UNICA UNIVERSITÀ DEGLI STUDI DI CAGLIARI

This is the Author's manuscript version of the following contribution: Luca Saba, Riccardo Cau, Alessandro Murgia, Andrew N. Nicolaides, Max Wintermark, Mauricio Castillo, Daniel Staub, Stravos Kakkos, Qi Yang, Kosmas I. Paraskevas, Chun Yuan, Myriam Edjlali, Roberto Sanfilippo, Jeroen Hendrikse, Elias Johansson, Mamood Mossa-Basha, Niranjan Balu, Martin Dichgans, David Saloner, Daniel Bos, Rolf H. Jager, Ross Naylor, Gavino Faa, Jasjit S. Suri, Justin Costello, Dorothee P. Auer, Scott McNally, Leo H. Bonati, Valentina Nardi, Aad van der Lugt, Maura Griffin, Bruce A. Wasserman, M. Eline Kooi, Jonathan Gillard, Giuseppe Lanzino, Dimitri P. Mikhailidis, Danny M. Mandell, John Benson, Dianne van Dam-Nolen, Anna Kopczak, Jae Song, Ajay Gupta, J. Kevin DeMarco, Seemant Chaturvedi, Renu Virmani, Tom Hatsukami, Martin Brown, Alan R. Moody, Peter Libby, Andreas Schindler, Tobias Saam, Carotid Plaque-RADS, a novel stroke risk classification system, JACC: Cardiovascular Imaging, 2023,

The publisher's version is available at:
https://doi.org/10.1016/j.jcmg.2023.09.005

When citing, please refer to the published version.

This full text was downloaded from UNICA IRIS https://iris.unica.it/

Carotid Plaque-RADS, a novel stroke risk classification system

Running title: Carotid Plaque-RADS classification

Word count: 4997

Luca Saba[1] MD, Riccardo Cau[1] MD, Alessandro Murgia[1] MD, Andrew N. Nicolaides[2] MD, PhD, Max Wintermark[3] MD, Mauricio Castillo[4] MD, Daniel Staub[5] MD, Stravos Kakkos[6] MD, PhD, Qi Yang[7] MD, PhD, Kosmas I. Paraskevas[8] MD, Chun Yuan[9] MD, PhD, Myriam Edjlali[10] MD, PhD, Roberto Sanfilippo[11] MD, Jeroen Hendrikse[12] MD, PhD, Elias Johansson[13] MD, Mamood Mossa-Basha[14] MD, Niranjan Balu[15] MD, PhD, Martin Dichgans[16] MD, David Saloner[17] MD, PhD, Daniel Bos[18,19,20] MD, PhD , Rolf H. Jager[21] MD, Ross Naylor[22] MD, Gavino Faa[23] MD, Jasjit S.Suri[24] PhD, Justin Costello[25] MD, Dorothee P. Auer[26] MD, Scott McNally[27] MD, PhD, Leo H. Bonati[28] MD, Valentina Nardi[29] MD, Aad van der Lugt[18] MD, Maura Griffin[30] MD, Bruce A. Wasserman[31] MD, M. Eline Kooi[32] MD, Jonathan Gillard[33] MD, Giuseppe Lanzino[34] MD, Dimitri P. Mikhailidis[35] MD, Danny M. Mandell[36] MD, PhD, John Benson[37] MD, Dianne van Dam-Nolen[18] MD, Anna Kopczak[38] MD, Jae Song[39] MD, Ajay Gupta[40] MD, J. Kevin DeMarco [41] MD, Seemant Chaturvedi[42] MD, Renu Virmani[43] MD, Tom Hatsukami[15] MD, Martin Brown[44] MD, Alan R. Moody[45] MD, Peter Libby[46] MD, Andreas Schindler[47]* MD, Tobias Saam[48]* MD.

*co-senior authors

1) Department of Radiology, University of Cagliari, Cagliari, Italy.

2) Vascular Screening and Diagnostic Centre, Nicosia, Cyprus; University of Nicosia Medical School, Nicosia, Cyprus and Department of Vascular Surgery, Imperial College, London, United Kingdom

3) Neuroradiology, Stanford University and Healthcare System, Stanford, CA, USA

4) Department of Radiology, University of North Carolina, Chapel Hill, NC 27599

5) Vascular Medicine/Angiology, University Hospital Basel and University of Basel, Basel, Switzerland

6) Department of Vascular Surgery, University of Patras Medical School, Patras, Greece

7) Department of Radiology, Xuanwu Hospital, Capital Medical University, Beijing, China

8) Department of Vascular Surgery, Central Clinic of Athens, Athens, Greece. Electronic address

9) Department of Radiology, University of Washington, Seattle, USA

10) Department of Neuroradiology, Université Paris-Descartes-Sorbonne-Paris-Cité, IMABRAIN-INSERM-UMR1266, DHU-Neurovasc, Centre Hospitalier Sainte-Anne, Paris, France.

11) Department of Vascular Surgery, University of Cagliari, Cagliari, Italy.

12) University Medical Center Utrecht, Utrecht, Netherlands

13) Clinical Science, Umeå University, Neurosciences, Umeå, Sweden

14) Department of Radiology (M.M.-B.), University of North Carolina, Chapel Hill, North Carolina

15) Department of Surgery, University of Washington, Seattle, WA, USA

16) Institute for Stroke and Dementia Research, University Hospital, LMU Munich, Munich, Germany; Munich Cluster for Systems Neurology (SyNergy), Munich, Germany; German Center for Neurodegenerative Diseases (DZNE), Munich, Germany

17) Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, USA

18) Department of Radiology and Nuclear Medicine, Erasmus MC Rotterdam, University Medical Center Rotterdam, Rotterdam, The Netherlands.

19) Department of Epidemiology, Erasmus MC, Rotterdam, the Netherlands.

20) Department of Cardiovascular Sciences, KU Leuven, Leuven, Belgium

21) Lysholm Department of Neuroradiology and the Neuroradiological Academic Unit, Department of Brain Repair and Rehabilitation, UCL Institute of Neurology, London, UK.

22) The Leicester Vascular Institute, Glenfield Hospital, Leicester UK LE3 9QP

23) Department of Pathology, University of Cagliari, Cagliari, Italy.

