USER MANUAL

StrokeSENS LVO
Version 1.3.1

StrokeSENS LVO

User Manual

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Regulatory Information

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UDI: *+B926SSSX10*

Manufactured by:

Circle Cardiovascular Imaging Inc.,
doing business as
Circle Neurovascular Imaging.

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Canada
Health Canada device license number: **107386**

United States of America
The following 510K clearance(s) applicable for this product:
K212261

Importer (UK)
Circle Cardiovascular Imaging UK Ltd.
Ty Menter Navigation Park,
Abercynon,
Mountain Ash, Wales, CF45 4SN

Importer (EU)
Circle Cardiovascular Imaging B.V.
SingelStaete, Singel 250
1016 AB Amsterdam
The Netherlands

European Union

CE
1639

StrokeSENS is qualified as a class IIa medical device.

EC REP

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CH REP

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IMPORTANT: 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	Australian Sponsor: **Siemens Healthcare Pty Ltd** Level 3, 141 Camberwell Road Hawthorn East, VIC 3123, Australia Ph: 1 (800) 310-300	ARTG number: 399398
CE Mark (MDD)	Circle Cardiovascular Imaging BV SingelStaete Singel 250 1016 AB Amsterdam The Netherlands	CE Mark Certificate US21/819944332 issued by SGS for StrokeSENS.
Health Canada	N/A	Health Canada device license number: 107386
US FDA	N/A	StrokeSENS LVO – K212261
UK	Circle Cardiovascular Imaging UK LTD. Ty Mentor, Navigation Park, Abercynon Mountain Ash, Mid Glamorgan, Wales, UK, CF45 4SN	MHRA registration: 22027

2 Introduction

This User Guide is also available:
• On the Internet at: www.circlenvi.com/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 info@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, analysis, viewing and communication of computed tomography (CT) scans of the brain in patients with suspected acute stroke. Analysis of contrast-enhanced CT images is provided by the StrokeSENS LVO module, which includes automated detection of suspected large vessel occlusion (LVO).

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.
	**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.

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.
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 devices. The compatible radiological software solution may also provide other radiological functionalities outside the scope of the StrokeSENS LVO 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 (ie. ICA – MCA vessels).

3 Basic Components and Indication for Use

3.1 Indication for Use

StrokeSENS LVO is a radiological computer-aided triage and notification (CADt) software indicated for use in the analysis of CTA head images. The device is intended to assist hospital networks and trained clinicians in workflow triage by flagging and communication of suspected positive findings of Large Vessel Occlusion (LVO) in head CTA images.

StrokeSENS LVO uses a software algorithm to identify suspected LVO findings. In the case of a suspected LVO, the system will send a notification to a pre-configured destination(s), notifying the clinicians 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.

Notifications may include a compressed preview of images. Notifications are meant for informational purposes only and are not intended for diagnostic use beyond notification. The StrokeSENS LVO device does not alter the original medical image and is not intended to be used as a diagnostic device.

The results of StrokeSENS LVO are intended to be used in conjunction with other patient information and based on professional judgement, to assist with triage / prioritization of medical images. Notified clinicians are responsible for viewing full images per standard of care.

3.2 Patient population

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

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

3.3 Intended user population

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.

3.4 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.

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, 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 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 Clinical Benefits

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.

6 Contraindications

None

7 Undesirable Side Effects

None

8 System Hardware and Software Specifications

8.1 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 scanner systems in the market, including:

- Siemens (Somatom Definition series, Sensation series, Somatom Force)
- General Electric (Discovery series, Lightspeed series, Revolution series, Optima series)
- 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. Comprehensive testing of the StrokeSENS LVO software in the StrokeSENS Platform has been conducted, verifying the performance of the StrokeSENS LVO software in the compatible system. This document provides user instructions and labelling for the StrokeSENS LVO software as integrated into the compatible StrokeSENS Platform.

