NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Software with artificial intelligence derived algorithms for analysing CT brain scans in people with a suspected acute stroke

Final scope

July 2021

1 Introduction

The topic selection oversight panel identified software with artificial intelligence derived algorithms for analysing CT brain scans as potentially suitable for evaluation by the Diagnostics Assessment Programme based on a briefing that was published as a NICE medtech innovation briefing. The artificial intelligence neuroimaging software platforms described in the briefing have algorithms that can process brain scan images for several indications including dementia, traumatic brain injury or stroke. However, the main use presented in the briefing appears to be most developed in stroke, so the scope of this assessment will focus on the use of artificial intelligence for processing CT brain scans in people suspected to have a stroke. All of the software identified for this assessment uses fixed (or static) algorithms in clinical practice and they do not replace the role of a healthcare professional in reporting brain images. Artificial intelligence is used only to derive each version of the fixed algorithm.

The final scope was informed by discussions at the scoping workshop held on 26th May 2021 and the assessment subgroup meeting held on 9th June 2021.

A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technologies

This section describes the properties of the diagnostic technologies based on information provided by companies to NICE and information available in the public domain. NICE has not carried out an independent evaluation of these descriptions.

2.1 Purpose of the medical technology

Software with artificial intelligence (AI) derived algorithms can be used to analyse computed tomography (CT) images of the brain to detect and report irregularities associated with conditions such as stroke. The result of this analysis is not intended for making or confirming diagnosis, but to support brain scan review and reporting by a trained healthcare professional. A clinician uses this report alongside other patient information to make a treatment decision. The software may speed up the review of CT scans for suspected stroke by identifying, quantifying, and notifying about clinically relevant brain structures related to acute stroke. Some software has features that can prioritise the review of stroke CT scans on the radiology workflow.

The software solutions are typically designed to be incorporated into standard radiology CT workstations. This means they can work with existing forms of brain imaging (including non-contrast CT [non-enhanced], CT angiography [CTA] and CT perfusion [CTP] imaging), radiology information systems (RIS) and picture archiving and communication systems (PACS). They are typically hosted on a web cloud which is separate from image exchange portals used to transfer images between care providers.

Stroke-related changes in the brain highlighted by the AI-derived algorithms, may assist in confirming a stroke and support clinical decisions about suitability of an appropriate 'time-sensitive' treatment such as thrombolysis and thrombectomy. The use of the software in the radiology workflow may lead to improved report turnaround time (that is, time between the CT scan and report), quicker review of scans by a multi-site clinical team, improved decisions about treatment, expedited patient transfer, reduced time to treatment and improved patient outcomes. In addition, the software may be beneficial in spotting unsuspected findings related to a stroke, for example, in people presenting with non-stroke-like symptoms. The benefits of the software are likely to be different depending on which scan is being reported (non-enhanced, CTA or CTP), and whether a neuroradiologist is available (or needed) to report the scan, or not.

2.2 Product properties

Several companies offer software with artificial intelligence derived algorithms for analysing CT brain scans in people with a suspected acute stroke. Some companies offer software that can be used to analyse non-enhanced, CTA and CTP scans (or have agreements between companies to offer their algorithms as a package), whereas others have software that can only analyse one of these types of scans. Some software packages do not have a dedicated platform through which they are delivered but may be housed on

multivendor platforms for example Blackford analysis. Each of the technologies identified is described in the following sections. Where less detail is given this is because only information available in the public domain was able to be used.

Table 1. Summary of types of CT scans analysed by AI platforms included in this assessment.

Platform	Available to the NHS	Type of CT scan analysed		
		Non-enhanced CT	CTA	CTP
icobrain ct	✓			✓
Aidoc	✓	✓	✓	
Aidoc + icobrain	NYD	✓	✓	✓
RapidAI	✓	✓*	✓	✓
e-stroke	✓	✓*	✓	✓
Viz	✓	✓	✓	✓
qER**	NYD	✓		
Zebra-Med	TBC	✓		
CT Perfusion 4D	TBC			✓
Brainscan	TBC	✓		
Cercare stroke**	NYD			✓
Cina head**	✓	✓*	✓	
Accipio**	✓	✓	✓	
Biomind	TBC	✓		

CT- computed tomography, CTA- CT angiography, CTP- CT perfusion *Gives ASPECTS score by assessing non-enhanced CT, NYD- Not yet deployed, **Provided through a multivendor platform, Blackford analysis.

Clinical experts highlighted potential difficulties in using software from different vendors. This included the need to ensure that such programs could operate without disrupting workflow.

The Royal College of Radiologists released a position statement and published a guidance on Integrating artificial intelligence with the radiology reporting workflows (RIS and PACS) which specifies the standards that a radiology department should meet for the integration of AI into its established systems. The guidance notes that “artificial intelligence must be integrated in reporting (radiology information system and picture archiving and communication system) workflows seamlessly and in a way that does not add

extra burden to radiologists. It further states that the accuracy of the AI algorithms must be clearly declared for radiologists and others making decisions on patient management." In addition, it notes that currently worklists are prioritised based on referral location, type of scan required, speciality of referrer and referrer's urgency and that AI abnormalities and alerts should be added to data fields for worklist prioritisation.

