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Evaluation of Carotid Atherosclerotic Plaque Surface Characteristics Utilizing Simultaneous Noncontrast Angiography and Intraplaque Hemorrhage (SNAP) Technique

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Abstract

Purpose—To evaluate the feasibility of the Simultaneous Noncontrast Angiography and intraPlaque hemorrhage (SNAP) technique in identification of carotid plaque surface characteristics compared with the conventional multicontrast vessel wall imaging protocol.

Materials and Methods—Thirty symptomatic patients with carotid plaque were recruited and underwent carotid artery magnetic resonance imaging (MRI) (3.0T) using a conventional multicontrast protocol and SNAP sequence. As an intrinsic multicontrast sequence, SNAP could generate a gray blood reference (Ref) image set, a black blood corrected real (CR) image set, and a bright blood MR angiography (MRA) image set. A bright blood SNAP Ref2 image was implemented by combining Ref and MRA images for facilitating plaque surface characteristics evaluation. The presence/absence of calcification (CA), juxtaluminal calcification (JCA), and ulceration was assessed. The agreement between SNAP and multicontrast vessel wall protocol in identifying CA, JCA, and ulceration was analyzed using Cohen's kappa analysis. The interreader and intrareader reproducibility of SNAP imaging in identifying plaque surface characteristics was also assessed.

Results—Good to excellent agreement was found between SNAP and conventional multicontrast protocol in identifying CA ($\kappa = 0.74$, 95% confidence interval [CI]: 0.54–0.93), JCA ($\kappa = 0.81$, 95% CI: 0.66–0.97), and ulceration ($\kappa = 0.82$, 95% CI: 0.65–0.99). In addition, excellent intrareader and interreader reproducibility was found for SNAP imaging in identification of CA, JCA, and ulceration.

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Conclusion—SNAP imaging showed excellent agreement with multicontrast imaging and high reproducibility in identification of both JCA and ulceration, suggesting that SNAP imaging may be a time-efficient, alternative tool in identification of plaque surface characteristics in carotid arteries.

Carotid vulnerable atherosclerotic plaque is one of the major causes of cerebrovascular events, such as transient ischemic attack (TIA) and stroke.^{1,2} Previous studies have shown that carotid plaque compositional characteristics, particularly intraplaque hemorrhage (IPH) and large lipid-rich necrotic core (LRNC), are associated with plaque progression,^{3,4} vulnerability,^{5,6} and subsequent symptoms.⁷ In addition to high-risk plaque compositional features, plaque surface characteristics, such as juxtaluminal calcification (JCA) and ulceration, has also been demonstrated to be correlated with cerebrovascular events.^{8,9} Although the role of deep calcification (CA) in plaque vulnerability is still controversial,^{10,11} JCA has been recognized as a high-risk plaque feature.^{12,13} In addition, plaque ulceration, which may act as a source of cerebral emboli, is believed to be an indicator for vulnerable plaque.^{14–16} Therefore, characterizing carotid plaque surface characteristics accurately is important for prevention of cerebrovascular events.

Multicontrast magnetic resonance vessel wall imaging has been utilized to identify JCA and ulceration validated by histology.^{17,18} However, the conventional multicontrast protocol has a small longitudinal coverage (32 mm around carotid bifurcation) with a long scan time, limiting its application in clinical settings. It has been shown that computed tomography angiography (CTA) is capable of detecting plaque ulceration¹⁹ and JCA.^{20,21} However, for CTA examination, an iodine contrast agent has to be used, which may not be applicable for patients with iodine allergy or renal dysfunction.

Recently, a Simultaneous Non-contrast Angiography and intraPlaque hemorrhage (SNAP) magnetic resonance imaging (MRI) sequence was proposed for carotid artery imaging with large longitudinal coverage.²² Previous studies showed excellent agreement between SNAP and a conventional multicontrast protocol in identifying IPH²² and luminal stenosis.²³ Notably, as an intrinsic multicontrast sequence, SNAP contains a proton density (PD)-weighted reference acquisition (Ref) without blood suppression, which is used for phase-sensitive reconstruction only. This Ref image together with the black blood corrected real (CR) image and MR angiography (MRA) image generated from SNAP provide an opportunity to identify surface characteristics of carotid plaque. However, the feasibility of SNAP in evaluating surface characteristics, such as ulceration and JCA, has not been investigated.

In this study we sought to evaluate the usefulness of SNAP imaging in identification of carotid plaque surface characteristics compared with conventional multicontrast protocol.

Materials and Methods

Study Sample

In total, 30 patients (mean age: 63.7 ± 9.5 years; 24 males) with recent cerebrovascular symptoms (<2 weeks) and carotid atherosclerotic plaque (>30% stenosis) diagnosed by

duplex ultrasound were recruited in this study. Patients with carotid artery occlusion and contraindications to MRI examination were excluded. All patients underwent MRI of the carotid arteries. The study protocol was approved by the Institutional Review Board and written consent form was obtained from all subjects.

