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MRI of Carotid Atherosclerosis

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Introduction

Stroke is a serious public health problem and is one of the leading cause of morbidity and mortality worldwide. Ischemic stroke accounts for the majority of all strokes. Patients with substantial carotid narrowing are at increased risk for major stroke; however, the degree of stenosis alone is a relatively poor prediction of neurological events.¹⁻⁵ A great deal of research has been dedicated to investigating and identifying plaque instability: the so-called “vulnerable plaque.” However, to understand the mechanisms behind vulnerable plaque, a reliable in vivo imaging method which can monitor both plaque progression and components is needed.

Because of its proximity to the skin and the availability of atherosclerotic specimens from carotid endarterectomy, the carotid artery provides an excellent location for imaging arterial plaques and study of disease progression or regression. Beyond overall luminal stenosis (the current clinical standard for measuring disease severity), recent pathological studies of both coronary and carotid specimens confirm that large necrotic core with thin fibrous caps, plaque neovasculation, and increased inflammation are all features associated with vulnerable plaques.¹⁻⁷ Pathological classification of atherosclerotic plaque has shown some unique features of carotid plaque morphology due to the high flow rates and the shear forces caused by the bifurcation of the common carotid artery into the internal and external carotids. Virmani et al³, in their recent article, described distinct differences between coronary and carotid atherosclerotic plaques. Plaque ulceration, intraplaque hemorrhage, and calcified nodules may occur more frequently in the carotid than the coronary vascular beds. Another feature of carotid atherosclerosis is the infrequency of total occlusion compared to the coronary beds.

In order to detect and further study the increasingly complex findings on atherosclerotic plaques, a robust, reproducible, high-resolution imaging method which can quantify plaque morphology, distinguish tissue components, and detect other pathological features associated with vulnerable plaque is needed. Ultimately, the imaging method should have the potential to not only be used as a screening tool for the presence of atherosclerosis but also to distinguish stable from vulnerable plaques and distinguish patients with high risk of cardiovascular complications.

High-resolution magnetic resonance imaging (MRI) is one of the most promising modalities for visualizing the carotid atherosclerotic plaque, as MR allows direct visualization of the diseased vessel wall, has excellent soft tissue contrast, is capable of characterizing plaque

morphology, and can potentially monitor progression of the disease.⁸⁻¹⁴ MR imaging is non-invasive, does not involve ionizing radiation, and is highly reproducible.

This article focuses on the current state-of-the-art in MR carotid atherosclerotic plaque imaging to evaluate plaque morphology and composition and identify the features of vulnerable plaques. It also focuses on current new potential including 3T MRI and dynamic contrast enhanced MRI. Finally, the status of several current applications of MRI of carotid atherosclerosis will be reviewed.

Multi-Contrast MRI

A technique which is well-established for plaque characterization is 1.5T multi-contrast MRI, which utilizes several MR contrast weightings at a single location to identify and characterize plaque components. For carotid MRI, the multi-contrast approach includes three basic contrast weightings (T1, PD, T2) obtainable with black blood imaging and complementary bright blood imaging, producing angiographic data.^{8,15,16} In addition, contrast enhancement (CE) of carotid atherosclerosis can quantify vessel wall morphology and key plaque components with excellent accuracy and reproducibility.¹⁷⁻²⁰ By using multi-contrast MRI we can image key features of carotid plaques, including differentiating between American Heart Association (AHA) classification of lesion types, intraplaque hemorrhage, fibrous cap and other plaque components and vessel wall thickness.

Lesion type

The ability of multi-contrast high resolution MRI to determine plaque composition *in vivo* enables the classification of human carotid atherosclerotic plaque into categories designated by the American Heart Association (AHA). Cai et al⁸ modified the AHA classification specifically for MRI. In this classification scheme, types I and II of the AHA classification were combined into type I-II. The current resolution of MRI does not allow for the differentiation of discrete foam cells in type I and the multiple foam cell layers of the fatty streak in type II. Types IV and V in the AHA classification were similarly combined into type IV-V, because the ability of MRI to distinguish between the proteoglycan composition of the type IV cap and the dense collagen of the type V cap has not been demonstrated. Type VI, VII, and VIII were easily distinguishable on MRI and remained separate classifications. In this study, 60 patients who underwent endarterectomy were scanned prior to surgery. The resulting high-resolution MR images and subsequent histology specimens were independently reviewed and classified. Overall, the classification obtained by MR imaging and the AHA classifications showed good agreement, with Cohen's $\kappa=0.74$ and weighted $\kappa=0.79$. See Figure 1 for an example of a Type VI lesion.

