

How can MRI of Mouse Models provide value for cardiovascular studies?

Frederick H. Epstein, Ph.D.

Professor

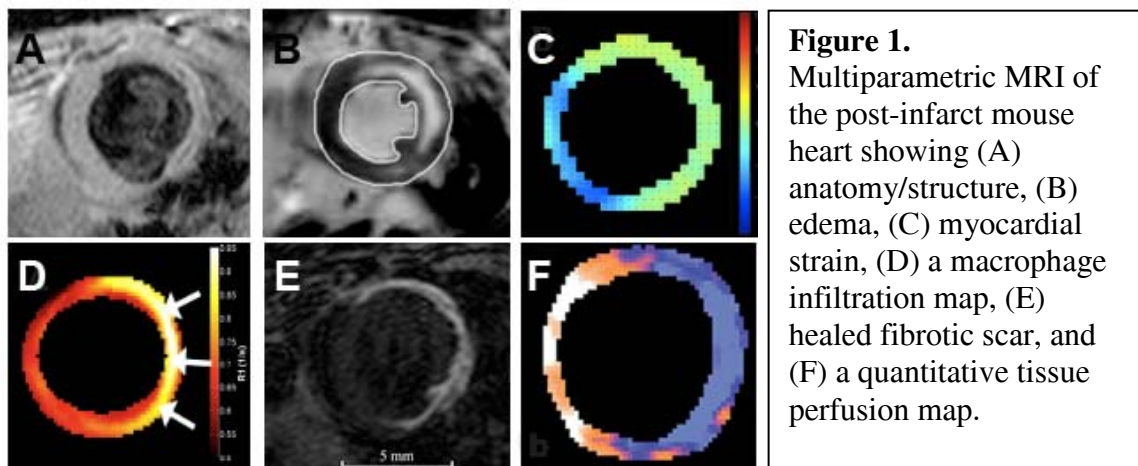
Departments of Biomedical Engineering and Radiology, University of Virginia

Mice are widely used to study molecular and cellular mechanisms underlying cardiovascular disease and to evaluate experimental therapies. The wide variety and availability of gene-modified mice as well as their low cost facilitates their use. In addition, many surgical, genetic, and diet-induced mouse models of human cardiovascular diseases have been developed, and the combination of genetic manipulation with disease models provides a powerful platform for testing mechanisms and evaluating novel therapies.

In this context, small-animal MRI provides serial noninvasive quantitative readouts of many parameters that are critical to the assessment of the cardiovascular system in mice. The multiparametric MRI exam for the mouse heart can assess cardiac anatomy, global and regional function, strain, myocardial perfusion, infarction, edema, and scar. Additional cardiac parameters that can be measured include macrophage infiltration, aspects of tissue microstructure quantified by diffusion tensor MRI, and aspects of metabolism. In the blood vessels, blood flow can be quantified, wall shear stress can be estimated, and aortic plaque can be imaged.

A substantial body of work has used small-animal MRI to test hypotheses regarding left ventricular (LV) remodeling in mouse models of myocardial infarction. These studies have utilized MRI of LV anatomy, infarction, and function to elucidate the roles of various receptors and enzymes in healing, scar formation and remodeling, and to evaluate the potential of experimental therapies such as small molecules and stem cells for modulating the natural LV remodeling process.

Recently there has been growing interest in the effects of obesity and diabetes on the heart, and mice fed a high fat diet have emerged as an important model of diet-induced human obesity and type II diabetes. Recent MRI studies in mice fed a high fat diet have demonstrated reduced myocardial perfusion reserve, increased LV mass, and diastolic dysfunction, establishing a platform with great potential to reveal key molecular factors that link obesity, diabetes, and cardiomyopathies due to these conditions.



Suggested reading:

1. Epstein, Frederick H. "MR in mouse models of cardiac disease." *NMR in Biomedicine* 20, no. 3 (2007): 238-255.
2. Yang, Zequan, Christina M. Bove, Brent A. French, Frederick H. Epstein, Stuart S. Berr, Joseph M. DiMaria, Jennifer J. Gibson, Robert M. Carey, and Christopher M. Kramer. "Angiotensin II type 2 receptor overexpression preserves left ventricular function after myocardial infarction." *Circulation* 106, no. 1 (2002): 106-111.
3. Gilson, Wesley D., Frederick H. Epstein, Zequan Yang, Yaqin Xu, Konkal-Matt R. Prasad, Marie-Claire Toufektsian, Victor E. Laubach, and Brent A. French. "Borderzone contractile dysfunction is transiently attenuated and left ventricular structural remodeling is markedly reduced following reperfused myocardial infarction in inducible nitric oxide synthase knockout mice." *Journal of the American College of Cardiology* 50, no. 18 (2007): 1799-1807.
4. Winter, E. M., R. W. Grauss, B. Hogers, J. Van Tuyn, R. Van der Geest, H. Lie-Venema, R. Vicente Steijn et al. "Preservation of left ventricular function and attenuation of remodeling after transplantation of human epicardium-derived cells into the infarcted mouse heart." *Circulation* 116, no. 8 (2007): 917-927.
5. Sosnovik, David E., Choukri Mekkaoui, Shuning Huang, Howard H. Chen, Guangping Dai, Christian T. Stoeck, Soeun Ngoy et al. "Microstructural impact of ischemia and bone marrow-derived cell therapy revealed with diffusion tensor magnetic resonance imaging tractography of the heart in vivo." *Circulation* 129, no. 17 (2014): 1731-1741.
6. Naresh, Nivedita K., Xiao Chen, Rene J. Roy, Patrick F. Antkowiak, Brian H. Annex, and Frederick H. Epstein. "Accelerated dual-contrast first-pass perfusion MRI of the mouse heart: Development and application to diet-induced obese mice." *Magnetic Resonance in Medicine* (2014).
7. Abdurrachim, Desiree, Jolita Ciapaite, Bart Wessels, Miranda Nabben, Joost JFP Luiken, Klaas Nicolay, and Jeanine J. Prompers. "Cardiac diastolic dysfunction in high-fat diet fed mice is associated with lipotoxicity without impairment of cardiac energetics in vivo." *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids* 1841, no. 10 (2014): 1525-1537.