cleerlyhealth.com
info@cleerlyhealth.com
(646) 362-4255
110 16th Street
Suite 1400 #104
Denver, CO 80202

VIA electronic mail: olatokunbo.awodele@elevancehealth.com

April 19, 2023

National Government Services
Attn: Medical Policy Team
J6 & K A/B MAC LCD Reconsideration
P.O. Box 6474
Indianapolis, IN 46206-6474

Re: New LCD Request- Cleerly Labs

Dear NGS Medical Policy Team:

We appreciate the opportunity to submit a new LCD Request to National Government Services (NGS) for Cleerly Labs. This request seeks the creation of a new LCD to include the atherosclerosis imaging quantitative computed tomography (AI-QCT), based on published evidence on Cleerly Labs, for patients under evaluation for coronary artery disease (CAD) or suspected CAD. Cleerly, Inc. ("Cleerly"), developer of Cleerly Labs, is a digital health company innovating a new standard for evaluation of coronary artery disease (CAD). Cleerly goes beyond the traditional methods of diagnosing heart disease by using artificial intelligence (AI) to enable non-invasive, comprehensive quantification and characterization of atherosclerosis (plaque)—the primary disease process—in the heart arteries.

Background on Coronary Artery Disease

Heart disease is the leading cause of death in the United States for men and women with an estimated 697,000 dying from heart disease in 2020. According to the Centers for Disease Control and Prevention (CDC), coronary heart disease is the most common type of heart disease with approximately 20.1 million adults, aged 20 and older, having CAD.[1] Historically, primary methods of diagnosing heart disease have been through coronary angiograms and stress tests. It is estimated that one million invasive coronary angiograms and ten million stress tests are performed each year.[2] These tests have historically focused on the detection of stenosis (narrowing of the arteries) in the heart rather than the atherosclerosis (plaque) that causes the narrowings. However, a recent clinical trial by Maron et al. found that stenosis or stress test-guided treatment does not reduce heart attacks or death.[3]

The underlying cause of stenosis and ischemia is atherosclerosis, a disease of the arteries characterized by the deposition of plaques of fatty material on their inner walls. The evaluation of this disease, not the indirect consequences (e.g., stenosis, ischemia), optimally determines risk and guides the therapy for improved patient outcomes. Recent publications have highlighted that

[1] https://www.cdc.gov/heartdisease/facts.htm (Last visited December 31, 2022)
[2] Roth A, et al. Overuse of Cardiac Testing. *Am Fam Physician*. 2018 Nov 15;98(10):561-563.
[3] Maron DJ, et al. Initial Invasive or Conservative Strategy for Stable Coronary Disease. *N Engl J Med*. 2020 Apr 9;382(15):1395-1407.

atherosclerotic burden and composition are the most important determinants of future heart attack risk, with different types of plaque composition carrying different levels of risk. Patient management – lifestyle changes (e.g., diet and exercise) or medication therapy – driven by these determinants can lead to transformation in plaque composition in a manner that reduces heart attacks and avoids unnecessary downstream procedures (such as stress tests and invasive angiograms).[4]

Several prominent clinical practice guidelines recommend the use of coronary computed tomography angiography (CCTA) as a first line diagnostic tool for CAD. The ACC/AHA guidelines recommend CCTA as the 1st line test for evaluating CAD. However, these tests are currently used to evaluate stenosis alone, and not atherosclerosis. Lu, et al. and Choi, et al. have found that physician readers of CCTA consistently overestimate the cases of severe stenosis and are unable to quantify atherosclerotic burden or characterize type of plaque composition.[5] There has been an increasing recognition of this need to quantify and characterize plaque, with 2 positive recommendations in the 2021 ACC/AHA guidelines encouraging clinicians to leverage plaque information for improving risk stratification and monitoring disease over time. Further, the updated radiology CAD-RADS 2.0 guidelines recommend quantitative assessment of atherosclerosis in routine radiologic interpretation and reporting.[6]

Understanding a patient's atherosclerotic plaque burden and composition are the critically important determinants that drive effective CAD treatment – more important than understanding other existing measures of CAD, including stenosis and ischemia – because these existing approaches do not measure the actual disease (atherosclerosis). Until now, evaluation of CAD was for surrogate measures (stenosis, ischemia) of the disease. Quantification and characterization of coronary plaque is an analysis with a high degree of diagnostic accuracy in determining plaque burden and composition, measures the primary atherosclerotic disease process, and guides clinical decision making in a manner that improves event-free survival.

