510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K254115

B Applicant

Artera Inc.

C Proprietary and Established Names

ArteraAI Breast

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SHW	Class II	21 CFR 864.3755 Software algorithm device analyzing digital images for cancer prognosis	88 – PATHOLOGY

II Submission/Device Overview:

A Purpose for Submission:

1. New device
2. Establish a Predetermined Change Control Plan (PCCP) to add additional FDA-cleared interoperable scanners and file formats.

B Type of Test:

Software only device

III Intended Use/Indications for Use:

A Indication(s) for Use:

ArteraAI Breast is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from treatment-naive breast resection specimens prepared from formalin fixed paraffin-embedded (FFPE) tissue and stained using Hematoxylin & Eosin (H&E) stains. Additional inputs to ArteraAI Breast include the following physician-provided clinical variables:

- Age
- Tumor size
- Nodal status

ArteraAI Breast provides 5- and 10-year risks of distant metastasis and ArteraAI risk score for adult patients with HR+/HER2-, N0 or N1, early-stage invasive breast cancer without clinically or pathologically defined metastases after surgical tumor resection and who are candidates for standard of care adjuvant therapy. ArteraAI Breast is intended to assist physicians with prognostic risk-based decisions along with other clinicopathological factors.

ArteraAI Breast is intended to utilize WSIs acquired from FDA-cleared interoperable scanners and file formats that have been validated for use with this device.

B Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Warnings

1. The ArteraAI Breast should be used in conjunction with a complete standard of care evaluation.
2. The ArteraAI Breast patient report is to be utilized by trained physicians after being released by the pathology laboratory user.
3. The ArteraAI Breast results correctness is based on the quality requirements of the slide images and appropriate whole slide imaging scanner usage.
4. Ensure proper traceability of the scanned images to the patient using an anonymized patient ID.

Please refer to the device labeling for a complete list of Warnings and Precautions.

C Special Instrument Requirements:

Philips Ultra Fast Scanner (K172174) or Leica Aperio GT450 DX (K232202)

IV Device/System Characteristics:

A Device Description:

ArteraAI Breast is a software only device that utilizes artificial intelligence-based deep learning algorithms developed with WSIs of H&E-stained breast resection specimens to assess risk of distant metastasis in adult patients with hormone receptor positive (HR+)/Human Epidermal Growth Factor Receptor 2 negative (HER2-) breast cancer. The software performs an algorithmic assessment of clinical variables and features extracted from WSI using self-supervised learning. ArteraAI Breast consists of the AI Engine, consisting of multiple building block models that intake physician-provided clinical variables and image data to calculate an ArteraAI risk score, which is further binned to estimate observed 5- and 10-year distant metastasis rates in the clinical validation cohort. The product also outputs a categorical risk group (Low or High) based on the ArteraAI risk score. The algorithm is locked; it is not a continuous learning (continual machine learning model) algorithm.

Table 1: ArteraAI Breast Overview

Component Name	Description / Function
ArteraAI Platform	
ArteraAI Web Portal	This component allows users to interact with the platform to perform the following functions: 1. Select the test to be performed 2. Input the data 3. Pass the data to the ArteraAI Back-End component 4. Receive the report generated for the given ID 5. Manage the records from the previously executed tests 6. Access instructions for use and labeling information This component does not modify the image content or take any action other than transmitting WSIs to the back end.

Component Name	Description / Function
ArteraAI Back End	This component manages the task execution of other components. It performs the following functions: 1. Send and retrieve data associated with a given ID to/from the database 2. Start ArteraAI Image Converter jobs and pass the location of the WSI file to the ArteraAI Image Converter 3. Start AI jobs and pass location of slide images to the ArteraAI AI Engines 4. Compile PDF reports 5. Manage user authentication This component does not modify the image content or take any action other than transmitting WSI files to ArteraAI Breast AI Engine and ArteraAI Image Converter and populating the PDF reports with results from the ArteraAI Breast AI Engines.
ArteraAI Image Converter	The ArteraAI Image Converter converts WSI files to a file format usable by the ArteraAI Breast AI Engine (TIFF). The algorithms to process iSyntax images are in scripts provided by Philips and implemented using the Artera wrapper. The component is a software function solely intended to convert image formats (iSyntax to TIFF). This step is not required for WSIs in native SVS file format as these files do not need conversion to TIFF because they are already specialized, multi-resolution Tiled TIFF images.
ArteraAI Breast	
ArteraAI Breast AI Engine	Subject device that performs the medical function as described in the intended use.

Device Input:

The two inputs to the ArteraAI Breast device are listed below:

1. WSIs of H&E-stained breast resection specimen scanned to a digital image format via the Philips Ultra Fast Scanner (K172174) or Leica Aperio GT450 DX (K232202) with Settings below:
    - Philips Ultra Fast Scanner Settings:
      Magnification: 40x Resolution: 0.25 µm/pixel
      File format: iSyntax, Philips proprietary file format with either RAW or iSyntax compression
    - Leica Aperio GT450 Dx Settings:
      Magnification: 40x Resolution: 0.26 µm/pixel
      File format: SVS

2. Clinical Variable Inputs: Age, Tumor size and Nodal status

All WSIs from breast resection specimen slides with the same highest tumor grade as determined by the pathologist are uploaded to the ArteraAI web portal which are then analyzed by the ArteraAI Breast device. The above-mentioned clinical variables are also uploaded to the ArteraAI web portal. The ArteraAI Breast device initially calculates a raw score for a patient. Then one cut-off C1 is applied to the raw score for determination of the ArteraAI Breast risk categories:

Raw Score > C1, then category=High
Raw Score ≤C1, then category=Low
The highest ArteraAI Breast risk category is provided in the patient report.

Device Output:

The test output is a patient specific report, which includes the following:

- An ArteraAI Risk Score.
- An ArteraAI categorical risk group (Low or High), based on the ArteraAI Risk Score.
- Observed 5-Year Distant Metastasis (DM) Risk (in the clinical validation dataset)
- Observed 10-Year DM Risk (in the clinical validation dataset)

The ArteraAI Breast test report is intended to be interpreted by the treating clinician to aid in understanding the risk of distant metastasis in breast cancer patients. The results are provided to support risk-based decisions within the recommended professional guidelines.

B Principle of Operation

ArteraAI Breast is intended to be operated within a pathology laboratory with digital scanning capabilities. The ArteraAI Breast workflow is depicted in Figure 1 below.

