Journal of Cardiovascular Magnetic Resonance®, 3(3), 267–281 (2001)

Stress Cardiovascular Magnetic Resonance: Consensus Panel Report

Eike Nagel,[1] Christine Lorenz,[2] Frank Baer,[3] W. Gregory Hundley,[4] Norbert Wilke,[5] Stefan Neubauer,[6] Udo Sechtem,[7] Ernst van der Wall,[8] Roderic Pettigrew,[10] Albert de Roos,[9] Eckart Fleck,[1] Albert van Rossum,[11] Dudley J. Pennell,[12] and Samuel Wickline[2]

[1] *Department of Internal Medicine/Cardiology, Charité, Campus Virchow Clinicum, Humboldt University and German Heart Institute, Berlin, Germany*
[2] *Center for Cardiovascular MR, Cardiovascular Division, Barnes-Jewish Hospital at Washington University Medical Center, St. Louis, Missouri*
[3] *Internal Medicine III, Cardiology, University Hospital, Cologne, Germany*
[4] *Cardiology Section, The Wake Forrest University School of Medicine, Winston-Salem, North Carolina*
[5] *Center for Magnetic Resonance Research, University of Minnesota Medical School, Minnesota*
[6] *Department of Cardiovascular Medicine, John Radcliffe Hospital, Oxford, United Kingdom*
[7] *Internal Medicine 3, Cardiology/Pulmonology, Robert-Bosch Hospital, Stuttgart, Germany*
[8] *Department of Cardiology and* [9] *Department of Radiology, University Medical Center, Leiden, The Netherlands*
[10] *Frederik Philips MR Research Center, Emory University, Atlanta, Georgia*
[11] *Department of Cardiology, University Hospital VU, Amsterdam, The Netherlands*
[12] *Cardiovascular Magnetic Resonance Unit, Royal Brompton Hospital, London, United Kingdom*

Address correspondence and reprint requests to Eike Nagel.

INTRODUCTION

Cardiovascular magnetic resonance (CMR) has evolved into a new technique for the non-invasive detection of obstructive coronary artery disease. The ability of CMR to visualize global and regional wall motion and systolic thickening of the left ventricle with high spatial and temporal resolution enables the detection of wall motion abnormalities. In addition, perfusion defects and reduced coronary flow reserve can be assessed. With magnetic resonance spectroscopy it is possible to detect metabolic alterations. However, except for high-grade coronary artery stenosis, abnormalities can generally be identified only under stress conditions, which can be induced by physical exercise or standardized stress protocols with pharmacological agents such as dobutamine/atropine, dipyridamole, or adenosine infusion (Tab. 1). Exercise causes motion artifacts in standard encephalocardiogram (ECG)-triggered magnetic resonance images, but can this be overcome with real-time image acquisition. Given that real-time acquisition is not yet available on all commercial scanners, exercise is less well-suited than pharmacological stress for magnetic resonance. Pharmacological agents have been shown to be safe and well tolerated, and they reproducibly induce myocardial ischemia (1,2). To date, the most reliable clinical data exists on the analysis of left ventricular wall motion and thickening under pharmacological stress conditions. The goal of this overview is to present the results of recent studies and to establish recommendations for cardiologists, radiologists, and technologists for the performance of CMR stress testing.

Assessment of Wall Motion

For the assessment of wall motion, cine-loops of the heart are acquired with gradient-echo or segmented *k*-space turbo-gradient-echo sequences. More rapid image acquisition is possible by the use of echo planar imaging, which allows either reduced scan time or improved temporal resolution. Gradient-echo images provide high natural contrast between flowing blood and the myocardium, as well as the myocardium and surrounding structures such as lung parenchyma and thus allow a reliable delineation of the endo- and epicardial border. The heart can either be visualized with contiguous short axis slices or with a combination of several short (typically three to five) and long (typically horizontal and vertical) axis views (Fig. 1). A further reduction of acquisition time is possible with interactive or real-time CMR imaging (3,4), which has been shown to achieve similar or superior image quality when compared with echocardiography (4). It

Table 1

Stress Protocols

Stress Test	Patient Instructions	Protocol	Antidote
Dobutamine for the assessment of viability		5, 10 μg/kg BW per min for >3 min	
Dobutamine/atropine for the detection of coronary artery disease (wall motion)	No β-blockers and nitrates 24 h prior to the examination	(5), 10, 20, 30, 40 μg/kg BW per min for 3 min each, up to 1 mg atropine (4 × 0.25 mg) until submaximal heart rate [(220 − age) × 0.85] is reached. (half-life 2 min)	β-blocker (esmolol) 0.5 mg/kg as slowly injected bolus, additional bolus of 0.2 mg/kg as needed sublingual nitroglycerine
Dipyridamole (perfusion)	No caffeine (tea, coffee, chocolate, etc.) or medications such as aminophylline or nitrates 24 h prior to the examination	0.56 mg/kg BW per min for 4 min, maximal effect after approximately 3–4 min. (half-life 30 min)	Aminophylline 250 mg i.v. slowly injected with ECG monitoring sublingual nitroglycerine
Adenosine (perfusion)	Same as for dipyridamole	140 μg/kg BW per min for 6 min. (half-life 4–10 s)	Stop infusion (in occasional cases aminophylline 250 mg i.v. slowly injected with ECG monitoring)

BW = body weight.

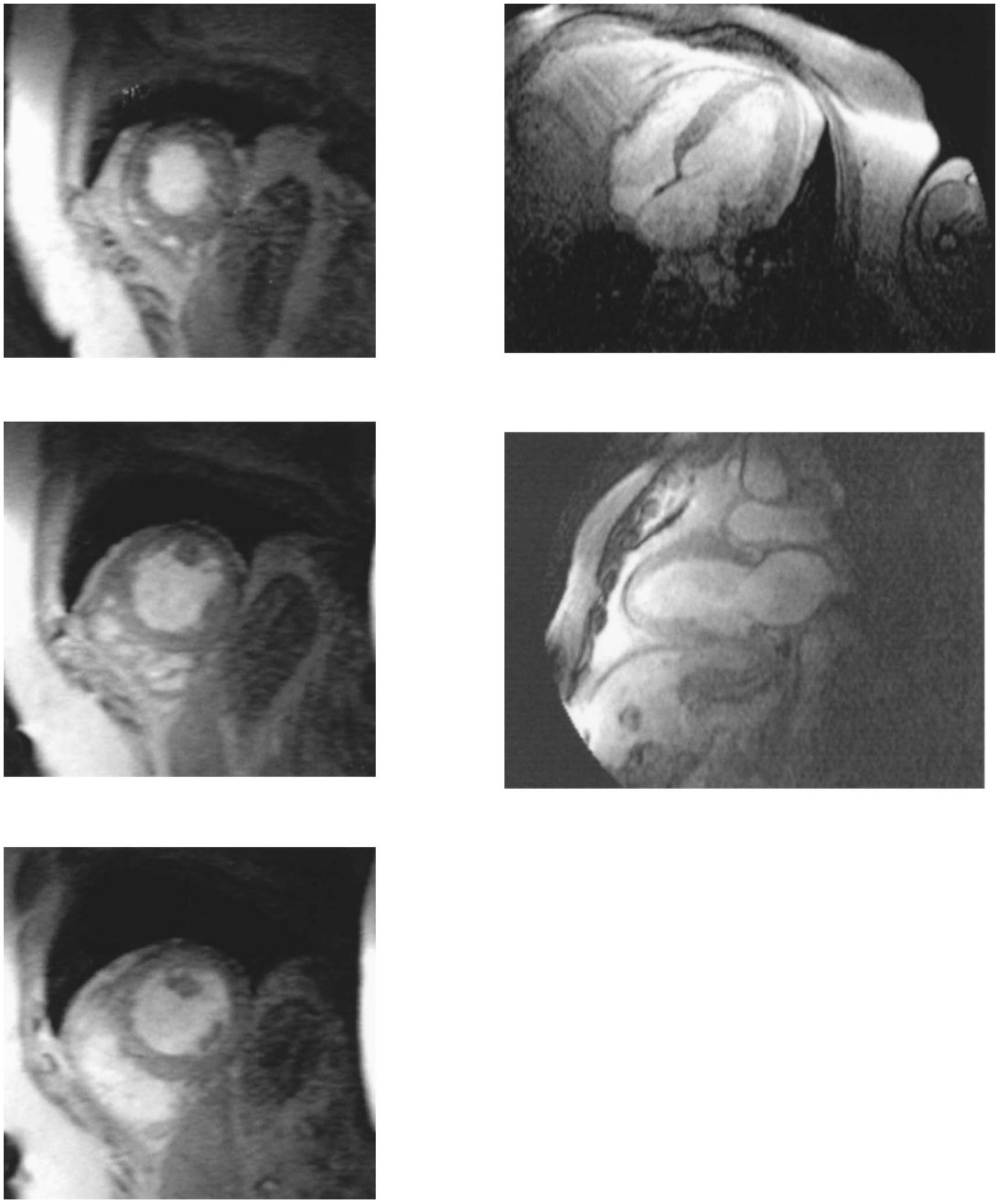

Figure 1. Segmented *k*-space spoiled gradient echo images at end-diastole acquired during breath holding of 16 heart beats (TE/TR/flip-angle: 2.1 ms/5.9 ms/25°, spatial resolution 1.3 × 1.3 mm, slice thickness 8 mm, temporal resolution 40 ms). One out of 18 cardiac phases is displayed. The left column shows short axis views at the apex (top), equator (middle), and base (bottom); the right column shows a horizontal (top) and a vertical (bottom) long axis view. No contrast agent was used.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

also permits an accurate determination of left ventricular ejection fraction (5,6). Real-time imaging may also allow the application of physical, rather than pharmacological, stress because these images are less sensitive to motion artifacts when compared with turbo-gradient-echo images.