8.2 DICOM requirements for Algorithm Processing

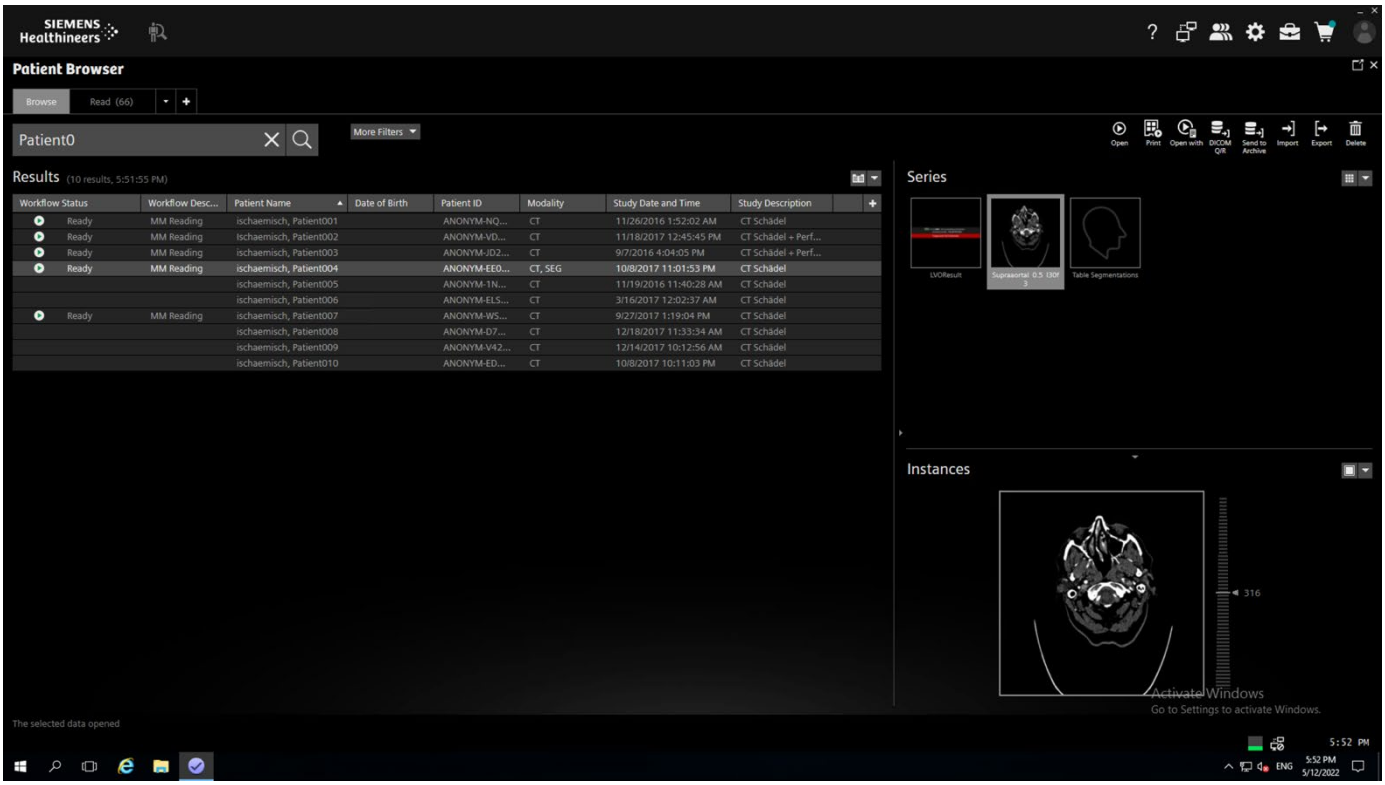
NOTICE: StrokeSENS was trained and tested with datasets acquired with the following parameters listed below. For accurate processing by the Artificial Intelligence (AI) algorithms, StrokeSENS requires DICOM standard CT images of the head that align with the following parameters

	CTA for LVO Detection
1.	ImageType = Original/Primary
2.	Modality = “CT”
3.	Volumes = 1 *a multi-volume CTA (ie. multi-phase CTA) is acceptable. Only the first phase is used for processing.
4.	SliceThickness <= 3.0 mm

In addition to the acceptable DICOM requirements listed above, 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.