24) Stroke Monitoring and Diagnostic Division, AtheroPoint™, Roseville, CA 95661, USA

25) Department of Neuroradiology, Walter Reed National Military Medical Center and Uniformed Services University of Health Sciences, 8901 Rockville Pike, Bethesda, MD 20889

26) Radiological Sciences, Division of Clinical Neuroscience, University of Nottingham, Nottingham, United Kingdom; NIHR Nottingham Biomedical Research Centre, University of Nottingham, Nottingham

27) University of Utah Department of Radiology, USA

28) Department of Neurology and Stroke Center, Department of Clinical Research, University Hospital Basel, University of Basel, Basel, Switzerland

29) Department of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota, USA

30) Vascular Screening and Diagnostic Centre, Nicosia, Cyprus; Vascular Noninvasive Diagnostic Centre, London, United Kingdom

31) The Russell H. Morgan Department of Radiology and Radiological Science, Johns Hopkins Hospital, 367 East Park building, 600 N Wolfe St, Baltimore, MD, 21287, USA

32) Department of Radiology and Nuclear Medicine, CARIM School for Cardiovascular Diseases, Maastricht University Medical Center, Maastricht, the Netherlands
33) Christ's College, Cambridge UK
34) Department of Neurosurgery, Mayo Clinic, Rochester, MN.
35) Department of Clinical Biochemistry, Royal Free Hospital Campus, University College London School, University College London, London, UK
36) Joint Department of Medical Imaging, University Health Network, Toronto, Ontario, Canada
37) Department of Radiology Mayo Clinic Rochester MN.
38) Institute for Stroke and Dementia Research, University Hospital, LMU Munich, Munich, Germany.
39) Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA.
40) Department of Radiology Weill Cornell Medical College New York NY.
41) Walter Reed National Military Medical Center and Uniformed Services University of the Health Sciences, Bethesda, Maryland, USA
42) Department of Neurology, University of Maryland Medical Center, Baltimore, Maryland, USA
43) Department of Cardiovascular Pathology, CVPath Institute, Gaithersburg, MD, USA
44) Department of Neurology and Neurosurgery, University College London Hospitals, London, UK
45) Department of Medical Imaging, University of Toronto, Toronto M5S 1A1, Canada
46) Division of Cardiovascular Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA
47) Institute of Neuroradiology, University Hospital, LMU Munich, Munich, Germany
48) Department of Radiology, University Hospital, LMU Munich, Munich, Germany & Die Radiologie, Rosenheim, Germany.

Disclosure paragraph

All authors agreed with the content and gave consent to submit.
The authors state that this work is not under consideration elsewhere and none of the paper's contents have been previously published.
The authors of this manuscript declare no relationships with any companies, whose products
or services may be related to the subject matter of the article.
This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
All authors read and approved the final manuscript.
The scientific guarantor of this publication is the corresponding author
The authors declare that they have no competing interests.
The views expressed in this article are those of the author and do not reflect the official policy of the Department of Army/Navy/Air Force, Department of Defense, or US Government.
The identification of specific products or scientific instrumentation does not constitute endorsement or implied endorsement on the part of the author, Department of Defense, or any component agency.
Author contribution: Conceptualization: L.S.; R.C.; A.M.; A.S.; T.S,;
Methodology: L.S.; A.S.; T.S,; A.N.N.; M.X.; M.C.; D.S.; S.K.; Q.Y.; K.I.P.; C.Y.; M.E.; R.S.; J.H.; E.J.; M.M.; N.B.; M.D.; D.S.; D.B.; R.H.J.: R.N.; G.F.; J.S.S; J.S.; D.P.A.; S.N.; L.H.B.; V.N.; A.V.D.L.; M.G.; B.A.W.; M.E.K.; J.G.; G.L.; D.P.M.; D.M.M.; J.B.; D.V.N.; A.K.; J.S.; A.G.; J.K.D.; S.C.; R.V.; T.H.; M.B.; A.R.M; P.L.;
Data curation: L.S.; R.C.; A.M.; A.S.; T.S
Writing— original draft preparation: L.S.; R.C.; A.M.; A.S.; T.S,; A.N.N.; M.X.; M.C.; D.S.; S.K.; Q.Y.; K.I.P.; C.Y.; M.E.; R.S.; J.H.; E.J.; M.M.; N.B.; M.D.; D.S.; D.B.; R.H.J.: R.N.; G.F.; J.S.S; J.S.; D.P.A.; S.N.; L.H.B.; V.N.; A.V.D.L.; M.G.; B.A.W.; M.E.K.; J.G.; G.L.; D.P.M.; D.M.M.; J.B.; D.V.N.; A.K.; J.S.; A.G.; J.K.D.; S.C.; R.V.; T.H.; M.B.; A.R.M; P.L.;
Writing—review and editing: L.S.; R.C.; A.M.; A.S.; T.S,; A.N.N.; M.X.; M.C.; D.S.; S.K.; Q.Y.; K.I.P.; C.Y.; M.E.; R.S.; J.H.; E.J.; M.M.; N.B.; M.D.; D.S.; D.B.; R.H.J.: R.N.; G.F.; J.S.S; J.S.; D.P.A.; S.N.; L.H.B.; V.N.; A.V.D.L.; M.G.; B.A.W.; M.E.K.; J.G.; G.L.; D.P.M.; D.M.M.; J.B.; D.V.N.; A.K.; J.S.; A.G.; J.K.D.; S.C.; R.V.; T.H.; M.B.; A.R.M; P.L.;
Supervision: L.S.; A.S.; T.S,; A.K.
Project administration: L.S.; R.C.; A.M.; A.S.; T.S,;

Please address correspondence to *Prof. Luca Saba*, University of Cagliari - Azienda Ospedaliero Universitaria di Cagliari – polo di Monserrato, Provincia di Cagliari, Italy; e-mail: lucasaba@tiscali.it

Acknowledgement: The authors thank Antonia Weingart for the pictorial presentation of the different Plaque-RADS categories.

Abstract

Objectives: The aim of this document is to establish a consistent and comprehensive approach for imaging and reporting carotid plaque by introducing the Plaque-Reporting And Data System (RADS) score.

Methods: A panel of experts recognized the necessity to develop a classification system for carotid plaque and its defining characteristics. Employing a multi-modality analysis approach, the Plaque-RADS categories were established through consensus, drawing on existing literature.

