Background

The current gold standard for the diagnosis of coronary artery disease is x-ray coronary angiography. Approximately 1 million cardiac catheterizations are performed each year in the western world. However, x-ray coronary angiography is expensive, invasive, and requires exposure of the patients to ionizing radiation. Moreover, there is a small but finite risk of serious complications to the patient and of operator exposure to radiation. Thus, there exists a strong need for a more cost-effective, non-invasive, and more patient friendly imaging modality. Coronary magnetic resonance angiography (MRA) overcomes a lot of the problems associated with x-ray angiography and has shown great potential for the diagnosis of coronary artery disease (CAD). In addition to being non-invasive, cost effective and patient friendly, it can survey in any image plane and has the ability to achieve high spatial resolution with no exposure to potentially harmful ionizing radiation.

The utility of coronary MRA has been investigated since the late 1980s [1, 2]. Although no coronary stenoses were identified in these early studies, the potential of MR imaging to assess the anatomy of the coronary vessels was demonstrated, and triggered further interest in this field. Simultaneously, it was suggested that coronary artery lumen narrowing is preceded by atherosclerosis and positive arterial remodeling of the vessel wall [3]. Hence, basic and clinical research findings have challenged the notion of flow limiting stenoses and studies have tried to focus away from the vessel lumen and towards the vessel wall. However, using x-ray angiography, the coronary artery vessel wall and hence, the remodeling cannot be visualized. This is where MRI, with its ability to differentiate between coronary lumen and the coronary artery vessel wall, offers great potential.

However, for successful coronary MRA and coronary vessel wall data acquisition, a series of major obstacles has to be overcome. The heart is subject to both intrinsic and extrinsic motion due to its natural periodic contraction and breathing. Both of these motion components exceed the dimensions of the coronary artery, resulting in the need for efficient motion suppression strategies if satisfactory acquisition of coronary MR data is to be achieved in the sub-millimeter range.

Enhanced contrast between the coronary lumen and the surrounding tissue is crucial for successful visualization of both the coronary lumen and the coronary vessel wall. In this chapter, we will discuss the hurdles that need to be overcome in order to acquire adequate coronary images using MRI, the technical details and clinical implications of coronary MRA and the approaches to coronary vessel wall imaging.

Technical Challenges associated with Coronary MRA

Motion Suppression in Coronary MRA

Cardiac Motion

Cardiac Motion, a major obstacle for obtaining adequate coronary MRA images, can be divided into two types: motion related to intrinsic cardiac contraction/relaxation and motion due to superimposed diaphragmatic and chest wall movement during respiration. Since the extent of each motion supercedes the diameter of the coronary artery, blurring artifacts of the coronary lumen occur unless adequate motion suppression techniques are used. To account for intrinsic cardiac motion, ECG gating is absolutely essential. However, considerable ECG signal degradation occurs because of radiofrequency field and gradient-switching noise. To overcome this, a vector ECG approach has been
found to be very robust for R-wave detection as compared to alternate gating strategies such as peripheral pulse detection. However, under the influence of a strong static magnetic field, the so called magnetohydrodynamic effect is enhanced and an artificial voltage overlaid to the T-wave of the ECG results. This artificial augmentation of the T-wave may frequently mislead the R-wave detection algorithm so that triggering is performed on the T-wave instead of the R-wave. This results in serious artifacts on coronary MRA and coronary vessel wall images. Since this artifact increases with field strength, this presents a major challenge for MRA, particularly at higher field strengths such as 3 Tesla. However, by analyzing the ECG vector in 3D space [4], the true T-wave can be separated from the artifactual T-wave augmentation. Moreover, reliable R-wave detection has recently been shown to be feasible even at higher field strength [5].

Another issue lies with actual coronary artery motion which occurs in a triphasic pattern during the cardiac cycle. Hence, mid-diastolic diastasis has been identified as the preferred time for image acquisition as it also coincides with the interval of rapid coronary filling. This period is inversely related to the heart rate and can be determined using a heart rate dependent formula. However, because of considerable interpatient variation, a recommendation is to determine a patient specific diastasis period which can be achieved by acquiring a cine image perpendicular to the long axis of the proximal/mid right coronary artery (RCA).

