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Clinical utility of two-dimensional magnetic resonance angiography in detecting coronary artery disease

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Aims The accuracy of magnetic resonance angiography in detecting proximal coronary artery stenoses is unclear. We postulated that fast magnetic resonance angiography is capable of (1) imaging proximal coronary arteries, and (2) detecting stenoses of ≥50% of their luminal diameter.

Methods and results Thirty-five patients, referred for analysis of angina pectoris, underwent both conventional angiography and magnetic resonance angiography of coronary arteries. A fast k-space segmented gradient-echo technique was used during breath-holds. Two observers, blinded to the results of conventional angiography, independently analysed the magnetic resonance studies for (1) length of visualized segments, and (2) presence of signal voids indicative of stenoses. From 140 proximal arteries, 15 (11%) were excluded because of incomplete imaging or degraded image quality. Mean length of the visualized segments was 9 ± 4 mm for the left main, 62 ± 16 mm for the left anterior descending, 21 ± 9 mm for the left circumflex and 89 ± 32 mm for the right coronary artery. Sensitivity for detecting ≥50% luminal diameter stenoses was 0·00 for the left circumflex, 0·53 for the left anterior descending coronary artery, 0·71 for the RCA and 1·00 for the left main artery. Specificity varied from 0·73 for the left anterior descending coronary artery to 0·96 for the left circumflex. Inter-observer agreement was 0·90.

Conclusion Thus, segmented magnetic resonance angiography is capable of non-invasive imaging of proximal coronary anatomy. Its good accuracy in detecting left main coronary artery disease, intermediate accuracy in detecting right coronary artery and left anterior descending coronary artery stenoses, and low accuracy in detecting left circumflex lesions fit within a range of sensitivities and specificities found by others. Further technical advances are necessary to make the technique clinically robust.
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Key Words: Magnetic resonance imaging, coronary disease, angiography, arteries.

Introduction

Visualization of the coronary arteries with X-ray techniques during selective injection of a contrast agent has had a great impact on the diagnosis and treatment of coronary artery disease. No other technique proved to be capable of directly visualizing the coronary arteries and depicting luminal stenoses. Although the clinical value of X-ray coronary angiography is beyond dispute, its (small) associated risks[1], the use of ionizing radiation, the necessary hospitalization and the inherent expense have been the impetus for investigation of novel diagnostic techniques that potentially provide the same or more information without the drawbacks.

Magnetic resonance angiography is such a novel technique. With the advent of fast imaging techniques, problems associated with cardiac and respiratory motion have been successfully dealt with. The application of these techniques to the imaging of coronary arteries has recently been reported[2–9]. However, the clinical value of magnetic resonance angiography in the detection of coronary artery disease is still uncertain. Only two full-text reports have been published on the accuracy of fast magnetic resonance angiography in detecting proximal coronary artery stenoses[10,11]. There is little consistency between the results of these two studies. Manning *et al.* were the first to report on the subject and found the sensitivity and specificity of the technique to be as high as 90% and 92%, respectively[10]. In a later study by Duerinckx *et al.* distinctly lower

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values were reported: sensitivity varied from 0–55% for 'probable' detection and 0–31% for 'certain' detection[11]. More data are needed to determine the clinical value of this promising technique. In this study we present the results of our experience.

We postulated that fast magnetic resonance angiography is capable of: (1) imaging the proximal coronary arteries, and (2) detecting significant (≥50% of the luminal diameter) coronary artery stenoses. This hypothesis subsequently was tested in a prospective, blinded study in a group of patients referred for cardiac catheterization and conventional X-ray coronary angiography.

Methods

Patients

Informed consent to perform magnetic resonance angiography of the coronary arteries was obtained from patients referred for elective conventional coronary angiography because of angina pectoris. Exclusion criteria were atrial fibrillation, an indwelling pacemaker, presence of intracranial vascular clips, severe claustrophobia, and unstable angina pectoris or myocardial infarction within the last 3 months. When no outpatient could be scheduled at times that the magnetic resonance system was available for cardiac magnetic resonance angiography, a patient from the ward was referred for imaging. The investigators performing the magnetic resonance angiography were unaware of the results of conventional X-ray coronary angiography. A total of 35 patients was investigated (27 men, eight women). Mean age was 58 ± 10 years (range 34–76 years). The mean interval between conventional coronary angiography and magnetic resonance angiography was 15 ± 8 days (range: 0–29 days). A short history was taken to be sure that no coronary events had occurred between the two investigations. All studies were performed in accordance with guidelines of the Hospital Committee on Medical Ethics and Clinical Investigations.

