Journal Website: https://www.icjn.net/cl ISSN: 3106-5058 | EISSN: 3106-5066

ICJN Press

Cytotherapy and Longevity (CL)

Volume. 01 | Issue. 02 | Nov. 2026 DOI: 10.66729/cl202605008



REVIEW

Mechanomedicine: Fundamental Mechanisms, Clinical Applications and Future Directions

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Abstract

Mechanomedicine has developed from advances in mechanobiology toward a broader field that spans diagnosis, treatment, and tissue regeneration. This review summarizes the biological basis of mechanosensing and mechanotransduction and examines how these processes contribute to disease progression, tissue repair, and treatment responses. Particular attention is given to the clinical and regenerative applications of mechanical regulation and to the factors that influence treatment responses and translational potential. Current evidence shows marked differences in translational maturity among these approaches, highlighting the need to distinguish established clinical applications from strategies that remain experimental or at an early stage of translation. The review also discusses the importance of mechanical dose, therapeutic windows, disease stage, and tissue condition in determining treatment outcomes, together with the growing role of mechanical biomarkers in diagnosis and patient stratification. In regenerative medicine, mechanical regulation may provide new ways to improve cell function and tissue repair, while age-related changes in tissue mechanics may influence regenerative capacity and healthy longevity. Finally, emerging developments in artificial intelligence, mechanogenomics, gene editing, and wearable sensing are discussed as tools for improving the measurement, interpretation, and personalization of mechanical interventions. Overall, mechanomedicine is moving toward a more evidence-based and clinically oriented framework that integrates mechanistic understanding with diagnosis, treatment, and regeneration.

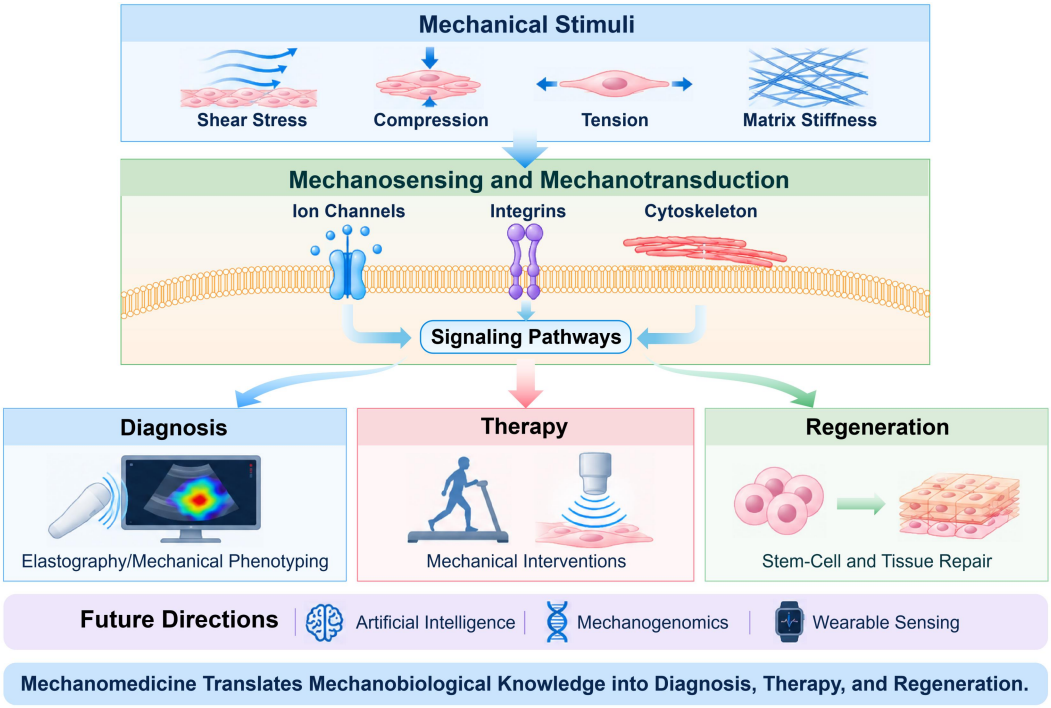
Keywords

Mechanomedicine; Mechanical forces; Mechanotransduction; Clinical application; Regenerative medicine

Citation: Xinle Li, Xuetong Wang and Ping Zhang. Mechanomedicine: Fundamental Mechanisms, Clinical Applications and Future Directions. *Cytotherapy and Longevity*. 2026, 01 (2): 1-11. doi: 10.66729/cl202605008.

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Received 11 May 2026; Revised 18 June 2026; Accepted 2 November 2026; Available online 16 November 2026.

