Neuroimaging of Stroke. The Complementary Roles of CT and MRI

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Abstract

Cerebral ischemia or stroke is now considered a treatable medical emergency. This has created the need for powerful diagnostic tools for its determination with accuracy. Computed tomography (CT) and Magnetic resonance imaging (MRI) have known great technological improvements that have paralleled the clinical successes with treatment modalities. While overall equivalent, both techniques have their pros and cons and tend to be more and more accepted as complimentary techniques that may be used either alone or sequentially depending on the question that is being asked. This paper deals with their use alone and in combination for the diagnosis.

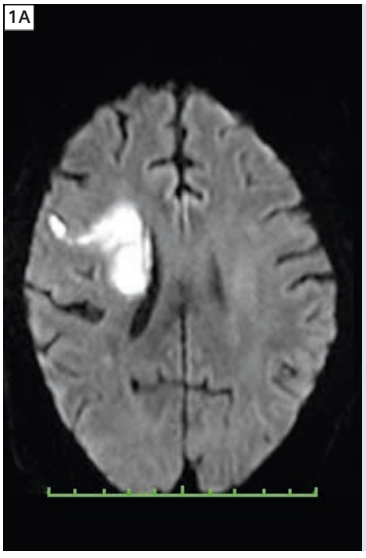
Introduction

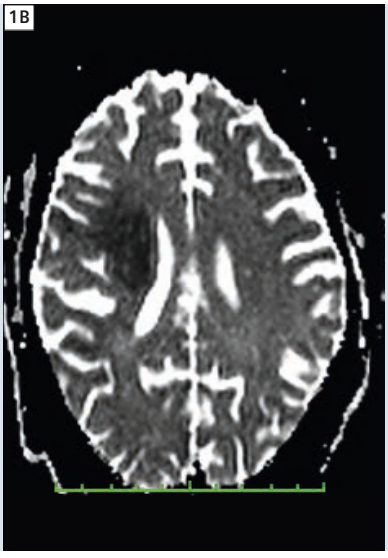
Cerebral ischemia and its resultant pathology, stroke, is one of the leading causes of morbidity and mortality in industrialized countries. This is in part due to the fact that it shares common causes with cardiovascular diseases such as arteriosclerosis among others. While stroke was for a long time considered an untreatable entity for which there was no treatment and where the only outcome at best was a long and difficult period in rehabilitation, over the last two decades, parallel advances in both therapies and imaging have provided the clinician with new options when confronted with these patients.

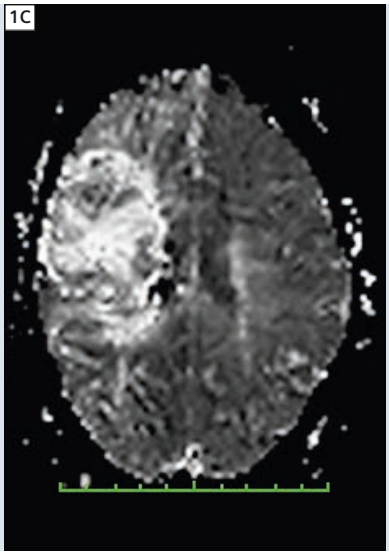
The main objective when confronted with a patient who has acute signs referable to a possible stroke is to exclude another possible pathology that could cause identical symptoms [1].

In the emergency situation, imaging has to perform many roles while being short and not interfering with the time window: it has to exclude another pathology (primarily hemorrhage), detect ischemia, demonstrate occlusion, show hypoperfusion and eventual penumbra and finally determine hemorrhagic risk and eventual outcome.

Since its introduction in the 70's, computed tomography has always played an important role in the management of patients with neurological diseases [2, 3]. Initially for patients with acute symptoms it was mainly used to exclude a very clear cause of neurological dysfunction such as cerebral hemorrhage. However, as knowledge and experience with the use of CT has increased, it has proved itself to be a very powerful tool in experienced hands (or eyes) [4]: one can see early signs of loss of differentiation between white and grey matter as well as signs of sulcal effacement that will eventually precede hypodensity; hypodensity will correspond to the accumulation and increase in water content in the tissue. Frank hypodensity when encompassing more than 33% of the MCA territory

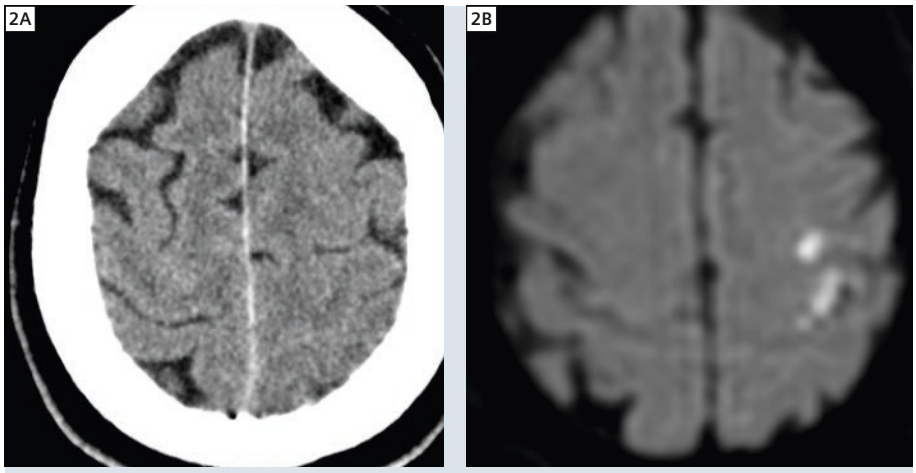






1 Patient with left-sided weakness: there is a right-sided hyperintensity on the DWI image corresponding to ischemia **(1A)** along with a decrease in the ADC **(1B)**, as well as hypoperfusion **(1C)**. The difference between the diffusion lesion and the perfusion area corresponds to the penumbra.