2.2.1 icobrain ct

icobrain ct (Icometrix) is a CE marked (class 1 medical device) neuroimaging platform which uses static AI algorithms to detect abnormalities in brain CT scans in clinical practice. icobrain ct can generate an output report related to stroke diagnosis:

- Report 1, from icobrain ctp (ct perfusion), details a quantitative assessment of perfusion in the brain based on a CT scan done with contrast. It analyses the flow of blood in areas of the brain to determine the presence of potentially salvageable tissues in ischaemic stroke. The analysis includes a calculation of abnormality in parameters such as mean transit time (MTT), cerebral blood flow (CBF), cerebral blood volume (CBV) and time to maximum (Tmax) of residue function.

- Report 2, from icobrain tbi (traumatic brain injury): The company states that this algorithm can give a quantitative assessment of intracranial haemorrhage (ICH) based on a non-enhanced CT scan. However, icobrain tbi has been validated only in people with traumatic brain injury. Some of the non-contrast CT parameters measured include midline shift and asymmetry index between the left and right lateral ventricle.

The company notes that its AI neuroimaging platform integrates with existing RIS and PACS. The software is intended for automatic labelling, visualization and volumetric quantification of segmentable brain structures from a set of CT images. It receives digital images as input and generates an electronic report on quantitative parameters and annotated images. Results can be viewed as visual reports through DICOM (digital imaging and communication in medicine) output images, email notifications and on a web browser. The report highlights stroke-related changes that guide clinician diagnosis. Data transfer from and into the PACS is done securely over a software icobridge, installed on site. Icobrain ct has had 2 major releases, versions 4.0 and 5.0. The company notes that performance of icobrain in detecting ICH and for CT perfusion analysis has been tested on a series of scenarios that cover specific aspects of the software performance. Icobrain ct algorithms send and receive

information over a secure cloud ‘icometrix’. icometrix is ISO13485 and ISO27001 certified and GDPR and HIPAA compliant for privacy and security.

The company provides a training manual for health professionals which gives guidance on how to use the software and interpret reports. Customer support is also available from the company. Prior to deployment in clinical practice the company carries out a clinical and technical test phase. Icobrain ct is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.2 Aidoc ICH, Aidoc LVO, Aidoc mobile

The Aidoc software (also called “BriefCase” [Aidoc]) is a CE marked (class 1 medical device) AI triage and notification platform. This neuroimaging platform uses static AI algorithms to detect abnormalities in brain CT scans in clinical practice. Algorithms related to stroke diagnosis include:

- Aidoc ICH for detecting suspected intracranial haemorrhage on non-contrast head CT
- Aidoc LVO for detecting suspected large vessel occlusions (LVO) on CT angiography

The third component of the platform relevant to stroke diagnosis is Aidoc mobile, which is for communication between clinical stakeholders in the stroke pathway to facilitate peer review.

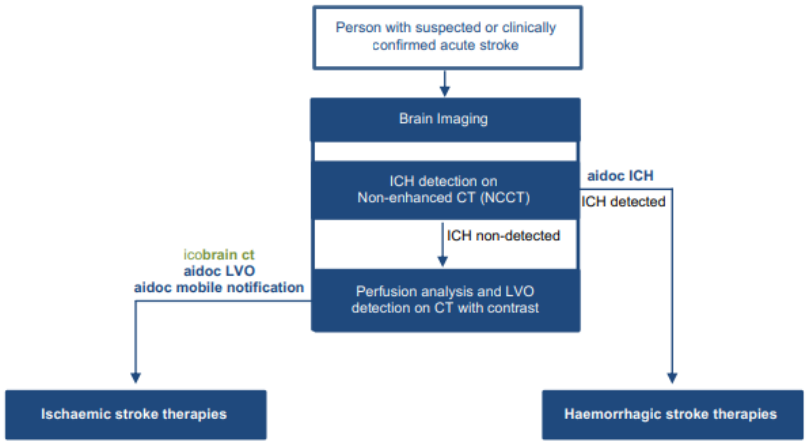
The company notes that its software can integrate with existing radiology workstation including PACS, reporting system and radiology workflow solutions. The platform can prioritise worklist, triage, and generate notification on suspected stroke cases. Analysis done by the AI software is intended to supplement CT scan review by a neuroradiologist or stroke specialist.

The company provides an initial product training which lasts around 30 minutes and where necessary additional training on specific workflows can be provided. A recurring annual training is also available to review new features, enhancements, and algorithms. Prior to deployment of the software on a site, the company through its AI operations centre carries out an automated performance assessment. Aidoc is ISO13485 and ISO27001 certified. The Aidoc software is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.3 Icometrix and Aidoc 'comprehensive stroke solution'

Aidoc and icometrix have partnered to provide a stroke solution in which the Aidoc software detects intracranial haemorrhage and large vessel occlusion in ischaemic stroke while the icobrain software is used for CT perfusion analysis in ischaemic stroke. Figure 1 shows how the technologies are intended to be implemented in clinical practice.