MR angiography

Imaging was performed on a whole-body imaging system (Magnetom SP, Siemens Medical Systems, Erlangen, Germany), operating at 1·5 T. A standard circularly polarized radiofrequency receiver coil was used. Patients were studied in the prone position, with the heart above the surface coil. Signal acquisition was electrocardiographically (ECG) triggered, and gated to mid-diastole. A flow-compensated gradient echo sequence with incremental excitation flip angle (a= 22–90°) and k-space segmentation was used, with an echo time of 7·0 ms and a repetition time of 12·6 ms. The principles of this technique have been described[4]. Field of view was 260 × 260 mm^2 and matrix size 256 × 140 or 256 × 144, resulting in an in-plane spatial resolution of 1·8 × 1 0 mm^2. Slice-thickness was 4 mm. As a standard, nine phase-encoding steps per cardiac cycle were obtained (data acquisition window: 113 ms), resulting in a scan time of 16 cardiac cycles per image. If a patient's RR interval was less than 800 ms, seven phase-encoding steps per cardiac cycle were performed in order to reduce the window of data acquisition in mid-diastole to 88 ms; scantime then changed to 20 cardiac cycles. One fat-selective saturation pulse per cardiac cycle was applied before the imaging pulse train, to suppress the strong signal from epicardial fat surrounding the coronary arteries. The acquisition was performed during a breath-hold in end-expiration. Before the acquisition, several minutes were dedicated to instructing the patient how to perform end-expiratory breath-holding. Patients were video-monitored and each acquisition was only started when the patient was seen to have completed expiration and when the respiratory variation in the recorded ECG signal had disappeared.

Imaging protocol

In all patients, a standard imaging protocol was used, based on preliminary work. First, a series of 1 mm overlapping parallel transverse images was obtained at the level of the aortic root, followed by series of overlapping oblique images perpendicular to the transverse plane and oriented through the left and right atrioventricular grooves, and through the interventricular groove. We have previously shown that the proximal epicardial coronary arteries may be reliably imaged in this set of images[12]. Total imaging time amounted up to 60 min on average.

Image analysis

For analysis the sets of parallel, overlapping images were mounted in oscillating cine-loops to optimize appreciation of the continuity of the coronary artery segments. The patient studies were recorded without patient data in random order on VHS videotape. Both cine-loops and still frame images on hard copies were reviewed. All studies were analysed independently by two observers, who were both blinded to the results of conventional coronary angiography and to the results obtained by the other observer. For each patient study the length of the coronary artery segment that had been visualized was measured and the presence of stenoses within this segment assessed. A vessel was judged to be significantly stenosed if a focal area of marked intraluminal attenuation or loss of signal was present on the magnetic resonance angiogram. When in a cine-loop signal loss was seen to occur at the site of contiguity between segments visualized on two consecutive parallel images, a positive score was only assigned when signal loss occurred at the same site in the second perpendicular set of images depicting the same artery. Analysis was performed at two different levels of confidence. With level A, a positive score was assigned to coronary arteries which were judged to contain 'probably' a significant stenosis, i.e. when partial signal loss was detected. Analysis at confidence level B, assigned a positive score only to coronary arteries with focal complete signal loss, which was judged to represent 'certainly' significant stenosis. The results of magnetic resonance angiography were compared to those of conventional angiography.

In an additional analysis, sensitivity and specificity of the technique in the detection of stenoses were calculated at three different cutoffs of stenosis severity (≥50%, ≥70% and ≥90% luminal diameter reduction) on the conventional angiogram.

