Radiological investigation of acute stroke 2: the multimodal approach

Stroke is an important condition with high mortality and morbidity. Radiology plays a central part in the acute stroke management pathway, with its role now widened beyond establishing the diagnosis. This article reviews radiological techniques beyond the non-enhanced computed tomography brain scan.

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 by swift and appropriate management, with imaging central to the management pathway.

The role of radiology has moved beyond the diagnostic role of confirming the diagnosis and differentiating ischaemia from non-vascular aetiologies. Advances in magnetic resonance imaging and computed tomography can provide valuable information regarding salvageable brain parenchyma. Furthermore, interventional neuroradiology, in selected cases, now has a central role in stroke management as treatment has progressed from supportive care to brain reperfusion. The previous article (p. 379) discussed the role of the non-enhanced computed tomography brain scan in recognizing the evolving ischaemic territory, particularly in the hyper-acute setting. This article reviews the radiological techniques beyond the non-enhanced computed tomography brain scan.

Advanced imaging: beyond the non-enhanced computed tomography brain scan

While the non-enhanced computed tomography brain scan is the first-line radiological investigation in managing patients presenting clinically with stroke, improvements in technology have given rise to a multimodal radiological approach. These techniques, using computed tomography and magnetic resonance imaging, can provide valuable information by assessing any potentially salvageable brain tissue. Magnetic resonance imaging is more accurate in demonstrating infarct site and size and, importantly, more sensitive in the early recognition of ischaemic stroke. However, magnetic resonance imaging availability, longer scanning times, patient claustrophobia and specific contraindications currently limit its use as the primary investigation in the acute setting.

The multimodal radiological approach

The multimodal approach using computed tomography and/or magnetic resonance imaging has been summarized as an assessment of 'the 4 Ps': parenchyma, pipes (neurovasculature), perfusion and penumbra (Rowley, 2001). At the authors' institution the multimodal approach uses computed tomography, with the entire investigation and data acquisition process complete within 10 minutes. This comprises:

- Non-enhanced computed tomography: parenchymal assessment and exclusion of haemorrhage
- Computed tomography angiography: evaluation of the cranial and neck vessels
- Computed tomography perfusion: evaluation of potentially salvageable brain tissue.

Radiological evaluation of the cranial and neck vessels

Arterial vessels

Spontaneous dissection of the internal carotid artery and vertebral arteries is an increasingly recognized cause of stroke in young and middle-aged patients (Schievink, 2001). Therefore this diagnosis is important to consider in this patient population presenting with stroke symptoms associated with headache or neck pain in the absence of trauma. Furthermore, imaging the extracranial vessels is an important component of the stroke management pathway, since severe carotid artery stenosis (70–99% by North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria) is a major, yet treatable, risk factor for ischaemic stroke (Grau et al, 2001; Goldstein et al, 2006; Sacco et al, 2006).

Conventional angiography has been historically considered the gold standard for the diagnosis of cervical artery dissection, but non-invasive imaging techniques are now commonly used. Computed tomography angiography produces images of the entire neurovasculature axis, typically from the aortic arch to the circle of Willis (*Figure 1*). The acquired data are used to create multiplanar reformatted images, which are particularly helpful in planning interventional stroke procedures. Internal carotid artery dissections commonly occur just distal to

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the carotid bifurcation or just below the skull base, whereas vertebral artery dissections are most commonly seen at the C1–C2 level. Dissections typically appear as narrowing or tapering occlusion of the contrast-filled lumen, either alone or combined with a contrast-filled false lumen. Another sign is the presence of an isodense mural haematoma causing an eccentric appearance of the lumen.

Figure 1. a. Sagittal and (b) axial computed tomography angiogram images of normal intracranial vessels.

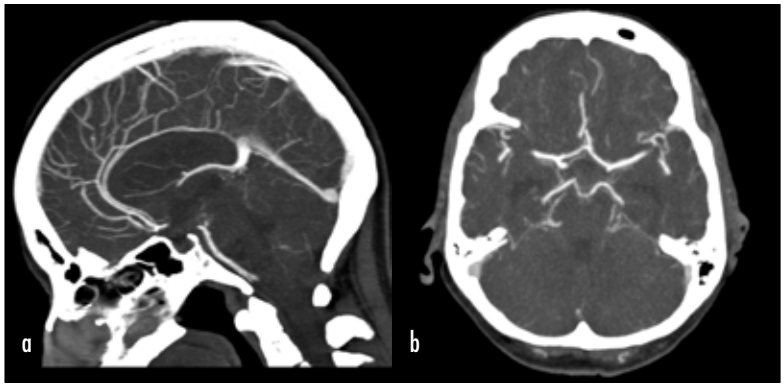


Figure 2. Magnetic resonance images demonstrating a left internal carotid artery dissection. a. On contrast-enhanced magnetic resonance angiogram the dissection is visualized by attenuation of the true lumen of the left internal carotid artery (arrow); compare to the normal right internal carotid artery. b. Standard axial T2W brain image demonstrates a hyperintense clot within the false lumen, adjacent to the flow void of the narrowed vessel lumen (arrow).