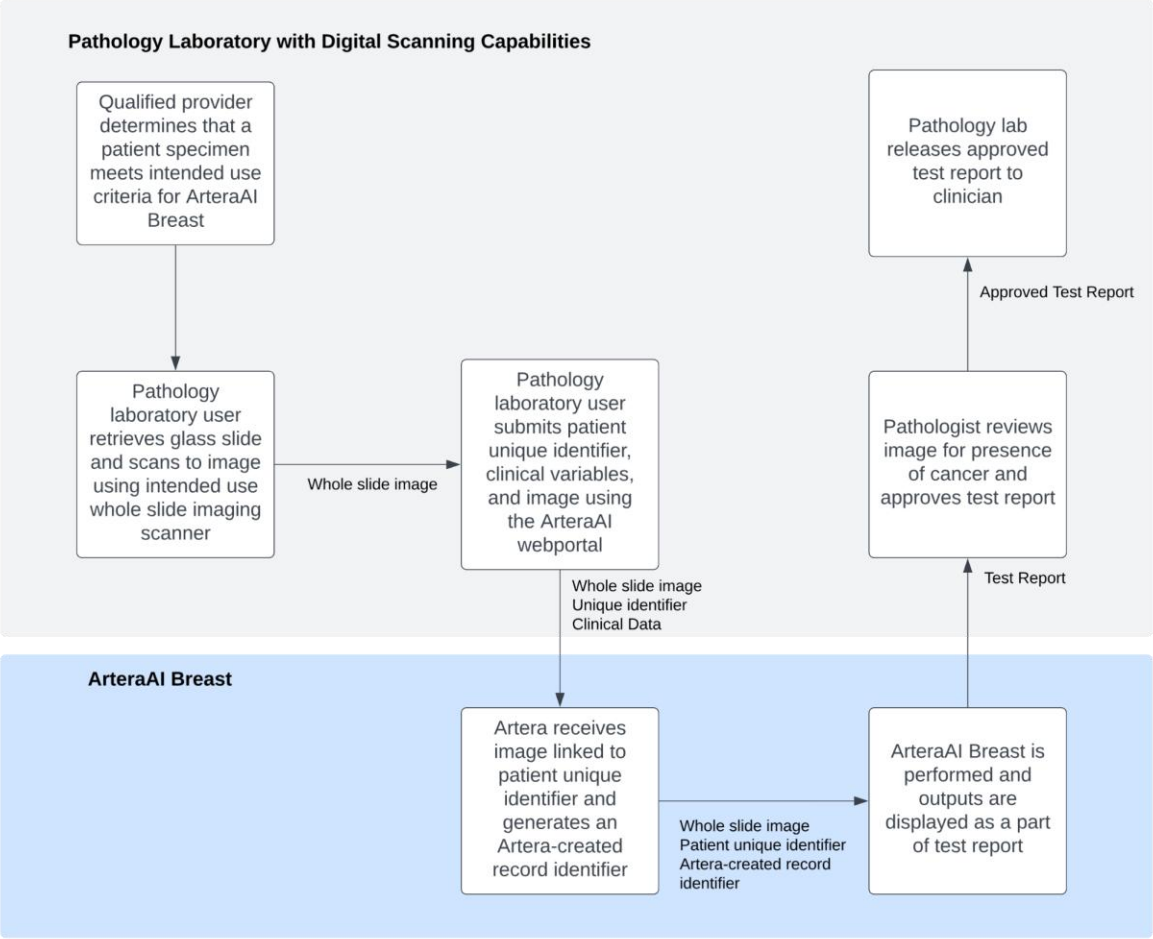


Figure 1. Workflow depicting the steps to operate ArteraAI Breast

ArteraAI Breast is operated as follows:

1. ArteraAI Breast is performed on WSI images of breast resection specimens after a patient's diagnosis of breast cancer per standard of care. A qualified pathologist must have already determined that breast cancer is present in the patient's breast resection specimen.
2. WSIs of glass slides of H&E stained FFPE tissue from breast resection specimens are obtained using intended use scanners (FDA-cleared Philips Ultra Fast scanner or Leica Aperio GT450 Dx) at 40x magnification in accordance with the scanner's Instructions for Use.
3. The WSIs are reviewed to verify that the image is not blurry, no defects are present and the whole tissue region is included in the image. Additional image and other related quality control steps are performed per the ArteraAI Breast Instructions for Use.
4. All WSIs from breast resection specimen slides with the same highest tumor grade as determined by the pathologist are uploaded as inputs to the ArteraAI web portal along with a unique patient identifier and the clinical variables specified in the device input section above. This information is then transferred to Artera's back-end infrastructure.

The patient identifier is intended to provide end-to-end traceability while protecting patient health information privacy.

5. During the WSI transfer process, a web worker (thread), which is a web browser feature, is used to manage the upload of the WSI to parallelize the data transfer. This allows the image and other data upload to proceed in the background, allowing the operator to continue interacting with the system without interruption.
6. ArteraAI Breast produces a test report that summarizes the ArteraAI Breast results and transfers the test report to the pathology laboratory via the ArteraAI web portal.
7. The pathologist will confirm the presence of cancer within the uploaded WSI, review and approve the report in accordance with the local laboratory procedures and release the test report to the requesting clinician.

C. ArteraAI Breast Algorithm Model Development

The AI algorithm used in the ArteraAI Breast was developed using deep learning machine learning algorithms trained on WSIs of H&E- stained breast resection specimen slides from multiple, multi-center, prospective randomized controlled clinical trials and clinical studies to assess 5-year and 10-year risk of DM. ArteraAI Breast was trained on a dataset comprising digitized pre-treatment biopsy and surgical slides from 8,549 patients from four trials — WSG ADAPT, WSG PlanB, NSABP B34, and ABCSG 6 — incorporating specific image-based features alongside clinical variables including age, tumor size, nodal status to predict risk of DM. Once a final model candidate was selected, a cut-off for the prognostic score to determine the Low and High-risk groups was developed using a subset of held out prognostic model validation data (n=946) as well as 2,188 patients from NSABP B14 and 1,198 patients from NSABP B39. Cut-off between risk groups were chosen to ensure sufficient sample sizes within risk categories, balancing statistical power for future validation and clinical interpretability. There were 997 distant metastasis events in the dataset used to develop the model. Detailed information about training and calibration datasets is presented in Table 2 below:

Table 2: Characteristics of Training Dataset

	Study Name					
Characteristic	**ADAPT** N = 4,475	**PlanB** N = 2,872	**B-34** N = 2,485	**ABCSG-6** N = 1,144	**B-14** N = 3,830	**B-39** N = 1,747
Sample Type, n (%)						
Baseline Biopsy	4,475 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Baseline Resection	0 (0.0%)	2,872 (100.0%)	2,485 (100.0%)	1,144 (100.0%)	3,830 (100.0%)	1,747 (100.0%)
Randomization Year						
Range	2012 - 2019	2009 - 2017	2001 - 2004	1990 - 1996	1981 - 1988	2005 - 2013

Study Name						
Characteristic	**ADAPT** N = 4,475	**PlanB** N = 2,872	**B-34** N = 2,485	**ABCSG-6** N = 1,144	**B-14** N = 3,830	**B-39** N = 1,747
Race						
Black	0 (0.0%)	0 (0.0%)	169 (6.8%)	0 (0.0%)	180 (4.7%)	83 (4.8%)
White	0 (0.0%)	0 (0.0%)	2,102 (84.6%)	0 (0.0%)	3,481 (90.9%)	1,626 (93.1%)
Other	0 (0.0%)	0 (0.0%)	207 (8.3%)	0 (0.0%)	120 (3.1%)	21 (1.2%)
Unknown/Missing	4,475 (100.0%)	2,872 (100.0%)	7 (0.3%)	1,144 (100.0%)	49 (1.3%)	17 (1.0%)
Age at Baseline (year)						
Median (Range)	55 (20 - 85)	55 (25 - 77)	54 (24 - 86)	64 (40 - 80)	57 (21 - 76)	56 (25 - 89)
Unknown/Missing	756	0	0	0	0	0
Menopausal Status, n (%)						
Pre/peri-menopausal	1,478 (33.0%)	905 (31.5%)	734 (29.5%)	0 (0.0%)	1,135 (29.6%)	632 (36.2%)
Post-menopausal	2,241 (50.1%)	1,451 (50.5%)	899 (36.2%)	1,144 (100.0%)	2,675 (69.8%)	1,115 (63.8%)
Unknown/Missing	756 (16.9%)	516 (18.0%)	852 (34.3%)	0 (0.0%)	20 (0.5%)	0 (0.0%)
Tumor Size (cm)						
Median (Range)	1.7 (0.0 - 18.0)	1.9 (0.1 - 18.0)	1.7 (0.0 - 10.0)	1.8 (0.2 - 10.0)	2.0 (0.1 - 13.5)	1.2 (0.0 - 3.0)
Unknown/Missing	859	302	5	4	295	159
T Stage, n (%)						
Tis	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (0.3%)
T1	2,109 (47.1%)	1,424 (49.6%)	1,686 (67.8%)	669 (58.5%)	2,234 (58.3%)	1,361 (77.9%)
T2	1,507 (33.7%)	1,044 (36.4%)	747 (30.1%)	440 (38.5%)	1,218 (31.8%)	222 (12.7%)
T3	84 (1.9%)	86 (3.0%)	47 (1.9%)	31 (2.7%)	83 (2.2%)	0 (0.0%)

