Radiological investigation of acute stroke 1: non-enhanced computed tomography

Radiology plays a central part in the acute stroke management pathway, with its role now widened beyond establishing the diagnosis. This article reviews the role of the non-enhanced computed tomography brain scan, particularly focusing on the hyper-acute presentation of stroke from a radiological perspective.

Stroke affects approximately 110 000 people in England per year. It accounted for 11% of all deaths in England and Wales in 1999 (Stevens et al, 2010), and may be considered the largest cause of complex disability in adults (Adamson et al, 2004). The prognosis of patients presenting with an acute stroke can be significantly improved following swift and appropriate management, with imaging central to the management pathway.

There are numerous causes of stroke, which in the majority of cases are clinically indistinguishable (*Table 1*). Broadly these are classified as ischaemia (75%) or haemorrhage (25%). Previously the primary role of imaging was to confirm the diagnosis, and differentiate ischaemia from haemorrhage and other non-vascular causes. Radiology is now a critical part of stroke management as advances in patient management move from supportive care to brain reperfusion. This article discusses the role of the non-enhanced computed tomography brain scan, particularly focusing on the hyper-acute radiological signs of stroke. In order to consider the role of imaging it is necessary to briefly discuss the pathophysiology of stroke.

Table 1. Causes of stroke

Ischaemia	Cerebrovascular thrombotic and embolic events
	Small vessel disease
	Global hypoperfusion
	Venous infarction
	Cervical artery dissection
	Vasculitis
	Substance abuse
	Metabolic disorders, e.g. mitochondrial cytopathies
	Sickle cell disease
	Moyamoya disease
Haemorrhage	Hypertension
	Amyloid angiopathy
	Ruptured arteriovenous malformation
	Ruptured aneurysm
	Coagulopathy
	Tumour
	Venous infarction
	Abscess
	Traumatic
	Illicit drug use
	Sickle cell disease
	Vasculitis
	Encephalitis

Pathophysiology of imaging changes and the ischaemic penumbra

Brain parenchyma perfusion is autoregulated over a range of perfusion pressures. Below these perfusion cannot be maintained potentially leading to ischaemia. Ischaemia results in cell membrane ion pump failure and the redistribution of extracellular water into the intracellular space. This development of cytotoxic oedema is responsible for radiological changes, which occur within minutes of cerebral hypoxia, reaching a maximum at 2–4 days.

Brain parenchymal ischaemia usually results in changes within well-demarcated vascular territories, the middle cerebral artery being the commonest territory affected. These ischaemic areas produce characteristic radiological patterns of injury which help differentiate ischaemia from stroke differentials.

The concept of the ischaemic penumbra has evolved to explain the pathological parenchymal changes, and can be represented radiologically (Earnshaw et al, 2009). The ischaemic penumbra represents a region of potentially salvageable brain tissue surrounding a central irreversible 'infarct core' (*Figure 1*). Thrombolysis aims to restore circulation to the ischaemic penumbra, so it is critical that reperfusion therapy is initiated as soon as possible.

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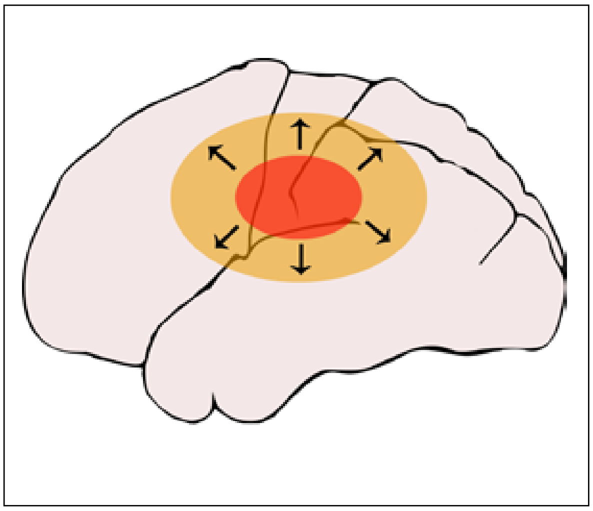

Figure 1. The ischaemic penumbra. Following a stroke the central irreversibly damaged infarct core (red region) expands into the hypoperfused, but potentially reversible ischaemic area (orange region).

