Current perspective

Magnetic resonance coronary angiography: present clinical applications

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Coronary angiography is presently considered the gold standard test for the assessment of coronary artery disease. However, owing to the exposure to ionizing radiations, the invasiveness, and the incidence of major complications (0.3-1.1%), investigators are attempting to develop safer, non-invasive techniques. Cardiovascular magnetic resonance proved to be an extremely safe tool with a wide range of clinical applications. Its flexibility and non-invasiveness allow the evaluation of the heart and coronary arteries in one single setting, with the possibility of quantifying several cardiac physiological parameters. Multiple techniques have been applied to overcome the substantial difficulties in coronary artery imaging: respiration artifacts are suppressed by breath-holding or respiratory gating, cardiac motion artifacts are reduced by diastolic gating with ultra fast sequences and the signal-to-noise ratio can be increased with contrast agents. In several clinical trials, magnetic resonance coronary angiography has been successfully used to assess coronary artery stenoses, coronary artery bypass grafts and anomalous coronary artery origins and course. Considering the continuing developments in magnet coils, in software technology and in innovative imaging approaches, it is likely that magnetic resonance coronary angiography will in the future play an important role in the evaluation of coronary artery disease.

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Introduction

The first manuscripts regarding the applications of magnetic resonance (MR) for diseases of the cardiovascular system were published in the early '80s[1]. Over the following years, cardiovascular MR proved to be an extremely flexible tool, far more versatile than any other technique currently used in the clinical practice[2-7].

In fact, cardiovascular MR could be widely used to study both the heart morphology and function, i.e. the quantification of the left ventricular mass, wall thickness, systolic myocardial thickening, chamber volume, ejection fraction, and other parameters of global and regional systolic and diastolic functions[8-10]. Furthermore, cardiovascular MR provides an optimal tool for the assessment of myocardial ischemia, postinfarction scars, left ventricular remodeling, aneurysms, septal defects, mural thrombi, valvular regurgitations, and the patency of bypass grafts[11-14]. High resolution MR is also used for the imaging and quantification of atherosclerotic plaque composition *in vivo*. Recently, intravascular MR devices to be used when performing imaging-guided balloon angioplasty have been developed[15-17].

However, the most attractive fields for cardiovascular MR applications are the assessment of myocardial perfusion and non-invasive coronary angiography[18-21]. Currently, the only clear indication for magnetic resonance coronary angiography (MRCA) consists of the visualization of congenital coronary anomalies. On the other hand, conventional coronary angiography is considered the gold standard for the detection of coronary artery stenoses in patients with ischemic heart disease[22-24]. Nevertheless, coronary angiography is invasive, expensive and it requires a substantial X-ray exposure for patients and operators. It is not risk-free, bearing the risk of arrhythmias, stroke and adverse reactions to contrast agents. Furthermore, it necessitates patient hospitalization[15,16,25].

In view of the above-mentioned reasons, many researchers are currently examining alternative, non-invasive clinical tools and, among them, MRCA is considered the most promising method. The advantage of this technique lies in its flexibility and it allows the evaluation of both the

anatomy and function of the heart. However, some impediments limit the routine clinical use of MRCA: difficulties are due to cardiac and respiratory movements, to the small size and tortuous course of coronary arteries, and to the low contrast between vessels and surrounding structures such as the epicardial fat and myocardium[26].

New technologies have been introduced with the aim of overcoming these problems: the development of cardiac and respiratory gating, of an ultra fast two- or three-dimensional gradient system, of echoplanar, spiral or parallel imaging sequences and of contrast agents have significantly changed the diagnostic potential of cardiovascular MR.

Moreover, the injection of paramagnetic contrast agents can be used for the assessment of myocardial perfusion, a crucial step in the management of patients with ischemic heart disease. Indeed, nuclear medicine perfusion techniques are widely used, although they are burdened by a limited spatial resolution.

Therefore, cardiovascular MR could become, in this field, an effective and valid clinical tool[15-17].

Anatomical and physiological aspects of coronary artery disease

The left main coronary artery (LMCA) arises from the left aortic sinus and then passes behind the right ventricular outflow tract to give rise to the left anterior descending (LAD) and circumflex (LCx) arteries. In normal subjects its diameter is between 3 and 6 mm. From the LMCA bifurcation, the LAD passes down towards the apex of the heart in the anterior interventricular groove. The right coronary artery (RCA) arises from the right aortic sinus and passes down along the anterior atrioventricular groove towards the crux of the heart.

During the cardiac cycle, especially in mid systole and early diastole, the coronary arteries undergo substantial displacement producing vessel blurring. To avoid that, images are acquired in mid-late diastole, during a period of relative cardiac stasis. In general, the acquisition time should be limited to < 100 ms. Strategies to achieve this temporal resolution include segmenting "k-space" (the multiple data acquired for the creation of the image) or acquiring "k-space" with either spiral or echoplanar techniques[15,16,26].

Besides, even the respiratory cyclic movements, related to the diaphragmatic vertical excursions, influence the quality of the image by producing respiratory artifacts and vessel blurring. To solve this problem, researchers initially used two-dimensional breath-hold gradient-echo strategies, based on multiple thin slice acquisitions aligned in plane with the artery. This approach requires several breath-holds and some patients with cardiorespiratory diseases are unable to comply with this technique. Moreover, breath-holds at different levels produce image misregistration. Following these initial attempts, an alternative strategy based on respiratory-gating was developed. Liu et al.[27] introduced a two-dimensional radiofrequency pulse (navigator echo) to monitor the diaphragmatic motion during respiration. By setting a narrow navigator acceptance window in which data are accepted, the patient can breath freely, without changing the quality of the images obtained. Furthermore, the scan times are prolonged, especially in patients with bradycardia and variable respiratory patterns[16,26-28].

