

# Diagnostic Accuracy of a Clinical Carotid Plaque MR Protocol Using a Neurovascular Coil Compared to a Surface Coil Protocol

Waleed Brinjikji, MD,<sup>1,2\*</sup> J. Kevin DeMarco, MD,<sup>3</sup> Robert Shih, MD,<sup>3</sup>  
Giuseppe Lanzino, MD,<sup>1,2</sup> Alejandro A. Rabinstein, MD,<sup>4</sup>  
Christopher A. Hilditch, MBbCh,<sup>5</sup> Patrick J. Nicholson, MBbCh,<sup>5</sup> and  
John Huston III, MD<sup>1</sup>

**Background:** Carotid plaque imaging with MRI is becoming more commonplace, but practical challenges exist in performing plaque imaging with surface coils.

**Purpose:** To compare the diagnostic performance of a carotid plaque MRI protocol using a standard neurovascular coil (Neurovascular Coil Protocol) to a higher-resolution carotid plaque MRI using carotid surface coils (Surface Coil Protocol) in characterizing carotid plaque.

**Study Type:** Prospective study comparing two MR techniques in plaque characterization.

**Population:** Thirty-eight consecutive carotid artery disease patients.

**Field Strength/Sequence:** Patients underwent 3T MRI using 1) a Neurovascular Coil Protocol including the following sequences: 3D-FSE T<sub>1</sub> pre/postcontrast and precontrast 3D IR-FSPGR, and 2) a Surface Coil Protocol using standard multicontrast MRI sequences.

**Assessment:** Plaque characteristics analyzed by two independent neuroradiologists included intraplaque hemorrhage (IPH), lipid-rich necrotic-core (LRNC), and thin/ruptured fibrous cap (TRFC).

**Statistical Tests:** Diagnostic performance of the Neurovascular Coil Protocol was compared to the Surface Coil Protocol reference standard using receiver-operating curves.

**Results:** For IPH, sensitivity, specificity, and area under the curve (AUC) of the Neurovascular Coil Protocol were 91.1% (95% confidence interval [CI] = 78.8–97.5%), 87.0% (95% CI = 66.4–97.2%), and 0.92, respectively. For LRNC without IPH sensitivity, specificity, and AUC were 73.3% (95% CI = 44.9–92.2%), 85.7% (95% CI = 67.3–96.0%), and 0.84, respectively. For TRFC, sensitivity, specificity, and AUC were 35.3% (95% CI = 14.2–61.7%), 97.6% (95% CI = 87.4–99.9%), and 0.66 respectively. Interobserver agreement for IPH, LRNC, and TRFC using the Neurovascular Coil Protocol were  $k = 0.87$  (95% CI = 0.75–0.99),  $k = 0.54$  (95% CI = 0.29–0.80), and  $k = 0.41$  (95% CI = 0.08–0.74), respectively.

**Data Conclusion:** Our Neurovascular Coil Protocol has high sensitivity, specificity, and accuracy in identifying IPH and LRNC but is limited in assessment of TRFC.

**Level of Evidence:** 1

**Technical Efficacy:** Stage 2

J. MAGN. RESON. IMAGING 2018;00:000–000.

Carotid artery stenosis is a well-established risk factor for ischemic stroke, contributing to 10–20% of strokes or transient ischemic attacks (TIA).<sup>1</sup> Randomized clinical trials comparing medical therapy to surgical intervention have primarily selected patients by degree of stenosis.<sup>2–7</sup> However,

roughly 10–20% of patients with acute ischemic stroke have nonstenotic, complex plaque ipsilateral to the territory of the ischemic event.<sup>8</sup> On magnetic resonance imaging (MRI), these plaques often demonstrate variable risk factors such as intraplaque hemorrhage (IPH), lipid-rich necrotic

View this article online at [wileyonlinelibrary.com](http://wileyonlinelibrary.com). DOI: 10.1002/jmri.25984

Received Nov 28, 2017, Accepted for publication Jan 30, 2018.

\*Address reprint requests to: W.B., Mayo Clinic, Department of Radiology, 200 1st St. SW, Rochester, MN 55905. E-mail: [Brinjikji.waleed@mayo.edu](mailto:Brinjikji.waleed@mayo.edu)

From the <sup>1</sup>Department of Radiology, Mayo Clinic, Rochester, Minnesota, USA; <sup>2</sup>Department of Neurosurgery, Mayo Clinic, Rochester, Minnesota, USA; <sup>3</sup>Department of Radiology, Walter Reed Army Institute, Bethesda, Maryland, USA; <sup>4</sup>Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA; and <sup>5</sup>Joint Department of Medical Imaging, Toronto Western Hospital, Toronto, Ontario, Canada

Additional supporting information may be found in the online version of this article.

core (LRNC), and thin/ruptured fibrous cap (TRFC).<sup>8</sup> Furthermore, many patients with a high degree of stenosis have stable plaques that are thought to be at low risk of rupture and resultant ischemic stroke.<sup>9</sup> Because of such findings, over the past decade there has been a paradigm shift that now emphasizes plaque characterization in addition to degree of stenosis in the diagnosis and risk stratification of carotid artery disease.

A majority of studies examining the utility of carotid plaque imaging have depended on carotid surface coils to provide high-resolution images of the plaque and vessel wall.<sup>8,10</sup> Despite the excellent results of these studies, a vast majority of centers have yet to integrate carotid plaque protocols using surface coils into standard clinical practice, citing barriers such as lack of availability of carotid surface coils and challenges related to positioning of carotid surface coils due to their small coverage. Meanwhile, while many groups have begun to perform carotid plaque imaging using standard neurovascular coils in clinical practice, little is known regarding the diagnostic accuracy of these multicontrast protocols in identifying LRNC, IPH, and TRFC. Understanding the strengths and limitations of such protocols when compared to surface coil imaging is important. The purpose of this study was to compare the diagnostic performance of a carotid plaque MRI protocol using a standard neurovascular coil (Neurovascular Coil Protocol) to that of higher-resolution carotid plaque MRI using a carotid surface coil in characterization of carotid plaque (Surface Coil Protocol).

