



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

I Background Information:

A 510(k) Number

K260023

B Applicant

SimBioSys, Inc.

C Proprietary and Established Names

TumorSight Risk

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
SHW	Class II	21 CFR 864.3755 - pathology software algorithm device analyzing digital images for cancer prognosis	Pathology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Type of Test:

Software only device

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

TumorSight Risk is an artificial intelligence based software only device that analyzes data from previously diagnosed invasive breast cancer patients to assess the risk of recurrence. TumorSight Risk utilizes the following data: age, race, cancer stage, nodal status, and grade, combined with Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) data to generate 5- and 10-year risks of breast cancer recurrence and a proprietary prognostic score.

TumorSight Risk is intended for use in adult women with hormone receptor positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-), lymph node negative (N0) or positive (N1), Stage I-IIIa breast cancer to inform a physician in prognostic risk-based decisions in conjunction with other relevant clinicopathological factors.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Contraindications

TumorSight Risk is contraindicated for the following:

- Patients with breast implants.
- Patients with prior mastectomy.
- MRI images acquired with unilateral DCE breast protocols.
- MRI images acquired post-treatment.
- Pediatric patients (age < 22 years old).
- Patients with no DCE MRI prior to initiation of therapy (in the neoadjuvant setting) or surgery (in the adjuvant setting).
- Patients where the DCE MRI does not meet ACR guidelines for contrast enhanced breast imaging.
- Poor quality DCE MRI (inadequate image quality, insufficient number of images).
- Patients with cN2 or higher clinical nodal status.
- Laboratory test results and clinicopathological characteristics that determine estrogen receptor (ER) status, progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER2) status, Tumor Grade, Tumor Stage and Nodal Stage that do not comply with American Society of Clinical Oncology (ASCO), College of American Pathologists (CAP) and American Joint Committee on Cancer (AJCC) guidelines.

Refer to the labeling for a complete list of contraindications, precautions and limitations.

IV Device/System Characteristics:

A Device Description:

TumorSight Risk employs artificial intelligence (AI) algorithms and image processing to analyze data from previously diagnosed invasive breast cancer patients. TumorSight Risk integrates standard of care (SOC) diagnostic pathology data with clinical and medical imaging data to provide a proprietary prognostic score (named as TSR score) ranging from 0-100 that is used to determine a risk category and prognostic risk estimate of recurrence of disease within 5 years and 10 years from diagnosis.

The table below shows the TSR score range and the associated risk category.

TSR Score Range	TumorSight Risk Category
>35	High
>20 to ≤35	Intermediate
≤20	Low

TumorSight Risk is a web-based application that is accessed using a standard web browser.

TumorSight Risk is intended to be used with the following MRI Manufacturer/field strength:

MRI Manufacturer	Magnetic Field Strengths
General Electric (GE)	1.5T, 3T
Siemens	1.5T, 3T

Device Input:

1. Age, race, clinical tumor (T) stage, clinical nodal (N) stage, tumor histologic grade.
2. Multi-tissue segmentation map which is derived from processing the patient's pre-treatment dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) acquired according to American College of Radiology (ACR) guidelines. This input is a validated output of the TumorSight Viz device (K251766).

Additional patient information is required by the device, but are not inputs to the device. These include ER/PR/HER2 status, which is used to determine case eligibility criteria per indications for use. They are not used by the AI algorithm for device output generation (Risk Category or TSR Score). Additionally, cancer laterality information is used to ensure that the appropriate multi-tissue segmentation map is retrieved from TumorSight Viz. It is a processing input used to associate the DCE MRI images with the correct segmentation output, rather than an input feature of the TumorSight Risk AI model itself. Patient clinical data, i.e., age, race, clinical T stage, clinical N stage, tumor histologic grade, and multi-tissue segmentation map obtained from DCE-MRI are utilized by the TumorSight Risk AI algorithm to compute the device output (TumorSight Risk (TSR) Score and Risk Category).

A summary of the device operation is as follows:

1. DCE MRI data (e.g., in DICOM format) is input into the previously cleared TumorSight Viz device. TumorSight Viz processes the data and generates a multi-tissue segmentation.
2. The multi-tissue segmentation is automatically input into TumorSight Risk from the TumorSight Viz device.
3. Intermediate imaging values are computed from the multi-tissue segmentation.
4. The intermediate imaging values are combined with clinical and pathologic data and input into a machine learning algorithm that generates a proprietary TSR Score and risk category ("High Risk", "Intermediate Risk", or "Low Risk").

Device Output:

1. Proprietary TSR Score ranging from 0-100 that is used to determine a risk category
2. Categorical assessment of "High Risk", "Intermediate Risk" or "Low Risk"

3. Observed 5-Year Risk of recurrence (in the clinical validation dataset)
4. Observed 10-Year Risk of recurrence (in the clinical validation dataset)

This output is displayed in a report format (“Risk Report”) which also describes the TumorSight Risk methodology and provides a summary of the validation results.

