August 19, 2024

Nano-X AI Ltd.
℅ Neta Sherman
Associate VP Regulatory Affairs and Quality
Shlomo Shmeltzer Road 94
Po Box 3486
PETAH TIKVA, 4970602
ISRAEL

Re: K241440
Trade/Device Name: HealthCCSng
Regulation Number: 21 CFR 892.1750
Regulation Name: Computed tomography x-ray system
Regulatory Class: Class II
Product Code: JAK
Dated: May 21, 2024
Received: May 21, 2024

Dear Neta Sherman:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Lu Jiang

Lu Jiang, Ph.D.
Assistant Director
Diagnostic X-Ray Systems Team
DHT8B: Division of Radiologic Imaging
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Office of Product Evaluation and Quality
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Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K241440

Device Name
HealthCCSng

Indications for Use *(Describe)*
The HealthCCSng device is intended for use as a non-invasive post-processing software to evaluate calcified plaques in the coronary arteries, which present a risk for coronary artery disease.
The HealthCCSng device analyzes routine non-gated, non-contrast CT studies that include the entire heart of adult patients of age 30-85.
The device generates an exact calcium score and a four coronary artery calcium detection category output representing the estimated quantity of calcium detected together with preview axial images of the detected calcium meant for informational purposes only.
The device output will be available to the radiologist as part of their standard workflow. A list of studies that received a successful algorithm analysis result will also be available for further clinician assessment (such as by a cardiologist, general practitioner etc.).
The HealthCCSng results are not intended to be used on a stand-alone basis for risk attribution, clinical decision-making or otherwise preclude clinical assessment of CT studies.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510 (k) Summary

510(K) Summary - HealthCCSng
Nano-X AI Ltd.

510(k) Number - K241440

Applicant's Name: Neta Sherman, AVP Regulatory Affairs and Quality
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Date Prepared: August 16, 2024

Trade Name: HealthCCSng

Modified Device:

Proprietary Name	Nano-X AI HealthCCSng device
Premarket Notification	K241440
Classification Name	Computed tomography x-ray system.
Regulation Number	21 CFR §892.1750
Product Code	JAK
Regulatory Class	II

Cleared Device:

The HealthCCSng V2.0 device is substantially equivalent to the following cleared Device:

Proprietary Name	Cleared Device: Nano-X AI HealthCCSng device
Premarket Notification	K210085
Classification Name	Computed tomography x-ray system.
Regulation Number	21 CFR §892.1750
Product Code	JAK
Regulatory Class	II

Performance Standards:
No performance standards have been established for such device under Section 514 of the Federal Food, Drug, and Cosmetic Act.

Intended Use/Indication for Use:

The HealthCCSng device is intended for use as a non-invasive post-processing software to evaluate calcified plaques in the coronary arteries, which present a risk for coronary artery disease.
The HealthCCSng device analyzes routine non-gated, non-contrast CT studies that include the entire heart of adult patients of age 30-85.
The device generates an exact calcium score and a four coronary artery calcium detection category output representing the estimated quantity of calcium detected together with preview axial images of the detected calcium meant for informational purposes only.
The device output will be available to the radiologist as part of their standard workflow. A list of studies that received a successful algorithm analysis result will also be available for further clinician assessment (such as by a cardiologist, general practitioner etc.).
The HealthCCSng results are not intended to be used on a stand-alone basis for risk attribution, clinical decision-making or otherwise preclude clinical assessment of CT studies.

Device Description:

HealthCCSng product is a software device that automatically estimates the coronary artery calcium category from non-cardiac-gated adult CT scans. The product is aimed to leverage the high utilization of CT scans in the medical care environment (both inpatient and outpatient), including lung cancer screening programs, in order to automatically detect calcification in the coronary arteries of patients in an opportunistic manner.

