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Atherosclerosis Imaging Using MR Imaging: Current and Emerging Applications

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Atherosclerosis remains the leading cause of death in industrialized societies, and its incidence is projected to increase worldwide in the next 2 decades [1]. It is recognized as a systemic disease affecting the vessel walls of all the major arteries, including the aorta, coronary, carotid, and peripheral arteries, and leads to a myriad of diseases, including stroke, myocardial infarction, peripheral vascular disease, aortic aneurysms, and sudden death [2]. Traditionally, clinicians have focused on atherosclerotic lesions that cause flow-limiting stenoses. During the last 2 decades, however, it has been shown that the process of atherosclerosis begins as an extraluminal phenomenon in the blood vessel wall, and the flow-limiting stenoses constitute a much later stage in the process of atherosclerosis [3]. Also, studies have demonstrated that the benefits of therapy-related decreased clinical events are not proportional to parallel reductions in vessel stenoses [4]. Therefore, the concept of flow-limiting stenoses has been challenged, and studies now focus more on the progressively atherosclerotic vessel wall. The American Heart Association created a detailed classification scheme designed to be used as a histologic template for images obtained by a variety of invasive and noninvasive techniques in the clinical setting [5,6]. It has been demonstrated that a vast majority of the thromboembolic events result from plaque rupture or erosion [7,8], which is characterized by thinning and rupture of the fibrous cap overlying the thrombogenic lipid core [9,10]. Accurate in vivo tracking of progressive lesions would be extremely useful clinically to determine the status of patients' atherosclerotic disease.

Because a major limitation of X-ray angiography is being a "luminogram," alternative imaging modalities to detect atherosclerotic plaque have been investigated. Intravascular ultrasound has been used to discern plaque components accurately [11], but it is an invasive procedure and is associated with procedure-related complications, and its ability to image the vessel wall downstream from a stenosis is limited. Furthermore, because of its high cost, intravascular ultrasound cannot be justified as a screening tool in an asymptomatic population. B-mode ultrasonography has been used to measure plaque volume in the carotid arteries, but its accuracy is limited by the plane of acquisition and the fact that atherosclerosis is a focal process [12,13]. CT has been used to detect and quantify coronary calcification, but its ability to detect soft, noncalcified plaques is not yet fully determined [14]. MR imaging, because of its high resolution, three-dimensional (3-D) capabilities, noninvasive nature, and capacity for soft tissue characterization, is emerging as a powerful modality to assess the atherosclerotic plaque burden in the arterial wall and has been used to monitor atherosclerosis in vivo [15,16]. This article reviews the technical principles and current status of in vivo MR imaging of atherosclerosis in various arterial beds and briefly discusses ongoing research in this field.

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Technical considerations for MR imaging of atherosclerosis

To visualize the atherosclerotic plaque by MR imaging accurately, many factors need to be taken into consideration. Accurate imaging must obtain adequate spatial resolution and adequate tissue contrast, avoid or minimize artifacts, be highly reproducible to facilitate longitudinal studies, and at the same time cause little or no discomfort to the subjects.

A normal artery wall is extremely thin (around 1 mm for the coronaries and thicker for the aorta and carotids), but with progressive arterial remodeling this thickness can vary from a few millimeters to more than a centimeter. An important imaging consideration is the ability to discern different plaque components, including the fibrous cap, lipid core, hemorrhage, and calcification. To do so, a spatial resolution in the submillimeter range is necessary. With the advent of sophisticated receiver coils and improvements in hardware, it is now possible to achieve an in-plane resolution in the order of 0.25×0.25 mm^2 in the carotids, 0.8×0.8 mm^2 in the aorta, and 0.46×0.46 mm^2 in the coronaries, with a 2- to 5-mm slice thickness [17–19] on a 1.5-T MR scanner. In 3-D coronary vessel wall imaging, an isotropic resolution of $1.0 \times 1.0 \times 1.0$ mm^3 has also been reported [20]. The use of phased-array surface coil techniques has proven to be effective in improving the signal-to-noise ratio (S/N) [21,22]. The widespread availability of 3-T MR scanners will probably help improve the S/N, which can be partially traded for an improved spatial resolution.

Histologic studies have shown that different plaque components co-exist, and these different components produce differences in the MR signal based upon their physical properties [23]. T1 and T2 relaxation times vary among tissue types, enabling the generation of tissue contrast. Thus, to achieve tissue contrast and hence plaque characterization, images obtained using different weightings are necessary [18,24]. Another technical aspect to consider is the suppression of the signal obtained from the blood flow; this suppression enhances the conspicuity of the vessel wall and its components against the backdrop of a hypointense lumen. Currently, the most effective flow-suppression (black-blood) method in plaque imaging is thought to be the double inversion recovery (IR) technique [25]. IR, in combination with fast spin echo (FSE) techniques, has been used to image the carotid, aortic, and coronary vessel wall [17–19,26]. To reduce the scan time related to this technique, multislice techniques have been developed that reduce the imaging time by two- to fourfold without significantly compromising the S/N [27,28].

