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# 3d-printing applications in bone fabrication: a review

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## ABSTRACT

Bone scaffolding is an alternative solution to bone therapy, which is currently being developed in tissue engineering. This effort aims to produce a bone scaffold with a shape and specification according to bone therapy's needs. 3D printing is a scaffold fabrication method with promising prospects because it can produce scaffolding with physical characteristics as needed, both pore and physical. The method used in this article is a formal review to review various national and international literature using articles from 2000 to 2020 with the keywords "scaffold," "3D-printing", "bone," and "natural sources." The results of this article present various aspects regarding the use of 3D printing for scaffolding. Some aspects that are considered are how 3D printing works, the type of material used, and the scaffold's characteristics. It aims to get a clearer picture of the use of 3D printing, both its prospects/potential, application challenges, and future developments.

Keywords: 3D-printing, bone, scaffolding

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## INTRODUCTION

Bone scaffolding is an alternative solution to bone therapy, which is currently being developed in tissue engineering. The scaffold has various advantages over conventional bone therapy solutions such as allografts and autografts, which are prone to donor scarcity.

In addition to the aspects of the type of material used that must be biocompatible, an essential factor that must be considered in the fabrication of bone scaffolding is related to the morphology and structure of the scaffold produced (Castilho, *et al.*, 2014). According to Karageorgiou & Kaplan (2005), a suitable scaffold must have a pore size between 100–800 µm, because the exchange of nutrients and cell growth is highly dependent on the characteristics of the pores (Karageorgiou & Kaplan, 2005). Therefore, to produce scaffolding with a good structure, various new methods such as 3D-printing have been developed. It is because conventional methods have many limitations, often resulting in inappropriate pore sizes, high interconnectivity levels, and unsuitable mechanical properties (Wüst, Müller, & Hofmann, 2011).

3D-printing technology is a technology that continues to be developed today in the fields of agriculture, health, the automotive industry, and the aerospace industry (Keleş, Blevins, & Bowman, 2017). In the health sector, 3D-printing technology has been widely applied, especially in bone scaffolding. In 1993, the concept of tissue engineering began when Larger and Vacanti published a paper describing the characteristics and applications of biodegradable 3D-scaffolding in detail (An, Teoh, Suntornnond, & Chua, 2015). Ideally, the 3D scaffold should be porous, have a very well connected pore network, and be consistent. Pore size will affect the migration and infiltration of cells associated with the bone therapy process (Loh & Choong, 2013). The scaffold's architectural design also significantly influences the mechanical sophistication and behavior of cells (Hollister, 2005). Therefore, the use of 3D-printing technology in the fabrication of bone scaffolding has various advantages, including the scaffold can be fabricated into a structure with a high degree of accuracy (through CAD-based software) so that it can adjust the shape according to the needs of the bone therapy process (Do, Khorsand, Geary, & Salem, 2015).

In this paper, we conduct a study related to essential aspects of developing 3D-printing method bone scaffolding, including how 3D-printing works, the types of materials that can be used, and the resulting scaffold's characteristics. The study aims to obtain a clearer picture regarding the use of 3D-printing for the fabrication of bone scaffolding both in light of application challenges and potential future developments.

## RESEARCH METHODS

In writing this article, the method used is a formal review to review various national and international literature by searching through google scholar. The initial phase of the search for items obtained was 54 articles from 2000 to 2020 with the keywords "scaffold", "3D-printing", "bone" and "natural sources." Then do the identification and relevance of articles for writing, namely the 3D printing applications in bone fabrication. From the initial number of searches, 27 relevant items were obtained.

