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Validation of a machine learning software tool for automated large vessel occlusion detection in patients with suspected acute stroke

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Abstract

Purpose CT angiography (CTA) is the imaging standard for large vessel occlusion (LVO) detection in patients with acute ischemic stroke. Stroke*SENS* LVO is an automated tool that utilizes a machine learning algorithm to identify anterior large vessel occlusions (LVO) on CTA. The aim of this study was to test the algorithm's performance in LVO detection in an independent dataset.

Methods A total of 400 studies (217 LVO, 183 other/no occlusion) read by expert consensus were used for retrospective analysis. The LVO was defined as intracranial internal carotid artery (ICA) occlusion and M1 middle cerebral artery (MCA) occlusion. Software performance in detecting anterior LVO was evaluated using receiver operator characteristics (ROC) analysis, reporting area under the curve (AUC), sensitivity, and specificity. Subgroup analyses were performed to evaluate if performance in detecting LVO differed by subgroups, namely M1 MCA and ICA occlusion sites, and in data stratified by patient age, sex, and CTA acquisition characteristics (slice thickness, kilovoltage tube peak, and scanner manufacturer).

Results AUC, sensitivity, and specificity overall were as follows: 0.939, 0.894, and 0.874, respectively, in the full cohort; 0.927, 0.857, and 0.874, respectively, in the ICA occlusion cohort; 0.945, 0.914, and 0.874, respectively, in the M1 MCA occlusion cohort. Performance did not differ significantly by patient age, sex, or CTA acquisition characteristics.

Conclusion The Stroke*SENS* LVO machine learning algorithm detects anterior LVO with high accuracy from a range of scans in a large dataset.

Keywords Machine learning · Large vessel occlusion · Stroke · Automatic detection

Abbreviations

AUC	Area under the curve
CI	Confidence interval
CNN	Convolutional neural network
EVT	Endovascular treatment
ICA	Internal carotid artery
ICH	Intracranial hemorrhage
LVO	Large vessel occlusion
MCA	Middle cerebral artery
ROC	Receiver operator characteristics

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Introduction

Patients with acute ischemic stroke due to large vessel occlusions (LVO), on average, may account for around 15–20% of all acute ischemic stroke patients [1]. However, LVO strokes contribute to 90% of stroke mortality and severe clinical disability if left untreated [2]. Recent advances in endovascular stroke treatment (EVT) have led to significant reduction in disability in these patients in comparison to best medical management [3]. Because of the robust evidence from clinical trials confirming its efficacy and safety, EVT has become the standard of care in patients with anterior circulation stroke due to LVO [3].

Contrast-enhanced CT angiography (CTA) has been widely adopted as the imaging standard for LVO detection in order to identify eligible patients for endovascular treatment [4–6]. Timely CTA interpretation and LVO detection remain challenging especially in smaller, more rural hospitals where physicians with experience in stroke imaging are not always available [7]. Since any delay in the treatment of patients with LVO directly affects patient outcomes [8], automated detection and notification of suspected LVO can help improve patient outcomes by directly reducing the time to diagnosis and clinical decision-making [6].

Stroke*SENS* LVO (Circle Neurovascular Imaging, Calgary, Canada) is a computer-aided triage and notification (CADt) tool which utilizes machine learning to automatically detect LVO on CTA head images. The automated software is intended to notify clinicians of patients with suspicious LVO via pre-determined communication protocols, thus allowing them to get involved in the case sooner than they may have been able to if using standard diagnostic workflows. The aim of this retrospective cohort study was to evaluate the software's performance in LVO detection, when compared to a neuroradiologist expert consensus assessment on imaging data from a large multicenter image database.

Methods

Software development dataset

The Stroke*SENS* LVO algorithm was developed using a dataset of 874 CTA cases (development dataset) of pooled de-identified imaging data from three clinical trials initiated from the University of Calgary (INTERRSeCT[9], PRove-IT[10], ESCAPE[11]). The primary goal for the software development was a reliable detection of the anterior LVO including intracranial ICA and M1 MCA occlusions. The subset of data used for development was selected from the pooled database according to the following inclusion criteria: age of 18 years or older who underwent baseline CTA imaging for suspected acute stroke with image slice thickness between 0.5 and 2.5 mm.

The imaging data for development were acquired from multiple institutions and multiple CT scanners, manufactured by four different CT vendors (GE, Siemens, Philips, Toshiba). Scans determined to be technically inadequate (e.g., invalid DICOM image or inappropriate head coverage or no contrast) or with significant patient motion were excluded. Images in the development dataset included 553 subjects with anterior LVO [internal carotid artery (ICA) and the M1 segment of the middle cerebral artery (MCA)] and 321 subjects with other/no occlusions [negative cases (non-occlusions), distal occlusions (i.e., M2, M3 MCA), and non-anterior circulation occlusions (i.e., occlusions in the vertebrobasilar territory)]. There was no scan with intracranial hemorrhage (ICH) in the development dataset. The manually labeled data points annotating the occlusion were used for the algorithm development.

Image preprocessing and convolutional neural network

A preprocessing pipeline was used to transform the raw CTA volume into a normalized space suitable for use as inputs to a convolutional neural network. This is required so that the network is always presented with images of the same resolution, field of view, and range of intensity values; and so, it does not have to account for these factors of variation as they are standardized. To this end, the volumes were cropped 181 mm from the top of the raw volume and then resampled to a voxel spacing of 1.13 mm^3, leading to an input shape of $160 \times 192 \times 160$ voxels. Furthermore, the image intensities were clipped to the range of 0 to 1000 Hounsfield units (HU).

