USER MANUAL

StrokeSENS
Version 2.2

circle
CARDIOVASCULAR
IMAGING

StrokeSENS 2.2

User Manual

July 2024

Regulatory Information

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UDI

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European Union

CE
1639

StrokeSENS is qualified as a class IIa medical device. It complies with the requirements of the European Medical Device Directive 93/42/EEC under the transitional provisions of Article 120 of the Medical Device Regulation 2017/745.

EC REP

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QDossier B.V.
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euar@celegence.com

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CAUTION: US Federal law restricts this device to sale by or on the order of a licensed healthcare practitioner.

℞ Only

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1 Regulatory

1.1 Regulatory Information

Agency	Authorized Representative	Approval / Clearance Reference
Australia TGA ARTG	**KD&A Pty Ltd** 286 Flinders Street Adelaide SA 5000	ARTG number: 380409
CE Mark (MDD)	**EU Authorized Representative** QDossier B.V. Cartografenweg 28C 5141 MT Waalwijk, The Netherlands euar@celegence.com	CE Mark Certificate US21/819944332 issued by SGS for StrokeSENS.
Health Canada	N/A	Health Canada device license number: 107386
FDA	**US Agent** ComplianceAcuity, Inc. 485 Clinton St, #888 Ridgway, CO 81432	StrokeSENS LVO – 510k (K212261)
UK	**Celegence Limited** Kemp House, 128 City Road, London, EC1V 2NX United Kingdom	MHRA registration: 32312

2 Introduction

This User Guide is also available:
• On the Internet at: https://www.circlecvi.com/strokesens-documentation

A paper copy of this User Guide can be ordered at no additional cost. Please, send a request to your Sales or Service representative. They will transfer your request to support@circlecvi.com. In application of the EU Commission Regulation on electronic instructions for use of medical devices, in European Union, your request should be treated within 7 days.

2.1 Product Description

StrokeSENS is a decision-aid software package to be used by clinicians to perform image processing of contrast-enhanced computed tomography (CT) scans of the brain in patients with suspected acute stroke. Different acquisition types can be processed by different modules within the software package:

- Analysis of non-contrast CT (NCCT) images is provided by the StrokeSENS ASPECTS module, which assesses regions with suspected acute ischemic tissue for Alberta Stroke Program Early CT (ASPECT) scoring
- Analysis of contrast-enhanced CT (CTA) images is provided by the StrokeSENS LVO module, which detects suspected large vessel occlusions (LVO)

StrokeSENS is a software-only device designed with standard APIs for operation within a compatible radiological software platform.

The StrokeSENS software package is responsible for:

1. Organizing and filtering input NCCT, CTA, and mCTA images received from the host system
2. Processing input NCCT images for identification of ASPECTS scoring
3. Processing input CTA images for identification of LVO
4. Communicating results/outputs to the host system for generation of notification/triage workflow

The compatible host system is responsible for:

1. Running or installing the StrokeSENS device within the host system radiological platform,
2. Providing the necessary NCCT input images to the StrokeSENS ASPECTS software package,
3. Providing the necessary CTA input images to the StrokeSENS LVO software package,
4. Receiving the output/result indication and generating the desired workflow (including notification/triage and viewing of DICOM results, if applicable)

2.2 Symbols used in documentation

Symbol	Description
	**Consult Instructions for Use**: Indicates that the user shall read Instructions for Use.
	**Manufacturer**: Indicates the medical device manufacturer's name and address.
	**Distributor:** Indicates the entity distributing the medical device into the locale
	**Importer:** Indicates the entity Importing the medical device into the locale
	**Unique device identifier (UDI):** Indicates a carrier that contains Unique Device Identifier information
	**General caution**: Used to highlight the fact that there are specific warnings or precautions associated with the application, which are not otherwise found on the label.
	**Medical Device**: Indicates this product is a medical device.
	**Authorized representative in the European Community:** Indicates the authorized representative in the European Community.
	**Authorized representative in Switzerland:** Indicates the authorized representative, physical or legal, with registered office in Switzerland acting on behalf of Medical Devices Manufacturers based outside the Swiss territory.

2.3 Terms and Definitions

Term	Definition
StrokeSENS LVO	The StrokeSENS LVO software device is a computer-aided triage and notification software intended to flag and communicate findings of suspected LVO in head CTA images. It consists of algorithms and processing methods intended to be used as part of an integrated compatible radiological software platform such as StrokeSENS platform, or other compatible radiological software platform solutions.
StrokeSENS ASPECTS	The StrokeSENS ASPECTS software device is a computer-aided diagnosis (CADx) software device used to assist the clinician in the assessment and characterization of brain tissue abnormalities by predicting the ASPECT (Alberta Stroke Program Early CT) score based on CT image data. It consists of algorithms and processing methods intended to be used as part of an integrated compatible radiological software platform such as StrokeSENS platform, or other compatible radiological software platform solutions.
Compatible Radiological Software Platform	A compatible radiological software platform solution is responsible for providing the electronic medium for communication, storage, and transfer of medical images as well as may be responsible for the coordination of email/notification results, as specified by the requirements of the StrokeSENS LVO device. The compatible radiological software solution may also provide other radiological functionalities outside the scope of the StrokeSENS LVO device functionality including image review functionality and image processing/analysis workflow.
CTA	CTA or Computed Tomography Angiography is a type of medical imaging in which contrast-enhanced images are acquired by computed tomography devices. CTA of the head (and neck) are commonly acquired in suspected acute stroke patients.
DICOM	Digital Imaging and Communications in Medicine (DICOM) is the standard for the communication and management of medical imaging information and related data. DICOM is most commonly used for storing and transmitting medical images enabling the integration of medical imaging devices such as scanners, servers, workstations, printers, network hardware, and picture archiving and communication systems (PACS) from multiple manufacturers.
Large vessel occlusion (LVO)	Common pathology of acute ischemic stroke, wherein a large arterial vessel in the brain is occluded by a clot. StrokeSENS LVO is indicated for large vessel occlusions in the anterior circulation only (i.e. ICA – MCA vessels).
Alberta Stroke Program Early CT Score (ASPECTS)	10-point quantitative score used to assess early ischemic changes on non-contrast CT head scan.
PACS	Picture Archiving and Communication System

3 Basic Components and Indication for Use

3.1 Intended Use / Intended Purpose

StrokeSENS is intended to be used by qualified medical professionals for viewing and evaluation of computed tomography (CT) images in a Digital Imaging and Communications in Medicine (DICOM) standard format, for the purpose of obtaining diagnostic information as part of a comprehensive diagnostic decision-making process.

3.2 Indications for Use

StrokeSENS is a decision-aid software package to be used by clinicians to perform image processing, analysis, viewing and communication of computed tomography (CT) scans of the brain in patients with suspected acute stroke. Data and images are acquired through DICOM-compliant imaging devices prior to processing and analysis in StrokeSENS.