Assessment of Myocardial Perfusion and Contrast Agent Kinetics

Perfusion CMR is mainly performed by a rapid series of images during the first pass of a contrast bolus injection. With state-of-the-art scanners, several slices (typically three to five) are imaged every heart beat using turbo gradient-echo, echo-planar, or a combination of turbo-gradient-echo and echo planar imaging (hybrid sequence) (7,8). A prepulse (inversion or saturation) is used to suppress the signal of the myocardium before injection of a Gd-DPTA bolus. The contrast agent passes through the right and left ventricular cavity and then into the myocardium, causing an increase in signal intensity (9) (Figs. 2 and 3).

METHODS

Even though rapid progress has been made and more information about the following topics is available, no broad consensus about the value of these techniques in clinical practice has been reached to date.

Quantitative Regional Wall Motion

A quantitative analysis of wall motion and systolic thickening is possible and has shown good results in small studies (10,11). Further improvements of diagnostic accuracy and reproducibility may be achieved with online or rapid offline analysis or myocardial tagging (12), which allows quantification of regional three-dimensional myocardial motion.

Assessment of Myocardial Perfusion from T1 and T2 Changes without Contrast Agents

From the signal loss after the injection of a T2-shortening agent (13) or the differences of oxygenated and nonoxygenated blood without the use of contrast agents, myocardial perfusion can be assessed (14–16). Advantages of these techniques are the possibility of quantification and the lack of contrast agents.

Assessment of Viability from Contrast Enhancement

The distribution kinetics of contrast agents have been used to detect myocardial infarction and to define viable myocardium (17,18). In some patients, after myocardial infarction a hypoenhanced zone in the core of a region with hyperenhancement has been found in the equilibrium phase (1–2 min after injection) (19). This hypoenhanced core has been explained by the occlusion of capillaries with dying blood cells and debris (= microvascular obstruction or nonreflow region) and was a strong predictor for cardiac morbidity and mortality after myocardial infarction (19). In the experimental animal, enhancement patterns correlate well with reversible and irreversible myocardial ischemia (20). In another study, different patterns of contrast agent kinetics after myocardial infarction have been assigned to different pathophysiological situations, such as irreversible myocardial defect, predominantly viable myocardium, and a mixture of viable and necrotic myocardium (21). The amount of data seems as yet insufficient for broad clinical use and the underlying mechanisms for these observations have not been fully understood so far. Since this manuscript deals with the application of stress during cardiac MR examinations, the assessment of viability from perfusion studies will not be elaborated any further.

Assessment of Flow

Up to now, the assessment of coronary artery flow has only been performed by a limited number of centers (22–24). Segmented *k*-space turbo-gradient-echo sequences or echo-planar imaging are used during breath holding or free breathing in combination with navigator gating to suppress breathing motion artifacts (25,26). The velocity of the flowing blood can be determined from the velocity encoded (phase contrast) images. Peak flow and volume flow can be calculated and a flow reserve can be determined from measurements before and after dipyridamole or adenosine.

It has also been shown that the peak flow acceleration in the aorta is a marker of ischemia in patients with coronary artery disease (27); the change in peak flow acceleration from baseline to stress has been shown to correlate to the extent of ischemic burden. Further studies are required to determine the clinical utility of this technique, which to date has only been reported from one center.

Due to their investigational status, no recommendations concerning flow measurements will be given in this article.

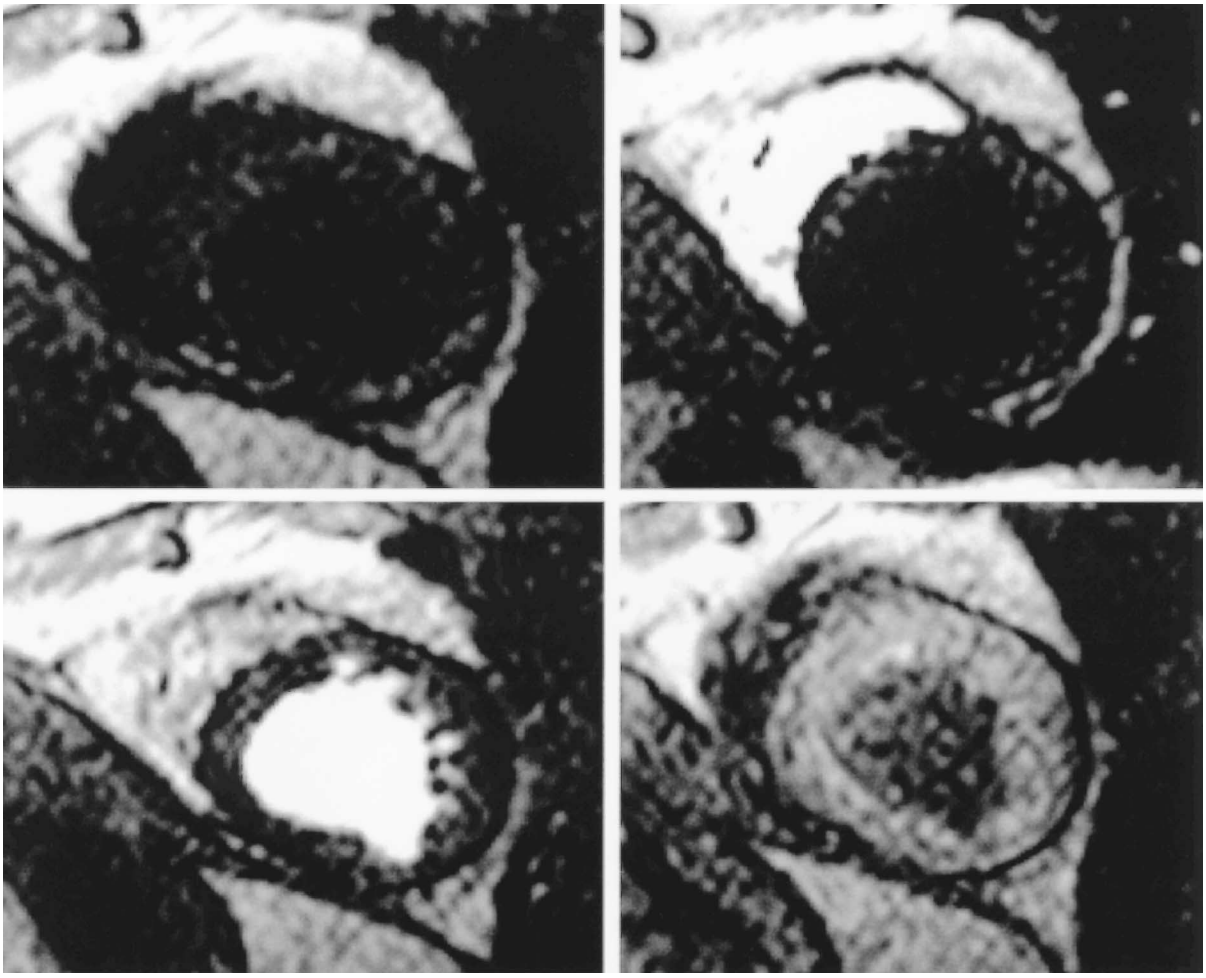

Figure 2. Perfusion images acquired with a segmented *k*-space spoiled gradient echo-echo-planar read out hybrid sequence (TE/TR/flip-angle: 3.3 ms/12.5 ms/30°, EPI-factor 11). For each heart beat, five short axis images are acquired. Four images of a series of 60 dynamics are displayed. Before contrast agent injection (top left), the myocardial signal is suppressed using an inversion prepulse, then the contrast agent bolus arrives in the right (top right) and left ventricle (bottom left). The myocardium is enhanced (bottom right) after the first pass of the contrast agent bolus has left the left ventricular cavity.

