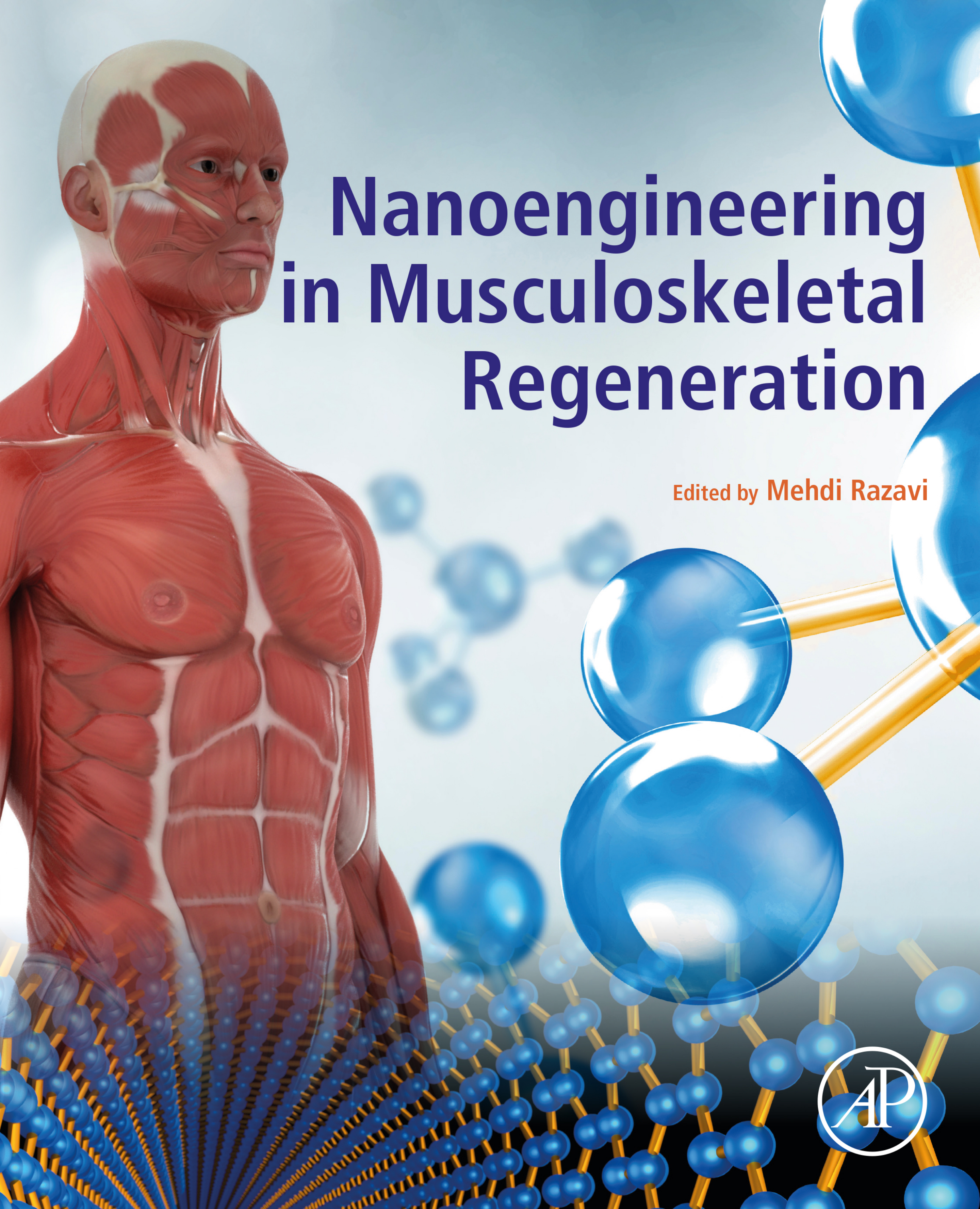

Nanoengineering in Musculoskeletal Regeneration

Edited by Mehdi Razavi

NANOENGINEERING IN MUSCULOSKELETAL REGENERATION

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Preface

Musculoskeletal degeneration and complications from injuries have become more prevalent as people live longer and increasingly participate in rigorous athletic and recreational activities. Additionally, defects in skeletal tissues may immobilize people and cause inflammation and pain. There is therefore a tremendous need for new strategies to promote the regeneration of musculoskeletal tissues, due to the large number of patients suffering from disease or trauma to these tissues. Regenerative medicine focuses on using stem cell biology to advance medical therapies for devastating disorders. In this area, musculoskeletal regenerative medicine provides solutions to repair, restore, or replace skeletal elements and associated tissues that are affected by acute injury, chronic degeneration, genetic dysfunction, and cancer-related defects. *Musculoskeletal Regenerative Nanomedicine* book provides a basic level of understanding of important areas related to the application of nanotechnology in musculoskeletal regenerative medicine, starting from key nanobiomaterials, nanoscaffolds and surface nanopatterns, technology transfer aspects that include testing both in vitro and in vivo, and stem cell nanoengineering. A discussion of the potential benefit of nanotechnology for future research has also been presented. The ultimate goal of this book is to give an updated summary of therapeutic pipeline from biomedical discovery to clinical implementation, improving treatments for patients with conditions of the muscles, tendons, cartilage, meniscus, and bone. We hope by combining existing knowledge with new discoveries, this book can suggest innovative treatments to basic scientists or clinicians working on the gamut of musculoskeletal disorders. This book is a reference book for undergraduate and graduate courses, bioengineers, materials engineers, medical students, and clinical laboratories. Content includes basic, translational, and clinical researches addressing musculoskeletal repair and regeneration for the treatment of diseases and injuries of the skeleton and its associated tissues. Finally the efforts of all the contributors and the publisher are appreciated.