Figure 1 Icometrix and Aidoc 'comprehensive stroke solution' pathway



2.2.4 Rapid ASPECTS, Rapid ICH, Rapid CTA, Rapid LVO, Rapid CTP

RapidAI (Ischemaview) is a CE marked (class 2a medical device) neuroimaging platform which uses static AI algorithms for detecting abnormalities in brain CT scans in clinical practice. The CT algorithms relevant to stroke diagnosis are:

- Rapid ICH is an image processing software that analyses non-enhanced CT head scans to detect, and flag suspected intracranial haemorrhage. Cases with suspected findings can be notified through email and the mobile application. The notification includes compressed images that are for information purposes only and not intended to be diagnostic. The notified clinician is responsible for viewing non-compressed images on a diagnostic viewer and carrying out necessary patient evaluation.

- Rapid CTA is an image processing software that analyses head CT angiograms scans to provide neurologic vasculature maps with indications of hemispheric differences in the intracranial ICA/MCA (internal carotid artery/ middle cerebral artery) region which may indicate a large vessel occlusion.

- Rapid LVO is an image processing software that analyses head CT angiograms scans to highlight and notify cases with suspected large vessel occlusion

- Rapid CTP enables the assessment of salvageable brain tissue through the delivery of quantified and colour-coded CT perfusion maps that identify brain regions with reduced cerebral blood flow, volume, and transit time that exceed pre-specified thresholds. Imaging datasets acquired from CT or Cone Beam Computed Tomography (CBCT) or MR Perfusion and Mismatch, MR Diffusion, and CT/MR Angiography are anlysed to measure parameters that determine suitability for thrombectomy.

- RAPID ASPECTS is not intended for the primary interpretation of CT images. It assists the clinician in evaluating patients presenting for diagnostic imaging with known MCA or ICA occlusion, to assess the extent of disease on non-contrast CT scans. Extent of disease refers to the number of ASPECTS (Alberta Stroke Program Early CT Score) regions affected. Image data and AI analysis of morphological features is used to generate a single ASPECT score. This score is useful in characterizing early signs of brain ischaemia, areas of irreversible tissue injury and to help the clinician assess patient eligibility for thrombectomy or thrombolysis.

The RapidAI platform runs on a standard computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis. The software receives DICOM compliant images as input primarily CT, CTA, CBCT and Magnetic Resonance (MR). Results from on Rapid platform can be viewed as visual reports through PACS, email notifications and the Rapid mobile app. Notifications have a sound option for positive cases and can be set to user defined thresholds to enable prioritisation. Results from multiple sites can be viewed and organised in one location. RapidAI is ISO certified and complies with GDPR and data security requirements.

The company provides training which includes online role-based product training, virtual instructor-led sessions led by clinical experts and performance support content.

2.2.5 e-ASPECTS, e-CTP, e-CTA

The e-Stroke platform (Brainomix) is a CE marked (class 2a medical device) neuroimaging platform that utilises AI for detecting anomalies in brain CT

scans. The platform includes the following algorithms relevant to stroke diagnosis:

- e-ASPECTS which analyses non-contrast CT scans for clot detection, signs of hypodensity and generates a heat map of regional ischaemic change, volume of the change, and an automatic ASPECTS score.

- e-CTP which analyses CT perfusion scans to generate perfusion summary maps, report parameters such as mismatch volume and ratio, hypoperfusion intensity ratio, and assesses eligibility for mechanical thrombectomy.

- e-CTA which analyses CT angiogram scans to detect the location of large vessel occlusions and to generate a CT collateral score which is used to assesses eligibility for mechanical thrombectomy.

The software integrates with current imaging systems and results can be viewed as visual reports through DICOM output images, email notifications and a web browser.

2.2.6 Viz

The Viz platform (Viz.ai) is a CE marked (class 1 medical device) software which uses static AI algorithms to detect abnormalities in brain scans in clinical practice. The algorithms relevant to stroke detection include:

- Viz LVO which analyses CT angiogram images of the brain and sends notification to the clinician if a suspected large vessel occlusion has been detected. Notifications include compressed images that can be previewed for information purposes only. They are not intended to be diagnostic. The notified clinician is responsible for viewing non-compressed images on a diagnostic viewer and carrying out necessary patient evaluation.

- Viz ICH which analyses non-contrast CT images of the brain and sends notification to the clinician if a suspected intracranial haemorrhage has been detected.

- Viz CTP has communication and analysis capabilities for CT perfusion scans. The analysis includes the calculation of parameters related to tissue perfusion and tissue blood volume.

The company notes that the Viz platform integrates with currently available CT scanners and is designed to receive DICOM images which can be transferred securely to Viz.ai's GDPR-compliant Amazon Web Services cloud. Within the cloud, Viz.ai will analyse the imaging data for specific

neurovascular disease. The platform can be used by hospital networks and trained clinicians.

The Viz platform is GDPR/HIPAA compliant and has ISO and SOC-2 certifications. Viz is currently a self-certified class 1 medical device under the Medical Device Directive, the company notes that it will be up classified to a class 2a medical device under the Medical Device Regulation, in line with the transition from the Medical Device Directive to the Medical Device Regulation.