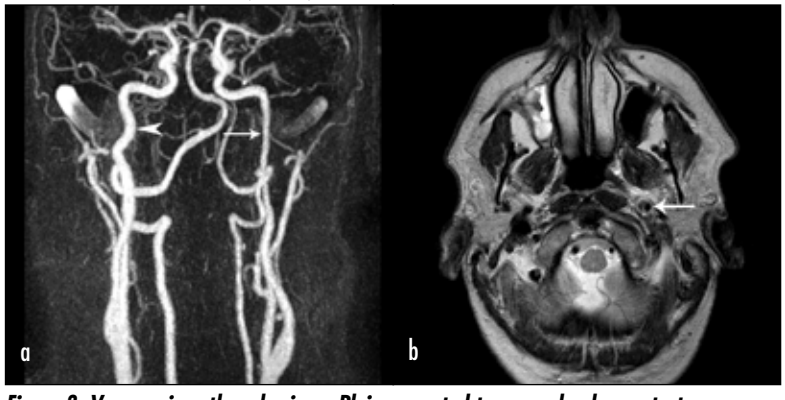
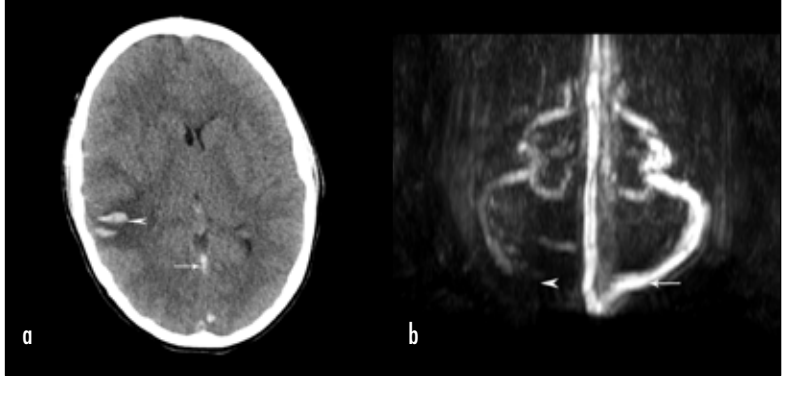


Figure 3. Venous sinus thrombosis. a. Plain computed tomography demonstrates a hyperdense clot within the straight sinus (arrow). A further clot within the transverse sinus (not seen on this slice) resulted in haemorrhagic change (arrowhead) within the surrounding, hypodense infarcted middle cerebral artery and posterior cerebral artery territories. b. Magnetic resonance venography demonstrates a patent left transverse sinus (arrow) and an absent right transverse sinus (arrowhead) as a result of the presence of thrombus.



There are two types of magnetic resonance imaging techniques which assess the vasculature: contrast-enhanced magnetic resonance angiography and time of flight. Contrast-enhanced magnetic resonance angiography acquires images during the first pass of intravenous contrast agent through the arteries whereas time of flight images depend on flowing blood which appears brighter than stationary blood. Contrast-enhanced magnetic resonance angiography is better than time of flight, as time of flight images may not visualize well areas where flow is slow or which are not in an optimal plane. There are potential limitations of magnetic resonance techniques in the first few days following a dissection, such as the hyperintense signal of thrombus obscuring the mural haematoma, and on T1-weighted images a lack of hyperintense signal within the mural haematoma.

Both computed tomography and magnetic resonance techniques are used to investigate craniocervical dissections (*Figure 2*). Computed tomography angiography has been reported to visualize features of cervical artery dissection, such as intimal flaps and pseudoaneurysms, more frequently than magnetic resonance imaging, particularly in cases of vertebral artery dissection (Vertinsky et al, 2008). However, there is currently no clear evidence to support which technique is superior (Provenzale and Sarikaya, 2009). The choice of technique is generally influenced by individual factors such as scanner availability in relation to the urgency of the clinical scenario, other potential coexisting diagnoses and radiologist preference. With respect to the investigation of severe carotid artery stenosis contrast-enhanced magnetic resonance angiography has been reported as the most accurate non-invasive imaging test for carotid artery stenosis (Chappell et al, 2009), therefore contrast-enhanced magnetic resonance angiography is currently more likely to be performed as part of the investigation of transient ischaemic attacks.