Conventional X-ray coronary angiography

Conventional X-ray contrast coronary angiography was performed by the Judkins technique. The images were all interpreted by consensus by two cardiologists from the cardiac catheterization laboratory, who were blinded to the magnetic resonance angiography findings. The reports included the presence, severity and site of the angiographic coronary artery stenoses. A stenosis was considered to be haemodynamically significant when luminal diameter reduction was ≥50%. Stenoses with a luminal diameter reduction of ≥70% and ≥90% were separately specified to be included in the additional analysis assessing the influence of stenosis severity on the accuracy of magnetic resonance lesion detection.

Results

In all patients both conventional X-ray coronary angiography and magnetic resonance angiography of the proximal coronary artery tree were performed. From the total of 140 major epicardial coronary arteries, eight arteries (6%) were excluded from analysis because they had not been imaged during magnetic resonance angiography due to time constraints or patient discomfort: three left anterior descending, three left circumflex, one right and one left main coronary artery. Another seven (5%) were excluded because severe degrading of magnetic resonance image quality had occurred, for which reason reliable analysis of these arteries was not deemed feasible (two left anterior descending coronary arteries, two left circumflex, three right coronary artery). Reasons for degraded images in these patients were either frequent ventricular or supraventricular ectopy, or triggering problems due to the induction of magnetohydrodynamic effects. Thus, 125 arteries were analysed: 34 left main coronary arteries, 30 left anterior descending coronary arteries, 30 left circumflex and 31 right coronary arteries.

Conventional coronary angiography

Conventional X-ray coronary angiography demonstrated proximal stenoses of ≥50% luminal diameter to be present in 35 arteries (28%). In Table 1 the distribution of these stenoses as well as the distribution in two subsets of arteries with a more severe degree of stenosis on the conventional angiogram are summarized.

***Table 1** Classification according to severity of stenosis*

	LMCA	LAD	LCx	RCA	All
≥50%	4	15	2	14	35
≥70%	2	11	2	11	26
≥90%	1	5	0	5	11

LMCA=left main coronary artery; LAD=left anterior descending coronary artery; LCx=left circumflex artery; RCA=right coronary artery.

***Table 2** Sensitivity, specificity and predictive values of 2D MRA in the detection of ≥50% coronary artery stenoses*

Artery	CL	Sens	Spec	PPV	NPV
LMCA	A	1·00	0·93	0·67	1·00
	B	0·75	0·97	0·75	0·97
LAD	A	0·53	0·73	0·67	0·61
	B	0·33	0·93	0·83	0·58
LCx	A	0·00	0·96	0·00	0·93
	B	0·00	0·96	0·00	0·93
RCA	A	0·71	0·82	0·77	0·78
	B	0·43	1·00	1·00	0·68

CL=confidence level; A='possible' stenosis; B='certain' stenosis (see text); sens=sensitivity; spec=specificity; NPV=negative predictive value; PPV=positive predictive value.

MR angiography

The mean length of the segments that were imaged was 9 ± 4 mm for the left main coronary artery, 62 ± 16 mm for the left anterior descending coronary artery, 21 ± 9 mm for the left circumflex and 89 ± 32 mm for the right coronary artery.

The sensitivity of the technique in detecting stenoses of ≥50% luminal diameter was 0·00 for the left circumflex, 0·53 for the left anterior descending coronary artery, 0·71 for the right coronary artery and 1·00 for the left main coronary artery when a positive score was assigned to arteries which were judged to have 'possibly' a significant proximal stenosis (confidence level A). Specificity in detecting such a stenosis varied from 0·73 for the left anterior descending coronary artery to 0·96 for the left circumflex. When a positive score was assigned only to arteries in which a stenosis was judged to be 'certainly' present (confidence level B), sensitivity decreased to 0·00 for the left circumflex, 0·33 for the left anterior descending coronary artery, 0·43 for the right coronary artery and 0·75 for the left main coronary artery. Specificity at this level of confidence in the analysis varied from 0·93 for the left anterior descending coronary artery to 1·00 for the right coronary artery (Figs 1 and 2). Sensitivities, specificities and predictive values are summarized in Table 2. At both levels of confidence inter-observer agreement for the detection of proximal coronary artery stenoses by magnetic resonance angiography was 0·90.