Results: We present a universal classification that is applicable to both researchers and clinicians. The Plaque-RADS score offers a morphological assessment in addition to the prevailing quantitative parameter of "stenosis". The Plaque-RADS score spans from grade 1 (indicating complete absence of plaque) to grade 4 (representing complicated plaque). Accompanying visual examples are included to facilitate a clear understanding of the Plaque-RADS categories.

Conclusion: Plaque-RADS is a standardized and reliable system of reporting carotid plaque composition and morphology via different imaging modalities, such as US, CT, and MRI. This scoring system has the potential to help in the precise identification of patients who may benefit from exclusive medical intervention and those who require alternative treatments, thereby enhancing patient care. A standardized lexicon and structured reporting promise to enhance communication between radiologists, referring clinicians, and scientists.

Key words: Carotid plaque; atherosclerosis; stroke; plaque imaging; Plaque-RADS; reporting and data system; carotid stenosis; complicated plaque.

Condensed Abstract

The Plaque-RADS (Plaque-Reporting and Data System) score was created to standardize the reporting of carotid plaque characteristics, and to offer new aspects for the tailored management of individuals with asymptomatic and symptomatic atherosclerotic carotid lesions. Reduced variability in reporting facilitates communication between interpreting and referring clinicians, and generates robust data for auditing, data mining, quality improvement, research, and education. In addition to the degree of carotid stenosis Plaque-RADS may help to specifically identify patients who might or might not benefit from best medical treatment alone and thus improve patient care.

The Plaque-RADS classification is an intuitive nomenclature for several imaging modalities that reflects the severity of plaque instability and – if successfully implemented - could be an important tool to provide specific recommendations for the management of atherosclerotic carotid disease.

Abbreviations

CTA	Computed tomography angiography
FC	Fibrous Cap
IPH	Intraplaque hemorrhage
LRNC	Lipid-rich necrotic core
MRI	Magnetic resonance imaging
MWT	Maximum wall thickness
RADS	Reporting And Data System
US	Ultrasound

Highlights

- Carotid plaque structure and composition are critical determinants of plaque vulnerability.
- A universal and complementary approach of non-invasive imaging facilitates plaque characterization.
- Plaque-RADS has a high inter-observer reliability and can be easily implemented in routine clinical reporting.
- Standardized terminology and structured reporting across different imaging modalities may improve risk stratification of carotid plaques.

Introduction

Non-invasive carotid imaging modalities have demonstrated their ability to characterize plaque features as predictors of future events, offering a significant contribution to risk stratification and patient management[1]. Translation of the present knowledge on plaque vulnerability into routine clinical practice requires a standardized reporting system.

The 2017 European Society of Cardiology (ESC) clinical practice guidelines have recognized these developments and recommend to evaluate the presence of plaque imaging characteristics that may indicate an increased risk of ipsilateral stroke additionally to the degree of carotid stenosis in asymptomatic individuals[2]. These include, amongst others, intraplaque hemorrhage (IPH) or lipid-rich necrotic core (LRNC) on magnetic resonance imaging (MRI and large or echolucent plaques or increased juxta-luminal black (hypoechoic) areas on carotid ultrasound[2]. Similarly, the European Society for Vascular Surgery (ESVS) clinical practice guidelines emphasize the importance of plaque vulnerability assessment[3]. Even though scoring systems for singular modalities have been suggested (e.g. American Heart Association [AHA] lesion-types [4], modified AHA lesion-types for MRI[5], Carotid plaque score for ultrasound[6], etc.), there is still no universal classification system for various imaging modalities that scores the severity of an atherosclerotic lesion based on plaque morphology and composition. The proposed Plaque-RADS score aims to create an intuitive, accurate, reliable and standardized scoring system that can be used with various imaging modalities to provide risk estimates for first-time or recurrent large artery cerebrovascular events.

The rationale of new image-based classification

As shown with previous scores, such as the Lung-RADS[7], BI-RADS[8], PI-RADS[9], LI-RADS[10], and CAD-RADS[11] score for lung, breast, prostate, liver, and coronary artery imaging, the use of a standardized reporting system improves communication and patient selection by reducing differences in terminology, harmonizing classification formats between different institutions, and facilitating the exchange of clear and systematic information between imaging and referring physicians and researchers.

To date there is no such system for a standardized classification of atherosclerotic carotid plaque. Instead, most clinical reports of CTA mention the degree of carotid stenosis, but despite their increasingly recognized value, specific plaque features are accounted for in only a minority of cases[12]. This lack of reporting, may be at least partly due to gaps in knowledge of high-risk plaque features and their associated risk and possible therapeutic consequences.

Consequently, the introduction of a standardized classification system for carotid atherosclerotic plaque (Plaque-RADS)

1. will level the differences across the various institutions regarding the use of terminology and patient evaluation criteria, serving as a reference format in everyday clinical practice,
2. facilitates data mining and allow researchers across different institutions to collect information in a more homogenous and synergistic way; for example, in the course of time stratified prognostic data could be collected for each Plaque-RADS category and help clinicians design agreed-upon treatment flowcharts, and
3. draws attention to imaging findings representative of plaque morphology and composition beyond the mere degree of stenosis underscoring a paradigm shift.

Plaque-RADS reporting system

Plaque-RADS categories are based on specific imaging features of plaque composition and other characteristics. The score is applied on a per vessel basis and can be established by ultrasound, CTA, and MRI. **Figures 1 and 2** provide a flow-chart and schematic overview of the Plaque-RADS categories. Categories range from Plaque-RADS 1 (absence of atherosclerosis) to Plaque-RADS 4 (plaque with features of complicated plaque) and should represent

the clinically most relevant finding per vessel. Further sub-specifications (a, b, c) can be provided for Plaque-RADS categories 3 and 4. Not all imaging modalities are currently equally suited to identify the individual categories. Therefore, the modality used to obtain the score should always be provided. In addition, the Plaque-RADS categories may be supplemented by "ancillary features" of carotid plaque vulnerability, namely plaque inflammation and neovascularization, positive carotid artery remodeling, plaque burden, progression of stenosis, and carotid plaque calcifications (see Supplemental material, Supplemental Table 1, and supplemental Figure 1-4).

Table 1 summarizes the characteristic imaging features of the Plaque-RADS categories and the attributable risk of developing symptoms.