Venous vessels

Venous infarction secondary to venous sinus thrombosis accounts for 1% of all strokes, and has been included as it is often misdiagnosed or overlooked. Thrombosis may be directly visualized on non-enhanced computed tomography and computed tomography venography, where thrombus is seen as a filling defect within a contrast-filled vessel (*Figure 3*). Subsequent venous infarcts appear as low-density areas, often sparing the cortex, but unlike arterial infarcts are not confined to arterial vascular territories. The most common radiological pattern is thrombosis of the vein of Labbe and the transverse sinus which causes oedema in the posterior temporal lobe. Haemorrhagic transformation and prominent cerebral oedema are common features, often more pronounced than in arterial infarction. Venous imaging can also be obtained using magnetic resonance with or without contrast.

Radiological evaluation of potentially salvageable brain tissue

Non-enhanced computed tomography shows ischaemic changes of hypodensity which usually delineate areas of established ischaemia, but it cannot demonstrate the potentially salvageable penumbral tissue which thrombolytic therapy aims to benefit. Images derived from computed tomography and magnetic resonance imaging perfusion studies can demonstrate these changes and are therefore of growing interest.

Advanced computed tomography imaging

A computed tomography perfusion study is a dynamic study where a volume of brain tissue is sequentially scanned during injection of intravenous contrast (*Figure 4*). The different components affecting blood supply are displayed on three colour coded 'maps':

- Mean transit time: time taken for blood to flow from the arterial to the venous system or time to peak: time taken for contrast to reach maximal concentration from first arrival
- Cerebral blood flow: rate of blood flow (ml/100g/min)
- Cerebral blood volume: percentage volume of blood in the region of interest.

Mean transit time and time to peak are sensitive indicators of vascular disease and rise early in infarction. Cerebral blood volume may be preserved, or slightly increased in an early infarct or chronic stenosis by regulatory mechanisms, whereas cerebral blood flow in this situation usually falls. The ratio of cerebral blood flow to cerebral blood volume closely correlates with final infarct size, while a severely reduced cerebral blood volume indicates irreversible ischaemia. In simple terms, penumbral tissue is suggested by high time to peak, high mean transit time, low cerebral blood flow and normal or mildly reduced cerebral blood volume. Recently there have been attempts to quantify mean transit time, time to peak, cerebral blood flow and cerebral blood volume levels for ischaemic core *vs* penumbral tissue, but these are not in widespread use.

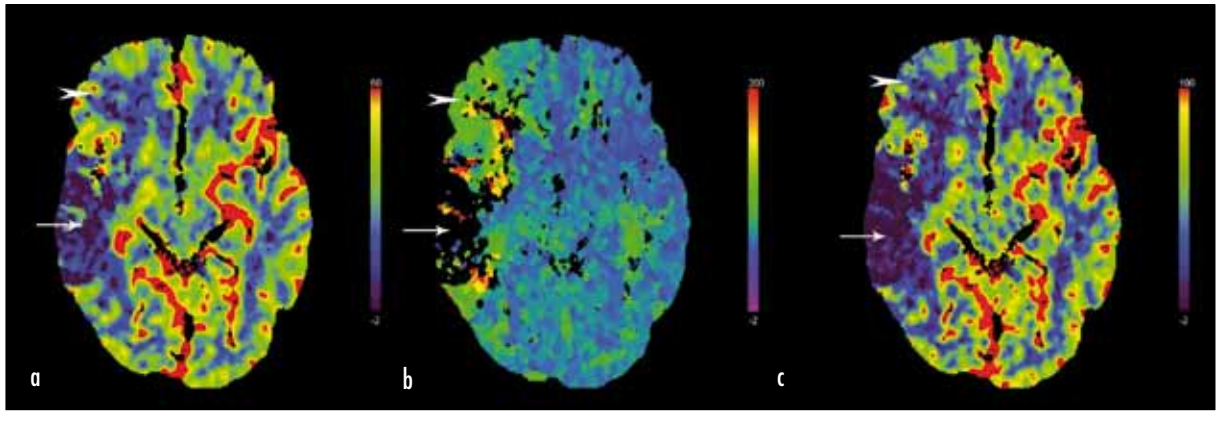
Advanced magnetic resonance imaging

While not the mainstay of acute stroke imaging, advanced magnetic resonance imaging techniques confer certain advantages in diagnostically challenging patients (*Figure 5a*). Specifically, diffusion weighted imaging and perfusion weighted imaging can, taken together, provide superior clinico-pathological information within minutes of an event, and may offer additional prognostic information.

