REVIEW

Neuro-imaging of cerebral ischemic stroke
Imagerie de l’accident cérébral ischémique

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Summary  Major progress has recently been made in the neuro-imaging of stroke as a result of improvements in imaging hardware and software. Imaging may be based on either magnetic resonance imaging (MRI) or computed tomography (CT) techniques. Imaging should provide information on the entire vascular cervical and intracranial network, from the aortic arch to the circle of Willis. Equally, it should also give information on the viability of brain tissue and brain hemodynamics. CT has the advantage in the detection of acute hemorrhage whereas MRI offers more accurate pathophysiological information in the follow-up of patients.

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Résumé  Des avancées majeures ont été réalisées récemment en imagerie de l’accident vasculaire cérébral (AVC) en raison de l’amélioration des techniques d’acquisition et de post-traitement. L’exploration peut être réalisée soit par des techniques d’imagerie par résonance magnétique (IRM) soit par scanner. L’imagerie doit pouvoir fournir des informations non seulement sur l’ensemble de la vascularisation cervicale et intracrânienne, mais également sur la viabilité du tissu cérébral. Le scanner reste intéressant pour la détection de l’hémorragie à la phase aiguë alors que l’IRM permet une meilleure appréciation des altérations physiopathologiques dans le suivi des patients.

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Introduction

Stroke has been considered a medical emergency for over a decade. This is in part due to progress in therapeutics, but also in diagnostics [1]. Both magnetic resonance
Multimodality imaging of a left middle cerebral artery (MCA) stroke. There is a large hyperintensity on diffusion-weighted imaging (DWI), with a reduction in ADC; the lesion is visible on the T2-weighted image (c), but there is no blood on the T2* images (d). The coronal Flair image shows the extent of the infarct in the frontal and temporal lobes. Contrast-enhanced (f) and intracranial time-of-flight MR angiography show a left MCA occlusion.

Imagerie multimodale chez un patient présentant un infarctus dans le territoire de l’artère cérébrale moyenne (ACM) gauche : sur la séquence de diffusion, il existe une plage étendue hyperintense intéressant le territoire de l’ACM (a) associée à une diminution de l’ADC(b); la lésion est visible sur la séquence en pondération T2 (c), mais il n ’y a pas d’hémorragie visible sur la séquence T2* (d). L ’image Flair coronale démontre l ’extension de l ’ischémie au niveau des lobes frontal et temporal. L ’angio grammie par RM (ARM) avec injection de gadolinium (f) et l ’ARM en « temps de vol » (g) montrent une occlusion de l ’artère cérébrale moyenne gauche.

Imaging (MRI) and computed tomography (CT) have contributed to enormous leaps in neuro-imaging over the past few years. Previously, functional studies of stroke were acquired using nuclear medicine techniques such as PET and SPECT [2]. As for MR, echoplanar imaging began the first revolution by providing ultrafast techniques such as diffusion and perfusion imaging. The development of multiarray CT technology made it possible to achieve both angiographic and perfusion mapping quickly and satisfactorily. Since the principal modern treatment for stroke is thrombolysis, the first goal of imaging is to exclude hemorrhage; it must also demonstrate ischemia itself and then, to determine whether viable tissue is at risk of further infarction, make an assessment of cerebral hemodynamics. Finally, to identify any possible cases of such an event, angiography should be performed. From a technological point of view, the increased availability of even higher-powered field scanners (3 T and more) for clinical use should further increase the diagnostic potential of MRI. Also, in any situation where stroke is clinically and radio-

DWI in a patient with an acute left MCA infarction. On the T2-weighted image, the lesion is visible (a). DWI shows a large hyperintensity on the left MCA territory(b), with a decreased EDC in the corresponding area (c).

IRM de diffusion chez un patient présentant un accident ischémique aigu de l’artère cérébrale moyenne (ACM) gauche. La lésion est visible sur la séquence en pondération T2 (a). En diffusion, il existe une large plage hyperintense intéressant le territoire de l’ACM (b), avec à une diminution de l’ADC dans le même territoire (c).
logically atypical, it may be necessary to also investigate the venous side of the cerebral circulation in search of a thrombosis.

