July 1, 2025

Circle Cardiovascular Imaging Inc.
Kyle Mayr
Director - Regulatory Affairs & Quality Management Systems
Suite 1800, 707 8 Avenue SW
Calgary, AB T2P 1H5
Canada

Re: K250221
Trade/Device Name: StrokeSENS ASPECTS Software Application
Regulation Number: 21 CFR 892.2060
Regulation Name: Radiological Computer-Assisted Diagnostic Software For Lesions Suspicious Of Cancer
Regulatory Class: Class II
Product Code: POK
Dated: May 30, 2025
Received: June 2, 2025

Dear Kyle Mayr:

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

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

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

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

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

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn

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

Sincerely,

Jessica Lamb, Ph.D.
Imaging Software Team
Assistant Director
DHT8B: Division of Radiological Imaging
Devices and Electronic Products
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
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: 07/31/2026
*See PRA Statement below.*

Submission Number *(if known)*

K250221

Device Name

StrokeSENS ASPECTS Software Application

Indications for Use *(Describe)*

StrokeSENS ASPECTS is a computer-aided diagnosis (CADx) software device used to assist the clinician in the assessment and characterization of brain tissue abnormalities using CT image data.

The Software automatically registers images and uses an Atlas to segment and analyze ASPECTS Regions. StrokeSENS ASPECTS extracts image data from individual voxels in the image to provide analysis and computer analytics and relates the analysis to the atlas defined ASPECTS regions. The imaging features are then synthesized by an artificial intelligence algorithm into a single ASPECT (Alberta Stroke Program Early CT) Score.

StrokeSENS ASPECTS is indicated for evaluation of patients presenting for diagnostic imaging workup with known MCA or ICA occlusion, for evaluation of extent of disease. Extent of disease refers to the number of ASPECTS regions affected which is reflected in the total score. StrokeSENS ASPECTS provides information that may be useful in the characterization of ischemic brain tissue injury during image interpretation (within 12 hours from time last known well).

StrokeSENS ASPECTS provides a comparative analysis to the ASPECTS standard of care radiologist assessment by providing highlighted ASPECTS regions and an automated editable ASPECTS score for clinician review. StrokeSENS ASPECTS presents the original and annotated images for concurrent reads. StrokeSENS ASPECTS additionally provides a visualization of the voxels contributing to the automated ASPECTS score.

Limitations:
1. StrokeSENS ASPECTS is not intended for primary interpretation of CT images. It is used to assist physician evaluation.
2. StrokeSENS ASPECTS has been validated in patients with known MCA or ICA occlusion prior to ASPECTS scoring.
3. Use of StrokeSENS ASPECTS in clinical settings other than brain ischemia within 12 hours from time last known well, caused by known ICA or MCA occlusions, has not been tested.
4. StrokeSENS ASPECTS has only been validated and is intended to be used in patient populations aged over 21.

Contraindications:
• StrokeSENS ASPECTS is contraindicated for use on brain scans displaying neurological pathologies other than acute ischemic stroke, such as tumors or abscesses, hemorrhagic transformation, and hematoma.

Cautions:
• Patient Motion: Excessive patient motion leading to artifacts that make the scan technically inadequate.

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

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

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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# StrokeSENS ASPECTS 510(k) Summary

The following 510(k) summary of safety and effectiveness information is submitted in accordance with the requirements of the Safe Medical Device Act 1990 and 21 CFR 807.92(c).

## I. SUBMITTER


| | |
|---|---|
| **Submitter's Name:** | Circle Cardiovascular Imaging, Inc. |
| **Address:** | Suite 1800 – 707 8th Ave SW, Calgary, AB, Canada, T2P 1H5 |
| **Date Prepared:** | January 23 2025 |
| **Telephone Number**: | +1 587 686-0787 |
| **Contact Person :** | Kyle Mayr |
| **Email:** | kyle.mayr@circlecvi.com |


## II. DEVICE

| | |
|---|---|
| **Name of the Device:** | StrokeSENS ASPECTS software application |
| **Short Brand Name:** | StrokeSENS ASPECTS |
| **Classification Name:** | Radiological computer-assisted diagnostic software for lesions suspicious of cancer. |
| **Proposed Classification:** | Device Class: II<br>Product Code: POK<br>Regulation Number: 21 CFR 892.2060 |

## III. PREDICATE DEVICE

The predicate device is Brainomix 360 e-ASPECTS manufactured by Brainomix Limited and cleared under K221564.