Study Name						
Characteristic	**ADAPT** N = 4,475	**PlanB** N = 2,872	**B-34** N = 2,485	**ABCSG-6** N = 1,144	**B-14** N = 3,830	**B-39** N = 1,747
T4	16 (0.4%)	16 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Unknown/Missing	759 (17.0%)	302 (10.5%)	5 (0.2%)	4 (0.3%)	295 (7.7%)	159 (9.1%)
Nodal Stage, n (%)						
N0	3,198 (71.5%)	1,778 (61.9%)	1,911 (76.9%)	711 (62.2%)	3,811 (99.5%)	1,494 (85.5%)
N1	455 (10.2%)	933 (32.5%)	420 (16.9%)	299 (26.1%)	19 (0.5%)	253 (14.5%)
N2-3	62 (1.4%)	161 (5.6%)	154 (6.2%)	130 (11.4%)	0 (0.0%)	0 (0.0%)
Unknown/Missing	760 (17.0%)	0 (0.0%)	0 (0.0%)	4 (0.3%)	0 (0.0%)	0 (0.0%)
Tumor Grade, n (%)						
G1	302 (6.7%)	127 (4.4%)	552 (22.2%)	191 (16.7%)	0 (0.0%)	559 (32.0%)
G2	2,073 (46.3%)	1,608 (56.0%)	1,013 (40.8%)	647 (56.6%)	0 (0.0%)	677 (38.8%)
G3	1,342 (30.0%)	1,122 (39.1%)	873 (35.1%)	228 (19.9%)	0 (0.0%)	489 (28.0%)
Unknown/Missing	758 (16.9%)	15 (0.5%)	47 (1.9%)	78 (6.8%)	3,830 (100.0%)	22 (1.3%)

Note that the sample size indicated in this table is based on patient cases with available WSIs. some patients may have been excluded due to missing DM information, confirmed HR-/ HER2+ status, or failed score generation. Overall, 11,935 patients from the above datasets were used to develop the model.

D. Software and Cybersecurity

ArteraAI Breast software documentation and software verification and validation testing demonstrate that the device followed all recommendations for basic documentation level as outlined in the FDA guidance document, "*Content of Premarket Submissions for Device Software Functions," issued on June 14, 2023*. A description of the testing protocols, including pass/fail criteria, and report of results were provided for the verification and validation activities and all testing results met design specifications and passed the acceptance criteria.

ArteraAI Breast cybersecurity documentation demonstrated that the device met the

cybersecurity requirements as outlined in Section 524B of Federal Food, Drug, and Cosmetic Act (FD&C Act). This includes a threat model, software bill of materials, data security training, validation and mitigation of cybersecurity risks, cyber risk management, labeling, cyber testing, and post market cyber vulnerabilities and other information for safeguarding the algorithms.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ArteraAI Prostate

B Predicate 510(k) Number(s):

DEN240068

C Comparison with Predicate(s):

Device & Predicate Device(s):	K254115 ArteraAI Breast	DEN240068 ArteraAI Prostate
General Device Characteristic Similarities		
	Software-only medical device (AI-based image analysis plus clinical variables) that uses a deep learning model trained on FFPE tissue / H&E whole-slide images to generate risk scores, risk of distant metastasis, and risk categorization (Low / High).	Software-only medical device (AI-based image analysis) that uses a deep learning model trained on FFPE tissue / H&E whole-slide images to generate risk scores, risk of distant metastasis, and risk categorization (Low / Intermediate / High).
Intended Use/Indications For Use	ArteraAI Breast is a software only device intended to analyze scanned histopathology whole slide image (WSI) from treatment-naïve breast resection specimens prepared from formalin fixed paraffin-embedded (FFPE) tissue and stained using Hematoxylin &	ArteraAI Prostate is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from treatment-naïve prostate core needle biopsies prepared from formalin fixed paraffin-embedded (FFPE) tissue and stained using

	Eosin (H&E) stains. Additional inputs to ArteraAI Breast include the following physician-provided clinical variables: ● Age ● Tumor size ● Nodal status ArteraAI Breast provides 5- and 10-year risks of distant metastasis and ArteraAI risk score for adult patients with HR+/HER2-, N0 or N1, early-stage invasive breast cancer without clinically or pathologically defined metastases after surgical tumor resection and who are candidates for standard of care adjuvant therapy. ArteraAI Breast is intended to assist physicians with prognostic risk-based decisions along with other clinicopathological factors. ArteraAI Breast is intended to utilize WSIs acquired from FDA-cleared interoperable scanners and file formats that have been validated for use with this device.	Hematoxylin & Eosin (H&E) stains. ArteraAI Prostate provides 10-year risks of distant metastasis and prostate cancer specific mortality and is intended to assist physicians with prognostic risk-based decisions along with other clinicopathological factors in non-metastatic prostate cancer patients. ArteraAI Prostate is intended for males 55 years of age or older without clinically or pathologically defined metastases, and who are candidates for curative intent management (surgery, radiation therapy with or without systemic therapy, or active surveillance). ArteraAI Prostate is intended to utilize WSIs acquired from an FDA-cleared interoperable scanner with which ArteraAI Prostate has been authorized for use or a 510(k)-cleared scanner that has been assessed in accordance with the Predetermined Change Control Plan (PCCP) for qualifying additional interoperable scanners.
General Device Characteristic Differences		
Indication	Breast Cancer	Prostate Cancer
Risk Groups	Low, High	Low, Intermediate, High

Specimen Type	FFPE breast resection sample	FFPE prostate biopsy sample

Predetermined Change Control Plan (PCCP):

In addition to the similarities and differences between the candidate and predicate devices listed in the table above, the candidate device has an authorized PCCP with the following modification:

Addition of additional FDA-cleared interoperable whole slide image (WSI) scanners and file formats that have been validated for use with this device. See Section VIII for more information.

VI Standards/Guidance Documents Referenced:

1. Guidance for the Content of Premarket Submissions for Device Software Functions; June 2023
2. CLSI document EP05- A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition; September 2014
3. CLSI document EP12-Ed3: Evaluation of Qualitative, Binary Output Examination Performance; March 2023
4. Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions; September 2023
5. The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]; July 2014
6. Guidance for Industry and FDA Staff: De Novo Classification Process (Evaluation of Automatic Class III Designation); October 2021
7. Acceptance of Clinical Data to Support Medical Device Applications and Submissions Frequently Asked Questions; February 2018
8. Guidance for Industry and Food and Drug Administration Staff - Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications; August 2019
9. Guidance for Off-the-Shelf Software Use in Medical Devices; August 2023
10. ISO 14971 Third Edition 2019-12 Medical devices - Application of risk management to medical devices
11. IEC 62304 Edition 1.1 2015-06 (2015). Medical device software – Software life cycle processes
12. IEC 62366-1 Edition 1.1 2020-06 CONSOLIDATED VERSION – Medical devices – Part 1: Application of usability engineering to medical devices

VII Performance Characteristics:

A Analytical Performance:

1. Precision/Reproducibility:

The precision of ArteraAI Breast device was evaluated in a between-site reproducibility study which was performed at three laboratory sites in the United States. At each site, slides were scanned by a single operator on a Philips Ultra Fast scanner and Leica Aperio GT 450 DX at 40x objective, with one scan per day, over five non-consecutive days (15 replicates in total for 3 sites for the two different scanner models). Fifty samples (including 6 borderline samples based on ArteraAI Breast raw score cut-off) were included in the between-site reproducibility study and these patient samples were selected from intended use population. The sample characteristics are provided in Table 3 below.