The StrokeSENS software provides analysis capabilities for imaging datasets acquired with standard CT imaging and contrast enhanced CT Angiography (CTA) modalities. Analysis of non-contrast CT images includes assessment of regions with suspected acute ischemic tissue. Analysis of contrast-enhanced CT images includes automated detection of anterior circulation Large Vessel Occlusion (LVO).

In the case of a suspected anterior circulation LVO, the system will send a notification to a pre-configured destination(s) (members of the acute stroke team), notifying them of the existence of a suspected LVO that requires review. The notification system is intended to be used in parallel to the standard of care workflow to notify clinicians of the existence of the case earlier than they may have been notified as part of the standard of care workflow. Images are available for viewing on a mobile device and on a standard radiology workstation. Images that are previewed on a mobile device are for informational purposes only and are not intended for diagnostic use beyond notification.

3.3 Contraindications

None

3.4 Intended users

The intended users of StrokeSENS shall be clinicians and hospital networks involved in the management of acute stroke patients. Specifically, the intended users of StrokeSENS shall be clinicians including radiologists, neurologists, neuro-interventionalists, emergency physicians, and neurocritical care specialists.

3.5 Patient population / Target population

StrokeSENS is intended to be used on adults (22 years and older) with suspected acute stroke.

The StrokeSENS ASPECTS module is intended to be used on adults with confirmed ICA or MCA occlusion within 6 hours of symptom onset.

The StrokeSENS LVO module is intended to be used on adults to detect anterior circulation Large Vessel Occlusions (LVO).

3.6 Training required for use of this device

Training for the StrokeSENS device is satisfied through this User Manual in the form of the Indications For Use / Intended Use, the system and image requirements, workflow / configuration instructions (with screenshots), and Device Operating Instructions. Detailed installation instructions and on- or off-site support are provided to the IT Administrators upon installation. The intended users of the software are specialists trained in the diagnosis and management of acute stroke and are familiar with the use of radiological software environments. No additional formal training is necessary to effectively use the software.

3.7 Clinical Benefits

StrokeSENS ASPECTS provides automated ASPECTS scoring to aid clinicians in their assessment of early ischemic changes (ASPECTS) on non-contrast CT images. This standardizes ASPECT scoring across clinicians from different sub-specialties.

StrokeSENS LVO allows clinicians and hospital networks to be notified of time-sensitive and potentially dangerous cases earlier than they may have been in the standard of care pathway.

3.8 Undesirable Side Effects

None

4 Warnings and Cautions

Safety notice legends

WARNING:
This indicates a potentially hazardous situation, which, if not avoided, could result in serious injury.

CAUTION:
This indicates a potentially hazardous situation which, if not avoided, may result in minor or moderate injury.

NOTICE:
This indicates a non–hazardous situation, which, if not avoided, could result in equipment damage, lost time, or reduced image quality.

WARNING: Patient Data
The displayed study/patient data as well as information used for processing images are initially derived from the DICOM information where available. Note that editing these values in the original DICOM may affect the calculations in the software. It is the responsibility of the user to verify the results before being used for making diagnostic or treatment decisions.

WARNING: Artificial Intelligence (AI) algorithms are used to produce visualizations and identify suspicious findings in CT images for the purpose of aiding the clinician in the assessment of patients with suspected acute stroke. Inaccurate results may be produced. Results are not to be considered a primary diagnosis. Users are intended to review all available information, including the original CT images, before making patient management decisions.

WARNING: StrokeSENS is a parallel workflow tool intended to be used in conjunction with standard of care procedures. StrokeSENS should not replace the standard of care procedure.

WARNING: Misleading information due to user error, inadequate source images, and/or inaccurate Artificial Intelligence predictions may lead to misdiagnosis.

CAUTION: StrokeSENS relies on the quality and correctness of the image source data, for the software to satisfy its intended use. Clinicians are intended to confirm findings on original images prior to making diagnostic or treatment decisions. Information provided by StrokeSENS is intended to be used as an adjunct to standard of care procedures and should not be considered as primary diagnosis.

CAUTION: StrokeSENS undergoes rigorous Cybersecurity and Systems testing prior to release. Once deployed on-site, the security and connectivity of the StrokeSENS system within the hospital IT infrastructure is managed by the on-site/customer's IT and Security professionals. It is therefore the responsibility of the customer to ensure appropriate security measures are in place to promote safe and effective use of the product within their local and jurisdictional regulations.

CAUTION: No known susceptibilities to other software applications have been identified, however, it is the end-user's responsibility to ensure the environment in which the StrokeSENS application is installed is maintained and free of other applications that may jeopardize the safe and effective use of the software.

CAUTION: This user manual is considered adequate training for the safe and effective use of the product. Training will be made available to the customer at time of installation and for major product upgrades, however training is not mandatory or required. Ongoing technical support and customer service is available. See Technical Support section below.

CAUTION: StrokeSENS is not for use in patients younger than 22 years of age. Use of this device in a population outside of the intended use, could result in incorrect outputs from the device, potentially leading to minor Harm of the patient or minor functionality failure.

NOTICE: **Note on IEC 60601-1:** As a software-only solution, StrokeSENS does not fall under the safety and compliance considerations of the IEC 60601-1 standard. Complying with these standards for medical electrical equipment used in conjunction with StrokeSENS is the responsibility of the relevant clinicians and institutions.

NOTICE: Software may slow down when other applications are being run on the same machine.

5 System Hardware and Software Specifications

5.1 Compatible Imaging Systems

StrokeSENS does not have a user interface. Results of the StrokeSENS modules are used for the purpose of early identification and notification of potentially time-sensitive cases. Results and notifications are intended to be incorporated into other radiological platforms and enterprise workflow environments (such as PACS, radiology workstations, and mobile stroke triage workflows) through well-defined APIs or standard communication protocols (i.e. DICOM services). Compatible host systems are responsible for communicating the triage and/or notification from the StrokeSENS modules findings through various workflow mechanisms. These mechanisms can include but are not limited to push notifications, worklist prioritization, UI indicators, email notification, and/or DICOM display, depending on the desired existing workflow of the host system. Access to view the original input images is the responsibility of the host system.

StrokeSENS modules have been tested on CT images from a variety of different scanner systems in the market, including:

- General Electric (Discovery series, Lightspeed series, Revolution series, Optima series)
- Siemens (Somatom Definition series, Sensation series, Somatom Force)
- Philips (Brilliance series, iCT series, Ingenuity series, MX8000 series)
- Toshiba (Aquilion series)

This document provides user instructions and labelling for the StrokeSENS software as integrated into compatible host application environments. Additional host system-specific user information may be available and provided by the host system or by Circle as a supplement to the existing user manual. Please contact support@circlecvi.com with any questions regarding system-specific workflows and supported radiological environments.

5.2 Software architecture

All computation, and storage is handled by StrokeSENS on the server it is installed on. All communication with StrokeSENS is done through TCP, or HTTP requests. The server requirements are outlined below.

