A new heart

A nationwide breakthrough for surgeons using 3D hearts

By Lisa Robbins, ASU News
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Each year, around 1.3 million children are born with congenital heart disorders, malformations that can include missing chambers or misplaced vessels. It’s the most common birth defect globally, and about one-third of cases require surgery, often just weeks after birth.

The structural defects vary widely. Often, surgeons must rely on 2D images of a heart the size of a walnut from CT scans.

As one of the largest pediatric heart centers in the U.S., Phoenix Children’s performs dozens of surgeries for congenital heart disorders every year. In 2012, it launched the Cardiac 3D Print Lab, a pioneering initiative with ASU that used 3D-printed models of patients’ hearts to guide complex pediatric heart surgeries.

Holding the heart

In 2009, Justin Ryan, an intermedia student at ASU learning 3D modeling and animation in what was then called the Katherine K. Herberger College of Fine Arts, attended a guest lecture by David Frakes, a professor in the Ira A. Fulton Schools of Engineering, and his career changed course.

“He needed someone to do 3D modeling, printing and casting,” says Ryan, who now leads the 3D Innovations Lab at Rady Children’s Hospital in San Diego.

Ryan, ’10 BA, ’14 MS, ’15 PhD, worked in Frakes’ lab. In 2010, Frakes, Ryan and a small group of collaborators at ASU recognized they could deliver 3D prints directly to surgeons.

“We could give the surgeon the opportunity to quite literally hold a patient’s heart in their hand before operating,” Ryan says.

The basic idea was to transform images of a patient’s heart taken from CT scans into 3D models that could then be printed in plastic using commercially available 3D printers. These color-coded models would help surgeons quickly understand the patient’s specific structural defects and plan their operations accordingly.

By 2012, Ryan and his colleagues at the Fulton Schools had secured a grant for a 3D printer at Phoenix Children’s. A retrospective study published by Ryan in the journal 3D Printing in Medicine showed that the models had a meaningful impact on reducing the amount of time the patient spent in surgery. To date, more than 500 heart models have been created at Phoenix Children’s.

“If you can do a surgery faster, it reduces anesthesia time and risk,” Ryan says. The faster surgeries were attributed to better surgeon preparedness, which itself reduces the chance of complications and improves the likelihood of good patient outcomes.

When Ryan and his colleagues launched their 3D printing initiative in 2010, you could count the number of 3D print labs in U.S. hospitals on one hand. Today, there are more than 100 3D printing centers at hospitals around the U.S. as research pioneered at ASU has become standard practice.

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> ’10 BA, ’14 MS, ’15 PhD in bioengineering

Growing new tissue

While Ryan’s models help surgeons see damaged hearts, Mehdi Nikkhah is working to repair heart tissue itself.

Nikkhah, a professor in the School of Biological and Health Systems Engineering, has spent more than a decade on cardiac regeneration and disease modeling. His goal is to create engineered heart tissues in the lab that can be transplanted to repair damage from heart attacks.

“Myocardial infarction — a heart attack — is one of the leading causes of death nationwide,” Nikkhah says. “For severe cases, the expected survival is often limited to only a few years, as they go through catastrophic heart failure.”

Nikkhah’s lab is attacking this problem from two directions. First, he’s growing replacement tissue. His team combines stem cells with gold nanoparticles in a gel to create engineered heart tissues or patches that beat in the lab. The gold nanoparticles make the tissue electrically conductive, allowing cells to contract together like healthy heart muscle does. The goal is to transplant these patches onto damaged hearts, replacing scar myocardium with functional tissue that can pump blood.

The work has earned support from the Arizona Biomedical Research Commission, Phoenix Children’s and most recently, a major NIH grant with Dr. Wuqiang Zhu at Mayo Clinic of Arizona.

“The collaboration is moving toward animal trials that can pave the way for preclinical studies,” Nikkhah says.

Meanwhile, his heart-on-a-chip technology uses microfluidic devices the size of only a few millimeters to model cardiovascular disease. These chips contain human stem cells embedded in three-dimensional hydrogels or the same conductive materials used in the transplantable patches, creating miniature hearts.

Nikkhah can simulate a heart attack on the chip, then test whether his engineered tissues can repair the damage. If a treatment works on the chip, it's worth pursuing.

"This microengineering platform enables us to recapitulate the disease and interrogate its mechanism in the lab," Nikkhah says. "Then we can potentially do drug screening, and we can come up with better therapeutics for treatment of heart disease in the future."

