Myocardial infarction (MI) is a leading cause of death and disability. In addition to the immediate incidence of death in acute infarction caused by pump failure or arrhythmias related to the immediate loss of functioning cardiac tissue and the possibility of later progression to intractable pump failure in the subacute or chronic phases of infarction, a significant number of patients with prior MI have sudden death, presumably largely caused by arrhythmias related to the infarction. There are various theories about the mechanisms of infarction-related arrhythmias, many centering around the idea that the altered transmission through the region of the infarction can alter the propagation of waves of electric activation in such a way that they can set up self-perpetuating foci of electric activity. However, there is still much uncertainty about the area.

In MI, there is ischemia of a portion of the heart wall that is sufficiently severe and prolonged that cells in the heart wall start to die. Whereas the myocytes, with their relatively high metabolic demands, are likely to be irreversibly damaged by such a significant period of ischemia and thus lost from the wall, the fibroblasts in the heart wall are more resistant to the effects of ischemia and thus are more likely to survive. In the healing phases of MI, these fibroblasts can become activated and effectively “patch” the wall with a meshwork of collagen. The resistance of the heart wall to the effects of ischemia is species-dependent, in part reflecting the different capacities of different species for supplying collateral blood to myocardium at risk. A correlate of this is seen in the degree of definition of the infarcted myocardium from the adjacent spared myocardium. Species such as dogs or rats, which have excellent collateral blood supply, develop irregular and patchy margins between infarcted and preserved myocardium, whereas animals such as sheep, which have poor collateral blood supply, develop much more sharply delineated boundaries between infarcted and preserved myocardium; human beings fall somewhere in between these extremes.

The architecture of the normal heart wall is highly ordered, with a very regular arrangement of the muscle fibers. The muscle fibers are wound around the wall in a helical way that changes smoothly with depth, changing from being oriented obliquely with respect to the long axis of the ventricle in the subepicardium, to running circumferentially in a “hoop-like” manner in the mid wall, to being oblique in the opposite direction in the subendocardium. There are also additional secondary, but well-defined, “sheet-like” organizations of the fibers. The muscle fibers are held in their organizational structures by a hierarchical network of collagen fibers. The muscle fibers are the force-generating elements of the heart wall and can only generate active tension along their length; these forces get distributed through the heart wall by the collagenous fibers that hold them together. Thus, the spatial distribution of the fibers is an important determinant of the way that the heart generates tension in the wall and thus the way that it pumps blood. In addition, the heart fibers propagate their electric depolarization and thus the initiation of mechanical contraction, from one to another. This propagation of electric activation proceeds more rapidly along the direction of the fibers than across them, which also produces an important link between their spatial arrangement and the development of mechanical contraction.

MRI is playing an increasingly important role in the management of MI and its complications. MRI is becoming accepted as the gold standard way to assess global cardiac function due to its ability to provide reliable measurements of such aspects of function as the end-diastolic volume, the stroke volume, and the ejection fraction. In addition, through the use of contrast agents that are seen to be retained relatively longer in regions of fibrosis, MRI can provide images of late gadolinium enhancement that correlate extremely well with the areas of fibrosis in animal models of MI and that have prognostic significance in human MI. Although not yet of practical utility, MRI can also provide unique information on the spatial arrangement of the cardiac muscle fibers through diffusion-weighted imaging. In diffusion MRI, strong pulses of magnetic field gradients are applied in such a way that they reduce the signal from diffusing water molecules, even though they may move distances that are only on the order of tens of microns but leave the signal from stationary molecules unchanged. Because the diffusion along the direction of the fibers is more rapid than it is across them, the use of a suitable range of directions and strengths of these diffusion-sensitizing gradients allows us to calculate the underlying distribution of the fiber orientations within the region being imaged. These methods have had only limited application to in vivo imaging, due to technical difficulties such as their sensitivity to patient motion and their relatively long acquisition times, although they have been used to demonstrate the interruption of the
normal orderly arrangement of the muscle fibers in the setting of prior MI. However, they have been able to be used for detailed mapping of the fiber arrangements in ex vivo heart specimens (eg, reference 9). These fiber data can be obtained in full 3D and provide information that would be difficult to obtain with traditional serial-section histological methods.

In the article by Sosnovick et al10 in this issue of Circulation: Cardiovascular Imaging, a variant MRI diffusion method, diffusion spectrum MRI tractography, was used for myocardial fiber mapping. This approach seeks to recover information on both the distribution fiber directions within each voxel imaged and the connections of the fibers between them. In particular, diffusion spectrum MRI tractography was used to study the effects of infarction on the myofiber architecture in a rat model of MI; infarction was created by permanent coronary artery ligation for 3 weeks. After MRI study of the heart specimens, representative sections were also examined with conventional histological methods. After the tractographic analysis is performed, the resulting processed images are elegant and striking, with clear demonstration of both the 3D arrangement of the normal helical fibers and the interruption of this arrangement by the infarction. The irregular boundary between the infarcted and preserved heart wall, expected in this infarct model, is also clearly seen. In addition, the authors claim to have discovered a novel feature of the infarction through their tractographic analysis, “nodes of orthogonal myofiber intersection or contact” (NOMIC). In these regions, fibers with nearly orthogonal orientations, which would normally be well separated from each other, are found close together in portions of the region of the infarction. They also identified similar-appearing regions in the corresponding conventional histological sections.

The fiber mapping results presented here are a technical tour de force, with the detailed depiction of the diffusion effects of the cellular architecture potentially providing an effective understanding of structures well below the nominal resolution of the imaging method itself. The question arises as to the nature and significance of the new structures reported here. Rather than new fibers growing into the infarct, it seems likely that these are residual surviving muscle fibers that were “trapped” in the contracting fibrosis of the healing infarct. However, their electric and mechanical significance is still uncertain. Electrically, even though they are close together, it is not clear whether these fibers will be able to form true electric connections, with the capacity to effectively reroute waves of electric activation in ways that could lead to self-sustaining foci of electric activation that could produce potentially fatal arrhythmias. Mechanically, they will potentially have locally much more rapidly varying directions of contraction force than would be present in the normal heart, with its gradual changes in fiber orientation. However, the significance of this is also uncertain, as the amount of force that can be generated by such relatively isolated fibers embedded in dense fibrosis is probably relatively small. The relevance of the rat model of MI used to the kinds of MI occurring in human beings is also uncertain. Furthermore, it is not at all clear that these methods will be able to be extended to clinical human studies. Nevertheless, the new availability of such effectively high-resolution methods for investigating the boundaries of infarctions, and for correlating them with their functional consequences (at least in animal models, for now), should lead to greater insight into the mechanisms of both the electric and mechanical consequences of MI, and, we hope, to improved means to treat them.

Disclosures
None.

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MRI of the Microarchitecture of Myocardial Infarction: Are We Seeing New Kinds of Structures?
Leon Axel

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