StrokeSENS
Version 1.4 – GE Integration
Not for USA

# USER GUIDE

CIRCLE
NEUROVASCULAR IMAGING

# StrokeSENS

# User Guide

*September 2022*

*GEHC P/N 5922506-1EN revision 1*

# Regulatory Information

MD

**Circle Cardiovascular Imaging Inc.**
doing business as **Circle Neurovascular Imaging**
1100, 800 5th Avenue SW Calgary,
Alberta, T2P 3T6, Canada
**Telephone:** 1 (587) 747-4692
**Website:** circlenvi.com

**European Union**

CE
1639

For EU: StrokeSENS is qualified as a class IIa medical device.

UDI **UDI:** *+B926SSSX10*

EC REP

**EU Authorized Representative**

Circle Cardiovascular Imaging BV
SingelStaete
Singel 250
1016 AB Amsterdam
The Netherlands

CH REP

**CH Authorized Representative**

Arazy Group Swiss GmbH
Bruderholzallee 53
4059 Basel, Switzerland
swiss.ar@arazygroup.com

**EU Distributor:**

GE Medical Systems SCS
283, rue de la Miniere
78530 Buc
FRANCE
Tel : +33 1 30 70 40 40

**USA Distributor:**

GEXPRO
12221 W. Feerick St.
Milwaukee, WI 53222
USA

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

# Table of Contents

# 1 Regulatory Approvals

## 1.1 Regulatory Information

This product has the following regulatory approvals.

| AGENCY | Authorized Representative | Approval/Clearance Reference |
|---|---|---|
| **Australia TGA ARTG** | Australian Sponsor:<br>GE Healthcare Australia Pty Ltd.<br>32 Phillip St, Parramatta NSW 2150,<br>Australia | ARTG number: 387024 |
| **CE Mark (MDD)** | Circle Cardiovascular Imaging BV<br>SingelStaete<br>Singel 250<br>1016 AB Amsterdam<br>The Netherlands | CE Mark Certificate US21/819944332 issued by SGS for StrokeSENS |
| **Health Canada** | N/A | License number: 107386 |
| **India** | Taevas Life Sciences Private Limited<br>H.No: 2-3/AC/83, Aparna County,<br>Behind Mathrusri Nagar Miyapur,<br>Hyderabad-500049, India | SUGAM registration: Circle-CAN/I/MD/007603 |
| **UK** | Circle Cardiovascular Imaging UK LTD.<br>Ty Mentor, Navigation Park,<br>Abercynon Mountain Ash, Mid<br>Glamorgan, Wales, UK, CF45 4SN | MHRA registration: 22027 |

# 2 Introduction

This User Guide is also available:

- On the Internet at: https://www.gehealthcare.com/documentationlibrary
    1. Click **Enter Customer Documentation Portal**.
    2. Enter the part number of this User Guide in the Search field.
    3. Click **Search**.
- On AW VolumeShare:
    1. Click on the **?** tab.
    2. Select a document.
- On AW Server:
    1. Enter the URL for AW Server in your favorite web browser (for example, http://3.70.211.103/).
    2. Select the link for User Documentation.

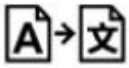
Language codes are listed in the following tables.

| Language code | Language |
|---|---|
| BG | Bulgarian |
| CS | Czech |
| DA | Danish |
| DE | German |
| EL | Greek |
| EN | English |
| ES | Spanish |
| ET | Estonian |
| FI | Finnish |
| FR | French |
| HR | Croatian |
| HU | Hungarian |

| Language code | Language |
|---|---|
| IT | Italian |
| LT | Lithuanian |
| LV | Latvian |
| NL | Dutch |
| NO | Norwegian |
| PL | Polish |
| PT-PT | Portuguese |
| RO | Romanian |
| SK | Slovakian |
| SR | Serbian |
| SV | Swedish |

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 CEMEURDIST@med.ge.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.

