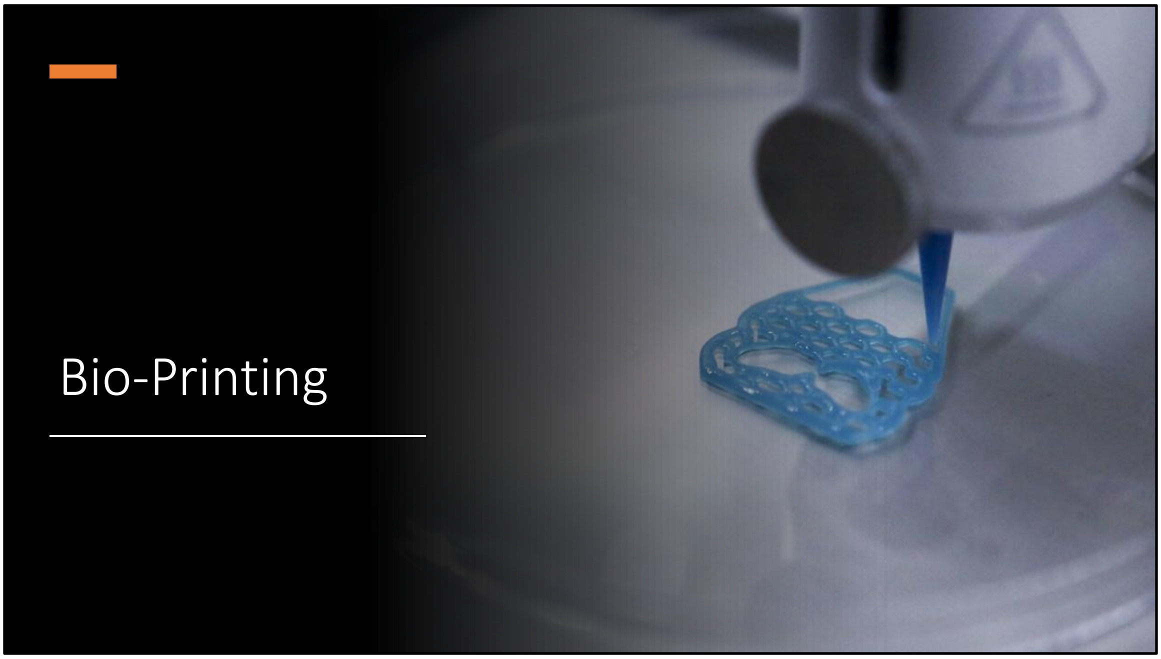


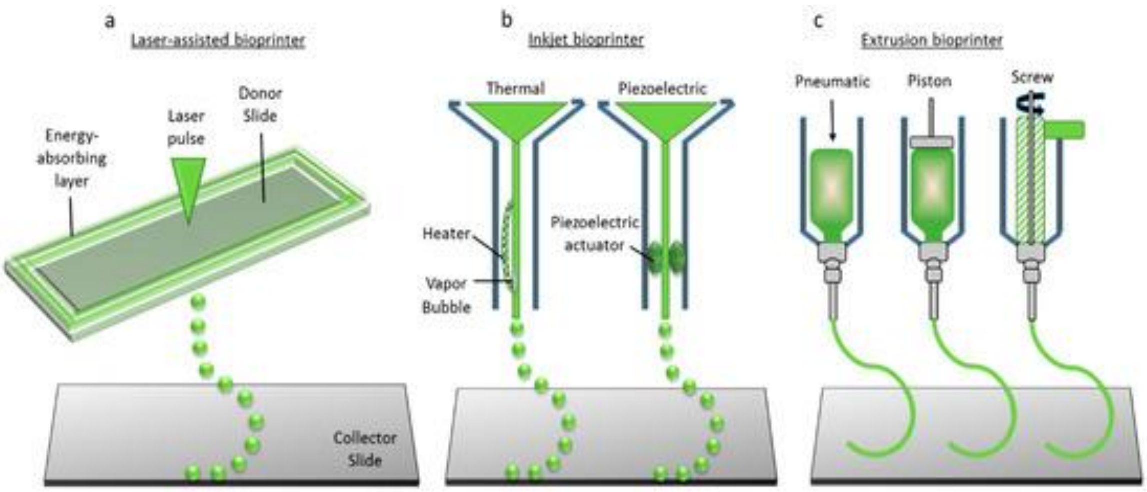
Whats is Bio-Printing?

