3-DIMENSIONAL BIOPRINTING:

A REVOLUTIONIZING APPROACH TO HEALTHCARE

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ABSTRACT

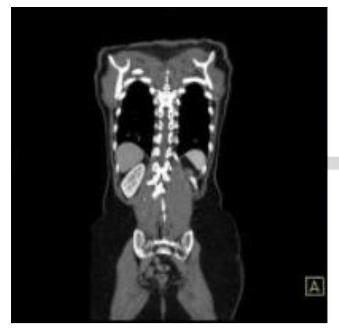
Recent technological developments have allowed for three-dimensional printing to be used within the healthcare system to create scaled prototype organs for surgeons to practice operating on in anomalous cases. This is done using silicon printing with the design derived from CT scans and gives doctors a chance to assess the issue and figure out the best means of operating. The current use is now expanding to using three-dimensional printing to allow the printing and replication of biomaterials through stem cell reproduction, such as creating skin grafts and small blood vessels. Due to the great demand for transplant organs in the United States and worldwide as well as the natural obstacles in transplantation of donor matching and rejection, biolabs are now attempting to further this and complete the replication of organ systems using the recipient's own stem cells taken from converted blood cells. In the future, it will hopefully advance to the production of complex organ systems, although it will have to fight the obstacles of cell density issues, the complexity of printing specified functional cells, and the issue of printing vascular systems to keep the tissue alive throughout the printing process. This paper will discuss the current control and breadth of bioprinting and its uses in advanced surgeries, its shortcomings and sustainability concerns, and its potential to expand to customized organ creation and transplantation.

ORGAN MODELLING

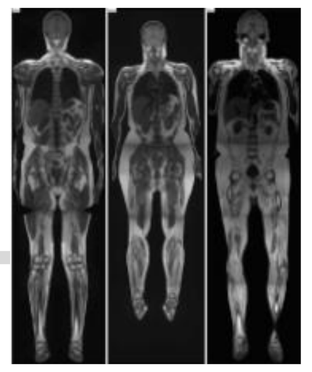
CREATING AN ORGAN MODEL VIA IMAGING

- Organ modeling is the exercise of capturing and processing a 3D graphic image of an organ or bodily system, and then using that computerized image to manufacture a perfect replica of that organ system for a healthcare professional to use to their benefit. The driving force of organ modeling technology is the ability to obtain detailed computer-imaged structures within the body. These types of images have been used for decades to help medical professionals develop diagnoses, and only up until recently have they been used to create physical models of the structures they capture.

OBTAINING 3D REPRESENTATIVE IMAGES



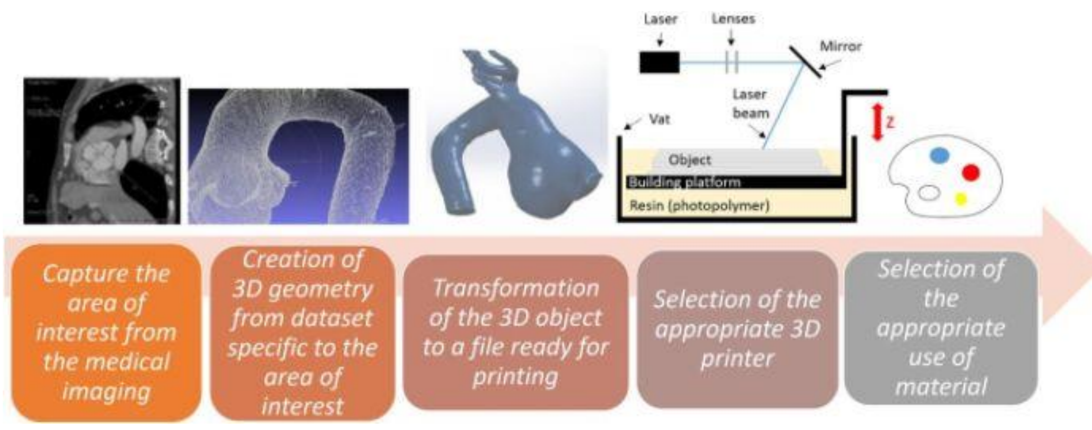
COMPUTED TOMOGRAPHY SCANS (CT)



MAGNETIC RESONANCE IMAGING (MRI)

These provide the necessary data required to build a full 3D model in a software, such as AutoCad.