Graphical Abstract



Highlights

- Mechanosensing and mechanotransduction form the biological basis of mechanomedicine.
- Mechanomedicine integrates diagnostic, therapeutic, and regenerative applications with different levels of clinical evidence.
- Mechanical dose, tissue context, and emerging technologies are central to the future development of personalized mechanomedicine.

1. Introduction

Mechanical forces are ubiquitous in biological systems and play a key role in maintaining tissue homeostasis and contributing to disease pathogenesis[1,2]. Shear stress, compression, and tension regulate cellular behavior across multiple scales. Rather than acting solely as passive physical inputs, these forces can actively influence gene expression, cell fate, and tissue organization. Mechanomedicine examines how mechanical cues and the physical microenvironment influence cellular behavior, tissue development, disease progression, and therapeutic responses through cell-matrix interactions and tissue mechanics[3,4].

The conceptual development of mechanomedicine has progressed from classical biomechanics to mechanobiology and, more recently, toward clinical translation[5,6]. Classical biomechanics primarily focuses on the physical properties, forces, and mechanical behavior of biological systems, whereas mechanobiology extends this perspective by investigating how cells and tissues sense and respond to mechanical cues[1,3]. Mechanobiology therefore provides the fundamental basis for understanding how mechanical forces regulate cellular behavior from the molecular to the organ scale and how mechanical inputs are converted into biochemical signals through mechanosensing and mechanotransduction[5]. Mechanomedicine builds on these principles by translating mechanobiological discoveries into diagnostic techniques, medical devices, therapeutic interventions, and regenerative strategies[6]. Mechanotherapy refers more specifically to the therapeutic use of mechanical or physical interventions and can therefore be considered one component of the broader mechanomedicine framework[7]. Within the broader framework of mechanomedicine, different interventions may operate through distinct therapeutic principles. Direct mechanical interventions act primarily through the physical manipulation, removal, or modification of tissues or pathological structures. Mechanical thrombectomy, for example, restores blood flow by physically removing an occluding thrombus[8]. By contrast, mechanotransduction-based interventions regulate cellular behavior through mechanically sensitive signaling pathways[1,9]. Biomechanics, mechanobiology, mechanotherapy, and mechanomedicine are therefore closely related but conceptually distinct, with mechanosensing and mechanotransduction providing the biological link between mechanical stimuli and cellular responses[7,9].

Advances in mechanobiology, biomaterials, bioengineering, and medical devices have substantially expanded the scope of mechanomedicine. Liu *et al.* recently provided a comprehensive overview of the field, including its fundamental principles, diagnostic and therapeutic applications, tissue regeneration, and clinical translation[6]. The present review extends this discussion by linking mechanosensing and mechanotransduction more closely to clinical and regenerative applications, while considering differences in the translational maturity and context dependence of mechanical interventions. We also discuss the therapeutic mechanical window, cytotherapy and regenerative medicine, aging and healthy longevity, as well as emerging approaches involving artificial intelligence, mechanogenomics, gene editing, and wearable sensing. The overall framework is summarized in **Figure 1**.

