

3D imaging points to possible cause of sudden cardiac death

An imaging technique developed by Freiburg researchers provides insights into cardiac arrhythmias that can cause sudden cardiac death in animal models. The changes discovered could explain why even seemingly healthy people are sometimes affected.

Medical professionals in Freiburg have discovered a possible reason why young people who appear to be healthy can suffer sudden cardiac death. Using a new three-dimensional imaging method, they demonstrated in an animal model that scar tissue in the heart can alter electrical signals in a way that remains unnoticeable during periods of rest but can lead to dangerous arrhythmias during exertion. Collectively with members of the National Research Council of Italy, researchers at the University of Freiburg's Faculty of Medicine were able to visualise this mechanism. The results were published on 6 October 2025 in the journal *Nature Cardiovascular Research*. The findings could help to better understand previously unexplained cases and to make diagnostics more targeted for high-risk patients.

"Our study shows that scar tissue in the heart does not simply interfere with the heart's function; it actively influences how the heart works overall," says Prof. Dr. Peter Kohl, Director of the Institute for Experimental Cardiovascular Medicine at the Medical Centre – University of Freiburg. "This helps us to better understand the electrical causes of arrhythmias – and, in the long term, to make diagnosis and treatment more targeted."

When scars alter the heart's electrical signal

The study focused on mice with a genetically determined form of heart muscle disease, as also occurs in humans – especially in young patients at high risk of sudden cardiac death. Using a newly developed combination of high-resolution 3D imaging and optical measurements of electrical excitation, the researchers were able to show that scar tissue that develops in such diseases does not alter the propagation of electrical signals in the heart across the board, but rather depending on the heart rate. During a normal heartbeat, the electrical impulses passed largely unimpeded. However, as soon as the heart beat faster – for example, during physical exertion or emotional stress – the signals were weakened or blocked by the scarred tissue.

This effect is comparable to a technical "low-pass filter": fast impulses are specifically attenuated, while slower ones remain unaffected. This previously unknown mechanism could explain why patients appear normal in resting examinations, even though they are at high risk of dangerous arrhythmias during exercise.

The foundation for cardiac digital twins

Another key finding of the study is that the structure of the heart alone is not sufficient to reliably predict the risk of arrhythmia. "We need digital models that take into account not only the anatomy but also the electrical properties of the various heart cells," explains Dr. Francesco Giardini, a scientist at the Institute for Experimental Cardiovascular Medicine at the Medical Centre – University of Freiburg. The study provides an important basis for this. The aim is to develop so-called digital twins, which are individual computer models created for individual patients. These should make it possible to better assess risks and treat them in a targeted manner before life-threatening events occur.

Next steps: The path to clinical application

The current results are based on an established animal model that replicates key features of the human disease. However, an important limitation is that the data has so far only been collected in murine models. The next step will therefore be to investigate larger animal models in order to further test the transferability to humans.

The long-term goal is to further develop the imaging techniques so that they can be used clinically – for example, for individual risk assessments or therapy planning in patients with heart muscle disease and scar tissue. The research was funded as part of the CRC 1425 "The Heterocellular Nature of Cardiac Lesions" collaborative research centre at the University

of Freiburg. An ERC Advanced Grant was recently awarded to Dr. Leonardo Sacconi, senior author of the study and visiting scientist at the Institute for Experimental Cardiovascular Medicine, for the further development of the method.

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Correlative imaging integrates electrophysiology with three-dimensional murine heart reconstruction to reveal electrical coupling between cell types. DOI: doi.org/10.1038/s44161-025-00728-9

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