The two-dimensional approach has a low spatial resolution, with poor depiction of small and tortuous vessels and with the incorrect evaluation of stenoses (for example, interpretative difficulties related to contiguous sections misregistration due to inconsistent breath-hold positions). On the other hand, the three-dimensional technique has a higher spatial resolution because it is based on the acquisition of volumetric datasets of the heart in a single breath-hold or using respiratory gating[29].

Another problem arises from the differentiation of the coronary arteries from surrounding structures. Spin-echo techniques produce a "black-blood" vessel against the perivascular fat and arterial wall. Gradient-echo techniques produce a "white-blood" vessel: the signal regained from blood can be amplified with additional suppression of the perivascular fat and myocardium or with the administration of gadolinium-based contrast agents[17,26,30,31] (Figs. 1 and 2).

Clinical indications for magnetic resonance coronary angiography

The development of MRCA in coronary artery disease is currently the primary goal of the research endeavor: in fact, this technique may be employed for patients with ischemic heart disease, to detect coronary artery stenoses, for preoperative screening and for the follow-up of myocardial revascularization procedures (coronary angioplasty or coronary artery bypass grafting). The sensitivity of MR angiograms is such that the identification of significant stenoses within two thirds of the major coronary artery course is possible; in fact, MRCA permits adequate visualization of the following segments: the LMCA, the proximal and mid tracts of the LAD and of the LCx arteries and the RCA as far as the crux of the heart. The visualization of the coronary arteries, even if limited to the proximal and mid segments, provides sufficient information for a clinical assessment. For example, the tortuosity of these vessels is an index of atherosclerosis, such that if MRCA is suggestive of linear and non-stenotic arterial tracts, it may be assumed that in 85% of these patients the entire coronary artery tree is free from atherosclerotic lesions. Thus, MRCA may be employed for screening purposes in selected groups of patients with two or more cardiovascular risk factors[32].

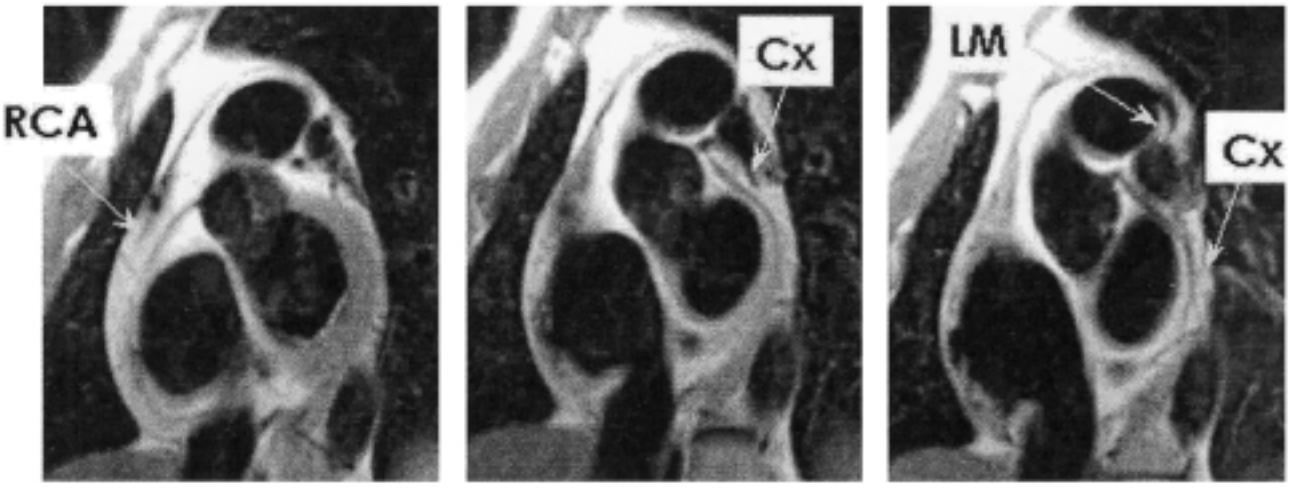

Figure 1. *By using the spin-echo sequence, it is possible to obtain a "black-blood" image of the coronary arteries. Cx = left circumflex coronary artery; LM = left main coronary artery; RCA = right coronary artery.*

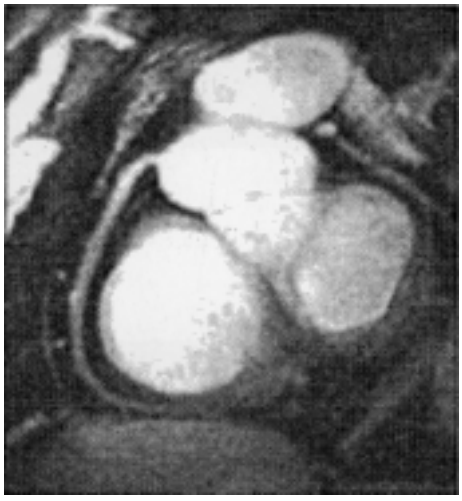

Figure 2. *By using the gradient-echo sequence, a "white-blood" image of the coronary lumen is visualized.*

Recent studies of atherosclerotic plaques demonstrate that high resolution MRCA permits the non-invasive visualization of the artery wall and the assessment of plaque composition. It is thus conceivable that in the future vulnerable plaques will be identified before their rupture, thus preventing acute coronary syndromes[17,27,33,34].