Bio printing is a additive manufacturing procedure very similar to regular 3D printing , however instead of using some sort of plastic or resin to create the structure, bio-printing use bioink or hydrogels infused with cells. Using a digital file as a blueprint the printer builds up the model layer by layer until the model is complete. The models are made with various cells and biomaterials to mimic living tissues.

It comprises of 3 main steps
- pre-bioprinting
- Bioprinting
- Post-bioprinting

Bioprinting is a relatively new technology that can have many useful benefits and applications we'll explain later on.

Printer Types

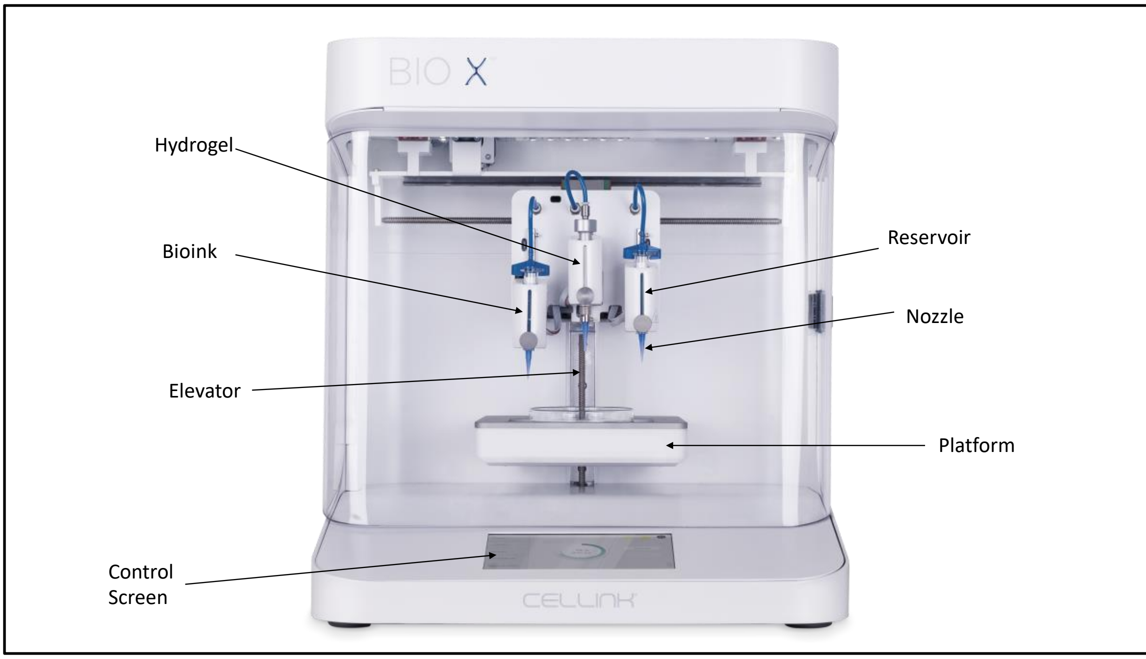


As for the anatomy of the printer, there are 3 major types.

1. Laser-assisted bioprinter
   - focuses laser pulses of the donor slide creating a pressure that forces bioink droplets onto the collector slide.

2. Inkjet bioprinter
   - ejects droplets of bioink by one if two methods.
     a. using thermal energy to create bubbles that force of the hydrogels from the nozzle or,
     b. using a piezoelectric actuator that actuates at high energy level frequencies to push the droplets out.
   - most commonly used in bio printing

