**Subject:** Magnetization-Prepared Rapid Acquisition Gradient Echo Magnetic Resonance Imaging (MPRAGE MRI)
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## Description/Scope

This document addresses magnetization-prepared rapid acquisition gradient echo (MPRAGE) magnetic resonance imaging (MRI).

## Position Statement

**Investigational and Not Medically Necessary:**

The use of magnetization-prepared rapid acquisition gradient echo magnetic resonance imaging (MPRAGE MRI) is considered **investigational and not medically necessary** for all indications.

## Rationale

It has been hypothesized that visualizing and characterizing high-intensity carotid plaques using MPRAGE MRI can predict future cerebral ischemic events or coronary events in individuals with clinically stable coronary artery disease (CAD). High-intensity signals in carotid plaques can be observed using the bright T1 signals in an MRI of the carotid arteries. It can be challenging to measure plaque vulnerable to rupture, but this technique focuses on the bright T1 signals in an MRI of the carotid arteries. It is believed that the bright T1 signal is from intraplaque hemorrhage and the degradation of hemorrhage into methemoglobin. Methemoglobin shortens the longitudinal relaxation time (T1) and gives the bright signals in T1-weighted images such as MPRAGE. MPRAGE MRI has been shown to successfully identify vulnerable carotid plaques as high-intensity signals; however, it is unknown if the presence of these high-intensity plaques is associated with a higher risk of coronary or ischemic events.

A retrospective review by Yamada and colleagues (2007) looked at 222 individuals with suspected or known carotid plaque who had MPRAGE MRI (392 carotid arteries). The purpose of the study was to investigate an association between ischemic events (in the previous 6 months) and MPRAGE MRI signal hypersensitivity according to the severity of stenosis in the carotid artery. Ischemic events were defined as cerebral infarctions, transient ischemic attack, and retinal ischemia. Of the 392 carotid arteries with carotid plaque, 370 carotid arteries were included in the evaluation of association with previous ischemic events. A total of 170 carotid arteries were found to have high signal intensity on MPRAGE MRI. The frequency of ischemic events was noted to have increased in individuals who were found to have high signal intensity plaques on MPRAGE MRI. It was noted that MPRAGE MRI hyperintense signals persist for months but longer studies are needed to clarify whether MPRAGE MRI hyperintense signals indicate a risk of subsequent cerebral ischemic events.

Noguchi and colleagues (2011) examined the intensity signals of carotid plaques in 217 individuals with clinically stable CAD using MPRAGE MRI. Stable CAD was defined as the absence of angina at rest with angiographically documented stenosis less than 50% in at least one of the major coronary arteries. In this particular study, a high-intensity plaque was determined if any region of the plaque had a signal intensity greater than 200% of the adjacent muscle. Participants were split into two groups; those found to have high-intensity plaques (n=116) and those without high-intensity plaques (n=101). Ultrasound was performed to measure intima media thickness of the carotid artery. Left ventricular ejection fraction was measured by single photon emission-computed tomography before MRI. The 217 individuals with clinically stable CAD were followed for a period of 12 to 72 months or until the occurrence of a clinical coronary event; cardiac death, nonfatal acute myocardial infarction, unstable angina pectoris, or unplanned hospitalization for recurrent angina. Of the 116 individuals in the high-intensity plaque group, 31 had coronary events, while there were 5 events in the non high-intensity plaque group. The authors suggested that the presence of high-intensity plaque visualized by MPRAGE MRI is a predictor of future coronary events in individuals with stable CAD. This study had limitations including the fact that all of the individuals studied had confirmed CAD. Translation of the study findings to a more general high-risk population could be challenging. The authors conclude that “more substantial, longer-term study with more patients is needed to clarify the short- and long-term prognostic roles of MRI as well as the role of MRI screening for high-risk asymptomatic patients.”

Saito and colleagues (2012) compared MPRAGE MRI to three other MRI techniques (non-gated spin echo, cardiac-gated black-blood fast-spin echo, and three-dimensional time-of-flight magnetic resonance angiography) in 31 individuals with known carotid stenosis who were candidates for carotid endarterectomy. The purpose was to determine the best technique for visualizing the intraplaque characteristics. The investigators concluded that the non-gated spin echo images more accurately characterized the intraplaque components when compared with the cardiac-gated, MPRAGE MRI, and magnetic resonance angiography images.