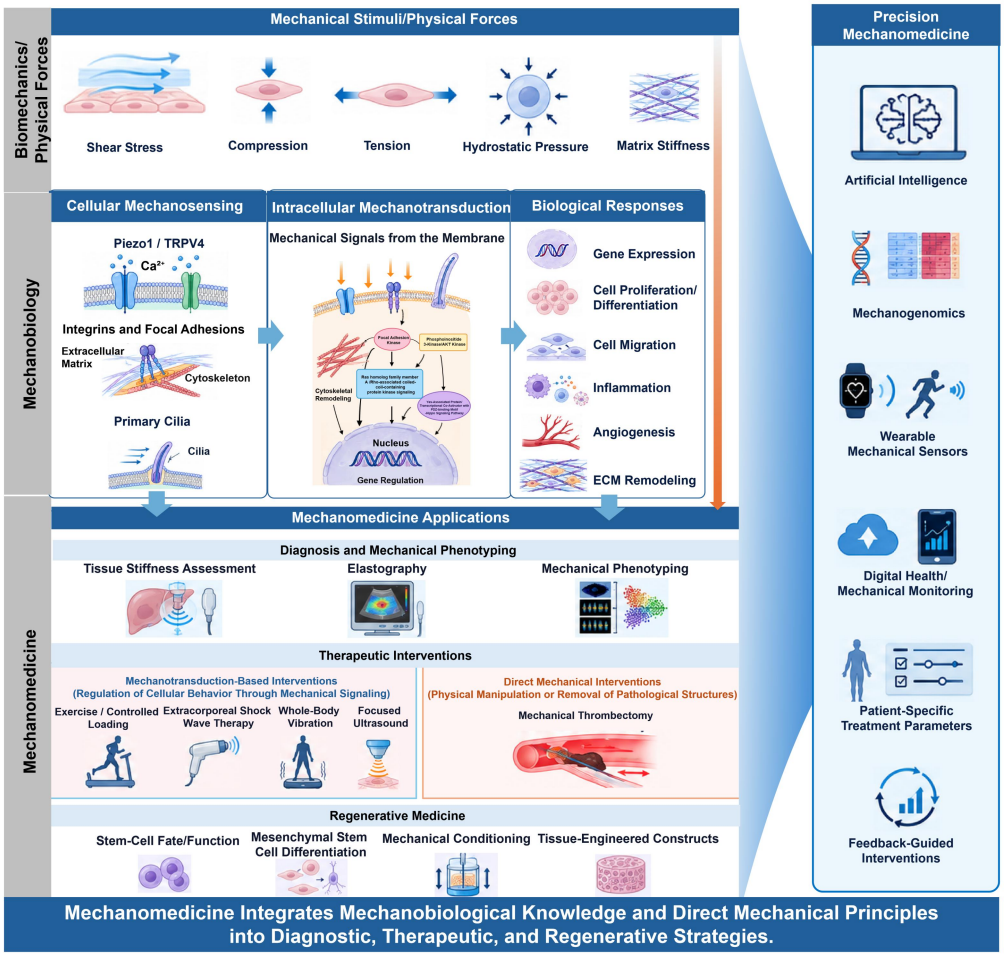


Figure 1. Conceptual framework of mechanomedicine. Mechanical stimuli can influence cellular behavior through mechanosensing and intracellular mechanotransduction, leading to biological responses and subsequent diagnostic, therapeutic, and regenerative applications. Mechanomedicine also includes direct mechanical interventions, such as mechanical thrombectomy, in which therapeutic effects arise primarily from physical manipulation rather than cellular mechanotransduction. Some interventions may involve both direct physical effects and secondary mechanobiological responses. **NOTE:** ECM: extracellular matrix; Piezo1: Piezo-type mechanosensitive ion channel component 1; TRPV4: Transient receptor potential cation channel subfamily V member 4. Copyright: Created by the authors using WPS Presentation (WPS Office, version 12.1.0.29161, 32-bit).

2. Mechanosensing and Mechanotransduction: Biological Basis of Mechanomedicine

2.1 Cellular Mechanosensing

Cells have a variety of mechanosensitive structures and molecules that enable them to sense and respond to mechanical stimuli. Mechanosensitive ion channels, including piezo-type mechanosensitive ion channel component 1 (Piezo1) and transient receptor potential cation channel subfamily V member 4 (TRPV4), are key factors in converting mechanical forces into electrochemical signals. For example, Piezo1 is widely expressed in endothelial cells and is activated by fluid shear stress, leading to calcium influx and downstream signaling that regulates vascular tone, inflammation, and angiogenesis[10,11]. Recent studies have shown that gain-of-function mutations in Piezo1 can lead to cardiac hypertrophy and fibrosis, highlighting its physiological importance[12].

Integrins connect the extracellular matrix (ECM) with the cytoskeleton and play a crucial role in mechanosensing[13,14]. When cells are subjected to mechanical force, integrins cluster and activate focal adhesion kinase (FAK), triggering a series of intracellular signaling events that regulate cell migration, proliferation, and differentiation. FAK activation further recruits adaptor proteins, such as talin and vinculin, to form mature focal adhesions that serve as signaling hubs[15-17]. These complexes not only transmit forces but also integrate mechanical and growth-factor signals. Primary cilia also function as mechanosensory organelles in various cell types, including renal epithelial cells and chondrocytes. Defects in ciliary mechanosensing have been associated with skeletal and renal disorders[18,19].

2.2 Intracellular Mechanotransduction

Once mechanical signals are sensed at the cell surface, they are converted into biochemical signals that regulate cellular function. The cytoskeleton is a dynamic network composed of actin filaments, intermediate filaments, and microtubules and functions as both a mechanical scaffold and a signaling sensor[20]. Mechanical forces can induce cytoskeletal remodeling, and thereby alter the activity of intracellular signaling molecules. Yes-associated protein (YAP) and transcriptional co-activator with PDZ-binding motif (TAZ) are crucial downstream effectors of mechanotransduction. Changes in ECM stiffness or cell shape can regulate the nuclear translocation of YAP/TAZ, thereby regulating the expression of genes related to cell growth, survival, and differentiation[21-23]. The Hippo signaling

pathway, traditionally known for its role in organ size control, is also highly responsive to mechanical cues. Hippo pathway activation promotes YAP/TAZ phosphorylation, leading to their cytoplasmic retention and degradation in soft environments. In contrast, rigid substrates promote YAP/TAZ nuclear localization and activate the transcription of growth-promoting genes[24-26].

