Cardiac MRI: Where Are We?

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Introduction

To date, cardiac magnetic resonance imaging (MRI) has occupied a valuable niche in the diagnosis of uncommon cardiovascular diseases. Cardiac MRI is key in characterizing cardiac masses, in defining the cardiac anatomy in congenital heart disease, in diagnosing certain cardiomyopathies, such as arrhythmogenic right ventricular dysplasia, and in imaging the pericardium in constrictive cardiac syndromes. Because of the expense of MRI technology and its previously limited applications, cardiac MRI has remained in the hands of cardiovascular imaging subspecialists at tertiary care institutions. In the future, however, it is likely that cardiovascular MRI will have an ever-expanding role in everyday cardiology practice. Recent advances promise to make cardiac MRI the imaging modality of choice to assess myocardial viability, myocardial ischemia, the severity of peripheral vascular and coronary artery disease and the extent of atherosclerosis, including the identification of the vulnerable plaque (Table 1). A real advantage of cardiac MRI is that it can provide a complete cardiovascular assessment of a patient in a single setting.

Myocardial Viability

Several methods are now available for the noninvasive detection of myocardial viability by cardiac MRI: (1) contrast-enhanced MRI; (2) low-dose dobutamine MRI and (3) metabolic imaging using MR spectroscopy. MR imaging with standard gadolinium-based intravenous contrast agents can distinguish infarcted from viable myocardium and can characterize infarct size and extent of microvascular obstruction post myocardial infarction (MI). The kinetics of gadolinium uptake are different in infarcted vs. viable myocardium. The "washout" of gadolinium is delayed in necrotic myocardium, and thus infarcted myocardium appears bright or hyperenhanced compared to viable myocardium during MRI imaging 5–10 minutes after injection of gadolinium. As shown in numerous animal studies comparing the detection of infarction by MRI with pathology, contrast-enhanced MRI can image the entire range of infarction from small subendocardial or subepicardial infarcts to transmural myocardial damage, with unparalleled spatial resolution. In fact, the resolution of this new MRI viability imaging is so advanced that MRI may redefine our current view of viability. Contrast-enhanced MRI can determine not only whether a region is viable but also what percentage of a territory is irreversibly damaged.

The group from Northwestern University recently investigated myocardial viability assessment by contrast-enhanced MRI in a group of 41 patients before and after a revascularization procedure. They identified 804 dysfunctional myocardial segments at baseline in these patients. The likelihood of functional improvement after revascularization increased as the extent of transmural hyperenhancement (i.e., infarcted myocardium) decreased. Specifically, contractility increased in 256 of 329 segments (78%) with no hyperenhancement before revascularization compared with improvement in only 1 of 58 segments (1.7%) with hyperenhancement of greater than 75% of tissue in that segment (Figure 1). Segments with intermediate degrees of hyperenhancement showed increased functional recovery as the extent of hyperenhancement decreased. This study shows that myocardial viability is not a binary phenomenon—segments are not either viable or not. Instead, there is a spectrum of viability dependent on the transmural extent of damage. Because of its superior spatial resolution, contrast-enhanced MRI is poised to become the imaging method of choice for assessment of myocardial viability.

This same technique of contrast-enhanced MRI can provide accurate assessment of both infarct size and microvascular obstruction (MO) after MI. Both acute and chronic infarcts appear as hyperenhanced regions when imaged on delayed gadolinium-enhanced MRI. As explained above, these hyperenhanced regions by MRI are precisely correlated with pathological evidence of infarction. In the post-MI setting, MO, or the "no-reflow" phenomenon seen on coronary angiography, represents an area of severe infarction characterized by myocyte and endothelial cell necrosis with obstruction of capillaries by inflammatory cells and necrotic debris. The presence of MO predicts adverse ventricular remodeling, worse ventricular function, and poorer clinical outcomes. MO appears as dark or hypoenhanced regions of myocardium when imaged early after injection of intravenous gadolinium. The infarcted zone appears hyperenhanced when imaged later, several minutes, after gadolinium injection. Using this technique, Wu et al. imaged 44 post-MI patients and showed that the risk of adverse cardiac events increased as infarct size, as defined by the extent of hyperenhancement, increased. Also, they showed that the presence of MO predicted adverse clinical events (Figure 2). Finally, the presence of MO was a predictor of adverse events independent of infarct size.