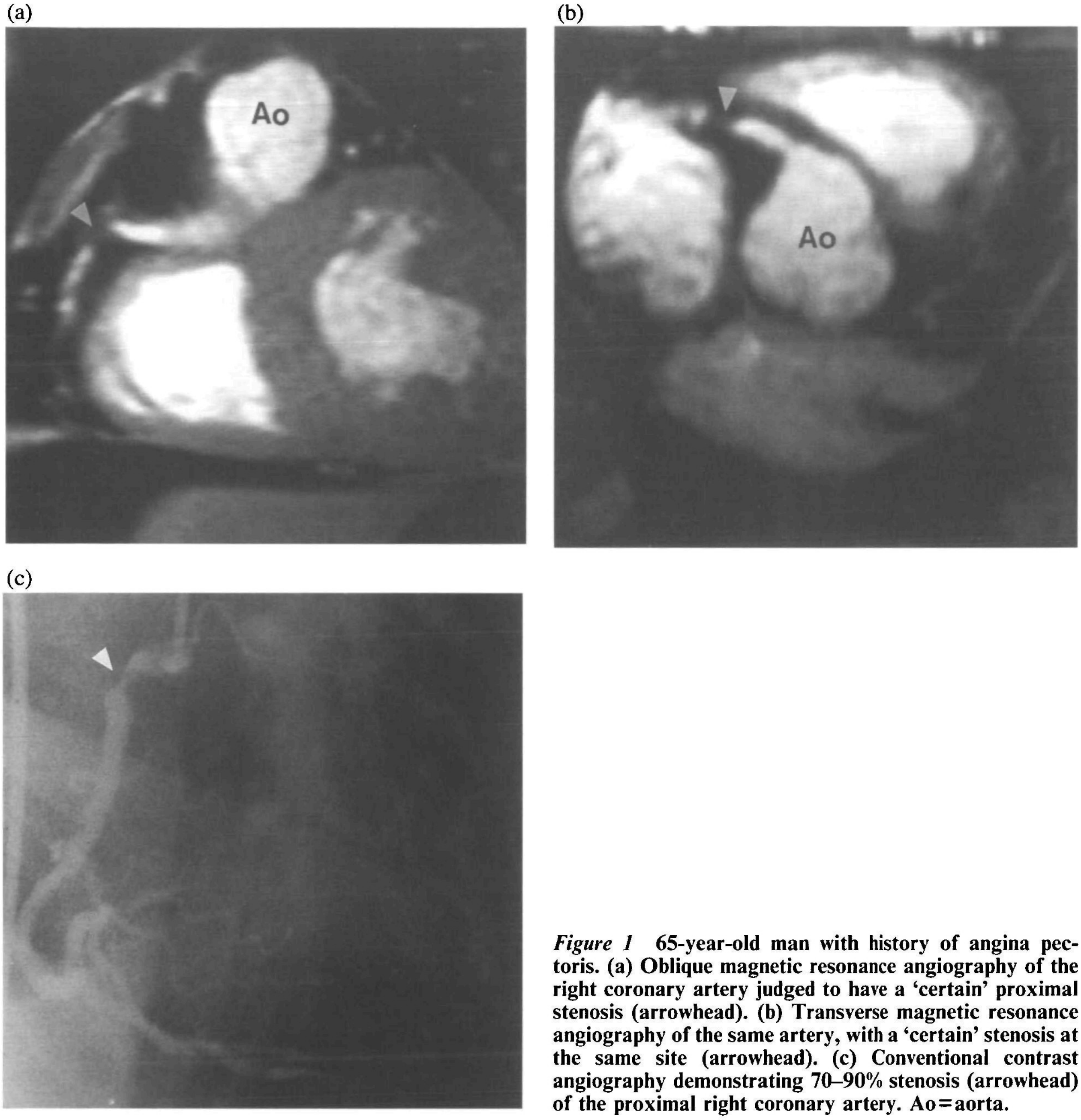


Figure 1 **65-year-old man with history of angina pectoris. (a) Oblique magnetic resonance angiography of the right coronary artery judged to have a 'certain' proximal stenosis (arrowhead). (b) Transverse magnetic resonance angiography of the same artery, with a 'certain' stenosis at the same site (arrowhead). (c) Conventional contrast angiography demonstrating 70–90% stenosis (arrowhead) of the proximal right coronary artery. Ao=aorta.**