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CHAPTER

1

Challenges toward musculoskeletal injuries and diseases

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1 Musculoskeletal system

Musculoskeletal system is mainly used for exercise and functional physical tasks, as well as mechanical support and protection of body organs. It is composed of skeleton that is composed of bone, joint, and skeletal muscle of exercise joint (Fig. 1) [2]. This chapter will discuss the biological characteristics of musculoskeletal tissue and its damage and summarize the common musculoskeletal diseases in various body parts. Finally, it will introduce the application of orthopedic implants in the treatment of musculoskeletal diseases.

1.1 Skeletal system

The skeletal system is one of the organ systems of vertebrates, including the body's cartilage, bone, and bone connection [3]. It is derived from the proliferation and differentiation of mesenchymal cells, which are derived from mesoderm. Its function is to support and protect the body, make red and white blood cells, and store minerals. Bones are made up of various shapes and have complex internal and external structures, which can reduce weight and keep hard at the same time. One of the components of bone is mineralized bone tissue, which is a hard honeycomb-like solid structure inside. Other tissues of bone include bone marrow, periosteum, nerves, blood vessels, and cartilage. The human skeleton has the function of supporting the body, in which both the hard bone tissue and the cartilage tissue are part of the human connective tissue (while the hard bone is the only one of the connective tissue with relatively hard intercellular substance). There are 206 bones in adults and 213 in children. For

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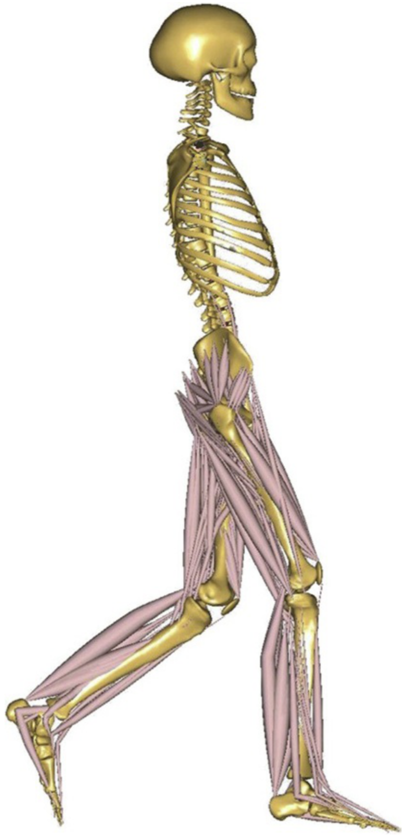

FIG. 1 Lower limb part model of musculoskeletal system, including the hip, knee, and ankle joints and 318 muscles [1]. *With permission from Yubo F. Lower limb joint motion and muscle force in treadmill and over-ground exercise, under Creative Commons Attribution (CCA) 4.0, copyright 2019.*

example, the skulls will heal with age, so it is normal for adults to have one or two less or one or two more skeletons [4].

1.1.1 Cartilage

Cartilage is the prerequisite tissue for the development of many bones in the fetus [5]. In adult bones, it exists almost between all bones. Cartilage is a kind of flexible connective tissue that can be weighed. Except for the bone support under the joint surface and the synovium cover on the joint surface, the rest of cartilage is wrapped by fibrocartilage. In new and young bodies, cartilage has rapid growth capacity. It is mainly divided into three categories: muscle cartilage, white fibrocartilage, and yellow elastic cartilage, which are composed of chondrocytes and extracellular matrix rich in collagen and elastic fibers. Cartilage is usually avascular, is formed in the embryonic mesenchyme, and grows through substance and sedimentary matrices [6].

1.1.2 Bone

Bone is a kind of strong and rigid connective tissue that ensures the body can move fast on land. Its strength provides support and protection for the body, and its rigidity makes its joint surface not twisted under load and keeps its shape accurate and ensures a strong number of muscles in rapid limb movement without bending the bone. Unlike cartilage, the bone is a vascular tissue with high cell density, which can adapt to the changing mechanical requirements and regeneration after injury [5]. The living bone is white, which includes the compact bone or cortical bone outside and the spongy bone or trabecular bone with honeycomb structure inside. In general, tendons attach to rough bone surfaces. Muscle fibers do not connect directly to periosteum or bone. The transmission of force is through the connective tissue to load and package all muscles. Bone generally contains mineralized extracellular matrix collagen, which embeds a series of specialized cells, including osteoblasts, osteoclasts, and osteoclasts. Most of the bone is formed through the process of osteogenesis in cartilage, that is, the preformed cartilage membrane defines the initial shape and position of bone, and cartilage is replaced by bone in a regular order [7].