MRI

All MR scans were performed on a 3T whole-body MR scanner (Achieva TX, Philips Healthcare, Best, The Netherlands) with an 8-channel carotid dedicated phased-array surface coil (Chenguang Medical Technologies, Shanghai, China). Both SNAP sequence and conventional multicontrast vessel wall imaging protocol (T_1 -weighted [W], T_2 W, magnetization-prepared rapid-acquisition gradient-echo [MP-RAGE], and time of flight [TOF]) were acquired using the following parameters: SNAP: turbo field echo (TFE) sequence, coronal acquisition, repetition time (TR) 10 msec, inversion recovery repetition time (IRTR) 1987 msec, echo time (TE) 4.5 msec, inversion time (TI) 490 msec, flip angle $11^\circ/5^\circ$, number of signal averages (NSA) 1, bandwidth 241 Hz/pixel, field of view (FOV) $160 \times 160 \times 32 \text{ mm}^3$, spatial resolution $1 \times 1 \times 1 \text{ mm}^3$, scan time 1 minute 59 seconds; T_1 W: turbo spin echo (TSE) sequence, axial acquisition, quadruple-inversion-recovery (QIR) prepared, TR 800 msec, TE 10 msec, NSA 1, bandwidth 181 Hz/pixel, FOV $160 \times 160 \text{ mm}^2$, resolution $0.6 \times 0.6 \text{ mm}^2$, slice thickness 2 mm, scan time 7 minutes 28 seconds; T_2 W: TSE sequence, axial acquisition, multislice double inversion-recovery (MDIR) prepared, TR 4800 msec, TE 50 msec, NSA 1, bandwidth 212 Hz/pixel, FOV $160 \times 160 \text{ mm}^2$, resolution $0.6 \times 0.6 \text{ mm}^2$, slice thickness 2 mm, scan time 4 minutes 19 seconds; MP-RAGE: TFE sequence, inversion recovery, TR 13.2 msec, TE 4.6 msec, TI 304 msec, flip angle 15° , NSA 1, bandwidth 217 Hz/pixel, FOV $160 \times 160 \text{ mm}^2$, resolution $0.6 \times 0.6 \text{ mm}^2$, slice thickness 2 mm, scan time 1 minute 23 seconds; TOF: fast field echo (FFE) sequence, TR 20 msec, TE 5 msec, flip angle 20° , NSA 1, bandwidth 288 Hz/pixel, FOV $160 \times 160 \text{ mm}^2$, resolution $0.6 \times 0.6 \text{ mm}^2$, slice thickness 2 mm, scan time 1 minute 59 seconds. The total scan time of conventional multicontrast vessel wall imaging protocol was 15 minutes 9 seconds. The longitudinal coverage of conventional multicontrast protocol was 32 mm.

Image Processing

For SNAP imaging data, the inversion recovery (IR) and Ref images were directly generated from two successive TFE acquisition shots. Corrected real (CR) images, in which blood presented negative signal, were generated using phase-sensitive reconstruction. By setting all positive values to zero and inverting all the negative values in a CR image, an MRA image was generated. The proton density (PD)-weighted Ref image demonstrated bright blood signal. The contrast between lumen and vessel wall in Ref was low, obscuring the lumen boundary. To enhance the contrast between lumen and wall, a Ref2 image was generated by combining Ref image with an MRA image (Fig. 1). The coronal SNAP images including CR, MRA, Ref, and Ref2 images were then reformatted to cross-sectional plane with the same slice thickness and location with conventional multicontrast protocol.

Image Analysis

To determine the feasibility of SNAP imaging in identification of surface characteristics, the axial SNAP images and conventional multicontrast images were independently reviewed by

one trained reader (S.C., 5 years of experience with MRI) blinded to the other image type and clinical information with a 1-month interval. The presence (yes or no) of calcification (CA), JCA, and ulceration were identified using multicontrast vessel wall images and SNAP images separately. The criteria of CA, JCA, and ulceration on multicontrast MR images were as follows: 1) calcification was identified as hypointense signal on all contrast-weighted images using a conventional multicontrast protocol²⁴; 2) JCA was identified as surface calcification in contact with the lumen boundary.^{25,26} The lumen boundary was determined by T₁W, T₂W, and TOF images. 3) Ulceration was defined as plaque surface irregularity on multicontrast vessel wall images.^{27,28} The criteria of CA, JCA, and ulceration on SNAP images were as follows: i) calcification was identified as hypointense signal on Ref and Ref2 images, and a neutral signal on CR image²⁹; ii) JCA was defined as calcification in contact with the lumen boundary. The lumen boundary was determined by CR, MRA, and Ref2 images using SNAP imaging; iii) ulceration was defined as plaque surface irregularity with blood extension into the plaque.^{22,23} Blood in the lumen showed hyperintense signal on MRA and Ref2 images, and hypointense signal on CR image. For plaque with JCA detected by both methods, the contrast-to-noise ratio (CNR) between the lumen and JCA was calculated with the standard deviation of sternocleidomastoid muscle region as noise in SNAP Ref2 images and TOF images.

