review of piezoelectric material power supply, 2021 International Conference on Electronics, Circuits and Information Engineering (ECIE), 2021;136–139.
62. Marino A, Genchi GG, Sinibaldi E, Ciofani G. Piezoelectric Effects of Materials on Bio-Interfaces. ACS Appl Mater Interfaces. 2017;9(21):17663–80.
63. Percival KM, Paul V, Husseini GA. Recent Advancements in Bone Tissue Engineering: Integrating Smart Scaffold Technologies and Bio-Responsive Systems for Enhanced Regeneration. Int J Mol Sci. 2024;25(11):6012.
64. Starr MB, Wang X. Coupling of piezoelectric effect with electrochemical processes. Nano Energy. 2015;14:296–311.
65. Mohammadkhah M, Marinkovic D, Zehn M, Checa S. A review on computer modeling of bone piezoelectricity and its application to bone adaptation and regeneration. Bone. 2019;127:544–55.
66. Alvarez-Lorenzo C, Zarur M, Seijo-Rabina A, Blanco-Fernandez B, Rodríguez-Moldes I, Concheiro A. Physical stimuli-emitting scaffolds: The role of piezoelectricity in tissue regeneration. Materials Today Bio. 2023;22: 100740.
67. Brohawn SG. How ion channels sense mechanical force: insights from mechanosensitive K2P channels TRAAK, TREK1, and TREK2. Ann N Y Acad Sci. 2015;1352(1):20–32.
68. Ryo N, Shang M, Takayuki N, Tomoki C, Ryota K, Hiroki O, Merissa O, Chisa S, Noriyuki F, Guan W, Errol M, Yannis PP, Toshifumi O, Darryl D'L, Martin L, Ardem P, Asahara H. The mechanosensitive ion channel PIEZO1 is expressed in tendons and regulates physical performance. Sci Translat Med. 2022;14(647):eabj5557.
69. Fernandez-Yague MA, Trotier A, Demir S, Abbah SA, Larranaga A, Thirumaran A, Stapleton A, Tofail SAM, Palma M, Kilcoyne M, Pandit A, Biggs MJ. A Self-Powered Piezo-Bioelectric Device Regulates Tendon Repair-Associated Signaling Pathways through Modulation of Mechanosensitive Ion Channels. Adv Mater. 2021;33(40): e2008788.
70. Ge Z, Qiao Y, Zhu W, Xu Y, Fang Q, Wang D, Tang Y, Zhao R, Deng X, Lin W, Wang G, Xiang Y, Hu X. Highly stretchable polyester-based piezoelectric elastomer for simultaneously realization of accelerated regeneration and motion monitoring for Achilles tendon rupture. Nano Energy. 2023;115: 108751.
71. Fang Q, Wang D, Lin W, Ge Z, Deng X, Zhao R, Tang Y, Liu W, Xiong Z, Duan A, Zhang Z, Xiang Y, Hu X, Wang G. Highly Stretchable Piezoelectric Elastomer for Accelerated Repairing of Skeletal Muscles Loss. Adv Funct Mater. 2024;2313055.
72. Zhang Q, Zhu J, Fei X, Zhu M. A Janus nanofibrous scaffold integrated with exercise-driven electrical stimulation and nanotopological effect enabling the promotion of tendon-to-bone healing. Nano Today. 2024;55: 102208.
73. Sasikala ARK, Kaliannagounder VK, Alluri NR, Shrestha BK, Kim S-J, Ali-Boucetta H, Park CH, Unnithan AR. Development of self-powered multifunctional piezomagnetic nanoparticles for non-invasive post-surgical osteosarcoma theranogeneration. Nano Energy. 2022;96: 107134.

74. Wang W, Wang P, Li Q, Dai W, Yi B, Gao Z, Liu W, Wang X. Piezoelectrically-enhanced composite membranes mimicking the tendinous electrical microenvironment for advanced tendon repair. Nano Today. 2024;57: 102381.