**Symbols used in documentation and labeling**

| Symbol | Description |
|---|---|
|  | **Consult Instructions for Use**:<br>Indicates that the user shall read Instructions for Use. |
|  | **Manufacturer**:<br>Indicates the medical device manufacturer's name and address. |
|  | **Distributor:**<br>Indicates the entity distributing the medical device into the locale. |
|  | **Translation:**<br>To identify that the original medical device information has undergone a translation which supplements or replaces the original information. |
|  | **Unique device identifier (UDI):**<br>Indicates a carrier that contains Unique Device Identifier information. |
|  | **General caution:**<br>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**:<br>Indicates this product is a medical device. |
|  | **Authorized representative in the European Community:**<br>Indicates the authorized representative in the European Community. |
|  | **Authorized representative in Switzerland:**<br>Indicates the authorized representative in Switzerland. |

## 2.1 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 and ASPECTS devices. The compatible radiological software solution may also provide other radiological functionalities outside the scope of the StrokeSENS LVO and ASPECTS devices 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) | A 10-point quantitative score used to assess early ischemic changes on non-contrast CT head scan. |

## 2.2 Product Description

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. Analysis of non-contrast CT images is provided by the StrokeSENS ASPECTS module, which includes assessment of regions with suspected acute ischemic tissue (ie. ASPECTS scoring). Analysis of contrast-enhanced CT images is provided by the StrokeSENS LVO module, which includes automated detection of suspected large vessel occlusion (LVO).

StrokeSENS ASPECTS and StrokeSENS LVO decision-aid tools are made available within the GE FastStroke software application. The GE FastStroke software application is considered a Compatible Radiological Software Platform which provides the electronic medium for communication, storage, and transfer of medical images, as well as the coordination of notification outputs from the StrokeSENS LVO device. The GE FastStroke software application provides an automated workflow that includes StrokeSENS ASPECTS and StrokeSENS LVO alongside other relevant radiological information of the head and neck for the diagnostic workup of patients with suspected acute stroke.

# 3 Intended 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 that 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.

# 4 User Profile

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

# 5 Patient Population

StrokeSENS is intended to be used on adults (22 years and older) with suspected acute stroke.
StrokeSENS ASPECTS is intended to be used on adults with confirmed anterior circulation Large Vessel Occlusion (LVO) within 6 hours of symptom onset.
StrokeSENS LVO is intended to be used on adults to detect anterior circulation Large Vessel Occlusion (LVO).

# 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 / user management / 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.

# 7 Warnings and Cautions

**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, predict scores, 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 LVO is a parallel workflow tool intended to be used in conjunction with standard of care procedures. StrokeSENS LVO 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 is intended to be used on adults (22 years and older). 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.

**CAUTION**: This user manual is considered adequate training for the safe and effective use of the product. Training may 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.

**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 software applications are being run on the same machine.

### Safety notice legends

**WARNING**: This indicates a potentially hazardous situation, which, if not avoided, could result in death or 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.

# 8 Software Safety-Related Messages

Messages giving information and warnings relating to the current system status are displayed on the screen.

Some of these messages may be related to safety issues. For example, a message may warn that a screen or printed image will be enlarged or reduced, and this must be taken into consideration in the care decision process. It is important that users take note of and act on the information given in these messages.

In user guides intended for use in countries where the on–screen language is different from the local language, the table shows the displayed messages and gives a translation in the local language. In user guides intended for use in countries in which the on-screen language is available in the local language, the right side of the table is left blank.

| **ASPECTS** | |
|---|---|
| ASPECTS results auto-generated and intended for use in patients with ICA/MCA occlusions. | |
| For use in ICA/MCA occlusion. | |
| Dataset not compatible for ASPECT Scoring. | |
| ASPECT Scoring has failed. | |
| Patient age is less than 22, StrokeSENS is intended to be used on adults 22 years and older. | |
| Patient age is not identified, StrokeSENS is intended to be used on adults 22 years and older. | |

| **LVO** | |
|---|---|
| LVO result is for notification purposes only and is not intended for primary diagnosis. | |
| Dataset not compatible for LVO detection. | |
| LVO detection has failed. | |
| Patient age is less than 22, StrokeSENS is intended to be used on adults 22 years and older. | |
| Patient age is not identified, StrokeSENS is intended to be used on adults 22 years and older. | |

# 9 Clinical Benefits

StrokeSENS ASPECTS provides automated ASPECTS scoring to aid clinicians in their assessment of early ischemic changes (ASPECTS) on non-contrast CT. This standardizes ASPECT scoring across clinicians from different sub-specialties. The clinical study referenced in section Validation of StrokeSENS ASPECTS Performance provides evidence that the use of StrokeSENS ASPECTS enables less-experienced readers to improve their ability to read ASPECTS, approaching the performance of expert readers.

