

Scientists prove feasibility of 'printing' replacement tissue

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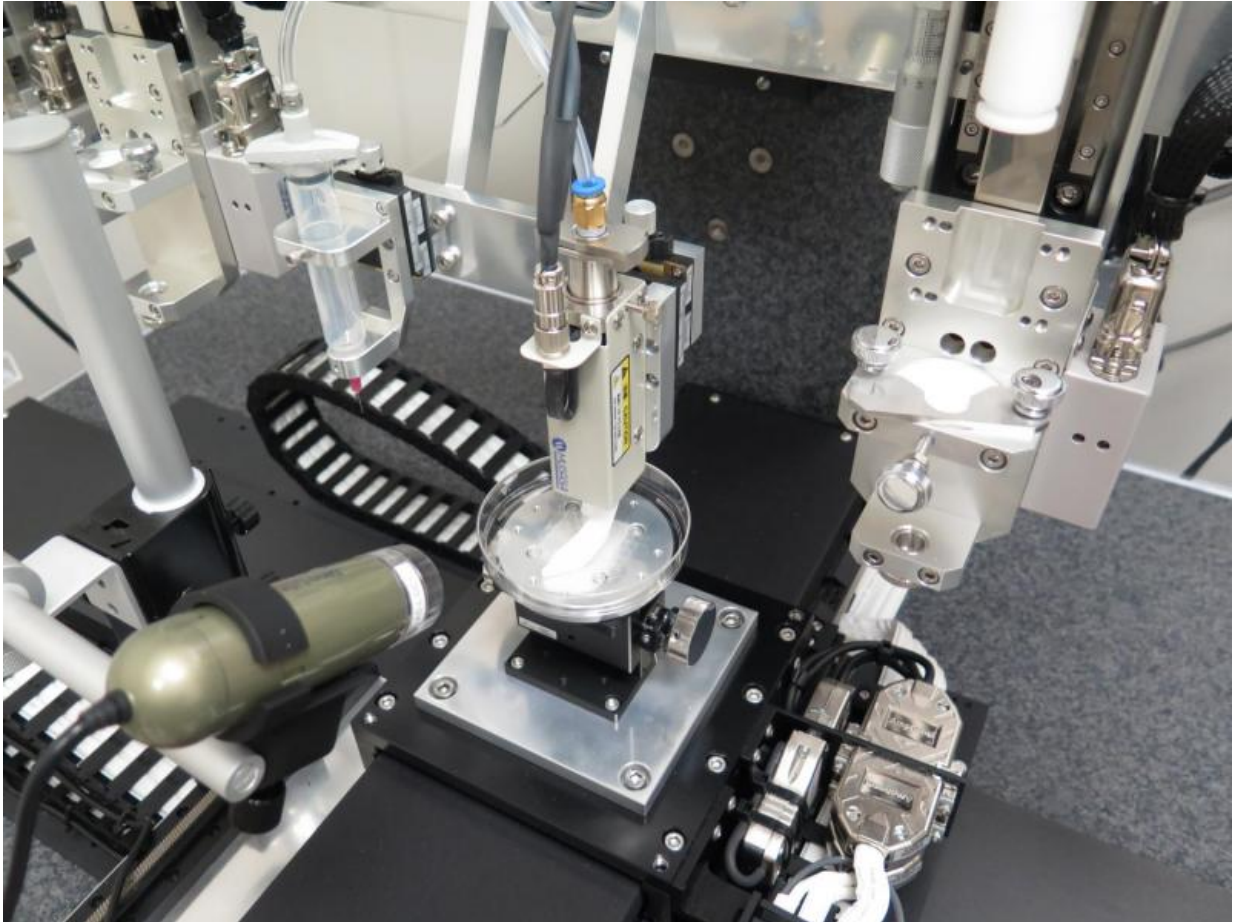
The Integrated Tissue-Organ Printing System at work printing a jaw bone structure. Credit: Wake Forest Institute for Regenerative Medicine

Using a sophisticated, custom-designed 3D printer, regenerative medicine scientists at Wake Forest Baptist Medical Center have proved that it is feasible to print living tissue structures to replace injured or diseased tissue in patients.

