

# Role of diagnostic radiology in the management of acute stroke

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## Abstract

This article discusses the clinical efficacy of diagnostic imaging in acute stroke. It compares computed tomography (CT) with magnetic resonance imaging (MRI) according to six different levels of clinical efficacy.

1. Brain imaging will reduce healthcare costs if it prevents the disability and death of stroke victims
2. Brain imaging will improve the clinical outcome of stroke patients if it can identify patients who will benefit from an effective treatment - e.g. thrombolysis
3. To identify patients who will benefit from a certain treatment, brain imaging must provide information relevant to the choice of treatment that is unavailable from other sources
4. This might include imaging techniques that allow the exclusion of brain haemorrhage and other diseases that mimic ischaemic stroke and permit the assessment of ischaemic oedema and perfusion disturbance, mass effect, arterial wall pathology and obstruction
5. The imaging modality should be sensitive and specific for stroke pathology soon after symptom onset
6. In this way, the imaging modality should be technically capable of reliably detecting the relevant stroke pathology

The feasibility of MRI is limited. Both CT and MRI have the technical capacity to exclude acute brain haemorrhage. CT detects irreversibly injured brain tissue with moderate reliability but high specificity. MRI displays ischaemic tissue highly conspicuously and with good sensitivity but cannot reliably distinguish between reversible and irreversible brain damage within the first hours following stroke onset. Both CT and MRI have great therapeutic impact by differentiating haemorrhagic from ischaemic stroke, thus allowing specific treatment to take place. CT has been shown to improve patients' outcome within the first 6 hours following stroke onset and thereby reduce healthcare costs. The extent of early ischaemic oedema that is apparent on CT may identify patients who will not benefit from recanalisation therapy. MRI assessment of acute stroke patients may allow efficacious treatment beyond currently accepted time-windows by applying the perfusion-diffusion mismatch and assessment of arterial occlusion.

## Introduction

It is well established that non-contrast computed tomography (NCCT) identifies patients with acute cerebral ischaemia among patients with a stroke syndrome and thus enables effective thrombolytic therapy.<sup>1</sup> However, there is controversy regarding whether the further information beyond the exclusion of haemorrhage provided by computed tomography (CT) or magnetic resonance imaging (MRI), CT- or MR-angiography (CTA, MRA) or perfusion imaging with CT (CTPI) or MRI (MRPI) can really improve patients' clinical outcome and reduce healthcare costs. In theory, CT – like MRI – can be clinically effective in acute stroke patients on six different levels:<sup>2</sup>

## Feasibility and technical capacity

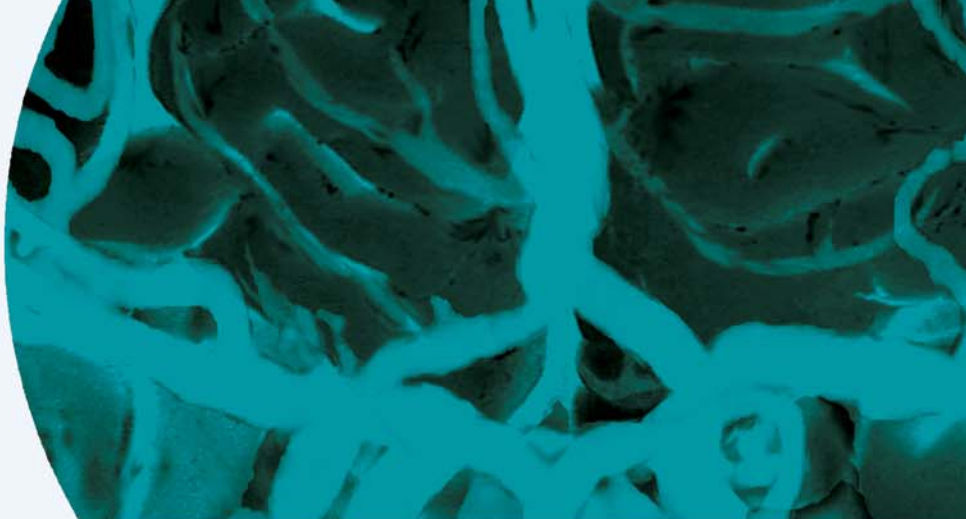
CT is the standard of care in acute stroke imaging. It is widely available, fast and practical, and therefore feasible for routine clinical use. The feasibility of MRI in stroke is limited. Even if 100% availability of MRI is assumed for stroke centres in the near future, it appears that 20–30% of acute stroke patients either cannot tolerate this examination or face specific risks during scanning.<sup>3–6</sup> Consequently, CT should be the preferred modality in patients with severe stroke, MRI contraindications or claustrophobia.