75. Wang A, Ma X, Yang Y, Shi G, Han L, Hu X, Shi R, Yan J, Guo Q, Zhao Y. Biophysical-driven piezoelectric and aligned nanofibrous scaffold promotes bone regeneration by re-establishing physiological electrical microenvironment. Nano Res. 2024;1–18.
76. Chen S, Zhu P, Mao L, Wu W, Lin H, Xu D, Lu X, Shi J. Piezocatalytic Medicine: An Emerging Frontier using Piezoelectric Materials for Biomedical Applications. Adv Mater. 2023;35(25):2208256.
77. Ganeson K, Tan Xue May C, Abdullah AAA, Ramakrishna S, Vigneswari S. Advantages and Prospective Implications of Smart Materials in Tissue Engineering: Piezoelectric, Shape Memory, and Hydrogels. Pharmaceutics. 2023;15(9):2356.
78. Meysam TC, Thinh TL, Feng L, Tra V, Ritopa D, James FS, Caitlyn M, Jinyoung P, Khanh TMT, Yang L, Jacob P, Rachel T, Wu H, Menka JM, Daniela M-A, Osama RB, Kazem K, Horea I, Nguyen TD. Highly piezoelectric, biodegradable, and flexible amino acid nanofibers for medical applications. Science Advances. 2023;9(24):eadg6075.
79. Yang C, Ji J, Lv Y, Li Z, Luo D. Application of Piezoelectric Material and Devices in Bone Regeneration. Nanomaterials. 2022;12(24):4386.
80. Haider ST, Shah MA, Lee D-G, Hur S. A Review of the Recent Applications of Aluminum Nitride-Based Piezoelectric Devices. IEEE Access. 2023;11:58779–95.
81. Li H, Lim S. Self-poled and transparent polyvinylidene fluoride-co-hexafluoropropylene-based piezoelectric devices for printable and flexible electronics. Nanoscale. 2023;15(9):4581–90.
82. Li Z, Yi X, Yang J, Bian L, Yu Z, Dong S. Designing Artificial Vibration Modes of Piezoelectric Devices Using Programmable, 3D Ordered Structure with Piezoceramic Strain Units. Adv Mater. 2021;34(2):2107236.
83. Sun Y, Zeng K, Li T. Piezo-/ferroelectric phenomena in biomaterials: A brief review of recent progress and perspectives. Science China Physics, Mechanics & Astronomy. 2020;63(7): 278701.
84. Wu Y, Zou J, Tang K, Xia Y, Wang X, Song L, Wang J, Wang K, Wang Z. From electricity to vitality: the emerging use of piezoelectric materials in tissue regeneration. Burns & Trauma. 2024;12:tkae013.
85. Lin Y, Bariya M, Javey A. Wearable Biosensors for Body Computing. Adv Func Mater. 2020;31(39):2008087.
86. Hu D, Yao M, Fan Y, Ma C, Fan M, Liu M. Strategies to achieve high performance piezoelectric nanogenerators. Nano Energy. 2019;55:288–304.
87. Xu Z, Hao Y, Luo A, Jiang Y. Technologies and applications in wireless biosensors for real-time health monitoring. Med-X. 2024;2(1):24.
88. Sekhar MC, Veena E, Kumar NS, Naidu KCB, Mallikarjuna A, Basha DB. A Review on Piezoelectric Materials and Their Applications. Cryst Res Technol. 2022;58(2):2200130.
89. Li J, Carlos C, Zhou H, Sui J, Wang Y, Silva-Pedraza Z, Yang F, Dong Y, Zhang Z, Hacker TA, Liu B, Mao Y, Wang X. Stretchable piezoelectric biocrystal thin films. Nat Commun. 2023;14(1):6562.