Combination of Methods

In general, a combination of imaging methods can be used within a CMR examination. The combined determination of wall motion and perfusion has been shown in animals (28) and in small numbers of patients (29,30).

MR Spectroscopy

^{31}P-spectrospcopy is the only technique for the noninvasive study of cardiac high-energy phosphate metabolism, allowing the measurement of adenosine triphosphate (ATP) and phosphocreatine in the human heart (31,32). On theoretical grounds, testing for alterations of regional high-energy phosphate content in patients with suspected coronary artery disease is attractive because the myocardial phosphocreatine concentration is one of the most sensitive indicators of myocardial ischemia, decreasing significantly within 12 s after the onset of ischemia (33). In normal human myocardium, high-energy phosphate levels do not change with mild and moderate degrees of cardiac stress induced by handgrip exercise (34) or low-dose dobutamine (35), and only decrease slightly with high levels of stress (high-dose dobutamine

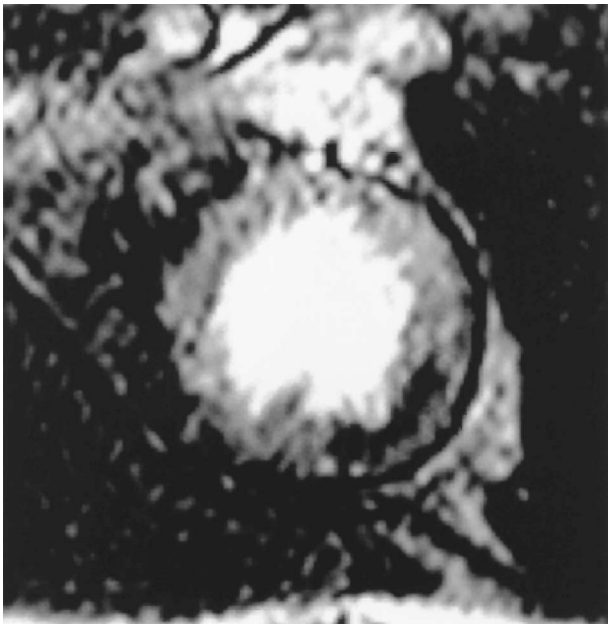

Figure 3. Pathological perfusion image. Acquisition technique identical to Figure 2. A reduction of myocardial perfusion can be seen during the first pass of the contrast agent in the inferolateral wall as a dark zone in a patient with high-grade (>75%) stenosis of the left circumflex artery.

plus atropine). In patients with high-grade stenosis of the left anterior descending (LAD) artery, Weiss et al. (34) have demonstrated that, in principle, a ''biochemical stress test'' is possible. In patients (but not volunteers) the myocardial phosphocreatine/ATP ratio decreased from 1.5 ± 0.3 to 0.9 ± 0.2 during handgrip exercise and returned toward normal during recovery from exercise. After revascularization, phosphocreatine/ATP ratios did not change any further with exercise. These results were reproduced by Yabe et al. (36). In 20% of women with normal coronary angiograms but chest pain, subnormal phosphocreatine to ATP ratios during handgrip exercise were found, possibly due to microvascular coronary artery disease (37). For detection of regional myocardial ischemia, a spatial resolution of <5 cm^3 would be a prerequisite. Unfortunately, on 1.5-Tesla magnetic resonance (MR) systems, the intrinsically low MR sensitivity of the ^{31}P nucleus limits resolution to voxel sizes of about 30 cm^3, and it is unlikely that technical improvements in coil design or localization techniques will increase resolution to the required level. For this reason, MR spectroscopy is not described in further detail here. On the other hand, at 3 or 4 Tesla, 4–5 cm^3 resolution for ^{31}P-MR spectroscopic imaging during cardiac stress testing is achievable (38), and it is entirely possible that in the future, with improvements in high-field magnet technology, cardiac ^{31}P-MR stress testing will become an important clinical tool. Such a method would, for example, allow the non-invasive study of the effectiveness of revascularization procedures or various antianginal therapies. The ''phosphocreatine threshold'' may emerge as a clinically relevant parameter, representing the level of exercise achievable without a decrease of myocardial phosphocreatine concentrations.

Accuracy of Stress Testing

Viability

By using low-dose dobutamine, which stimulates wall thickening without inducing ischemia (10 μg/kg body weight per minute), CMR has shown good results for the detection of viable myocardium when compared with PET (39) and transesophageal echocardiography (sensitivity 81%, specificity 100%) in a study of 43 patients (40). The prediction of functional recovery 4 to 6 months after revascularization yielded a sensitivity of 89% and a specificity of 94% when an increase of systolic wall thickening of ≥2 mm was observed during stress CMR, which is essentially identical to the sensitivity and specificity of PET (41).

Thus, low-dose dobutamine stress CMR is a valid tool for the detection of viable myocardium and can compete with transesophageal echocardiography and PET; however, current data stems from a single center only and multicenter studies in larger numbers of patients are required to fully evaluate this technique.

Stress-Induced Wall Motion Abnormalities for the Diagnosis of Ischemia

Echocardiographic detection of wall motion abnormalities during high-dose dobutamine stress or during exercise has been shown to be an accurate diagnostic tool for the screening of patients with suspected coronary artery disease. Sensitivities and specificities have been reported to lie within the ranges of 54–96% and 60–100%, respectively (42), depending on the pretest likelihood of disease and the experience of the stress centers. However, the value of stress echocardiography is limited by a rate of 10–15% for nondiagnostic results (42) and low specificities for the basal-lateral and the basal-inferior segments of the left ventricle (43).

With CMR, good results have been found for the detection of wall motion abnormalities at intermediate doses of dobutamine (maximum 20 μg/kg BW per min-

ute i.v.) (44–46). However, echocardiographic studies have shown that high-dose dobutamine and additional atropine are required to ensure high sensitivity. In a recent prospective study of 208 patients with suspected coronary artery disease, high-dose dobutamine/atropine (40 μg/kg body weight per minute plus up to 1 mg atropine i.v.) stress was used and echocardiography and CMR (Figs. 3 and 4) were compared with angiography for the detection of significant coronary artery disease (>50% angiographic diameter stenosis) (47). In this study, a significant improvement of sensitivity (86% vs. 74%), specificity (86% vs. 70%), and diagnostic accuracy (86% vs. 73%) of CMR versus transthoracic echocardiography was found. These differences were most pronounced in patients who had moderate echocardiographic image quality (48). The results were comparable when echocardiographic image quality was high. In a different study by Hundley et al. (49) patients with nondiagnostic echocardiograpic image quality were assessed with a similar protocol and 94% of them could be adequately examined with CMR, yielding a sensitivity and specificity of 83% in those patients who also underwent angiographic assessment.

Since high-dose dobutamine stress CMR is highly accurate and can be performed in less than 30 min, it has the potential to replace dobutamine stress echocardiography for the detection of coronary artery disease in patients with non-diagnostic or suboptimal echocardiographic image quality. Further studies with larger numbers of patients are required.

Perfusion for the Diagnosis of Ischemia

The kinetics of the first pass of a contrast agent bolus can be used to quantify or semiquantify myocardial perfusion (50–55). From alterations of the signal intensity curves during infusion of adenosine or dipyridamole, an assessment of perfusion reserve can be made (56). Recent reports have shown high sensitivity and specificity of this technique for the detection of coronary artery disease (57–62) and a good correlation with coronary artery luminal narrowing (63). To date, data have been published from more than 400 patients who have been examined with MR firstpass perfusion studies using either dipyridamole or adenosine. Direct comparison with SPECT resulted in sensitivities ranging from 77% (64) to 90% (65,66) and specificities from 86% (57) to 97% (64). Currently, large prospective trials in unselected patients are under way in several institutions. The preliminary results from these studies are highly promising and the assessment of myocardial perfusion with magnetic resonance may progress to routine clinical use, but studies with large numbers of patients are required, and the necessary postprocessing must be made widely available.