5.3 System hardware and software specifications

The following specification can be applied to provision one virtual machine:

Requirement	Recommendations
CPU	Intel(R) Xeon(R) CPU E5-2680 v3 @ 2.50Hz, 2500 Mhz, 4 Core(s), 4 Logical Processor(s)(Analysis of a single study requires 2 cores to support incoming studies, and an additional 2 cores to perform machine learning computation tasks)
RAM	16 GB DDR3 to support study analysis (or better for faster processing)
Storage	64 GB SSD (Depending on the number and the sizes of studies stored, this number may be varied.)
OS	Linux Kernel 3.10 minimum requirement for Docker
Network	1 GB ethernet minimum

6 Sorting and Classification of DICOM Series

6.1 Default Series Classifier

All study DICOM images received by the StrokeSENS application will be processed by a default classification algorithm. This serves to retrieve only adequate head CT volumes for processing by the StrokeSENS modules. Please refer to **Section 7.2** for the recommended acquisition parameters for the optimal processing of the StrokeSENS modules. The criteria for the default classifier are as follows:

NCCT for ASPECTS
1. Modality = CT
2. Orientation = Axial (calculated from the Image Orientation Patient DICOM tag)
3. Image Type = Original/Primary
4. Field of View along the Z axis > 50 mm
5. Volumes = 1
6. Window Width <= 210

- Modality and Orientation are hard requirements, i.e., Can not be bypassed via the classifier bypass (see **Section 6.2**).
- NCCT series with a slice thickness of >=2.5 mm will take priority over series that are <2.5 mm.

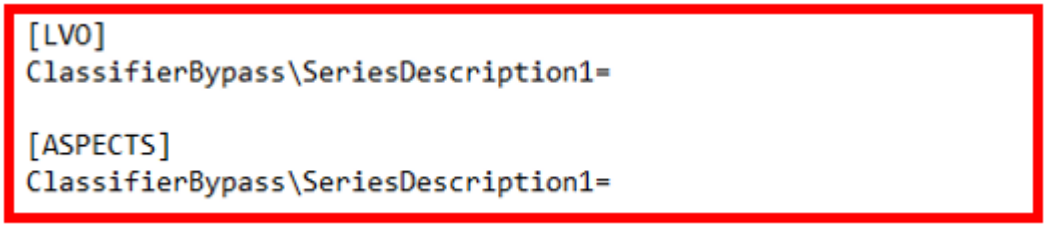
CTA for LVO Detection
1. Modality = CT
2. Orientation = Axial (calculated from the Image Orientation Patient DICOM tag)
3. Image Type = Original/Primary
4. Field of View along the Z axis > 50 mm
5. Volumes = 1 or 3 * If a multi-phase CTA is provided, exactly 3 phases are required. Only the first phase will be used for processing. If the 3 CTA volumes are provided as separate series, the Acquisition Data and Acquisition Time (or Acquisition DateTime) DICOM tags must be specified to identify the earliest series.
6. 210 < Window Width <= 1200

- Modality and Orientation are hard requirements, i.e., Can not be bypassed via the classifier bypass (see **Section 6.2**).

Note, studies that do not contain a series that satisfies the above criteria will not be processed. This will be logged, and no result will be produced.

6.2 Classifier Bypass

If the default classifier fails to correctly classify a series that the user wants processed by any of the StrokeSENS modules, then the site admin may configure the **ClassifierBypass** to select the series via Series Description. These settings can be found in the config file as shown below.



These settings take a series description string as the value; multiple of these lines can be added to the config file for matching multiple descriptions. Any series that contains the listed series description configured here will automatically be sent through to the assigned module for processing.

7 Device Operating Instructions

7.1 How to Communicate with StrokeSENS

Only image data, acquired through Digital Imaging and Communication in Medical Images (DICOM)-compliant imaging devices, may be sent to StrokeSENS for processing. There are two mechanisms by which DICOM images may be sent: the DICOM protocol or through a REST API call. The REST API may also be used for communications beyond receiving and sending DICOM images, like pinging for service status.

7.1.1 DICOM Message Protocol

The StrokeSENS DICOM service is available for sites to transmit DICOM study images to the StrokeSENS application. For configuration details please refer to the StrokeSENS Integration Guide.

7.1.2 REST API

There are three requests that are available through the StrokeSENS REST API. These are the GET /status, POST /process, and POST /modifyaspects requests. StrokeSENS, by default, reserves port 8082 for its REST API, although this is configurable (See Integration Guide).

7.1.2.1 Typical workflow

1. Integrating partner calls a POST /process request indicating the input/output directory for DICOM files, and providing a callback URL to send an API response to when StrokeSENS is complete processing.
2. DICOM study images are picked up from the input directory specified and are automatically processed by StrokeSENS.
3. StrokeSENS stores the post-processing output DICOM images in the output directory specified.
4. StrokeSENS sends a response to the callback URL specified to indicate that processing of the study request is completed, along with results embedded in the body of the call.

7.1.2.2 StrokeSENS API Descriptions

Refer to the StrokeSENS Integration Guide for a description of the StrokeSENS APIs.

7.2 Recommended acquisition parameters for input DICOM images.

NOTICE: StrokeSENS was developed and tested with datasets acquired with the following parameters listed below. For accurate processing by the Artificial Intelligence (AI) algorithms, StrokeSENS requires DICOM standard CT images of the head that align with the following parameters.

In addition to the acceptable DICOM requirements listed below, accurate processing of CT images relies on technically adequate input images. Technically inadequate CT input images may result in reduced performance (potential increase in false positive and/or false negative findings). Reasons a CT input image may be technically inadequate include severe motion, poor contrast timing, and inaccurate anatomical coverage of the head. To ensure accurate processing, CT images should encompass the entire head with no severe artifacts.

Any deviation from the recommended acquisition parameters below will result in warning messages that will be displayed in the QC output of the StrokeSENS modules.

7.2.1 Recommended parameters for the LVO Module

CTA for LVO Detection
1. Slice Thickness within [0.5, 1.5] mm
2. Pixel Spacing along the X/Y axis within [0.35, 0.7] mm
3. Field of View along the Z axis >=100 mm
4. Field of View along the X/Y axis >=150 mm
5. Slice Gap <=0.1 mm (Slice Gap is defined as an area between adjacent slices that is not covered by neither slice).
6. Slice Overlap <=0.5 mm (Slice Overlap is defined as an area between adjacent sliced this is covered by both slices).
7. KVP within [100, 140] kV
8. X-Ray Tube Current within [150, 850] mA

7.2.2 Recommended parameters for the ASPECTS Module

NCCT for ASPECTS
1. Slice Thickness within [0.625, 5] mm
2. Pixel Spacing along the X/Y axis within [0.35, 0.55] mm
3. Field of View along the Z axis >=110 mm
4. Field of View along the X/Y axis >=180 mm
5. Slice Gap <=0.1 mm (Slice Gap is defined as an area between adjacent slices that is not covered by neither slice).
6. Slice Overlap <=0.5 mm (Slice Overlap is defined as an area between adjacent sliced this is covered by both slices).
7. KVP within [100, 140] kV
8. X-Ray Tube Current within [140, 680] mA