The HealthCCSng product analyzes cases using an artificial intelligence algorithm for the automated detection and estimation of coronary calcium and outputs a result for review by the clinician. The device works in parallel to and in conjunction with the standard of care workflow. The final diagnosis is made by the clinician after reviewing the scan independently of the software. The device is intended for use by the clinicians as a non-diagnostic analysis software in conjunction with additional patient information and professional judgment.

HealthCCSng receives a non-gated, non-contrast CT study from the storage application, Nanox AI's Imaging Analytics Platform (IMA)/ other platforms. For each CT study received, the software shall validate at least one compliant series in which the entire heart is present and performs an analysis. For each complaint study, the software shall output:

1. Estimated Coronary Calcium Detection, based on the measurement of calcium deposits in the coronary arteries.
2. A corresponding Estimated Coronary Calcium Detection Category, based on the Estimated Coronary Calcium measurements.

Product Output:
The software output will include the following calcium categories:

Estimated Coronary Calcium Detection	Corresponding Estimated Coronary Calcium Detection Category
0	Zero Calcium
1-99	Low
100-399	Medium
≥400	High

For patients in which calcium was detected, the user will be presented with representative key images - all the slices containing the measured coronary calcifications (130 HU and above). On these images, the calcified areas will be annotated.

The following modules compose the HealthCCSng software:

1) **Data input and validation:** DICOM validation receives imaging study from hosting application and the validation feature assessed the input data (i.e. age, modality, view, etc.) to ensure compatibility for processing by the algorithm.
2) **HealthCCSng algorithm:** Once a study has been validated, the algorithm analyzes the CT for analysis and quantification.
3) **IMA Integration feature:** The results of a successful study analysis are provided to the hosting application.
4) **Error codes feature:** In the case of a study failure during data validation or the analysis by the algorithm, an error is provided to the system.

The product operates in the following manner:

1. A CT scan is sent to the Image Analytics Platform (IMA).
2. The Image Analytics Platform (IMA) forwards the scan to the HealthCCSng algorithm for analysis.
3. The scan is analyzed, with the following possible results sent back to IMA:

a. **Non-compliant**: the scan is not compliant with the input criteria of the product and is therefore not analyzed.
b. **Success** -
    1. Success – A Zero calcium, Low, Medium or High Coronary Calcium Detection has been identified.
    2. Success No Category - Cause: metal artifact(s) suggestive of known cardiac disease is suspected.
c. **Failure:** the scan has been analyzed. An error prevented the device from completing the analysis and therefore there is no output available.

In all cases of success, HealthCCSng will provide key images of visualization of the detected coronary calcium (except for zero category), the category name and the exact score.

Technological Characteristics Compared to Cleared Device:

We believe that the HealthCCSng modified device is substantially equivalent to the Nano-X AI HealthCCSng cleared device K210085.

	Modified Device: **HealthCCSng Device**	**Cleared Device:** **Nano-X AI Ltd. HealthCCSng Device (K210085)**
Intended Use/ Indications for Use	The HealthCCSng device is intended for use as a non-invasive post-processing software to evaluate calcified plaques in the coronary arteries, which present a risk for coronary artery disease. The HealthCCSng device analyzes routine non-gated, non-contrast CT studies that include the entire heart of adult patients of age 30-85. The device generates an exact calcium score and a four coronary artery calcium detection category output representing the estimated quantity of calcium detected together with preview axial images of the detected	The HealthCCSng device is intended for use as a non-invasive post-processing software to evaluate calcified plaques in the coronary arteries, which present a risk for coronary artery disease. The software generates an estimated coronary artery calcium detection category. The HealthCCSng device analyzes existing non-cardiac-gated CT studies that include the heart of adult patients above the age of 30. The device generates a three-category output representing the estimated

	calcium meant for informational purposes only. The device output will be available to the radiologist as part of their standard workflow. A list of studies that received a successful algorithm analysis result will also be available for further clinician assessment (such as by a cardiologist, general practitioner etc.). The HealthCCSng results are not intended to be used on a stand-alone basis for risk attribution, clinical decision-making or otherwise preclude clinical assessment of CT studies.	quantity of calcium detected together with preview axial images of the detected calcium meant for informational purposes only. The device output will be available to the radiologist as part of their standard workflow. The HealthCCSng results are not intended to be used on a stand-alone basis for risk attribution, clinical decision-making or otherwise preclude clinical assessment of CT studies.

