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Reproducibility of black-blood coronary vessel wall MR imaging

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Purpose. New magnetic resonance imaging (MRI) methods can provide high spatial resolution images of the coronary artery wall, and statistically significant differences in coronary vessel wall thickness between atherosclerotic disease patients and control subjects have been shown. The aim of this study is to assess inter-study reproducibility (i.e., repeatability) of the cross-sectional 2D coronary vessel wall MRI using a black-blood technique. *Methods and Results.* Twelve healthy adult subjects were studied with the use of a commercial 1.5 T CMR system. A double inversion recovery fast spin-echo (FSE) sequence (black blood) was used. Each subject was scanned twice on different days. The mean RCA lumen area difference between study 1 and study 2 was 0.004 mm^2, and the coefficient of repeatability (COR) was ± 0.06 mm^2. The mean RCA wall thickness difference between study 1 and study 2 was 0.02 mm, and the COR was ± 0.39 mm. *Conclusion.* Cross-sectional coronary vessel wall imaging with 2D double-IR FSE is highly reproducible for serial evaluation of coronary vessel walls and atherosclerotic coronary artery disease.

Key Words: Vessel wall imaging; Coronary MRA; Black blood imaging; Reproducibility

1. Introduction

Coronary angiography is the method of choice for the imaging of coronary vasculature. However, it only demonstrates the degree of luminal narrowing. During the early stages of atherosclerotic disease, the coronary vessel wall thickens with little change in the diameter of the vessel lumen, referred to as "positive remodeling" or the "Glagov effect" (1). Moreover, acute coronary syndromes are frequently caused by rupture of the mild-to-moderately stenotic vulnerable plaques (2–4). Detection of anatomical changes in the coronary vasculature due to positive remodeling of the arterial wall may provide the basis for pharmacological therapy and lifestyle modifications to prevent future cardiovascular events in early atherosclerosis. Coronary angiography is not useful for early detection of atherosclerotic disease due to the invasive nature of the examination and because positive remodeling is not detected by coronary angiography.

Use of MRI for noninvasively imaging the coronary artery vessel wall and assessing plaque composition has been demonstrated (5–9). Despite the challenges of cardiac and respiratory motion, small size and tortuosity of coronary arteries, high-resolution MRI has been able to provide submillimeter spatial resolution images to detect coronary wall thickness associated with atherosclerosis. The so-called "black blood" techniques using double inversion-recovery (DIR) fast spin-echo (FSE) are particularly promising in this regard as they maximize the signal difference between the static vessel wall and the flowing blood, which is intentionally suppressed (5–9). Using this technique, statistically significant differences in coronary vessel wall thickness between atherosclerotic disease patients and control subjects have been reported (6–8).

Inter-study reproducibility of measuring vessel wall thickness and lumen size of the coronary artery wall using MRI has not been assessed. The aim of this study was to determine inter-study reproducibility as well as reader reproducibility for assessment of the coronary artery wall by MRI.

2. Methods

2.1. *Subjects*

We scanned 12 healthy subjects (mean age 37, range 24–50, 10 men) with no history of coronary artery disease after obtaining informed consent as part of a protocol approved by the institutional review board. Each subject underwent two

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MRI scans. Minimum and maximum time between the two scan were 24 hours and 11 days, respectively. MRI studies were performed in a 1.5 T whole-body MRI system (Signa CVi, General Electric Medical Systems, Waukesha, WI) equipped with 40 mT/m gradients. A four-element anterior-only phased-array coil was used for signal reception. ECG gating was performed to minimize effects of cardiac and vessel motion and all subjects were instructed to suspend breathing at end-expiration to minimize physiological motion artifacts. Subject heart rates ranged from 60 to 84 beats per minute. Of the 12 subjects, the scan on one volunteer could not be completed due to claustrophobia. Inspection of the ECG for two other subjects did not show a rest period in mid or late diastole, and the right coronary artery (RCA) was not well visualized in these subjects. Thus, images from nine subjects were used for subsequent analysis.