The next technical issue to consider is that of artifacts, including those caused by cardiac contraction, breathing, blood flow, and random motion such as swallowing or tremors, all of which can significantly deteriorate image quality. To counter these artifacts, cardiac gating is used to improve the quality of the scan. For aortic and coronary imaging, along with cardiac gating, breathing also is an issue, which is countered by breath-holding or use of respiratory navigators [18–20]. Also, perivascular fat, which can obscure signal from the vessel wall, particularly in the coronaries, needs to be suppressed [29]. An interesting development is the use of contrast agents to enhance plaque components. Usually gadolinium-based agents are used in association with double IR imaging or spoilt gradient echo sequences [30,31]. With the use of novel contrast agents such as ultrasmall paramagnetic particles of iron oxide (USPIOs) or fibrin-specific agents, new data are being acquired rapidly [32–34].

The final technical aspect that needs to be considered is the processing of the MR images that are obtained. Plaque analysis is generally separated into two domains: assessment of morphology (plaque dimensions) and assessment of tissue characteristics. In general, these variables are considered in continuous rather than categorical form so that inferences can be drawn about the longitudinal regression or progression of plaque.

Assessment of plaque morphology using MR imaging

Accurate quantification of vessel wall dimensions depends upon the ability to discern the inner and outer boundaries of the vessel wall. Once these boundaries have been determined, the dimensions can be recorded as thickness or area (difference between outer contour and inner contour). Several semiautomatic image-processing tools have been proposed for vessel boundary detection [35,36]. Atherosclerosis, however, is generally not a uniform process, and there can be sudden variations in regional plaque surfaces. The measurements of thickness and area are less accurate and more vulnerable to anatomic mismatches because only a single slice is measured, and an entire anatomic rematch of the patient's prior scanning position is virtually impossible. Thus, to reduce the variation in plaque dimensions from study to study, plaque volume becomes the morphologic assessment of choice. Generally, multiple (five or six) slices are obtained with the center slice in the middle of the thickest part of the plaque. A modification of Simpson's formula is used to calculate plaque volume. In this process, the emphasis is on the middle slices rather than the outer slices, and minimal errors of registration do not significantly alter the volume measurements. In a carotid artery study, the variability in plaque volume assessment was found to be between 4% and 6% [37]. In a recent study of aortic atherosclerosis, the authors were able to demonstrate that the reproducibility of plaque volume assessment (intraclass correlation coefficient, 0.95; coefficient of variation, 5.7%) was significantly superior to that of plaque thickness (intraclass correlation coefficient, 0.82; coefficient of variation, 18.9%) or plaque area (intraclass correlation coefficient, 0.90; coefficient of variation, 21.3%). Based on these findings, the authors concluded that changes of less than 4.6% in aortic plaque volume could be considered as accurately measured by MR imaging [38].

Characterizing plaque using MR imaging

The difference in MR signal between hydrogen protons in different chemical environments make it ideally suited for noninvasive characterization of the different components of a given plaque. Techniques focused on lipid assessment using spectroscopy and chemical-shift imaging have been found less useful in the in vivo setting because of the relatively low lipid concentration in the tissue and hence poor S/N [39–41]. Most of the newer techniques use water protons to generate the MR signal. Different plaque components have been characterized by T1, T2, and proton-density weightings in animals [42,43], ex vivo specimens [41,44], in vivo carotids [44,45], in vivo aortas [18], and, more recently, the coronaries [19,22].

The characteristic appearance of different plaque components on MR imaging has been previously validated (Figs. 1 and 2) [17,23,44]. Generally, lipid components appear as isointense regions within the plaque on T1- and proton density–weighted images but hypointense on T2-weighted images. On the other hand, the fibrous cap appears bright, and calcium appears very hypointense on all three weightings. Thrombus appears hyperintense (albeit less so than fibrous cap) on all three weightings. Perivascular fat, which predominantly consists of triglycerides, has a different MR appearance than the lipid core, which generally consists of unesterified cholesterol and cholesterol esters [23,41].

Recent studies have demonstrated that the use of paramagnetic contrast agents, such as gadolinium, enables subtle distinctions between different plaque components to be detected (Fig. 3). Increases in T1 relaxation by gadolinium leads to increased contrast enhancement on T1-weighted pulse sequences. There is evidence of neovascularization and inflammation in atherosclerotic plaque [46], and it has been proposed that contrast-enhanced MR imaging can aid in plaque characterization by helping to detect these changes [30,31]. These studies demonstrated that pre- and postcontrast MR imaging helped differentiate between the necrotic core and fibrous tissue. In the study by Wasserman et al [31] the S/N of fibrous cap was twice that of the lipid core. Another study demonstrated that postcontrast signal enhancement in carotid arteries and aorta is associated with elevated serum levels of interleukin-6, C-reactive protein, and cell adhesion molecules [47].

USPIOs alter the relaxation times of adjacent tissue and are avidly taken up by macrophages. It has been demonstrated that injection of USPIO into hyperlipidemic rabbits is associated with the appearance of signal voids on the luminal surface of the aorta [48]. Another active area of research is the detection of thrombus or fibrin, which has been demonstrated to play a role in plaque progression [7]. Contrast agents that can detect and characterize thrombi have been developed, and fibrin has been identified by lipid-encapsulated perfluorocarbon paramagnetic nanoparticles in vitro [33,49] as well as in vivo [33]. In a recent report, the feasibility of a gadolinium-based fibrin-binding contrast agent, EP-2104R (EPIX Medical, Inc., Cambridge, Massachusetts) was demonstrated in a swine model of coronary thrombus and in-stent thrombosis (Fig. 4) [34]. Potential applications include detection of coronary in-stent thrombosis or thrombus burden in patients with acute coronary syndromes.