The sensitivity and specificity of the technique calculated in an additional analysis of subgroups of arteries with a more severe degree of stenosis are reproduced in Fig. 3. A tendency of the sensitivity to increase with a more severe degree of stenosis was found at both confidence levels. However, the higher sensitivity occurred at the expense of a concomitant loss of specificity, due to the increased detection of stenoses with a severity below the cut-off.

Discussion

Clinical applicability of non-invasive coronary angiography would be one of the greatest advances in cardiac imaging of this decade. Our results confirm earlier findings that non-invasive imaging of substantial proximal and mid-segments of the coronary arteries is feasible using fast magnetic resonance angiography[2–9]. The current accuracy in detecting significant atherosclerotic lesions, however, seems to depend on the artery, being high for left main coronary arteries, intermediate for left anterior descending and right coronary arteries and low for left circumflex arteries.

Previous work

Several different spin-echo and gradient-echo techniques have already been applied in magnetic resonance

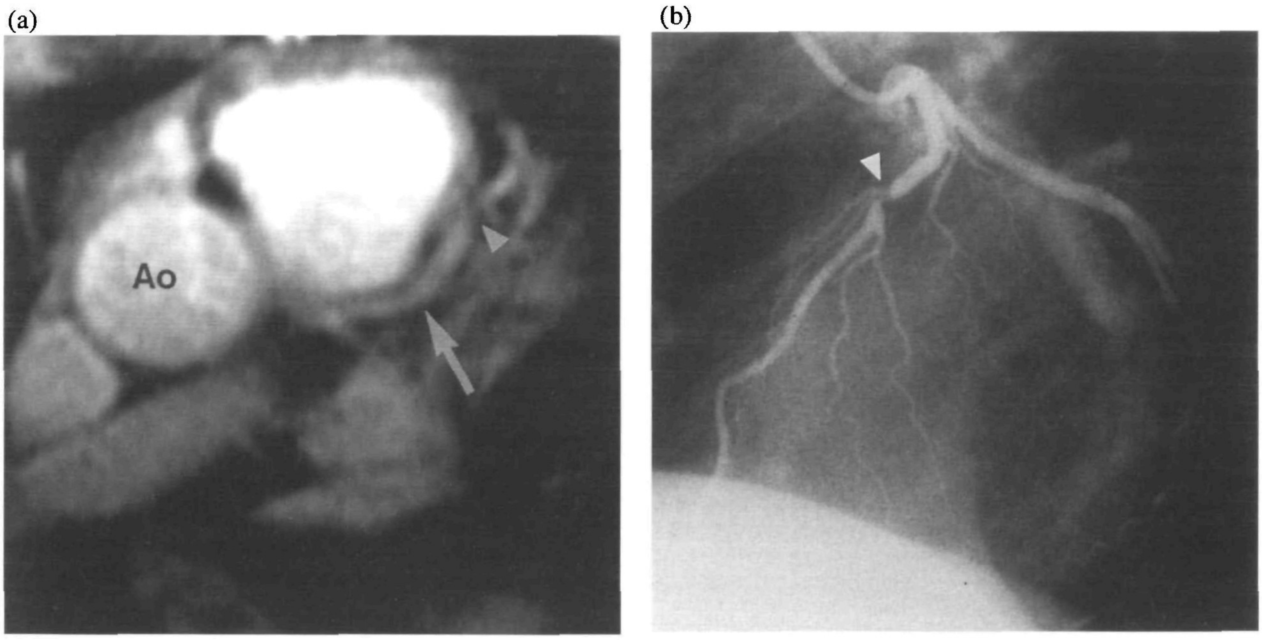


Figure 2 **34-year-old man with history of angina pectoris. (a) Transverse magnetic resonance angiography of the left anterior descending coronary artery (arrow) demonstrating a 'certain' stenosis (arrowhead). (b) Conventional contrast angiography demonstrating a 90–99% stenosed mid-segment of the left anterior descending coronary artery (arrowhead). Ao=aorta.**