Reporting in *Nature Biotechnology*, the scientists said they printed ear, bone and muscle structures. When implanted in animals, the structures matured into functional tissue and developed a system of blood vessels. Most importantly, these early results indicate that the structures have the right size, strength and function for use in humans.

"This novel tissue and organ printer is an important advance in our quest to make replacement tissue for patients," said Anthony Atala, M.D., director of the Wake Forest Institute for Regenerative Medicine (WFIRM) and senior author on the study. "It can fabricate stable, human-scale tissue of any shape. With further development, this technology could potentially be used to print living tissue and organ structures for surgical implantation."

With funding from the Armed Forces Institute of Regenerative Medicine, a federally funded effort to apply [regenerative medicine](#) to battlefield injuries, Atala's team aims to implant bioprinted muscle, cartilage and bone in patients in the future.



The Integrated Tissue-Organ Printing System at work printing a jaw bone structure. Credit: Wake Forest Institute for Regenerative Medicine

Tissue engineering is a science that aims to grow [replacement tissues](#) and organs in the laboratory to help solve the shortage of donated tissue available for transplants. The precision of 3D printing makes it a promising method for replicating the body's complex tissues and organs. However, current printers based on jetting, extrusion and laser-induced forward transfer cannot produce structures with sufficient size or strength to implant in the body.

The Integrated Tissue and Organ Printing System (ITOP), developed

over a 10-year period by scientists at the Institute for Regenerative Medicine, overcomes these challenges. The system deposits both bio-degradable, plastic-like materials to form the tissue "shape" and water-based gels that contain the cells. In addition, a strong, temporary outer structure is formed. The printing process does not harm the cells.

A major challenge of [tissue engineering](#) is ensuring that implanted structures live long enough to integrate with the body. The Wake Forest Baptist scientists addressed this in two ways. They optimized the water-based "ink" that holds the cells so that it promotes cell health and growth and they printed a lattice of micro-channels throughout the structures. These channels allow nutrients and oxygen from the body to diffuse into the structures and keep them live while they develop a system of blood vessels.

It has been previously shown that tissue structures without ready-made blood vessels must be smaller than 200 microns (0.007 inches) for cells to survive. In these studies, a baby-sized ear structure (1.5 inches) survived and showed signs of vascularization at one and two months after implantation.

"Our results indicate that the bio-ink combination we used, combined with the micro-channels, provides the right environment to keep the cells alive and to support cell and tissue growth," said Atala.

Another advantage of the ITOP system is its ability to use data from CT and MRI scans to "tailor-make" tissue for patients. For a patient missing an ear, for example, the system could print a matching structure.



Completed ear structure printed with the Integrated Tissue-Organ Printing System. Credit: Wake Forest Institute for Regenerative Medicine

Several proof-of-concept experiments demonstrated the capabilities of ITOP. To show that ITOP can generate complex 3D structures, printed, human-sized external ears were implanted under the skin of mice. Two months later, the shape of the implanted ear was well-maintained and cartilage tissue and [blood vessels](#) had formed.

To demonstrate the ITOP can generate organized soft [tissue structures](#), printed [muscle tissue](#) was implanted in rats. After two weeks, tests confirmed that the muscle was robust enough to maintain its structural

characteristics, become vascularized and induce nerve formation.

And, to show that construction of a human-sized bone structure, jaw bone fragments were printed using human stem cells. The fragments were the size and shape needed for facial reconstruction in humans. To study the maturation of bioprinted bone in the body, printed segments of skull bone were implanted in rats. After five months, the bioprinted structures had formed vascularized bone [tissue](#).

Ongoing studies will measure longer-term outcomes.

More information: A 3D bioprinting system to produce human-scale tissue constructs with structural integrity, *Nature Biotechnology*, [DOI: 10.1038/nbt.3413](#)

Provided by Wake Forest University Baptist Medical Center

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