Respiratory Motion

The second major impediment to coronary MRA is respiratory motion. Early approaches to suppressing respiratory motion involved the use of breath-hold techniques. Two-dimensional (2D) breath-hold coronary MRA relied on acquiring contiguous images, with the goal of surveying the proximal segments of the coronary arteries during serial breath-holds. More recently, three-dimensional (3D) breath-hold techniques for coronary MRA have also been implemented [6-10]. Breath-hold approaches offer the advantage of rapid imaging and are technically easy to implement in compliant subjects. For coronary MRA techniques that utilize the first-pass enhancement of intravenously injected extracellular contrast agents, breath-holding is a requirement at the present time. However, breath-holding strategies have several limitations. Some patients may have difficulty sustaining adequate breath-holds, particularly when the duration exceeds a few seconds. Additionally, it has been shown that during a sustained breath-hold there is cranial diaphragmatic drift [11], which may be substantial in many cases (~1cm). Among serial breath-holds, the diaphragmatic and cardiac positions frequently vary by up to 1 cm, resulting in registration errors [6,12]. Misregistration results in apparent gaps between the segments of the visualized coronary arteries, which could be misinterpreted as signal voids from coronary stenoses. Finally, the use of signal enhancement techniques, such as signal averaging or fold-over suppression is significantly restricted by the duration of the applicable breath-hold duration. Using breath-holding techniques, the spatial resolution of the images is also governed by the patient’s ability to hold his/her breath. Thus, while breath-hold strategies are often successful with motivated volunteers, their applicability to the broad range of patients with cardiovascular disease is more limited.

To overcome limitations associated with breath-holding, different methods such as MR navigators [13] have been developed to allow for free-breathing coronary MRA. With vertical positioning of the navigator at the dome of the right hemidiaphragm (lung-liver interface), the diaphragmatic cranio-caudal displacement can be monitored. These data can be used to gate coronary MRA acquisitions. The gating process can be either prospective (i.e. before data acquisition) or retrospective (i.e. following data acquisition, but before image reconstruction). Although navigator approaches greatly improve patient comfort and do not require significant subject motivation, their use prolongs the scan duration since coronary MRA data are collected during 50% of the RR intervals on average [14]. To overcome problems associated with narrow gating windows and prolonged scans, coronary MRA with prospective navigator correction has been implemented and has been shown to maintain or improve image quality both for 2D and 3D approaches to coronary MRA [15-17], while scanning time can be shortened. However, it is of utmost importance that the navigator is positioned in close temporal proximity to the imaging part of the sequence [18]. Typical examination times with free-breathing 3D real-time navigator approaches are ~7min.

Currently, inversion-recovery techniques seem to be emerging as the method of choice for contrast-enhanced coronary MRA [19-22]. However, the inversion-pre-pulse precedes the navigator thereby reducing the magnetization at the location of the navigator, which may adversely affect navigator performance. Therefore, countermeasures have been proposed [23] and successfully applied [22].

Spatial Resolution

Even though great progress has been made with regard to motion suppression, MRI hardware, soft-
Coronary Magnetic Resonance Angiography

Contrast-Enhancement in Coronary MRA

Using MRI, the contrast between the coronary blood-pool and the surrounding tissue can be manipulated using the in-flow effect [29] or by the application of MR pre-pulses. Non-exogenous contrast enhancement between the coronary arteries and the surrounding tissue has been obtained by the use of fat-saturation pre-pulses [29], magnetization transfer contrast pre-pulses (MTC) [30] or more recently T2 preparatory pulses (T2Prep) [31, 32] which take advantage of natural T2 differences between blood and the surrounding myocardium. With these techniques, the coronary lumen appears bright while the surrounding myocardium appears with reduced signal intensity. An alternative to bright-blood visualization of the coronary arteries is black-blood coronary MRA, in which the coronary lumen appears signal attenuated while the surrounding tissue displays with high signal intensity [33].

