

Table 2
Statistical Comparison (Mann-Whitney U Test) of K^{trans} Produced by Directly Measured AIF Between Any Two of the Plaque Components (P Value)*

K^{trans} U test P value	NC	Hem	LM	CA	FIB
NC	1				
Hem	<0.001	1			
LM	<0.001	<0.001	1		
CA	<0.001	0.384	<0.001	1	
FIB	<0.001	<0.001	<0.001	<0.001	1

*P value <0.05 for values in bold italic.

illustrated in Fig. 3a,b. Statistical comparisons between any two of the components are summarized in Tables 2 and 3 for K^{trans} and v_p , respectively. LM and FIB have relatively high values of K^{trans} (LM: 0.0962 ± 0.0180 [mean ± 95% confidence interval], FIB: 0.0581 ± 0.0040) and v_p (LM: 0.1736 ± 0.0389, FIB: 0.0915 ± 0.0067). In contrast, NC, Hem, and CA have relatively low values of K^{trans} (NC: 0.0236 ± 0.0055, Hem: 0.0041 ± 0.0081, CA: 0.0111 ± 0.0069) and v_p (NC: 0.0475 ± 0.0118, Hem: 0.0288 ± 0.0161, CA: 0.0224 ± 0.0159). In paired comparison of K^{trans} and v_p , CA and Hem showed no significant differences between them, but the K^{trans} and v_p values for any other pair of components were significantly different.

The estimations using the population-derived AIF had similar results as those generated by the measured AIF. The mean K^{trans} and v_p values for each component are shown in Fig. 3c,d, again demonstrating relatively high values in LM and FIB (K^{trans} : LM: 0.1124 ± 0.0162, FIB: 0.0661 ± 0.0039; v_p : LM: 0.1201 ± 0.0533, FIB: 0.0682 ± 0.0079). Also, NC, Hem, and CA have relatively low values of K^{trans} (NC: 0.0270 ± 0.0053, Hem: 0.0077 ± 0.0074, CA: 0.0131 ± 0.0060) and v_p (NC: 0.0354 ± 0.0142, Hem: 0.0241 ± 0.0156, CA: 0.0138 ± 0.0144). In statistical comparisons between any two of the components (Table 4 for K^{trans} and Table 5 for v_p), CA and Hem also present no significant differences between them, while any other pair of components was significantly different in the K^{trans} and v_p values.

DISCUSSION AND CONCLUSIONS

The results of this analysis indicate that DCE-MRI exhibits its differences in K^{trans} and v_p within plaque regions with different compositions, reflecting different perme-

Table 3
Statistical Comparison (Mann-Whitney U Test) of v_p Produced by Directly Measured AIF Between Any Two of the Plaque Components (P Value)*

v_p U test P value	NC	Hem	LM	CA	FIB
NC	1				
Hem	0.020	1			
LM	<0.001	<0.001	1		
CA	0.006	0.817	<0.001	1	
FIB	<0.001	<0.001	<0.001	<0.001	1

*P value <0.05 for values in bold italic.

Table 4
Statistical Comparison (Mann-Whitney U Test) of K^{trans} Produced by Population-Derived AIF Between Any Two of the Plaque Components (P Value)*

K^{trans} U test P value	NC	Hem	LM	CA	FIB
NC	1				
Hem	<0.001	1			
LM	<0.001	<0.001	1		
CA	<0.001	0.630	<0.001	1	
FIB	<0.001	<0.001	<0.001	<0.001	1

*P value <0.05 for values in bold italic.

ability and vascular blood supply. LM is a loosely organized region of FIB with high water content and permeability that leads to the highest measured K^{trans} and v_p . FIB contains rich microvasculature with relatively high permeability, also leading to high K^{trans} and v_p . In contrast, NC, Hem, and CA do not generally contain living cells and exhibit little vascularization, leading to substantially lower values of K^{trans} and v_p .

One implication of this result is that the derived V-V image from DCE-MRI could be used in differentiating plaque composition. NC, Hem, and CA usually appears dark in V-V images, with very low K^{trans} and v_p . LM usually appears light green in V-V images, with highest K^{trans} and v_p . These characteristics could be added to those established for standard MRI contrast weightings (10) to potentially improve plaque characterization.

More significantly, with localized K^{trans} and v_p measurements, DCE-MRI has the ability to assess plaque perfusion characteristics in specific plaque regions. This may enable quantitative DCE-MRI to replace or augment the use of ultrasound superparamagnetic particles of iron oxide, which localize the presence of macrophages in atherosclerotic plaque (15,16). This also may provide more localized information than positron emission tomography to evaluate the role of inflammation in atherosclerosis plaque progression and rupture. Previous studies have established that global perfusion characteristics are strongly dependent on global macrophage content (6) and systemic markers of inflammation (12). Assuming that local perfusion characteristics are primarily driven by local inflammatory cell content, localized K^{trans} and v_p measurements could be used to quantify inflammation where it is most likely to lead to plaque disruption. The shoulder region of the plaque could be one such region. A previous study (17) suggested that plaque rupture

Table 5
Statistical Comparison (Mann-Whitney U Test) of v_p Produced by Population-Derived AIF Between Any Two of the Plaque Components (P Value)*

v_p U test P value	NC	Hem	LM	CA	FIB
NC	1				
Hem	0.017	1			
LM	<0.001	<0.001	1		
CA	0.005	0.679	<0.001	1	
FIB	<0.001	<0.001	<0.001	<0.001	1

*P value <0.05 for values in bold italic.

occurs most frequently at regions heavily infiltrated by foam cells. Macrophages are capable of degrading the extracellular matrix by phagocytosis or by secreting proteolytic enzymes such as plasminogen activators and the family of matrix metalloproteinases, which may cause a rupture. These macrophages, together with the neovasculatures that facilitate the infiltration of the macrophages, are observed frequently in the plaque shoulders (18).

In this study, we sought to establish an automatic procedure to measure the localized K^{trans} reliably. Although the DCE-MRI images of some cases have bad image quality that has no clear lumen boundary and some cases have very big misalignment between DCE-MRI and other weightings due to the movements of patients, the success rate of the location registration algorithm is over 75%, and over 70% of all the slices do not need manual adjustment when mapping contours to V-V images. The result shows that the established registration algorithms are working and can avoid manual operation most of the time.

This study also compared the influence of two different AIF extraction methods: a cluster algorithm to directly measure the AIF from signal enhancement inside the blood vessel and a model-based population-derived AIF. Differences were observed, depending on the AIF methodology. In Fig. 3, we observe that average K^{trans} values are 15% higher with the population-derived AIF (median difference = 15%) and v_p is lower (median difference = 29%). Nevertheless, nearly identical relative values were observed when comparing modeling results from different tissue types. Thus, the choice of AIF methodology did not appear to alter the conclusion that variations in perfusion parameters are localizable within atherosclerotic plaque.

A limitation of this study is the lack of histologic data. Thus, the relative accuracies of the two AIF methodologies cannot be compared. Also, the hypothesis that localized measurements of K^{trans} and v_p indicate local inflammatory burden cannot be directly verified with histology. However, the result of this study was indirectly verified because the components used in this analysis were defined with a histologically verified protocol on multi-contrast MRI (10) and directly mapped to DCE-MRI, and DCE-MRI has been shown to be sensitive to inflammatory content within plaque in studies with histologic verification (6,7).