90. Shu S, An J, Chen P, Liu D, Wang Z, Li C, Zhang S, Liu Y, Luo J, Zu L, Tang W, Wang ZL. Active-Sensing Epidermal Stretchable Bioelectronic Patch for Noninvasive, Conformal, and Wireless Tendon Monitoring. Research. 2021.
91. Panda S. Biomolecular Piezoelectric Materials for Biosensors. Prabha Materials Science Letters. 2022;1(1):37–49.
92. Chen S, Tong X, Huo Y, Liu S, Yin Y, Tan ML, Cai K, Ji W. Piezoelectric Biomaterials Inspired by Nature for Applications in Biomedicine and Nanotechnology. Adv Mater. 2024;36(35):2406192.
93. Duan S, Wu J, Xia J, Lei W. Innovation Strategy Selection Facilitates High-Performance Flexible Piezoelectric Sensors. Sensors. 2020;20(10):2820.
94. Zhou H, Zhang Y, Qiu Y, Wu H, Qin W, Liao Y, Yu Q, Cheng H. Stretchable piezoelectric energy harvesters and self-powered sensors for wearable and implantable devices. Biosens Bioelectron. 2020;168: 112569.
95. Fu S, Lan Y, Wang G, Bao D, Qin B, Zheng Q, Liu H, Wong VKW. External stimulation: A potential therapeutic strategy for tendon-bone healing. Frontiers in Bioengineering and Biotechnology. 2023;11:1150290.
96. Kwon HJ, Lee GS, Chun H. Electrical stimulation drives chondrogenesis of mesenchymal stem cells in the absence of exogenous growth factors. Sci Rep. 2016;6:39302.
97. Zhou Z, Zheng J, Meng X, Wang F. Effects of Electrical Stimulation on Articular Cartilage Regeneration with a Focus on Piezoelectric Biomaterials for Articular Cartilage Tissue Repair and Engineering. Int J Mol Sci. 2023;24(3):1836.
98. de Carla CC, Denise CZ, Neves LMG, Mendonça JS, Joazeiro PP, Esquisatto MAM. Effects of microcurrent stimulation on Hyaline cartilage repair in immature male rats (Rattus norvegicus). BMC Complement Altern Med. 2013;13:1–9.
99. Casagrande SM, Biondo-Simões MDLP, Ioshii S, Robes RR, Biondo-Simões R, Boeno BRDO. Histological evaluation of the effect of low-frequency electric stimulation on healing Achilles tendons in rats. Acta Cirúrgica Brasileira. 2021;36(1):e360103.
100. Labanca L, Rocchi JE, Giannini S, Faloni ER, Montanari G, Mariani PP, Macaluso A. Early Superimposed NMES Training is Effective to Improve Strength and Function Following ACL Reconstruction with Hamstring Graft regardless of Tendon Regeneration. J Sports Sci Med. 2022;21(1):91–103.
101. Ferrigno B, Bordett R, Duraisamy N, Moskow J, Arul MR, Rudraiah S, Nukavarapu SP, Vella AT, Kumbar SG. Bioactive polymeric materials and electrical stimulation strategies for musculoskeletal tissue repair and regeneration. Bioact Mater. 2020;5(3):468–85.
102. Yu Y, Fan Y, Han F, Luan G, Wang Q. Transcranial direct current stimulation inhibits epileptic activity propagation in a large-scale brain network model. SCIENCE CHINA Technol Sci. 2023;66(12):3628–38.
103. Filmer HL, Dux PE, Mattingley JB. Applications of transcranial direct current stimulation for understanding brain function. Trends Neurosci. 2014;37(12):742–53.
104. Figueiredo JGS, de Sousa BM, Soares Santos MP, dos Vieira SI. Gathering Evidence to Leverage Musculoskeletal Magnetic Stimulation Towards Clinical Applicability. Small Science. 2024;4(5):2300303.
105. Noruzi K, Swami P, Frejo L, Wright J, Wong J, Grande D, Datta-Chaudhuri T. Effect of uniform capacitively coupled electric fields on matrix metabolism of osteoarthritic cartilage. Bioelectronic Medicine. 2022;8(1):14.