The predicate device has not been subject to a design-related recall.

## IV. DEVICE DESCRIPTION

StrokeSENS ASPECTS is a stand-alone software device that uses machine learning algorithms to automatically process NCCT (non-contrast computed tomography) brain image data to provide an output ASPECTS score based on the Alberta Stroke Program Early CT Score (ASPECTS) guidelines.

The post-processing image results and ASPECTS score are identified based on regional imaging features and overlayed onto brain scan images. StrokeSENS ASPECTS provides an automated ASPECTS score based on the input CT data for the physician. The score includes which ASPECTS regions are identified based on regional imaging features derived from non-contrast computed tomography (NCCT) brain image data. The results are generated based on the Alberta Stroke Program Early CT Score (ASPECTS) guidelines and provided to the clinician for review and verification. At the discretion of the clinician, the scores may be adjusted based on the clinician's judgement.

StrokeSENS ASPECTS can connect with other DICOM-compliant devices, to transfer NCCT scans for software processing.

Results and images can be sent to a PACS via DICOM transfer and can be viewed on a PACS workstation or via the StrokeSENS UI or other DICOM-compatible radiological viewer.

StrokeSENS ASPECTS provides an automated workflow which will automatically process image data received by the system in accordance with pre-configured user DICOM routing preferences.

StrokeSENS ASPECTS principal workflow for NCCT includes the following key steps:

- Receive NCCT DICOM Image
- Automated image analysis and processing to identify and visualize the voxels which have been included in the ASPECTS score (Also referred to as a 'heat map' or 'VCTA; Voxels Contributing to ASPECTS Score').
- Automated image analysis and processing to register the subject image to an atlas to segment and highlight ASPECTS regions and to display whether or not each region is qualified as contributing to the ASPECTS score.
- Generation of auto-generated results for review and analysis by users.
- Generation of verified/modified result summary for archiving, once the user verifies or modifies the results.

Once the auto-generated ASPECTS score results are available, the physician is asked to confirm that the case in question is for an ICA or MCA occlusion and is able to modify/verify the ASPECTS regional score. The ASPECTS auto-generated results, including the ASPECTS score, indication of affected side, affected ASPECTS regions and voxel-wise analysis (shown as a heatmap of voxels 'contributing to ASPECTS score'), along with the user-verified/modified result summary can be sent to the Picture Archiving and Communications System (PACS).

## V. INDICATIONS FOR USE

StrokeSENS ASPECTS is a computer-aided diagnosis (CADx) software device used to assist the clinician in the assessment and characterization of brain tissue abnormalities using CT image data.

The Software automatically registers images and uses an Atlas to segment and analyze ASPECTS Regions. StrokeSENS ASPECTS extracts image data from individual voxels in the image to provide analysis and computer analytics and relates the analysis to the atlas defined ASPECTS regions. The imaging features are then synthesized by an artificial intelligence algorithm into a single ASPECT (Alberta Stroke Program Early CT) Score.

StrokeSENS ASPECTS is indicated for evaluation of patients presenting for diagnostic imaging workup with known MCA or ICA occlusion, for evaluation of extent of disease. Extent of disease refers to the number of ASPECTS regions affected which is reflected in the total score. StrokeSENS ASPECTS provides information that may be useful in the characterization of ischemic brain tissue injury during image interpretation (within 12 hours from time last known well).

StrokeSENS ASPECTS provides a comparative analysis to the ASPECTS standard of care radiologist assessment by providing highlighted ASPECTS regions and an automated editable ASPECTS score for clinician review. StrokeSENS ASPECTS presents the original and annotated images for concurrent reads. StrokeSENS ASPECTS additionally provides a visualization of the voxels contributing to the automated ASPECTS score.

Limitations:

1. StrokeSENS ASPECTS is not intended for primary interpretation of CT images. It is used to assist physician evaluation.
2. StrokeSENS ASPECTS has been validated in patients with known MCA or ICA occlusion prior to ASPECTS scoring.
3. Use of StrokeSENS ASPECTS in clinical settings other than brain ischemia within 12 hours from time last known well, caused by known ICA or MCA occlusions, has not been tested.
4. StrokeSENS ASPECTS has only been validated and is intended to be used in patient populations aged over 21.