B TumorSight Risk Algorithm Development:

The TumorSight Risk algorithm is a regression-based machine learning model that integrates clinical, demographic, pathologic and imaging features. The model was trained/tuned using a dataset of N=1,133 samples from 6 sites geographically distributed throughout the United States (US). The development (training plus tuning) dataset was representative of the US population (see Table 1). The training portion of the development dataset was used to generate candidate models, while the tuning portion of the development dataset was used to select the final model. The candidate model was tested for repeatability, reproducibility, accuracy, and stability. The algorithm was locked after model training and prior to analytical precision testing and clinical validation.

Table 1: Demographics of the training/tuning dataset

Factor	Training/Tuning N=1,133 (%)
Institution	
Site 1	159 (14.0%)
Site 2	397 (35.0%)
Site 3	102 (9.0%)
Site 4	48 (4.2%)
Site 5	20 (1.8%)
Site 6	407 (35.9%)
Age	
22-29	8 (<1%)
30-39	91 (8%)
40-49	307 (27%)
50-59	343 (30%)
60-69	238 (21%)
70-79	124 (11%)
80+	20 (2%)
Unknown	2 (<1%)
Race	
White	844 (75%)
Black or African American	204 (18%)
Asian	21 (2%)
Native Hawaiian or Other Pacific Islander [†]	0 (0%)
American Indian or Alaska Native [†]	5 (<1%)
Other [†]	50 (4%)
Unknown [†]	9 (<1%)
Cancer Grade	

1	242 (21%)
2	606 (54%)
3	255 (22%)
Unknown	30 (3%)
Clinical Tumor Stage	
T1	537 (47%)
T2	404 (36%)
T3	138 (12%)
T4	1 (<1%)
Unknown	53 (5%)
Clinical Nodal Stage	
N0	752 (66%)
N1	277 (24%)
N2	0 (0%)
N3	0 (0%)
Unknown	104 (9%)
Breast Laterality	
Left	577 (50.9%)
Right	556 (49.1%)
Recurrence (Any Time)	
True	144 (12.7%)
False	989 (87.3%)

V Substantial Equivalence Information:

A Predicate Device Name(s)

ArteraAI Breast

B Predicate Device Number(s)

K254115

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K260023</u>	<u>K254115</u>
Device Trade Name	TumorSight Risk	ArteraAI Breast
General Device Characteristic Similarities		

Intended Use/Indications For Use	TumorSight Risk is an artificial intelligence based software only device that analyzes data from previously diagnosed invasive breast cancer patients to assess the risk of recurrence. TumorSight Risk utilizes the following data: age, race, cancer stage, nodal status, and grade, combined with Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) data to generate 5- and 10-year risks of breast cancer recurrence and a proprietary prognostic score. TumorSight Risk is intended for use in adult women with hormone receptor positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-), lymph node negative (N0) or positive (N1), Stage I-IIIa breast cancer to inform a physician in prognostic risk-based decisions in conjunction with other relevant clinicopathological factors.	ArteraAI Breast is a software only device intended to analyze scanned histopathology whole slide images (WSIs) from treatment-naïve 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.
Physical Characteristics	Artificial intelligence/machine learning (AI/ML) based software only Device	Same
General Device Characteristic Differences		
Data Source (Input)	DCE-MRI and Clinicopathological data	Scanned histopathology whole slide images (WSIs) from treatment-naïve breast resection specimens prepared from formalin fixed paraffin embedded (FFPE) tissue and stained using Hematoxylin & Eosin (H&E) stains
Output	• Proprietary TSR Score ranging from 0-100 that is used to determine a risk category • Categorical assessment of "High Risk", "Intermediate Risk" or "Low Risk" • Observed 5-Year Risk of recurrence (in the clinical validation dataset) • Observed 10-Year Risk of recurrence (in the clinical validation dataset)	• 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)

VI Standards/Guidance Documents Referenced:

1. Guidance for Industry and Food and Drug Administration Staff: Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions (June 2025).
2. Guidance for Food and Drug Administration Staff: Content of Premarket Submissions for Device Software Functions (June 2023).

