Revascularization interventions in evolving myocardial infarctions have their rationale in the assumption that viable myocardial cells persist in the ischemically injured area. Consequently, intensive work has been directed over the past decade toward the development of noninvasive imaging methods to identify and quantify myocardial viability.

See p 744

In this regard, the temporal pattern of myocardial contrast enhancement on MRI is reported in this issue of Circulation to be a predictive index of potential myocardial viability for reperfused myocardial infarctions.1 With fast MRI, the first-pass distribution of MRI contrast media indicated that despite patency of the target coronary artery with TIMI 3 flow in all patients, reperfusion at the tissue level was impeded in more than half of the injured regions. This sign of impeded perfusion (“no-reflow” phenomenon) was predictive of poorer contractile recovery 7 weeks after the acute event. These results are similar to earlier reports, such as that of Ito et al.,2 that used myocardial contrast echocardiography to assess myocardial reperfusion after patency of acutely occluded epicardial coronary arteries was established. Recovery of regional and global LV function was worse in the group of patients with residual contrast defects. MRI and echocardiographic estimates of tissue perfusion after coronary recanalization seem to reflect the severity of microvascular disruption, occlusion, or extravascular compression by edema or hemorrhage. Thus, the depicted perfusion pattern serves as a surrogate of the severity of myocardial injury rather than a direct indicator of myocardial cellular viability.

A number of other promising MRI techniques for predicting myocardial viability of potentially salvageable myocardium in a region of acute ischemic injury have been proposed. These MRI approaches can be conveniently divided into 3 categories: assessment of tissue perfusion after recanalization, evaluation of myocardial contractile reserve, and characterization of myocardial cellular membrane function.

The report by Rogers et al.1 exemplifies the first approach. It examined the myocardial contract enhancement pattern on both first-pass and pseudoequilibrium-phase (delayed) MRI images and identified that hypoenhancement on first-pass imaging was an indicator of poorer recovery of function 7 weeks after the acute event. A prior report by Wu et al.3 suggested that contrast-enhanced MRI could estimate the extent of microvascular obstruction after acute coronary occlusion in 44 patients using pseudoequilibrium-phase (1 to 2 minutes after injection) images. MRI performed 10 to 6 days after infarction demonstrated hypoenhanced areas within the infarct zone in 11 patients who were therefore considered to have microvascular obstruction in the core of the infarction. Hypoenhancement was observed in the periphery of the infarction in these 11 patients, whereas hyperenhancement of the entire infarction was present in the remaining patients. The group with hypoenhanced regions, which was presumed to represent microvascular obstruction, had significantly more future cardiovascular event and more severe LV remodeling. Saeed et al.4 also demonstrated in an animal model of reperfused myocardial infarction that reperfusion at the tissue level is characterized on inversion recovery echo-planar imaging as enhancement to a level approaching that of normal myocardium 20 seconds after injection, followed by progressive further enhancement, whereas the signal intensity of normal myocardium declines. This study, using methodology with high temporal resolution, actually demonstrated that the first-pass enhancement kinetics of even adequately reperfused myocardium is not identical to normal myocardium, but rather there is decreased upslope and delay in the early peak of enhancement of the infarcted compared with normal myocardium. It seems clear from a number of studies that lack of enhancement of the core of acute infarctions after recanalization either on first-pass or pseudoequilibrium MRI acquisitions is predictive of more severe injury, less recovery of regional function, and poorer outcome.

The second MRI approach for predicting myocardial viability simulates techniques used with echocardiography by demonstrating residual contractile response to inotropic drugs in an ischemically injured or chronically ischemic region. This MRI approach to predicting viability not only assesses contractile response but also incorporates the precise measurement of wall thickness afforded by MRI as an additional parameter. MRI-defined diastolic wall thickness ≥5.5 mm and dobutamine-induced systolic wall thickening ≥2 mm were shown to be predictive of contractile recovery after myocardial revascularization.5,6 Quantitative assessment of dobutamine-induced systolic wall thickening on cine MRI was shown to be a reliable indicator of improvement of regional LV function and ejection function after revascularization.5 With the use of 18F-fluorodeoxyglucose PET as the determinant of residual viability, dobutamine transesophageal echocardiography (TEE) and dobutamine cine MRI were compared in 43 patients with prior myocardial infarction.6 Sensitivity and specificity of dobutamine TEE and cine MRI for PET-defined viability were 77% versus 81% and 94% versus 100%, respectively. A potential advantage of the MRI
approach is that it is quantitative; the edge definition of the endocardial and epicardial surface provides for precise measurement of systolic wall thickening. Another morphological indicator of likely viability is end-diastolic wall thickness of an ischemically impaired region. An end-diastolic wall thickness of >5.5 to 6.0 mm as measured by cine MRI in ischemically dysfunctional segments has correlated with viability as defined by radionuclide imaging or favorable response to revascularization.5–8

