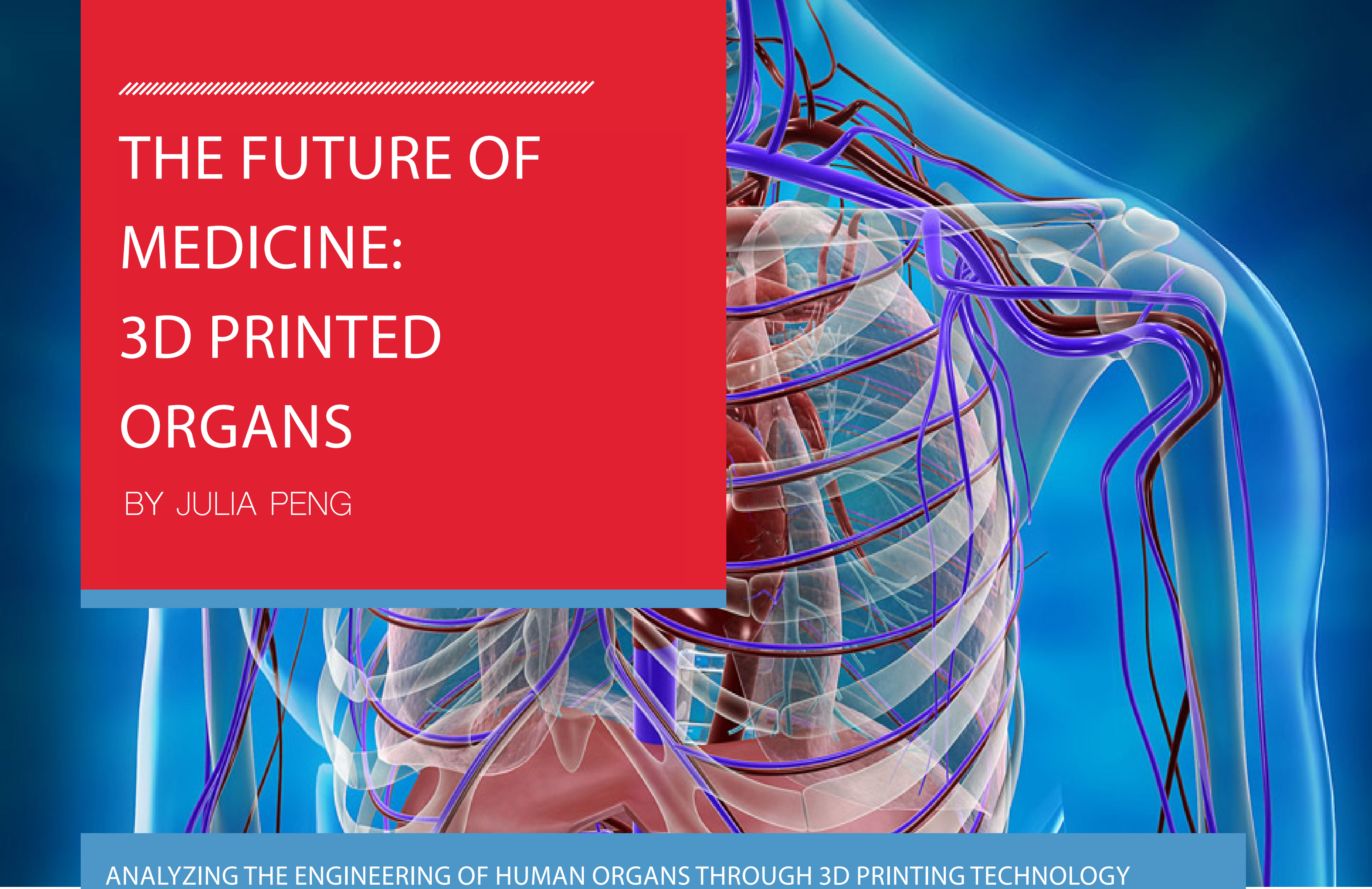


THE FUTURE OF MEDICINE: 3D PRINTED ORGANS

BY JULIA PENG

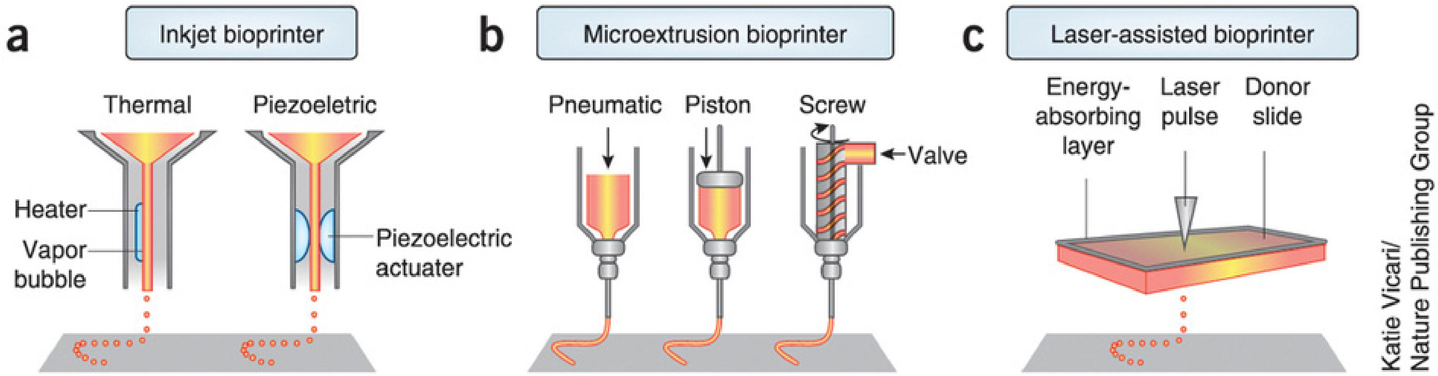
ANALYZING THE ENGINEERING OF HUMAN ORGANS THROUGH 3D PRINTING TECHNOLOGY

Three years--that's how long New Yorker Tim McCabe has been waiting for a kidney transplant. Diagnosed with ulcerative colitis as a teenager, McCabe has been suffering from deteriorating kidneys ever since. Each day, McCabe waits by the phone, anticipating news of an available kidney, but each day, he is met with disappointment. Having left his job as a highway inspector due to his declining physical condition, McCabe now spends his days confined by nonstop dialysis treatments, hoping to survive long enough to watch his two sons grow up.[1]

This is the unfortunate reality for many Americans awaiting organ transplants, as there is a seemingly perpetual organ shortage crisis in the U.S. In the last ten years, the number of patients required a transplants has more than doubled, yet the actual number of transplants performed has remained stagnant. There are currently over 119,000 people awaiting an organ transplant, but in 2015, only 30,970 transplants were performed, with the wait time for each transplant averaging 3 to 5 years. Every 10 minutes, another person is added to the waiting list, and every day, 22 people die waiting for a transplant.[6]