2.2.7 qER

qER (Qure.ai) is a CE marked (class unknown) triage and notification tool that detects and quantifies a range of brain abnormalities intracerebral bleeds and their subtypes, infarcts, mass effect, midline shift and cranial fractures following non-contrast CT imaging. The software populates a radiology reporting template with preliminary findings, patient prioritisation and alert systems including mobile notifications. It integrates with current imaging systems.

2.2.8 CINA head

CINA head (Avicenna) uses CE marked (class 1 medical device) artificial intelligence software for detecting abnormalities in brain CT scans. The algorithms in CINA head include:

- CINA-ICH which identifies suspected intracranial haemorrhage on non-contrast CT scans and prioritises them on the radiologist's worklist
- CINA LVO detects and prioritises the review of suspected large vessel occlusions on CT angiography.
- CINA ASPECTS analyses non-contrast CT and creates heat maps that indicate signs of hypodensity which help characterise early ischaemic brain tissue injury

2.2.9 ACCIPIO

Accipio suite (MaxQ AI) is a CE marked (class 2a medical device) AI-derived software that can identify, analyse, prioritise, annotate and triage both positive and negative findings of suspected intracranial haemorrhage on non-contrast CT scans and large vessel occlusions on contrast CT scans.

2.2.10 Zebra triage

Zebra-Med (Zebra Medical Vision) is a CE marked (class 1 medical device) software that detects and annotates intracranial haemorrhage after non-contrast CT imaging and automates patient prioritisation and a real-time alert system. It integrates with the current imaging worklist and viewer with an accompanying alert widget.

2.2.11 CT Perfusion 4D Neuro

CT Perfusion 4D (GE Healthcare) is a CE marked (class unknown) medical device for CT perfusion image analysis of images obtained by cine imaging (in the head and body) after the intravenous injection of contrast. It produces image data and generates information regarding changes in image intensity over time and in calculation of the various perfusion-related parameters (including regional blood flow, regional blood volume, mean transit time and capillary permeability).

2.2.12 Brainscan

The Brainscan system is a CE marked (class 2a medical device) AI platform that enables automatic detection and classification of pathological changes occurring in CT examinations of the brain.

2.2.13 Cercare stroke

Cercare stroke (Cercare Medical) is a CE marked (class not available publicly) AI enabled stroke CT and MRI imaging software. The technology uses inputs from perfusion maps and additional maps of oxygen extraction and metabolism to provide an overview of brain tissues status in stroke.

2.2.14 Biomind

Biomind (Biomind.ai) is a CE marked (class not available publicly) AI derived software used for detecting the location of intracerebral haemorrhage on CT scans and assessing its severity.

3 Target condition

A stroke is a serious life-threatening medical condition that occurs when blood supply to a part of the brain is severely compromised. When blood flow to a part of the brain is stopped or restricted, the flow of oxygen and nutrients needed by the brain is impeded, leading to the death of brain cells. A stroke often occurs without any warning and the symptoms a person experiences depends on the part of the brain that is affected. Common symptoms include a drooping of one side of the face, problems speaking, problems with vision, loss of sensation in an arm or leg, slurred or garbled speech.

There are 2 main types of stroke:

- Ischaemic stroke – This happens when blood vessels are blocked by a clot or become too narrow for blood to pass through.
- Haemorrhagic stroke – This happens when a weakened blood vessel bursts and blood leaks into soft brain tissues.

A stroke can occur at any age, but the incidence increases with age. Approximately 57,000 people in England experienced stroke for the first time in 2016 (First incidence of stroke. Estimates for England 2007 to 2016). It is estimated that more than 100,000 strokes occur in the UK every year, causing around 38,000 deaths (NICE impact stroke). Stroke is the third most common cause of premature death and a leading cause of disability in the UK.

The specific treatment for stroke depends on the cause and severity of the condition. Stroke can cause long-term disability. The sooner the stroke is treated, the less severe the clinical outcomes.

3.1 Ischaemic stroke

Ischaemic stroke is the most common type of stroke, accounting for 85% of all stroke cases. It is caused when blood clot forms in areas where arteries have been narrowed or blocked because of the build-up of fatty deposits overtime. This results in a loss of neurological function leading to numbness of the face, arm or leg on one side of the body. Other factors that may cause narrowing of the arteries include smoking, high blood pressure, obesity, high levels of cholesterol, diabetes and excessive alcohol intake. Irregular heartbeat known as atrial fibrillation can cause ischaemic stroke because they can cause blood clots in the heart to break up, escape from the heart and become lodged in the blood vessels supplying the brain.

3.2 Haemorrhagic stroke

Haemorrhagic stroke is less common than ischaemic stroke. It occurs when a weakened blood vessel in the skull ruptures and bleeds into the brain. A haemorrhagic stroke is mainly caused by high blood pressure which can weaken arteries in the brain. Another common cause of haemorrhagic stroke is the rupture or leak of a brain aneurysm (a balloon like expansion of a blood vessel in the brain) and poorly formed blood vessels in the brain.

4 Diagnostic and care pathway

4.1 Stroke care services

The NHS Long Term Plan, identifies stroke as a clinical priority, section 3.78 of the plan, sets out the NHS's ambition to support the national scaling of technology that will assist the expansion of life-changing treatments to more patients, which includes CT perfusion scans to assess the reversibility of brain damage, improved access to MRI scanning and the potential use of artificial intelligence in the interpretation of CT and MRI scans to support clinical decisions regarding suitability for thrombolysis and thrombectomy.