In 2009, Singh and colleagues reported on a retrospective chart review of 75 asymptomatic men (98 carotid arteries) with 50-70% carotid stenosis based on Doppler ultrasound that had MPRAGE MRI for detection of intraplaque hemorrhage. Thirty-six of the carotid arteries were found to have intraplaque hemorrhage on MPRAGE MRI and six cerebrovascular events occurred compared to no clinical events in the 62 carotid arteries without intraplaque hemorrhage. Mean follow-up time was 24.92 months. This study is limited by its retrospective design and the sample group included only asymptomatic men from a single institution.

A 2011 study by Cheung and colleagues reported on 217 individuals (434 carotid arteries) who had Doppler ultrasound imaging or magnetic resonance angiography that showed carotid stenosis at 50% or less. These individuals were referred for MPRAGE MRI for assessment of intraplaque hemorrhage. A total of 233 carotid arteries were associated with unilateral neurologic symptoms and intraplaque hemorrhage was found by MPRAGE MRI in 31 of those carotid arteries. Fourteen carotid arteries were shown by MPRAGE MRI to have intraplaque hemorrhage in the arteries contralateral to the neurologic symptoms.

Kurosaki (2011) reported on a retrospective review of 735 individuals who presented with stroke or transient ischemic attack and underwent carotid artery MRI procedure screening. A total of 639 individuals were found to have negative screening results, 66 individuals were found to have positive screening results with 62 of those individuals having severe stenosis of greater than 70%. Data was analyzed for 96 participants; 32 participants with positive screening and severe stenosis, 30 participants with negative screening and with severe stenosis, 34 participants with positive screening without severe stenosis. The individuals in the severe stenosis group were followed for a mean period of 9.1 months. Recurrent events occurred in 7 of the participants (three strokes and four transient ischemic attacks). Individuals in the positive screening group without severe stenosis were followed for a mean period of 12.1 months. Recurrent events occurred in 5 of those participants.

McNally and colleagues (2012) reported on 159 individuals (318 carotid arteries paired with brain images) who presented with suspected acute stroke and were scanned with MPRAGE MRI. A total of 266 arteries were eligible for analysis. There were 56 positive brain diffusion tensor images involving the ipsilateral internal carotid artery. The relative risk of an acute territorial ischemic event with an MPRAGE-positive carotid artery was 6.4 when compared to an MPRAGE-negative carotid artery. Of the 266 carotid artery MPRAGE images, 38 were considered to be positive.

A study by Larson and colleagues (2022) looked at individuals with and without acute ischemia to assess whether signal intensity ratio of intraplaque hemorrhage showed a relationship between higher signal intensity ratio and acute ischemic cerebral events. In this retrospective chart review, all subjects had magnetic resonance angiography (MRA) of the neck with MPRAGE. There were 106 participants who had at least one carotid artery with intraplaque hemorrhage with a signal intensity ratio greater than 1.5. A history of an ischemic event was noted in 91 of those participants with 15 participants with no prior ischemic events. Of those with a prior ischemic event, 70 of the subjects had intraplaque hemorrhage in the carotid artery ipsilateral to the ischemic event with 21 subjects who had intraplaque hemorrhage within the contralateral carotid artery. This led to 85 participants with intraplaque hemorrhage (70 with plaque ipsilateral to an ischemic event and 15 with plaque without an ischemic event). On MPRAGE, mean signal intensity ratio values for those with an ipsilateral event was 3.0 ± 1.1 and mean signal intensity ratio for those without an ipsilateral event was 3.3 ± 1.1.

While some of the published literature shows that MPRAGE MRI may identify individuals at risk of clinical events (Cheung, 2011; Kurosaki, 2011; McNally, 2012; Singh, 2009), how this imaging would be used in risk-stratifying individuals for possible intervention has not been established. There is also a lack of information regarding improvement of the net health outcome based on test results.

## Background/Overview

Originating from the brachiocephalic artery and the aortic arch the carotid arteries in the neck supply blood to the brain. Plaque in the carotid arteries can lead to stroke. For those individuals found to have plaque in the carotid arteries, management could include carotid artery stenting or carotid endarterectomy.

## Definitions

Carotid arteries: Arteries originating from the aorta that pass through the neck flowing up to the brain. The carotid arteries and their subsequent branches supply approximately 80% of the brain’s blood supply.

Magnetic resonance imaging (MRI): An imaging test that uses powerful magnets and radio waves to create pictures of the body without the use of radiation.