OVERVIEW OF CLEERLY LABS

Cleerly Labs is an FDA-cleared, web-based software application that is intended to be used by trained medical professionals as an interactive tool for viewing and analyzing cardiac computed tomography (CT) data for determining the presence and extent of coronary plaques and stenosis in patients who underwent CCTA for evaluation of CAD or suspected CAD.[7] The Cleerly Labs analysis is a separate and distinct service from CCTA, providing significantly additional information, critical to patient care management decisions for that patient, that cannot be provided by the CCTA alone. More specifically, Cleerly quantifies and characterizes sub-voxel (3D pixel)-level data from CCTA scans - beyond the capabilities of human readers – to determine the presence, extent and type of coronary plaque and stenosis. Cleerly Labs was cleared by FDA following premarket review under K190868 and K202280.

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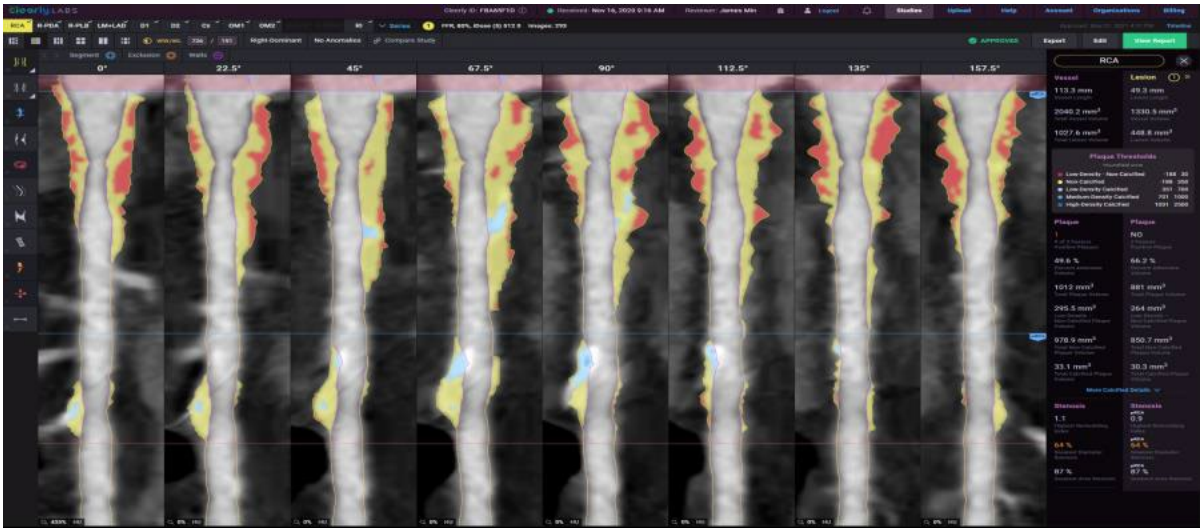
[4] Williams MC, et al. Low-Attenuation Noncalcified Plaque on Coronary Computed Tomography Angiography Predicts Myocardial Infarction: Results From the Multicenter SCOT-HEART Trial (Scottish Computed Tomography of the HEART). *Circulation*. 2020 May 5;141(18):1452-1462. doi: 10.1161/CIRCULATIONAHA.119.044720. Epub 2020 Mar 16.

[5] Choi AD, et al. CT Evaluation by Artificial Intelligence for Atherosclerosis, Stenosis and Vascular Morphology (CLARIFY): A Multi-center, international study. *J Cardiovasc Comput Tomogr*. 2021 Nov-Dec;15(6):470-476. doi: 10.1016/j.jcct.2021.05.004. Epub 2021 Jun 12.