MR imaging of carotid atherosclerosis

The carotid artery has become the most common target vessel for MR imaging of

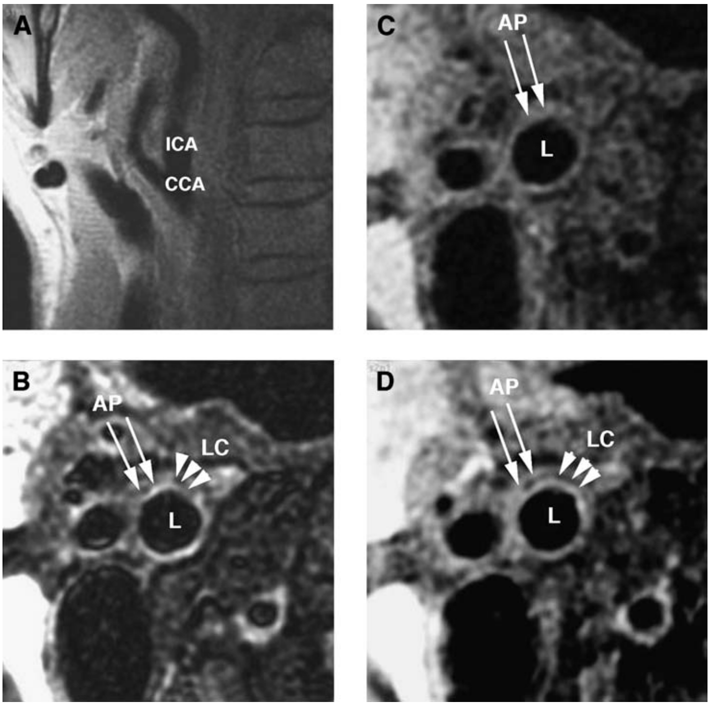

Fig. 1. High-resolution MR images of the right carotid artery of a 72-year-old man with advanced atherosclerosis. (*A*) Oblique proton-density image through the proximal internal and external carotid arteries. This image was used to prescribe subsequent images. CCA, common carotid artery ICA, internal carotid artery. (*B*) T2-weighted precontrast, (*C*) T1-weighted precontrast and (*D*) T1-weighted postcontrast FSE images of the right internal carotid artery demonstrating arterial wall remodeling caused by atherosclerotic plaque (AP). Note the lipid core (LC) within the atherosclerotic plaque on T2-weighted and postcontrast T1-weighted images. L, lumen.

atherosclerosis (see Figs. 1–3). This application has become widespread because of the use of phased-array coils, well-validated multicontrast imaging protocols [17,44], and the existence of a reference based on histologic examination of atherosclerotic lesions obtained surgically during carotid endarterectomy [50].

MR imaging accurately identifies the adventitial layer of the carotid artery and thus aids in measurement of vessel wall dimensions with high accuracy (4%–6% error of vessel volume measurement) [16,37,51]. MR imaging has also been used to demonstrate the state of carotid plaque substructure, including the fibrous cap. In one study, the in vivo state of the fibrous cap was characterized based on its appearance on MR images (intact and thin, intact and thick, or ruptured), and there was a high level of agreement between the MR images and the histologic state of the fibrous cap [45]. When multicontrast MR imaging has been compared with histology, a sensitivity of 81% and specificity of 90% has been demonstrated for identification of an unstable fibrous cap [52]. A ruptured fibrous cap identified on MR imaging was highly associated with a stroke or a transient ischemic attack [53]. MR imaging also has a high sensitivity and specificity in detecting lipid core, hemorrhage, and calcification in ex vivo imaging of endarterectomy specimens (90%–100%) [54] and in vivo imaging (85%–92%) [24,55]. The role of contrast-enhanced MR imaging in characterizing carotid plaque has been described previously in this article.

MR imaging of aortic atherosclerosis

The feasibility of detecting atherosclerosis of the thoracic aorta using surface receiver coils has been demonstrated, using transesophageal echocardiography (TEE) as a reference [18]. MR assessment of the aorta correlated well with TEE for assessment of plaque thickness, extent, and composition. This technique has been found to be

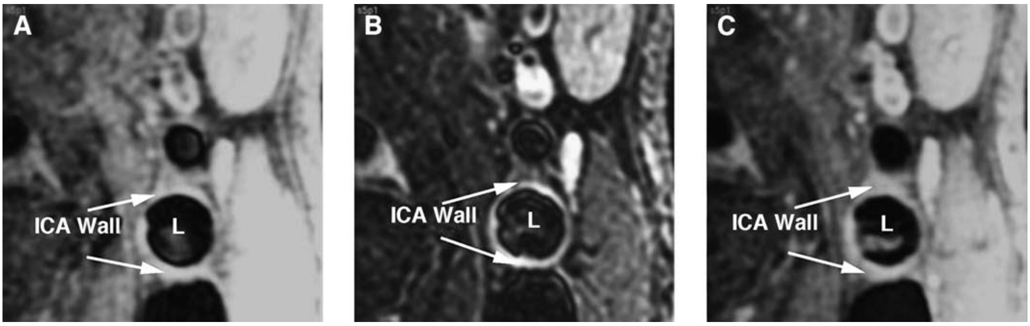

Fig. 2. High-resolution MR images of the right carotid artery of a 75-year-old man with advanced atherosclerosis. (*A*) T2-weighted precontrast, (*B*) T1-weighted precontrast, and (*C*) T1-weighted postcontrast FSE images of the right internal carotid artery (ICA) demonstrating only arterial wall remodeling caused by atherosclerotic plaque (*arrows*). Note the lipid core is absent. L, lumen.

