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MRI of the Coronary vasculature: Imaging the Lumen, Wall and Beyond

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Abstract

The characteristics of coronary artery disease (CAD) are gradual thickening of the coronary walls and narrowing of the vascular lumen due to the built-up of atherosclerosis plaques. Those morphological changes can be noninvasively detected by coronary MRI/MRA. In addition, functional changes, such as coronary wall distensibility and flow changes may also be evaluated with MRI. However, the application of current MRI/MRA techniques is limited in clinical practice due to several adverse technical and physiological factors, such as cardiac motion and respiratory motion. Many technical innovations have been adopted to address those problems from multiple aspects.

Keywords

Coronary artery disease; magnetic resonance imaging; noninvasive

Introduction

Coronary artery disease (CAD) is the leading cause of death on the world. The characteristics of CAD are gradual thickening of the coronary walls and narrowing of the vascular lumen due to the build-up of atherosclerosis plaques. Subclinical CAD may “silently” progress over a long time period until coronary events, a group of symptoms attributed to myocardial ischemia, affect patients^{1,2}. Therefore, the detection of CAD in its early stage is clinically significant. However, the morphological and functional features of the remodeled coronary artery, which may convey risk of subclinical CAD, have not been comprehensively investigated in asymptomatic individuals who do not have documented or suspected structural cardiovascular disease. This knowledge gap exists mainly because clinical examinations for detecting coronary wall are either invasive or require X-ray exposure. Therefore, noninvasive imaging methods for the evaluation of coronary artery are

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highly desired for optimal cardiovascular prevention. Over the past decade, magnetic resonance imaging/angiography (MRI/MRA) has emerged as a promising noninvasive method for observing both morphological and functional changes on coronary walls^{3,4}. In this review chapter, we will summarize state-of-art coronary MRI/MRA techniques for detecting CAD from various aspects, including luminal stenosis, coronary wall plaques and coronary functional changes. In addition, clinical application and limitations of current coronary MRI techniques in clinical practice will also be discussed.

Imaging of coronary lumen using MRI

Traditionally, stenosis of the coronary lumen is an indicator of obstructive CAD and subsequent treatments, such as coronary artery bypass graft surgery (CABG) and percutaneous transluminal coronary angioplasty (PTCA), is based on extent and severity of disease. Multiple bright-blood MRI pulse sequences can be used to rapidly image coronary lumen and detect coronary stenosis, such as spoiled gradient echo and steady-state free precession (SSFP)⁵. (Box 1)

Regenfus et al. evaluated 50 patients with suspected CAD using a turbo FLASH sequence within one single breath-hold. The authors reported that 268 of 350 (76.6%) coronary segments could be evaluated. In those coronary segments, 48 of 56 luminal stenoses could be detected by MRI⁶. With T1-shortening contrast agents, such as gadolinium, spoiled gradient echo sequences can be used to depict contours of the coronary lumen. In a study with 16 healthy volunteer, Li et al. demonstrated that gadolinium may significantly increase the image quality of coronary MRA in 2 breath-holds. However, spatial resolution and coverage of coronary MRA may be limited by the length of breath-hold and the duration of sustainable blood pool enhancement generated by contrast agents⁷. Using a free-breathing technique and a scheme of slow infusion (0.3 ml/s) of the contrast agent (for prolonged T1 contrast between vessel wall and the blood pool), Bi et al. demonstrated that coronary MRA (FLASH sequence) is capable of imaging the whole coronary tree within a relatively short period (4.5 +/- 0.6 min) for 8 volunteers⁸. In a single center study, Yang et al. performed contrast-enhanced whole-heart MRA in 69 consecutive patients with suspected CAD. The authors found that whole-heart MRA could identify clinically significant coronary stenosis in 32 patients and could rule out CAD in 23 patients. On a per-segment basis, MRA had high sensitivity (91.6%), specificity (83.1%), and accuracy (84.1%) for the detection of CAD (using X-ray angiography as the “gold standard”). On a per-patient basis, these values for accurate CAD diagnosis were 94.1%, 82.1%, and 88.7%, respectively⁹. Recently, the same group also demonstrated a comparable diagnostic accuracy for the detection of CAD (significant coronary luminal stenosis) in 110 patients using similar imaging techniques with a 32 channel coil¹⁰.