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.

# 10 Contraindications

None.

# 11 Undesirable Side Effects

None.

# 12 System Hardware and Software Requirements

## 12.1 Compatible Imaging Systems

StrokeSENS is a CT vendor-agnostic post-processing software that leverages artificial intelligence (AI) to process CT medical images of the head for suspected acute stroke, for the purpose of early identification and notification of potentially time-sensitive cases.
StrokeSENS has been tested on CT images from a variety of different CT 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)

The StrokeSENS LVO notification system is intended to be used as part of an integrated medical imaging system. Integration into a compatible imaging system is necessary to provide infrastructure and services such as DICOM handling, login and user management, and basic image viewing.

This release of the StrokeSENS LVO and ASPECTS software is integrated into the GE FastStroke software application. Comprehensive testing of the software in the GE FastStroke software application has been conducted, verifying the performance of the StrokeSENS LVO and ASPECTS software in the compatible system. This document provides user instructions and labelling for the StrokeSENS LVO and StrokeSENS ASPECTS software as integrated into the compatible GE FastStroke system.

## 12.2 Hardware Requirements

StrokeSENS is fully integrated within the FastStroke software application which runs on the GE Healthcare AW VolumeShare and AW Server platforms. Refer to GE Healthcare AW VolumeShare and AW Server user guides. For information about the minimum RAM required, refer to the GE Volume Viewer applications user guide addendum.

## 12.3 Required Image Parameters for Algorithm Processing

If the images do not meet the following requirements, the series will not be processed.

| **Image Requirements for ASPECT Scoring** |
|---|
| Non-contrast head CT (automatically determined by Window Width ≤ 210 HU (Hounsfield Unit)) |

| **Image Requirements for LVO Detection** |
|---|
| Head CT Angiography* (automatically determined by 210 HU < Window Width ≤ 1170 HU (Hounsfield Unit)) |

* When CTA is a multi-phase acquisition, the algorithm will utilize the first phase

## 12.4 Recommended Image Parameters for Algorithm Processing

**NOTICE**: StrokeSENS was developed and tested with datasets with the following parameters, therefore the use of these recommended parameters will ensure optimal performance of StrokeSENS.

| | **ASPECTS** | **LVO** |
|---|---|---|
| **Scan Range** | CT head volume covering the whole head (vertex to base) is recommended. | CTA head volume covering the whole head (vertex to base) is recommended. |
| **Matrix Size** | 512x512 | 512x512 |
| **Slice Thickness** | 0.625-5 mm | 0.5-2.5 mm |
| **DFOV along the X/Y axis** | 180-324 mm | 180-412 mm |

# 13Workflow and Instructions for Use

StrokeSENS ASPECTS and StrokeSENS LVO are made available through the GE FastStroke software platform.

## 13.1 StrokeSENS ASPECTS

Provided that the StrokeSENS ASPECTS license is present and a compatible non-contrast CT volume is available, ASPECTS (Alberta Stroke Program Early CT Score) will be automatically processed by the StrokeSENS ASPECTS module upon FastStroke session launch regardless of whether the session was launched manually or automatically using preprocessing.

StrokeSENS ASPECTS will only process images that meet the StrokeSENS ASPECTS image requirements, as outlined in the Required Image Parameters for Algorithm Processing section of this guide as well as in the FastStroke user guide. Additionally, it is advised to use the recommended parameters as outlined in the Recommended Image Parameters for Algorithm Processing section of this guide.