Table 3: Characteristics of Samples Used in Analytical Studies

Characteristic	**N = 50**	
Age (year), Median, (Range)	63, (28, 81)	
Age <50	15 (30.0%)	
Age 50+	35 (70.0%)	
Tumor Size (cm), Median, (Range)	2.0, (0.2, 7.2)	
N Stage		
N0, n (%)	34 (68.0%)	
N1, n (%)	16 (32.0%)	
ArteraAI Risk Group (Case-Level Mode)	**Philips Ultra Fast Scanner**	**Leica Aperio GT 450DX Scanner**
Low Risk, n (%)	25 (50.0%)	26 (52.0%)
High Risk, n (%)	25 (50.0%)	24 (48.0%)
Borderline Group (Case-Level Mean)	**Philips Ultra Fast Scanner**	**Leica Aperio GT 450DX Scanner**
Borderline Case, n (%)	7 (14.0%)	6 (12.0%)
Non-Borderline Case, n (%)	43 (86.0%)	44 (88.0%)

Summary of Analytical Validation Study Results:

a. Analysis of numeric values of the raw score using both scanners (Philips Ultra Fast and Leica Aperio GT 450DX) was performed according to CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures, 3rd Edition. Within-laboratory, between-site and reproducibility were calculated; in addition, a qualitative analysis (percent of each ArteraAI categories among 15 replicates) was performed and results of these analyses are presented in Table 4 (Philips Ultra Fast) and Table 5 (Leica Aperio GT 450DX).

b. The %CV for the within-site precision for the Philips Ultra Fast Scanner (the same scanner on different days) ranged from 0.2% to 8.4%; the %CV for the between-site precision component ranged from 0.0% to 3.9% and %CV for reproducibility (which includes within-site precision and between-site component) ranged from 0.4% to 8.4%.

Table 4: Within-Site Precision and Reproducibility of ArteraAI Raw Score (Philips Ultra Fast Scanner)

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results	
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent High
1	10.5	Low	Non-Borderline	0.887	8.4	0.000	0.0	0.887	8.4	100.0%	100.0%	100.0%	100.0%	0.0%
2	19.8	Low	Non-Borderline	0.558	2.8	0.084	0.4	0.564	2.9	100.0%	100.0%	100.0%	100.0%	0.0%
3	20.7	Low	Non-Borderline	0.222	1.1	0.165	0.8	0.276	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
4	21.1	Low	Non-Borderline	0.311	1.5	0.201	1.0	0.370	1.8	100.0%	100.0%	100.0%	100.0%	0.0%
5	21.2	Low	Non-Borderline	0.641	3.0	0.185	0.9	0.667	3.1	100.0%	100.0%	100.0%	100.0%	0.0%
6	21.3	Low	Non-Borderline	0.612	2.9	0.000	0.0	0.612	2.9	100.0%	100.0%	100.0%	100.0%	0.0%
7	21.9	Low	Non-Borderline	0.331	1.5	0.161	0.7	0.368	1.7	100.0%	100.0%	100.0%	100.0%	0.0%
8	22.6	Low	Non-Borderline	0.508	2.2	0.671	3.0	0.842	3.7	100.0%	100.0%	100.0%	100.0%	0.0%
9	24.1	Low	Non-Borderline	0.731	3.0	0.000	0.0	0.731	3.0	100.0%	100.0%	100.0%	100.0%	0.0%
10	24.3	Low	Non-Borderline	0.569	2.3	0.169	0.7	0.594	2.4	100.0%	100.0%	100.0%	100.0%	0.0%
11	25.9	Low	Non-Borderline	0.533	2.1	0.279	1.1	0.602	2.3	100.0%	100.0%	100.0%	100.0%	0.0%
12	26	Low	Non-Borderline	0.263	1.0	0.221	0.9	0.343	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
13	26.4	Low	Non-Borderline	0.199	0.8	0.296	1.1	0.356	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
14	26.5	Low	Non-Borderline	0.369	1.4	0.333	1.3	0.497	1.9	100.0%	100.0%	100.0%	100.0%	0.0%
15	26.6	Low	Non-Borderline	0.237	0.9	0.253	0.9	0.346	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
16	26.7	Low	Non-Borderline	0.392	1.5	0.000	0.0	0.392	1.5	100.0%	100.0%	100.0%	100.0%	0.0%
17	27.3	Low	Non-Borderline	0.335	1.2	0.046	0.2	0.338	1.2	100.0%	100.0%	100.0%	100.0%	0.0%
18	27.4	Low	Non-Borderline	0.143	0.5	0.208	0.8	0.252	0.9	100.0%	100.0%	100.0%	100.0%	0.0%
19	27.5	Low	Non-Borderline	0.329	1.2	0.338	1.2	0.472	1.7	100.0%	100.0%	100.0%	100.0%	0.0%
20	27.8	Low	Borderline	0.217	0.8	0.278	1.0	0.353	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
21	27.9	Low	Borderline	0.433	1.6	0.268	1.0	0.509	1.8	100.0%	100.0%	100.0%	100.0%	0.0%
22	27.9	Low	Borderline	0.375	1.3	0.335	1.2	0.503	1.8	100.0%	100.0%	100.0%	100.0%	0.0%
23	28	Low	Borderline	0.408	1.5	0.000	0.0	0.408	1.5	100.0%	100.0%	100.0%	100.0%	0.0%

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results	
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent High
24	28.4	Low	Borderline	0.145	0.5	0.425	1.5	0.449	1.6	100.0%	100.0%	100.0%	100.0%	0.0%
25	30.4	Low	Borderline	0.482	1.6	1.175	3.9	1.270	4.2	60.0%	100.0%	0.0%	53.0%	47.0%
26	31.6	High	Borderline	1.07	3.4	0.458	1.5	1.164	3.7	60.0%	100.0%	100.0%	13.0%	87.0%
27	33.3	High	Non-Borderline	1.235	3.7	1.143	3.4	1.683	5.0	80.0%	100.0%	100.0%	7.0%	93.0%
28	36.1	High	Non-Borderline	0.683	1.9	0.645	1.8	0.939	2.6	100.0%	100.0%	100.0%	0.0%	100.0%
29	36.2	High	Non-Borderline	0.77	2.1	0.847	2.3	1.145	3.2	100.0%	100.0%	100.0%	0.0%	100.0%
30	39.7	High	Non-Borderline	1.353	3.4	0.683	1.7	1.516	3.8	100.0%	100.0%	100.0%	0.0%	100.0%
31	43.4	High	Non-Borderline	1.083	2.5	0.466	1.1	1.179	2.7	100.0%	100.0%	100.0%	0.0%	100.0%
32	43.9	High	Non-Borderline	1.277	2.9	1.400	3.2	1.895	4.3	100.0%	100.0%	100.0%	0.0%	100.0%
33	44	High	Non-Borderline	0.706	1.6	0.225	0.5	0.741	1.7	100.0%	100.0%	100.0%	0.0%	100.0%
34	45.2	High	Non-Borderline	0.549	1.2	0.799	1.8	0.970	2.1	100.0%	100.0%	100.0%	0.0%	100.0%
35	45.6	High	Non-Borderline	0.393	0.9	0.497	1.1	0.634	1.4	100.0%	100.0%	100.0%	0.0%	100.0%
36	46.1	High	Non-Borderline	0.413	0.9	0.537	1.2	0.678	1.5	100.0%	100.0%	100.0%	0.0%	100.0%
37	49.1	High	Non-Borderline	0.182	0.4	0.547	1.1	0.577	1.2	100.0%	100.0%	100.0%	0.0%	100.0%
38	51.7	High	Non-Borderline	0.637	1.2	0.000	0.0	0.637	1.2	100.0%	100.0%	100.0%	0.0%	100.0%
39	52.4	High	Non-Borderline	0.219	0.4	0.151	0.3	0.267	0.5	100.0%	100.0%	100.0%	0.0%	100.0%
40	52.4	High	Non-Borderline	1.023	2.0	0.254	0.5	1.054	2.0	100.0%	100.0%	100.0%	0.0%	100.0%
41	53.2	High	Non-Borderline	0.153	0.3	0.148	0.3	0.213	0.4	100.0%	100.0%	100.0%	0.0%	100.0%
42	54.9	High	Non-Borderline	0.383	0.7	0.384	0.7	0.542	1.0	100.0%	100.0%	100.0%	0.0%	100.0%
43	56.6	High	Non-Borderline	0.81	1.4	0.832	1.5	1.161	2.1	100.0%	100.0%	100.0%	0.0%	100.0%
44	57.6	High	Non-Borderline	0.585	1.0	0.419	0.7	0.719	1.2	100.0%	100.0%	100.0%	0.0%	100.0%
45	57.7	High	Non-Borderline	0.453	0.8	0.000	0.0	0.453	0.8	100.0%	100.0%	100.0%	0.0%	100.0%
46	58	High	Non-Borderline	0.569	1.0	0.357	0.6	0.672	1.2	100.0%	100.0%	100.0%	0.0%	100.0%
47	60.1	High	Non-Borderline	0.161	0.3	0.209	0.3	0.264	0.4	100.0%	100.0%	100.0%	0.0%	100.0%
48	61.7	High	Non-Borderline	0.343	0.6	0.493	0.8	0.600	1.0	100.0%	100.0%	100.0%	0.0%	100.0%
49	63.3	High	Non-Borderline	0.278	0.4	0.529	0.8	0.597	0.9	100.0%	100.0%	100.0%	0.0%	100.0%
50	72.2	High	Non-Borderline	0.167	0.2	0.497	0.7	0.524	0.7	100.0%	100.0%	100.0%	0.0%	100.0%
n=50														