Intraplaque hemorrhage

in vivo MR imaging is able to depict carotid intraplaque hemorrhage with good sensitivity and moderate to good specificity.^{9,15,20-22} Furthermore, it has been shown that MR imaging can differentiate between hemorrhage ages using a modified criteria for cerebral hemorrhage.²² The authors categorized three stages of intraplaque hemorrhage: fresh, recent, and old. Fresh hemorrhage (<1 week) corresponds to early subacute cerebral hemorrhage and produces hyperintensity on T1W/TOF images and isointensity or hypointensity on T2W/PD images. Recent hemorrhage (1 to 6 weeks) corresponds to late subacute brain hemorrhage and produces hyperintensity on all 4 contrast weightings. Old hemorrhage (>6 weeks) corresponds to the late chronic brain hemorrhage and produces hypointensity on all 4 contrast weightings. (Figure 1)

Fibrous cap status

Several studies highlight the ability of MR to not only detect the presence or absence of the fibrous cap, but also to differentiate between cap types. Hatsukami et al¹² were the first to report the use of a 3D TOF “bright-blood” imaging technique to help identify ruptured fibrous caps *in vivo* in atherosclerotic human carotid arteries. By using preoperative images of 22 consecutive endarterectomy patients, the *in vivo* state of the fibrous cap was characterized on the basis of its appearance in MR images as being intact and thick, intact and thin, or ruptured (Figure 2). The authors found a high level of agreement between the MR findings and the histologic state of the fibrous cap, with Cohen $\kappa = 0.83$ (95% confidence interval = 0.67, 1.00) and weighted $\kappa = 0.87$ with the appearance of a hypointense juxtaluminal band seen on the TOF MR images. An MR investigation by Mitsumori et al²³ demonstrated that *in vivo* MR imaging has high test sensitivity (81%) and specificity (90%) for the identification of a thin or ruptured cap. In a prospective cohort study validating *in vivo* MRI against histological analysis of excised carotid plaques, Trivedi et al²⁴ used 2D TOF MR images to demonstrate that the intra-class correlation coefficients between two MR readers were 0.94 and 0.88 for quantifying the fibrous cap and lipid core components, respectively, and there was good agreement between MR- and histology-derived quantification of both fibrous cap and lipid core content; the mean % difference for the fibrous cap was 0.75% ($\pm 2.86\%$) and for the lipid core was 0.86% ($\pm 1.76\%$). Cai et al¹⁷ used un-enhanced T1-weighted and contrast-enhanced T1-weighted images to measure the intact fibrous cap, showing a moderate to good correlation between the MR findings and the excised histologic specimen: maximal thickness ($r = 0.78$, $P < .001$), length ($r = 0.73$, $P < .001$), and area ($r = 0.90$, $P < .001$) of the intact fibrous cap.

Quantification of plaque composition

Saam et al^{saam13} recently demonstrated that the *in vivo* capabilities of MRI to quantify all the major components of advanced human carotid atherosclerotic plaque by comparing measurement of plaque components using MRI with histology. The MRI measurements of the plaque composition were statistically equivalent to those of histology for Lipid Rich Necrotic Core (LR/NC), loose matrix, and dense (fibrous) tissue. Calcification differed significantly when measured as a percentage of wall area (9.4 versus 5%; $P < 0.001$), possibly due to either calcification shrinking less than other components during histological processing, or underestimation by MRI of areas showing hypointense signal due to the signal averaging of voxels that only partially contain calcification. Intra-reader and inter-reader reproducibility was good to excellent for all tissue components, with ICCs ranging from 0.73 to 0.95. (Figure 3)

Wall thickness

Underhill et al²⁵ demonstrated the first comparison between wall thickness measurements by MRI and B-mode US. The authors found a very high Pearson correlation coefficient ($r = 0.93$; $P < 0.001$) between Intima Media Thickness (IMT) by B-mode US and automated Mean Wall Thickness (MWT) by MRI, which strongly indicates that it is possible to use carotid MRI as a tool for assessing systemic atherosclerotic disease. Mani et al. proved the viability of MWT measurement by showing good correlation of MWT to carotid IMT.²⁶ A major difference between MRI and Ultrasound is the ability of MRI to measure the entire circumference of the wall at any location in the artery.

