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REVIEW ARTICLE

3-D bioprinting technologies in tissue engineering and regenerative medicine: Current and future trends

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Abstract Advances in three-dimensional (3D) printing have increased feasibility towards the synthesis of living tissues. Known as 3D bioprinting, this technology involves the precise layering of cells, biologic scaffolds, and growth factors with the goal of creating bioidentical tissue for a variety of uses. Early successes have demonstrated distinct advantages over conventional tissue engineering strategies. Not surprisingly, there are current challenges to address before 3D bioprinting becomes clinically relevant. Here we provide an overview of 3D bioprinting technology and discuss key advances, clinical applications, and current limitations. While 3D bioprinting is a relatively novel tissue engineering strategy, it holds great potential to play a key role in personalized medicine.

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Introduction

Advances in computer-aided design (CAD) and fabrication technologies have brought rapid progress to the field of three-dimensional (3D) printing in recent years. Also known as additive manufacturing (AM), rapid prototyping (RP), and free form fabrication (FFF), 3D printing was initially conceived by Charles Hull in 1986.[1,2] Hull's concept was based on the idea that successive layers of a base material could be applied on top of each other to 'print' objects. Since its inception, 3D printing has impacted several fields including engineering, manufacturing, and medicine. In recent years, the development of biocompatible systems for 3D printing have been especially promising for tissue engineering applications. The field of tissue engineering has conventionally involved culturing cells, seeding them into biocompatible scaffolds, and allowing growth and maturation (in vitro or via bioreactor) to form the desired tissues.[3] We use the term 3D bioprinting to describe the precise layering of cells, biologic scaffolds, and biologic factors with the goal of recapitulating a biologic tissue. Compared to traditional tissue engineering methods, the technologies utilized by 3D bioprinting systems allow for greater precision in the spatial relationship between the individual elements of the desired tissue. 3D bioprinting holds great promise for regenerative medicine applications (see Fig. 1).

General approaches

Three central approaches to bioprinting are biomimicry, autonomous self-assembly, and a microtissue-based method. These general strategies are not exclusive to bioprinting and are broadly applied to many investigational areas within the larger scope of regenerative medicine. In many cases, these are used for tissue engineering applications unrelated to bioprinting. However, a discussion of these fundamental strategies is necessary when considering the optimal approach to bioprinting objectives. Each of these may applied to specific bioprinting applications to varying degrees based on factors such as target tissue type, user experience, and printing method. It is not uncommon to combine strategies for more complex tissue types.[1] We discuss each of these in detail below.

Biomimicry

With the understanding that function will follow form, a biomimetic approach attempts to engineer each individual component of native tissue. While it is the most conceptually straightforward approach, it is extremely difficult to reproduce all elements that make up the milieu of a given target tissue. Even for relatively simple tissue types, the sheer volume and dynamic nature of cellular interactions that occur reach staggering complexity. In addition to the numerous cell types, signaling molecules, and structural elements within the tissue itself, all environmental factors including pressure, temperature, and electrical forces must be considered.[4,5] As tissues become more complex, the 3D structure and resultant mechanical forces add yet more complexity.

There are several ways that these complexities are minimized when utilizing a biomimetic approach to bioprinting project design. The selection of an appropriate scaffold material is crucial. An optimal scaffold can closely approximate many of the structural and mechanical requirements of a target tissue. Scaffold choice also heavily influences signaling through cellular interactions with the extracellular matrix component (ECM).[5] The use of bioreactors to regulate environmental parameters is also critical to successful biomimicry. Bioreactors essentially create an environment or a set of microenvironments that mimic that of the target tissue.[3] Depending on specific needs, a bioreactor can regulate any combination of chemical, mechanical, and electrical variables.[5] These variables may also change over time to create an appropriately dynamic environment that allows for sequential

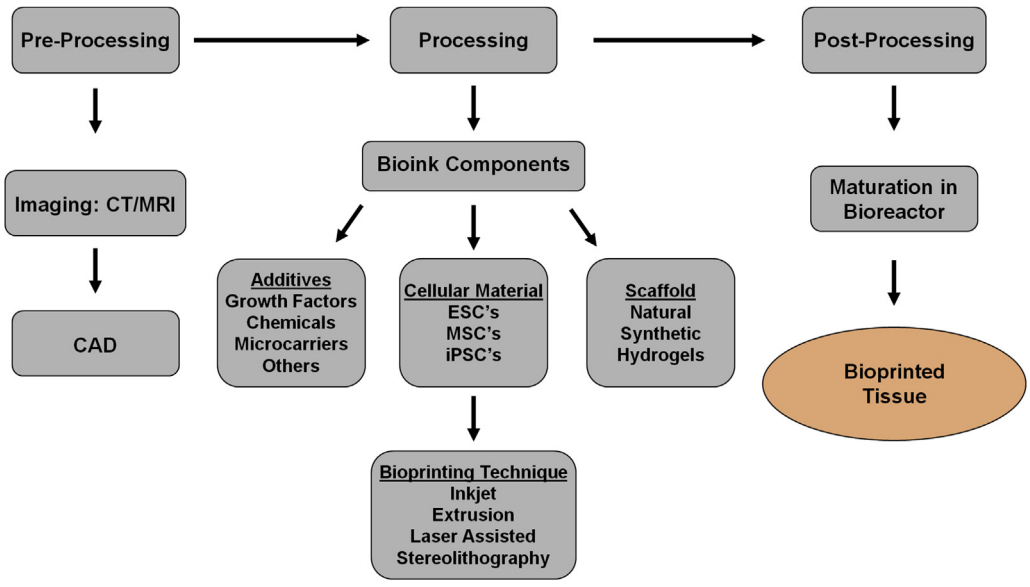

Figure 1 Bioprinting overview schematic.

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