## Materials and Methods

### Patient Population

Following Institutional Review Board approval, patients scheduled to undergo MR angiography (MRA) for evaluation of carotid artery disease were prospectively enrolled in our study. Inclusion criteria were the following: 1) adult patients aged 40 and older; 2) no contraindication to gadolinium contrast administration (ie, gadolinium allergy, low estimated glomerular filtration rate [eGFR], pregnant patients, etc.); and 3) patient scheduled to undergo a neck MRA for evaluation of symptomatic or asymptomatic carotid artery disease. There was no minimum degree of carotid artery needed for inclusion in this study. All potential subjects were asked to give written informed consent for enrollment in the study.

### Imaging

All included patients underwent two MR angiographic studies spaced no more than 3 months apart. Same-day scans were not performed due to an institutional policy forbidding more than one gadolinium administrations for nonemergent MRIs in 1 day. The MRI examinations performed were 1) a Neurovascular Coil Protocol, and 2) carotid plaque MRI using a surface coil (Surface Coil Protocol).

The Neurovascular Coil Protocol images were acquired on a 3T MRI scanner (GE 750, GE Healthcare, Milwaukee, WI) with a 16-channel HNS coil covering the head and neck area and

included five sequences: 1) 2D time of flight (TOF); 2) 3D fast spoiled gradient echo (3D-IR-FSPGR) acquired in the coronal plane; 3) 3D fast spin-echo T<sub>1</sub> imaging with variable flip angles and fat saturation acquired in the coronal plane with and without contrast; 4) gadolinium bolus carotid MRI acquired in the coronal plane. The total image acquisition time was 40 minutes.

The reference standard Surface Coil Protocol was acquired on a 3T MRI scanner (GE HDxt, GE healthcare) with a 6-channel carotid coil (NeoCoil, Pewaukee, WI, 3T) and included eight sequences: 1) axial precontrast quadruple inversion recovery (QIR) T<sub>1</sub>-weighted (T<sub>1</sub>W); 2) axial 3D-FSPGR; 3) axial multislice double inversion recovery T<sub>2</sub>-weighted (T<sub>2</sub>W); 4) oblique sagittal proton density multislice double inversion recovery; 5) 3D TOF; 6) axial QIR contrast-enhanced T<sub>1</sub>W (CE-T<sub>1</sub>W); 7) axial 2D TOF; and 8) axial 2D spoiled gradient recall (SPGR) with dynamic imaging. The total image acquisition time was 42 minutes. Details of the scan parameters are provided in Supplementary Tables 1 and 2.

### Imaging Analysis

The Neurovascular Coil Protocol MRIs were reviewed by two independent neuroradiologists with 1 year (R.S.) and 5 years (J.H.) experience in interpreting carotid plaque MRI blinded to the clinical history and findings on the Surface Coil Protocol MRI. An image-quality rating was assigned to each carotid artery (4-point scale: 1 = poor, 4 = excellent). Arteries with an image quality = 1 were excluded. Studies with poor image quality were those in which there was substantial motion artifact and/or insufficient black blood suppression. Arteries with severe motion artifact or poor black-blood suppression were excluded. Each MRI was reviewed for the presence of IPH, LRNC, calcification (CA), ulceration, and fibrous cap thickness, which are defined in Supplementary Table 3. In cases where there was no appreciable plaque, there was no fibrous cap recorded. The review was recorded on a Microsoft Excel spreadsheet. Because there are no software packages for quantification of plaque composition on imaging protocols using standard neurovascular coils, no quantifiable measurements were obtained. Following independent review of each vessel, differences between the two neuroradiologists were resolved by consensus to determine the final read.

All Surface Coil Protocol carotid plaque exams were reviewed by a neuroradiologist with 10 years' experience interpreting carotid plaque MRI (J.K.D.) and a neuroradiologist with 1 year of experience (W.B.) previously trained in interpretation of research carotid plaque MRI. Both authors were blinded to the clinical history and findings on the clinical carotid plaque MRI. The two neuroradiologists reached a consensus decision for each plaque feature using a previously described protocol.<sup>11</sup> An image-quality rating was assigned to each carotid artery (4-point scale: 1 = poor, 4 = excellent). Arteries with an image quality = 1 were excluded. Studies with poor image quality were those in which there was substantial motion artifact and/or insufficient black blood suppression. The extracranial bifurcation was used as a landmark for matching the five different weightings. LRNC, IPH, and CA were identified based on histologically validated criteria. Details of these criteria are listed in Supplemental Table 3. Area measurements of LRNC, IPH, and CA were obtained using an imaging analysis tool

for carotid plaque MRI (MRI-PlaqueView; VP Diagnostics, Seattle, WA). Each artery was assigned an American Heart Association (AHA) classification according to modified MRI criteria in the Surface Coil Protocol, but not the Neurovascular Coil Protocol due to lack of multicontrast MRI.<sup>12</sup>

### Clinical Data

Baseline demographic data collected included age and gender. Cardiovascular risk factors collected included hypertension, hyperlipidemia, coronary artery disease, diabetes mellitus, history of cigarette smoking (never, current, former), and presence of peripheral artery disease. Symptomatic status of the carotid artery lesion was also recorded. Symptomatic patients were defined as those with a history of stroke or TIA within 30 days of initial imaging, while asymptomatic patients were defined as those who either never had a stroke or TIA or had a stroke/TIA at >30 days of initial imaging.

### Assessment of Generalizability

In order to assess the generalizability of the results of our study, we had two independent neuroradiologists with no prior experience in carotid plaque imaging assess a subgroup of 24 carotid plaques from the Neurovascular Coil Protocol. These two reviewers (C.H. and P.N.) independently assessed each plaque for the above-listed features and sensitivity, specificity, accuracy, and interobserver variance for each reviewer was assessed.

