UK & ROI ACUTE STROKE SIMULATION COURSE

Acute Ischaemic Stroke:

Thrombolysis and Thrombectomy

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Outline

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- Stroke Definitions
- Ischaemic Stroke Subtypes
- Stroke Clinical Syndromes By Vascular Territory
- Thrombolysis
- Thrombectomy

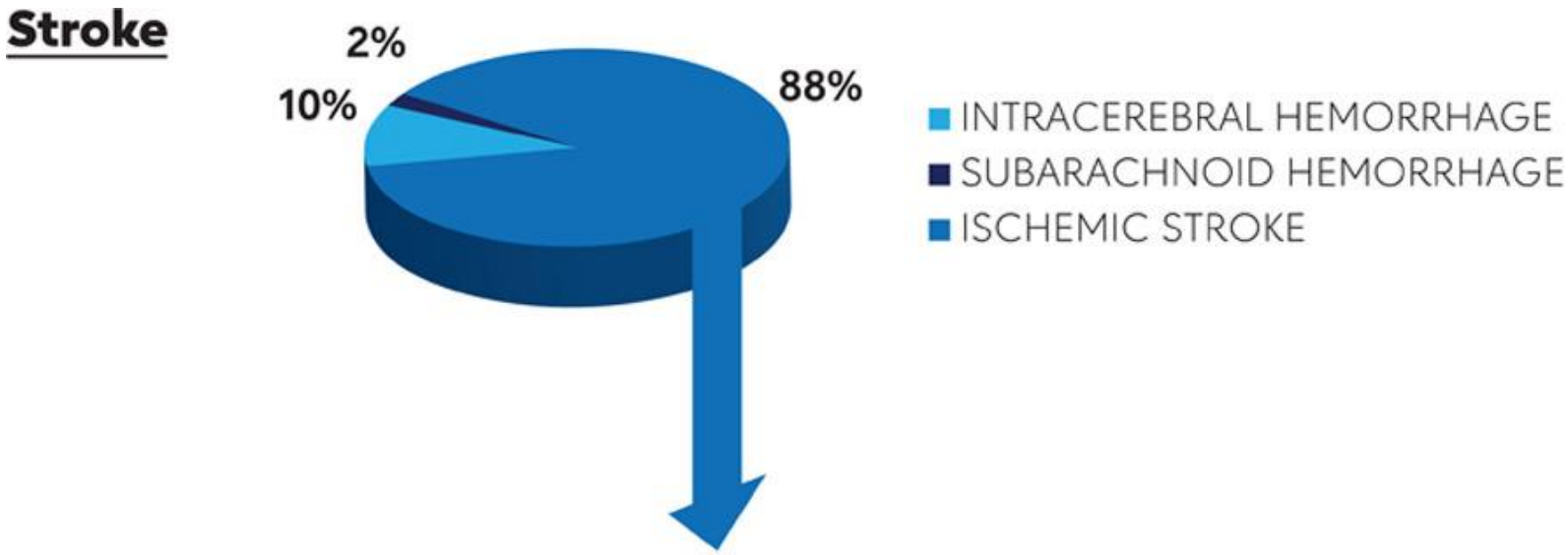
Definitions

Stroke[1] is a clinical syndrome of presumed vascular origin characterized by rapidly developing signs of focal or global disturbance of cerebral functions which lasts longer than 24 hours or leads to death.

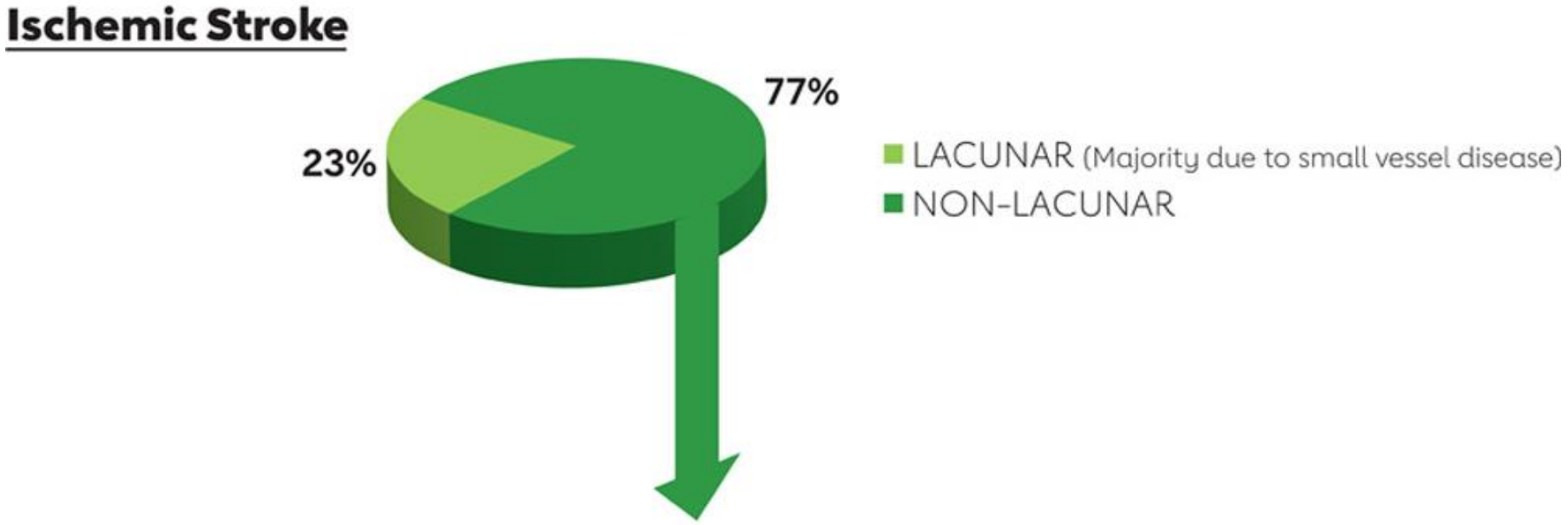
- **Ischaemic stroke** — an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal cell death due to infarction following vascular occlusion or stenosis.

- **Haemorrhagic stroke** — rapidly developing neurological dysfunction due to a focal collection of blood from within the brain parenchyma or ventricular system (intracerebral haemorrhage), or bleeding into the arachnoid space (subarachnoid haemorrhage) that is not caused by trauma.