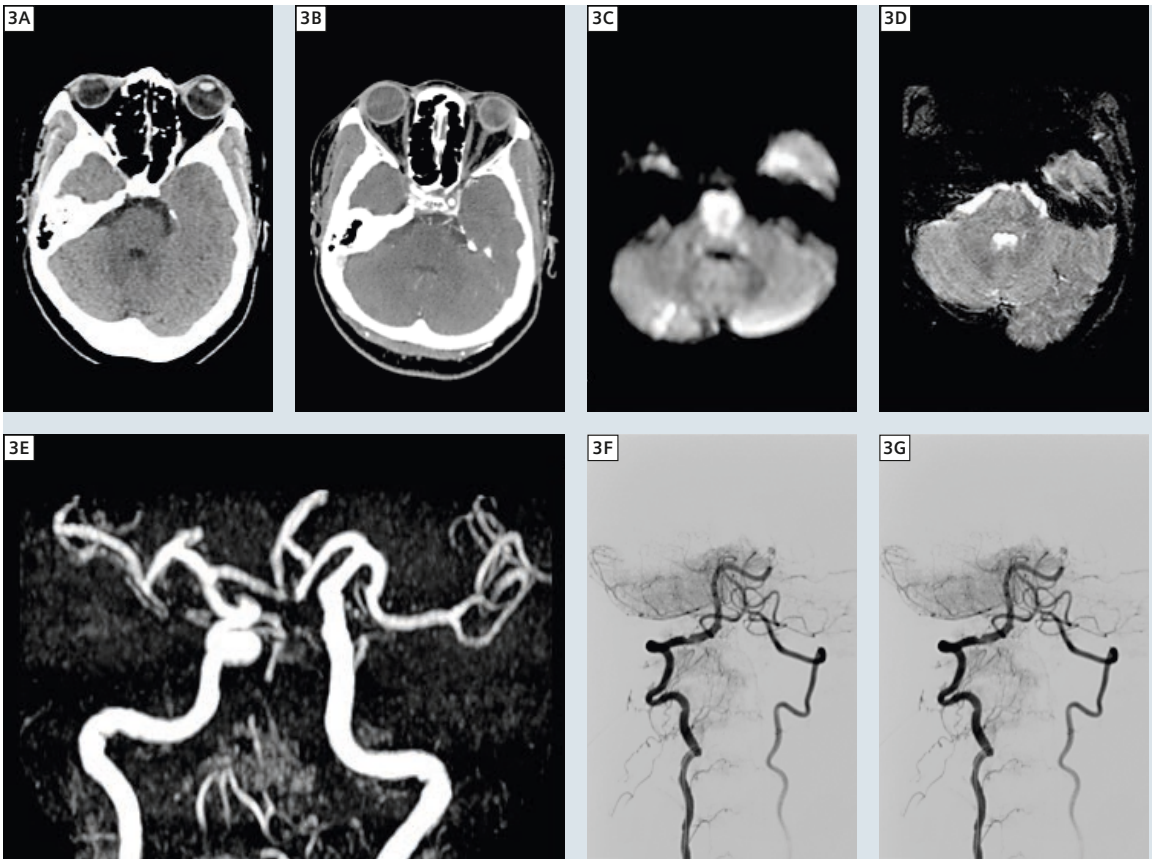
was found to be a contra-indication to the administration of thrombolysis since there was a subsequent increase in mortality [5].
After the publication of the initial NINDS thrombolysis trial [6], as well as the ECAS trial [7], intravenous thrombolysis slowly became accepted as a standard of care for patients with acute stroke. It had the main drawback that therapy was initially considered to be effective only 3 hours after symptom onset (considered to be the 'therapeutic window'). This had two impacts. The first was to look for a way of not just diagnosing but of certifying that one was treating a patient with acute stroke: thus began a new era for neuroimaging to become a marker for acute stroke. The second was to search for more effective drugs and to try to expand the therapeutic window.
Recent evaluation of thrombolysis data has shown that for rTPA at least the therapeutic window is now 4.5 hours [8]. Also there is mounting evidence that mechanical non pharmacological may be performed with improved outcomes [9].



2 Patient with right-sided weakness. The CT shows possible sulcal effacement in the left frontal lobe **(2A)**. The diffusion image shows without doubt that there are many small hyperintense lesions **(2B)**.

