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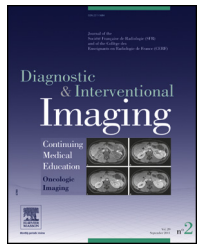

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Patient ''candidate'' for thrombolysis: MRI is essential

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Abstract Because of its excellent sensitivity and specificity to diagnose arterial ischemic stroke (AIS) in the acute phase, MRI answers the main questions to guide treatment in ''candidates'' for thrombolysis. It lasts less than ten minutes, can confirm the diagnosis of AIS and distinguish it from hematomas and other ''stroke mimics''. It can identify the ischemic penumbra (perfusion-diffusion mismatch), determine the site of occlusion and provide prognostic information to adapt treatment in some cases in which the indications are poorly defined. In light of the most recent scientific findings, MRI can guide the treatment turning it into the investigation of choice in ''candidates'' for thrombolysis.

Clinical studies showing the effectiveness of intravenous (IV) rt-PA (recombinant tissue plasminogen activator) in arterial ischemic stroke (AIS) have selected patients based on brain CT. In this case the purpose of imaging was to exclude an intracranial hemorrhagic lesion. The NINDS [1] study, the princeps IV thrombolysis study, was published in 1995 and many improvements have been made in imaging since then. Currently, more sophisticated imaging is often preferred to select candidates for thrombolysis.

The French National Health Authority guidelines published in May 2009 [2] on the management of AIS in the acute phase state: ''patients suspected of having acute AIS must have priority access (24/24 h 7/7 d) to cerebral imaging [...]. MRI is the best investigation to show early signs of ischemia and visualize intracranial hemorrhage. This should be

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performed as the first line examination. If MRI is available as a first line investigation it should be accessible in the emergency settings and short protocols should be preferred [...]. If urgent access to MRI is not available, a cerebral CT should be performed''.

These guidelines stress the importance of accessibility and speed of MRI, which are the prerequisite conditions, in order to avoid delaying intravenous thrombolytic therapy. Rapid MRI sequences (PROPELLER, Echo planar), which are of slightly poorer quality compared to the images used in other situations, can reduce the length of the investigation consistent with the adage ''time is brain'' [3]. MRI can therefore be performed without delaying patient care. The investigation protocol lasts between five and ten minutes and covers the entire brain without radiation. Patient agitation may deteriorate image quality although the information obtained is often sufficient for treatment decision (Fig. 1). Only 10—15% of patients therefore cannot access MRI (severe agitation, unstable hemodynamics or contra-indication) [4].

Some information provided by MRI are essential whereas others await validation, apart from some specific situations (> 4.5 h, age over 80 years old, unknown time of onset, etc.).

The purposes of MRI are listed below:

Primary objectives:
- to exclude hematoma;
- to confirm the positive diagnosis of AIS;
- to exclude differential diagnoses.

Secondary objectives:
- to characterize the infarction;
- to date the infarction;
- to assess the ''core'' of the infarction (necrosis);
- to establish the site of occlusion and collaterality;
- to assess the penumbra.

Primary objectives

To exclude hematoma

In order to exclude intraparenchymal hematoma, the main differential diagnosis from AIS [5—8], MRI performs as well as CT, including during the first few hours after the onset of symptoms. The pattern of hematoma in the acute phase is:
- diffusion-weighted imaging hyperintensity and reduced apparent diffusion coefficient. These can occasionally be confused with those of an AIS although a hematoma presents a more heterogeneous pattern, with magnetic susceptibility effects and a brighter diffusion-weighted hyperintensity than an acute ischemic lesion. This heterogeneous appearance is also seen on the T1-weighted image (performed as the localizing sequence) with a T1-weighted hypointensity (whereas a hyperacute ischemic lesion is usually not seen on T1-weighted sequence) and a leaflike appearance in the periphery;
- pronounced FLAIR hyperintensitity (the FLAIR hyperintensity is unusual in ischemic lesions before 3 hours);
- peripheral T2*-weighted hypointensity consistent with the presence of deoxyhemoglobin (Fig. 2).

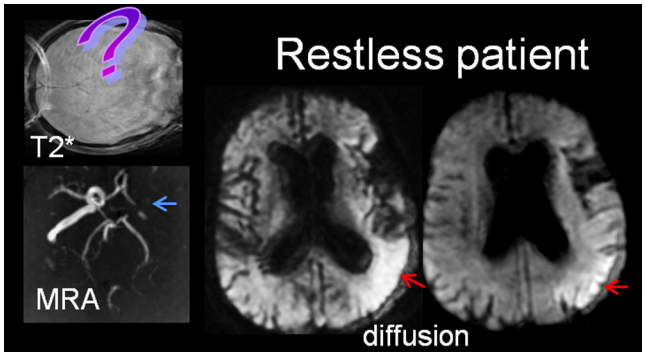

Figure 1. Restless patient during MRI: the diffusion-weighted image shows a hyperintensity in the superficial territory of the left middle cerebral artery (red arrows); MRA shows ipsilateral carotid and middle cerebral artery occlusion (blue arrow); the T2* image shows no hemorrhagic lesion. This information is sufficient to decide a treatment intervention.

Combined analysis of the different sequences, particularly diffusion-weighted and T2*-weighted images avoid missing the diagnosis of hematoma which is a contra-indication to thrombolytic therapy.

Apart from symptomatic intraparenchymal hematoma, the T2*-weighted image may show one or several chronic microbleeds (Fig. 3). These are not seen on CT and may be single or multiple, lying deeply (hypertensive origin), or peripherally (in that case they are suggestive of amyloid angiopathy [9]). In a meta-analysis of 570 patients, Fiehler et al. [10] found no additional risk of hemorrhage from thrombolysis in patients with microbleeds (it should be noted that very few patients had multiple microbleeds in this meta-analysis [10]). The issue of the risk of hemorrhagic transformation and/or cerebral hemorrhage after thrombolysis in patients with numerous microbleeds is still unanswered as this population was not represented in the study reported by Fiehler et al. A trend towards greater risk appeared in a more recent meta-analysis [11], although this did not reach statistically significance.

T2*-weighted images can also assess the presence of hemorrhagic changes and is more sensitive than CT, classifying hemorrhagic changes more severely according to the ECASS classification [12] compared to CT [13] (Fig. 4).

Confirming the diagnosis of AIS

MRI can confirm the positive diagnosis of acute AIS: hyperintensity on the diffusion-weighted images, distributed within an arterial territory, with a homogeneous reduction of the apparent diffusion coefficient (Fig. 5). MRI is more sensitive than CT particularly in the early phase of ischemia [14]. False negatives however can be seen with the diffusion-weighted images: posterior cerebral fossa lesions, small strokes and recent lesions or transient symptoms [15]. An ''optimized'' diffusion-weighted sequence can reduce the number of false negatives [16] (Fig. 6).

Excluding the differential diagnoses

Based on the clinical presentation or even some imaging appearances, a number of diseases may mimic AIS. These differential diagnoses (''stroke mimics'') need to be excluded to avoid inappropriate thrombolysis. Other