Chapter 1

General introduction and outline
Ischemic heart disease remains the leading cause of morbidity and mortality in the Western world. Ischemic cardiomyopathy is a frequent cause of chronic heart failure and has become a major problem in clinical cardiology. Recent estimations show that 4.9 million patients in the United States have (chronic) heart failure, with 550,000 new patients diagnosed annually, resulting in 970,000 hospitalizations. Coronary artery disease (CAD) is the underlying cause of heart failure in >70% of patients; obstructive atherosclerosis of the coronary arteries may result in a regional reduction of blood flow to the myocardium. Thus, an imbalance between oxygen supply and demand arises, leading to the so-called ischemic cascade of CAD.

In recent years, magnetic resonance imaging (MRI) has been applied increasingly, in the evaluation of patients with CAD. A comprehensive cardiac MRI study including assessment of myocardial perfusion, myocardial function, both at rest and under stress, and delayed contrast-enhancement for myocardial viability imaging, and coronary magnetic resonance angiography for detecting stenosis can now be performed in a relatively short time. Therefore, MRI can be used to evaluate most aspects of the ischemic cascade. Moreover, MRI provides additional information for the surgeon needed to select the optimal surgical strategy, for instance including information on left and right ventricular function, the presence of aneurysms and ischemic mitral regurgitation.

Delayed contrast-enhanced MRI of myocardial infarction was first described more than 20 years ago and was defined as regions of increased signal intensity, in the infarcted region on T1-weighted images, acquired more than 5 minutes after the intravenous administration of a gadolinium based contrast agent. The mechanisms at cellular level underlying hyperenhancement have not been fully elucidated. It has been postulated that after an acute myocardial infarction, membranes of necrotic myocytes are ruptured, allowing gadolinium to diffuse into the intracellular space. Chronic infarcts however are characterized by a dense collagenous scar. It has been hypothesized that at a cellular level, interstitial space between collagen fibers may be significantly greater than the interstitial space between densely packed myocytes in normal myocardium. Hence, the gadolinium concentration in scar would be greater than in normal myocardium. Both mechanisms result in an increased concentration of gadolinium based contrast agents in the damaged tissue after (acute) infarction, resulting in increased signal intensity on delayed magnetic resonance images. It has been described that delayed contrast-enhanced MRI enables differentiation between reversible and irreversible myocardial damage and thus can be used to predict whether
regions of abnormal ventricular contraction will improve after revascularization in patients with CAD (assessment of viability)\(^6\). Furthermore, MRI has an excellent spatial resolution and is currently the only imaging modality that allows distinction between transmural and subendocardial ischemic injury. More recently, the prognostic significance of delayed contrast-enhanced MRI was described among patients with a clinical suspicion of CAD but without a history of myocardial infarction. It was concluded that delayed contrast-enhanced MRI could provide incremental prognostic value to major adverse cardiac events (cardiac death, acute myocardial infarction, etc.) beyond common clinical, angiographic, and functional predictors\(^7\).

The hallmark of viability is the improvement of contraction in dysfunctional myocardium that is elicited by the infusion of low dosages of dobutamine. MRI can be used to investigate the presence or absence of contractile reserve. Baer et al\(^8\) extensively explored this approach and demonstrated that dobutamine stress MRI can adequately predict improvement of regional left ventricular (LV) function after revascularization. It was shown that an increased systolic wall thickening >2 mm during dobutamine infusion was a reliable predictor of functional recovery after revascularization.

**Purpose and outline of this thesis**

The purpose of this thesis is to evaluate the value of various MRI techniques for the assessment myocardial viability in patients with acute and chronic myocardial infarction. In addition, we investigated and evaluated remodeling of the left or right ventricle in patients with chronic ischemic cardiomyopathy.

Chapter 2 contains a review that describes the value of MRI techniques for assessment of coronary arteries, the ischemic cascade, and myocardial infarction in CAD. Chapter 3 compares visual and quantitative analysis of infarct transmurality on delayed contrast-enhanced MRI. In addition, infarct transmurality was related to the severity of wall motion abnormalities at rest. Chapter 4 presents a head-to-head comparison between delayed contrast-enhanced MRI and low-dose dobutamine MRI in patients with ischemic LV dysfunction. Chapter 5 relates various MRI parameters (LV ejection fraction, volumes, transmurality and spatial extent of scar tissue, etc.) to the presence or absence of Q waves on the echocardiogram (ECG). Chapter 6 discusses various strategies using MRI (such as dobutamine stress, end-diastolic wall thickness and delayed contrast-enhancement) to provide information on myocardial
viability. In chapter 7, delayed contrast-enhanced MRI is evaluated for the assessment of right ventricular infarction in patients with acute inferior myocardial infarction. In chapter 8, the value of delayed contrast-enhanced MRI to predict LV dilatation after acute myocardial infarction is evaluated. Chapter 9 proposes a new MRI approach to predict β-blocker therapy effect on LV function. In chapter 10, the relationship between improved regional and global myocardial function in patients with ischemic cardiomyopathy in response to β-blocker therapy or revascularization is described. In chapter 11 the relationship between transmural posterolateral scar tissue and response to cardiac resynchronization therapy is evaluated.

References