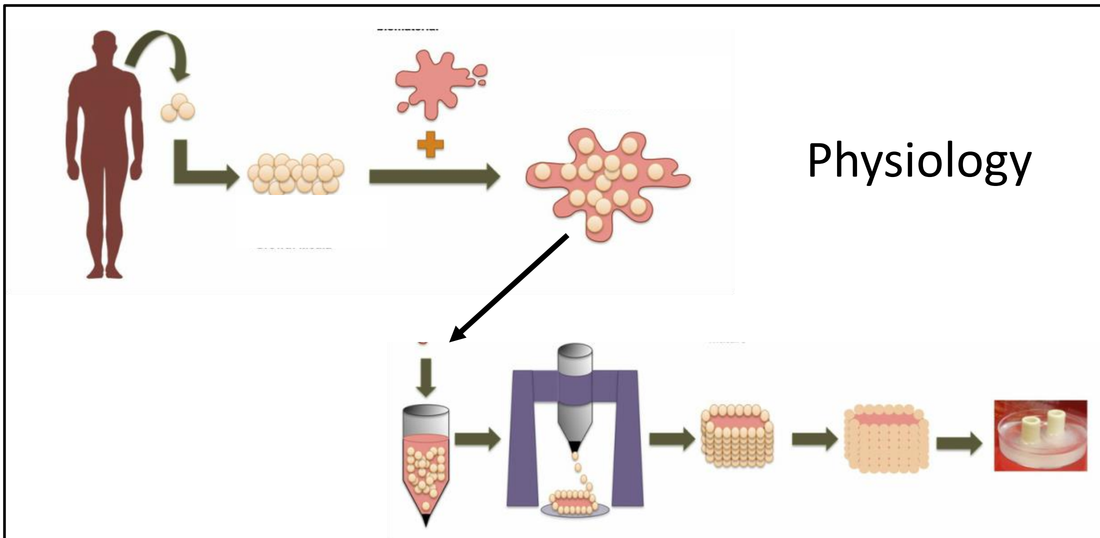
3. Extrusion bioprinter
   - extrude the bioink by air pressure, mechanical pressure or with a screw type mechanism.



The bioprinter components are as follows

- Hydrogel: Gel used to provide the bioink with nutrients and oxygen so it doesn't die.
- Bioink: biomaterials used to created simulated tissue, they are infused with the cells of what they're trying to mimic.
- Elevator: Metal shaft in the back of the printer to move the print up and down so multiple layers can be stacked
- Control Screen: Screen to see the progress and duration of the print and other information.
- Platform: Holds the printed tissue duirng the print, often containing a petri dish.
- Nozzle: where the bioink is ejected from.
- Reservoir: holds the bioink and hydrogel during the printing process.

Physiology



To create a bio-printed materiel one must follow a number of steps.

1. Extract healthy cells from a patient
2. Culture cells in a growth solution
3. Mix the cells the with the hydrogel to creating the bioink
4. Transfer the bioink into the reservoir and load the nozzle
5. Start printing the bioink into the desired tissue layer by layer
6. Take the printed tissue and transfer it into a growth media so that it can grow and mature.
7. After maturation the tissue can be used for transplant or drug development studies

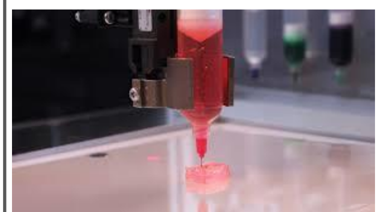
Pathology

The pathology for bioprinting may vary depending on your use for it.

First case: Transplant
- In some cases 3D printed tracheas have been transplanted into a patient with Tracheobronchomalacia.
- In other cases the transplants were purely cosmetic, such as an ear or nose transplant.

Second case: Testing
- Bio printed tissue may also be used in drug testing, since the tissue is suppose the mimic live human tissue it can be a good candidate in early drug testing when the effects are uncertain.

Since bioprinting isn’t limited to one tissue/ organ the pathology is quite extensive ranging from diseases to cancers to personal cosmetic appearance to drug testing.