Contrast Enhancement MRI

Contrast-enhanced MR has also demonstrated its usefulness in distinguishing certain plaque tissues. A gadolinium contrast agent can improve the accuracy of MR in differentiating the lipid-rich necrotic core from surrounding fibrous tissue. The lipid-rich necrotic core shows little if any enhancement on post-contrast T1-weighted images, facilitating differentiation from

the surrounding enhancing fibrous tissue¹⁹. Using pre- and post-contrast T1-weighted images, Cai et al¹⁷ showed that the lipid-necrotic core, measured as proportion of the vessel wall, was similar on MR images and histologic specimens, with values of $30.1\% \pm 12.5$ (standard deviation) and $32.7\% \pm 12.3$, respectively. Furthermore, the area measurements were strongly correlated ($r = 0.85$; $P < .001$).

Two independent studies also point to the importance of CE MRI in characterizing the fibrous cap. Kramer et al²⁷ demonstrated that contrast enhancement improved the delineation of the fibrous cap, which was found to be hyperintense relative to the lipid-necrotic core on T2-weighted images. Wassermann et al²⁸ found that gadolinium-enhanced T1-weighted images helped differentiate the fibrous cap from the lipid-necrotic core, with a contrast-to-noise ratio as good as or better than that of T2-weighted MR images but with approximately twice the signal-to-noise ratio.

Furthermore, Cai et al¹⁷ demonstrated that the use of a gadolinium contrast agent not only allows for the identification of the intact fibrous cap, but, more importantly, also allows for the accurate morphological measurements of the fibrous cap. The authors used un-enhanced T1-weighted and contrast-enhanced T1-weighted images to measure the intact fibrous cap, and showed a moderate to good correlation between the MR findings and the excised histologic specimen for the maximal thickness length and area measurements of the intact fibrous cap. Quantitative measurement of cap thickness is a promising step towards better identifying plaques with weakened fibrous caps.

Dynamic contrast-enhanced MRI

Recent studies have linked inflammation with the pathogenesis and destabilization of atherosclerotic lesions.²⁹⁻³¹ Non-invasive identification of inflammation in atherosclerosis has been challenging. Circulating inflammation markers, such as high-sensitivity C-reactive protein, are useful for evaluating systemic inflammation and a risk stratification for cardiovascular diseases,³² but not for the identification of inflammation of individual local lesions.

Dynamic Contrast Enhancement (DCE), a modality which uses repeated fast image acquisition techniques to measure contrast uptake and blood flow, offers one possibility for imaging biomarkers of inflammation in arterial plaques. Strong contrast enhancement suggests the presence of a vascular supply to the plaque and increased endothelial permeability facilitating the entry of the contrast agent from the blood plasma. Because neovasculature growth into the plaque and increased endothelial permeability are associated with plaque inflammation,³³⁻³⁶ Quantitative measurement of plaque enhancement has been argued to provide information about plaque inflammation.

The ability to extract quantitative measurements from contrast enhancement is only beginning to be explored in plaque imaging. Kerwin et al. demonstrated that DCE MRI showed a strong correlation between the rate of carotid plaque contrast enhancement and histological evidence of neovasculature and macrophage infiltration of the human atherosclerotic lesion.^{37,38} Time varying signal intensities within the plaques were used to estimate the fractional plasma volume (v_p) and transfer constant, (K^{trans}) into extracellular space. Results showed K^{trans} correlated with histologic markers of inflammation, suggesting that K^{trans} and v_p measurement via DCE MRI is capable of imaging markers of plaque inflammation.

