Bioprinting of Human Organs

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While bioprinting of living tissue has been possible for some time, the creation of functional organs has been limited by the ability to vascularise these tissues – until now.

Imagine walking into a hospital and asking your doctor: "Could you please print me a new liver?" It may sound like science fiction, but this is essentially the objective of our work. And every day we are closer to bringing it into reality. For instance, we have developed a way of printing out a network of blood vessels that could support the growth and maintenance of such an organ.

Patients around the world are placed on long organ transplant lists to have another chance in life. In the US alone a new name is added to the national transplant waiting list every 12 minutes.

Hence there is a tremendous need to develop technologies that will allow parts of human tissues to be created in the lab. But how could we fabricate human organs from scratch to alleviate such high demand? 3D printing of living cells may be the answer.

The basic idea is that if we are able to keep cells alive outside of the body for long enough, and can manipulate how they behave and are arranged in three-dimensions, we should be able to control how these cells mature to form living organs.

How does that translate into a health care solution? If we are able to create functional organs in the lab, we may not need to wait until one patient dies to have an organ available for transplantation.

Difficulties in Fabricating Organs

The difficulties in creating parts of living tissues in the lab are numerous. One of them is finding materials to act as frameworks – commonly known as scaffolds – that the body can tolerate while keeping cells alive for long periods of time. Replicating the complexity of natural living tissues is another. And understanding the interactions that occur between different cell types and growth factors in an organ is yet another great challenge.

While we have come a long way in addressing some of these issues, what we are struggling with now is how to recreate the three-dimensional architecture that allows cells to mature into organs.

For instance, keeping cells in a Petri dish while they divide and differentiate is something that we have been able to do for a long time. However, in the body many different cells are organised in complex three-dimensional structures. This is very different from simple layers of cells laid on a Petri dish, and this is where the idea of 3D bioprinting comes into play.

3D printers have been used to fabricate a number of things in our daily lives, from simple mobile phone cases to parts of cars and complex machinery. In 3D printing, thin layers of a material are sequentially dispensed to form 3D objects. While this technique has been used to print objects with molten plastics and metals, the critical challenge now is to adapt these technologies to the printing of living cells and biological materials.

In a recent set of studies performed with our colleagues from Harvard University and the Massachusetts Institute of Technology, we have developed a set of techniques that overcome some of these challenges. And our results show that printing living tissues and organs in the lab bench may be more than just a promise.

Printing Living Tissues

Currently, three systems are used to print living tissues – laser-based bioprinters, inkjet-based bioprinters and extrusion-based bioprinters. Much like common personal desktop printers, bioprinting involves taking a 3D digital image from a computer and reproducing it by dispensing an ink onto a substrate. In bioprinting the ink – typically referred to as "bio-ink" – consists of solutions made up of cells, or cells in combination with biomaterials: typically proteins or synthetic polymers that the body can tolerate.

Inkjet-based bioprinting involves droplets of living cells maintained in cartridges, much like common ink-jet personal printers. In fact, the first attempt to print cells used a simple HP printer to dispense a suspension of cells instead of the regular ink.

Extrusion-based bioprinters, on the other hand, dispense continuous filaments either made up of cells tightly bound to one another, or dispersed in a cell-friendly material of controlled viscosity. Typically, a pneumatic system or a moving piston controls the extrusion of these materials from a syringe at pre-defined locations. During printing, the biomaterial is then precisely layered in sequence, thus forming the desired 3D structure.

Laser-based bioprinting uses the high energy of lasers to transfer cells deposited on a platform onto a collector below. This process is repeated several times to create a 3D structure.

Although all existing bioprinting methods show great promise, certain limitations still exist. For instance, problems may arise in laser-based systems from cell interactions with the laser light. In inkjet-based systems, controlling the consistency and fusion of bio-ink droplets can be difficult. Similarly, in extrusion-based systems, a limited selection of materials allows both reproducible printing and cell survival.

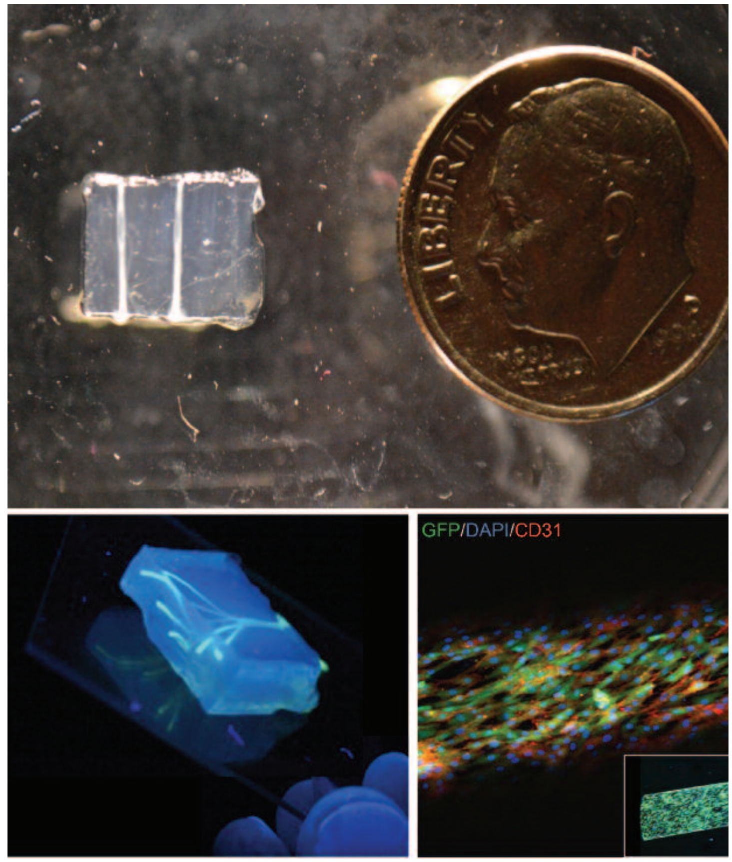
Furthermore, the time required to print tissues at clinically relevant dimensions using the existing methods is still far from what one would like. These aspects represent important hurdles before this technology can be effectively translated into the clinic.

Vascularisation: The Critical Challenge

Cells need ready access to nutrients, oxygen and an effective "waste disposal" system to sustain life. This is why vascularisation – a functional network of blood vessels and capillaries – is central to recreating biological tissues and organs.

To address this challenge, we have developed a 3D bioprinting technique to create tiny blood vessels and capillaries for tissues created in the lab. We have 3D-printed tiny interconnected fibres that serve as a mould for artificial blood vessels. We then covered the 3D-printed structures with a cell-rich protein-based material that was solidified by applying light to it. We then removed the bioprinted fibres to leave behind a network of empty channels.

When we flushed these channels with cells that we collected from the blood vessels of patients, the cells rapidly covered the inside of the channel walls and formed nicely structured blood capillaries. We hope that these promising results will enable us to fabricate tissues and whole organs with their own vascular networks.



3D bioprinted blood capillaries enclosed in a protein hydrogel.

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How Long Before 3D Bioprinted Organs Becomes a Reality?

This question is rather difficult to answer, as 3D bioprinting is a field that expands rapidly towards clinical application. While we believe we have the right tools to create "organs on demand", the reality is that much research is still required.

Simple 2D-printed tissues are already available, mostly for research purposes, but are not widely used clinically. Hollow organs may be the next step towards full organ fabrication. But certainly solid organs with complex functions, such as the heart, liver or lungs, are still a long way from being effectively developed.

It may be quite a long journey, but what an exciting journey it will be!

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