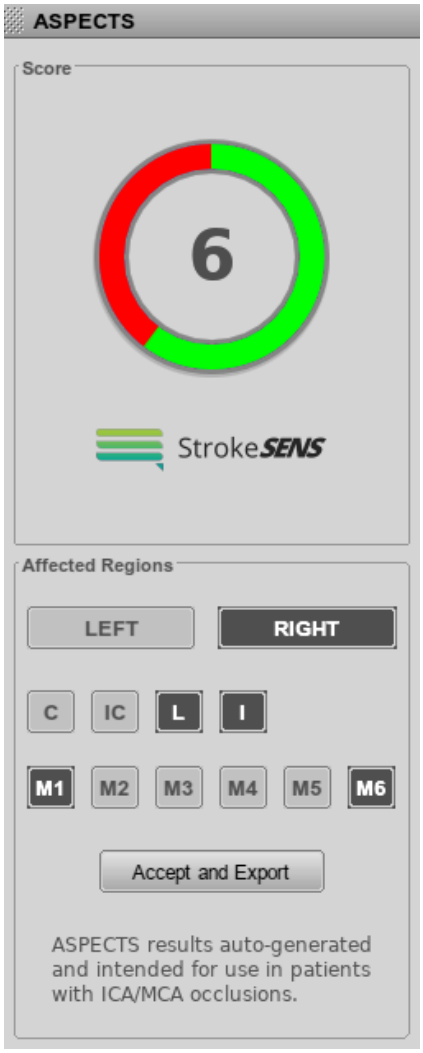
When available, ASPECTS summary results are displayed in the ASPECTS report panel to the right of the FastStroke non-contrast CT viewports, while the ASPECTS overlay appears on the axial view along with the score. In the case ASPECTS is calculated, the top left viewport (on single screen configuration, top right on dual screen) will display an axial view of the non-contrast CT series without the ASPECTS overlay, for side-by side comparison within the default Non-Contrast CT review step.

**Note**: ASPECTS results are automatically generated and are intended for use in non-contrast images of patients with ICA/MCA occlusion.

The ASPECT Score is a 10-point quantitative score used to assess early ischemic changes on non-contrast CT head. Each area/region of grey white loss constitutes 1 deduction point from 10 total points.

| | | | |
|---|---|---|---|
| Caudate (C) | -1 | M2 - Anterior temporal lobe | -1 |
| Internal Capsule (IC) | -1 | M3 - Posterior temporal lobe | -1 |
| Lentiform Nucleus (L) | -1 | M4 - Anterior MCA | -1 |
| Insula (I) | -1 | M5 - Lateral MCA | -1 |
| M1 - Frontal operculum | -1 | M6 - Posterior MCA | -1 |

**Visit the *aspectsinstroke.com* website for detailed review of the ASPECTS imaging construct including interactive educational sessions and modules.**

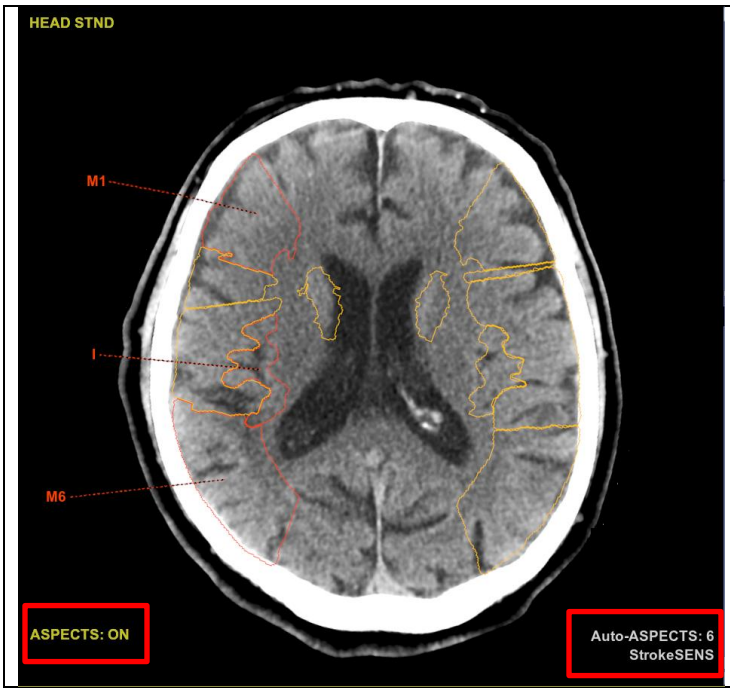



Per ASPECTS guidelines, 10 ROIs are identified per hemisphere of the brain and are delineated on the image and outlined in yellow. ROIs determined by the ASPECTS algorithm to be affected by early ischemic changes are outlined in red and identified in the ASPECTS report panel.

