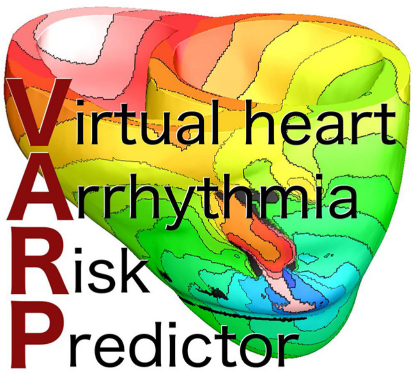
amazing things PODCAST

USING A PERSONALIZED, VIRTUAL HEART TO PREVENT SUDDEN CARDIAC DEATH

More than 350,000 people each year will experience an out of hospital cardiac arrest. Cardiac arrest is an extremely dangerous circumstance that requires immediate treatment. In cardiac arrest, death results when the heart suddenly stops working properly. This may be caused by abnormal, or irregular, heart rhythms (called arrhythmias). Since prior heart attack, or myocardia infarction, is a major risk factor for arrhythmia, these patients are prime candidates for surgically implanted defibrillators, which monitor heart rhythm and deliver an electric shock if needed to keep the heart beating regularly.

The current tools for assessing whether a patient is likely to actually suffer an arrhythmia and therefore benefit most from the defibrillator (which carries its own risks) are not highly predictive. Dr. Natalia Trayanova, the Murray B. Sachs Professor of Biomedical Engineering and Medicine at Johns Hopkins University, and a team of researchers are working to change this. They have developed a computational model for predicting which heart patients are at greatest risk for arrhythmia. Called VARP, for virtual arrhythmia risk predictor, Dr. Trayanova's virtual heart uses MRI and other patient-specific cardiac data to create a personalized geometrical model of the heart. The model incorporates not just the wall of the heart, but also all the structural remodeling that occurs after a heart attack. That computer model, coupled with mathematical equations that express the dynamics of the human cells of the heart, is then stressed in a variety of different ways and locations to see if a patient is at risk for sudden cardiac death due to arrhythmia.



A groundbreaking retrospective study published in *Nature Communications* in May 2016 demonstrated the accuracy of the VARP model. In this study, Dr. Trayanova and her team looked at 41

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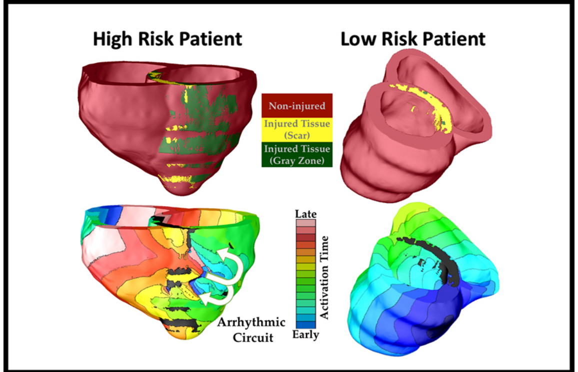
patients who had received a defibrillator because they were deemed at risk for arrhythmia based on current clinical predictors. Using their virtual replica of each patient's heart, they then set out to predict which patients were at highest risk and eventually compared their predictions to the defibrillator recipients' post-implantation records. Patients who tested positive for arrhythmia risk by VARP were four times more likely to develop arrhythmia than those who tested negative. VARP also predicted arrhythmia occurrence in patients four to five times better than existing clinical predictors.

This study provided important proof of concept for VARP. Although more study is needed before VARP reaches the clinic, Dr. Trayanova is excited about the possibility it represents to save lives and direct healthcare intervention and spending to where they will have the greatest impact.

Dr. Trayanova's research has been supported by the National Institutes of Health and other organizations. She particularly credits receipt of an NIH Director's Pioneer Award for giving her the freedom to pursue an idea that some might have thought unworkable, but which has turned out to be potentially transformative, as having the greatest impact on her academic career.

The Virtual Heart Arrhythmia Risk Prediction for Two Patients



The virtual heart methodology classified one patient as high risk of developing a life-threatening arrhythmia, and the other as low risk. Top panels show the geometric replicas of the patient hearts, reconstructed from their MRI scans. Shown is normal tissue as well as injured tissue left by an earlier heart attack in each heart. The injured tissue consists of scar and a semi-viable border zone between normal tissue and scar (also called gray zone because of its gray appearance in the MRI scan). Bottom panels show propagation of electrical wave in the virtual hearts, with lines representing times at which the electrical wave arrived at given locations in the heart (called activation times). In the low-risk heart, despite the presence of injury, the electrical wave swept uniformly though the heart, triggering strong uniform contraction and blood pumping. In the high-risk heart, arrhythmia developed. The electrical wave was "stuck" at the scar, rotating around it over and over again, which is called arrhythmia (arrows show direction of rotation, i.e. the arrhythmia "circuit"). The rotational wave was unable to cause coordinated contraction and prevented the heart from pumping blood effectively, which results in sudden cardiac death unless a defibrillation shock is given.

GRAPHIC BY HERMENEGILD AREVALO AND NATALIA TRAYANOVA

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United for Medical Research has undertaken the Amazing Things Podcasts because America's investment in medical research — through the National Institutes of Health — is making amazing things possible. Listen to the full story of Natalia Trayanova's groundbreaking efforts to improve cardiac care at www.amazingthingspodcast.com.

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