

## Technical Note

# Intra- and Interstudy Reproducibility of Coronary Artery Diameter Measurements in Magnetic Resonance Coronary Angiography

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**Purpose:** To determine the intra- and interstudy reproducibility of right coronary artery diameter assessment using serial magnetic resonance (MR) coronary angiography.

**Materials and Methods:** Two-dimensional (2D) navigator-gated segmented fast low angle shot (FLASH) images of the proximal right coronary artery were acquired three times in 11 healthy volunteers, the first two times in the same study session and the third time after repositioning the subject in the scanner. Coronary artery diameters were determined using automated segmentation software and intra- and interstudy reproducibility calculated as the standard deviation (SD) of the signed differences between measurements within and between study sessions, respectively. The reproducibility of the segmentation software was determined by repeated analysis of each individual scan.

**Results:** One subject was excluded from the study due to poor-quality images. In the remaining 10 subjects, the mean ( $\pm$  SD) intrastudy difference in coronary artery diameters was  $-0.05 \pm 0.12$  mm, a value that is very similar to between-frame (same-film) differences reported in quantitative coronary angiography (QCA). The mean ( $\pm$  SD) interstudy difference in coronary artery diameters was  $0.16 \pm 0.43$  mm, although this was greatly skewed by one subject with poor image plane repositioning. Excluding that subject resulted in a mean ( $\pm$  SD) interstudy difference of  $0.04 \pm 0.20$  mm. The reproducibility of the segmentation software was excellent, with the mean difference between repeat analyses of the images being  $0.00 \pm 0.03$  mm.

**Conclusion:** The intrastudy variability of coronary artery diameter measurements is low, potentially allowing MR coronary angiography to be used as a tool for the noninvasive assessment of serial changes following pharmacological intervention. A major contributing factor to this is the

high reproducibility of the segmentation software. Interstudy variability is approximately three times the intrastudy variability.

**Key Words:** reproducibility; coronary; diameter; magnetic resonance; angiography

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ENDOTHELIAL VASODILATOR DYSFUNCTION is an early marker of atherosclerosis, which is assessed by the vessel diameter changes induced by pharmacological intervention (1). Patients with angiographically normal coronary arteries and those with atherosclerosis both show a vessel diameter increase of approximately 25% in response to the endothelium-independent vasodilator nitroglycerin. However, in response to the endothelium-dependent vasodilator acetylcholine, those with normal arteries show a dose-dependent diameter increase (typically to a maximum of 10%), whereas those with atherosclerosis exhibit paradoxical vasoconstriction, the degree of which is dependent on the severity of the disease (2). The prognostic significance of endothelial dysfunction has recently been shown in patients both with (3,4) and without (4) coronary artery disease, and a number of trials have documented improvements in function in response to lipid-lowering therapies and lifestyle modification (1).

Vessel diameter is generally assessed in the catheter laboratory using quantitative coronary angiography (QCA) or intravascular ultrasound (IVUS), both of which are invasive techniques with an associated overall complication rate of 0.8% and a small, but significant, mortality rate of 0.12% (5). Compared to these techniques, the spatial resolution of magnetic resonance (MR) coronary angiography (6) is limited and imaging is complicated by respiratory and cardiac motion, both of which result in image blurring. Despite these drawbacks, as a noninvasive technique, MR would be a very attractive alternative for assessing coronary artery dimensions. The lack of x-radiation is also highly beneficial, as repeat investigations would not be limited by ionizing radiation regulations and could be performed, as required, within the framework of the

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local ethics committee. Although the vasodilatory effect of nitroglycerin has been demonstrated with MR imaging (MRI) in conference proceedings (7), no reports on the inter- and intrastudy variabilities of the technique have been found in the literature, and consequently, its reproducibility is unknown. The purpose of this study, therefore, is to determine the within- and between-study reproducibility of MR coronary angiography for the assessment of coronary artery diameter.

## MATERIALS AND METHODS

This study was carried out on a Siemens Sonata scanner with gradients having a maximum strength of 40 mT/m and maximum slew rate of 200 mT/m/msec on each axis independently.