Yet, phase-contrast MR could be used for the non-invasive detection of restenoses in patients with recurrent chest pain after percutaneous revascularization (such an event occurs in 25 to 60% of subjects having a successful percutaneous coronary arterial revascularization procedure). When a hemodynamically significant stenosis is present, phase-contrast MR evaluation is sufficiently accurate for the correct identification of a reduced flow reserve in the distal vessels and of an increased blood velocity at the site of stenosis. This technique is particularly useful in patients with coronary stents, because the metal causes a signal void and conventional gradient-echo techniques do not permit the correct assessment of the severity of stenosis[16,34,35].

Coronary artery bypass grafts. With the increase in coronary artery bypass surgery, a higher frequency of graft stenoses and occlusion due to early thrombosis, intimal hyperplasia and accelerated atherosclerosis has been observed. At the moment, the only tool available for the assessment of graft disease is X-ray cardiac catheterization. Different types of MR techniques have been tested as non-invasive alternatives to X-ray angiography of grafts. Spin-echo techniques depict grafts as black vessels, but stenoses cannot be reliably assessed (the sensitivity for the detection of graft patency was 86-98%, the specificity was lower at 59-85%). In contrast, using cine gradient-echo sequences, patent grafts appear white (with this approach the sensitivity is reported to be as high as 88-98%, with a specificity of 86-100%). The addition of gadolinium-based contrast agents with rapid breath-hold three-dimensional sequences can produce angiographic quality images of the aorta and grafts, although the assessment of the distal insertion and the detection of significant stenoses remain limited. However, both techniques provide some functional information about the flow down the grafts: preliminary studies have suggested that MR flow measurements may differentiate grafts with significant stenoses and patent grafts. Thus, the combined use of MR angiography techniques and phase-contrast flow velocity mapping offers the potential of a safe, non-invasive diagnostic tool for the detection of graft dysfunction[15,17,27,36-38]. Furthermore, with the increasing use of intracoronary stents in interventional cardiology, it will be important that MRCA be improved so as to permit accurate assessment of the blood flow proximal and distal to a patent or stenosed

stent. Even if the stents may produce some artifacts, MRCA is safe for the patient, even if performed soon after stent implantation[15,17]. The accurate flow assessment in combination with intravascular contrast agents will allow a wider utilization in the evaluation of stents.

Anomalous coronary arteries. The incidence of anomalous coronary arteries in patients with a normal cardiac anatomy is 0.3-0.9%. This condition is clinically benign in the majority of cases, but it is associated with sudden death if the LAD passes between the pulmonary artery and ascending aorta. Because of the lack of three-dimensional information about the anatomical relationship with the great vessels, the assessment of anomalous coronary vessels at conventional X-ray angiography can be incomplete. MRCA can be orientated in any spatial plane and allows optimal definition of the relationship of the anomalous vessel with the aorta and right ventricular outflow tract. So, MRCA has been recognized as a valuable tool for the identification of anomalous coronary arteries[15-17,25,39,40].

Contraindications. Electromagnetic interference causes malfunction of implanted devices; therefore, MR is contraindicated in patients with: a) pacemakers; b) defibrillators; c) metallic vascular clips (especially intracranial); d) cochlear implants.

Dental or hip prostheses may provoke image degradation, but they do not constitute an absolute contraindication to MR.

Patients with claustrophobia cannot be studied using the MR technique unless under sedation[41,42].

Magnetic resonance coronary angiography sequences

Both spin-echo and gradient-echo techniques have been employed for the imaging of the heart and coronary arteries. With spin-echo imaging, the signal from blood-filled compartments can be suppressed, producing "black-blood" images. On the contrary, the gradient-echo technique provides the opposite contrast by making use of the signal enhancement possible from the inflow of non-saturated blood to the region of interest, to produce "white-blood" images. This method provides greater flexibility for MRCA. Several variants have been explored using two- and three-dimensional scans combined with breath-hold and free-breathing measurements[15,17,26,30].

Breath-hold techniques. Three breath-hold techniques have been conceived: 1) two-dimensional; 2) spiral; 3) echoplanar.

The two-dimensional breath-hold fat-suppressed gradient-echo technique represents the first attempt to resolve the coronary arteries. It is based on the acquisition of image planes oriented parallel to each of the coronary vessels; scans are performed while the patient holds his breath; images are reviewed *in situ* so as to evaluate the entire course of the studied coronary vessel. In case of interpretative difficulties (for example, MR signal inhomogeneity), it is possible to acquire additional images in planes perpendicular to the vessel; in fact, such images take full advantage of the inflow effects, achieving a higher flow signal and better resolution for the visualization of any possible narrowing along the way[43]. In 1993, Manning et al.[22] presented the initial encouraging results on a group of adult volunteers. This clinical study was performed on 39 patients, 74% of whom presenting with coronary artery stenoses. Stenoses were identified as signal loss in the vessel lumen. The degree of vessel stenoses was taken to be proportional to the degree of signal loss. In a blinded analysis, the overall sensitivity and specificity were 90 and 92% respectively. However, trials performed by Post et al.[24] and by Sardanelli et al.[30] pointed out a large variability in the results obtained[16,43,44]. In our recent clinical study[45] on 40 patients, the overall sensitivity and specificity were 79 and 78% respectively (Figs. 3-5).