There are also some potential improvements in several technical areas. First, a dynamic protocol lasting about 3.8 min was chosen to not extend the already long scan protocol for carotid plaque imaging. The relatively short duration time requires us to use a linearized kinetic model that ignores efflux effect of the contrast agent (19) and avoids potential fit failures that often occur with more complicated models. However, the linearized model cannot differentiate the parameter for partial volume of extravascular extracellular space (v_e) and the transfer rate (K_{ep}) that compose K^{trans} (12). Second, to obtain sufficient coverage, signal-to-noise ratio and spatial resolution, we chose a relative long interval of 19 sec, which could affect the accuracy of the kinetic analysis by undersampling the AIF and tissue uptake curves. Further improvement on the temporal resolution could

greatly benefit the kinetic analysis. Last, we assume the T_1 -dependent signal intensity change in DCE images can be used in place of contrast agent concentration with the spoiled gradient recalled echo imaging sequence and saturation band used in this study. This may produce bias in the kinetic parameters. With further improvement such as measuring the change in longitudinal relaxation rate instead of signal intensity, we could indicate the concentration of contrast agent more accurately. Despite these technical limitations, we were able to demonstrate that kinetic parameters provide local information, a conclusion that is likely to apply to improved DCE techniques as well.

In conclusion, the results of this analysis indicate that DCE-MRI exhibits differences in K^{trans} within plaque regions of different compositions. If the results of further studies with histology verify the association between the derived parameters (K^{trans} and v_p) and inflammation in localized regions, DCE-MRI will be of value for studying the dependence of plaque progression and rupture on local inflammatory processes. Moreover, DCE-MRI could be useful for studies evaluating the effectiveness of novel therapies intended to inhibit plaque inflammation.

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ORIGINAL
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A Noninvasive Imaging Approach to Assess Plaque Severity: The Carotid Atherosclerosis Score

BACKGROUND AND PURPOSE: The presence of IPH and/or FCR in the carotid atherosclerotic plaque indicates a high-risk lesion. The aim of this multicenter cross-sectional study was to establish the characteristics of lesions that may precede IPH and/or FCR. We further sought to construct a CAS that stratifies carotid disease severity.

MATERIALS AND METHODS: Three hundred forty-four individuals from 4 imaging centers with 16%–99% carotid stenosis by duplex sonography underwent carotid MR imaging. In approximately 60% of the study sample (training group), multivariate analysis was used to determine factors associated with IPH and FCR. Statistically significant parameters identified during multivariate analysis were used to construct CAS. CAS was then applied to the remaining arteries (40%, test group), and the accuracy of classification for determining the presence versus absence of IPH or, separately, FCR was determined by ROC analysis and calculation of the AUC.

RESULTS: The maximum proportion of the arterial wall occupied by the LRNC was the strongest predictor of IPH ($P < .001$) and FCR ($P < .001$) during multivariate analysis of the training group. The subsequently derived CAS applied to the test group was an accurate classifier of IPH (AUC = 0.91) and FCR (AUC = 0.93). Compared with MRA stenosis, CAS was a stronger classifier of both IPH and FCR.

CONCLUSIONS: LRNC quantification may be an effective complementary strategy to stenosis for classifying carotid atherosclerotic disease severity. CAS forms the foundation for a simple imaging-based risk-stratification system in the carotid artery to classify severity of atherosclerotic disease.

ABBREVIATIONS: AH = Anzhen Hospital; AUC = area-under-the-curve; CAS = Carotid Atherosclerosis Score; CE = contrast-enhanced; CE-MRA = contrast-enhanced MR angiography; CE-T1WI = contrast-enhanced T1-weighted imaging; CI = confidence interval; FCR = fibrous cap rupture; FSE = fast spin-echo; FSPGR = fast SPGR; FSRS = Framingham Stroke Risk Score; IMT = intima-media thickness; Inf = infinite; IPH = intraplaque hemorrhage; JV = jugular vein; LRNC = lipid-rich necrotic core; Max = maximum; MDIR = multisection double inversion recovery; Min = minimum; MRA = MR angiography; MRI = MR imaging; MSU = Michigan State University; NWU = normalized wall index; OR = odds ratio; PD = proton density; PLA = People's Liberation Army General Hospital; QIR = quadruple inversion recovery; ROC = receiver operating characteristics; SPGR = spoiled gradient-recalled echo; T1WI = T1-weighted imaging; T2WI = T2-weighted imaging; TOF = time-of-flight; TVA = total vessel area; UW = University of Washington

Carotid atherosclerotic disease is a leading cause of stroke. Disease severity and risk of stroke have been traditionally determined by measures of luminal occlusion.¹ Findings from randomized prospective investigations, however, have indicated that stenosis may be an uncertain measure of stroke risk

in symptomatic patients with <70% stenosis² and across all levels of stenoses in asymptomatic patients.³ Concurrently, atherosclerotic plaques in the coronary arteries associated with sudden cardiac death have been differentiated from lesions not associated with infarcts by histologic findings from within the vessel wall.⁴ In accord, considerable effort has been directed at identifying features of the carotid arterial wall that may provide complementary information to lumenography to evaluate disease severity better.

MR imaging of the carotid arteries has been validated with histology to be an effective method to identify and measure atherosclerotic vessel morphology and plaque composition.^{5–7} Recent carotid MR imaging–based cross-sectional^{8–10} and prospective^{11–13} studies of carotid atherosclerosis have offered exciting evidence that among many plaque features, IPH and FCR are some of the key determinants of the high-risk lesion—plaques associated with cerebrovascular events. Beyond the differentiation of high-risk lesions, however, a critical component of disease assessment is the recognition of lesions that may precede the development of IPH and/or FCR. The aim of this multicenter cross-sectional study was to determine which imaging features or combination of imaging features

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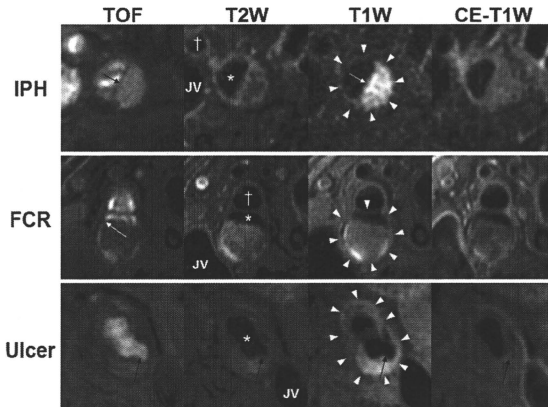


Fig 1. In vivo identification of IPH, FCR, and ulceration. Each row contains multicontrast axial images from a single location in the carotid artery. The outer wall boundary (white arrowheads) of either the internal or common carotid artery, the lumen of the internal or common (asterisk) carotid artery, the external (cross, where applicable) carotid artery, and the JV are identified. The top row is of the right internal carotid artery from a 69-year-old man imaged at MSU. IPH (arrows) is characterized by a hyperintense signal intensity on TOF and T1WI. The second row is of the right internal carotid artery from an 80-year-old man imaged at PLA. An FCR (white arrow) is evident on TOF imaging by the hyperintense signal intensity extending from the lumen into the plaque and the absence of a fibrous cap on T2WI and CE-T1WI. The third row is of the left common carotid artery from a 74-year-old man imaged at PLA. An ulceration (black arrows) is present. Notably, the varying appearance of the ulcer between the different contrast weightings is due to reduced flow suppression caused by turbulent flow in the ulcerated region, particularly after contrast administration.

has the highest association with the presence of IPH and/or FCR. We further sought to construct an imaging-based CAS that characterizes features of precursor lesions and provides evidence for an improved method to stratify carotid disease severity compared with the traditional stenosis measurement. This simple scoring system is intended to combine lesion morphologic and compositional information quantitatively, to provide easy tracking of the status of plaques, and to be used in large-scale prospective studies that link plaque features with clinical outcomes.

Materials and Methods

Study Sample

Multicontrast carotid MR images from 435 individuals with 16%–99% stenosis by duplex sonography in at least 1 carotid artery were pooled from 4 institutions: 1) AH, Capital Medical University, Beijing, China (n = 78; stenosis, >50%); 2) MSU, East Lansing, Michigan (n = 90; stenosis, >50%); 3) PLA, Beijing, China (n = 67; stenosis, >50%); and 4) UW, Seattle, Washington (n = 80; stenosis, 16%–49%; n = 120; stenosis, 50%–79%). The study procedures and consent forms were reviewed and approved by the institutional review board at each institution before study initiation. The artery with the greatest stenosis by duplex sonography, termed the index artery, was selected for image review because image acquisition was centered on that artery. Arteries were excluded from review if there was the following: 1) prior carotid endarterectomy on the index carotid artery, 2) prior radiation therapy to the neck, 3) insufficient coverage (<10 mm including the bifurcation) by MR imaging, or 4) poor image quality by MR imaging. Clinical information was obtained through chart review.