highly reproducible [26]. In subjects from the Framingham heart study, aortic plaque burden increases with age [56]. After 1 year of lipid-lowering therapy, MR imaging of the aorta has demonstrated plaque regression by 8% without a change in the cross-sectional area of the arterial lumen [15,57].

Transesophageal MR imaging (TEMRI) using a loopless antenna coil has been developed for aortic MR imaging. The rationale behind TEMRI comes from a specific limitation for surface MR receiver coils: the trade-off between depth of penetration and S/N. To detect and visualize distant structures such the thoracic aorta adequately, a strong local signal could be of paramount importance; such a signal was achieved by using a TEMRI coil [58]. The feasibility and utility of this technique was demonstrated in patients with aortic atherosclerosis [59]. The authors have recently demonstrated that the addition of the TEMRI coil increases the signal in the aortic arch and descending aorta by 157% to 225% above that attained by surface coils alone (Fig. 5) [38]. Furthermore, using the combined surface MR imaging and TEMRI, the authors also have demonstrated recently that aortic plaque regression of about 12% can be detected as early as 6 months (as compared with 1 year or longer) following lipid-lowering therapy [60]. The disadvantage of this approach is that the technique is invasive and requires a skilled operator to position the TEMRI probe.

MR imaging of coronary atherosclerosis

Until recently, the acceptance of MR imaging for coronary imaging has been hampered by many

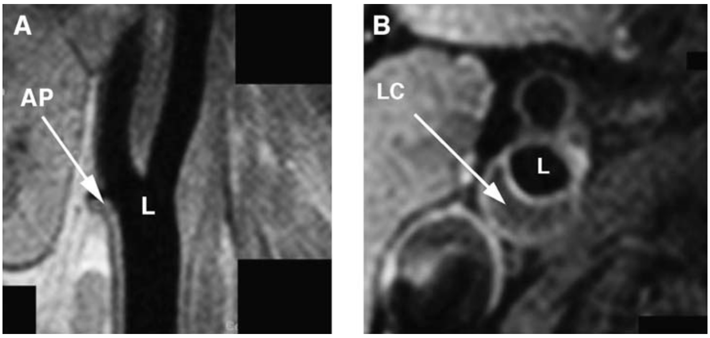

Fig. 3. High-resolution MR images of the right carotid artery of another patient with advanced atherosclerosis. (*A*) Oblique proton density image through the proximal internal and external carotid arteries. This image was used to prescribe subsequent images. AP, atherosclerotic plaque; L, lumen. (*B*) T1-weighted postcontrast FSE image of the right internal carotid artery demonstrating significant arterial wall remodeling caused by atherosclerotic plaque with an excellent postcontrast delineation of the lipid core (LC). L, lumen.

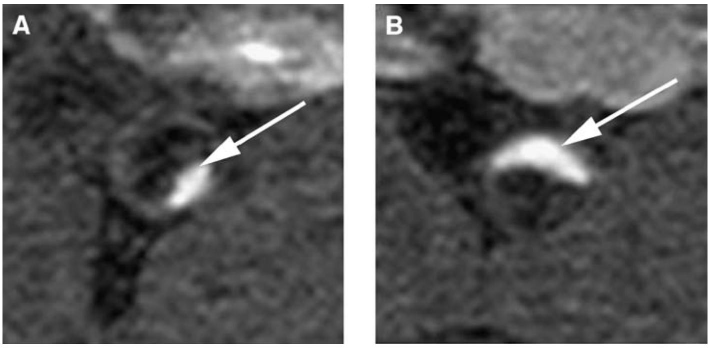

Fig. 4. (*A* and *B*) Two mural thrombi (*arrows*) observed at different levels of the aorta, with good contrast between thrombus (*arrow*), arterial lumen, and vessel wall, 20 hours after administration of EP-1873 contrast agent. (Courtesy of Dr. Phillip Graham, EPIX Medical Inc, Cambridge, MA.)

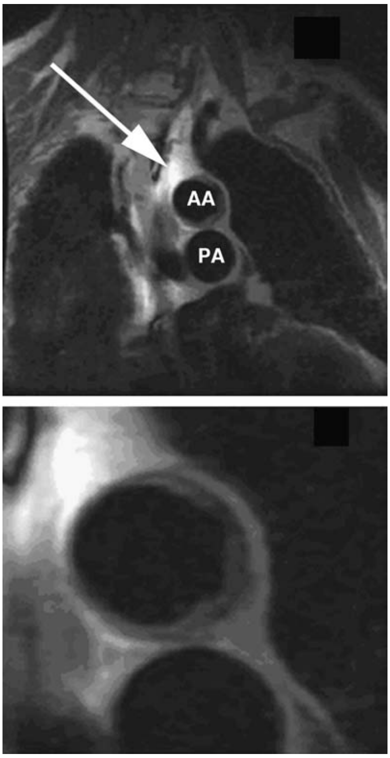

Fig. 5. Double IR FSE proton-density images of the aortic arch, in a patient with advanced atherosclerosis, obtained using a combination of surface and transesophageal MR imaging, demonstrating excellent delineation of the atherosclerotic plaque. The arrow points to the hyperintense signal related to the transesophageal receiver coil. AA, aortic arch; PA, pulmonary artery.

