The article by Zhao et al is the first definitive study to describe the use of high-resolution MRI to monitor the effects of intensive drug treatment on the dimensions and composition of atherosclerotic plaques in human carotid arteries. (An earlier brief rapid communication by Corti and coworkers described the effect of lipid-lowering therapy on carotid and aortic vessel dimensions but not plaque composition.) In this small case-control study, eight untreated patients with coronary artery disease were compared with eight patients treated for 10 years with triple lipid-lowering therapy (two carotids each). From the MR image slice that showed the largest plaque area in each carotid, the authors made both dimensional (total area, lumen area, and wall area) and compositional (area occupied by lipid deposits, fibrous tissue, and calcification) measurements. None of the dimensional measurements were significantly different in the two groups. Only the plaque lipid core areas were significantly reduced by lipid therapy (P=0.01), although calcium content tended to be higher in treated patients. However, when the carotids were stratified according to their percent luminal area reduction, the upper tertile (n=12 with 66% to 83% reduction) was significantly different from the other lower tertiles with respect to carotid wall area (P<0.01), lumen area (P<0.01), fibrous area (P<0.05), calcified area (P<0.1), and calcified/lipid-rich area (P<0.1).

Although the lack of statistically significant differences for these parameters in the total, unstratified group is disappointing, this problem may possibly be overcome by using global plaque measurements (eg, total plaque volume) rather than those restricted to the most stenosed slice, which may not be sufficiently representative of disease in the entire lesion. Whereas total plaque volume and plaque composition probably should be used as primary endpoints for larger trials, other parameters, such as longitudinal and radial position of the plaque, will be useful secondary or tertiary endpoints. The outcome of the study may also have been affected by the case-control design.

Case-control studies are susceptible to bias when sampling subjects from two populations, in this instance a decade apart. The two groups may have different kinds of disease, different susceptibilities to disease, and different receptivities to treatment. The bias could be in either direction. These problems emphasize the advantages of the controlled trial in which patients are recruited from the same population, randomly assigned to multiple groups, validated by baseline examination before treatment, and then closely monitored in their treated and untreated states by blinded observers.

This report has far-reaching significance and implications for evaluating the efficacy of lipid-lowering intervention. The study is an excellent illustration of the advantages that MRI affords for assessing plaque conditions. It is non-invasive and non-irradiative, allowing multiple serial measurements over time without the hazards that attend some other imaging techniques, such as intravascular ultrasonography and angiography. Its potential for measuring structural and functional features of the atherosclerotic vessel far exceeds that of B-mode ultrasound. But arguably, the most valuable characteristic of MRI is its inherent remarkable capacity for distinguishing tissue components of differing chemical composition (eg, lipid, calcification, thrombus, extracellular matrix, connective tissue, cells). Segmentation of these components is achieved by the judicious use of T1-weighted, T2-weighted, proton density–weighted, and/or diffusion-weighted images. In the present study, the authors have used this approach to measure the composition of carotid lesions, a measurement useful for estimating the vulnerability of a plaque to rupture.

The carotid bed affords multiple advantages for monitoring atherosclerosis. Stenosing carotid lesions are a major cause of stroke and transient ischemic attacks; hence, direct monitoring of these vessels provides valuable information for guiding medical and surgical intervention. The carotids are also appropriate surrogates for the coronary arteries, which are considerably more difficult to image because of their smaller size and greater motion. Carotid endarterectomy provides tissues with dimensional and compositional properties similar to those of the carotid plaque in vivo. Their ex vivo images can be directly compared with the in vivo images and corresponding histologic sections. Carotid disease is remarkably symmetrical in terms of plaque volume and calcification as assessed by MRI and electron beam computed tomography of cadaveric vessels. This observation implies that the MR image and histology of a tissue resected at endarterectomy is a reasonable reflection of disease in the contralateral vessel.
This small study by Zhao and coworkers¹ raises important questions about the requirements for the broad application of MRI to multi-site trials. Foremost among these requirements is standardization of hardware, software, and procedures for image acquisition, transmission, storage, processing, and analysis. Computer-assisted algorithms for boundary detection will be especially important for assuring accurate and reproducible quantitation of image features, minimizing analysis time, and eliminating operator error. Tight control over these parameters will enable execution of clinical trials with fewer patients than is currently required using other imaging technologies. Finally, a prospective double-blind randomized trial is likely to be more instructive and conclusive than a retrospective case-control study.

References


Evaluating Atherosclerotic Lesions by Magnetic Resonance Imaging: From Dimensional to Compositional Quantitation

Joel D. Morrisett and William Insull, Jr

Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/21/10/1563

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at: http://atvb.ahajournals.org//subscriptions/