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Medical Policy Manual | Radiology, Policy No. 61

Artificial Intelligence Augmented Analysis of Atherosclerotic Plaque from Computed Tomography Scan

Effective: January 1, 2026

Next Review: November 2026
Last Review: November 2025

DESCRIPTION

This policy addresses the application of artificial intelligence augmented technologies that analyze computed tomography angiography scans to assess arterial disease risk through post image processing arterial plaque quantification and characterization analysis.

MEDICAL POLICY CRITERIA

Quantification and characterization of arterial plaque using artificial intelligence augmented analysis of computed tomography scans is considered **investigational** for <u>all</u> indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Computed Tomography to Detect Coronary Artery Calcifications, Radiology, Policy No. 06
2. Ultrasonographic Measurement of Carotid Artery Intima-Media Thickness as an Assessment of Atherosclerosis, Radiology, Policy No. 37

BACKGROUND

Coronary computed tomography angiography (CCTA) is a non-invasive imaging technique that visualizes coronary arteries and assesses atherosclerotic plaque characteristics to evaluate cardiovascular risk. Artificial intelligence-enabled quantitative CCTA analysis software (AI-QCT) uses data from an existing coronary CT angiography to quantify and characterize the structure and topography of the coronary arteries as well as arterial plaque buildup for coronary heart disease risk assessment. These AI enabled software packages are post-processing tools.

Post processing AI enabled software tools have also been developed to characterize plaque from noncoronary computed tomography for arterial disease risk assessment.

REGULATORY STATUS

Examples of AI-QCT include (but are not limited to) Cleerly Labs (Cleerly, Inc), HeartFlow Plaque analysis (HeartFlow, Inc), Elucid PlaqueIQ (Elucid.com) and Cari-Plaque (Caristo Diagnostics). Artificial intelligence enabled plaque analysis technologies are required to receive clearance from the food and drug administration (FDA) before marketing for use in the United States.

The following are some examples of technologies that have received FDA clearance:

Cleerly Labs – FDA clearance March 2025 (K242338) – Original clearance February 2019
HeartFlow Analysis (HeartFlow, Inc) – July 2025 (K250902) – Original clearance August 2019
Elucid PlaqueIQ (Elucid, Inc) – Original clearance September 2024 (K241524)
Cari-Plaque (Caristo, Inc) – Original clearance February 20, 2025 (K242240)
The Cari-Heart (Caristo, Inc) is not currently available for market in the United States

This list is not intended to be inclusive of all applicable technologies.

The FDA clearance typically includes a clarification that the software is not intended to replace the skill and judgment of a qualified medical practitioner and should only be used by people who have been appropriately trained in the software's functions, capabilities and limitations.[1] Users should be aware that certain views make use of interpolated data. This is data that is created by the software based on the original data set. Interpolated data may give the appearance of healthy tissue in situations where pathology that is near or smaller than the scanning resolution may be present.

EVIDENCE SUMMARY

Evidence for artificial intelligence (AI) augmented technologies that analyze computed tomography angiography scans to quantify and characterize arterial plaque to assess disease risk must fulfill three parameters:

1. Establish technical feasibility, typically assessed with two types of studies, those that compare test measurements with a gold standard and those that compare results taken with the same device on different occasions (test-retest). Normally conducted in the preclinical setting, the focus of this parameter is on test reproducibility and establishment of the test protocol.

2. Demonstrate diagnostic performance (sensitivity, specificity, positive and negative predictive values) of the test compared with the gold standard.
3. Evaluate clinical outcomes based on the performance of the test versus the standard of care. While in some cases, new diagnostic tests can be adequately evaluated using technical and diagnostic performance, when a test identifies a new or different group of patients with a disease, randomized trials are needed to demonstrate the impact of the test on net health outcomes (balance of benefits and harms).

For the evaluation of clinical validity and utility, this evidence review is focused on large studies that reported on the accuracy of the marketed version of the technology, included a suitable reference standard, and described participant selection criteria and clinical characteristics.