A 3D convolutional neural network (CNN) [12] was used to extract valuable features from the normalized volume and to perform the detection of LVO. It was composed of 4 down blocks, each of which was composed of 2 convolutional layers with 8 kernels. The activation function for each convolutional layer was the rectified linear unit (ReLU) function [13]. At the end of each down block, a batch normalization operation was performed [14]. After the last convolutional layer, all nodes were flattened, and a single fully connected layer was applied to compute the output layer. The output layer encoded information about both the existence of an LVO and the location of the clot from the manually labeled data points on the source scans.

The training of the model was performed using an Adam optimizer [15] with a learning rate of 1e-3 and a batch size of 16 for 2700 epochs. In each epoch, the entire training

set was backpropagated through the model. During training, several data augmentation operations were performed. These include (1) rotation of up to + -45 degrees on the axial plane, (2) rotation of + -20 degrees in the coronal/sagittal planes, (3) flipping along the *x* axis only, and (4) translation of up to + -40 voxels in all axes.

The loss function was necessary to guide the training process of the model and was not used during the deployment of the model. It was based on the softmax cross entropy function between the output layer and the reference encoding, both of which contained information about the existence of an LVO and the location of the clot. (Of note, the occlusion location was used for the software development, but only to a limited extent, and the information about the occlusion location is not provided to the end-users).

Software validation dataset (test set)

This test data was independent of the development dataset and was retrospectively selected from the following studies, namely, ESCAPE-NA1[16], ALIAS[17], TEMPO-1[18], and PREDICT [19]. Additional inclusion criteria for the test set included subjects aged 18 years or older, who underwent baseline CTA imaging for acute stroke with image slice thickness between 0.5 and 2.5 mm. Similar to the derivation dataset, the imaging data for the test set were acquired from multiple CT scanner models, manufactured by four different CT scanner vendors (GE, Siemens, Philips, Toshiba), as well as from multiple hospital sites and geographies. Scans determined to be technically inadequate (e.g., invalid DICOM image or inappropriate head coverage or no contrast) or with significant patient motion were excluded.

Based on data from similar marketed devices, it was determined that a lower bound 95% confidence interval (CI) of 80% for both sensitivity and specificity is required to demonstrate the clinical utility of the device. Using the normal approximation interval, and assuming that the sensitivity/specificity point estimates would be at 85% (5% above the acceptance criteria), a sample size of 200 LVO and 200 other/no occlusion was deemed necessary to meet this performance goal.

Random selection with purposive sampling was performed to achieve a balanced number of LVO and other/no occlusion cases and to ensure representation of cases acquired on multiple scanner manufacturers. The sampling was automated and informed by patient-level metadata which included only the scanner manufacturer and the clinical reference label (LVO yes/no) from the originating clinical study.

Expert consensus was used as ground truth to establish the reference dataset labels. Three board-certified neuroradiologists (with > 5 years of experience in stroke imaging) independently read all CTA images. A LVO scan was defined as containing an ICA or M1 MCA occlusion. A other/no occlusion scan was defined as any scan that does not contain an LVO, i.e., it may either had other more distally located intracranial occlusions or no occlusions at all. In addition to reporting "LVO" vs "other/no occlusion," the readers were also asked to report the site of occlusion (anatomical location including any intracranial ICA segment, M1 MCA segment, and/or other occlusion/distal occlusions; the MCA bifurcation/trifurcation was used as the anatomical cutoff between M1 and M2 MCA segments) as well as the presence of any intracranial hemorrhage (ICH). The readers interpreted the scans blinded to any clinical information. The consensus was determined when at least two of three readers agreed on the presence or absence of LVO. This study was approved by the University of Calgary Conjoint Health Research Ethics Board.

StrokeSENS LVO detection and notification

Stroke*SENS* generates a binary prediction of the presence or absence of LVO on CTA images of the brain. CTA head scans were automatically routed to the Stroke*SENS* LVO processing engine where they were processed and analyzed. In the case of a positive finding, i.e., a LVO detection by the software, the Stroke*SENS* user interface stated that a LVO was suspected (Fig. 1). In the case of a positive finding, the system also automatically generates a notification which is sent to a prespecified email list. In a typical clinical scenario, the notification would be configured to be sent to physicians at a treating hospital parallel to the standard of care workflow. In the current setting, the notifications are sent only for suspected LVO cases.

Statistical analysis

Baseline characteristics of patients with LVO vs. other/no occlusion were compared using a chi-square test or Wilcoxon rank-sum test as appropriate. Expert reads on the presence or absence of LVO were considered as the ground truth. Software performance for LVO detection was assessed using ROC analysis, reporting area under the curve (AUC), sensitivity, and specificity. The level of softmax cross entropy was used to calculate the AUC. False-negative and false-positive cases were retrospectively analyzed, and the reason for the false-negative/false-positive result was identified.

Subgroup analyses were performed to evaluate software performance in the detection of M1 and ICA segment occlusions separately. Software performance was also tested on data stratified by patient sex (female versus male), age (< 70 years or ≥ 70 years or), slice thickness (< 1.0 mm or ≥ 1.0 mm), kilovoltage tube peak (< 120 kVp or ≥ 120 kVp) of the scan, and scanner manufacturer (GE Medical, Siemens, Philips, Toshiba). As no cases with ICH were used

