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NEWS BIOMEDICAL

Bioprinting Inside the Body, Without Breaking the Skin

› Ultrasound enables minimally invasive 3D-printing of tissues, therapies, and more

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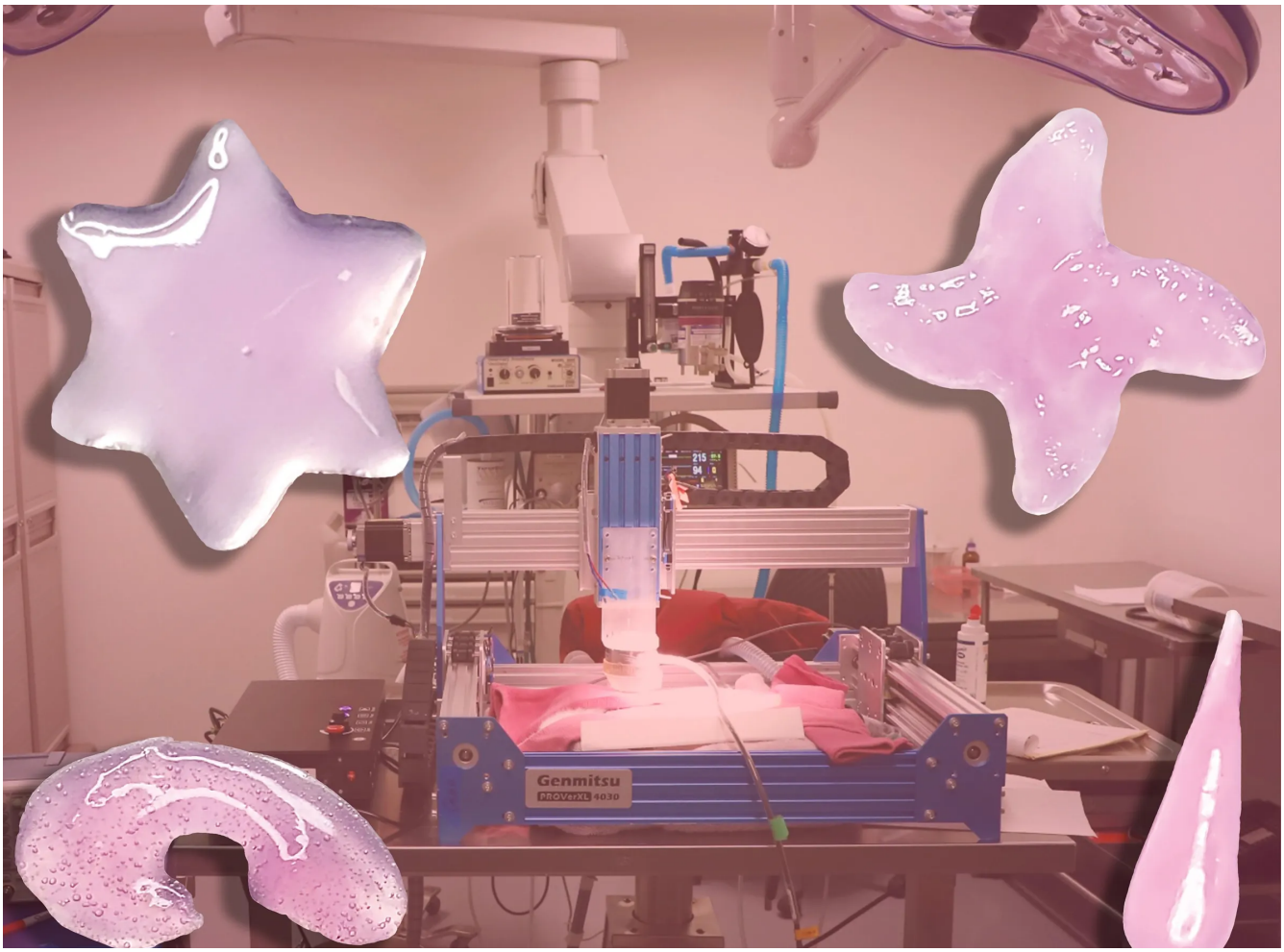

NEW TECHNIQUE FOR 3D PRINTING SOFT

A materials directly inside the body could allow the creation of complex structures deep within tissue—without making a single incision.

