3D Bioprinting Technology

Standardizing the 3D bioprinting of organs has more challenges, in comparison to 3D printing with melted plastic. Each human organ has different components to consider and its own unique physical structure. Scientists also need to consider the combination of various cell types and connecting organ components together. However, precision printing is no longer a problem, because earlier advancements in 3D printing have already developed several high-precision Cartesian robots that will also work for bioprinting (Cubo, Garcia, Cañizo, Velasco and Jorcano, 2016).

Currently, research labs throughout the world tackle a slightly different challenge within 3D bioprinting, such as developing different bioinks, standardizing the artificial production for an organ, and researching or testing 3D bioprinted organs or organ parts.

Bioink Variations

Bioink is malleable material typically used to create the matrix-like scaffolds where cells can then grow in vitro. Currently, hydrogels, polymers, and ceramics are the most well-studied bioinks. Hydrogels are best used in the development of soft tissues, such as skin, while ceramic-based bioinks support the generation of harder tissues, like bones (Cubo *et al.* 2016). At Harvard, researchers developed a bioprinting method that prints several bioinks at the same time to achieve 3D tissue structures (Kolesky, Truby, Gladman, Busbee, Homan, and Lewis, 2014). Bioink can also be the biological material itself. A technique developed at University of Iowa prints tissue spheroids in tissue strands at the scale 500-700µm. This bioink and system allows bioprinting technology to be easily scalable, and therefore more standardized (Yu & Ozbolat 2014).

Bioprinting Skin

In 3D bioprinting, skin has seen the most developments, because the natural layering of skin cells require less complicated bioprinting methods. A common strategy has appeared, which shows skin bioprinting has become the most standardized, relative to other organs. Strong, successful developments in skin bioprinting indicate a promising future for other organs.

A large number of skin injuries indicate an urgent need for effective and available treatment. According to the World Health Organization, there are 11 million burn injuries, each year, that require medical attention. Over 250,000 cases of burn injury result in death. Other skin injuries include chronic ulcers, infections, surgeries, and genetic diseases (Cubo *et al.* 2016). In addition, 3D printed skin can also be used to for testing.

Figure 2 shows a 3D bioprinter for human skin. Scientists in Madrid modified this bioprinter to use a hydrogel bioink embedded with cells. According to their results, the bioprinter was able to "demonstrate that 3D bioprinting is a suitable technology to generate bioengineered skin for therapeutical and industrial applications in an automated matter" (Cubo *et al.* 2016). It was based off the open source 3D printer model, Printrbot, a project similar to RepRap, and "most of the structural parts were generated by a normal 3D printer" (Cubo *et al.* 2016). The open source, systematic manufacturing of a successful skin bioprinter suggests that similar methods will be developed for more geometrically-complicated organs soon.

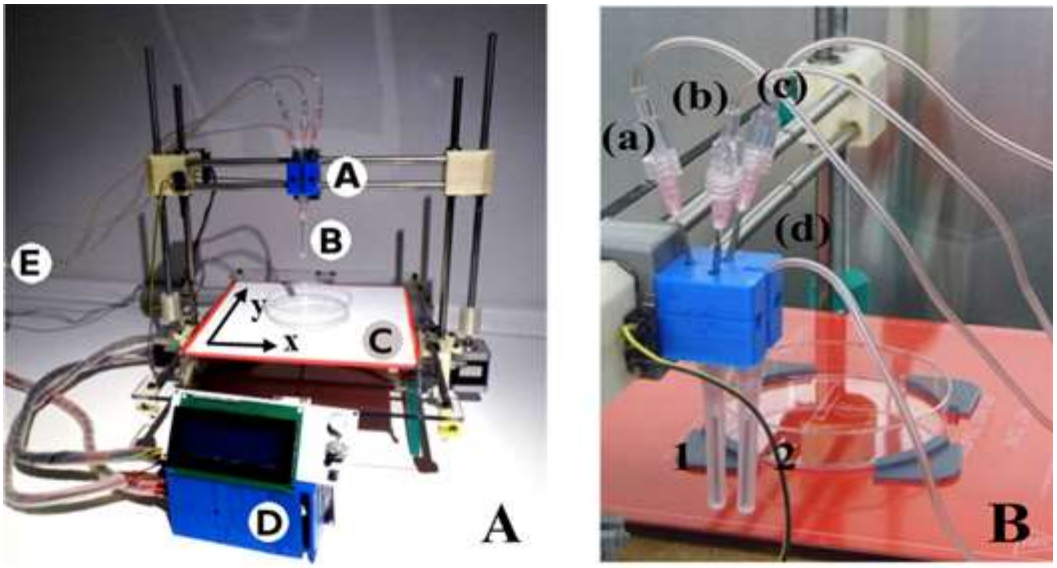

Figure 2. A 3D bioprinter used for printing human skin (Cubo *et al.* 2016)