Total ASPECTS is presented in the report panel, which reflects the number of regions out of 10 determined to be unaffected (illustrated in green), while the number of regions out of 10 determined to be affected is illustrated in red.

In addition, the user can toggle on/off the image overlay ROIs and interact with the input non-contrast CT image by clicking on the “ASPECTS: ON/OFF” annotation within the viewport (see image below).

The bottom right corner of the ASPECTS viewport displays annotations based on the status of the score:

<table>
<tr>
<td> 
</td>
<td>
<ul>
<li>Automated score, not modified nor accepted by user:<br>Auto-ASPECTS: [score]</li>
</ul>
<ul>
<li>Score modified but not accepted by user:<br>ASPECTS: [score]</li>
</ul>
<ul>
<li>Score accepted without modification by user:<br>ASPECTS: [score]<br>[username]</li>
</ul>
<ul>
<li>Score accepted after modification by user:<br>ASPECTS*: [score]<br>[username]</li>
</ul>
</td>
</tr>
</table>

With [username] being the login used to log in to the platform (AWS/AW) at the time the score was accepted and exported.
The product name **StrokeSENS** is always displayed, indicating that StrokeSENS ASPECTS device, manufactured by Circle Neurovascular Imaging, was used to generate the results.


While the StrokeSENS ASPECTS algorithm is processing, the panel shows a processing wheel, and all regions are greyed out while waiting for the results. During this time, users can still interact with the images.

Similarly, when StrokeSENS ASPECTS predicts a score of 10, no region is determined to be affected. Therefore, no region/hemisphere is selected on the report panel and all regions overlays in the viewport are illustrated in yellow.

If the ASPECTS algorithm fails or the data does not meet ASPECTS image requirements, an error message is displayed in the panel.


Use the **Accept and Export** button to accept the automated ASPECT score and save the ASPECTS images as a new series in the database, with the following series description: "*ASPECTS – [XX] – [username]*", in which *[XX]* will automatically be replaced by the ASPECT score and *[username]* by the login of the user logged into the platform at the time the series was exported/saved.

The series will be saved as a SCPT and will include the ASPECTS contours on the images as well as the related ASPECT score and annotations. The slice thickness and image spacing used to generate the series will be the ones from the input series used to process the ASPECTS.

After the **Accept and Export** button was clicked, it will change to **Accepted and Exported** and will be greyed out to let the user know the action was performed.

The ASPECT score is editable if judged necessary.

To edit the processed score, simply select/deselect the desired regions/hemisphere by clicking the corresponding buttons as needed. Buttons representing the different regions and hemispheres remain available at anytime to allow ASPECTS modifications.
If a user modifies a region/hemisphere after clicking on the **Accept and Export** button, the greyed out button will become active again to allow for the edited score to be accepted and exported as a new series.

**Note**: Do not forget to export the edited series if desired. Previously exported series will not be updated nor automatically deleted. It is the user responsibility to delete any previously saved and potentially wrong series to avoid confusion.

If a user loads a session with a previous save state including an ASPECTS processing, ASPECTS editions and buttons state will have been kept as they were when the save state was created.
If a user loads a session without a previous compatible ASPECTS save state, the ASPECTS processing will start from scratch.

### 13.2 StrokeSENS LVO

Provided that the StrokeSENS LVO license is present, the StrokeSENS LVO detection algorithm will be triggered automatically upon FastStroke session launch, regardless of whether the session was launched manually or automatically using preprocessing, when a compatible series is detected (see Required Image Parameters for Algorithm Processing and Recommended Image Parameters for Algorithm Processing).

If a LVO (Large Vessel Occlusion) is suspected by the algorithm, the "**Suspected LVO**" notification will be displayed in red in the viewport(s) displaying the CTA, or the 1st phase of the mCTA series (i.e. Carotids and Collaterals review steps when available/applicable).

This notification is followed by the "**StrokeSENS**" annotation to let the user know that this result is generated by StrokeSENS.