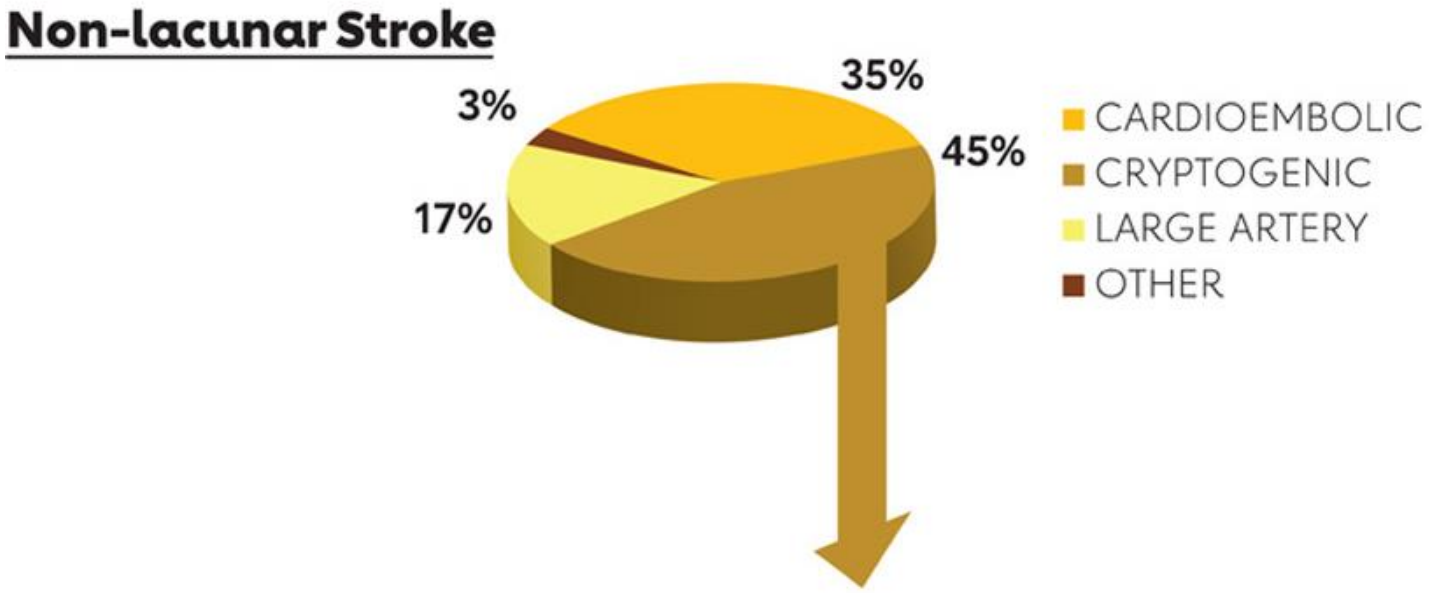
Stroke Subtypes[2]



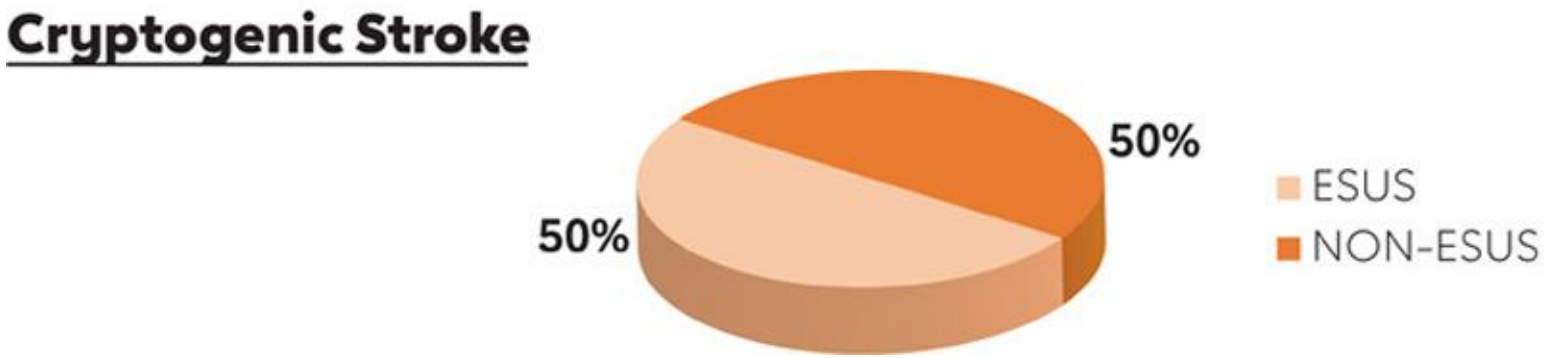
Ischaemic Stroke Subtypes[2]



Non-Lacunar Stroke Subtypes[2]



Cryptogenic Stroke[2]



Ischaemic Stroke Subtypes[2]