The imaging revolution

During the 90's the first real revolution was the clinical implementation of echo-planar imaging capable scanners [10] that would thus allow diffusion [11] and perfusion imaging [12] techniques to move into the clinical arena. This led to the capacity of performing whole brain datasets demonstrating both diffusion lesion and perfusion deficit [13] (Fig. 1).
Diffusion imaging relies on the capacity of a diffusion sequence to demonstrate changes in water distribution between the intra- and extra-cellular compartments that may occur in stroke [14]: on the so-called diffusion-weighted images (DWI) this is associated with a signal increase that can be quantified by assessing the maps of the apparent diffusion coefficient (ADC) that are usually generated at the same time. Initially this led to great enthusiasm due to the high sensitivity [15] and specificity of DWI for stroke and it was even hoped that it might constitute the first step towards the equivalent of an ECG for cerebral ischemia [16].
A very simple MR protocol consists of a T2-weighted image, a T2*-weighted image a Time-of-flight (TOF) MR angiography (MRA) sequence and the diffusion and perfusion sequences, all of which can be done in 20 minutes or less.
Computed tomography had also made some advances since its debut with the development of spiral scanning [16]. While this was initially applied to do examinations of the chest and abdomen, it set the standard for future potential uses in imaging of the neck vessels. Here it was the additional development of multi-slice scanners that allowed one to cover larger and larger areas in shorter times, thus enabling both implement accurate angio-CT of the head and neck vessels as well a brain CT perfusion imaging [17].
Due to a certain facility of use, CT became the leading technique. Indeed, along with some difficulties in its use (magnetic fields, claustrophobia, many sequences), MRI was also considered more difficult to read when it came to the detection of hemorrhage in inexperienced hands. Also, since its use is slightly less time consuming, it has been widely adopted for screening patients with acute stroke that are enrolled in clinical trials or even in clinical routine of thrombolysis protocols.
However, magnetic resonance imaging, due to its capacity to provide a better visual delineation of acute and especially small infarcts [18] (Fig. 2), has become a preferred tool for drug trial where very often an accurate assessment of ischemic lesion volume is absolutely necessary in order to assess drug safety and efficacy [19].
After years of debate and controversy, it has finally been established that MRI can demonstrate hemorrhage probably as well as CT and is better at demonstrating ischemic lesions with DWI (Fig. 2).
The penumbra concept, which has evolved substantially from its initial description, has been a cause of some controversy. Indeed, it was first a situation in which neuronal dysfunction was caused by decreased blood flow and thus cellular damage [20]. Since it was somewhat unclear in its scope and exact definition the area was called the penumbra. From this initial description of this entity, the clinical concept has evolved towards an imaging-driven one where the penumbra is seen as an area of hemodynamically impaired brain and not one of synaptic dysfunction. However since it is the hemodynamics that are at its basis, both kinds of penumbra – overall, or at least from a clinical point-of-view – can be considered the same in order to have a working hypothesis towards implementation of treatment. It is for this reason also that one prefers to speak about tissue at risk and not just about penumbra.



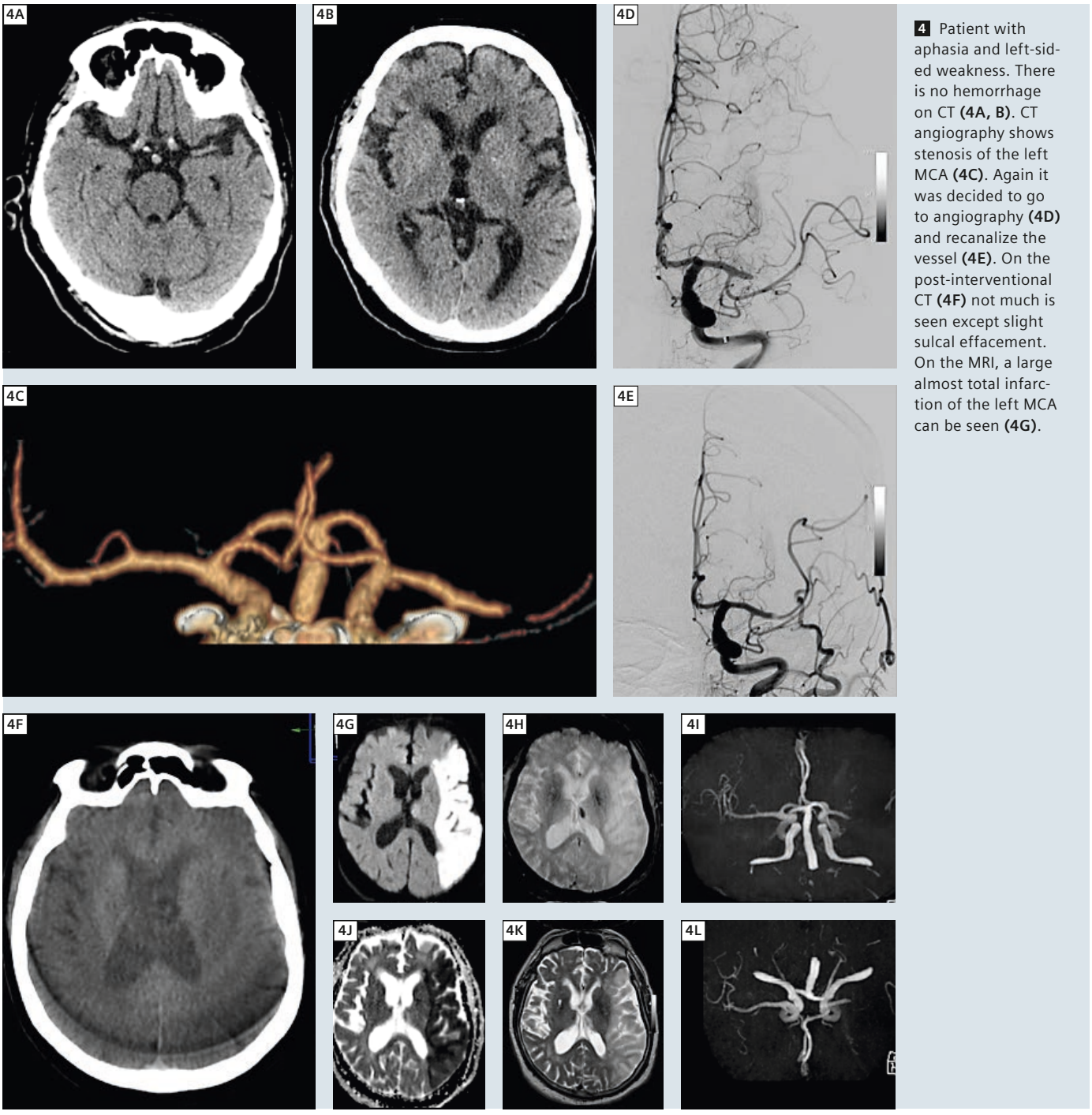
3 Patient with acute posterior fossa symptoms. The CT is not conclusive and does not show any clear signs of hypodensity **(3A, B)** while there is non-opacification of the basilar artery **(3B)**. The diffusion image **(3C)** shows a clear ischemia in the central pons but no signs of hemorrhage on the T2*-weighted image **(3D)**. Angio-MRI confirms occlusion of the basilar artery **(3E)**. Based on the presence of ischemia and occlusion but no hemorrhage it was decided to go to angiography and intervention **(3F)**. After intervention there was reperfusion of the basilar artery **(3G)**.