2.2. *Imaging protocol*

Sagittal and axial scout images were acquired using a gradient-echo sequence and were used to verify coil positioning and to prescribe the volume containing the RCA. From an axial image, a slice was prescribed along the vertical long axis of the right ventricle between the midpoint of the tricuspid valve and the apex of the right ventricle. A gated, fast, 2D, single slice, cine steady-state free precession (SSFP) sequence was used and resulted in cine images of the proximal and distal cross-sectional view of the RCA. These images were used to identify the range of motion of the RCA during the cardiac cycle and to select the optimum delay time corresponding to the rest period in mid or late diastole. A 3D volume containing the RCA was then acquired using a breath-hold SSFP bright blood angiogram (10) with the following imaging parameters: TR/TE = 4.7/1.9 ms; Matrix = 256 × 192; FOV = 28 × 22.4 cm; flip angle = 65°; NSA = 0.5; slice thickness = 2 mm; number of partitions = 12. No contrast agent was used. A set of three slices with a separation of 1 cm between them, and the first slice approximately 1 cm from the origin of the RCA was planned from these images. Thus, the most distal image acquired was at a distance of 4 cm from the origin. The vessel wall images were acquired using a gated, 2D FSE sequence with a double inversion pulse preparation for nulling the blood and suppressing the signal from the myocardium (11). A spectrally selective fat suppression pre-pulse was also used to increase the contrast between the vessel wall and the epicardial fat. The imaging parameters were: TR = 2R–R; TE = 5.1 ms; Matrix = 256 × 224 with zero filling to 512 × 448; FOV = 18 × 13.5 cm; ETL = 16; slice thickness = 3 mm. The total examination scan time ranged from 25–47 min (mean: 34 min).

2.3. *Data analysis*

The images depicting the vessel cross-sectional views were analyzed offline using custom software (CINE Tool, GE Medical Systems). Since the prescription between scan 1 and scan 2 could not be matched perfectly, only the image pair between the two scans that best matched each other based on anatomical landmarks was analyzed. The images were zoomed to magnify the vessel boundaries. The outer and inner boundaries of the vessel wall were traced manually by two observers (TH and MM) on each image using freehand regions of interest. The software reported the area of the outer and the inner regions of interest. The lumen area (equal to the inner area) and the vessel wall area (equal to the difference between the outer and the inner area) were then calculated. The lumen diameter and mean vessel wall thickness were also calculated assuming a circular cross-section.

Image signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were measured from each image as follows: three circular regions of interest were placed in the bright vessel wall, in the background air in front of the chest wall, and in

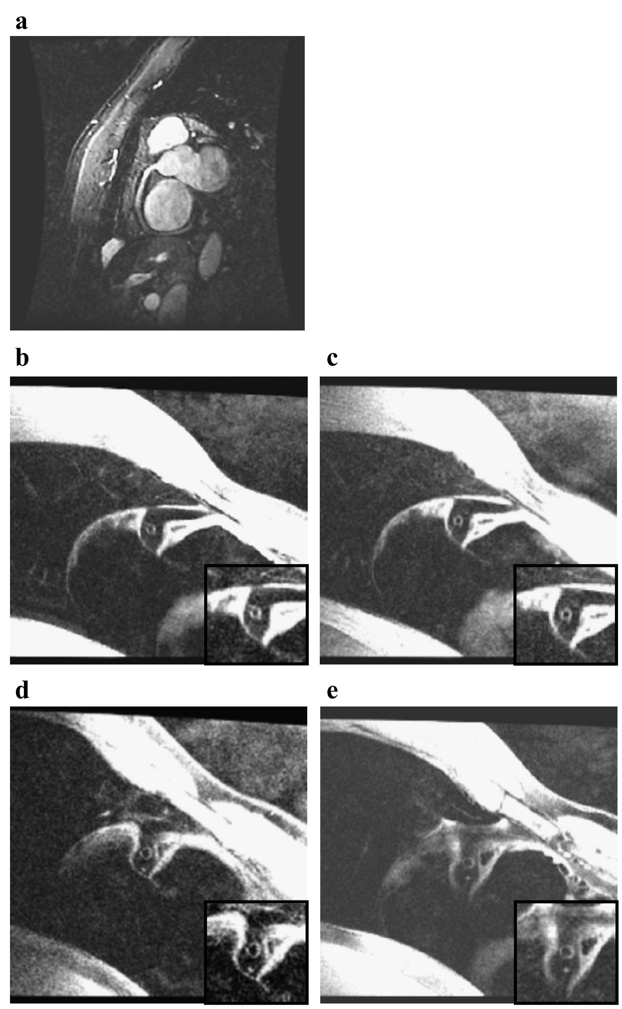

Figure 1. (a) One slice from a 3D MRA view of the RCA from one subject. (b,c): RCA vessel wall images from two studies from the same subject. (d,e): RCA vessel wall images from two studies from another subject.

the suppressed epicardial fat adjacent to the vessel wall. These regions of interest yielded respectively the vessel signal S, the noise N (from the standard deviation of the pixels in the noise ROI), and the fat signal S_{fat}. SNR and CNR were then calculated as: SNR = S/N, and CNR = $(S - S_{fat})/N$.

The resulting data from the two scans and from the two observers were analyzed using Pearson's correlation and Bland-Altman reproducibility analysis (12). Coefficient of repeatability (COR) for 95% confidence intervals (using 1.96 times the standard deviation of the differences) is reported.