### Statistical Analysis and Outcomes

The purpose of this study was to assess the diagnostic performance of the Neurovascular Coil Protocol when compared to the Surface Coil Protocol. For each plaque component, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy were calculated. In addition, receiver operator characteristic (ROC) analysis was performed and area under the curve (AUC) was reported to evaluate the ability of the clinical Neurovascular Coil Protocol to differentiate the plaque components. Cut-off values for quantitative plaque components (ie, IPH, LRNC, and CA) were determined using the Youden index. The Youden index is also known as Youden's J statistic and is a single statistic that captures the performance of a diagnostic test. The index is defined for all points of an ROC curve and the maximum value of the index may be used as a criterion for selecting the optimum cut-off point when the diagnostic test gives a numeric rather than dichotomous result. This statistic was used in this study because volumes are not dichotomous and we wished to identify what volumes of hemorrhage, LRNC, and CA are optimally identified on the clinical plaque protocol.

Interobserver agreement for assessment of the various plaque components in the clinical carotid plaque protocol were assessed using Cohen's kappa.  $k < 0$  was interpreted as no agreement and 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 as almost perfect agreement. Agreement in location of the specific tissue was required and all reviewers documented which slice numbers they identified with certain imaging findings. Statistical analyses were performed using the SAS-based statistical software package JMP13.0 (www.jmp.com, Cary, NC).

**TABLE 1. Patient Characteristics**

|                               | N (%)       |
|-------------------------------|-------------|
| Mean age (standard deviation) | 71.0 (11.1) |
| Gender                        |             |
| Male                          | 27 (71.1)   |
| Female                        | 11 (28.9)   |
| Comorbidities                 |             |
| Hypertension                  | 23 (60.5)   |
| Hyperlipidemia                | 25 (65.8)   |
| Coronary artery disease       | 11 (28.9)   |
| Diabetes mellitus             | 6 (15.8)    |
| Peripheral artery disease     | 4 (10.5)    |
| Smoking                       |             |
| Current                       | 8 (21.1)    |
| Former                        | 17 (44.7)   |
| Never                         | 13 (34.2)   |
| Symptomatic patients          | 21 (55.3)   |
| Symptomatic vessels           | 21 (27.6)   |

## Results

### Patient Population

Of the 40 patients who provided informed consent for participation in this study, 38 (95.0%) underwent both the Neurovascular Coil Protocol and Surface Coil Protocol. Two were excluded because they received endarterectomy prior to completing both studies. Indications for the initial neurovascular MRI were as follows: 1) recent ischemic event/symptomatic carotid artery atherosclerotic lesion in 21 patients; 2) screening in a setting of prior known asymptomatic stenosis of  $\geq 50\%$  in 11 patients; and 3) incidental discovery of asymptomatic carotid artery atherosclerosis in a setting of workup for other neurovascular conditions including aneurysm or vertebral artery stenosis. Median time between the two examinations was 1 day (range = 1–87 days). Mean age was  $71.0 \pm 11.1$  years; 27 patients (71.1%) were male; 21 patients (55.3%) had symptomatic carotid artery disease; and 17 patients (44.7%) were asymptomatic. None of the asymptomatic patients had any history of ischemic events. Twenty patients had at least 50% stenosis of at least one carotid artery. Mean degree of stenosis was  $29\% \pm 31\%$ . This is summarized in Table 1.

### Plaque Characteristics on High-Resolution MRI

Of the 76 vessels scanned with the Surface Coil Protocol, 72 (94.7%) were of acceptable image quality. Four vessels in three patients were excluded due to the presence substantial

**TABLE 2. Baseline Plaque Characteristics on High-Resolution Surface Coil Protocol and Clinical Plaque Protocol**

| Variable  | Surface coil protocol <i>N</i> (%) | Neurovascular coil protocol <i>N</i> (%) |
|---|------------------------------------|--|
| Number scanned  | 76 (100.0)                         | 76 (100.0)                               |
| Number acceptable image quality                           | 72 (94.7)                          | 72 (94.7)                                |
| American Heart Association type                           |                                    |  |
| 1   | 0 (0.0)                            | NA                                       |
| 2   | 0 (0.0)                            | NA                                       |
| 3   | 15 (19.7)                          | NA                                       |
| 4   | 0 (0.0)                            | NA                                       |
| 5   | 17 (22.4)                          | NA                                       |
| 6   | 24 (31.6)                          | NA                                       |
| 7   | 16 (21.1)                          | NA                                       |
| Intraplaque hemorrhage                                    | 24 (33.3)                          | 25 (34.7)                                |
| Type 1  | 15 (20.8)                          | NA                                       |
| Type 2  | 24 (33.3)                          | NA                                       |
| Lipid rich necrotic core                                  | 41 (56.9)                          | 39 (54.2)                                |
| Calcification   | 55 (76.4)                          | 14 (23.0)                                |
| None  | 24 (33.3)                          | 47 (77.0)                                |
| Intimal   | 18 (25.0)                          | NA                                       |
| Subintimal  | 30 (40.0)                          | NA                                       |
| Nodule  | 2 (2.8)                            | NA                                       |
| Fibrous cap status  |                                    |  |
| Thick   | 19 (26.4)                          | 21 (29.2)                                |
| Thin/ruptured   | 19 (26.4)                          | 7 (9.7)                                  |
| None  | 34 (47.2)                          | 44 (61.1)                                |
| Ulceration  | 9 (12.5)                           | 9 (12.5)                                 |
| Mean volume hemorrhage (standard deviation)               | 55.3 (121.9)                       | NA                                       |
| Mean volume lipid rich necrotic core (standard deviation) | 134.7 (208.8)                      | NA                                       |
| Mean volume calcium (standard deviation)                  | 72.1 (132.8)                       | NA                                       |
| Image quality   |                                    |  |
| Poor  | 4 (5.3)                            | 4 (5.3)                                  |
| Fair  | 17 (22.4)                          | 20 (26.3)                                |
| Good  | 26 (34.2)                          | 18 (23.7)                                |
| Excellent   | 29 (38.2)                          | 34 (44.7)                                |