Low-dose dobutamine cardiac MRI techniques can also be used for viability assessment via determination of contractile reserve. An advantage of cardiac MRI is its superior detection of endocardial and epicardial borders to give precise measurements of wall thickness. Baer et al. per-

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Table 1. Applications of Cardiovascular MRI

Cardiac masses	Myocardial viability
Pericardial disease	Contrast-enhanced MRI
Cardiomyopathies	Low-dose dobutamine MRI
Right ventricular dysplasia	Metabolic imaging
Sarcoid	Myocardial ischemia
Hemochromatosis	Perfusion imaging
Congenital heart disease	Dobutamine stress MRI
Anatomy	MRI coronary flow reserve
Quantification of shunts	Peripheral vascular imaging
Anomalous coronary arteries	Carotid
Aortic disease	Renal
Dissection	Lower extremity
Intramural hematoma	Coronary artery imaging
Coarctation	MRA
Aneurysm	Black-blood MRI
Quantification of LV mass, volume, function	Atherosclerosis imaging
	Black-blood MRI
	Transesophageal MRI
	Intravascular MRI

formed rest and low-dose dobutamine MRI in 43 patients with chronic infarcts who were scheduled to undergo revascularization. Based on prior studies, they defined viability as dobutamine-induced systolic wall thickening of ≥2mm in over half of the infarcted region and a diastolic wall thickness (DWT) of ≥5.5 mm. In this setting, dobutamine MRI had a sensitivity of 89% and a specificity of 92% for recovery of function after revascularization.

Finally, a future application of cardiac MRI in detecting myocardial viability is the metabolic assessment of the myocardium using MR spectroscopy. These techniques take advantage of alternative electromagnetically active nuclei, such as sodium or phosphorous, to image regional myocardial metabolic function. For instance, phosphorus 32 (^{32}P) spectroscopy can detect depletion of high-energy phosphates (ATP) in ischemic myocardium. Infarcted myocardium appears bright on sodium 23 (^{23}Na) MRI as myocytes lose cell membrane function and intracellular sodium concentrations increase.

Myocardial Ischemia

In addition to assessing myocardial viability and quantifying myocardial infarction, cardiac MRI can detect myocardial ischemia. In analogy to other non-invasive methods of ischemia detection, MRI can detect both perfusion defects induced by vasodilators such as dipyridamole and abnormal wall motion responses to inotropic stimuli such as dobutamine. Furthermore, MRI can directly assess the physiologic significance of coronary stenoses through the