Reproducibility

To assess the interreader reproducibility of SNAP in identification of CA, JCA, and ulceration, the SNAP images of all subjects were evaluated by a second reviewer (J.L., 3 years of experience with MRI) independently blinded to the multicontrast vessel wall images and the first review's results. Three months after the initial review, the first reviewer (S.C.) reevaluated the SNAP images to identify CA, JCA, and ulceration for determining the intrareader reproducibility of SNAP imaging blinded to the multicontrast images and the results of the first round of review.

Statistical Analysis

Cohen's kappa analysis was used to determine the agreement between SNAP and conventional multicontrast protocol in identification of CA, JCA, and ulceration based on the first reviewer's result. A kappa value (κ) 0.8 was considered excellent agreement. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of SNAP imaging in detecting CA, JCA, and ulceration were calculated by using a conventional multicontrast protocol as the reference standard. The intrareader and interreader agreement was also evaluated. A per-plaque-based CNR of lumen and JCA were compared between SNAP Ref2 and TOF using a paired *t*-test. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed with Medcalc (v. 11.4.2.0, MedCalc Software, Mariakerke, Belgium).

Results

Of the 60 arteries of the 30 recruited patients, five (8.3%) were excluded because of insufficient image quality ($n = 1$) or total occlusion ($n = 4$). Of the remaining 55 arteries, 38 (69.1%) had CA, 31 (56.4%) had JCA, and 14 (25.5%) had ulceration on multicontrast MRI.

The SNAP imaging showed good agreement with the multicontrast protocol in identification of CA ($\kappa = 0.74$, 95% confidence interval [CI]: 0.54–0.93) (Table 1). Excellent agreement was found in identification of JCA ($\kappa = 0.81$, 95% CI: 0.66–0.97) and ulceration ($\kappa = 0.82$, 95% CI: 0.65–0.99) between SNAP imaging and the multicontrast protocol (Table 1). SNAP imaging yielded moderate to high sensitivity, specificity, PPV, and NPV in identification of CA (94.7%, 76.5%, 90.0%, and 86.7%), JCA (96.8%, 83.3%, 88.2%, and 95.2%) and ulceration (92.9%, 92.7%, 81.3%, and 97.4%). Typical images of JCA and ulceration are shown in Figs. 2 and 3.

For SNAP imaging, excellent intrareader agreement (κ : 0.81–0.92) was found in identification of CA, JCA, and ulceration (Table 2). Similarly, excellent interreader agreement (κ : 0.81–0.92) was observed in identification of CA, JAC, and ulceration by SNAP imaging (Table 2). There was no significant difference of lumen-JCA CNR between SNAP Ref2 and TOF (SNAP Ref2: 117.5 ± 19.9 ; TOF: 113.7 ± 27.7 , $P = 0.34$).

Discussion

This study investigated the agreement between SNAP imaging and conventional multicontrast imaging in identification of surface characteristics of carotid plaques, such as JCA and ulceration. We found that SNAP imaging showed excellent agreement with multicontrast imaging in identification of both JCA and ulceration. In addition, SNAP imaging had excellent intrareader and interreader agreement in detecting the above surface characteristics features. Moreover, the scan time of SNAP was 87% shorter than that of a conventional multicontrast protocol (SNAP: 1 min 59 sec, conventional multicontrast protocol: 15 min 9 sec). Our findings suggest that SNAP imaging may be a time-efficient, alternative tool in identification of plaque surface characteristics in carotid arteries within a large longitudinal coverage.

In the present study, compared with the multicontrast protocol, SNAP showed excellent agreement in detecting JCA and ulceration. The identification of JCA and ulceration depended on plaque surface morphology and signal intensity on bright and black blood images.^{26,27} As an intrinsically multicontrast sequence, the SNAP sequence can generate coregistered multicontrast images sets via image reconstruction and processing, including black blood heavy T_1W CR image, MRA, bright blood Ref, and proposed lumen-boundary-enhanced bright blood Ref2. The identification of JCA is based on the identification of calcification and the luminal boundary. As the signal of atherosclerotic calcification is near zero in all contrast-weighted images, the multicontrast SNAP images can be used to detect calcification. Calcification showed hypointense signal on Ref and Ref2 images, in which the signal of blood and vessel wall is positive. In contrast, calcification showed a neutral signal on the CR image in which the blood signal is negative and vessel wall signal is positive. Furthermore, high lumen-to-wall contrast can be achieved by SNAP, which is critical for lumen boundary delineation. The identification of JCA and ulceration would benefit from the conspicuous lumen boundary using SNAP imaging.