Contraindications:

- StrokeSENS ASPECTS is contraindicated for use on brain scans displaying neurological pathologies other than acute ischemic stroke, such as tumours or abscesses, haemorrhagic transformation, and hematoma.

Cautions:

- Patient motion: Excessive patient motion leading to artifacts that make the scan technically inadequate.

## VI. COMPARISON WITH PREDICATE DEVICE

The detailed analysis of the subject device and the predicate device (shown in **Table 1** and **Table 2**) demonstrates that the subject device is substantially equivalent in indications for use / intended use, technological characteristics, functionality, and operating principles with the predicate (K221564). Of the three characteristics (technical, biological, and clinical) required for the demonstration of equivalence, biological characteristics are not applicable since both the subject device and predicate device are software as a medical device application with no tangible component interfacing with the body.

Both proposed and predicate devices have the same intended use. Both devices are computer-aided diagnosis (CADx) software devices used to assist clinicians in the assessment and characterization of brain tissue abnormalities using CT image data.

Both devices segment and identify ASPECTS regions and use machine learning algorithms to analyze image data to facilitate the evaluation of extent of disease and to identify and count the affected ASPECTS regions to generate an ASPECTS score.

Both devices display and highlight the affected ASPECTS regions along with the automatically generated ASPECTS score. Both devices are not intended for primary interpretation of CT images and both require that cases processed meet prerequisite criteria such that a primary diagnosis of ICA or MCA occlusion has already been made by clinicians prior to accessing the processing results and the resulting ASPECTS score.

Both devices include a gating condition requiring users to confirm that the case in question is for a confirmed ICA or MCA occlusion before processing results are made available.

Both devices include pre-processing steps to normalize NCCT scan orientation in order to identify and segment ASPECTS regions on the subject NCCT scan.

In both cases, the devices identify signs indicative of ischemic damage and relate these to the segmented ASPECTS regions in order to determine whether or not individual ASPECTS regions are included as contributing to a reduced ASPECT score. In both cases, the segmented ASPECTS regions are labelled and presented to users in the software User Interface with the regions highlighted depending on whether they have been determined to affect the ASPECT score or not. In both cases, users can manually edit the automated result for one or more ASPECTS regions.

The following principal difference exists between StrokeSENS ASPECTS and the predicate device:

- StrokeSENS ASPECTS is indicated for cases within 12 hours from time last known well, the predicate is indicated for cases within 6 hours from time last known well.
- StrokeSENS ASPECTS is not limited to Siemen’s Somatom Definition CT scanners

StrokeSENS ASPECTS has similar technological characteristics and indications for use as the predicate device.