Some CAD patients may have varying degrees of co-existing kidney dysfunction¹¹. Therefore, noncontrast coronary MRA techniques may provide added benefits in that patient population by avoiding nephrotoxic contrast agents and risk of Nephrogenic Systemic Fibrosis (NSF). The high T2/T1 ratio of the blood provides strong blood signal and may serve as an intrinsic contrast agent for the SSFP technique in coronary MRA^{12,13}. Using noncontrast whole-heart coronary MRA, Kato et al. detected significant CAD in 138

patients with suspected CAD with high sensitivity and high negative predictive value (88%)¹⁴. Using quantitative analysis of coronary MRA, Yonezawa et al. found that ROC curve analysis in a segment-based analysis for identifying significant coronary stenosis was 0.96¹⁵. In a multi-center study, coronary MRA provided an accuracy of 72 % (95 CI, 63% to 81%) in diagnosing CAD¹⁶. Stuber et al. demonstrated good agreement of anatomy and pathology between coronary MRA and X-ray angiography in depicting the coronary tree in 7 CAD patients confirmed by X-ray angiography and 15 healthy adult volunteers¹⁷. Indicated by higher sensitivity, specificity and area under the ROC curve (AUC), Liu et al. found that noncontrast coronary MRA is superior to coronary CTA for delineating luminal narrowing of the coronary artery in the segments with heavy calcification¹⁸. Yoon et al. studied 207 patients with suspected CAD using noncontrast whole-heart coronary MRA. The authors observed 10 coronary events (half of them were deadly events) in 84 patients with significant coronary stenosis identified with MRA during a follow-up of 25 months. While only 1 coronary event happened in 123 patients without CAD (also defined using MRA findings). Cox regression demonstrated that a coronary stenosis on MRA is an independent risk factor associated with significant increase for all cardiac events (RR= 20.78, p = 0.001)¹⁹. Figure 1 and 2 demonstrate that coronary MRA (with and without contrast enhancement) is able to show coronary stenosis.

Imaging coronary dilation and flow using MRI

Coronary MRA may also be used to evaluate coronary dilation or stiffness (indicated by changes on lumen area). Terashima et al. studied 12 CAD patients and 20 healthy controls before and after the administration of vasodilator (sublingual nitroglycerin, NTG)²⁰. In 20 healthy adults and 17 patients with CAD, Hays et al. observe impaired coronary endothelial function associated with CAD (indicated by less cross-sectional coronary dilation after the administration of vasoactive medication)²¹. Similar impaired endothelial function could also be found in CAD patients before and after isometric handgrip exercise, another endothelial-dependent stressor, by the same group²². Using 3D coronary MRA pictures acquired at diastole and systole, Lin et al. calculated coronary dispensability index (CDI), an index of coronary stiffness, within cardiac cycles based on the differences of cross-sectional coronary lumen areas. The authors found that older type 2 diabetes mellitus (T2DM) patients without documented cardiovascular disease have lower CDIs in all coronary branches than healthy elderly²³. Figure 3 shows the measurement of coronary distensibility.

Coronary flow is another important index for evaluating coronary atherosclerosis and endothelial function of the coronary wall. Altered blood flow usually accompanies luminal narrowing. Phase contrast (PC)-MRI is a traditional technique for quantifying 2D blood flow in the vessel. Shibata et al. demonstrate good agreement between MRI-derived coronary flow velocity reserve (calculated with flow difference before and after the administration of dipyridamole) and that measured using Doppler guide wire in 19 patients with heart disease ($r = 0.91$)²⁴. Insufficient coronary flow reserve (calculated on measurements before and after stress) was identified in diagnosed CAD patients (with flow-limiting luminal stenosis) as compared to healthy volunteers^{21,22}.

Imaging coronary wall using MRI

As a major manifestation of CAD, coronary remodeling involves the long-term, active modification of the vessel structure in response to pathological changes in its milieu, such as the development of atherosclerotic plaques. Because remodeled coronary wall (positive or negative) is the underlying source of myocardial ischemia, coronary remodeling becomes a reliable indicator of CAD and serves as a strong predictor of near-term coronary events²⁵. Coronary “culprit” plaque is the immediate source of cardiovascular events^{25,26}. Therefore, imaging of the coronary artery is of great clinical significance because it proves the existence of coronary plaques. The patterns of coronary remodeling have been found to be associated with clinical presentations of CAD. Currently, X-ray angiography is the standard clinical examination for the diagnosis of CAD. With X-ray angiography, Nahser et al. observed a reduction in coronary vasodilation and impaired regulation of coronary flow in T2DM patients²⁷. However, angiography shows only the coronary lumen, whereas CAD is a disease that originates in the vessel wall. Actually, many acute coronary events were triggered by superficial plaque erosion or rupture without obstructive lesions^{28,29}. Coronary artery plaques with positive remodeling (a nearly normal lumen gauge with compensatory vessel enlargement) have higher plaque vulnerability, indicated by a higher macrophage count and lipid content³⁰. That means a substantial burden of atherosclerosis can exist without producing stenosis³¹. Those individuals with increasing cardiovascular risk may have low-grade narrowing in coronary arteries, which may be ignored by X-ray angiography. Existing studies have demonstrated the relationships between morphological changes of coronary plaques and risk of coronary events. Unfortunately, current clinical methods for coronary wall examination, such as IVUS, are limited by invasiveness. As a noninvasive imaging method, MRI may address this unmet clinical need by detecting risky coronary plaques without significant lumen stenosis. Over the past decade, MRI has emerged as a radiation-free, noninvasive method for the accurate detection of *in situ* atherosclerotic lesions on the coronary wall^{32,33}. (Box 2)