RECOMMENDATIONS FOR MR STRESS TESTING

Image Acquisition

Viability (Low-Dose Dobutamine)

Since time for image acquisition is not limited by the stress regime, low-dose dobutamine (≤10 μg dobutamine/kg body weight/min) studies can be performed with standard gradient echo sequences. However, examination time can be reduced by the use of segmented *k*-space turbo-gradient-echo or echo-planar imaging techniques. Five standard views (vertical long axis, horizontal long axis, basal short axis, mid short axis, and apical short axis) should be acquired. Alternative approaches, such as complete coverage of the left ventricle with short axis views, may be performed. It is essential, however, to cover all coronary perfusion territories. Temporal resolution needs to be equal to or better than 20 frames/second with a spatial resolution below 2 × 2 mm and a slice thickness of 6–10 mm to allow the detection of small alterations of myocardial thickening. Images are acquired at rest and during each stress level. The stress protocol is shown in Table 1. Monitoring and contraindications are listed in Tables 2 and 3.

Wall Motion Abnormalities (High-Dose Dobutamine)

For high-dose dobutamine stress tests, breath-hold cine imaging using turbo-gradient-echo techniques, echo-planar imaging, or real-time imaging should ideally be used in preference to conventional nonbreathhold techniques. These fast techniques significantly reduce the scan time, improve image quality, and enable rapid detection of wall motion abnormalities. The same views as recommended for low-dose dobutamine studies should be imaged. Imaging starts immediately after increasing the dobutamine dose at each cardiac level. To achieve an adequate number of phases during tachycardia, temporal resolution needs to be approximately 25 frames/second (<40 ms). Studies published so far have used a spatial resolution of around 2 × 2 mm or better, with a slice thickness of 6–10 mm. Images are acquired and reviewed at rest and during each stress level. For the stress protocol

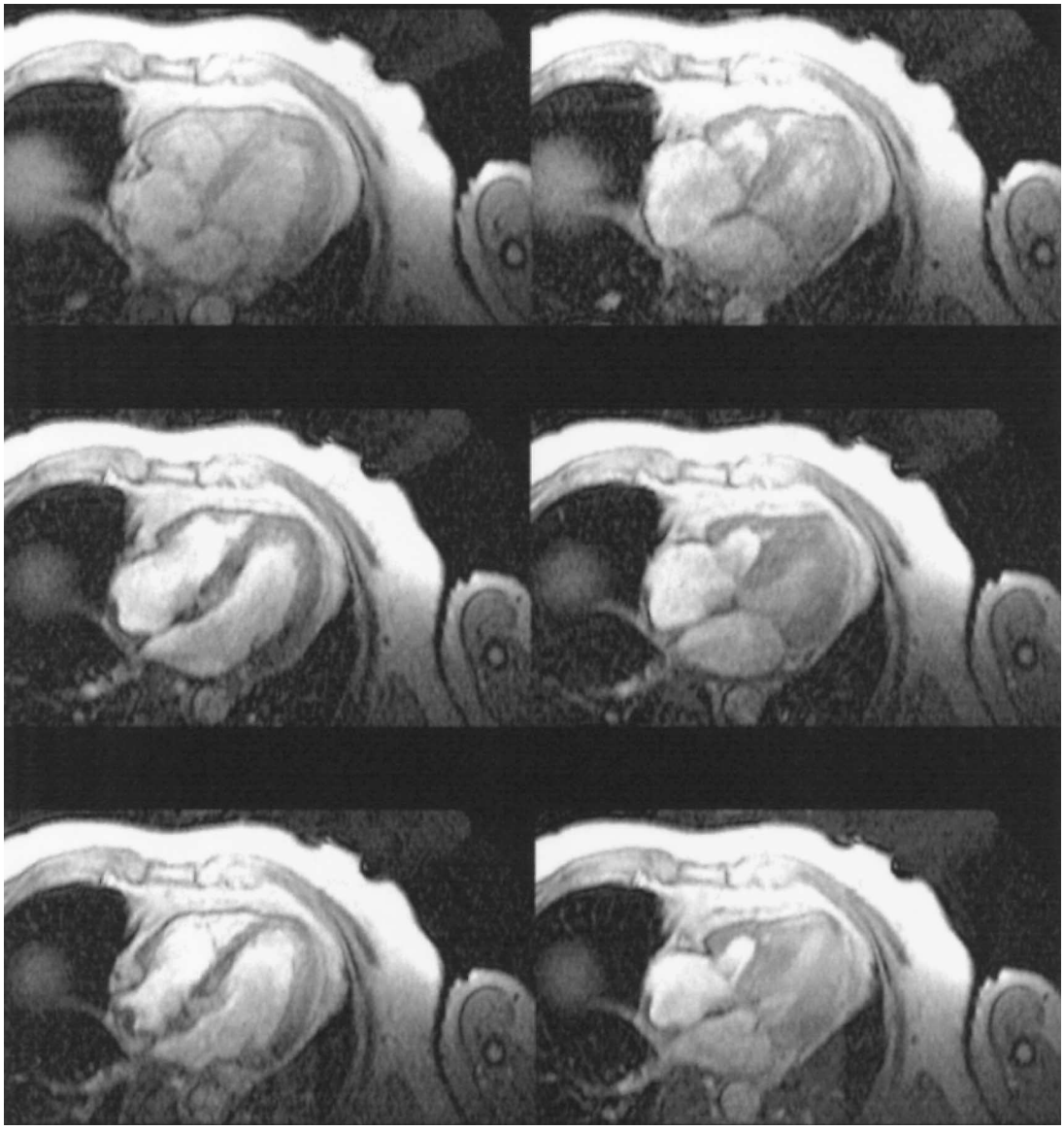

Figure 4. Horizontal long axis views during dobutamine stress. Imaging technique identical to Figure 1. Left column: end-diastole; right column: end-systole. Top row: rest; middle row: intermediate stress (20 μg/kg/min), note the increased contraction and wall thickening in all segments; bottom row: maximal stress, there is a significant wall motion abnormality at the apical septum in a patient with significant coronary artery disease.

and details concerning monitoring, contraindications and termination criteria refer to Tables 1–4.

Perfusion (Dipyridamole/Adenosine)

Perfusion imaging before and after dipyridamole or adenosine infusion requires the acquisition of a rapid series of several images per heartbeat during the first pass of a contrast agent bolus. Most centers use either turbo gradient echo, echo planar imaging, or a combination of both. Three to five slices are acquired every—or at least every other—heart beat. This temporal resolution is essential to allow a determination of the upslope of the signal intensity curve. A spatial resolution of 3×3 mm or better with a slice thickness of 6–10 mm is recommended. See Tables 1–4 for details. An inversion or saturation prepulse is generally used to suppress the myocar-

Table 2

Monitoring Requirements for Stress MR Imaging

	Dobutamine + Atropine	Dipyridamile/ Adenosine
Heart rate and rhythm (single lead ECG)	Continuously	Continuously
Blood pressure	Every minute	Every minute
Pulse oximetry	Continuously	Continuously
Symptoms	Continuously	Continuously
Wall motion abnormalities	Every dose increment	At peak stress

Table 3

Contraindications for MR Stress Tests

MR examination	Incompatible metallic implants (e.g., pacemakers, retroorbital metal, cerebral artery clips)
	Claustrophobia
Dobutamine	Severe arterial hypertension (≥220/120 mm Hg)
	Unstable angina pectoris
	Significant aortic stenosis (aortic valve gradient >50 mm Hg or aortic valve area <1 cm^2)
	Complex cardiac arrhythmias
	Significant hypertrophic obstructive cardiomyopathy
	Myocarditis, Endocarditis, Pericarditis
	Other major disease
Dipyridamole/adenosine	Myocardial infarction <3 days
	Unstable angina pectoris
	Severe arterial hypertension
	Asthma or severe obstructive pulmonary disease
	AV-block >IIa

Table 4

Dobutamine Termination Criteria

- Submaximal heart rate reached [(220 − age) × 0.85]
- Blood pressure decrease >20 mm Hg systolic below baseline systolic blood pressure or decrease >40 mm Hg from a previous level
- Blood pressure increase >240/120 mm Hg
- Intractable symptoms
- New or worsening wall motion abnormalities in at least 2 adjacent left ventricular segments (out of 16)
- Complex cardiac arrhythmias

dial signal before contrast agent injection. Most centers use a dose of Gd-DPTA 0.025–0.05 mmol/kg body weight rapidly injected into an antecubital vein, and flushed with approximately 10 mL saline for quantitative approach, which includes the signal intensity curves of the left ventricular cavity for calculation. Doses of Gd-DPTA 0.05–0.2 mmol/kg are rapidly injected for a more visual approach. Injection is performed manually or (preferably) with an injection pump. To facilitate image analysis, it is an option to acquire images during breath holding during the first pass of the contrast agent through the left ventricular cavity and the myocardium. Alternatively, post processing techniques may help to remove respiratory motion in nonbreathhold imaging. Optimal breath holding can be achieved by injecting the contrast agent at the beginning of two breathing cycles before breath holding for approximately 20 s.

