MOLECULAR IMAGING

MRI of carotid atherosclerosis: clinical implications and future directions

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Abstract | Atherosclerosis is now widely recognized as a multifactorial disease with outcomes that arise from complex factors such as plaque components, blood flow, and inflammation. Despite recent advances in understanding of plaque biology, diagnosis, and treatment, atherosclerosis remains a leading cause of morbidity and mortality. Further research into the development and validation of reliable indicators of the high-risk individual is greatly needed. Carotid MRI is a histologically validated, noninvasive imaging method that can track disease progression and regression, and quantitatively evaluate a spectrum of parameters associated with *in vivo* plaque morphology and composition. Intraplaque hemorrhage and the lipid-rich necrotic core are the best indicators of lesion severity currently visualized by carotid MRI. However, MRI methods capable of imaging other important aspects of carotid atherosclerotic disease *in vivo*—including inflammation, neovascularization, and mechanical forces—are emerging and may aid in advancing our understanding of the pathophysiology of this multifactorial disease.

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Introduction

The AHA currently estimates that about 795,000 people suffer a new or recurrent stroke each year in the US. The morbidity and long-term disability of stroke result in direct and indirect costs of US$68.9 billion per year.[1] Multiple randomized, prospective studies[2–4] have associated carotid stenosis with symptomatic neurological events. However, luminal stenosis is probably not the best criterion for stratification of disease severity, since, in the European Carotid Surgery Trial,[5] 43.8% of the 3,018 trial participants with symptomatic carotid disease had <30% stenosis. Furthermore, in the North American Symptomatic Carotid Endarterectomy Trial (NASCET),[2] the 5-year rate of any ipsilateral stroke was 22.2% for patients with <50% stenosis. Accordingly, the application of stenotic severity for managing carotid atherosclerotic disease has resulted in only a 7% reduction in incident stroke during the interval 1996–2006,[1] and 8–83 carotid endarterectomies are necessary to prevent a single stroke within 2 years of surgery.[6]

The phenomenon of adaptive arterial remodeling,[7] an initial outward expansion of plaque burden to preserve lumen diameter, has directed the search for alternate or complementary strategies to improve carotid disease evaluation toward the vessel wall. Noninvasive approaches to carotid vessel wall imaging have included ultrasonography (both two-dimensional[8,9] and three-dimensional[10]), CT,[11] and MRI.[12] Compared with ultrasonography and CT, the key advantage that MRI affords is the opportunity to acquire and combine multiple different contrast weightings, both bright blood (such as time-of-flight) and black blood (such as T1-weighted with blood-flow suppression), to distinguish tissue composition within the arterial wall. The utilization of multiple, high spatial resolution contrast weightings for the *in vivo* assessment of carotid atherosclerotic disease has been termed 'carotid MRI'. Importantly, carotid MRI has been systematically validated with histology to quantify the principal components of carotid lesions: the lipid-rich necrotic core (LRNC),[13–17] calcification,[13,14] intraplaque hemorrhage (IPH),[13,14,16,18–21] and surface disruption.[17,22–24] In addition, the intrareader and inter-reader,[14,18,20,25,26] as well as the interscan,[25,27–30] reproducibility of quantitative measures associated with both morphology and composition have also been extensively reported. Although carotid MRI is presently an established imaging tool dedicated to research, the burgeoning data from prospective studies has placed carotid MRI at the precipice of translation to clinical practice.

The hardware, sequence design, and imaging criteria associated with carotid MRI have been previously summarized.[31–34] In this Review, we move beyond technical development and validation to examine the current understanding and potential clinical implications of *in vivo* carotid atherosclerotic disease consequent of carotid MRI. First, we examine the two plaque features that have emerged as the most critical carotid-MRI-visualized components for discriminating lesion severity—IPH and LRNC—including gaps in our current knowledge about these elements. We then go on to explore new MRI techniques that may expand the current potential of *in vivo* plaque imaging by enabling the *in vivo* assessment of inflammation, neovasculature, and mechanical wall forces, and discuss the expansion of MRI studies to evaluate additional potential outcomes of carotid disease. These

Competing interests
The authors declare no competing interests.

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