Botnar et al. acquired coronary wall images in 5 healthy volunteers and 5 CAD patients (confirmed by X-ray angiography). Fayad et al. also detected significant difference of maximal coronary wall thickness between subjects with and without CAD (4.38 ± 0.71 mm vs. 0.75 ± 0.17 mm) using 2-dimensional (2D) FSE sequence. In a cross-sectional study, Kim et al found that subjects with type 1 diabetes mellitus (T1DM) and diabetic nephropathy (DN) had a thicker coronary wall than those T1DM patients free of kidney involvements using a three-dimensional (3D) TSE sequence³⁴. Coronary wall MRI has also been adopted as a quantitative tool for cardiovascular risk estimation in epidemiological studies. In the Multi-Ethnic Study of Atherosclerosis (MESA) study, Miao et al. detected positive coronary remodeling, a predictor for future cardiovascular events, in asymptomatic older adults using MRI ($n = 179$)³⁵. Pericardial fat volume, an index of cardiovascular vulnerability, was also found to strongly relate to coronary plaque eccentricity (detected with MRI) in healthy older adults³⁶. Lin et al. demonstrated the differences of coronary wall thickness and stiffness between subjects with primary hypertension (HTN) and healthy controls³⁷. Those results suggest that coronary wall features have the potential to serve as quantitative imaging

biomarkers in evaluating cardiovascular risks. Figure 4 shows positive remodeling of the coronary wall in an asymptomatic subject with type 2 diabetes mellitus (T2DM).

Application and limitations of MRI/MRA for CAD management in clinical practice

Currently, coronary MRI/MRA has not been widely accepted as a regular examination in clinical practice. Many factors may affect image quality of coronary arteries, which may compromise clinical diagnosis. Such a situation is due to several technical limitations of this technique. At the same time, many novel technical innovations have been developed to solve those problems. (Box 3)

When an acute coronary syndrome (ACS) happens, “*time is myocardium and time is outcome.*”³⁸ Therefore, MRI is not suitable for CAD diagnosis under acute situations due to long scan times. Although MRI can be a useful tool for screening subclinical CAD, MRI may need more time than other noninvasive imaging tools, such as coronary CTA, for the detection of CAD. In addition, a long scan may adversely affect image quality of coronary MRI/MRA due to unexpected motion artifacts and will potentially lower coronary MRI's clinical value. During the last few decades, many technical advances have been applied to shorten coronary MRI scan times. Parallel imaging takes advantages of spatial encoding from multiple parts of phase-array receive coils to shorten the MRI acquisition time³⁹. Huber et al. reported the implementation and evaluation of sensitivity-encoding (SENSE) free-breathing navigator-gated 3D coronary MRA at 3T. The authors found that SENSE could significantly reduce MRI scan time for the coronary tree in 11 healthy volunteers⁴⁰. However, there is usually a trade-off between short acquisition time and lower SNR (representing inferior visualization of coronary branches)⁴¹. Using a 32-channel coil, Nehrke et al. acquired free-breathing whole-heart coronary MRA in 4 minutes with the use of SENSE and partial Fourier encoding for k-space acceleration⁴². In a recent study, Akçakaya et al applied a novel B(1) -weighted compressed sensing (CS) technique in 3D whole-heart coronary MRA. With a CS-based acquisition and reconstruction strategy (low-dimensional-structure self-learning and thresholding [LOST]), the authors acquired high resolution coronary MRA in 7 healthy volunteers with a shorter acquisition time than that of the traditional SENSE technique⁴³.