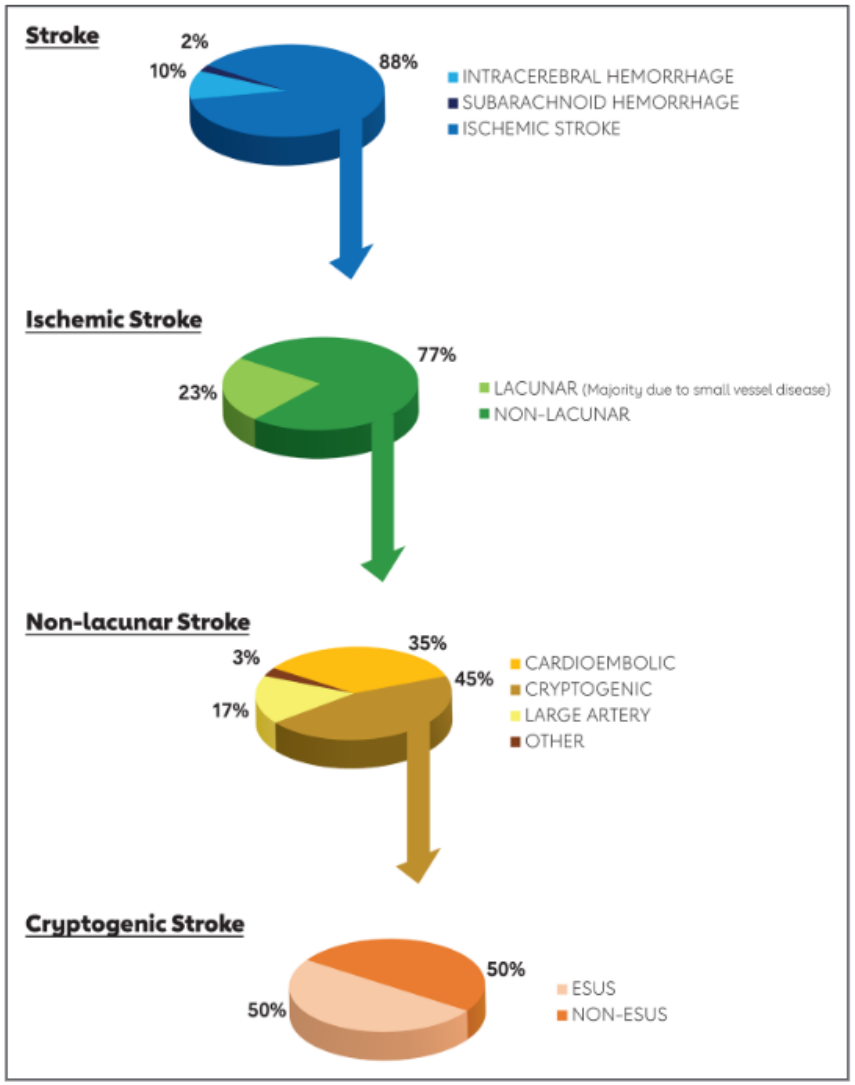
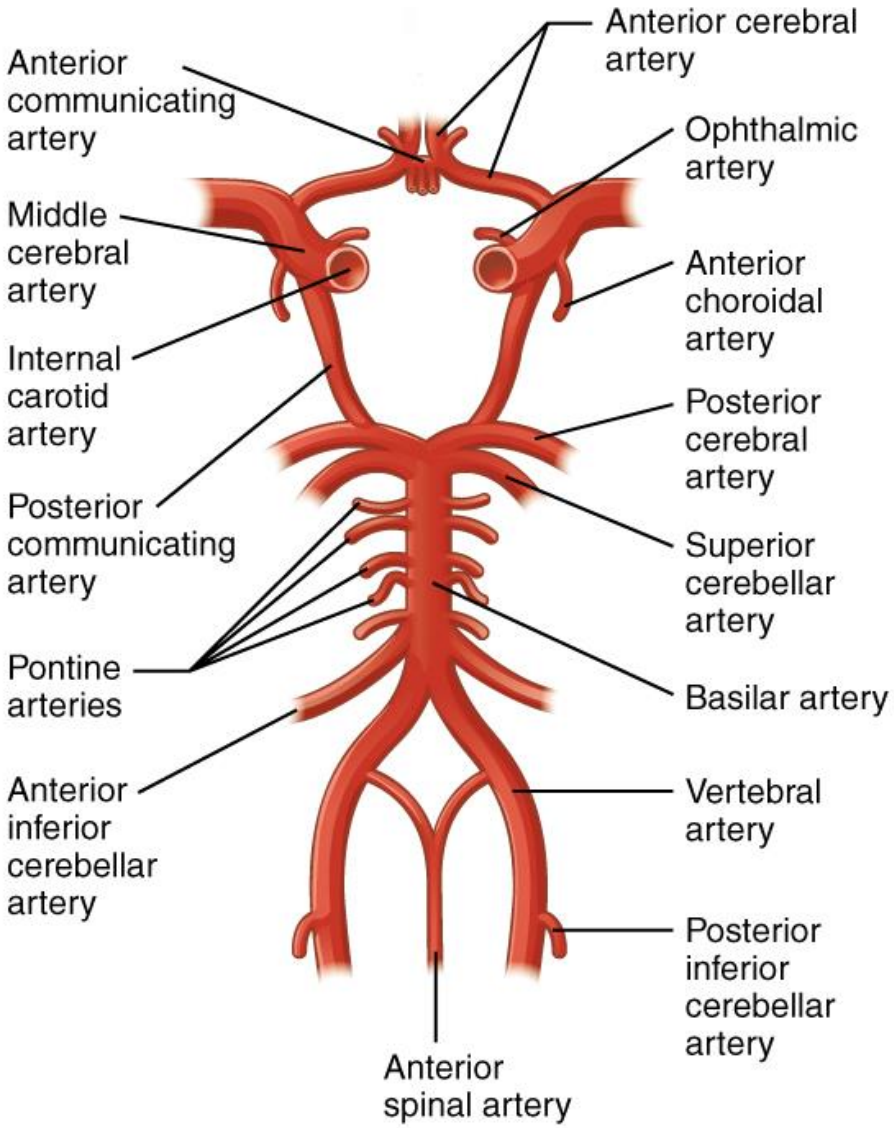


Figure 1. Conceptual representation of ischemic stroke subtypes. Percentages are approximate and are informed by Kolominsky-Rabas et al[36] and Gardener et al.[37] Precise percentages will depend on extent of testing and patient populations. Ischemic stroke subtype definitions are informed by the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification scheme[38] unless otherwise indicated. ESUS indicates embolic stroke of undetermined source.

Anatomy: Circle of Willis[3]



Anatomy: Vascular Territories[4,5]

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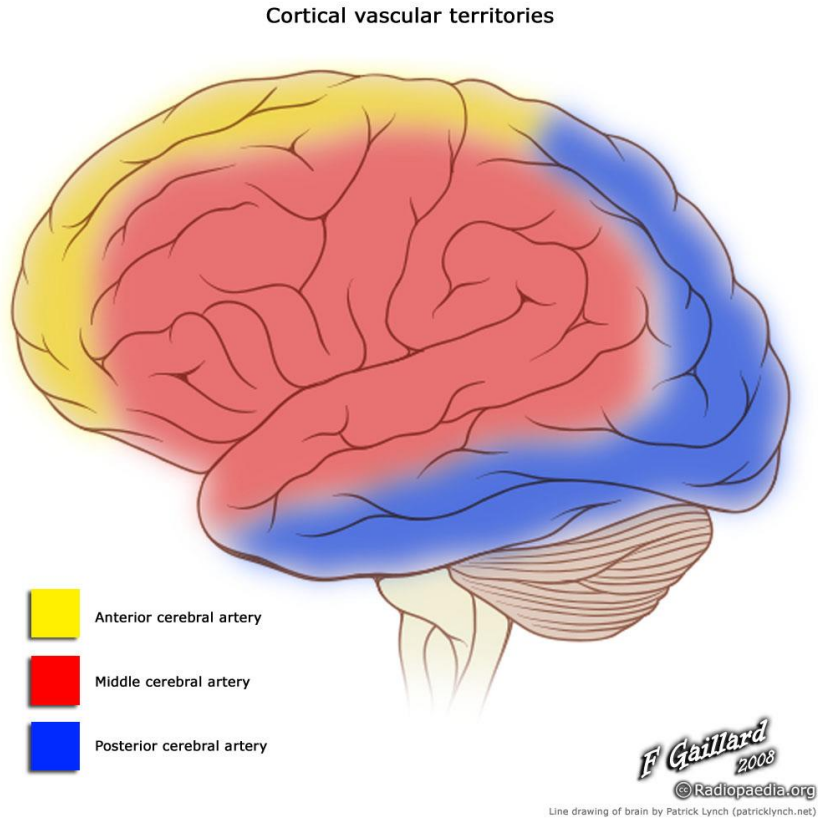