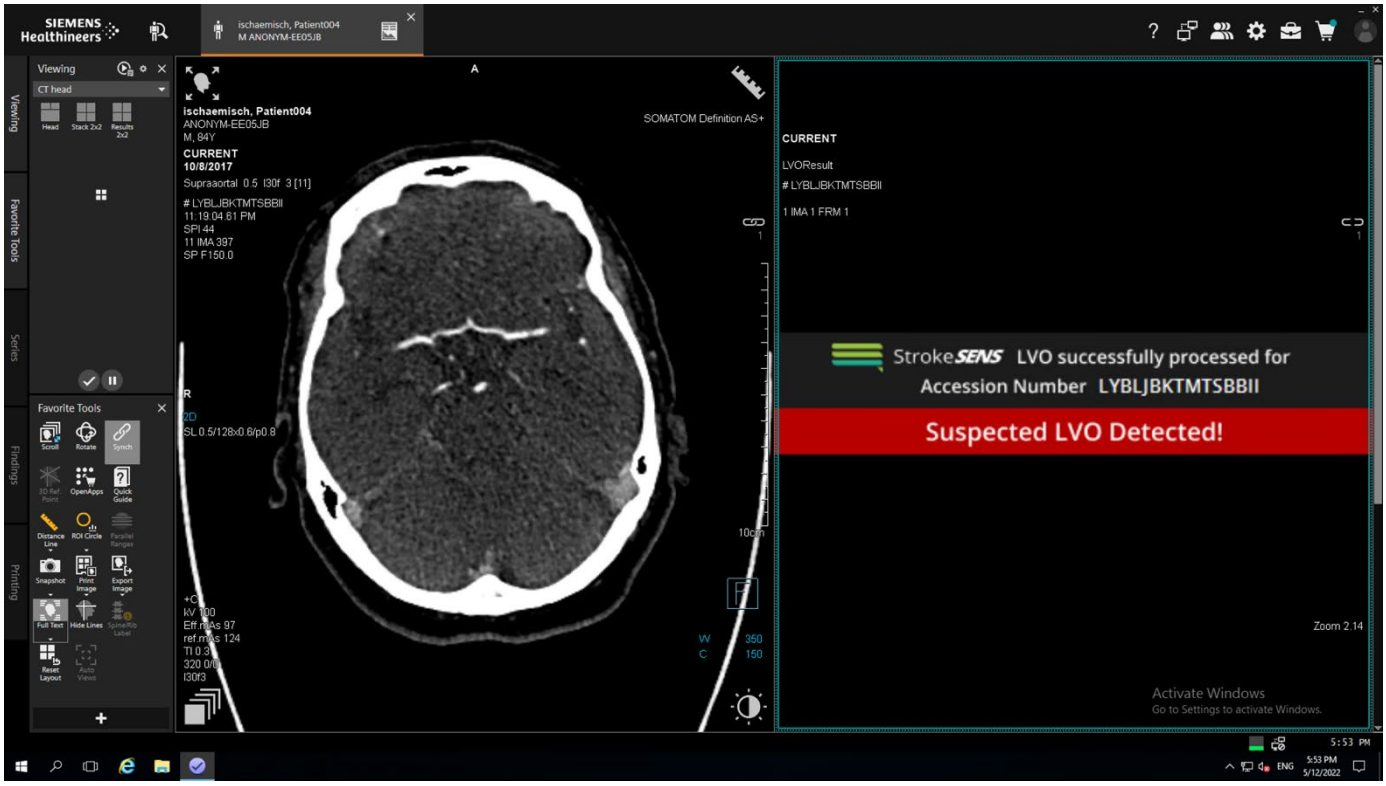
9 LVO Detection

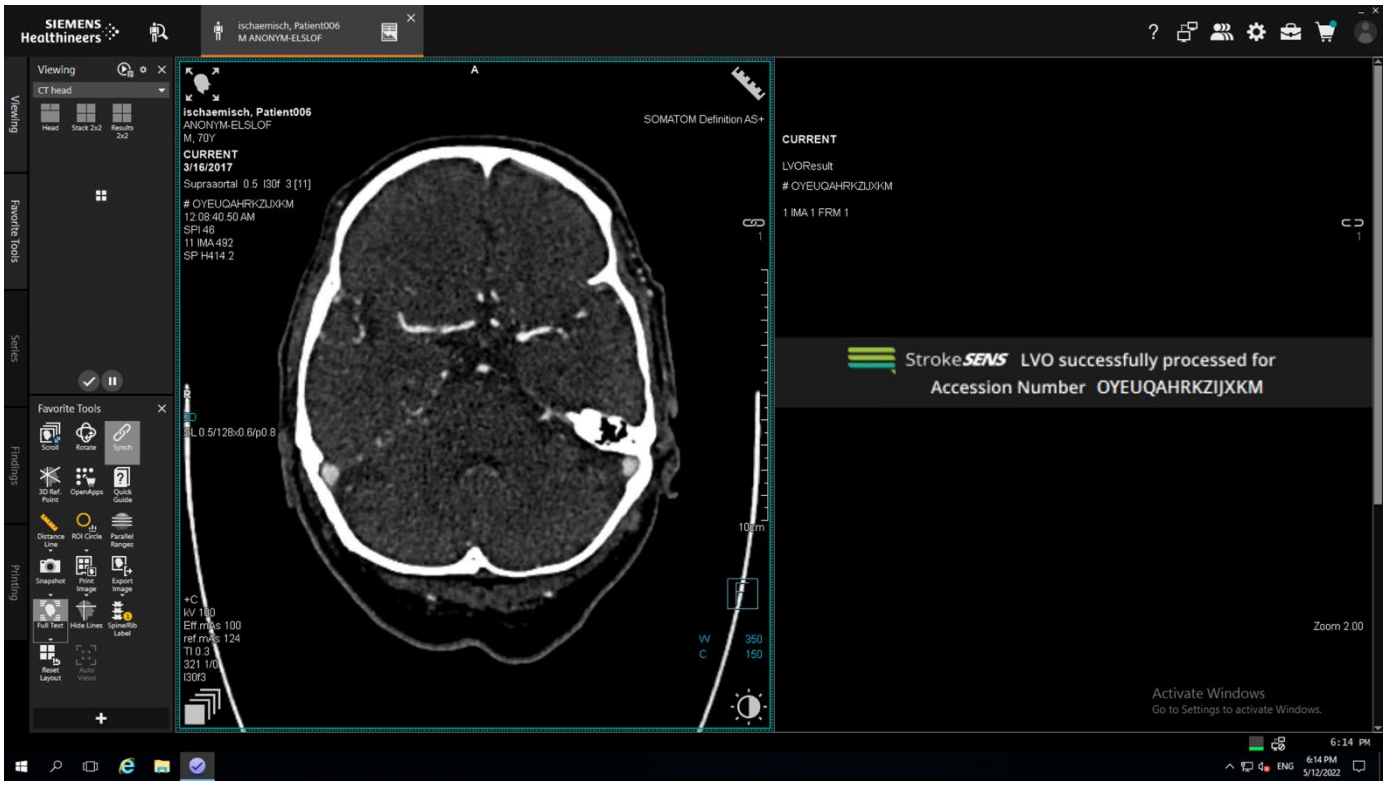
CTA Head scans appropriate for LVO detection (see 8.6 above) will be identified by syngo.via and shared with the StrokeSENS LVO algorithm for processing. Once LVO Detection post-processing is complete, the results will be saved as a single-image Series in the same Study to which the CTA source images belong. Both the original CTA and the LVO Detection results will be available to the user via the Patient Browser (see below).



Head CT Angiogram (CTA) and LVO Detection results Series made available for viewing from the Patient Browser

The LVO Detection results indicate that processing was successfully completed, provide an Accession Number for the user's reference, and in the case a suspected LVO is detected, that is indicated. (see below for cases where an LVO was and was not detected, respectively).





10 Summary of data and device performance

10.1 StrokeSENS LVO

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 three clinical study/trial databases, namely the Prove-IT clinical study (ClinicalTrials.gov Identifier: NCT02184936), the INTERRSeCT clinical study (JamaNetwork.com Identifier: 2702146) and ESCAPE randomized controlled trial (ClinicalTrials.gov Identifier: NCT01778335). The development dataset was composed of 63% anterior large vessel occlusion (ICA and M1), while the remaining cases included a variety of anterior LVO-negative cases (no occlusion, distal occlusions, and non-anterior circulation occlusions i.e., Basilar, posterior, vertebral, and hemorrhage) typically seen in the intended clinical population. 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 operational point of the algorithm (0.8) was selected to optimize sensitivity and specificity on a subset of the development dataset.