With the use of MR contrast agents, the T1 relaxation of blood can be shortened, allowing for increased contrast-to-noise ratio (CNR) for coronary MRA [19, 21]. The contrast agents currently available for coronary MRA are the traditional extracellular gadolinium-based contrast agents. However, because extracellular agents quickly extravasate into the extravascular space, their use requires rapid first-pass imaging, thereby necessitating breath-holding [8]. First-pass coronary MRA with extravascular contrast agents is also limited by the need for repeated contrast injections when more than one slab is imaged. With each subsequent injection, the CNR will be lower, as the signal from the extracellular space continuously increases following initial contrast administration.

An attempt to overcome the inherent limitations of extracellular contrast agents has seen the development of newer intravascular agents (the so-called blood-pool agents) based either on gadolinium (e.g. B22956 and MS-325) or iron oxide (e.g. AMI 227 and NC100150) [19-21, 34, 35]. The use of intravascular agents has the advantage of allowing image acquisition over longer time periods after intravenous administration of the contrast agent. Thus, non-breath-hold schemes can be employed, and repeated scans have similar CNR values thereby obviating the need for repeated injections [21]. Figure 1 displays a left coronary arterial system with high contrast acquired with B-22956 (Bracco Imaging S.p.A., Milan, Italy) and a previously described free-breathing navigator-gated and corrected 3D inversion technique [21]. Using this specific intravascular contrast agent, a substantial (50%) enhancement of the SNR was accompanied by a 160% improvement in CNR when compared to a standard non-contrast enhanced technique [22, 36]. Simultaneously, a 20% improvement in vessel sharpness suggested superior vessel

![Fig. 1. Left (a) and right (b) coronary arterial systems acquired with the intravascular contrast agent B-22956 (Bracco Imaging S.p.A., Milan, Italy) and a free-breathing navigator gated and corrected 3D inversion technique [21]. The images were acquired as part of an international collaboration: IBT ETH Zurich, Switzerland, German Heart Center, Berlin, Germany, Bracco Imaging SpA, Italy, Beth Israel Deaconess Medical Center, MA, USA, Philips Medical Systems, Best, The Netherlands](image-url)
delineation post contrast [22]. These findings are visually supported by the images displayed in Fig. 1. Similar results were found in a parallel volunteer study using the contrast agent SH L 643A (Schering, Berlin, Germany) [37].

Identification of Coronary Stenosis

Although current breath-hold coronary MRA techniques have relatively limited in-plane spatial resolution, the technique has proven adequate for the identification of proximal coronary stenoses in several clinical series. Gradient-echo techniques depict focal stenoses as signal voids. In one of the earliest patient studies comparing coronary MRA prospectively with x-ray coronary angiography [38], a segmented k-space 2D breath-hold ECG-gated gradient-echo sequence was used. Overall sensitivity and specificity values of the 2D coronary MRA technique for correctly ascertaining whether individual vessels had or did not have significant CAD (50% diameter on conventional contrast angiography) were 90% and 92%, respectively. Subsequent studies [39-43] have reported variable sensitivity and specificity values for the detection of significant CAD. Explanations for this variability in these single center studies include differences in the utilized MR sequences, inadequate patient cooperation with regards to breath-holding, and irregular rhythms, all of which contribute to image degradation. Newer breath-hold [10] and non-breath-hold approaches to 3D coronary MRA have also demonstrated the ability of this technique to detect coronary stenoses. The first international multicenter trial prospectively comparing coronary MRA and the gold standard x-ray coronary angiography using common methodology and identical hardware and software has recently been completed [36]. The major finding of the study was that free-breathing sub-millimeter 3D coronary MRA is able to accurately identify significant proximal and mid coronary disease, while non-significant coronary disease can be excluded with high confidence (Fig. 2). Drawbacks that need to be resolved include a relatively low specificity (false positive readings) while the potential for accurate quantitative grading of stenosis has still to be investigated.

Recent Technical Developments

Spiral Coronary MRA

Although early attempts to acquire coronary MRA data in the sub-millimeter range resulted in 2D spiral acquisitions with outstanding image quality [44], this technique has not been widely employed. An advantage of spiral techniques is that efficient sampling of k-space can be performed with high SNR while minimizing adverse effects due to flow artifacts. An extension of spiral coronary MRA using a 3D acquisition strategy [45, 46], an interleaved segmented approach [46], and real-time navigator technology for free-breathing coronary MRA data acquisition has proven to be a very valuable alternative for high-resolution coronary MRA [47]. An image of a left coronary arterial system acquired with a dual-interleaved free-breathing 3D spiral technique is shown in Figure 3.