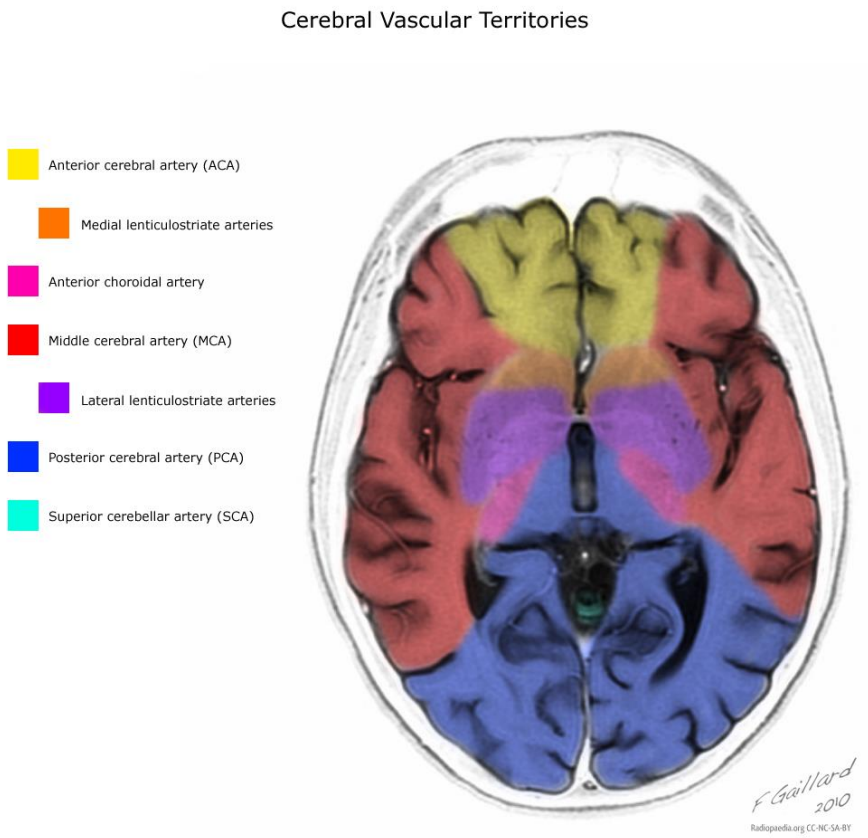

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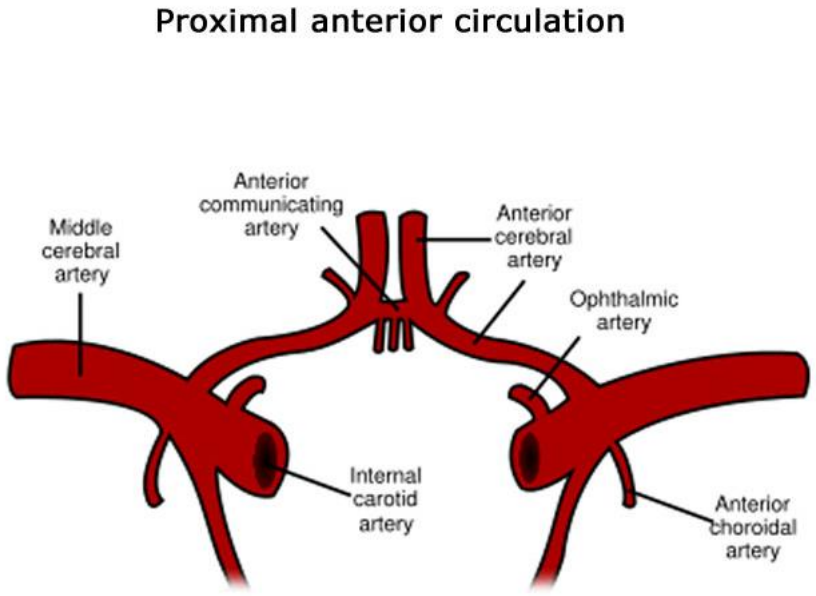
Stroke Clinical Syndromes by Vascular Territory

Anterior Cerebral Artery[6,7]

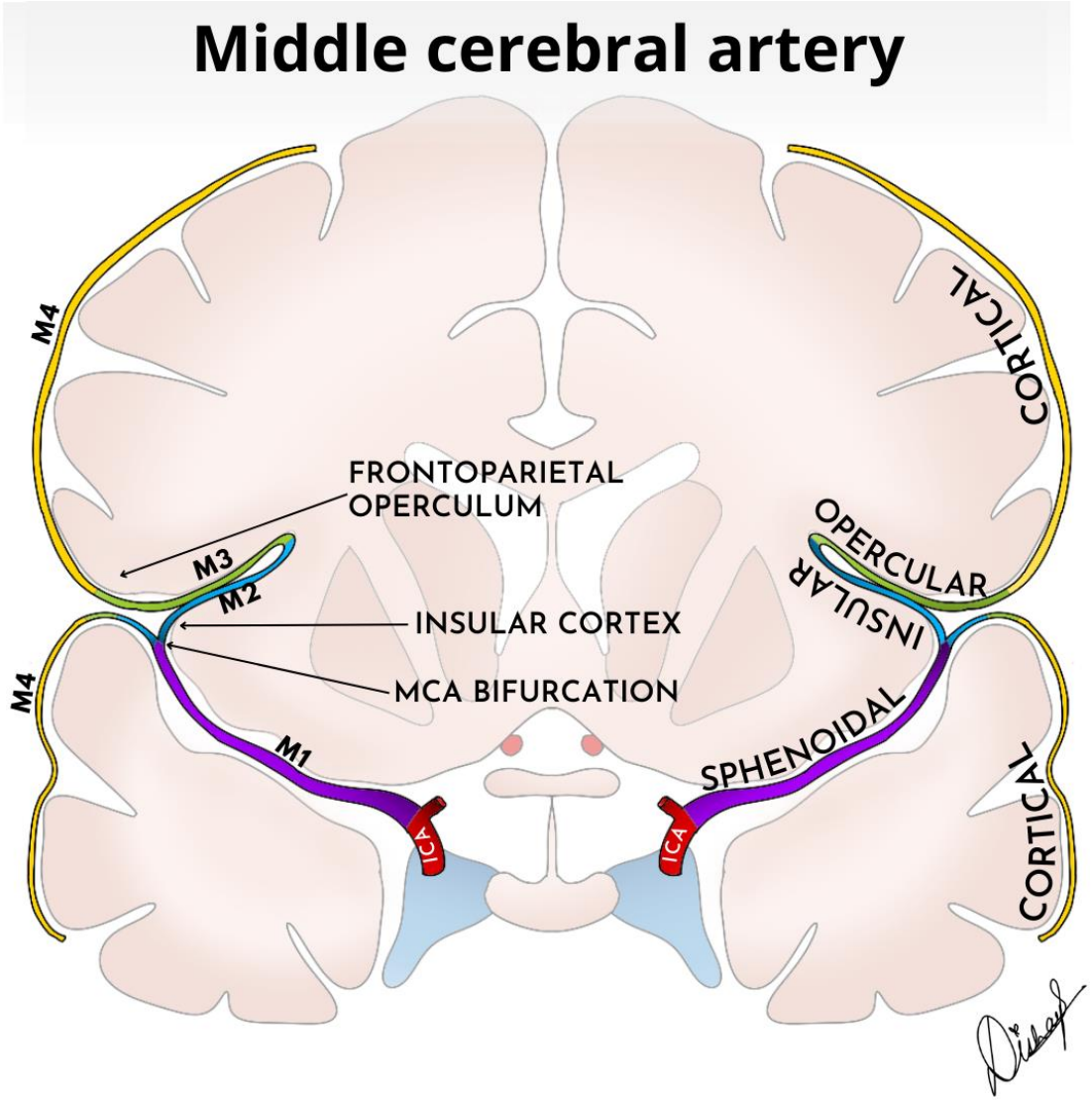
- Leg more than arm involvement with hand sparing
- Urinary incontinence
- Gait apraxia
- Akinetic mutism



Middle Cerebral Artery[6]