According to the National Stroke Service Model: Integrated Stroke delivery Networks guidance which outlines best practices for stroke care, people with a suspected stroke should typically receive care within 4 hours in a hospital with a:

- Comprehensive stroke centre that provides hyper-acute, acute and inpatient rehabilitation including thrombectomy and neurosurgery services or in an

- Acute stroke centre which provides hyper-acute, acute and inpatient rehabilitation, but *excluding thrombectomy and neurosurgery*. All acute stroke centres are expected to have an intra hospital thrombectomy transfer pathway to transfer patients from acute stroke centres to comprehensive stroke centres.

Hyper-acute stroke care usually covers the first 72 hours after a person is admitted. Services provided in the hyperacute phase include specialist clinical assessment, urgent imaging and skilled clinical interpretation of images, delivery of intravenous thrombolysis 24 hours a day, 7 days a week and transfer or treatment for thrombectomy. Imaging ensures that appropriate diagnosis is made, and time-dependent interventions are delivered. The guidance describes an optimal stroke imaging pathway (see section 4.3 for further details) and encourages the use of artificial intelligence at specified points along the pathway.

4.2 Initial assessment

The NICE guideline on stroke and transient ischaemic attack in over 16s: diagnosis and initial management recommends that people with sudden onset of neurological symptoms outside hospital should be screened using a validated tool such as FAST (Face Arm Speech Test). On admission to emergency department with a suspected stroke, a validated tool ROSIER

(Recognition of Stroke in the Emergency Room) is used to establish diagnosis before referral to a specialist stroke unit.

Clinical experts noted that initial stroke assessment (using FAST) is done by paramedics who pick up a patient in an ambulance and pre-alert the stroke team in a hospital with an acute or comprehensive stroke centre. On arrival the patient follows the stroke pathway where the stroke team (usually a stroke specialist) carries out an assessment of signs, symptoms, blood tests and clinical history to confirm suspicion of stroke. A CT scan is booked by the stroke team. Some patients may self-present to the emergency department, or have had a negative FAST result from the paramedic assessment, in which case, the emergency department clinician does a clinical assessment, organises a scan and then refers the patient to the stroke unit, if appropriate.

4.3 Brain imaging

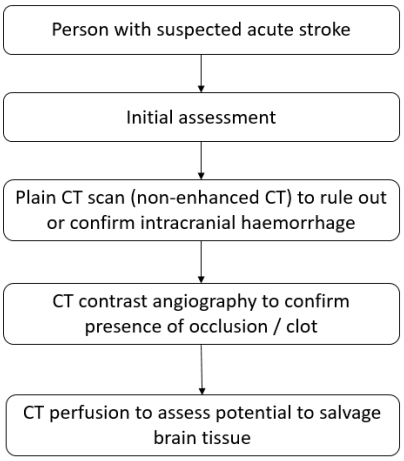
The NICE guideline on stroke and transient ischaemic attack in over 16s: diagnosis and initial management recommends brain imaging with non-enhanced CT immediately if any of the following apply:

- indications for thrombolysis or thrombectomy
- on anticoagulant treatment
- a known bleeding tendency
- a depressed level of consciousness (Glasgow Coma Score below 13)
- unexplained progressive or fluctuating symptoms
- papilloedema, neck stiffness or fever
- severe headache at onset of stroke symptoms.

The guideline also recommends that if thrombectomy might be indicated, imaging with CT contrast angiography should be performed following initial non-enhanced CT. Add CT perfusion imaging (or MR equivalent) if thrombectomy might be indicated beyond 6 hours of symptom onset. Scanning is recommended within 24 hours of symptoms onset in everyone with suspected acute stroke without indications for immediate brain imaging.