Two-dimensional MRCA has many limits: low signal-to-noise ratio, low spatial resolution and difficult

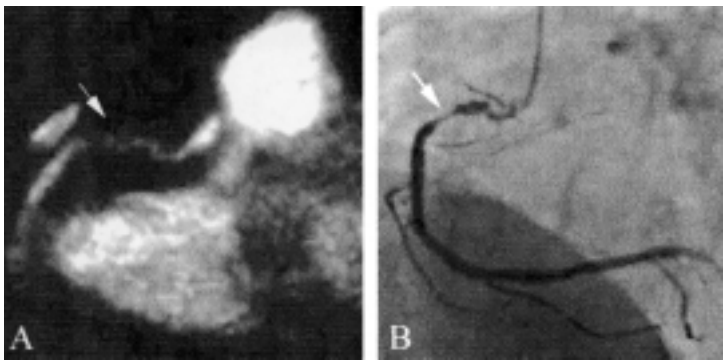

Figure 3. A: *magnetic resonance coronary angiography of a 52-year-old male patient, showing a long stenosis of the right coronary artery* (arrow). B: *conventional coronary angiogram showing the corresponding stenosis.*

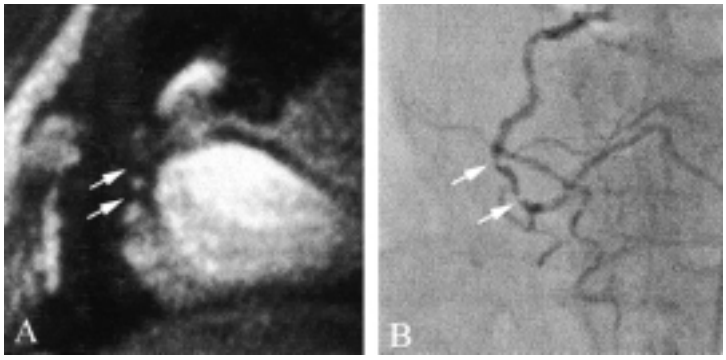

Figure 4. A: *magnetic resonance coronary angiography of a 58-year-old male patient, showing two stenoses in the right coronary artery* (arrows). B: *conventional coronary angiogram showing the corresponding stenoses.*

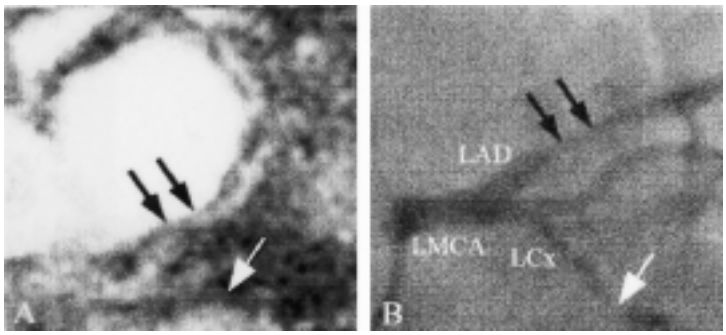

Figure 5. A: *magnetic resonance coronary angiography of a 65-year-old female patient, showing two significant long distance stenoses of the left anterior descending coronary artery (LAD,* black arrows*) and of the circumflex artery (LCx,* white arrow*).* B: *the corresponding stenoses as visualized at conventional angiography. LMCA = left main coronary artery.*

differentiation of the LAD and of the LCx from the great cardiac veins; besides, it requires significant operator experience for the differentiation of real from spurious information. In fact, focal coronary stenoses are perceived indirectly through signal fluctuations along the vessel or through the absence of any signal because of flow turbulence. Sometimes, in case of tortuous vessels or of an inconstant breath-hold position, it is possible to observe false stenoses. Instead, three-dimensional MRCA allows the acquisition of a volume slab containing several thin slices and consequently a high spatial resolution. It allows an operator-independent setup and the image review can be performed after the acquisition has been completed. At present, the trend in MRCA techniques is to acquire a volume data set in a single breath-hold. One of the most promising methods is "volume coronary angiography with targeted scans", which allows the acquisition of small three-dimensional slabs along the course of the coronary vessels during breath-holds. Breath-hold techniques also include spiral and echoplanar scans. Since the arterial movement during the acquisition causes image degradation, the sequence acquisition speed is important. Segmented gradient-echo techniques have an acquisition duration of 100 ms; spiral and echoplanar sequences are much faster, with a duration of 30-40 ms. These techniques produce higher quality coronary artery images but require specialized scanner hardware[43,44].

Free-breathing techniques. Many patients perform badly with breath-holds, especially if they suffer from impaired cardiac or respiratory function. To improve patient comfort, several free-breathing schemes were evaluated, using both two- and three-dimensional techniques. These comprise: a) averaging multiple acquisitions; b) retrospectively ordered respiratory gated data; c) prospectively synchronized respiratory data collection. The latter two use navigator echoes to monitor the diaphragm position[46].

The method of averaging acquisitions without respiratory synchronization was among the first three-dimensional MRCA techniques used. Because averaging does not provide images at any particular diaphragm position, significant blurring was reported. Respiratory navigator gating synchronizes the acquisition of the MR signals with the cardiac and respiratory cycle: only data acquired at a predefined diaphragm position (usually end-expiration) are used for image reconstruction. This approach allows the visualization of the coronary arteries while the patient breathes freely, producing high resolution images, but its clinical use is limited by the long scan times (up to 30-40 min)[29].

New techniques in magnetic resonance coronary angiography

Fat-suppressed three-dimensional volume sequence. The coronary arteries are embedded in pericardial fat through most of their course. Fat-suppression techniques enhance the signal of the coronary artery lumen from the surrounding perivascular fat and improve vessel visibility. With the recent introduction of fat-suppressed three-dimensional volume sequences, it is possible to produce high quality, non-contrast-enhanced images of the coronary arteries.

Volume selective imaging with tracking. The ability to selectively excite a small volume within an imaging plane can allow the acquisition of a reduced number of lines of "k-space" and also reduce image blurring. When combined with slice tracking, a wider navigator acceptance window may be used to increase the efficiency of data acquisition whilst achieving an optimal image quality.