USPIOs

Ultra-small super paramagnetic particles of iron oxide (USPIO) enhanced MRI imaging is another interesting non-invasive method which may hold promise for identifying vulnerable

plaque inflammation *in vivo* in humans, in which areas of focal signal loss on MR images have been shown to correspond to the accumulation of iron particles in plaque macrophages^{39,40}. USPIO is thought to accumulate predominantly in activated macrophages either at the shoulders or in the necrotic lipid core of ruptured and rupture-prone human atherosclerotic lesions, and is considered to be a marker of the degree of inflammation within the plaque⁴¹. USPIO particles, when clumped in the phagolysosomes, produce a strong T2* susceptibility effect visible on T2* weighted sequences as magnetic susceptibility artifacts or signal voids.

Kooi et al⁴² was the first to demonstrate that the accumulation of USPIOs in human atherosclerotic lesions caused signal decreases in *in vivo* MR images. In her study, eleven symptomatic patients scheduled for carotid endarterectomy received MRI scans before, 24 hours after (n=11), and 72 hours after (n=5), the administration of USPIOs (Sinerem) at a dose of 2.6 mg Fe/kg. Histological and electron microscopical analyses of the plaques showed the USPIOs within the plaques in 10 of 11 patients, occurring primarily in macrophages. Histological analysis showed USPIOs in 27 of 36 (75%) of the ruptured and rupture-prone lesions and 1 of 14 (7%) of the stable lesions. In the post-USPIO MRI scans, two observers found signal changes in the vessel walls of the patients with USPIO uptake in 67 of 123 (54%) and 19 of 55 (35%) quadrants of the T2*-weighted MR images acquired after 24 and 72 hours, respectively. For the quadrants with changes, there was a significant signal decrease of 24% (95% CI, 33% to 15%) in regions of interest in the images acquired after 24 hours, whereas no significant signal change was found after 72 hours. Subsequently, Howarth et al. used USPIO-enhancement to demonstrate inflammation as well as corroborate fibrous cap thinning at points of highest wall stress.⁴³

3T Carotid MR Imaging

Although most of the MR plaque imaging methods have been developed for 1.5T scanners, 3T MR scanners are now becoming common in clinical practice. Several studies have demonstrated the advantages of 3T MRI for plaque imaging and interpretation compared to 1.5T methods.

Yarnykh et al. demonstrated the viability of 3T plaque imaging by showing significant improvement in the signal-to-noise ratio, contrast-to-noise ratio, and image quality, as well its ability to reduce scan time and increase spatial resolution. The morphologic measurements taken at 3T were shown to be compatible with those at 1.5T for the high-resolution black blood imaging of the carotid arteries.⁴⁴

Recently, Underhill et al. reported a prospective study comparing the interpretations and quantifications of carotid vessel wall morphology and plaque composition between 1.5 and 3T MRI. The author demonstrated a strong level of agreement between field-strengths for all morphological variables with intraclass correlation coefficient values ranging from 0.88 to 0.96. Agreement in the identification of the presence or absence of plaque components was very good for calcification, the lipid-rich necrotic core, and hemorrhage. The findings presented support the translation of the histologically validated 1.5T carotid image interpretation criteria to 3T multi-sequence images.⁴⁵

Current Applications of carotid MRI of Atherosclerosis

Carotid Lesion features and their association with neurological symptoms

A landmark study shows that MRI identification of fibrous cap rupture is highly associated with a recent history of Transient Ischemic Attack (TIA) or stroke⁴⁶. In this study, Yuan et al. used the standard multi-contrast MRI techniques to examine 28 symptomatic and 25 asymptomatic subjects to determine whether fibrous cap thinning or rupture, as identified on

MR images, is associated with a history of recent transient ischemic attack or stroke. When compared with patients with a thick fibrous cap, patients with a ruptured cap were 23 times more likely to have had a recent transient ischemic attack or stroke, further highlighting the ability of MRI to detect vulnerable plaque.