Challenges for Bioprinting Other Organs

Problems with the current organ donor process drives research for some organs more than others. Although there are labs that work on other body parts, such as different kinds of cartilage, eyeballs, or lungs parts, kidneys and livers a lot more studied. Kidneys and livers are in greater demand, especially with challenges on the organ donor list. However, the challenge still depends on the geometry and cell types of the organ or other body part. Although heart transplants are widely needed, hearts have complicated internal structures, but "livers, which have a natural tendency to regenerate anyway, should arrive reasonably soon" ("Printed human body parts could soon be available for transplant," 2017).

In Japan, researchers found that "a mixture of human liver precursor cells and two other cell types can spontaneously form three-dimensional structures dubbed 'liver buds'". Although the liver buds did not have all the functionality of an entire liver, mice survived, for a month, with this transplanted liver tissue grown from stem cells. In the future, liver buds could be transplanted into human patients through a large vein for the partial treatment of liver failure, restoring around 30% of liver function (Rojahn 2013).

For kidneys, 3D bioprinted kidneys have achieved greater functionality than ever before. Researchers were able to 3D print the proximal tubule, which is a part of the nephron. The nephron is the part of the kidney that filters blood, which provides the kidney with its basic functionality (Orcutt 2016). The new 3D printed kidney tissues could also be used for drug testing. 10% of the global population is affected by chronic kidney disease (World Kidney Day 2017), so the development, research, and testing of 3D printed kidney tissue is positively impacting a large fraction of the world.

Abstracting the process of creating more complicated structures with any kind of bioink advances the research to develop all kinds of organs and other body parts. A general 3D bioprinter was described in 2015, with designs and features comparable to previous generations of other 3D printers (Korzinski, Primmer, and Ulrey). Successful artificial organs are promising, but the high cost and need for specialized researchers significantly limit production (Cubo *et al.* 2016). 3D bioprinting itself is the base technique to mitigate issues around different cell types being involved in a printable body part. Figure 3 shows a 3D printed lattice structure from a lab, printed with several different inks at the same time. When this lab used bioinks instead of plastic, they were able to develop the blood vessels for general 3D bioprinted organs (Rojahn 2014).

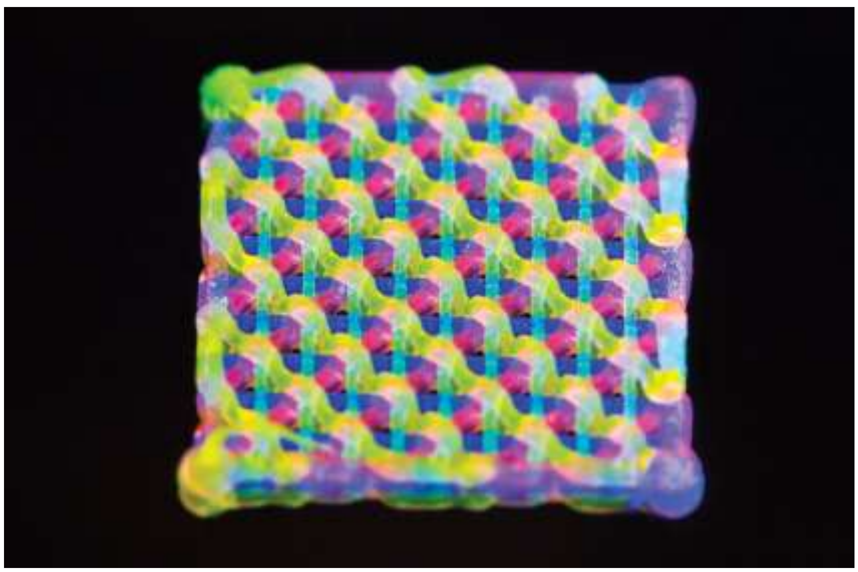

Figure 3. A 3D printed lattice using three different inks (Kolesky *et al.* 2014)

Accomplishments in 3D bioprinting and the testing of various 3D bioprinted organs reveal this technology to be promising for the future of organ donation. As researchers test and develop 3D bioprinting methods for in-demand organs, their methods and techniques also perpetuate research for less-common parts. Root Analysis, a medical technology consultancy, estimates the 3D bioprinting of entire organs will happen in about six years ("Printed human body parts could soon be available for transplant," 2017).