Table 1: Signal intensity of plaque features across different contrast weightings*

	TOF	T2WI	PD	T1WI	CE-T1WI
Calcification	– ^b	– ^b	– ^b	– ^b	–
LRNC	0/+	–/0	–/0	0/+ ^b	– ^b
IPH	+ ^b	–/0	–/0	+ ^b	–/0

* Intensity relative to the sternocleidomastoid muscle – indicates hypointense; 0, isointense; +, hyperintense.
^b Principal criteria for identification of a feature.

MR Imaging Acquisition

Participants underwent carotid MR imaging on either a 1.5T or 3T scanner by using bilateral phased-array carotid surface coils. Previously published multicontrast carotid imaging protocols^{14,15} were adapted for each study center. Sequences and imaging parameters are detailed in On-line Table 1. Notably, at 2 sites (AH and MSU) participants also underwent CE-MRA (On-line Table 1).

Image Analysis

All images of the index carotid artery from each subject were interpreted at a core laboratory by teams of 2 reviewers, all with >1.5 years’ experience in vascular MR imaging, via consensus opinion and blinded to clinical information. At each axial location, image quality was assessed with a 4-point scale (1 = poor, 2 = adequate, 3 = good, 4 = excellent). For arteries with image quality ≥2, image analysis software¹⁶ was used to draw the lumen and outer wall boundaries at each axial location. Lumen area, wall area, total vessel area, maximum wall thickness, and NWI (wall area/total vessel area) were recorded. In addition, the presence or absence of calcification, LRNC, IPH (Fig 1, top row), and fibrous cap status was determined by using multicontrast imaging criteria that have been previously validated with histol-

ogy^{6,17-19} and collectively depicted in a recently published atlas of carotid MR imaging and histology.²⁰

Signal-intensity criteria for identifying calcification, LRNC, and IPH are summarized in Table 1. Fibrous cap status was identified as 1) intact thick if fibrous tissue was evident on CE-T1WI or T2WI between the LRNC and the lumen, 2) intact thin if fibrous tissue was not evident on CE-T1WI or T2WI between the LRNC and lumen, and 3) ruptured if there was an absence of a fibrous cap on CE-T1WI and T2WI and juxtaluminar IPH on TOF (Fig 1, middle row). Area measurements of the LRNC and calcification, when present, were also collected, and the proportion of each component relative to the wall area (eg, percentage LRNC area = 100% × LRNC area / wall area) was subsequently calculated for each MR imaging location. Proportional measurements of plaque composition normalized the data for arterial size. Percentage stenosis was determined from the CE-MRA by using the established North American Symptomatic Carotid Endarterectomy Trial criterion²¹: 100% × (1 – luminal diameter at the point of maximal narrowing / the diameter of the normal distal internal carotid artery).

Statistical Analysis

All statistical analyses were performed with SPSS for Windows (Version 12.0, SPSS, Chicago, Illinois). Due to differences among institutions in longitudinal coverage of the artery, the maximum arterial value for each continuous metric was used during data analysis (as opposed to mean arterial values or volume data), except for lumen area, in which case the minimum arterial value was used. Individuals with ulceration, defined as a surface disruption with invagination into the plaque, were excluded from analysis (Fig 1, bottom row). Ulceration alters the morphology and composition of the plaque, which obscures the conditions that existed before the development of ulceration. To account for differences among imaging protocols, field-strengths, and patient demographics at different sites, we randomly divided the remaining evaluable study sample into 2 datasets with an intended ratio of 60:40 (training set/test set) by using the random selection of data command in SPSS. This method of creating a training and test set through random subsection creates 2 datasets that are equivalent to 2 independent random draws from the source collection of patients.²² Although measures of reproducibility for carotid MR imaging parameters have been previously reported (intra- and inter-reader^{6,19}, interscan^{15,23,24}), partitioning of the dataset in this manner, after image interpretation had been complete for all arteries, enabled the unbiased evaluation of reproducibility of the results obtained from the training set on the test set. To verify the randomness of allocation between the training and test sets, we evaluated differences in the baseline demographic and arterial characteristics with the independent *t* test for continuous variables and the Fisher exact test for categorical variables. Statistical significance, based on 2-sided tests, was defined as *P* < .05.

The CAS was constructed via the following steps: Step 1, with the training set, univariate binary logistic regression for continuous variables or the Fisher exact test for categorical variables was used to identify potential predictors of IPH and FCR from each of the clinical and arterial parameters listed in Table 2. IPH and FCR were not considered in the univariate analysis because they were the target, dependent variables used as indicators of a high-risk lesion. Step 2, with the training set, we created a multivariate model separately for IPH and FCR by using backward elimination of predictor variables, starting from all parameters with an association (*P* < .10) identified during univariate analysis and by using *P* < .10 (*F* test) to retain a variable in

Table 2: Demographic information (n = 334)

	Training Set (n = 196)	Testing Set (n = 138)	<i>P</i> Value
Age (yr)	69.0 ± 10.1	69.5 ± 9.5	.61
Male sex (%)	74.0	76.1	.70
History of			
Hypertension (%)	79.1	75.2	.43
Diabetes mellitus (%)	20.4	27.5	.15
Coronary artery disease (%)	34.3	39.3	.41
Smoking status			
Never (%)	28.2	31.9	.59
Quit (%)	49.7	44.2	
Current (%)	22.1	23.9	
Imaging center			
AH (%)	19.9	21.7	.27
MSU (%)	21.4	13.0	
PLA (%)	13.8	15.9	
UW (%)	44.9	49.3	
Intraplaque hemorrhage (%)	24.0	19.6	.35
Fibrous cap rupture (%)	7.1	10.9	.24
Min lumen area (mm ²)	17.2 ± 10.4	17.9 ± 9.1	.51
Max wall area (mm ²)	61.1 ± 21.6	63.8 ± 24.5	.29
Max total vessel area (mm ²)	113.0 ± 35.7	117.4 ± 38.3	.29
Max wall thickness (mm ²)	3.93 ± 1.79	4.00 ± 1.70	.72
Max normalized wall index	0.696 ± 0.139	0.674 ± 0.142	.16
Presence of calcification (%)	72.4	73.9	.80
Max percentage calcification (%) ^a	14.7 ± 10.4	16.1 ± 10.7	.31
Presence of LRNC (%)	59.7	63.7	.49
Max percentage LRNC ^a (%)	35.8 ± 18.3	31.3 ± 17.9	.09
MRA stenosis (%)	47.6 ± 29.3	48.8 ± 32.4	.83

^a Only for arteries with calcification (n = 244) or LRNC (n = 206) present.

the model. OR and the 95% CI are reported for results from univariate and multivariate analysis. Step 3, by using the training set, we assessed the accuracy of classification for each statistically significant parameter selected in the multivariate analysis with ROC curves and the AUC. Step 4, parameters identified during multivariate analysis of the training set were used to construct the CAS. Notably, methods used to construct the CAS were dependent on the results and are, thus, described in the "Results" section. Step 5, after formulation of the CAS from the training set was complete, performance of CAS was evaluated with the test set. ROC curves and AUC were used to determine the strength of the classification for identifying lesions with IPH or, separately, FCR in the test set.

Prevalence of calcification, LRNC, IPH, and fibrous cap status (thick, thin, or ruptured) are reported for each level of CAS separately for the training and the test sets. The prevalence of IPH, FCR, and measures used to construct the CAS were computed at each imaging location (relative to the bifurcation) for the entire dataset (training + test). Finally, in all participants with a CE-MRA, strength of classification for determining the presence of IPH and FCR was determined for both MRA stenosis and CAS.