MRI of carotid artery affords bilateral data acquisition, which provides an opportunity to study atherosclerotic lesion features of both carotids at the same time. Using bilateral acquisition, Saam et al.⁴⁷ showed significant differences between symptomatic and asymptomatic plaques in the same patient. Compared with asymptomatic plaques, symptomatic plaques had a higher incidence of fibrous cap rupture ($P = .007$), juxtaluminal hemorrhage or thrombus ($P = .039$), type I hemorrhage ($P = .021$), and complicated AHA type VI lesions ($P = .004$), and a lower incidence of uncomplicated AHA type IV and V lesions ($P = .005$). Symptomatic plaques also had larger hemorrhage ($P = .003$) and loose matrix ($P = .014$) areas and a smaller lumen area ($P = .008$).

In a study examining contralateral carotid artery features in symptomatic patients by Tang et al.⁴¹, twenty symptomatic patients underwent multisequence MRI before and 36 hours after USPIO infusion. The images were manually segmented into quadrants, and the signal change in each quadrant was calculated after USPIO administration. A mixed mathematical model was developed to compare the mean signal change across all quadrants in the 2 groups. Patients had a mean symptomatic stenosis of 77% as measured by conventional angiography, compared with 46% on their asymptomatic side.

All symptomatic carotid stenoses had inflammation, as shown by USPIO-enhanced imaging. On the contralateral sides, inflammatory activity was found in 19 (95%) patients. Contralaterally, there were 163 quadrants (57%) with a signal loss, compared with 217 quadrants (71%) on the symptomatic side ($P = 0.007$). The author concludes that contralateral asymptomatic plaques also seem to demonstrate inflammation, though not to the extent of the symptomatic side. Inflammatory activity may be a significant risk factor in asymptomatic disease.

The author also compared 20 symptomatic patients with contralateral disease with 20 completely asymptomatic patients.⁴⁸ The mean percentage of quadrants showing signal loss was 53% in the contralateral of the symptomatic group, compared with 31% in the asymptomatic individuals ($p = 0.025$). The mean percentages showing enhancement were 44% and 65%, respectively ($p = 0.024$), and the mean signal difference between the two groups was 8.6% (95% CI 1.6% to 15.6%; $p = 0.017$). This study suggests inflammatory activity may be a significant risk factor in asymptomatic disease.

Plaque progression

Noninvasive imaging of carotid plaque has proven to be particularly powerful in longitudinal studies designed to evaluate the natural history of disease progression and its association with patient symptoms or the response to pharmacological interventions.

A recent natural history study of carotid atherosclerosis points to the significant role of intraplaque hemorrhage in plaque rupture and clinical symptoms. Takaya et al.⁴⁹ demonstrated the utility of high-resolution MRI in a prospective study of the association between plaque composition and cerebrovascular events in asymptomatic patients who had 50% to 79% stenosis in the carotid artery. They demonstrated that the presence of a thin or ruptured fibrous cap, intraplaque hemorrhage, or a larger lipid-rich necrotic core accounted for an increased risk of subsequent ipsilateral cerebrovascular events in a mean follow up period of 38.2 months. The danger posed by the fibrous cap and lipid-rich necrotic core have already been documented, but this study also points to intraplaque hemorrhage as an topic for investigation.

In a recent 18-month prospective natural history study, Saam et al⁵⁰ demonstrated the capabilities of *in vivo* MRI to quantify changes in atherosclerotic carotid artery wall morphology and identify potential factors that may influence the progression rate in plaque burden. Averaged across the 68 subjects in this study, the mean wall area increased by 2.2% per year ($P = 0.001$) and the mean lumen area decreased by 1.9% per year ($P = 0.02$). Measurements of the location with the most severe disease, such as the maximum wall and minimum lumen areas, showed even larger changes (3.2 and -4.3% per year, respectively), indicating that atherosclerotic disease progression and remodeling is focally enhanced. Two factors were significantly associated with decreased wall progression rate: statin therapy ($P = 0.01$) and larger lesions, as defined by a Normalized Wall Index > 0.64 ($P = 0.001$). Normalized Wall Index (NWI) is defined as the wall area (WA) over the sum of the wall area plus the lumen area (LA) [$NWI = WA / (WA + LA)$]. The rate of progression for mean wall area and for NWI was approximately four-times greater amongst the subjects who were not treated with statins, compared to the statin-treated group (4.4% versus 1.2% per year, and 3.6% versus 0.8% per year, respectively).