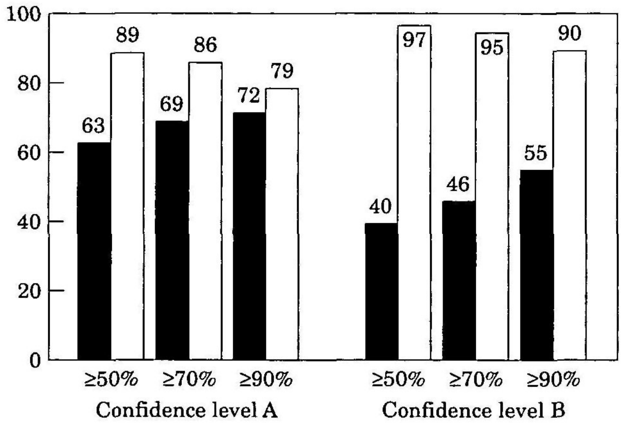
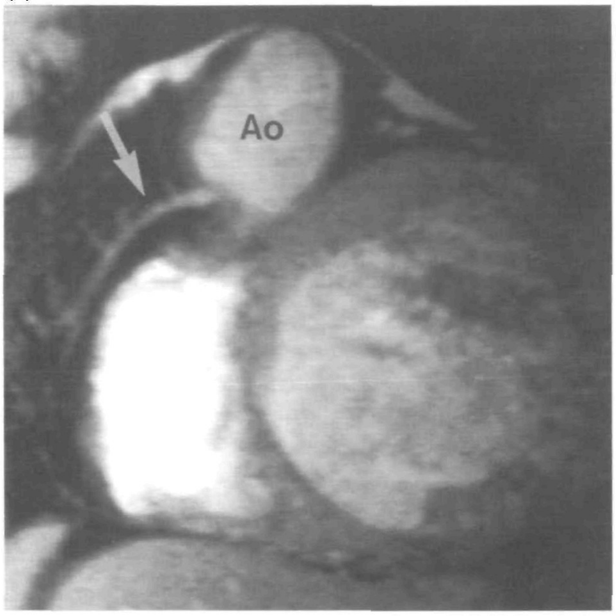


Figure 3 **Sensitivity (■) and specificity (□) of magnetic resonance angiography in the detection of proximal coronary artery disease according to increasing stenosis severity.**

coronary angiography. Conventional spin-echo magnetic resonance imaging has been used for the early visualization of proximal coronary artery segments[13], but has a poor sensitivity in the detection of proximal coronary artery disease[14]. Since 1991, magnetic resonance coronary angiography has been performed almost exclusively with faster 'bright blood' gradient-echo techniques. Various approaches have been described. Multiple thin slice 2D acquisitions with post-processing[2,3], subtractive methods based on selective tagging of arterial blood[5], spiral k-space scanning[6], and three-dimensional coronary angiography[7] have been reported to be capable of imaging the proximal coronary arteries in volunteers. Most clinical work, however, has been performed using a k-space segmented fast 2D technique which facilitates imaging within a breath-hold. Originally developed for coronary angiography by Edelman and co-workers[4], it was tested in patients by Manning *et al.* from the same group[8,10]. They reported the overall sensitivity and specificity of the technique for identifying vessels with significant stenosis to be 90 and 92%, respectively[10]. However, distinctly lower values were reported by Duerinckx *et al.*, who used the same technique[11].

