Noninvasive In Vivo Human Coronary Artery Lumen and Wall Imaging Using Black-Blood Magnetic Resonance Imaging

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Background—High-resolution MRI has the potential to noninvasively image the human coronary artery wall and define the degree and nature of coronary artery disease. Coronary artery imaging by MR has been limited by artifacts related to blood flow and motion and by low spatial resolution.

Methods and Results—We used a noninvasive black-blood (BB) MRI (BB-MR) method, free of motion and blood-flow artifacts, for high-resolution (down to 0.46 mm in-plane resolution and 3-mm slice thickness) imaging of the coronary artery lumen and wall. In vivo BB-MR of both normal and atherosclerotic human coronary arteries was performed in 13 subjects: 8 normal subjects and 5 patients with coronary artery disease. The average coronary wall thickness for each cross-sectional image was $0.75 \pm 0.17$ mm (range, 0.55 to 1.0 mm) in the normal subjects. MR images of coronary arteries in patients with $\geq 40\%$ stenosis as assessed by x-ray angiography showed localized wall thickness of $4.38 \pm 0.71$ mm (range, 3.30 to 5.73 mm). The difference in maximum wall thickness between the normal subjects and patients was statistically significant ($P<0.0001$).

Conclusions—In vivo high-spatial-resolution BB-MR provides a unique new method to noninvasively image and assess the morphological features of human coronary arteries. This may allow the identification of atherosclerotic disease before it is symptomatic. Further studies are necessary to identify the different plaque components and to assess lesions in asymptomatic patients and their outcomes. (Circulation. 2000;102:506-510.)

Key Words: atherosclerosis ♦ magnetic resonance imaging ♦ coronary disease

Acute ischemic coronary syndromes often result from the rupture of a mildly to moderately stenotic coronary artery plaque, leading to thrombus formation.1–3 Currently available imaging techniques for the diagnosis of coronary artery disease are limited. For example, coronary angiography demonstrates only the degree of luminal narrowing and fails to visualize the arterial wall. Moreover, arteries accommodate plaque growth through outward displacement of the vessel wall, thereby preserving lumen cross-sectional area.4 Other imaging techniques, such as intravascular ultrasound,5 fast CT,6 and angiography,7 have all advanced our understanding of atherosclerosis, but these techniques are invasive and yield limited information about plaque composition.

Recent in vivo studies of atherosclerotic plaques in animal models,8,9 carotid arteries,10,11 and aorta12 demonstrate that high-resolution MRI can noninvasively image the artery wall and assess plaque composition. Preliminary studies in a porcine model of atherosclerosis showed that the major difficulties of MR coronary wall imaging are due to the combination of cardiac and respiratory motion artifacts, the nonlinear course of the coronary arteries, and their relatively small size and location.13 Thus, an effective in vivo MRI technique for coronary artery imaging must overcome artifacts related to blood flow and cardiac, respiratory, and vessel wall motion to achieve high-resolution and high-contrast imaging.

Current white-blood non–contrast-enhanced MR coronary angiography (gradient-echo,14 echo planar,15 spiral,16 etc) provide no information about the coronary wall structure or atherosclerotic plaque characteristics. In this context, the concept of black-blood MRI (BB-MR) is promising, because the signal from static tissue is maximized and the transverse magnetization of flowing blood is made intentionally incoherent, leading to blood signal void.17,18

Therefore, by combining BB-MR with high-spatial-resolution and fast-data-acquisition imaging, both lumen and wall imaging of the coronary arteries should be possible. A number of different methods are available for BB-MR.17–21 However, none of these methods have been used for coronary lumen and wall imaging.

In this in vivo study of normal and atherosclerotic human coronary arteries, we use long-echo-train-length (ETL) fast-spin-echo (FSE) imaging with “velocity-selective” inversion preparatory pulses22,23 to nullify the signal from flowing...
blood. A cardiac phased-array surface coil for high-resolution coronary imaging (460- to 750-μm in-plane spatial resolution) is also used. The results of this study clearly demonstrate that normal and atherosclerotic human coronary wall imaging can be performed with high-resolution BB-MR methods.