Plaque regression

Because of the comprehensive information provided by carotid MRI, this technique is also ideal for monitoring vessel wall changes under treatment. Carotid MRI has been extensively validated for its ability to monitor plaque regression⁵¹ Corti et al was the first to demonstrate a decrease in carotid and aortic plaque burden and increase in luminal area after 2 years of monotherapy with simvastatin⁵² In a later investigation, they extended their observations to note that intensive dosing of simvastatin, compared with traditional dosing, did not effect a greater change in plaque size.⁵³

Two recent clinical trials highlight the use of multi-contrast carotid MRI to identify changes in plaque tissue composition under treatment. The first, the Familial Atherosclerosis Treatment Study (FATS)⁵⁴, as a pilot case control study, followed 16 patients: 8 who had received intensive lipid-lowering treatment for 10 years, and 8 who were selected as controls and had never been treated with lipid-lowering drugs, but were matched for age, baseline low density lipoprotein, and triglycerides. Carotid MRI images were acquired from the subjects and quantitative measurements included plaque area, area of fibrous tissue, calcium, and lipid deposits. This study showed that prolonged intensive lipid lowering therapy is associated with a markedly decreased lipid content; a characteristic of clinically stable plaque. Figure 4 shows comparisons of carotid plaque tissue components and composition from treated vs. untreated patients.

The Outcome of Rosuvastatin treatment on carotid artery atheroma: a magnetic resonance Imaging Observation (ORION) trial was a randomized double-blind trial to assess the effects of rosuvastatin on carotid plaque volume and composition. The trial used a 1.5T MRI scanner to image carotid atherosclerotic plaques at baseline and after 24 months of treatment. Forty-three patients with low-density lipoprotein cholesterol and 16% to 79% carotid stenosis were randomized to receive either a low (5 mg) or high (40/80 mg) dose of rosuvastatin. This study showed that rosuvastatin treatment was associated with a reduction in lipid-rich necrotic core size, whereas the overall plaque burden remained unchanged over the course of 2 years of treatment⁵⁵. Figure 5 shows the effects of rosuvastatin on LRNC as measured by multi-contrast MRI. Both of these studies highlight the importance of examining both plaque morphology and tissue composition in order to fully understand the effects of treatment on atherosclerosis progression/regression.

Flow and stress

Another application of carotid MRI is to extract quantitative vessel wall morphology and composition information from MRI to be used for hemodynamic and tissue mechanical analysis. Biomechanical stress is also considered to be a major determinant of plaque vulnerability⁵⁶. The fibrous cap rupture of atherosclerotic plaque can be considered to be a structural failure when the structure of plaque cannot resist the pressure and hemodynamic shear stress.⁵⁷ Li et al⁵⁸ have previously shown the feasibility of using combined finite element analysis and high resolution MR imaging to perform stress analysis on carotid plaques and demonstrated that mean maximal stresses were found to be higher in symptomatic plaques compared to the asymptomatic ones. Tang D et al⁵⁹ has developed a 3D model of vessel wall strain /stress analysis method based on carotid MRI data and a preliminary study indicates that lipid rich necrotic cores covered by thin plaque caps are associated with both extreme maximum (stretch) and minimum (compression when negative) stress/strain levels, adding to the evidence that fibrous cap is an indicator of vulnerable plaque. Furthermore very recently, Tang et al⁶⁰ demonstrated that there is an association between biomechanical stress and USPIO enhanced MR-defined inflammation within carotid plaque, both known risk factors for plaque vulnerability. This underlines the complex interaction between physiological processes and biomechanical mechanisms in the development of carotid plaques. Groen H., provided further evidence that plaque rupture may be linked to flow stress in their study which used MRI to locate a ruptured fibrous cap within an area of high wall shear stress.⁶¹ The ability of MRI to visualize different plaque components and morphology make it a promising candidate to test models of flow and biomechanical stress on carotid plaque.