- Homonymous hemianopia/quadrantonopia
- Face-arm-leg involvement
- Aphasia (Broca's = superior division; Wernicke's = inferior division)
- Inattention
- Gaze paralysis (usually indicates a large area of frontal damage)

Middle Cerebral Artery[8]



Vertebrobasilar[6]

- Occipital lobe: homonymous hemianopia, cortical blindness, other cortical visual deficits
- Cerebellum: ataxia, nystagmus
- Brainstem cranial nerve palsies: diplopia, facial numbness/weakness, vertigo, dysphagia, dysphonia
- Spinal tracts: hemiparesis and hemisensory loss

Lacunar Stroke Syndromes[6,9]
(due to occlusion of deep perforating small arteries)

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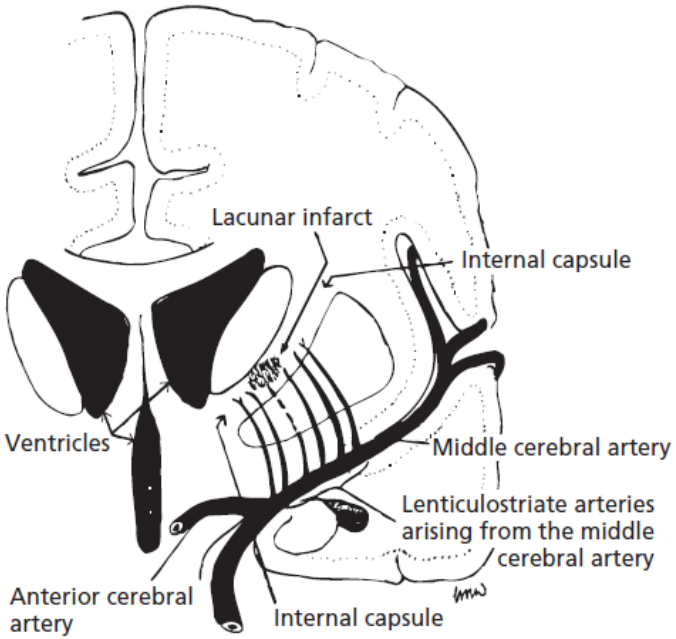
- Pure motor hemiparesis
- Pure sensory stroke
- Sensorimotor stroke
- Ataxic hemiparesis



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Reperfusion Therapies

Aim of Reperfusion Therapies

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- To restore blood flow to ischaemic area of the brain

- To improve functional outcome for the patient

Initial Assessment

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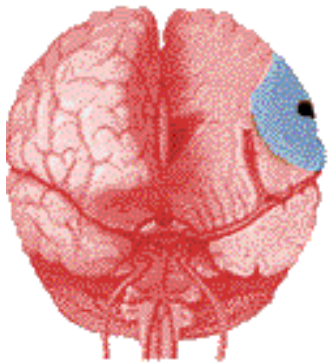
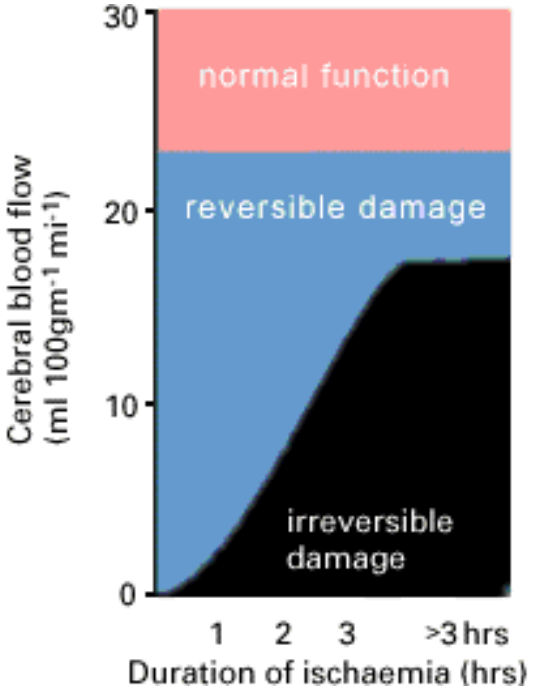
1. Focused history taking, need to include:
    - Time of onset/time last known to be well
    - Pre morbid function
    - Medications (any anticoagulants?)

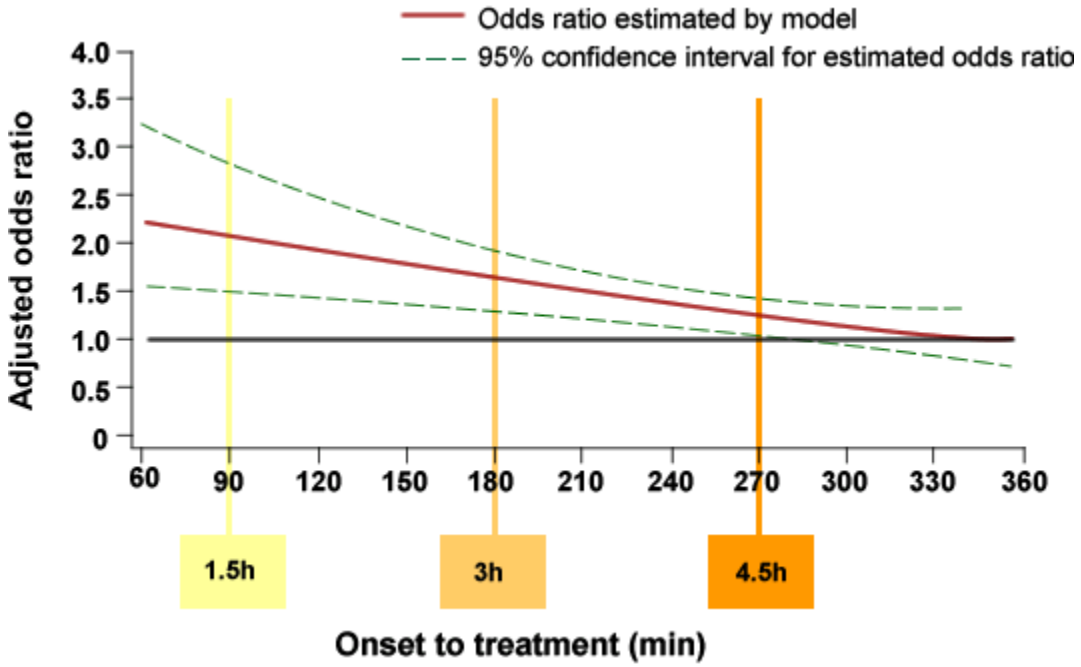
2. Focused examination using NIHSS

3. Imaging: CT Head +/- CT Angiogram if thrombectomy is an option

Time Is Brain[10,11]







Model estimating odds ratio for favourable outcome at 3 months in tPA treated patients compared with controls by onset to treatment. Adjusted for age, baseline glucose concentration, baseline National Institutes of Health Stroke Scale (NIHSS) measurement, baseline diastolic blood pressure, previous hypertension, and interaction between age and baseline NIHSS measurement.