c. The %CV for the within-site precision for the Leica Aperio GT450 Dx scanner (the same scanner at different days) ranged from 0.2% to 4.0%; the %CV for the between-site precision component ranged from 0.0% to 3.5% and %CV for reproducibility ranged from 0.4% to 4.7%.

Table 5: Within-Site Precision and Reproducibility of ArteraAI Raw Score (Leica Aperio GT450 Dx Scanner)

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results	
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent High
1	10.5	Low	Non-Borderline	0.423	4.0	0.027	0.3	0.424	4.0	100.0%	100.0%	100.0%	100.0%	0.0%
2	21.3	Low	Non-Borderline	0.346	1.6	0	0.0	0.346	1.6	100.0%	100.0%	100.0%	100.0%	0.0%
3	18.7	Low	Non-Borderline	0.316	1.7	0.082	0.4	0.326	1.7	100.0%	100.0%	100.0%	100.0%	0.0%
4	20.9	Low	Non-Borderline	0.171	0.8	0.015	0.1	0.171	0.8	100.0%	100.0%	100.0%	100.0%	0.0%
5	19.8	Low	Non-Borderline	0.401	2.0	0.196	1.0	0.446	2.3	100.0%	100.0%	100.0%	100.0%	0.0%
6	22	Low	Non-Borderline	0.242	1.1	0.433	2.0	0.496	2.3	100.0%	100.0%	100.0%	100.0%	0.0%
7	21.2	Low	Non-Borderline	0.205	1.0	0.287	1.4	0.352	1.7	100.0%	100.0%	100.0%	100.0%	0.0%
8	21.5	Low	Non-Borderline	0.31	1.4	0.422	2.0	0.524	2.4	100.0%	100.0%	100.0%	100.0%	0.0%
9	24	Low	Non-Borderline	0.25	1.0	0.147	0.6	0.29	1.2	100.0%	100.0%	100.0%	100.0%	0.0%
10	24.8	Low	Non-Borderline	0.209	0.8	0.141	0.6	0.252	1.0	100.0%	100.0%	100.0%	100.0%	0.0%
11	23.5	Low	Non-Borderline	0.262	1.1	0.256	1.1	0.366	1.6	100.0%	100.0%	100.0%	100.0%	0.0%
12	25.2	Low	Non-Borderline	0.151	0.6	0.152	0.6	0.214	0.9	100.0%	100.0%	100.0%	100.0%	0.0%
13	25.6	Low	Non-Borderline	0.23	0.9	0.283	1.1	0.365	1.4	100.0%	100.0%	100.0%	100.0%	0.0%
14	26.5	Low	Non-Borderline	0.241	0.9	0.241	0.9	0.341	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
15	25	Low	Non-Borderline	0.242	1.0	0.196	0.8	0.312	1.2	100.0%	100.0%	100.0%	100.0%	0.0%
16	26	Low	Non-Borderline	0.068	0.3	0.101	0.4	0.122	0.5	100.0%	100.0%	100.0%	100.0%	0.0%
17	25	Low	Non-Borderline	0.172	0.7	0	0.0	0.172	0.7	100.0%	100.0%	100.0%	100.0%	0.0%
18	27.3	Low	Non-Borderline	0.281	1.0	0.269	1.0	0.388	1.4	100.0%	100.0%	100.0%	100.0%	0.0%
19	27.4	Low	Non-Borderline	0.248	0.9	0.067	0.2	0.257	0.9	100.0%	100.0%	100.0%	100.0%	0.0%
20	27.3	Low	Non-Borderline	0.168	0.6	0.14	0.5	0.219	0.8	100.0%	100.0%	100.0%	100.0%	0.0%
21	28.1	Low	Borderline	0.298	1.1	0.202	0.7	0.36	1.3	100.0%	100.0%	100.0%	100.0%	0.0%
22	26.1	Low	Non-Borderline	0.219	0.8	0.337	1.3	0.402	1.5	100.0%	100.0%	100.0%	100.0%	0.0%

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results	
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent High
23	26.5	Low	Non-Borderline	0.23	0.9	0.408	1.5	0.469	1.8	100.0%	100.0%	100.0%	100.0%	0.0%
24	27.8	Low	Borderline	0.141	0.5	0.037	0.1	0.146	0.5	100.0%	100.0%	100.0%	100.0%	0.0%
25	33.6	High	Non-Borderline	0.514	1.5	0.618	1.8	0.804	2.4	100.0%	100.0%	100.0%	0.0%	100.0%
26	28.3	Low	Borderline	0.273	1.0	0.422	1.5	0.502	1.8	100.0%	100.0%	100.0%	100.0%	0.0%
27	29.3	Low	Borderline	0.229	0.8	0.179	0.6	0.291	1.0	100.0%	100.0%	100.0%	100.0%	0.0%
28	31.4	High	Borderline	0.49	1.6	1.047	3.3	1.156	3.7	40.0%	100.0%	100.0%	20.0%	80.0%
29	38.5	High	Non-Borderline	0.595	1.5	0.182	0.5	0.622	1.6	100.0%	100.0%	100.0%	0.0%	100.0%
30	31	High	Borderline	0.985	3.2	1.083	3.5	1.464	4.7	20.0%	100.0%	60.0%	40.0%	60.0%
31	43.8	High	Non-Borderline	0.576	1.3	0.139	0.3	0.593	1.4	100.0%	100.0%	100.0%	0.0%	100.0%
32	46.2	High	Non-Borderline	0.686	1.5	0.409	0.9	0.799	1.7	100.0%	100.0%	100.0%	0.0%	100.0%
33	42	High	Non-Borderline	0.304	0.7	0.635	1.5	0.704	1.7	100.0%	100.0%	100.0%	0.0%	100.0%
34	46	High	Non-Borderline	0.435	0.9	0.621	1.4	0.758	1.6	100.0%	100.0%	100.0%	0.0%	100.0%
35	43.6	High	Non-Borderline	0.275	0.6	0.071	0.2	0.284	0.7	100.0%	100.0%	100.0%	0.0%	100.0%
36	43.3	High	Non-Borderline	0.341	0.8	0.282	0.7	0.443	1.0	100.0%	100.0%	100.0%	0.0%	100.0%
37	46.8	High	Non-Borderline	0.616	1.3	0.574	1.2	0.842	1.8	100.0%	100.0%	100.0%	0.0%	100.0%
38	50	High	Non-Borderline	0.27	0.5	0.591	1.2	0.65	1.3	100.0%	100.0%	100.0%	0.0%	100.0%
39	49.5	High	Non-Borderline	0.487	1.0	0.48	1.0	0.684	1.4	100.0%	100.0%	100.0%	0.0%	100.0%
40	48.9	High	Non-Borderline	0.327	0.7	0.654	1.3	0.731	1.5	100.0%	100.0%	100.0%	0.0%	100.0%
41	50.4	High	Non-Borderline	0.12	0.2	0.291	0.6	0.315	0.6	100.0%	100.0%	100.0%	0.0%	100.0%
42	51.8	High	Non-Borderline	0.634	1.2	0.332	0.6	0.716	1.4	100.0%	100.0%	100.0%	0.0%	100.0%
43	53	High	Non-Borderline	1.231	2.3	0.231	0.4	1.253	2.4	100.0%	100.0%	100.0%	0.0%	100.0%
44	55.8	High	Non-Borderline	0.241	0.4	0.093	0.2	0.258	0.5	100.0%	100.0%	100.0%	0.0%	100.0%
45	55.3	High	Non-Borderline	0.143	0.3	0.17	0.3	0.222	0.4	100.0%	100.0%	100.0%	0.0%	100.0%
46	56	High	Non-Borderline	0.399	0.7	0.209	0.4	0.45	0.8	100.0%	100.0%	100.0%	0.0%	100.0%
47	58.8	High	Non-Borderline	0.205	0.3	0.258	0.4	0.33	0.6	100.0%	100.0%	100.0%	0.0%	100.0%
48	60.5	High	Non-Borderline	0.403	0.7	0.276	0.5	0.489	0.8	100.0%	100.0%	100.0%	0.0%	100.0%
49	60.3	High	Non-Borderline	0.345	0.6	0.408	0.7	0.534	0.9	100.0%	100.0%	100.0%	0.0%	100.0%