[6] Cury, R. C., Leipsic, J., Abbara, S., Achenbach, S., Berman, D., Bittencourt, M., Budoff, M., Chinnaiyan, K., Choi, A. D., Ghoshhajra, B., Jacobs, J., Koweek, L., Lesser, J., Maroules, C., Rubin, G. D., Rybicki, F. J., Shaw, L. J., Williams, M. C., Williamson, E., … Blankstein, R. (2022). CAD-RADS™ 2.0 – 2022 coronary artery disease-reporting and Data System. *JACC: Cardiovascular Imaging*, *15*(11), 1974–2001. https://doi.org/10.1016/j.jcmg.2022.07.002

[7] https://www.accessdata.fda.gov/cdrh_docs/pdf19/K190868.pdf, https://www.accessdata.fda.gov/cdrh_docs/pdf19/K202280.pdf

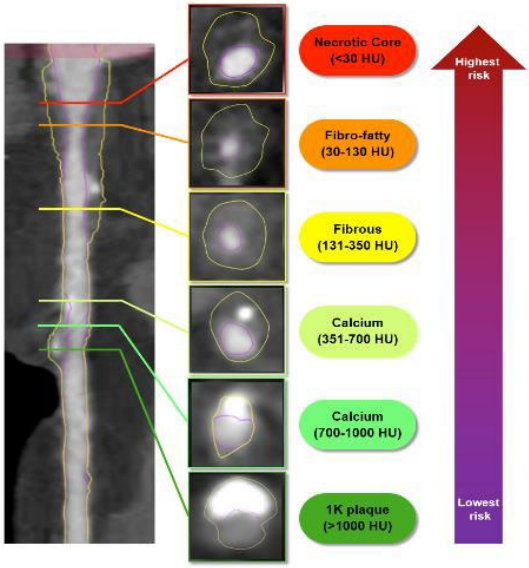
Exhibit 1. Quantification and Characterization of Atherosclerotic Plaque Types and Burden in Coronary Vessel



Using data from the underlying CCTA, Cleerly Labs quantifies and characterizes atherosclerosis, performing whole-heart quantitation and characterization of atherosclerotic plaque. (See **Exhibit 1**) This quantification and characterization of the atherosclerotic burden enables physicians to determine the risk of heart attacks.[8] Beyond this, Cleerly Labs also quantifies stenosis more accurately than humans with results comparable to an invasive angiography.[9] Kim, *et al*. found that Cleerly Labs reduces human reader overestimation of severe stenosis by 54%, which subsequently reduces downstream testing and interventions by 95%, with total costs being reduced by 34%.[10]

[8] Ferencik M *et al*. *JAMA Cardiol*. 2018.
[9] Griffin, William F., Andrew D. Choi, et. al. "AI Evaluation of Stenosis on Coronary CT Angiography, Comparison With Quantitative Coronary Angiography and Fractional Flow Reserve: A CREDENCE Trial Substudy." JACC: Cardiovascular Imaging, 2022. https://doi.org/10.1016/j.jcmg.2021.10.020.
[10] Kim Y, Choi A, Telluri A. Atherosclerosis Imaging Quantitative Computed Tomography (AI-QCT) to Guide Referral to Invasive Coronary Angiography in the Randomized Controlled CONSERVE Trial. In Press. Clinical Cardiology 2023

Exhibit 2. Different Types of Coronary Atherosclerotic Plaque and Associated Level of Risk



An additional clinical benefit of Cleerly Labs is that it reduces unnecessary healthcare services or healthcare waste. Lipkin *et al*. and Chang *et al*. found that Cleerly Labs reduces unnecessary invasive angiograms by 87 - 95%.[11] When compared to non-invasive nuclear stress tests, Cleerly Labs reduces referrals to invasive angiograms by 49%.

SUMMARY OF EVIDENCE

As a medical device company that is currently offering its services in the states covered by NGS, Cleerly respectfully requests that NGS create a new LCD to include AI-QCT given the evidence demonstrating the high degree of diagnostic accuracy for detecting the presence, extent, and type of atherosclerotic plaque, stenosis severity, and coronary ischemia. This service gives diagnostic detail and information not possible with CCTA alone, and that positively influences the treatment pathways considered for the patient and effectively reduces healthcare waste.