Predicting heart problems

In the School of Computing and Augmented Intelligence, Associate Research Professor Ayan Banerjee and Professor Sandeep Gupta are developing digital tools to predict and prevent heart disease before damage occurs, especially in women.

When doctors analyze exercise stress electrocardiograms, they look for specific markers for evidence of heart disease. But in women, hormonal changes and other physiological factors create a baseline depression in the ST segment, one of the key markers doctors use to identify coronary artery disease. Women's ECGs can look abnormal even when they're healthy, leading to false positives and unnecessary invasive testing. Or sometimes, real problems get missed.

It's a big problem. Cardiovascular disease affects more women than all forms of cancer combined, causing one in three deaths each year. Yet the disparities in testing accuracy mean that although women are less likely to suffer from heart disease than men, they are far more likely to die from it.

Banerjee and Gupta, who lead ASU's Intelligent Mobile and Pervasive Applications and Communication Technologies Lab, are tackling this with a hybrid approach to artificial intelligence. The team received multiple grants from the Arizona New Economy Initiative, the Mayo Clinic Cardiovascular Research Award and, more recently, the National Institutes of Health, to work with collaborators at Mayo Clinic. They conducted a study of more than 1,200 patients who had undergone both exercise stress ECGs and coronary angiography. Rather than simply feeding data into a neural network, their approach combines patient data with decades of medical expertise about how the heart works and what doctors look for in ECG readings.

"The innovation was to not just utilize the data but also experts' knowledge at various stages of model development and validation," Gupta says.

Why this research matters

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The results from the Mayo Clinic study were striking. When tested on 227 patients not included in the training data, the AI achieved 94% accuracy in detecting severe coronary artery disease. More importantly, it eliminated the gender gap. The system improved sensitivity from 50% to 91% in women and from 50% to 94% in men. For the first time, the test worked equally well for both sexes.

“What we could do with AI is level the playing field,” Banerjee says.

Importantly, the AI can explain its reasoning in terms doctors understand, showing which features led to a diagnosis.

“Our main idea is not just use AI as a data-churning machine, but integrate the human experts’ knowledge into AI,” Banerjee says.

Monitoring for life

In addition to using AI for improved ECG analysis, Banerjee and Gupta are working on building digital twins of patients’ hearts.

These mathematical models capture the unique electrical and mechanical properties of a patient’s heart, which Gupta hopes will one day allow physicians to detect problems long before they become life-threatening.

“Heart attacks occur very infrequently, but when they occur, they are life-threatening,” Banerjee says.

To catch them before they happen may require around-the-clock monitoring that provides a complete picture of how a person’s heart changes over time.

The challenge with lifelong monitoring is too much data. That’s where the digital twin comes in. The team’s approach uses physiological models based on decades of cardiac research.

“A year or two years’ worth of data can be only stored using 15 parameters,” Banerjee says, “instead of millions of data points.”

Hearts change slowly over a lifetime. When significant changes occur, the system detects them and adjusts the digital twin model.

The digital twin can help doctors understand what’s happening with a specific patient’s heart. The team is working on techniques to run these models on portable devices, making continuous monitoring practical. The digital twin tools are now in pilot studies at Mayo Clinic.

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Dorothy Sears
Professor, College of Health Solutions

“Our goal is to basically eliminate deaths from heart failure,” Gupta says.

But collecting real-world data still plays an important role in prevention. For years, Dorothy Sears, a professor in the College of Health Solutions, has studied how sedentary behavior damages cardiovascular health and how behavioral interventions can reduce the risk of cardiovascular problems. In one study, Sears used data from wearable sensors worn by 518 postmenopausal women who were overweight and discovered that their sitting behavior was associated with levels of blood sugar and fats linked to heart disease risk. Data from a more recent study on postmenopausal women highlighted a simple solution to improving their cardiovascular health.

“We showed that just breaking up sitting time with an eight-minute break once an hour improved vascular function in a single day,” Sears says. “Our evidence is showing that any way that you can break up your sitting time or maybe just walk around or stand up will benefit your blood vessels.”

A coordinated effort

ASU researchers are working at every stage of heart care. None of these innovations happened in isolation. Each breakthrough required collaboration across disciplines, among universities and hospitals, and researchers who understood that solving heart disease means addressing it from the operating room to the research lab.