Eleven healthy subjects (seven male) were studied supine with a 20-cm-diameter loop surface coil positioned anteriorly on the chest. The mean age was 32.3 years (range = 20–47 years), and all subjects gave informed consent, as required by the local ethics committee. Vessel diameter measurements were made from images acquired transaxial to the vessel using double-oblique angulation, as follows. Multiple (typically three) contiguous low-resolution ( $1.1 \times 2.2 \times 7$  mm) transverse images were acquired during free breathing with a right hemidiaphragm navigator and an acceptance window of  $\pm 3$  mm positioned around the end-expiratory pause position. From these, the path of the right coronary artery in the atrio-ventricular groove was determined and an in-plane image piloted showing a length of the right coronary artery and its origin on the aortic root. Each low-resolution image took approximately 30 seconds to acquire. High-resolution imaging of the vessel perpendicular to the imaging plane was then performed on a straight section of artery 10–20 mm from its origin, the exact position being determined by the vessel tortuosity. This careful positioning was necessary to reduce partial-volume effects at the vessel boundary. The distance from the origin of the artery on the aortic root was noted for accurate repositioning of the high-resolution image plane in subsequent scanning sessions. For the high-resolution studies, the navigator acceptance window was reduced to  $\pm 2$  mm. The imaging field of view (FOV) was 125 mm with a matrix size of  $256 \times 256$  pixels, resulting in an in-plane resolution of  $0.49 \times 0.49$  mm. The slice thickness was 6 or 7 mm, depending on the image signal-to-noise ratio (SNR), and fat suppression was achieved using a chemical-shift-selective prepulse. The sequence echo time (TE) was 5.7 msec, and the acquisition of five views per segment resulted in an acquisition window of 65 msec. This was positioned in mid-diastole when the heart was relatively stationary, as determined for each subject by a trueFISP cine acquisition in the four-chamber view. The imaging time for the high-resolution studies was approximately two minutes, assuming a respiratory efficiency of 40%. Two high-resolution images were acquired and the subject then removed from the scanner. The subject was then repositioned and a further high-resolution image acquired after repiloting the image plane. The high-resolution image plane was positioned the same distance from the origin of the artery on the