Other signaling pathways, including the Ras homolog (Rho)/Rho-associated coiled-coil-containing protein kinase (ROCK) pathway and the phosphoinositide 3-kinase (PI3K)/protein kinase B (PKB) pathway, are also activated by mechanical force[27,28]. Rho GTPases regulate actomyosin contractility and influence cell morphology and motility. Mechanical stretching or compression can activate Ras homolog gene family member A (RhoA), leading to actin polymerization and increased myosin II activation, thereby enhancing cell tension. Mechanical loading can also enhance angiogenesis and osteogenesis through the PI3K/PKB signaling pathway in experimental osteoporosis models[29].

These mechanosensitive pathways provide a mechanistic basis for many of the therapeutic approaches discussed below. Piezo1-mediated and integrin-mediated mechanosensing is particularly relevant to vascular responses to shear stress and mechanical loading, whereas integrin-FAK and cytoskeletal signaling contribute to load-dependent cell migration, differentiation, and matrix remodeling. YAP/TAZ links matrix stiffness and cell shape to transcriptional programs involved in proliferation, differentiation, and tumor progression, while PI3K/PKB signaling participates in loading-induced angiogenic and osteogenic responses. Thus, the biological effects of mechanical interventions depend not only on the applied mechanical stimulus but also on the mechanosensors and downstream signaling networks engaged in specific tissues.

3. Clinical and Regenerative Applications of Mechanomedicine

3.1 Musculoskeletal Disorders

3.1.1 Osteoarthritis

Osteoarthritis (OA) is characterized by progressive cartilage degeneration, subchondral bone remodeling, and synovitis, and is a representative condition for mechanical loading-based interventions[30]. Experimental studies suggest that appropriately controlled mechanical loading can promote anabolic responses in cartilage. In clinical OA, however, the benefits of exercise are most consistently demonstrated in pain relief and improvement of physical function, whereas evidence that exercise delays structural disease progression remains limited and inconclusive[31]. Low-impact aerobic exercise, such as swimming, cycling and walking, can relieve joint pain and improve function by enhancing muscle strength, reducing joint stiffness and stimulating chondrocyte metabolism[32-36]. Personalized exercise therapy can reduce OA-related pain and improve physical function[37].

Pulsed electromagnetic fields (PEMFs) have also been investigated for their effects on ion-channel activity, inflammation, and ECM synthesis[38-41]. Mechanical loading can regulate the inflammatory microenvironment and promote endogenous stem-cell migration in experimental OA models[42-44]. Extracorporeal shock wave therapy (ESWT) has also demonstrated beneficial effects on pain and function in clinical studies[45-47]. At the cellular level, these loading-induced responses are mediated by mechanosensitive ion channels and integrin-associated adhesion complexes, which transmit mechanical cues to cytoskeletal and downstream signaling pathways involved in chondrocyte metabolism and matrix remodeling[13,14,48].

However, the evidence supporting these interventions is not equivalent. Exercise therapy is supported by substantial clinical evidence, whereas several mechanisms involving direct mechanical loading, macrophage regulation, and stem-cell recruitment are mainly derived from preclinical studies. Therefore, mechanistic efficacy should be distinguished from established clinical effectiveness.

3.1.2 Tendon Injury

Tendon diseases, including Achilles and rotator cuff tendinopathy, are common overuse injuries characterized by impaired healing and collagen disorganization[49-51]. Mechanical loading therapy, particularly eccentric training, has become an important treatment strategy[52-55]. Mechanical stimulation promotes tendon-cell activity, collagen synthesis, and fiber rearrangement, thereby improving tendon structure and mechanical properties.

Tissue engineering based on bioreactors further extends this concept by applying cyclic tensile loading to engineered tendon constructs containing mesenchymal stem cells (MSCs) or tendon cells[56-60]. Such mechanical conditioning improves collagen organization and mechanical properties and provides a link between mechanotherapy and regenerative medicine.

3.1.3 Osteoporosis

Osteoporosis is characterized by low bone mass, microstructural deterioration and increased fracture risk[61,62]. Bone is a highly mechanosensitive organ, and osteocytes act as key sensors of mechanical loading[63-68]. Weight-bearing exercise and resistance training stimulate bone formation through mechanosensitive cellular responses.