**Methods**

**Subjects**

We studied 13 subjects: 8 healthy subjects (mean age, 30 years; range, 25 to 37 years; 4 men) without a history of cardiovascular disease and 5 consecutive coronary artery disease patients (mean age, 68 years; range, 50 to 78 years; 3 men) with ≥40% stenosis as documented by x-ray angiography. The MRI studies were performed within 24 hours of the coronary contrast x-ray angiogram. Written informed consent was obtained from all subjects, and the institutional review board approved the protocol.

**MR Imaging**

MRI was performed on a 1.5-T whole-body MRI system (General Electric Medical Systems, Signa) equipped with high-performance gradient (40-mT/m amplitude, 150-mT·m⁻¹·ms⁻¹ slew rate) and a multichannel receiver with a maximal bandwidth of 250 kHz. A 4-element (2 anterior and 2 posterior) specially designed cardiac phased-array receiver surface coil was used for signal reception. A multichannel receiver with a maximal bandwidth of 250 kHz. A first IR pulse inverts the inversion recovery (IR) pulse followed immediately by a slice-suppression consisted of 2 inversion pulses: 1 nonselective 180° blood and bright wall signal of the coronary arteries. The flow artifacts and providing a strong contrast between the dark flowing blood. A cardiac phased-array surface coil for high-resolution coronary imaging (460- to 750-μm in-plane spatial resolution) is also used. The results of this study clearly demonstrate that normal and atherosclerotic human coronary wall imaging can be performed with high-resolution BB-MR methods.

**Selective 180° inversion pulse.** The first IR pulse inverts the inversion recovery (IR) pulse followed immediately by a slice-suppression consisted of 2 inversion pulses: 1 nonselective 180° blood and bright wall signal of the coronary arteries. The flow artifacts and providing a strong contrast between the dark flowing blood. A cardiac phased-array surface coil for high-resolution coronary imaging (460- to 750-μm in-plane spatial resolution) is also used. The results of this study clearly demonstrate that normal and atherosclerotic human coronary wall imaging can be performed with high-resolution BB-MR methods.

**Velocity-selective inversion preparatory pulses**

Velocity-selective inversion preparatory pulses were used to suppress the signal from flowing blood, thereby avoiding possible flow artifacts and providing a strong contrast between the dark flowing blood and bright wall signal of the coronary arteries. The flow suppression consisted of 2 inversion pulses: 1 nonselective 180° inversion recovery (IR) pulse followed immediately by a slice-selective 180° inversion pulse. The first IR pulse inverts the magnetization of the entire body, including all of the blood. The second IR pulse reinserts the imaging slice but leaves the blood outside the slice inverted. The section thickness of the selective inversion pulse was set to 3 times the slice thickness to accommodate possible misregistration of tissue between the preparatory pulses and data acquisition. The noneselective pulse consisted of a rectangular “hard” pulse 1024 μs long. The selective pulse was a hyperbolic-secant pulse 8640 μs long. This provided good B1 insensitivity and inversion profile. The velocity-selective inversion pulses were placed at end diastole (after the detection of the ECG trigger), and the data acquisition occurred during diastole. This process maximized the blood flow suppression due to outflow and also minimized artifacts due to vessel motion. Image acquisition started after a predetermined inversion time (TI). The delay time or TI for the velocity-selective inversion preparatory pulses was determined close to the null point of the blood signal (see equation). TI is based on the T1 relaxation value of the blood and the TR interval:

\[ TI = -\frac{1 - e^{-TR/T1}}{e^{T1}} \]

With TR=2 RR=1000 ms (heart rate=60 bpm) and T1=1200 ms, from the equation, TI is 625 ms.

