Imaging techniques in acute disabling stroke

RAD Magazine, 36, 427, 25-26

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Stroke is one of the leading causes of long-term disability and death worldwide. Over the last two decades, acute disabling stroke [ADS] has become a treatable condition with significant improvements in outcome, largely due to stroke unit care and revascularisation with thrombolytics. IV thrombolysis has been shown to significantly improve mortality and morbidity if administered up to 4.5 hours after the onset of symptoms. However, treatment with IV lytics can be complicated by serious side effects, due mostly to either intracranial haemorrhage (6.2% excess of symptomatic ICH from updated Cochrane systematic review) or failure of clot lysis. It is therefore desirable to differentiate between acute stroke sufferers who are likely to benefit from thrombolysis and those unlikely to benefit or who may actually be harmed by the treatment.

Diagnostic work-up aims to stratify the risk of such complications and consists of two main elements: A, exclusion of intracranial haemorrhage and B, accurate assessment of the vascular, morphological +/- physiological status of the brain. We briefly review state-of-the-art imaging strategies and their potential application in the management of patients with ADS. The UK approach to the diagnostic work-up of stroke is driven by the National Institute for Health and Clinical Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN) and the Department of Health through guidelines which state that the main purpose of imaging is to determine whether stroke is haemorrhagic or ischaemic and to exclude stroke mimicking conditions, while identifying people eligible and suitable for thrombolysis.

Non-contrast CT brain imaging (NCCT) remains the principal modality in the urgent investigation of ADS, being accurate, quick and widely available. 24-hour access to NCCT is required and, for those with an appropriate indication, brain imaging should be performed as soon as possible after arrival at hospital (next available suitable scan slot in hours or within one hour at most out-of-hours). The diagnosis of very recent stroke on CT relies on detection subtle signs such as hypoattenuation of cortical or deep grey matter and the presence of brain swelling or oedema. All of these can range from very mild to severe and therefore appear from very subtle to overt on imaging – see figure 1. Identification of a dense vessel such as the middle cerebral artery is suggestive of thrombus and obstruction of blood flow but does not necessarily correlate with infarct size or severity.

The identification of an infarct can be further complicated by the presence of chronic infarction, small vessel disease or other structural brain abnormality. Diagnosing acute infarction on CT can therefore be difficult and may require specialist interpretation to pick up. It has been demonstrated that neuroradiologists are more accurate at diagnosing acute stroke on NCCT. Unfortunately, hyperacutely, NCCT signs of infarct are often very subtle and specialist expertise is not always available; therefore, the main application of NCCT in ADS remains exclusion of intracranial haemorrhage or stroke mimics.

More advanced CT techniques, including CT perfusion (CTP), CT angiography (CTA) and CT venography (CTV), have become widely available over the last few years and the addition of these techniques can further improve detection of infarct, potentially may identify patients with the best potential outcome after thrombolysis and may contribute to widening of the thrombolysis time window in the future. It has to be remembered, however, that the addition of any advanced imaging technique implies a time penalty and delay to treatment in a situation where ‘time means brain tissue’.

CT perfusion (CTP) increases the sensitivity of CT for diagnosing stroke and can provide useful information regarding the penumbra (potentially salvageable ischaemic tissue) and core infarct (irretrievably ischaemic brain tissue). This is done by imaging brain tissue repeatedly following a contrast bolus and deriving cerebral blood flow (CBF), cerebral blood volume (CBV) and mean transit time (MTT) of blood for a given volume of brain tissue using mathematical modelling processing of the time density curve obtained – see
Nowadays, such processing is built into most manufacturers’ software packages. CTP can be a very useful adjunct, particularly in posterior fossa ischemia, which is notoriously difficult to evaluate on NCCT. CTP interpretation relies on the concept that prolonged contrast transit time (either MTT or Time to Peak) identifies ischemic brain whereas cerebral blood volume reduction identifies core infarct. In ischemic but not irretrievably damaged brain CBV is preserved and may even be increased (figure 2). Conversely, in core infarct, cerebral autoregulation breaks down and CBV is reduced. CBF/MTT analysis can be aided by additional reference to CBF maps and values, though the CBF threshold level for differentiating infarct core from ischemic penumbra and normal brain are not clear cut in humans in clinical practice. To date, most studies show expert eyeballing of the colour maps in CTP (or MRP) is as reliable as simple ROI quantitative analysis. Deconvolution algorithms for CTP produce absolute CBF values but other techniques, especially those relying on TTP and utilising only part of the contrast time density curve, provide only relative CBF, analogous to MR Perfusion. Obtaining and interpreting a CTP study can be complex and requires specific training.