Systematic Reviews

Du (2025) published a systematic review and meta-analysis assessing the diagnostic performance of artificial intelligence in detecting coronary artery stenosis and calcified plaque on CT angiography, comparing AI performance with that of radiologists across 17 studies involving 5,560 patients and images.[2] The study employed a bivariate random-effects model to determine combined sensitivity and specificity, assessed heterogeneity using I^2 statistics, evaluated risk of bias using the revised QUADAS-2 tool, and graded evidence level using the GRADE system. For coronary artery stenosis ≥50%, AI demonstrated sensitivity of 0.92 (95% CI 0.88-0.95), specificity of 0.87 (95% CI 0.80-0.92), and area under the curve (AUC) of 0.96 (95% CI 0.94-0.97), outperforming radiologists who achieved sensitivity of 0.85 (95% CI 0.67-0.94), specificity of 0.84 (95% CI 0.62-0.94), and AUC of 0.91 (95% CI 0.89-0.93). For stenosis ≥70%, AI achieved sensitivity of 0.88 (95% CI 0.70-0.96), specificity of 0.96 (95% CI 0.90-0.99), and AUC of 0.98 (95% CI 0.96-0.99), while in calcified plaque detection, AI demonstrated sensitivity of 0.93 (95% CI 0.84-0.97), specificity of 0.94 (95% CI 0.88-0.96), and AUC of 0.98 (95% CI 0.96-0.99). The study was limited by retrospective study designs and heterogeneity in CTA technologies, with the authors emphasizing the need for external validation through prospective, multicenter trials.

Jie (2024) published a systematic review and meta-analysis evaluating the diagnostic accuracy of artificial intelligence-assisted computed tomography angiography for atherosclerotic plaque assessment, including 11 studies comprising 1,484 patients.[3] The review examined radiomics, machine-learning, and deep-learning techniques applied to CTA images for detecting stenosis, calcification, and plaque vulnerability, with quality and risk of bias assessed using the QUADAS-2 tool and meta-analysis conducted using STATA software version 17.0. The overall pooled area under the receiver operating characteristic curve for atherosclerotic plaque assessment was 0.96 (95% confidence interval 0.94-0.97) across 21 trials, with specific performance metrics showing an AUROC of 0.95 (95% CI 0.93-0.96) for detecting ≥50% stenosis in five studies, an AUROC of 0.96 (95% CI 0.94-0.97) for identifying ≥70% stenosis in six studies, and an AUROC of 0.92 (95% CI 0.90-0.94) for calcium detection in six studies. The analysis demonstrated low risk of bias but revealed substantial heterogeneity among included studies.

Nonrandomized Studies

Rinehart (2024) published a clinical utility study evaluating the impact of Artificial Intelligence Plaque Analysis (AI-QCPA; HeartFlow, Inc) on clinical decision-making in 100 patients with varying levels of coronary artery disease, reviewed by 3 experienced cardiologists.[4] The study found that adding AI-QCPA to coronary computed tomography angiography (CCTA) resulted in a reclassification rate of 66% (95% CI, 56.72%-75.28%), with higher rates observed in patients with calcium scores greater than 400 (96%), CAD-RADS 4 scores (94%), and coronary stenoses of 50% or greater (89.5%), primarily leading to intensification of preventative medical therapy. Limitations include the study's reliance on experienced level 3 Society of Cardiovascular Computed Tomography (SCCT) readers which may not reflect broader clinical practice, the relatively small sample size of 100 cases, and the lack of long-term clinical outcome data to validate whether the reclassifications led to improved patient outcomes. Additional real-world, prospective, observational data and potentially randomized controlled trials are needed to evaluate the associated with changes in down-stream cardiovascular outcomes.