Comparison with other work

Our results are intermediate between those observed by Manning *et al.* and those of Duerinckx *et al.* We agree with Manning *et al.* that the technique appears to be accurate in the detection of left main coronary artery disease. The sensitivity of 75–100% (at confidence level B and A, respectively) is in the same range as the 100% found by Manning *et al.* Duerinckx *et al.* included two left main coronary artery lesions and neither were detected by magnetic resonance angiography at the confidence levels we used. For the other arteries, Manning found sensitivities of 71%, 87%, and 100% for the left circumflex, left anterior descending and right coronary artery, respectively, whereas Duerinckx found distinctly lower values for 'sure' and 'probable' detection: 0% for the left circumflex, 9–55% for the left anterior descending, and 31–46% for the right coronary artery. Our results of 0%, 33–53% and 35–59%,



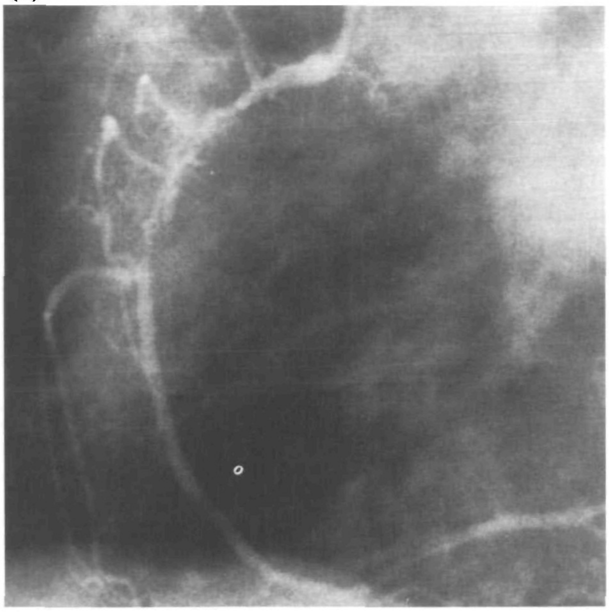


Figure 4 **51-year-old man with history of angina pectoris. (a). Oblique magnetic resonance angiography of the proximal right coronary artery (arrow) showing a delicate right coronary artery that was, however, judged not to be stenosed. (b) Conventional contrast angiography demonstrating subtotal stenosis of the proximal right coronary artery possibly due to a recanalized thrombotic occlusion. Ao=aorta.**

for left circumflex, left anterior descending and right coronary artery lesions, respectively, are in between.

We have no satisfactory explanation for this difference in results. A great deal of the difference might be attributable to patient selection bias. Manning *et al.* selected patients from among those scheduled for outpatient testing. We and Duerinckx *et al.* studied consecutive patients, although we did include patients from the ward when no outpatient was scheduled at times that the magnetic resonance unit was available for cardiac research. It is possible that the proportion of motivated, cooperative patients differed in the populations studied or that stenosis severity was unequal among patient groups.

Pennell *et al.* in a recent study reported on the ability of magnetic resonance angiography to localize stenoses in coronary arteries and assess their severity and length[15]. The study had a different design, in that only selected arteries known to be stenosed were included. Therefore, the 85% success rate in identifying stenoses in this study cannot be directly compared with previous data on the accuracy of the technique. An interesting finding was that stenoses were correctly localized and that the amount of signal loss was positively correlated to stenosis severity. The length of stenoses was overestimated with magnetic resonance angiography for more severe stenoses.

Stenosis detection

The capability of a magnetic resonance angiographic technique to detect luminal stenoses depends on a variety of factors. Spatial resolution is an important factor (Fig. 4). Visualizing anatomical luminal diameter narrowing in small-diameter cardiac vessels at currently attainable spatial resolution might easily result in being insensitive, due to partial volume effects. On the other hand, because complex flow distal to high-grade stenoses causes signal loss, this might contribute to stenosis detection[16–18]. Increasing stenosis severity and increasing blood flow velocity tend to increase signal loss[15,19–21]. Stenosis morphology is also expected to influence signal loss, with sharp-edged stenoses producing more signal loss than smoothly-shaped stenoses, although this remains to be proven in patients. Turbulent fluctuation velocity seems to be the major determinant of signal voiding at stenoses in magnetic resonance angiographic images[22]. In addition, system parameters like echo time — or, more specifically: gradient strength and duration — voxel size, and the application of flow compensation influence the sensitivity of a technique to signal loss due to turbulent low[17,20,21,23,24].

