Characterization of atherosclerotic plaque by magnetic resonance imaging

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Background Atherosclerosis, the most common disease in the industrialized world, is still one of the most poorly explained and little understood problems in medicine. It is important to obtain reliable images of lipid-rich type IV and Va plaques, which, upon rupture, are most likely to cause acute ischemic events. The development of noninvasive methods to detect atherosclerotic plaque lesions and assess their composition promises to play an important role in the management of patients in the future.

Methods This review highlights the advantages and disadvantages of magnetic resonance imaging (MRI) and intravascular ultrasound, compared with histopathologic findings, in detecting and determining the extent of atheromatous plaques.

Results Compared with intravascular ultrasound, MRI has been found to be superior in delineating lipid plaque components. Intravascular ultrasound, despite its better spatial resolution, is an invasive method and does not provide information on complex features of stenotic vessels. In vitro studies show that MRI of atherosclerotic plaques makes it possible to characterize the lesions in detail in terms of size, shape, and plaque tissue components.

Conclusions Although MRI is in its early stages, it shows potential as a noninvasive method that can be used to evaluate atherosclerotic plaque and distinguish its components. (Am Heart J 2001;141:S45-8.)

Atherosclerosis, the most common disease in the industrialized world, is still one of the most poorly explained and little understood problems in medicine. The risk factors are known; however, the mechanism that triggers plaque deposition, differences in plaque composition, plaque growth, and the rupture of atherosclerotic plaque are unknown or speculative. Atherosclerosis research is therefore currently focusing on the physiopathologic characteristics of atheroma growth and plaque rupture as well as on new imaging techniques for the assessment of plaque composition. Noninvasive techniques for the recognition and characterization of different atherosclerotic lesions and their composition would therefore be extremely valuable. Imaging modalities are needed to characterize plaque components, lipid content, and the extent of the lipid core and the fibrous capsule.

Atherosclerotic plaque disease represents a chronic inflammatory response to injury, culminating in an acute event induced by plaque rupture. It is believed to originate with the incorporation of fatty streaks into the vessel intima and to evolve later into its typical appearance of a central region of necrosis covered by a fibrous cap. Variations in the appearance and composition of plaque, which consists of lipid and fibrous tissue as well as calcifications, are considerable. There is mounting evidence that the makeup of an atherosclerotic plaque represents an important determinant of the clinical risk and outcome.

Atherosclerotic plaques consisting predominantly of collagen-rich fibrous tissue may progress over a period of many years and may lead to the development of collaterals. Acute coronary occlusion and myocardial infarction, in contrast, evolve most frequently from mild to moderate stenosis of lipid-rich lesions. These lipid plaques typically have a core of foam cells, in which lipids are predominantly in the form of liquid and liquid-crystalline cholesterol esters, which are covered by a fibrous cap. Such lesions fracture easily, and the exposed lipid surface increases thrombogenicity, leading to vascular occlusion.

In most patients acute ischemic events appear to be caused by the disruption of type IV and Va lipid-rich lesions, which are often not even angiographically visible. Therefore it is important to visualize these less obstructive lipid-rich plaques vulnerable to rupture to identify their presence before a clinical event occurs. The development of a noninvasive method for detecting atherosclerotic plaque lesions and for assessing their structural significance promises to play an important role in the management of patients in the future.

Magnetic resonance imaging of the plaque in vitro

Magnetic resonance imaging (MRI) has been shown to be an ideal tool for imaging the arterial wall. The 3-layer

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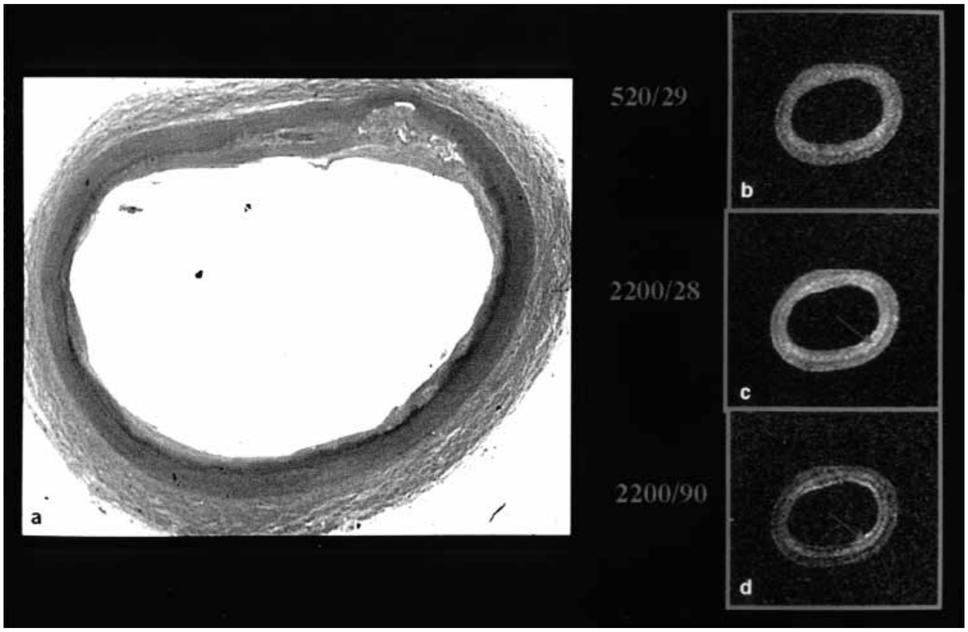
Figure 1