technical limitations, including constant cardiac motion caused by contraction/relaxation, diaphragmatic/chest wall motion caused by respiration, the small caliber of the coronary vessels, the tortuosity of the coronary arteries, and signal from surrounding epicardial fat and myocardium [61]. With the following refinements of MR techniques, however, coronary imaging has become technically feasible. To account for bulk cardiac motion, ECG gating (particularly the vector ECG approach) has been used with unprecedented results [62]. Because coronary artery motion is minimal at mid-diastole, it has become the preferred time for imaging [61]. Several different approaches have been used to minimize the effect of respiratory motion. These methods include sustained or multiple brief breath-holds, coached breathing, free breathing using multiple averages, and chest wall bellows. A more recent innovation is the positioning of MR navigators at any interface that accurately depicts respiratory motion (eg, the dome of the right hemidiaphragm) [61,63]. Advanced MR pulse sequences have been developed that can suppress the signal from surrounding epicardial fat and the myocardium, thus enabling visualization of the coronary arteries with contrast [29]. Finally, to improve in-plane spatial resolution to image the coronaries, newer cardiac-specific coils have been developed that support an improved S/N [61].

Fayad et al [19] have demonstrated the feasibility of in vivo imaging of the coronary vessel wall using a 2-D black-blood technique [19]. The reproducibility of this technique, which must be excellent for this imaging method to become a useful clinical tool, has only recently been studied at John Hopkins University. The authors have recently demonstrated that coronary vessel wall imaging (Fig. 6) using the double IR FSE (2-D black-blood pulse sequence) was reproducible ($r = 0.87$) with good inter- and intraobserver agreement [64]. This technique allows only limited spatial coverage, however. To overcome this problem, Botnar et al [65] have attempted to image the coronary vessel wall using 3-D black-blood coronary MR imaging, along with a local inversion prepulse to suppress unwanted signal (ventricular blood, myocardium, and chest wall tissue) outside a user-defined region of interest, and a spiral imaging technique. They were able to show the phenomenon of outward arterial remodeling noninvasively [20]. This technique enables the imaging of a long segment of the coronary artery wall and might be a useful screening technique for measuring plaque burden.

Role of intravascular MR imaging

The ability of MR imaging to generate high-resolution images of the vessel wall, delineate perivascular soft tissue structures, and generate multiplanar images in real time have generated interest in MR imaging as a replacement for X-ray angiography [66]. In a recent study on swine, an intravascular MR coil/guide wire (Surgi-Vision, Gaithersburg, Maryland), introduced through the external iliac vein into the inferior vena cava generated excellent images in vivo that correlated well with histologic findings (Fig. 7) [67]. Preliminary studies have also demonstrated the feasibility of MR-guided percutaneous angioplasty in rabbit aorta [68], stent deployment in pig femoral arteries [69] and pig coronary arteries [70], and monitoring of catheter-based gene therapy in pig femoral arteries [71].

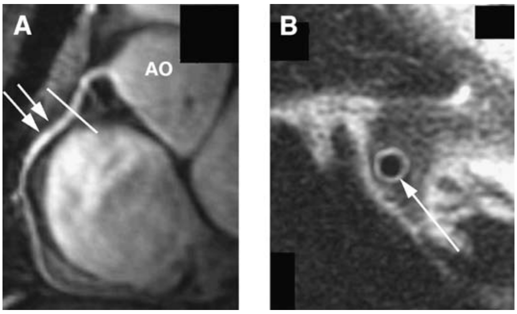

Fig. 6. (*A*) MR angiogram of the right coronary artery (*arrows*). AO, aorta. The bold line indicates where the image of the vessel wall was obtained. (*B*) Double IR FSE image of the right coronary artery (*arrow*) in a healthy volunteer.

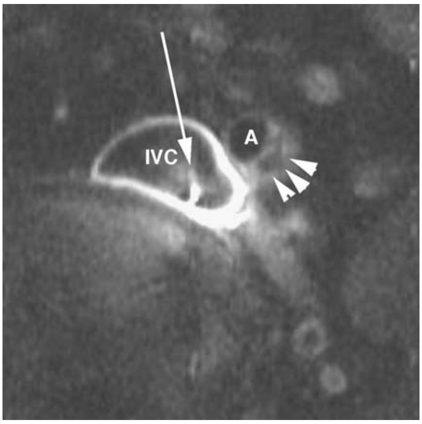

Fig. 7. Double IR FSE image of the abdominal aorta (A) in a patient with advanced atherosclerosis, obtained using an intravascular coil positioned in the inferior vena cava (IVC). Notice the bright signal emanating from the coil (*arrow*). The atherosclerotic changes in the aortic wall (*arrowheads*) are well delineated.