So what can we do to solve this issue? What if there were a way to make a new organ on demand, eliminating the need for donor compatibility and absolving the waiting list crisis? The solution may lie in 3D bioprinting, the manufacturing of new tissues and organs using 3D printing technology. This would involve taking a sample of a patient's cells and using those cells to 'print' a new organ by depositing cells and biomaterial layer by layer, creating a tissue structure identical to that of natural human tissue. Over the years, researchers have developed and improved upon methods of printing vital human tissue, and this engineering technology has now advanced to a point where systematic organ printing may be on the horizon.

The general 3D tissue printing process that researchers have been using does not deviate much from traditional 3D printing; the major difference is that the printer deposits cellular biomaterial instead of synthetic material. The printing process involves three major steps: preprocessing, or the development of the computer blueprint; processing, the depositing of biomaterial; and post-processing, or tissue maturation and conditioning. In the processing stage, there are currently three main approaches to depositing biomaterial: inkjet, microextrusion, and laser assisted printing. Thermal inkjet printers heat the printhead electrically, forcing droplets of material out of the nozzle. Microextrusion printers use pneumatic (operated by air pressure), piston, or screw dispensing systems to extrude beads of material from the nozzle. Laser assisted printers use laser-induced pressure to propel cell materials onto a collector. Each printer type has its own set of advantages and disad-