Administration of contrast agents is a common way to improve image quality. Paetsch et al successfully use an intravascular contrast agent, B-22956, to significantly improve the image quality of 3D coronary MRA⁴⁴. Yu et al. performed contrast enhanced whole-heart coronary MRA (with SENSE) in 11 healthy volunteers. The authors found that a longer left anterior descending artery (LAD) could be depicted as compared with that presented by noncontrast coronary MRA⁴⁵. Many solutions could be applied to jointly improve the performance of coronary MRI/MRA.

Compared to imaging other solid organs, continues motion of the coronary tree in the 3D space is a specific challenge for coronary imaging. Heartbeat and breathing are major sources of coronary motion. In order to minimize the adverse effects of motion on coronary image quality, segmented acquisition schemes were designed to collect imaging data over multiple heartbeat and respiration cycles. Only the signal received within a highly selected “acquisition window” for minimal coronary motion will be accepted for filling *k*-space. An

ideal “acquisition window” should be both “cardiac motion-free” (a “rest period of regional cardiac motion” chosen with ECG) and “respiratory freezing” (identified with 2D motion-adapted navigator [NAV] echo)”⁴⁶⁻⁴⁸. Unfortunately, current motion correction/suppression strategies are still unable to eliminate the adverse effects of motion on cardiovascular MR scans completely. Severe cardiac motion, associated with faster heart rates and shortened “rest periods” in cardiac cycles, has already been proven to be a prominent determinant of poor image quality in coronary wall MRI⁴⁹. Beta-blockers can significantly lower heart rate and increased rest duration in cardiac cycle⁵⁰. SSFP is a fast MR imaging pulse sequence (4). With identical spatial resolution and gross imaging time as that used for TSE (FSE), SSFP can therefore acquire data in a shorter time window in a single cardiac cycle. Such a physical characteristic can be particularly utilized in cardiac imaging which is affected by severe cardiac motion. Using a black-blood SSFP sequence, Lin et al. significantly increased image quality of coronary wall under conditions of fast heart rate (> 80 beats/minute) in healthy subjects⁵¹. Compared with traditional TSE(FSE) sequences for coronary wall imaging, SSFP also had better performance in directly observing the coronary wall for the detection of potential cardiac allograft vasculopathy (CAV) in heart transplant (HTx) recipients who usually have extremely fast heart rates due to denervation of “foreign” hearts⁵². Figure 5 shows a coronary wall image in an HTx recipient.

Limited by the length and stability of breath-holding, breath-hold MRI is not suitable for all coronary examinations. Free-breathing coronary MRI/MRA has become the preferred choice in most large-scale clinical/epidemiological studies for guiding cardiovascular prevention, such as the MESA study³⁵. However, changes of breathing patterns (indicated by changes of the location of diaphragm during the scan) may significantly affect image quality^{46,48,53}. Irregular breathing modes may widely exist in healthy populations. Older subjects were more likely to have inconsistent breathing modes⁵⁴. Advanced Respiratory Motion Compensation has been used to suppress such adverse effects due to motion⁵⁵. Using 3D-NAV and 3D affine correction, Henningson et al. demonstrated 100% scan efficiency in performing high-resolution whole-heart 3D coronary MRA with high image quality in a recent study⁵⁶. Pang et al. developed a whole-heart coronary MRA technique using motion-corrected sensitivity encoding with 3D projection reconstruction⁵⁷. Such a sequence can be used to image the whole coronary tree in 5 minutes with good image quality despite the adverse effects of respiratory motion. In addition, some adjuncts, such as abdominal belts, have been applied to stabilize respiratory motion during coronary MRI/MRA. Ishida et al. used an dedicated abdominal belt to regulate respiratory motion during coronary scans and therefore resulted in a higher scan efficiency, shorten scan time and better image quality^{14,58,59}.

Future directions

Since coronary MRI/MRA may provide a cluster of quantitative measurements to evaluate the progression of coronary atherosclerosis, it will become more and more important in cardiovascular disease diagnosis and management. In addition, CAD may also be considered as a secondary target-organ involvement of nephrology, endocrinology and rheumatology disorders, including chronic kidney disease (CKD), T2DM and systemic lupus erythematosus (SLE)⁶⁰⁻⁶². A noninvasive, standardized approach to measure subclinical

CAD and related cardiac changes from multiple aspects is important for guiding CAD management and improving patient survival by measuring individual responses to comprehensive target-organ protection. In a recent study, Pang et al. developed a self-gated 4D whole-heart imaging technique to detect coronary anatomy and cardiac function simultaneously⁶³. However, although coronary MRI/MRI has been developed for CAD estimation for more than 10 years, many technical and physiological conditions still significantly affect its performance in clinical practice. Further work is needed to optimize the technique and extend its clinical application for patient care.