Exhibit 3 gives an overview of two clinical studies highlighted in the peer-reviewed evidence below that supports the coverage of AI-QCT where clinically appropriate and reasonable and necessary.

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[11] Lipkin I, Telluri A, Kim Y, et al. Coronary CTA With AI-QCT Interpretation: Comparison With Myocardial Perfusion Imaging for Detection of Obstructive Stenosis Using Invasive Angiography as Reference Standard. *AJR Am J Roentgenol* 2022;219(3):407-419. (In eng). DOI: 10.2214/ajr.21.27289.

Chang HJ, Lin FY, Lee SE, et al. Coronary Atherosclerotic Precursors of Acute Coronary Syndromes. J Am Coll Cardiol. 2018 Jun 5;71(22):2511-2522. doi: 10.1016/j.jacc.2018.02.079. PMID: 29852975; PMCID: PMC6020028.

Exhibit 3. CLARIFY and CREDENCE Clinical Trials

Trial Name	CT EvaLuation by ARtificial Intelligence For Atherosclerosis, Stenosis and Vascular MorphologY (CLARIFY)	Computed TomogRaphic Evaluation of Atherosclerotic Determinants of Myocardial IsChEmia Trial (CREDENCE) (NCT02173275)
Study Design	Prospective, multicenter, controlled clinical trial conducted	Prospective, multicenter, controlled clinical trial conducted
Study Objective	To evaluate whether AI-aided analysis would allow for rapid accurate evaluation of vessel morphology and stenosis when compared to consensus of L3 expert readers	To estimate compare the diagnostic accuracy of comprehensive anatomic (obstructive and nonobstructive atherosclerotic plaque) vs functional imaging measures for estimating vessel-specific fractional flow reserve
Total Patients	232	307 (derivation cohort)
Interventions	▪ CCTA ▪ AI-QCT	▪ CCTA ▪ Quantitative coronary angiography (QCA) ▪ Invasive fractional flow reserve (FFR)
Patient Demographics	Age: 60 years $\pm$ 12 Male: 86.0% BMI, kg/m^2: 27.5 $\pm$ 6 Hypertension: 61% Hyperlipidemia: 69% Diabetes: 29% Current smoker: 38%	Age: 64 years $\pm$ 10 Male: 71.0% BMI, kg/m^2: 26 $\pm$ 4 Hypertension: 64% Hyperlipidemia: 44% Diabetes: 31% Current smoker: 17%
Funded by Cleerly	Yes	No

Griffin et al.

Using the CREDENCE data, Griffin et. al.[12] conducted a retrospective analysis to evaluate the performance of AI-QCT in detecting and grading coronary stenoses when compared to CCTA, dedicated core-lab invasive QCA, and invasive FFR. Invasive QCA and invasive FFR are widely considered the 'gold standards' for stenosis and ischemia, respectively.

CCTA	Conducted using a CT scanner with $\geq$64-detector rows and in accordance with SCCT guidelines
Invasive QCA	Performed, in a dedicated core lab, two orthogonal views on a per-lesion basis of every lesion visually for $\geq$30% diameter stenosis in vessels with a reference vessel diameter $\geq$2.0 mm
Invasive FFR	Interrogated all major coronary arteries or branches with lesion between 40% and 90%
AI-QCT (Cleerly Labs)	Automated analysis of CCTA using series of validated convolutional neural network models for image quality assessment, coronary segmentation and labeling, lumen wall evaluation and vessel contour determination, and plaque characterization

[12] Griffin, William F., Andrew D. Choi, et. al. "AI Evaluation of Stenosis on Coronary CT Angiography, Comparison With Quantitative Coronary Angiography and Fractional Flow Reserve: A CREDENCE Trial Substudy." JACC: Cardiovascular Imaging, 2022. https://doi.org/10.1016/j.jcmg.2021.10.020.

To evaluate the performance of the AI-based diameter stenosis, Griffin analyzed the sensitivity, specificity, and diagnostic accuracy relative to the determination of ≥50% and ≥70% stenosis on a per-segment, per-vessel, per-territory, and per-patient base, using QCA as the reference standard. Areas under the receiver-operating characteristic curve (AUC) were used to evaluate the diagnostic performance for ≥50% and ≥70% stenosis per QCA as well as to evaluate the prediction of FFR for both QCA and AI-QCT.