Plaque-RADS categories

Plaque-RADS 1

This category represents the normal vessel wall with no evidence of localized atherosclerotic plaque (Figure 3). Population-based cohort studies including the Rotterdam Study, the Tromsø Study, and the Multi-Ethnic Study of Atherosclerosis (MESA) study have shown that patients without carotid plaque are not at risk of atherosclerosis-related cardiovascular or cerebrovascular events[13–16]. Vessels of this category are consistent with AHA lesion-type I/II plaques.

Plaque-RADS 2

This category is defined by an eccentric plaque with a maximum wall thickness (MWT) <3 mm and the absence of complicated plaque features such as IPH, fibrous cap (FC) rupture, and intraluminal thrombus (Figure 4).

Plaques in this category may consist mainly of fibrous tissue, small lipid pools, a small LRNC, calcifications, or a combination of these tissue types.

These plaque features are hallmarks of relatively stable plaques although they are also potential precursors of more advanced lesions. The presence of these features results in an increase in wall thickness that has been shown to be associated with increased cerebrovascular and cardiovascular risk, but less than that associated with complicated plaque features[17]. In this regard, total plaque thickness, as determined by ultrasound, has been shown to improve the prediction of future atherosclerotic cardiovascular events over and above that provided by traditional risk factors alone[18,19].

The risk of Plaque-RADS 2 lesions is higher than Plaque-RADS 1 lesions, but it is still relatively low.

This category contains plaques of AHA-lesion types III, IV/V (small), VII and VIII.

The rationale of choosing a cut-off of MWT <3mm is discussed in the Supplement.

Plaque-RADS 3

This category represents a carotid plaque with a MWT of ≥3 mm which may consist of a moderate to large LRNC, calcifications, healed ulcerations and fibrous tissue. Complicated plaque features, such as IPH, thrombus and plaque rupture are absent. Further subclassification may be undertaken with dedicated imaging. This category contains plaques of AHA lesion-types IV/V, VII, and VIII.

Plaque-RADS 3a

This subcategory represents a carotid plaque with a moderate to large LRNC, a thick FC, and a MWT of ≥3 mm in the absence of complicated plaque features (Figure 5).

Currently, data on the risk of LRNC is limited. Nonetheless a Meta-analysis by Gupta et al. showed an increased risk for future ipsilateral cerebrovascular events when LRNC is present with a HR of 3.00 (1.511 – 5.945; p = 0.002)[20]. Besides an increased downstream cerebrovascular risk the presence of a LRNC is also associated with an increase in cardiovascular risk[21].

Plaque-RADS 3b

This subcategory contains carotid plaque with a MWT ≥3 mm with a moderate to large LRNC with thin and intact FC (Figure 6).

It must be emphasized that the capability of contemporary imaging to accurately assess thin FCs lacks evidence. Thus, for assigning a score 3b in the Plaque-RADS classification system, the thin FC may be either directly visualized (if the spatial resolution of the modality in use allows that) or inferred by the presence of a LRNC without visualization of a thick and intact FC. Most importantly, what distinguishes this class from higher-risk class 4 is the absence of complicated plaque features.

With regard to FC integrity, several studies have emphasized its determinant role in plaque stability[20,22]. A thick FC is associated with a low risk of plaque rupture, while the risk of rupture increases for a thin FC[20,23].

Plaque-RADS 3c

The defining feature of this category is plaque ulceration regardless of plaque thickness, in the absence of IPH, FC-disruption or intraluminal thrombus (Figure 7).

Thus, for what pertains to the designation of score 3c in the Plaque-RADS classification system, the term ulceration must be intended as ulceration not associated with the presence of IPH (score 4a), visible FC disruption (score 4b) or intraluminal thrombus (score 4c); rather, the term ulceration in this context refers to a surface cavity most likely secondary to previous extrusion of atheromatous material in the context of a healed plaque rupture.

Plaque-RADS 4

Plaque-RADS score 4 is assigned in the presence of at least one of the following findings independent of plaque thickness: IPH, a ruptured FC or an intraluminal thrombus. When feasible, a further subclassification can be used, differentiating IPH, ruptured FC, and intraluminal thrombi into classes 4a, 4b, and 4c, respectively. Subclasses may provide important information in future studies to better understand statistical correlations between such specific entities and clinical events. This category contains plaques of AHA lesion-type VI.

Plaque-RADS 4a

The defining feature of this category is IPH (Figure 8).

In the Carotid Plaque Imaging in Acute Stroke (CAPIAS) study, IPH was the most common feature of complicated plaques and present in 89% of all complicated plaques ipsilateral to acute ischemic stroke[24]. In the recent prospective Plaque At RISK (PARISK) study of 244 patients with a recent symptomatic mild-to-moderate carotid stenosis during a mean follow-up period of 5.1 years the presence of IPH was associated with recurrent cerebrovascular events (HR 2.12, 95%CI 1.02-4.44)[25]. Along the same lines pooled individual patient data from 7 cohort studies of 560 patients with symptomatic and 136 patients with asymptomatic carotid stenosis found MRI-detected IPH in 51.6% of the symptomatic and 29.4% of the asymptomatic patients. Multivariate analysis identified IPH (HR 11.0, 95%CI 4.8-25.1) and severity of stenosis (HR 3.3, 95%CI 1.4-7.8) as independent predictors of recurrent ipsilateral stroke. Presence of IPH increased the risk for first-time stroke in asymptomatic patients with carotid stenosis by almost 8-fold (HR 7.9, 95%CI 1.3-47.6)[26].

Plaque-RADS 4b

The defining feature of this category is a ruptured FC, usually accompanied by juxtaluminal plaque hemorrhage[27](Figure 9).

Disruption of the FC, with the resultant exposure of thrombogenic subendothelial plaque constituents, can precipitate thromboembolic complications both in the carotid and coronary vascular bed[28]. It appears that plaque rupture represent a dynamic process of rupture, thrombus formation, healing, and remodeling of the plaque[29]. A meta-analysis of 363 carotid arteries from asymptomatic and symptomatic patients showed that a thin or ruptured FC (HR 5.93, 95%CI 2.65–13.29, P<0.01) is associated with future cerebrovascular events[20].