So far, reperfusion strategies have been shown to be beneficial only in acute stroke,<sup>7–11</sup> while neuroprotective drugs have not shown an effect. Consequently, imaging modalities that can reliably exclude brain haemorrhage or assess arterial occlusion, cerebral perfusion deficit

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or ischaemic tissue damage may identify patients who can benefit from thrombolysis. Kidwell *et al* have shown that MRI can detect primary brain haemorrhage as reliably as CT in acute stroke patients and is superior to CT in detecting chronic haemorrhages within the brain parenchyma.<sup>12</sup>

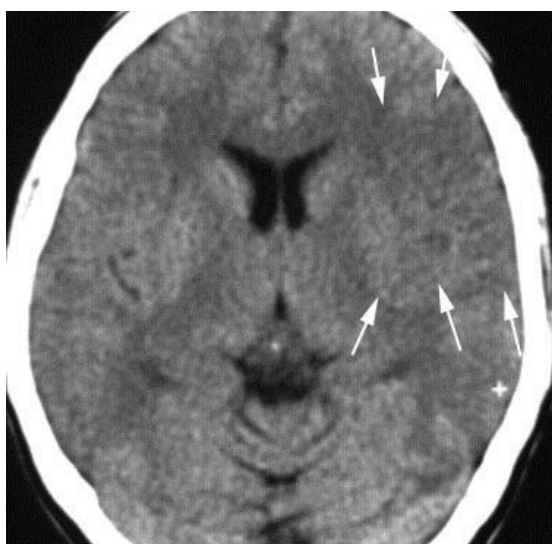


Figure 1. CT in a 37-year-old woman obtained 0.5 h after the onset of aphasia and right hemiparesis witnessed by her husband. The arrows indicate an area with subtle hypo-attenuating brain tissue.

Early after arterial occlusion occurs, it is difficult to detect ischaemic damage, even under the microscope. However, it has been shown that severely ischaemic brain tissue, below the blood flow threshold for structural integrity, takes up water immediately after arterial occlusion.<sup>13,14</sup> CT can detect and measure the change in brain tissue water content and, in this way, determine the volume of irreversibly injured brain tissue.<sup>15,16</sup> Because of the subtlety of the changes (Figure 1), early ischaemic oedema is recognised with only moderate inter-observer reliability within the first hours following stroke onset.<sup>17-19</sup> However, it has been demonstrated that training in CT reading, altering the window width and the use of a semi-quantitative score considerably improves the sensitivity for detecting ischaemic oedema.<sup>20-22</sup>

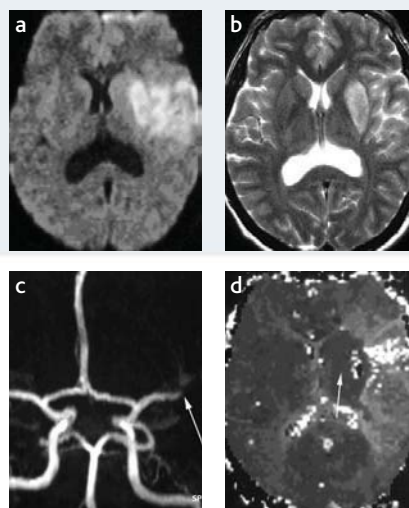


Figure 2. Same patient as in Figure 1. MRI was performed 3 h after CT. On DWI (2a), an almost identical region to that demonstrated with CT shows increased signal. On T2-weighted spin echo sequences (2b), the signal is increased within the lentiform nucleus and the insular cortex. The time-of-flight MR angiography (2c) shows an occlusion of the distal MCA trunk (arrow) resulting in a perfusion deficit on the time-to-peak-parameter map (2d). Remarkably, the left lentiform nucleus (arrow) appears as already hyper-perfused at this timepoint.

The signal of spin echo MRI sequences is relatively insensitive for ischaemic brain oedema, and diffusion-weighted MR-imaging (DWI) does not directly show the volume of irreversible brain injury (Figure 2). The apparent diffusion coefficient (ADC) declines at cerebral blood flow (CBF) values of 30 ml/100 g/min, exactly at the CBF threshold where the extracellular fluid space shrinks due to ischaemic cell swelling.<sup>13,23,24</sup> That means that brain tissue volume with increased signal on DWI and associated decreased ADC may include both irreversibly damaged brain tissue and tissue that can recover if CBF is restored. The increase in DWI signal can be detected with very good intra- and inter-observer reliability.<sup>25</sup>

#### Diagnostic accuracy

Digital subtraction angiography is the accepted gold standard for CTA and MRA in the assessment of arterial obstructions, revealing high accuracy for both modalities.<sup>26-28</sup> However, for the assessment of intracranial haemorrhage and ischaemic oedema,

## Role of diagnostic radiology in the management of acute stroke *continued*

Imanuel Dzialowski and Rüdiger von Kummer

a reference standard is unavailable because surgery or autopsy is, fortunately, not performed in most of these patients.

In summary, NCCT seems to have a rather low sensitivity for brain ischaemia that does not affect the structural integrity of the tissue but a high specificity for irreversible ischaemic injury, whereas diffusion-weighted MRI has a high sensitivity for ischaemia but limited specificity for irreversible tissue damage.

### Diagnostic impact

The diagnostic impact of stroke imaging can be measured by the percentage of patients in whom the diagnosis made without it is changed when imaging information is received.<sup>29</sup> In acute haemorrhagic stroke, MRI does not increase the frequency of this diagnosis, if all patients were examined with CT, but MRI may clarify the cause of brain haemorrhage if gradient echo sequences are applied.