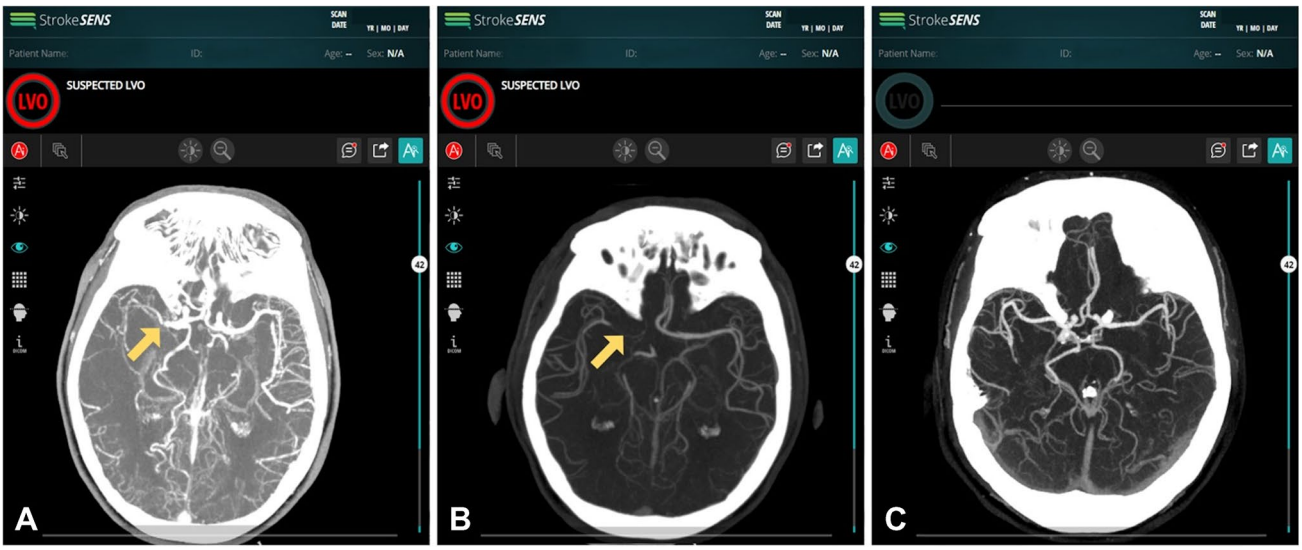

Fig. 1 Exemplary cases of Stroke*SENS LVO* software performance. In case A and B, Stroke*SENS* LVO correctly detected a large vessel occlusion (demonstrated as a red circle in the upper left corner) in the right M1 middle cerebral artery (A, *yellow arrow*) and right terminal internal carotid artery (B, *yellow arrow*). In case C, *StrokeSENS* LVO correctly predicted that no large vessel occlusion was present. (Of note, the occlusion sites are marked with *yellow arrows* for clarity, it is not part of the software analysis)

for the development, a sensitivity analysis to evaluate an impact of the ICH presence on the software performance was performed. Separate logistic regression models were used to test if the association between software prediction and ground truth (expert reads of LVO vs. not) were modified by either patient age, sex, presence or absence of ICH, slice thickness, kVp, or scanner manufacturer. Additionally, the mean, the maximum, and the minimum processing times for positive cases (both true positive and false positive) were reported as a representative measure of time to notification (representing the time from the moment the scan is received in Stroke*SENS* to the notification send to the end-user). No imputation was performed for missing data since there were no missing data. Data analysis was performed using Stata 16.1 (Stata LLC Corp).

The Checklist for AI in Medical Imaging (CLAIM) guidelines was followed [20].

Results

Out of 2779 eligible stroke cases, 1205 cases with identified baseline CTA and initial core lab reading were included into the preliminary dataset (excluded scans: 1339 cases with no baseline CTA, 52 scans with missing age information, and 183 scans with missing initial core lab read). Scans with inappropriate head coverage ($n=12$), no contrast ($n=11$), or corrupted DICOM ($n=4$) were additionally excluded and 400 cases randomly selected for expert consensus read (200 scans allocated in the primary LVO cohort and 200 scans allocated to the primary other/no occlusion cohort). In total, 17 scans were reclassified by the consensus as LVO, and a total of 400 cases (217 allocated to a LVO cohort and 183 allocated to other/no occlusion cohort) were included in the test set (Fig. 2).

Baseline characteristics of patients stratified by presence or absence of LVO are shown in Table 1. Patients with LVO presented with more severe stroke symptoms (expressed with higher National Institutes of Health Stroke Scale [NIHSS]) and had lower Alberta Stroke Program Early CT Score (ASPECTS) on non-contrast CT. The distribution of intracranial occlusion site in patients with LVO was terminal ICA (35.5%, $n=77$) and M1 MCA (64.5%, $n=140$). In the patients without LVO, there were 183 scans with either no occlusion (21.3%), a more distally located MCA occlusion (15.8%), or an occlusion in the posterior circulation (2.7%). The intracranial hemorrhage was present in 110 cases (60.1% of other/no occlusion cohort).

Of the 217 LVO cases evaluated, 194 (89.4%) were correctly identified as LVO by the software. Of 23 falsely negative cases, there were seven cases with ICA occlusion but normally opacified terminal ICA through the circle of Willis, six cases with short-segment M1 MCA occlusions and good collaterals, three with M1 MCA occlusion, and one case with ICA occlusion demonstrated good collaterals and also early venous opacification that may contribute to "richer" vasculature beyond the occlusion; four cases demonstrated a distal M1 MCA occlusion with a prominent anterior temporal artery, and one case had a nonocclusive M1 MCA thrombus. Poor contrast opacification was present in one case.