Diagnostic Performance AI-QCT Versus Invasive QCA, Per Patient (n=303)

AI-QCT vs. Invasive QCA	Sensitivity	Specificity	PPV	NPV	Accuracy	AUC
≥50% Stenosis	94%	68%	81%	90%	84%	0.88
≥70% Stenosis	94%	82%	69%	97%	86%	0.92

See Table 2 in Griffin *et al*.

Griffin et al found comparable sensitivity, accuracy, and negative predictive value at both 50% and 70% stenosis with higher specificity with ≥70% versus ≥50% stenosis when comparing AI-QCT versus QCA on a per-patient basis. When analyzing on a per vessel basis, invasive QCA and AI-QCT had comparable and statistically significant specificity, negative predictive value and AUC while QCA had high specificity.

Diagnostic Performance of QCA and AI-QCT Stenosis to predict FFR, Per Vessel (n=848)

Diagnostic Performance, >70% Stenosis to Predict FFR, per Vessel	Invasive QCA (% (n/n) (95% CI)	AI-QCT % (n/n) (95% CI)	P Value
Accuracy	85.0 (721/848) (81.8-87.1)	86.2 (731/848) (83.2-88.2)	< 0.2173
AUC	0.953	0.916	0.001

See Table 3 in Griffin *et al*.

Of the 157 vessels that were determined by AI-QCT to be ≥70%, sixty-two vessels were considered false positives because the QCA was <70%. However, two-thirds (66.1%) of these vessels were found to have an invasive FFR value of <0.8, indicating the higher concordance of AI-QCT to invasive FFR than invasive QCA. Overall, an AI-based evaluation of the stenosis – the detection and grading – demonstrated high diagnostic performance for the identification, exclusion, discrimination, and correlation to a QCA reference standard. Moreover, the findings from this study are in direct accordance with a prior study that assessed the performance of AI-QCT compared to level 3 expert readers' consensus. The study authors concluded that the use of AI-QCT "may augment clinical coronary CTA interpretation", particularly given the speed with which the services can be performed and given its demonstrated superior performance to previous CCTA core lab and site readers.

Choi et al.

Choi et. al.[13] conducted a prospective study – CLARIFY – of patients with acute, stable chest pain undergoing CCTA at high volume centers of excellence. The CCTAs were analyzed by expert level III readers with 7-17 years of experience and by AI-QCT for:

- Percent of maximal diameter stenosis;
- Plaque volume and composition;

[13] Choi AD et al. "CT EvaLuation by Artificial Intelligence For Atherosclerosis, Stenosis and Vascular MorphologY (CLARIFY): A Multi-center, international study." Journal of Cardiovascular Computed Tomography, https://doi.org/10.1016/j.jcct.2021.05.004.

- Presence of high-risk plaque; and
- Coronary Artery Disease Reporting & Data System (CAD-RADS) category

Diagnostic performance of Artificial Intelligence vs Level 3 Expert Consensus

THRESHOLD	BASIS	% AGREE	SENSITIVITY	SPECIFICITY	PPV	NPV
>50% Stenosis	Per vessel	97.5%	77.1%	98.3%	64.3%	99.1%
	Per patient	94.8%	80.0%	97.0%	80.0%	97.0%
>70% Stenosis	Per vessel	99.7%	90.9%	99.8%	83.3%	99.9%
	Per patient	99.1%	88.9%	99.6%	88.9%	99.6%

See Table 2 in Choi *et al*.

As demonstrated above, there was close census between Cleerly Labs and L3 readers for determination of % of maximal diameter stenosis. Choi et al also found close consensus on CAD-RADS scores, with 98.3% and 99.9% agreement with 1 CAD-RADS category per patient and per vessel respectively for L3 and AI depicted. Additionally, AI depicted high risk plaques in 53% more patients than found by expert readers.

Lipkin et al.