Comparison of Technological Characteristics

Technological Characteristics	**Modified Device: HealthCCSng Device**	**Cleared Device: Nano-X AI Ltd. HealthCCSng Device (K210085)**	**Summary**
Regulation			
Product Code	JAK	JAK	Same
Regulation Number	21 CFR §892.1750	21 CFR §892.1750	
General			
Modality	Computed tomography (CT)	Computed tomography (CT)	Same
Image format	DICOM	DICOM	Same
Supported CT scan	Non-contrast CT scan	Non-cardiac-gated CT scan	Similar. The inclusion criteria are the same: in

			both devices algorithm is intended to run on non-contrast non-gated CT scans.
Slice thickness	Up to 5.1 mm	Up to 3.1 mm	Similar, the modified HealthCCSng supports all the slice thickness range as in the cleared device and in addition can support a wider variety of scans. The expansion of the slice thickness range was validated and performnance was found similar to the cleared device.
Intended users	Radiologists, Interpretive Clinicians	Radiologists, Interpretive Clinicians	Same
Intended population	Patients aged 30-85 years	Patients aged 30 years and above	Similar, both modified and cleared devices are intended for adult population at the age of 30 and older; the modified device has an upper limit as part of product scope focus on relevant population.
Analysis and Measurement			

Detection of target organ	Yes, detection of the heart	Yes, detection of the heart	Same
Segmentation of organ	Deep-learning-based segmentation of the heart	Deep-learning-based segmentation of the heart	Same
Calcification detection	Automatic	Automatic	Same
Default threshold of calcium	130 HU (Hounsfield Units)	130 HU (Hounsfield Units)	Same
Coronary artery calcification quantification method	Coronary Calcium Detection Category and exact detected calcium score on side bar	Coronary Calcium Detection Category Detected and calcium score mark on side bar	Similar, both devices provide calcium category; both the cleared device and the modified device mark the calcium score on a side bar; the modified device also provides the detected calcium score number as an output, which was validated and was found similar to the cleared device.
Reporting			
Annotation of detected calcium	Yes	Yes	Same
Generate patient report	Optional to add the results to the report, DICOM Secondary Capture, Insight UI application	DICOM Secondary Capture, Insight UI application	Similar, the modified device also enables the option to add the

			results to the radiology report.
Device output	1) Estimated Coronary Calcium Detection, based on the measurement of calcium deposits in the coronary arteries, precise score is indicated besides the arrow on the side scale bar. 2) A corresponding Estimated Coronary Calcium Detection Category, based on the Estimated Coronary Calcium measurements 4 categories: 0 – Zero Calcium 1-99 – Low 100-399 – Medium ≥400 - High	1) Estimated Coronary Calcium Detection, based on the measurement of calcium deposits in the coronary arteries, score is presented as an arrow on the side scale bar. 2) A corresponding Estimated Coronary Calcium Detection Category, based on the Estimated Coronary Calcium measurements 3 categories: 0-99 – Low 100-399 – Medium 400 - High	Similar, both devices provide calcium category; The modified HealthCCSng device provides a more precise representation of coronary calcium score, and separating the category 0 from the other from the 'low' category.

Performance Data:

The HealthCCSng was designed and manufactured under the Quality System Regulations as outlined in 21 CFR § 820.
Safety and performance of HealthCCSng has been evaluated and verified in accordance with software specifications and applicable performance standards through Software Development and Validation & Verification Process to ensure performance according to specifications, User Requirements and Federal Regulations and Guidance documents, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices".