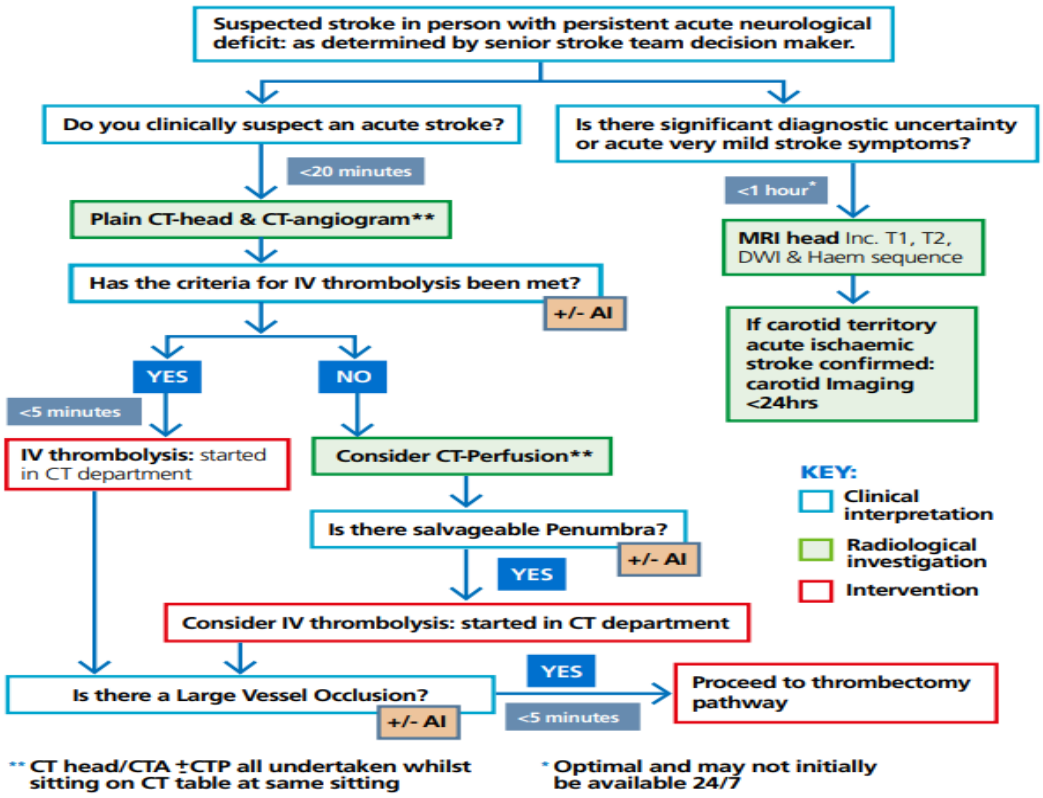
Expert advice during scoping indicated that practice has changed since the guideline was published and the National Stroke Service Model guidance (see below) recommends that stroke imaging, interpretation and transfer decisions are made within 20 minutes of patient's arrival.

Figure 2 – summary of CT imaging pathway



The National Stroke Service Model: Integrated Stroke delivery Networks guidance describes an optimal stroke imaging pathway with recommended time standards and points in the pathway where AI could play a role, see figure 3.

Figure 3 - National optimal stroke pathway



Source: The National Stroke Service Model: Integrated Stroke delivery Networks

During scoping clinical experts noted that suspected stroke cases are always prioritised for CT scan. The time from completing an examination to reviewing the CT images and sending the report to a clinician for intervention varies across hospitals but is generally under 1 hour. In some hospitals, a non-enhanced CT scan is used to confirm a stroke, detect intracranial bleeding and to rule out stroke mimics, for example, a brain tumour. Subsequently, results of the none-enhanced CT scan are used to determine if CT angiography or CT perfusion should be done (figure 2). In other hospitals everyone with a suspected acute stroke referred for a CT brain scan has a plain CT, CT angiography and CT perfusion done.

Image interpretation for confirmed diagnosis of a suspected stroke is typically done by a neuroradiologist or an interventional neuroradiologist, especially where mechanical thrombectomy is being considered. Depending on the organisation of stroke care in some hospitals, other clinical experts including a radiologist, a diagnostic radiologist, a reporting radiographer or a stroke physician may interpret images for stroke diagnosis. Clinical experts noted that in some instances, during the radiologist's out of office hours CT scan reporting may be outsourced to commercial teleradiology and report from a remote radiologist obtained within 1 hour. Some hospitals have an on-call rota using their own radiologists.

In a radiology setting where AI-augmented analysis has been implemented, when CT imaging is done, DICOM images from the scan are sent to the AI software for pre-analysis before display on PACS for review. In settings without AI capability or at times when the AI software is not working, DICOM images are sent directly to PACS.

4.4 Reperfusion treatment

4.4.1 Thrombolysis

Thrombolysis is the use of a clot-bursting drug to disperse a clot and restore blood flow in the affected blood vessel of the brain in people who have had an ischaemic stroke. It can help improve survival. The NICE technology appraisal guidance on Alteplase for treating acute ischaemic stroke recommends that treatment with Alteplase is started as soon as possible within 4.5 hours of the onset of stroke symptoms after excluding intracranial haemorrhage using appropriate imaging techniques. The National Stroke Service Model guidance recommends that thrombolysis should be given within 60 minutes and ideally within 20 minutes of admission (door to needle time).

During scoping, a clinical expert noted that based on clinical judgement, thrombolysis may still be of benefit if done within 6 hours of the onset of

stroke symptoms. It may however become less effective as more time passes by. Although beneficial if done early, thrombolysis carries a risk of bleeding in the brain for 1 in 25 people within 7 days of therapy (Stroke Association).

4.4.2 Thrombectomy

Thrombectomy (also known as mechanical thrombectomy) involves the use of a catheter inserted into a cerebral artery to pull or suck out a clot with the aim of restoring blood flow and minimising brain tissue damage in people who have had a stroke caused by a major vessel occlusion. Thrombectomy is time sensitive and can remove clots that are too big to be broken by clot-bursting drugs. The NICE guideline on stroke and transient ischaemic attack in over 16s: diagnosis and initial management recommends thrombectomy as soon as possible and within 6 hours for people who have acute ischaemic stroke and confirmed occlusion of the proximal anterior circulation. This may be done together with intravenous thrombolysis, if not contraindicated. The NICE interventional procedures guidance on mechanical clot retrieval for treating acute ischaemic stroke recommends thrombectomy to treat ischaemic stroke.