motion artifact. The three most common AHA plaque types were Type V (17 vessels, 22.4%), Type VI (24 vessels, 33.6%), and Type VII (16 vessels, 21.1%). IPH was found in 24 vessels (33.3%) and LRNC in 41 (56.9%). Calcifications were found in 55 vessels (76.4%). Nineteen patients (26.4%) had a TRFC. Mean volume of IPH was  $55.3 \pm 121.9 \text{ mm}^3$ , mean volume of LRNC was  $134.7 \pm 208.8 \text{ mm}^3$ . This is summarized in Table 2.

#### **Diagnostic Performance of Clinical Carotid Plaque Protocol**

Data on diagnostic performance of the Neurovascular Coil Protocol are summarized in Table 3. ROC curves are provided in the Supplementary File.

For IPH, sensitivity of the clinical carotid plaque protocol was 91.1% (95% confidence interval [CI] = 78.8–97.5%) and specificity was 87.0% (95% CI = 66.4–97.2%).

TABLE 3. Diagnostic Performance of Neurovascular Coil Protocol Versus Surface-Coil Protocol

|                           | Intraplaque hemorrhage | Lipid rich necrotic core | Lipid rich necrotic core without hemorrhage | Thin ruptured fibrous cap | Thick fibrous cap | Ulcer            | Calcium          |
|---------------------------|------------------------|--------------------------|---|---------------------------|-------------------|------------------|------------------|
| Sensitivity               | 91.1 (78.8–97.5)       | 84.6 (69.5–94.1)         | 73.3 (44.9–92.2)                            | 35.3 (14.2–61.7)          | 52.9 (27.8–77.0)  | 83.3 (35.9–99.6) | 28.9 (16.4–44.3) |
| Specificity               | 87.0 (66.4–97.2)       | 85.7 (67.3–96.0)         | 85.7 (67.3–96.0)                            | 97.6 (87.4–99.9)          | 70.0 (53.5–83.4)  | 98.1 (89.9–99.9) | 91.7 (61.5–99.8) |
| Positive predictive value | 93.2 (82.6–97.5)       | 89.2 (76.8–95.4)         | 73.3 (51.4–87.8)                            | 85.7 (43.8–97.9)          | 42.9 (28.1–59.0)  | 83.3 (41.0–97.3) | 92.9 (65.3–98.9) |
| Negative predictive value | 83.3 (65.9–92.8)       | 80.0 (65.4–89.5)         | 85.7 (71.9–93.4)                            | 78.9 (72.3–84.2)          | 77.8 (67.0–85.8)  | 98.1 (89.7–99.7) | 25.6 (21.1–30.7) |
| Accuracy                  | 89.7 (80.0–95.8)       | 85.1 (74.7–91.7)         | 81.4 (67.4–90.3)                            | 79.7 (67.2–89.0)          | 64.9 (51.1–77.1)  | 96.6 (88.3–99.6) | 42.1 (30.2–55.0) |
| Area under curve          | 0.92                   | 0.93                     | 0.84  | 0.66                      | 0.61              | 0.91             | 0.59             |
| Agreement (kappa)         | 0.87 (0.75–0.99)       | 0.72 (0.55–0.90)         | 0.54 (0.29–0.80)                            | 0.41 (0.08–0.74)          | 0.55 (0.33–0.77)  | 0.47 (0.19–0.74) | 0.36 (0.11–0.61) |

Overall accuracy was 89.7% (95% CI = 80.0–95.8%) and the AUC was 0.92 (Supplementary File). Agreement between the two independent reviewers was almost perfect, with  $k = 0.87$  (95% CI = 0.75–0.99). The cutoff volume which maximized the Youden Index for intraplaque hemorrhage was 15.0 mm<sup>3</sup>. Figure 1 provides examples of plaque hemorrhage detection with the Neurovascular Coil Protocol and Surface Coil Protocol.