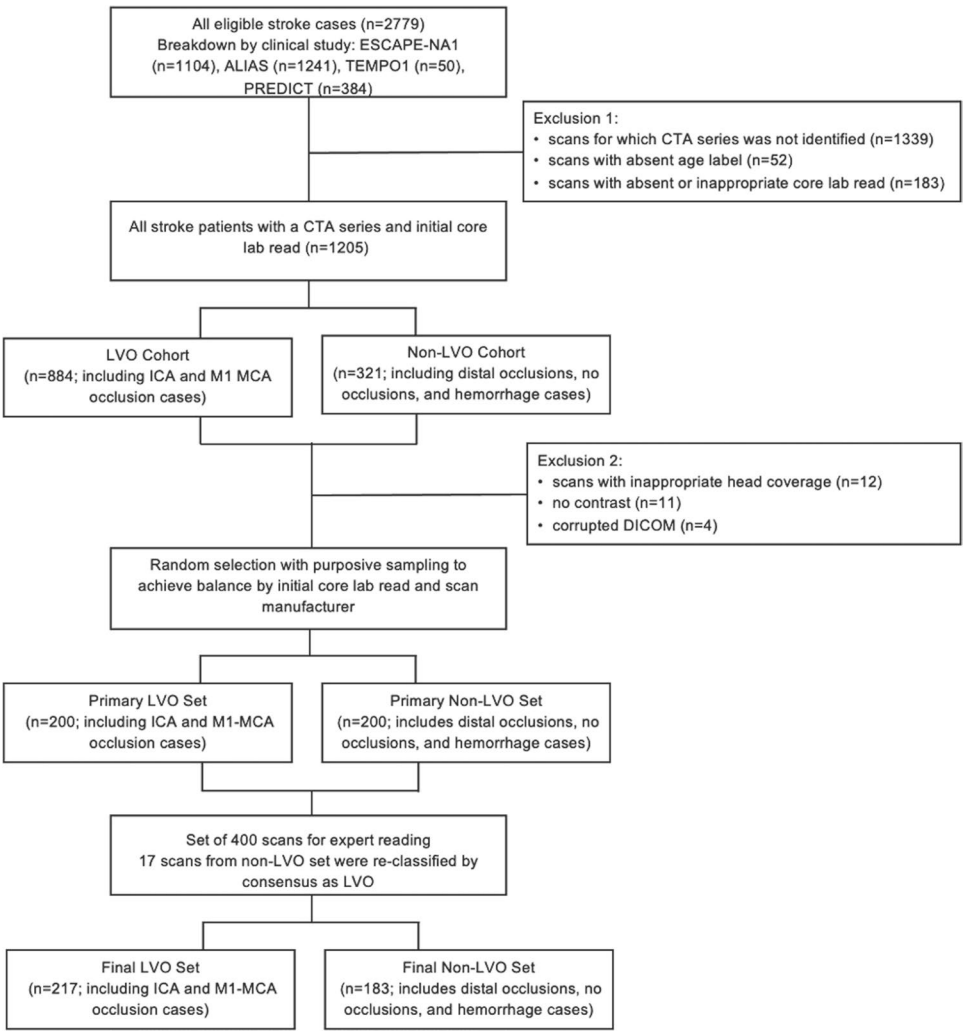

Fig. 2 Scan selection of the test set that was used for evaluation of large vessel occlusion detection with Stroke*SENS* LVO. Note: ICA, internal carotid artery; LVO, large vessel occlusion; M1 MCA, M1 segment of the middle cerebral artery

Table 1 Baseline clinical and imaging characteristics of subjects in the test set

Baseline characteristic	LVO ($n=217$)	Other/no occlusion ($n=183$)	p value
Age, median (IQR)	70 (61–78)	69 (58–78)	0.671[a]
Sex, female, n (%)	97 (44.7)	86 (46.7)	0.687[b]
Baseline NIHSS, median (IQR)	17 (11–21)	8 (6–16)	<0.001[a]
Baseline ASPECTS, median (IQR)	8 (7–9)	10 (9–10)	<0.001[a]
Onset to CT, min, median (IQR)	134 (71–253)	115 (72–195)	0.261[a]

[a]Derived from Wilcoxon rank sum test

[b]Derived from chi-square test

Note: ASPECTS, Alberta Stroke Programme Early CT Score; IQR, interquartile range; LVO, large vessel occlusion; NIHSS, National Institutes of Health Stroke Scale

Of the 183 other/no occlusion cases, 23 (12.6%) were incorrectly identified as LVO by the software. A review identified multiple possible reasons for the false-positive findings: scan asymmetry at the level of the circle of Willis was present in six cases; four cases had an M2 segment occlusion and either relatively short M1 MCA segment or a dominant M2 MCA branch occlusion; three cases had M1 MCA segment stenosis; beam hardening artifact obscured the ICA/MCA segment in three cases; one case was with a M1 MCA aneurysm adjacent to the M1 segment occlusion; and two cases had low-quality scans (poor contrast filling, incomplete study). No obvious reason for

the false-positive finding was found in the remaining four cases.

The sensitivity and specificity for LVO detection were 0.894 (95% CI: 0.854–0.932) and 0.874 (95% CI: 0.817–0.919), respectively, and the AUC was 0.939 (95% CI: 0.915–0.962). The results of subgroup analyses for the M1 and ICA segment occlusion detection were comparable to the main analysis (Table 2). In an analysis stratified by patient sex, age, slice thickness, kVp, and scan manufacturer, the sensitivity, specificity, and AUC ranged from 0.843 to 0.945, 0.83 to 1.0, and 0.928 to 0.970, respectively (Table 2). There was also no difference found in the software performance when the cases with ICH were excluded from the other/no occlusion cohort (Supplementary Table 1). No statistically significant interactions were noted between age, sex, presence/absence of ICH, slice thickness, kVp, and software prediction of LVO in logistic regression models testing for association between software prediction and ground truth (all $p > 0.05$).

The mean processing time for the sum of 217 true and false-positive cases was 44.5 s (standard deviation ± 11 s), the minimum time was 18.4 s, and the maximum time was 77.9 s.

Discussion

In this study, we test the ability of Stroke*SENS* LVO in detecting LVO of the anterior circulation automatically in patients presenting with acute stroke. The accuracy (sensitivity and specificity of 0.894 and 0.874 overall, with similar results across various subgroups, Fig. 3) and speed of detection of the software in a large dataset from multiple centers and geographies, using a variety of vendor machines and protocols for CTA image acquisition, supports the generalizability of the software's use in routine clinical practice.