A third MRI approach for determining myocardial viability in a region of ischemic injury uses MRI contrast media to probe cellular membrane integrity. Most MRI contrast media have a molecular size so that they freely exist from the vascular space and rapidly distribute in the extracellular space. These media can increase or decrease signal intensity, depending on the type and concentration of the media in a tissue and the MRI parameters used. Gd-based contrast media, such as GdDTPA, usually increase the MRI signal of tissues, whereas another agent, dysprosium DTPA (Dy-DTPA), decreases the signal of tissues. Both of these contrast media have extracellular distribution and are excluded from myocardial cells with intact membranes. In fact, the signal attenuation caused by Dy-DTPA depends on the microheterogeneity of distribution in tissue because the media resides in the extracellular but not intracellular space. Experiments in rats with reperfused myocardial infarctions demonstrated that the loss of myocardial cellular membrane integrity was reflected in a decreased potency of Dy-DTPA in infarcted tissue compared with normal myocardium.9,10 On T2-weighted images, the signal of normal myocardium was profoundly attenuated by Dy-DTPA, whereas the signal of the infarcted myocardium was maintained, causing the infarcted region to have higher relative intensity. Decreased potency of this agent was consistent with the loss of cellular membrane integrity, permitting the media to reside in the extracellular but not intracellular space. Gd-based contrast media have extracellular distribution and are excluded from myocardial cells with intact membranes. In fact, the signal attenuation caused by Dy-DTPA depends on the microheterogeneity of distribution in tissue because the media resides in the extracellular but not intracellular space. 

A series of inversion-recovery echo-planar images acquired rapidly provides a method for defining the inversion time at which signal is nulled in normal and ischemically injured myocardium and the differential effect of MRI contrast media on this value in normal and injured myocardium. This methodology provides reasonably precise in vivo measurement of T1 relaxation time (rate) of myocardium and provides an estimate of T1 relaxivity of Gd MRI contrast media. Recent reports have used this approach to estimate the distribution volume of Gd chelates in normal and ischemically injured myocardium.11,12 It has been proposed that under optimal circumstances, measurement of distribution volume provides an index of the percentage of necrotic myocardial cells within a zone of ischemic injury.11 Evidence that these MRI contrast media, which serve as indicator material, achieve a nearly equilibrium state in tissues is recognized on contrast-enhanced MRI and apparently is a poor prognostic sign of itself.3 Myocardial hemorrhage is also a circumstance in which there may be low intensity within the core of the infarction and thereby confound estimation of distribution volume of T1-enhancing contrast media.

During the past year, clinical trials have begun using high-molecular-weight MRI contrast media; the molecular size of these agents is such that the media remain in the blood pool for several hours. A major impetus to the development of these blood pool agents is their anticipated use to improve coronary MRI angiography. An additional use suggested by recent studies is the estimation of the severity and extent of microvascular injury caused by acute myocardial infarction. A prototype of these blood pool MRI contrast media is GdDTPA albumin. A recent report showed that in a rat model with reperfused ischemic injury of graded severity, blood pool contrast media caused enhancement of the periphery of the infarct zone and demarcated a less enhanced central core.14 The size of the central core increased in relationship to the duration of ischemic before reperfusion. On the other hand, standard extracellular MRI contrast media produced nearly homogeneous enhancement of the entire ischemic zone at 3 minutes after injection. It seems likely that delivery of the blood pool agent to the core of the infarction is dependent on intact microvasculature, whereas the lower-
molecular-size extracellular agents can reach the core by diffusion despite microvascular damage.

Although MRI was reported to be useful in the evaluation of ischemic heart disease >15 years ago, use of the modality in this disease has been meager. This is likely due to the familiarity and ubiquity of echocardiography and radionuclide imaging, which accomplish many of the same diagnostic goals in ischemic heart disease. It has been proposed by proponents of MRI that this modality can serve as a comprehensive noninvasive imaging modality in ischemic heart disease and thereby be more or at least as cost-effective as the competing technique. The article by Rogers et al provides evidence of another facet of MRI in ischemic heart disease: prediction of myocardial viability after ischemic injury. However, it is my opinion that neither the current paper nor previous ones discussed in this editorial will open the gate for widespread use of MRI in ischemic heart disease. The utilization of the multiple capabilities of MRI in ischemic heart disease will likely remain dormant until robust and uncomplicated methodology is developed for MRI angiography of the coronary arteries. The coupling of noninvasive angiography and flow quantification should move MRI to a prominent position in the diagnosis of coronary artery disease.

References

Key Words: Editorials • magnetic resonance imaging • contrast media • reperfusion
Prediction of Myocardial Viability by MRI
Charles B. Higgins

*Circulation*. 1999;99:727-729
doi: 10.1161/01.CIR.99.6.727

*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/99/6/727

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Circulation* is online at:
http://circ.ahajournals.org//subscriptions/