Initially the MR penumbra concept was based on a simple visual subtraction between the hypoperfused area and the smaller central initial DWI lesion. While rather imprecise and probably inexact, it provided the clinicians with an initially functioning model to use to monitor disease and interventions.
When considering the ischemic brain, one point that has always been considered elusive, at least with CT and MRI, has been the capacity to detect collateral flow. Indeed, since from a physiological point-of-view, a drop in blood flow is very quickly followed by neuronal death, perfusion is maintained at least by a collateral system of present. This is an observation that is very often made by interventional neuroradiologists, and an area where planar (CT and MRI) imaging has failed somewhat. However it is becoming increasingly evident that at least a partial image of collateral flow can be seen on post-contrast CT images where very often dilated collateral vessels will appear or on MRI where arterial spin labeling (ASL) seems to be able to demonstrate at least in some instances the presence of collateral circulation. This may be especially relevant in cases that arrive at the hospital beyond the therapeutic window: indeed, in any case, based on imaging there may still be a potential tissue at risk, or little signs of secondary hemorrhage so that these patients may indeed benefit from the use of a non-pharmacological intervention. The typical case will be a patient arriving with symptoms after 5 hours where intravenous rTPA is thus contra-indicated but where MRI reveals only a small lesion with a surrounding hypoperfusion: this candidate may be amenable to clot extraction and/or stenting based on imaging findings.

The strengths of CT and MRI

A strength of magnetic resonance imaging is clearly its capacity to demonstrate even small lesions that will be often invisible or only visible to the trained eye.

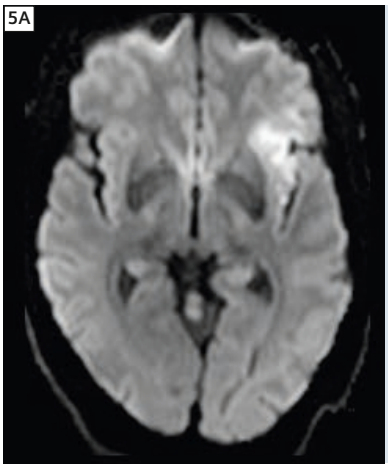
Magnetic resonance provides whole brain coverage with both diffusion and perfusion sequences; additional techniques such as ASL and susceptibility-weighted imaging (SWI) can provide unique information on the ischemic brain. Very often MRI can provide a diagnostic result in patients where the initial CT is not conclusive (Fig. 3). MRI also remains non-ionizing, which is of prime importance if one considers patients that require frequent follow-ups. This is why, even in patients who have had an initial CT, MRI is to be preferred for follow-up: on the second day DWI will be able to demonstrate the exact extent of the lesion and thus allow one to obtain a better delineation of the final lesion extent (Fig. 4). As already explained, arterial spin labeling is a technique using labeled blood as an endogenous tracer: this has been shown to produce images of cerebral blood flow but also shown able – at least in part – to obtain images containing information about collateral flow [21] (Fig. 5); this could be of advantage