1.1.3 Articulation

An articulation is an adjacent and connective area between two or more bones. These bonds are supported by a series of soft tissues, and their basic function is to help grow or facilitate the movement between bones. These connections include fibrous joint, cartilaginous connection, and synostosis [8].

1.2 Muscle

Muscles are made up of muscle cells. Actin, myosin, and related proteins are overflowing in muscle cells, almost filling the whole cell. They are mainly arranged in one direction and interact to form a linear contraction of the whole cell at the molecular level. Contractile muscle cells assemble into muscles, which convert chemical energy into mechanical work. Muscle force can move limbs; muscle tissue accounts for 40%–50% of body weight.

Humans have about 639 muscles. According to the different structure and function, it can be divided into smooth muscle, cardiac muscle, and skeletal muscle. Skeletal muscle and cardiac muscle are also called striated muscle because their actin and myosin are combined into regular repeating units, which make the cells present the appearance of fine striations that can be observed under the microscope. Smooth muscle contraction speed is very slow, but it is never tired; while striated muscle contraction speed is very fast, but it is easy to produce burnout. As for the cardiac muscle, not only it can contract rapidly, but also it can never be tired. It is a very strong muscle, so it can make the heart beat continuously until the end of life. Among them the skeletal muscle accounts for 40%–45% of the total body mass, which is the dynamic part of the exercise system. It is divided into white and red muscle fibers. The white muscle contracts or stretches rapidly depending on rapid chemical reaction, while the red muscle relies on continuous oxygen supply. It transforms the chemical energy produced by food intake into the production of mechanical force, which helps the basic functions of the body, such as the production of calories; the regulation of blood sugar; and the storage of lipids, carbohydrates, and amino acids. The structure of muscle is muscle → muscle bundle → muscle fiber (muscle cell) → myofibril → sarcomere (actin and myosin) [9].

1.3 Tendons

Muscles are usually attached to bones with strong tendons, the fibers of which branch deep in the abdomen. Tendons are composed of bundles of collagen, which in turn form larger bundles. They are usually covered with synovial tissue, which soaks tendons in a thin layer of aponeurosis fluid for lubrication and nutrient delivery. Others are only covered by dense sheaths of connective tissue called peritoneum proteins. Most muscle strains occur at myotendinous junction. These may be near the end of the muscle's abdomen, where it tapers down to become the main tendon tissue, or along the tendon fibers into the muscle interior. Tendons are usually damaged at the attachment [10] of bone and in particularly high stress areas (i.e., they wrap around bone protrusions) or in areas with low blood vessels (such as the middle substance of Achilles tendon) [11].

1.4 Ligament

Ligament connects bone to bone. In the process, they form joint capsules that provide stability and help to save energy. For example, the lateral branch of the knee joint, which is firm and minimum elastic, provides structural stability. And the ligament of the shoulder joint capsule (scapula and humerus), which is thin and flexible, allows a wide range of motion. The iliofemoral (Y) ligament provides support when standing, thus reducing muscle activity. It controls the external rotation during flexion and the internal and external rotation during extension. This stores energy when the hip joint is straightened for a more efficient gait [12].

2 Musculoskeletal injuries

2.1 Work-related musculoskeletal disorders (WMSD)

Musculoskeletal injuries are often referred to as work-related musculoskeletal disorders (WMSD), which means the injuries of muscles, bones, nerves, and other systems (Fig. 2) caused by long-term stress, repetitive operation, poor posture, static load, heavy lifting, heavy physical labor and vibration, unreasonable labor organization process, and adverse social and psychological factors in professional activities. WMSD, characterized by pain, discomfort, and limited movement, are mainly manifested as pain; rigidity; spasm; and numbness in the lower back, shoulder, neck, forearm, and hand. The most common WMSD are low back pain (LBP), neck-shoulder-wrist syndrome (CTS), and carpal tunnel syndrome (CTS).

WMSD has been listed as an occupational disease by the International Labor Organization (ILO) since 1960. At present the countries and regions that listed the diseases in the list of occupational diseases mainly include the United States, the United Kingdom, Germany, the Netherlands, Sweden, Argentina, Brazil, Italy, Portugal, Romania, Hong Kong, and China. ILO has listed eight kinds of diseases, including tenosynovitis of neck of radius, chronic tenosynovitis of wrist, olecranon bursitis of elbow, prepatellar bursitis, epicondylitis, meniscus injury, CTS, and musculoskeletal system diseases not mentioned earlier in the latest list of international occupational diseases in 2010 [14].