## RESULTS AND DISCUSSION

### Basic Concept of 3D-Printing

3D printing technology was developed by MIT (Massachusetts Institute of Technology). 3D printing involves the deposition of successive layers through a computerized process (Do, Khorsand, Geary, & Salem, 2015). The 3D printing method, or often known as additive manufacturing, makes a three-dimensional solid object from a digital model (Hakim, Sa-

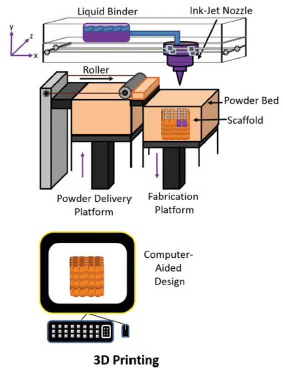


**Figure 1**. 3D-printing schematic (Do, *et al.,* 2015)

putra, Utama, & Setyoadi, 2019). Building the structure is carried out by adding layers of material layer by layer in succession (Putra & Sari, 2018). Compared to traditional machining methods, the 3D-printing method is more efficient because the product manufacturing process uses materials as needed without any final disposal processes (Hakim, Saputra, Utama, & Setyoadi, 2019). The schematic part of 3D-printing can be seen in Figure 1.

In the 3D printing process, the design is made using CAD software. After completion, the design data is entered into the CAM software and imported into 3D print for production processing (Hakim, Saputra, Utama, & Setyoadi, 2019). Meanwhile, the principles of technology in 3D-printing are divided into 2, namely:

a) The printing technique by extrusion this technique will melt the polymer binder layer by layer.

b) The printing technique with powder (binder) is almost similar to the extrusion technique. The 3D printing binder uses an inkjet nozzle to affix the material that forms the layer of the object being made. The difference from the extrusion technique, the binder technique uses two materials that will form a layer of the printed object. The material consists of dry powder and liquid glue or adhesive material (binder). The first stage of the 3D printer will be to apply a powder coating to do the printing. Then the second stage of the nozzle will apply the adhesive. This process is repeated until the object is finished printing. The binder technique is faster than the extrusion technique because less material is needed. Besides, it allows more diverse materials in the process, such as metal and ceramics, and coloring (Ikhsanto & Zainuddin, 2019).

The use of 3-D printing in the medical field can be made to manufacture tissues and organs; manufacture prosthetics, implants, and customized anatomical models; and pharmaceutical research on dosage forms, delivery, and discovery. The application of 3D printing in medicine has advantages such as customization and personalization of medical products, medicines, and equipment, cost-effectiveness, increased productivity, design and manufacturing, and enhanced collaboration. Besides having biocompatibility and mechanical properties, materials for hard tissue applications require architectural properties in pore size, pore interconnectivity, and porosity. Because of its complex shape, a method is needed to meet architectural requirements, and 3-D printing can meet it (Putra & Tontowi, 2019).

There are three types of 3D printing, including powder-based 3D-printing, ink-based 3D-printing, and polymer-based printing. 3D-printing technology has an up-and-coming prospect in tissue engineering because it can produce complex structures with high resolution and can produce customized medical products through a combination with image reconstruction techniques (Liu & Yan, 2018). A network similar to the original structure is essential in scaffolding fabrication to produce scaffolding identical to the original scaffold (Geckil, Xu, Zhang, Moon, & Demirci, 2010).

## Characteristics of 3D-Printing Scaffolding

In making 3D-printing scaffolding, several critical criteria must be considered, including biocompatibility, biodegradability, pore interconnectivity, pore size, porosity, and mechanical properties (Do, Khorsand, Geary, & Salem, 2015). In the manufacture of scaffolding, biocompatibility and biodegradability are significant properties to ensure that they are degraded into non-toxic products and leave the essential and appropriate living tissue needs. Then the material must induce an inflammatory response so that there is no rejection by the host immune system. Besides, mechanical properties have an important role in scaffolding. The scaffold must be able to withstand the forces applied by the cell as it grows. Otherwise, it will cause brittleness before the cell is fully developed and will result in low diffusion and inefficient tissue formation (Thomas, Thomas, Kalarikkal, & Jose, 2018).

In recent decades, porous scaffolding has been the preferred scaffold. In making scaffolding, pores are essential because they function as space for cells to attach and grow into new tissue (Aufan, Daulay, Indriani, Nuruddin, & Purwasasmita, 2012). The combination of powder, material, and structure size will also affect the 3D printing capability of scaffolding (Do, Khorsand, Geary, & Salem, 2015).