Whole-body vibration (WBV) provides high-frequency, low-amplitude mechanical stimulation and has been investigated as a non-invasive intervention for osteoporosis[69,70]. Mechanical loading also regulates osteogenic signaling and vascular remodeling in experimental models[71,72]. Mechanical signals are transmitted through osteocyte mechanosensors and downstream pathways, including PI3K/PKB and other osteogenic signaling networks, thereby linking mechanical loading to bone formation and vascular remodeling[29,64,72]. Low-intensity pulsed ultrasound (LIPUS) has been explored for fracture healing through the regulation of osteoblast activity and angiogenesis[73-75]. Clinical evidence, however, has been less convincing. In the large multicenter Trial to Re-evaluate Ultrasound in the Treatment of Tibial Fractures (TRUST), which enrolled 501 patients with surgically managed tibial fractures, LIPUS did not improve functional recovery or accelerate radiographic healing compared with sham treatment[76]. A subsequent BMJ clinical practice guideline issued a strong recommendation against the routine use of LIPUS for fracture or osteotomy healing[77]. These results indicate that the biological effects observed in experimental models do not necessarily translate into meaningful clinical benefit.

Together, these studies demonstrate the therapeutic potential of mechanical regulation in musculoskeletal disorders and further highlight its relevance to regenerative medicine. Mechanical loading can influence endogenous stem-cell migration, MSCs differentiation, and tissue-engineered constructs, suggesting that mechanomedicine may provide a complementary strategy for cell-based and regenerative therapies. Nevertheless, treatment effects are strongly dependent on loading intensity, frequency, duration, disease stage, and tissue condition, and defining an appropriate therapeutic mechanical window therefore remains a central challenge.

3.2 Cardiovascular, Neurovascular, and Cancer Applications

3.2.1 Cardiovascular and Neurovascular Disorders

The cardiovascular system is continuously exposed to cyclic tension, shear stress and hydrostatic pressure. Endothelial cells sense blood-flow-associated shear forces through Piezo1, integrins and other mechanoreceptors. Physiological laminar shear stress contributes to vascular homeostasis, whereas abnormal hemodynamics, including turbulence and low shear stress, can induce endothelial dysfunction, oxidative stress and inflammation, thereby contributing to atherosclerosis[78,79]. These responses illustrate how Piezo1- and integrin-mediated mechanosensing can translate hemodynamic forces into vascular signaling and functional adaptation[14,78,79].

Beyond mechanotransduction-mediated regulation of vascular homeostasis and disease, mechanomedicine also includes direct mechanical interventions with different therapeutic principles. Mechanical thrombectomy is a representative example, in which therapeutic benefit is achieved primarily through the physical removal of an occluding thrombus and restoration of blood flow rather than through the modulation of cellular mechanotransduction. It therefore represents an established direct mechanical intervention within the broader mechanomedicine framework[8,80,81].

Mechanical regulation is also relevant to neurovascular disorders. Changes in vascular shear stress, endothelial mechanosensing, and blood-brain barrier mechanics can influence cerebrovascular function and neurological injury[82]. In addition to mechanical thrombectomy, mechanically assisted approaches such as focused ultrasound have also been explored to transiently modulate blood-brain barrier permeability for therapeutic delivery[83].

3.2.2 Cancer

The mechanical properties of the tumor microenvironment play important roles in cancer initiation, progression, and metastasis[84-87]. Increased matrix stiffness, solid stress, and abnormal interstitial fluid pressure of tumor tissue can promote the proliferation, invasion, and epithelial-mesenchymal transition of tumor cells through the integrin-YAP pathway. Stromal sclerosis can also induce the activation of cancer-associated fibroblasts, which further promote the deposition of collagen and fibronectin and contribute to a positive feedback loop within the tumor microenvironment. Changes in matrix stiffness and mechanical stress may also influence the tumor immune microenvironment by modulating immune-cell infiltration, activation, and function, thereby linking tumor mechanobiology to immune regulation[88]. The mechanical microenvironment can also favor the selection of more aggressive tumor-cell phenotypes and contribute to mechanical adaptation and memory. For example, cancer cells previously exposed to a stiff matrix may retain enhanced migratory and stem-like properties even after returning to a softer environment, suggesting that mechanical memory may be maintained through epigenetic mechanisms[87]. Mechanical drug delivery systems, such as ultrasound-responsive nanoparticles, can improve targeted drug delivery to diseased tissues and reduce systemic side effects[89,90]. When focused ultrasound (FUS) is combined with microbubbles, it can transiently increase blood-brain barrier (BBB) permeability, thereby facilitating the delivery of chemotherapeutic agents or gene therapies to the brain. FUS-mediated BBB modulation is currently being investigated clinically in brain tumors and neurodegenerative diseases[91,92].