SYNTHESIS OF MODEL ORGANS

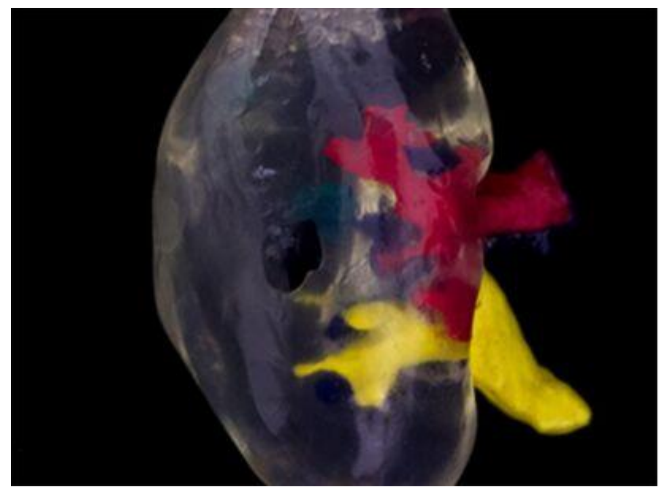


TYPES OF MATERIAL USED IN MODEL

TYPE OF MATERIAL	BENEFITS	CONSEQUENCES
PLASTIC	Low cost	Poor representation
ELASTOMERIC (rubber)	Can be used in practice surgeries	Expensive
POWDERS (starch, plaster)	Low cost & excellent detail	Inaccurate material properties

APPLICATIONS OF MODEL ORGANS

- Surgeons facing difficult and complex procedures can make use of model organs to improve their quality of performance. Each surgery that a certain induvial requires may be unique in some fashion that complicates the ease of surgical methods. Organ models have begun to be used in practice surgeries to allow medical professionals to attempt difficult procedures. A remarkable use of organ modeling was done at a hospital in Belfast, Ireland, as a team of surgeons were faced with a patient requiring an immediate kidney transplant. The patient's father was the only acceptable donor available; however, his kidney contained a potentially dangerous cyst. The surgeons turned to axial3D, a 3D printing company, and they created a model of the kidney using CT scans. The model contained a dyed representation of the cyst, and the surgeons were able to practice removing it before doing so on the real kidney. The real surgery was a complete success, and the patient received a completely functional and healthy kidney.



3D Printed Kidney Model from axial3D

BIOPRINTING CELLS

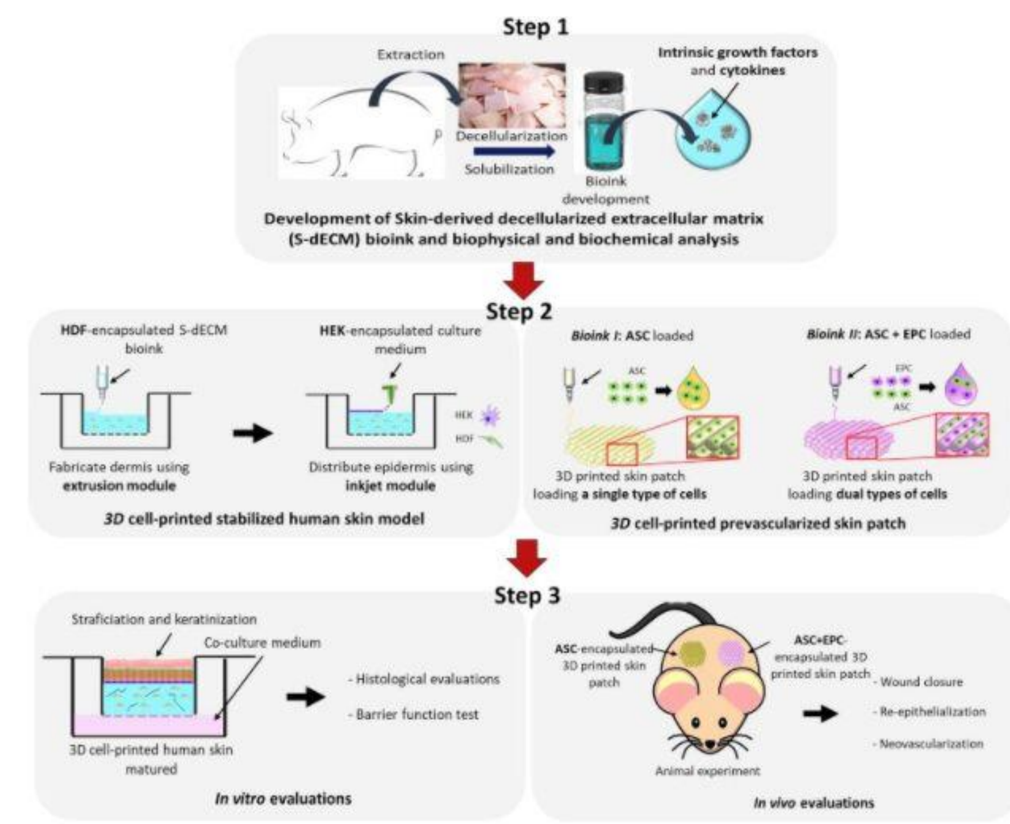
3D BIOPRINTING METHODS

LASER-BASED PRINTERS	Have the best resolution	Laser shock induced cell deformation
INKJET-BASED PRINTERS	Versatile, affordable, print multiple cell types	Can cause cell damage due to printing nozzle
EXTRUSION-BASED PRINTERS	Better structural integrity, fastest method	Low resolution, restricted biomaterial selection