Various materials used in making 3D scaffolding include metal, ceramics, polymers, and composites (Do, Khorsand, Geary, & Salem, 2015). Metals have mechanical strength similar to bone and are safe to use in vivo (Vasconcellos, *et al.*, 2008; Chou, *et al.*, 2013). Behind the advantages, metals have disadvantages, such as being difficult to degrade. It causes metal ion toxicity due to corrosion and degradation at high concentrations in the body (Wataha, *et al.*, 2010; Davis, *et al.*, 2009).

Ceramics are a material that can make scaffolding because of its apatite mineralization ability (Wu, *et al.*, 2012). Hydroxyapatite (HA) is usually contained in bones and teeth. Hydroxyapatite is an attractive material for scaffolding, with properties similar to natural bone. HA has become a concern in regenerative medicine with its biocompatibility and ability to promote profitable cell growth and survival (Leukers, *et al.*, 2005). The scaffold with ceramic material such as HA produces a pore size of 300 μm, which is sufficient to transfer nutrients to the cells. It makes HA one of the most suitable ceramic materials for a porous 3D printing bone scaffold.

Polymers are the main category of material used in the manufacture of 3D scaffolding for tissue engineering. It is because polymers are used as adhesives (Hribar, Soman, Warner, Chung, & Chen, 2014). In addition to the three types of materials above, the latter is a composite, which has an important role, especially in increasing the mechanical strength of the 3D bone scaffolding (Do, Khorsand, Geary, & Salem, 2015; Afriani, *et al.*, 2020). Composite is the primary material in making 3D scaffolding, which is more comprehensive for bone tissue engineering. The synthesized biomaterial composites have the potential to pave the way for 3D scaffolding with> 99% precision, 100% interconnectivity, adjustable pore size, good mechanical strength (Do, Khorsand, Geary, & Salem, 2015). Composite materials have the potential to be developed with 3D scaffolding by combining ceramic materials with materials that have good mechanical strength and the addition of polymers that have good biocompatibility and biodegradable properties when applied in bone tissue.

### Challenges and Further Developments

Although 3D printing has its advantages, several aspects of challenges and developments need to be studied so that this method can be widely applied. Adhesives and powders are some of the main challenges that must be faced with this method.

### Binder

In the 3D method, the type of adhesive is essential. It is because the adhesive used must be biocompatible, biodegradable, and non-toxic. Also, it is necessary to develop advanced methods capable of perfectly decomposing adhesives in a scaffold. In general, this can be done by sintering with temperatures above the melting point of the adhesive material. Then the adhesive concentration also plays an essential role in the 3D-printing fabrication process. If the concentration is too little, the resulting scaffold adhesive will not be evenly distributed. Meanwhile, if the adhesive is too much, it can cover the nozzle mouth of the 3D-printing tool used (Shirazi, *et al.*, 2015).

### Powder

Powder size is one of the things that need to be considered in scaffolding fabrication. The powder size, which is too fine, will cause the coating process to take a long time. Meanwhile, large powders will make it difficult for the printer to follow a precise pattern. So it takes a powder size that suits the needs and capabilities of the printer. Likewise, with the powder's level of wetness, which must be adjusted to the needs and capabilities of the printer. Then a further development is needed that examines various in-vivo and in-vitro tests so that the resulting scaffold can meet all the predetermined requirements (Hapgood, Litster, Biggs, & Howes, 2002; Bandyopadhyay, Bose, & Das, 2015).

## CONCLUSION

Bone scaffolding is an alternative solution to bone therapy, and its fabrication through 3D -printing technology can be further developed because 3D-printing technology can produce scaffolds with complex structures. From several types of materials, composite is the most suitable material to use by the characteristics of scaffold fabrication. Several types of 3D-printing can be used, such as powder, inkjet, and polymer-based types. The choice of 3D-printing depends on the properties of the material used and the challenges related to the adhesive material and the powder's characteristics. Therefore, the development of 3D-printing is still comprehensive, and there are still various aspects that need to be studied further to obtain knowledge regarding the application of 3D-printing for bone scaffolding in depth.

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