3. IEC 62304 Edition 1.1 2015-06 CONSOLIDATED VERSION, Medical Device Software – Software Life Cycle Processes (recognition Number 13-79).
4. ISO 14971 Third Edition 2019-12, Medical devices – Applications of risk management to
5. medical devices (recognition Number 5-125).
6. CLSI document EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition; 2014
7. CLSI document EP12-Ed3: Evaluation of Qualitative, Binary Output Examination Performance – Third Edition; 2023
8. CLSI document EP49-Ed1: Framework for Developing Evidence of Clinical Validity of Medical Laboratory Test Methods – First Edition; 2026

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility from MRI

A study using simulated noise added to MRIs was conducted to assess the precision/reproducibility of the TumorSight Risk algorithm. One hundred twenty (120) patient images were selected which were evenly split across GE/1.5T, GE/3T, Siemens/1.5T, Siemens/3T MRI machines. These images were processed through the system three times with 3% added Rician noise. One hundred nineteen (119) samples were successfully processed and 0.83% (1/120) samples were not successfully processed. The reproducibility study included a minimum of 4 samples near the cutoff C1[20] between low and intermediate and 4 samples near the cutoff C2 [35] between intermediate and high (borderline cases). The sample characteristics are provided in Table 2 below.

Table 2: Characteristics of Samples Used in Reproducibility Study

Characteristic	GE/1.5T N=30	GE/3T N=30	Siemens/1.5T N=30	Siemens/3T N=30
# Successfully Processed	30 (100%)	30 (100%)	30 (100%)	29 (97%)
Age (mean ± std)	57 ± 12	51 ± 13	53 ± 14	60 ± 12
Age < 50	11 (37%)	17 (57%)	10 (33%)	8 (27%)
Age ≥ 50	19 (63%)	13 (43%)	20 (67%)	22 (73%)
Race				
White	25 (83%)	16 (53%)	12 (%)	29 (%)
Black	4 (13%)	1 (3%)	18 (%)	0 (0%)
Other [†]	1 (3%)	13 (43%)	0 (0%)	1 (3%)
Cancer Grade				
1	7 (23%)	6 (20%)	6 (20%)	6 (20%)
2	21 (70%)	20 (67%)	18 (60%)	16 (53%)
3	2 (7%)	4 (13%)	6 (20%)	8 (27%)
Clinical Tumor Stage				
T1	10 (33%)	10 (33%)	10 (33%)	10 (33%)
T2	10 (33%)	10 (33%)	10 (33%)	11 (36%)

Characteristic	GE/1.5T N=30	GE/3T N=30	Siemens/1.5T N=30	Siemens/3T N=30
T3	10 (33%)	10 (33%)	10 (33%)	9 (30%)
Clinical Nodal Stage				
N0	15 (50%)	15 (50%)	15 (50%)	25 (83%)
N1	15 (50%)	15 (50%)	15 (50%)	5 (17%)
Laterality				
Left	15 (50%)	14 (47%)	16 (53%)	18 (60%)
Right	15 (50%)	16 (53%)	14 (47%)	12 (40%)
TumorSight Risk Category				
High Risk	17 (57%)	19 (63%)	19 (63%)	12 (41%)
Intermediate Risk	4 (13%)	7 (23%)	5 (17%)	6 (21%)
Low Risk	9 (30%)	4 (13%)	6 (20%)	11 (38%)
Borderline Group				
Borderline Case	9 (30%)	7 (23%)	10 (33%)	10 (34%)
Non-Borderline Case	21 (70%)	23 (77%)	20 (67%)	19 (66%)

Summary precision statistics for: i) the variability of SD standard deviation (SD) (mean values of SD, the median of SD); ii) the variability of percent coefficient of variation (%CV) ((mean values of %CV, the median of %CV)), and iii) the percent agreement are shown in Table 3 below. The average SD is less than 0.25 risk units, and the average %CV is less than 1.1% across all manufacturer/field strength combinations. Overall percent agreement was 99.4% (only 2 out of 119 patients exhibited less than perfect agreement).

Table 3: Summary Precision Results for the Processed Cases (n=119) for the TSR Score

Parameter	Overall N=119	GE/1.5T N=30	GE/3T N=30	Siemens/1.5T N=30	Siemens/3T N=29
SD (mean, median)	0.23 (0.12)	0.25 (0.09)	0.21 (0.11)	0.21 (0.17)	0.25 (0.12)
%CV (mean, median)	0.61 (0.31)	0.48 (0.25)	0.44 (0.26)	0.51 (0.36)	1.06 (0.33)
%Agreement (N *3 replicates)	99.4% (355/357)	98.9% (89/90)	100% (90/90)	98.9% (89/90)	100% (87/87)
%Disagreement (N*3 replicates)	0.6% (2/357)	1.1% (1/90)	0% (0/90)	1.1% (1/90)	0% (0/87)

Precision profiles, including average SD vs. mean score of TSR, and %CV vs. mean score of TSR for the overall dataset are shown in the following Figure 1.