106. Lee M, Lee Y, Choi JH, Kim H, Jeong D, Park K, Kim J, Park J, Jang WY, Seo J, Lee J. Postoperative Long-Term Monitoring of Mechanical Characteristics in Reconstructed Soft Tissues Using Biocompatible, Immune-Tolerant, and Wireless Electronic Sutures. ACS Nano. 2024;18(19):12210–24.
107. Capone F, Salati S, Vincenzi F, Liberti M, Aicardi G, Apollonio F, Varani K, Cadossi R, Di Lazzaro V. Pulsed Electromagnetic Fields: A Novel Attractive Therapeutic Opportunity for Neuroprotection After Acute Cerebral Ischemia. Neuromodulation: Technology at the Neural Interface. 2022;25(8):1240–1247.
108. Kim Y, Cho H-J, Park H-S. Technical development of transcutaneous electrical nerve inhibition using medium-frequency alternating current. J Neuroeng Rehabil. 2018;15(1):1–12.

109. Aldayel A, Jubeau M, McGuigan M, Nosaka K. Comparison between alternating and pulsed current electrical muscle stimulation for muscle and systemic acute responses. J Appl Physiol. 2010;109(3):735–44.
110. Vinhas A, Rodrigues MT, Gonçalves AI, Reis RL, Gomes ME. Pulsed Electromagnetic Field Modulates Tendon Cells Response in IL-1β-Conditioned Environment. J Orthop Res. 2019;38(1):160–72.
111. de Girolamo L, Viganò M, Galliera E, Stanco D, Setti S, Marazzi MG, Thiebat G, Corsi Romanelli MM, Sansone V. In vitro functional response of human tendon cells to different dosages of low-frequency pulsed electromagnetic field. Knee Surg Sports Traumatol Arthrosc. 2014;23(11):3443–53.
112. Dolkart O, Kazum E, Rosenthal Y, Sher O, Morag G, Yakobson E, Chechik O, Maman E. Effects of focused continuous pulsed electromagnetic field therapy on early tendon-to-bone healing. Bone & Joint Research. 2021;10(5):298–306.
113. Flodin J, Reitzner SM, Emanuelsson EB, Sundberg CJ, Ackermann P. The effect of neuromuscular electrical stimulation on the human skeletal muscle transcriptome. Acta Physiol. 2024;240(5): e14129.
114. Dohnert MB, Novaski NdOC, Deves JR, Soares ARdO, Silveira MMd, Santos JVEd, Kuplich PA, Daitx RB. High frequency transcutaneous electrical stimulation in the immediate postoperative period of anterior cruciate ligament reconstruction: a randomized clinical trial. ABCS Health Sciences. 2022;47:e022229.
115. Chang C-Y, Weng YH, Chang C-H, Yang J-L, Chen P-T, Lin J-J. Neuromuscular electrical stimulation of humeral adductors in subjects with rotator cuff tear. Arch Orthop Trauma Surg. 2024;1–8.
116. Shi H, Li F, Zhang F, Wei X, Liu C, Duan R. An electrical stimulation intervention protocol to prevent disuse atrophy and muscle strength decline: an experimental study in rat. J Neuroeng Rehabil. 2023;20(1):84.
117. Tu K, Bao R, Wang L, Guo Z, Jiang C, Su Y, Liu S, Liu J. Stimulation of Sympathetic Nerve Using Ultraflexible Cuff Electrodes Inhibits Inflammation Caused by Tendon Rupture. Adv Funct Mater. 2024;2306666.
118. Wu P, Shen L, Liu H-F, Zou X-H, Zhao J, Huang Y, Zhu Y-F, Li Z-Y, Xu C, Luo L-H, Luo Z-Q, Wu M-H, Cai L, Li X-K, Wang Z-G. The marriage of immunomodulatory, angiogenic, and osteogenic capabilities in a piezoelectric hydrogel tissue engineering scaffold for military medicine. Mil Med Res. 2023;10(1):35.