About the author

A former staff writer at Wired magazine and founder of the deep tech PR and marketing agency HAUS, he is an ASU alumnus, ’15 BA in English (creative writing) and philosophy, and a graduate of Barrett, The Honors College.

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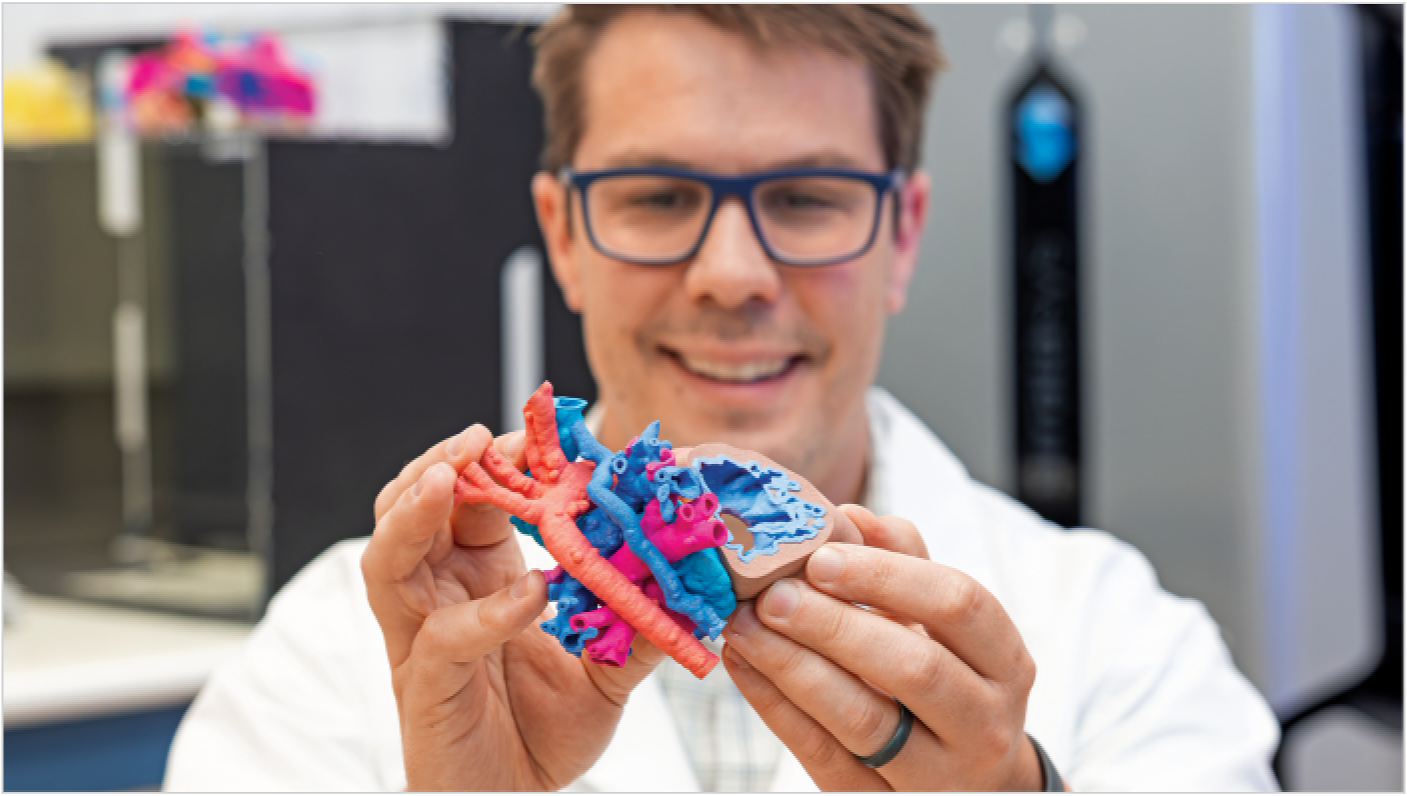
Main image



ASU alum Justin Ryan holds a 3D printed heart model in his hands. The models help guide complex pediatric heart surgeries at Phoenix Children's. Photo by Sabira Madady

Text image(s)

ASU alum Justin Ryan uses a 3D heart innovation from ASU to save lives at Rady Children's Hospital in San Diego. Photo by Sabira Madady

Gallery

Shaun Wootten, ’17 BS and BSE, is a PhD student working in Mehdi Nikkhah’s laboratory.

The heart-on-a-chip technology uses microfluidic devices the size of only a few millimeters to model cardiovascular disease.