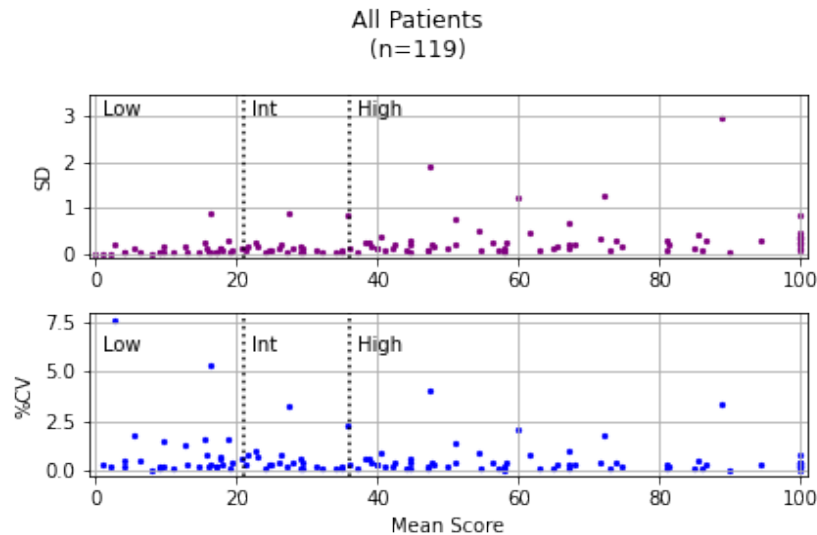


Figure 1: Precision profiles for all N=119 subjects included in the study for the TSR Score.

B Clinical Performance:

The clinical performance of TumorSight Risk device was evaluated in a retrospective clinical performance study which included a total of 2,129 patients across 4 sites in the US. Enrollment included identification of patients that were diagnosed between January 1, 2010, and December 31, 2024, and had a pre-treatment MRI available. The clinical, pathologic and recurrence data elements were extracted from the medical record and/or cancer registry. The cases were selected based on the inclusion and exclusion criteria described below.

Inclusion criteria:

- Subject has previously granted the institution consent for their data to be used for additional research purposes
- Adult (≥ 22 years) female subjects with biopsy proven early-stage or locally advanced invasive breast cancer
- Any race/ethnicity
- Clinical node negative (cN0) and node positive (cN1) patients are eligible
- Hormone receptor positive (HR+)
- Human epidermal growth factor receptor 2 negative (HER2-)
- Pre-treatment DCE MRI available
- Patient received treatment and was followed for first recurrence
- GE or Siemens MRI manufacturer
- 1.5T or 3T field magnetic strength
- Imaging conforms to ACR guidelines for contrast enhanced breast imaging

Exclusion criteria:

- HR- or HER2+ disease
- No DCE MRI prior to initiation of therapy (in the neoadjuvant setting) or surgery (in the adjuvant setting)
- Distant metastases at the time of diagnosis
- Bilateral disease

- T4 disease
- cN2 or higher clinical nodal status
- Patients meeting the following criteria:
 - Breast implants
 - Patients with prior mastectomy
 - Unilateral DCE breast protocols
 - Post-treatment DCE breast MRI
 - Pediatric patients (age < 22 years old)
- Poor quality images (inadequate image quality, insufficient number of images)
- DCE MRI does not meet ACR guidelines for contrast enhanced breast imaging

The summary of patient characteristics for the clinical validation dataset is presented in Table 4 below.

Table 4: Summary of Clinical Validation Patient Cohort Characteristics

Variables	Validation N=2129 (%)
Institution	
Site A	712 (33.4%)
Site B	718 (33.7%)
Site C	447 (21.0%)
Site D	252 (11.8%)
Age*	
22-29	16 (<1%)
30-39	128 (6%)
40-49	505 (24%)
50-59	580 (27%)
60-69	567 (27%)
70-79	300 (14%)
80+	33 (2%)
Race**	
White	1532 (72%)
Black or African American	338 (16%)
Asian [†]	182 (9%)
Native Hawaiian or Other Pacific Islander [†]	65 (3%)
American Indian or Alaska Native [†]	6 (<1%)
Other [†]	6 (<1%)
Unknown	0 (0%)
Cancer Grade*	
1	736 (35%)
2	1084 (50%)
3	309 (15%)
Unknown	0 (0%)
Clinical Tumor Stage***	
T1	1299 (61%)
T2	681 (32%)
T3	149 (7%)

Variables	Validation N=2129 (%)
T4	0 (0%)
Unknown	0 (0%)
Clinical Nodal Stage^{***}	
N0	1811 (85%)
N1	318 (15%)
N2	0 (0%)
N3	0 (0%)
Unknown	0 (0%)
Recurrence (Any Time)	
True	181 (8.5%)
False	1948 (91.5%)

^{***}Within the TumorSight Risk device and algorithm, races other than White and Black are categorized as “Other”. The measures of the clinical performance for the device with three outputs (High, Intermediate, Low) are i) Predictive Value (PV) for each output and ii) percentage of the results for each output. Predictive Values are evaluated using Kaplan-Meier analyses, from the “High”, “Intermediate” and “Low” populations, respectively.