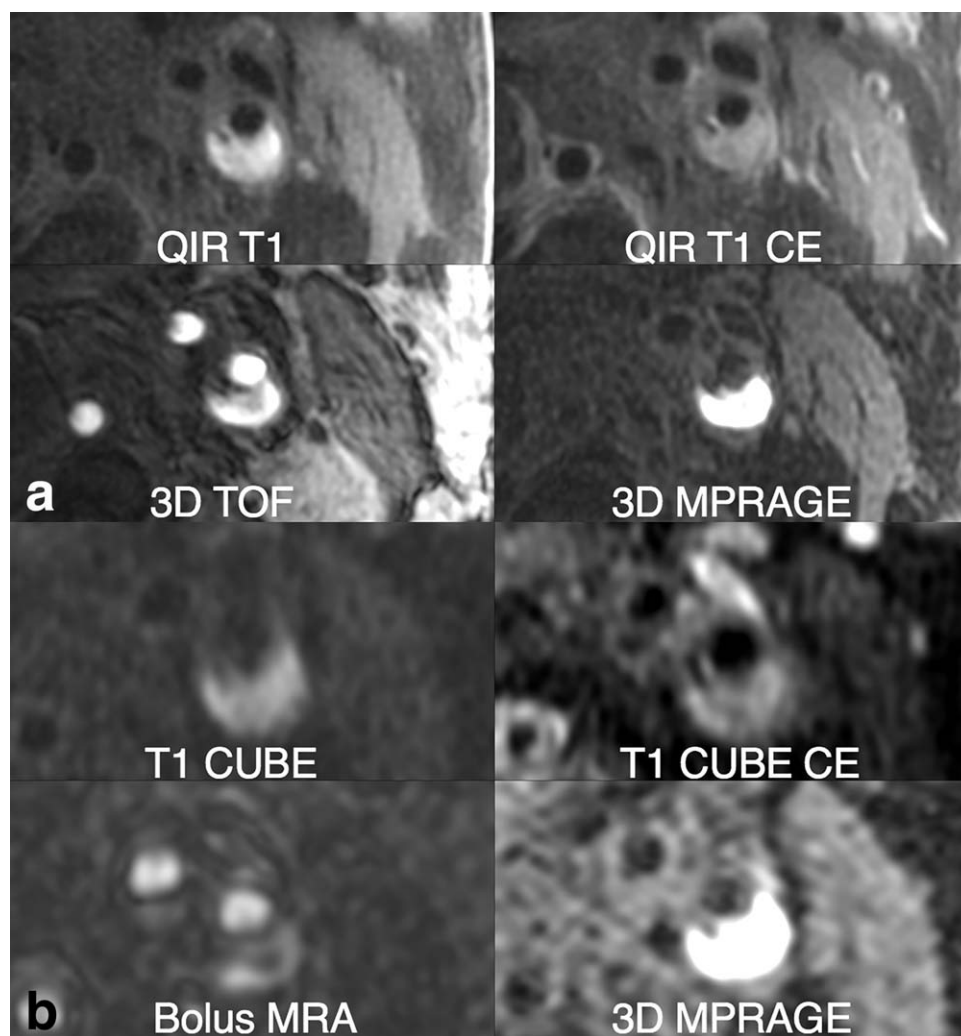
For LRNC (including patients with and without IPH), sensitivity of the Neurovascular Coil Protocol was 84.6% (95% CI = 69.5–94.1%) and specificity was 85.7% (95% CI = 67.3–96.0%). Overall accuracy was 85.1% (95% CI = 74.7–91.7%) and the AUC was 0.93 (Supplementary File). Agreement between the two independent reviewers was substantial with  $k = 0.72$  (95% CI = 0.55–0.90). The cutoff volume which maximized the Youden Index for LRNC was 24.2 mm<sup>3</sup>.

For LRNC in the absence of plaque hemorrhage, sensitivity of the Neurovascular Coil Protocol was 73.3% (95% CI = 44.9–92.2%) and specificity was 85.7% (95% CI = 67.3–96.0%). Overall accuracy was 81.4% (95% CI = 67.4–90.3%) and the AUC was 0.84 (Supplementary File). Agreement between the two independent reviewers was moderate, with  $k = 0.54$  (95% CI = 0.29–0.80). The cutoff volume which maximized the Youden Index for LRNC without plaque hemorrhage was 24.2 mm<sup>3</sup>. Figure 2 provides examples of LRNC detection with the clinical carotid plaque protocol and high-resolution exam.

For TRFC, sensitivity of the Neurovascular Coil Protocol was 35.3% (95% CI = 14.2–61.7%) and specificity was 97.6% (95% CI = 87.4–99.9%). Overall accuracy was 79.7% (95% CI = 67.2–89.0%) and the AUC was 0.66 (Supplementary File). Agreement between the two independent reviewers was moderate, with  $k = 0.41$  (95% CI = 0.08–0.74). Figure 3 provides examples of TRFC detection with the Neurovascular Coil Protocol and Surface Coil Protocol.

For plaque calcification, sensitivity of the Neurovascular Coil Protocol was 28.9% (95% CI = 16.4–44.3%) and specificity was 91.7% (95% CI = 61.5–99.8%). Overall accuracy was 42.1% (95% CI = 30.2–55.0%) and the AUC was 0.59 (Supplementary File). Agreement between the two independent reviewers was fair, with  $k = 0.36$  (95% CI = 0.11–0.61). The cutoff volume that maximized the Youden Index for LRNC without plaque hemorrhage was 58.0 mm<sup>3</sup>.

**ASSESSMENT OF GENERALIZABILITY.** Two independent reviewers with no prior experience in plaque imaging assessed a subset of 24 carotid plaques. When compared to the reference standard, the mean sensitivity, specificity, and accuracy in assessment of IPH were 100.0%, 100.0%, and 100.0%. Agreement between the two reviewers was



**FIGURE 1:** Example of intraplaque hemorrhage using the Surface Coil and Neurovascular Coil Protocol. **A:** Surface coil exam with (quadruple inversion recovery) QIR T<sub>1</sub>, QIR T<sub>1</sub> with contrast, 3D TOF, and 3D magnetization-prepared rapid gradient-echo (MPRAGE) demonstrates a large plaque with intrinsic high T<sub>1</sub> signal consistent with plaque hemorrhage. **B:** The Neurovascular Coil Protocol exam with T<sub>1</sub> CUBE with and without contrast, gadolinium bolus MRA, and 3D MPRAGE demonstrates high intrinsic T<sub>1</sub> signal consistent with plaque hemorrhage.