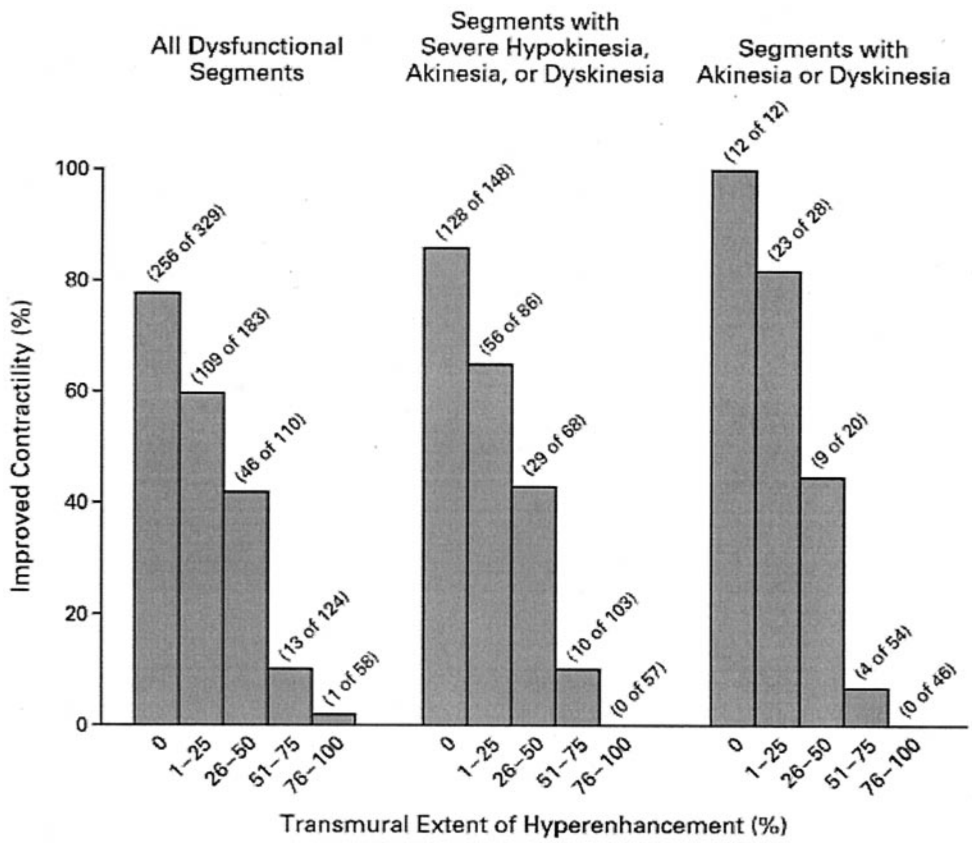

Figure 1. Relation between the transmural extent of hyperenhancement before revascularization and the likelihood of increased contractility after revascularization. Data are shown for all 804 dysfunctional segments and separately for the 462 segments with at least severe hypokinesia and the 160 segments with akinesia or dyskinesia before revascularization. For all three analyses, there was an inverse relation between the transmural extent of hyperenhancement and the likelihood of improvement in contractility. Kim et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53. Copyright 2000 Massachusetts Medical Society. All rights reserved.