While the StrokeSENS LVO algorithm is processing, the information "**LVO processing...**" is displayed in the viewport(s) and users can still interact with the images.

If the LVO detection algorithm successfully processed and the result is negative, no notification is displayed.

If the LVO detection algorithm fails or the data does not meet LVO image requirements, a pop up displays an error message (see Software Safety-Related Messages chapter).

**Note**: The "Suspected LVO" annotation is for notification purposes only and should not be considered diagnosis. The default slice location of the viewport is not determined by the output of the StrokeSENS LVO algorithm, nor does the algorithm indicate the location of the suspected occlusion. No images are marked up by the StrokeSENS LVO module.

# 14 Summary of Device Performance

## 14.1 Validation of StrokeSENS LVO Performance

**Description of Data Used for Development**

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 development dataset was composed of 476 positive cases with an anterior large vessel occlusion (i.e., intracranial ICA and M1-MCA) and 195 negative no-occlusion cases. The imaging data was acquired from multiple CT scanner models, manufactured by four different CT scanner vendors (GE, Siemens, Philips, Toshiba) from multiple sites across North America (Canada and USA), EU and Asia.

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, 1.5] | 652 | 378 |
| (1.5, 2.5] | 14 | 22 |
| >2.5 | 5 | 0 |
| **kVp** | | |
| [80, 100] | 151 | 80 |
| (100, 120] | 482 | 281 |
| (120, 140] | 38 | 39 |
| **Age** | | |
| ≤50 | 77 | 40 |
| 51-60 | 117 | 67 |
| 61-70 | 167 | 107 |
| 71-80 | 157 | 113 |
| 81-90 | 131 | 60 |
| 91-100 | 16 | 13 |
| Data not available | 6 | 0 |
| **Sex** | | |
| Male | 351 | 217 |
| Female | 308 | 183 |
| Data not available | 6 | 0 |

| | | |
|---|---|---|
| **Geography** | | |
| Canada | 326 | 179 |
| US | 236 | 153 |
| Europe | 81 | 43 |
| Asia | 3 | 1 |
| Australia | 22 | 24 |
| Data not available | 3 | 0 |
| **Site of Occlusion** | | |
| ICA | 106 | 77 |
| M1-MCA | 370 | 140 |
| Non-LVO | 195 | 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, 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 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 mean sensitivity of 90.3% CI = [86.4%,94.3%], and mean specificity of 95.1% 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 1.94 minutes (S.D: ±0.06 mins, Min: 1.79 mins, Max: 2.14 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: 1.94 mins<br>S.D: ±0.06 mins<br>Min: 1.79 mins<br>Max: 2.14 mins |

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

| Sub-Group | # of LVO | # of Non-LVO | Total | Sensitivity [95% CI] | Specificity [95% CI] |
|---|---|---|---|---|---|
| Full cohort | 217 | 183 | 400 | 0.903 [0.864, 0.943] | 0.951 [0.919, 0.982] |
| **Site of Occlusion** | | | | | |
| ICA Set | 59 | 183 | 242 | 0.872 [0.798, 0.946] | - |
| M1-MCA Set | 158 | 183 | 341 | 0.921 [0.876, 0.966] | - |
| Hemorrhage Set | 217 | 109 | 326 | - | 0.973 [0.923, 0.991] |
| Non-LVO-Non-Hemorrhage Set | 217 | 74 | 291 | - | 0.918 [0.855, 0.981] |
| **Age** | | | | | |
| ≥ 70 years old | 109 | 88 | 197 | 0.881 [0.82, 0.942] | 0.943 [0.874, 0.975] |
| < 70 years old | 108 | 95 | 203 | 0.926 [0.877, 0.975] | 0.958 [0.897, 0.984] |
| **Sex** | | | | | |
| Male | 120 | 97 | 217 | 0.900 [0.846, 0.954] | 0.959 [0.899, 0.984] |
| Female | 97 | 86 | 183 | 0.907 [0.849, 0.965] | 0.942 [0.871, 0.975] |
| **Slice Thickness** (mm) | | | | | |
| 0.5mm - 0.8mm | 108 | 95 | 203 | 0.880 [0.818, 0.941] | 0.958 [0.897, 0.984] |
| 0.9mm - 2mm | 109 | 88 | 197 | 0.927 [0.878, 0.976] | 0.943 [0.874, 0.975] |
| **Manufacturer** | | | | | |
| GE Medical | 62 | 84 | 146 | 0.958 [0.897, 0.984] | 0.958 [0.897, 0.984] |
| Siemens | 63 | 80 | 143 | 0.958 [0.897, 0.984] | 0.958 [0.897, 0.984] |
| Other | 92 | 19 | 111 | 0.958 [0.897, 0.984] | 0.958 [0.897, 0.984] |