**Short Optimized RF Pulses**

The data acquisition is performed with an FSE sequence. As usual for the FSE sequence, the time between the 90° excitation pulse and the first refocusing pulse is half the time between the neighboring refocusing pulses (the echo spacing; ESP). The strong and fast gradients made possible very compact echo trains. To further shorten the ESP, short radiofrequency (RF) pulses optimized by use of the Shinnar-LeRoux algorithm were used. The RF excitation pulses were 1.2 ms long. The refocusing pulse had a flip angle of 155°. With a data acquisition sampling of 125 kHz and 256 frequency points, an ESP as short as 3.9 ms was achievable. These pulses provided reduced power deposition and reduced echo amplitude unstabilities.

**Optimized Fat Suppression**

In acquiring images of the coronary artery wall, the velocity-selective inversion pulses were immediately followed by a chemical shift-selective (CHESS) pulse. This pulse eliminated the epicardial fat signal and thus enhanced the definition of the outer boundary of the arteries. To take account of the multicomponent nature of the fat signal, the CHESS pulse was optimized according to Kuroda et al and resulted in improved fat suppression and coronary wall visualization.

**Long-ETL FSE Imaging**

The preparatory pulses (velocity-selective inversion pulses and CHESS pulse) were followed by an ECG-gated, long-ETL FSE imaging sequence. The short ESP allowed the use of long-ETL data acquisition without the disadvantage of T2 relaxation blurring. From the initial scout images of the coronary arteries, 5 contiguous transverse (cross-sectional) images of the lumen and wall of the proximal segments of the right (RCA) and left anterior descending (LAD) coronary arteries were acquired in 13 subjects. Imaging was performed during short periods of suspended respiration of 12 to 18 heartbeats per slice. One way to restrict the number of phase-encoding steps is to reduce the field of view (FOV) in the phase-encoding direction. However, for a small FOV, this may result in back-folding artifacts. Therefore, when this was the case, we disabled the 2 posterior coil elements of our 4-coil-elements anterior and posterior phased-array coil by a user-controlled variable just before imaging.

The imaging parameters were TR=2 RR intervals, TE=40 ms, asymmetric (3/4) FOV in the phase encoding direction (in some of the images), 18- to 29-cm FOV, 3- to 5-mm slice thickness, noninterslice gap, 384×384 or 384×256 acquisition matrix, number of signals averaged (NSA) 1, 32 ETL, 125-kHz data sampling. The in-plane resolution was 0.46 to 0.75 mm.

**Image Analysis**

The MR images were transferred to a Macintosh computer for analysis. The inner (ie, lumen) and outer (eg, adventitial-medial) boundaries of the vessels were traced semiautomatically with ImagePro Plus (Media Cybernetics). The semiautomated tracing tool works by following an edge (ie, boundary) of significant contrast. The maximal wall thickness was determined from each cross-sectional image. The data were then analyzed with a 2-tailed unpaired Student’s t test. A value of P<0.05 was considered to be statistically significant. Values are mean±SEM.

**Results**

All the images demonstrated excellent flow suppression and high contrast and signal-to-noise in the coronary arteries and clearly delineated the coronary wall. Cross-sectional images of normal coronary artery wall showed a circular lumen surrounded by a uniform thin wall (Figure 1). A transverse lumen image obtained without fat saturation (Figure 1A) and wall image obtained with fat saturation (Figure 1B) of the
proximal LAD from a normal subject are shown. In this subject, the maximum wall thickness of the LAD measures \(\approx 0.8\) mm.

Figure 2 shows the ectatic atherosclerotic coronary arteries and thickened coronary wall of a 45-year-old male patient. The BB-MR cross-sectional lumen image reveals a circular lumen and an anterior plaque (arrow, Figure 2A). The cross-sectional image of the wall clearly reveals a variably thick proximal RCA, with the wall thinner around the 6 o’clock position and thicker in the other sectors (Figure 2B). In that patient, the maximum wall thickness is 3.3 mm. Figure 3A shows mild disease in the proximal LAD as seen on x-ray angiography in a 78-year-old female patient. The BB-MR cross-sectional lumen image reveals a circular lumen (Figure 3B), and the wall image shows a concentric plaque (maximum thickness 4.13 mm) (Figure 3C). In that patient, the maximum wall thickness is 4.13 mm. Figure 4A shows high-grade stenosis in the proximal LAD on the x-ray angiogram in a 75-year-old male patient. The BB-MR wall image obtained with fat saturation reveals a large eccentric plaque measuring 5.73 mm with heterogeneous signal intensity, possibly due to the different tissue composition (Figure 4C).