Parallel imaging techniques. In standard sequences, the data from separate coils in a phased-array device are summed to produce the final image. "Simultaneous acquisition of spatial harmonics" and "sensitivity encoding" take advantage of arrays of small coils to increase image efficiency. Normally, image acquisitions with a small field of view will result in wrap-around or fold-over artifacts due to aliasing. However, parallel imaging techniques use the spatial arrangements of multiple coils to eliminate these aliasing artifacts thus increasing imaging efficiency. This improved efficiency reduces the imaging time and increases the spatial resolution in a constant imaging time. This has been demonstrated, for example, with the use of a three-dimensional contrast-enhanced MRCA sequence to acquire a volume data in half the normal time or else to double the spatial resolution in a constant breath-hold time.

Vessel wall imaging. Conventional coronary angiography does not provide information about the vessel wall and about the atheroma and cannot differentiate stable atherosclerotic plaques from vulnerable ones. With the development of new techniques, MRCA now allows the assessment of atherosclerotic plaques on the vessel wall by using long-echo-train-length fast spin-echo imaging with inversion preparatory pulses to null the blood signal as well as additional selective perivascular fat suppression. This may be useful to monitor disease treatment or for improving the delineation of potential lesions identified as areas of signal loss at gradient-echo coronary angiography[33-35].

Magnetic field strength. For over a decade, 1.5 Tesla has been the gold standard magnetic field strength for clinical MR systems. The use of higher fields was confined to research and not designed for routine clinical use. The introduction of the 3.0 Tesla MR system offers a higher potential for MRCA: the increase in field strength provides a higher signal-to-noise ratio and enhances image contrast. So, scan times could be shortened substantially, delivering an increased diagnostic certainty and patient throughput.

Contrast agents in magnetic resonance coronary angiography

Dynamic MRCA has been improved by using extracellular gadolinium-based paramagnetic contrast agents; however, the short intravascular half-life of these agents limits the resolution and the possibility of repeated scans. To overcome this problem, intravascular contrast media have been tested both in MRCA and in the cardiovascular MR evaluation of myocardial perfusion[47,48]. The advantages of blood pool contrast agents are: a) blood pool retention allowing the use of a contrast agent at a lower concentration; b) prolonged blood pool enhancement allowing a longer acquisition time; this may be used to increase the signal-to-noise ratio and image resolution or to take multiple scans after one contrast injection.

The first gadolinium-based blood pool contrast agent applied was Angiomark (MS-325). This is a small chelate molecule that permits an excellent visualization of the vessels; it reversibly binds to human serum albumin, has a long half-life and is eliminated by the kidneys. Clariscan (NC100150) is an ultrasmall superparamagnetic iron particle (USPIO), with a half-life of 3-4 hours, is taken up by macrophages and is metabolized by the liver. Both gadolinium-based and USPIO agents can reduce the T1 of blood to values < 100 ms; however, gadolinium-based agents are more advantageous because they maintain a longer T2 in blood with similar T1 shortening (shortening the T2 results in a decreased signal intensity).

No serious side effects have been reported after the injection of blood pool contrast agents. Transient nausea and paresthesia were reported in one third of patients after bolus injection of Angiomark over 30 s.

Similar to other iron oxide-based contrast agents, Clariscan interferes with iron metabolism; moreover, it has been occasionally associated with mild headache and abdominal pain[35,41,44,49-53].

A new group of MR contrast agents is the necrosis-specific agents that bind to necrotic tissue or cellular debris and are thus distinct from the inert extracellular MR contrast agents. These tissue specific contrast agents can provide persistent enhancement of acutely infarcted myocardium[54], but at present, owing to their high toxicity they are not approved for clinical use.

Another approach to the imaging of cell death is the use of antibodies such as monocristalline iron oxidate nanoparticle-antimyosin, a superparamagnetic iron oxide agent containing antibodies against myosin[55].

Assessment of myocardial perfusion

Cardiovascular MR techniques allow the study of myocardial perfusion and should be designed to demonstrate: a) the extent of the ischemic area; b) the distinction between occlusive and reperfused infarctions, even after coronary artery bypass grafting or coronary angioplasty (Fig. 6); c) the distinction between healthy and infarcted, non-viable myocardium; d) the differentiation between stunned and hibernated myocardium; e) myocardial viability.

The "bolus tracking technique" is the most widely used protocol in MR perfusion studies designed to follow the first-pass distribution of a contrast agent in the myocardium. This can be achieved by applying ultrafast MR sequences (FLASH, turboFLASH, ECHOPLANAR)[46,56].

The turboFLASH technique provides repeated sub second acquisitions at the same slice (usually the mid left ventricular short-axis) in 1-2 s. Even if the anatomical study is limited to one or a few tomograms, the short-axis plane imaged at the mid ventricular level usually reveals perfusion defects in the major coronary regions.

A new technique, ECHOPLANAR imaging, has been recently implemented with the aim of imaging the whole heart with an improved temporal resolution. With ECHOPLANAR imaging, acquisition times can be decreased to 40-80 ms, thus allowing the coverage of 8-10 contiguous short-axis sections in 1-2 R-R intervals.

The MR contrast agents currently applied in these studies are "extracellular relaxation agents", employing the T1 shortening effects of gadolinium. "Relaxation" agents increase the signal intensity in normally perfused myocardium while the ischemic zone appears with a delayed and lower signal enhancement. The addition of stress agents (dipyridamole, adenosine) improves the evaluation of perfusion defects[56].

MR contrast agents have been used for the quantification of the regional blood flow: after injecting a contrast agent, the first-pass enhancement of the myocardium is imaged and the signal intensity measured. Wilke et al.[57] provided quantitative values of myocardial perfusion using MR.

However, there is growing evidence in the literature that MR is at least as effective as radionuclide studies, but MR has a higher spatial resolution, uses no radiopharmaceuticals and can be combined with functional studies. The ultimate goal is to combine the assessment of myocardial perfusion with the visualization of the coronary vessels[21,34,58-61].