Future of MR-based atherosclerosis imaging

As described in this article, the past decade has seen significant developments in the MR imaging of atherosclerosis. Most of the studies, however, have involved a small number of subjects, and there is paucity of multicenter data. Because there is considerable institutional variation in acquisition and in analysis techniques, it is difficult to classify current findings as anything other than preliminary. Nonetheless, current results open an exciting window of opportunity that can be used to devise an optimal treatment strategy, monitor the effect of therapy, and understand better the pathophysiology of atherosclerosis.

Potential applications of MR atherosclerosis imaging might include its use in longitudinal studies looking at the effects of newer drug therapies on plaque composition and morphology. Advantages would include noninvasive or minimally invasive monitoring of plaque regression with MR imaging and the potential to reduce the sample size compared with intravascular ultrasound. MR imaging also can be used to monitor disease progression in high-risk patients. Further refinements of the technique and in image analysis will be necessary before the use of MR imaging for this purpose becomes widespread.

Other potential applications include individually tailored therapy for patients based on their plaque characteristics and plaque burden. Because of advances in MR hardware and software, MR imaging could be used as a screening tool to stratify patients based on their cardiovascular risk. Finally, the high resolution of MR imaging and the development of sophisticated contrast agents offer tremendous promise of in vivo molecular imaging of the atherosclerotic plaque.

Summary

Because of its high resolution, 3-D capabilities, noninvasive nature, and capacity for soft tissue characterization, MR imaging has emerged as a powerful modality to assess the process of atherosclerosis comprehensively in different arterial beds, including the coronary arteries. It holds great promise in studies involving longitudinal follow-up of plaque progression and for detection of therapeutic intervention-related changes. With the development of newer, target-specific contrast agents and molecular imaging applications, an exponential growth in its current applications is anticipated.

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References

[1] Michaud CM, Murray CJ, Bloom BR. Burden of disease–implications for future research. JAMA 2001;285(5):535–9.

[2] Ross R. Atherosclerosis–an inflammatory disease. N Engl J Med 1999;340(2):115–26.

[3] Glagov S, Weisenberg E, Zarins CK, et al. Compensatory enlargement of human atherosclerotic coronary arteries. N Engl J Med 1987;316(22):1371–5.

[4] Brown BG, Zhao XQ, Chait A, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. N Engl J Med 2001;345(22):1583–92.

[5] Stary HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation 1995;92(5):1355–74.

[6] Stary HC, Chandler AB, Glagov S, et al. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Arterioscler Thromb 1994;14(5):840–56.

[7] Virmani R, Kolodgie FD, Burke AP, et al. Lessons from sudden coronary death: a comprehensive morphological classification scheme for atherosclerotic lesions. Arterioscler Thromb Vasc Biol 2000;20(5):1262–75.

[8] Shah PK. Pathophysiology of coronary thrombosis: role of plaque rupture and plaque erosion. Prog Cardiovasc Dis 2002;44(5):357–68.

[9] Falk E. Why do plaques rupture? Circulation 1992;86(6 Suppl):III30–42.

[10] Davies MJ, Thomas AC. Plaque fissuring–the cause of acute myocardial infarction, sudden ischaemic death, and crescendo angina. Br Heart J 1985;53(4):363–73.

[11] Nissen SE, Yock P. Intravascular ultrasound: novel pathophysiological insights and current clinical applications. Circulation 2001;103(4):604–16.

[12] O'Leary DH, Polak JF. Intima-media thickness: a tool for atherosclerosis imaging and event prediction. Am J Cardiol 2002;90(10C):18L–21L.

[13] Spence JD. Ultrasound measurement of carotid plaque as a surrogate outcome for coronary artery disease. Am J Cardiol 2002;89(4A):10B–5B [discussion: 15B–16B].

[14] Fayad ZA, Fuster V, Nikolaou K, et al. Computed tomography and magnetic resonance imaging for noninvasive coronary angiography and plaque imaging: current and potential future concepts. Circulation 2002;106(15):2026–34.

[15] Corti R, Fuster V, Fayad ZA, et al. Lipid lowering by simvastatin induces regression of human atherosclerotic lesions: two years' follow-up by high-resolution noninvasive magnetic resonance imaging. Circulation 2002;106(23):2884–7.

[16] Yuan C, Beach KW, Smith LH Jr, et al. Measurement of atherosclerotic carotid plaque size in vivo using high resolution magnetic resonance imaging. Circulation 1998;98(24):2666–71.

[17] Yuan C, Mitsumori LM, Beach KW, et al. Carotid atherosclerotic plaque: noninvasive MR characterization and identification of vulnerable lesions. Radiology 2001;221(2):285–99.

[18] Fayad ZA, Nahar T, Fallon JT, et al. In vivo magnetic resonance evaluation of atherosclerotic plaques in the human thoracic aorta: a comparison with transesophageal echocardiography. Circulation 2000;101(21):2503–9.

[19] 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(5):506–10.

[20] Kim WY, Stuber M, Bornert P, et al. Three-dimensional black-blood cardiac magnetic resonance coronary vessel wall imaging detects positive arterial remodeling in patients with nonsignificant

coronary artery disease. Circulation 2002;106(3): 296–9.

[21] Hayes CE, Mathis CM, Yuan C. Surface coil phased arrays for high-resolution imaging of the carotid arteries. J Magn Reson Imaging 1996;6(1):109–12.