Nurmohamed (2024) published a retrospective cohort study examining the association between atherosclerotic plaque characteristics determined by AI-QCT (Cleerly, Inc) and cardiovascular outcomes in patients from the ISCHEMIA trial.[5] The study analyzed CCTA data from 3,711 participants (mean age 64 years, 21% female, 79% with multivessel coronary artery disease) over a median follow-up of 3.3 years. Using multivariable Cox regression, researchers found that total plaque volume was most strongly associated with the primary outcome of cardiovascular death or myocardial infarction (adjusted hazard ratio 1.56, 95% CI 1.25-1.97 per interquartile range increase). Adding AI-QCT plaque quantification to baseline risk factors improved the model's predictive value at 6 months (AUC 0.688 vs. 0.637; P=.006), 2 years (AUC 0.660 vs. 0.617; P=.003), and 4 years (AUC 0.654 vs. 0.608; P=.002). While the study demonstrated that AI-QCT-derived measures of plaque volume and composition modestly improved event prediction in this high-risk population, limitations included the retrospective design, the highly selected nature of the ISCHEMIA trial population (predominantly male with advanced coronary disease), and the modest improvement in predictive value despite statistical significance.

Kim (2023) published a retrospective analysis of data from the CONSERVE Trial comparing clinical CCTA interpretation versus a semi-automated AI and machine learning approach (AI-QCT; Cleerly, Inc) for patients referred for non-emergent invasive coronary angiography (ICA).[6] The study included 747 stable patients (mean age 60 ± 12.2 years, 49% women) and found that AI-QCT identified no coronary artery disease in 9% of patients compared to 34% with clinical CCTA interpretation. Application of AI-QCT to identify obstructive coronary stenosis would have reduced ICA by 87% (for >50% stenosis threshold) and 95% (for >70% threshold), with no cardiovascular death or acute myocardial infarction occurring in 78% of patients with maximum stenosis <50%. The AI-QCT referral management approach would have reduced overall costs by 26% (using <50% stenosis threshold) and 34% (using <70% threshold) with no change in 1-year major adverse cardiovascular events. Limitations included the post-hoc nature of the analysis, lack of a blinded CCTA core laboratory, absence of quantitative coronary angiography analysis for direct comparison with AI-QCT, and assumptions in the decision model that all severe stenoses would trigger ICA referral and that ICA has perfect sensitivity and specificity.

Jones (2022) published a retrospective study examining the inter-observer variability among expert-level readers for quantifying coronary plaque and plaque components on CCTA, using artificial intelligence-enabled quantitative analysis software (AI-QCT; Cleerly, Inc) as a reference.[7] The study analyzed CCTA imaging from 232 patients enrolled in the CLARIFY Trial, with readers quantifying overall plaque volume and percentage breakdown of noncalcified and calcified plaque on a per-vessel basis. Results showed that expert readers achieved moderate-to-high inter-observer consistency for total plaque volume (ICC=0.78 for single reader, 0.91 for mean scores), but demonstrated significant variability and high discordance with AI-QCT when quantifying plaque composition (weighted kappa coefficients between 0.17-0.34 for high-risk plaque identification). Limitations included the post-hoc nature of the analysis, use of established Hounsfield unit thresholds without adjustment for high luminal contrast enhancement, exclusion of poor-quality CCTAs deemed uninterpretable by expert readers, and the unknown prognostic significance of AI-quantified atherosclerotic plaque.

Jonas (2021) published a retrospective analysis examining whether CCTA scanning parameters influence the diagnostic performance of AI-based quantitative CT analysis software for identifying coronary lesions with ≥50% stenosis.[8] The study analyzed CCTA and quantitative coronary CT data from 303 stable patients (64 ± 10 years, 71% men) from the derivation arm of the CREDENCE Trial using FDA-cleared AI-enabled software. Results showed that on a per-vessel basis, significant differences in sensitivity for detecting ≥50% stenosis were found only based on contrast type (iso-osmolar 70.0% versus non-iso-osmolar 92.1%, p=0.0345) and iodine concentration (ranging from 70.0% to 95.2% across different concentrations, p=0.0287) in the context of low injection flow rates. On a per-patient basis, there were no significant differences in AI diagnostic performance across all measured scanner, scan technique, patient preparation, contrast, and individual patient parameters. Limitations included the post-hoc nature of the analysis, focus solely on stenosis severity rather than other CAD metrics like plaque volume and composition, and use of core-lab interpreted QCA for stenosis >30% as ground truth, which prevented assessment of AI performance for milder stenoses that may still have prognostic significance.