119. Xia G, Song B, Fang J. Electrical Stimulation Enabled via Electrospun Piezoelectric Polymeric Nanofibers for Tissue Regeneration. Research. 2022.
120. Chen C, Bai X, Ding Y, Lee IS. Electrical stimulation as a novel tool for regulating cell behavior in tissue engineering. Biomater Res. 2019;23(1):25.
121. Dong C, Qiao F, Hou W, Yang L, Lv Y. Graphene-based conductive fibrous scaffold boosts sciatic nerve regeneration and functional recovery upon electrical stimulation. Appl Mater Today. 2020;21: 100870.
122. Zhang P, Zhu B, Du P, Travas-Sejdic J. Electrochemical and Electrical Biosensors for Wearable and Implantable Electronics Based on Conducting Polymers and Carbon-Based Materials. Chem Rev. 2023;124(3):722–67.
123. Na Li QY, Duan S, Du Y, Shi X, Li X, Jiao T, Qin Z, He X. Anti-Swelling, High-Strength, Anisotropic Conductive Hydrogel with Excellent Biocompatibility for Implantable Electronic Tendon. Advanced Functional Materials. 2024;34(12):2309500.
124. Tang X, Saveh Shemshaki N, Vernekar VN, Prabhath A, Kuyinu E, Kan H-M, Barajaa M, Khan Y, Laurencin CT. The Treatment of Muscle Atrophy After Rotator Cuff Tears Using Electroconductive Nanofibrous Matrices. Regenerative Engineering and Translational Medicine. 2020;7(1):1–9.
125. Shemshaki NS, Kan H-M, Barajaa MA, Lebaschi A, Otsuka T, Mishra N, Nair LS, Laurencin CT. Efficacy of a Novel Electroconductive Matrix To Treat Muscle Atrophy and Fat Accumulation in Chronic Massive Rotator Cuff Tears of the Shoulder. ACS Biomater Sci Eng. 2023;9(10):5782–92.
126. Yang S, Cheng J, Shang J, Hang C, Qi J, Zhong L, Rao Q, He L, Liu C, Ding L, Zhang M, Chakrabarty S, Jiang X. Stretchable surface electromyography electrode array patch for tendon location and muscle injury prevention. Nat Commun. 2023;14(1):6494.
127. Petersen R. Carbon Fiber Biocompatibility for Implants Fibers. 2016;4(1):1.
128. Arambula-Maldonado R, Mequanint K. Carbon-based electrically conductive materials for bone repair and regeneration. Materials Advances. 2022;3(13):5186–206.
129. Shin M, Lim J, Park Y, Lee J-Y, Yoon J, Choi J-W. Carbon-based nanocomposites for biomedical applications. RSC Adv. 2024;14(10):7142–56.
130. Islam M, Lantada AD, Mager D, Korvink JG. Carbon-Based Materials for Articular Tissue Engineering: From Innovative Scaffolding Materials toward Engineered Living Carbon. Adv Healthcare Mater. 2021;11(1):2101834.
131. Pan L, Wang F, Cheng Y, Leow WR, Zhang Y-W, Wang M, Cai P, Ji B, Li D, Chen X. A supertough electro-tendon based on spider silk composites. Nat Commun. 2020;11(1):1332.
132. Wang L, Wan F, Xu Y, Xie S, Zhao T, Zhang F, Yang H, Zhu J, Gao J, Shi X, Wang C, Lu L, Yang Y, Yu X, Chen S, Sun X, Ding J, Chen P, Ding C, Xu F, Yu H, Peng H. Hierarchical helical carbon nanotube fibre as a bone-integrating anterior cruciate ligament replacement. Nat Nanotechnol. 2023;18(9):1085–93.