In general, sensitivity is important metrics to indeed capture as many positive cases as possible and consider them for lifesaving EVT treatment; on the flip side, specificity is very important, especially in hospital sites in which the prevalence of LVOs is very low, since the positive predictive value (precision) is directly influenced by it. In turn, low PPV values can lead clinicians to not trust the tool which can, in turn, lead them to ignore the notifications of the tool entirely [21]. Given that, we aimed at maximizing both the sensitivity and specificity of the model equally.

The test set in this analysis was purposively sampled to include a higher prevalence of common pathologies (i.e., ICH, distal occlusions, and posterior circulation occlusions)

Table 2 Area under the curve, sensitivity, and specificity for automated LVO detection using the machine learning-based algorithm

Group	# of LVO	# of other/no occlusion	Total	Sensitivity [95% CI]	Specificity [95% CI]	AUC [95% CI]
Full cohort	217	183	400	0.894 [0.854, 0.932]	0.874 [0.817, 0.919]	0.939 [0.915, 0.962]
Site of occlusion						
ICA + other/no occlusion	77	183	260	0.857 [0.759, 0.927]	0.874 [0.817, 0.919]	0.927 [0.888, 0.965]
M1 MCA + other/no occlusion	140	183	323	0.914 [0.855, 0.955]	0.874 [0.817, 0.919]	0.945 [0.918, 0.972]
Age						
< 70 years	108	95	203	0.843 [0.760, 0.901]	0.916 [0.841, 0.963]	0.928 [0.891, 0.965]
≥ 70 years	109	88	197	0.945 [0.884, 0.980]	0.83 [0.735, 0.901]	0.951 [0.923, 0.980]
Sex						
Male	120	97	217	0.875 [0.802, 0.928]	0.866 [0.782, 0.927]	0.936 [0.905, 0.968]
Female	97	86	183	0.918 [0.844, 0.964]	0.884 [0.797, 0.943]	0.940 [0.903, 0.977]
Slice thickness						
< 1.0 mm	120	100	220	0.883 [0.812, 0.935]	0.850 [0.765, 0.914]	0.936 [0.904, 0.967]
≥ 1.0 mm	97	83	180	0.939 [0.849, 0.983]	0.924 [0.832, 0.975]	0.939 [0.902, 0.977]
Tube voltage						
< 120 kVp	76	4	80	0.908 [0.819, 0.962]	1.0 [0.398, 1.0]	0.970 [0.923, 1.0]
≥ 120 kVp	141	179	320	0.887 [0.822, 0.934]	0.872 [0.814, 0.917]	0.935 [0.905, 0.965]
Scanner manufacturer						
GE Medical	62	84	146	0.903 [0.801, 0.964]	0.869 [0.778, 0.933]	0.956 [0.924, 0.987]
Siemens	63	80	143	0.857 [0.746, 0.933]	0.90 [0.812, 0.956]	0.924 [0.875, 0.972]
Other (Philips, Toshiba)	92	19	11	0.913 [0.836, 0.962]	0.79 [0.544, 0.94]	0.927 [0.871, 0.983]

Note: AUC, area under the curve; CI, confidence interval; ICA, internal carotid artery; kVp, kilovoltage peak; LVO, large vessel occlusion; M1 MCA, M1 segment of the middle cerebral artery

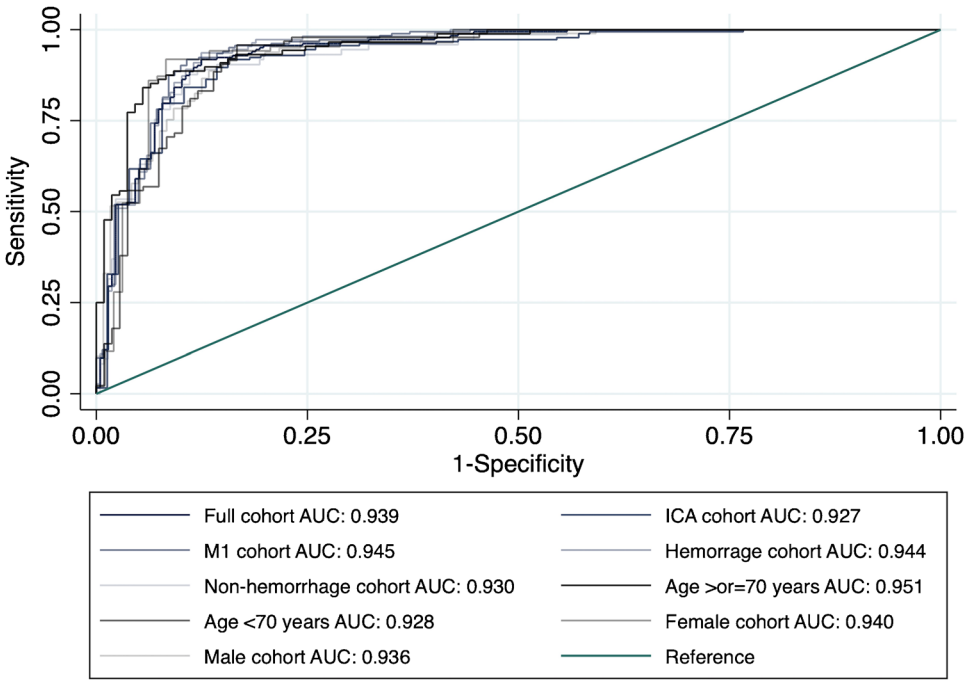

Fig. 3 Areas under the receiver operating characteristic curves (AUC) for the *StrokeSENS* LVO. Model performance is demonstrated in the full dataset and in data stratified by occlusion site (internal carotid artery [ICA] and M1 segment of the middle cerebral artery [MCA]), age (< 70 years and ≥ 70 years), sex, and presence/absence of intracranial hemorrhage

than is typically encountered in consecutive suspected acute stroke cases in the anterior circulation. The objective of the purposive sampling was to test the model's diagnostic performance in a dataset with a large representation of less straightforward cases (i.e., ICH and "other" occlusions) that are expected to be encountered by the algorithm in the clinical practice. A high proportion of hemorrhagic scans in the other/no occlusion cohort was included in order to test the consistency of the software's performance in LVO detection and verified the consistency of the tool. We considered this to be a valid feature of the software tool as the presence of the ICH, or other pathologies such as intracranial tumors can lead to a false-positive finding due to tissue distortion resulting in a change of the vessel course [22]. Although ICH cases can be detected on NCCT scan and will most likely be excluded from further imaging in many diagnostic settings, the fact that other settings include a CTA after NCCT in patients with ICH (for detection of neurovascular abnormalities or spot sign identification) means that even with diagnostic pathways including such cases being sent to the algorithm, the performance continues to be good.