Cardiovascular disease and carotid plaque features

The association between the carotid artery features, specifically intima-media thickness, and coronary artery disease has been previously well described in the ultrasound literature.^{57, 62-65}

Recently, Underhill et al⁶⁶ studied the morphological and compositional differences in the carotid arteries between subjects with angiographically defined obstructive coronary artery disease ($\geq 50\%$ stenosis, cases) and those with normal coronary arteries (no lumen irregularities, controls). Carotid MRI was performed on ninety-four participants with a 1.5T scanner. At each axial imaging location, lumen area (LA), total vessel area (TVA), wall area (WA), mean wall thickness (MWT) and normalized wall index ($NWI = WA/[LA+WA]$) were determined. Area measurements of calcification (CA) and lipid-rich necrotic core (LRNC) were also recorded. The authors found that in the internal carotid artery (ICA), CAD cases demonstrated a smaller mean LA and TVA, while having a larger MWT, NWI and CA. In the distal bulb, CA and LRNC were larger in CAD cases. CAD cases also demonstrated a greater prevalence (9.9% vs. 2.9%, $p=0.004$) of CA in the ICA. No differences between groups were identified in the common carotid artery. They conclude that the statistically significant structural and compositional differences in the carotid artery exist between subjects with and without CAD. These findings provide compelling evidence that carotid MRI may be an effective screening tool for identifying subjects at risk from coronary artery disease.

Summary

MRI of carotid atherosclerosis provides a unique method to characterize plaque morphology and tissue composition and to a certain extent, plaque inflammation. Because of its noninvasiveness, it has many current and potential applications; the fact that it is the only technique that can examine the fibrous cap status in vivo makes it a powerful tool to identify high-risk plaques. With quantitative measurement achievable on a series of plaque compositional and morphological features, this technique is also well suited for studying

atherosclerosis progression and regression. This technique can also be combined with other imaging modalities such as ultrasound and nuclear medicine to create a comprehensive evaluation of carotid atherosclerosis from tissue compliance, composition, to inflammation.

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Figure 1.

Example of type VI lesion just distal to carotid bifurcation (acute to subacute mixed hemorrhages were detected by histology). On multicontrast-weighted MR images, acute and subacute mixed hemorrhage had high SI on both TOF and T1WI images, iso-SI to slightly high SI on PDWI and T2WI images (arrow). * indicates lumen. Original magnification $\times 10$.

Figure 2.

Example of plaque with fibrous cap rupture on gross section, histology (Masson's trichrome stain), and MRI. On gross and histological sections, there is an area of cap rupture (arrow 1) next to a region where fibrous cap is thick (arrow 3). Cap rupture site corresponds to region where dark band is absent, and hyperintense, bright region is seen adjacent to lumen on MRI. Hyperintense region in plaque core on MRI corresponds to region of recent intraplaque hemorrhage on gross and histological cross sections (arrow 2). Reprinted with permission from *Circulation*. 2000;102:959.

Figure 3.

Plaque composition calculated as the percentage of the vessel wall area, calculated per artery, and then averaged across all arteries for MRI and histology.

Figure 4.

Comparisons of carotid plaque tissue components and composition. The treated plaques contained significantly less lipid than did the untreated plaques ($p=0.01$). Fibrous tissue, calcium and calcium plus lipid were not statistically different between the 2 groups. Reprinted, with permission, from Zhao XQ et al. Effects of prolonged intensive lipid-lowering therapy on the characteristics of carotid atherosclerotic plaques *in vivo* by MRI: a case-control study. *Arterioscler. Thromb. Vasc. Biol.* 2001; 21: 1623-1629. Ref 7.

Figure 5.

Multi-contrast weighted images from the same subject that compare the 2 baseline scans with the 2-year follow-up scan at a single location in the left common carotid artery. Notice that the hypointense signal (arrow) on the T2W images from the baseline scans, interpreted as LRNC, has changed to a hyperintense signal at follow-up. This change is representative of a LRNC being replaced by fibrous tissue *, Lumen; JV, jugular vein; PD, proton density; T1W, T1-weighted; T2W, T2-weighted; TOF, time-of-flight. Underhill H, AHJ, 2008.