There is substantial variation between perfusion algorithms and CT manufacturers, so caution is required in interpreting the results obtained. Most importantly, because current techniques on most installed scanners do not include the whole brain in a single acquisition, infarction can be erroneously excluded if the tissue evaluated does not include the affected brain. Slice placement on older scanners relies on accurate clinical information from experienced stroke physicians/neurologists, which is also not always available in practice. Use of CTP plus the absence of positive signs of infarct on NCCT is an area of clinical practice under active investigation as part of the ongoing IST3 trial.

CTA provides detailed information regarding vascular anatomy and site of vessel obstruction, while collateral circulation and impact on perfusion can be assessed from base images. In cases of haemorrhagic stroke, CTA provides diagnostic information regarding the source of haemorrhage. CTV, is relatively quick and easy to obtain and at least as accurate as MRV in diagnosing cases of suspected cerebral venous occlusion.

In the UK, MRI is less readily available than CT and comparatively more expensive. It is more time consuming and less well tolerated, with 30-40% of ADS patients either failing to tolerate MRI or having a contra-indication to it. The current NICE/DoH recommended indication for MRI is for cases of delayed presentation (more than seven days), though MRI/MRA is often preferred in cases of suspected dissection. The advent of techniques such as diffusion weighted imaging (DWI) and perfusion weighted imaging (PWI) has revolutionised stroke related imaging with MR. DWI can delineate infarcted brain tissue within minutes of the insult (figure 3), while PWI is able to define an area of cerebral hypoperfusion. While it is hypothesised that DWI/PWI mismatch may aid in identifying patients who will benefit from thrombolysis, a recent review found that currently published data do not yet support the routine use of the mismatch hypothesis in clinical practice. Definitive diagnosis of intracranial haemorrhage is possible on MRI with gradient echo sequences and susceptibility weighted imaging.

**FIGURE 2** Identifying “ischaemic penumbra” on CTP. NCCT (a) demonstrates obvious low density right MCA territory with a focal area of prolonged perfusion in the right posterior temporal region on MTT map (blue area in (b) with corresponding reduced area on CBF map (dark blue area on right side in (c). In comparison, the CBV map (d) demonstrates CBV is maintained here, an indication that, notwithstanding the NCCT appearance, this may be salvageable brain tissue. (e) is the CTA from same patient confirming occluded right MCA but with good collateral vessels present (another sign indicating potential for good outcome with active treatment).

**FIGURE 3** (a) T2 image showing right hemisphere oedema from stroke and (b) corresponding DWI image.
imaging (Figure 4). These can delineate micro haemorrhages through detection of the paramagnetic effects of haemoglobin.\textsuperscript{18,19} Micro haemorrhages are considered a risk factor for haemorrhagic transformation, which can impact upon decisions regarding eligibility for thrombolysis.

There are free web-based materials to assist with improving infarct detection and scan reading – the British Association of Stroke Physicians hosts a tutorial on CT interpretation in acute stroke at http://www.neuroimage.co.uk/basp/. The ACCESS study, which informed this article about interpreting CT scans, is ongoing at http://www.neuroimage.co.uk/access/. There, you have the opportunity to review 63 acute stroke CT scans and compare your assessments with those of experts and colleagues in relevant specialties. More clinically focused online teaching via Thrombolysis Masterclass Modules is available at http://www.strokeadvancingModules.org/labyrinth_thrombo/, which embeds imaging within complete, real, clinical cases (supported by Chest, Heart and Stroke Scotland). Strategies in stroke imaging can be explored in more detail via CPD modules or whole courses associated with the University of Edinburgh’s online MSc in Neuroimaging for research – see http://www.neuroimage.ed.ac.uk/eLearninfo/cpd/bitesized.asp.

**Conclusion**

There is little doubt that advanced imaging techniques in acute stroke will have an increasingly vital role in managing stroke patients, in particular in helping to determine the most appropriate intervention(s) for any individual. However, there are some logistical problems such as availability, time delays and specialist interpretative support to overcome in many UK centres.

**References**