**Magnetic resonance imaging**

Initially, MRI was extremely motion-sensitive and associated with long acquisition times, so it was difficult to perform in a clinical setting of stroke. Then, the advent of faster imaging techniques such as echoplanar imaging rendered it possible to perform an appropriate stroke MR protocol in 20 min or less (Fig. 1) [3]. The main weakness of MRI when used in the diagnostic chain of ischemic stroke management is its unreliability in detecting hemorrhage. However, it is possible to acquire fast diffusion imaging using field strengths of less than 1.5-T and other acquisition schemes such as line-scan imaging [4—7]. In fact, most modern stroke protocols are carried out using 1.5-T echoplanar-capable magnets. However, with the current availability of higher-powered clinical scanners, MRI will again become important: indeed, along with the increasing field strength comes an increase in signal, which should be of great benefit to MR perfusion and angiographic techniques.

**Diffusion imaging**

Diffusion imaging was developed initially by Le Bihan, and uses a modified spin-echo sequence in which diffusion-sensitizing pulses are placed around the pulses [8]. Diffusion imaging with MRI was rendered possible by faster imaging, as it is inherently motion-sensitive. The early onset of ischemia is associated with redistribution of water between compartments, leading to diminished diffusion which, in turn, reduces the apparent diffusion coefficient and increases signaling on so-called diffusion-weighted images (DWI). This has been shown to be highly accurate in detecting early stroke in both animals and humans [9—12]. Diffusion imag-
Right-hemispheric stroke. There is disorganization of the fibers on the reconstructed tractogram in the right hemisphere.

AVC hémisphérique droit. On retrouve une désorganisation des fibres de l’hémisphère droite sur la reconstruction de la tractographie.

has also been shown to be positive as early as 40 min after onset (Fig. 2). However, these lesions may be partially [13] or completely reversible, depending on reperfusion. Thus, the lesion as seen on DWI is neither a stable nor reliable indicator of the final lesion if imaging is performed too early, as the decreases in the apparent diffusion coefficient (ADC) occur in an onion-ring pattern, with the deepest ischemia at the center [14]. However, as time goes by, and the lesion reaches its maximum size and intensity [15,16], DWI will correlate well with both clinical status and outcome [17].

A recent prospective study has demonstrated the superiority of DWI MR-based protocols for the detection of acute ischemia [18]. While most territorial infarcts are well visualized, DWI can reveal the small cortical infarcts (Fig. 3) or lacunes (Fig. 4) that may be missed on CT; in addition, MRI sensitivity allows it to better demonstrate diffuse cortical ischemia or lesions due to hypotension [19]. False-positive findings are few, but do occur, and may involve tumors or infectious processes [20].

Diffusion imaging has also been used to monitor neurovascular interventions [21,22] as well as to demonstrate edema that might occur in venous disorders of the brain [23,24]. The location and multiplicity of the lesions may sometimes help to point towards a possible cause of embolism, be it carotid or cardioembolic [25].

A further development of diffusion imaging is diffusion tensor imaging (DTI) where, in each voxel, small tensors represent the direction and strength of molecular motion. This provides a map of fractional anisotropy, which is of interest as anisotropic changes have been shown to be among the earliest in the development of an ischemic lesion [26].

Wallerian degeneration after stroke. The patient, who suffered a left-sided MCA infarction, shows asymmetry on tractography.

Dégénérescence Wallérienne secondaire à un AVC. Chez ce patient, il existe une asymétrie de la tractographie postis-chémique dans le territoire de l’artère cérébrale moyenne gauche.
Figure 7 Penumbra model. The central ischemic core is seen as a hyperintensity on DWI (a). This area, also visible on the ADC map (b), is surrounded by a larger area of hypoperfused tissue (c).

Figure 7 Concept de la pénombre : le centre de la lésion ischémique est visible sous forme d’une hyperintensité en IRM de diffusion (a). Cette lésion, visible également sur l’ADC (b), est entourée d’une zone plus large de tissu cérébral hypoperfusé (c).

Figure 8 Subacute left MCA infarction. CT perfusion shows hypoperfusion (a). On DWI, there is an area of hyperintensity involving the basal ganglia on the left (b). Susceptibility-weighted imaging (SWI) shows no hemorrhage (c), and there is a slight hyperperfusion due to reperfusion a few days later, seen on arterial spin labeling (ASL) angiography (d).