Using the CREDENCE trial, Lipkin et. al.[14] conducted a retrospective analysis of patients with stable myocardial ischemia referred to invasive angiography. Patients underwent CCTA and rest or stress myocardial perfusion imaging (MPI) prior to QCA and invasive FFR. Cardiologists at the labs interpreted each MPI examination with summed stress scores (SSS) to determine the severity of ischemia.

Among the patients with no ischemia based on the stress MPI, AI-QCT identified non-obstructive (1-49%) and obstructive (50%+) ischemia in 46% and 54% respectively. Where the stress MPI identified moderate to severe ischemia, AI-QCT identified mild, moderate, and severe ischemia in 10%, 24% and 76% respectively.

	Stress MPI				
AI-QCT	No Ischemia (n = 102)	Any Ischemia (n = 199)	Minimal / Mild Ischemia (n = 100)	Moderate Ischemia (n = 42)	Severe Ischemia (n = 57)
0% Stenosis (n = 1)	0 (0)	1 (< 1)	1 (1)	0 (0)	0 (0)
1–49% Stenosis (n = 94)	47 (46)	47 (24)	37 (37)	5 (12)	5 (9)
50–69% Stenosis (n = 84)	35 (34)	49 (25)	35 (35)	7 (17)	7 (12)
≥ 70% Stenosis (n = 122)	20 (20)	102 (51)	27 (27)	30 (71)	45 (79)

See Table 2 in Lipkin *et al*.

When comparing AI-QCT to stress MPI using either QCA or invasive FFR as the reference standard, AI-QCT maintained higher or comparable sensitivity and higher specificity, PPV, and NPV relative to stress MPI for patients with QCA > 50% stenosis, or QCA > 70% stenosis, or FFR < 0.80. Lipkin et al. also generated receiver operating characteristic curves for AI-QCT (percent stenosis) and stress MPI (score from 0 to 4). In their ROC analysis, they found that the AI-QCT AUC was significantly higher than that for stress MPI for:

- Prediction of ≥ 50% stenosis by QCA (0.88 [0.84–0.92] vs 0.66 [0.60–0.72], $p < .001$);

[14] Lipkin, et. al. "Coronary CTA With AI-QCT Interpretation: Comparison With Myocardial Perfusion Imaging for Detection of Obstructive Stenosis Using Invasive Angiography as Reference Standard." American Journal of Roentgenology 2022 219:3, 407-419.

- Prediction of ≥ 70% stenosis by QCA (0.92 [0.90–0.95] vs 0.81 [0.76–0.87], $p < .001$); and
- Prediction of FFR < 0.80 (0.90 [0.87–0.94] vs 0.71 [0.66–0.77, $p < .001$).

Finally, the authors tested four different sequential approaches (e.g., MPI versus AI-QCT first) to assess the potential for AI-QCT to reduce invasive angiography. Based on the analysis, an AI-QCT first approach set at a ≥ 70% severe obstructive threshold allows for a 26% reduction in expected downstream invasive angiography when compared to a nuclear MPI first strategy. By incorporating AI-QCT into the diagnostic paradigm, it allows for "substantial reduction in unnecessary downstream invasive angiography procedures."[15]

Jonas et al.

Using the CREDENCE trial data, Jonas, et. al.[16] evaluated whether AI-QCT performance was affected by variability in CCTA scanning parameters including but not limited to scanning vendor, model, scan preparation, contrast, and patient-based parameters. The performance of AI-QCT was analyzed by assessing the accuracy, sensitivity, and specificity for identifying >50% using QCA as the reference standard. analysis found that the innovative AI-QCT technology was not impacted by CCTA scanning parameters for diagnosing moderate to high grade stenosis. This analysis was performed at both at the patient level and at the vessel level.

The authors found no significant difference in the AI-QCT performance at the patient level based on variations in:

- Scanner type
- Gating technique
- Bolus type
- Contrast features
- Radiation features
- Image generation
- Medication administration prior to imaging; or
- Clinical patient characteristics.

When evaluating at the vessel level, the only significant differences were in sensitivity in detecting >50% stenosis by iodine concentration and contrast type. For all other parameters, there was no significant difference in sensitivity, specificity or accuracy.

Kim et al.