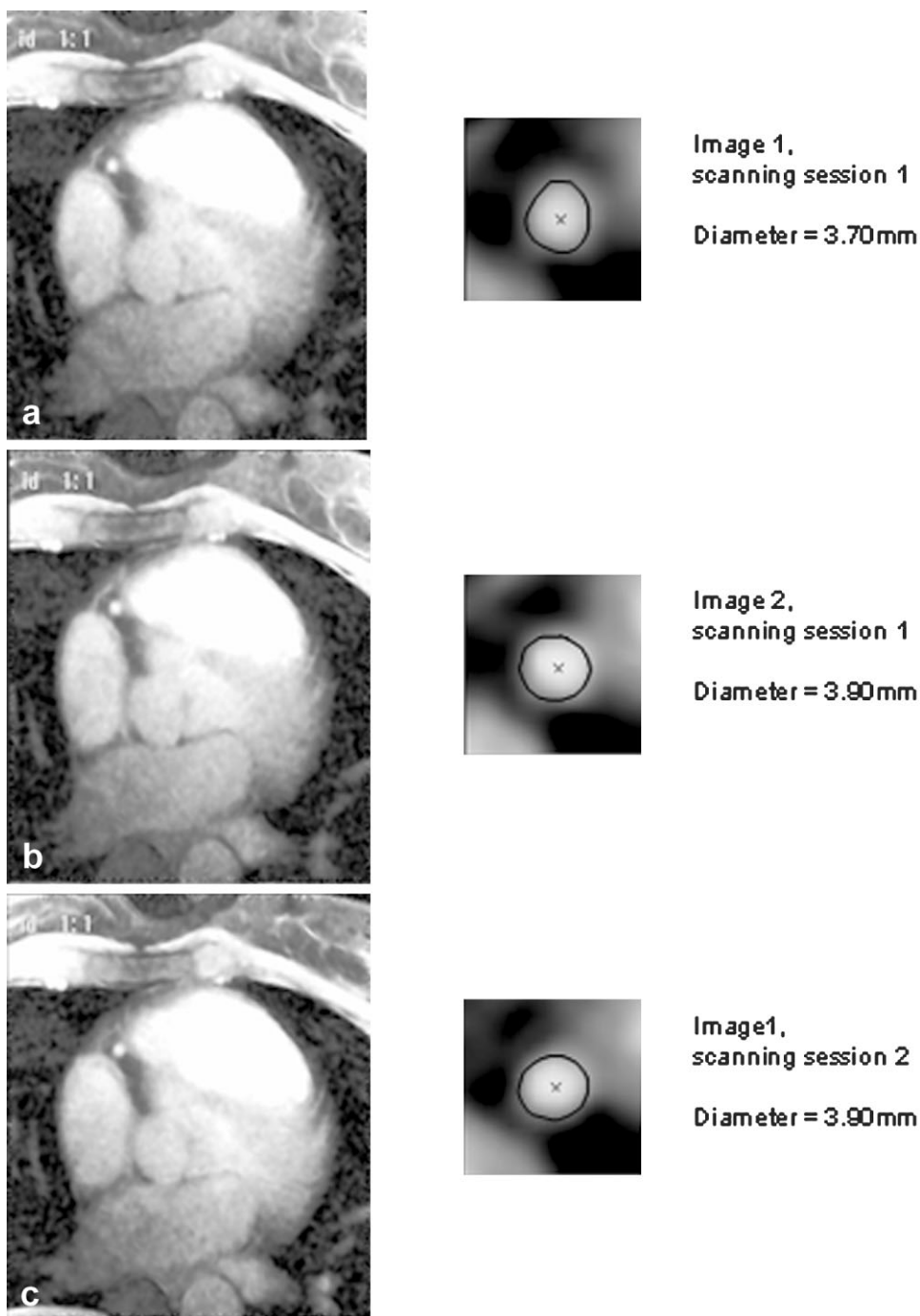
aortic root as in the first scanning session. In three of the subjects, two images were acquired in the second scanning session, which allowed the within-study variability to be assessed for both sessions. Heart rate was noted in each scanning session.

## Image Analysis

On each high-resolution image on each subject, the coronary artery cross-sectional area was determined using an automated segmentation technique based on a statistical shape model (8). The model was trained using manually delineated vessel contours, demarcated by an experienced observer on 65 images from healthy subjects. Each contour was uniformly sampled with arc-length parameterization and the set of labeled samples aligned to the local reference coordinates using iterative linear least squares. Principal component analysis was then applied to the training set to derive a statistical point distribution model that represented a robust parametric deformable structure that captured the plausible variations of the training set. The model deformed to fit unseen shapes in a new image using specific constraints found in the training process. Structural adaptive anisotropic filtering (9) of the image prior to segmentation minimized the sensitivity of the results to the initial user-defined starting point. Unlike a conventional isotropic filter, such as the Gaussian kernel, this filter provided a satisfactory result even in the low SNR cases, while still preserving structural features well. To aid the precision of the segmentation process, each image was zoomed by a factor of six (equivalent to zero filling the raw data), resulting in a pixel size of 0.081 mm. The images were then histogram equalized and the user required to mark the approximate center of the vessel with the cursor. Once the initial pose of the vessel model was established, local deformation was applied by following the active shape model approach. The area of the extracted contour was then determined analytically and the vessel diameter calculated, assuming that the cross-sectional area was circular. This approach has been validated at different levels of SNR (3.4, 6.7, and 10.0) using coronary artery phantoms of different diameters (3.11, 3.67, and 4.55 mm), where repeat acquisitions were performed as the imaging FOV was shifted in 0.2-mm increments in first one, and then the other, in-plane direction. The accuracy of the technique, defined as the standard deviation (SD) of the differences between the actual and measured diameters as a percentage of the actual diameter, varied between 1% and 2%, depending on the vessel size and the SNR (8).