133. Yu X, Wu G, Cai P, Ding Y, Cui J, Wu J, Shen Y, Song J, Yuan Z, El-Newehy M, Abdulhameed MM, Chen H, Mo X, Sun B, Yu Y. Carbon Fiber-Mediated Electrospinning Scaffolds Can Conduct Electricity for Repairing Defective Tendon. ACS Appl Mater Interfaces. 2024;16(39):52104–15.
134. Gao Y, Wang X, Fan C. Advances in graphene-based 2D materials for tendon, nerve, bone/cartilage regeneration and biomedicine. Science. 2024;27(7):110214.
135. Bao D, Sun J, Gong M, Shi J, Qin B, Deng K, Liu G, Zeng S, Xiang Z, Fu S. Combination of graphene oxide and platelet-rich plasma improves tendon-bone healing in a rabbit model of supraspinatus tendon reconstruction. Regen Biomater. 2021;8(6):rbab045.
136. Derakhshi M, Daemi S, Shahini P, Habibzadeh A, Mostafavi E, Ashkarran AA. Two-Dimensional Nanomaterials beyond Graphene for Biomedical Applications. Journal of Functional Biomaterials. 2022;13(1):27.
137. Murali A, Lokhande G, Deo KA, Brokesh A, Gaharwar AK. Emerging 2D nanomaterials for biomedical applications. Mater Today. 2021;50:276–302.
138. Chen J, Sheng D, Ying T, Zhao H, Zhang J, Li Y, Xu H, Chen S. MOFs-Based Nitric Oxide Therapy for Tendon Regeneration. Nano-Micro Letters. 2020;13(1):1–17.
139. Garg R, Driscoll N, Shankar S, Hullfish T, Anselmino E, Iberite F, Averbeck S, Rana M, Micera S, Baxter JR, Vitale F. Wearable High-Density MXene-Bioelectronics for Neuromuscular Diagnostics, Rehabilitation, and Assistive Technologies. Small Methods. 2022;7(8):2201318.

140. Yu J, Lv X, Wang K. Applications of Triboelectric Nanogenerators in Medical Recovery: A Review. ACS Applied Electronic Materials. 2024;6(8):5465-5478.
141. Cao X, Jie Y, Wang N, Wang ZL. Triboelectric Nanogenerators Driven Self-Powered Electrochemical Processes for Energy and Environmental Science. Adv Energy Mater. 2016;6(23):1600665.
142. Conta G, Libanori A, Tat T, Chen G, Chen J. Triboelectric Nanogenerators for Therapeutic Electrical Stimulation. Adv Mater. 2021;33(26):2007502.
143. Radhakrishnan S, Joseph N, Vighnesh NP, Sabarinath PJ, John J, John H, Padmanabhan NT. Recent updates on triboelectric nanogenerator based advanced biomedical technologies: A short review. Results Eng. 2022;16:100782.
144. Fang H, Guo J, Wu H. Wearable triboelectric devices for haptic perception and VR/AR applications. Nano Energy. 2022;96: 107112.
145. Chen A, Zhang C, Zhu G, Wang ZL. Polymer Materials for High-Performance Triboelectric Nanogenerators. Advanced Science. 2020;7(14):2000186.
146. Zhang W, Li G, Wang B, Zhu Q, Zeng L, Wen Z, Yang C, Pan Y. Triboelectric Nanogenerators for Cellular Bioelectrical Stimulation. Adv Func Mater. 2022;32(34):2203029.
147. Zhou X, Li G, Wu D, Liang H, Zhang W, Zeng L, Zhu Q, Lai P, Wen Z, Yang C, Pan Y. Recent advances of cellular stimulation with triboelectric nanogenerators. Exploration. 2023;3(4):20220090.
148. Hu W, Wei X, Zhu L, Yin D, Wei A, Bi X, Liu T, Zhou G, Qiang Y, Sun X, Wen Z, Pan Y. Enhancing proliferation and migration of fibroblast cells by electric stimulation based on triboelectric nanogenerator. Nano Energy. 2019;57:600–7.