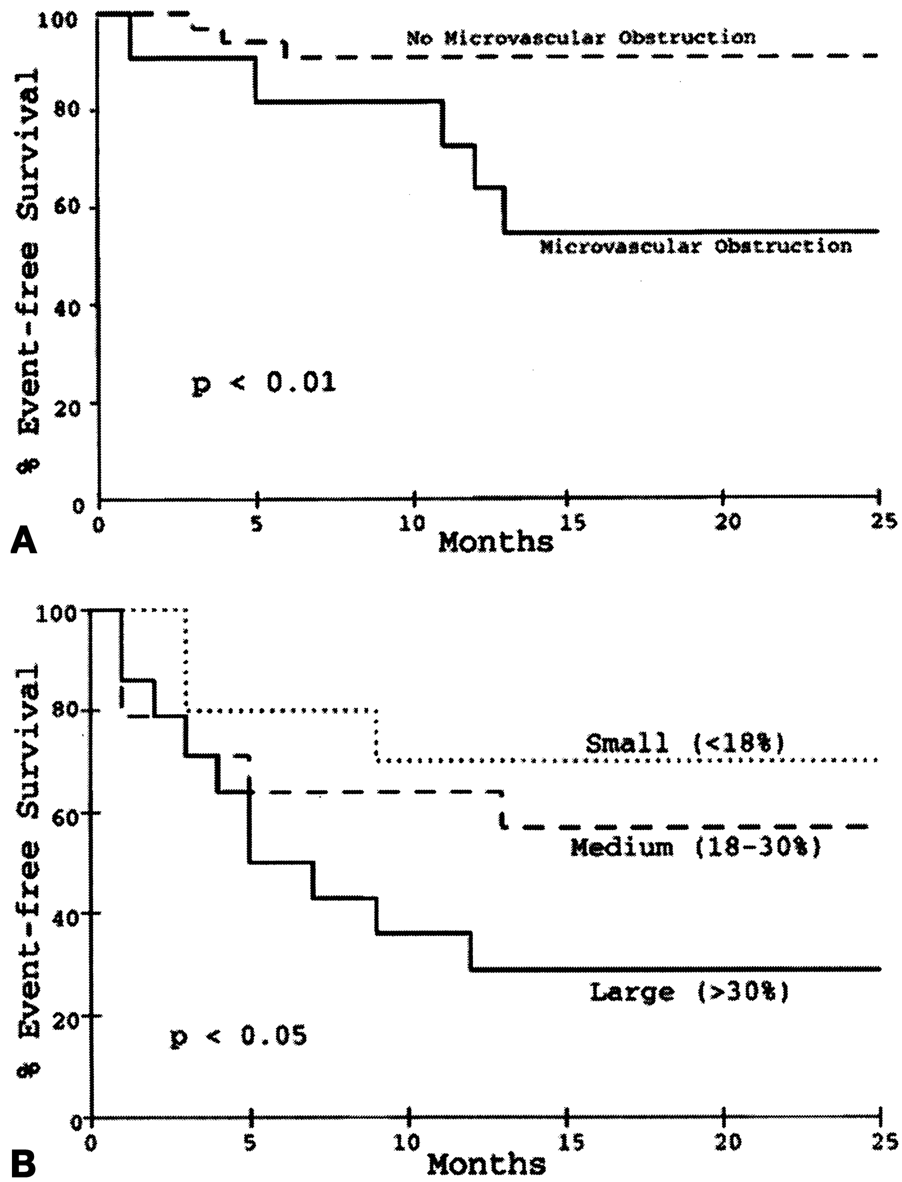

Figure 2. A) Event-free survival (clinical course without cardiovascular death, reinfarction, congestive heart failure or stroke) for patients with and without MRI microvascular obstruction. B) Event-free survival (clinical course without cardiovascular death, reinfarction, congestive heart failure, stroke or unstable angina requiring hospitalization) for patients grouped by MRI infarct size. Wu et al. Prognostic Significance of Microvascular Obstruction by Magnetic Resonance Imaging in Patients With Acute Myocardial Infarction. Circulation 1998;97:765–72. Copyright 1998 Lippincott Williams & Wilkins.

non-invasive measurement of coronary flow reserve. Cardiac MRI has the capability to demonstrate perfusion reserve like a dipyridamole thallium study, contractile reserve like a dobutamine echocardiogram, and coronary flow reserve like an intracoronary Doppler wire.

First-pass MRI imaging, immediately after the intravenous injection of gadolinium, can assess resting myocardial perfusion. Ischemic myocardium appears darker than normal myocardium on early images due to reduced perfusion of these ischemic areas. This can be quantified by comparing the time-intensity curves of ischemic versus normal zones. However, the preferred method is detection of perfusion reserve using a vasodilating agent such as dipyridamole. Al-Saadi, et al., calculated perfusion reserve by MRI using dipyridamole in a cohort of 34 patients undergoing cardiac catheterization. They found that using a perfusion reserve value of 1.5, MRI had a sensitivity of 90% and a specificity of 83% for the detection of coronary artery stenoses greater than 75% by angiography.

Another method of ischemia detection that has been extensively investigated is cardiac dobutamine MRI. In many institutions, dobutamine MRI is now routinely used as the first-line method to determine myocardial ischemia in certain patient populations. Dobutamine MRI may be a preferred method of ischemia detection because it provides high quality images of left ventricular function in a wide variety of patients. In 1999, Nagel, et al., reported on 208 patients referred for cardiac catheterization who underwent both dobutamine echo and dobutamine MRI before their catheterization. Dobutamine MRI was performed using the same dobutamine-atropine protocol commonly employed for clinical dobutamine echo studies. Near real-time cine MRI was then used to image left ventricular function in multiple views. They found that, with coronary angiography as the gold standard, dobutamine MRI had a higher sensitivity and specificity for the detection of significant coronary artery disease than dobutamine echo.

Dobutamine MRI has particular advantage over dobutamine echo in patients who have poor acoustic windows by echocardiography. MRI can usually give an accurate assessment of ventricular function even in patients with large body habitus, pulmonary disease, or prior cardiothoracic surgery. Hundley, et al., demonstrated that routine use of dobutamine MRI is feasible in the clinical setting. They reported on 153 patients referred for dobutamine MRI after a non-diagnostic dobutamine echo. The dobutamine MRI was completed in an average of 53 minutes, and had a sensitivity and specificity of 83% and 83% for detecting coronary artery stenoses >50%. At the most recent American College of Cardiology meeting, this group reported having completed over 850 dobutamine MRI studies, now with an average scan time of 25 minutes.

