ISMRM 2013 syllabus
Session: Myocardial Tissue Characterization
Talk: Research Promises: What Can We Expect in the Future ?

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Take home messages
Over the next years we can expect novel cardiac MRI technology that

- does not rely on the use of an exogenous contrast agent,
- provides quantitative readouts of myocardial tissue status,
- enables in vivo imaging of myocardial fiber remodeling,
- integrates multi-parametric information on heart anatomy, function and physiology,
- and is sufficiently fast for routine clinical use.

Cardiovascular diseases (CVDs) are the major cause of mortality globally, fueled by spreading of the western life-style into the developing countries [1]. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Particularly, ischemic heart disease has become the leading cause of death worldwide (7.3 million in 2008). The predominant cause of ischemic heart disease is the occlusion of a coronary artery in the cardiac microcirculation by either a stenotic atherosclerotic plaque or a thrombus formed after rupture of a vulnerable lesion. Also, non-ischemic heart diseases of the cardiac muscle, such as dilated, hypertrophic and restrictive cardiomyopathies, have a high mortality rate.

CVDs have in common that they cause changes in size, shape, structure and physiology of the myocardium and the heart as a whole, processes that commonly are collectively referred to as remodeling of the heart. The cardiomyocyte is the major cell involved in remodeling. Also fibroblasts, collagen, the extracellular matrix, the coronary vessels and the nervous system of the heart play a role. Adverse cardiac remodeling eventually may lead to a progressive inability of the heart to sustain blood circulation at levels that meet the body's needs.

There are gaps in our understanding of the importance of cardiac remodeling as a pathogenic mechanism, and cause and effect relations [2]. Critical to our understanding of this disorder are observations that the progression of this disease is related to progressive alterations in structure and function of the heart. With continued application of imaging techniques to study CVD, there has been increased understanding of the various patterns of cardiac remodeling and their relationship to underlying etiology and prognosis. Nevertheless, novel, more specific and quantitative imaging techniques are still needed.

Molecular MRI of the heart enables imaging of relevant processes in CVD, including apoptosis [3,4], necrosis [3], macrophage infiltration [5], enzyme activity [6], angiogenesis [7] and development of fibrosis [8]. Abundant targets, such as collagen in fibrotic myocardium, may be imaged with peptides linked to small Gd chelates. A number of studies in preclinical setting have demonstrated imaging of less abundant targets with nanoparticle-based technology [9]. It is expected that some of these molecular MRI technologies eventually will find their way in clinical research or practice, but concerns about safety on the use of nanotechnology in humans motivates the search for new contrast mechanisms in the heart that do not require the use of an exogenous agent.

Clinically, T1-weighted and T1-mapping cardiovascular MRI after injection of a Gd-chelate contrast agent can be used to detect and characterize myocardial fibrosis [10]. However, these measurements are based on an increased distribution volume and prolonged washout of the contrast agent in fibrotic tissue and therefore do not offer a direct window on fibrotic tissue components. Novel MR imaging techniques that provide a more direct measurement of fibrosis – preferably without the need for a contrast agent – are therefore relevant. Such techniques could improve risk stratification and aid in the evaluation of new treatment strategies aiming to reduce fibrosis. Recently, T2 was demonstrated to significantly correlate with the extent of diffuse fibrosis in a mouse model of diabetic cardiomyopathy [11]. T2* imaging was demonstrated to be significantly altered in chronic infarcts for which late gadolinium enhancement (LGE) was inconclusive [12]. Ex vivo ultra short echo time (UTE) imaging was employed to visualize the collagenous scar remaining after myocardial infarction in rats and mice [13]. Also, T1-rho imaging was used for infarct characterization without contrast agent administration [14].

Diffusion tensor imaging (DTI) of myocardial fiber architecture is rapidly emerging as a technique to characterize the myofiber architecture of the living heart [15]. In vivo application of the technique has long been problematic because of the challenge to separate the micrometer-scale diffusional motion of water molecules in the myocardium from bulk motion in the contracting heart and the respiration cycle. Recent improvements in hardware, sequence design and post-processing have made it possible to reproducibly study the myofiber architecture of the healthy and diseased heart in living subjects [16,17]. This technique may offer diagnostic utility of the differential diagnosis of adverse left ventricular remodeling and enable researchers to test hypotheses on structure-function relations of the mammalian heart [15].

Arrhythmia is one of the major concerns in heart failure and emerging cellular therapies. It can occur as a side effect of cell transplantation technique, or because of the absence of electrical coupling of transplanted cells with endogenous myocytes. Functional MRI techniques that determine local electrical tissue properties may become of great value to assess the presence of abnormal electrical activation and conductivity in the heart. Also the use of high fields MRI scanners (7T and higher) for cardiovascular imaging may result in unexpected and novel contrast mechanisms that may warrant further exploration.

It can be foreseen that novel imaging techniques will be combined with existing cardiac MRI protocols – such as LGE and perfusion measurements – for a full structural, function and physiological assessment of CVDs. For such multi-parametric assessment to be successful the speed and ease of acquisition need to be improved. Novel data acquisition and reconstruction strategies will be developed that increase the overall MR-efficacy, including retrospective imaging, parallel imaging using multiple receiver coils and in particular novel reconstruction algorithms for temporally undersampled data.

The distant future is generally difficult to predict, but with reasonable certainty no end in the developments and (clinical and research) applications of cardiovascular MRI to characterize the myocardium in health and disease can be expected in the near future.

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