## Statistics

Intrastudy reproducibility in the coronary artery diameter was calculated as the SD of the signed differences in the vessel diameter measured in the two serial scans within a study session (10). Similarly, interstudy reproducibility was calculated as the SD of the signed differences between the vessel diameter as measured in the first scans in each of the two study sessions. To determine the reproducibility of the segmentation technique,



**Figure 1.** Example study in a subject with a 3.8-mm-diameter artery with segmented vessel boundaries and areas. **a,b:** acquired serially in the same scanning session. **c:** acquired in a second scanning session after repositioning the subject. Note the equivalence of the image planes in the two scanning sessions.

each high-resolution scan was analyzed twice and the variability determined as the SD of the signed differences between the two results.

## RESULTS

Of the 11 subjects, 1 was excluded from analysis due to very poor image quality in both scanning sessions, which resulted from a highly variable breathing pattern and poor navigator gating. In the remaining 10 subjects, the mean SNR in the high-resolution images was 6.4 (SD = 1.6, range = 4.4–12.3) and the mean vessel diameter was 3.8 mm (SD = 0.8 mm, range = 2.4–4.8

mm). There were no changes in heart rate between the two study sessions for any subject.

The segmentation software was highly reproducible with the mean ( $\pm$  SD) difference between repeat analyses of the high-resolution images being 0.0 mm ( $\pm$  0.03 mm), with 95% confidence limits of 0.06 and  $-0.07$  mm.

An example of a study on a typical vessel (diameter = 3.8 mm) is shown in Fig. 1. Table 1 shows the mean vessel diameter and the percentage difference in vessel diameter within and between scanning sessions for the 10 subjects included in the study. In nine of these subjects, the images acquired in each of the two separate scanning sessions were visually very similar, as in

Table 1  
Intra- and Inter-study Diameter Differences in 10 Healthy Subjects\*

Subject	Vessel diameter mm	Intra-study diameter difference		Inter-study diameter difference	
		%	mm	%	mm
1	2.4	-7.1%	+0.17mm	+6.5%	+0.16mm
1 (session 2)	2.4	-3.1%	-0.07mm	-	-
2	3.1	+0.3%	+0.01mm	-2.4%	-0.07mm
2 (session 2)	3.1	-1.0%	-0.03mm	-	-
3	3.1	-6.8%	-0.21mm	+8.6%	+0.27mm
4	3.6	-7.1%	-0.26mm	+0.4%	+0.01mm
5 (Fig. 2)	3.6	-0.1%	-0.00mm	<b>+37.8%</b>	<b>+1.25mm</b>
6 (Fig. 1)	3.8	+5.3%	+0.20mm	+5.1%	+0.19mm
7	4.4	-0.7%	-0.03mm	+6.0%	+0.26mm
8	4.7	+0.6%	+0.03mm	-3.5%	-0.16mm
9	4.7	+1.2%	+0.06mm	+0.4%	+0.02mm
9 (session 2)	4.7	-0.9%	-0.04mm	-	-
10	4.8	-2.2%	-0.11mm	-6.7%	-0.32mm
Mean $\pm$ SD	3.8 $\pm$ 0.8	-1.7 $\pm$ 3.6%	-0.05 $\pm$ 0.12mm	5.2 $\pm$ 12.5% 1.6 $\pm$ 5.2% <sup>a</sup>	0.16 $\pm$ 0.43mm 0.04 $\pm$ 0.20mm <sup>a</sup>

\*In three subjects (1, 2 and 9) multiple acquisitions in the second scanning session enabled intra-study variability to be calculated for both sessions.

<sup>a</sup>Excluding subject 5, see Fig. 2 and text.

The inter-study diameter differences in the subject with poor image plane repositioning (subject 5) are highlighted in bold.

the example in Fig. 1. However, in one subject (subject 5), the positioning of the image plane in the second scanning session was poor, with the vessel being clearly oblique to the imaging plane, as shown in Fig. 2. This resulted in a greater measured vessel diameter and a large interstudy percentage difference (highlighted in bold in Table 1). The mean ( $\pm$  SD) intrastudy percentage difference in diameters for the group is  $-1.7 \pm 3.6\%$ . The mean ( $\pm$  SD) interstudy percentage change in diameter is  $5.2 \pm 12.5\%$ , although this is greatly skewed by subject 5. Excluding that subject, the mean ( $\pm$  SD) interstudy percentage change is  $1.6 \pm 5.2\%$ .