Several automated standalone acute stroke software platforms are available for use in the clinical practice, such as iSchemaView (RAPID CTA), Viz.ai (VIZ LVO), Brainomix (e-CTA), Canon (^{AUTO}Stroke Solution LVO), or StrokeViewer (NICO.LAB). These platforms use different artificial intelligence (AI) including machine-learning (ML) methods for automatic detection of LVOs. Strategies for computer-aided detection of LVO include the direct identification of occlusion site using local vascular features (i.e., detect the clot directly by identifying the discontinuity of the contrast-enhanced vessel) and the indirect identification of occlusion site based on the regional vessel density asymmetry between the affected hemisphere and the unaffected hemisphere. The 3D CNN that is at the core of Stroke*SENS* LVO was trained using information about the existence of LVO and the location of the clot, which allows it to extract both global (image-level) features as well as local features of the clot. Additional analysis is required to assess the trade-off between these two strategies, but it is expected that an ideal device will take both strategies into consideration, similar to how a clinician typically reviews a CTA scan. More specifically, it is well known that in LVO cases with good collateral flow, the downstream effect of the occlusion on the opacification of the peripheral vasculature might not be easily detectable; in contrast, a bundle of vessels around the site of occlusion in LVO cases, or an intracranial MCA stenosis or aneurysm in other/no occlusion cases, may influence a detection of the clot features and result in false-negative/positive findings.

Different methodologies for the computer-aided detection of LVO are discussed in a systematic review by Murray et al. [23] published in 2019. Of the previously mentioned commercial LVO detection platforms, most have undergone validation studies that describe the software's performance in LVO (ICA and M1 MCA) occlusion detection (Table 3). The reported sensitivity and specificity of the software tools ranged from 0.72 to 0.97 and 0.74 to 0.96, respectively. The performance of the software tools was tested on various datasets, and therefore a direct comparison is not possible. However, with regard to this limitation, the available data suggest that Stroke *SENS* with its sensitivity and specificity

Table 3 The summary of available automatic software tools for LVO detection

Software	Number of cases (LVO/all)	Detected occlusion site	Sensitivity	Specificity	AUC	False negative	False positive	Processing time, seconds
Stroke*SENS*	217/400	ICA & M1 MCA	0.894	0.874	0.939	23 (6 ICA occlusions with normally opacified terminal ICA segment; 6 short-segment occlusions; 4 distal M1 MCA occlusion with prominent ATA; 3 good collaterals and arterio-venous phase; 1 non-occlusive thrombus; 1 poor contrast filling)	23 (6 axial scan asymmetry; 4 M2 occlusions; 3 MCA stenosis; 3 beam hardening artifact; 1 MCA aneurysm; 5 unclear reason)	44.5 (mean)
Viz LVO (Viz.ai) [24]	163/2544	Not specified	0.963	0.938				345 (median)
Viz LVO (Viz.ai) [22]	75/1167	ICA & M1 MCA	0.81	0.96	0.91	14	56 (12 M2 and M3 MCA occlusions; 12 hemorrhage; 9 > 50% MCA stenosis; 4 scans with tumor; 19 no pathology)	
Viz LVO (Viz.ai) [22] *Stroke protocol*	72/404	ICA & M1 MCA	0.82	0.90		13	-	
RAPID CTA [25] (iSchema-View)	320/926	ICA & M1 MCA	0.969	0.743	0.941	9 (3 short-segment occlusions; 5 robust collaterals; 1 ICA at skull base)	11 (4 variant MCA anatomy; 1 subdural hematoma with severe midline shift; 1 MCA aneurysm;3 M2 MCA stenosis; 1 incomplete TICI 2b reperfusion after MT	158 (median)
e-CTA (Brainomix) [26]	(160/301)	ICA & M1 MCA,	0.92	0.98		26		
Stroke Solution LVO (Canon) [27]	202/303	ICA / M1 MCA	0.90/0.77	0.98/0.98		55	2	71.5 (for LVO cohort)
StrokeViewer (NICO.LAB) [28] *MR CLEAN Registry*	952 [a]	ICA / M1 MCA	0.88/0.94			65 (8 ICA occlusions; 13 M1 occlusions; 44 incorrect location marked)	0	299 (mean)
StrokeViewer (NICO.LAB) [28] *PRESTO*	76/581[a]	ICA/M1 MCA	0.80/0.95	-	-	6 (2 ICA occlusions; 4 incorrect location marked)	55 (24 no occlusion; 2 extracranial ICA, 29 unknown data	

[a]Data from the sensitivity analysis with excluded M2 MCA occlusions

[b]Mean processing time for the pooled dataset of patients from MR CLEAN Registry and PRESTO study

Note: ATA, anterior temporal artery; AUC, area under the curve; CI, confidence interval; ICA, internal carotid artery; LVO, large vessel occlusion: MCA, middle cerebral artery; MT, mechanical thrombectomy; NPV, negative predictive value; PPV, positive predictive value

of 0.89 and 0.87, respectively, is likely comparable to the currently available tools.