Steady-state with free-precession Coronary MRA

With this sequence, high SNR and very high contrast between the ventricular blood-pool and the myocardium can be obtained without the need for exogenous contrast enhancement. The application of SSFP is therefore highly promising for contrast enhancement in 3D coronary MRA, in which the in-flow effect is generally reduced due to relatively thick slab excitations [48]. Presently, more and more cardiac MRI centers are adopting SSFP sequences either in conjunction with a single breath-hold [48] or based on free-breathing with navigators [49]. A first evaluation in an animal model demonstrated that SSFP imaging permits high quality coronary MRA during free breathing with substantial improvements in SNR, CNR and vessel sharpness when compared with standard T2-prepared gradient-echo imaging [49]. Although spiral imaging achieved the highest SNR, SSFP imaging was considered better for image quality and vessel definition. In a small volunteer study to evaluate theoretical considerations concerning the T1-lowering characteristics of contrast agents [50], consistent fat suppression and a 78% increase in blood-myocardial CNR was found post contrast using SSFP.

Black-blood Coronary MRA

Artifacts originating from metallic implants such as clips or sternal wires are accentuated on gradient echo based bright blood coronary MRA. Furthermore, thrombus, vessel wall and various plaque components may appear with high signal intensity on bright blood coronary MRA [51]. As a result, luminal stenosis may be obscured on bright blood images. To overcome this potential drawback, ‘black-blood’ fast spin-echo coronary MRA techniques have recently been introduced [23, 33]. With these techniques, the coronary lumen appears signal attenuated while the signal of surrounding tissue including epicardial fat and my-
Fig. 2a-h. Left (a, c, e, g) and right (b, d, f, h) coronary arterial systems acquired in the first international multicenter trial prospectively comparing x-ray coronary angiography and coronary MRA [32]. The image data were acquired in patients referred to x-ray angiography using a T2-Prep [19] 3D navigator-gated and corrected free-breathing coronary MRA technique [12].

Fig. 3. 3D spiral image of a left coronary arterial system. The image was acquired with real-time navigator technology using a dual-interleaved spiral imaging technique.
occardium appears enhanced. Initial results obtained in patients suggest that artifacts originating from metallic implants can be minimized. However, a principal disadvantage of dual-inversion black-blood coronary MRA is that calcifications appear signal attenuated resulting in the possibility for misinterpretation of calcified stenosis. On the other hand, black-blood coronary MRA has proven very useful for the visualization of the vessel wall as discussed below.

**Parallel Imaging for Coronary MRA**

An alternative method to compensate for respiratory motion, and thus to allow for free-breathing coronary MR imaging, would be to decrease the acquisition time so that the entire data set is obtained in one cardiac cycle. The development of such rapid strategies is an active field of research in cardiac MRI [52, 53]. Early introductions to parallel imaging for coronary MRA include techniques termed 'SMASH' and 'SENSE'. These parallel imaging approaches are able to reduce the scanning time for cardiac MRI substantially [54] and therefore have great potential. However, a principal trade-off for reduced acquisition time is a reduced SNR and this has to be evaluated carefully for each individual application. On the other hand, magnets with higher field strengths may overcome some of these limitations while maintaining a suitably short acquisition time.

**High Field (3T) Coronary MRA**

Currently, the vast majority of research into coronary MRA as well as most technical innovations and clinical applications are performed on 1.5T systems. For many of these applications, limited SNR or lengthy examination times are impediments. The recent availability of high field systems (3T) equipped with dedicated cardiac hardware (real-time spectrometer, parallel receiver technology with high bandwidth, body RF send coil, vector ECG, etc.) and software (SENSE, navigators, interactive interface, SSFP) will permit a major step forward for coronary MRA. Preliminary in vivo findings obtained in two healthy adult subjects evaluated on a commercial 3T system (Philips Medical Systems, Best, NL) are displayed in Figure 4. The images were acquired using an ECG trig-