Plaque-RADS 4c

This category is characterized by carotid plaque with an intraluminal thrombus (Figure 10). Other features such as IPH or FC rupture may also be present. Intraluminal carotid artery thrombi are associated with neurologic symptoms in up to 92% of cases[30], and a recognized predictor of stroke of carotid origin[17,31–33]. McNally et al. conducted a retrospective cross-sectional study of 726 carotid-brain MRI examinations in patients undergoing stroke workup. After the exclusion of non-carotid-plaque stroke, occlusions, and near-occlusions the strongest predictor of carotid-source stroke was intraluminal thrombus (OR 103.6, 95%CI 8.64-710.8, P<0.001)[17].

Supplemental Table 2 provides an overview of previous studies examining carotid plaque characteristics according to Plaque-RADS categories and attributable risk for symptom development.

Reporting the Plaque-RADS score

For the structured reporting of a Plaque-RADS score we recommend to use the following syntax, which will be further detailed in the following paragraphs:

Side of carotid: stenosis degree/ imaging modality Plaque-RADS score/ MWT/ Ancillary Features/ Modifiers.

Stenosis degree

It is important to stress that the Plaque-RADS score is not meant to replace the measurement of stenosis but rather integrate synergistically with it. Indeed, the independent association between the degree of carotid stenosis in both symptomatic[34,35] and asymptomatic patients[36,37,38] is well known. The degree of luminal stenosis should be reported using the North American Symptomatic Carotid Endarterectomy Trial (NASCET), as it is widely used and already harmonized across modalities.

Stenosis [%] = (Diameter of the normal distal ICA – Narrowest ICA Diameter in the stenotic segment) / Diameter of the normal distal ICA

Imaging modality

The imaging modality used to obtain the Plaque RADS score should be indicated. In the final evaluation, all modalities used should be listed, with the one leading to the highest score mentioned first. The supplemental material contains suggestions regarding which imaging modalities should be used for optimal assessment of each plaque RADS category. Supplemental **table 3** summarizes key plaque features across different imaging modalities. However, a detailed discussion of ideal imaging practice of the atherosclerotic plaque is beyond the purpose of this paper but can be found in the Consensus document by the ASNR Vessel Wall Imaging Study group[1].

Maximum wall thickness (MWT)

The MWT [mm] is derived via a linear measurement of the greatest thickness of the vessel wall as measured on axial images perpendicular to the vessel's long axis and includes the arterial vessel wall and both calcified and non-calcified components of the plaque.

Ancillary features

To accommodate the variety of other imaging vulnerability markers that have been well studied and validated in the scientific literature, and with an open mind for future advancements, we propose an optional sub-classifier of plaque RADS: AnFe. We suggested to report each assessed individual AnFe in the final score.

Modifiers

Similar to CAD-RADS[11], categories can be complemented by modifiers, including limited-diagnostic study ("L"), the presence of a stent ("Stent"), and previous carotid endarterectomy ("CEA").

The Modifier "L" can be applied if the study is not fully diagnostic, for example in case of blooming artifacts on CT, or motion artifacts or metal-induced artifacts on CT or MRI.

Overestimation of restenosis using non-invasive imaging is a potential risk in stented carotid arteries and assessment of plaque morphology is limited in stented vessels. Therefore, the application of the Modifier "Stent" may be useful in clinical practice.

Following the logic above, a plaque in a symptomatic patient with ipsilateral 50% stenosis with IPH with positive remodeling would be classified as:

- Right carotid: 50%/***MRI Plaque-RADS 4a***/ 5mm/ Positive Remodeling.

It is important to emphasize that AnFE do not determine the main Plaque-RADS score. Therefore, the assessment of the AnFe is not mandatory in the Plaque-RADS score but rather serve as a complementary tool when available, also for research purpose.

Finally, it is fundamental to consider the appropriateness of the modality used for each Plaque-RADS score. Whenever practitioners find that the study could not definitively exclude the possibility of a relevant score upgrade, further investigation should be considered. By means of example, the identification of a Plaque-RADS score 3a on CT may require further investigation on MRI to rule out the presence of IPH (which would upgrade to score 4a). Rather than adding a classification category dedicated to the imaging modality, we suggest that "Consider MRI examination" is reported in the score and further information is provided in the impressions; in this case a plaque in an asymptomatic patient with 70% carotid stenosis and a MWT of 5 mm, a positive rim sign and positive remodeling would read as:

- Left carotid: 70%/***CT Plaque-RADS 3a***/MWT=5mm/ Positive rim sign AND Positive Remodeling/Consider MRI examination

Inter-observer agreement

A score is only helpful if it is straightforward and reliable. As confirmation of applicability and reliability Plaque-RADS categories were assigned by blinded experts in the field of plaque imaging to 100 vessels on US, CT, and MRI, each. The inter-observer agreement was retrospectively assessed based on Cohen κ test to investigate the reproducibility of Plaque-RADS categories (0.00 = poor, 0.00–0.20 = slight, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = substantial, and 0.81–1.00 = almost perfect)[39]. The study included evaluation of 100 vessels on US, 100 vessels on CT, and 100 vessels on MRI. The analysis was based on data from previously published studies approved by the Institutional Review Boards and informed consent was waived owing to its retrospective nature. Inter-observer agreement for US, CT, and MRI images ($\kappa = 0.804$, $p < 0.001$; $\kappa = 0.868$, $p < 0.001$; and $\kappa = 0.876$, $p < 0.001$; respectively) was excellent. Additionally, the overall inter-reader agreement among the readers across different modalities was excellent ($\kappa = 0.856$, $p < 0.001$). The results are presented in more detail in **Supplemental Table 4**.

Conclusion

Plaque-RADS is a standardized cross-modality system for reporting carotid plaque composition and morphology. This structured system aims to provide an in-depth insight into carotid imaging markers of vulnerability, to better evaluate carotid artery disease and predict the risk of cerebrovascular events. The main purpose of Plaque-RADS is to create a standardized lexicon and structured reporting for carotid artery disease, and improve communication between those interpreting images, referring clinicians, and researchers by providing a clear and reproducible, personalized risk stratification of patients.

Clinical perspective

COMPETENCY IN MEDICAL KNOWLEDGE: Plaque-RADS is an intuitive and reliably assessable tool which enables standardized description of a given atherosclerotic carotid lesion in symptomatic and asymptomatic patients. The system, which can be applied by readers of any experience, helps to detect critical hallmarks of atherosclerotic plaques and translates the findings into the attributable risk. This facilitates interpretation of findings in both clinical routine and research. This may allow improvement in diseases risk stratification and adequate therapy.