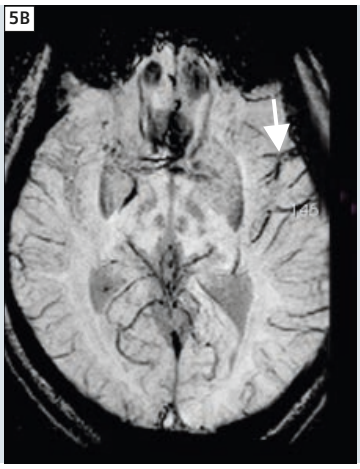


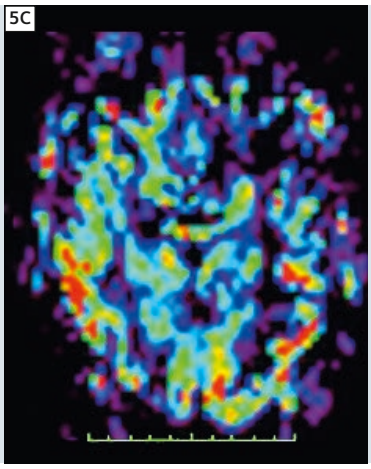
4 Patient with aphasia and left-sided weakness. There is no hemorrhage on CT **(4A, B)**. CT angiography shows stenosis of the left MCA **(4C)**. Again it was decided to go to angiography **(4D)** and recanalize the vessel **(4E)**. On the post-interventional CT **(4F)** not much is seen except slight sulcal effacement. On the MRI, a large almost total infarction of the left MCA can be seen **(4G)**.

in cases of strokes again beyond the therapeutic window and where the outcome could be improved by some kind of treatment. SWI, due to its inherently strong T2* weighting, could help to demonstrate the well known venous stasis that is present in severe cases of stroke [22]; it can also demonstrate small bleeds better, and there have been some instances where it has been shown to demonstrate changes referable to the altered oxygenation in these tissues [23] (Fig. 6). The use of higher fields such as 3T has enabled an improvement in perfusion techniques and the implementation of SWI and ASL clinically [24]. In addition, new high-resolution angiography techniques should allow one to investigate the vessels both intra- and extracranially (Figs. 7 and 8).

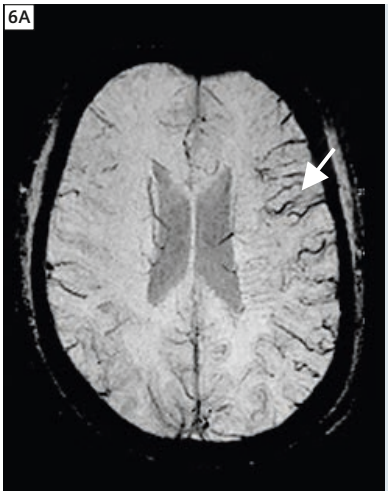
A CT is very often more accessible since there is no need to screen often unconscious or uncooperative patients for metallic implants; the room can also be entered more quickly by an emergency team that does not have to remove pens, scissors and wallets from their pockets

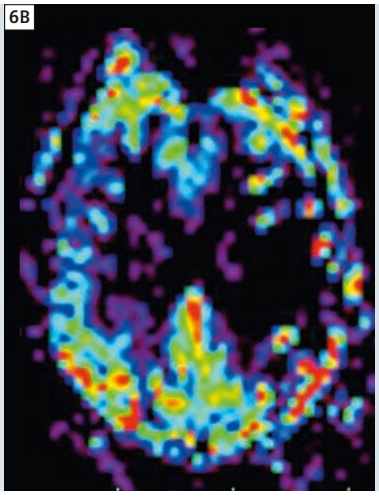


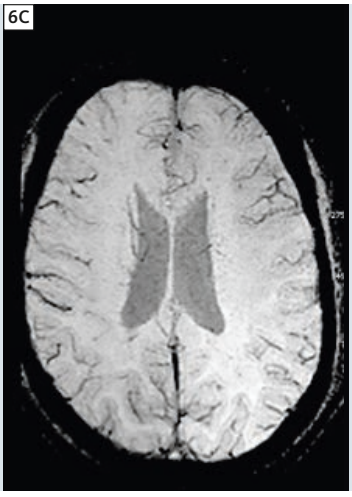




5 Patient with left-hemispheric stroke: on DWI there is a small cortical lesion **(5A)**, as well as some dilated vessels seen on SWI **(5B)** (arrow), ASL shows a large area of hypoperfusion.







6 Patient with a left hemispheric stroke: on initial SWI **(6A)** there are cortical dark prominent vessels (arrow) in the area of hypoperfusion seen on ASL **(6B)**; after thrombolysis these dark vessels have disappeared **(6C)**. Also after thrombolysis the left MCA territory is more hyperintense, reflecting the changes in local oxygenation.

before placing the patient on the table. Also, until recently the gantries of CT scanners gave the team a better view of the often unstable and sometimes intubated patients so that they could be monitored more safely during the examination.