Conclusions

Cardiovascular MR is a rapidly developing field. By allowing a combination of morphologic and functional images, flow and perfusion data, non-invasive visualization of the coronary arteries and *in vivo* metabolic information, cardiovascular MR could be the most complete examination tool of the heart. Its flexibility

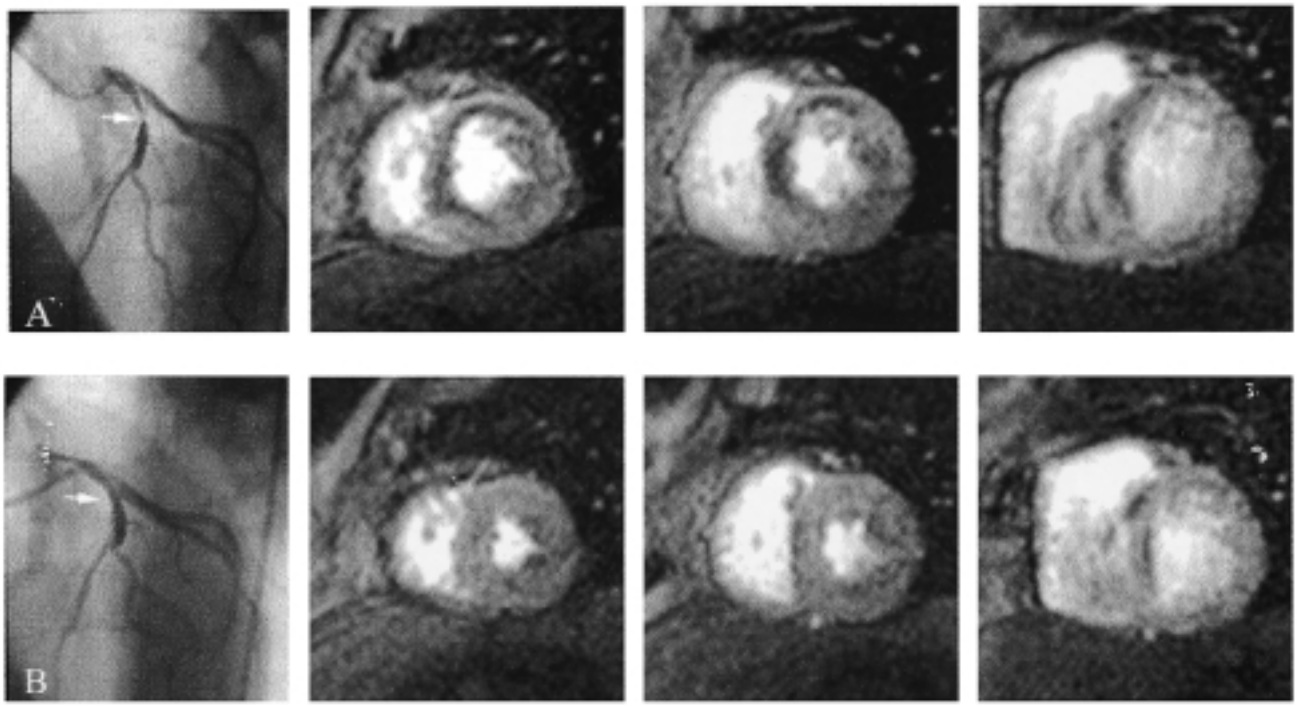

Figure 6. *Dynamic first-pass magnetic resonance study of the myocardial perfusion in a 61-year-old male patient during the adenosine stress test before* (A) *and after* (B) *a revascularization procedure (coronary angioplasty + stent) on the anterior descending coronary artery.*

and non-invasiveness open the door for the evaluation of the heart and of the coronary arteries in one single setting with a high anatomical definition. Finally, MRCA has the potential to be used as a unique screening non-invasive tool in preventive medicine for the detection of significant atherosclerotic lesions in patients with one or more risk factors.

The progress made over the past 15 years in the development and applications of cardiovascular MR indicate the areas of future developments if the clinical usefulness of cardiovascular MR is to be further improved. A critical point consists in the standardization of the examination protocol; researchers should compare the different protocols currently used among the various cardiovascular MR centers. MR systems should be optimized in order to reduce the imaging processing time and thus provide very fast and interactive scans.

For being experts in this technique that requires the combined study of physics, chemistry and medicine, training activities are recommended to both cardiologists and radiologists. In view of the continual improvements made in cardiovascular MR, the next years will possibly witness the routine clinical use of this unique technique.