Image Interpretation

Viability

For viability studies, quantitative assessment is required. A minimal end diastolic wall thickness of >5 mm with resting thickening or resting akinesis, with an improvement of systolic wall thickening of ≥2 mm during dobutamine stimulation, are the diagnostic criteria for viable myocardium used in published studies (39–41).

Wall Motion Abnormalities for the Diagnosis of Ischemia

For optimal image interpretation, multiple cine loop display is recommended, with perhaps five slices at each dose level viewed simultaneously. The ventricle is analyzed by segments. Schemes vary from a nine-segment model (44) to that recommended for echocardiography, with 16 (or 17) left-ventricular segments per stress level, which are visually or quantitatively evaluated according to the standards suggested by the American Society of Echocardiography (67). Image quality is graded as good, acceptable, or bad, and the number of diagnostic segments is reported. Segmental wall motion is classified as normokinetic, hypokinetic, akinetic, or dyskinetic, and assigned one to four points. The sum of points is divided by the number of analyzed segments and yields a wall motion score. Normal contraction results in a wall motion score of 1, a higher score being indicative of wall motion abnormalities. During dobutamine stress with increasing doses, a lack of increase in the wall motion or systolic wall thickening or a reduction of the wall motion or thickening are both regarded as pathological findings.

Perfusion

Up to now, no optimal approach for the analysis of perfusion images has been defined. Image interpretation ranges from a simple visual approach (62) to the calculation of a perfusion reserve index from the linear fit of the upslope of the myocardial signal intensity curves (61,63,68,69) or the maximal signal intensity (69) to a more complex, quantitative calculation of myocardial perfusion using a gamma variate fit or tracer kinetic models correcting for the extraction of the contrast agent and fast as well as slow water exchange (53,70). Similar segments as used for wall motion are evaluated. In addition, differences between endo- and epi-cardial perfusion can be assessed. Perfusion reserve index is calculated as the relative difference of perfusion before and after vasodilation.

SAFETY RECOMMENDATIONS

During stress examinations using low- or high-dose dobutamine, dipyridamole, or adenosine, monitoring of the patient within the magnet is mandatory. In general, monitoring during a MR examination requires the same precautions and emergency equipment as any other stress examination. A physician trained in cardiovascular emergencies and resuscitation needs to be at the scanner. Specific recommendations are listed in Table 2. Apart from specific contraindications for MR, such as retro-orbital metal, cerebral clips, or pacemakers, the contraindications are identical to those for stress echocardiography and are listed in Table 3.

Dobutamine

Dobutamine is a sympathomimetic drug with beta-1, beta-2, and slight alpha-1 receptor stimulation properties. Infusion of the drug increases cardiac contractility and heart rate, and decreases systolic vascular resistance. Whereas, during low-dose infusion ($\leq$10 μg/kg/min), the increase of contractility is the major effect, at higher doses the increased consumption of oxygen causes contraction abnormalities in myocardial segments supplied by stenotic coronary arteries.

While only minimal side effects are to be expected during low-dose dobutamine, high-dose dobutamine stress may cause severe complications in 0.25% of patients, which include infarction (0.07%), ventricular fibrillation (0.07%), and sustained ventricular tachycardia (0.1%) (1,2). Thus, although adverse events are rare, preparation and practice for rapid removal of the patient from the magnet needs to be borne in mind in addition to a close compliance with test truncation criteria (Tab. 4). In most other modalities, eye-to-eye contact exists between patient and examiner, but in CMR, communication is usually via a microphone system and video cameras, although it can also be conducted personally. Remote communication does not hinder the safety process if symptoms, blood pressure, pulse oximetry, and the occurrence of wall motion abnormalities are carefully monitored (Tab. 2). This can be done either by placing standard equipment outside the scanner room connected to the patient with special extensions through a waveguide in the radiofrequency cage, or by using special CMR compatible equipment that currently exists at many CMR sites. A defibrillator and all medications for emergency treatment must be available at the CMR site. A specific problem for monitoring within the magnet is that of assessing the changes of ST-segments from the ECG. Possible improvements may be achieved by the use of ECG tracings that are based on the spatial information of the vector cardiogram (71). However, since wall motion abnormalities precede ST changes (72,73) and such abnormalities can be readily detected with fast CMR, monitoring is effective without a diagnostic ECG and can also be performed in patients with left bundle branch block who are routinely evaluated with dobutamine stress echocardiography despite nondiagnostic ST segments. With conventional imaging, such wall motion abnormalities can be detected immediately after image reconstruction, which is completed 5–10 s after image acquisition. In addition, real-time imaging permits immediate detection of wall motion abnormalities and can be used for monitoring; however, it is not yet ready for the diagnostic visualization of wall motion abnormalities. In the experience of the consensus panel, with more than 500 patients examined with low-dose and more than 1000 patients examined with high-dose dobutamine stress CMR, wall motion abnormalities were readily detected during the stress examination. In two cases (0.2%) cardiopulmonary resuscitation due to ventricular fibrillation was required. These complications are within the expected range and were safely handled with a good patient outcome.

Dipyridamole/Adenosine

Dipyridamole and adenosine cause vasodilation, which is more pronounced in normal arteries in comparison with those with stenosis creating perfusion heterogeneity. The vasodilatory effect may lead to mild-to-moderate reduction of systolic, diastolic, and mean arterial blood pressure of approximately 10 mm Hg. In addition,

a depressant effect on the SA and AV node is exerted. Thus, for dipyridamole (74) and adenosine stress tests, monitoring of heart rate and rhythm, blood pressure, and the patient's symptoms is required, and patients with AV-block >IIa need to be excluded. Mild side effects such as hypotension or bradycardia are common (0.85%). Severe side effects are to be expected in only 0.07% of patients and include asystole, ventricular tachycardia, persistent angina pectoris, and myocardial infarction (75–77). The stimulation of respiration may lead to an increase in minute ventilation, reduction in arterial PCO_2, and respiratory alkalosis. Thus, this test is not suitable for patients with asthma or poor pulmonary function. Contraindications and examination termination criteria are listed in Tables 3 and 4. The experience of the consensus panel consists of more than 200 examinations with dipyridamole and 250 with adenosine for the assessment of myocardial perfusion. No side effects requiring significant medical treatment were observed.

Training

For adequate image acquisition and interpretation as well as patient care during stress, specific training is required. This includes the ability to perform the scan, to interpret the images immediately after acquisition during the scan, to stop the test if new wall motion abnormalities occur, and to perform cardiopulmonary resuscitation, as well as the ability to react adequately to other emergency situations that may occur during stress testing, such as severe angina pectoris, cardiac arrhythmias, or bronchoconstriction. Further information and recommendations for training will form the subject of future reports.

CONCLUSION

CMR is a rapidly developing new modality with applications in clinical cardiology for detection and assessment of myocardial ischemia and viability. With currently available techniques it is possible to assess viability from wall motion studies with low-dose dobutamine with similar diagnostic accuracy to transesophageal echocardiography or PET. High-dose dobutamine examinations are safe, yield a high diagnostic accuracy, and can be used in patients with nondiagnostic or moderate echocardiographic image quality to detect stress-induced wall motion abnormalities. Perfusion measurements with dipyridamole or adenosine are safe and robust and may develop into a clinically useful examination. Thus, while some further developments remain to be performed—mainly in image postprocessing and display—stress techniques are now ready for full clinical evaluation in large patient numbers.