Sample	Mean Raw score	ArteraAI Risk Group (Case-Level Mode)	Borderline Cases	Within-Site		Between-Site		Reproducibility (Total)		Percent Category Agreement Results based on Case-Level Category Call Mode			Percent Category Agreement Results	
				SD	%CV	SD	%CV	SD	%CV	Site 1	Site 2	Site 3	Percent Low	Percent High
50	69.3	High	Non-Borderline	0.808	1.2	0.505	0.7	0.953	1.4	100.0%	100.0%	100.0%	0.0%	100.0%
n=50														

B Clinical Performance:

The clinical performance of ArteraAI Breast was evaluated in a retrospective clinical study which included a total of 1,271 patients across three sites in the US. The dataset for pivotal clinical performance study included patients with HR+/HER2- early-stage invasive breast cancer (pT1-T3, pN0-N1, pM0) diagnosed between 2006 and 2019 without metastatic disease (pM1). The datasets for testing included patients who met the following criteria were considered eligible:

- Age at diagnosis was ≥18 years.
- Have undergone breast cancer surgery since 2006
- Have at least one baseline pre-treatment H&E-stained slide (or FFPE) specimen) from a surgical specimen of the primary tumor, representing the highest-grade tumor available with most tumor content.
  - For patients with multiple primary site tumors, the highest grade and tumor volume slide was chosen.
- Have received endocrine therapy (tamoxifen or aromatase inhibitors)
- Patients may have also received additional standard-of-care treatments.

Patients were considered ineligible if any of the following criteria were met:

- Prior or concurrent malignancy (except non-melanoma skin cancer) within the 5 years prior to breast cancer diagnosis
- Non-invasive breast cancer (pTis)
- pT4
- pN2-3
- Recurring cancer
- Metastatic disease at diagnosis or surgery
- Confirmed HER2-positive disease
- Prior systemic or local treatment for primary breast cancer under investigation, or
- Received only palliative care.

The summary of patient characteristics for the pivotal clinical performance study is presented in Table 6 below.

Table 6: Summary of Clinical Validation Patient Cohort Characteristics

Variables	Overall N = 1271[1]
Institution	
Site 1	186 (15%)
Site 2	54 (4.2%)
Site 3	1,031 (81%)
Age at Time of Surgery	
Median (Q1 - Q3)	62 (54 - 70)
Min - Max	23 - 94
Age at Time of Surgery	
< 50	201 (16%)
>= 50	1,070 (84%)
Sex	
Female	1,260 (99%)
Male	11 (0.9%)
Race	
White	1,069 (84%)
African American	140 (11%)
Asian American and Pacific Islander AAPI	36 (2.8%)
Other/Unknown	26 (2.0%)
Ethnicity	
Hispanic or Latino	32 (2.6%)
Not Hispanic or Latino	1,179 (97%)
Missing	60
Tumor Size (mm)	
Median (Q1 - Q3)	13 (8 - 20)
Min - Max	1 - 125
T-Stage	
T1	845 (67%)
T1a	11 (0.9%)
T1b	29 (2.3%)
T1c	70 (5.6%)
T1mi	1 (<0.1%)
T2	275 (22%)
T3	26 (2.1%)
Missing	14

Variables	Overall N = 1271[1]
N-stage	
N0	1,064 (84%)
N1	207 (16%)
Surgery Type	
Breast conserving	676 (53%)
Mastectomy	409 (32%)
Other/Unknown	186 (15%)
Adjuvant Systemic Therapy Type	
Any chemotherapy received	292 (23%)
Endocrine therapy only	832 (65%)
Other systemic therapy or systemic therapy unknown	147 (12%)
Pathological Tumor Grade	
1	363 (34%)
2	588 (55%)
3	121 (11%)
Missing	199
ArteraAI Risk Group	
ArteraAI Low	827 (65%)
ArteraAI High	444 (35%)
[1]n (%). Note that some percentages may not add up to a hundred percent due to rounding	

Summary of Clinical Validation Results:

a. 5-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

The prognostic ability of the ArteraAI Breast was evaluated for 5-year risk of DM.
The estimates of 5-year risks of DM for ArteraAI Breast Risk categories, sub-group analysis for 5-Year risk of DM for ArteraAI Breast Risk Groups based on race and treatment along with two-sided 95%CI are presented in Table 7-9 below.
The results of the pivotal clinical performance study are presented in the tables below:

i. 5-year risk of DM for ArteraAI Breast Risk category High (8.7%) is statistically significantly higher than the overall risk (3.6%) and this difference (5.1%) is clinically significant.

ii. 5-year risk of DM for ArteraAI Breast Risk category Low (0.9%), is statistically significantly lower than the overall risk (3.6%) and this difference (2.7%) is clinically significant.

Table 7: 5-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

ArteraAI Risk Category	Total Number	Number of DM for 5 Years	Estimated 5-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
Low	827	7	0.9% (0.4%-1.8%)	65.1%
High	444	38	8.7% (6.4%-11.8%)	34.9%
Total	1,271	45	3.6% (2.7%-4.8%)	100.0%

iii. A sub-group analysis was performed based on race (Table 8). This analysis shows that the overall 5-year DM risk estimates were similar between White and African American groups (3.6% vs 3.7%). Among patients in the Low-risk group, African American patients had 5-year DM risk of 1.4% and White patients had 0.9%. In the High-risk group, African American patients had a lower observed risk compared to the White patients (6.4% vs 9.7%). In each subgroup, patients classified as High-risk had higher estimated 5-year DM risk compared to the overall risk and those classified as Low-risk had lower estimated 5-year DM risk compared to the overall risk.