Results

Of the 435 index arteries available for review, 388 (89.2%) had ≥10-mm longitudinal coverage, which included the bifurcation and sufficient image quality for identification of the vessel boundaries and plaque composition. An additional 54 arteries were excluded due to the presence of ulceration on the index artery. The remaining 334 arteries were used to form the training and testing datasets. Of these 334 arteries, 116 arteries had corresponding CE-MRA from AH and MSU. The mean lon-

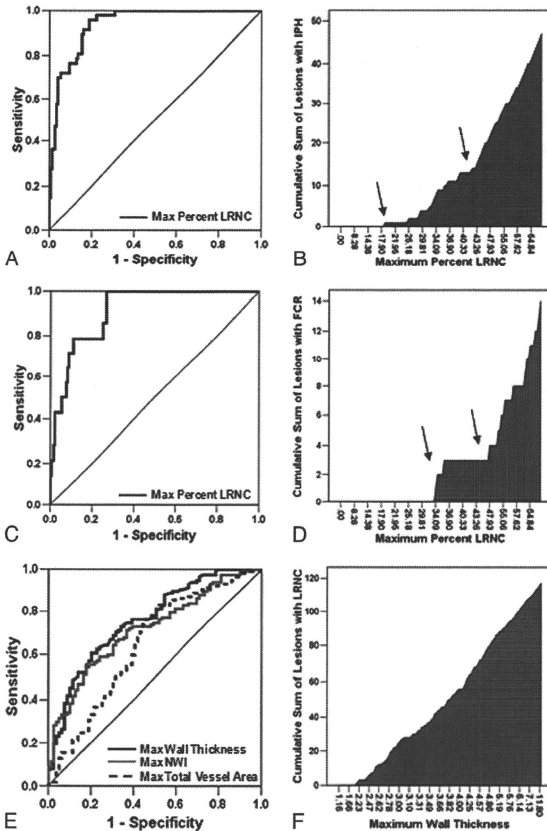


Fig 2. ROC curve analyses for the classification of IPH (A) and FCR (C) in the training set by maximum percentage LRNC. Adjacent to each ROC curve is a cumulative prevalence plot for IPH (B) and FCR (D) versus maximum percentage LRNC. The cumulative prevalence plots clearly depict changes in slope (arrows) for both IPH (B) and FCR (D), which were subsequently used to construct the CAS. E, ROC curve analysis for prediction of the presence of LRNC in the training set by maximum wall thickness, maximum total vessel area, and maximum NWI. F, In the cumulative prevalence plot for LRNC by maximum wall thickness, LRNC was absent in lesions with a maximum wall thickness <2 mm.

gitudinal coverage of the 334 evaluable scans was 23.4 ± 7.8 mm (range, 10–36 mm). There were no significant differences in demographic data, arterial morphology, and plaque composition between the training and test groups (Table 2).

Metrics that were associated with the presence of IPH or FCR, as identified during univariate analyses of the training set, are presented in On-line Table 2. Analysis in the training set through backward elimination in multivariate logistic regression selected the maximum percentage LRNC as the sole statistically significant predictor of both IPH (OR for 10% increase in maximum percentage LRNC, 3.3; 95% CI, 2.3–4.7; $P < .001$) and FCR (OR for 10% increase in maximum percentage LRNC, 2.5; 95% CI, 1.6–3.8; $P < .001$). Of note, MRA stenosis was available for only a subset of arteries in the train-

ing set, so multivariate analysis was performed twice for FCR: 1) on the subset of arteries for which MRA stenosis could be used as a covariate, and 2) on the entire training set without MRA stenosis as a covariate. In both instances, maximum percentage LRNC was the sole statistically significant predictor of FCR. ROC analysis of the training set found maximum percentage LRNC to be a strong classifier of both IPH (AUC = 0.94, Fig 2A) and FCR (AUC = 0.91, Fig 2C).

CAS

In evaluating the cumulative prevalence of IPH at different levels of maximum percentage LRNC within the training set, the curve (shown in Fig 2B) showed 2 distinguishable jumps at approximately 20% and 40%. Evidentiary change in the cu-

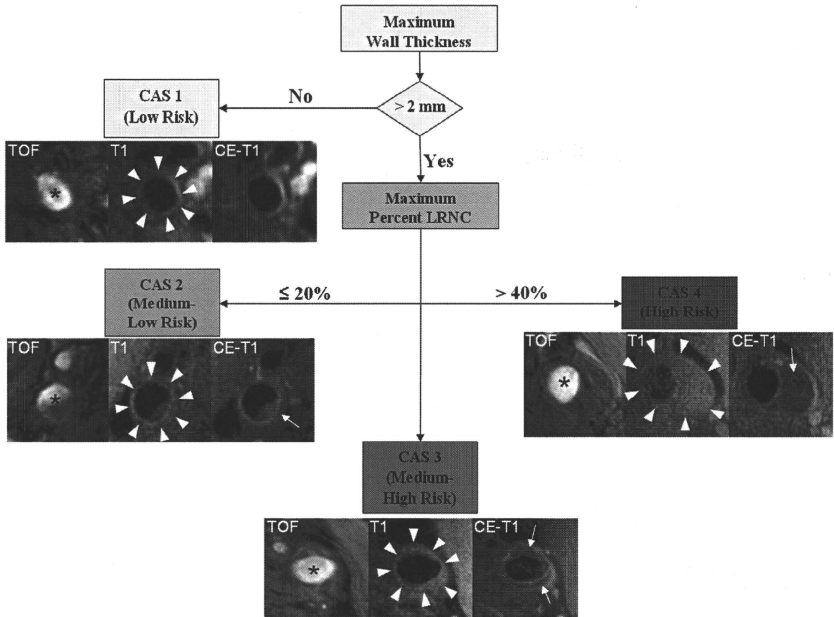


Fig 3. Flow diagram of CAS. Subjects with a maximum wall thickness >2 mm require additional evaluation. Further categorization of lesions can be determined by the size of the maximum percentage LRNC. Examples of matched cross-sectional images from 3 contrast weightings (TOF, T1WI, and CE-T1WI) for each category are provided. Images corresponding to CAS 1 (maximum wall thickness <2 mm) are from the left common carotid artery of a 69-year-old man imaged at MSU. The plaque in the CAS 2 (maximum percentage LRNC, $\leq 20\%$) example is from the right internal carotid artery of a 63-year-old man imaged at UW. There is a small LRNC (arrow) present on postcontrast imaging. Of note, there are also flow artifacts visible in the lumen—common artifacts in images distal to the bifurcation. The lesion in CAS 3 (maximum percentage LRNC, $>20\%$ and $\leq 40\%$) is from the left common carotid artery of a 65-year-old man imaged at AH. A noticeable LRNC (arrows) is present in both the anterior and posterior arterial wall. An example of a large LRNC (arrow) without IPH in the left common carotid artery of a 64-year-old man imaged at PLA is shown for CAS 4 (maximum percentage LRNC, $>40\%$). Arrowheads indicate the outer wall boundary, asterisk, the lumen.

Table 3: Prevalence of features for each level of CAS				
	1	2	3	4
Training set ($n = 196$)				
No.	16	90	42	48
Calcification (%)	12.5	80.0	78.6	72.9
LRNC (%)	0.0	30.0	100.0	100.0
IPH (%)	0.0	1.1	28.6	70.8
Fibrous cap status				
Thick (%)	0.0	21.1 (66.7) ^a	23.8	12.5
Thin (%)	0.0	10.0 (33.3) ^a	69.1	64.6
Ruptured (%)	0.0	0.0	7.1	22.9
Testing Set ($n = 138$)				
No.	17	62	34	25
Calcification (%)	17.6	83.9	79.4	80.0
LRNC (%)	11.8	43.5	100.0	100.0
IPH (%)	0.0	0.0	29.4	68.0
Fibrous cap status				
Thick (%)	11.8 (100.0) ^a	30.7 (66.7) ^a	29.4	4.0
Thin (%)	0.0	14.5 (33.3) ^a	64.7	44.0
Ruptured (%)	0.0	0.0	5.9	52.0

^a Lesions with an LRNC.

mulative prevalence of FCR occurred at maximum percentage LRNC values equal to approximately 30% and 45% (Fig 2D).

