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Perspective

The Role of Biomechanics in Tissue Engineering

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Introduction

In the 80's tissue engineering and regenerative medicine emerged as scientific fields with a massive potential to understand the complexity inherent to the biological tissues [1]. Bridging the gap between tissue anatomy with its physiology is a paramount challenge to be solved and one of the main goals in biomechanics is to explore functional biological problems using the principles of mechanics. The United States National Committee on Biomechanics formed a subcommittee to study the principles of functional tissue engineering arguing that the biomechanical properties of the implants are critical to their proper function *in vivo*, [2]. It became clear that the field of tissue engineering needs to establish functional criteria to help the design and manufacturing for tissue repairs and replacements. Nowadays, we have several research groups spread worldwide trying to develop constructs that could mimic native tissues. Due to its nature, they gathers scientists, engineers and physicians in multidisciplinary teams using a variety of fields to construct tailored biological substitutes [3].

A Multidisciplinary Team for a Multidisciplinary Problem

Under a first look, biological tissues may seem a simple type of tissue, but its complex organization makes it a major challenge for its repair and regeneration. For instance, cartilage is a both strong and flexible type of connective tissue of the body. It is a dynamic and responsive tissue with low metabolic activity and relatively poor ability to heal. Additionally, there is no vascularization in cartilage to support the chondrocytes with nutrients. Thus, nutrients must diffuse through different layers in order to produce large amounts of extracellular matrix. In fact, the complete repair of damaged cartilage is a nowadays difficult procedure [4].

Cartilage is a biological tissue with a huge complexity, which is present in the human body in three types: hyaline cartilage, fibrocartilage and elastic cartilage [5]. Apart to some resemblances, these types are quite different and play unlike roles for human functionality. For instance, the hyaline cartilage, also known as articular cartilage, has a major role in providing joints with a surface that combines low friction with high lubrication [6]. On the other hand, fibrocartilage (e.g. in the temporomandibular joint disc) spreads the intra-articular load, stabilizes the joints during translation and decreases the wear of the articular surface [7]. Even though, getting a deeper knowledge on cartilage characterization and understanding, bridging the gap between anatomy and physiology, may lead the way for better implants aiming cartilage repair and regeneration. This is of even more interest as cartilage is an avascular tissue of the human body, hence with an extremely low capability for tissue regeneration [5]. However, this ground-breaking issue can only be successfully achieved with the establishment of multidisciplinary research teams.

These multidisciplinary research teams are mandatory for a multidisciplinary scientific field like tissue engineering. Thus, research teams can apply a wide variety of methodologies and provide suitable inputs for its development. Being the major goal to produce biological substitutes to restore, maintain or improve tissue function, using biocompatible and biodegradable support structures, i.e. scaffolds, in conjunction with human cells, researchers have been interested on developing alternative approaches for restoring functionality. For instance, the creation of constructs with a structure and composition resembling native cartilage and yielding similar mechanical behavior [8]. To do so, one of the most promising methodologies involves the use of Additive Manufacturing (AM) processes. AM technologies allow the production of complex 3D structures with a high level of control, predefined geometry, size and interconnected pores, in a reproducible way. This controlled organization enhances the combination of biomaterials throughout the whole structure, providing an suitable biomechanical environment for tissue regeneration [9].

The Role of Biomechanics

Overlapping the mentioned issues, constructed implants must be validated alongside with *in vivo* results for clinical applications. However, the amount of research that focus in the in vitro analysis is way higher than the long-lasting *in vivo* regeneration, even though, several methodologies can be used to examine the recovery of movements after tissue regeneration, for instance of the nerve [10]. In fact, when in vitro systems cannot provide a reproducible approximation of the real-life *in vivo* or clinical setting, *in vivo* models (i.e., animal models) are required [11]. Although several studies have used animal models to evaluate bone, cartilage, nerve or muscle regeneration, we are far from having a full understanding of relationship between the load-bearing, muscle actions and resultant movement. Complementarily, biomaterials should be designed based to mimic the native tissue, thus, comprising several criteria as mechanical behavior and biological performance.

One of the common procedures for examining tissue regeneration in the animal model is through the movement analysis. Bearing in mind the different fields of biomechanical evaluation, the kinematical analysis is a non-invasive, low-cost and fast-forward methodology that provides important outputs from the resultant movement [10]. Furthermore, it may be used to infer about the kinetics via inverse kinematics. However, some considerations should be taken: (i) researchers should look up for 3D analysis instead of 2D; (ii) alongside

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with time comes morphological changes (e.g. weight) in the animal that should be considered in repeated measures; (iii) bilateral analysis must be considered to identify possible mechanisms of compensation in the non-injured limb.

Concluding, tissue engineering and regenerative medicine may have huge benefits in having multidisciplinary teams. That exchange of knowledge regarding the mechanics, biology, veterinary, health sciences, etc… may lead to a place where function becomes more important than structure, and ultimately a step closer to clinical translation.

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