REFERENCES

1. Picano, E.; Mathias, W.J.; Pingitore, A.; Bigi, R.; Previtali, M. Safety and Tolerability of Dobutamine-Atropine Stress Echocardiography: A Prospective, Multicentre Study. Echo Dobutamine International Cooperative Study Group. Lancet **1994**, *344*, 1190–92.
2. Mertes, H.; Sawada, S.G.; Ryan, T.; Segar, D.S.; Kovacs, R.; Foltz, J.; Feigenbaum, H. Symptoms, Adverse Effects, and Complications Associated with Dobutamine Stress Echocardiography. Experience in 1118 Patients. Circulation **1993**, *88*, 15–19.
3. Lorenz, C.H.; Fischer, S.E.; Mens, G.; Johansson, L.O.; van Vaals, J.J. Interactive Cardiac Scan Planning on a Standard Clinical MR Scanner. Proceedings of the ISMRM, Sydney, 1998; 1958 (abstract).
4. Yang, P.C.; Kerr, A.B.; Liu, A.C.; Liang, D.H.; Hardy, C.; Meyer, C.H.; Macovski, A.; Pauly, J.M.; Hu, B.S. New Real-Time Interactive Cardiac Magnetic Resonance Imaging System Complements Echocardiography. J. Am. Coll. Cardiol. **1998**, *32*, 2049–56.
5. Scheidegger, M.B.; Spiegel, M.; Stuber, M.; Bonetti, P.; Dubach, P.; Boesiger, P. Assessment of Cardiac Wall Thickening and Ejection Fraction from Real Time Cardiac MR Images in Patients with Left Ventricular Dysfunction. Proceedings of the ISMRM, Sydney, 1998; 554 (abstract).
6. Nagel, E.; Schneider, U.; Schalla, S.; Ibrahim, T.; Schnackenburgm B.; Bornstedtm A.; Kleinm C.; Lehmkuhl, H.; Fleck, E. Magnetic Resonance Real Time Imaging for the Evaluation of Left Ventricular Function. J. Cardiovasc. Magn. Reson. **2000**, *2*, 7–14.
7. McKinnon, G.C. Ultrafast Interleaved Gradient-Echo-Planar Imaging on a Standard Scanner. Magn. Reson. Med. **1993**, *30*, 609–616.
8. Fischer, S.E.; Wickline, S.A.; Lorenz, C.H. Multiple Slice Hybrid Imaging Sequence for Myocardial Perfusion Measurement. Proceedings of the ISMRM, New York, 1996; 682 (abstract).
9. Manning, W.J.; Atkinson, D.J.; Grossman, W.; Paulin, S.; Edelman, R.R. First-Pass Nuclear Magnetic Resonance Imaging Studies Using Gadolinium-DTPA in Patients With Coronary Artery Disease. J. Am. Coll. Cardiol. **1991**, *18*, 959–65.
10. van Rugge, F.P.; van der Wall, E.E.; Spanjersberg, S.J.; de Roos, A.; Matheijssen, N.A.; Zwinderman, A.H.; van Dijkman, P.R.; Reiber, J.H.; Bruschke, A.V. Magnetic Resonance Imaging During Dobutamine Stress for Detection and Localization of Coronary Artery Disease. Quan-

titative Wall Motion Analysis Using a Modification of the Centerline Method. Circulation **1994**, *90*, 127–38.
11. van der Geest, R.J.; Buller, V.G.M.; Jansen, E.; Lamb, H.J.; Baur, L.H.B.; van der Wall, E.E.; de Roos, A.; Reiber, J.H.C. Comparison between Manual and Semiautomated Analysis of Left Ventricular Volume Parameters from Short-Axis MR Images. J. Comp. Assist. Tomogr. **1997**, *21*, 756–65.
12. Power, T.P.; Kramer, C.M.; Shaffer, A.L.; Theobald, T.M.; Petruolo, S.; Reichek, N.; Rogers, W.J. Breath-Hold Dobutamine Magnetic Resonance Myocardial Tagging: Normal Left Ventricular Response. Am. J. Cardiol. **1997**, *80*, 1203–1207.
13. Beache, G.; Kulke, S.; Kantor, H.; Niemi, P.; Campbell, T.; Chesler, D.; Gerwirtz, H.; Rosen, B.; Brady, T.; Weisskoff, T. Imaging Perfusion Deficits in Ischemic Heart Disease with Susceptibility-Enhanced T2-Weighted MRI: Preliminary Human Studies. Magn. Reson. Imaging **1998**, *16*.
14. Li, D.; Dhawale, P.; Rubin, P.; Haacke. E.; Gropler, R. Myocardial Signal Response to Dipyridamole and Dobutamine: Demonstration of the BOLD Effect Using Double-Echo Gradient-Echo Sequence. Magn. Reson. Med. **1996**, *36*, 16–20.
15. Bauer, W.; Nadler, W.; Bock, M.; Schad, L.; Wacker, W.; Hartlep, A.; Ertl, G. Theory of the BOLD Effect in the Capillary Region: An Analytical Approach for the Determination of T2* in the Capillary Network of Myocardium. Magn. Reson. Med. **1999**, *41*, 51–62.
16. Niemi, P.; Poncelet, B.; Kwong, K.; Weisskoff, R.; Rosen, B.; Brady, T.; Kantor, H. Myocardial Intensity Changes Associated with Flow Stimulation in Blood Oxygenation Sensitive Magnetic Resonance Imaging. Magn. Reson. Med. **1996**, *36*, 78–82.
17. Judd, R; Lup-Olivieri, C.; Arai, M.; Kondo, T.; Croisille, P.; Lima, J.; Mohan, V.; Becker, L.; Zerhouni, E. Physiological Basis of Myocardial Contrast Enhancement in Fast Magnetic Resonance Images of 2-Day-Old Reperfused Canine Infarcts. Circulation **1995**, *92*, 1902–1910.
18. Kim, R.; Fieno, D.; Parrish, T.; Harris, K.; Chen, E.; Simonetti, O.; Bundy, J.; Finn, J.; Klocke, F.; Judd, R. Relationship of MRI Delayed Contrast Enhancement to Irreversible Injury, Infarct Age and Contractile Function. Circulation **1999**, *100*, 1992–2002.
19. Wu, K.C.; Zerhouni, E.A.; Judd, R.M.; Lugo Olivieri, C.H.; Barouch, L.A.; Schulman, S.P.; Blumenthal, R.S.; Lima, J.A. Prognostic Significance of Microvascular Obstruction by Magnetic Resonance Imaging in Patients with Acute Myocardial Infarction. Circulation **1998**, *97*, 765–72.
20. Kim, R.J.; Chen, E.L.; Lima, J.A.; Judd, R.M. Myocardial Gd-DTPA Kinetics Determine MRI Contrast Enhancement and Reflect the Extent and Severity of Myocardial Injury after Acute Reperfused Infarction. Circulation **1996**, *94*, 3318–26.
21. Rogers, W.J.; Kramer, C.M.; Geskin, G.; Hu, Y.-L.; Theobald, T.M.; Vido, D.A.; Petruolo, S.; Reichek, N. Early Contrast-Enhanced MRI Predicts Late Functional Recovery after Reperfused Myocardial Infarction. Circulation **1999**, *99*, 744–50.
22. Hundley, W.G.; Lange, R.A.; Clarke, G.D.; Meshack, B.M.; Payne, J.; Landau, C.; McColl, R.; Sayad, D.E.; Willett, D.L.; Willard, JE.; Hillis, L.D.; Peshock, R.M. Assessment of Coronary Arterial Flow and Flow Reserve in Humans with Magnetic Resonance Imaging. Circulation **1996**, *93*, 1502–1508.
23. Clarke, G.D.; Eckels, R.; Chaney, C.; Smith, D.; Dittrich, J.; Hundley, W.G.; NessAiver, M.; Li, H.F.; Parkey, R.W.; Peshock, R.M. Measurement of Absolute Epicardial Coronary Artery Flow and Flow Reserve with Breath-Hold Cine Phase-Contrast Magnetic Resonance Imaging. Circulation **1995**, *91*, 2627–34.
24. Davis, C.P.; Liu, P.F.; Hauser, M.; Gohde, S.C.; von Schulthess, G.K.; Debatin, J.F. Coronary Flow and Coronary Flow Reserve Measurements in Humans with Breath-Held Magnetic Resonance Phase Contrast Velocity Mapping. Magn. Reson. Med. **1997**, *37*, 537–44.
25. Hofman, M.B.; van Rossum, A.C.; Sprenger, M.; Westerhof, N. Assessment of Flow in the Right Human Coronary Artery by Magnetic Resonance Phase Contrast Velocity Measurement: Effects of Cardiac and Respiratory Motion. Magn. Reson. Med. **1996**, *35*, 521–31.
26. Nagel, E.; Bornstedt, A.; Hug, J.; Schnackenburg, B.; Wellnhofer, E.; Fleck, E. Non- Imaging: Comparison of Breath-Hold and Navigator Techniques with Intravascular Invasive Determination of Coronary Blood Flow Velocity with Magnetic Resonance Ultrasound. Magn. Reson. Med. **1999**, *41*, 544–49.
27. Pennell, D.J.; Firmin, D.N.; Burger, P.; Yang, G.Z.; Manzara, C.C.; Ell, P.J.; Swanton, R.H.; Walker, J.M.; Underwood, S.R.; Longmore, D.B. Assessment of Magnetic Resonance Velocity Mapping of Global Ventricular Function During Dobutamine Infusion in Coronary Artery Disease. Br. Heart J. **1995**, *74*, 163–70.
28. Kraitchman, D.L.; Wilke, N.; Hexeberg, E.; Jerosch Herold, M.; Wang, Y.; Parrish, T.B.; Chang, C.N.; Zhang, Y.; Bache, R.J.; Axel, L. Myocardial Perfusion and Function in Dogs with Moderate Coronary Stenosis. Magn. Reson. Med. **1996**, *35*, 771–80.
29. Bremerich, J.; Buser, P.; Bongartz, G.; Muller-Brand, J.; Gradel, C.; Pfisterer, M.; Steinbrich, W. Noninvasive Stress Testing of Myocardial Ischemia: Comparison of MRI Perfusion and Wall Motion Analysis to 99mtcmimi SPECT, Relation to Coronary Angiography. Eur. Radiol. **1997**, *7*, 990–95.
30. Sensky, P.; Jivan, A.; Hudson, N.; Keal, R.; Morgan, B.; Tranter, J.; de Bono, D.; Samani, N.; Cherryman, G. Coronary Artery Disease: Combined Stress MR Imaging Protocol: One-Stop Evaluation of Myocardial Perfusion and Function. Radiology **2000**, *215*, 608–614.
31. Neubauer, S.; Krahe, T.; Schindler, R.; Horn, M.; Hillenbrand, H.; Entzeroth, C.; Mader, H.; Kromer, E.P.; Rieg-