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Box 1

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MRI sequences used in the evaluation of coronary luminal stenosis (bright-blood)*				Need contrast agent?
Spoiled gradient echo	FLASH (Fast low angle shot magnetic resonance imaging)	SPGR (Spoiled Gradient Recall Acquisition using Steady States)	T1 FFE (T1-weighted Fast Field Echo)	<i>Yes</i>
SSFP	FISP (Fast Imaging with Steady-state Precession)	GRASS (Gradient Recall Acquisition using Steady States)	FFE (Fast Field Echo)	<i>No</i>

* Names vary from different MRI scanner manufacturers

Box 2

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MRI sequences used in the evaluation of coronary wall*		Need contrast agent?
FSE (fast spin echo)	TSE (turbo spin echo)	No

* Names vary from different MRI scanner manufacturers

Box 3

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Major challenges for current coronary MRI/MRA techniques	Possible solutions
Long scan time	Developing fast imaging techniques
Low spatial resolution and SNR	Using high magnetic field and administrating of contrast agents
Adverse physiological conditions, such as fast heart rate and irregular breath-modes	Developing novel imaging techniques, suppressing adverse patho-physiological conditions

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Key points

1. MRI is a useful noninvasive tool for the detection of coronary stenosis.
2. MRI can detect morphological and functional changes of remodeled coronary artery.
3. Many technical advances have been adopted to improve the performance of coronary MRI/MRA for cardiovascular risk estimation.

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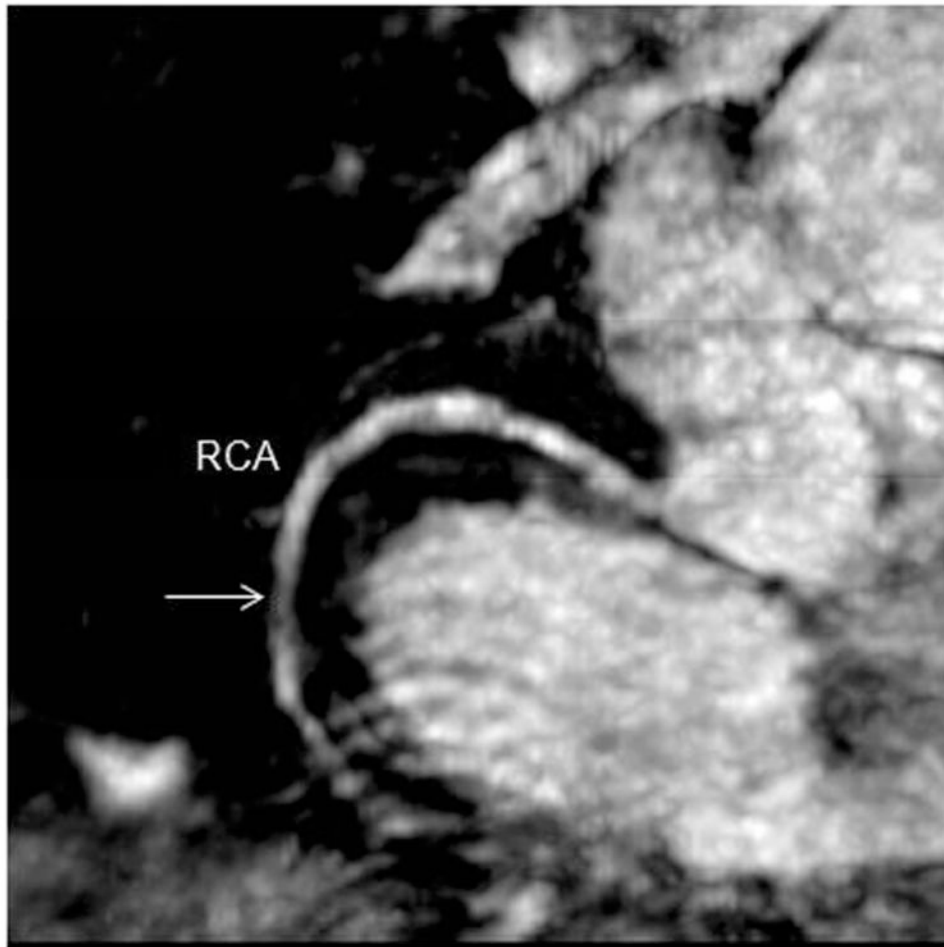