Dobutamine MRI can be further enhanced by a technique called tissue tagging. This method allows for quantitative calculation of regional ventricular wall motion, by applying non-invasive grid lines on the left ventricle that deform with the myocardium during systole. The degree of deformation of these tag lines can be calculated and reported as myocardial shortening or myocardial strain. Using a recently developed technique, called harmonic phase (HARP) imaging, this quantitative assessment of regional wall motion can be calculated rapidly. Our group at Johns Hopkins has shown the feasibility of using HARP to quantify regional wall motion during human dobutamine stress MRI studies.

Finally, preliminary studies have examined the role of phase-contrast MRI in determining coronary flow reserve, a measure of the physiologic significance of coronary stenoses. Using this MRI technique, one can non-invasively assess coronary blood flow at rest and after the infusion of an intravenous vasodilator such as adenosine. The coronary flow reserve can be calculated by phase-contrast MRI in a similar way as with an intracoronary flow wire in the catheterization lab. A recent study by Hundley, et al., examined this technique in a cohort of patients with suspected restenosis after coronary intervention. They found phase-contrast MRI to have a sensitivity of 100% and a specificity of 89% for the detection of coronary lesions >70% by cardiac catheterization.

Vascular Imaging

Magnetic resonance angiography (MRA) has an increasing role in the diagnosis and management of vascular disease. Most physicians are familiar with MRI/MRA as a diagnostic alternative to CT and transesophageal echocardiography for the diagnosis of aortic dissection. In addition, MRA is useful in the screening and preoperative assessment of carotid, renal and lower extremity vascular disease. Compared with standard angiography, MRA is noninvasive, uses nontoxic contrast agents and does not use ionizing radiation. Furthermore, there are specific clinical situations, such as infrapopliteal vascular imaging, in which MRA is superior to angiography.

MRA has found broader clinical application with the development of several imaging techniques. Time-of-flight MRA (TOF) records moving blood as a bright signal and is useful in imaging distal lower extremity vessels. Phase-contrast MRA (PC-MRA) relies on the effect of flowing blood on a magnetic field to estimate the velocity of blood flow and therefore the hemodynamic significance of a lesion. Finally, contrast-enhanced MRA (CE-MRA) uses a 3D gradient echo sequence and a peripheral intravenous injection of gadolinium to give a complete 3D picture of the vascular system.

Frequently, MRA is used in conjunction with Doppler ultrasound for screening and preoperative assessment of carotid artery stenosis, reducing the need for carotid angiography. MRA is especially valuable in the noninvasive imaging of intracerebral carotid disease, areas not well imaged by ultrasound. A recent analysis of 11 studies comparing carotid MRA to angiography determined that MRA has a sensitivity of 93% and a specificity of 88%.

In many centers, MRA is becoming the screening test of choice for renal artery stenosis over ultrasound or nuclear methods. Unlike prior MRA techniques, CE-MRA reliably images accessory renal arteries and branch vessels. Recent studies using CE-MRA show a sensitivity and specificity of 96% and 94%, respectively, for the detection of a high-grade renal artery stenosis at angiography. Also, PC-MRI can been used to noninvasively determine the hemodynamic significance of a renal artery lesion.

3D CE-MRA can provide a detailed "road map" of the peripheral vascular system. Surface coils that cover patients from abdomen to ankles allow "run-off" MRA imaging without the need for coil repositioning. TOF techniques are particularly valuable for preoperative imaging in preparation for distal leg bypass procedures. TOF MRA can image infra-popliteal vessels that are difficult to opacify with contrast during standard angiography. MRA gives such a comprehensive view of the peripheral vascular system that some centers are now abandoning routine preoperative angiography and performing peripheral vascular surgery based on MRA imaging alone.