Process

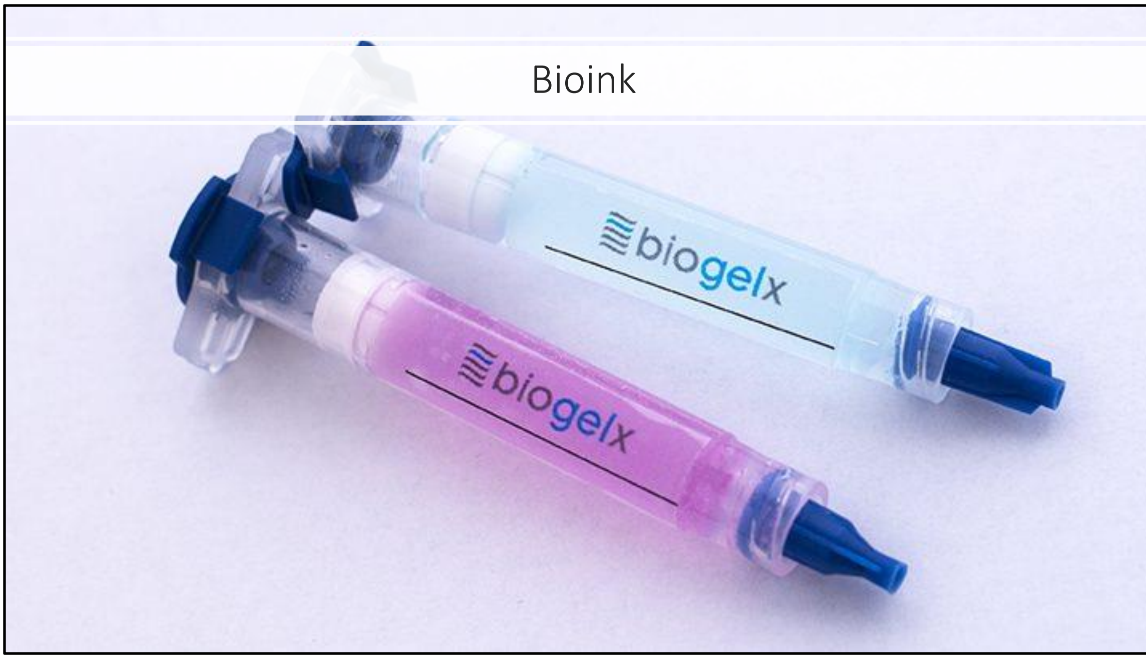
The bioprinting process happens in 3 main steps

1. Pre-Bioprinting
   - Doctors take a MRI or CT scan to get a 3D image
   - A 3D model is made using a CAD software
   - Slice by slice layers are made
   - Bioink is prepared with the patients cells and the hydrogel containing all the nutrients the cells need to grow

2. Bioprinting
   - The prepared bioink is loaded in the printer
   - The nozzle or nozzles are selected based on what is being printed
   - The speed of the print is based on the tissue being printed
   - Layer are printed at 0.5mm thickness
   - The bioink come out of the nozzles as a highly viscous fluid

3. Post-Bioprinting
   - Crosslinked with UV light or an ionic solution to become stable/ hardening
   - The composition of the tissue determines the crosslink
   - Finally the tissue is placed in a incubation to mature and grow

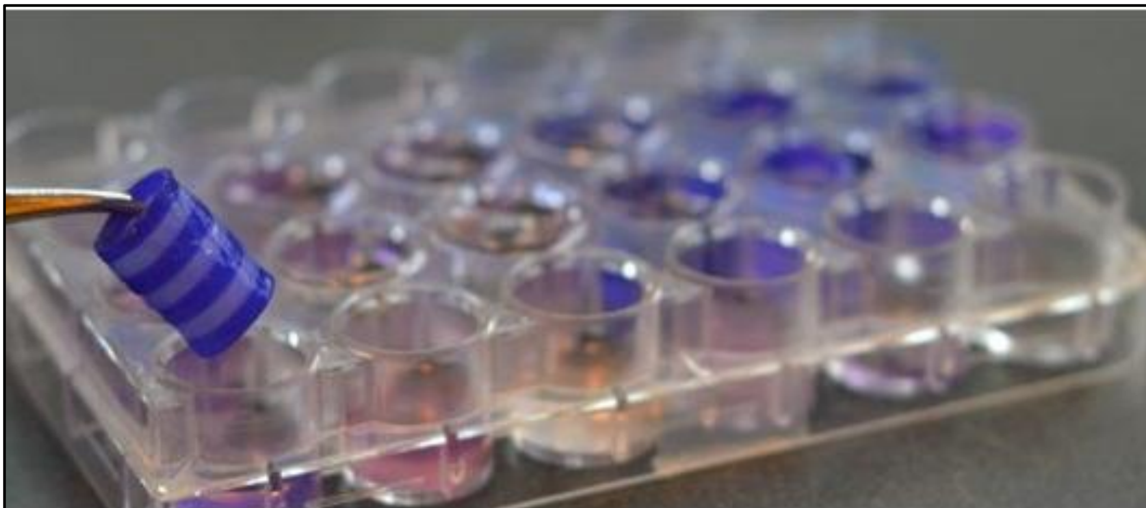
Bioink



Bioinks contains cells and other biomaterials to mimic the extracellular matrix of a human. These bioink are gels rather than the normal filament one would use for 3D printing.
These bioinks must support:
- Proliferation
- Cell adhesion
- Differentiation

Bioinks must also follow different rules than regular 3D printing which are:
- Print temperature cannot be too high or the cells in the bioink will die
- Must have crosslinking abilities
- Bioactive materials that can be modified by cells after printing
- All materials must be non-toxic

Some of the building blocks for bioinks include: agarose, alginate, chitosan, collagen, fibrin, gelatin, decellularized ECM, etc



Applications – Drug Testing

One big application of 3D printing tissues is the ability to test new drugs on them.