Figure 1.
A 75 year-old male patient with atypical chest pain. A lumen stenosis on the LCX was identified by contrast-enhanced MRA (courtesy of Dr. Debiao Li)
Source of the figure: reference # 9, with permission of Dr. Debiao Li

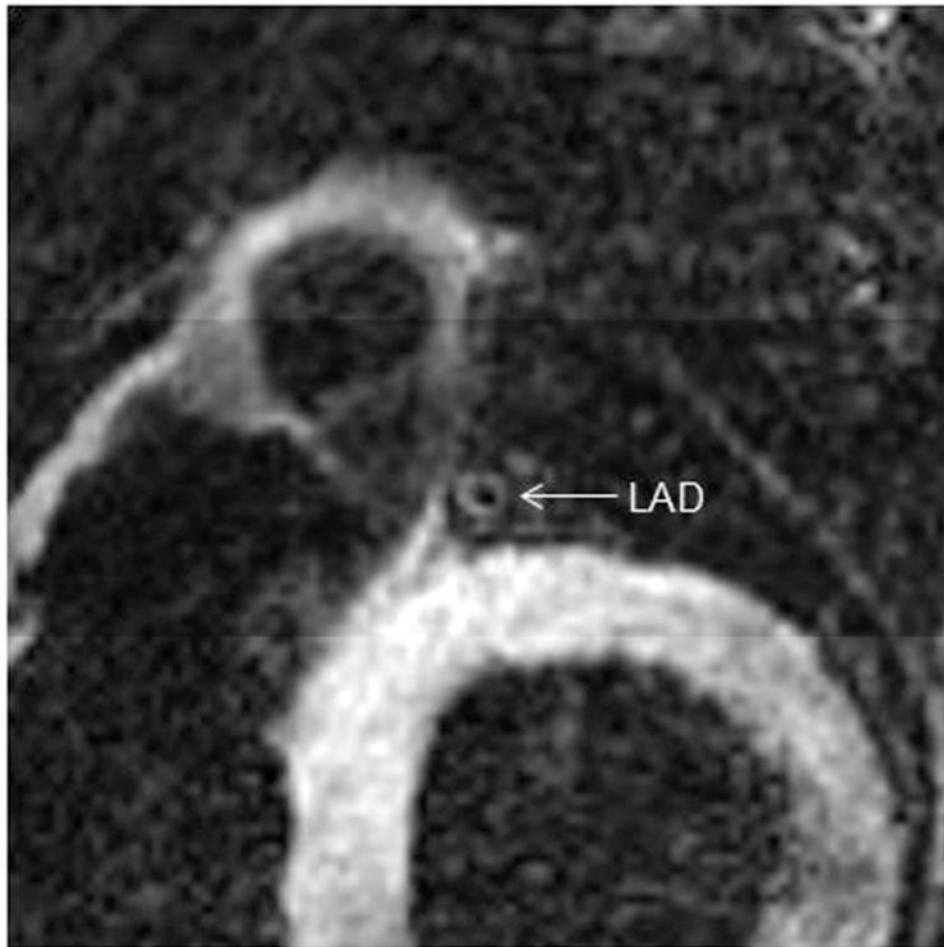


Figure 2.
A 74 year-old asymptomatic male. A lumen stenosis on the RCA could be identified by noncontrast MRA (confirmed by coronary angiogram)
Source of the figure: unpublished data of our group.