However, these approaches are at different stages of translation. FUS-based approaches are under clinical investigation, whereas most tumor-mechanics-targeted strategies remain predominantly preclinical.

3.3 Cytotherapy and Regenerative Medicine

Mechanical regulation is directly relevant to cytotherapy and regenerative medicine because therapeutic stem cells continuously interact with the physical and mechanical properties of their surrounding microenvironment. Mechanical cues, including matrix stiffness, strain, shear stress, and cell-matrix interactions, can regulate stem-cell fate, proliferation, and functional behavior through mechanotransduction pathways involving integrin-associated adhesion signaling, cytoskeletal remodeling, and YAP/TAZ activation[93,94].

Several experimental studies suggest that mechanical conditioning can improve the therapeutic performance of transplanted cells. In a mouse model of myocardial infarction, cyclic mechanical preconditioning of muscle-derived stem cells enhanced cardiac function and peri-infarct angiogenesis compared with non-stimulated cells[95]. Mechanobiological conditioning of human MSCs through controlled mechanical strain and modulation of Smad2 and Smad3 and YAP signaling also enhanced vascular regeneration after implantation, including in an ischemic hindlimb model[96]. More recently, mechanically preconditioned adipose-derived stem cells showed improved survival and immunoregulatory activity and accelerated chronic wound healing after transplantation[97]. These studies indicate that mechanical preconditioning can influence not only stem-cell phenotype but also regenerative outcomes *in vivo*. Nevertheless, most evidence remains preclinical, and the optimal mechanical stimulus, durability of the induced phenotype, and clinical benefit require further investigation.

Aging is also accompanied by substantial changes in tissue mechanics and mechanotransduction. Progressive ECM remodeling and stiffening, altered cytoskeletal tension, and impaired cell-matrix interactions can disrupt mechanosensing and pathways such as integrin-FAK and YAP/TAZ, contributing to cellular senescence and reduced regenerative capacity[4,98]. These changes may also alter the mechanical niche encountered by transplanted or endogenous stem cells, thereby limiting tissue repair in older individuals. Modulating matrix mechanics or restoring appropriate mechanotransduction may therefore provide a strategy to preserve regenerative function and improve healthspan. However, direct evidence that mechanomedicine interventions improve human healthspan or lifespan remains limited. At present, this area should therefore be viewed as an emerging rather than established therapeutic direction.

3.4 Diagnostic Applications and Mechanical Phenotyping

Mechanical properties can also serve as diagnostic biomarkers. Elastography is one of the most established examples, providing non-invasive measurements of tissue stiffness using ultrasound- or magnetic resonance-based approaches. Its clinical application is particularly well developed in chronic liver disease, where transient elastography, shear-wave elastography, and magnetic resonance elastography are used for fibrosis assessment and risk stratification[99,100]. Large-scale evidence supports their diagnostic value, especially for advanced fibrosis and cirrhosis, although performance varies with disease etiology, technical platform, and clinical context.

Elastography is also being explored in tumors and other tissues, where changes in stiffness may complement conventional imaging and provide information on disease progression or treatment response. However, stiffness measurements are not disease-specific and may be influenced by inflammation, congestion, tissue composition, acquisition conditions, and operator-dependent or platform-dependent variability. Standardized protocols, validated cut-off values, and external validation across patient populations therefore remain important for broader clinical use[99,100].

At the cellular level, mechanical phenotyping approaches, including atomic force microscopy and deformability-based cytometry, can quantify cell stiffness and deformability and have shown potential for identifying disease-associated cellular states. Their clinical translation remains less mature than tissue-level elastography. Differences in sample preparation, cell size, viscoelastic behavior, measurement platforms, and analytical models can lead to substantial variability across studies, and standardized mechanical biomarkers and prospective clinical validation are still needed[101]. Thus, diagnostic mechanomedicine currently spans clinically established uses of tissue-scale stiffness measurement in selected settings and emerging cell-scale mechanical biomarkers with different levels of translational maturity. Representative mechanomedicine strategies, together with their current translational status and major limitations, are summarized in **Table 1**.