## Coding

*The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.*

**When services are Investigational and Not Medically Necessary:**
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

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| **CPT** | |
| 76498 | Unlisted magnetic resonance procedure (eg, diagnostic, interventional) [when specified as MPRAGE MRI]<br>**Note:** when a procedure described by an anatomic MRI code is identified as MPRAGE, the service will be considered investigational and not medically necessary. |
| | |
| **ICD-10 Diagnosis** | |
| | All diagnoses |

## References

**Peer Reviewed Publications:**


1. Cheung HM, Moody AR, Singh N, et al. Late stage complicated atheroma in low-grade stenotic carotid disease: MR imaging depiction--prevalence and risk factors. Radiology. 2011; 260(3):841-847.
2. Hishikawa T, Iihara K, Yamada N, et al. Assessment of necrotic core with intraplaque hemorrhage in atherosclerotic carotid artery plaque by MR imaging with 3D gradient-echo sequence in patients with high-grade stenosis. J Neurosurg. 2010; 113(4):890-896.
3. Kurosaki Y, Yoshida K, Endo H, et al. Association between carotid atherosclerosis plaque with high signal intensity on T1-weighted imaging and subsequent ipsilateral ischemic events. Neurosurgery. 2011; 68(1):62-67.
4. Larson AS, Brinjikji W, Kroll NJ, et al. Normalized intraplaque hemorrhage signal on MP-RAGE as a marker for acute ischemic neurological events. Neuroradiol J. 2022; 35(1):112-118.
5. Larson AS, Brinjikji W, Savastano L, et al. Carotid intraplaque hemorrhage and stenosis: at what stage of plaque progression does intraplaque hemorrhage occur, and when is it most likely to be associated with symptoms? AJNR Am J Neuroradiol. 2021; 42(7):1285-1290.
6. McNally JS, Kim S, Yoon H, et al. Carotid magnetization-prepared rapid acquisition with gradient-echo signal is associated with acute territorial cerebral ischemic events detected by diffusion-weighted MRI. Circ Cardiovasc Imaging. 2012; 5(3):376-382.
7. Noguchi T, Yamada N, Higashi M, et al. High-intensity signals in carotid plaques on T1-weighted magnetic resonance imaging predict coronary events in patients with coronary artery disease. J Am Coll Cardiol. 2011; 58(4):416-422.
8. Saito A, Sasaki M, Ogasawara K, et al. Carotid plaque signal differences among four kinds of T1-weighted magnetic resonance imaging techniques: a histopathological correlation study. Neuroradiology. 2012; 54(11):1187-1194.
9. Singh N, Moody AR, Gladstone DJ, et al. Moderate carotid artery stenosis: MR imaging-depicted intraplaque hemorrhage predicts risk of cerebrovascular ischemic events in asymptomatic men. Radiology. 2009; 252(2):502-508.
10. Yamada N, Higashi M, Otsubo R, et al. Association between signal hyperintensity on T1-weighted MR imaging of carotid plaques and ipsilateral ischemic events. AJNR Am J Neuroradiol. 2007; 28(2):287-292.
11. Zwanenburg JJ, Hendrikse J, Takahara T, et al. MR angiography of the cerebral perforating arteries with magnetization

prepared anatomical reference at 7 T: comparison with time-of-flight. J Magn Reson Imaging. 2008; 28(6):1519-1526.

## Websites for Additional Information

1. Centers for Disease Control and Prevention. Heart disease facts. October 14, 2022. Available at: https://www.cdc.gov/heartdisease/facts.htm. Accessed on March 14, 2023.
2. National Heart Lung and Blood Institute. Carotid artery disease. Available at:https://www.nhlbi.nih.gov/health-topics/carotid-artery-disease. Accessed on March 14, 2023.

## Document History

| Status | Date | Action |
|---|---|---|
| Reviewed | 05/11/2023 | Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Websites for Additional Information section. |
| Reviewed | 05/12/2022 | MPTAC review. Updated Rationale and References sections. |
| Reviewed | 05/13/2021 | MPTAC review. Updated Websites for Additional Information section. |
| Reviewed | 05/14/2020 | MPTAC review. |
| Reviewed | 06/06/2019 | MPTAC review. Updated Description/Scope section. |
| Reviewed | 07/26/2018 | MPTAC review. The document header wording updated from "Current Effective Date" to "Publish Date." Updated Background/Overview, References, and Websites sections. |
| Reviewed | 08/03/2017 | MPTAC review. Updated Rationale section. |
| Reviewed | 08/04/2016 | MPTAC review. Updated Reference section. Removed ICD-9 codes from Coding section. |
| Reviewed | 08/06/2015 | MPTAC review. Updated References section. |
| Reviewed | 08/14/2014 | MPTAC review. Updated References section. |
| Reviewed | 08/08/2013 | MPTAC review. Updated Rationale, Background/Overview, and References sections. |
| New | 08/09/2012 | MPTAC review. Initial document development. |

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