The National Stroke Service Model guidance recommends that "All potential thrombectomy patients should have a CT angiogram as part of their initial brain scan; with image interpretation for thrombectomy referral completed by the referring team, supported by AI and off-site expertise as required."

4.5 Pharmacological treatment

The NICE guideline on stroke and transient ischaemic attack in over 16s: diagnosis and initial management recommends the use of aspirin (or an alternative antiplatelet agent if there is intolerance to aspirin) within 24 hours in people with acute stroke in whom a diagnosis of intracerebral haemorrhage has been excluded. Anticoagulant therapy with heparin and then warfarin is recommended for people diagnosed with cerebral venous sinus thrombosis (including those with secondary cerebral haemorrhage).

The guideline recommends a reversal of anticoagulation treatment using a combination of prothrombin complex concentrate and intravenous vitamin K, in people with a primary intracerebral haemorrhage who were receiving warfarin before their stroke. Supplemental oxygen, blood sugar control and blood pressure control may be offered to people with acute stroke.

4.6 Patient issues and preferences

Catching a stroke early and managing it within the specified treatment window for relevant therapy options will help reduce the likelihood of subsequent

strokes, improve survival and quality of life, and reduce the likelihood of disability. Deciding what treatment options, a person can have may depend on whether they can tell the clinician when symptoms began and whether there are other underlying conditions such as bleeding disorders.

There may be a slight delay in the time to diagnosis of stroke, for people who self-present to hospital with non-stroke-like symptoms as the stroke team will not be pre-alerted of their arrival, temporarily delaying them from going directly onto the stroke pathway. This group of patients may spend some time in the emergency department before referral to the stroke unit.

Software updates, system crashes or delays may impact the benefits of getting reassurance about a stroke diagnosis from an AI software. False negative AI-assisted analysis can lead to poor patient outcomes, given the time sensitive nature of stroke. False positive results may delay diagnosis of other possible conditions and lead to increase resource use. Clinical experts commented that false positive brain CT scans, in the stroke context, may be because of the presence of brain tumours and that false negative results would require repeat imaging on the same day with an MRI scan if symptoms persist and no alternative diagnosis are made.

5 Comparator

The alternative to software-assisted review of CT brain scans is an unassisted review of CT brain scans by a healthcare professional.

6 Scope of the assessment

Table 2 Scope of the assessment

Decision questions	**Question 1:** Does software assisted review of non-enhanced CT brain scans for guiding thrombolysis treatment decisions for people with suspected acute stroke represent a clinically and cost-effective use of NHS resources? **Question 2a:** Does software assisted review of CT angiography brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke represent a clinically and cost-effective use of NHS resources? **Question 2b:** Does software assisted review of CT perfusion brain scans for guiding mechanical thrombectomy treatment decisions for people with an ischaemic stroke after a CT angiography brain scan represent a clinically and cost-effective use of NHS resources?

<table>
<tr><td>Populations</td><td>
Question 1: People referred to or attending secondary care with a suspected acute stroke who were last known to be well within 24 hours

Question 2a: People with an ischaemic stroke who were last known to be well within 6 hours
Question 2b: People with an ischaemic stroke who were last known to be well within the last 6 -24 hours who have already had a CTA brain scan

Depending on the availability of evidence, the following subpopulation may be considered:
People over the age of 80 with small vessel disease and calcification of the cerebrovasculature
</td></tr>
<tr><td>Interventions</td><td>
AI-derived software-assisted CT brain scan review by a healthcare professional using any of the following software/platforms:
<table>
<tr><td></td><td>Non-enhanced CT</td><td>CTA</td><td>CTP</td></tr>
<tr><td rowspan="2">Interventions</td><td colspan="3">Thrombolysis</td></tr>
<tr><td></td><td colspan="2">Thrombectomy</td></tr>
<tr><td>icobrain ct</td><td></td><td></td><td>✓</td></tr>
<tr><td>Aidoc</td><td>✓</td><td>✓</td><td></td></tr>
<tr><td>Aidoc + icobrain</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>RapidAI</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>e-stroke</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>Viz</td><td>✓</td><td>✓</td><td>✓</td></tr>
<tr><td>qER</td><td>✓</td><td></td><td></td></tr>
<tr><td>Zebra-Med</td><td>✓</td><td></td><td></td></tr>
<tr><td>CT Perfusion 4D</td><td></td><td></td><td>✓</td></tr>
<tr><td>Brainscan</td><td>✓</td><td></td><td></td></tr>
<tr><td>Cercare stroke</td><td></td><td></td><td>✓</td></tr>
<tr><td>Cina head</td><td>✓</td><td>✓</td><td></td></tr>
<tr><td>Accipio</td><td>✓</td><td></td><td></td></tr>
<tr><td>Biomind</td><td>✓</td><td></td><td></td></tr>
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Comparator	• CT brain scan review by a healthcare professional without assistance from AI-derived software. Note: non-enhanced CT scans may be reviewed by a radiologist, specialist radiologist, radiographer, stroke physician or emergency medicine physician, depending on availability of staff. CTA and CTP scans are more likely to be reviewed by a radiologist, neuroradiologist or an interventional neuroradiologist.
Healthcare setting	Comprehensive stroke centre Acute stroke centre
Outcomes	Intermediate measures for consideration may include: • Diagnostic accuracy for the detection of intracranial haemorrhage, ischaemic stroke (patients suitable for pharmacological clot-busting therapies), large vessel occlusion (patients suitable for thrombectomy) • Number of positive and negative cases of intracranial haemorrhage or large vessel occlusion • Turnaround time (that is, time between CT scan and radiology report) • Time to diagnosis • Time to treatment (thrombolysis, thrombectomy or surgical intervention) • Rate of reperfusion • Length of hospital stay (emergency department and inpatient stay) • Time from arrival to discharge • Ease of use/acceptability of AI software by clinicians
	Clinical outcomes for consideration may include: • Morbidity (including modified ranking score) • Mortality
	Patient-reported outcomes for consideration may include: • Health related quality of life
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of annual subscription for AI software • Cost of staff training • Cost of treatment • Costs related to adverse events from treatment