Normal iliac artery. **a,** Histologic section showing normal pattern in intima, media, and adventitia. MRI of normal vessel with T1-weighted imaging (SE 520/29) **(b)**, spin-density (SE 2200/28) **(c),** and T2-weighted imaging (SE 2200/90) **(d)**. In T2-weighted images, 3-layered appearance of vessel is clearly visible, with excellent delineation of media (*arrows* in **c** and **d**).

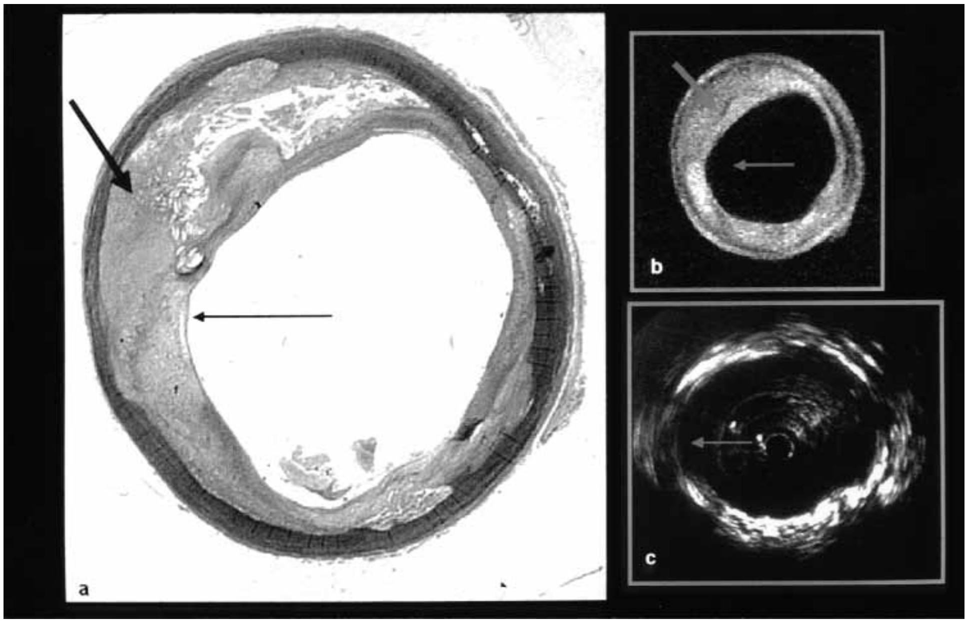
appearance of the vessel wall is detectable in MR images, especially in T2-weighted images, with a clear delineation of the intima and medial zone. The first studies were performed with high field intensity magnets; these images delineated atherosclerotic plaque lesions and made it possible to distinguish fibrous tissue from lipid-rich plaque tissue.[1] Spin-density-weighted pulse sequences have been shown to be superior to T1- or late T2-weighted pulse sequences in the delineation and differentiation of the plaque components.

MRI of atherosclerotic plaques makes it possible to characterize the lesions in detail in terms of size, shape, and even plaque tissue components. The results of in vitro studies have demonstrated the higher sensitivity and specificity of MRI in detecting fibrous and lipid plaque components compared with histologic methods. Plaque tissue can be distinguished thanks to the increased signal of fibrous plaque components in spin-density and T2-weighted images, whereas lipid plaque tissue typically appears as hypointense in these pulsed sequences. Calcifications have shown lack of signal in T1- and T2-weighted images. MRI can thus clearly delineate fibrous tissue, lipid plaque components, and calcifications. Compared with histologic techniques, MRI has shown a sensitivity of 97% in the visualization of fibrous tissue and a sensitivity of 66% for lipid plaques (Figure 1).

Plaque imaging by intravascular ultrasound and MRI

Intravascular ultrasound (IVUS) is used widely in human peripheral and coronary arteries to diagnose, quantitate, and characterize atherosclerotic plaques and is the only clinically established method for imaging atherosclerotic plaque lesions. This technique provides detailed pictures of the structure of arterial cross-sectional anatomy and accurately reflects the size of the atherosclerotic plaque. As well as making it possible to measure plaque size, IVUS image patterns may show correspondence with the composition of the atherosclerotic plaque. As described in several IVUS studies, echolucent plaques have increased levels of lipids but also higher fractions of loose fibrous, thrombotic, or necrotic elements, whereas echogenic plaques have a higher collagen and calcium content. Hiro et al[2] examined whether the descriptors of tissue components by IVUS predict the properties of human atherosclerotic plaques. The sensitivity in detecting calcified plaques was high; however, discrimination between fibrous and fatty plaque on the basis of intensity of the signals had a