In summary, MRA is becoming an established tool in the clinical management of vascular disease. MRA is particularly useful in the non-invasive screening and preoperative imaging of carotid, renal, and lower-extremity atherosclerotic disease. Further validation studies are needed to confirm the advantages of MRA over conventional angiography seen in small single-center trials. However, MRA is an attractive alternative to standard angiography because it is noninvasive and avoids both ionizing radiation and iodinated contrast. With improvements in intravascular MRA contrast agents and imaging speed, the clinical use of MRA for vascular imaging is likely to grow.

Coronary Artery Imaging

Cardiac MRI can image the coronary arteries and promises to become a noninvasive alternative to coronary angiography. Coronary MRA has already become a standard for imaging anomalous coronary arteries and coronary artery bypass graft patency. However, significant challenges to the widespread application of coronary MRA include cardiac and respiratory motion, limited spatial resolution, tortuous coronary vessels with surrounding epicardial fat, and MRI artifacts produced by intracoronary stents and sternal wires. Recent advances in MRI techniques have overcome many of these challenges. Currently, there are two general approaches to coronary imaging: (1) MRA using gradient-echo sequences to give “bright blood” images of the vessel lumen analogous to angiography and (2) “black blood” MRI using spin-echo sequences with dual inversion recovery pulses to negate the signal from flowing blood providing images of the coronary vessel wall.

Since the initial report in 1993 comparing coronary MRA to conventional coronary angiography, numerous studies have been conducted showing the benefits of new MRI techniques in this field. Specifically, modifications of pulse sequences, such as a T2 preparation prepulse, have improved the contrast-to-noise ratio of MR angiography, allowing for improved image quality. Navigator-echo techniques, which eliminate the requirement for patient breath holding, have allowed for longer image acquisition times. Increased scan time allows for improved image resolution and 3D image acquisition. Using these technological improvements, recent studies report that on average coronary MRA can image the proximal 8 cm of the LAD and the RCA.

A second approach to coronary imaging is the technique of black blood MRI. As discussed in the next section, black blood MRI images the coronary wall and the atherosclerotic plaque as it encroaches on the lumen from the outside. Further improvements in intravascular contrast agents, surface coils, pulse-sequence design, and image reconstruction techniques promise to advance coronary MRA and black blood MRI to the forefront of noninvasive coronary imaging.

Atherosclerotic Plaque Imaging

Great strides have been made in cardiology over the last several decades in the identification of coronary artery disease as manifest by severe intraluminal coronary stenoses. However, over half of acute coronary syndromes occur due to rupture of atherosclerotic plaques that if visualized by angiography would be considered non-critical. Or, restated, the vulnerable atherosclerotic plaque may appear benign by angiography because most of the early process of plaque formation takes place outside the lumen and inside the vessel wall. The current gold standard imaging technique, coronary angiography, only images the lumen and cannot image the atherosclerotic plaque. Thus, the future of cardiology lies outside the vessel lumen and inside the vessel wall where the atherosclerotic plaque is initiated, formed, and ruptures causing a clinical cardiovascular event. The goal of the plaque-focused approach to cardiology is to develop an imaging modality that can identify plaques at high risk of causing a clinical event and to intervene with mechanical or medical therapies to stabilize these vulnerable plaques.

Of the many imaging techniques under development for this application, MRI is one of the most promising. Cardiac MRI is able to noninvasively image the entire vessel wall and identify atherosclerotic plaques using techniques such as black-blood MRI. Also, cardiac MRI can use different tissue markers, proton-density and T2 weighting, to distinguish intra-plaque lipid from calcium, thrombus and the fibrous cap. Studies of carotid artery plaque before and after carotid endarterectomy have shown that MRI plaque characterization is similar to histological analysis of plaque components. Similar studies comparing MRI and histology in autopsy specimens have shown that MRI can characterize plaque in the thoracic aorta. These preliminary investigations show that MRI can identify plaques that are lipid-rich, that have a thin fibrous cap or that have adherent thrombus. These are characteristics that may predispose plaques to rupture, triggering a clinical event.

