

Advances in Experimental Medicine and Biology 881

Luiz E. Bertassoni
Paulo G. Coelho *Editors*

Engineering Mineralized and Load Bearing Tissues

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Engineering Mineralized and Load Bearing Tissues

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Preface: Engineering Mineralized and Load-Bearing Tissues: Progress and Challenges

From cartilage and bones, which enable body growth, calcium storage, and a range of hematopoietic functions, all the way to teeth and ligaments, which are elegantly structured to bear a range of functional loads in the most diverse conditions, mineralized and load-bearing tissues represent a unique category of biological materials that perform a range of critical functions in the human body.

Treatment of diseases and injuries associated with these tissues results in a yearly financial burden of hundreds of billions of dollars worldwide. Tissue engineering has emerged as an exciting alternative for the treatment of these conditions. By bringing together principles of life sciences, biology, engineering, and clinical medicine and dentistry, the regeneration of mineralized and load-bearing tissues has gradually become a clinical reality.

Recent research has shown that the regeneration of truly biomimetic, clinically relevant, and functional load-bearing tissues will only be achieved through a complex combination of novel biomanufacturing methods, smart engineering solutions, supported by solid biological foundations. This book carefully outlines each of these individual aspects to offer a comprehensive overview of recent progresses and challenges toward effective regeneration of functional tissues, including the bone, cartilage, dentin, enamel, cementum, and periodontal ligament.

We present recent progress on the fabrication of load-bearing tissues using emerging biomanufacturing methods. Jeong and Atala provide a comprehensive overview of 3D printing strategies focusing primarily on the fabrication of bone and cartilage tissue constructs. Prof Nikkhah and Maas cover recent developments relative to lithography-based microfabrication of cell-laden hydrogels. In Chap. 3, Araujo et al. offer their insights into the synthesis of bioinspired polymeric nanofibrils for the regeneration of cartilage, bone, and dental structures. Combined, these emerging methods have changed the landscape of regenerative medicine in recent years. For instance, these methods have enabled recent strategies which are primarily focused on the fabrication of 3D tissue constructs, with more clinically relevant dimensions, which is a substantial development from earlier methods relying on thin scaffolds and cells seeded on planar 2D culture substrates.

In the second part of this book, applied strategies for bone, cartilage, and dental regeneration are presented. Clinical and surgical challenges associated with regeneration of oral and maxillofacial tissues are described by Young et al. Recent attempts to engineer pre-vascularized bone scaffolds are

reviewed by Bertassoni and colleagues, while osteointegration of implants via unique healing pathways is discussed by Coelho et al. in Chap. 7. Exciting methods to chemically synthesize cell-laden hydrogels functionalized or conjugated with bone morphogenic peptides are presented by Jabbari and his group. Arguably, these latter methods represent the future of smart polymeric delivery platforms for tissue regeneration, which take advantage of bioinspired growth factors in ECM-mimetic 3D microenvironments for functional tissue engineering. A similar pathway is explored by George and co-workers, who focus their attention on dentin matrix proteins and their role in bone mineralization and regeneration.

Exploring the interface between the mechanics of load-bearing tissues and approaches to regenerate them, Armitage and Oyen offer a unique perspective of the challenges associated with engineering stiff and tough tissues, such as the ligament and bone, while using comparatively soft and brittle scaffold materials, such as hydrogels and ceramics, respectively. Correia, Reis, and Mano present recent strategies for the regeneration of cartilage using multiphase, multistructured, and hierarchical scaffolds, which appear as a highly effective method for fabrication of multilevel hierarchical tissues, such as the cartilage and bone. In a more focused review, Deghani's group address current challenges and regenerative treatments for injuries of the anterior cruciate ligament.

In a separate section, the regeneration of dental tissues is comprehensively covered by Bartold and colleagues, Tsuji's group, and Prof. Uskokovic, who address recent progress and challenges toward effective cementum and periodontal ligament regeneration, enamel tissue engineering, and, lastly, whole tooth regeneration as a future dental treatment, respectively.

Overall this book brings together researchers from diverse backgrounds, from materials science, engineering, and biology to clinical medicine and dentistry, to discuss various aspects of mineralized and load-bearing tissue engineering. We argue that this collection of manuscripts will represent a unique platform stimulating progress toward the regeneration of functional mineralized and load-bearing tissues on the lab bench and facilitate the translation of these strategies into a clinical reality in the near future.

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Engineering Mineralized and Load Bearing Tissues

Scope, Target Audience and Highlights

Mineralized and load-bearing tissues represent some of the most important structural entities in the animal kingdom. They provide shape to all individuals, enabling foremost steps in evolution, such as gait, nutrition, development, and immune response. Diseases related to load-bearing tissues yield an annual economic burden of over \$20 billion/year in America, a cost that is expected to quadruple with an increase in the aging population. A large part of such conditions involve load-bearing bone, cartilage, and/or dental structures requiring assisted repair. Tissue engineering has long held great promises as improved treatment options for these conditions. Tremendous progress has been achieved in the last decade; these have included successful strategies in materials sciences, biology, engineering, and, most importantly, the interface among these fields. Here, we aim to address recent developments in engineering of fully functional mineralized and load-bearing tissues. We envision this will represent a valuable reference for researchers in their endeavors to fabricate biomimetic load-bearing tissues. Similarly, by bringing together high-caliber scientists from bone, cartilage, and dental fields – integrating backgrounds in materials sciences, engineering, biology, mechanics, fluidics, etc. – we will provide a unique platform to facilitate the functional regeneration of mineralized and load-bearing tissues.

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