In the normal subjects, the average maximum coronary wall thickness was \(0.75 \pm 0.17\) mm (range, 0.55 to 1.0 mm; \(n=40\)). MR images of coronary arteries in coronary artery disease patients showed atherosclerotic plaques 3.30 to 5.73 mm in maximum wall thickness (4.38 \(\pm 0.71\) mm; \(n=25\)). The difference in maximum coronary wall thickness between the normal subjects and patients was statistically significant (\(P<0.0001\)).

**Discussion**

This study demonstrates, for the first time, that in vivo MRI can provide high-spatial-resolution images of the coronary artery wall in normal and diseased human arteries. Vessel lumen and wall morphology in normal and atherosclerotic human coronary arteries was assessed with a high-resolution...
Possible Further Improvements

The slice thickness of the MR image (3 to 5 mm) causes volume averaging (ie, partial-volume effect) and can contribute to an overestimation of the coronary wall. Thinner slice thickness, as used with 3D acquisition techniques, could further improve our coronary artery wall imaging.\(^\text{18,37}\) Moreover, zero-filled interpolation of the 256×256 images can be used to create 512×512 images to reduce or prevent cardiovascular disease.

Other coil designs, such as a smaller anterior 4-element phased-array coil, may improve the spatial resolution and allow the identification of the substructures within atherosclerotic coronary lesions.

The BB FSE sequence used in this study has flexible multicontrast capabilities (ie, proton-density or T2 weighting through direct manipulation of TE), which, with improvements in spatial resolution and image contrast,\(^\text{39–43}\) may allow the characterization of the different coronary plaque components.\(^\text{9,11,12,44,45}\)

A misalignment of the imaging plane and the long axis of the vessel can lead to inaccurate cross-sectional images and lead to errors in wall thickness measurements and plaque imaging. Careful planning in this study minimized these errors. A 3D imaging sequence\(^\text{18,37}\) will allow image reformatting in any desired plane direction and thus ensure the proper alignment between the imaging plane and the course of the coronary arteries.

The effect of slowly flowing blood near the vessel walls is another phenomenon that could potentially degrade the accuracy of vessel wall imaging with BB techniques. However, preliminary results in our study and with a similar BB-MR sequence in the coronary arteries\(^\text{36}\) and in the brain\(^\text{46}\) suggest that this effect is minimal.

Breath-holding was used to suppress respiratory motion. This limits the maximal duration of the scan and may not be possible in certain patients. We have limited the breath-holding duration to 12 to 18 heartbeats (12 to 18 seconds for heartbeats of 60 bpm), which was well tolerated by all subjects. Adequate breath-holding was confirmed by respiratory bellows. Short breath-holding limits the achievable spatial resolution and data sampling for each image, which in turn leads to vessel wall imaging. These problems can be overcome only by a prolongation of the duration of the breath-holds, which is well tolerated in some patients, or by the use of navigator techniques to avoid breath-holding altogether.\(^\text{47,48}\) The reduction of the ESP will also lead to shorter breath-holds and reduction of vessel motion blurring.

We have visualized the major epicardial coronary arteries but not the side branches. However, coronary atherosclerosis most often involves the proximal portion of the coronary arteries, usually at or near branch sites.\(^\text{49}\) Evaluation of the whole extent of the epicardial coronary arteries will be developed in future studies. Moreover, validation and repeatability studies of the MRI findings need to be performed, possibly in patients undergoing intravascular ultrasound.

Clinical Implications

Atherosclerotic coronary artery plaque rupture is a key event leading to acute coronary syndromes. In vivo MRI provides a means to noninvasively image and assess the morphological features of atherosclerotic and normal human coronary arteries. Future work will certainly aim at the identification of the different plaque components. This may allow the identification of the vulnerable plaques before they rupture and may provide a way to target pharmacological intervention to reduce or prevent cardiovascular disease.
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