Magnetic Resonance Carotid Plaque Imaging

Kiyofumi Yamada and Shinichi Yoshimura

MRI is able to visualize the wall and vessel lumen and has good soft tissue contrast which allows for the assessment of morphologic and compositional features of carotid artery plaques. It has been reported that presence of vulnerable plaque is related with an increased incidence of cerebral ischemic events. It is also reported that unstable carotid plaques which contain large amount of lipid-rich necrotic core (LRNC) and intraplaque hemorrhage (IPH) are related with an increased incidence of ischemic complications during or after carotid artery stenting (CAS). MRI assessment of LRNC and IPH has a good sensitivity and specificity. Also, it enables a volumetric analysis. In this review, we describe the current understanding of the magnetic resonance (MR) carotid plaque imaging and its clinical application for CAS.

Keywords ▶ carotid artery stenosis, magnetic resonance imaging, carotid plaque imaging, carotid artery stenting

Introduction

MRI is suitable for carotid plaque imaging because it is less invasive and it enables to visualize the carotid plaque components. It has advantages over other modalities in that it can visualize the vessel wall and lumen and has good soft tissue contrast which allows for the assessment of morphologic and compositional features of carotid artery plaques. Using multicontrast MRI sequences, they can visualize plaque components such as lipid-rich necrotic core (LRNC), intraplaque hemorrhage (IPH), and calcification (CA).1–5) Recently, it has been reported that unstable carotid artery plaques which contain a large size of LRNC and IPH are related to an increased incidence of embolic complications after carotid artery stenting (CAS). Therefore, the clinical implication of preoperative magnetic resonance (MR) carotid plaque imaging is expected to improve the outcome of CAS.6)

MR Carotid Plaque Imaging

Identification of carotid artery disease is based on measurements of the degree of luminal stenosis and surface irregularities by ultrasound, CT, MRI, and DSA.

Over other modalities, MRI has many advantages in that it is able to visualize the vessel wall and lumen and has good soft tissue contrast which realizes evaluation of morphologic and compositional features of carotid artery plaques.1–4) Plaque components could be detected by identifying combinations of signal intensities visualized by each component in multicontrast MRI. In experiments of the ex vivo imaging of carotid endarterectomy (CEA) specimen, including the LRNC, IPH, and CA, components could be differentiated with sensitivities and specificities ranging from 84% to 100%.5) Translation of these results to in vivo imaging, the sensitivity was 85% and a specificity was 92%3) (Table 1 and Fig. 1). It is reported that the in vivo capability of MRI to quantify carotid plaque components by comparing results with histological findings. MRI assessment of plaque components was statistically equivalent to those of histology for fibrous tissue and LRNC. Intra- and inter-observer reproducibility was good to excellent for all carotid plaque components, with intraclass correlation...
coefficients ranging from 0.73 to 0.95. Multicontrast MRI assessment using T1-weighted (T1W), T2-weighted (T2W) images and time of flight (TOF) images can visualize plaque components (e.g., LRNC, IPH, and CA) without administration of contrast media.

Intraplaque Hemorrhage

IPH is considered as one of the important features of vulnerable plaque. Numerous studies reported the relation between the presence of IPH and cerebrovascular ischemic events, and IPH is associated with the progression of carotid plaque. Gupta et al. reported on their meta-analysis about MR carotid artery plaque imaging and ischemic stroke risk that IPH was related with significantly increased risk for transient ischemic attack or ischemic stroke (hazard ratio: 4.40; 95% CI: 2.10–9.23; and hazard ratio: 5.04; 95% CI: 2.15–11.85, respectively). MR carotid plaque imaging is considered the best imaging technique for IPH detection.

IPH appears blight on T1-weighted image (T1WI) due to the relatively short T1 of methemoglobin. IPH can be identified on T1WI sequences such as T1WI sampling perfection with application optimized contrasts using different flip angle evolutions (SPACE), T1WI fast spin-echo, TOF, a highly T1W sequence such as magnetization prepared rapid gradient echo (MP-RAGE) is able to produce higher sensitivity and specificity for IPH detection (Fig. 2).

As clinical settings, we previously reported that maximum intensity projection (MIP) images from routine TOF-MRA can identify IPH as a high intensity signal in the plaque. MIP images from TOF-MRA are widely used for screening of carotid artery stenosis and allow for rapid determination of the stenotic degree and other anatomical findings at the same time using rotational views. Therefore, this finding provides the potential of an additional application of MIP images from TOF-MRA used for the assessment of carotid artery stenosis for the routine clinical use (Fig. 3).