BIOPRINTING WITH STEM CELLS

Stem cells are cells that can differentiate into specialized cell types, making them ideal for use in bioprinting. After stem cells are extracted from tissue samples, they are prepared with growth factors and multiplied. Embryonic stem cells (ESCs) are extracted from human embryos created in an in vitro fertilization clinic. In order to control the use of ESCs, the National Institutes of Health created guidelines for stem cell research, stating that they can only be used when the embryo is no longer needed and with informed consent from the donors. Current research has shown that regular adult cells can be reprogrammed as induced pluripotent stem cells (iPSCs), which mimic embryonic stem cells, which would be the best solution because they do not carry with them ethical controversy.

CURRENT RESEARCH OF SMALL CELL PRINTING



Results from a study done with extracted porcine tissue decellularized into a bioink suggest that skin-derived bioink contains growth factors that accelerate wound healing. In these studies, researchers have successfully 3D bioprinted vascularized tissues and skin patches that can have revolutionary health applications. This research is vital for engineers to move forward in the journey toward 3D printed organs.

CREATING A REAL ORGAN

SIX THEORETICAL STEPS OF ORGAN DESIGN

BLUEPRINT THE ORGAN
This will probably occur through a three-dimensional configuration of CT scans, as they are used currently to model and print accurate surgical prototypes.

CREATE A PLAN
This would follow with the design of a printing plan based on cell material, location within the organ, cell density and the changing of the bioink throughout the printing process.

CREATE SPECIALIZED CELLS
Since all of the body's cells share the same DNA sequence, DNA can be isolated from blood cells and transformed into specialized cells.

CREATE BIOINK WITH CELLS
The cells are then placed into a substrate that allows for the support and distribution of cells.

PRINT THE ORGAN
The printing process occurs then as the bioink is transfused with cells to ensure that all specialized cells are being placed properly within the organ.

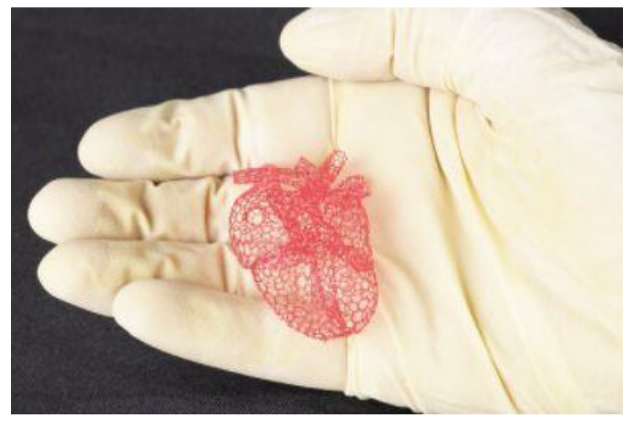
TRANSPLANT THE ORGAN
The organ is then transferred from a sterile printing station and the patient's body in a surgical procedure.

THE SHORTCOMINGS OF ORGAN PRODUCTION

SCAFFOLD STRUCTURE

Scaffold printing requires a printer to layer the substrate, resulting in the printed object's multi-dimensionality. These scaffolded structures do not occur within the confines of nature, as things grow through the accumulation of cells. Using sugar as a base for the degradable structure, it is currently being investigated as to whether this could be a possible means of collapsing a structure.

A 3D-printed heart exterior printed with a sugar substrate



CELL DENSITY

Cell densities are also a factor that needs to be modified in order to print operating organ bodies. Organs consist of differing cell types, which each have differing, yet corresponding cell densities. For example, liver tissue is far denser than most with 1.3*108 cells per gram. These densities need to be accounted for when replicating cells via the viscosity of the printing substrate: the bioinks. To account for this, viscosity needs to be considered when utilizing the bioinks and altered accordingly,

VASCULARIZATION

Arguably one of the most pressing unanswered questions to successfully complete a bioprinted organ, there must be a readily accessible vascular network to supply the organ with blood supply as it is being built. The vascular system provides the cells with nutrients and much needed oxygen to survive