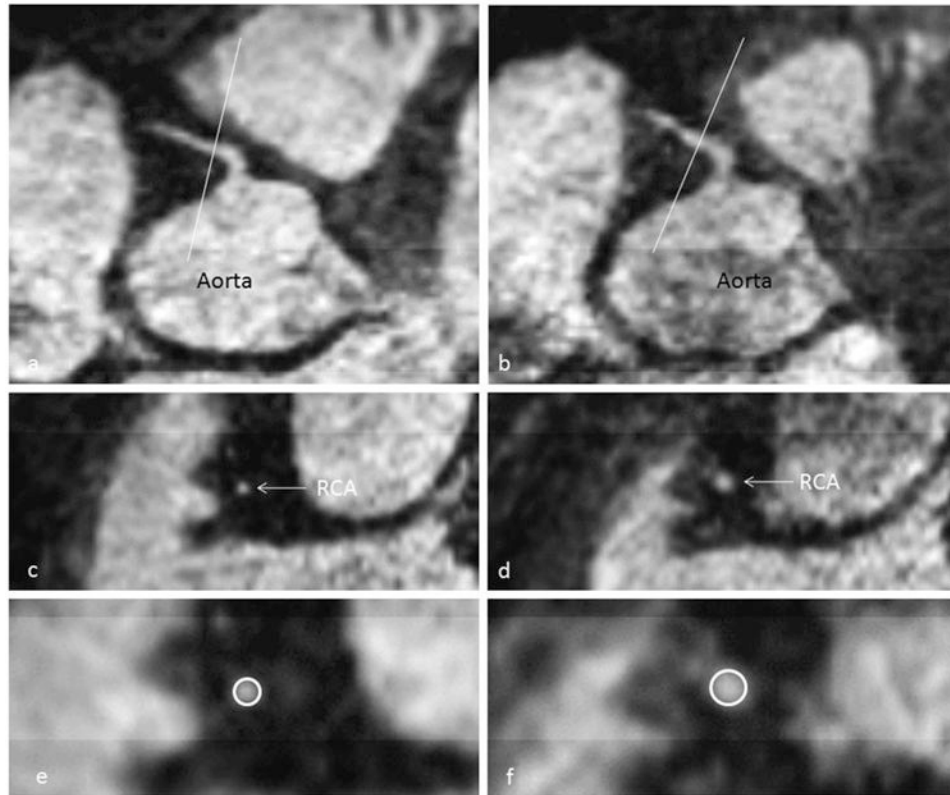


Figure 3.

A 73 year-old healthy male. His peripheral blood pressure was 130/70 mmHg (PP= 60mmHg). **(a)** Longitudinal view of the RCA in mid-diastole **(b)** Longitudinal view of the RCA in end-systole. **(c)** Transverse view of lumen in mid-diastole **(d)** Transverse view of lumen in end-systole **(e)** Zoomed diastolic lumen with contour shows the area is 7.61mm². **(f)** Zoomed systolic lumen with contour shows the area is 15.05 mm². $CDI = (15.05 - 7.61) / 7.61 / 60 \times 1000 = 16.29 \text{ (mmHg}^{-1}\text{)}$

Source of the figure: reference #23 from our group

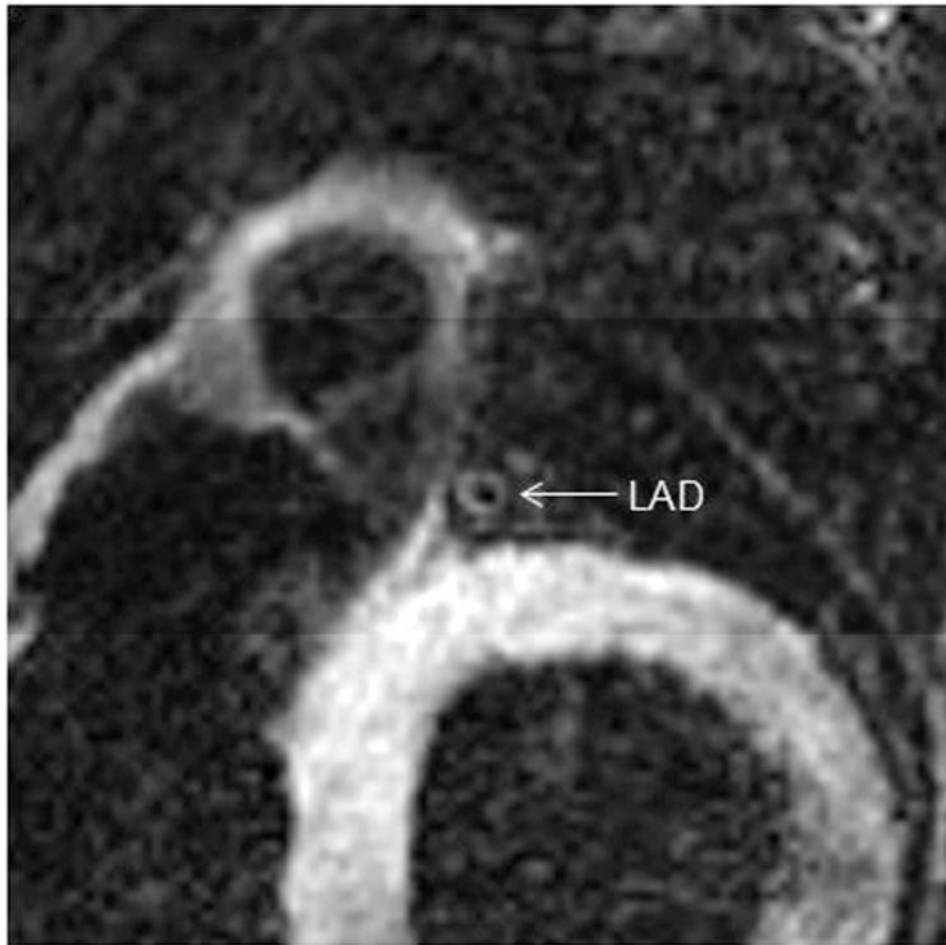


Figure 4.