### Table 1 MRI criteria used to identify plaque components

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<th>TOF</th>
<th>T1W</th>
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<td>Calcification</td>
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<td>LRNC with no or little IPH</td>
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The classification is based on the following signal intensities relative to sternocleidomastoid muscle. Hyper: hyperintense; Hypo: hypointense; IPH: intraplaque hemorrhage; Iso: isointense; LRNC: lipid-rich necrotic core; MP-RAGE: magnetization prepared rapid gradient echo; T1W: T1 weighted; T2W: T2 weighted; TOF: time of flight
Fibrous Cap Rupture and LRNC

The fibrous cap, which separates LRNC from the lumen, is considered as one of the identifying features of the vulnerable plaque. Vulnerable plaques are composed of the presence of a thin fibrous cap covering a large size of LRNC with IPH. The size of LRNC was considered a strong predictor of fibrous cap disruption.\(^{17,18}\) Fibrous cap rupture exposes the LRNC to luminal blood, activating the thromboembolic cascade. Therefore, fibrous cap status and LRNC are expected to be related with a risk of cerebrovascular ischemic events.\(^{12,19}\) On T2W image, LRNC can be detected as a focal hypointense lesion.\(^{20}\) In multiple studies, it has been confirmed the improved detection of LRNC seen as a focal non-enhancing lesion in the plaque on contrast-enhanced T1WI.\(^{21,22}\) A fibrous cap is visualized by the presence of a juxtaluminal band of low signal on TOF-MR image. Therefore, ulceration or ruptured fibrous cap can be clearly visualized on TOF-MRI (Fig. 4). Contrast-enhanced MRA followed by post-contrast-enhanced wall imaging will improve the detection of LRNC and depiction of the fibrous cap\(^{23}\) (Fig. 5).

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**Fig. 2** An example of a HIS-positive plaque on MIP images of 3D TOF-MRA. HIS in the plaque was observed on MIP images on TOF-MRA (A) (arrow). (B) The matching histology Masson’s trichrome staining showed large regions of intraplaque hemorrhage. HIS: high-intensity signal; MIP: maximum intensity projection; TOF: time of flight.

**Fig. 3** An example of ruptured fibrous cap with ulcer. (A) Digital subtraction angiography showed internal carotid stenosis with ulcer (black arrow). (B) Axial image of time of flight-MRA showed discontinuity of juxtaluminal band of low signal (white arrow) and ulcer (white arrowhead).
Clinical Implications of MR Carotid Plaque Imaging for CAS

CAS has recently emerged as a potential alternative to CEA because it is less invasive. A randomized controlled trial, Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) showed that the risk of stroke, myocardial infarction, or death did not differ significantly between CAS and CEA in the patients at any risk for CEA. Moreover, The Asymptomatic Carotid Trial 1 (ACT-1) demonstrated that the primary end point (MI, stroke, or death within 30 days or ipsilateral stroke within 1 year) occurred in 3.8% of CAS and 3.4% of CEA (p = 0.01 for non-inferiority). Although several advantages of CAS have been reported, one of its disadvantages is a relatively high incidence of distal embolism. It has been reported that plaque vulnerability, such as the presence of IPH and LRNC, is related with an increased number of emboli after CAS; therefore, preoperative MR carotid plaque imaging is important.

Presence of large LRNC and IPH is considered to be the important factors determining the amount of debris produced or the presence of plaque protrusion through the stent strut during carotid stenting. Therefore, preoperative evaluation and exclusion of such vulnerable plaques are necessary to reduce the ischemic complications during or after CAS.

In the recent meta-analysis using retrospective single-center observational studies, Brinjikji et al., reported higher rates of new DWI lesions after CAS, as well as of a composite outcome of perioperative ischemic stroke, in patients with IPH on preoperative MR carotid plaque imaging before CAS. Those studies emphasized the potential of preoperative MR carotid plaque imaging for predicting ischemic complications during or after CAS. However, these studies were performed in a retrospective manner, single center, including the small number of patients. Prospective multicenter studies with the large number of patients will be required in the future. In addition, those studies also did not perform a volumetric analysis of plaque and its components such as LRNC and IPH. The volumes of LRNC, IPH, or plaque itself may be important factors for distal embolism as these might correlate with the amount of debris produced during CAS and will be a part of future work.

Conclusion

In this review, we described to highlight the recent results of MR carotid plaque imaging and the relation between the
result of it and CAS. Due to its less invasiveness and good visualization of the carotid arterial wall, and quantification of plaque components, MRI is suitable for preoperative carotid plaque imaging. The prospective study will be needed to establish the effectiveness of preoperative MR carotid plaque imaging to reduce the complications during or after CAS.

**Disclosure Statement**

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