![Fig. 4. Preliminary in vivo coronary MRA image acquired at 3T. The 3D image data were obtained during free breathing with a T2-Prep and 2D selective real-time navigator technique. The image of the right coronary system (a) was acquired with a 6-element cardiac phased-array surface coil while the image of the left coronary system (b) was acquired using a body coil](image)

![Fig. 5. Arterial spin labeling enables an exclusive and selective 3D visualization of the coronary arterial lumen [42]. The left coronary system (a, b, c) is displayed at 3 incremental viewing angles about the left-right axis of the examined healthy adult subject. Signal from the surrounding tissue (chest wall, atria, great cardiac vessels, coronary veins etc.) is entirely suppressed](image)
Coronary Vessel Wall Imaging

Coronary Artery Disease and Atherosclerosis

Despite advances in both treatment and prevention, complications of atherosclerotic disease remain the leading cause of morbidity and mortality in the Western World [56]. More than 50% of atherosclerotic deaths can be attributed to coronary heart disease with estimated socioeconomic costs of $112 billion in the year 2002 in the United States alone. While atherosclerosis may progress slowly over years or decades, the occurrence of thrombosis as a consequence of sudden plaque rupture often leads to abrupt life threatening complications. Such acute events may explain why many people who die from coronary artery disease die suddenly without manifestation of typical symptoms. As reported by Glagov et al [3], the initial response to endothelial injury and initial development of atherosclerosis is outward remodeling of the artery, with relative preservation of lumen diameter. Such findings have been confirmed in living patients with invasive [57] and non-invasive techniques [58, 59]. Over 50% of all future myocardial infarctions occur in vascular regions with atherosclerotic thickening but non-critical luminal narrowing [60, 61]. This was confirmed in a prospective study of 4476 elderly subjects for whom carotid wall thickness, assessed non-invasively by high-resolution B-mode ultrasound, was a stronger predictor of future stroke and myocardial infarction than were conventional coronary atherosclerotic risk factors [62]. The inference was that carotid wall thickening was a marker for diffuse atherosclerosis and thus correlated or predicted concomitant disease in the coronaries. The prognostic value of coronary wall thickness for predicting future events is probably very high. However, this has not yet been demonstrated because ultrasound evaluation of coronary wall thickness can only be performed invasively (intravascular ultrasound) and such studies are precluded in large, prospective, long-term endpoint trials. However, coronary wall disease, indexed by coronary calcium, can be detected by rapid computed tomography (CT) and this approach has also been useful in predicting future cardiac events [63, 64]. The approach, however, does not directly measure wall thickness and cannot identify or characterize common, non-calcified atherosclerotic plaques. Conventional x-ray angiography is the current gold standard for the detection and treatment of intra-luminal (flow-limiting) coronary artery stenosis, but x-ray “luminography” provides minimal information on the magnitude of underlying atherosclerotic plaque burden. For these reasons, a non-invasive technique capable of measuring coronary wall thickness has great potential not only for the identification of disease at an early stage, but also for the prediction of future events and the evaluation of therapeutic strategies.