Figure 2



Comparison of MRI and IVUS with histologic image of a plaque. **a,** Histologic section of mixed plaque shows lipid plaque tissue with cholesterol crystals *(thick arrow)* covered by fibrous tissue *(thin arrow)*. **b,** T2-weighted MRI distinguishes between lipid tissue, which appears as hypointense areas *(thick arrow)* and fibrous tissue, which appears as bright signal *(thin arrow)*. **c,** Corresponding IVUS image showing moderately echogenic mixed plaque and hypoechogenic signal, indicating soft plaque tissue *(arrow)*.

sensitivity of only 50% and 40%, respectively. This means that tissue characterization by IVUS distinguishes calcified from noncalcified plaque; however, soft echoes, although indicative of a material assumed to be less firm than calcium, do not necessarily correspond to soft tissue. IVUS can thus delineate the thickness and the echogenicity of vessel wall structure but does not provide full histopathologic information.

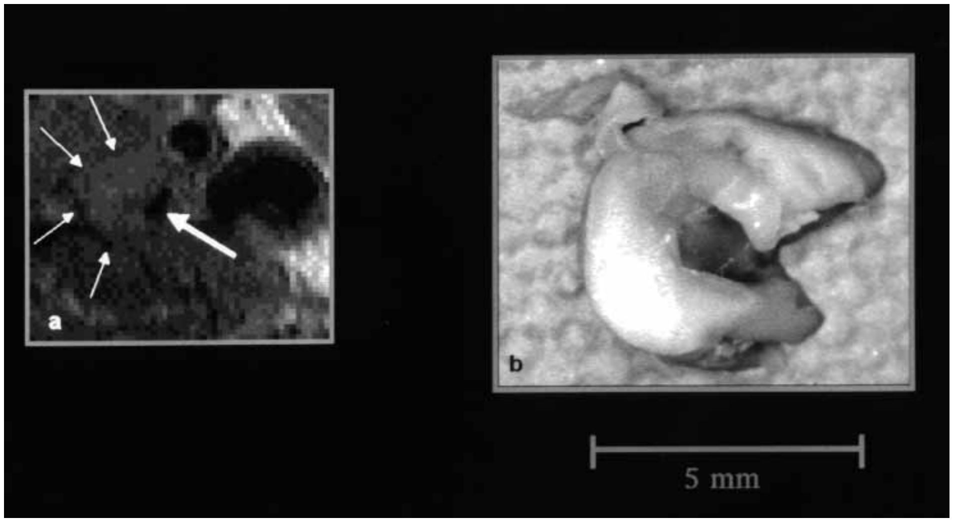
In a study that compared the ability of IVUS and MRI to distinguish plaque tissue in postmortem iliac arteries, the latter was shown to be superior in delineating lipid plaque components. In the diagnosis of fibrous plaque tissue and calcifications, both methods showed the same diagnostic sensitivity.[3]

However, both methods have limitations. IVUS has a better spatial resolution but is an invasive technique with all attendant complications, including deterioration of plaque stability, which may lead to acute vessel occlusion. IVUS is not able to visualize plaque tissue behind calcifications because of the intense shadowing caused by calcified plaque components. Furthermore, IVUS is not able to penetrate heavily stenotic sections and thus does not provide information on the complexities of the whole stenosis. MRI, on the other hand, is a noninvasive method and is able to provide images of atheromas even with low field intensity systems. However, its spatial resolution needs to be improved, and imaging time needs to be shortened. Further advances in MRI software and new algorithms are needed to enhance the level of detail in these images (Figure 2).

MRI of atheromas in vivo

In vivo MRI of atherosclerotic lesions was also performed in patients with severe carotid artery stenosis following endarterectomy to assess the usefulness of this method in a clinical setting. These patients were examined with a 1.5-T magnet with a head-neck coil. Three-dimensional MR angiography images were initially obtained, and T1- and T2-weighted sequences were planned on acquired maximum intensity projection images at the site of the stenosis. The results with MRI were then compared with the pathologic findings. In all patients, MRI was able to visualize the size and shape of the stenosis and delineate the different plaque components. The technique has demonstrated the capability to visualize the complex composition of an atherosclerotic plaque with its fatty, fibrous, and calcified components. Because slice thickness is only 3 mm,

Figure 3



In vivo MRI of carotid artery stenosis. **a,** MRI showed atherosclerotic plaque *(small arrows)* in internal carotid artery, which led to severe stenosis of vessel lumen *(large arrow)*. Plaque tissue was assessed as fibrous tissue because of its hyperintense signals in spin-density image. **b,** After endarterectomy, examination of pathologic specimen confirmed fibrous plaque tissue.

tissue changes in the atheroma were easily detectable. Lipid plaque tissue typically appeared as hypointense areas in spin-density and T2-weighted images. In vivo studies of carotid artery plaques have documented the same behavior of signal intensity of the different plaque tissue components, as was found in in-vitro studies (Figure 3).[4]

Summary and future developments

MRI of atherosclerotic lesions is in its early stages, but it nonetheless has potential for evaluating plaque and distinguishing plaque tissues. This noninvasive technology provides a comprehensive assessment of atherosclerosis and is a potentially useful tool for detecting the disease and studying its natural history, risk factors, and the effects of pharmaceutical treatment.

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