Table 2. Hyper-acute ischaemic stroke signs on plain computed tomography

Sign	Comment
Loss of definition of deep grey matter structures	Grey/white matter attenuation difference is lost, particularly within the basal ganglia, internal capsule or insular ribbon
Generalized hypoattenuation in a vascular territory	
Dense artery sign	Acute thrombus is visualized within the affected artery. However, this sign is of low sensitivity, and can be mimicked by age calcification and a raised haematocrit
Hyperattenuating 'dots'	Represents occlusion of distal middle cerebral artery branches
Sulcal effacement or swelling	

Radiological investigation of stroke

Since its introduction in the early 1970s the non-enhanced computed tomography brain scan has been the mainstay of stroke imaging. It confers a number of benefits when managing an acutely ill patient, being easily accessible, allowing rapid image acquisition and not requiring intravenous contrast.

The role of the non-enhanced computed tomography brain scan

Non-enhanced computed tomography aims to answer a series of clinical questions, guiding further management.

Is there evidence of an acute ischaemic stroke?

The non-enhanced computed tomography brain scan is of limited sensitivity (14–43%) (von Kummer et al, 1996), and may be completely normal following an acute stroke. However, there are a number of, albeit subjective, signs described in the hyper-acute stage (0–3 hours) (Hoggard et al, 2001) (*Table 2* and *Figure 2*). If present, they can increase the sensitivity of non-enhanced computed tomography, and have prognostic value, as they are associated with poorer outcomes (Wardlaw and Mielke, 2005).

In ischaemic stroke non-enhanced computed tomography appearances become more conspicuous over time. In addition haemorrhagic changes may develop. Risk factors for parenchymal haemorrhage include patients receiving aspirin before thrombolysis, those treated with recombinant tissue plasminogen activator, extent of parenchymal hypoattenuation on baseline computed tomography, congestive heart failure, advanced age and raised baseline systolic blood pressure (Larrue et al, 2001). This so-called haemorrhagic transformation can be classified according to the European Cooperative Acute Stroke Study into 'haemorrhagic infarcts' without space-occupying effect and 'parenchymal haematomas'

Figure 2. The evolving non-enhanced computed tomography signs of ischaemic stroke. a. Subtle loss of grey/white matter differentiation and hypoattenuation of brain parenchyma (red highlighted area). b. The 'dense artery' sign within the left middle cerebral artery (arrow). c. Non-enhanced computed tomography scan of the same patient from Figure 2b *the following day, demonstrating the true extent of ischaemic changes. Note the mass effect and sulcal effacement secondary to cerebral oedema complicating the area of ischaemia.*

with space-occupying effect (Renou et al, 2010). The former group are divided into two further subgroups: changes of small petechiae along the periphery of the infarct (HI1 changes) or confluent petechiae within the infarcted area (HI2 changes). The latter are further subdivided into <30% of the infarcted area is affected (PH1 changes) or >30% of the infarcted area (PH2 changes) (Renou et al, 2010). Of these, PH2 changes are important to recognize as they are associated with both an increased risk of deterioration 24 hours following the onset of a stroke and increased mortality at 3 months (Berger et al, 2001).

To thrombolyse or not?

The thrombolysis therapeutic window now extends up to 4.5 hours after symptom onset (Bluhmki et al, 2009). A number of contraindications for thrombolysis, detectable on computed tomography, need to be excluded. These include the size of the infarct, presence of a haemorrhagic stroke, and differentiating stroke mimics.

Infarct size

The infarct size is important following results of the European Cooperative Acute Stroke Study I, which demonstrated that infarcts greater than one third of the middle cerebral artery territory had a 3.5-fold increase in parenchymal haemorrhage (Hacke et al, 1995). Consequently, an infarct of this size or greater may be considered a contraindication to thrombolysis.

The extent of infarcted tissue may be assessed on clinical grounds using the National Institutes of Health Stroke Scale (Fischer et al, 2005). In addition, there are several methods to radiologically quantify the infarct size. Perhaps the most noteworthy is the Alberta Stroke Programme Early CT Score (ASPECTS) (Barber et al, 2000). ASPECTS, a 10-point score, divides the middle cerebral artery territory into 10 anatomical areas, with a point deducted for each affected area; a score of ≤7 is sometimes used as a contraindication for thrombolysis (*Figure 3*).