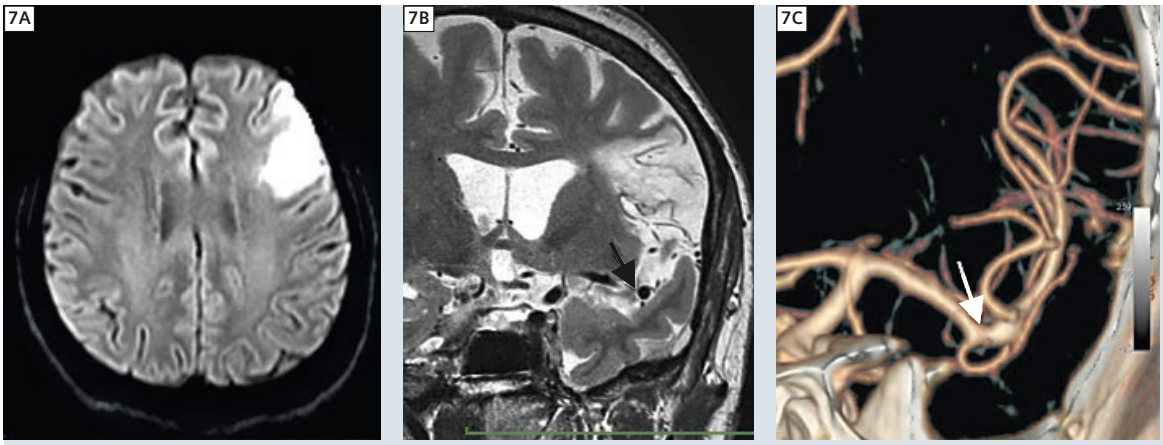
The typical situation where CT and MRI are both going to be necessary are the cases of less acute situations, where an initial CT and CT angiography (CTA) shows a lesion maybe not amenable to thrombolysis but which necessitates a more thorough work-up because of the underlying disease. This is the case in carotid disease, where patients either present with a stroke or with stroke-like symptoms. The initial CT may initially be normal despite the patient having certain clinical signs of acute stroke: in these cases going to MRI can be very helpful. This will be the case for small cortical lesions. It will typically be the case in patients with severe carotid stenosis, where CT has often been done since CTA will provide the best delineation of vascular calcification, but where MRI can provide two additional findings: the demonstration of small ischemic emboli in the brain and local demonstration of the presence of plaque hemorrhage (Figs. 9 and 10).

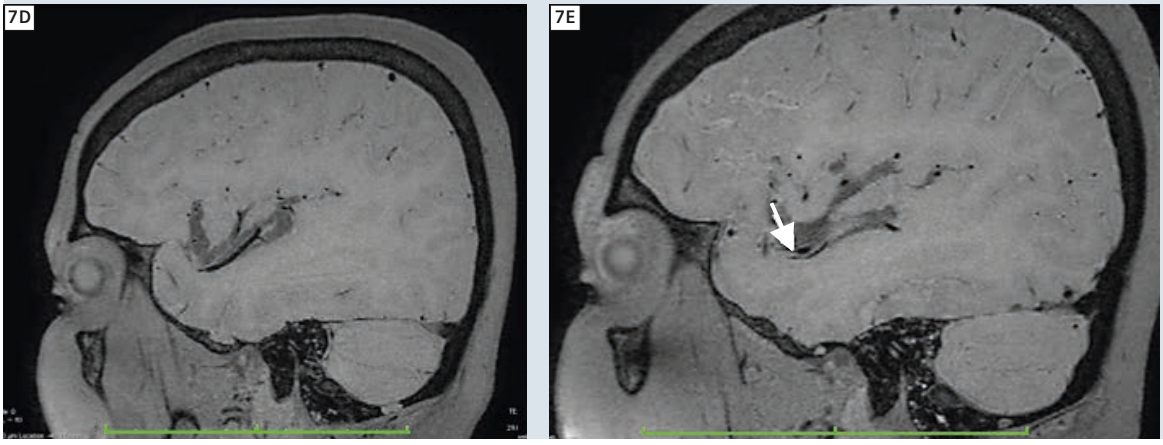
Future perspectives

Whenever one considers the etiologies of stroke, local carotid plaque vulnerability is going to be a key factor. Thus, the idea of performing any kind of 'molecular' imaging that would allow to determine which plaque is more 'active' and more prone to eventually seed emboli is very seductive. This could be done either by MRI using either SPIO contrast materials, or even by conventional contrast media or some combination of a nuclear medicine technique with a radiological method (CT or MRI) to produce combined hybrid imaging.