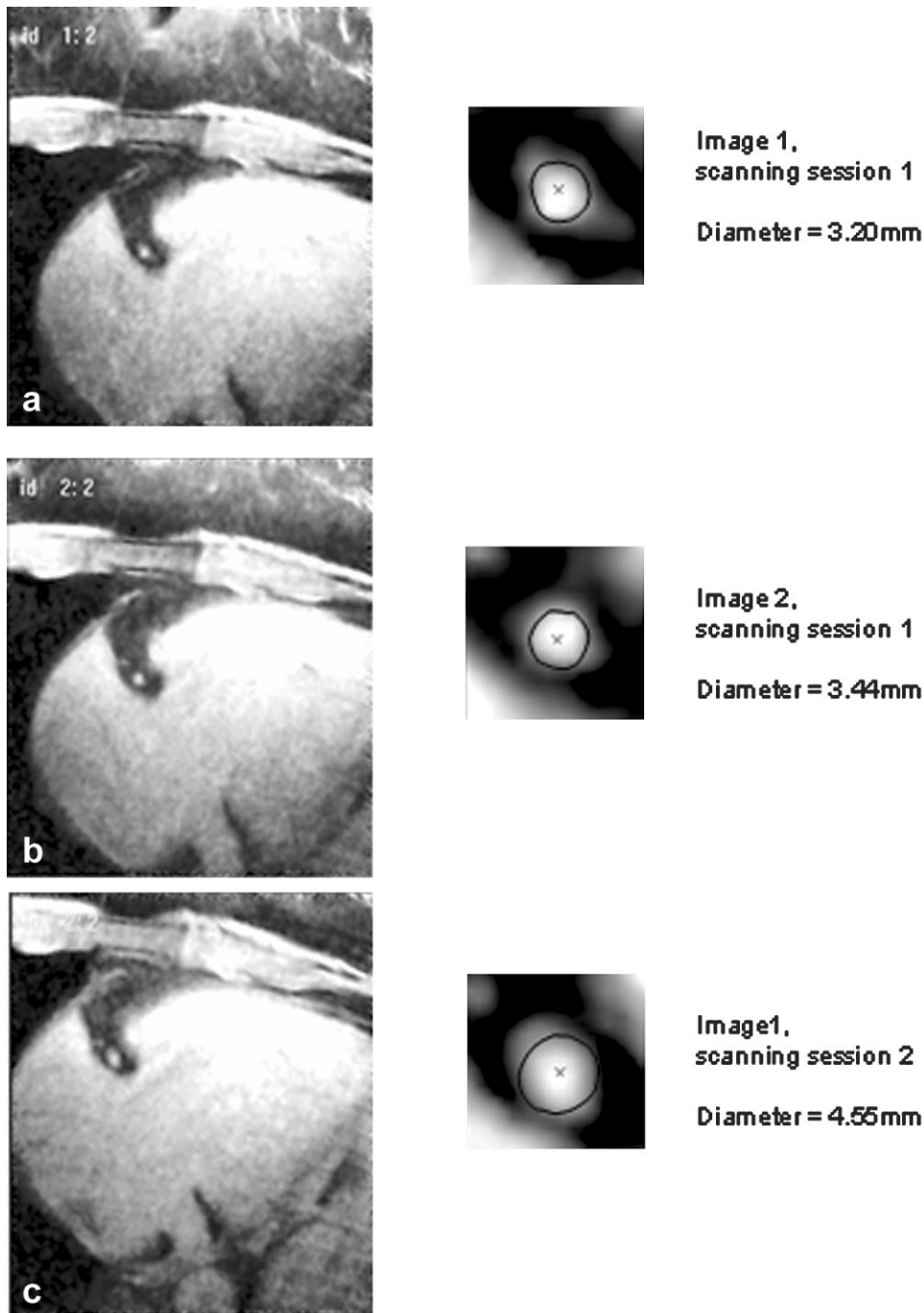
The results of Bland-Altman analysis for within-study session and between-study session diameter differences are shown in Fig. 3. For serial acquisitions within a study session, the mean difference in diameters is  $-0.05 \pm 0.12$  mm, with 95% confidence limits of 0.19 and  $-0.28$  mm. For acquisitions in different studies sessions, the mean difference in diameters is  $0.16 \pm 0.43$  mm with 95% confidence limits of 1.02 and  $-0.69$  mm. Excluding the outlying data point (subject 5, Fig. 2), the mean difference in diameters between studies is  $0.04 \pm 0.20$  mm, with 95% confidence limits of 0.44 and  $-0.36$  mm.