Diffusion weighted imaging is much more sensitive and specific in detecting hyperacute ischaemic changes than non-enhanced computed tomography, although the sensitivity of diffusion weighted imaging in cases of small brainstem lacunar infarcts can be poor. Changes demonstrated by diffusion weighted imaging are visualized within minutes of a stroke and persist for 7–10 days. Diffusion weighted imaging detects the diffusion capabilities of protons within water. In areas of cytotoxic oedema the movement of water molecules is restricted as a result of swelling reducing the volume of extracellular spaces. This effect generates a high/bright diffusion weighted imaging signal (*Figure 5b*), but a high diffusion weighted imaging signal may also be seen if the affected area also has high signal on a standard T2 magnetic resonance imaging image ('T2 shine through'). In order to negate this effect it is important to review the accompanying apparent diffusion coefficient map. On the apparent diffusion coefficient map areas of true restricted diffusion (i.e. ischaemic areas) appear dark (*Figure 5c*). This acute drop in apparent diffusion coefficient signal gradually normalizes by 5–10 days, thereby helping to differentiate the age of a lesion.

Perfusion weighted imaging also provides information about the perfusion status of brain parenchyma using the non-diffusable contrast material, gadolinium. In acutely infarcted tissue, there is a reduction in the amount of

Figure 4. A computed tomography perfusion study demonstrating a right middle cerebral artery territory infarct resulting in areas of (a) decreased cerebral blood volume (arrow), (b) increased time to peak (arrow) and (c) decreased cerebral blood flow (arrow) representing the 'infarct core'. More anteriorly in the right middle cerebral artery territory (arrowheads) cerebral blood volume is relatively well preserved, despite a clear increase in the time to peak and slight decrease in cerebral blood flow, representing areas of penumbral tissue.



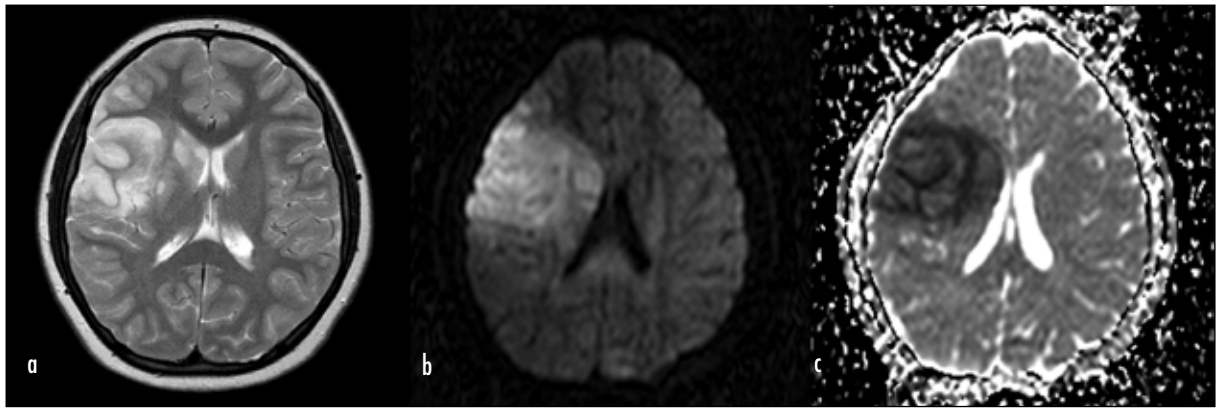
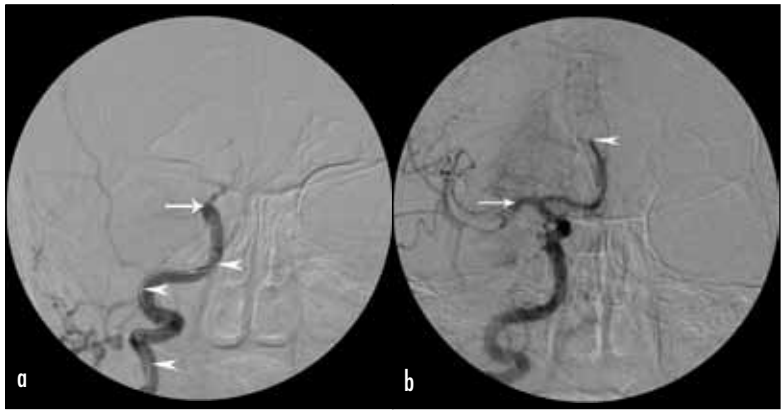