In the present study, SNAP showed high sensitivity in the identification of calcification and JCA. The specificity of SNAP in identifying calcification and JCA were lower than the

sensitivity. One reason might be that the outer wall boundary of plaque in SNAP CR and Ref2 images may be not clear due to insufficient wall-to-muscle contrast and low signal-to-noise ratio in some patients. The specificity of SNAP in detecting calcification and JCA could be improved by applying motion compensation technique and further optimization of the TI of the SNAP sequence.

This study demonstrated good agreement between SNAP and a conventional multicontrast method in the detection of plaque ulceration. SNAP detected more ulcerations than the multicontrast method within the coverage of the multicontrast protocol. One possible interpretation might be that SNAP can achieve a better blood suppression effect and a higher wall-to-lumen contrast than conventional multicontrast sequences, which result in an accurate plaque surface depiction insensitive to blood flow condition and velocity.^{22,23}

In consideration of the capability of SNAP in IPH detection and stenosis quantification simultaneously, SNAP can detect multiple high-risk plaque features with a single scan. Notably, the SNAP sequence possessed a larger longitudinal coverage than the conventional multicontrast protocol (SNAP 160 mm, multicontrast protocol 32 mm), which can provide a plaque characterization overview for the extracranial carotid arteries. The coverage of the SNAP sequence may potentially be extended to covering both intra- and extracranial arteries with a dedicated head/neck neurovascular coil.³⁰ Furthermore, there was also a substantial reduction in scan time by using SNAP than the conventional multicontrast method. The high scan efficiency of SNAP may facilitate its application of carotid artery imaging in clinical practice. Moreover, as all image sets generated by SNAP are coregistered, SNAP may serve as a promising sequence for automatic plaque components segmentation.

This study has several limitations. First, a per-artery instead of per-slice-based analysis was performed. Per-slice-based analysis may introduce bias due to the potential misregistration between SNAP and the conventional multicontrast protocol. Second, the spatial resolutions of SNAP and conventional multicontrast protocol were different in this study. Limited by isotropic resolution of SNAP sequence and the total scan time, the same resolution could not be achieved in this study. Similar findings are expected should the same resolution be adopted by both techniques. Third, we used the histology-validated conventional multicontrast MRI protocol as a reference for identifying plaque surface characteristics. A comparison with CT or histology, which was not available in this study, would further improve the confidence level of SNAP in surface characteristics evaluation.

In conclusion, as a fast imaging technique, SNAP imaging showed excellent agreement with multicontrast imaging and high reproducibility in identification of both JCA and ulceration. Our findings suggest that SNAP imaging may be a time-efficient, alternative tool in identification of plaque surface characteristics in carotid arteries within a large longitudinal coverage.

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FIGURE 1.
Flowchart of SNAP reconstruction and image processing.

FIGURE 2.

Images from a 70-year-old male with carotid plaque juxtaluminal calcification (arrow). Juxtaluminal calcification was identified by both conventional multicontrast sequences (a: T₁W; b: T₂W; c: MP-RAGE; d: TOF) and SNAP (e: CR; f: MRA; g: Ref; h: Ref2).

FIGURE 3.

Images from a 62-year-old male with carotid plaque ulceration (arrow) detected by both conventional multicontrast protocol and SNAP. Multicontrast protocol: a: T₁W; b: T₂W; c: MP-RAGE; d: TOF; e: TOF MRA. SNAP: f: CR; g: MRA; h: Ref; i: Ref2; j: CR (curved multiplanar reconstruction); k: sagittal MRA. Dashed lines: the longitudinal coverage of conventional multicontrast protocol.

TABLE 1
Agreement Between SNAP and Multicontrast MRI in Assessing Surface Characteristics

		Conventional multicontrast protocol					
		CA		JCA		Ulceration	
		Presence	Absence	Presence	Absence	Presence	Absence
SNAP	Presence	36	4	30	4	13	3
	Absence	2	13	Presence	20	1	38

CA: calcification; JCA: juxtaluminal calcification.

TABLE 2

Intra- and Interreader Agreement of SNAP Imaging in Assessing Surface Characteristics

	Cohen's kappa κ (95% CI)	
	Intrareader	Interreader
CA	0.87 (0.72–1.0)	0.81 (0.63–0.99)
JCA	0.81 (0.65–0.97)	0.81 (0.65–0.97)
Ulceration	0.92 (0.80–1.0)	0.92 (0.81–1.0)

CA: calcification; JCA: juxtaluminal calcification; CI: confidence interval.