Thus, cutoff values for maximum percentage LRNC were selected at 20% and 40% to provide 3 tiers ($<20\%$, $20\%–40\%$, and $>40\%$) of stratification of risk for both IPH and FCR.

Because only lesions with an LRNC would be eligible for classification beyond the first tier, an additional univariate/multivariate analysis was performed to determine predictors of the presence of an LRNC (On-line Table 2). Among the 3 variables identified during multivariate analysis (On-line Table 2), accuracy of classification of arteries (LRNC present versus absent, Fig 2E) was strongest for maximum wall thickness (AUC = 0.76), followed by maximum NWI (AUC = 0.72) and maximum total vessel area (AUC = 0.65). From a plot of cumulative prevalence of arteries with LRNC versus maximum wall thickness for the training set (Fig 2F), LRNC did not occur in arteries with a maximum wall thickness ≤ 2 mm. As such, lesions with a maximum wall thickness ≤ 2 mm were classified as the first tier of CAS followed by the 3 tiers dependent on the size of the maximum percentage LRNC (Fig 3).

Applied to the test set ($n = 138$), the 4-tier CAS was a strong classifier of both IPH (AUC = 0.91) and FCR (AUC = 0.93). The prevalence of each compositional feature for each

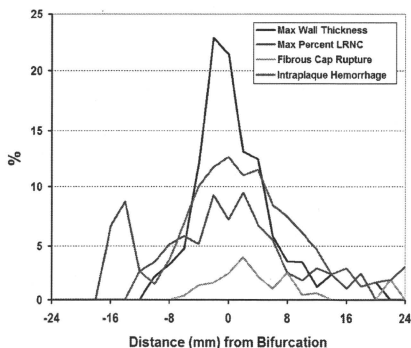


Fig 4. Prevalence of key features in the carotid artery is shown for each MR imaging location relative to the bifurcation. Distance from the bifurcation (0) is labeled on the x-axis, where positive and negative integers represent locations within the internal and common carotid arteries, respectively.

category of CAS applied to both the training and test sets is detailed in Table 3.

Anatomic Location of Key Features

An analysis of the prevalence of plaque features at different locations in the artery, including all evaluable arteries without an ulcer ($n = 3898$ sections from 334 arteries) demonstrated that the maximum wall thickness and maximum percentage LRNC, IPH, and FCR occurred predominantly at or adjacent to the carotid bifurcation (Fig 4).

CAS versus MRA Percentage Stenosis

In the subcohort of individuals with CE-MRA ($n = 116$), CAS was a stronger classifier than stenosis for both IPH (AUC = 0.87 versus 0.57, respectively; Fig 5A) and FCR (AUC = 0.85 versus 0.67, respectively; Fig 5B).

Discussion

This study used a standardized carotid MR imaging protocol implemented at multiple centers to evaluate a spectrum of in vivo carotid atherosclerotic disease. While carotid MR imaging enables the assessment of a multitude of morphologic and

compositional imaging parameters, this cross-sectional study distinguished the maximum percentage LRNC as the variable with the strongest association with the presence of IPH and FCR. In addition, our data indicate that in the absence of high-risk features (IPH, FCR, and/or ulceration), plaques with a maximum percentage LRNC $>40\%$ may also be considered high-risk (CAS 4) due to the high prevalence of IPH and/or FCR observed in this subset of arteries. A simple imaging-based risk assessment system derived from these findings, such as CAS, may prove clinically useful for stratifying atherosclerotic disease severity in the carotid artery. These results form the basis for large prospective studies that target the LRNC as the key parameter for determining the risk of developing IPH and/or FCR and for evaluating the risk of cerebrovascular events along with IPH, FCR, ulceration, and stenosis.

Compared with stenosis, the traditional measure of carotid atherosclerotic disease severity, CAS was a stronger classifier for the presence of IPH and FCR. Outward remodeling²⁵ coupled with an enlarged luminal area of the carotid bulb, the location where these features were most prevalent (Fig 4), may enable the development of high-risk features before detectable luminal encroachment. Babiarz et al²⁶ described a wide range of plaque burden in lesions with minimal stenosis as determined by CE-MRA. Saam et al²⁷ found that IPH or FCR or both were present in 8.7% of lesions with 1%–15% stenosis and 21.7% of lesions with 16%–49% stenosis. Most recently, Dong et al²⁸ reported the occurrence of both IPH and FCR in angiographically normal (0% stenosis) arteries. Collectively, these previous studies^{26–28} highlight the potential limitations of traditional risk-stratification systems that use stenosis as the principal criterion for discriminating lesion severity. Accordingly, alternate methods for assessing carotid atherosclerotic disease severity, such as CAS, may be clinically constructive, particularly in patients with $<70\%$ stenosis.

Our findings demonstrated that arterial wall thickness measurements were effective for discriminating between lesions with and without a LRNC. This is interesting because it may create a natural connection point between sonography and MR imaging in a clinical setting. Measures of carotid wall thickness by sonography have been previously associated with stroke. O'Leary et al²⁹ found that a maximum internal carotid IMT ≥ 1.81 mm was associated with an adjusted relative risk of 2.4 for incident stroke. Touboul et al³⁰ found the presence of

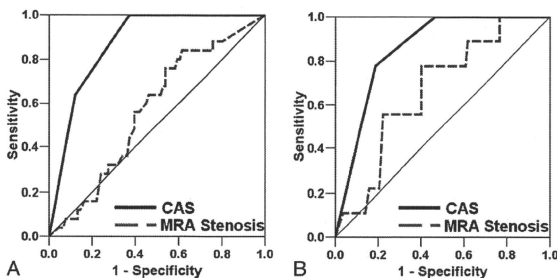


Fig 5. ROC curve analyses for IPH (A) and FCR (B) by using either CAS or MRA stenosis.

carotid plaque that encroached into the vessel >1 mm to be independently associated with stroke risk. However, discrimination of plaque stability solely on morphology (eg, wall thickness) may be insufficient. Prati et al³¹ recently reported that inclusion of carotid findings (eg, IMT >1 mm and at least 1 plaque) into the FRS resulted in a higher predictive power of incident stroke only in subjects with an FRS >20%. Accordingly, we found wall thickness to be an appropriate measure for differentiation between stable and potentially unstable carotid disease, but parameters beyond arterial morphology were necessary to classify severity accurately. Nevertheless, evaluation of wall thickness measurements, particularly with sonography, may be a cost-effective strategy for identifying individuals to evaluate with multicontrast high-resolution carotid MR imaging.

There are several limitations that merit discussion. First, the imaging protocol used in this study was not uniform across study centers. However, randomly partitioning the data into training and test sets accounts for differences that may occur due to the site. Furthermore, the heterogeneity within the dataset suggests that CAS may be sufficiently robust to overcome differences that may occur as a result of image acquisition. Second, the current CAS is limited to predicting the presence of IPH and FCR in the carotid atherosclerotic lesion. While the scoring system may require further optimization based on future prospective studies linked to clinical (eg, stroke) and/or imaging (eg, development of a new IPH) outcomes, the proposed system may already be relevant. The data presented herein and the subsequently derived CAS point to ways to improve carotid MR imaging efficiency and accuracy by focusing imaging strategies on the detection of the LRNC, IPH, FCR, and ulceration. Sequences used during this investigation were part of a broad multicontrast protocol to comprehensively evaluate carotid disease. Selecting sequences to focus on quantification of the specific features (eg, CE-T1WI¹⁸ for LRNC; TOF¹⁹ or magnetization-prepared rapid acquisition of gradient echo³² for IPH) necessary for severity assessment may substantially decrease scanning time and increase translatability of carotid MR imaging to clinical practice.