## 14.2 Validation of StrokeSENS ASPECTS Performance

### Description of Data Used for Development

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 development dataset was composed of 57% anterior large vessel occlusion (ICA, M1, proximal M2), while the remaining cases included a variety of other cases (no occlusion, distal occlusions, and non-anterior circulation occlusions i.e., Basilar, posterior, vertebral) typically seen in the intended clinical population. The imaging data was acquired from multiple CT scanner models, manufactured by two different CT scanner vendors (GE & Siemens) from multiple sites across North America and EU.

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

| | Development Set | Test Set (MRMC) |
|---|---|---|
| Total | 438 | 200 |
| **Manufacturer** | | |
| GE Medical Systems | 404 | 93 |
| Siemens | 34 | 44 |
| Philips | 0 | 34 |
| Toshiba | 0 | 29 |
| **Slice Thickness** | | |
| [2.5, 3.75] | 49 | 69 |
| (3.75, 5] | 389 | 131 |
| **KVP** | | |
| [100, 120] | 273 | 164 |
| (120, 140] | 165 | 36 |
| **ASPECTS** | | |
| 0 | 0 | 3 |
| 1 | 0 | 5 |
| 2 | 1 | 8 |
| 3 | 3 | 11 |
| 4 | 4 | 7 |
| 5 | 3 | 19 |
| 6 | 19 | 16 |
| 7 | 30 | 21 |
| 8 | 36 | 36 |
| 9 | 70 | 27 |
| 10 | 272 | 47 |
| **Age** | | |
| ≤30 | 1 | 1 |
| (30, 40] | 9 | 7 |
| (40, 50] | 31 | 22 |
| (50, 60] | 56 | 26 |
| (60, 70] | 94 | 43 |

| | | |
|---|---|---|
| (70, 80] | 137 | 64 |
| (80, 90] | 92 | 34 |
| (90, 100] | 12 | 3 |
| NA | 6 | 0 |
| **Sex** | | |
| Male | 224 | 89 |
| Female | 208 | 111 |
| NA | 6 | 0 |
| **Geography** | | |
| Canada | 365 | 77 |
| US | 0 | 59 |
| Europe | 73 | 51 |
| Asia | 0 | 11 |
| Australia | 0 | 2 |
| **Onset to CT Time (minutes)** | | |
| ≤60 | 55 | 28 |
| (60, 120] | 154 | 77 |
| (120, 180] | 60 | 33 |
| (180, 240] | 50 | 29 |
| (240, 300] | 30 | 26 |
| (300, 360] | 20 | 7 |
| (360, 420] | 10 | 0 |
| (420, 480] | 9 | 0 |
| (480, 540] | 10 | 0 |
| (540, 600] | 10 | 0 |
| (600, 660] | 5 | 0 |
| (660, 720] | 7 | 0 |
| ≥720 | 18 | 0 |
| **NIHSS Score** | | |
| [0, 4] | 78 | 6 |
| (4, 8] | 87 | 21 |
| (8, 12] | 63 | 19 |
| (12, 16] | 59 | 47 |
| (16, 20] | 68 | 61 |
| (20, 24] | 52 | 24 |
| (24, 28] | 21 | 18 |
| (28, 32] | 2 | 4 |
| (32, 36] | 1 | 0 |
| NA | 7 | 0 |

