AT THE HEART OF INNOVATION

CMU Researchers Solve Hard Problem of 3-D Printing Soft Tissue

AUGUST 1, 2019

A team of researchers from Carnegie Mellon University published a paper in *Science* that details a new technique allowing anyone to 3-D bioprint tissue scaffolds out of collagen, the major structural protein in the human body. This first-of-its-kind method brings the field of tissue engineering one step closer to being able to 3-D print a full-sized, adult human heart.

Arthur Hamerschlag Career Development Professor and Professor of Biomedical Engineering and Materials Science & Engineering Adam Feinberg and a team of Carnegie Mellon researchers invented a new 3-D bioprinting method that brings the dream of bioengineered human hearts one step closer to reality.

The technique, known as Freeform Reversible Embedding of Suspended Hydrogels (FRESH), has allowed the researchers to overcome many challenges associated with existing 3-D bioprinting methods, and to achieve unprecedented resolution and fidelity using soft and living materials.

Each of the organs in the human body, such as the heart, is built from specialized cells that are held together by a biological scaffold called the extracellular matrix (ECM). This network of ECM proteins provides the structure and biochemical signals that cells need to carry out their normal functions. However, until now, it has not been possible to rebuild this complex ECM architecture using traditional biofabrication methods.

"What we've shown is that we can print pieces of the heart out of cells and collagen into parts that truly function, like a heart valve or a small beating ventricle," said Adam Feinberg, Arthur Hamerschlag Career Development Professor and professor of biomedical engineering (BME) and materials science & engineering in the College of Engineering, whose lab performed this work. "By using MRI data of a human heart, we were able to accurately reproduce patient-specific anatomical structure and 3-D bioprint collagen and human heart cells."

More than 4,000 patients in the United States are waiting for a heart transplant, while millions of others worldwide need hearts but are ineligible for the waitlist. The need for replacement organs is immense, and new approaches are needed to engineer artificial organs that are capable of repairing, supplementing or replacing long-term organ function. Feinberg, who is a member of Carnegie Mellon's Bioengineered Organs Initiative and the Next Manufacturing Center, is working to solve these challenges with a new generation of bioengineered organs that more closely replicate natural organ structures.

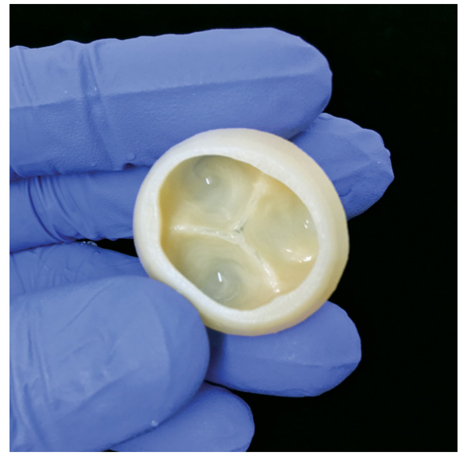
"Collagen is an extremely desirable biomaterial to 3-D print with because it makes up literally every single tissue in your body," said Andrew Hudson, a BME Ph.D. student in Feinberg's lab and co-first author on the paper. "What makes it so hard to 3-D print is that it starts out as a fluid, so if you try to print this in air, it just forms a puddle on your build platform. We've developed a technique that prevents it from deforming."

The FRESH 3-D bioprinting method developed in Feinberg's lab allows collagen to be deposited layer by layer within a support bath of gel, giving the collagen a chance to solidify in place before it is removed from the support bath. With FRESH, the support gel can be easily melted away by heating the gel from room temperature to body temperature after the print is complete. This way, the researchers can remove the support gel without damaging the printed structure made of collagen cells.

This method is truly exciting for the field of 3-D bioprinting because it allows collagen scaffolds to be printed at the large scale of human organs. It is not limited to collagen, as a wide range of other soft gels including fibrin, alginate and hyaluronic acid also can be 3-D bioprinted using the FRESH technique, providing a robust and adaptable tissue engineering platform. Importantly, the researchers also developed open-source designs so that anyone from medical labs to high school science classes can build and have access to low-cost, high-performance 3-D bioprinters.

"We're making real progress toward engineering functional human tissues and organs. This Science paper is one step along that path."
— Adam Feinberg, Arthur Hamerschlag Career Development Professor and Professor of Biomedical Engineering and Materials Science & Engineering

Looking forward, FRESH has applications in many aspects of regenerative medicine, from wound repair to organ bioengineering, but it is just one piece of a growing biofabrication field.



A valve component for an adult human heart now can be 3-D printed using a new method pioneered at CMU.

"We're talking about the convergence of technologies — not just what my lab does in bioprinting but also from other labs and small companies in the areas of stem cell science, machine learning and computer simulation," Feinberg said.

"It is important to understand that there are many years of research yet to be done, but there should still be excitement that we're making real progress toward engineering functional human tissues and organs. This *Science* paper is one step along that path."

Other collaborators on the paper include co-first author Andrew Lee, a BME Ph.D. student in Feinberg's lab; BME postdoctoral researcher Dan Shiwarski; BME Ph.D. students Joshua Tashman, T.J. Hinton, Sai Yerneni and Jacqueline Bliley; and BME Research Professor Phil Campbell.