[22] Botnar RM, Stuber M, Kim WY, et al. Magnetic resonance coronary lumen and vessel wall imaging. Rays 2001;26(4):291–303.

[23] Yuan C, Petty C, O'Brien KD, et al. In vitro and in situ magnetic resonance imaging signal features of atherosclerotic plaque-associated lipids. Arterioscler Thromb Vasc Biol 1997;17(8):1496–503.

[24] Yuan C, Mitsumori LM, Ferguson MS, et al. In vivo accuracy of multispectral magnetic resonance imaging for identifying lipid-rich necrotic cores and intraplaque hemorrhage in advanced human carotid plaques. Circulation 2001;104(17):2051–6.

[25] Edelman RR, Chien D, Kim D. Fast selective black blood MR imaging. Radiology 1991;181(3): 655–60.

[26] Chan SK, Jaffer FA, Botnar RM, et al. Scan reproducibility of magnetic resonance imaging assessment of aortic atherosclerosis burden. J Cardiovasc Magn Reson 2001;3(4):331–8.

[27] Song HK, Wright AC, Wolf RL, et al. Multislice double inversion pulse sequence for efficient black-blood MRI. Magn Reson Med 2002;47(3):616–20.

[28] Yarnykh VL, Yuan C. Multislice double inversion-recovery black-blood imaging with simultaneous slice reinversion. J Magn Reson Imaging 2003; 17(4):478–83.

[29] Li D, Paschal CB, Haacke EM, et al. Coronary arteries: three-dimensional MR imaging with fat saturation and magnetization transfer contrast. Radiology 1993;187(2):401–6.

[30] Yuan C, Kerwin WS, Ferguson MS, et al. Contrast-enhanced high resolution MRI for atherosclerotic carotid artery tissue characterization. J Magn Reson Imaging 2002;15(1):62–7.

[31] Wasserman BA, Smith WI, Trout HH III, et al. Carotid artery atherosclerosis: in vivo morphologic characterization with gadolinium-enhanced double-oblique MR imaging initial results. Radiology 2002; 223(2):566–73.

[32] Kooi ME, Cappendijk VC, Cleutjens KB, et al. Accumulation of ultrasmall superparamagnetic particles of iron oxide in human atherosclerotic plaques can be detected by in vivo magnetic resonance imaging. Circulation 2003;107(19):2453–8.

[33] Flacke S, Fischer S, Scott MJ, et al. Novel MRI contrast agent for molecular imaging of fibrin: implications for detecting vulnerable plaques. Circulation 2001;104(11):1280–5.

[34] Botnar RM, Buecker A, Wiethoff AJ, et al. In vivo magnetic resonance imaging of coronary thrombosis using a fibrin-binding molecular magnetic resonance contrast agent. Circulation 2004;110:1463–6.

[35] Yuan C, Lin E, Millard J, et al. Closed contour edge detection of blood vessel lumen and outer wall boundaries in black-blood MR images. Magn Reson Imaging 1999;17(2):257–66.

[36] Ladak HM, Thomas JB, Mitchell JR, et al. A semi-automatic technique for measurement of arterial wall from black blood MRI. Med Phys 2001;28(6): 1098–107.

[37] Zhang S, Hatsukami TS, Polissar NL, et al. Comparison of carotid vessel wall area measurements using three different contrast-weighted black blood MR imaging techniques. Magn Reson Imaging 2001;19(6):795–802.

[38] Steen H, Warren W, Desai MY, et al. Combined transesophageal and surface MRI provides optimal imaging and high reproducibility of aortic atherosclerosis imaging. J Cardiovasc Magn Reson, in press.

[39] Mohiaddin RH, Firmin DN, Underwood SR, et al. Chemical shift magnetic resonance imaging of human atheroma. Br Heart J 1989;62(2):81–9.

[40] Vinitski S, Consigny PM, Shapiro MJ, et al. Magnetic resonance chemical shift imaging and spectroscopy of atherosclerotic plaque. Invest Radiol 1991; 26(8):703–14.

[41] Toussaint JF, Southern JF, Fuster V, et al. T2-weighted contrast for NMR characterization of human atherosclerosis. Arterioscler Thromb Vasc Biol 1995;15(10):1533–42.

[42] Skinner MP, Yuan C, Mitsumori L, et al. Serial magnetic resonance imaging of experimental atherosclerosis detects lesion fine structure, progression and complications in vivo. Nat Med 1995;1(1): 69–73.

[43] Helft G, Worthley SG, Fuster V, et al. Atherosclerotic aortic component quantification by noninvasive magnetic resonance imaging: an in vivo study in rabbits. J Am Coll Cardiol 2001;37(4):1149–54.

[44] Toussaint JF, LaMuraglia GM, Southern JF, et al. Magnetic resonance images lipid, fibrous, calcified, hemorrhagic, and thrombotic components of human atherosclerosis in vivo. Circulation 1996;94(5): 932–8.

[45] Hatsukami TS, Ross R, Polissar NL, et al. Visualization of fibrous cap thickness and rupture in human atherosclerotic carotid plaque in vivo with high-resolution magnetic resonance imaging. Circulation 2000;102(9):959–64.

[46] de Boer OJ, van der Wal AC, Teeling P, et al. Leucocyte recruitment in rupture prone regions of lipid-rich plaques: a prominent role for neovascularization? Cardiovasc Res 1999;41(2):443–9.

