Coronary Vessel Wall Imaging

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Introduction

Cardiovascular diseases remain the leading cause of morbidity and mortality in the western world and developing countries. Coronary artery disease causes the majority of events resulting in cardiovascular mortality and morbidity. In clinical practice, early identification and characterization of unstable atherosclerotic lesions that might cause these complications remains challenging. Evidence is mounting that a substantial part of ruptured plaques reside in vessels with less than 60% stenosis. A priori detection of vulnerable plaques is therefore an increasing clinical need, but requires new imaging techniques that provide information on plaque composition and biological processes associated with plaque progression and destabilization. Imaging methods, limited to the assessment of arterial luminal diameter, are still considered the reference standard for the diagnosis of clinically significant coronary and carotid artery disease and guidance of treatment. Severe atherosclerotic vessel wall changes can be missed on X-ray angiography, as positive remodeling can occur without visually apparent luminal narrowing. Atherosclerotic plaques with positive remodeling were shown to be associated with a higher risk of rupture.

In clinical practice, atherosclerotic plaque components in the carotid, aortic and coronary artery can be differentiated and characterized using unenhanced MR imaging techniques. Using clinically approved nonspecific contrast agents additional information on plaque composition can be gained. Targeted MR contrast agents, which enhance specific molecules or cells, allow visualization and characterization of pathological processes at a molecular level and thus may allow for early disease detection, guidance of treatment and monitoring of treatment response.
Vessel Wall Imaging of the Coronary Arteries

Technical Challenges

Coronary artery plaques are associated with the majority of cardiovascular events and complications. Unenhanced and contrast enhanced MRI of coronary vessels is technically more demanding compared to other arterial beds. Coronary arteries have a considerably smaller luminal area and are subject to substantial respiratory and cardiac motion. Several approaches have been proposed to correct for this movement. Initially, breath-hold techniques were used to compensate for respiratory motion. As breath-hold duration is usually limited to less than 20 seconds, and a considerable portion of the coronary artery tree needs to be imaged, the achievable spatial resolution is relatively low. Diaphragmatic drift may also occur during breathholds, resulting in additional motion artifacts, if these are not compensated for. To address these limitations, navigator echoes have been implemented that monitor respiratory motion and data acquisition during free breathing. In addition to gating, real-time motion correction can be performed in all three directions using navigator echoes by adjustment of the receiver frequency, phase and RF frequency offset to reduce remaining misregistration in the gating window. Recent improvements in navigator technology include ultrafast motion tracking, motion-adapted gating strategies, use of multiple navigators or use of image navigators. Due to the intrinsic motion of coronary arteries during the cardiac cycle, ECG synchronization of data acquisition is always required.

Unenhanced Vessel Wall Imaging

The clinical assessment of coronary artery disease using X-ray angiography is focused on the assessment of the severity of luminal narrowing. Early arterial changes can
lead to a compensatory enlargement of both the outer vessel wall and lumen (positive remodeling) and can be missed on X-ray angiography\textsuperscript{5,15}.

Several studies have shown that positive remodeling is associated with plaque vulnerability and rupture\textsuperscript{3,4}. Lipid-lowering treatment with atorvastatin was shown to reduce the progression of coronary atherosclerosis assessed by percentage change in atheroma volume\textsuperscript{16}. Coronary vessel wall size and remodeling therefore is an important marker for screening of subclinical disease in a large population.

Intravascular ultrasound, which is considered the reference standard for the assessment of the coronary wall, is limited by its invasive nature. Multidetector computed tomography, which has already been successfully used for the assessment of coronary remodeling does not allow direct visualization of the coronary vessel wall and is limited by the use of ionizing radiation and the administration of iodinated contrast agent, especially if frequent follow up investigations are needed\textsuperscript{17}.