TRANSLATIONAL OUTLOOK: The introduction of the Plaque-RADS classification and its broad application will facilitate communication in clinical routine and may serve as basis for studies, which advance the management of carotid atherosclerotic disease.

References

1. Saba L, Yuan C, Hatsukami TS, et al. Carotid Artery Wall Imaging: Perspective and Guidelines from the ASNR Vessel Wall Imaging Study Group and Expert Consensus Recommendations of the American Society of Neuroradiology. *Am J Neuroradiol*. 2018;39(2). doi:10.3174/ajnr.A5488
2. Aboyans V, Ricco J-B, Bartelink M-LEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal. *Eur Heart J*. 2018;39(9):763-816. doi:10.1093/eurheartj/ehx095
3. Naylor R, Rantner B, Ancetti S, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg*. 2023;65(1):7-111. doi:10.1016/j.ejvs.2022.04.011
4. Stary HC, Chandler AB, Dinsmore RE, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation*. 1995;92(5):1355-1374. doi:10.1161/01.cir.92.5.1355
5. 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(11):1368-1373. doi:10.1161/01.CIR.0000028591.44554.F9
6. Hollander M, Bots ML, del Sol AI, et al. Carotid Plaques Increase the Risk of Stroke and Subtypes of Cerebral Infarction in Asymptomatic Elderly. *Circulation*. 2002;105(24):2872-2877. doi:10.1161/01.CIR.0000018650.58984.75
7. Version 1.1. American College of Radiology. https://www.acr.org/-/media/ACR/Files/RADS/Lung-RADS/LungRADSAssessmentCategoriesv1-1.pdf?la=en. Published 2019. Accessed September 5, 2019.
8. Sickles EA, D'Orsi CJ, Bassett LW, Appleton CM, Berg WA, Burnside ES. Acr bi-rads® mammography. *ACR BI-RADS® atlas, breast imaging Report data Syst*. 2013;5:2013.
9. Weinreb JC, Barentz JO, Choyke PL, et al.. PI-RADS Prostate Imaging-Reporting and Data System, v2.1 [homepage on the Internet]. American College of Radiology; 2019. [cited 2021 Mar 15]. Available from: https://www.acr.org/-/media/ACR/Files/RADS/Pi-RADS/PI.
10. https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS/CT-MRI-LI-RADS-v2017, accessed 2018/01/05.
11. Cury RC, Abbara S, Achenbach S, et al. CAD-RADSTM Coronary Artery Disease – Reporting and Data System. An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NA. *J Cardiovasc Comput Tomogr*. 2016;10(4):269-281. doi:10.1016/j.jcct.2016.04.005
12. Baradaran H, Foster T, Harrie P, et al. Carotid artery plaque characteristics: current reporting practices on CT angiography. *Neuroradiology*. 2021;63(7):1013-1018. doi:10.1007/s00234-020-02610-w
13. Gepner AD, Young R, Delaney JA, et al. Comparison of coronary artery calcium presence, carotid plaque presence, and carotid intima-media thickness for cardiovascular disease prediction in the Multi-Ethnic Study of Atherosclerosis. *Circ Cardiovasc Imaging*. 2015;8(1):e002262. doi:10.1161/CIRCIMAGING.114.002262
14. Zavodni AEH, Wasserman BA, McClelland RL, et al. Carotid Artery Plaque Morphology and Composition in Relation to Incident Cardiovascular Events: The Multi-Ethnic Study of Atherosclerosis (MESA). *Radiology*. 2014;271(2):381-389. doi:10.1148/radiol.14131020
15. Mathiesen EB, Johnsen SH, Wilsgaard T, Bønaa KH, Løchen M-L, Njølstad I. Carotid Plaque Area and Intima-Media Thickness in Prediction of First-Ever Ischemic Stroke. *Stroke*. 2011;42(4):972-978. doi:10.1161/STROKEAHA.110.589754
16. Van Den Bouwhuijsen QJA, Bos D, Ikram MA, et al. Coexistence of calcification, intraplaque hemorrhage and lipid core within the asymptomatic atherosclerotic carotid plaque: The Rotterdam study. *Cerebrovasc Dis*. 2015;39(5-6):319-324. doi:10.1159/000381138
17. McNally JS, McLaughlin MS, Hinckley PJ, et al. Intraluminal thrombus, intraplaque hemorrhage, plaque thickness, and current smoking optimally predict carotid stroke. *Stroke*. 2015;46(1):84-90. doi:10.1161/STROKEAHA.114.006286
18. Nicolaides AN, Panayiotou AG, Griffin M, et al. Arterial Ultrasound Testing to Predict Atherosclerotic Cardiovascular Events. *J Am Coll Cardiol*. 2022;79(20):1969-1982. doi:10.1016/j.jacc.2022.03.352
19. Selwaness M, Bos D, van den Bouwhuijsen Q, et al. Carotid Atherosclerotic Plaque Characteristics on Magnetic Resonance Imaging Relate With History of Stroke and Coronary Heart Disease. *Stroke*. 2016;47(6):1542-1547. doi:10.1161/STROKEAHA.116.012923
20. Gupta A, Baradaran H, Schweitzer AD, et al. Carotid plaque MRI and stroke risk: a systematic review and meta-analysis. *Stroke*. 2013;44(11):3071-3077. doi:10.1161/STROKEAHA.113.002551
21. Brunner G, Virani SS, Sun W, et al. Associations Between Carotid Artery Plaque Burden, Plaque Characteristics, and Cardiovascular Events: The ARIC Carotid Magnetic Resonance Imaging Study. *JAMA Cardiol*. 2021;6(1):79-86. doi:10.1001/jamacardio.2020.5573
22. van Dijk AC, Truijman MTB, Hussain B, et al. Intraplaque Hemorrhage and the Plaque Surface in Carotid Atherosclerosis: The Plaque At RISK Study (PARISK). *AJNR Am J Neuroradiol*. 2015;36(11):2127-2133. doi:10.3174/ajnr.A4414
23. Sun J, Zhao X-Q, Balu N, et al. Carotid Plaque Lipid Content and Fibrous Cap Status Predict Systemic CV Outcomes: The MRI Substudy in AIM-HIGH. *JACC Cardiovasc Imaging*. 2017;10(3):241-249. doi:10.1016/j.jcmg.2016.06.017
24. Kopczak A, Schindler A, Bayer-Karpinska A, et al. Complicated Carotid Artery Plaques as a Cause of Cryptogenic Stroke. *J Am Coll Cardiol*. 2020;76(19):2212-2222. doi:10.1016/j.jacc.2020.09.532
25. Kopczak A, Schindler A, Sepp D, et al. Complicated Carotid Artery Plaques and Risk of Recurrent Ischemic Stroke or TIA. *J Am Coll Cardiol*. 2022;79(22):2189-2199. doi:10.1016/j.jacc.2022.03.376
26. Schindler A, Schinner R, Altaf, Nishaf, et al. Prediction of Stroke Risk by Detection of Hemorrhage in Carotid Plaques. *JACC Cardiovasc Imaging*. 2020;13(2_Part_1):395-406. doi:10.1016/j.jcmg.2019.03.028
27. Kampschulte A, Ferguson MS, Kerwin WS, et al. Differentiation of Intraplaque Versus Juxtaluminal Hemorrhage/Thrombus in Advanced Human Carotid Atherosclerotic Lesions by In Vivo Magnetic Resonance Imaging. *Circulation*. 2004;110(20):3239-3244. doi:10.1161/01.CIR.0000147287.23741.9A
28. Cademartiri F, Balestrieri A, Cau R, et al. Insight from imaging on plaque vulnerability: similarities and differences between coronary and carotid arteries—implications for systemic therapies. *Cardiovasc Diagn Ther*. 2020;10(4):1150-1162. doi:10.21037/cdt-20-528
29. Carr S, Farb A, Pearce WH, Virmani R, Yao JST. Atherosclerotic plaque rupture in symptomatic carotid artery stenosis. *J Vasc Surg*. 1996;23(5):755-766. doi:https://doi.org/10.1016/S0741-5214(96)70237-9
30. Bhatti AF, Leon LRJ, Labropoulos N, et al. Free-floating thrombus of the carotid artery: literature review and case reports. *J Vasc Surg*. 2007;45(1):199-205. doi:10.1016/j.jvs.2006.09.057
31. Eesa M, Hill MD, Al-Khathaami A, et al. Role of CT Angiographic Plaque Morphologic Characteristics in Addition to Stenosis in Predicting the Symptomatic Side in Carotid Artery Disease. *Am J Neuroradiol*. 2010;31(7):1254 LP - 1260. doi:10.3174/ajnr.A2078
32. Paraskevas KI, Veith FJ, Spence JD. How to identify which patients with asymptomatic carotid stenosis could benefit from endarterectomy or stenting. *Stroke Vasc Neurol*. 2018;3(2):92-100. doi:10.1136/svn-2017-000129
33. Markus HS, King A, Shipley M, et al. Asymptomatic embolisation for prediction of stroke in the Asymptomatic Carotid Emboli Study (ACES): a prospective observational study. *Lancet Neurol*. 2010;9(7):663-671. doi:10.1016/S1474-4422(10)70120-4
34. Messas E, Goudot G, Halliday A, et al. Management of carotid stenosis for primary and secondary prevention of stroke: state-of-the-art 2020: a critical review. *Eur Heart J Suppl*. 2020;22(Suppl M):M35-M42. doi:10.1093/eurheartj/suaa162
35. Strömberg S, Nordanstig A, Bentzel T, Österberg K, Bergström GML. Risk of Early Recurrent Stroke in Symptomatic Carotid Stenosis. *J Vasc*