Figure 8 AVC subaigu du territoire de l’artère cérébrale moyenne gauche. Le scanner de perfusion montre une hypoperfusion (a). En IRM de diffusion, il existe un hypersignal des noyaux gris centraux (b). Absence d’hémorragie sur la séquence de susceptibilité (SWI) (c) et discrète hyperperfusion liée à la reperfusion après quelques jours, visible sur l’angiographie par marquage des spins (ASL) (d).

Figure 9 Left occipital hematoma. In the acute phase (a), the lesion is hypo-intense on the T2-weighted image, and iso-intense on the T1-weighted image. In the subacute stage (b), the hematoma appears hyperintense on T1- and T2-weighted images while, in the late stage (c), it is hyperintense on the T2-weighted image, and hypo-intense on the T1-weighted image.

Figure 9 Hématome occipital gauche. À la phase aiguë (a), la lésion est hypo-intense en pondération T2 et iso-intense en pondération T1. À la phase subaiguë (b), l’hématome est hyperintense en pondération T1 et T2. À la phase tardive (c), il reste hyperintense en pondération T2 et devient hypo-intense en pondération T1.
Figure 10  Left-sided deep hematoma due to hypertension. CT shows high-density signals (a) whereas brain MRI shows a hypo-intense lesion on T2-weighted (b) and T2*-weighted (c) images, and on SWI (d).

Figure 10  Hématome profond gauche d’origine hypertensive. Le scanner montre une hyperdensité de l’hématome (a) alors que l’IRM cérébrale montre une lésion hypo-intense en pondération T2 (b), T2* (c) et susceptibilité (SWI) (d).

(Fig. 5). Also, these DTI data sets allow the reconstruction of fiber tracts, which could be important when assessing recovery and reorganization after stroke (Fig. 6).

Perfusion imaging

Perfusion with MRI has the advantage of providing whole-brain coverage with the most commonly used techniques, using either gadolinium-based chelates or the endogenous contrast of flowing blood. Perfusion with contrast agents is still the MR perfusion technique that results in the most robust data. Indeed, the use of gadolinium chelation leads to a strong signal drop due to secondary changes in local susceptibility [27,28]. Most packages now offer automatic reconstruction of maps of cerebral blood flow (CBF) and cerebral blood volume (CBV) as well as of the mean transit time (MTT) and time to peak (TTP).

The mismatch and the penumbra

Over the years, the exact definition of the penumbra has varied considerably [29], having grown from a neurophysiological model into one that involves compromised hemodynamics. The so-called MR-based diffusion—perfusion mismatch is based on the simple idea that the early central diffusion lesion constitutes an ischemic core that is surrounded by an area of hypoperfusion (Fig. 7) [30]. However, problems with this model arise when confronted by a hemodynamic penumbra instead of the traditional metabolic one. While the mismatch model is not perfect, it is still a working one that allows management of patients. In fact, variations in the mismatch correspond to changes in clinical status. The earlier the imaging is done, the greater the mismatch will usually be, with mismatch alterations occurring over time: the core will tend to expand outwards in the absence of treatment.

Figure 11  Normal time-of-flight MR angiography at both 1.5-T and 3 T. With the latter, the distal branches of the MCA are much more visible.

Figure 11  Angiographie « temps de vol » normale en IRM 1.5-T et 3 T. À 3 T, les branches distales de l’artère cérébrale moyenne sont mieux visibles.
Arterial spin labeling (ASL) techniques

Arterial spin labeling (ASL) allows mapping of cerebral blood flow by labeling blood protons [31—37]. Although the technique has been validated, it does suffer from a decreased signal-to-noise ratio; it will, however, benefit from being acquired at 3 T (Fig. 8).

This technique may also be of great interest due to the current concerns over nephrogenic systemic fibrosis: perfusion without contrast is now possible even in elderly patients who have diffuse vascular disease that may include the kidneys and who are also at risk of kidney failure. In addition, ASL may be able to demonstrate collateral flow, which has been one of the inherent weaknesses of perfusion MRI and which is indispensable when trying to assess cerebral viability [33].