Time Is Brain[12]

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Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

Rationale for Thrombolysis

Cerebral angiography performed soon after onset of stroke demonstrates arterial occlusion in 80% of acute infarctions

Recanalization of occluded arteries may reduce the degree of injury to brain if done before process of infarction is irreversible- ischaemic penumbra

Thrombolysis

- Intravenous thrombolysis is the only approved systemic reperfusion treatment for patients with ischaemic stroke[9]

- Thrombolysis is now administered to between 10 and 11% of patients with acute stroke in the UK and Ireland[13]

Indications For Thrombolysis

- Time of onset and IVT treatment can be commenced within 4.5 hours of onset
- Age ≥ 18 years
- BM > 3
- No contraindications for IV alteplase (do not wait for lab results)

Absolute Contraindications

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- Previous stroke in last 14 days
- Presence of haemorrhage or extensive early ischaemic changes on CT (ASPECTS 0-2)
- Major head injury or intracranial/intraspinal surgery in the last 3 months
- Major surgery or trauma in the past 14 days
- Intracranial neoplasm or cerebral venous thrombosis
- Arterial puncture of a non-compressible blood vessel in the past 7 days
- Recent (<10 days) obstetric delivery, traumatic external heart massage
- Symptoms suggestive of subarachnoid haemorrhage even if CT is normal
- Significant bleeding disorder at present or within the past 6 months. Known harmorrhagic diathesis
- Severe liver disease, oesophageal varices, acute aortic dissection, bacterial endocarditis, acute pancreatitis
- Platelet count below 100 x 10*9/L
- Patients on warfarin, need to urgently check INR, must be <1.7
- Patients on heparin – send urgent aPTT and discuss with haematology oncall. Do not proceed if aPTT outside of normal limits
- Confirmed taken DOAC within 24 hours of symptom onset

Relative Contraindications

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- Previous stroke in the last 3 months
- Previous primary intracerebral haemorrhage
- Evidence of early ischaemic change on CT or hyperdensity > 1/3 MCA territory
- Minor neurological deficit (NIHSS < 4) or symptoms rapidly improving before start of infusion
- Seziure as presenting symptom or at onset of stroke
- Cerebral amyloid angiopathy with >10 microhaemorrhages, AV malformation or aneurym (>10mm)
- Unexplained severe anaemia or recent GI or GU bleeding in the last 21 days
- Persistent blood pressure elevation (>185mmHg systolic or 110mmHg diastolic) despite management
- BM <2.7 mmol/L or >30 – correct and reassess
- Confirmed taken DOAC within 24-48 hours of symptom onset – send urgent aPTT and thrombin time

Extended Thrombolysis[14]

- Introduced as part of the new stroke clinical guideline

- This will vary locally depending on access to CT/MR perfusion or MRI (DWI-FLAIR mismatch)

- This is applicable to:
    1. Patients with an acute ischaemic stroke, regardless of age or severity
    2. Patients last known to be well >4.5 hours earlier

- Treatment must be started within 4.5 and 9 hours of known onset OR within 9 hours of the midpoint of sleep when they have woken up with symptoms

- There must be evidence on perfusion scans or MRI of the potential to salvage brain tissue. This is irrespective of whether they require a thrombectomy

Extended Thrombolysis[14]

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Table 3.5.1 Eligibility criteria for extending thrombolysis to 4.5-9 hours and wake-up stroke

	Time window	Imaging	Imaging criteria
Wake-up stroke	>4.5 hours from last seen well, no upper limit	MRI DWI-FLAIR mismatch	DWI lesion and no FLAIR lesion
Wake-up stroke or unknown onset time	>4.5 hours from last seen well, and within 9 hours of the midpoint of sleep. The midpoint of sleep is the time halfway between going to bed and waking up	CT or MRI core-perfusion mismatch	Suggested: mismatch ratio greater than 1.2, a mismatch volume greater than 10 mL, and an ischaemic core volume <70 mL
Known onset time	4.5-9 hours	CT or MRI core-perfusion mismatch	Suggested: mismatch ratio greater than 1.2, a mismatch volume greater than 10 mL, and an ischaemic core volume <70 mL

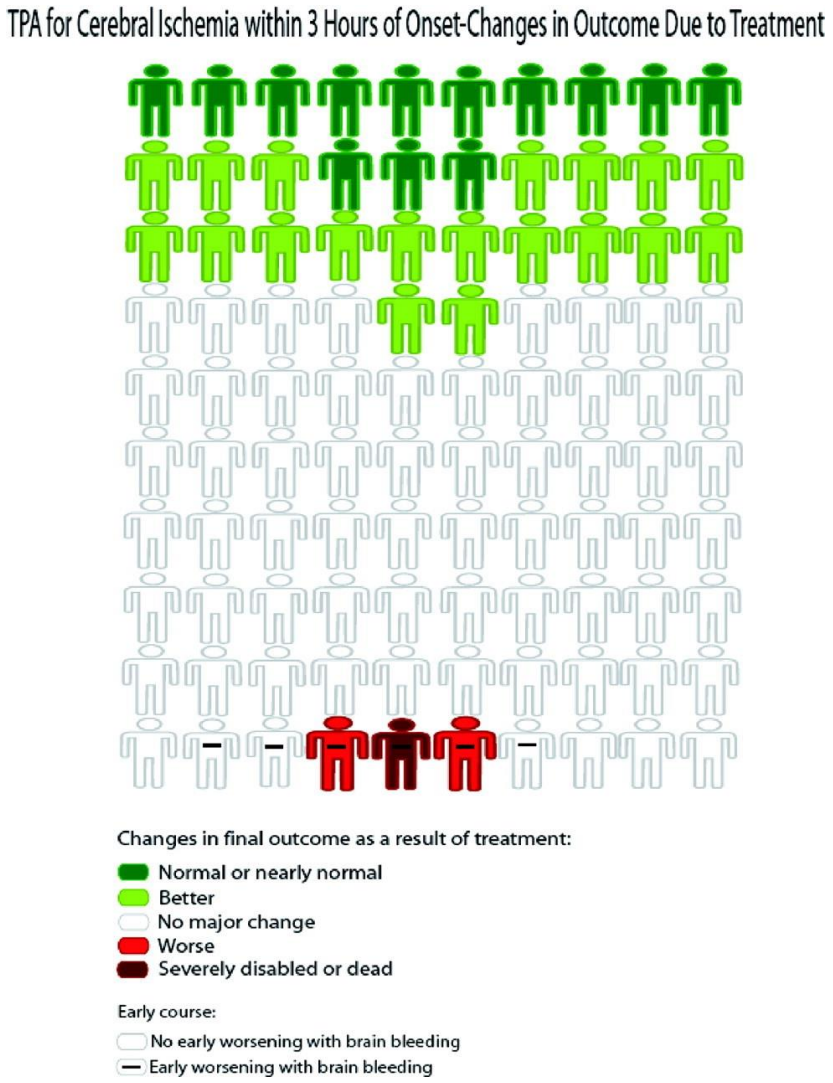
Limitations to IVT

- Success is dependent on the length and size of the clot
- E.g 35% recanalization for middle cerebral arteries vs 14% for internal carotid arteries
- Historically, small time window (most stroke patients don’t receive it, need advanced imaging for extended thrombolysis)

Consenting for IVT

- Establish if patient is able to consent to treatment with thrombolysis
- Good practice to discuss with next of kin particularly if patient lacks capacity
- If patient lacks capacity, best interests decision
- One third of patients will do better than they would have done without thrombolysis
- Risks: Symptomatic haemorrhage (around 7%), major potential life-threatening bleed (around 3%), allergic reaction
- May give more nuanced information on a case by case basis

What do I tell patients?[15]



All physicians use different resources, these are some of the figures quoted:

- ***1 in 3*** ***some benefit***
- ***1 in 10*** ***significant benefit***
- ***1 in 35*** ***harm***

- **2%** **fatal intracranial bleed**
- **5%** **bleed**

What do I prescribe?