**Summary of Standalone Performance Assessment**

To demonstrate the standalone performance of the StrokeSENS ASPECTS software a retrospective case study was conducted. 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), multiple CT scanner models manufactured by different CT scanner vendors (GE, Siemens, Toshiba, Philips), slice thickness of 2.5-5mm, and kVp value range of 100-140. The test data were representative of a wide range of clinical severities (ASPECT 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 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. Receiver Operating Characteristics (ROC) analysis was used to assess the region-level accuracy of the StrokeSENS automated ASPECT score prediction vs the expert annotation, achieving a per-region clustered AUC of 83.5%. Further analysis shows the StrokeSENS ASPECTS module performed with a side classification accuracy of 97.3% and an ICC of 74.6%.

| ASPECT Score Performance | |
|---|---|
| Clustered AUC | 0.835 [0.802, 0.869] |
| Intraclass correlation coefficient (ICC) | 0.746 [0.680, 0.800] |

| Side Prediction Summary | |
|---|---|
| Accuracy | 0.973 [0.932, 0.989] |
| Sensitivity | 0.989 [0.956, 0.997] |
| Specificity | 0.942 [0.904, 0.980] |

The predetermined operational points (OPs) were selected on a subset of the development dataset based on (1) manual EIC segmentations performed by an expert neuroradiologist, (2) automatic ASPECTS region segmentation generated by the algorithm, and (3) the reference ASPECTS read. For each of the ten ASPECTS regions, the receiver operating characteristics (ROC) curve is calculated, and the point that was closest to the point of the perfect classifier (i.e., the top left corner of the ROC) was selected as the operational point for that region. The following table specifies the OP for each of the 10 ASPECTS regions, and the corresponding performance of the device on the test dataset (N=200).

| Affected Region Performance | | | | |
|---|---|---|---|---|
| Region | AUC | Selected OP | Sensitivity | Specificity |
| M1 | 0.837 | 0.026797961 | 0.773 [0.715, 0.831] | 0.843 [0.793, 0.894] |
| M2 | 0.821 | 0.048311334 | 0.850 [0.801, 0.899] | 0.608 [0.541, 0.676] |
| M3 | 0.892 | 0.067800194 | 0.852 [0.803, 0.901] | 0.757 [0.698, 0.817] |
| M4 | 0.85 | 0.004963366 | 0.867 [0.820, 0.914] | 0.761 [0.702, 0.820] |
| M5 | 0.865 | 0.017413441 | 0.907 [0.867, 0.948] | 0.699 [0.635, 0.762] |
| M6 | 0.801 | 0.051263440 | 0.857 [0.809, 0.906] | 0.743 [0.682, 0.804] |
| Caudate | 0.761 | 0.015985325 | 0.609 [0.541, 0.676] | 0.877 [0.831, 0.922] |
| Lentiform | 0.786 | 0.058007717 | 0.808 [0.753, 0.862] | 0.615 [0.547, 0.682] |
| Insula | 0.872 | 0.016447369 | 0.883 [0.838, 0.927] | 0.611 [0.544, 0.679] |
| Internal Capsule | 0.799 | 0.255516827 | 0.375 [0.308, 0.442] | 0.917 [0.878, 0.955] |

**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 ASPECT score ≤5) also improved when aided with StrokeSENS (AUC=84.2%) vs unaided (AUC=78.1%) in reference to the truther consensus aspects.

### 14.3 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-Siemens 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.

Young 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.

### 14.4 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, 2500Mhz, 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 |

# 15 Technical Support

### Reporting of Serious Incidents:

Any serious incident related to the use of this device should be reported to both GE Healthcare and the health authority/competent authority where the device is installed. GE Healthcare is responsible to notify the manufacturer (Circle Neurovascular Imaging) of the serious incident.

- To report to GE Healthcare:
  - Either contact your local service representative
  - Or report to: In-box.complaints@ge.com

- Please provide the following information:
  - The catalogue number* or the model designation of the device as stated on its identification plate affixed on the device
  - The System ID/serial number/lot number of the device
  - The date of incident
  - The description of incident, including any patient or user impact/injury
  - Your contact information (facility, address, contact name, title, and telephone number)

* For eDelivery digital kits:

1. Go to eDelivery Software portal (https://gehealthcare.flexnetoperations.com/flexnet/operationsportal/logon.do) and log in using your UserID and your password.
2. In the Recent Entitlements section, click See all to display the list of products you have purchased. Product names and their catalogue number are both displayed in the Product column.

For technical questions please contact your GE representative.