Using “black-blood” techniques and plaque characterization methods, cardiac MRI has become a valuable tool for the study of vascular remodeling and plaque regression in animal models. Recently, cardiac MRI plaque imaging techniques have been used in human studies of atherosclerosis. Several groups have imaged human atherosclerotic plaques in the carotid arteries, the thoracic aorta, and even the coronary arteries. A major challenge to MRI imaging is that the sub-millimeter resolution needed to characterize individual plaque components limits image quality. Our group at Johns Hopkins has attempted to solve this limitation of atherosclerosis imaging in the thoracic aorta with the technique of transesophageal MRI. Using a miniaturized receiver coil placed in the esophagus through a small-caliber nasogastric tube, we are able to increase the signal-to-noise ratio in the thoracic aorta and improve image quality. We have shown that this technique of transesophageal MRI is superior to transesophageal echo for aortic plaque imaging (Figure 3).

This same miniaturized receiver coil can also be used intravascularly, the technique of invasive MRI, to give even higher resolution images of the vessel wall. Real-time MRI techniques have recently been used in animal studies to perform MRI-based intravascular interventions. Radiofrequency (RF) ablation has been performed using real-time

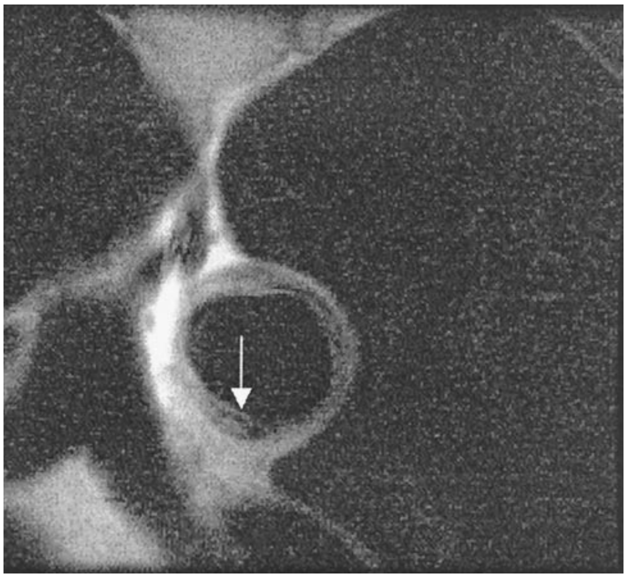

Figure 3. Transesophageal MRI of the distal aortic arch of a 77-year-old male with remote stroke, showing heterogeneous atherosclerotic thickening and intraplaque calcification or hemorrhage (arrow). Reprinted with permission from The American College of Cardiology (J Am Coll Cardiol 2001;37:2031–5).

MR visualization of the RF catheter and direct visualization of the RF lesion. Preliminary studies show that catheter tracking, angioplasty balloon positioning and balloon deployment are feasible. For now, human applications of these techniques will require many technical advances. However, one day, MRI could be used in both the electrophysiology lab and the angioplasty suite.

The next frontier in cardiology is the development of techniques to identify the unstable atherosclerotic plaque and to reduce the risk of plaque rupture with medical therapy or with coronary intervention. With continued improvements in coil technology and advances in image acquisition techniques, cardiac MRI is poised to usher in this next era of cardiology. In this new paradigm, the focus of cardiology will be not on the lumen as depicted by angiography, but on the atherosclerotic plaque itself as visualized by MRI. Thus, the goal will be to non-invasively identify and subsequently modify the vulnerable atherosclerotic plaque.

Conclusion

Because of these advances in MRI viability assessment, MRI stress testing, noninvasive vascular and coronary MRA and atherosclerotic plaque imaging, cardiac MRI is on the cusp of widespread clinical applicability. Currently, contrast-enhanced MRI is a standard technique for determination of infarct size and assessment of myocardial viability. Dobutamine MRI is a viable alternative for assessment of myocardial ischemia, especially in the significant subset of patients with poor acoustic windows by dobutamine echocardiography. Carotid, renal and peripheral vascular MRA are gaining acceptance in the screening and preoperative settings. Coronary MRA is the current gold standard for imaging coronary anomalies and bypass graft patency. Ongoing studies are using MRI atherosclerosis imaging techniques to evaluate the role of statins and other therapies in the modification of the vulnerable plaque.