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References

1. Ernst RR, Anderson WA. Application of Fourier transform spectroscopy to magnetic resonance. Rev Sci Instrum 1966; 37: 93-9.
2. Dinsmore RE, Wismer GL, Levine RA, Okada RD, Brady TJ. Magnetic resonance imaging of the heart: positioning and gradient angle selection for optimal imaging planes. AJR Am J Roentgenol 1984; 143: 1135-42.
3. Higgins CB, Stark D, McNamara M, Lanzer P, Crooks LE, Kaufman L. Multiplane magnetic resonance imaging of the heart and major vessels. AJR Am J Roentgenol 1984; 142: 661-7.
4. Higgins CB, Kaufman L, Crooks LE. Magnetic resonance imaging of the cardiovascular system. Am Heart J 1985; 109: 136-52.
5. Schulthess von GK, Fisher M, Crooks LE, Higgins CB. Gated MR imaging of the heart: intracardiac signals in patients and healthy subjects. Radiology 1985; 156: 125-32.
6. Akins EW, Hill JA, Fitzsimmons JR, Pepine CJ, Williams CM. Importance of imaging plane for magnetic resonance imaging of the normal left ventricle. Am J Cardiol 1985; 56: 366-72.
7. Pohost GM, Canby RC. Nuclear magnetic resonance imaging: current applications and future prospects. Circulation 1987; 75: 88-95.
8. Gaudio C, Reale A. Nuclear magnetic resonance of the cardiovascular system: our experience in 112 subjects. Cardiologia 1988; 33: 907-16.
9. Gaudio C, Miccheli A, Ricci R, Pizzuto F, Puddu PE, Reale A. Angulated transverse tomographic sections to measure cardiac dimension by magnetic resonance imaging: a comparison with 2D-echocardiography. Cardiologia 1989; 34: 513-6.
10. Axel L, Dougherty L. Heart wall motion: improved method of spatial modulation for magnetization for MR imaging. Radiology 1989; 172: 349-50.
11. Bigren HG, Klipstein RH, Firmin DN, et al. Quantitation of anterograde and retrograde blood flow in the human aorta by magnetic resonance velocity mapping. Am Heart J 1989; 117: 1214-22.
12. Buser PT, Auffermann W, Holt WW, et al. Noninvasive evaluation of global left ventricular function with use of cine nuclear magnetic resonance. J Am Coll Cardiol 1989; 13: 1294-300.
13. Semelka RC, Tomei E, Wagmer S, et al. Interstudy reproducibility of dimensional and functional measurements between cine magnetic resonance studies in the morphologically abnormal left ventricle. Am Heart J 1990; 119: 1367-72.
14. Bogaert J, Bosmans H, Maes A, Suetens P, Marchal G, Rademakers FE. Remote myocardial dysfunction after acute anterior myocardial infarction: impact of left ventricular shape on regional function. A magnetic resonance myocardial tagging study. J Am Coll Cardiol 2000; 35: 1525-34.
15. Bunce NH, Pennel DJ. Magnetic resonance of coronary arteries. Eur Radiol 2001; 11: 721-31.
16. Sinitsyn V. Magnetic resonance imaging in coronary heart disease. Eur J Radiol 2001; 38: 191-9.
17. Bunce NH, Lorenz CH, Pennell DJ. MR coronary angiography: 2001 update. Rays 2001; 26: 1: 61-9.
18. Saeed M, Wendland MF, Yu KK, et al. Identification of myocardial reperfusion using echo-planar MR imaging: discrimination between occlusive and reperfused infarctions. Circulation 1994; 90: 1492-501.
19. Edelman RR, Mattle HP, Atkinson DJ, Hoogewoud HM. MR angiography. AJR Am J Roentgenol 1990; 154: 937-46.
20. Yamada T, Tada S, Harada J. Aortic dissection without intimal rupture: diagnosis with MR imaging and CT. Radiology 1988; 168: 347-52.
21. Sensky PR, Jivan A, Hudson NM, et al. Coronary artery disease: combined stress MR imaging protocol. One-stop evaluation of myocardial perfusion and function. Radiology 2000; 215: 608-14.
22. Manning WJ, Li W, Edelman RR. A preliminary report comparing magnetic resonance coronary angiography with conventional angiography. N Engl J Med 1993; 328: 828-32.
23. Duerinckx AJ, Atkinson D, Hurvitz R, Mintorovitch J, Whitney W. Coronary MR angiography after stent placement. AJR Am J Roentgenol 1995; 165: 662-4.
24. Post JC, van Rossum AC, Hofman MBM, Valk J, Visser CA. Three-dimensional respiratory-gated MR angiography of coronary arteries comparison with conventional coronary angiography. AJR Am J Roentgenol 1996; 166: 1399-404.
25. Taylor AM, Thorne SA, Rubens MB, et al. Coronary artery imaging in grown up congenital heart disease. Complementary role of magnetic resonance and X-ray coronary angiography. Circulation 2000; 101: 1670-8.
26. Van Geuns RJM, Wielopolski PA, de Bruin HG, et al. MR coronary angiography with breath-hold targeted volumes: preliminary clinical results. Radiology 2000; 217: 270-7.
27. Liu YL, Riedere SJ, Rossman PJ, Grimm RC, Debbins JP, Ehman RL. A monitoring, feedback and triggering system for reproducible breath-hold MR imaging. Magn Reson Med 1993; 30: 507-11.