Finally, CAS was not applied to neurologic symptom status. Because patient examinations were pooled from multiple different institutions, inclusion criteria for the carotid MR imaging varied. For example, only asymptomatic patients were imaged at UW compared with MSU, which imaged both asymptomatic and symptomatic individuals. In addition, findings from several large population-based studies indicate a much greater prevalence of subclinical strokes compared with clinically overt events.^{33,34} To accurately determine the ability of CAS to classify risk, future prospective investigations should integrate brain MR imaging to account for all strokes (silent and overt) that occur within the carotid vascular supply.

Conclusions

We conclude that the maximum percentage LRNC is an effective parameter for classifying the severity of carotid atherosclerotic disease. In the absence of FCR, IPH, and ulceration, a plaque with a maximum percentage LRNC >40% may be a high-risk lesion. The findings from this cross-sectional study form the basis for large long-term prospective studies that

evaluate the effectiveness of CAS in predicting disease progression, development of FCR and IPH, and future ischemic events.

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MRI を用いたプラークイメージング

大田英揮

金原出版

MRI を用いたプラークイメージング

大田英揮*

■ はじめに

現在、頸動脈の動脈硬化性病変に対する外科的あるいは血管内治療の適応は、主に頸動脈の狭窄度に基づいている¹⁾。これは、North American Symptomatic Carotid Endarterectomy Trial (NASCET)²⁾ や European Carotid Surgery Trial (ECST)³⁾ といった大規模臨床研究の結果により、頸動脈の動脈硬化性高度狭窄病変が脳梗塞のリスクファクターであると考えられているためである。しかし、必ずしも狭窄度のみが動脈硬化性病変の重症度を反映しているわけではない。近年、血管内皮に生じた動脈硬化性プラークの破綻と、それに引き続く血栓形成が脳梗塞の原因の一つとして注目されている。破綻しやすい不安定なプラーク、いわゆる“vulnerable plaque”⁴⁾ を同定し、プラークの破綻の機序を明らかにすることが、脳梗塞を予測するために重要となってきた。

動脈硬化性病変を評価するためのイメージングモダリティとしては、MRI、CT、超音波、PET等があげられる。特にMRIは、高い組織コントラスト、空間分解能を有しており、壁内のプラーク成分を良好に描出することができる。本稿では、MRIを用いた頸動脈のプラークイメージングについて、今まで報告されてきている論文とともに、自験例を提示しつつ解説する。

① MRI プロトコール

プラークの様々な構成成分は、それぞれが異なる信号パターンを呈するため、複数のシークエンスを撮像する必要がある⁵⁾。プラークを含んだ血管壁の信号を評価するためには、血管内腔とのコントラストを明瞭にするため、血液の信号を抑制した black-blood imaging が必須となる。black-blood imaging の方法は幾つかあり⁶⁾、主なものとして、presaturation preparatory pulse 法、double inversion recovery (DIR) 法、motion-sensitized driven-equilibrium (MSDE) 法⁷⁾ などがある。また、black-blood imaging には血管壁と周囲とのコントラストを明瞭にするために、脂肪抑制も併用する。

そのほか、bright-blood imaging である time-of-flight (TOF) も、プラーク表面の形態（表面の不整、潰瘍、内腔に近接した石灰化）やプラーク内出血の評価に用いられる。造影 T1 強調像は lipid-rich/necrotic core の評価、および線維性被膜の評価に有用である。また、3D magnetization prepared rapid acquisition gradient echo (3D MPRAGE)、(Moody らの原著⁸⁾ では MR direct thrombus imaging (MRDTI) は、プラーク内出血の同定に有用である。このシークエンスは、血液信号が null になるように T1 を設定し、脂肪抑制を併用した三次元グラジエントエコー T1 強調法である。

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[索引用語: MRI, プラークイメージング]

② 動脈硬化プラークの性状

動脈硬化プラーク内の様々な成分のうち、主に MRI で同定されるものとしては lipid-rich/necrotic core、線維性被膜、石灰化、プラーク内出血、loose matrix が挙げられる。組織所見をゴールドスタンダードにした場合、これらのプラーク構成成分の同定における MRI の感度、特異度は 85 ~ 92% と報告されている⁹⁾¹⁰⁾。以下にそれぞれの成分について信号パターンを含めて解説する。

1) Lipid-rich/necrotic core と線維性被膜

MRI で lipid-rich/necrotic core として同定される成分は、組織学的に extracellular lipid, cholesterol crystals, necrotic debris で構成されている¹¹⁾。動脈硬化が進行すると、lipid-rich/necrotic core は徐々に増大していく。Lipid-rich/necrotic core を被うようにして、血管内腔との間に介在する線維組織を線維性被膜と呼ぶ¹¹⁾。線維性被膜は平滑筋細胞によって形成され、炎症細胞を伴う場合もある。線維性被膜が厚い場合は、それだけ被膜の破綻しにくいプラークであると考えられる。一方、線維性被膜が菲薄化 (thin-cap fibroatheroma: TCFA) すると、線維組織の層が薄く、平滑筋細胞も欠如してくる。線維性被膜が菲薄化したプラークでは、lipid-rich/necrotic core のサイズが大きくなり、プラーク内出血もしばしば認められるようになる^{12) 13)}。菲薄化した線維性被膜を有するプラークは、破綻しやすい不安定なプラークであると考えられている。

プラーク内出血を伴わない lipid-rich/necrotic core は、T1 強調像にて等信号～やや高信号を呈する。T2 強調像では、低信号を呈するという報告や⁹⁾、中間信号～高信号を呈するとの報告もあり⁶⁾、一定していない。また、後述するプラーク内出血を伴う lipid-rich/necrotic core でも、T2 強調像にて様々な信号を呈する。一方、lipid-rich/necrotic core は血管構造に乏しい成分であることから、造影 T1 強調像で増強効果に乏しい低信号域として認められる¹⁴⁾ (図 1)。

線維性被膜は定性的に厚い被膜、菲薄化した被膜、破綻した被膜と分類できる^{14) 15)}。厚い線維性被膜の場合、血管内腔と lipid-rich/necrotic core との間に帯状構造が認められる。この帯状構造は、TOF

で低信号を呈し、造影 T1 強調像で増強される。線維性被膜が菲薄化すると、この帯状構造が欠損、途絶する (図 1)。破綻した線維性被膜では、帯状構造の欠損 / 途絶に加えて、内腔表面の不整が認められ、TOF 画像においては、内腔から連続するようにプラーク内に進展する高信号が認められる。

Yuan ら¹⁶⁾ は、頸動脈 MRI でプラークの線維性被膜を評価し、最近生じた臨床症状 (脳梗塞 / 一過性脳虚血発作) の有無との関連性について検討している。それによると、菲薄化した、あるいは破綻した線維性被膜が MRI で同定された群は、厚い線維性被膜を有する群と比較して有症状の患者が有意に多かった。不安定な線維性被膜が臨床症状と関連している可能性が示唆されている。

2) プラーク内出血

プラーク内出血は赤血球内のメトヘモグロビンによる T1 短縮効果により、T1 強調像にて高信号を呈する⁸⁾。スピエコー系の T1 強調像や TOF で高信号を呈するが、MPRAGE ではさらに高信号が明瞭になる (図 1)。3T MRI において、fast spin echo T1 強調像、TOF、MPRAGE を用いてプラーク内出血の診断能を比較した場合、MPRAGE が最も感度、特異度、および定量的評価に優れている¹⁰⁾。MPRAGE はプラーク内出血を同定する特異的なシークエンスとして有用と考えられる。