Summary of Clinical Validation Results:

1. Measures of Clinical Performance

Clinical performance of the TumorSight Risk device is described by Table 5 below.

Predictive Value (PV) for output “X” is the probability that a Target Condition (Recurrence) occurs within a specific time frame (5 years and 10 years) given the device output for the patients is “X” (this PV for output “X” is called also “risk of recurrence”)

Table 5: Recurrence Rate by TumorSight Risk Category for 5 years and 10 years

Risk Category by TumorSight Risk device	Total number	Percentage of patients with the Risk Category	Number of recurrences for 5 years	Risk of Recurrence within 5 years (95% CI)	Number of recurrences for 10 years	Risk of Recurrence within 10 years (95% CI)
High	534	25.1%	46	9.8% (7.4%, 12.9%)	70	26.4% (20.2%, 34.1%)
Intermediate	559	26.3%	28	5.7% (4.0%, 8.2%)	43	13.4% (9.6%, 18.5%)
Low	1036	48.7%	27	3.0% (2.0%, 4.3%)	52	8.6% (6.4%, 11.5%)
Total	2129	100.0%	101	5.4% (4.5%, 6.5%)	165	13.5% (11.4%, 15.9%)

- The risks of recurrence for TumorSight Risk category “High” patients were 9.8% (95%CI: (7.4%, 12.9%)) for 5 years and 26.4% (95%CI: (20.2%, 34.1%)) for 10 years. The TumorSight Risk output “High” is *statistically and clinically informative* because i) the 5-year risk is higher than the pre-test risk of 5.4% (the lower bound of the 95%CI, 7.4%, is higher than the pre-test risk of 5.4% (7.4% > 5.4%), and ii) the 10-year risk is higher than

the pre-test risk of 13.5% (the lower bound of the 95%CI, 20.2%, is higher than the pre-test risk of 13.5% (20.2% > 13.5%).

- The risks of recurrence for TumorSight Risk category “Low” patients were 3.0% (95%CI: (2.0%, 4.3%)) for 5 years and 8.6% (95%CI: (6.4%, 11.5%)) for 10 years. The TumorSight Risk output “Low” is *statistically and clinically informative* because i) the 5-year risk is lower than the pre-test risk of 5.4% (the upper bound of the 95%CI, 4.3%, is lower than the pre-test risk of 5.4% (4.3% < 5.4%)) and ii) the 10-year risk is lower than the pre-test risk of 13.5% (the upper bound of the 95%CI, 11.5%, is lower than the pre-test risk of 13.5% (11.5% < 13.5%).
 - The risk of recurrence for TumorSight Risk category Intermediate is similar to the pre-test risk for both 5 years (5.7% vs 5.4%) and 10 years (13.4% vs 13.5%. Percents of patients with “intermediate” results in the clinical performance study was 26.3% (559/2129).
2. Figure 2 below shows the risk of recurrence curves of the “High”, “Intermediate” and “Low” categories patients along with all subjects in the study population through 10 years:

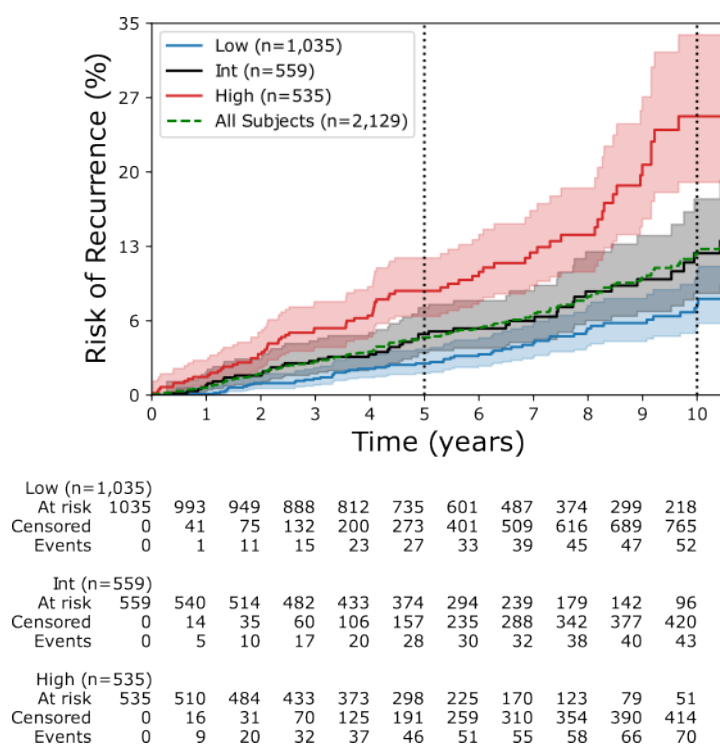


Figure 2: Kaplan-Meier curves for 5- and 10-year risk of recurrence for TumorSight Risk categories (High, Intermediate (Int), and Low), and the whole study population (N=2,129). The vertical lines delineate the 5-year and 10-year analysis endpoint.

