DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
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January 13, 2016

Heartflow, Inc.
Windi Hary
Director Quality And Regulatory
1400 Seaport Boulevard, Building B
Redwood City, California 94063

Re: K152733
Trade/Device Name: FFRct
Regulation Number: 21 CFR 870.1415
Regulation Name: Coronary Physiologic Simulation Software Device
Regulatory Class: Class II
Product Code: PJA
Dated: December 10, 2015
Received: December 11, 2015

Dear Windi Hary:

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 (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. 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.

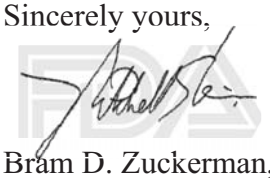
Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's 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 803); good manufacturing practice requirements as set forth in

the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,



for Bram D. Zuckerman, M.D.
Director
Division of Cardiovascular Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K152733

Device Name
FFRct v2.0

Indications for Use *(Describe)*
HeartFlow FFRCT is a post-processing software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for clinically stable symptomatic patients with coronary artery disease. It provides FFRCT, a mathematically derived quantity, computed from simulated pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. FFRCT analysis is intended to support the functional evaluation of coronary artery disease.

The results of this analysis are provided to support qualified clinicians to aid in the evaluation and assessment of coronary arteries. The results of HeartFlow FFRCT are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

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)

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5.0 510(K) SUMMARY

This 510(k) summary of safety and effectiveness information is submitted in accordance with the requirements of 21 CFR Part 807.87(h).

5.1 Submitter Information

Submitter / Manufacturer Name: HeartFlow, Inc.
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Date Prepared: September 21, 2015

5.2 Device Identification

Device Name:	FFR_{CT} v2.0
Device Trade Name:	FFR_{CT} v2.0
Common Name:	HeartFlow FFR_{CT}
Classification Name:	Coronary Physiologic Simulation Software Device
Product Code:	PJA
Product Class:	Class II (21 CFR 870.1415)

5.3 Predicates

HeartFlow FFR_{CT} v1.4 (DEN130045) is the identified predicate for the HeartFlow FFR_{CT} v2.0 product. This is discussed further in *VOL_002 SEC 013 Substantial Equivalence*.

5.4 Device Description

FFR_{CT} v2.0 is post-processing image analysis software developed for the clinical quantitative and qualitative analysis of CT DICOM data. It is a tool for the analysis of CT DICOM-compliant cardiac images and data, to assess the anatomy and function of the coronary arteries.

The software displays the anatomy combined with functional information using graphics and text, including computed and derived quantities of blood flow, pressure and velocity, to aid the clinician in the assessment of coronary artery disease.

FFR_{CT} is independent of imaging equipment, imaging protocols and equipment vendors; the clinical validation report (*VOL_003 FFR_{CT} v2.0 Clinical Validation Report*) includes identification of vendors and equipment used in the clinical validation of the product. This data is summarized in the product labeling, and can be found in the Clinical User Instructions for Use (*Attachment VOL_003 Instructions for Use - Customers*). HeartFlow FFR_{CT} analyses are performed on previously physician-acquired

image data and are unrelated to acquisition equipment and clinical workstations.

5.5 Intended Use

HeartFlow FFR_{CT} is a post-processing software for the clinical quantitative and qualitative analysis of previously acquired Computed Tomography DICOM data for clinically stable symptomatic patients with coronary artery disease. It provides $FFR_{CT,}$ a mathematically derived quantity, computed from simulate pressure, velocity and blood flow information obtained from a 3D computer model generated from static coronary CT images. FFR_{CT} analysis is intended to support the functional evaluation of coronary artery disease.

The results of this analysis are provided to support qualified clinicians to aid in the evaluation and assessment of coronary arteries. The results of HeartFlow FFR_{CT} are intended to be used by qualified clinicians in conjunction with the patient's clinical history, symptoms, and other diagnostic tests, as well as the clinician's professional judgment.

5.5.1 Contraindications

The FFR_{CT} v2.0 Customer Instructions for Use (*VOL_003 Instructions for Use – Customers*) clearly identify for which patient populations and CT scanner manufacturers the product has been clinically validated.