Table 8: Subgroup Analysis for 5-Year risk of DM for ArteraAI Breast Risk Groups (Low and High) patients by Race

Race	ArteraAI Risk Category	Total Number	Number of DM for 5 Years	Estimated 5-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
White	Low	718	6	0.9% (0.4%-1.9%)	67.2%
	High	351	33	9.7% (7.0%-13.3%)	32.8%
	Total	1,069	39	3.7% (2.7%-5.1%)	100.0%
African American	Low	77	1	1.4% (0.2%-9.2%)	55.0%
	High	63	4	6.4% (2.4%-16.1%)	45.0%
	Total	140	5	3.6% (1.5%-8.5%)	100.0%
Others	Low[1]	32	0	0.0% (0%-10.7%)[3]	51.6%
	High	30	1	3.3% (0.5%-21.4%)	48.4%

Race	ArteraAI Risk Category	Total Number	Number of DM for 5 Years	Estimated 5-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
	Total[2]	62	1	1.6% (0.2%-10.9%)	100.0%
[1]No events were observed with ArteraAI Low for patients with race AAPI, Other and Unknown.					
[2]Among the 62 patients, 36 patients have race "AAPI", 25 patients have race "Other", 1 patient has race "Unknown"					
[3]Wilson Score method was used to calculate the 95% CI.					

iv. A subgroup analysis was performed based on treatment (Table 9): any chemotherapy received (n=292), endocrine therapy only (n=832), and other systemic therapy or unknown (n=147). In each subgroup, patients classified as High-risk had higher estimated 5-year DM risk compared to the overall risk and those classified as Low-risk had lower estimated 5-year DM risk compared to the overall risk.

Table 9: Subgroup Analysis for 5-Year risk of DM for ArteraAI Breast Risk Groups (Low and High) patients by Treatment

Treatment	ArteraAI Risk Category	Total Number	Number of DM for 5 Years	Estimated 5-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
Any chemotherapy received	Low	96	2	2.1% (0.5%-8.1%)	32.9%
	High	196	17	8.8% (5.6%-13.8%)	67.1%
	Total	292	19	6.6% (4.2%-10.1%)	100.0%
Endocrine therapy only	Low	622	4	0.7% (0.3%-1.8%)	74.8%
	High	210	15	7.3% (4.4%-11.8%)	25.2%
	Total	832	19	2.3% (1.5%-3.6%)	100.0%
Other systemic therapy or systemic therapy unknown	Low	109	1	0.9% (0.1%-6.3%)	74.1%
	High	38	6	17.6% (8.3%-35.2%)	25.9%
	Total[1]	147	7	4.9% (2.4%-10.0%)	100.0%
[1]Among the 147 patients, 5 patients have treatment "Other", 142 patients have treatment "Unknown"					

b. 10-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

The prognostic ability of the ArteraAI Breast was evaluated for 10-year risk of DM.

The estimates of 10-year risks of DM for ArteraAI Breast Risk categories, sub-group analysis for 10-Year risk of DM for ArteraAI Breast Risk Groups based on race and treatment along with two-sided 95%CI are presented in Table 10-13 below.

The results of the pivotal clinical performance study are presented in the tables below:

i. 10-year risk of DM for ArteraAI Breast Risk category High (16.6%) is statistically significantly higher than the overall risk (7.6%) and this difference (9.0%) is clinically significant.

ii. 10-year risk of DM for ArteraAI Breast Risk category Low (2.8%), is statistically significantly lower than the overall risk (7.6%) and this difference (4.8%) is clinically significant.

Table 10: 10-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

ArteraAI Risk Category	Total Number	Number of DM for 10 Years	Estimated 10-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
Low	827	15	2.8% (1.6%-4.7%)	65.1%
High	444	57	16.6% (12.8%-21.5%)	34.9%
Total	1,271	72	7.6% (6.0%-9.7%)	100.0%

iii. A subgroup analysis was performed based on race (Table 11). This analysis shows that overall, 10-year DM risks for African American patients were lower (4.5%) than the White patients (8.5%). Among patients in the Low-risk group, African American and White patients had a similar 10-year DM risk (3.2% vs 2.8%). In the High-risk group, African American patients had a lower observed 10-year DM risk compared to the White patients (6.4% vs 20.1%). In each subgroup, patients classified as High-risk had higher estimated 10-year DM risk compared to the overall risk and those classified as Low-risk had lower estimated 10-year DM risk compared to the overall risk.

Table 11. Subgroup Analysis for 10-Year risk of DM for ArteraAI Breast Risk Groups (Low and High) patients by Race

Race	ArteraAI Risk Category	Total Number	Number of DM for 10 Years	Estimated 10- year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
White	Low	718	13	2.8% (1.6%-5.1%)	67.2%
	High	351	52	20.1% (15.3%-26.3%)	32.8%
	Total	1,069	65	8.5% (6.6%-10.9%)	100.0%
African American	Low	77	2	3.2% (0.8%-12.3%)	55.0%
	High	63	4	6.4% (2.4%-16.1%)	45.0%
	Total	140	6	4.5% (2.1%-9.9%)	100.0%
Others	Low[1]	32	0	0.0% (0%-10.7%)[2]	51.6%
	High	30	1	3.3% (0.5%-21.4%)	48.4%
	Total[3]	62	1	1.6% (0.2%-10.9%)	100.0%

[1]No events were observed with ArteraAI Low for patients with race AAPI/Other/Unknown.

[2]Wilson Score method was used to calculate the 95% CI.

[3]Among the 62 patients, 36 patients have race "AAPI", 25 patients have race "Other", 1 patient has race "Unknown"

iv. A sub-group analysis was performed based on treatment (Table 12): (any chemotherapy received (n=292), endocrine therapy only (n=832), and other systemic therapy or unknown (n=147). In each subgroup, patients classified as High-risk had higher estimated 10-year DM risk compared to the overall risk and those classified as Low-risk had lower estimated 10-year DM risk compared to the overall risk.

Table 12. Subgroup Analysis for 10-Year risk of DM for ArteraAI Breast Risk Groups (Low and High) patients by Treatment

Treatment	ArteraAI Risk Category	Total Number	Number of DM for 10 Years	Estimated 10-year Risk of DM (95% CI)	Percentage of Patients with the Risk Category
Any chemotherapy received	Low	96	3	3.3% (1.1%-9.9%)	32.9%
	High	196	28	17.02% (11.9%-24.0%)	67.1%
	Total	292	31	12.4% (8.8%-17.3%)	100.0%
Endocrine therapy only	Low	622	10	2.8% (1.5%-5.4%)	74.8%
	High	210	20	12.4% (7.8%-19.4%)	25.2%
	Total	832	30	5.2% (3.5%-7.6%)	100.0%
Other systemic therapy or systemic therapy unknown	Low	109	2	2.6% (0.6%-10.7%)	74.1%
	High	38	9	44.5% (21.3%-76.5%)	25.9%
	Total[1]	147	11	12.1% (6.1%-23.1%)	100.0%

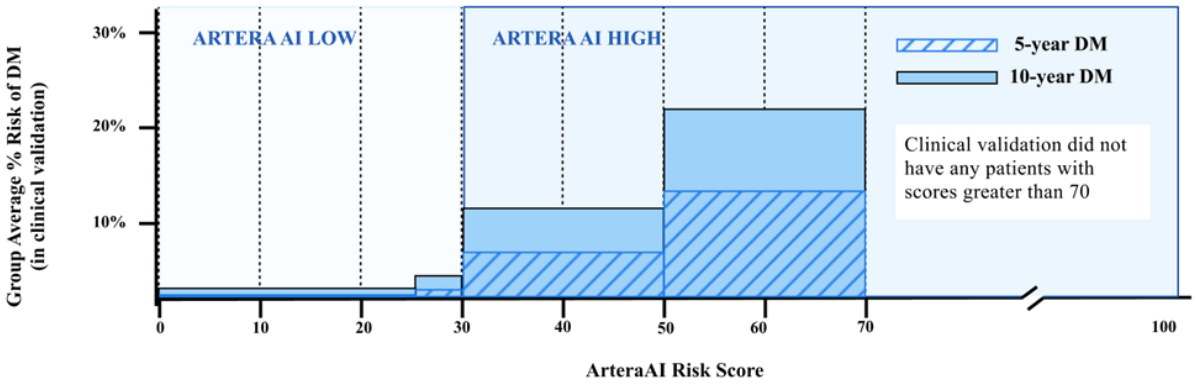
[1]Among the 147 patients, 5 patients have treatment "Other", 142 patients have treatment "Unknown"

iii. The analysis of ArteraAI Risk Score bins demonstrate:

- A monotonic increase is observed for 5-year DM risk and 10-year DM risk.
- There are two bins in the Low-risk group ([5.9, 25) and [25, 30]). Within the Low-risk group, patients with the lowest score bin [5.9, 25] had 3.2 times lower 5-year DM risk (0.4% vs 1.4%) and 1.7 times lower 10-year DM risk (2.1% vs 3.5%) compared to the patients with the second Low-risk bin [25, 30].
- There are two bins in the High-risk group (30,50) and [50,68]. Within the High-risk group, patients in the second High-risk bin [50,68] had 2.3 times higher 5-year DM risk (15.6% vs 6.6%) and 2.1times higher 10-year DM risk (27.7% vs 13.1%) compared to the first High-risk bin (30,50).