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

	Development Set	Test Set
Total	874	400
Manufacturer		
GE Medical Systems	633	146
Siemens	179	143
Philips	34	47
Toshiba	28	64
Slice Thickness (mm)		
[0.5, 1.5]	839	378
(1.5, 2.5]	19	22
>2.5	16	0
kVp		
[80, 100]	130	80
(100, 120]	742	281
(120, 140]	2	39
Age		
<=50	71	40
51-60	112	67
61-70	190	107
71-80	260	113
81-90	179	60
91-100	16	13
Data not available	46	0
Sex		
Male	429	217
Female	398	183
Data not available	47	0
Geography		
Canada	640	179
US	26	153
Europe	186	43
Asia	21	1
Australia	1	24

Site of Occlusion		
ICA	146	77
M1-MCA	407	140
Non-LVO	321	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 the clinical study/trial databases, namely ESCAPE NA1 randomized controlled trial (ClinicalTrials.gov Identifier: NCT02930018), Predict study (PMID: 22405630), Tempo1 open label clinical trial (ClinicalTrials.gov Identifier: NCT01654445) and Alias randomized clinical trial (ClinicalTrials.gov Identifier: NCT00235495). The negative (non-LVO) subgroup was supplemented with challenging cases including anterior LVO-negative cases (no occlusion, distal occlusions, and non-anterior circulation occlusions i.e., Basilar, posterior, vertebral, and hemorrhage) typically seen in the intended clinical population.

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 89.4% CI = [85.3%, 93.5%], and mean specificity of 87.4% CI = [82.6%, 92.2%] 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 0.75 minutes (S.D: ±0.21 mins, Min: 0.26 mins, Max: 1.33 mins)

Test	**Test Results**
Sensitivity	0.894, 95% CI = [0.853, 0.935]
Specificity	0.874, 95% CI = [0.826, 0.922]
Processing Time	Mean: 0.75 mins S.D: ±0.21 mins Min: 0.26 mins Max: 1.33 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	0.894 [0.853, 0.935]	0.874 [0.826, 0.922]
Site of Occlusion					
ICA Set + Non-LVO Set	77	183	260	0.857 [0.779, 0.935]	0.874 [0.826, 0.922]

M1-MCA Set + Non-LVO Set	140	183	323	0.914 [0.868, 0.961]	0.874 [0.826, 0.922]
LVO Set + Hemorrhage Set	217	110	327	0.894 [0.853, 0.935]	0.891 [0.833, 0.949]
LVO Set + Non-LVO-Non-Hemorrhage Set	217	73	290	0.894 [0.853, 0.935]	0.849 [0.767, 0.931]
Age					
>= 70 years old	109	88	197	0.945 [0.902, 0.988]	0.830 [0.751, 0.908]
< 70 years old	108	95	203	0.843 [0.774, 0.911]	0.916 [0.860, 0.972]
Sex					
Male	120	97	217	0.875 [0.816, 0.934]	0.866 [0.798, 0.934]
Female	97	86	183	0.918 [0.863, 0.972]	0.884 [0.816, 0.951]
Slice Thickness (mm)					
0.5mm - 0.8mm	108	95	203	0.880 [0.818, 0.941]	0.863 [0.794, 0.932]
0.9mm - 2mm	109	88	197	0.908 [0.854, 0.962]	0.886 [0.820, 0.953]
Manufacturer					
GE Medical	62	84	146	0.903 [0.830, 0.977]	0.869 [0.797, 0.941]
Siemens	63	80	143	0.857 [0.771, 0.944]	0.900 [0.834, 0.966]
Other	92	19	111	0.913 [0.855, 0.971]	0.789 [0.567, 0.915]

10.2 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 StrokeSENS LVO
- Young adults (<50) were underrepresented in the data used for training and testing LVO detection algorithms

10.3 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, 2 Core(s), 2 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

11 Technical Support

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

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