3. Results

3.1. *Image quality*

Overall, there was excellent blood and epicardial fat suppression, with well-defined borders between vessel wall and suppressed epicardial fat and between vessel wall and blood (Fig. 1). The mean signal-to-noise ratio (SNR), and standard deviation of the SNR were 9.8 and 3.07, respectively. Mean contrast-to-noise ratio (CNR), and standard deviation of the CNR were 5.74 and 2.11, respectively.

3.2. *Inter-observer variability*

Figures 2a and 2b show Bland-Altman plots for inter-observer differences for the RCA vessel wall thickness and lumen area, respectively. The mean RCA wall thickness measured by observers 1 and 2 were 1.066 mm (range 0.65–1.42 mm) and 1.135 mm (range 0.63–1.74 mm), respectively. The mean RCA wall thickness difference between observer 1 and observer 2 was 0.07 mm, and COR was ±0.28 mm (Fig. 2a). Pearson correlation coefficient between observer 1 and observer 2 was 0.87. For RCA lumen area, the difference

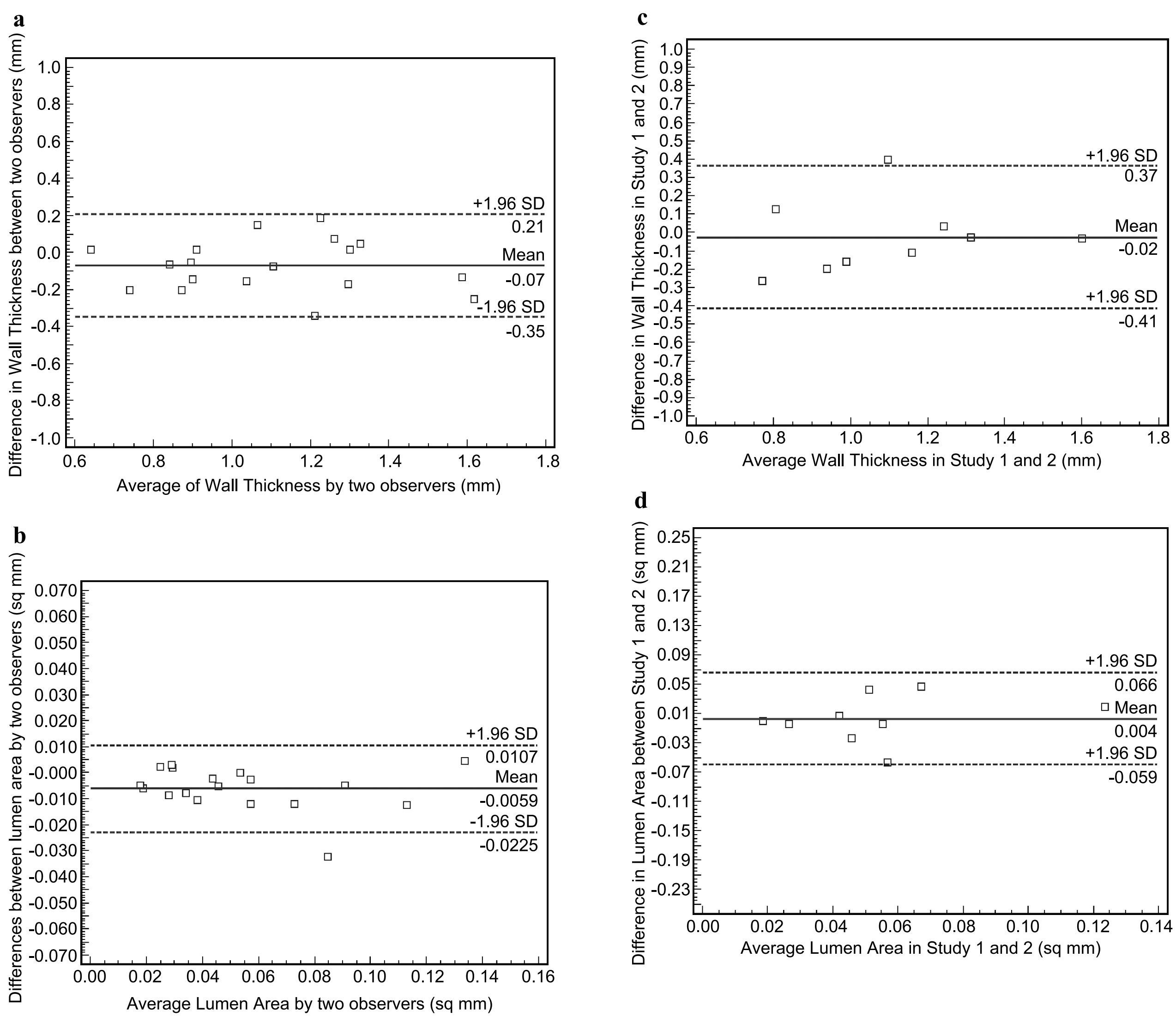

Figure 2. Bland-Altman plots for inter-observer and inter-study repeatability of RCA wall thickness and lumen area measurements.

between observer 1 and observer 2 was 0.0059 mm^2, and the COR was ± 0.0166 mm^2 (Fig. 2b). Pearson correlation coefficient between observer 1 and observer 2 was 0.97.