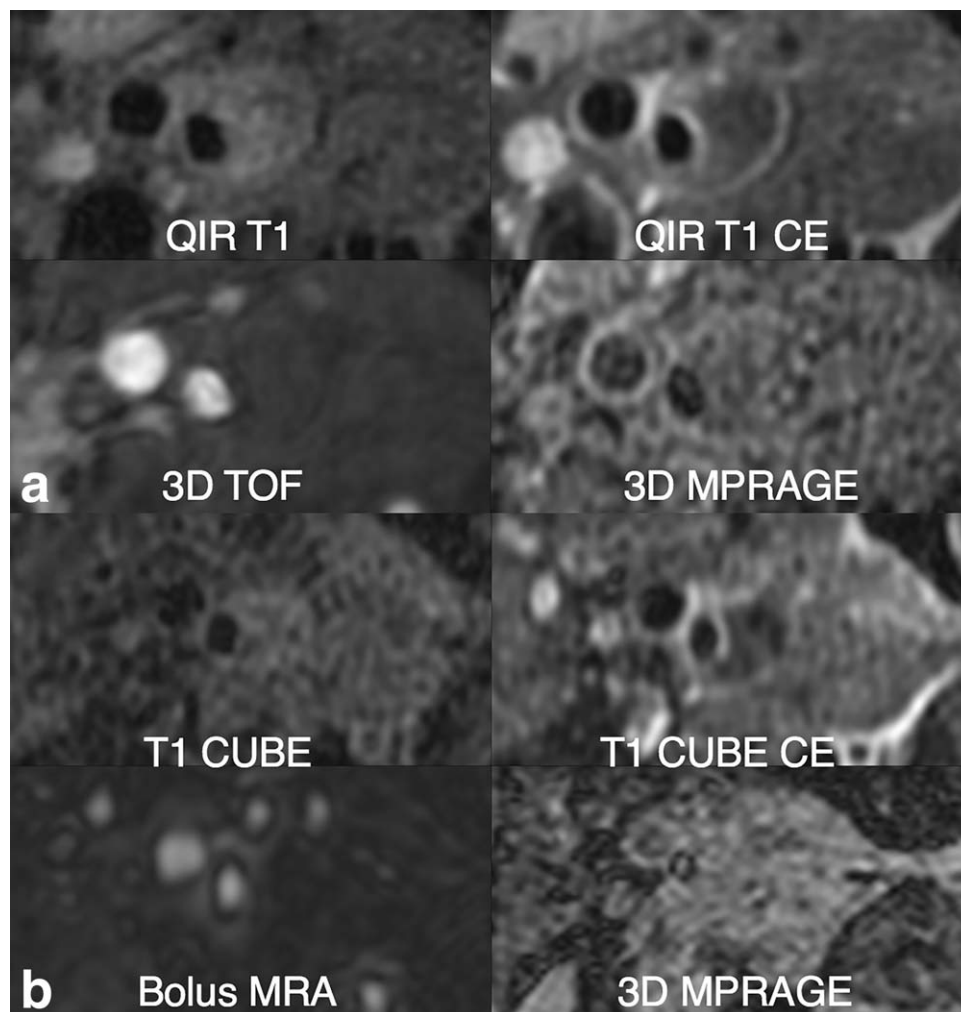
excellent, with  $k = 1.0$ . For LRNC, mean sensitivity, specificity, and accuracy were 74.2%, 71.1%, and 70.3% and agreement was moderate, with  $k = 0.52$ . For TRFC, mean sensitivity, specificity, and accuracy were 54.5%, 100%, and 78.5% and agreement was moderate, with  $k = 0.56$ . For plaque calcification, mean sensitivity, specificity, and accuracy were 45.4%, 100.0%, and 56.4% and agreement was fair, with  $k = 0.39$ .

## Discussion

Our study evaluating the diagnostic performance of a 3.0T Neurovascular Coil Protocol when compared to a Surface Coil MR Protocol demonstrated a number of interesting findings. First, the diagnostic performance of the Neurovascular Coil Protocol in identifying high-signal IPH was excellent, with high levels of interobserver agreement and sensitivity, specificity, and accuracy rates around 90%. The volume threshold that maximized diagnostic performance

was low, at just 15 mm<sup>3</sup>. The Neurovascular Coil Protocol also performed well in evaluating the presence of LRNC in the absence of plaque hemorrhage with sensitivity, specificity, and accuracy rates of 73%, 86%, and 81%, respectively, and moderate interobserver agreement. While the Neurovascular Coil Protocol had excellent performance in evaluating the presence of plaque ulceration, there was difficulty in characterization of fibrous cap and evaluating the presence of calcium. These findings suggest that our Neurovascular Coil Protocol is a potentially useful tool in carotid plaque characterization in the clinical setting, particularly when evaluating for the presence of intraplaque hemorrhage, large lipid-rich necrotic cores, and plaque ulcerations, but is limited in detection of more subtle abnormalities in the fibrous cap.

While multicontrast high-resolution carotid plaque imaging using carotid surface coils is the standard in carotid plaque characterization, there are many practical limitations