The HealthCCSng modified device performance was evaluated in a retrospective, simulated use, standalone performance study of its performance compared to the established ground truth and relative to the cleared device. The ground truth (Coronary Artery Calcium Category) was determined by the majority agreement of two out of three US board certified radiologists, experienced in identifying coronary calcium on non-gated CT studies.

The validation dataset included a truthed and enriched sample of at least 400 anonymized CT scans that include the heart from 4 healthcare institutions: Intermountain Healthcare (US), Clalit Health System (OUS), Northewell Health (US) and USARAD (US). The sample was engineered to contain sufficient cases within all coronary artery calcium categories.

The validation dataset included 436 cases, of which the algorithm returned a result on 427 cases, a yield of 97.94% (30-85 years old;mean age of 61.89 years; SD=13.11; male=58.31% (249)). The validation dataset represented the following imaging parameters: Modality (CT), Slice Thickness (0.5, 0.6, 0.625, 1, 1.25, 1.5, 2, 2.5, 3.75, 4, and 5 mm), Slice Increment (0.625, 1, 1.25, 1.5, 2, 2.5 and 3 mm), Exposure in mAs (Radiation Dose) i(15-966), KVP (100, 120, 130, 135 and 140), and four (4) manufacturers of CT devices (GE, Philips, Siemens and Toshiba). CT data across all, slice thickness, slice increment, exposure, KVP and manufacturers were well supported by the HealthCCSng device.

The HealthCCSng device demonstrated an overall agreement between HealthCCSng coronary calcium category and the ground truth category of 89.46% (95% CI: [86.15%, 92.21%]). The lower bound of the confidence interval for the primary endpoint of overall agreement is greater than the success criterion of 85%, thus the null hypothesis is rejected, and the acceptance criterion met.

- Agreement for the **Zero category** was: 86.63% (95% CI: [80.61%, 91.33]), the point estimate for the Zero category is greater than 85%, the acceptance criterion is met.
- Agreement for the **Low category** was: 87.65% (95% CI: [78.47%, 93.92%]), the point estimate for the Low category is greater than 85%, the acceptance criterion is met.
- Agreement for the **Medium category** was: 87.36% (95% CI: [78.50%, 93.52%]), the point estimate limit for the Medium category is greater than 76%, the acceptance criterion is met.
- Agreement for the **High category** was: 98.85% (95% CI: [93.76%, 99.97%]), the point estimate for the High category is greater than 60%, the acceptance criterion is met.

The HealthCCSng estimated coronary calcium score was compared to the corresponding ground truth (GT) score.
The HealthCCSng device demonstrated a statistically significant correlation (Pearson's correlation coefficient) between the GT and HealthCCSng scores of r=0.959 (95% CI: [0.9499, 0.9655], p<0.0001.

The device validation also demonstrated good correlation between the algorithm results on paired non-gated and gated scans, as summarized in table 1 and figures 1-2 below.

In addition, the device performed as well as radiologists did, however the user should note that Coronary Calcium Scoring on non-gated CT scans, is not as accurate as on gated CT scans.

Table 1: Categorical Agreement

	HealthCCSng CAC Category [HU] Non-Gated								Total	
	0		1-99		100-399		400+			
	N	%	N	%	N	%	N	%	N	%
HealthCCSng CAC Category [HU] Gated										
0	16	88.89%	1	5.56%	1	5.56%	.	.	18	100.00%
1-99	12	44.44%	13	48.15%	2	7.41%	.	.	27	100.00%
100-399	.	.	8	36.36%	12	54.55%	2	9.09%	22	100.00%
400+	.	.	.	.	6	18.18%	27	81.82%	33	100.00%
Total	28	28.00%	22	22.00%	21	21.00%	29	29.00%	100	100.00%