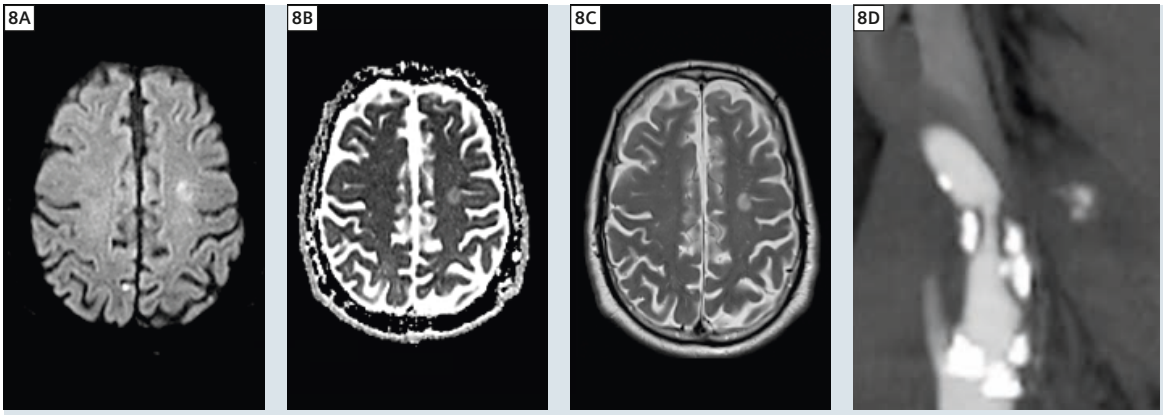
Conclusions

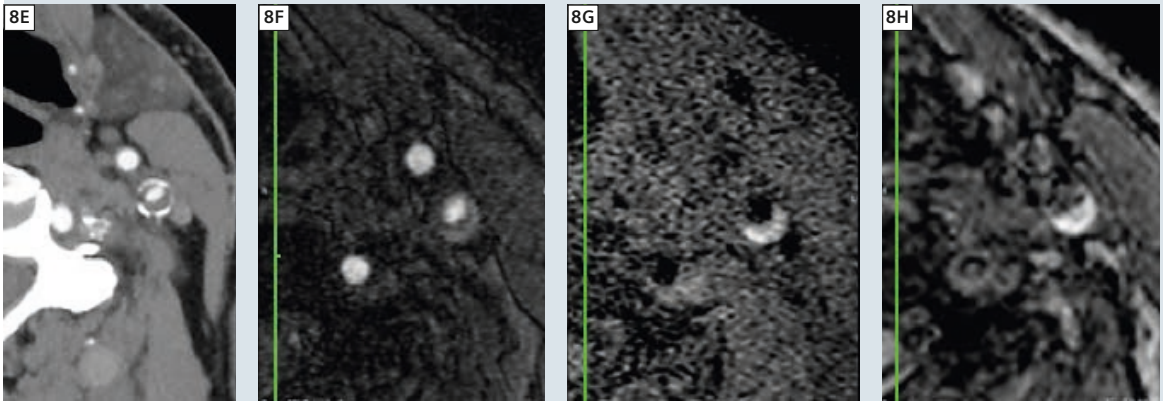
From a radiological point of view we are now at a crossroads where we deploy two advanced techniques, CT and MRI. These techniques are equally useful since they have complementary pros and cons: MRI is more sensitive to ischemia, but CT can more clearly demonstrate hemorrhage; CT angiography may provide a more correct luminographic effect and demonstrate plaque calcification better. Both techniques can be utilized in first intention with almost comparable results, but this depends often on local logistics. However, in complex vascular situations it becomes increasingly clear that one needs both