149. Li G, Zhu Q, Wang B, Luo R, Xiao X, Zhang Y, Ma L, Feng X, Huang J, Sun X, Wen Z, Pan Y, Yang C. Rejuvenation of Senescent Bone Marrow Mesenchymal Stromal Cells by Pulsed Triboelectric Stimulation. Advanced Science. 2021;8(18):2100964.
150. Wang H, Wang J, He T, Li Z, Lee C. Direct muscle stimulation using diode-amplified triboelectric nanogenerators (TENGs). Nano Energy. 2019;63:103844.
151. Sharma A, Panwar V, Mondal B, Prasher D, Bera MK, Thomas J, Kumar A, Kamboj N, Mandal D, Ghosh D. Electrical stimulation induced by a piezo-driven triboelectric nanogenerator and electroactive hydrogel composite, accelerate wound repair. Nano Energy. 2022;99: 107419.
152. Wu Y, Zhang K, Li S, Xiang Z, Jiang G, Zhang R, Qi Y, Ji X, Cai X, Zhang C, Li J, Yan R, Jin H, Dong S, Luo J, Feng G. Self-powered wearable electrical stimulation patch with integrated triboelectric nanogenerator for tendinopathy treatment. Nano Energy. 2024;121: 109234.
153. Wang W, Sun W, Du Y, Zhao W, Liu L, Sun Y, Kong D, Xiang H, Wang X, Li Z, Ma Q. Triboelectric Nanogenerators-Based Therapeutic Electrical Stimulation on Skin: from Fundamentals to Advanced Applications. ACS Nano. 2023;17(11):9793–825.
154. Tang Y, Wang Z, Xiang L, Zhao Z, Cui W. Functional biomaterials for tendon/ligament repair and regeneration. Regenerative Biomaterials. 2022;9:rbac062.
155. Chen P, Wang A, Haynes W, Landao-Bassonga E, Lee C, Ruan R, Breidahl W, Shiroud Heidari B, Mitchell CA, Zheng M. A bioinductive collagen scaffold that supports human primary tendon-derived cell growth for rotator cuff repair. Journal of Orthopaedic Translation. 2021;31:91–101.
156. Luo S, Zhang C, Xiong W, Song Y, Wang Q, Zhang H, Guo S, Yang S, Liu H. Advances in electroactive biomaterials: Through the lens of electrical stimulation promoting bone regeneration strategy. Journal of Orthopaedic Translation. 2024;47:191–206.
157. Liu Y, Lu J. Research trends of piezoelectric biomaterials in osteochondral tissue engineering. Materials Today Communications. 2024;41: 110264.
158. Freedman BR, Rodriguez AB, Leiphart RJ, Newton JB, Ban E, Sarver JJ, Mauck RL, Shenoy VB, Soslowsky LJ. Dynamic Loading and Tendon Healing Affect Multiscale Tendon Properties and ECM Stress Transmission. Sci Rep. 2018;8(1):10854.
159. Liu Y, He K, Chen G, Leow WR, Chen X. Nature-Inspired Structural Materials for Flexible Electronic Devices. Chem Rev. 2017;117(20):12893–941.
160. Harris KD, Elias AL, Chung HJ. Flexible electronics under strain: a review of mechanical characterization and durability enhancement strategies. J Mater Sci. 2015;51(6):2771–805.
161. Zhang Y, Le Friec A, Zhang Z, Müller CA, Du T, Dong M, Liu Y, Chen M. Electroactive biomaterials synergizing with electrostimulation for cardiac tissue regeneration and function-monitoring. Mater Today. 2023;70:237–72.
162. Mokhtari F, Azimi B, Salehi M, Hashemikia S, Danti S. Recent advances of polymer-based piezoelectric composites for biomedical applications. J Mech Behav Biomed Mater. 2021;122: 104669.