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- Alteplase:

  0.9mg/kg (max 100kg)
  10% bolus given over 1-2 minutes IV
  Then rest of infusion over 1 hour

OR

- Tenecteplase:

  0.25mg/kg (max 25mg)
  Single bolus given over 5 seconds
  Global shortage currently

Door to needle times

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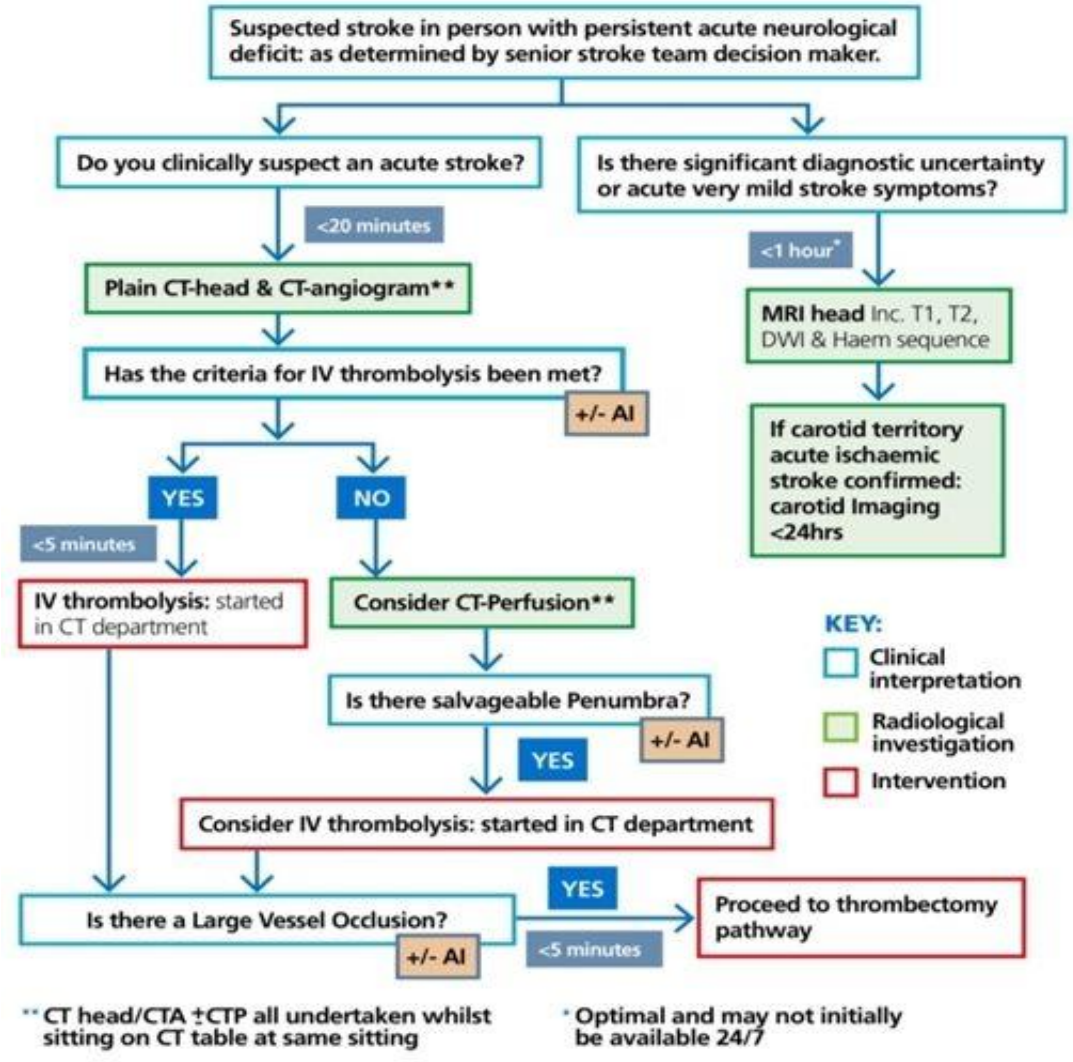
- In hours target: <30 mins
- Out of hours target: Within 60 mins
- Don’t forget: TIME IS BRAIN

National Optimal Stroke Imaging Pathway[16]



Post Thrombolysis

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Need to avoid:

- Urethral catheters for 24 hrs, ideally
  - If vital wait for 30mins post infusion
- Venous puncture during infusion
- Arterial puncture, IM injections or central lines for 24 hours
  - Unless absolutely necessary)

Thrombolysis Complications

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Neurological deterioration:

- Not always due to haemorrhage
- If NIHSS increases by 2 or more:
    1. Stop the infusion
    2. Repeat CT Head
- Low threshold for repeat CT Head if:
    1. New nausea and vomiting
    2. Any new neurology
    3. Acute severe hypertension
    4. New headache

Thrombolysis Complications

Other complications:

- Bleeding
  - Stop infusion, send bloods, D/W Haem if indicated, may need imaging depending on site and severity
- Allergic reaction
  - Stop infusion, anaphylaxis treat as per ALS, if not compromised: chlorphenamine and hydrocortisone
- Hypertension
  - Stop infusion, keep <185/110mmHg with labetalol/GTN)

Eligibility For Mechanical Thrombectomy: Anterior Circulation[14]

- Previously independent (mRS 0 - 2)
- Proximal intracranial large artery occlusion (confirmed on CTA)
- NIHSS 6 or more
- Procedure can begin within 6 hours of known onset

Eligibility For Mechanical Thrombectomy: Anterior Circulation[14]

- Previously independent (mRS 0 or 1)
- Proximal intracranial large artery occlusion (confirmed on CTA)
- NIHSS 6 or more
- Onset 6 – 24 hours ago (including wake up symptoms)
- If the following criteria are met (next slide)

Eligibility For Mechanical Thrombectomy: Anterior Circulation[14]*

Criteria if onset 6-24 hours ago:

- 6-12 hours: an ASPECTS score of 3 or more, irrespective of core infarct size

- 12-24 hours: an ASPECTS score of 3 or more and CT/MR Perfusion mismatch of greater than 15ml, irrespective of core infarct size

*This will depend on local referral pathways and options available

Eligibility For Mechanical Thrombectomy: Posterior Circulation[14]*

- Within 12 hours of onset
- Confirmed intracranial vertebral or basilar artery occlusion
- NIHSS 10 or more
- Combined with favourable ASPECTS score and Pons-Midbrain Index