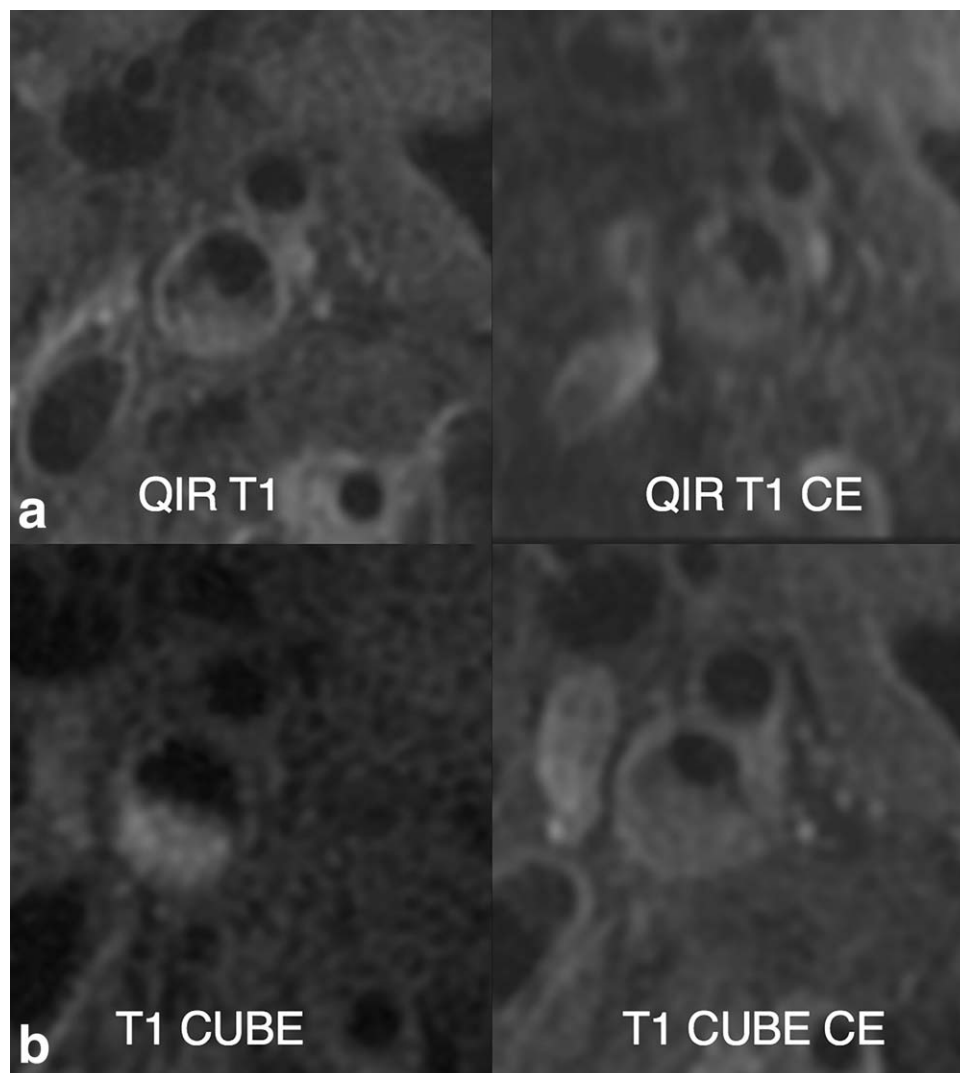
**FIGURE 2:** Example of lipid-rich necrotic core using the Surface Coil and Neurovascular Coil Protocol. **A:** Surface coil exam with QIR T<sub>1</sub>, QIR T<sub>1</sub> with contrast, 3D TOF, and 3D MPRAGE demonstrates a large plaque which is peripherally enhancing and internally has low T<sub>1</sub> signal. There is no evidence of plaque hemorrhage on MPRAGE. Note the smooth continuous enhancement of the fibrous cap at the plaque–vessel interface consistent with a thick fibrous cap. **B:** The Neurovascular Coil Protocol with T<sub>1</sub> CUBE with and without contrast, gadolinium bolus MRA, and 3D MPRAGE demonstrates a large plaque which is peripherally enhancing and internally has low T<sub>1</sub> signal. There is no evidence of plaque hemorrhage on the MPRAGE. Note the smooth continuous enhancement of the fibrous cap at the plaque–vessel interface consistent with a thick fibrous cap.

to its widespread implementation. First, given the small coverage area of such surface coils it is relatively easy to miss the carotid lesion due to improper coil positioning. In addition, there are time limitations in the clinical setting, as the scan time for a complete multicontrast carotid plaque protocol typically lasts about 45 minutes, not including the added time for additional brain scanning if necessary. Given the ubiquity of standard neurovascular coils in clinical practice and the ability to easily switch from cervical to cerebral imaging, our protocol promises to be a useful tool in evaluation of carotid plaque.

Carotid plaque imaging using the protocol described in this study is not without limitations. As described previously, our protocol does not allow for a high degree of accuracy in characterizing plaque surface characteristics. The AUCs for thin/ruptured fibrous cap and thick fibrous cap were mediocre and interobserver agreement rates were

moderate. In addition, sensitivity for detection of plaque calcium was low. In retrospect, challenges in identification of plaque calcium could have been mitigated by the addition of a 3D-TOF to the clinical carotid plaque protocol due to the typical jet-black appearance of plaque calcium on these sequences. Nonetheless, with further refinement of carotid plaque imaging protocols using neurovascular coils and further training of radiologists in interpretation of these images, the diagnostic performance of these protocols in assessment of plaque surface characteristics will improve.

Expanding the use and availability of carotid plaque imaging is important for a number of reasons. In a systematic review and meta-analysis of nearly 800 patients, Gupta et al found that IPH was associated with a hazards ratio of 4.6 for TIA and stroke.<sup>13</sup> The presence of IPH is associated with symptomatic events independent of degree of stenosis, as one study found that IPH was associated with a 17.7%



**FIGURE 3:** Example of thin and ruptured fibrous cap using the Surface Coil and Neurovascular Coil Protocol. **A:** Surface coil exam with QIR T<sub>1</sub>, QIR T<sub>1</sub> with contrast, 3D TOF, and 3D MPRAGE demonstrates lack of continuous enhancement at the plaque–vessel interface consistent with a thin and ruptured fibrous cap. **B:** The Neurovascular Coil Protocol with T<sub>1</sub> CUBE with and without contrast, gadolinium bolus MRA, and 3D MPRAGE demonstrates lack of continuous enhancement at the plaque–vessel interface consistent with a thin and ruptured fibrous cap.

stroke rate per year of follow-up, regardless of degree of stenosis.<sup>14</sup> Thus, identifying the presence of IPH is particularly important. Our study shows the ability to detect IPH with neurovascular coils using the histologically validated multi-contrast carotid surface coil MR protocol as the reference standard. The presence of LRNC and TRFC was associated with hazards ratios of respectively 3 and 5.9 as well.<sup>13</sup> Other longitudinal studies have also found that the size of LRNC and the presence of plaque ulceration are independent predictors of symptomatic events.<sup>15</sup> Given the excellent diagnostic performance of our 3T clinical carotid plaque protocol in detecting IPH, LRNC, and ulceration, our findings suggest that this easily standardized protocol could be a useful tool in risk stratification of carotid artery disease.

Another potential application of carotid plaque imaging is in the diagnostic workup of cryptogenic stroke.