T2 weighted black blood coronary vessel wall MRI was successful used for detection and quantification of increased coronary vessel wall thickness and positive remodeling in patients with coronary artery disease confirmed by x-ray angiography\textsuperscript{18-20}. High inter-study reproducibility has been shown for this method\textsuperscript{21}. As coronary vessel wall imaging does not require the use of ionizing radiation or the administration of iodinated contrast agents, it is especially appealing as a screening method in an asymptomatic patient population. In a pilot study, MR vessel wall imaging was able to assess an increase in coronary vessel wall thickness with preservation of lumen size in a patient population with subclinical coronary artery disease, consistent with positive remodeling\textsuperscript{20}. In a cross-sectional study in asymptomatic subjects with long-standing type 1 diabetes, MR vessel wall imaging revealed a significantly greater coronary plaque burden in patients with nephropathy.
compared with those with normoalbuminuria. In a recent study in a large asymptomatic multi ethnic population MR vessel wall imaging identified positive coronary remodeling in a significant number of individuals with no prior history of coronary artery disease. A different study confirmed the prevalence of coronary artery thickening in asymptomatic adults with no history of coronary artery disease. In this study, various subjects exhibited significant coronary stenosis in addition to positive coronary remodeling. These studies demonstrate the potential of coronary MR vessel wall imaging for early detection of atherosclerotic disease.

For coronary plaque characterization and intracoronary thrombus detection unenhanced T1-weighted coronary MR vessel wall imaging can be used. While hyperintense signal on unenhanced T1-weighted coronary vessel wall images was observed in the past, it has not been systemically evaluated until recently. In this study, hyperintense coronary plaques on unenhanced T1-weighted coronary vessel wall images were compared to measurements from MDCT, intravascular ultrasound and coronary flow by X-ray angiography. Hyperintense coronary plaques were shown to be associated with positive coronary remodeling, ultrasound attenuation, lower Hounsfield units, spotty calcification and transient slow flow after percutaneous coronary intervention. All these features have been associated with unstable plaques.

In a recent study, the feasibility of direct intracoronary thrombus imaging was demonstrated in patients with acute coronary syndrome using black blood unenhanced T1 weighted MRI. The paramagnetic effect of methemoglobin containing 5 unpaired electrons, which is present in acute thrombus, was used to visualize intracoronary thrombus. The detection of coronary thrombus could be achieved with a sensitivity of 91% and specificity of 88%.
Functional changes of the coronary artery have also been investigated by vessel wall MRI. Coronary endothelial function, represented by changes in cross-sectional coronary lumen area and blood flow, was investigated in healthy subjects and patients with coronary artery disease. During isometric handgrip exercise endothelial dependent coronary artery dilation and an increase in blood flow could be visualized and quantified noninvasively in healthy subjects. The absence of these coronary reactions was demonstrated in patients with coronary artery disease. These different unenhanced coronary vessel wall imaging techniques may improve risk stratification in patients with clinical or subclinical coronary artery disease and offer novel insights regarding the importance of local coronary endothelial function.

**Nonspecific Contrast Enhanced Vessel Wall Imaging**

Delayed contrast enhanced MRI represents an alternative imaging approach for coronary vessel wall imaging. This technique allows the direct assessment of contrast agent uptake in the coronary vessel wall. Nonspecific extracellular contrast agents used in clinical practice rapidly extravasate into the vessel wall and are thought to enhance areas with either increased distribution volume, delayed clearance or increased neovascularization. Areas of delayed contrast enhancement were shown to correlate with the severity of atherosclerosis in comparison to multislice computed tomography and quantitative coronary angiography. In patients with giant cell arteritis and Takayasu’s arteritis, transient contrast uptake was measured, potentially linking this pattern to acute inflammation and edema formation. A similar pattern of atherosclerotic plaque enhancement was observed in patients after acute myocardial infarction. It was shown that coronary vessel wall contrast uptake is significantly increased early after myocardial infarction as compared to 3 months.
follow-up scans \(^3\). The decrease in contrast agent uptake was most likely associated with a regression of inflammation. These studies demonstrate that both plaque composition (e.g. fibrous vs. atheromatous) \(^2\) and inflammation \(^3,4\) may be associated with the retention of extracellular contrast agents.

As only limited data are available on unenhanced and contrast enhanced coronary vessel wall MRI, further prospective studies are needed to investigate the clinical role of these techniques for the better diagnosis and characterization of coronary artery disease.
Conclusion

MR vessel wall imaging has progressed substantially in the past decade and considerable technical improvements have been made that allow for reliable visualization and characterization of the aortic and carotid vessel wall. Small single center pilot studies have demonstrated the feasibility of coronary MR vessel wall imaging. These studies demonstrated the potential of this technique for the non-invasive quantification of coronary plaque burden and positive arterial remodeling, which could lead to improved risk stratification in patients with coronary artery disease. With further developments in MR imaging techniques and contrast agents, this technique has potential to be increasingly useful for the non-invasive assessment of atherosclerosis and for monitoring response to treatment in clinical practice.
References