Kim et. al.[17] used CCTA data from 747 individuals enrolled into the randomized controlled CONSERVE trial, each of whom had an ACC/AHA Guideline Indication for invasive coronary angiography (ICA). Site interpretation and clinical recommendation for further ICA testing of CCTAs were compared to AI-QCT. CCTA interpretation and AI-QCT guided findings were also related to MACE at 1-year follow-up. Application of AI-QCT to identify obstructive coronary stenosis at the >50%

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[15] Lipkin, et. al. "Coronary CTA With AI-QCT Interpretation: Comparison With Myocardial Perfusion Imaging for Detection of Obstructive Stenosis Using Invasive Angiography as Reference Standard." American Journal of Roentgenology 2022 219:3, 407-419.

[16] Jonas, et. al. "The effect of scan and patient parameters on the diagnostic performance of AI for detecting coronary stenosis on coronary CT angiography." Clinical Imaging, Volume 84, 2022, Pages 149-158. https://doi.org/10.1016/j.clinimag.2022.01.016.

[17] Kim Y, Choi A, Telluri A. Atherosclerosis Imaging Quantitative Computed Tomography (AI-QCT) to Guide Referral to Invasive Coronary Angiography in the Randomized Controlled CONSERVE Trial. In Press. Clinical Cardiology 2023

and >70% threshold would have reduced ICA by 87% and 95%, respectively. Compared to CCTA alone, Cleerly enables reduction of referral to unnecessary ICA by 53% (13 vs 28% @ 50% threshold) and 71% (5 vs 16% @ 70% threshold). When compared to CCTA clinical reads, AI-QCT reduces ICA referral by 53% (13 vs 28% @ 50% threshold) and 71% (5 vs 16% @ 70% threshold).

Clinical outcomes for patients without AI-QCT-identified obstructive stenosis was excellent; for the 78% of patients identified by AI-QCT to possess a maximum stenosis <50% (i.e., non-obstructive disease), no cardiovascular death or acute myocardial infarction occurred. These data support the concept of AI-QCT as an effective 'gatekeeper' to unnecessary, expensive and potentially harmful procedures for patients being considered for ICA.

When applying an AI-QCT referral management approach to avoid ICA in patients with <50% or <70% stenosis, overall costs were reduced by 26% and 34%, respectively. This cost reduction was calculated using the Cleerly list price of $1500. When recalculated using the newly assigned new tech APC 1551 at $950, the cost savings grows to 46% and 54% respectively.

Overall, the evidence detailed above demonstrates not only the accuracy, sensitivity and specificity of AI-QCT compared to QCA as a reference of care, but also its advantages over CCTA alone, over stress MPI, and its potential to reduce downstream unnecessary invasive procedures when sequenced appropriately.

NEW LCD REQUEST

As a medical device company that is currently doing business in states covered by NGS, Cleerly respectfully requests that NGS create a new LCD to include AI-QCT given the evidence demonstrating the high degree of diagnostic accuracy for detecting the presence, extent, and type of atherosclerotic plaque, stenosis severity, and coronary ischemia. This service gives diagnostic detail and information not possible with CCTA alone, and that influence the treatment pathways considered for the patient. We request the following language to be included in the new LCD:

SECTION	REQUESTED LANGUAGE
LCD Title	Atherosclerosis Imaging Quantitative Computed Tomography (AI-QCT)
Abstract	Current available body of evidence demonstrates that Atherosclerosis Imaging Quantitative Computed Tomography (AI-QCT) can reliably detect with a high degree of diagnostic accuracy the presence, extent, and type of coronary atherosclerotic plaque, stenosis severity, and coronary ischemia in patients under evaluation for CAD or suspected CAD. AI-QCT adds reproducible diagnostic detail not possible with CCTA alone, and the additional diagnostic information influences the treatment options for the patient.
Indications	*<u>Indications for AI-QCT</u>* *In the absence of professional clinical guidelines, a standing order for AI-QCT for every patient undergoing a CCTA is not reasonable and necessary, and is not a covered Medicare service. Only the treating physician or qualified non-physician healthcare professional may determine the medical necessity of the test and the timing at which the AI-QCT should be ordered. Specific documentation must justify the medical necessity for the AI-QCT in the patient's medical record.* *AI-QCT may be ordered concurrently with CCTA as a reasonable and necessary diagnostic study to:* *a. Further assess atherosclerotic plaque burden and characteristics for symptomatic patients with elevated risk for a major cardiac event with ASCVD (Atherosclerotic Cardiovascular Disease) > 7.5%*