Cryptogenic stroke occurs in up to 30% of ischemic stroke patients and one-third of these patients have nonstenotic carotid plaques ipsilateral to the stroke. On MRI, these plaques often demonstrate IPH, TRFC, and luminal thrombosis, suggesting that a high proportion of these strokes are due to rupture or erosion of nonstenotic high-risk plaques.<sup>16</sup> In one recently published study including patients with unilateral anterior circulation infarction with <50% stenosis, they found that 22% of patients had a hemorrhage-positive plaque ipsilateral to the stroke.<sup>17</sup> Identifying such patients could go far in preventing extensive workup for other sources of stroke.<sup>18</sup> By integrating this plaque protocol in the standard neck MRA/brain MRI/MRA workup of stroke, centers can potentially improve their evaluation of cryptogenic stroke patients without the added cost and time of a dedicated surface coil exam.



One of the main limitations of our study was the small number of patients included (38 patients), which can limit the power of our study to detect differences between modalities. Our study was performed using 3.0T GE scanners and GE protocols, which limits generalizability of our results to centers that do not have access to such scanners and protocols. There were hardware differences and software differences in the two MRI protocols, which can limit comparisons. Another limitation stems from the fact that volumetric analysis of plaque components using the large field of view exam was not performed, due to the fact that programs available for plaque analysis of protocols, such as our Neurovascular Coil Protocol, are not yet available. The Neurovascular Coil Protocol was not histologically validated. The strengths of our study include the representation of symptomatic and asymptomatic patients and different types of plaques (ie, calcified, LRNC, and IPH), and the review of all imaging studies by two independent neuroradiologists blinded to the clinical status of the patient.

Our novel study comparing our Neurovascular Coil Protocol to the high-resolution coil exam demonstrated that the Neurovascular Coil protocol has high sensitivity, specificity, and accuracy in identifying IPH, LRNC, and plaque ulcerations with moderate to excellent interobserver agreement. The Neurovascular Coil Protocol was suboptimal in the assessment of fibrous cap and plaque calcium. Based on these results, we feel that, with proper training, widespread use of carotid plaque imaging with standard neurovascular coils is both effective and feasible. Further research is needed to refine and standardize large field of view carotid plaque imaging techniques.

## Funding

This work was funded by the Radiological Society of North America Resident and Fellow Research Grant which was awarded to Dr. Waleed Brinjikji.

## References

1. Fairhead JF, Rothwell PM. The need for urgency in identification and treatment of symptomatic carotid stenosis is already established. *Cerebrovasc Dis* 2005;19:355–358.
2. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Barnett HJM, Taylor DW, Haynes RB, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445–453.
3. [No authors listed.] Endarterectomy for asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. *JAMA* 1995;273:1421–1428.
4. [No authors listed.] Randomised trial of endarterectomy for recently symptomatic carotid stenosis: Final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;351:1379–1387.
5. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Barnett HJ, Taylor DW, Eliasziw M, et al. Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. *N Engl J Med* 1998;339:1415–1425.
6. Halliday A, Mansfield A, Marro J, et al. Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: Randomised controlled trial. *Lancet* 2004;363:1491–1502.
7. Hobson RW 2nd, Weiss DG, et al. Efficacy of carotid endarterectomy for asymptomatic carotid stenosis. The veterans affairs cooperative study group. *N Engl J Med* 1993;328:221–227.
8. Brinjikji W, Huston J 3rd, Rabinstein AA, Kim GM, Lerman A, Lanzino G. Contemporary carotid imaging: From degree of stenosis to plaque vulnerability. *J Neurosurg* 2016;124:27–42.
9. Horie N, Morikawa M, Ishizaka S, et al. Assessment of carotid plaque stability based on the dynamic enhancement pattern in plaque components with multidetector CT angiography. *Stroke* 2012;43:393–398.
10. Cai JM, Hatsukami TS, Ferguson MS, Small R, Polissar NL, Yuan C. Classification of human carotid atherosclerotic lesions with in vivo multicontrast magnetic resonance imaging. *Circulation* 2002;106:1368–1373.
11. Takaya N, Yuan C, Chu B, et al. Association between carotid plaque characteristics and subsequent ischemic cerebrovascular events: A prospective assessment with MRI—initial results. *Stroke* 2006;37:818–823.
12. Lopez-Cancio E, Galan A, Dorado L, et al. Biological signatures of asymptomatic extra- and intracranial atherosclerosis: The Barcelona-Asia (asymptomatic intracranial atherosclerosis) study. *Stroke* 2012;43:2712–2719.
13. Gupta A, Baradaran H, Schweitzer AD, et al. Carotid plaque MRI and stroke risk: A systematic review and meta-analysis. *Stroke* 2013;44:3071–3077.
14. Saam T, Hetterich H, Hoffmann V, et al. Meta-analysis and systematic review of the predictive value of carotid plaque hemorrhage on cerebrovascular events by magnetic resonance imaging. *J Am Coll Cardiol* 2013;62:1081–1091.
15. Chu B, Kampschulte A, Ferguson MS, et al. Hemorrhage in the atherosclerotic carotid plaque: A high-resolution MRI study. *Stroke* 2004;35:1079–1084.
16. Freilinger TM, Schindler A, Schmidt C, et al. Prevalence of nonstenosing, complicated atherosclerotic plaques in cryptogenic stroke. *JACC Cardiovasc Imaging* 2012;5:397–405.
17. Gupta A, Gialdini G, Lerario MP, et al. Magnetic resonance angiography detection of abnormal carotid artery plaque in patients with cryptogenic stroke. *J Am Heart Assoc* 2015;4:e002012.
18. Gates MJ, Brinjikji W, Williams L, Lanzino G. Mild carotid stenosis with recurrent symptoms triggered by eating. *World Neurosurg* 2017;97:750 e711–750 e713.