

Transparent 3D Heart Tissue Reveals Its Complexity

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LONDON, UK — A technique borrowed from neuroscience to see through brain tissue is helping scientists to visualize the myocardium at the multicellular level, which might one day prove helpful in the diagnosis and monitoring of patients with heart disease^[1].

Researchers at Imperial College London in the UK used free-of-acrylamide SDS-based tissue clearing (FASTClear) to visualize adult human and canine myocardial slices in 3D. "This is the first time such an optical clearing method has been used on adult cardiac tissue," first author Dr Filippo Perbellini notes in a news release.

"The myocardium is a very complex multicellular structure that is regulated at the molecular, cellular, and multicellular level. The latter may be responsible for a variety of pathological events, including arrhythmia, fibrosis, inflammation, and disturbances of blood perfusion, but the 3D multicellular structure is difficult to visualize," Perbellini and Prof Cesare Terracciano, who led the research, added in a joint email to *theheart.org* | *Medscape Cardiology*.

"The FASTclear technique has the potential to permit the assessment of microscale 3D multicellular structure during routine characterization of myocardial biopsies. Given the fast and simple approach, it is likely to be useful in the diagnosis and monitoring of patients, but this has to be tested," the researchers said.

They published their work online July 12, 2017 in *Nature Scientific Reports*.

Transparent Heart Tissue

Given that cardiac tissue is very dense and opaque in nature, 3D imaging is tough to achieve, and structural analysis of diseased myocardial tissue is often limited to 2D images of thin myocardial sections, the researchers explain in their article.

"Using standard microscopy methods, we are able to image the surface of the samples about 20 to 30 μm from the surface. With more sophisticated methods we can achieve 50- to 80- μm depth, but we were never able to image a whole myocardial slice," Dr Perbellini explains in the news release.

With FASTClear, the researchers have been able to visualize samples 300 μm thick.



A process of optical clearing renders myocardium slices transparent. [Source: Dr Filippo Perbellini]

Using this technique they could see the position of blood vessels and the scaffold of the heart, as well as fibrotic tissue, which changes with cardiac disease, they report. They used a sample taken from human heart during heart transplantation, but say they could do the same with tissue from a biopsy.

"As a diagnostic tool, it would be able to us tell how fibrotic the tissue is, showing the changes in structure of a failing human heart and how this disrupts it from beating as the heart becomes less elastic," Terracciano notes in the release.

"At this stage we envisage that the main short-term application of this technique will be the screening of the effects of drugs or other treatments (eg, gene/cell therapy) ex vivo, particularly to study fibrosis and the effects on the microcirculation. For these applications the combination with the myocardial slice technique, which allows the preparation of several viable samples from the same biopsy, is particularly useful," Perbellini and Terracciano said in an emailed response.

"Pioneering" Work

There are several future steps to this research, they added. "First, more aspects of cardiac morphology need to be studied with this technique: the visualization of inflammatory cells and the relationship with other structures is a very interesting and topical area," they note.

"Another aspect is to bring together a structure-function relationship assay where the myocardium is first challenged functionally (our laboratory is pioneering several techniques to study the functional properties of myocardial slices) and then subjected to the FASTclear technique to determine the detailed multicellular structure that underpins the function of

the tissue. Improving some technical aspects, which include controlling shrinkage and obtaining visualization of very large transmural human biopsies, are also future goals of this research," Perbellini and Terracciano said.

Reached for comment, Dr Jeremy Pearson (British Heart Foundation, London, UK) said, "By adapting a method originally designed to study brain tissue, Terracciano's group has been able to produce 3D images of heart tissue. These illustrate in more detail than has previously been possible the complex relationships between heart muscle cells and the small blood vessels running between them.

"This pioneering method will give us a much clearer picture of the complex structure of the heart and a window into the changes that occur when hearts are failing," Pearson said.

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References

Perbellini F, Liu AKL, Watson SA, et al. Free-of-acrylamide SDS-based tissue clearing (FASTClear) for three dimensional visualization of myocardial tissue. *Nat Sci Rep* 2017; DOI: 10.1038/s41598-017-05406-w. [Article](#)

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