[47] Weiss CR, Arai AE, Bui MN, et al. Arterial wall MRI characteristics are associated with elevated serum markers of inflammation in humans. J Magn Reson Imaging 2001;14(6):698–704.

[48] Ruehm SG, Corot C, Vogt P, et al. Magnetic resonance imaging of atherosclerotic plaque with ultrasmall superparamagnetic particles of iron oxide in hyperlipidemic rabbits. Circulation 2001;103(3): 415–22.

[49] Yu X, Song SK, Chen J, et al. High-resolution MRI characterization of human thrombus using a novel fibrin-targeted paramagnetic nanoparticle contrast agent. Magn Reson Med 2000;44(6):867–72.

[50] Thackray BD, Burns DH, Ferguson MS, et al. A new method for studying plaque morphology. Am J Card Imaging 1995;9(3):149–56.

[51] Kang X, Polissar NL, Han C, et al. Analysis of the measurement precision of arterial lumen and wall areas using high-resolution MRI. Magn Reson Med 2000;44(6):968–72.

[52] Mitsumori LM, Hatsukami TS, Ferguson MS, et al. In vivo accuracy of multisequence MR imaging for identifying unstable fibrous caps in advanced human carotid plaques. J Magn Reson Imaging 2003;17(4): 410–20.

[53] Yuan C, Zhang SX, Polissar NL, et al. Identification of fibrous cap rupture with magnetic resonance imaging is highly associated with recent transient ischemic attack or stroke. Circulation 2002;105(2): 181–5.

[54] Shinnar M, Fallon JT, Wehrli S, et al. The diagnostic accuracy of ex vivo MRI for human atherosclerotic plaque characterization. Arterioscler Thromb Vasc Biol 1999;19(11):2756–61.

[55] Cai JM, Hatsukami TS, Ferguson MS, et al. Classification of human carotid atherosclerotic lesions with in vivo multicontrast magnetic resonance imaging. Circulation 2002;106(11):1368–73.

[56] Jaffer FA, O'Donnell CJ, Larson MG, et al. Age and sex distribution of subclinical aortic atherosclerosis: a magnetic resonance imaging examination of the Framingham Heart Study. Arterioscler Thromb Vasc Biol 2002;22(5):849–54.

[57] Corti R, Fayad ZA, Fuster V, et al. Effects of lipid-lowering by simvastatin on human atherosclerotic lesions: a longitudinal study by high-resolution, noninvasive magnetic resonance imaging. Circulation 2001;104(3):249–52.

[58] Shunk KA, Lima JA, Heldman AW, et al. Transesophageal magnetic resonance imaging. Magn Reson Med 1999;41(4):722–6.

[59] Shunk KA, Garot J, Atalar E, et al. Transesophageal magnetic resonance imaging of the aortic arch and descending thoracic aorta in patients with aortic atherosclerosis. J Am Coll Cardiol 2001;37(8):2031–5.

[60] Lima JA, Desai MY, Steen H, et al. Statin induced cholesterol lowering and plaque regression after 6 months of mri monitored therapy. Circulation 2004;10:2336–41.

[61] Manning WJ, Stuber M, Danias PG, et al. Coronary magnetic resonance imaging: current status. Curr Probl Cardiol 2002;27(7):275–333.

[62] Fischer SE, Wickline SA, Lorenz CH. Novel real-time R-wave detection algorithm based on the vectorcardiogram for accurate gated magnetic resonance acquisitions. Magn Reson Med 1999;42(2): 361–70.

[63] Stuber M, Botnar RM, Danias PG, et al. Submillimeter three-dimensional coronary MR angiography with real-time navigator correction: comparison of navigator locations. Radiology 1999;212(2): 579–87.

[64] Hazirolan T, Gupta SN, Mohamed MA, et al. Reproducibility of black-blood coronary vessel wall MR imaging. J Cardiovasc Magn Reson, in press.

[65] Botnar RM, Kim WY, Bornert P, et al. 3D coronary vessel wall imaging utilizing a local inversion technique with spiral image acquisition. Magn Reson Med 2001;46(5):848–54.

[66] Ladd ME, Debatin JF. Interventional and intravascular MR angiography. Herz 2000;25(4):440–51.

[67] Hofmann LV, Liddell RP, Arepally A, et al. In vivo intravascular MR imaging: transvenous technique for arterial wall imaging. J Vasc Interv Radiol 2003;14(10):1317–27.

[68] Yang X, Atalar E. Intravascular MR imaging-guided balloon angioplasty with an MR imaging guide wire: feasibility study in rabbits. Radiology 2000;217(2): 501–6.

[69] Dion YM, Ben El Kadi H, Boudoux C, et al. Endovascular procedures under near-real-time magnetic resonance imaging guidance: an experimental feasibility study. J Vasc Surg 2000;32(5):1006–14.

[70] Spuentrup E, Ruebben A, Schaeffter T, et al. Magnetic resonance–guided coronary artery stent placement in a swine model. Circulation 2002;105(7): 874–9.

[71] Yang X, Atalar E, Li D, et al. Magnetic resonance imaging permits in vivo monitoring of catheter-based vascular gene delivery. Circulation 2001; 104(14):1588–90.