Surg. 2015;61(2):570. doi:10.1016/j.jvs.2014.12.017
36. Nadareishvili ZG, Rothwell PM, Beletsky V, Pagniello A, Norris JW. Long-term Risk of Stroke and Other Vascular Events in Patients With Asymptomatic Carotid Artery Stenosis. *Arch Neurol*. 2002;59(7):1162-1166. doi:10.1001/archneur.59.7.1162
37. Chang RW, Tucker L-Y, Rothenberg KA, et al. Incidence of Ischemic Stroke in Patients With Asymptomatic Severe Carotid Stenosis Without Surgical Intervention. *JAMA*. 2022;327(20):1974-1982. doi:10.1001/jama.2022.4835
38. Howard DPJ, Gaziano L, Rothwell PM. Risk of stroke in relation to degree of asymptomatic carotid stenosis: a population-based cohort study, systematic review, and meta-analysis. *Lancet Neurol*. 2021;20(3):193-202. doi:10.1016/S1474-4422(20)30484-1
39. McHugh ML. Interrater reliability: the kappa statistic. *Biochem medica*. 2012;22(3):276-282.

Figure legends

Figure 1: Step by step flowchart to classify carotid atherosclerotic plaques into the different Plaque-RADS categories.

Figure 2: Schematic representation of the different Plaque-RADS categories 1 to 4.

MWT = maximum wall thickness; LRNC = lipid-rich / necrotic core; FC = fibrous cap; IPH = intraplaque hemorrhage; CEA = Carotid endarterectomy

Figure 3: Plaque-RADS 1.

US: Regular wall in the common carotid artery (CCA) and bifurcation. The vessel wall in ultrasound is homogenous and thin (a-c).

CT: Regular wall in the CCA and bifurcation on axial (d), coronal (e), and sagittal (g) reconstructions.

MRI: Regular wall of the CCA (g-j).

Histology: Normal vessel wall (k,l). High magnification of the boxed area (l) shows tunica media and intima with mild intimal thickening which cannot be visualized with current in vivo imaging modalities.

Figure 4: Plaque-RADS 2.

US: Eccentric wall thickening with speckled calcifications and acoustic shadowing (arrows). (a) Axial image; (b) Color Doppler image; (c) Longitudinal image.

CT: Diffuse carotid wall thickening with and without calcifications (f; open arrow).

MRI: Eccentric wall thickening and small calcification (arrow in g-k; hypointense in all weightings) of the right internal carotid artery.

Histology: Eccentric plaque with a wall thickness <3 mm. The magnification shows thickening of the intima (m).

Figure 5: Plaque-RADS 3a.

US: Large plaque of the carotid bifurcation with uniform isoechoic echogenicity on B-mode ultrasound imaging (arrowhead) consistent with LRNC and thick FC. a) longitudinal and b) transverse view; c) micro-flow imaging.