On average, MRI scanner time cost $400 per hour, with study lengths ranging from 30 to 90 minutes. Usual professional fees are $100 per study. These charges for MRI are more than for a standard ultrasound evaluation. However, this is equivalent to the charges for a stress or dobutamine echo and less than a standard nuclear study. States often require a certificate of need before allowing the purchase of an MRI magnet. Although many states have relaxed these requirements, certain ones such as Massachusetts and Michigan remain quite strict in limiting the expansion of MRI technology. These restrictions are likely to change as the costs of MRI are reduced and as the role of MRI becomes more widely accepted in the practice of cardiovascular medicine.

A particular advantage of cardiac MRI is that it is a very versatile tool. With future advances, MRI will provide similar information to an echocardiogram, a nuclear stress test, a coronary flow wire and a coronary angiogram. Additionally, MRI will be able to image the atherosclerotic plaque unlike any currently available technique. A single imaging tool, cardiac MRI, will be able to assess ischemic, infarcted and viable myocardium, detect coronary and peripheral vascular stenoses, determine coronary flow reserve and characterize individual atherosclerotic plaques. Cardiac MRI, therefore, will offer a complete cardiac evaluation, tailored to the individual patient's need, in a single exam.

Suggested Reading

Kim RJ, Wu E, Rafael A, et al. The use of contrast-enchanced MRI to identify reversible myocardial dysfunction. N Engl J Med 2000;343:1445–53.

Wu KC, Zerhouni EA, Judd RM, et al. Prognostic significance of microvascular obstruction by MRI in patients with acute myocardial infarction. Circulation 1998;97:765–72.

Baer FM, Theissen P, Schneider CA, et al. Dobutamine MRI predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. J Am Coll Cardiol 1998;31:1040–8.

Weiss RG, Bottomley PA, Hardy CJ, Gersenblith G. Regional myocardial metabolism of high-energy phosphates during isometric exercise in patients with coronary artery disease. N Engl J Med 1990;323:1593–600.

Kim RJ, Judd RM, Chen E-L, Fieno DS, Parrish TB, Lima JAC. Relationship of elevated (^{23} Na) MRI intensity to infarct size after acute reperfused myocardial infarction. Circulation 1999;100:185–92.

Al-Saadi N, Nagel E, Gross M, et al. Noninvasive detection of myocardial ischemia from perfusion reserve based on cardiovascular magnetic resonance. Circulation 2000;101:1379–83.

Nagel E, Lehmkuhl H, Bocksch W, et al. Noninvasive diagnosis of ischemia-induced wall motion abnormalities with the use of

high-dose dobutamine stress MRI. Circulation 1999;99:763–70.
Hundley WG, Hamilton CA, Thomas MS, et al. Utility of fast cine MRI and display for the detection of myocardial ischemia in patients not well suited for second harmonic stress echocardiography. Circulation 1999;100:1697–702.
Garot J, Bluemke DA, Osman NF, et al. Fast determination of regional myocardial strain fields from tagged cardiac images using harmonic phase MRI. Circulation 2000;101:981–8.
Hundley GW, Hillis DL, Hamilton CA, et al. Assessment of coronary arterial restenosis with phase-contrast MRI measurements of coronary flow reserve. Circulation 2000;101:2375–81.
Manning WJ, Li W, Edelman RR. A preliminary report comparing magnetic resonance coronary angiography with conventional angiography. N Engl J Med 1993;328:828–32.
Toussaint JF, LaMuraglia GM, Southern JF, Fuster V, Kantor HL. Magnetic resonance images lipid, fibrous, calcified, hemorrhagic and thrombotic components of human atherosclerosis in vivo. Circulation 1996;94:932–8.
Correia LCL, Atalar E, Kelemen MD, et al. Intravascular MRI of aortic atherosclerotic plaque composition. Arterioscl Thromb Vasc Biol 1997;17:3626–32.
Shunk KA, Garot J, Atalar E, Lima JAC. Transesophageal MRI of the aortic arch and descending thoracic aorta in patients with aortic atherosclerosis. J Am Coll Cardiol 2001;37:2031–5.

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