3. Subgroup Analyses

Subgroup analysis of recurrence rates observed in the clinical validation study at 5- and 10-years post diagnosis were performed based on race, age, nodal stage, treatment, MRI Manufacturer/ Magnetic Field Strength, as shown in tables 6 - 10.

a. Subgroup Analysis by Race

Clinical performance of the TumorSight Risk device analyzed by race: (White, African American and Other) is described below:

Table 6: Subgroup Analysis of Recurrence Risks at 5- and 10-years Post Diagnosis by Race

Race	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N (% of subjects)
White	High	11.1% (7.6%, 16.0%)	26.5% (18.5%, 37.1%)	268 (17.5%)
	Intermediate	5.4% (3.4%, 8.4%)	11.3% (7.4%, 17.1%)	381 (24.9%)
	Low	3.1% (2.1%, 4.6%)	9.3% (6.3%, 12.5%)	883 (57.6%)
	Overall	5.0% (4.0%, 6.3%)	12.2% (10.0%, 14.9%)	1532 (100.0%)
African American	High	4.8% (2.2%, 10.3%)	13.8% (7.3%, 24.5%)	134 (39.6%)
	Intermediate	7.8% (3.8%, 15.7%)	22.9% (12.7%, 39.3%)	102 (30.2%)
	Low	2.2% (0.6%, 8.6%)	3.9% (1.2%, 12.0%)	102 (30.2%)
	Overall	5.0% (3.0%, 8.2%)	15.1% (9.6%, 23.3%)	338 (100.0%)
Other	High	12.8% (7.9%, 20.5%)	42.0% (24.4%, 65.2%)	132 (51.0%)
	Intermediate	4.3% (1.4%, 12.9%)	6.8% (2.5%, 17.9%)	76 (29.3%)
	Low	2.4% (0.4%, 16.1%)	2.4% (0.3%, 16.1%)	51 (19.7%)
	Overall	8.2% (5.3%, 12.7%)	21.7% (13.6%, 33.6%)	259 (100.0%)

b. Subgroup Analysis by Age

Clinical performance of the TumorSight Risk device analyzed by age: (<50 years and ≥50) is described below:

Table 7: Subgroup Analysis of Recurrence Risks at 5- and 10-years Post Diagnosis by Age

Age	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N (% of subjects)
<50	High	9.7% (6.0%, 15.4%)	24.5% (16.3%, 35.7%)	179 (27.6%)
	Intermediate	6.6% (3.3%, 12.7%)	21.6% (12.0%, 37.0%)	146 (22.5%)
	Low	1.8% (0.7%, 4.2%)	5.6% (2.7%, 11.1%)	323 (49.8%)
	Overall	5.1% (3.6%, 7.3%)	13.8% (10.1%, 18.6%)	648 (100%)
≥50	High	9.9% (7.0%, 13.9%)	26.8% (19.0%, 37.0%)	356 (24.0%)
	Intermediate	5.4% (3.5%, 8.3%)	11.0% (7.4%, 16.3%)	413 (27.9%)
	Low	3.5% (2.3%, 5.3%)	9.9% (7.2%, 13.6%)	712 (48.1%)
	Overall	5.5% (4.4%, 6.9%)	13.4% (11.0%, 16.3%)	1481 (100%)

c. Subgroup Analysis by Nodal Stage

Clinical performance of the TumorSight Risk device analyzed by nodal stage: (cN0 and cN1) is described below:

Table 8: Subgroup Analysis of Recurrence Risks at 5- and 10-years Post Diagnosis by Nodal Stage

Nodal Stage	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N (% of subjects)
cN0	High	7.3 % (4.6%, 11.3%)	20.2% (12.4%, 31.8%)	278 (15.4%)
	Intermediate	5.5% (3.7%, 8.2%)	13.0% (9.0%, 18.4%)	504 (27.8%)
	Low	3.0% (2.1%, 4.3%)	8.7% (6.5%, 11.6%)	1028 (56.8%)
	Overall	4.4% (3.4%, 5.5%)	11.1% (9.1%, 13.6%)	1810 (100%)
cN1	High	12.6% (8.8%, 17.8%)	32.8% (23.9%, 44.0%)	257 (80.6%)
	Intermediate	7.9% (3.0%, 19.8%)	17.3% (7.4%, 37.5%)	55 (17.2%)
	Low	0.0% (0.0%, 0.0%)	0.0% (0.0%, 0.0%)	7 (2.2%)
	Overall	11.4% (8.2%, 15.8%)	28.6% (21.3%, 37.8%)	319 (100%)

d. Subgroup Analysis by Treatment

Clinical performance of the TumorSight Risk device analyzed by treatment: (chemo-endocrine therapy and endocrine therapy) is described below.