Haemorrhagic stroke

Haemorrhagic stroke can be broadly classified as intraparenchymal and subarachnoid. Intraparenchymal haemorrhage typically appears as a hyper-dense mass, often distorting or displacing surrounding structures (*Figure 4*). Subarachnoid haemorrhage typically results in blood within the basal cisterns, interhemispheric fissures and cerebral sulci. Over time these hyper-dense areas become isodense; this only takes days in cases of subarachnoid haemorrhage, whereas for parenchymal bleeds isodensity develops in 2–6 weeks.

Stroke mimics

The diagnosis of stroke mimics is often straightforward, but there are a number of non-vascular conditions which can present with stroke-like symptoms. Non-enhanced computed tomography also plays a role in differentiating stroke from these so-called 'stroke mimics'. There are a number of conditions which may clinically mimic stroke (*Table 3*). The incidence of stroke mimics has been reported as 17% in adults (Hopyan et al, 2010) and 21% (Shellhaas et al, 2006) in the paediatric population. The commonest stroke mimics are

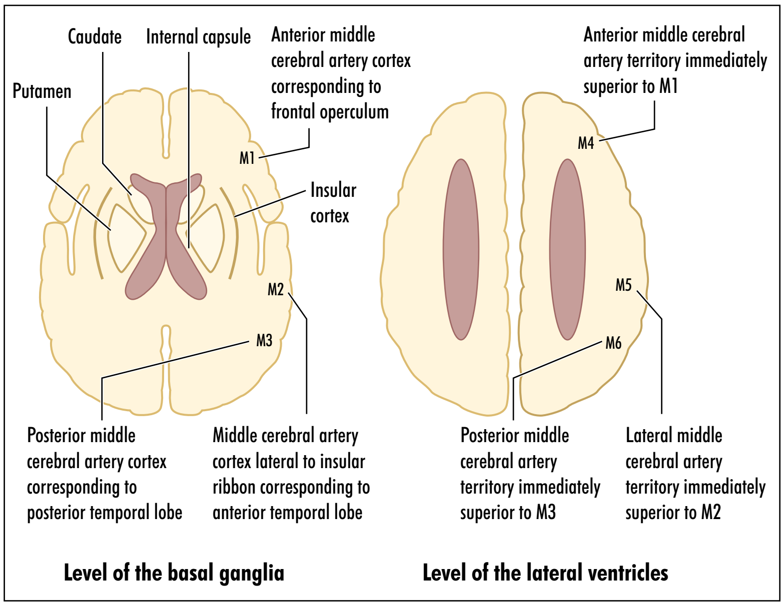

Figure 3. Alberta Stroke Programme Early CT (ASPECTS) anatomical areas.

Figure 4. A hyper-dense focus (arrow) in the left basal ganglia representing an acute intraparenchymal haemorrhage.

reported to be in those presenting with the post-ictal state following an unrecognized or un-witnessed seizure (Norris and Hachinski, 1982; Libman et al, 1995). These can present with transient focal neurological signs including hemiparesis (Todd's paralysis) and hemisensory deficits. Other common conditions responsible for the majority of stroke mimics include systemic infections, brain tumours and toxic-metabolic disturbances (Libman et al, 1995).

Conclusions

The non-enhanced computed tomography brain scan is the first imaging technique for investigation of patients presenting with stroke-like symptoms and signs. In the hyper-acute phase a number of radiological signs reflect the developing ischaemic penumbra, and may also have prognostic value. Their recognition and interpretation, in the given clinical context, are a critical contribution in providing effective brain reperfusion therapy. BJHM

Table 3. Stroke mimics
Post-ictal state
Mass lesion
Primary CNS tumour
Metastatic CNS tumour
Infection
Encephalitis
Brain abscess
Toxic-metabolic problems
Hypoglycaemia
Hyperglycaemia
Hepatic encephalopathy
Subdural haematoma
Hypertensive encephalopathy
Multiple sclerosis
Hemiplegic migraine
Psychiatric problems

Conflict of interest: none.