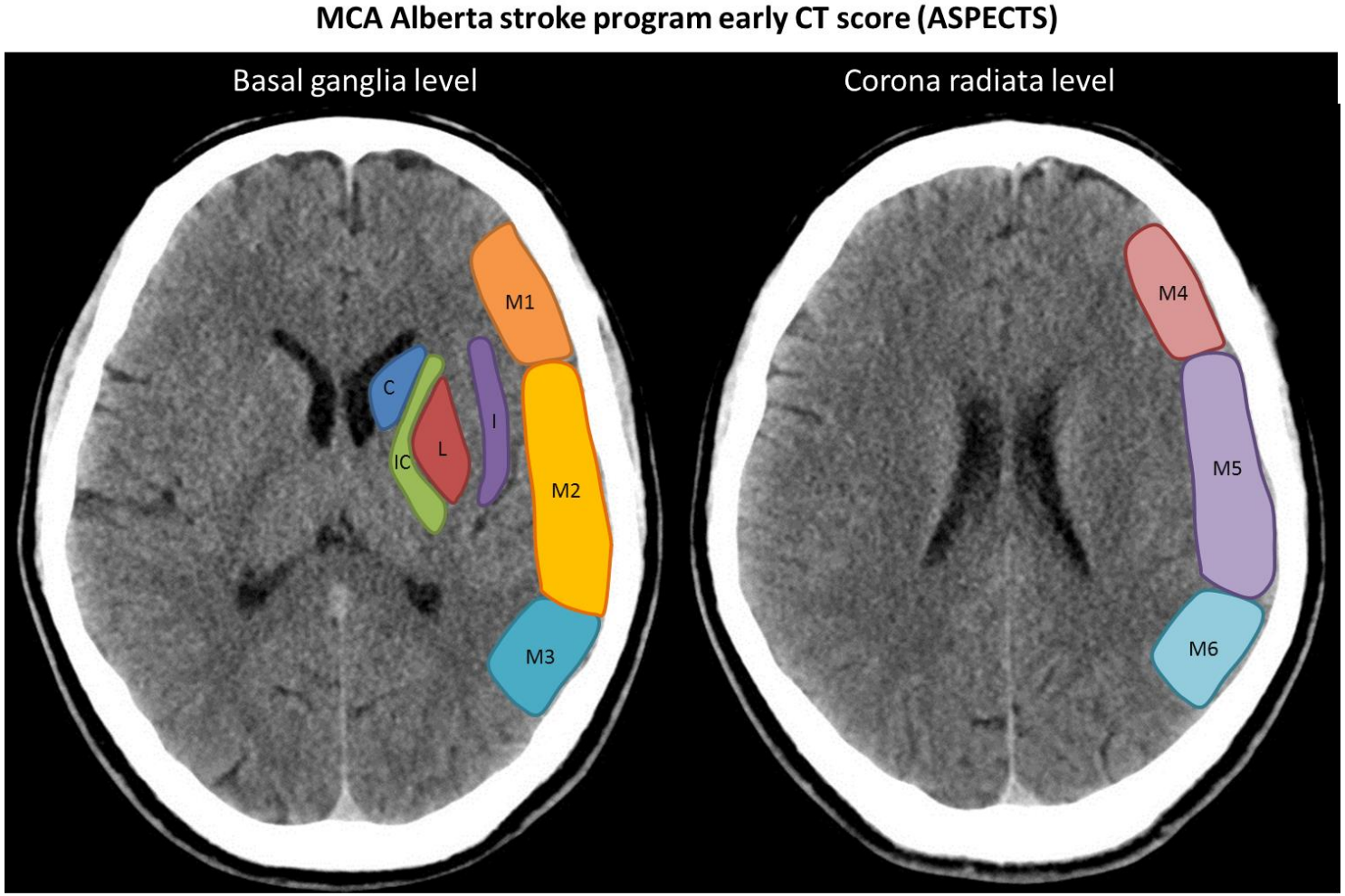
* Caution should be exercised when considering mechanical thrombectomy for patients presenting between 12-24 hours of onset &/or over the age of 80 owing to the paucity of data

ASPECTS Score[17]

- Alberta Stroke Programme Early CT Score
- 10 point quantitative CT Scan score used for MCA stroke patients
- Can be adjusted for posterior circulation strokes
- The MCA vascular territory is divided into regions. Where there is evidence of regional involvement 1 point is deducted from an initial score of 10

NB You are not expected to score patients, this will be done by neuroradiologists when considering thrombectomy

ASPECTS Score[18]



C: Caudate; IC: internal capsule; L: lentiform nucleus; I: Insular Cortex.

Thrombectomy Consent

- Establish if patient is able to consent to thrombectomy
- Good practice to discuss with next of kin particularly if patient lacks capacity
- If the patient lacks capacity, best interests decision
- Around 40% of patients will do better than they would have done without thrombectomy
- Risks: worsening/new stroke (1%), brain haemorrhage (<4%), allergic reaction to contrast, puncture site complications, anaesthetic risk

Can a patient have thrombolysis and thrombectomy?

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- Yes

- In patients that are eligible for both, they should be given both treatments. Some patients will be ineligible for thrombolysis but eligible for thrombectomy

- Thrombolysis should be started and then the patient transferred/taken for thrombectomy

- The protocols for this will vary locally e.g. if a stroke nurse can accompany the patient whilst the infusion runs in the ambulance

Thrombolysis or Thrombectomy?

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JAMA | Original Investigation

Effect of Endovascular Treatment Alone vs Intravenous Alteplase Plus Endovascular Treatment on Functional Independence in Patients With Acute Ischemic Stroke

The DEVT Randomized Clinical Trial

Stroke

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Abstract

Introduction

Thrombectomy Versus Combined Thrombolysis and Thrombectomy in Patients With Acute Stroke

A Matched-Control Study

Xu Tong, Yilong Wang, Jens Fiehler, Clayton T. Bauer, Baixue Jia, Xuelei Zhang, Xiaochuan Huo, Gang Luo, Anxin Wang, Yuesong Pan, Ning Ma, Feng Gao, Dapeng Mo, Ligang Song, ... See all authors and on behalf of the ANGEL-ACT Study Group

Originally published 4 Mar 2021 | https://doi.org/10.1161/STROKEAHA.120.031599 | Stroke. 2021;52:1589–1600

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Thrombectomy alone versus intravenous alteplase plus thrombectomy in patients with stroke: an open-label, blinded-outcome, randomised non-inferiority trial

Prof Urs Fischer, MD * • Johannes Kaesmacher, MD * • Daniel Strbian, MD • Prof Omer Eker, MD • Christoph Cognard, MD • Patricia S Plattner, MSc • et al. Show all authors • Show footnotes

Published: July 09, 2022 • DOI: https://doi.org/10.1016/S0140-6736(22)00537-2 • Check for updates

Thrombolysis or Thrombectomy?

- No superiority trials
- All non-inferiority trials
- No clear evidence to show that one is superior
- No clear evidence to suggest that one is inferior
- Therefore patients should be offered both treatments

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17. Case courtesy of Osamah A. A. Alwalid, Radiopaedia.org, rID: 72706