A 71 year-old asymptomatic female with a history of T2DM for 10 years. An eccentrically remodeled coronary segment on the LAD (without significant lumen stenosis) could be identified by MRI.

Source of the figure: unpublished data of our group.

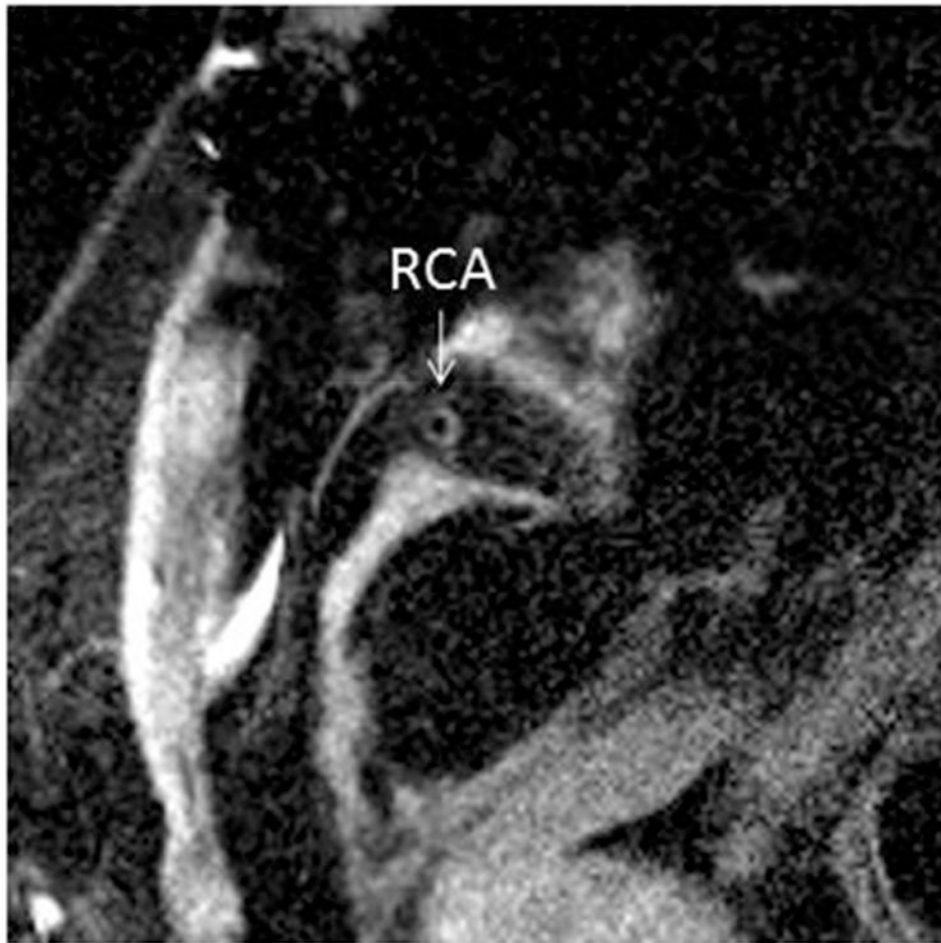


Figure 5. a 61-year-old female, who had a HTx 7 years ago. Her heart rate is 108 beats/minute. We can clearly see the RCA using black-blood SSFP MRI technique. Source of the figure: reference #52 from our group.

MRI sequences used in the evaluation of coronary luminal stenosis (bright-blood)*				Need contrast agent?
Spoiled gradient echo	FLASH (Fast low angle shot magnetic resonance imaging)	SPGR (Spoiled Gradient Recall Acquisition using Steady States)	T1 FFE (T1-weighted Fast Field Echo)	<i>Yes</i>
SSFP	FISP (Fast Imaging with Steady-state Precession)	GRASS (Gradient Recall Acquisition using Steady States)	FFE (Fast Field Echo)	<i>No</i>

* Names vary from different MRI scanner manufacturers

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MRI sequences used in the evaluation of coronary wall*		Need contrast agent?
FSE (fast spin echo)	TSE (turbo spin echo)	<i>No</i>

* Names vary from different MRI scanner manufacturers

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Major challenges for current coronary MRI/MRA techniques	Possible solutions
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