7.3 DICOM and Non-DICOM Outputs (Clinical User)

7.3.1 LVO Module

7.3.1.1 DICOM Output

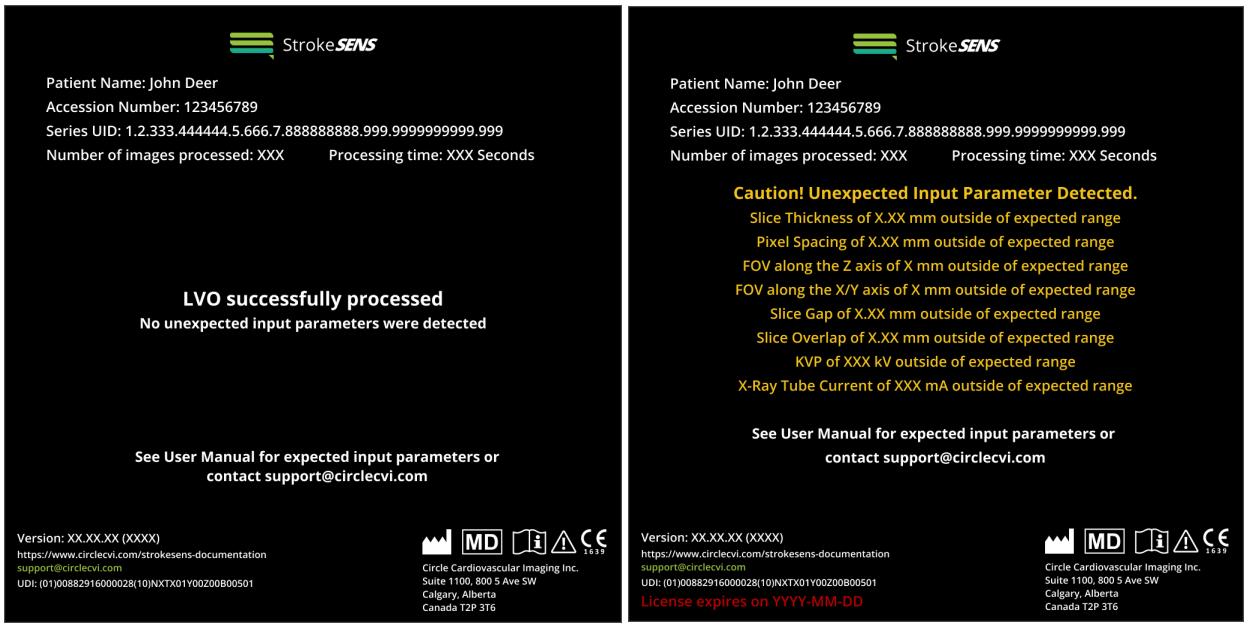
For every successfully processed study, one output series with two output DICOM images will be produced in accordance with the DICOM Conformance standard. The first image will contain a single Maximum Intensity Projection (MIP) image of 24mm covering the anatomical area of the large vessels. This provides a preview of the vasculature to the user based purely on the anatomical region and is not intended to represent the presence or location of an occlusion. If the algorithm identified a suspected LVO, a red banner will be presented on the top of the image notifying the clinician that a suspected LVO was identified. If the algorithm processed but did not identify a suspected LVO, there will be no red banner present on the top of the image.

The second image in the series conveys quality control information of the LVO module processing and complements the first image. The LVO output DICOM is assigned Instance Number 1, whereas the quality control image will be assigned Instance Number 2.

Example screenshot of the StrokeSENS LVO Output DICOM. On the left is a no LVO detected case. On the right is a LVO detected case.

The second DICOM output image in the series will contain relevant details about the processed study like Patient Name, Accession Number, Series UID, number of images processed, processing time, any quality control warnings/notifications, license expiry information, and About Box information.

Quality control warnings/notifications will be visible if certain acquisition parameters are outside the recommended range of values that are specified in Section 7.2. If a single flag is triggered, the message will appear on the output result image describing the specific criteria that was flagged. Also, the red software license expiration warning will appear notifying the user when there are 30 days or less before the expiration date of the StrokeSENS license.



Example screenshot of the StrokeSENS LVO Quality Control Output DICOM. On the left is a case with no warnings. On the right is a case showing study warnings in yellow, as well as the expiry date warning label in red.

7.3.1.2 Non-DICOM Output

A non-DICOM output will be automatically generated as JSON-format file and intended to accompany the DICOM outputs. This file is routed to a user-configured path within the file system defaulted to "/var/opt/strokesens/output". The JSON gives valuable machine-readable information to the host system, which is intended to be used to generate notification or triage workflows, when configured in the host system. The details within the file mirror the information provided by the output DICOMS like LVO detection result, study information, and warning messages, if any. In the case of a suspected LVO the Results/LVO value will be populated, otherwise it will be blank. Likewise, for all other keys in the JSON, if no value is available then they will be left blank.


```
{
    "ProcessingStatus": {
        "AccessionNumber": "2303493130527506",
        "NumberOfImagesProcessed": "270",
        "OriginalSeriesInstanceUID": "1.2.826.0.1.3680043.9.2842.289497046591054447282458491009894090 3",
        "OriginalStudyInstanceUID": "1.2.826.0.1.3680043.9.2842.101256985876705895817654186020359754 9",
        "PatientName": "PRoVe-IT-01-008",
        "ProcessingTime": "67",
        "Title": "StrokeSENS LVO processing completed"
    },
    "Results": {
        "LVO": "Suspected LVO Identified!"
    },
    "Software": {
        "Address": "Suite 1100, 800 5 Ave SW Calgary, Alberta Canada T2P 3T6",
        "Documentation": "https://www.circlenvi.com/documentation.html",
        "ExpiryDate": "2024-09-07",
        "Manufacturer": "Circle Cardiovascular Imaging Inc. Doing business as Circle Neurovascular Imaging",
        "ManufacturerModelName": "StrokeSENS",
        "SoftwareVersion": "2.1.0_(-1)",
        "SupportEmail": "support@circlecvi.com",
        "UDI": "(01)00882916001025(10)SSXX02Y01Z00B0-1"
    },
    "TimeStamp": "2024-01-02-11-26-51",
    "UnexpectedInputParameters": {
    }
}
```


Example screenshot of the StrokeSENS JSON Non-DICOM from a study where LVO processed.