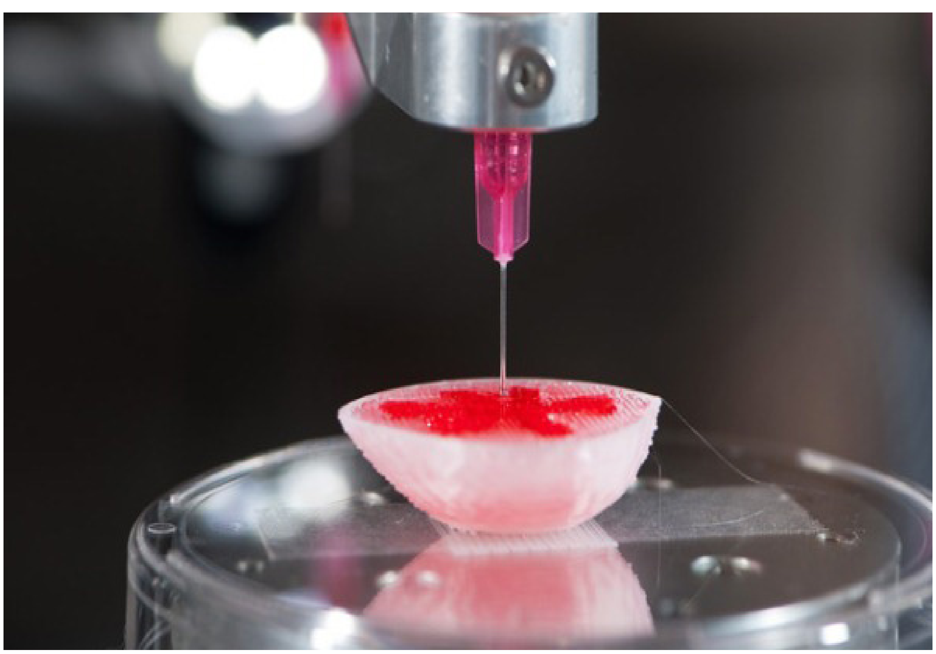


vantages. For instance, microextrusion printers have limitations on material crosslinking (molecular bonding in the material) inkjet printers have limitations on material viscosity.[3]

Compared with non-biological 3D printing, 3D bioprinting does involve some additional complexities, including cell types, growth factors, and sensitivities of living cells. Due to these complexities, many studies of bioprinting only use a limited range of materials, mostly involving collagen, hyaluronic acid, alginate, and modified acrylates.[4] The material used in the printing process needs to be easily manipulated by the machine to maintain its cellular functions and provide support for the overall structure. But current bioprinting technology already has the capacity to revolutionize modern medicine as we know it, as there have been records of its potential for success.

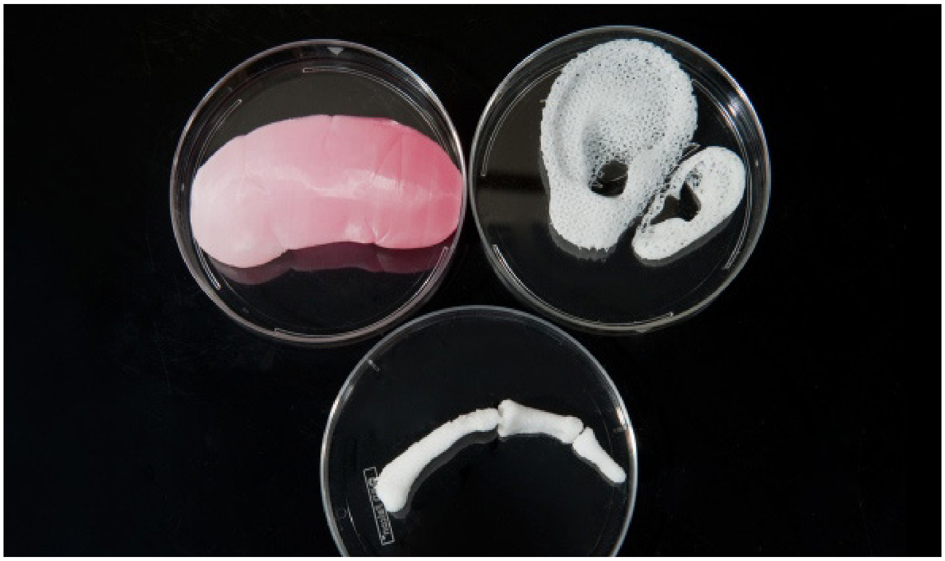
In 2011, six-month old infant Kaiba Gionfriddo suddenly stopped breathing due to a collapsed windpipe. After the life-threatening attack recurred for several weeks, doctors and researchers at the University of Michigan, Ann Arbor harnessed the power of advanced engineering technology and 3D printed a tracheal apparatus--a tubular device that wrapped around the infant's tracheal tube to keep the airways open. Constructed via inkjet printer from biomaterials compatible with the infant's body, the tube was successfully integrated into the infant's respiratory system, where it was eventually dissolved and reabsorbed by the body.[5]

