

Layer by Layer:  
The Science Behind 3D Bioprinting Vascularized Organs

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## What is 3D Bioprinting?

3D Bioprinting is the production of three dimensional structures that imitate human tissue and organs.

## What are Vascular Organs?

Vascular organs are part of the circulatory system which circulate blood and other fluids throughout the body

- Heart
- Blood Vessels:
  - **Arteries**
  - **Veins**
  - **Capillaries**

## History

**1984** - Charles Hull invented stereolithographing, the first version of 3D printing

**1988** - Dr. Robert J. Klebe used a common inkjet printer to demonstrate his process of **cytoscribing**. This paved the way for 3D bioprinting.

**1999** - First example of 3D bioprinting seen with the creation of scaffolding covered in the patient's cells providing the framework for them to grow into a bladder. This project was led by Dr. Anthony Atala at Wake Forest Institute of Regenerative Medicine and marked the first 3D bioprinted organ to be transplanted into the human body. This is not the same as the modern version of 3D bioprinting.

**2002** - The same institution successfully printed a miniature working kidney

**2003** - Dr. Thomas Boland Patented the process of using an ink-jet printer for printing cells

**2008** - Excursion based bioprinting was introduced

**2010s** - techniques such as sacrificial templating, coaxial printing, and angiogenic factor in

order to make organs **perfusable** were created

**2016** - invention of **sacrificial inks** to create hollow channels. This allows functional vascular channels to be embedded in tissue

**2020s** - 4D bioprinting where printed structures have the ability to change shape and/or function when responding to different stimuli

## How does it work?

1) Imaging

The patients organs shape and structure is captured by MRI or CT scans

2) Design

Software known as, Computer-Aided Design or CAD, is used in order to design the structure of the specific organ including its vascular networks

3) Bioink Preparation

Bioink is a combination of cells and biocompatible materials that are mixed together by scientists. Different cells and materials are used for different parts of the organ, so they are placed into the printer in separate cartridges.

4) Printing

There are multiple different methods used for the printing of organs but it is generally accomplished layer by layer through depositing bioinks.

<u>Method</u>	<u>How It Works</u>
Excursion Based Bioprinting	Bioink is extruded layer by layer from a nozzle
Inkjet Bioprinting	Ejects droplets of bioink onto substrate
Laser Assisted Bioprinting	Laser transfers bioink to substrate
Stereolithography and Digital Light Processing	Uses light on photosensitive bioresin
Sacrificial Templating	Temporary ink is printed into tissue that is later removed, making it <b>perfusable</b>
Coaxial Bioprinting	Uses a dual-layer nozzle allowing it to print the organs

	core and shell at the same time for creating hollow tubes
Self-Assembly via Angiogenesis	Cells are printed close together and induced in order to develop into blood vessels
Modular Tissue Engineering	Built from small, pre-vascularized tissue that fuse together

#### 5) Testing

The testing process includes ensuring that each organ is functional by pumping nutrient rich liquid through the vessels for **perfusion**, and by testing to see if the organ performs its duty.

<u>Advantages</u>	<u>Disadvantages</u>
<ul style="list-style-type: none"> <li>● Lack of organ donors</li> <li>● Patient specific Implants</li> <li>● Advanced drug testing models</li> <li>● Customizable design</li> <li>● Reduces animal testing</li> <li>● Reduces organ trafficking</li> </ul>	<ul style="list-style-type: none"> <li>● Cost</li> <li>● Maturation time</li> <li>● Demand issues</li> <li>● Regulatory and safety issues</li> </ul>

### The Future of 3D Bioprinting Vascularized Organs

- Miniature versions of organs have been created, however, the goal is to create full scale working organs
- Hope to create transplantable organs that are fully 3D printed
- Still need to focus on improvements with the vascularization of the organs
- 4D bioprinting is still a fairly new concept still being explored by scientists
- Regulations and ethics surrounding the topic requires further discussion

### Key words

**Arteries** - blood vessels carrying blood away from the heart

**Veins** - blood vessels carrying blood to the heart

**Capillaries** - connect arteries to veins

**Perfusion** - process of delivering blood to the body's organs and tissue

**Sacrificial inks** - temporary material used to create hollow channels

**Cytoscribing** - cells are placed in a specific pattern onto a surface

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