ger, G.A.; Lackner, K.; et al. ^{31}P Magnetic Resonance Spectroscopy in Dilated Cardiomyopathy and Coronary Artery Disease. Altered Cardiac High-Energy Phosphate Metabolism in Heart Failure. Circulation **1992**, *86*, 1810–18.

32. Bottomley, P. MR Spectroscopy of the Human Heart: The Status and the Challenges. Radiology **1994**, *191*, 593–612.
33. Clarke, K.; O'Connor, A.; Willis, R. Temporal Relation Between Energy Metabolism and Myocardial Function During Ischemia and Reperfusion. Am. J. Physiol. **1987**, *253*, H412–21.
34. Weiss, R.; Bottomley, P.; Hardy, C.; Gerstenblith, G. Regional Myocardial Metabolism of High-Energy Phosphates During Isometric Exercise in Patients with Coronary Artery Disease. N. Engl. J. Med. **1990**, *323*, 1593–1600.
35. Lamb, H.; Beyerbacht, H.; Doornbos, J.; van der Wall, E.; van der Laarse, A.; de Roos, A. Metabolic Response of Normal Human Myocardium to High-Dose Atropine-Dobutamine Stress Studied by 31P-MRS. Circulation **1997**, *96*, 2969–77.
36. Yabe, T.; Mitsunami, K.; Okada, M.; Morikawa, S.; Inubushi, T.; Kinoshita, M. Detection of Mycardial Ischemia by 31P Magnetic Resonance Sprectroscopy During Handgrip Exercise. Circulation **1994**, *89*, 1709–1716.
37. Buchthal, S.; den Hollander, J.; Merz, C.; Rogers, W.; Pepine, C.; Reichek, N.; Sharaf, B.; Reis, S.; Kelsey, S.; Pohost, G. Abnormal Myocardial Phosphorus-31 Nuclear Magnetic Resonance Spectroscopy in Women with Chest Pain but Normal Coronary Angiograms. N. Engl. J. Med. **2000**, *342*, 829–35.
38. Hetherington, H.; Luney, D.; Vaughan, J.; Pan, J.; Ponder, S.; Tschendel, O.; Twieg, D.; Pohost, G. 3D 31P Spectroscopic Imaging of the Human Heart at 4.1 T. Magn. Reson. Med. **1995**, *33*, 427–31.
39. Baer, F.M.; Voth, E.; Schneider, C.A.; Theissen, P.; Schicha, H.; Sechtem, U. Comparison of Low-Dose Dobutamine-Gradient-Echo Magnetic Resonance Imaging and Positron Emission Tomography with [18F]Fluorodeoxyglucose in Patients with Chronic Coronary Artery Disease. A Functional and Morphological Approach to the Detection of Residual Myocardial Viability. Circulation **1995**, *91*, 1006–1015.
40. Baer, F.M.; Voth, E.; LaRosee, K.; Schneider, C.A.; Theissen, P.; Deutsch, H.J.; Schicha, H.; Erdmann, E.; Sechtem, U. Comparison of Dobutamine Transesophageal Echocardiography and Dobutamine Magnetic Resonance Imaging for Detection of Residual Myocardial Viability. Am. J. Cardiol. **1996**, *78*, 415–19.
41. Baer, F.M.; Theissen, P.; Schneider, C.A.; Voth, E.; Sechtem, U.; Schicha, H.; Erdmann, E. Dobutamine Magnetic Resonance Imaging Predicts Contractile Recovery of Chronically Dysfunctional Myocardium after Successful Revascularization. J. Am. Coll. Cardiol. **1998**, *31*, 1040–48.
42. Geleijnse, M.L.; Fioretti, P.M.; Roelandt, J.R. Methodology, Feasibility, Safety and Diagnostic Accuracy of Dobutamine Stress Echocardiography. J. Am. Coll. Cardiol. **1997**, *30*, 595–606.
43. Bach, D.S.; Muller, D.W.; Gros, B.J.; Armstrong, W.F. False Positive Dobutamine Stress Echocardiograms: Characterization of Clinical, Echocardiographic and Angiographic Findings. J. Am. Coll. Cardiol. **1994**, *24*, 928–33.
44. Pennell, D.J.; Underwood, S.R.; Manzara, C.C.; Swanton, R.H.; Walker, J.M.; Ell, P.J.; Longmore, D.B. Magnetic Resonance Imaging During Dobutamine Stress in Coronary Artery Disease. Am. J. Cardiol. **1992**, *70*, 34–40.
45. Baer, F.M.; Voth, E.; Theissen, P.; Schicha, H.; Sechtem, U. Gradient-Echo Magnetic Resonance Imaging During Incremental Dobutamine Infusion for the Localization of Coronary Artery Stenoses. Eur. Heart J. **1994**, *15*, 218–25.
46. van Rugge, F.P.; van der Wall, E.E.; de Roos, A.; Bruschke, A.V. Dobutamine Stress Magnetic Resonance Imaging for Detection of Coronary Artery Disease. J. Am. Coll. Cardiol. **1993**, *22*, 431–39.
47. Nagel, E.; Lehmkuhl, H.B.; Bocksch, W.; Klein, C.; Vogel, U.; Frantz, E.; Ellmer, A.; Dreysse, S.; Fleck, E. Noninvasive Diagnosis of Ischemia-Induced Wall Motion Abnormalities with the Use of High-Dose Dobutamine Stress MRI: Comparison with Dobutamine Stress Echocardiography. Circulation **1999**, *99*, 763–70.
48. Nagel, E.; Lehmkuhl, H.B.; Klein, C.; Schneider, U.; Frantz, E.; Ellmer, A.; Bocksch, W.; Dreysse, S.; Fleck, E. Influence of Image Quality on the Diagnostic Accuracy of Dobutamine Stress Magnetic Resonance Imaging in Comparison with Dobutamine Stress Echocardiography for the Noninvasive Detection of Myocardial Ischemia. Z. Kardiol. **1999**, *88*, 622–30.
49. Hundley, W.; Hamilton, C.; Thomas, M.; Herrington, D.; Salido, T.; Kitzman, D.; Little, W.; Link, K. Utility of Fast Cine Magnetic Resonance Imaging and Display for the Detection of Myocardial Ischemia in Patients Not Well Suited for Second Harmonic Stress Echocardiography. Circulation **1999**, *100*, 1697–1702.
50. Diesbourg, L.; Prato, F.; Wisenberg, G.; Drost, D.; Marshall, T.; Carroll, S.; O'Neill, B. Quantification of Myocardial Blood Flow and Extracellular Volume Using a Bolus Injection of Gd-DPTA: Kinetic Modeling in Canine Ischemic Disease. Magn. Reson. Med. **1992**, *23*, 239–53.
51. Jerosch Herold, M.; Wilke, N. MR First Pass Imaging: Quantitative Assessment of Transmural Perfusion and Collateral Flow. Int. J. Card. Imaging **1997**, *13*, 205–218.
52. Wilke, N.; Simm, C.; Zhang, J.; Ellermann, J.; Ya, X.; Merkle, H.; Path, G.; Luckmann, H.; Bache, R.J.; Ugurbil, K. Contrast-Enhanced First Pass Myocardial Perfusion Imaging: Correlation between Myocardial Blood