T2* techniques

As already mentioned above, despite the literature showing a clear advantage of MR in the detection of acute hemorrhage, in practice, it remains unreliable. While helpful in assessing the presence of hematoma, whether old or new, MR techniques are known to be more reliable in revealing old hemorrhagic changes [38]: the sensitivity of the method to follow the changes induced by blood degradation makes it the ideal technique for the follow-up of hemorrhagic lesions (Fig. 9). This has been further improved by the development of so-called susceptibility-weighted imaging (SWI) techniques (Fig. 10). While these will also demonstrate hematoma, they are of greatest interest for the investigation of patients who have vascular disease associated with chronic bleeding such as microbleeds.
Figure 14  Cortical venous thrombosis. This large edematous lesion in the right hemisphere shows hypo-intensity on DWI (a), and hyperintensity on coronal Flair imaging (b). MR phlebography shows a thrombosed cortical vein (c).

MR angiography

Traditionally, time-of-flight MR angiography (TOF MRA) provides high-resolution images of the intracranial circulation. For the carotid vessels, a contrast-enhanced sequence that covers the vasculature from the aortic arch to the circle of Willis is preferred [39]. Post-contrast intracranial TOF MRA may be performed if stent or endovascular procedures have been used to assess post-procedural patency of the vessels. MRA techniques are much improved by the increase in signal achieved by imaging at 3 T (Fig. 11).

Spectroscopy and fMRI

MR spectroscopy has the potential to reveal metabolic alterations in cerebral tissue by using either monovoxel or multivoxel chemical shift imaging (Fig. 12). These metabolite maps are better able to show the alterations that may sometimes still be reversible. Also of interest is the use of functional MRI (fMRI) to assess the ischemic cerebrum and its functional recovery (Fig. 13).

Venous disease should also be considered in cases where the ischemic lesion does not respect the usual vascular ter-

Figure 15  Early CT signs of ischemic stroke: there is loss of corpus striatum on the left side.
Figure 15  Signes d’ischémie précoce au scanner : perte de la différenciation des noyaux gris centraux du côté gauche.
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Figure 16 Hyperdense MCA signals (a) and loss of corpus striatum (b) on the right. On perfusion CT (MTT map), there is a large area of diminished perfusion (c). DWI performed the next day shows a massive MCA infarction (d).

Figure 16 Signe de l’artère cérébrale moyenne (ACM) hyperdense à droite (a) avec perte de la différenciation du striatum droit (b). Sur le scanner de perfusion (cartographie du MTT), on met en évidence une diminution de la perfusion (c). L’IRM de diffusion effectuée le jour suivant montre un infarctus étendu dans le territoire de l’ACM (d).

Computed tomography

The main strength of computed tomography (CT) has been its capacity to detect acute bleeding with a high degree of sensitivity as well as to demonstrate the earliest signs of ischemia [40—43]. The accumulation of water in tissue causes the normally gray tissue structures to disappear (loss of gray–white matter differentiation and loss of corpus striatum) (Figs. 15 and 16), and there will also be signs of hypodensity, an important feature because, if hypodensity is found in more than 33% of the territory of the middle cerebral artery (MCA), thrombolysis with rTPA will cause an increase in fatal hemorrhage [40].

Moreover, CT has been revolutionized by the development of multiarray units that allow an even quicker acquisition of an increasing number of slices.

CT angiography

This has the advantage of being able to better, and more easily, demonstrate the difference between calcified and fibrous plaques (Figs. 17 and 18).

CT perfusion

At present, most CT scanners do not provide coverage for more than four slices, which may be insufficient in many cases, especially where cortical or infratentorial areas are involved. However, this technique does provide an acceptable means of mapping blood flow in the MCA circulation (Fig. 19) [44,45]. These measurements have been validated against nuclear medicine methods [46], and have been shown to be highly reliable and to compare well with MR methods [47,48]. In the future, it could even be combined to create some form of PET–CT.

