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The machinery of medicine

How medicine's new tools advance research and care

ALSO
6 Medicine from the Amazon
40 Greek drama helps veterans
44 Helping doctors help themselves

New artery? We can print that

Mark Michalski, M.D., HS '15, on call late one night in 2013, was browsing through *Wired* when he came across an article about 3D printing. It is, as the name suggests, a technology for printing—not ink on a sheet of paper but structures made of diverse materials in three dimensions. Then a radiology resident at Yale-New Haven Hospital, Michalski spent many working hours examining cross-sectional images of the human body and body parts. These images, taken from computed tomography (CT) and magnetic resonance imaging (MRI) scans, depict the body as if it were cut up into many thin slices; taken together, they represent three-dimensional structures. Most of the time, surgeons scroll through these images to create mental pictures of the anatomy that they will meet in 3D only in the operating room. 3D printing, Michalski realized, offered a new possibility: custom-printed 3D models, which surgeons could handle and experiment with, of the structures that they would later cut, stitch, and screw together.

"I thought to myself, 'Well, I have a lot of the raw materials here; I wonder if I can just start printing things,'" recalls Michalski. "Of course, it wasn't that simple."

Since then, Michalski and other radiologists at Yale have used 3D printing to make models in both plastic and plaster of knees, feet, pelvises, shoulder blades—"just about anything bony," says Michalski. Physicians use these models to teach young doctors, plan surgeries, and communicate with patients. In the department of surgical research, doctors are using Bio3D printers, which print live cells, to make not models but the organs themselves, starting with blood vessels. 3D-printed organs, doctors hope, could eventually be used in organ transplants.

Invented in the 1980s, 3D printers build up objects layer by layer. The printer draws out one layer of "ink" (which can be plastic, metal, plaster powder, wood composite, even chocolate); the platform moves downward, and the printer adds another layer atop the first. Successive strata form a three-dimensional object in the same way that a surgeon may use multiple cross-sectional images to envision a 3D form. The printer follows a digital template; and luckily for doctors, software can turn radiological data from MRI and CT scans into these very guides.

In 2013, the raw materials that Michalski had at his disposal included not just troves of radiological scans but also 3D printers in the Yale Center for Engineering Innovation and Design (CEID). The CEID has five 3D printers, three of which are available to any Yale student or faculty member. These open-access printers, produced by the New York City-based company MakerBot, extrude melted plastic through a heated tip that moves around the platform, creating a design in the same the way a baker writes with frosting on a cake.

In mid-2013, Michalski started printing anatomical objects on the MakerBot printers; his first print was a blue plastic model of the chambers of a child's heart. It was not long before Michalski began to collaborate with the CEID's assistant director, Joseph Zinter, Ph.D., M.H.S. '11, to 3D-print models that could help surgeons. In June 2013, for example, they printed a model of the tumor-invaded tibia of a patient scheduled for surgery at Yale. "We brought the model to the orthopaedic surgeon and said, 'This is the case you have on Thursday,'" recalls Zinter. The model helped the surgeon plan an operative approach that would avoid cutting the patient's patellar tendon, says Zinter.

Based on the success of Michalski's work at the CEID, the Department of Diagnostic Radiology acquired its own 3D printers in 2014. Radiology uses powder printers, a different type of 3D printer from those at the CEID. The powder printer lays down a bed of powdered plaster and the printer tip dispenses glue, causing the powder to stick together where the tip writes. By the end of the print job, the object is essentially buried in plaster dust, which supports the structure as it is being printed; the unused powder is then vacuumed away. (Since mid-2015, Michalski has worked full time for a medical device company, the Butterfly Network, of which he is president. As a research affiliate in the hospital's diagnostic radiology department, though, he maintains his ties to Yale and still does the occasional 3D print.)

Elliott Brown, M.D., HS '12, FW '13, who has led radiology's 3D-printing program since Michalski left Yale, explained how 3D printing helps physicians with their cases. Some things are easy to understand from looking at a radiological image, says Brown, but in tricky cases, "a 3D model is very helpful, because you get depth perception and you get proprioception, meaning you can understand the shape of an object by its feel." Since it's possible to drill into plaster, the models also allow orthopaedic surgeons, who may need to screw a patient's bones back together, to test various surgical approaches.

Beyond models, researchers want to print living organs for patients awaiting organ transplants. In the ideal case, these could be printed from cultured cells taken from the recipient, eliminating both the wait for a donor organ and the risk of immune system rejection.

This past summer, Yale's department of surgical research joined the effort to 3D-print organs when they acquired a Bio3D printer through a partnership with the bioprinting company Organovo. John Geibel, D.Sc., M.D., M.S., vice chair of surgery, director of surgical research, professor of surgery and of cellular and molecular physiology, and his colleagues began by printing blood vessels using mixtures of rat smooth muscle, fibroblasts, and endothelial cells. In a laboratory hood, the bioprinter lays down the "bio ink," strips of cells resembling ground meat, supported by strips of a water-based gel. The result: a cylinder of cells around a gel interior, which later can be removed to become the lumen of the blood vessel. The next benchmark, says Geibel, is to implant 3D-printed vessels into rats.

Eventually, Geibel would like to print a liver. During his career, Geibel hopes to create a 3D-printed "assist liver" that could be transplanted into patients and help them survive while they await a donor's liver. "If we get that far," says Geibel, "it's not impossible to think that we could eventually create a complete replacement organ."

—*Ashley P. Taylor*

ROBERT LISAK

A year ago Mark Michalski was finishing up his residency. Now he's heading a startup with millions of dollars in financing and dozens of employees.