The approach, unveiled this week in *Science*, uses focused ultrasound to sculpt injected "bio-ink" into tissue-like structures, opening the door to minimally invasive applications in cancer therapy, bioelectronics, and regenerative medicine.

Developed by engineers at the California Institute of Technology, the method eliminates the need for surgical cutting or surface-access printing. Instead, researchers simply inject a custom-designed liquid ink into the body through a needle or catheter.

Then, using real-time ultrasound imaging to guide placement, they direct a second focused beam of high-frequency sound to gently heat the target site by just a few degrees—enough to trigger a molecular chain reaction that turns the liquid into a gel.

"It's quite exciting," says Yu Shrike Zhang, a biomedical engineer at Harvard Medical School and Brigham and Women's Hospital in

Cambridge, Mass., who was not involved in the research. "This work has really expanded the scope of ultrasound-based printing and shown its translational capacity."

No Nozzle, No Problem

To make the method work, the Caltech team—led by biomedical engineer Wei Gao and his former postdoc Elham Davoodi—had to rethink nearly every step of conventional 3D printing.

Traditional printers rely on physical nozzles to deposit material layer by layer. The new technique—termed Deep tissue In vivo Sound Printing, or DISP—gets rid of the nozzle altogether, using tightly focused beams of sound to generate controlled temperature spikes that kick-start a printing-like process.

At the heart of the system are liposomes: tiny fat-based capsules similar to those used in mRNA vaccines. These remain intact at normal body temperature but rupture when briefly warmed. "You only need a few degrees Celsius," Gao explains, "and then it will release."

Inside, the liposomes carry cross-linking agents. Once activated by the warming energy of ultrasound, these agents bind to loose polymer strands in the ink, such as alginate from seaweed or gelatin

from pigs—both staples of medical research and therapeutics. This rapidly forms a stable, biocompatible hydrogel.

Put It in Ink

To monitor the process in real time, the researchers added gas vesicles: protein-shelled nanostructures that scatter sound waves and illuminate under specialized ultrasound settings. These allow the team to visualize both the placement of the ink and whether it has successfully gelled.

The system offered impressive precision for an internal process, notes Gao. It could create patterns—stars, teardrops, pinwheels, and more—laying down hydrogel at speeds up to 40 millimeters per second, with a resolution of 150 micrometers, roughly the width of a coarse human hair.

Beyond printing shapes, the team also customized the ink with functional additives: electricity-conducting nanomaterials for sensing devices, living cells to promote tissue repair, and bioadhesives to help seal wounds or anchor implants in place.

“It’s quite versatile,” says Davoodi, a 3D-bioprinting researcher now at the University of Utah in Salt Lake City.

Bunny Prints and Tumor Hits

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To demonstrate DISP's potential in a medical setting, the researchers tested it in two animal models: mice and rabbits.

In mice, they printed a slow-release drug depot near a bladder tumor. Using bio-ink loaded with doxorubicin, a common chemotherapy drug, they created a soft reservoir designed to slowly release this therapeutic payload over time. The goal: to keep the drug concentrated at the tumor site far longer than standard bladder cancer therapies, which are often flushed out of the body within hours.

Additionally, they used rabbits to demonstrate the depth range of the approach, printing hydrogel scaffolds inside muscle tissue several centimeters below the skin.

The bio-ink appeared well tolerated, with no signs of adverse reactions. But in case removal were ever necessary, the researchers demonstrated—using pig and chicken tissues in the lab—that the printed hydrogels could be selectively dissolved with a chemical commonly used to treat heavy-metal poisoning.

Not only can we print in organs or tissue, but we can remove it," says Gao.

Scalpels Out, Sound Waves In

DISP wasn't the first attempt at in-body bioprinting. Initial approaches focused on infrared light but struggled with tissue penetration and light scattering. Meanwhile, later efforts that relied on ultrasound to directly trigger chemical reactions had serious drawbacks, such as microbubble formation or the generation of excess heat that could damage nearby tissues.

By instead using ultrasound to activate engineered liposomes and indirectly start the bioprinting reaction, with minimal thermal risk to surrounding tissue, the Caltech team sidestepped those issues, gaining greater control, faster printing speeds, and improved biocompatibility.

The technique remains far from clinical deployment. But it marks a major step toward more precise, less invasive treatments using 3D-bioprinted materials, notes Davoodi—particularly in cases where traditional surgery is risky, impractical, or undesired.

"It's a new research direction in the field of bioprinting," she says.