*Table 1. Indications comparison.*

| | **Subject Device**<br>*StrokeSENS ASPECTS*<br><br>Manufactured by Circle Cardiovascular Imaging Inc. | **Predicate Device**<br>*Brainomix 360 e-ASPECTS (K221564)*<br><br>Manufactured by Brainomix Limited |
|---|---|---|
| Indications for Use/Intended use | StrokeSENS ASPECTS is a computer-aided diagnosis (CADx) software device used to assist the clinician in the assessment and characterization of brain tissue abnormalities using CT image data.<br><br>The Software automatically registers images and uses an Atlas to segment and analyze ASPECTS Regions. StrokeSENS ASPECTS extracts image data from individual voxels in the image to provide analysis and computer analytics and relates the analysis to the atlas defined ASPECTS regions. The imaging features are then synthesized by an artificial intelligence algorithm into a single ASPECT (Alberta Stroke Program Early CT) Score.<br><br>StrokeSENS ASPECTS is indicated for evaluation of patients presenting for diagnostic imaging workup with known MCA or ICA occlusion, for evaluation of extent of disease. Extent of disease refers to the number of ASPECTS regions affected which is reflected in the total score. StrokeSENS ASPECTS provides information that may be useful in the characterization of ischemic brain tissue injury during image interpretation (within 12 hours from time last known well).<br><br>StrokeSENS ASPECTS provides a comparative analysis to the ASPECTS standard of care radiologist assessment by providing highlighted ASPECTS regions and an automated editable ASPECTS score for clinician review. StrokeSENS ASPECTS presents the original and annotated images for concurrent reads. StrokeSENS ASPECTS additionally provides a visualization of the voxels contributing to the automated ASPECTS score.<br><br>Limitations:<br>1. StrokeSENS ASPECTS is not intended for primary interpretation of CT images. It is used to assist physician evaluation.<br>2. StrokeSENS ASPECTS has been validated in patients with known MCA or ICA occlusion prior to ASPECTS scoring.<br>3. Use of StrokeSENS ASPECTS in clinical settings other than brain ischemia within 12 hours from time last known well, caused by known ICA or MCA occlusions, has not been tested.<br>4. StrokeSENS ASPECTS has only been validated and is intended to be used in patient populations aged over 21. | Brainomix 360 e-ASPECTS is a computer-aided diagnosis (CADx) software device used to assist the clinician in the assessment and characterization of brain tissue abnormalities using CT image data.<br><br>The software automatically registers images and uses an Atlas segment to analyze ASPECTS regions. Brainomix 360 e-aspects extracts image data from individual voxels in the image to provide analysis and computer analytics and relates the analysis to the atlas defined ASPECTS regions. The imaging features are then synthesized by an artificial intelligence algorithm into a single ASPECTS (Alberta Stroke Program Early CT) Score.<br><br>Brainomix 360 e-ASPECTS is indicated for evaluation of patients presenting for diagnostic imaging workup with known MCA or ICA occlusion, for evaluation of extent of disease. Extent of disease refers to the number of ASPECTS regions affected which is reflected in the total score. Brainomix 360 e-ASPECTS provides information that may be useful in the characterization of ischemic brain tissue injury during image interpretation (within 6 hours from time last known well).<br><br>Brainomix 360 e-ASPECTS provides a comparative analysis to the ASPECTS standard of care radiologist assessment by providing highlighted ASPECTS regions and an automated editable ASPECTS score for clinician review. Brainomix 360 e-ASPECTS additionally provides a visualization of the voxels contributing to the automated ASPECTS score and the voxels excluded from the automated ASPECTS score.<br><br>Limitations:<br>1. Brainomix 360 e-ASPECTS is not intended for primary interpretation of CT images. It is used to assist physician evaluation.<br>2. Brainomix 360 e-ASPECTS has ben validated in patients with known MCA or ICA occlusion prior to ASPECTS scoring.<br>3. Brainomix 360 e-ASPECTS is not suitable for use on brain scans displaying neurological pathologies other than acute stroke, such as tumours or abscesses, haemorrhagic transformation and hematoma.<br>4. Use of Brainomix 360 e-ASPECTS Module in clinical settings other than brain ischemia within 6 hours from time last known well, caused by known ICA or MCA occlusions has not been tested. |

| | **Subject Device**<br>*StrokeSENS ASPECTS*<br><br>Manufactured by Circle Cardiovascular Imaging Inc. | **Predicate Device**<br>*Brainomix 360 e-ASPECTS (K221564)*<br><br>Manufactured by Brainomix Limited |
|---|---|---|
| | Contraindications:<br>• StrokeSENS ASPECTS is contraindicated for use on brain scans displaying neurological pathologies other than acute ischemic stroke, such as tumours or abscesses, haemorrhagic transformation and hematoma.<br><br>Cautions:<br>• Patient motion: Excessive patient motion leading to artifacts that make the scan technically inadequate. | 5. Brainomix 360 e-ASPECTS has only been validated and is intended to be used in patient populations aged over 21.<br>6. Brainomix 360 e-ASPECTS has been validated and is intended to be used on Siemens Somatom Definition scanners.<br>7. Brainomix 360 e-ASPECTS is not intended for mobile diagnostic use. Images viewed on a mobile platform are compressed preview images and not for diagnostic interpretation.<br><br>Contraindications/Exclusions/Cautions:<br>• Patient motion: Excessive patient motion leading to artifacts that make the scan technically inadequate.<br>• Haemorrhagic Transformation, Hematoma. |