3.3. *Inter-study reproducibility*

The average wall thickness and lumen area from the two observers was compared between study 1 and study 2 using Bland-Altman analysis and the results are shown in Figs. 2c and 2d. The mean RCA wall thickness difference between study 1 and study 2 was 0.02 mm, and the COR was ± 0.39 mm (Fig. 2c). The mean RCA lumen area difference between study 1 and study 2 was 0.004 mm^2, and the COR was ± 0.06 mm^2 (Fig. 2d).

4. Discussion

MRI can provide high spatial resolution images of the RCA wall in normal and diseased human arteries, and statistically significant differences in coronary vessel wall thickness between atherosclerotic disease patients and control subjects has been shown (6–8). However, the inter-study repeatability of RCA vessel wall MR imaging has not previously been determined. Our study showed that there is high inter-study repeatability and low inter-observer variability for both right coronary vessel wall thickness and right coronary artery luminal area in healthy subjects. Although it will be important to extend these results by imaging the other major vessels of the coronary tree, it should be pointed out that if presence of calcium in the RCA is used as a surrogate marker of atherosclerosis, then it is justifiable to look at the vessel wall measurements from RCA alone.

An animal study showed an excellent correlation between coronary wall images and histopathology sections for average wall thickness (5). However, there is small but consistent overestimation of mean wall thickness and vessel wall area by MRI in comparison to histopathology (5). This overestimation may relate to shrinkage of the vessel during histopathologic preparation (5) and excluded adventitial layer during IVUS measurement (7). The main reasons for overestimation are the lower in-plane and through-plane spatial resolution of MRI, and residual respiratory and cardiac motion during scanning (6, 7, 9). Incomplete blood suppression of slow flowing blood located close to the vessel wall, may mimic signal from the vessel wall, thereby causing an additional overestimation of the true vessel wall thickness, but this effect is expected to be small, because double IR prepulse was optimized to decrease the blood signal (6, 13).

Low-resolution images tend to overestimate the arterial wall thickness and underestimate the lumen area by increasing the partial volume effect (8, 9, 14). The in-plane spatial resolution in this study was 0.7 × 0.6 mm. This may result in a vessel wall area overestimation of < 45% (between 30%–45%) for a normal coronary artery wall (14). One method to increase spatial resolution is to lengthen the breath hold duration so that additional phase encode steps could be obtained. Longer breath-hold times, however, may not be tolerable by certain patients. Free breathing coronary vessel wall imaging with navigator sequences may be used to increase spatial resolution in both cross-sectional and long-axis coronary vessel wall imaging (2, 8). A limitation of our study is that only healthy volunteers were imaged in this study. When extending the results to the imaging of patients, it may be necessary to use navigator sequences, particularly in less cooperative patients.

Through-plane resolution in coronary vessel wall imaging varied between 3–5 mm in previous researches, which causes volume averaging and contributes to an overestimation of the coronary wall thickness. In this study, the slice thickness was 3 mm. Thin slice thickness decreases partial volume effects. However, it causes a reduction in SNR. 3D acquisition techniques (8), higher magnetic strengths (3T), and prone position (15) provide higher SNR, and could further improve accuracy of the coronary artery vessel wall imaging.

Study limitations include two subjects who had no discernible rest periods of coronary wall motion, and the RCA walls of these subjects were not seen clearly. The coronary artery wall is clearly seen only when the images are obtained in a short period of decreased motion (“rest period”) in mid or late diastole (16). A short acquisition window and subject-specific trigger delay are necessary to decrease the blurring effects of the residual cardiac motion (16, 17). The rest period is inversely proportional to the heart rate so that the success rate of coronary wall imaging is likely to be low for tachycardiac subjects. In addition, only the right coronary artery was assessed. The right coronary can frequently be imaged in a single oblique imaging plane, which decreases the duration of the MRI examination. Finally, we evaluated only normal subjects. If patients with documented coronary atherosclerosis were included, mean wall thickness would be higher than we have observed. The variation we observed may thus perhaps represent a worse case scenario since the coronary walls in these healthy subjects were presumably thin and without significant atherosclerotic disease.

5. Conclusion

Cross-sectional coronary artery wall imaging with breath hold 2D double MR FSE is a reproducible method and may be suited to serial evaluation of the coronary vessel wall and atherosclerotic coronary artery disease.

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