Testing is usually done on artificial tissue and then on animals, however this tissue are often very different than and human tissues meaning that when testing on humans results could wildly vary.

Using printed tissues scientist can closely reassemble human tissues needed for testing.

This will also:
- Reduce the amount of animal testing needed
- Fast track testing time
- Reduce research costs because they can determine the effectiveness of the drug earlier on in the testing process.

Another useful application is surgical planning/ training.

This process can be used when the surgery will be difficult for the surgeon and having a 3D simulated model of the organ the doctor is trying to perform on will help him visualize how the approach the surgery.

This is done in 4 steps:

- First, a image must be taken of the organ that needs to be operated on using a MRI or CT scan
- Second, the image must be processed and segmented into layer so that the printer can print the organ
- Third, the printing process takes place based on the required materials and properties needed, different organ are built with different materials and different properties
- Forth, base on the type of print supports may need to be remove and other materials may be added to enhance features of the printed organ.

Prosthesis

Another use for 3D printed tissues is prosthesis.

One of the main advantages over normal prostheses is the cost and customizability.

These have jumped over the hurdle that normal prostheses face as well. If a young child needs a prosthetic they will often outgrow the prosthetic many time over the time of there life.

With a 3D printed it’s a living tissue and can grow and adapt with the child over their life and 5 children in a study found that they had greater range of motion with a missing digit they had.

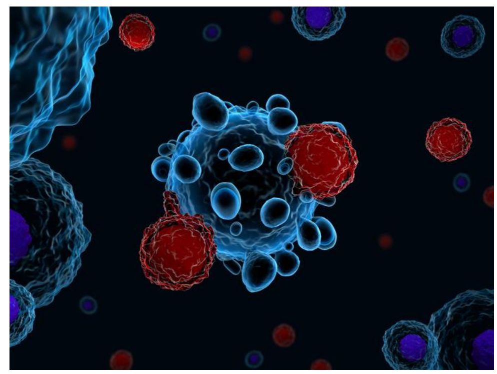
One last application is tissue constructs

There have been many successful tissues that have been bioprinted and reported in medical journals such as:
- Bone
- Skin
- Cartilage
- Heart valves

In there future these could play a significant role in regenerative medicine and it much easier and faster to print a tissue than to find a suitable donor.

However this tissues are reported at the laboratory level and still need some time before they clinically avaible due to the challenges that still need to be surmounted.

Advantages



As bioprinting continues to evolves certain advantages could arise that may change the face of medicine that we see today.

1. Bioprinting could replace organ donation
   - Printing would reduce the wait time
   - More people on the organ donation list would receive the life saving organs they need
   - Won't have to rely on someone else dying

2. Bioprinting could be more compatible with the recipient
   - With organ donation there is a chance the recipient immune system will reject the organ
   - Printed organ will use the recipients cells, so there is a much higher chance they wont be rejected.

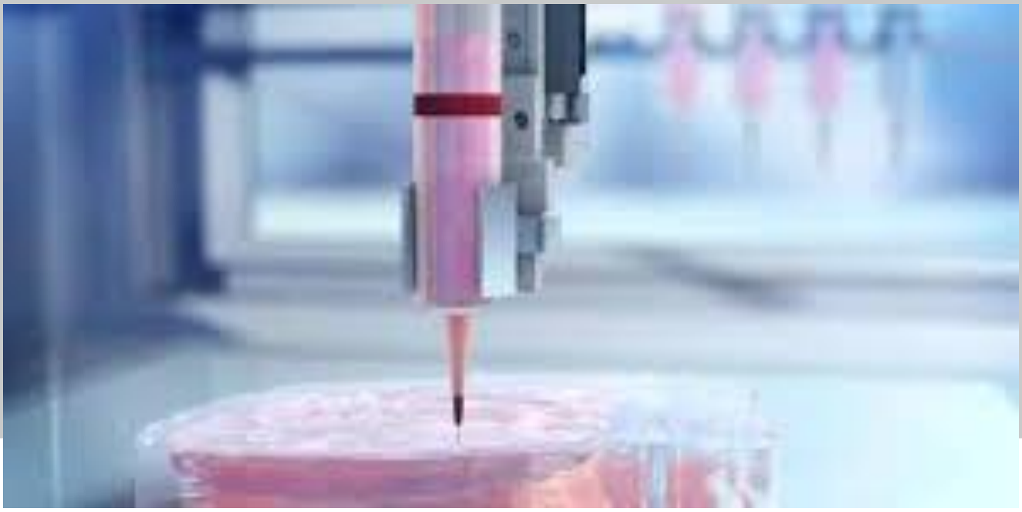
Advantages

More advantages include:

