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A novel dual-frequency loading system for studying mechanobiology of load-bearing tissue

Chunqiu Zhang [a,b,*], Lulu Qiu [a], Lilan Gao [a], Yinjie Guan [b], Qiang Xu [a], Xizheng Zhang [a], Qian Chen [b,**]

[a] Tianjin Key Laboratory of the Design and Intelligent Control of the Advanced Mechatronical System, Tianjin University of Technology, Tianjin 300384, China
[b] Cell and Molecular Biology Laboratory, Department of Orthopaedics, Alpert Medical School of Brown University/Rhode Island Hospital, Providence, RI, USA

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ABSTRACT

In mechanobiological research, an appropriate loading system is an essential tool to mimic mechanical signals in a native environment. To achieve this goal, we have developed a novel loading system capable of applying dual-frequency loading including both a low-frequency high-amplitude loading and a high-frequency low-amplitude loading, according to the mechanical conditions experienced by bone and articular cartilage tissues. The low-frequency high-amplitude loading embodies the main force from muscular contractions and/or reaction forces while the high-frequency low-amplitude loading represents an assistant force from small muscles, ligaments and/or other tissue in order to maintain body posture during human activities. Therefore, such dual frequency loading system may reflect the natural characteristics of complex mechanical load on bone or articular cartilage than the single frequency loading often applied during current mechanobiological experiments. The dual-frequency loading system is validated by experimental tests using precision miniature plane-mirror interferometers. The dual-frequency loading results in significantly more solute transport in articular cartilage than that of the low-frequency high-amplitude loading regiment alone, as determined by quantitative fluorescence microscopy of tracer distribution in articular cartilage. Thus, the loading system can provide a new method to mimic mechanical environment in bone and cartilage, thereby revealing the in vivo mechanisms of mechanosensation, mechanotransduction and mass-transport, and improving mechanical conditioning of cartilage and/or bone constructs for tissue engineering.

1. Introduction

Mechanobiology is an emerging research field at the interface of biology and engineering. It focuses on the way that load-bearing tissues are produced, maintained and adapted by cells as an active response to biophysical stimuli in their environment [1]. The main goals of research in the field of mechanobiology are threefold: (1) to quantify or estimate the mechanical environment to which cells are subjected in health and disease, (2) to identify and quantify mechanosensitive responses and the molecular mechanisms of mechanically induced pathological conditions, and (3) to ultimately apply the knowledge obtained to the development of new therapies [2]. Mechanobiological research can produce the tools and knowledge to benefit development of medical devices, biomaterials, and engineered tissues for tissue repair and reconstruction. To achieve these goals, proper mechanical environment should be recreated at tissue and/or cellular levels. Moreover, functional tissue engineering also requires loading comparable to the in vivo mechanical environment of load-bearing tissue for tissue engineering [3].

Currently, there are various loading devices which provide mechanical stimulus mimicking gravitational and muscular force particularly for musculoskeletal tissues. For load-bearing tissues of bone and articular cartilage, there are different types of mechanical devices at organ, tissue and/or cellular levels. The mechanical stimuli includes direct compression [4–8], tension [9,10], shear [11], rolling [12,13], dynamic hydrostatic pressure [14,15], centrifugal force [16] and vibration [17]. There are fluid-induced shear stress such as the perfusion systems [18–22], the spinner flask [23] and rotating vessel bioreactors [23,24,26]. Bioreactor that mimics the native mechanical conditions, have played a crucial role in recent approaches to tissue engineering, providing an environment that promotes efficient cell seeding, nutrient and

* Correspondence to: C. Zhang, Tianjin Key Laboratory of the Design and Intelligent Control of the Advanced Mechatronical System, Tianjin University of Technology, Tianjin 300384, China.
** Corresponding author.
E-mail addresses: zhang_chunqiu@126.com (C. Zhang), Qian_chen@brown.edu (Q. Chen).

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waste transport, and essential physical stimuli [25]. A combination of two or more mechanical stimuli can also be used to improve the mechanical conditions in order to mimic the in vivo mechanical environment that tissues experience [27–31]. A biaxial mechanical loading bioreactor for tissue engineering can produce different frequency and amplitude of both shear and compression simultaneously [29]. The bioreactor system for load- and perfusion-controlled tissue engineering of chondrocyte-constructs also can be used [28]. Over the past decade, the development of functional tissue engineering is deeply rooted in the challenges and questions of the role of mechanobiology in tissue engineering.