The retrospective review of false-negative cases revealed imaging characteristics that the algorithm did not overcome such as normally opacified terminal ICA segment in the presence of more proximally located ICA occlusion or presence of short-segment occlusion and good collaterals. The same reasons for the false-negative finding were mentioned by the authors of the RAPID CTA validation study [25]. This suggests that an early opacification of the vasculature beyond the occlusion through collateral flow remains a challenge for automatic software. Similar to the previously reported reasons for false-positive findings in literature [22, 25], intracranial MCA stenosis or the presence of an MCA aneurysm led to falsely positive results also in our dataset. However, the most common reason identified in this study that likely led to false-positive results was an asymmetric projection of the circle of Willis on the axial scan caused by lateral tilt. This is important information that could be incorporated into the further development of the software tool. In three cases, M2 occlusions were identified as LVO and marked as false-positive result while the validated software version was primarily developed to identify ICA and M1 MCA occlusions.

Automated software systems utilizing AI for detection of stroke signs can potentially accelerate the triage, diagnosis, and treatment initiation of stroke patients significantly [29]. Current methods of notifying the treating physician result in delays in treatment that negatively impact patient outcomes [30]. A recent study showed that utilizing an automated LVO detection software together with a notification system resulted in an average reduction of 22.5 min in triage and transfer times between the spoke primary stroke center and the hub comprehensive stroke center [31]. While CTA is often the only advanced imaging modality in primary centers, a tool for automated LVO detection and notification that would streamline the clinical workflow can aid in accurate and timely patient selection for rapid EVT at spoke hospitals. The Stroke*SENS* LVO showed excellent performance in speed of potential notification with a mean processing/notification time of 44.5 s in this study. Although a short processing time is a promising feature, the time for data transfer from the CT machine to the processing computer needs to be evaluated in the real world.

This study has some limitations. First, the current version of the software has been developed to identify only LVOs in the anterior circulation, and its primary evaluation was therefore focused only on detection of such LVOs. With increasing evidence of endovascular treatment benefit in more distally located occlusions and occlusions in the posterior territory, further software development is warranted to reliably identify such intracranial occlusions. Second, the software performance was evaluated in a retrospective fashion on data from clinical studies that may have excluded patients with stroke mimics and other non-stroke pathologies that are detected routinely in real-life practice. Our study dataset consisted of an artificially high LVO prevalence (54%) as we optimized the model with as many LVO cases as possible while matching those with an equal number of examples of other/no occlusion findings. The real-world LVO prevalence is approximately 15–30%; therefore, the evaluation of the software performance in real-world data is warranted. The Stroke*SENS* LVO's performance in LVO detection and potential speed of notification in this validation dataset will need to be supported by tests in real-life conditions done in a prospective manner. Such studies are planned. Finally, the impact of tools such as Stroke*SENS* will need to be compared with the current standard workflow in a randomized manner for us to understand the true benefit of such tools on the population of acute stroke patients.

Conclusion

Automated LVO detection and notification can aid in acute stroke management by quickly and accurately detecting patients with anterior LVO who may likely require immediate medical attention and benefit from EVT[19]. However, a further development including the full range of clinically relevant intracranial occlusions is as well as prospective studies exploring the impact of the software tools on acute stroke workflow and patient outcomes is warranted.

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Data availability Data generated or analyzed during the study are available from the corresponding author by request.

Declarations

Competing interests The author declares a conflict of interest.

Financial interests RG, AS, CD, IE, HE, SHM, and LASMN are employees of the Circle Neurovascular Imaging Inc. NK and MJ are consultants for the Circle Neurovascular Imaging Inc. BKM owns shares in the Circle Neurovascular Imaging Inc. and patent for systems of triage in acute stroke. JMO is a consultant for NICO.LAB and GE Healthcare.

Nonfinancial interests BKM is a member of the editorial board at stroke (assistant editor). JMO is a member of the editorial board at frontiers in neurology (guest associate editor).

Ethics approval Approval by the local Research Ethics Board was obtained.

Consent to participate Informed consent was obtained from all individual participants included in the clinical studies.

Consent for publication All individual participants have consented to publish data from the study by their agreement to participate in the clinical studies.