Identification of Plaque Components in the Vessel Wall by MRI

Findings from in vitro studies demonstrated the ability of MRI to identify various plaque components [65, 66] and T2-weighted sequences have shown promise for the differentiation of plaque components [65, 67]. Serfaty et al. [68] used T2-weighted MR imaging to measure fibrous cap thickness and lipid core volume. Unfortunately, their ex vivo study was limited by overestimation of the lipid core. Shinnar et al. [66] suggested the use of two echo times to differentiate the lipid core from fibrocellular areas that contain lipid. However, one limitation of T2-weighted MR imaging is an inherently low SNR. In vivo application of these techniques is supported by the strong agreement demonstrated between in vivo and ex vivo measurements of vessel wall thickness and T2 relaxation of plaque components [69, 70]. Wasserman et al. [71] used gadolinium (Gd) in combination with T1-weighted MRI to describe plaque morphology and demonstrated not only that delayed hyperenhancement preferentially occurs in fibrocellular tissue, but also that SNR is substantially enhanced.
compared to T2-weighted imaging. Similar results were reported by Yuan et al. [72] who showed that the strongest MRI signal enhancement was observed in fibrocellular tissue and that only modest contrast agent uptake occurred in the lipid core of the carotid vessel wall. A study by Jaffer et al. [73], which included participants who were free of clinically apparent coronary disease, revealed evidence of aortic atherosclerosis in 38% of the women and 41% of the men. Atherosclerotic prevalence was more apparent in the abdominal than in the thoracic aorta. These data demonstrate the ability of MR vessel wall imaging to detect subclinical atherosclerotic disease, and to better risk stratify patients with asymptomatic heart disease. However, it should be noted that all these studies were performed under ex vivo conditions, in animal models, or in the carotids or aorta as a surrogate for in vivo human coronary arteries, and that a clear correlation between carotid/aortic plaque and coronary events has not been established [73, 74]. Together with the current understanding that luminal disease underestimates plaque burden and that the majority of acute coronary syndromes occur at sites without previously flow-limiting stenoses (<50%) [60, 75], this demonstrates a clear need for an imaging method that allows direct and non-invasive access to the coronary or bypass graft vessel wall. However, coronary vessel lumen, and, especially wall imaging, are among the most challenging tasks for cardiovascular MRI. There are specific technical difficulties that have hampered the transfer of carotid or aortic plaque imaging approaches to the coronary vessel wall. These include the small dimensions (0.5–2mm) of the coronary vessel wall, a very complex geometry, cardiac and respiratory motion, and the proximity of the coronary artery walls to epicardial fat and coronary blood. As discussed above, recent advances in MRI hardware and new imaging software have made it possible to visualize the native coronary artery vessel wall in selected cases [58, 59, 76]. However, limited spatial resolution still hampers further progress and limits the accuracy and sensitivity of quantitative measurements [77]. A major step forward is expected with the availability of higher spatial resolution on 3T MRI systems and by simultaneously taking advantage of vessel wall hyperenhancement after contrast injection.

**Measurement of Plaque Regression after Pharmacological Intervention using MRI**

Non-invasive MRI has been shown to allow serial monitoring of atherosclerotic plaque size changes in the carotids after lipid-lowering pharmacological interventions [78]. Studies by Corti et al. [79, 80], revealed significant regression of established atherosclerotic carotid and aortic lesions in humans. These studies were performed at baseline and at 6 and 12 months after lipid-lowering therapy. The effects of the treatment on atherosclerotic lesions were measured as changes in lumen area, vessel wall thickness, and vessel wall area, a surrogate for atherosclerotic burden. At 6 months after pharmacological intervention, no changes in lumen area, vessel wall thickness, or vessel wall area were observed. However, at 12 months, significant reductions in vessel wall thickness and vessel wall area, without changes in lumen area, were observed in both aortic and carotid arteries. Unfortunately, the spatial resolution was still not optimal for coronary vessel wall imaging in these studies. In addition to improving spatial resolution, greater sensitivity for the measurement of progression and regression of wall thickness is needed. For this, direct imaging access to the coronary vessel wall is the goal.

**Coronary Vessel Wall Imaging using MRI**

Imaging of the coronary artery vessel wall is probably the most challenging task in cardiac MRI because of the small dimension and constant motion of the coronary arteries. Simultaneously, the need for high contrast between the coronary lumen blood pool and the surrounding coronary vessel wall is mandatory. However, this is very similar to the challenges faced by coronary MRA in general.