Choi (2021) published an industry sponsored, multicenter study of three sites and 232 patients that underwent coronary computed tomography angiography (CCTA) followed by analysis with the Cleerly Lab software (Cleerly, Inc).[9] The characterizations performed by the AI program were compared to three L3 readers. The results reported indicate the AI performance has high accuracy, sensitivity, specificity, positive predictive value and negative predictive values all at 90% or above. The CCTA interpretations between AI and L3 expert readers were reported to be close in agreement with a wide range of atherosclerosis identified through the AI. While the results from this study seem positive, non-industry sponsored randomized control trials and further basis of comparison for clinical utility for automated quantification of coronary atherosclerotic plaque are necessary.

Section Summary

Current evidence for AI-enabled quantitative coronary CT angiography analysis software demonstrates promising technical performance in detecting coronary stenosis and characterizing atherosclerotic plaque, with two systematic reviews and retrospective studies showing high diagnostic accuracy compared to expert readers. However, the existing literature is limited by retrospective study designs, post-hoc analyses, with significant heterogeneity in study populations and imaging protocols. While these AI technologies show potential for improving risk stratification and clinical decision-making, no high-quality prospective studies or randomized controlled trials have been conducted to establish whether their use translates into improved patient outcomes compared to standard care. Given that AI-QCT identifies different patient populations at risk and may lead to changes in clinical management, well-designed, multicenter randomized controlled trials are essential to determine the clinical validity and utility of these technologies in improving net health outcomes.

GUIIDELINE SUMMARY

AMERICAN COLLEGE OF CARDIOLOGY (ACC) AND AMERICAN HEART ASSOCIATION (AHA)

The 2021 joint committee on clinical practice guidelines for the evaluation and diagnosis of chest pain include a recommendation for determination of atherosclerotic plaque burden for intermediate risk patients with acute and stable chest pain with no known CAD (1A recommendation).[10] The guidelines state that the use of CCTA can help diagnose the extent and severity of nonobstructive and obstructive CAD. However, these guidelines do not address emerging technologies including using AI augmented post CCTA imaging processing for analysis of plaque burden.

SUMMARY

There is not enough high-quality evidence to show that artificial intelligence augmented quantification and characterization of atherosclerotic plaque from computed tomography scans to assess the severity of arterial disease improves health outcomes. No evidence-based clinical practice guidelines recommend artificial intelligence augmented quantification and characterization of atherosclerotic plaque to assess the severity of arterial disease. Therefore, quantification of arterial plaque using artificial intelligence augmented analysis of computed tomography scans is considered investigational for all indications.

REFERENCES

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CODES

Codes	Number	Description
CPT	0710T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; including data preparation and transmission, quantification of the structure and composition of the vessel wall and assessment for lipid-rich necrotic core plaque to assess atherosclerotic plaque stability, data review, interpretation and report
	0711T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; data preparation and transmission
	0712T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; quantification of the structure and composition of the vessel wall and assessment for lipid-rich necrotic core plaque to assess atherosclerotic plaque stability
	0713T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; data review, interpretation and report
	0992T	Noninvasive assessment of cardiac risk derived from augmentative software analysis of perivascular fat without concurrent computed tomography (CT) scan of the heart, including patient-specific clinical factors, with interpretation and report by a physician or other qualified health care professional
	0993T	Noninvasive assessment of cardiac risk derived from augmentative software analysis of perivascular fat with concurrent computed tomography scan of the heart, including patient-specific clinical factors, with interpretation and report by a physician or other qualified health care professional (List separately in addition to code for primary procedure)
	75577	Quantification and characterization of coronary atherosclerotic plaque to assess severity of coronary disease, derived from augmentative software analysis of the data set from a coronary computed tomographic angiography, with interpretation and report by a physician or other qualified health care professional
HCPCS	None	

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