プラーク内出血は、プラーク表面の亀裂やプラーク内の新生血管の破綻によって生じると考えられている¹⁷⁾。出血を伴った頸動脈プラークは経時的に増大傾向を示し、さらに、プラーク内出血を繰り返す可能性が高いと報告されている¹⁸⁾。すなわち、プラーク内出血はプラークの不安定化に大きく関与していると考えられる。Murphy ら¹⁹⁾ は、MRDTI (MPRAGE に相当) を用いて、脳梗塞 / 一過性脳虚血発作を有する患者群とコントロール群を撮影し、プラーク内出血に相当する MRDTI 高信号の有無を検討している。有症状群では 60% の患者に MRDTI 高信号が認められたのに対し、コントロール群では高信号は 1 例にも認められなかった。また、Yamada ら²⁰⁾ は、頸動脈の狭窄度を 0 ~ 29%、30 ~ 69%、70 ~ 99% の 3 群に分類し、各群において症候性患者と無症候性患者における、MPRAGE での高信号の頻度を比較している。この研究では、いずれの狭窄度群でも、

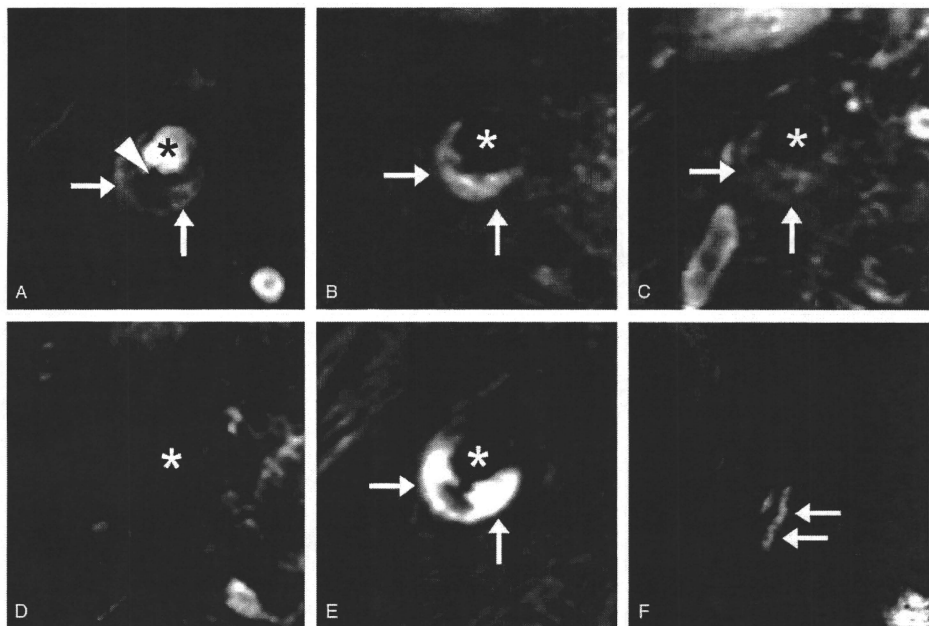


図1 70歳代、男性 右総頸動脈遠位端の軸切断画像

A TOF B T1強調画像 C 造影T1強調画像 D T2強調画像 E MPRAGE F T1強調の傍矢状断画像

TOF (A), T1強調 (B), MPRAGE 画像 (E) にて、高信号の領域が認められており (→)、この領域は造影T1強調画像 (C) にて、増強効果に乏しい。プラーク内出血を伴った lipid-rich/necrotic core と考えられる。傍矢状断画像 (F) で観察すると総頸動脈～内頸動脈近位部にかけて広範にプラーク内出血が認められる。血管内腔 (*) と、このプラーク内出血を伴った lipid-rich/necrotic core の間に介在する線維性被膜は、造影T1強調画像で同定できず、菲薄化した線維性被膜の可能性もある。また、TOF (A) にて内腔と接するように低信号の領域が認められ (▲)、内腔に近接した石灰化が疑われる。

MPRAGE 高信号の頻度が症候性患者群で高かった。これらより、プラーク内出血が症状と有意に関連していることが示唆される。

3) 石灰化病変

内膜の石灰化は、動脈硬化病変においてしばしば認められる所見である²¹⁾。石灰化とプラークの安定性という点においては様々な報告があるが、石灰化プラークは比較的安定している病変であると考えられていることが多い。過去の研究ではプラークの破綻は非石灰化プラークにより多く認められるとの報告や²²⁾、頸動脈プラークの石灰化が高度であればあるほど、脳梗塞の頻度が低いという報告がある²³⁾。

石灰化はいずれのシークエンスにおいても低信号を呈するため、比較的容易に同定できる。プラーク表面に存在する石灰化病変は、black-blood imaging では内腔の信号と同等になり、同定困難な場合があるため、bright-blood imaging である TOF を用いる必要がある (図2)。

4) Loose matrix

Loose matrix はプロテオグリカンに富む細胞外基質であり、冠動脈の病理学的研究において、プラーク破綻後の治癒過程に形成されるものと考えられている²⁴⁾。MRI では、T2強調画像と造影T1強調画像にて強い高信号を呈し⁹⁾、他のシークエンスでは低～等信

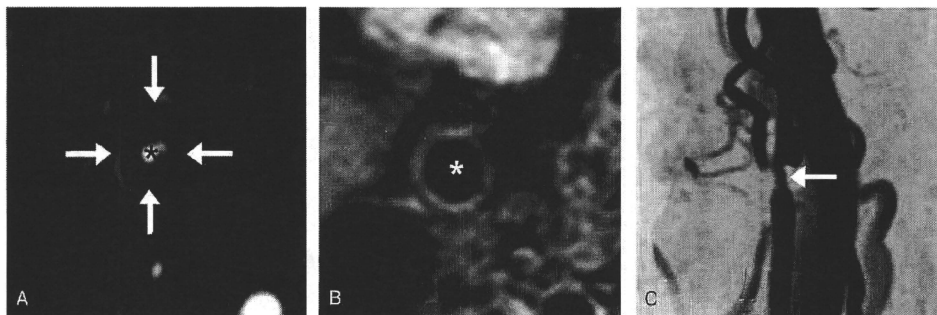


図2 70歳代, 男性 右総頸動脈遠位端の軸位断画像

A TOF B T1強調像 C 造影MRAのMIP画像 TOF (A) では内腔の狭小化と, 全周性の低信号構造(→)が認められ, 全周性の石灰化プラークによる狭窄病変と考えられる。Black-blood imagingのT1強調像(B)では, 信号抑制された内腔と, 石灰化の低信号の区別がつかず, 石灰化プラークの程度を評価するのは困難である。造影MRA (C) では, このレベルの狭窄(→)が明瞭に描出されている。*: 血管内腔

号を呈する(図3)。

症候性患者における責任病変側の頸動脈と, その反対側の頸動脈を比較した研究において, 責任病変側の loose matrix のサイズが有意に大きかったとの報告がある²⁵⁾。しかし, loose matrix の臨床的意義については, それ以外に明確な報告はない。

5) 血管壁厚

血管壁厚については, 超音波によるIMT (intima-media complex thickness) の評価がより簡便であり, 多くの研究が報告されている。MRIで計測した血管壁厚は, 超音波と比較して良好に相関する²⁶⁾。しかし壁厚計測のみを目的としてMRIを用いるのは非効率的であり, プラークイメージングと合わせて行われるべきものであろう。

③ 中等度以下の頸動脈狭窄病変におけるプラークイメージング

症候性頸動脈高度狭窄 (> 70%, NASCET法) に対する頸動脈内膜剥離術は, 確固たるエビデンス^{23) 31)}に基づき行われているが, 中等度以下の狭窄病変に対する治療法のエビデンスレベルは相対的に低い¹⁾。DeMarcoらは70%未満の狭窄を有する症例に頸動脈MRIを施行し, 無症候性群と比較して