Table 9: Subgroup Analysis of Recurrence Rates Observed in the Clinical Validation Study at 5- and 10-years Post Diagnosis by Treatment

Treatment	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N* (% of subjects)
Chemo-endocrine therapy	High	6.9% (3.8%, 12.6%)	20.2% (12.3%, 32.1%)	163 (37.8%)
	Intermediate	4.8% (2.0%, 11.2%)	9.7% (4.8%, 19.0%)	117 (27.1%)
	Low	3.6% (1.5%, 8.4%)	4.6% (2.1%, 10.0%)	150 (35.0%)
	Overall	5.2% (3.4%, 7.9%)	11.2% (7.8%, 15.9%)	430 (100.0%)
Endocrine therapy	High	3.0% (1.1%, 7.8%)	23.9% (13.5%, 40.3%)	157 (14.6%)
	Intermediate	4.4% (2.5%, 7.9%)	12.0% (7.3%, 19.4%)	293 (27.3%)
	Low	1.8% (1.0%, 3.3%)	9.0% (6.1%, 13.3%)	622 (58.0%)
	Overall	2.7% (1.8%, 4.0%)	11.4% (8.7%, 14.8%)	1072(100.0%)

*For 627 out of 2129 cases within the clinical validation study cohorts, treatment information was not available.

e. Subgroup Analysis by MRI Manufacturer/Field Strength

Clinical performance of the TumorSight Risk device analyzed by Manufacturer/Field Strength: (GE/1.5T, GE/3T, Siemens/1.5T, and Siemens/3T) is described below.

Table 10: Subgroup Analysis of Recurrence Risks at 5- and 10-years Post Diagnosis by MRI Manufacturer/magnetic Field Strength

MRI Manufacturer/ Magnetic Field Strength	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N* (% of subjects)
GE	High	12.2% (9.0%, 16.4%)	27.7% (21.1%, 35.8%)	361 (24.1%)
	Intermediate	6.4% (4.3%, 9.5%)	11.6% (7.9%, 16.9%)	388 (25.9%)
	Low	2.9% (1.9%, 4.4%)	9.2% (6.8%, 12.4%)	748 (50.0%)
	Overall	6.0% (4.8%, 7.4%)	13.5% (11.4%, 16.1%)	1497 (100.0%)
GE/1.5T	High	7.0% (3.9%, 12.3%)	21.8% (14.8%, 35.1%)	178 (16.8%)
	Intermediate	6.2% (3.8%, 9.9%)	11.1% (7.3%, 16.8%)	279 (26.4%)
	Low	3.0% (1.9%, 4.9%)	9.6% (7.1%, 13.1%)	601 (56.8%)
	Overall	4.5% (3.4%, 6.0%)	11.9% (9.6%, 14.6%)	1058 (100.0%)
GE/3T	High	17.3% (12.2%, 24.2%)	36.6% (21.1%, 58.3%)	183 (41.7%)
	Intermediate	6.9% (3.3%, 14.0%)	15.4% (5.1%, 41.4%)	109 (24.8%)
	Low	2.3% (0.7%, 7.0%)	3.6% (1.3%, 9.6%)	147 (33.5%)
	Overall	9.6%	19.0%	439

MRI Manufacturer/ Magnetic Field Strength	Risk Category	Recurrence Rate at 5 years (95% CI)	Recurrence Rate at 10 years (95% CI)	N* (% of subjects)
		(7.1%, 13.0%)	(12.2%, 28.9%)	(100.0%)
Siemens	High	4.4% (2.1%, 9.1%)	34.6% (12.6%, 73.9%)	173 (27.4%)
	Intermediate	4.1% (1.7%, 10.0%)	27.9% (14.0%, 50.8%)	171 (27.1%)
	Low	3.2% (1.7%, 6.7%)	3.2% (1.5%, 6.7%)	287 (45.5%)
	Overall	3.8% (2.4%, 6.0%)	17.1% (9.7%, 29.0%)	631 (100.0%)
Siemens/1.5T	High	5.0% (2.3%, 10.9%)	22.0% (5.7%, 65.5%)	126 (33.5%)
	Intermediate	4.5% (1.7%, 11.8%)	35.5% (16.9%, 64.6%)	106 (28.2%)
	Low	4.0% (1.7%, 11.8%)	4.0% (1.7%, 9.4%)	144 (38.3%)
	Overall	4.5% (2.7%, 7.3%)	17.5% (9.3%, 31.4%)	376 (100.0%)
Siemens/3T	High	2.8% (0.4%, 18.1%)	61.3% (19.1%, 98.6%)	47 (18.4%)
	Intermediate	3.8% (0.6%, 24.3%)	11.9% (2.8%, 42.6%)	65 (25.5%)
	Low	1.6% (0.4%, 6.4%)	1.6% (0.4%, 6.4%)	143 (56.1%)
	Overall	2.5% (0.9%, 7.1%)	16.6% (5.8%, 42.3%)	255 (100.0%)