Table 13: Observed 5- and 10-year risk of DM based on binned ArteraAI Risk Scores

ArteraAI Risk category	Bin	N	Mean ArteraAI Risk Score	Range ArteraAI Risk Score	Observed Risk of DM at 5 years (95% CI)	Observed Risk of DM at 10 years (95% CI)	Percentage of patients in the bin
Low	[5.9,25)	463	19.8	(5.9, 25.0)	0.4% (0.1% - 1.7%)	2.1% (0.9% - 4.9%)	36.4%
	[25,30]	364	27.3	(25.0, 30.0)	1.4% (0.6% - 3.4%)	3.5% (1.8% - 6.9%)	28.6%
High	(30,50)	341	41.2	(30.1, 49.9)	6.6% (4.4% - 9.9%)	13.1% (9.2% - 18.6%)	26.8%
	[50,68]	103	55.2	(50.1, 68.0)	15.6% (9.8% - 24.1%)	27.7% (19.0% - 39.3%)	8.1%
	Total	1271	30.6	(5.9, 68.0)	3.6% (2.7% - 4.8%)	7.6% (6.0% - 9.7%)	100%



Score Range	0-25	25-30	30-50	50-70	>70
Bin 5-year % DM Risk	0.4%	1.4%	6.6%	15.6%	*15.6%
Bin 10-year % DM Risk	2.1%	3.5%	13.1%	27.7%	*27.7%

*Estimates based on patients with risk scores 50-68

Figure 2. Observed 5- and 10-year risk of DM based on binned ArteraAI Risk Scores

c. Kaplan-Meier curves for 5- and 10-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

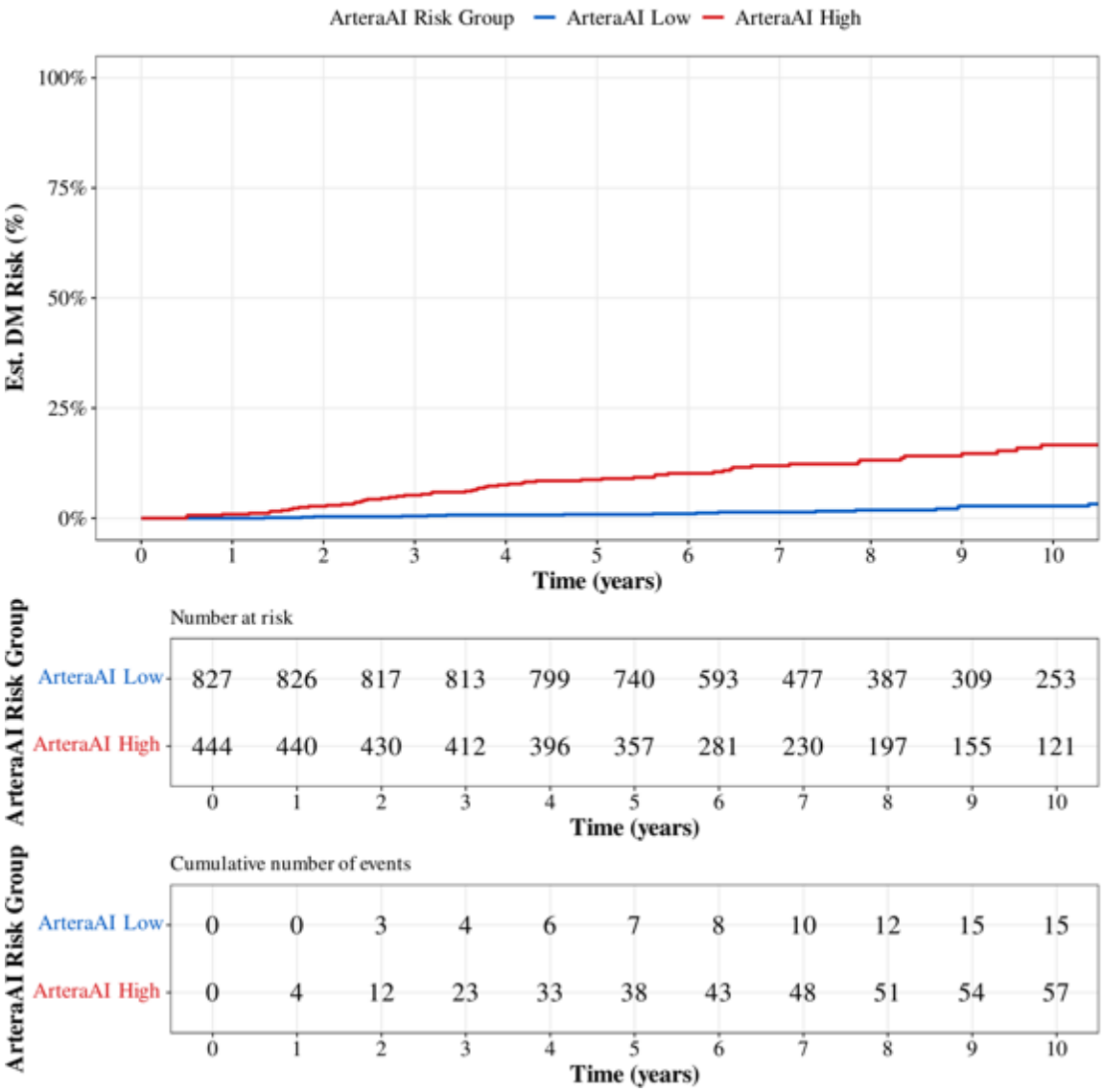


Figure 3. Kaplan Meier curve for 5- and 10-Year Risk of DM for ArteraAI Breast Risk Groups (Low and High)

VIII Pre-Determined Change Control Plan

The ArteraAI Breast includes a pre-determined change control plan (PCCP). The PCCP provides an overview of the planned modifications to add interoperable FDA cleared WSI scanners and file formats as intended use components. As outlined in the PCCP, each modification is designed

to address specific differences in device input, ensuring consistent performance and prognostic accuracy. Verification and validation testing will ensure that software updates made to add interoperability with additional FDA cleared scanners will not have an impact on existing interoperable scanners or other functionality. The verification/validation process for each additional scanner is same as the validation process used to show interoperability with the Philips Ultra Fast Scanner with the cleared device; the protocols and acceptance criteria detail performance characteristics necessary to ensure that the modified device is substantially equivalent to the cleared device.

Per ArteraAI's change control procedure, a change request for the following changes will be created:

i. Update the User Interface to include an additional interoperable scanner in the file upload workflow.
ii. Update the Back End to verify image metadata from files from the new interoperable scanner.
iii. If necessary: Update the Image Converter component to convert compatible files from the new scanner to the expected format for the AI Engine.

Upon successful validation, labeling will be updated in accordance with the authorized PCCP to provide users with current information regarding the device's interoperable scanner.

IX Proposed Labeling:

The labeling supports the substantial equivalence for this device.

X Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.