症候性群に, 薄い/破綻した線維性被膜, lipid-rich necrotic core, プラーク内出血の頻度が高かったと報告している²⁷⁾。Kweeらは²⁸⁾, 軽度~中等度狭窄を有する脳梗塞/一過性脳虚血発作の患者に頸動脈MRIを施行し, 軽度狭窄群と, 中等度狭窄群に分けてプラークの性状を比較している。その結果, 中等度狭窄を有する群のほうが, 薄い/破綻した線維性被膜, プラーク内出血の頻度が高く, lipid-rich/necrotic coreのサイズが大きく, 線維性組織のサイズが小さかった。

中等度以下の狭窄症例は, 外科的治療に至ることが少なく, 病理学的評価の難しい群であり, in vivo imagingの利点を生かせる領域である。また, この様な症例のなかで, 今後プラークイメージングを用いて, 外科的治療の有用なサブグループを同定できる可能性もあろう。

④ 頸動脈プラークイメージングを用いた前向き研究

in vivo imagingの大きな利点は, 病変と将来をイベント/変化を前向きに比較研究できることである。特にMRIは被曝がないため, 繰り返し検査を行うことに対するハードルが少ない。

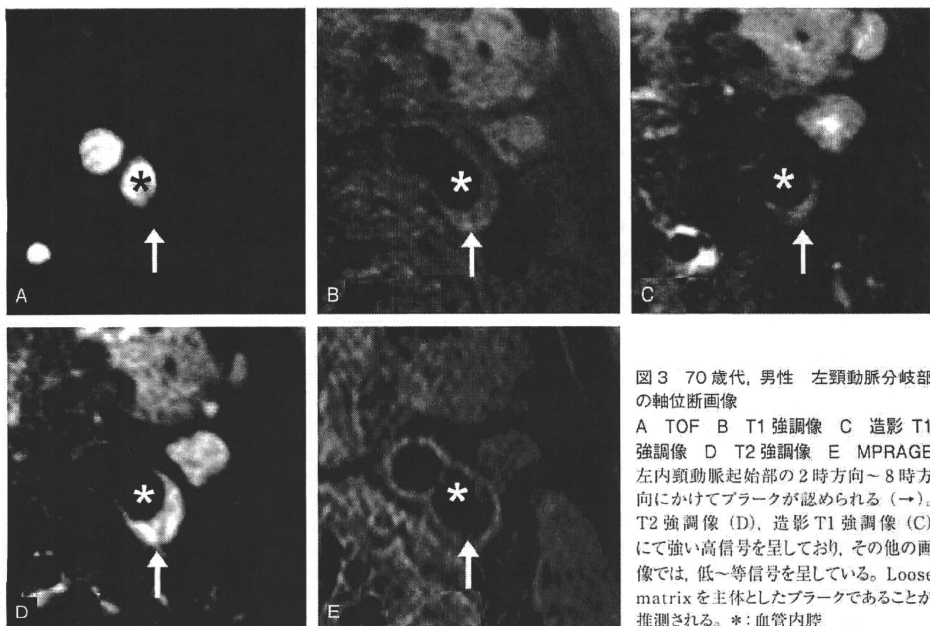


図3 70歳代、男性 左頸動脈分岐部の軸位断画像

A TOF B T1強調像 C 造影 T1強調像 D T2強調像 E MPRAGE
 左内頸動脈起始部の2時方向～8時方向にかけてプラークが認められる(→)。T2強調像(D)、造影T1強調像(C)にて強い高信号を呈しており、その他の画像では、低～等信号を呈している。Loose matrixを主体としたプラークであることが推測される。*:血管内腔

Takayaら³⁰⁾は、50～79%の頸動脈狭窄を有する無症状の154例に頸動脈MRIを施行後、12カ月以上の追跡調査を行った。追跡中12例に脳虚血性疾患が生じ、MRI所見を比較検討すると、特定のプラーク所見と症状との有意な関連が認められた。すなわち、プラーク要素のうち、非薄化/破綻した線維性被膜の頻度、プラーク内出血の頻度、lipid-rich/necrotic coreの大きさ、プラーク内出血の大きさが有意に将来のイベントと関連していた。Singhら³⁰⁾は、中等度狭窄を有する無症候性の男性において、プラーク内出血を有していると将来の脳虚血性イベントの発症率が高いと報告している。また、症候性患者においても、プラーク内出血があると、症状の再発率が有意に高いという報告がある^{31) 32)}。

この様に、脳虚血性疾患の予測因子として、頸動脈プラークイメージングが用いられうる可能性がある。

■ ま と め

MRIを用いた頸動脈のプラークイメージングでは、様々なプラーク成分を同定することができる。MRI所見に基づくと、lipid-rich/necrotic core、非薄化/破綻した線維性被膜の状態、プラーク内出血が頸動脈プラークの不安定化にかかわっていると考えられる。

今後、日本でも動脈硬化性疾患の増加に伴って、頸動脈のプラークイメージングの臨床的必要性が高まっていく可能性がある。プラーク診断に基づいて脳梗塞のリスク予測の他、外科的治療³⁰⁾・血管内治療³¹⁾の合併症予測が行える可能性を示唆する論文も報告されている。頸動脈疾患の治療方針決定に、今までの狭窄度に基づいた評価に加えて、プラーク診断が重要な要素となってくる可能性がある。

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Summary

Carotid plaque MR imaging

Although treatment strategy for carotid atherosclerotic disease has been based on the degree of its stenosis, vulnerable plaque prone to rupture is also considered as an important risk factor for subsequent thromboembolic ischemic events. MRI is a promising in vivo modality that can identify various plaque characteristics such as lipid-rich/necrotic core, fibrous cap, intraplaque hemorrhage and calcification. Recent studies revealed that unstable plaque characteristics such as thin/ruptured fibrous cap, intraplaque hemorrhage and larger lipid-rich/necrotic core were significantly associated with recent stroke as well as future ischemic events. Carotid MRI can be clinically used for the evaluation of carotid vulnerable plaque.

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臨床 MRI 撮像条件最適化援助ツールの開発

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A Tool to Aid Optimization of Imaging Parameters in Clinical MRI

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Key words : simulation, brain imaging, plaque imaging, FLAIR, MPRAGE

Optimization of imaging parameters in a clinical MRI examination requires basic understanding of the MRI pulse sequence and of the signals acquired by the sequence. We created a graphical tool to aid the optimization in clinical settings that could easily produce simulated signal intensities according to various changes in imaging parameters and operate interactively on the Web.

1. はじめに

MRIは、現在多くの保健医療施設において診断に用いられている検査法である。MRIには、様々な撮像法があり、さらに1つの撮像法においても、多くの撮像パラメータがあり、それらを適宜設定して検査が施行される。この際、パラメータの値により、得られる信号は様々に変化する。従って、臨床の場で、どのような撮像パラメータを選択すれば、最も診断価値の高い結果(画像)が得られるかを判断することが重要となる¹⁻⁴⁾。

このような撮像パラメータの最適化は必ずしも容易ではなく、各施設で何回も試行錯誤をして決定され、日常臨床に使用されている。そのようにして決定されたパラメータが、真に最適化されたものかどうかは、臨床経験の積み重ねや、他施設との情報交換などにより判断されることになる。このプロセスにおける試行錯誤の回数を減らし、

最適化を容易にするために、任意の撮像パラメータ値を与えたときに、どのようなMR信号が得られるかを、ウェブ上(http://www.nidi.med.tohoku.ac.jp/webMathematica/MRI_Notes/)で手軽に見ることができるようなツールを作成することを検討したので報告する。

2. 方 法

臨床MRIで基本となる、スピンエコー法・高速スピンエコー法を用いたT1、T2強調画像と反転回復法のほか、グラディエントエコー法のFast Low Angle Shot (FLASH)、Balanced Steady State Free Precession (SSFP)、Magnetization-Prepared Rapid Gradient-Echo (MPRAGE) Imaging⁵⁾、さらに、スピンエコー法を用いた拡散強調画像のシーケンスについて、緩和時間などの組織の性質と撮像パラメータを独立変数として、MRI信号強度を計算する関数を作成した。その具体的な形は以