The first successful implementation of coronary vessel wall imaging in humans involved the use of a dual-inversion fast spin echo sequence. Using this method, single slices of the coronary artery wall could be acquired during a prolonged breath-hold period, permitting the demonstration of relative wall thickening in selected cases [59]. Subsequently, and to overcome the limitations associated with breath-holding, this technique was adapted for use with navigators for free-breathing data acquisition [76]. More recently, the free-breathing navigator approach has been combined with 3D spiral imaging in conjunction with a ‘local inversion’ technique [81]. Using this method, excellent image quality can be obtained because of the high SNR associated with 3D imaging on the one hand and the signal-efficient spiral read-out on the other. This enables larger anatomical coverage with much thinner reconstructed slices than those of the earlier 2D approaches. Therefore, it is now possible to visualize long, contiguous sections of the coronary artery vessel wall as shown in Fig. 6. Additionally, the spiral approach permits data
acquisition within a short acquisition window of only 50 ms, permitting the effects of intrinsic myocardial motion to be suppressed more effectively while at the same time rendering the technique less susceptible to R-R variability. A disadvantage of the technique is a prolonged scanning time of ~12 min during free breathing with image acquisition during alternate R-R intervals. Preliminary evaluation of this local-inversion 3D spiral technique has been performed in 12 adult subjects comprising 6 clinically healthy subjects and 6 patients with non-significant coronary artery disease (10% to 50% diameter reduction on x-ray angiography). Examinations were performed on a commercial 1.5 Tesla scanner with free-breathing 3D coronary vessel wall imaging performed along the major axis of the right coronary artery with isotropic spatial resolution (1.0x1.0x1.0 mm³). The proximal vessel wall thickness and luminal diameter were objectively determined with an automated algorithm [32]. The 3D vessel wall scans allowed for visualization of the contiguous proximal right coronary artery in all subjects. The mean vessel wall thickness (1.7 ± 0.3 versus 1.0 ± 0.2 mm) was significantly increased in the patients compared with the healthy subjects (p<0.01). However, the lumen diameter measurement (3.6 ± 0.7 versus 3.4 ± 0.5 mm, p=0.47) was similar in both groups. The findings suggest that free-breathing 3D black-blood coronary MRI may serve as an appropriate non-invasive technique for the identification of increased coronary vessel wall thickness with preservation of lumen size in patients with non-significant coronary artery disease, consistent with “Glagov-type” outward arterial remodeling [3]. This novel approach may have the potential to quantify sub-clinical disease. Future developments will include the use of higher magnetic field strengths, contrast agents for plaque characterization [71, 72], and studies of vessel wall thickness following intervention [82].

Practical Recommendations

Because of the small dimensions and tortuosity of the coronary arteries, high-resolution imaging and sufficient volumetric coverage are essential. However, the need for high resolution and larger volumes results in dramatically lengthened scanning times of contemporary MRI techniques from a few seconds to a few minutes. Unfortunately, imaging of the heart is not practical on this timescale because of breathing and intrinsic myocardial motion. Therefore, ECG triggering, k-space segmentation, short acquisition intervals (Tacq <100ms), and imaging during quiescent periods in the cardiac cycle (typically in late diastole) are recommended, while respiratory artifacts must be suppressed by means of breath-holding or navigator technology. While k-space segmentation, abbreviated acquisition windows, and the use of navigators effectively suppress motion artifacts, a substantial increase in scanning time is inevitable (3-15 min). Breath-holding is an effective method to reduce scanning time, but compromises relating to the acquisition intervals (Tacq >120ms) and spatial resolution have to be made to accommodate practical breath-hold durations of <20 s. As is the case for CTA, improved coronary MRA image quality is achieved at lower heart rates while data collection during arrhythmias must be avoided.

At the present time, clinical multi-center experience only exists for free-breathing navigator approaches. Below are some practical recommendations for performing free-breathing navigator-gated and corrected coronary MRA at 1.5T. For coronary MRA with intravascular contrast agents, the T2-Prep sequence can simply be exchanged for an inversion pulse and a carefully adjusted inversion delay [22]. Parts of the protocols were provided by Marc Kouwenhoven from Philips Medical Systems. For breath-holding, black-blood imaging (coronary vessel wall imaging), and arterial spin label-
Table 1. Scout 3. Free-breathing navigator gated and corrected 3D SSFP

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Table 2. Targeted coronary MRA. High-resolution free-breathing navigator gated and corrected 3D SSFP

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<td>mm³</td>
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Scout Scanning

For localization of the coronary arteries and for identification of the period of minimal myocardial motion, 3 scout scans are recommended:

**Scout 1:** A low resolution 2D SSFP scan that covers the chest in 3 orthogonal views (coronal, sagittal, transverse). Multiple (10) 1 cm thick slices per view. The scan is performed during free-breathing.

**Scout 2:** On a mid-ventricular level (as identified on the first scout), a transverse 2D SSFP cine scan with 40 frames/s is acquired for the visual identification of the diastolic rest period. This scan can either be performed during free-breathing using signal averaging (total duration ~40 sec) or during one breath-hold of ~10 sec.