163. Liu T, Wang Y, Hong M, Venezuela J, Shi W, Dargusch M. Advances in biodegradable piezoelectrics for medical implants. Nano Today. 2023;52: 101945.
164. Zhao B, Qian F, Hatfield A, Zuo L, Xu T-B. A Review of Piezoelectric Footwear Energy Harvesters: Principles, Methods, and Applications. Sensors. 2023;23(13):5841.
165. Fanqi Dai, Qifan Geng, Tingyu Hua, Xing Sheng, Yin L. Organic biodegradable piezoelectric materials and their potential applications as bioelectronics. Soft Sci. 2023;3(1):7
166. Li J, Long Y, Yang F, Wang X. Degradable piezoelectric biomaterials for wearable and implantable bioelectronics. Curr Opin Solid State Mater Sci. 2020;24(1):100806.
167. Ali F, Koc M. 3D Printed Polymer Piezoelectric Materials: Transforming Healthcare through Biomedical Applications. Polymers. 2023;15(23):4470.
168. Chorsi MT, Curry EJ, Chorsi HT, Das R, Baroody J, Purohit PK, Ilies H, Nguyen TD. Piezoelectric Biomaterials for Sensors and Actuators. Adv Mater. 2018;31(1):1802084.
169. Ji J, Yang C, Shan Y, Sun M, Cui X, Xu L, Liang S, Li T, Fan Y, Luo D, Li Z. Research Trends of Piezoelectric Nanomaterials in Biomedical Engineering. Advanced NanoBiomed Research. 2022;3(1):2200088.
170. Kim H, Lee K, Jo G, Kim J-S, Lim MT, Cha Y. Tendon-Inspired Piezoelectric Sensor for Biometric Application. IEEE/ASME Trans Mechatron. 2021;26(5):2538–47.
171. Xu K, Lu Y, Takei K. Flexible Hybrid Sensor Systems with Feedback Functions. Adv Func Mater. 2020;31(39):2007436.
172. Kumar R, Bera S. Recent approaches in development of bio-based artificial piezoelectric constructs for biomedical applications. Giant. 2024;17: 100214.
173. Kamel NA. Bio-piezoelectricity: fundamentals and applications in tissue engineering and regenerative medicine. Biophys Rev. 2022;14(3):717–33.
174. Fernandez-Yague MA, Palma M, Tofail SAM, Duffy M, Quinlan LR, Dalby MJ, Pandit A, Biggs MJ. A Tympanic Piezo-Bioreactor Modulates Ion Channel-Associated Mechanosignaling to Stabilize Phenotype and Promote Tenogenesis in Human Tendon-Derived Cells. Advanced Science. 2024;11(45):2405711.
175. Huang Y, Yao K, Zhang Q, Huang X, Chen Z, Zhou Y, Yu X. Bioelectronics for electrical stimulation: materials, devices and biomedical applications. Chem Soc Rev. 2024;53(17):8632–712.
176. Chiu C-H, Lei KF, Yeh W-L. Development of a co-culture device for the study of human tenocytes in response to the combined stimulation of electric field and platelet rich plasma (PRP). Biomed Microdevice. 2017;19(3):1–10.

177. Liang Y, Qiao L, Qiao B, Guo B. Conductive hydrogels for tissue repair. Chem Sci. 2023;14(12):3091–116.
178. Wang L, Yu Y, Zhao X, Zhang Z, Yuan X, Cao J, Meng W, Ye L, Lin W, Wang G. A Biocompatible Self-Powered Piezoelectric Poly(vinyl alcohol)-Based Hydrogel for Diabetic Wound Repair. ACS Appl Mater Interfaces. 2022;14(41):46273–89.
179. Huang X, Zhang X. Recent Advance in Stretchable Self-Powered Piezoelectric Sensors: Trends, Challenges, and Solutions. Advanced Materials Technologies. 2023;8(24):2301226.

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