5.5.2 Warnings and Precautions

The warnings and precautions can be found in the FFR_{CT} v2.0 product labeling (*VOL_003 Instructions for Use – Customers*).

5.6 Technological Characteristics of Device

The HeartFlow FFR_{CT} device is a software medical device that allows for the quantitative and qualitative analysis of Coronary Computed Tomography Angiography (cCTA). FFR_{CT} v2.0 is the next generation of the predicate device FFR_{CT} v1.4 and has the same technological characteristics.

5.7 Alternative Practices and Procedures

A wide variety of non-invasive cardiac imaging modalities are available for the evaluation of patients with stable known or suspected coronary artery disease (CAD). These tests are aimed at (1) detection of CAD; (2) determining the severity of disease and risk stratification; and (3) helping to guide clinical decision-making. These modalities include electrocardiography (ECG), echocardiography (ECHO), nuclear myocardial perfusion imaging with single-photon emission tomography (SPECT) and positron emission computed tomography (PET), cardiac magnetic resonance imaging (MRI), and computed tomography coronary angiography (cCTA). Each of these modalities can be applied at rest or under stress conditions (exercise or pharmacologic stress). Non-invasive diagnosis of CAD can be accomplished by anatomic imaging of the coronary artery anatomy using cCTA or MRI or functional testing using SPECT, PET, stress ECHO and stress MRI to evaluate myocardial perfusion and/or wall motion abnormalities. While cCTA has primarily been used to detect the presence of anatomically obstructive coronary lesions, hybrid imaging strategies are now available which incorporate functional assessment with MPI stress testing and CT imaging.[1] This is in response to widespread recognition of the need for a non-invasive anatomic-functional test that can identify obstructive atherosclerotic plaques and also determine their functional significance.[2]

5.7.1 Diagnostic Performance of Non-invasive Cardiac Imaging Modalities

The diagnostic performance of non-invasive cardiac imaging modalities for the diagnosis of CAD is typically determined using invasive coronary angiography as the reference standard. The

determination of the presence or absence of significant coronary obstruction is usually made on the basis of visual estimates of angiographic percent lumen narrowing using a 50% stenosis threshold. However, it is well known that visual estimates of lumen stenosis have limited value in determining the hemodynamic or functional significance of coronary lesions, particularly for moderate coronary stenoses.[6] The determination, prior to coronary revascularization, of the functional significance of observed coronary lesions has been demonstrated to be the most important factor to influence clinical outcomes.[7, 8] Patients with hemodynamic or functionally significant-causing stenoses benefit from revascularization[6, 9] whereas patients with hemodynamically insignificant lesions require no intervention and experience favorable outcomes on medical therapy alone, with myocardial infarction and mortality rates of <1% per year.[10, 11] Thus, the determination of the hemodynamic significance of a lesion is of paramount importance in guiding treatment strategy, and this can be readily accomplished during ICA by measurement of fractional flow reserve (FFR).[12] The accuracy of angiographic visual assessment to determine the functional significance of a coronary stenosis was determined in 1,414 lesions in 509 patients in the FAME study.[13] Only 35% of angiographic stenoses 50-70% were functionally significant with FFR<0.80 and 65% were not. In the category of 71-90% stenosis by visual estimate, 80% were functionally significant and 20% were not. This inaccuracy of visual angiography as the reference standard for evaluating non-invasive imaging modalities tests has prompted calls for the use of FFR as the reference standard.[2]

5.7.1.1 Diagnostic performance of non-invasive cardiac imaging modalities vs visual angiography

The diagnostic performance of non-invasive cardiac imaging modalities using visual angiography as the reference standard is shown in Table 5-1 (data from the 2013 ESC Guidelines).[3]

Table 5-1. Diagnostic performance: visual angiography as reference standard

	DIAGNOSIS OF CAD	
	SENSITIVITY (%)	**SPECIFICITY (%)**
Exercise ECG[a]	45 – 50	85 – 90
Exercise stress echocardiography	80 – 85	80 – 88
Exercise stress SPECT	73 – 92	63 – 87
Dobutamine stress echocardiography	72 – 79	82 – 86
Dobutamine stress MRI[b]	79 – 88	81 – 91
Vasodilator stress echocardiography	72 – 79	92 – 95
Vasodilator stress SPECT	90 – 91	75 – 84
Vasodilator stress MRI	67 – 94	61 – 85
Coronary CTA[c]	95 – 99	64 – 83
Vasodilator stress PET	81 – 97	74 – 91

[a] Results without/with minimal referral bias.