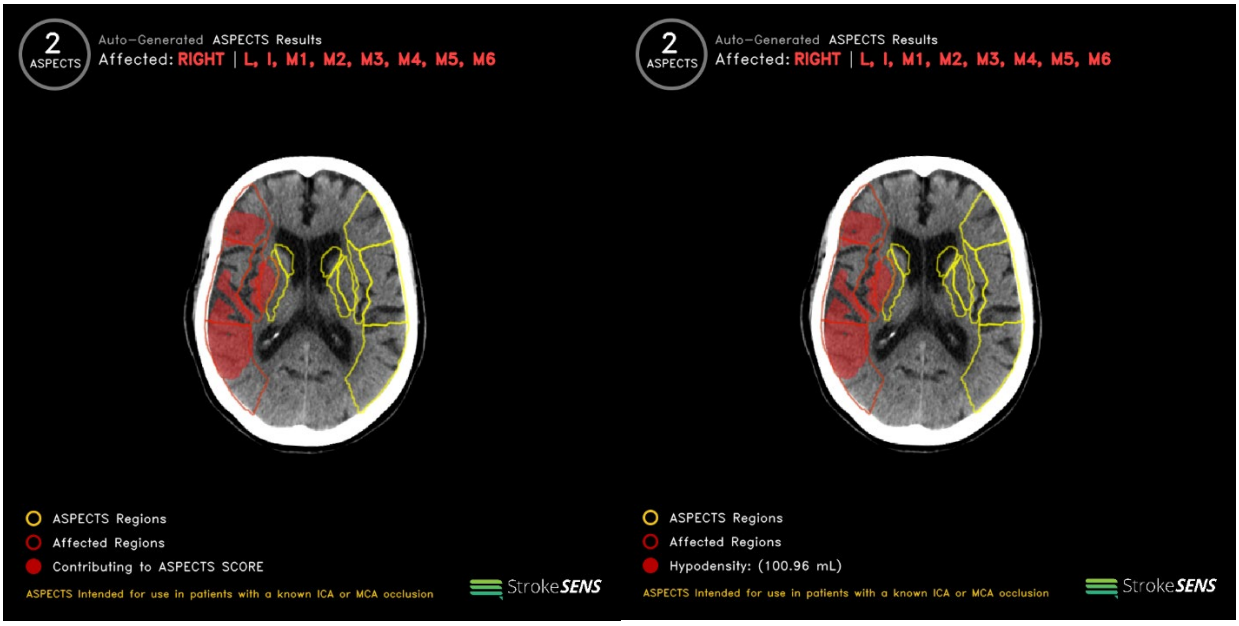
7.3.2 ASPECTS Module

7.3.2.1 DICOM Output

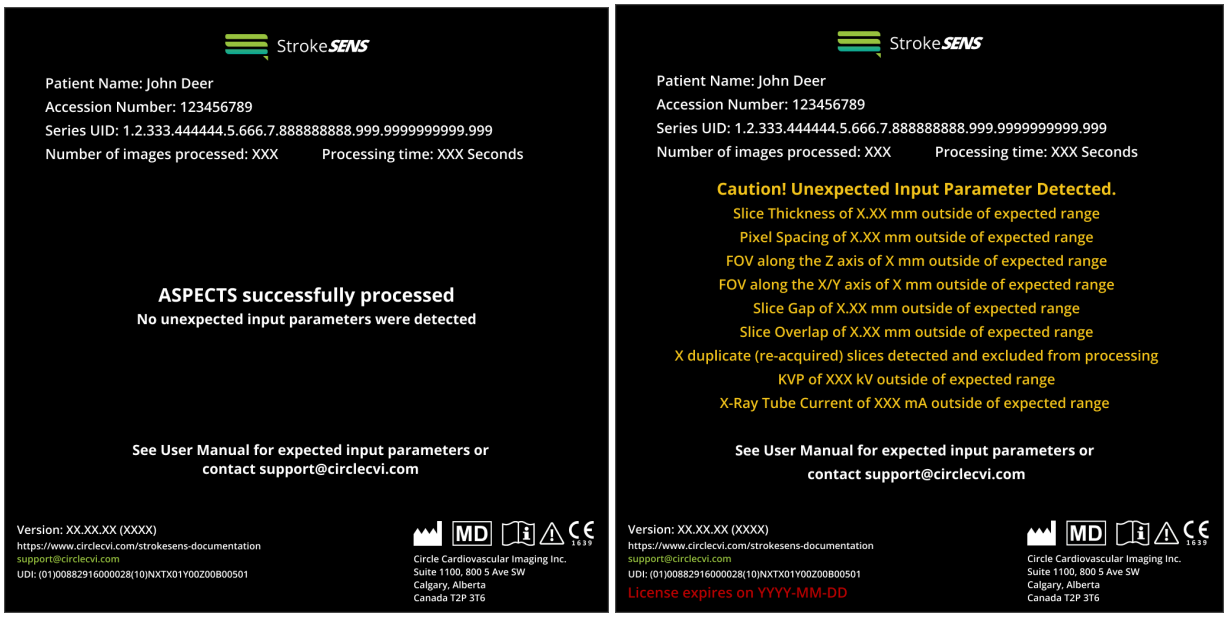
For every successfully processed study, one output series of Auto-generated ASPECT results will be produced in accordance with the DICOM Conformance standard. Auto-generated ASPECT results will contain images showing the overall ASPECTS score, affected side, and affected ASPECTS regions, along with a reconstructed non-contrast CT image overlaid with ASPECTS regions and voxels contributing to the ASEPCTS score. The last image in the series will contain relevant details about the processed study like Patient Name, Accession Number, Series UID, number of images processed, processing time, any quality control warnings/notifications, license expiry information, and About Box information.

Quality control warnings/notifications will be visible if certain acquisition parameters are outside the recommended range of values that are specified in **Section 7.2**. If a single flag is triggered, the message will appear on the output result image describing the specific criteria that was flagged. Also, the red software license expiration warning will appear notifying the user when there are 30 days or less before the expiration date of the StrokeSENS license.

In addition to warnings/notifications related to acquisition parameters, a scenario exists in which certain slices are re-acquired due to suboptimal acquisition (e.g., due to motion artifacts in the original acquisition). As a result, the NCCT series will contains duplicate (re-acquired) slices. Such re-acquired sliced will be excluded from processing and the following warning message will be shown to the user: “X duplicate (re-acquired) slices detected and excluded from processing”.



Example screenshot of the StrokeSENS ASPECTS auto generated results which include an example of ASPECTS scoring and related overlaid contours on a reconstructed version of the original image.



Example screenshot of the StrokeSENS Quality Control Output DICOM. On the left is a case with no warnings. On the right is a case showing study warnings in yellow, as well as the expiry date warning label in red.