Of course, this is only an example of a success in printing and implanting human tissue, as opposed to an actual organ. When it comes to printing a structure as complex as an organ, there are a number of additional factors to consider, including growth of cells, complex cell structure, and oxygen delivery. Organs are large structures, so billions of cells must be grown at a time; these cells not only assemble in multiple layers, but they also interact with each other. In addition, the organs need to be supplied with oxygen before implantation into the body, an oxygen supply system must be developed for each individual organ. But perhaps the most critical challenge in organ printing is the integration of a vascular system, or the assembly of blood vessels to enable nutrient and gas exchange.[4]



3D bioprinting of a kidney prototype

For Dr. Anthony Atala, director of the Wake Forest Institute for Regenerative Medicine at Wake Forest University, and his team of biomedical researchers, this posed the perfect challenge. Having already successfully printed bladders, cartilage, skin, and urine tubes that were implanted into patients, these researchers are currently working on printing an actual kidney. The first step of the proposed printing process would be to take a biopsy of the organ in question. Cells from the biopsy with regenerative potential would be isolated, multiplied, kept in a nutrient rich mixture, and transferred to a printer cartridge. A separate cartridge would then be filled with structural biomaterial. When the "print" button would be pressed, the biomaterial would deposit layer by layer to created the structure and the cells would be embedded between each layer. To resolve the issue of vascularization, a new fabrication technique would have to be implemented, involving the printing of multiple branched channels of bloods



Successfully 3D printed bone, ear, and kidney prototype, from Wake Forest Institute of Regenerative Medicine

> "The ultimate goal is to design a printing system utilizing the patient's own cells"

vessels. Bioreactors, chemicals that help preserve the state of the tissue in the vascularization process, would maintain tissue viability and "buy" time for vessel integration and blood transfusion in this post-processing stage. Under the right physiological conditions, the cells would perform as they would in a real organ. Although the researchers have successfully printed multiple 3D kidney prototypes using synthetically grown kidney cells, the process for printing an actual kidney is still in its developmental stages. For these scientists, the ultimate goal is to design a printing system utilizing the patient's own cells, so donor compatibility would not be an issue and rejection medications would no longer be needed.[4]

Even though 3D organ printing has very real implications in transforming the field of medicine, as of right now, only a small portion of the 3D printing industry's investment has been allocated towards biology and medicine. 3D printing has become hugely popular over the years. It's a 700 million dollar industry, but only 11 million dollars are currently invested in medical applications. However, over the next decade or so 3D printing is projected to be an 8.9 billion dollar industry, with 1.9 billion dollars invested in medical applications.2 With this emerging interest in 3D bioprinting for medicine, perhaps one day, made-to-order kidneys, bones, and hearts will be available for all.

REFERENCES

1. Bernstein, F. (Director), & Liu Y. (Director), McCann S. (Director), (2016). Waiting List [Motion Picture]. United States.
2. Kang, H., Lee, S. J., Ko, I. K., Kengla, C., Yoo, J. J., & Atala, A. (2016). A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. Nat Biotechnol Nature Biotechnology, 34(3), 312-319. doi:10.1038/nbt.3413
3. Kolesky, D. B., Truby, R. L., Gladman, A. S., Busbee, T. A., Homan, K. A., & Lewis, J. A. (2014). 3D Bioprinting of Vascularized, Heterogeneous Cell-Laden Tissue Constructs. Advanced Materials, 26(19), 3124-3130. doi:10.1002/adma.201305506Kamat P.V. J. of Phys. Chem. C. 2008, 112(48), 18737-53.
4. Murphy, S. V., & Atala, A. (2014). 3D bioprinting of tissues and organs. Nat Biotechnol Nature Biotechnology, 32(8), 773-785. doi:10.1038/nbt.2958
5. New Study Shows How Babies' Lives Were Saved by 3D Printing (with Video)." University of Michigan. N.p., n.d. Web. 05 Nov. 2016.
6. Organ Shortage Crisis: Problems and Possible Solutions. Transplantation Proceedings, 40(1), 34-38. doi:10.1016/j.transproceed.2007.11.067