	• Costs related to false results • Cost of patient transfer • Cost of managing disability
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

7 Other issues for consideration

Human errors may occur in radiological diagnosis, but it has been reported that software-assisted detection may help flag potential misdiagnosis (Chodakiewitz 2020). CT brain scan analysis by AI-derived software would typically be affected by the same factors that can influence the analysis done by a radiologist. This may include CT imaging being impacted by the presence of stents and dental implants which leads to streak artefacts and patient conditions such as convulsion which can lead to head motion artefacts and cardiac complications that may delay contrast getting to the brain.

Clinical experts highlighted that stroke is a diverse condition and there is a need to ensure that the population that an algorithm is trained or validated in is a good representation of the population it will be used on in practice, otherwise performance may be overestimated. They also stated that most of the software are designed to identify ischaemic strokes in anterior circulation and that patients with posterior circulation strokes or basilar artery occlusions may not benefit from them.

The reference standard for assessing the accuracy of the AI-derived software is a review by a neuroradiologist or a panel of neuroradiologists giving a consensus diagnosis.

It has been reported that artificial intelligence algorithm performance metrics for CT brain scans use different standards and this may prevent an objective comparison between algorithms (Murray 2020).

AI software may require periodic major updates. These updates may have an impact on the diagnostic accuracy of parameters used for the inference of a stroke. Evidence based on earlier versions of an AI-software may not accurately reflect the effectiveness of current versions.

There are variations in the diagnostic pathway for suspected acute stroke across the NHS. This is largely due to the variation in facilities available for stroke services. It is likely that the modelling will need to take into account scenarios where transfers are required to enable access to thrombectomy. It

should also consider the availability of healthcare professionals to review scans, that is scenarios where neuroradiologists are available, or not, to report CTA and CTP scans.

Some hospitals may opt to use 'comprehensive solutions,' which bring together interoperable AI software from different manufacturers to enable the analysis of plain CT, CTA and CTP. Other manufacturers may provide the full suite of algorithms for comprehensive CT scan analysis. Where algorithms can be bought directly from a company, and are also housed on a multi-vendor platform, the analysis should take into account the costs with and without the multivendor platform.

NHS Shared Business Services is undertaking a national procurement exercise for supply of AI software in neuroscience for stroke decision making support, which may help enable procurement of software in the future.

8 Potential equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

People who have had a stroke may have impaired cognitive function and physical disability that limits activity. Disability is protected characteristic under the equality act 2010.

Artificial intelligence algorithms for stroke diagnosis may have lower sensitivity in people over the age of 80 with small vessel disease and calcification of the cerebrovasculature.

Ability to assess the performance of AI algorithms in different age groups may be driven by the availability of training data in different age groups.

Some people may have limitations in their ability to co-operate with being scanned.

9 Potential implementation issues

IT issues

IT compatibility issues and capacity issues within NHS Trusts may be a potential barrier to the implementation of AI software. However, if hospitals

within a stroke network purchase the same AI software this may help overcome this barrier.

Procurement

The cost of procurement of AI platforms may be quite high for some hospitals. However, companies state that discrete packages can be purchased.

The cost of purchasing AI software will be an added cost for hospitals regardless of whether they use commercial teleradiology services or not during radiologist's out of office hours.

Clinician confidence

Confidence in the accuracy of the software can influence the choice to use it. False positive results may increase clinician's workload if several reviews must be done before overriding the results from software.

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Appendix A Glossary of terms

Aneurysm

A bulge in a blood vessel caused by a weakness in the blood vessel wall, usually where it branches.

Intracranial haemorrhage

Bleeding within the skull or between brain tissues

CT perfusion

A non-invasive imaging that shows which areas of the brain are adequately supplied with blood and provides detailed information on delivery of blood or blood flow to the brain.

CT angiography

Imaging done with a special dye to check the health of blood vessels in the brain and how blood flows through them.

Appendix B Abbreviations

AI	Artificial intelligence
ASPECTS	Alberta Stroke Program Early CT score
CT	Computed tomography
DICOM	Digital Imaging and Communications in Medicine
ICH	Intracerebral haemorrhage
LVO	Large vessel occlusion
MCA	Middle cerebral artery
ICA	Internal carotid artery
PACS	Picture Archive and Communication System

Appendix C References

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