[b] Results obtained in populations with medium-to-high prevalence of disease without compensation for referral bias.

[c] Results obtained in populations with low-to-medium prevalence of disease.

The diagnostic performance (sensitivity and specificity) of a given diagnostic test may vary depending on the disease prevalence in a given patient. Coronary CT is the most sensitive non-invasive test in identifying the presence of CAD, however CT has limited accuracy in determining the functional significance of a lesion and frequently overestimates the severity of a lesion. Even among high-grade stenoses identified by CT and confirmed by angiography, less than half of the lesions are ischemia-causing when compared to FFR.[4, 5]

5.7.1.2 Diagnostic performance of non-invasive cardiac imaging modalities vs Fractional Flow Reserve

The diagnostic performance of the various non-invasive cardiac imaging modalities using fractional flow reserve (FFR) as the reference standard is shown on Table 5-2. There is a significant reduction in diagnostic performance when these modalities are compared to FFR rather than visual angiography as the reference standard.

Table 5-2. Diagnostic performance: measured FFR as reference standard

DIAGNOSTIC PERFORMANCE vs mFFR	SENSITIVITY (%)	SPECIFICITY (%)
Stress ECHO – Jung 2008[14]	46	77
MPI-SPECT – Melikian 2010[15]	48	80
MPI-SPECT – Forster 2009[16]	62	90
MPI-CT+cCTA – Ko 2012[17]	68	98
cCTA – Meijboom 2008[4]	94	48
cCTA – Koo 2011[18]	91	40
cCTA – Min 2012[19]	84	42
Coronary angiography, visual – Meijboom 2008	55	62
Coronary angiography, visual - Park	66	67
Coronary angiography, QCA - Christou meta-analysis 2007[20]	78	51

Note: the sensitivity and specificity for visual angiography vs FFR in this study were 55% and 62% respectively; and for quantitative coronary angiography vs FFR were 57% and 69% respectively.

Summary of meta-analyses: A meta-analysis of 31 studies compared the results of quantitative coronary angiography (QCA) and/or non-invasive imaging of the same lesions versus FFR for the determination of the hemodynamic significance of coronary lesions.[20] Across 18 studies (1,522 lesions), QCA had a sensitivity of 78% (95% CI 67-86%) and specificity of 51% (95% CI 40-61%). In 21 studies (1,249 lesions) with non-invasive imaging, the sensitivity was 76% (95% CR 69-82%) and specificity was 76% (95%CI 71-81%). In the 15 studies with SPECT data (976 lesions), sensitivity was 75% (95% CI 66-82%) and specificity was 77% (95% CI 70-83%). In 6 studies with stress dobutamine echocardiography (273 lesions) sensitivity was 82% (95% CI 62-92%) and specificity was 74% (95% CI 66-81%).

5.8 Marketing History

In July 2011, HeartFlow received CE marking for an earlier version of the FFR_{CT} device and began commercialization of FFR_{CT} in several European countries and Australia. In November 2014, De Novo request for FFR_{CT} v1.4 (DEN130045) was granted by the U.S. Food and Drug Administration. We entered into Japan in 2014 prior to change of regulations and continue to market while the FFR_{CT} application is in process. HeartFlow received Canadian Medical Device License in August 2015. To date, FFR_{CT} has not been withdrawn from any foreign market for any reason relating to the safety and effectiveness of the device.

