

# 3D Organ construction: new trends and confronts

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## ABSTRACT

The end goal of 3D organ printing is to create fully functional organs that can entirely incorporate into the human body as if they were the part of it. It has the capability to mimic artificial tissues and organs and make them compatible with the human body.

*The authors declared no conflict of interest. Both authors contributed significantly to the writing of this editorial and agreed to be accountable for all aspects of the work.*

## INTRODUCTION

3D Bioprinting, also known as Additive Biomufacturing Technology, is a rapidly emerging field in regenerative medicine and is the preferred method for fabrication of organ models.<sup>1</sup>

Physical organ models are the objects that replicate the patient-specific anatomy and have played an important role in modern medical diagnosis, disease treatment and management.<sup>2</sup> 3D printing, as a powerful multi-function manufacturing technology, breaks the limitations of conventional methods and provides a great potential for manufacturing organ models.<sup>3</sup>

3D printing technology is a rapid prototyping method that constructs complex functional 3D structures layer by layer from various data fed from sources such as computer-aided-design (CAD), computer numerical control (CNC), mechanical technology, and material science, to be converted into a 3D physical model.<sup>4</sup>

## Historical Evolution of 3D Bioprinting

The first 3D printing was demonstrated by Charles W. Hull in 1986, which was named solid image processing or 'stereolithography', in which layers of materials were printed sequentially to form a 3D structure. Then, in 1988, Klebe stated that cells can be positioned precisely in a predetermined design by using a technique named "cytoscribing", where collagen and fibronectin are deposited using HP thermal drop-on-demand (DOD) inkjet printer.

Further upgraded technology was introduced by Thomas Boland and his team in 2003, in which they used a customized thermal inkjet printer to print cells in a viable condition. In the subsequent years, scientists have been trying different biological materials, from growth factors to decellularized extracellular matrix, to develop viable tissues. Nowadays, there are dozens of 3D printing technologies.

Hence, bioprinters are being modified to make them more advanced and accessible to everyone.<sup>5-9</sup>

## Emerging indications and applications of 3D Printing in the medical field

3D printing arose in the medical field as a tool for pre-planning complex surgeries, and with the advancement of technology in recent years, it is now possible to print life organs that can be implanted in the human body,<sup>10</sup> such as hearing aids, bones, jawbone, cranial bones, legs, lungs, heart, kidney, pancreas, and skin.<sup>11</sup> The 3D printer reproduces transcriptions that are similar in texture and size to the original organs, which aids physicians in practice and training on complex procedures. It can also be a useful tool for education and training to understand the human body.<sup>12</sup>

It is now being used to manufacture surgical instruments, which is very desirable because it will lower the cost of instruments while increasing their availability.<sup>13</sup> In Dentistry, it is easy to produce crowns, bridges, orthodontic appliances, and retainers.<sup>14</sup> With regards to printing pharmaceutical drugs, the first 3D printed drug, Sprintam (levetiracetam, for epilepsy treatment) has obtained U.S. Food and Drug Administration (FDA) approval. Some other recent achievements / advantages include:

- Facial surgery: in Belgium a full-face replacement was done.<sup>11</sup>
- Improved outcomes and reduced time in the operating room.<sup>15</sup>
- Decreased likelihood of transplant rejection.<sup>16</sup>
- May remove the need for immunosuppressive drugs after transplant.<sup>16</sup>
- Speed of productivity.<sup>17</sup>

## Challenges

3D bioprinting has to encounter various challenges such as limitations in the material selection, cell viability, ethical issues, and many more to make it clinically relevant or industrially attractive.<sup>18</sup>

The first issue that surfaces is whether there is anything that ought not to be printed. It is important to weigh the potential outcomes as well as mechanisms available for reducing the risk of negative consequences. Even after obtaining positive results during the testing protocols before the human trials, sustainable results are not guaranteed due to each patient's unique genetic makeup.<sup>19</sup>

## Submitted

June 10, 2022

## Accepted

June 22, 2022

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**Citation:** Nathaniel E, James

A. 3D Organ construction:

new trends and confronts.

[Editorial]. J Rehman Med

Inst. 2022 Apr-Jun;8(2):1-2.

3D printed organ models still remain in the stage of small-scale application, and existing studies reported some major challenges for further use. These are:

- 1) High cost, including time and expenses; some commercial 3D printers, materials and necessary software are very expensive, while some complicated image segmentation and model creating processes result in several days of labor and require a long learning period.
- 2) Limited simulation characteristic; it is still difficult for current materials to perfectly mimic the soft tissue. A few soft materials that mimic well are not suitable for direct 3D printing.

- 3) Low production accuracy. The accuracy is mainly affected by the resolution of imaging and 3D printing. At the same time, the available printing space of a 3D printer is limited.<sup>20-24</sup>

Unlike conventional manufacturing process that involves hand-made casts to build structures, 3D printing allows rapid fabrication of various structures, such as the shapes of organs and blood vessels, with almost no waste of excess material. Bioprinting has shown us a promising future for addressing the problem of organ transplantation globally.

Furthermore, organ models facilitate and grow a number of interdisciplinary researchers, doctors, and engineers, to exchange and cooperate between medicine and engineering, and promote the development of additive manufacturing in medicine, including artificial organs and biological 3D printing.

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