**Scout 3:** Transverse 3D SSFP scout scan for localization of the coronary arteries. Image acquisition is performed in late diastole, at the time-point of minimal myocardial motion as identified in Scout 2. The 3D volume of Scout 3 includes the whole heart including the apex and the pulmonary artery as seen on the coronal view of Scout 1. The navigator is localized at the dome of the right hemidiaphragm. Localization of the dome of the right hemidiaphragm is performed on the transverse and coronal views of Scout 1. The end-expiratory gating window for Scout 3 is 7 mm. The scan duration is ~1.5-2 min depending on the heart rate and the respiratory pattern of the patient (Table 1).

For high resolution coronary MRA, 3D volume-targeted SSFP or segmented k-space gradient echo imaging sequences are currently preferred. In the following protocols a compromise between bandwidth for signal-readout and TR was made. Therefore, not all the protocols run with the shortest possible TR values. Shortening of the TR is possible but at the cost of a reduced SNR (Table 2).
High-Resolution Coronary MRA

For accurate volume-targeting, it is important that the 3D scout scan (Scout 3) and 3D high-resolution coronary MRA are acquired at the same time-point in the cardiac cycle (identified from the images of Scout 2) and using the same suppression of respiratory motion. For high resolution imaging, the gating window should be reduced to ~5 mm and the localization of the navigator should remain unchanged when compared to Scout 3. Typically, the duration of the acquisition window is also reduced for high resolution coronary MRA (50 – 100 ms). Volume targeting for the right coronary system can be performed using a 3-point planscan tool. Three user-specified points (as viewed on Scout 3) on the proximal RCA, the mid-RCA and the distal RCA define the orientation and location of the center plane of the imaged volume. For the left coronary system, one point on the LM, and one point on the mid-LAD and mid-LCX prescribe a near-transverse view that includes the proximal segments of the left coronary arterial system. The highest (most cranial) point of the left coronary system is not always on the left main. Therefore, it is important to ensure that the prescribed volume encompasses the major proximal segments of the left coronary system. Alternative plane orientations parallel to the LCX and/or the LAD have also been used and long segments of the LCX are often visualized on scans of the RCA. These high resolution volume targeted MRAs provide ideal localizer scans for dual-inversion black-blood coronary vessel wall imaging. In whole-heart coronary MRA as described by Weber and co-workers [83], a transverse volume that encompasses the apex and the pulmonary artery as viewed on Scout 1 is planned. Although the whole-heart scan lasts 10-15 min, near-isotropic resolution is obtained (Tables 3, 4).

Navigator Pitfalls

To maximize navigator performance and efficiency, localization of the navigator at the dome of the right hemidiaphragm is important. Since the 3D shape of the diaphragm is individually dependent,
identification of the dome on 2 orthogonal planes is advised. Localization of the navigator with 1/3 above the lung-liver interface and 2/3 below is recommended. Caudal drift of the end-expiratory diaphragmatic position is sometimes observed which may adversely affect the efficiency of the scan. However, this is often related to sleep apnea or a low frequency pattern overlaid to the respiration, and in most cases the end-expiratory diaphragmic position returns to its original position. On average, the navigator efficiency should approach ~50% which prolongs the nominal scanning time by a factor of 2. Navigator efficiencies below 20% and above 80% are suboptimal meaning that the localization of the navigator may need to be adapted. Stopping and restarting the scan may help in some cases. General patient motion can be minimized by specifically informing the patient that changing the position of the legs (crossed vs. non-crossed) should be avoided during the scan session. Asking the patient to go to the restroom prior to the MR exam helps to minimize general patient motion and improves the respiratory pattern.

**Conclusion**

MR imaging, because of its non-invasive nature, 3D capabilities, and capacity for soft tissue characterisation, is emerging as a powerful modality for both coronary luminal and vessel wall imaging. With further refinement of the technique and improvements of the spatial resolution on high field MR scanners, there is hope of significantly improving our ability to detect and characterize the tissue and plaque components in the coronary vessel wall. Doing so may have far reaching implications for the management of patients with established coronary heart disease.

**References**

56. AHA, American Heart Association 2002 Heart and Stroke Statistical Update. 2002

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