References

1. Duloquin G, Graber M, Garnier L et al (2020) Incidence of acute ischemic stroke with visible arterial occlusion. Stroke 51:2122–2130. https://doi.org/10.1161/STROKEAHA.120.029949
2. Malhotra K, Gornbein J, Saver JL (2017) Ischemic strokes due to large-vessel occlusions contribute disproportionately to stroke-related dependence and death: a review. Front Neurol. https://doi.org/10.3389/fneur.2017.00651
3. Goyal M, Menon BK, Van Zwam WH et al (2016) Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 387:1723–1731. https://doi.org/10.1016/S0140-6736(16)00163-X
4. Powers WJ, Rabinstein AA, Ackerson T et al (2019) Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 50:E344–E418. https://doi.org/10.1161/STR.0000000000000211
5. Demchuk AM, Menon BK, Goyal M (2016) Comparing vessel imaging: Noncontrast computed tomography/computed tomographic angiography should be the new minimum standard in acute disabling stroke. Stroke 47:273–281. https://doi.org/10.1161/STROKEAHA.115.009171
6. Menon BK (2020) Neuroimaging in Acute Stroke. Contin Lifelong Learn Neurol 26:287–309. https://doi.org/10.1212/CON.0000000000000839
7. Almekhlafi MA, Kunz WG, Menon BK et al (2019) Imaging of patients with suspected large-vessel occlusion at primary stroke centers: available modalities and a suggested approach. Am J Neuroradiol 40:396–400. https://doi.org/10.3174/ajnr.A5971
8. Saver JL (2006) Time is brain—quantified. Stroke 37:263–266. https://doi.org/10.1161/01.STR.0000196957.55928.ab
9. Menon BK, Al-Ajlan FS, Najm M et al (2018) Association of clinical, imaging, and thrombus characteristics with recanalization of visible intracranial occlusion in patients with acute ischemic stroke. JAMA - J Am Med Assoc 320:1017–1026. https://doi.org/10.1001/jama.2018.12498
10. Menon BK, d'Esterre CD, Qazi EM, Almekhlafi M, Hahn L, Demchuk AM, Goyal M (2015) Multiphase CT angiography: a new tool for the imaging triage of patients with acute ischemic stroke. Radiology 275:510–520. https://doi.org/10.1148/radiol.15142256
11. Goyal M, Demchuk AM, Menon BK et al (2015) Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372:1–12. https://doi.org/10.1056/NEJMoa1414905
12. O'Shea K, Nash R (2015) An Introduction to Convolutional Neural Networks. ArXiv, abs/1511.08458. http://arxiv.org/abs/1511.08458
13. Agarap AF (2018) Deep Learning using Rectified Linear Units (ReLU). https://doi.org/10.48550/arxiv.1803.08375
14. Ioffe S, Szegedy C (2015) Batch normalization: accelerating deep network training by reducing internal covariate shift. 32nd Int Conf Mach Learn ICML 2015 1:448–456
15. Kingma DP, Ba JL (2015) Adam: a method for stochastic optimization. 3rd Int. Conf. Learn. Represent. ICLR 2015 - Conf. Track Proc
16. Hill MD, Goyal M, Menon BK et al (2020) Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1): a multicentre, double-blind, randomised controlled trial. Lancet 395:878–887. https://doi.org/10.1016/S0140-6736(20)30258-0
17. Ginsberg MD, Palesch YY, Hill MD, Martin RH, Moy CS, Barsan WG, Waldman BD, Tamariz D, Ryckborst KJ (2013) High-dose albumin treatment for acute ischaemic stroke (ALIAS) part 2: a randomised, double-blind, phase 3, placebo-controlled trial. Lancet Neurol 12:1049–1058. https://doi.org/10.1016/S1474-4422(13)70223-0
18. Coutts SB, Dubuc V, Mandzia J et al (2015) Tenecteplase-tissue-type plasminogen activator evaluation for minor ischemic stroke with proven occlusion. Stroke 46:769–774. https://doi.org/10.1161/STROKEAHA.114.008504
19. Demchuk AM, Dowlatshahi D, Rodriguez-Luna D et al (2012) Prediction of haematoma growth and outcome in patients with intracerebral haemorrhage using the CT-angiography spot sign (PREDICT): a prospective observational study. Lancet Neurol 11:307–314. https://doi.org/10.1016/S1474-4422(12)70038-8
20. Mongan J, Moy L, Kahn CE (2020) Checklist for artificial intelligence in medical imaging (CLAIM): a guide for authors and reviewers. Radiol Artif Intell 2:e200029. https://doi.org/10.1148/ryai.2020200029
21. Walach E (2019) Lies, damned lies and AI statistics. MedCity News. https://medcitynews.com/2019/08/lies-damned-lies-and-ai-statistics/. Accessed 6 May 2022
22. Dovrat AY, Saban M, Merhav G, Lankri I, Abergel E, Eran A, Tanne D, Nogueira RG, Hoffmann RS (2021) Evaluation of artificial intelligence-powered identification of large-vessel occlusions in a comprehensive stroke center. Am J Neuroradiol 42:247–254. https://doi.org/10.3174/ajnr.A6923
23. Murray NM, Unberath M, Hager GD, Hui FK (2020) Artificial intelligence to diagnose ischemic stroke and identify large vessel occlusions: a systematic review. J Neurointerv Surg 12:156–164. https://doi.org/10.1136/neurintsurg-2019-015135
24. Shalitin O, Sudry N, Mates J, Golan D (2020) AI-powered stroke triage system performance in the wild. JESTM 12:1–04
25. Amukotuwa SA, Straka M, Dehkharghani S, Bammer R (2019) Fast automatic detection of large vessel occlusions on CT angiography. Stroke 50:3431–3438. https://doi.org/10.1161/STROKEAHA.119.027076
26. Seker F, Pfaff JAR, Mokli Y, Berberich A, Namias R, Gerry S, Nagel S, Bendszus M, Herweh C (2021) Diagnostic accuracy of automated occlusion detection in CT angiography using e-CTA. Int J Stroke. https://doi.org/10.1177/1747493021992592
27. Rava RA, Peterson BA, Seymour SE et al (2021) Validation of an artificial intelligence-driven large vessel occlusion detection algorithm for acute ischemic stroke patients. Neuroradiol J. https://doi.org/10.1177/1971400921998952
28. Luijten SPR, Wolff L, Duvekot MHC et al (2021) Diagnostic performance of an algorithm for automated large vessel occlusion detection on CT angiography. J Neurointerv Surg 0:neurintsurg-2021–017842. https://doi.org/10.1136/neurintsurg-2021-017842

29. Amukotuwa SA, Straka M, Smith H, Chandra RV, Dehkharghani S, Fischbein NJ, Bammer R (2019) Automated detection of intracranial large vessel occlusions on computed tomography angiography a single center experience. Stroke 50:2790–2798. https://doi.org/10.1161/STROKEAHA.119.026259
30. Froehler MT, Saver JL, Zaidat OO et al (2017) Interhospital transfer before thrombectomy is associated with delayed treatment and worse outcome in the STRATIS registry (systematic evaluation of patients treated with neurothrombectomy devices for acute ischemic stroke). Circulation 136:2311–2321. https://doi.org/10.1161/CIRCULATIONAHA.117.028920
31. Hassan AE, Ringheanu VM, Rabah RR, Preston L, Tekle WG, Qureshi AI (2020) Early experience utilizing artificial intelligence shows significant reduction in transfer times and length of stay in a hub and spoke model. Interv Neuroradiol 26:615–622. https://doi.org/10.1177/1591019920953055

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