CT: Low-attenuating plaque with a mean HU value of 44 HU in the right internal carotid artery resembling a LRNC (d,e). The status of the FC cannot be assessed with CT.

MRI: Non-stenosing plaque of the left ICA. A large LRNC (arrowhead in f-j) appears isointense in TOF-images (hypointense in the T1w-CE images, and iso- to hyperintense in T1w pre-contrast, PDw, and T2w images. A thick and intact FC (arrow in f,h; hyperintense in T1w-CE and hypointense in TOF-imaging) separates the LRNC from the lumen.

Histology: Intimal thickening consistent with a thick FC over a LRNC (k, l). Panel m) shows a magnified view of a thick fibrous cap overlying the LRNC. Panel m is reproduced from Frank et al [PMID: 17826632]

Figure 6: Plaque-RADS 3b.

US: Complex plaque with presence of juxtaluminal black areas (JBA) in both the anterior and posterior component of the plaque with two discrete white areas (DWA) in the far wall component of the plaque consistent with a large LRNC or IPH at the origin of the left carotid bifurcation. Large sections of the plaque outline do not have a visible (i.e. thin) fibrous cap. a) and c) B-mode images; b) Color flow c) outlines the anterior and posterior plaque components.

MRI: Mildly stenosing plaque in the right ICA with a large LRNC (arrowheads; hypointense in contrast enhanced T1w-CE). The FC is thin and not in its entity delineated (arrow in T1w-CE).

Histology: Thin fibrous cap (arrows in magnified image from g) overlying a large LRNC (g,h).

Figure 7: Plaque-RADS 3c.

US: Mixed hyper- and hypoechogenic plaque at the carotid bulb on a) B-mode ultrasound imaging with ulceration (*) on micro-flow imaging , and B-mode 3D-US with b) longitudinal, c) axial, and d) coronal view.

CT: Axial and sagittal views of an ulcerated plaque in the left ICA, visible as contrast outpouching (≥1 mm) into the plaque (arrows in e-g). High grade stenosis.

Histology: Ulcerated plaque. The arrow (h) indicates the site of ulceration. Panel h is reproduced from Virmani et al [PMID: 18931283]

Figure 8: Plaque-RADS 4a.

MRI: Non-stenosing plaque of the right ICA. IPH Type I (arrowhead in a-d) resembled by hyperintense signal on T1w and TOF-images and isointense signal in PDw images. The FC cannot be delineated but no obvious plaque rupture is seen. IPH can be caused by "leaky" neovessels in a LRNC or by plaque rupture and is considered a hallmark of a high-risk lesion.

Histology: IPH in a LRNC. Panel e is reproduced from Kolodgie et al [PMID: 28818257].

Figure 9: Plaque-RADS 4b.

US: Ruptured plaque in the left carotid bulb. Calcified area on the anterior wall producing an acoustic shadow (white arrow in a). A free flap is visible in the lumen attached to the anterior wall on the left (white arrow in b). LRNC is not visible, presumably discharged, with color flow including flow reversal (blue area above the flap in b) between the flap and the near wall of the artery. This is a high-risk plaque.

MRI: Complex plaque in the left carotid bulb. Ulceration with rupture of the FC at the posterior end (solid arrow in c-g). The signal intensity of the ulcer is the same as that of the lumen. Large IPH in almost the entire plaque is seen as hyperintense on T1w, and TOF-images and isointense in PDw and T2w images (arrowhead in c-g) suggestive of fresh plaque hemorrhage. Speckled calcification appears as hypointense signal in all MRI sequences (open arrow in c-g). This is a high-risk plaque.

Histology: Ruptured fibrous cap (h,i). Magnification shows the area of fibrous cap rupture (red arrows in i) and adherent thrombus (asterisk in i)

Figure 10: Plaque-RADS IVc.

US: Severe stenosis in the proximal right carotid artery. DWA in the hypoechoic part of the plaque on the near wall without acoustic shadow indicates neovascularization (white arrow in b). Large JBA without a visible echogenic cap (open arrow in b) in the distal part of the stenotic area are compatible with intraluminal thrombus or LRNC indicating the need for further investigation with MRI. This is a high-risk plaque due to neovascularization, JBA, and severe stenosis. A) and b) B-mode image; c) Power Doppler image.

CT: Axial, sagittal, and coronal CT images demonstrating left carotid artery intraluminal thrombus and the "doughnut sign" defined as a filling defect surrounded by contrast (bold arrows in d-f).

MRI: Large thrombus (arrowhead in g-j) in the left carotid bulb, obstructing large parts of the origin of the ICA. The origin of the thrombus is most likely a rupture of the FC (not depicted). In TOF-imaging the thrombus causes a hypo-intense void of flow-signal (g).

Histology: Plaque rupture with intraluminal thrombus (arrow in k). Histological image is reproduced from Virmani et al [PMID: 18931283]

CT = Computed Tomography; DWA = Discrete white areas; FC = Fibrous Cap; HU = Hounsfield Unit; IPH = Intraplaque Hemorrhage; JBA= Juxtaluminal black areas; LRNC = Lipid-Rich Necrotic Core; MRI = Magnetic Resonance imaging; NC = necrotic core; US = Ultrasound. All histological images are stained with Movat pentachrome.

Tables

Table 1: Summary of Plaque-RADS categories based on imaging findings and the attributable risk of developing symptoms.

Plaque-RADS score		**Attributable Risk of ipsilateral cerebrovascular events**	**Imaging Findings**
1		Absent	Normal vessel wall
2		Low	MWT <3 mm
3		Moderate	MWT ≥ 3 mm or Healed Ulcerated plaque
	3a	Moderate	LRNC with intact thick FC (MWT ≥3 mm)

	3b	Moderate	LRNC with thin FC (MWT ≥3 mm)
	3c	Moderate	Healed Ulcerated plaque
4		High	Complicated plaque (irrespective of MWT)
	4a	High	IPH
	4b	High	Ruptured FC
	4c	High	Intraluminal thrombus
Ancillary features: Inflammation, Neovascularization, positive plaque remodeling, plaque progression, calcifications			
Modifiers: Limited diagnostic study (“L”), presence of a stent (“Stent”), previous carotid endarterectomy (“CEA”)			

FC = Fibrous Cap; IPH = Intraplaque Hemorrhage; LRNC = Lipid-Rich Necrotic Core; MWT = Maximum Wall Thickness.