7.3.2.2 Non-DICOM Output

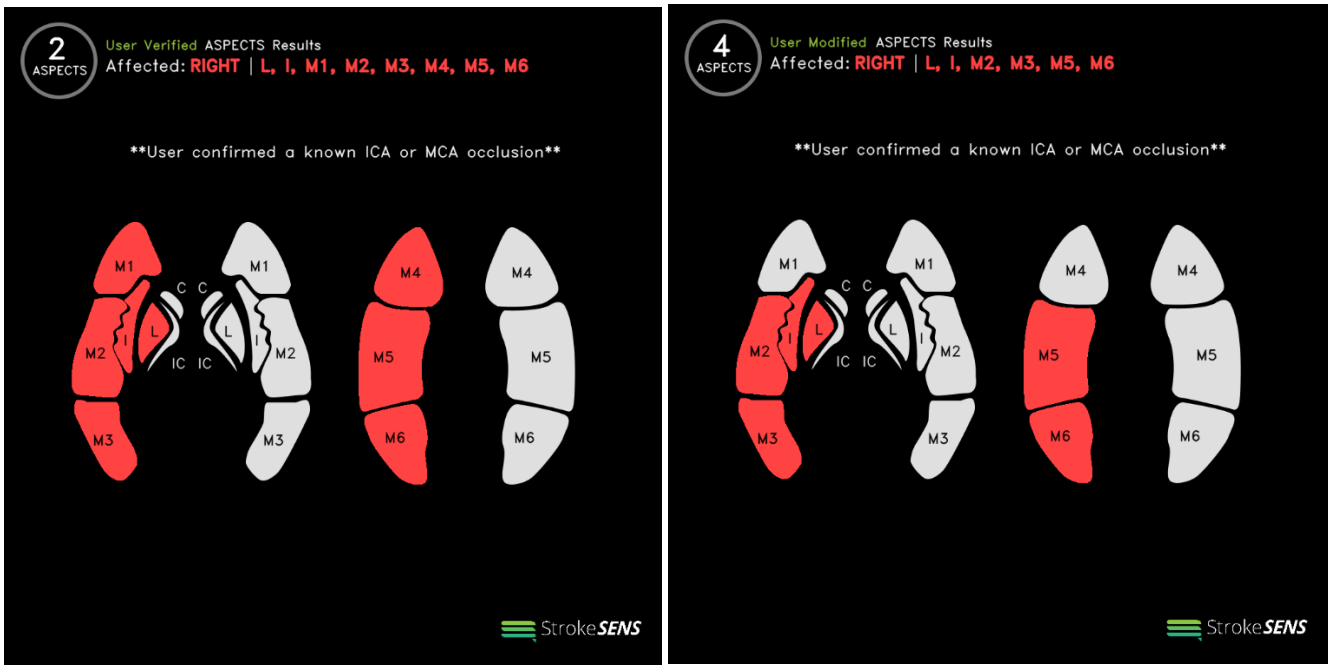
A non-DICOM output will be automatically generated as JSON-format file and intended to accompany the DICOM outputs. This file is routed to a user-configured path within the file system defaulted to "/var/opt/strokesens/output". The JSON gives valuable machine-readable information to the host system, which is intended to be used to generate notification or triage workflows, when configured in the host system. The details within the file mirror the information provided by the output DICOMS like ASPECTS region results, ASPECTS score, study information, and warning messages, if any. Likewise, for all other keys in the JSON, if no value is available then they will be left blank.


```
{
    "ProcessingStatus": {
        "AccessionNumber": "3866040791192985",
        "NumberOfImagesProcessed": "28",
        "OriginalSeriesInstanceUID": "1.2.276.0.7230010.3.1.4.3460997744.5648.1574723012.53432",
        "OriginalStudyInstanceUID": "1.2.276.0.7230010.3.1.2.3460997744.5648.1574723012.53419",
        "PatientName": "RSNA_01_031*",
        "ProcessingTime": "34",
        "Title": "StrokeSENS ASPECTS processing completed"
    },
    "Results": {
        "ASPECTS_Regions": "0, 0, 0, 0, 0, 0, 1, 1, 1, 1, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0",
        "ASPECTS_Score": "6"
    },
    "Software": {
        "Address": "Suite 1100, 800 5 Ave SW Calgary, Alberta Canada T2P 3T6",
        "Documentation": "https://www.circlenvi.com/documentation.html",
        "ExpiryDate": "2024-09-07",
        "Manufacturer": "Circle Cardiovascular Imaging Inc. Doing business as Circle Neurovascular Imaging",
        "ManufacturerModelName": "StrokeSENS",
        "SoftwareVersion": "2.1.0_(-1)",
        "SupportEmail": "support@circlecvi.com",
        "UDI": "(01)00882916001025(10)SSXX02Y01Z00B0-1"
    },
    "TimeStamp": "2024-01-15-11-51-59",
    "UnexpectedInputParameters": {
    }
}
```


Example screenshot of the StrokeSENS JSON Non-DICOM from a study where ASPECTS processed.

7.3.2.3 User Modify / Verify ASPECTS

For successfully processed ASPECTS results, the user can modify or verify the auto-generated outputs. Through the POST /modifyaspects API request (described in the StrokeSENS Integration Guide), a user can call on the StrokeSENS system to produce an additional DICOM output that will be prepended to the auto-generated ASPECTS series. This result will show up as the first image in the ASPECTS DICOM output series, and display user verified/modified ASPECTS score, affected side, and affected regions.



Example screenshot of the StrokeSENS User Verified/Modified Output. On the left is a case in which the user verified the auto-generated ASPECTS results. On the right is a case in which the user modified the auto-generated ASPECTS results. As shown, the green text at the top of the output will be User Verified if the ASPECTS scoring is the same as the auto-generated results, otherwise the green text will read User Modified to indicate the user has modified the auto-generated results. The ASPECTS score, affected side, affected regions, and contour illustration will represent the user verified/modified values. The contour illustration at the center of the output visualizes the ASPECTS regions, with the regions in red being the affected regions.

8 Summary of data and device performance

8.1 Validation of StrokeSENS LVO Performance

Description of Data Used for Development and Testing

The LVO detection module was developed using a pooled dataset composed of retrospective patient imaging data from five clinical study/trial databases, namely the Prove-IT clinical study (N=76, ClinicalTrials.gov Identifier: NCT02184936), ESCAPE randomized controlled trial (N=25, ClinicalTrials.gov Identifier: NCT01778335), ESCAPE-NA1 randomized controlled trial (N=451, ClinicalTrials.gov Identifier: NCT02930018), ALIAS randomized clinical trial (N=24, ClinicalTrials.gov Identifier: NCT00235495), and PREDICT study (N=95, PMID: 22405630).

The LVO test set was retrospectively collected from four clinical study/trial databases, namely the ESCAPE NA1 randomized controlled trial (N=219, ClinicalTrials.gov Identifier: NCT02930018), Predict study (N=110, PMID: 22405630), Tempo1 open label clinical trial (N=17, ClinicalTrials.gov Identifier: NCT01654445) and Alias randomized clinical trial (N=54, ClinicalTrials.gov Identifier: NCT00235495).