f. Subgroup analysis by Bins

Using TSR Score numeric values, patients with output “Low” were divided into two bins using: [0, 11) and [11, 21) and patients with output High” were divided into 2 bins: [36, 58) and [58, 100]. The recurrence risks and 95% confidence intervals at 5- and 10-years were estimated from the clinical study data (presented in Table 11 below) and plotted against TSR Score (Presented in Figure 3).

Table 11: Observed 5- and 10-year recurrence rate based on binned TSR Score

Risk Category	Device output (TSRS Range)	Device Output (Mean TSRS)	Bin	N	TSRS Range	Observed Recurrence Rate at 5 years (95% CI)	Observed Recurrence Rate at 10 years (95% CI)	Percentage of patients in the bin
High	[58, 100]	78.6	5	218	[58, 100]	13.6% (9.3%, 19.5%)	34.2% (24.4%, 46.4%)	10.2%
High	[36, 58)	44.2	4	316	[36, 57]	7.4% (4.9%, 11.1%)	21.1% (13.7%, 31.7%)	14.8%
Intermediate	[21, 36)	27.3	3	559	[21, 35]	5.7% (4.0%, 8.2%)	13.4% (9.6%, 18.5%)	26.3%
Low	[11, 21)	15.0	2	521	[11, 20]	3.7% (2.3%, 5.9%)	11.1% (7.8%, 15.8%)	24.5%

Risk Category	Device output (TSRS Range)	Device Output (Mean TSRS)	Bin	N	TSRS Range	Observed Recurrence Rate at 5 years (95% CI)	Observed Recurrence Rate at 10 years (95% CI)	Percentage of patients in the bin
Low	[0, 11)	5.2	1	515	[0, 10]	2.2% (1.2%, 4.1%)	6.2% (3.7%, 10.3%)	24.2%
	Total	26.7		2,129	[0, 100]	5.4% (4.5%, 6.5%)	13.5% (11.4%, 15.9%)	100.0%

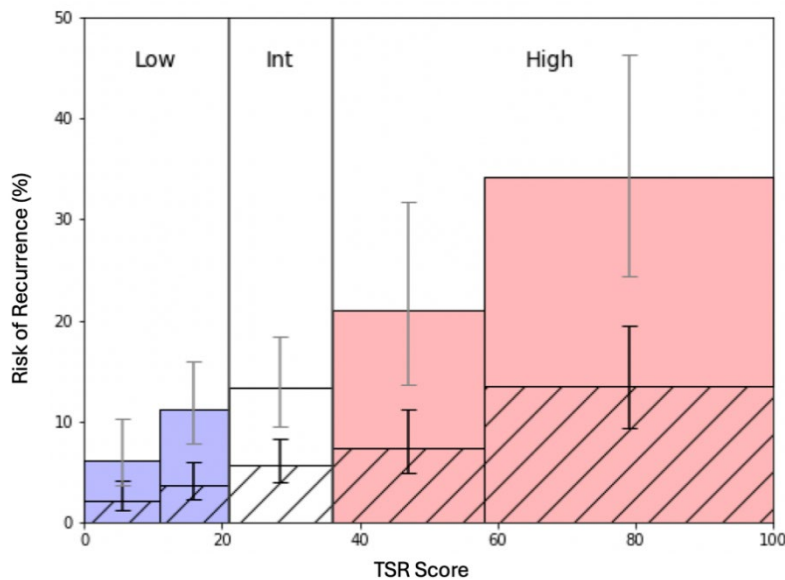


Figure 3: Observed 5- and 10-year risk of recurrence based on binned TSR scores

The empirically determined recurrence probability at 5-year and 10-years is plotted on the y-axis along with 95% CIs, versus TSR score on the x-axis. Hatched boxes and black error bars show 5-year recurrence probability. Open boxes and grey error bars show 10-year recurrence probability.

The analysis of TSR bins demonstrated that a monotonic increase is observed for 5-year and 10-year risks of recurrence.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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