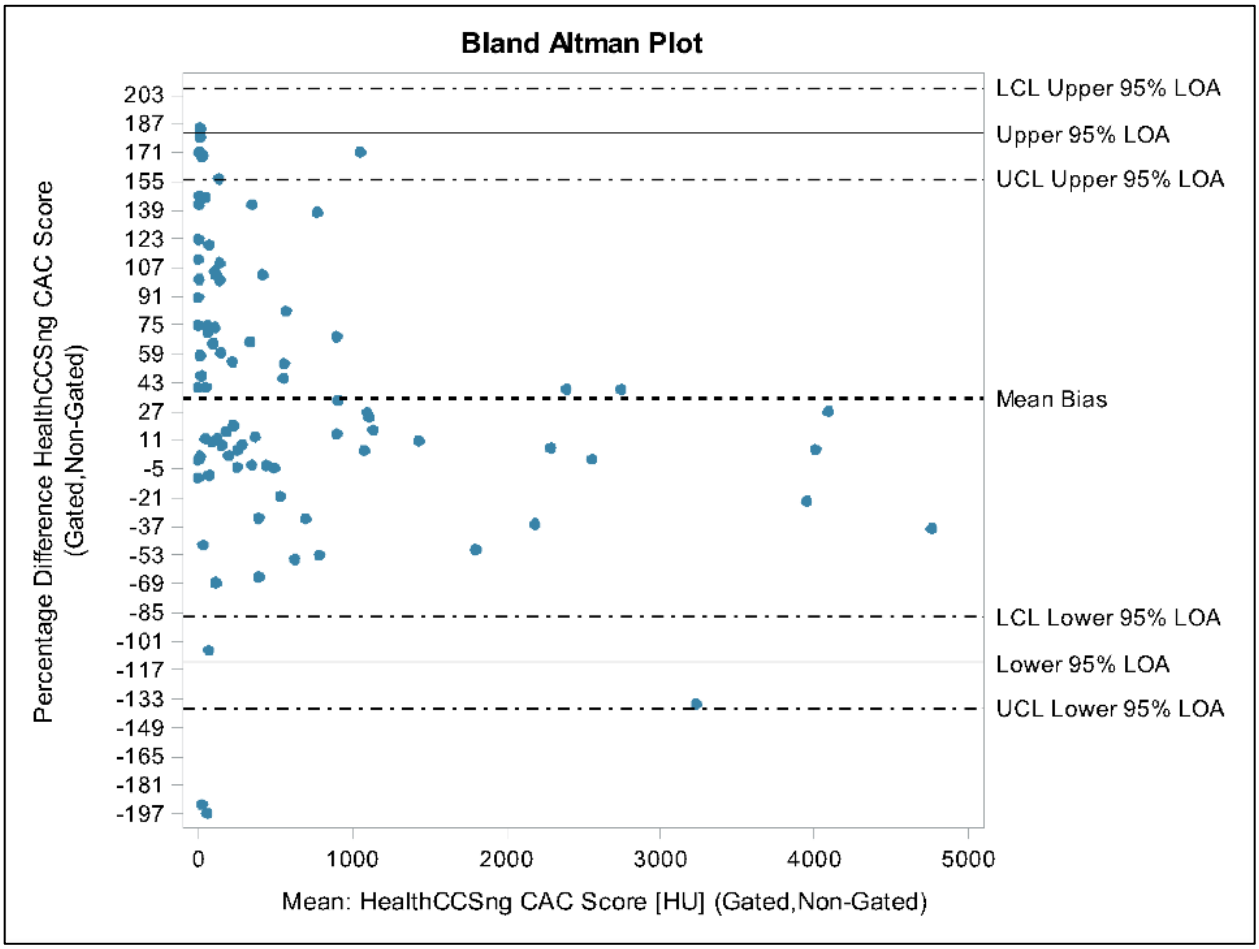

Figure 1: Paired Gated/ Non-Gated Bland Altman Plot

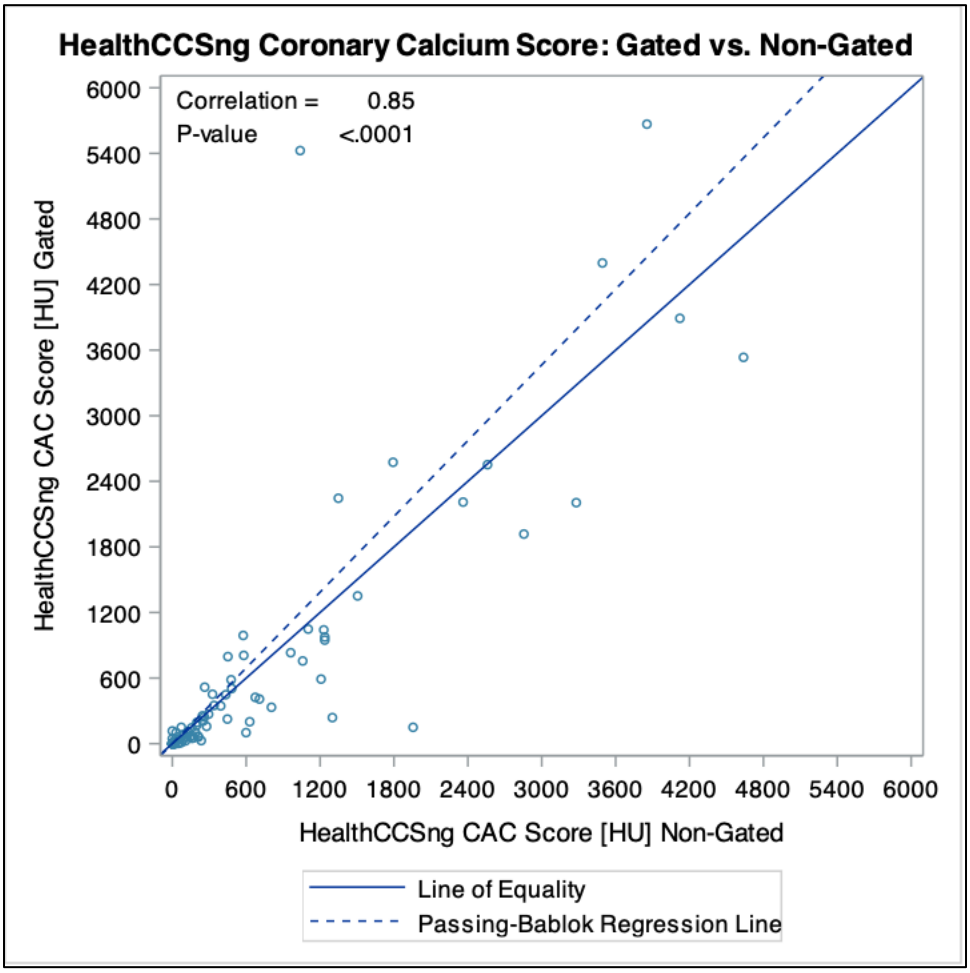

Figure 2: Scatter Plot of the HealthCCSng Algorithm Coronary Calcium Score in Hounsfield Units Gated versus non-Gated scans solid line is line of equality and the dotted line the Passing-Bablok regression line

In conclusion, this study demonstrated the HealthCCSng agreement of calcium score category measurements with the ground truth and established its safety and effectiveness, while demonstrating substantial equivalence to the cleared device. It also validated the performance of the HealthCCSng device across important cohorts, and applicable subsets of imaging acquisition characteristics.

Conclusion:

Based on the information submitted in this premarket notification, the modified HealthCCSng device does not constitute a new intended use. The modified device has very similar intended use and indications for use as the cleared device, with very similar technological characteristics and principles of operation. The minor differences supported by software and performance validation testing demonstrate that the modified device is as safe and effective as the cleared device and performs as intended. The minor technological differences between the modified HealthCCSng device and the cleared device raise no new issues or questions of safety or effectiveness, and the modified version is substantially equivalent.