*Table 2. Regulatory and technological features comparison.*

| **Feature** | **Subject Device**<br>*StrokeSENS ASPECTS*<br><br>Manufactured by Circle Cardiovascular Imaging Inc. | **Predicate Device**<br>*Brainomix 360 e-ASPECTS (K221564)*<br><br>Manufactured by Brainomix Limited |
|---|---|---|
| Device Class | II | II |
| Product Code(s) | POK | POK |
| Regulation Name | Radiological computer-assisted diagnostic software for lesions suspicious of cancer. | Radiological computer-assisted diagnostic software for lesions suspicious of cancer. |
| Regulation Number | 21 CFR 892.2060 | 21 CFR 892.2060 |
| DICOM Compliant? | Yes | Yes |
| Input Data Type | Non-contrast head CT scans | Non-contrast head CT scans |
| Clinical Application/Anatomic al Region | Stroke/Head | Stroke/Head |
| Standard of Care Representation | ASPECT Scoring | ASPECT Scoring |
| Alteration of original image data base | No | No |
| Alters Standard of Care Workflow | In parallel to | In parallel to |
| Technical Implementation | ML/AI (Deep Learning) | ML/AI (Random Forest) |
| Design: Computer Platform | Standard off-the-shelf server or virtual server | Standard off-the-shelf server or virtual server |
| Image Overlay | ASPECTS regions, highlighted by algorithms.<br>Voxel-wise analysis visualized as a heat map. | ASPECTS regions, highlighted by algorithms.<br>Voxel-wise analysis visualized as a heat map. |
| Gating Conditions | Users must confirm ICA or MCA occlusion prior to accessing ASPECTS results | Users must confirm ICA or MCA occlusion prior to accessing ASPECTS results |

## VII. PERFORMANCE DATA AND TESTING

Performance validation testing and software verification and validation activities were conducted to comply with specified design requirements in accordance with applicable consensus standards and to satisfy the special controls of the device classification.

Performance testing was conducted to verify compliance with specified design requirements in accordance with ISO 13485:2016+A11:2021, IEC 62304:2006+A1:2015, IEC 62366:2015+A1:2020 and ISO 14971:2019+A11:2021. DICOM conformance testing was performed to verify compliance with NEMA 3.1-3.20 (2021) standards. Verification and validation testing were conducted to ensure specifications and performance of the device and were performed per the FDA Guidance documents “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices” and “Content of Premarket Submission for Management of Cybersecurity in Medical Devices”. Software performance, verification and validation testing demonstrated that the StrokeSENS system met all design requirements and specifications. StrokeSENS has been developed and tested to meet cybersecurity requirements using design vulnerability Assessments (Threat Models), SBOM’s, NVD assessments, and Penetration Testing

This performance validation testing demonstrated that StrokeSENS ASPECTS provides accurate representation of key processing parameters under a range of clinically relevant parameters and perturbations associated with the intended use of the software. Software performance, validation and verification testing demonstrated that the StrokeSENS ASPECTS meets all design requirements and specifications. Design Verification and Validation according to 21 CFR 820.30 passed.

The results of software verification and validation and algorithmic testing demonstrate that StrokeSENS ASPECTS has met all design requirements and specifications associated with the intended use of the software. No deviations were found during the execution of the testing.

**Standalone Performance:** Stand-alone performance testing demonstrated that the proposed device provides accurate representation of key processing parameters under a range of clinically relevant parameters and perturbations associated with the intended use of the software. The stand-alone performance testing demonstrates the generalized performance for a range of typical patient demographics and a typical range of cases with confounding factors and including radiologically normal cases which is the same as for the predicate device.

The standalone validation dataset is comprised of 200 non-contrast CT scans from acute ischemic stroke patients with a confirmed ICA/MCA occlusion. Patients aged 21 years and younger were excluded. The median age was 71 years, and 55.5% were female. Patients were from multiple clinical sites including 77 from Canada, 59 from the United States, 51 from Europe, and 13 from Asia-Australia. Ground truth ASPECTS score was <7 in 69 patients and >6 in 131 patients. All patients presented within 6 hours of time last seen well. 164 patients had a proximal vessel occlusion (internal carotid artery or M1 segment of the middle cerebral artery) and 36 were non-proximal.

The primary standalone performance assessment was a region-level Clustered ROC Analysis to demonstrate the standalone performance of the ASPECTS device with respect to the expert consensus reference standard. The analysis demonstrated an AUC-ROC of 90.9% (95% CI = [88.7%, 93.1%]), with a accuracy of 90.6 [89.7%, 91.5%], a sensitivity of 70.6% [69.2%, 72.1%] and a specificity of 93.9% [93.2%, 94.7%].