Adamson J, Beswick A, Ebrahim S (2004) Is stroke the most common cause of disability? *J Stroke Cerebrovasc Dis* **13**(4): 171–7

Barber PA, Demchuk AM, Zhang J et al (2000) Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. *Lancet* **355**: 1670–4

Berger C, Fiorelli M, Steiner T et al (2001) Hemorrhagic transformation of ischemic brain tissue, asymptomatic or symptomatic? *Stroke* **32**(6): 1330–5

Bluhmki E, Chamorro A, Dávalos A et al (2009) Stroke treatment with alteplase given 3.0-4.5 h after onset of acute ischaemic stroke (ECASS III): additional outcomes and subgroup analysis of a randomised controlled trial. *Lancet Neurol* **8**(9): 1095–102

Earnshaw SR, Jackson D, Farkouh R, Schwamm L (2009) Cost-effectiveness of patient selection using penumbral-based MRI for intravenous thrombolysis. *Stroke* **40**(5): 1710–20

Fischer U, Arnold M, Nedeltchev K et al (2005) NIHSS score and arteriographic findings in acute ischaemic stroke. *Stroke* **36**(10): 2121–5

Hacke W, Kaste M, Fieschi C et al (1995) Intravenous thrombolysis with recombinant tissue plasminogen activator for acute hemispheric stroke. The European Cooperative Acute Stroke Study (ECASS). *JAMA* **274**(13): 1017–25

Hoggard N, Wilkinson ID, Griffiths PD (2001) The imaging of ischaemic stroke. *Clin Radiol* **56**(3): 171–83

Hopyan J, Ciarallo A, Dowlatshahi D et al (2010) Certainty of stroke diagnosis: incremental benefit with CT perfusion over noncontrast CT and CT angiography. *Radiology* **257**(3): 142–53

Larrue V, von Kummer R, Muller A, Blumki E (2001) Risk factors for severe hemorrhagic transformation in ischemic stroke patients treated with recombinant tissue plasminogen activator. *Stroke* **32**(2): 438–41

Libman R, Wirkowski E, Alvir J, Rao T (1995) Conditions that mimic stroke in the emergency department. Implications for acute stroke trials. *Arch Neurol* **52**(11): 1119–22

Norris J, Hachinski V (1982) Misdiagnosis of stroke. *Lancet* **i**(8267): 328–31

Renou P, Sibon I, Tourdias T et al (2010) Reliability of the ECASS radiological classification of postthrombolysis brain haemorrhage: a comparison of CT and three MRI sequences. *Cerebrovasc Dis* **29**(6): 597–604

Shellhaas RA, Smith SE, O'Tool E, Licht DJ, Ichord RN (2006) Mimics of childhood stroke: characteristics of a prospective cohort. *Pediatrics* **118**(2): 704–9

Stevens A, Raftery J, Mant J, eds (2010) *Health Care Needs Assessment: the Epidemiologically based Needs Assessment Reviews. First series.* 2nd edn. Radcliffe Medical Press, Oxford: 141–244

von Kummer R, Holle R, Gizyska U, Hofmann E, Jansen O, Petersen D, Schumacher M (1996) Interobserver agreement in assessing early CT signs of middle cerebral artery infarction. *Am J Neuroradiol* **17**(9): 1743–8

Wardlaw JM, Mielke O (2005) Early signs of brain infarction at CT: observer reliability and outcome after thrombolytic treatment – systematic review. *Radiology* **235**(2): 444–53

KEY POINTS

- In ischaemic stroke, subtle non-enhanced computed tomography signs may be seen in the hyperacute (0–3 hours) phase which may confirm the diagnosis and add prognostic information.
- The appearance of stroke on non-enhanced computed tomography is dynamic, and can be completely normal in the hyperacute phase.
- Non-enhanced computed tomography is crucial in differentiating ischaemic from haemorrhagic stroke.
- Non-enhanced computed tomography can be used to quantitatively assess infarct size, which may affect the decision to start thrombolytic therapy.
- Non-enhanced computed tomography frequently identifies unexpected pathology which can mimic the symptoms and signs of a stroke.