Combining CT or MRI tissue assessment with vascular imaging might allow for estimating tissue at risk for infarction<sup>30</sup> and thereby improve patient selection for thrombolytic therapy. The diagnostic impact of perfusion imaging still needs to be elucidated.<sup>31,32</sup>

The detection of areas with a high signal on DWI may allow assessment of the pattern of affected brain territories and the cause of stroke early on, and signals an increased risk for stroke in patients with transient ischaemic attacks.<sup>33</sup>

### Therapeutic impact

The therapeutic impact of stroke imaging is measured by the percentage of patients in whom the results of imaging changes the treatment originally planned without it. Both CT and MRI have enormous therapeutic impact in distinguishing between haemorrhagic and ischaemic stroke, thus permitting tailored treatment.

In acute cerebral ischaemia, the only effective treatment is intravenous thrombolysis with rt-PA applied within 3 hours of symptom onset or, in patients with middle cerebral artery (MCA) occlusion, intra-arterial infusion of pro-urokinase administered within 6 hours of symptom onset.<sup>7,10</sup> Whereas the National Institute of Neurological Disorders and Stroke (NINDS) rt-PA Study Group used CT only to exclude patients with intracranial haemorrhage, the Prolyse in Acute Cerebral Thromboembolism (PROACT) investigators excluded from the study patients with a hypo-attenuating area on CT exceeding one-third of the MCA territory. The European Cooperative Acute Stroke Studies (ECASS I and II) and prospective data on the use of the Alberta Stroke Program Early CT Score (ASPECTS) support the hypothesis that patients with such a large area of ischaemic oedema do not benefit from rt-PA treatment and have an increased risk for brain haematoma.<sup>8,9,22,34,35</sup>

The therapeutic impact of CTA and CTPI still needs to be proven. However, the finding, using MRI, of an extended brain perfusion deficit but relatively small tissue volume with impaired water diffusion (perfusion-diffusion mismatch) may allow treatment beyond currently accepted time windows. Parsons *et al.* showed a beneficial outcome after thrombolysis in patients with perfusion-diffusion mismatch within 6 hours of stroke onset but did not compare the effect of rt-PA with placebo treatment.<sup>36</sup>

### Impact on patients' clinical outcome

The combined analysis of prospective and randomised stroke thrombolysis trials that included 2,775 patients showed that thrombolysis improves outcome in patients with acute ischaemic stroke as demonstrated by NCCT in a highly time-dependent fashion.<sup>1</sup> The odds for favourable outcome were 2.8 if treated within 90 minutes and were approaching 1 after 270 minutes of stroke onset.



The Desmoteplase in Acute Ischaemic Stroke Trial (DIAS) was based on MRI and included patients with perfusion-diffusion mismatch up to 9 hours after symptom onset.<sup>11</sup> This study showed a beneficial effect of desmoteplase on reperfusion and clinical outcome. Using weight-adjusted doses, the frequency of symptomatic secondary haemorrhage was low. Patients without perfusion-diffusion mismatch were not studied.

Consequently, the impact of MRI findings on patients' clinical outcome remains unclear. However, the study shows that a beneficial treatment effect can be achieved based on MRI imaging only.

#### **Impact on healthcare costs**

Each disabling stroke that is prevented saves estimated lifetime costs of around US\$90,000.<sup>37</sup> It has been shown

that a strategy of CT examination immediately after stroke onset improves patients' clinical outcome and lowers healthcare costs compared with a strategy of scanning no-one. The gain is 78.2 quality adjusted life years and £560,324 per 1,000 acute stroke patients.<sup>38</sup>

#### **Conclusion**

CT is the current standard of care in acute stroke patients presenting within 3 hrs of symptom onset or with a severe stroke syndrome. MRI allows extending the time window for thrombolysis in selected patients and can help triaging patients with transient ischemic attacks. Current experience with imaging supports the view that a rigid time window for stroke interventions can be replaced by the imaging of stroke pathology and functional impairment.

#### **Key Learning**

- CT is the standard of care in acute stroke imaging since it is widely available, fast and practical. The feasibility of acute MRI is limited
- CT only has moderate sensitivity for brain ischaemia but high specificity for irreversible tissue injury
- Diffusion-weighted imaging on MRI has a high sensitivity for ischaemia but limited specificity for irreversible tissue damage
- Both CT and MRI have enormous therapeutic impact by distinguishing between ischaemic and haemorrhagic stroke thus enabling thrombolytic therapy within 3 hours from onset
- Patients with acute ischaemic stroke and extensive area of hypo-attenuation on CT are at higher risk for thrombolysis-related intracerebral haemorrhage if treated beyond 3 hours from onset
- A 'perfusion-diffusion mismatch' on MRI might identify patients suitable for thrombolysis beyond currently accepted time-windows

# Role of diagnostic radiology in the management of acute stroke *continued*

Immanuel Dzialowski and Rüdiger von Kummer

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