5.9 Potential Adverse Effects of the Device on Health

FFR_{CT} is a post-processing analysis of previously acquired CT images, such that there are no potential adverse effects of the device on health to the patient or requesting clinician. Risks related to the accuracy of the results and clinician interpretation/inclusion in their diagnosis and treatment are identified in the product labeling.

5.10 Summary of Studies

The software was designed, developed, tested and validated according to written procedures. These procedures specify individuals within the organization responsible for developing and approving

product specifications, coding, testing, validating and maintenance.

Validation studies included stress testing, and repeatability testing to ensure the safety and effectiveness of the device.

Software and medical device design validation has been completed. Medical device design included testing and evaluation using previously acquired diagnostic images received through HeartFlow sponsored clinical trials. The results concluded the device was acceptable for use.

5.10.1 Summary of Pre-clinical Studies

Pre-clinical studies of the computational methods underlying HeartFlow's FFR_{CT} technology were conducted at Stanford University in Dr. Charles A. Taylor's laboratory. The solver technology developed at Stanford University was licensed to HeartFlow. The pre-clinical studies performed at Stanford include extensive bench top experiments and *in-vivo* animal model validations. The results of these studies have been published in 6 peer-reviewed journal papers[21-26] and are summarized below. Additional pre-clinical studies have not been conducted at HeartFlow, since bench and animal models do not permit evaluation of our technology in relevant anatomic or physiologic models reflecting diseased human coronary vessels. Rather, we have validated our technology against measured fractional flow reserve, the standard of care *in-vivo* measurement in humans for the determination of hemodynamic significance of coronary lesions.

5.10.2 Summary of Clinical Studies

HeartFlow has conducted three primary clinical studies involving validation of FFR_{CT} to date. These studies were conducted with prior versions of the software. HeartFlowNXT provided the clinical validation for the predicate device, FFR_{CT} v1.4. The current version of software product represented in this 510(k), version 2.0, was clinically validated using the sequestered HeartFlowNXT dataset to evidence equivalence.

5.10.2.1 HeartFlowNXT

HeartFlow analysis of coronary blood flow using coronary CT angiography: NeXt sTeps (the HeartFlowNXT or HFNXT study) was a prospective, multicenter, non-randomized study. The overall objective of the HFNXT study was to determine the diagnostic performance of FFR_{CT}, as compared to cCTA alone, for the non-invasive determination of the presence of a hemodynamically significant coronary lesions using direct measurement of FFR (≤0.80) during cardiac catheterization as the reference standard. The rationale and design of the study is in press (*Attachment VOL_004 SEC 013 Gaur_JCCT_2013*) and the study reflects improvements in FFR_{CT} technology (software version v1.4) and a focus on quantitative image-quality analysis.

The study was conducted at 11 sites in 8 countries in Canada, Europe and Asia from September 2012 to August 2013, with 276 subjects enrolled. A total of 254 adult subjects with known or suspected coronary artery disease who were scheduled for clinically indicated invasive coronary angiography comprised the intention-to-diagnose (ITD) population. Subjects had an overall mean age of 63.7 years and 63.8% were men. A total of 22.8% had diabetes mellitus, 68.5% had hypertension, 78.7% had hyperlipidemia, 57.1% were current or former smokers. Also, 77.6% presented with angina in the 30 days prior to enrollment; 77.7% of subjects with angina had stable angina and 22.3% had unstable angina. Only 2% had documented prior history of myocardial infarction and no patients had renal dysfunction, defined as creatinine >1.5 mg/dL. The mean body mass index for enrolled subjects was 25.6 ± 3.7 kg/m^2. Left ventricular ejection fraction was reported for 76% of the enrolled subjects with a mean value of 61.8%. The time from the cCTA

scan to the ICA procedure was between 1 to 30 days in 87% of the ITD patients with a mean of 18.1 days. Sublingual or intravenous nitrates were administered in 99.6% of subjects undergoing coronary artery CT scanning. In 78% of the subjects beta blockers were administered to reduce heart rate prior to scan. The mean calcium score for ITD subjects was 302 (±468) Agatston units. A calcium score was reported for 84.3% of subjects, and of these, 25.7% had a calcium score > 400 Agatston units.