Flow in Dogs at Rest and during Hyperemia. Magn. Reson. Med. 1993, *29*, 485–97.
53. Wilke, N.; Jerosch Herold, M.; Wand, Y.; Huang, Y.; Christensen, B.V.; Stillman A.E.; Ugurbil, K.; McDonald, K.; Wilson, R.F. Myocardial Perfusion Reserve: Assessment with Multisection, Quantitative, First-Pass MR Imaging. Radiology **1997**, *204*, 373–84.
54. Larsson, H.B.; Stubgaard, M.; Sondergaard, L.; Henriksen, O. In Vivo Quantification of the Unidirectional Influx Constant for Gd-DTPA Diffusion across the Myocardial Capillaries with MR Imaging. J. Magn. Reson. Imaging **1994**, *4*, 433–40.
55. Fritz-Hansen, T.; Rostrup, E.; Ring, P.; Larsson, H. Quantification Of Gadolinium-DPTA Concentrations for Different Inversion Times Using an IR-turbo Flash Pulse Sequence: A Study on Optimizing Multislice Perfusion Imaging. Magn. Reson. Imaging **1998**, *16*, 893–99.
56. Keijer, J.T.; van Rossum, A.C.; van Eenige, M.J.; Karreman, A.J.; Hofman, M.B.; Valk, J.; Visser, C.A. Semiquantitation of Regional Myocardial Blood Flow in Normal Human Subjects by First-Pass Magnetic Resonance Imaging. Am. Heart J. **1995**, *130*, 893–901.
57. Lauerma, K.; Virtanen, K.S.; Sipila, L.M.; Hekali, P.; Aronen, H.J. Multislice MRI in Assessment of Myocardial Perfusion in Patients with Single Vessel Proximal Left Anterior Descending Coronary Artery Disease before and after Revascularization. Circulation **1997**, *96*, 2859–67.
58. Klein, M.A.; Collier, B.D.; Hellman, R.S.; Bamrah, V.S. Detection of Chronic Coronary Artery Disease: Value of Pharmacologically Stressed, Dynamically Enhanced Turbo Fast Low Angle Shot MR Images. Am. J. Roentgenol. **1993**, *161*, 257–63.
59. Eichenberger, A.C.; Schuiki, E.; Kochli, V.D.; Amann, F.W.; McKinnon, G.C.; von Schulthess, G.K. Ischemic Heart Disease: Assessment with Gadolinium-Enhanced Ultrafast MR Imaging and Dipyridamole Stress. J. Magn. Reson. Imaging **1994**, *4*, 425–31.
60. Hartnell, G.; Cerel, A.; Kamalesh, M.; Finn, J.P.; Hill, T.; Cohen, M.; Tello, R.; Lewis, S. Detection of Myocardial Ischemia: Value of Combined Myocardial Perfusion and Cineangiographic MR Imaging. Am. J. Roentgenol. **1994**, *163*, 1061–67.
61. Al-Saadi, N.; Nagel, E.; Gross, M.; Bornstedt, A.; Schnackenburg, B.; Klein, C.; Klimek, W.; Oswald, H.; Fleck, E. Noninvasive Detection of Myocardial Ischemia from Perfusion Reserve Based on Cardiovascular Magnetic Resonance. Circulation **2000**, *101*, 1379–83.
62. Wolff, S.; Day, R.; Santiago, L.; et al. Assessment of First-Pass Myocardial Perfusion Imaging During Rest and Adenosine Stress: Comparison with Cardiac Catheterization. Proc. Int. Soc. Magn. Reson. Med. **1999**, *7*, 305.
63. Cullen, J.; Horshfield, M.; Reek, C.; Cherryman, G.; Barnett, D.; Samani, N. A Myocardial Perfusion Reserve Index in Humans Using First-Pass Contrast Enhanced Magnetic Resonance Imaging. J. Am. Coll. Cardiol. **1999**, *33*, 1386–94.
64. Penzkofer, H; Wintersperger, B.; Knex, A.; Weber, J.; Reiser, M. Assessment of Myocardial Perfusion Using First-Pass and Color Coded Parameter Maps: A Comparison to 99Tc SestaMIBI SPECT and Systolic Myocardial Wall Thickening Analysis. Magn. Reson. Imaging **1999**, *33*, 161–70.
65. Wilke, N.; M. J.-H.; Stillman, A.E.; Kroll, K.; Tsekos, N.; Merkle, H.; Parrish, T.; Hu, X.; Wang, Y.; Bassingthwaighte, J.; et al. Concepts of Myocardial Perfusion Imaging in Magnetic Resonance Imaging. Magn. Reson. Q. **1994**, *10*, 249–86.
66. Matheijssen, N.A; Louwerenburg, W.; van Rugge, F.P.; Arens, R.P.; Kauer, B.; de Roos, A.; van der Wall, E.E. Comparison Of Ultrafast Dipyridamole Magnetic Resonance Imaging with Dipyridamole SestaMIBI SPECT for Detection Of Perfusion Abnormalities in Patients with One Vessel Coronary Artery Disease: Assessment by Quantitative Model Fitting. Magn. Reson. Med. **1996**, *35*, 221–28.
67. Rina, I.L.; Balody, G.J.; Hanson, P.; Labovitz, A.J.; Madonna, D.W.; Myers, J. Guidelines for Clinical Exercise Testing Laboratories. Circulation **1995**, *91*, 912.
68. Nagel, E.; Al-Saadi, N.; Foerster, S.; Paetsch, I.; Schalla, S.; Klein, C.; Schneider, U.; Schnackenburg, B.; Bornstedt, A.; Lehmkuhl, H.; Fleck, E. Magnetic Resonance Mycoardial Perfusion Reserve for the Detection of Coronary Artery Disease: Experience in 139 Patients. J. Cardiovasc. Magn. Reson. **1999**, *1*, 328–29 (abstract).
69. Keijer, J.T.; van Rossum, A.C.; van Eenige, M.J.; Bax, J,J.; Visser, F.C.; Teule, J.J.; Visser, C.A. Magnetic Resonance Imaging of Regional Myocardial Perfusion in Patients with Single-Vessel Coronary Artery Disease: Quantitative Comparison with 201Thallium—SPECT and Coronary Angiography. J. Magn. Reson. Imaging **2000**, *11*, 607–615.
70. Larsson, H.; Fritz-Hansen, T.; Rostrup, E.; Sondergaard, L.; Ring, P.; Henrikson, O. Myocardial Perfusion Modeling Using MRI. Magn. Reson. Med. **1996**, *35*, 716–26.
71. Fischer, S.; Wickline, S.; Lorenz, C. Novel Real-Time R-Wave Detection Algorithm Based on the Vectorcardiogram for Accurate Gated Magnetic Resonance Acquisitions. Magn. Reson. Med. **1999**, *42*, 361–70.
72. Heyndrickx, C.; Baic, H.; Nelkins, P.; Leusen, K.; Fishbein, M.; Vatner, S. Depression of Regional Blood Flow and Wall Thickening after Brief Coronary Occlusion. Am. J. Physiol. **1978**, *234*, H653–60.
73. Picano, E. *Symptoms and Signs of Myocardial Ischemia*; Springer Verlag: Berlin, 1997.
74. Pennell, D.; Underwood, R.; Ell, P.; Swanton, R.; Walker, J.; Longmore, D. Dipyridamole Magnetic Resonance Imaging: a Comparison with Thallium-201 Emission Tomography. Br. Heart J. **1990**, *64*, 362–69.
75. Picano, E.; Marini, C.; Pirelli, S.; Maffei, S.; Bolognese, L.; Chiriatti, G.; Chiarella, F.; Orlandini, A.; Seveso, G.;

Coloso, M.; et al. Safety of Intravenous High-Dose Dipyridamole Echocardiography. The Echo-Persantine International Cooperative Study Group. Am. J. Cardiol. **1992**, *70*, 252–58.

76. Abreu, A.; Mahmarian, J.; Nishimura, S.; Boyce, T.; Verani, M. Tolerance and Safety of Pharmacologic Coronary Vasodilation with Adenosine in Association with Thallium-201 Scintigraphy in Patients with Suspected Coronary Artery Disease. J. Am. Coll. Cardiol. **1991**, *18*, 730–35.
77. Cerqueira, M.; Verani, M.; Schwaiger, M.; Heo, J.; Iskandrian, A. Safety Profile of Adenosine Stress Perfusion Imaging: Results from the Adenoscan Multicenter Trial Registry. J. Am. Coll. Cardiol. **1994**, *23*, 384–89.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016