28. Gaudio C. 1984-1999: fifteen years of cardiovascular magnetic resonance imaging. State of the art and future strategies. G Ital Cardiol 1999; 29: 1239-45.
29. Wang Y, Rossman PJ, Grimm RC, Riederer SJ, Ehman RL. Navigator echo-based real-time respiratory gating and triggering for reduction of respiratory effects in three-dimensional coronary MR angiography. Radiology 1996; 198: 55-60.
30. Sardanelli F, Molinari G, Zandrino F, Balbi M. Three-dimensional, navigator-echo MR coronary angiography in detecting stenoses of the major epicardial vessels, with conventional coronary angiography as the standard of reference. Radiology 2000; 214: 808-14.
31. Worthley SG, Helft G, Fuster V, et al. High resolution ex vivo magnetic resonance imaging of in situ coronary and aortic atherosclerotic plaque in a porcine model. Atherosclerosis 2000; 150: 321-9.
32. Nikolaou K, Huber Armin, Knez A, et al. Navigator echo-based respiratory gating for three-dimensional MR coronary angiography: reduction of scan time using a slice interpolation technique. J Comput Assist Tomogr 2001; 25: 378-87.
33. Worthley SG, Helft G, Fuster V, et al. Noninvasive in vivo magnetic resonance imaging of experimental coronary artery lesions in a porcine model. Circulation 2000; 101: 2956-61.
34. Saeed M, Wendland MF, Watzinger N, Akbari H, Higgins CB. MR contrast media for myocardial viability, microvascular integrity and perfusion. Eur J Radiol 2000; 34: 179-95.
35. Hundley WG, Hillis LD, Hamilton CA, et al. Assessment of coronary arterial restenosis with phase-contrast magnetic resonance imaging measurements of coronary flow reserve. Circulation 2000; 101: 2375-81.
36. Fayad ZA, Fuster V, Fallon JT, et al. Noninvasive in vivo human coronary artery lumen and wall imaging using black-blood magnetic resonance imaging. Circulation 2000; 102: 506-10.
37. Vrachliotis TG, Aliabadi D, Bis KG, Shetty AN, London J, Farah J. Breath-hold electrocardiogram-triggered, contrast-enhanced, 3D MR angiography to evaluate patency of coronary artery bypass graft. (abstr) Radiology 1996; 201: 273.
38. Langerak SE, Kunz P, de Roos A, Vliegen HW, van der Wall EE. Evaluation of coronary artery bypass grafts by magnetic resonance imaging. J Magn Reson Imaging 1999; 10: 434-41.
39. Amparo EG, Hoddick WK, Hricak H, et al. Comparison of magnetic resonance imaging and ultrasonography in the evaluation of abdominal aortic aneurysms. Radiology 1985; 154: 451-6.
40. Gomes AS, Lois JF, Drinkwater DC, Corday SR. Coronary artery bypass grafts: visualization with MR imaging. Radiology 1987; 162: 175-9.
41. Bottomley PA. MR spectroscopy of the human heart: the status and the challenge. Radiology 1994; 191: 593-612.
42. Duerinckx AJ, Atkinson DP, Mintorovitch J, Simonetti OP, Vrman MK. Two-dimensional coronary MRA: limitations and artifacts. Eur Radiol 1996; 6: 312-25.
43. Sodickson DK, McKenzie CA, Li W, Wolff S, Manning WJ, Edelman RR. Contrast-enhanced 3D MR angiography with simultaneous acquisition of spatial harmonics: a pilot study. Radiology 2000; 217: 284-9.
44. Kroft LJM, de Roos A. Blood pool contrast agents for cardiovascular MR imaging. J Magn Reson Imaging 1999; 10: 395-403.
45. Gaudio C, Vittore A, Mancini P, et al. Detection of coronary artery stenoses using breath-hold magnetic resonance coronary angiography. Comparison with X-ray angiography. Am J Cardiol 2002, in press.
46. Atkinson DJ, Edelman RR. Cineangiography of the heart in a single breath hold with a segmented turboFLASH sequence. Radiology 1991; 178: 357-60.
47. Higgins CB, Saeed M, Wendalnd M. Contrast enhancement for the myocardium. Magn Reson Med 1991; 22: 347-65.
48. Wolf GL. Role of magnetic resonance contrast agents in cardiac imaging. Am J Cardiol 1990; 66: 59F-62F.
49. Regenfus M, Ropers D, Achenbach S, et al. Noninvasive detection of coronary artery stenosis using contrast-enhanced three-dimensional breath-hold magnetic resonance coronary angiography. J Am Coll Cardiol 2000; 36: 44-50.
50. Shaefer S. Clinical nuclear magnetic resonance spectroscopy: insight into metabolism. Am J Cardiol 1990; 66: 45F-50F.
51. Sandstede JJW, Lipke C, Beer M, et al. Analysis of first-pass and delayed contrast enhancement patterns of dysfunctional myocardium on MR imaging: use in the prediction of myocardial viability. AJR Am J Roentgenol 2000; 174: 1737-40.
52. Panting JR, Taylor AM, Gatehouse PD, et al. First-pass myocardial perfusion imaging and equilibrium signal changes using the intravascular contrast agent NC100150 injection. J Magn Reson Imaging 1999; 10: 404-10.
53. Li D, Zheng J, Weinmann HJ. Contrast-enhanced MR imaging of coronary arteries: comparison of intra and extravascular contrast agents in Swine. Radiology 2001; 218: 670-8.
54. Lund GK, Higgins CB, Wendland MF, et al. Assessment of nicorandil therapy in ischemic myocardial injury by using contrast-enhanced and functional MR imaging. Radiology 2001; 221: 676-82.
55. Weissleder R, Lee AS, Khaw BA, Shen T, Brady TJ. Antimyosin-labeled monocrystalline iron oxide allows detection of myocardial infarcts: MR antibody imaging. Radiology 1992; 182: 381-85.
56. Eichenberger AC, Schuiki E, Kochli DV, et al. Ischemic heart disease: assessment with gadolinium-enhanced ultrafast MR imaging and dipyridamole stress. J Magn Reson Imaging 1994; 4: 425-32.
57. Wilke N, Jerosch-Herold M, Wang Y, et al. Myocardial perfusion reserve: assessment with multisection, quantitative, first-pass MR imaging. Radiology 1997; 204: 373-84.
58. Passariello R, De Santis M. Magnetic resonance imaging evaluation of myocardial perfusion. Am J Cardiol 1998; 81 (12A): 68G-73G.
59. Keijer JT, van Rossum AC, van Eenige MJ, et al. Magnetic resonance imaging of regional myocardial perfusion in patients with single-vessel coronary artery disease: quantitative comparison with thallium-SPECT and coronary angiography. J Magn Reson Imaging 2000; 11: 607-15.
60. Sechtem U, Baer FM, Voth E, Theissen P, Schneider CA. Stress functional MRI detection of ischemic heart disease and myocardial viability. J Magn Reson Imaging 1999; 10: 667-75.
61. Canet EP, Janier MF, Revel D. Magnetic resonance perfusion imaging in ischemic heart disease. J Magn Reson Imaging 1999; 10: 423-33.