Figure 5. Advanced magnetic resonance studies. a. T2 axial image of an acute right middle cerebral artery infarct demonstrating high signal within the right middle cerebral artery territory. Corresponding areas of (b) high diffusion weighted image and (c) low apparent diffusion coefficient signal.

T1-shortening with gadolinium, seen as a reduction in parenchymal enhancement within the infarcted tissue. These signal changes are used to calculate cerebral blood volume and cerebral blood flow.

The combined diffusion weighted imaging and perfusion weighted imaging information allows a visual assessment of the hypothetical extent of the ischaemic penumbra. Here the ischaemic penumbra can be considered as an area of mismatch between a smaller diffusion weighted imaging abnormality and a larger perfusion weighted imaging abnormality. The timing of diffusion weighted imaging–perfusion weighted imaging is important with reports of up to 80% of ischaemic stroke patients having a diffusion weighted imaging–perfusion weighted imaging mismatch in the first 3–6 hours (Röther et al, 2002; Kidwell et al, 2003); these mismatch areas progressively decrease over time. Theoretically, patients demonstrating diffusion weighted imaging–perfusion weighted imaging mismatch are more likely to benefit from reperfusion therapy than those with a matched diffusion weighted imaging–perfusion weighted imaging defect, indicative of an irreversible ischaemic lesion. Currently there is limited evidence supporting the use of diffusion weighted imaging–perfusion weighted imaging in the acute setting, because of a lack of agreement in defining a mismatch threshold. This difficulty relates to the ischaemic penumbra volume being dependent on ischaemia duration, reperfusion and the presence of collaterals.

Figure 6. Catheter angiogram demonstrating recanalization in an acute stroke patient. a. Digital subtraction angiography demonstrates an occlusion (arrow) in the distal right internal carotid artery. A reperfusion catheter (arrowheads) is in situ and being advanced towards the occlusion. b. Following clot aspiration the internal carotid artery is patent. There is normal filling of the right middle cerebral artery (arrow). A smaller occlusion is now visible in the A2 segment of the anterior cerebral artery (arrowhead).



The role of interventional neuroradiology

Similar to the role of percutaneous revascularization in acute coronary syndromes, there is an emerging role for neurointerventional therapy in the acute stroke setting. These procedures include intra-arterial thrombolytic agents, and mechanical techniques, such as thrombus fragmentation, thromboaspiration, percutaneous transluminal angioplasty and stents (*Figure 6*).

Several studies report improved recanalization rates following intra-arterial thrombolysis compared to intravenous thrombolysis (Rha and Saver, 2007). These improved recanalization rates are also strongly associated with improved functional outcomes and reduced mortality (Rha and Saver, 2007). More recently it has been reported that recanalization rates are further improved following the addition of mechanical thrombolysis, although the effect on mortality and clinical outcome is still unclear (Shi et al, 2010). A drawback of intra-arterial thrombolysis is its association with complications and symptomatic intracranial haemorrhages (Wade et al, 2005). Furthermore, the time to commence neurointerventional therapy also delays the initiation of treatment.

Conclusions

Advanced computed tomography and magnetic resonance imaging techniques include a multimodal approach to assess the '4 Ps' and diffusion weighted imaging and perfusion weighted imaging magnetic resonance imaging technology. These radiological methods can provide superior clinico-pathological information in the diagnos-

tically challenging patient, delineate potentially salvageable brain tissue and treatable severe carotid artery stenosis. Last, the emerging role of neurointerventional radiology has an important role in the active management of brain reperfusion in acute stroke presentations. BJHM

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KEY POINTS

- The role of radiology in acute stroke can now provide greater information with respect to brain reperfusion.
- The radiological techniques beyond the non-enhanced computed tomography brain scan assess the '4 Ps': parenchyma, pipes, perfusion and penumbra.
- Advanced computed tomography and magnetic resonance imaging can demonstrate potentially salvageable brain parenchyma.
- There is an emerging role for interventional neuroradiology therapy in the acute stroke setting.