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# Development in additive printing for tissue-engineered bone and tendon regeneration

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**Abstract**

Additive printing, commonly known as additive manufacturing, presents transformative potential over conventional scaffold manufacturing methods in the repair of musculoskeletal tissues. With its ability to create complex geometries and microarchitectures that mimic tissue complexity, additive printing can offer various innovative methods for successful patient-specific tissue engineering applications. Here, we review the development in additive printing of the musculoskeletal tissues, in particular, bone and tendon tissue engineering. Promising technologies including (1) light-assisted-based, (2) nozzle-based, and (3) printer-based system, and materials which are involved in additive printing of bone and tendon tissues, will be presented. Lastly, a discussion of the future direction in this field is also provided.

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## Introduction

The musculoskeletal system is an organ system that provides the framework, support, stability, and movement to the human body, playing a pivotal role in our daily function. Among the musculoskeletal tissues, fractured bones and damaged tendons are the most common hard and soft tissue injuries, which account for ∼1,600,000 [1] and ∼800,000 [2] surgical treatments, respectively in the USA each year. When musculoskeletal defects are caused by disease or trauma and failed to heal on their own, transplant with autologous grafts obtained from the individual is required to regain its function. Despite being the gold standard, there are several disadvantages associated with autogenous grafts, for example in bone and tendon reconstruction, the additional surgical site, donor site morbidity, insufficient volume of bone and relative scarcity of tendon.

Musculoskeletal tissue reconstruction using synthetic materials is a promising alternative, but its usage is hindered by conventional manufacturing methods. Over the years, additive printing, commonly known as additive manufacturing, has been applied to tailor materials potentially for biomedical applications. With its ability to create complex geometries and microarchitectures that mimic tissue complexity, additive printing has offered many innovative methods for successful patient-specific tissue engineering applications [3–5]. Hence, this has led to the flourishing of research works in additive printing for musculoskeletal tissues. Here, we review the recent progress in additive printing of musculoskeletal tissues, in particularly, tendon and bone tissue engineering. Lastly, a discussion of the future direction of this field is provided.

## Basic elements of additive printing in biomedical engineering

Being a tool-free fabrication method, additive printing has versatile applicability in biomedical engineering due to having good control of the internal and external architectures of the fabricated product, in meeting the requirement of materials processing for scaffold fabrication. Based on the multiple digital cross-sections converted from computer aided design, the machine uses them as the guidelines to lay down successive layers of suitable material, which are selectively bonded at every layer to build precise and pre-defined scaffold. Depending on the machine and material used or the way that the binding or building material is deposited on the build bed, scaffold with different properties can be fabricated. As such, additive printing is determined by two important elements – technology and material that function alongside in shaping the scaffold.

## Technology

Despite sharing a common layer-by-layer deposition process concept, additive printing has evolved from a variety of technologies employing different process mechanics, which vary according to the material used and bonding mechanism to achieve specific outcome in biomedical engineering field (Figure 1) [6].

Different additive manufacturing processes build and consolidate layers of materials in different manners. Depending on the layer deposition and bonding of materials, process mechanics that are engaged in different technologies for bone and tendon tissue engineering are briefly summarized in three categories: (1) light-assisted-based, (2) nozzle-based, and (3) printer-based system.

Selective laser sintering/melting (SLS/SLM) and stereolithography apparatus (SLA) fall under the category of light-assisted-based system. SLS and SLM use thermal energy from laser to melt the polymer or sinter the metallic powder selectively within a powder bed, causing them to undergo a thermal transition in fixing the shape [7]. Powder bed is lowered by one layer thickness to allow the sequential building of the three-dimensional (3D) object layer by layer. Similarly, SLA uses ultraviolet light to realize the curing of the exposed material [8].

Nozzle-based system includes fused deposition modeling (FDM) and electrohydrodynamics jetting (E-jetting). Despite both techniques utilize nozzle to produce the material in filament form, material in FDM and E-jetting passes through the nozzle differently. The material is heated slightly above its melting point and gets extruded with the help of a pneumatic pump for FDM [9] whilst material is being pulled out by an electric field for E-jetting [10]. Each filament layer cures quickly and bonds with the surrounding material, of which each layer is piled on the previous layer, with the previous layer acting as the role of positioning and supporting [11].

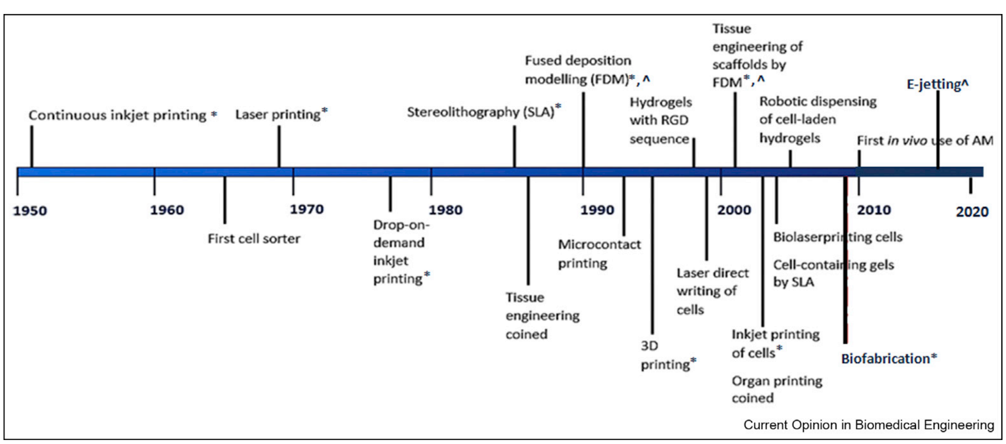
Printer-based system consists of three-dimensional printing (3DP) and inkjet printing. Instead using laser beam, 3DP uses a printhead to apply droplets of binder or solvent onto a powdered bed of ceramics or polymer to fuse the particles [12]. Binder or solvent are selectively deposited on the powdered bed, thereafter a new layer of powder is placed on top the previous one via a roller, and the platform holding powdered bed is lowered. The unbound powder in each layer provides support for the object being built. All these steps are repeated until the 3D object is finally built, and final 3D object is retrieved by depowdering the loose powders. On the other hand, inkjet printing uses a printhead that deposits droplets of material directly in a drop-on-demand or continuous manner, of which the construct is built up by the deposited material itself.

## Material

At the beginning of printing era, additive printing technology only uses resin and polymers for the design of models. As the technology for fabricating customized biomaterials and tissues has advanced, the range of materials has now expanded to include ceramics, and metals, which have high melting points that are difficult to prototype. Nevertheless, the selection of materials used for different technologies will still be dependent on the process mechanics.

Liquid photosensitive materials are required as the cured material for SLA, and these include low-molecular weight polyacrylates, epoxy macromers or monomers, hydrogels [13]. SLS and SLM have a wider selection of materials that ranges from thermoplastic, ceramics,

**Figure 1**




Evolution of additive printing technologies. * used for bone tissue engineering, ^ used for tendon tissue engineering (Figure is adapted with permission from [6]).