## DISCUSSION

Good-quality data were obtained in 10 (91%) of the 11 subjects studied, with the SD of the differences between consecutive scans in the same study session (intra-study reproducibility) being 0.12 mm. This compares well with QCA, where the SD of the differences measured in the same session but on different frames has been reported as 0.129 (11) and 0.22 (12) mm and is better than IVUS, where the SD of the diameters measured in repeated serial acquisitions is 0.345 mm (13). As such, it should be feasible to use serial MRI to de-

termine vessel diameter response to vasodilators, as used in studies of endothelial function (1), or to other pharmacological interventions (14). Data extracted from a previous conference proceeding have shown similar within-study diameter differences ( $0.05 \pm 0.12$  mm) with MRI, although in that case, successful imaging was obtained in only 7 (30%) of a group of 23 healthy volunteers (7).

When comparing diameters measured in two separate sessions, the results were considerably skewed by one subject in whom the reproducibility of the image plane positioning was poor. In this subject, the vessel is clearly in oblique cross section in the second session and a further attempt should have been made to reproduce the original plane. It is therefore arguable that this data should be rejected, and it clearly highlights the care required and the difficulties involved with repeat scanning sessions. The SD of the differences between sessions was 0.20 mm if the subject was excluded and 0.43 mm if included. For QCA, the SD of the differences obtained between sessions separated by less than a month is 0.219 mm (11). For repeated acquisitions in the same session but after changing the x-ray system settings and repositioning the views, an SD of the differences of 0.34 mm has been quoted (12). The data quoted for QCA variability is 10 years old, and it might be expected that improvements may have been made in recent years. However, these values are still quoted as standard in current review articles (15), and more recent data are not available. The higher variability of the MR technique (if all subjects are included) reflects the obvious difficulties in reproducing the same two-dimensional (2D) image plane in different sessions. The lower variability for QCA is possibly due to the more consistent appearance of the vessel from session to session when it is viewed as a projection after contrast administration.



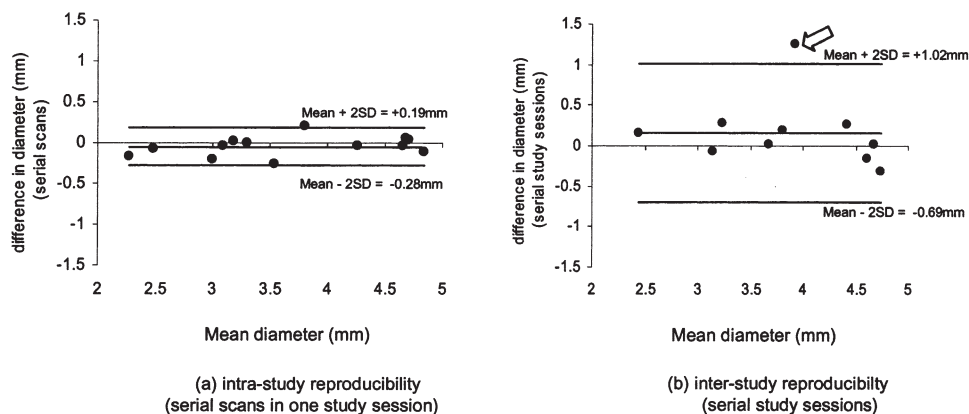
**Figure 2.** Study with poor interstudy variability (subject 5, Table 1). **a,b:** acquired serially in the same scanning session. **c:** acquired in a second scanning session after repositioning the subject. Note that despite the overall features of the image plane being similar in the two scanning sessions, the vessel is clearly oblique to the imaging plane in the second scanning session, resulting in an overestimate of vessel area.