Discussion

Neuro-imaging has recently taken giant leaps and this has had an especially major impact in stroke imaging. Using either CT or MRI, a “one-stop-shopping” approach can now be performed within an acceptable timeframe that will not delay treatment. The aims of imaging are beyond diagnosis, as it should both guide and monitor therapy. However, due to the still widespread use of rTPA for therapeutic thrombolysis, it is necessary first to exclude hemorrhage. Magnetic resonance techniques are more reliable in the follow-up of hematoma. After this subacute phase, and because of the lack of irradiation, MR techniques should be used. Thus, our suggested approach is to perform CT and perfusion CT on the first day at the first timepoint as this allows us to measure perfusion, obtain angiographic images and exclude hemorrhage. On the second day, when the ischemic core has become stabilized, MR will then provide the best indicator of outcome.

The next step is to reveal ischemia. In this case, MRI undoubtedly has advantages because it will clearly show hyperintensity on diffusion imaging, while CT scans are often open for discussion as to whether there is any hypodensity present. However, it is true that, with trained eyes, the early CT signs can often be detected.

MRI with diffusion should also be performed whenever a normal CT scan does not explain what was very likely a stroke. This may be seen in cases with deep and/or small cortical infarcts. Such lesions are rarely detectable with great accuracy by CT, whereas MRI reveals these lesions with the so-called “light-bulb” effect, where they stand out against the dark background.
It is also of major importance that these protocols allow the detection of patients in advance who might not benefit from treatment, but who might suffer secondary hemorrhage. At this time, this is possible using either MRI [49] or CT [40].

Assessing the penumbra is also important, as it is necessary to determine whether a lesion is a final infarction or still growing. So far, penumbra models have been developed based on the diffusion—perfusion mismatch, where only a relatively large mismatch area will benefit from any kind of treatment.

To optimize treatment strategies even further, it may become necessary to directly visualize the embolus to determine its extent and consistency. Indeed, this is especially important when confronted by long thrombi in the carotid that can migrate, and which may have to be extracted mechanically instead of with the use of thrombolysis. CT angiography already helps by demonstrating the type and extent of carotid plaque alterations, as excessive calcification will hinder the use of stents. In addition, the more up-to-date molecular imaging techniques such as PET—CT or MRI use paramagnetic particles that can help to determine the inflammatory or possibly fragile nature of a potentially embolic carotid plaque.

MRI may also provide more precise tissue characterization through the use of a combination of T2*, SWI and CSI techniques that will, in addition to the information provided by perfusion, help to assess the presence or not of a tissue.

Figure 17  Slightly hyperdense MCA sign on the left (a). Angio—CT shows a subocclusion at this level (b) that is also seen on the reconstructions (c).

Figure 17  Aspect discrètement hyperdense du segment M2 de l’artère cérébrale moyenne (ACM) gauche(a). L’angioscanner montre une subocclusion à ce niveau (b), que l’on retrouve sur les reconstructions (c).

Figure 18  Basilar artery stenosis. Narrowing is seen on both the CT reconstructions (a) as well as on digital subtraction angiography (DSA) (b). Axial CT images reveal a fibrous plaque (c).

Figure 18  Sténose du tronc basilaire. Diminution de la lumière visible sur les reconstructions scanographiques (a) et sur l’angiographie digitalisée avec soustraction(b). Les coupes scanographiques axiales mettent en évidence une plaque fibreuse (c).
at risk. This is of particular interest in patients who may be beyond the initial therapeutic 3-h window for rTPA. In these patients, other therapies such as endovascular recanalization may perhaps be considered; it is also important to know if there is a kind of "chronic" penumbra or tissue at risk.

These techniques may also be used in combination with less invasive modalities, such as transcranial ultrasound, to monitor the efficacy of thrombolysis itself while it is being done [50]. However, this cannot be done with either CT or MRI as neither is able to continuously nor safely monitor the flow through a vessel over a long period of time.

Further developments that may provide additional tissue characterization now include PET–CT and, in future, perhaps even PET–MRI (in development), as the possibility of measuring real-time flow rates as well as providing an idea of the local metabolism will certainly help to improve our understanding of these diseases.

Finally, none of these techniques should be used as a stand-alone, but should take into account all of the possible parameters such as the acute neurological status of the patient, the time to admission and the time to treatment. Only when these tools are successfully used in a multidisciplinary environment can their true impact on patient diagnosis and management be fully understood and optimally exploited.

References