SECTION	REQUESTED LANGUAGE
	b. Aid the physician in appropriate referral management of symptomatic patient (e.g., patient with known CAD presenting to the emergency room with new chest pain typical for angina) for further non-invasive testing, invasive testing and/or treatment *AI-QCT may be ordered after the CCTA has been performed and interpreted to obtain additional necessary diagnostic information in a symptomatic patient:* *a. To determine total plaque volume and type (non-calcified and calcified) in order to categorize the appropriate stage of atherosclerosis, which directs treatment management* *b. To further assess presence or absence of high-risk plaque (HRP) in patients with a CADRADS 2.0 plaque category of P2 (mild-moderate) or P3 (moderate)* *c. To further assess coronary stenosis severity or coronary ischemia where physiologic significance is unknown in patients with CADRADS 2.0 stenosis category of moderate (50-69% stenosis) or severe (70-99% stenosis)* *d. To obtain more precise diagnostic information to determine if the patient is considered in need of an invasive coronary angiogram* *e. To further assess for the progression or regression of disease and effectiveness of therapy compared to prior clinically-warranted CCTA studies*
Limitations	*<u>Limitations for AI-QCT</u>* *a. The test is never covered for screening, i.e., in the absence of signs, symptoms, or disease.* *b. All studies must be ordered by the physician/qualified non-physician practitioner treating the patient and who will use the results of the test in the management of the patient.* *c. The test will be considered not medically necessary if the anticipated results are not expected to provide new, additional information to that already previously obtained from other testing. New or additional information should facilitate the management decision by providing new diagnostic information not obtained from the underlying CCTA.* *d. The test may be denied, on post-pay review, as not medically necessary, when used for cardiac evaluation if there was pre-test knowledge of the extent and type of plaque and stenosis that would diminish the interpretive value.* *e. AI-QCT is not considered reasonable in the following clinical circumstances:* *i. Prior placement of prosthetic valves* *ii. Prior placement of grafts in coronary bypass surgery* *iv. Intracoronary metallic stent wherein the region of interest includes a stent* *v. Status post-heart transplantation* *vi. Recent MI (30 days or less)* *vii. Prior pacemaker or defibrillator lead placement* *viii. Newly diagnosed systolic heart failure, with no prior left heart catheterization* *ix. Non-obstructing stenosis (<50% of all major epicardial vessels) on CTA or catheterization in the past twelve months, in the absence of a new symptom complex.* *x. If turnaround times may impact prompt clinical care decisions* *This service should be performed solely in patients with symptomatic coronary syndrome. This test should be performed as an alternative to non-invasive stress testing, intravascular ultrasound, optical coherence tomography, invasive intracoronary pressure measurements (i.e., invasive FFR, iFR and others), near-field infrared spectroscopy, or invasive angiography-based computational modeling of FFR.*
References	*Bitar JA, Lakshmanan S, Manubolu VS, et al. Differential Effect of Apixaban versus Rivaroxaban on Atherosclerosis Plaque-Progression in Patients with Atrial Fibrillation. Journal of Cardiovascular Computed Tomography. July 2021;15(4): S47.*

SECTION	REQUESTED LANGUAGE
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Thank you again for your consideration of this reconsideration request. Should you have any questions, please do not hesitate to contact Lance Thrash, Vice President of Market Access and Reimbursement, at lance.thrash@cleerlyhealth.com. We welcome the opportunity to connect you with one or more members of Cleerly's clinical leadership team to discuss the latest clinical evidence on the use of Cleerly for patients with suspected CAD or under evaluation for CAD, and to further discuss the specifics of the requested language in the LCD and accompanying article.

Sincerely,

Lance Thrash, RN, BSN
VP, Market Access and Reimbursement
Cleerly Labs