This stand-alone performance testing demonstrates that StrokeSENS ASPECTS performance generalises to a range of image acquisition and reconstruction parameters encountered in multiple clinical sites and for a range of scanner types and manufacturers.

**Clinical Validation Reader Improvement:** The MRMC study dataset was comprised of 100 non-contrast CT scans from acute ischemic stroke patients with a confirmed ICA/MCA occlusion. Patients aged 21 years and younger were excluded. The median age was 72 years, and 53% were female. 50% of the patients were from 11 sites in Canada, and the other 50% were from 12 sites in the United States. Ground truth ASPECTS score was <7 in 27 patients and >6 in 73 patients. 88 patients presented within 6 hours of time last seen well, and the remaining 12 patients presented between 6 and 12 hours of time last seen well. 64 patients had a proximal vessel occlusion (internal carotid artery or M1 segment of the middle cerebral artery), and 36 had non-proximal MCA occlusions.

Comparison of the area under the curve (AUC) for each reader with and without the support of the StrokeSENS ASPECTS tool showed a statistically significant improvement of 5.7% from 68.6% to 74.3% (p-value<0.001) which was the primary endpoint for the study. When comparing reader performance with the ground truth, the improved AUC in the primary endpoint was driven by an increase in the sensitivity and specificity, derived from the mixed-effects logistic regression model, demonstrating (1) a statistically significant improvement in sensitivity of 9.7% (p-value<0.001) from 41.3% (unaided) to 51.0% (aided), and a statistically significant improvement in specificity of 1.6% (p-value<0.001) from 95.9% (unaided) to 97.5% (aided) when assisted by StrokeSENS ASPECTS compared to unassisted reading. Overall percentage agreement (accuracy) also improved in line with the AUC result by 2.6% (p-value<0.001) from 89.5% (unaided) to 92.0% (aided). Subgroup analysis based on the clinical training of the reader (radiologist versus neurologist) demonstrates a consistent improvement of StrokeSENS ASPECTS across reader groups.

The overall ASPECTS score was more consistent between readers with use of StrokeSENS ASPECTS with the Fleiss's Kappa value among the 8 readers in the study increased by 28.5%, from 32.3% (unaided) to 60.8% (aided). The range in AUC between users was also narrower with StrokeSENS ASPECTS than unassisted indicating a reduction in the variation of performance between different readers when StrokeSENS ASPECTS outputs are available.

The results showed statistically significant improvements in the agreement between the readers and a reference standard when using the StrokeSENS ASPECTS software compared to the conventional manual method used in routine clinical practice.

**Clinical Validation Voxels contributing to ASPECTS (VCTA):** The results of this VCTA verification study demonstrated a high Concordance Rate of 97.0% (i.e., the proportion of cases with a consensus score of Fair Concordance or above), with respect to the agreement between the device's auto-generated VCTA overlay and expert neuroradiologist assessment of ischemic tissue.

## VIII. CONCLUSION

StrokeSENS ASPECTS (subject device of this filing) is equivalent to the predicate (Brainomix 360 e-ASPECTS). It is intended to aid in the assessment of a specific disease state using standard of care scoring using machine learning/artificial intelligence algorithms. Both devices use ROI based assessments based on an ASPECTS defined atlas. Performance data demonstrates that StrokeSENS ASPECTS performs as intended within the same clinically relevant parameters for the intended use as the predicate device.

An MRMC clinical study was conducted to support substantial equivalence. The clinical data demonstrates that StrokeSENS ASPECTS shows a significant improvement in the agreement between the readers and a reference standard when using the StrokeSENS ASPECTS software compared to routine clinical practice. StrokeSENS ASPECTS is intended to improve reader performance in estimating an overall ASPECTS score. The risk/benefit profile of StrokeSENS ASPECTS remains favorable based on the positive impact on readers' overall aided performance in calculating an ASPECTS score (as measured in the reader study), and the standardization of ASPECTS reading between clinicians (higher inter-reader agreement) in identifying affected ASPECTS regions.

The company believes that StrokeSENS ASPECTS is substantially equivalent to the Brainomix 360 e-ASPECTS predicate.