Table 1. Representative diagnostic, therapeutic, and regenerative strategies in mechanomedicine, their translational status, and major limitations

Application/Disease Area	Mechanical Strategy	Evidence/Status	Major Limitation	References
Osteoarthritis	Exercise and controlled mechanical loading	Clinically supported for pain relief and functional improvement; structural benefit remains uncertain	Effects depend on loading parameters, disease stage, and tissue condition	[31,35-37,42-44,48]
Osteoarthritis	ESWT	Clinical evidence supports symptomatic benefit	Optimal dose and long-term structural effects remain unclear	[45-47]
Tendon Injury	Eccentric training/mechanical loading	Clinically used for selected tendinopathies	Response varies with tendon type and loading protocol	[49-55]
Tendon Regeneration	Cyclic mechanical conditioning of MSCs or tendon constructs	Preclinical/experimental	Limited clinical translation	[56-60]
Osteoporosis	Weight-bearing and resistance exercise	Recommended as part of non-pharmacological osteoporosis management	Exercise prescription depends on fracture risk and physical capacity	[61-68]
Osteoporosis	WBV	Clinical benefit remains uncertain	Heterogeneous protocols and inconsistent outcomes	[69,70]
Fracture Healing	LIPUS	Not supported for routine clinical use	High-quality clinical evidence shows no meaningful benefit	[73-77]
Acute Ischemic Stroke	Mechanical thrombectomy	Established clinical treatment	Benefit depends on patient selection and treatment conditions	[8,80,81]
Cancer	Tumor-mechanics- and mechanotransduction-targeted strategies	Predominantly preclinical/early translational	Tumor mechanical and biological heterogeneity	[84-88]
Cancer/Neurovascular Disorders	Focused ultrasound and mechanically assisted drug delivery	Emerging clinical translation	Safety, treatment parameters, and long-term effects require validation	[83,89-92]
Cytotherapy and Regenerative Medicine	Mechanical preconditioning of stem cells and regulation of the cellular mechanical microenvironment	Preclinical/early translational	Optimal stimulus and clinical efficacy remain uncertain	[93-97]
Aging and Regenerative Decline	Modulation of matrix mechanics and mechanotransduction	Emerging therapeutic concept	Direct evidence for improving human healthspan is limited	[4,98]
Chronic Liver Disease	TE, SWE, MRE	Established clinical diagnostic application	Performance and cut-offs vary with clinical and technical factors	[99,100]
Cellular Mechanical Phenotyping	AFM and deformability-based cytometry	Emerging diagnostic approach	Lack of standardized methods and validated biomarkers	[101]

NOTE: ESWT: extracorporeal shock wave therapy; MSCs: mesenchymal stem cells; WBV: whole-body vibration; LIPUS: low-intensity pulsed ultrasound; TE: transient elastography; SWE: shear-wave elastography; MRE: magnetic resonance elastography; AFM: atomic force microscopy.

4. Challenges and Future Directions

4.1 Clinical and Technical Challenges

Although significant progress has been made, many aspects of mechanotransduction are still poorly understood. The complexity of mechanical signals, including amplitude, frequency, duration, and direction, as well as the heterogeneity of cellular responses, makes it difficult to establish a clear causal relationship between mechanical inputs and biological outputs[102-104].

Optical tweezers, traction force microscopy (TFM), atomic force microscopy (AFM), and molecular tension sensors based on Förster resonance energy transfer (FRET) provide powerful approaches for quantifying cellular forces, but most remain difficult to translate directly into *in vivo* and clinical applications[105-108]. Finite element modeling and machine-learning approaches may help integrate mechanical measurements with tissue structure and biological responses[109-111].

Pathophysiological state, disease stage, and interindividual variability are also important determinants of therapeutic responses. The same mechanical stimulus may produce different biological responses depending on tissue condition and disease stage[112-118]. Therefore, accurate patient selection and individualized adjustment of mechanical parameters are important for clinical translation.

A major challenge is the lack of standardized definitions of

mechanical dose and therapeutic mechanical windows. Future studies should more clearly report the intensity, frequency, duration, and mode of mechanical intervention and distinguish evidence from *in vitro* studies, animal models, clinical trials, and established clinical practice.

4.2 Emerging Trends and Opportunities

Emerging technologies are expected to promote the development of mechanomedicine toward more quantitative and personalized approaches. Integrating artificial intelligence (AI) and machine-learning methods with mechanomedicine may facilitate the development of diagnostic algorithms and individualized treatment strategies[119,120]. AI can integrate large datasets containing mechanical and biological information, such as tissue stiffness, imaging features, gene-expression profiles, and clinical outcomes, to identify disease-associated patterns and predict therapeutic responses. In cancer, for example, tumor stiffness and perfusion measured by elastography and contrast-enhanced ultrasound have been incorporated into machine-learning models to predict treatment response[121]. However, the clinical applicability of these approaches still depends on the availability of standardized mechanical parameters, sufficiently large datasets, and external validation across different patient populations.