The following table summarizes the properties of both the development and test sets:

	Development Set	Test Set
Total	671	400
Manufacturer		
GE Medical Systems	410	146
Siemens	240	143
Philips	15	47
Toshiba	6	64
Slice Thickness (mm)		
[0.5, 1.0)	524	220
[1.0, 1.5)	122	151
[1.5, 2.0)	6	7
[2.0, 2.5)	7	18
[2.5, 3.0]	12	4
kVp		
[80, 100)	44	8
[100, 120)	108	72
[120, 140]	519	320
Age		
<50	68	37
[50, 60)	110	60
[60, 70)	162	106
[70, 80)	159	108
[80, 90)	140	72
[90, 100]	26	17
Data not available	6	0
Sex		
Male	357	217
Female	308	183

Data not available	6	0
Geography		
Canada	326	191
US	236	152
Europe	81	32
Asia	3	1
Australia	22	24
Data not available	3	0
Site of Occlusion		
ICA	107	59
M1-MCA	355	158
Non-LVO	209	183

Summary of Performance

To demonstrate the standalone performance of StrokeSENS LVO software, a retrospective case study was conducted to assess the sensitivity and specificity of StrokeSENS LVO for detecting anterior Large Vessel Occlusion (LVO). Performance was reported on a heterogenous dataset of 400 independent studies (217 LVO cases and 183 non-LVO cases). Patient cases consisted of baseline CT Angiography images acquired for suspected vessel occlusion or intracranial hemorrhage. This data was retrospectively collected from four clinical study/trial databases, as described in the previous section.

The positive LVO subgroup (N=217) included cases with occlusions in the intracranial ICA and M1-MCA arteries. The negative non-LVO subgroup (N=183) included challenging cases typically seen in the intended clinical population. These include non-LVO anterior circulation occlusion cases (i.e., more distal anterior occlusions), posterior circulation occlusions (i.e., basilar, vertebral, and more distal posterior occlusions), and no occlusion cases (i.e., with or without hemorrhage).

A 2+1 expert consensus was used for truthing to establish the reference dataset labels for each dataset. The expert truthers were US board-certified neuroradiologists experienced in clinical identification of the presence and location of vessel occlusion. Truthers were instructed to independently review all patient cases in the above test set (N=400). For each case, readers were asked to specify the presence or absence of a large vessel occlusion (LVO), presence or absence of hemorrhage, and site of occlusion (if occlusion present). Readers made their interpretations based on the provided single-phase CTA scan only. Readers were also asked to comment on the existence of other significant radiological findings and/or whether the scan was interpretable or not.

The device achieved a sensitivity of 90.3% (95% CI = [86.4%, 94.3%]), and specificity of 95.1% (95% CI = [91.9%, 98.2%]) for the binary LVO detection task on the test set (N=400, LVO=217, Non-LVO=183). In addition, an analysis of time to notify of suspicious cases was conducted by evaluating the average time for the StrokeSENS LVO device to process the CTA image and generate a notification (for LVO positive cases). The device achieved a mean value of 1.28 minutes (S.D: ±0.24 mins, Min: 0.95 mins, Max: 2.20 mins).

Test	Test Results
Sensitivity	0.903, 95% CI = [0.864, 0.943]
Specificity	0.951, 95% CI = [0.919, 0.982]

Processing Time	Mean: 1.28 mins S.D: ±0.24 mins Min: 0.95 mins Max: 2.20 mins

The results of the secondary analysis as well as a breakdown of the subgroups of interest are summarized below:

Sub-Group	LVO Count	Non- LVO Count	Sensitivity [95% CI]	Specificity [95% CI]
Full cohort	217	183	0.903 [0.864, 0.943]	0.951 [0.919, 0.982]
Site of Occlusion				
LVO: ICA Set	59	-	0.872 [0.798, 0.946]	-
LVO: M1-MCA Set	158	-	0.921 [0.876, 0.966]	-
Non-LVO: Hemorrhage Set	-	109	-	0.973 [0.923, 0.991]
Non-LVO: Non- Hemorrhage Set	-	74	-	0.918 [0.855, 0.981]
Age				
>= 70 years old	109	88	0.881 [0.82, 0.942]	0.943 [0.874, 0.975]
< 70 years old	108	95	0.926 [0.877, 0.975]	0.958 [0.897, 0.984]
Sex				
Male	120	97	0.900 [0.846, 0.954]	0.959 [0.899, 0.984]
Female	97	86	0.907 [0.849, 0.965]	0.942 [0.871, 0.975]
Slice Thickness (mm)				
0.5mm - 0.8mm	108	95	0.880 [0.818, 0.941]	0.958 [0.897, 0.984]
0.9mm – 2.5mm	109	88	0.927 [0.878, 0.976]	0.943 [0.874, 0.975]
Manufacturer				
GE Medical	62	84	0.919 [0.825, 0.965]	0.952 [0.884, 0.981]
Siemens	63	80	0.889 [0.811, 0.966]	0.950 [0.878, 0.98] 878,
Philips + Toshiba	92	19	0.902 [0.841, 0.963]	0.947 [0.754, 0.991]

Also, the Positive Predictive Values (PPVs) of the device at multiple prevalence values of LVO are as follows:

Prevalence of LVO (%)	Positive Predictive Value	Sample Size (Bootstrapping)
54.25%	0.956	205
40%	0.925	119.9
20%	0.82	50.1
10%	0.674	27.7
5%	0.482	17.4

8.2 Validation of StrokeSENS ASPECTS Performance

Description of Data Used for Development and Testing

Data were selected for development from a database composed of pooled imaging data from a multi- center clinical study, namely Prove-IT (ClinicalTrials.gov Identifier: NCT02184936), with subjects 22 years or older who underwent baseline non-contrast CT (NCCT) imaging for suspected acute ischemic stroke.

The test dataset is composed of 200 retrospective patient imaging data cases from two clinical trials and two randomized control trials, namely the Prove-IT clinical study (N=40, ClinicalTrials.gov Identifier: NCT02184936), the INTERRSeCT clinical study (N=59, JamaNetwork.com Identifier: 2702146), ESCAPE randomized controlled trial (N=16, ClinicalTrials.gov Identifier: NCT01778335), ESCAPE-NA1 randomized controlled trial (N=85, ClinicalTrials.gov Identifier: NCT02930018). Composition of the test data included different geographical regions (Canada, US, EU, Asia) and multiple CT scanner models manufactured by different CT scanner vendors (GE, Siemens, Toshiba, Philips). The test data were representative of a wide range of clinical severities (ASPECTS score range of 0-10, median ASPECTS = 8; NIHSS score range 0-30, median NIHSS score = 17) with an onset to CT time range <360 minutes.