Dynamic compression, a stimulus with strains from 0.1 to 25% at frequencies ranging from 0.0001 to 3 Hz [23], has produced significantly better results than many other types of mechanical stimuli for cartilage tissue engineering [3,19,23,30,32,33]. However, when the human body performs daily activities such as walking, bone tissue is subjected to the low-frequency high-amplitude loading [2,3,27,32,34], and at the same time, muscle are imposing high-frequency low-amplitude loading on bone in order to maintain body posture [17,34–36]. The normal strain measured on bone surfaces are in the range between approximately 400 and 3000 μ strain across many animal species at 0–3 Hz [3]. The high-frequency low-amplitude loading normally occurs at about a range of 6-90 Hz with 0–10 μ strain though there are different ranges from the low-frequency high-amplitude loading [34–36]. Therefore, from the perspective of bionics, the kind of loading of low-frequency high amplitude superimposing high-frequency low-amplitude loading, may be more suited to the needs of mechanobiology research in bone and cartilage or their tissue engineered constructs.

In this study, according to the loading characteristics of the human knee joint, we designed, validated, and tested a novel dual-frequency loading system. This loading system may facilitate further study and development of tissue constructs of artificial articular cartilage and bone.

2. Methods

2.1. Overall description

The dual-frequency loading system comprises two parts: a loading structure and a control component including computer and electric source. Its function includes the low-frequency high-amplitude control system based on cam and the high-frequency low-amplitude control system based on piezoceramics. The loading structure with the culture

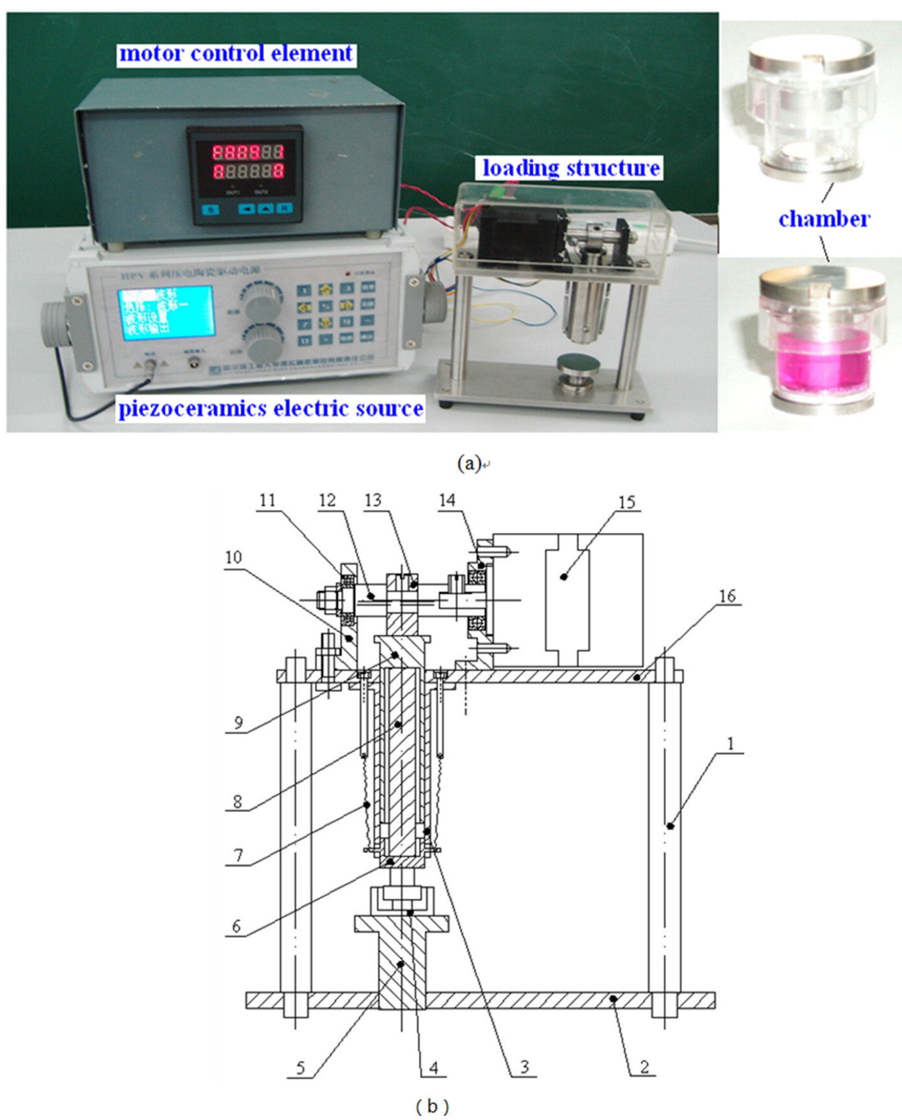

Fig. 1. The dual-frequency loading system. (a) The photograph of loading system with culturing chambers (one is empty, the other contains a scaffold culturing in culture medium). (b) Overall design of loading structure. 1 column, 2 floor, 3 sleeve, 4 culture chamber, 5 tables, 6 down-tappet blocks, 7 return spring, 8 piezoelectrics, 9 upper-tappet , 10 left side of the support plate, 11 rolling bearing, 12 eccentric shaft, 13 eccentric cam, 14 right side of the support plate, 15 stepping motor, 16 top plate.