3. Bioprinting could eliminate animal testing
   - printed tissues can be used to test cosmetic products as well once printing become more readily available

4. Bioprinting could replace drug testing volunteers
   - using printed tissues can reduce the risk to the volunteers as well as save money for the company

These advantages are still to come, but as the research progress bioprinting can become one of the most useful technology out there.



Challenges/ Limitations

While this technology can prove very beneficial, it also comes with its set of challenges as well.

Some of the challenges include:
Technology
- Need to increase the resolution and speed to bring it up to commercial level
- Printers need to be adapted to be able to use a variety of biomaterials

Biomaterials
- limited to a couple natural and synthetic bioinks

Type of cells
- the type of cells used to create the bioink help it differentiate, so stem cells are the best for the bioink but the hardest to get.

Vasculature and innervation of printed tissues
- these two key properties of living tissue are hard to mimic and therefore cause a problem for printed tissues

Ethical impacts

With every new technology come along with ethical concerns. Will 3D printed tissue be safe, or will it cause the richer to get richer and leave the poor in the dust, these are all good questions. Some of the more pressing concerns are:

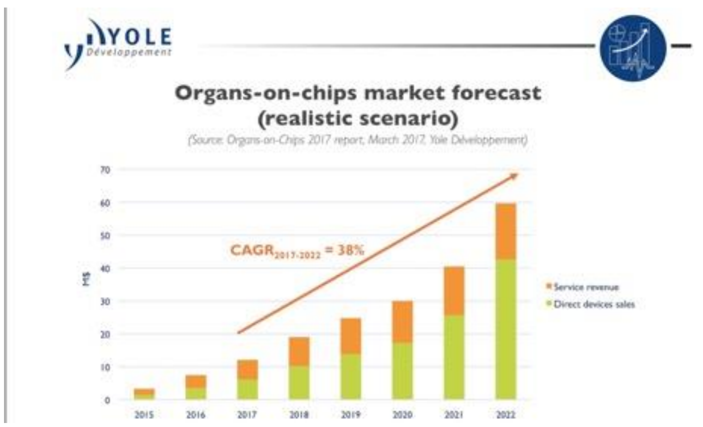
1. Equal treatment for everyone
    1. Bioprinting is more focus on personal healthcare rather than universal, so if people cant afford it will they still have equal access to this technology

2. Safety
    1. Safety is always a concern with medical devices, and 3D printed tissues are still under works, so will these tissues be safe enough to function inside a body

3. Enhancement
    1. Bioprinted tissues are supposed to replace the faulty ones, however what if people treat bioprinted organs as enhancements to better themselves

These all must be taken into consideration when the bioprinted tissues are commercially available.

Economic Value



Bioprinter has play a huge role in reducing the cost in the medical world. As of now a transplant can cost anywhere from \$500000 - \$1000000 which places a huge financial strain on everyone. If we are able to print organs for transplants we could give care t0 more people and well as cut the costs of the transplant because a printed organ will only cost tens of thousands od dollar instead. The wait time for a printed organ is only a week or two which causes less people to be in the hospital using the hospital resources.

The graph above is an estimate of revenue another company will get with their organ on chips. Which is bioprinted organs on a small scale to be used for drug testing as well as any other tests.