The following table summarizes the properties of both the development and test sets:

	Development Set	Test Set (MRMC)
Total	310	200
Manufacturer		
GE Medical Systems	285	93
Siemens	24	44
Philips	1	34
Toshiba	0	29
Slice Thickness		
[0.625, 2.5) *Reconstruction of existing patients	107	58
(2.5, 5]	310	200
KVP		
[100, 120]	200	164
(120, 140]	110	36
ASPECTS		
0	0	3
1	0	5
2	1	8
3	4	11
4	4	7
5	7	19
6	29	16
7	33	21
8	49	36
9	67	27
10	116	47
Age		
[22, 40)	5	5
[40, 50)	23	23
[50, 60)	41	24
[60, 70)	52	40

[70, 80)	104	67
[80, 90)	73	35
(90, 100]	8	6
NA	4	0
Sex		
Male	159	89
Female	146	111
NA	5	0
Geography		
Canada	228	77
US	0	59
Europe	82	51
Asia	0	11
Australia	0	2
Site of Occlusion		
ICA	58	46
M1-MCA	150	118
MeVO-MCA	86	36
Other sites of occlusion	8	0
No Occlusion	8	0
Onset to CT Time (minutes)		
<60	35	28
[60, 120)	96	76
[120, 180)	46	33
[180, 240)	37	29
[240, 300)	21	27
[300, 360)	17	7
[360, 420)	10	0
[420, 480)	8	0
[480, 540)	4	0
[540, 600)	8	0
[600, 660)	6	0
[660, 720)	5	0
>=720	17	0
NIHSS Score		
[0, 4)	10	4
[4, 8)	39	17
[8, 12)	49	18
[12, 16)	49	45
[16, 20)	60	56
[20, 24)	64	32
[24, 28)	30	23
[28, 32)	2	4
[32, 36)	2	0
NA	5	1

Summary of Standalone Performance Assessment

To demonstrate the standalone performance of the StrokeSENS ASPECTS software a retrospective case study was conducted on the N=200 cases of the test set. The truthing process involved a panel of three experts reporting the presence or absence of early ischemic changes on NCCT in each of the 10 regions of a standard ASPECTS template. The three experts (one neuroradiologist and two stroke neurologists; Canadian Board Certified) each have >15 years clinical experience scoring ASPECTS on head NCCT images of patients with acute ischemic stroke. Consensus was achieved by a process of majority rule. Specifically, all three expert truthers read all scans independent of each other. In cases of disagreement in assessing early ischemic changes at any region of the ASPECTS template, a final determination of whether that specific region is affected or not was determined by the majority rule (2/3) involvement for that specific region.

The standalone performance assessment was used to demonstrate the accuracy of the automated ASPECTS software with reference to the expert-annotated reference standard. The StrokeSENS ASPECTS software predicts the presence of early ischemic changes (EIC) in each of the 10 anatomical regions-of- interest (ROI) per hemisphere of the brain. As described in the Validation Protocol, Receiver Operating Characteristics (ROC) analysis was used to assess the region-level accuracy of the StrokeSENS automated ASPECT score prediction vs the expert annotation. Furthermore, region-wise sensitivity/specificity, side prediction accuracy, and total ASPECTS score mean difference and Intraclass Correlation Coefficient (ICC) are summarized here.

Regional ASPECT Score Performance	
Clustered AUC (N=2000)	84.4% [80.7%, 88.2%]
Sensitivity (N=579)	70.5% [68.5%, 72.5%]
Specificity (N=1421)	85.6% [84.1%, 87.2%]

Total ASPECTS Score Performance	
Side Prediction Accuracy (N=139)	100.0% [97.3%, 100.0%]
Mean Difference (Device minus Reference;	-0.165
ICC (N=200)	75.0% [68.0%, 80.0%]

Summary of Clinical Performance Assessment

To demonstrate the clinical performance of the StrokeSENS ASPECTS software, a concurrent read, fully-crossed multi-reader multi-case (MRMC) reader study was conducted on retrospective imaging data pooled from above mentioned PROVE-IT, INTERRSeCT, ESCAPE, ESCAPE NA1 trials. A sample of 100 non- contrast CT Head scans (2.5 - 5mm slice thickness) from subjects with a vessel occlusion of the anterior circulation with varying degrees of ischemic severity was randomly selected. There were a total 8 readers (4 female) with a range of clinical training as neurologists, radiologists and neuroradiologists of 0-10 years' experience. Each reader read all 100 cases (in randomized order) twice (once unaided and once aided by device) in two reading sessions separated by 2-4 weeks interval, in similar reading condition. The truthing process was identical to the one used in standalone performance assessment.

Descriptive analysis showed that the average improvement in the proportion of correctly rated regions when aided versus when unaided was 1.86%. Also, using a mixed effect model considering reader sequence, scan, and regions as a fixed effect, and readers as a random effect, the calculated area under the receiver operating characteristic curve (AUC) yielded 87.4% for aided with StrokeSENS, compared with an AUC of 86.3% when unaided. The overall sensitivity and specificity from the mixed model using Youden index showed 85.0% and 74.9% when aided with StrokeSENS vs 83.4% and 75% when unaided. The difference in AUC of 1.1% in favor of StrokeSENS was statistically significant (two-sided p-value <0.01) using bootstrap modeling. Further analysis showed that the overall intraclass correlation for reader level across reads was improved when aided by StrokeSENS (.65) vs when unaided (.48) meaning that StrokeSENS helps to introduce better consistency across reads for readers. The predictive accuracy of the readers' ratings for dichotomized total

ASPECTS (for total ASPECTs score <= 5) also improved when aided with StrokeSENS (AUC=84.2%) vs unaided (AUC=78.1%) in reference to the truther consensus aspects.

8.3 Potential Limitations of the Device Performance Assessment

The StrokeSENS LVO detection performance assessment had low representation of non-LVO cases from non-GE and non-Siemen's scanners.

The StrokeSENS LVO detection performance assessment was conducted on retrospective imaging data; no prospective clinical studies were conducted.

Ethnicity was not available in the patient-level data and therefore was not included in the subgroup analysis for either the ASPECTS or LVO modules.

adults (<50) were underrepresented in the data used for developing and testing the ASPECTS and LVO detection algorithms.

Interobserver variability in expert ASPECT scoring may limit the reliability of the reference standard; Inter- and intra-rater agreement is not available for the expert consensus reference standard.

8.4 Hardware Specifications for Testing Environment

Analysis was conducted on a machine with the specified requirements below:

	Hardware Specification
CPU	Intel(R) Xeon(R) CPU E5-2680 v3 @ 2.50GHz, 2500 Mhz, 4 Core(s), 4 Logical Processor(s)
RAM	16 GB
Storage	1 TB SSD
OS	Microsoft Windows Server 2019 Standard. Ver: 10.0.17763 Build 17763
Network	1 GB ethernet

9 Technical Support

For technical questions please contact our team by phone or e-mail:

Global:

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Calgary, Alberta, T2P 1H5
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NOTICE: Any serious incident* that occurs in relation to StrokeSENS must be reported to Circle and all relevant local regulatory authorities (e.g., Health Canada, the Competent Authority of the Member State in which the incident occurred, etc.).

**A serious incident means any incident that directly or indirectly led to: the death of a patient; the temporary or permanent serious deterioration of a patient's state of health; or a serious public health threat.*

Email: support@circlecvi.com

Website: circlecvi.com