In this study, segmented fast low angle shot (FLASH) was chosen as the imaging technique, as it is robust, and 0.49-mm in-plane resolution was relatively easily obtainable. Our initial choice of true fast imaging with steady state precession (FISP) (16) was impractical, since to obtain the high spatial resolution needed, the echo time was extended to a degree where reliability became a problem, with flow artifacts being frequently present. Dark-blood turbo spin-echo (17) was also considered but, in pilot examinations, proved to be less robust. If comparisons are to be made with IVUS and QCA, it is important to have an awareness of what is being imaged with the various techniques. QCA delineates the vessel lumen, whereas IVUS images the vessel

wall, the inner boundary of which demarcates the lumen. Dark-blood turbo spin-echo generally delineates the outermost extent of the vessel by imaging the high-intensity epicardial fat surrounding it, whereas segmented FLASH images both blood (lumen) and vessel wall with the blood signal being increased due to through-plane flow enhancement.

Navigator gating, rather than breath holding, was chosen as the method of respiratory suppression for this study, as it removed the limitation of needing to acquire the entire scan within the duration of a comfortable breath hold. It also removed problems of misregistration between scans due to different breath-hold positions. As we have seen, the majority of subjects

**Figure 3.** Bland-Altman analysis for intra- (a) and inter-study (b) reproducibility of coronary artery diameters. Note the outlying data point in b (arrow). The 95% confidence limits for the 10 subjects are  $-0.28$  to  $+0.19$  mm and  $-0.69$  to  $+1.02$  mm, respectively.



tolerated this well, although one had a highly irregular breathing pattern and failed to produce any good-quality data. This failure rate may be higher in the patient population where a combination of illness and anxiety may lead to respiratory control being poorer. The navigator acceptance window of  $\pm 2$  mm is slightly narrower than the 5-mm window typically used in coronary angiography studies and was chosen as a compromise between good respiratory control and respiratory efficiency. Real-time slice-following methods (18) were not implemented since accurate knowledge of the tracking factor (19), relating the motion of the coronary to that of the right hemidiaphragm, is highly subject specific (20) and difficult to obtain with accuracy.

All the studies performed were on the right coronary artery as in preliminary acquisitions, the image quality was found to be nearly always better than when imaging the left. There are several possible reasons for this. First, as the left coronary artery is further from the surface coil, the SNR is poorer than that for the right. Also, to avoid problems with wraparound with the small FOV, phase oversampling was required for the left artery, which extended the imaging time, potentially allowing more time for respiratory drift to develop. In addition, it is also likely that due to its location, the left coronary artery is more affected than the right by residual respiratory motion within the navigator window.

MR has the major advantages of being noninvasive and of not using ionizing radiation, and in this study, it has shown a similar reproducibility to QCA in serial acquisitions within the same study session. Of note, however, is that as the MR images are acquired over a period of approximately 2 minutes, they may be degraded if the heart rate is variable during the scanning period or if the heart rate is substantially increased with pharmacological intervention. The relatively long acquisition period also precludes the study of rapidly acting vasoactive agents. In addition, changes in coronary blood flow may also alter the degree of through-plane enhancement of the blood signal (while the vessel wall remains unchanged), and this may alter the appearance of the vessel and the area segmented. A further drawback is the relatively large slice thickness used—dictated by SNR considerations—which may result in partial-volume blurring of the vessel border. Lastly, it should also be taken into account that the

subjects studied here were healthy volunteers, and although the range of vessel diameters was large (2.4–4.8 mm), the absence of disease may have resulted in better image quality than would have been obtained in a population with coronary artery disease where image quality may be further compromised by poorer respiratory control (as noted earlier) and also by increased girth, which would result in reduced SNRs.

In conclusion, the reproducibility of diameter measurements on serial MR coronary imaging is very good and comparable with QCA. A large contributing factor to this is the very high reproducibility of the segmentation software, which eliminates the need for manual delineation of the vessel. A direct comparison of the results of MR and x-ray coronary angiography for assessing vessel diameter in the patient population will be undertaken as part of a larger study assessing coronary artery blood flow, for which ethics committee approval is currently being sought.

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