Federal Register Notice: 89 FR 51554, <u>Federal Register :: Networking and Information Technology</u> <u>Research and Development Request for Information on Digital Twins Research and Development</u>, June 18, 2024.

Request for Information on the National Digital Twins R&D Strategic Plan

Stephanie Armour

DISCLAIMER: Please note that the RFI public responses received and posted do not represent the views or opinions of the U.S. Government. We bear no responsibility for the accuracy, legality, or content of the responses and external links included in this document.

This copy is for your personal, non-commercial use only. Distribution and use of this material are governed by our Subscriber Agreement and by copyright law. For non-personal use or to order multiple copies, please contact Dow Jones Reprints at the second secon

https://www.wsj.com/health/healthcare/digital-heart-surgery-patient-treatment-c35ec4be

THE FUTURE OF EVERYTHING

A 'Digital Twin' of Your Heart Lets Doctors Test Treatments Before Surgery

Researchers create digital replicas of individual patients' organs using data from exams and wearable devices: 'You can run an infinite number of experiments'

By Stephanie Armour Follow

May 16, 2024 at 9:00 am ET

Patients diagnosed with heart disease, cancer and other ailments face myriad decisions: Which drug will be most effective? Will the side effects outweigh the benefits? Will surgery be enough?

Determining the best path forward may be far easier in years to come. Instead of trying a therapy and hoping it works, researchers are creating so-called digital twins to predict how a patient will respond before ever starting treatment.

"It's a paradigm change," says Emily Greenspan, a program director in the informatics and data science program at the National Cancer Institute. "You could be able to predict an

individual's disease trajectory."



Natalia Trayanova, a professor at Johns Hopkins, is leading a clinical trial using 'digital twins' of patients' hearts. PHOTO: JOHNS HOPKINS UNIVERSITY

In a Baltimore lab, Natalia Trayanova and her team at Johns Hopkins University are creating computational models of hearts. Each one mirrors the heart of a real patient with a potentially fatal arrhythmia, an irregular heartbeat that is often a result of scarring from heart attacks or other conditions.

The replicas, or "digital twins," appear as personalized 3-D hearts on computers, with areas of scarring shown in white. The team can use them to model how and where to make new tiny scars through a procedure called ablation to fix the arrhythmia.

"You can watch it on the screen," says Trayanova, a professor in the department of biomedical engineering at Johns Hopkins who is leading a clinical trial using these digital twins. "We want to know how to treat the patient in the most optimal way."

Federal agencies, startups and academics are pouring billions of dollars into bringing digital twins to the forefront of healthcare in the next five to 10 years. The global digital-twins healthcare market was valued at \$1.6 billion in 2023 and could reach \$21.1 billion by 2028, according to a report by MarketsandMarkets. The growth in North America is attributed to government funding and investment, as well as companies already providing digital-twin technology to represent healthcare data, physical hospitals, human physiology and other areas.

Digital twins for all?

Clinicians envision a tomorrow where nearly everyone could have a digital twin created by artificial intelligence, using information from medical exams, wearable data devices and medical records. AI could search through data of others with comparable issues and run simulations while providing continuous monitoring of a patient's health.

Like a crash-test dummy, a digital twin could be used to test drugs and conduct trials without harming the actual patient. A digital twin of a heart could allow surgeons to visualize the procedure and the patient's specific vessels before an operation. The technology could be used to design highly accurate prosthetics or determine the most effective rehabilitation exercises. Digital twins of a patient's uterus and cervix could help predict pregnancy outcomes.



Digital-twin models of uterine walls in pregnant women show levels of stretch as the baby grows. The digital twins are used to help predict the course of the pregnancies. PHOTO: ERIN LOUWAGIE AND KRISTIN MYERS/COLUMBIA UNIVERSITY

While the concept has been used for decades in other industries such as mechanical engineering, digital twins are still relatively new in healthcare because modeling a human organ or body—at times to the cellular level—is so complex. Collecting personal data with wearable devices and sensors also requires addressing concerns about how to preserve privacy. Machine learning, or artificial intelligence, is still evolving and can at times produce biased results.

Researchers say it is also hard to move ahead

because the concept involves so much agreement and buy-in from various stakeholders, including data scientists, doctors, engineers and others.

"There is a lot of trust that needs to happen," says Dr. David Spragg, an associate professor of medicine at Johns Hopkins Hospital in Baltimore specializing in cardiology and cardiac electrophysiology. He is also part of the team working on the clinical trial of digital twins for hearts.

Tackling tough questions

But the potential has generated enthusiasm from doctors and researchers who describe a not-too-distant future where digital twins could answer difficult medical questions. What side effects will a specific patient get from cholesterol-lowering drugs? How likely is a patient to get asthma or diabetes, and if so, how soon? How might a woman's specific pregnancy progress?

Researchers are already working on these ideas and, in some cases, putting them into novel use.

In the Johns Hopkins clinical trial on heart arrhythmia, the patients undergo a cardiac contrast-enhanced MRI. From the images, the biomedical engineering team reconstructs a three-dimensional model of the patient's heart, using artificial intelligence to put images together. The result is a 3-D heart that shows scarring and areas of damaged cells that can be rotated on the screen and looked at from different angles.

The digital heart is then populated with virtual cells that can each generate an electrical signal.

The team can then simulate a heartbeat in the heart digital twin, and poke and prod it by giving it small electrical signals here and there to see what happens with the heartbeat.

Using the digital twin, the team can predict the possible locations of disordered rhythms and identify the best locations for ablation before the procedure is carried out, says Trayanova, who is also a professor of medicine.

David Gakenheimer, an 80-year-old retired technology inventor who had arrhythmia, was a patient at Johns Hopkins and heard about the digital twin work. The hospital also has provided digital twins to patients who aren't in the clinical trial. So the team made one for Gakenheimer, who wanted to see how it would compare with the ablation procedure he underwent later from a doctor.

"I wanted to do a normal procedure and

compare it to her software," Gakenheimer says, referring to Trayanova. His successful treatment ended up matching the results from the digital twin: "The areas of her model accurately predicted them."

Previewing a pregnancy

Kristin Myers, a mechanical engineering professor at New York's Columbia University, is making digital copies of women's uteruses and cervixes, hoping this can help in determining how a pregnancy will go. To do this, Myers uses an ultrasound to create 3-D computational models as part of an effort to someday solve the problem of preterm births.

"The idea of digital twins in health is new," she says. "We can offer better diagnoses. You can run an infinite number of experiments."

At the National Cancer Institute, Greenspan envisions a novel way to treat oncology patients. Instead of trying a drug and hoping it works, doctors would create a digital twin of the patient to predict how the disease would respond to a certain drug.

The institute has been working on creating virtual twins for best treatments of lung cancer, for instance. In the next five years the technology will likely become part of clinical decision-making, Greenspan says.

"Predicting the best treatments and screening, these are blue-sky visions," she said. "There is a lot of foundational research that's needed."

Write to Stephanie Armour at