Another promising direction is the development of mechanogenomics, which combines mechanobiology with genomic and epigenomic approaches to understand how mechanical forces regulate gene expression[122,123]. By integrating chromatin accessibility, epigenetic status, and transcriptomic profiles with mechanical cues, mechanogenomics can reveal how force transmission through the integrin-cytoskeleton-nucleus axis reshapes chromatin organization and mechanosensitive transcriptional programs[124]. Single-cell and spatial transcriptomic approaches further enable the identification of heterogeneous cellular responses to mechanical cues such as compression and matrix stiffness[125-127]. Spatial transcriptomics combined with microscopic finite element analysis has linked local strain fields with regional gene-expression changes during fracture healing, providing a framework for identifying mechanosensitive targets in regenerative environments[127]. These approaches may therefore help map force-responsive regulatory networks and identify new therapeutic targets for mechanomedicine.

Clustered regularly interspaced short palindromic repeats (CRISPR)-Cas9 gene-editing technologies provide additional tools for investigating the functional roles of mechanosensitive genes[128-130]. Mechanosensitive regulators such as Piezo1 and YAP/TAZ represent potential targets for studying how alterations in mechanotransduction influence cardiovascular disease and cancer[131]. A magnetogenetic CRISPR platform using Piezo1-mediated mechanotransduction has further demonstrated remote Cas9 activation in cellular and *ex vivo* settings[132], providing proof-of-concept for integrating mechanical regulation with gene editing. However, these approaches remain largely experimental, and their therapeutic translation will require further evaluation of specificity, safety, and *in vivo* efficacy.

Wearable mechanical sensors and digital health platforms provide another route for translating mechanomedicine into longitudinal patient monitoring. Flexible piezoresistive, piezoelectric, capacitive, triboelectric, and optical sensors can continuously monitor parameters such as joint movement, tissue strain, pressure, and muscle activity during daily activities and rehabilitation[133-135]. Such devices may support the objective assessment of mechanical loading, muscle deformation, joint torque, and fatigue, while providing real-time feedback for rehabilitation and chronic disease management. Nevertheless, differences in sensor accuracy, placement, calibration, and data interpretation remain important barriers to routine clinical implementation.

Together, these emerging technologies address complementary components of precision mechanomedicine: AI enables integration and prediction, mechanogenomics facilitates identification of force-responsive molecular networks, gene editing provides tools for functional validation and targeted manipulation, and wearable sensors enable continuous mechanical monitoring. Their integration may ultimately support a transition from empirical mechanical interventions toward quantitative, patient-specific, and feedback-guided mechanomedicine.

5. Conclusion

Mechanomedicine provides a broad framework for translating mechanical principles and mechanobiological knowledge into diagnostic, therapeutic, and regenerative applications. Current evidence supports its potential across multiple disease settings and regenerative contexts, although the level of clinical validation varies considerably among different approaches. A clearer distinction between direct mechanical interventions and mechanotransduction-based strategies, together with careful evaluation of their translational status, is important for defining the scope and clinical relevance of the field. Mechanomedicine may also offer new perspectives for cytotherapy, regenerative medicine, and age-related changes in tissue repair and regenerative capacity.

Further progress will require better definition of mechanical dose and therapeutic windows, standardized methods for measuring mechanical biomarkers, and more rigorous clinical validation. Disease stage, tissue condition, and individual variability should also be considered when designing and interpreting mechanical interventions. Advances in artificial intelligence, mechanogenomics, gene editing, and wearable sensing may improve the characterization of mechanical signals and support more quantitative and individualized strategies. These developments may help bridge mechanistic understanding and clinical translation and support the broader application of mechanomedicine.

Author Contributions

Conceptualization, supervision: Ping Zhang; investigation, writing original draft: Xinle Li; writing-review, editing, visualization: Xuetong Wang; funding acquisition: Ping Zhang, Xinle Li and Xuetong Wang.

Artificial Intelligence (AI) Statements

ChatGPT (OpenAI) was used to generate selected illustrative elements in graphical abstract and Figure 1. The conceptual framework, scientific content, labels, annotations, and overall figure layout were independently developed by the authors. All AI-generated visual elements were reviewed and integrated by the authors to ensure their consistency with the scientific content. No original research data or images were modified using AI. The authors take full responsibility for the accuracy, originality, and integrity of the manuscript and its figures.

Conflicts of Interest

All authors state that they have no conflict of interest.

Funding

This work is supported by National Natural Science Foundation of China (No. 81772405, No. 81572100, No. 81601863), Heye Health

Technology Chong Ming Project (HYCMP-2021006, HYCMP-2022016, HYCMP-2026002), and Innovation Support Project for Post-graduates in Hebei Province (No. CXZZBS2027038).

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