Other factors that may have given rise to the false-negative results obtained are collateral supply of stenosed vessels, cardiac motion during the acquisition window of 88–113 ms in mid-diastole and misregistration due to inconsistent breath-holding. The results in the left circumflex are influenced by the relatively low signal-to-noise ratio in this posterior artery far away from the employed surface coil.

False-positive results, although less common than false-negative results, may have been due to minor luminal irregularities that, however, cause substantial local turbulence, resulting in loss of signal. Also potential signal loss associated with calcium depositioning in non-sigificant lesions or pronounced kinking of a vessel may have given rise to false-positive results.

Our imaging protocol is based on a previous study in which its efficacy was demonstrated[12]. In our experience, some imaging plane orientations used in conventional coronary angiography are not very useful in magnetic resonance angiography: the standard right anterior oblique orientation, although depicting large segments of the left anterior descending coronary artery in-plane, appeared to be of little value in the analysis. Differentiating the artery from the parallel cardiac vein, or from its side branches is difficult in these orientations. A standard transverse plane was more valuable. The same holds true for left anterior oblique equivalent orientations of the left circumflex artery. However, opinion varies and other authors have found these views for in-plane imaging of the arteries helpful[15].

Clinical value

Although patient numbers are small, the results obtained in this study group suggest that at this stage of development magnetic resonance angiography can be a valuable technique for the detection of left main coronary artery disease. This might be a clinical application of the technique, for example in patients with extensive ST-segment depression on exercise testing. Significant left main coronary artery stenosis could be demonstrated or excluded rapidly and non-invasively using magnetic resonance angiography. The clinical value of the technique seems still limited for the detection of left anterior descending coronary artery and right coronary artery disease. The results obtained in the left circumflex artery preclude diagnosis of stenoses in this artery at this stage of development.

Other studies have shown good results of the technique in the diagnosis of anomalous coronary anatomy[25,26]. In addition, magnetic resonance angiography of coronary arteries potentially provides more information than just a 'luminogram'. From the phase of the magnetic resonance signal blood flow velocities can be calculated. Coronary flow velocity and flow reserve measurement using pharmacological stress have been reported[27–32], facilitating assessment of the haemodynamic significance of detected lesions. These developments suggest that magnetic resonance angiography can develop into a versatile non-invasive diagnostic tool.

Limitations and new developments

Limitations inherent to the technique have been cited in previous reports[10,11], and include the dependence on a regular heart rhythm, problems with breath-holding in a minority of patients, and general contra-indications to magnetic resonance imaging.

Like Manning *et al.* and Duerinckx *et al.*, we have performed visual analysis of the X-ray coronary angiograms. Although quantitative assessment would have been superior, we do not believe that this would alter the main findings of the study. We investigated 35 patients in this study, a number that is intermediate to those investigated by Manning *et al.* and Duerinckx *et al.* A joint analysis of the results of various scientific centres would probably upgrade the significance of individual results. In this study, like in those by Manning *et al.* and Duerinckx *et al.*, a surface coil was used as the receiver antenna. Modern phased-array systems result in a better signal-to-noise ratio for arteries at the back of the heart, like the left circumflex artery. This might result in improved visualization of this artery.

Although images are acquired during the relative diastasis of mid-diastole, the data acquisition window of 88–113 ms should be decreased further. Faster gradient systems are under examination now. This development might well add to the technique's accuracy in detecting coronary stenoses.

A currently available alternative to breath-holding is navigator-echo-based respiratory gating[12,33]. Although this technique certainly offers several advantages, its incorporation into coronary imaging sequences had not yet resulted in a higher sensitivity in the detection of stenoses[34].

Conclusions

Fast segmented magnetic resonance angiography is capable of non-invasive imaging of proximal and mid-segment coronary anatomy. In our experience, it is probably accurate for the detection of left main coronary artery disease, has an intermediate accuracy for the detection of proximal and mid-segment left anterior descending artery and right coronary artery stenoses, and a low accuracy for the detection of left circumflex stenoses. Our findings fit within a range of sensitivity and specificity reported by a few other groups and indicate that further technical advances are necessary before confident clinical application in the general population of patients with coronary artery disease is possible. However, new developments are expected to further augment its clinical applicability in the near future.

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