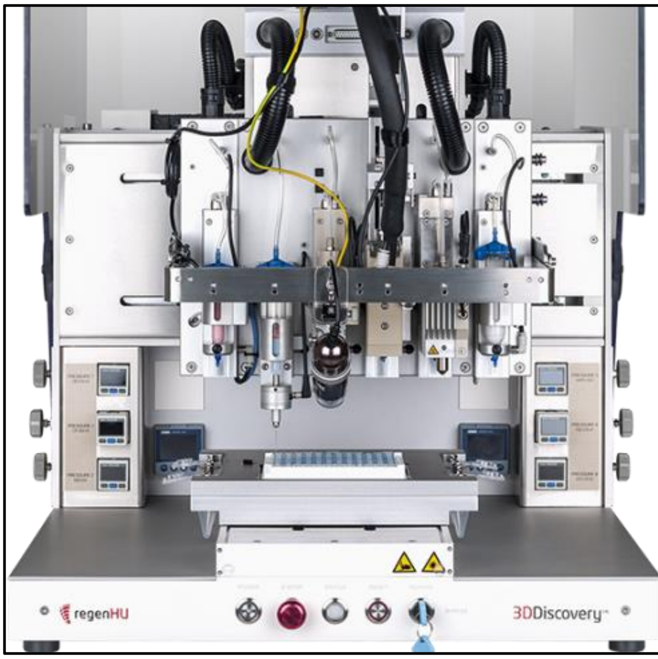
In the Beginning

- The first ancestor of the bioprinter today was made in 2003 by Thomas Boland who modified an inkjet printer to be able to be compatible with biomaterials

- A year later Gabor Forgacs created the first 3D bioprinter to use living cells without the need for scaffolding, this tech was so advanced that in 2009 the first commercial bioprinter was created.

- Over the next couple of year more tissues were being printed, one with blood networks and even a heart valve was made

- In 2015 a company called CELLINK created a bioprinter called INKREDIBLE which was not only cheap at $5000 but also aesthetically pleasing, INKREDIBLE became the new standard.



Moving Forward to Today

Recently a group of scientists from Israel have been about to 3D bioprint a heart with blood vessels. The heart was the size of a rabbits heart and was capable of contracting. This has been a breakthrough in the field of bioprinting because up until now printing a full functioning organ was a thing of the future.

Scientists In Poland have almost be able to make a functional prototype of a bionic pancreas using 3D bioprinting methods.

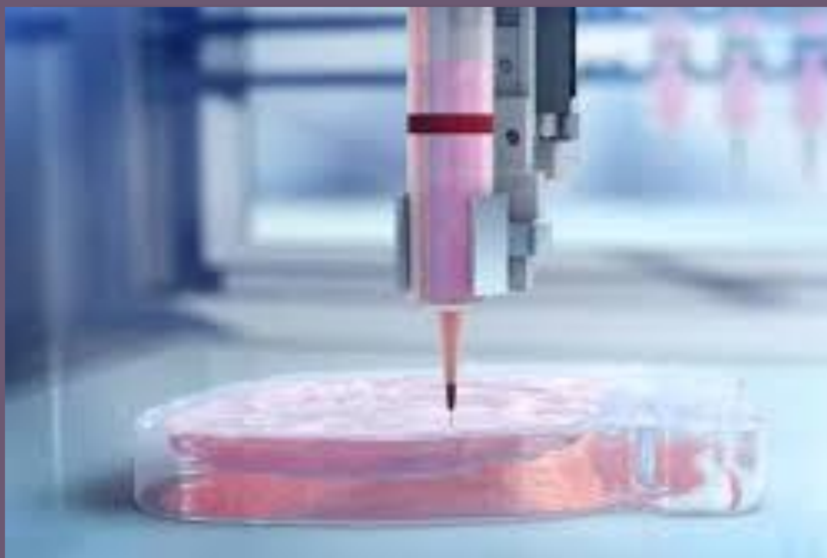
Printing in Space

The picture above is a model that NASA would use for a magnetic bioprinter.

- Using magnetic fields allows for tissue spheroids and synthetic microscaffolds and cell management.
- However gravity was found to limit the printer because it was always applying an opposing force.
- NASA wants to use microgravity along with magnetic fields to do the printer without scaffolds or a nozzle or magnetic nanoparticles in a process called biofrabrication.

This magnetic printer could revolutionize the bioprinter because the printed tissues would be much faster and they could have a more complex structure without the constraints of earths gravity.

NASA plans to launch this printer into outer space to be a part of the International Space Station so that test may be completed.



Conclusion

To wrap things up I would like to say that with some time 3D bioprinting could become the face of medicine as we know it today.

The possible benefits from bioprinter out way any of the costs to mass produce them to have them in every hospital.

Using bioprinter we can save lives one many animal and humans as treatment would be more readily available at a lower cost.

In the future I hope that one date Bioprinting become the norm for modern day medicine.

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