Direct comparison of invasive FFR and FFR_{CT} was performed in 484 vessels. At least one invasive FFR measurement was collected in all ITD subjects with an average of 1.9 measurements per subject. All invasive FFR data was reviewed by an independent FFR/QCA core laboratory.

The primary endpoint was the per-vessel sensitivity and specificity of FFR_{CT} to detect hemodynamically significant obstruction when FFR was used as the reference standard. The pre-specified target goals for sensitivity and specificity were 65% and 55%, respectively.

5.10.2.1.1 HeartFlow NXT study results

Primary endpoint success required both sensitivity and specificity hypotheses to be met. The per-vessel sensitivity of FFR_{CT} in the ITD population was 83.5% with a lower one-sided 95% CI of 75.3%. The per-vessel specificity of FFR_{CT} in the ITD population was 85.8% with a lower one-sided 95% CI of 81.5%. Both of the lower one-sided confidence limits for sensitivity and specificity were above the pre-specified target goals of 65% and 55%, respectively, therefore the primary endpoint was met. Results are shown in Table 5-3 below.

Table 5-3. HeartFlowNXT Primary Endpoint Results: Per-Vessel Sensitivity and Specificity of FFR_{CT} Intent To Diagnose Population

	ESTIMATE, %	LOWER ONE-SIDED 95% CONFIDENCE BOUND	TARGET RATE	MET[1] NOT MET
Sensitivity	83.5%	75.3%	65%	MET
Specificity	85.8%	81.5%	55%	MET
FFR is used as the reference standard FFR_{CT}: Diseased if hemodynamically-significant obstruction is ≤ 0.80 FFR: Diseased if hemodynamically-significant obstruction is ≤ 0.80 [1]MET if 95% LCL > Target Rate				

Per-subject FFR_{CT} specificity compared to site-read cCTA demonstrated superior diagnostic ability (p<0.001) in the intent to diagnose (ITD) subjects in one or more major epicardial coronary artery segments, using invasive FFR as the reference standard and defining hemodynamically-significant obstruction of a coronary artery (positive result) as an FFR ≤ 0.80 for both FFR and FFR_{CT} and as > 50% stenosis severity for site-read cCTA. Diagnostic performance of FFR_{CT} compared to site-read cCTA on the subject level is shown in Table 5-4 below.

Table 5-4. HeartFlowNXT Per-Subject Diagnostic Performance Analysis with FFR ≤ 0.80 as the Reference Standard. Intent to Diagnose Population.

	FFR_{CT} ≤ 0.80 ESTIMATE % (95% Wilson CI)	SITE-READ cCTA > 50% ESTIMATE % (95% Wilson CI)
Diagnostic Accuracy	81.1% (95.8%-85.4%)	52.8% (46.6%-58.8%)
Sensitivity	86.3% (77.0%-92.1%)	93.8% (86.2%-97.3%)
Specificity	78.7% (72.1%-84.2%)	33.9% (27.3%-41.2%)

PPV	65.1% (55.6%-73.5%)	39.5% (32.8%-46.6%)
NPV	92.6% (87.2%-95.8%)	92.2% (83.0%-96.6%)

The HeartFlowNXT study demonstrated good diagnostic performance for FFR_{CT} when all vessels were included, irrespective of size, location, or territory, and across a range of cCTA image quality measures. Further detail on the HeartFlowNXT study is provided in *Attachment VOL_003 HeartFlowNXT Clinical Study Report*.

Select published articles and in process manuscripts may be found in *VOL_004*.

5.10.2.2 FFR_{CT} v2.0 Clinical Validation

The sequestered HeartFlowNXT data was re-processed with FFR_{CT} v2.0, and analyzed per the HeartFlowNXT statistical analysis plan to demonstrate product equivalence through clinical validation. A summary of the results is presented below and in the Customer IFU (*Attachments VOL_003 Instructions for Use – Customers*); detailed results can be found in *Attachments VOL_003 FFR_{CT} v2.0 Clinical Validation Report*.

5.10.2.2.1 FFR_{CT} v2.0 Clinical Validation Results

Primary endpoint success required both sensitivity and specificity hypotheses to be met. The per-vessel sensitivity of FFR_{CT} in the ITD population was 84.2% with a lower one-sided 95% CI of 75.8%. As this was above the protocol specified target goal of 65%, the first null hypothesis was rejected and FFR_{CT} was considered to have met the sensitivity target goal. The per-vessel specificity of FFR_{CT} in the ITD population was 84.9%. The lower one-sided 95% CI was 80.4% and was above the protocol specified target goal of 55%, therefore the second null hypothesis was rejected and FFR_{CT} was considered to have met the specificity target goal.

Table 5-5. Primary Endpoint Analysis: Per-Vessel Sensitivity and Specificity of FFR_{CT} v2.0.2 Intent To Diagnose Population

	ESTIMATE, %	LOWER ONE-SIDED 95% CONFIDENCE BOUND	TARGET RATE	MET[1]/ NOT MET
Sensitivity	84.2%	75.8%	65%	MET
Specificity	84.9%	80.4%	55%	MET
FFR is used as the reference standard FFR_{CT}: Diseased if hemodynamically-significant obstruction is ≤ 0.80 FFR: Diseased if hemodynamically-significant obstruction is ≤ 0.80 [1]MET if 95% LCL > Target Rate				

Per-subject FFR_{CT} specificity compared to site-read cCTA demonstrated superior diagnostic ability (p<0.001) in the intent to diagnose (ITD) subjects in one or more major epicardial coronary artery segments, using invasive FFR as the reference standard and defining hemodynamically-significant obstruction of a coronary artery (positive result) as an FFR ≤ 0.80 for both FFR and FFR_{CT} and as > 50% stenosis severity for site-read cCTA. Diagnostic performance of FFR_{CT} compared to site-read cCTA on the subject level is shown in Table 5-6.

Table 5-6. HeartFlowNXT Per-Subject Diagnostic Performance Analysis with FFR ≤ 0.80 as the Reference Standard. Intent to Diagnose Population.

	FFR_{CT} ≤ 0.80 ESTIMATE % (95% WILSON CI)	**SITE-READ CCTA > 50% ESTIMATE % (95% WILSON CI)**
Diagnostic Accuracy	80.0% (74.4%-84.6%)	51.9% (45.5%-58.2%)
Sensitivity	87.8% (78.5%-93.5%)	93.2% (85.1%-97.1%)
Specificity	76.4% (69.3%-82.3%)	32.9% (26.1%-40.5%)
PPV	63.1% (53.5%-71.8%)	39.0% (32.1%-46.3%)
NPV	93.2% (87.5%-96.4%)	91.4% (81.4%-96.3%)

The validation study demonstrated good diagnostic performance for FFR_{CT} when all vessels were included, irrespective of size, location, or territory, and across a range of cCTA image quality measures. Further details can be found in *VOL_003 FFR_{CT} 2.0 Clinical Validation Report*.

5.11 Conclusions Drawn from Studies

5.11.1 Effectiveness Conclusions

Based on multiple studies conducted with FFR_{CT} and confirmed by clinical validation, FFR_{CT} analysis is additive to cCTA review alone by the physician when compared to an invasively measured standard.

5.11.2 Safety Conclusions

Safety was not a primary objective evaluated in any study conducted by HeartFlow given the non-invasive nature of the device; FFR_{CT} is just an additional data point for consideration in patient diagnosis and treatment. Data collected in HeartFlow's studies, and commercially, has not raised any new issues related to safety of FFR_{CT}.

5.11.3 Benefit-Risk Conclusions

FFR_{CT} analysis provides one additional data point to clinicians diagnosing coronary artery disease and can be performed without additional imaging, added radiation, modification of Society recommended image acquisition protocols, or administration of additional medications. The risks associated with FFR_{CT} are the same as all other non-invasive tests, a false negative or positive result. Given the increased specificity offered by FFR_{CT} over cCTA alone the benefits of using FFR_{CT} far outweigh the risks.

5.12 **Bibliography**

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