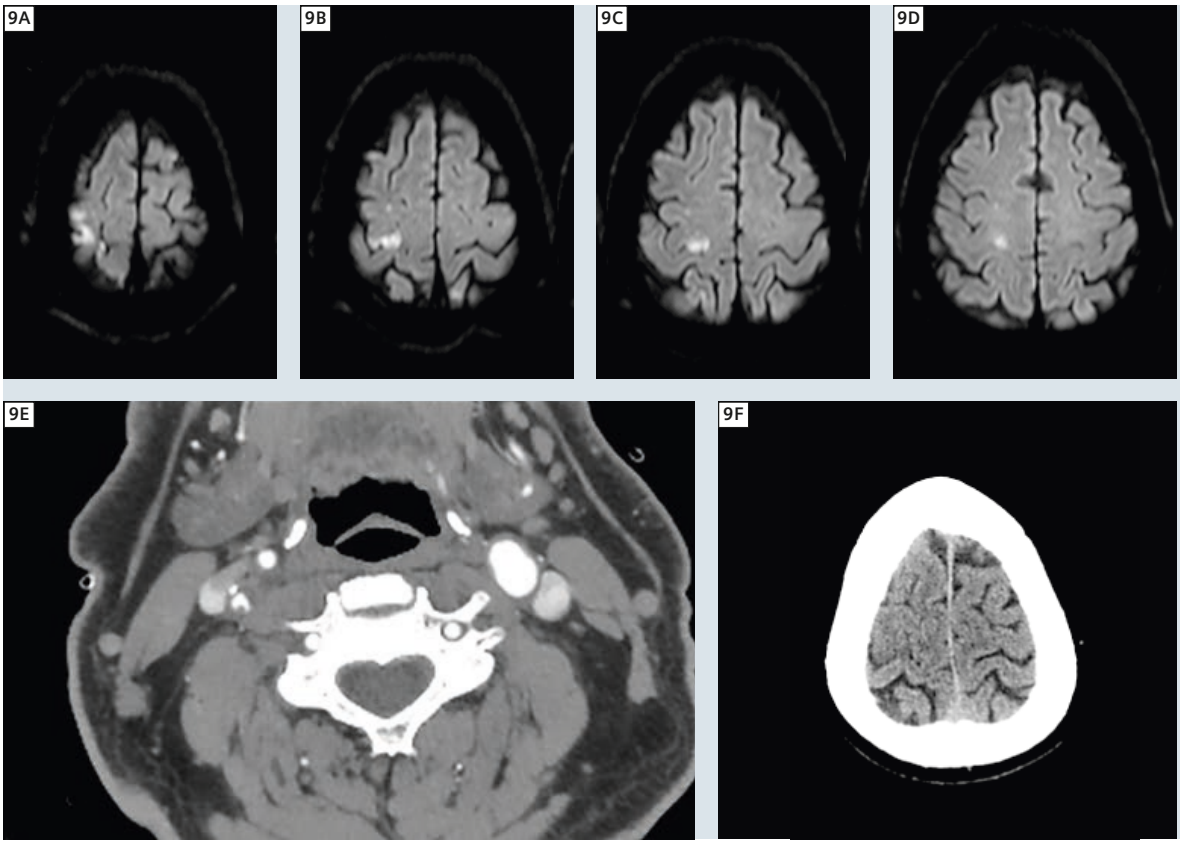


7 Patient with an intracranial stenosis and a frontal opercular infarction on the left. The DWI image shows a left frontal lesion **(7A)** and the high resolution MRA images show the stenosis (arrows).

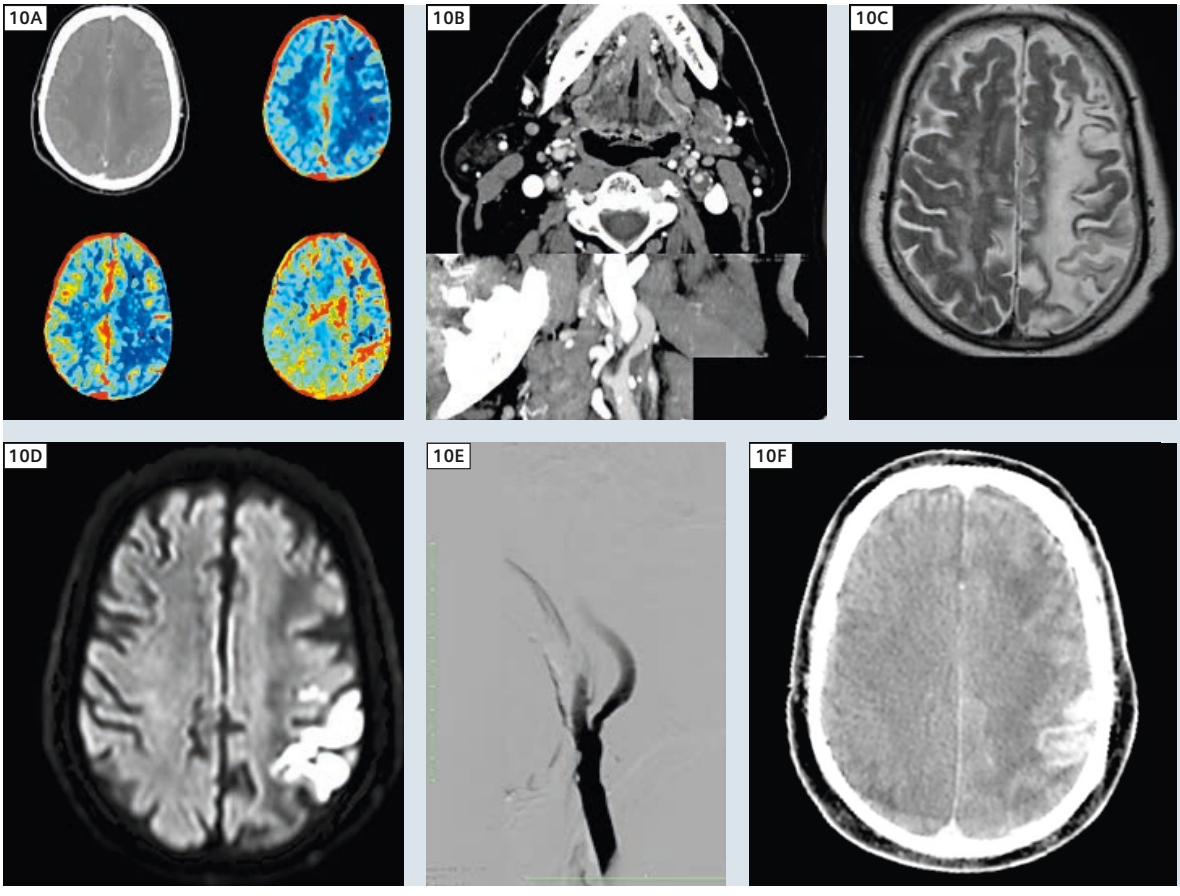




8 Patient with a tight stenosis of the left ICA, as well as cortical lesions **(8A–C)**. The carotid artery is calcified on CTA **(8D, E)** and on MRI there is a hemorrhage visible in the plaque **(8F–H)**.



9 Patient with a high-grade carotid stenosis on the right, seen on CTA. On the diffusion images one can clearly see the many ischemic cortical lesions **(9A–D)** that can only be seen retrospectively as a slight cortical swelling on the CT **(9F)**.



10 Patient with acute stroke. There is hypoperfusion on the perfusion CT but not clearly any new lesion visible **(10A)**. On T2 there are extensive alterations in the brain parenchyma **(10C)**. On DWI one can see that there is a recent ischemic cortical area that explains the new symptoms **(10D)**. Angiography revealed a carotid stenosis **(10E)** and CT after angiography showed luxury perfusion in the ischemic territory with contrast accumulation but no blood **(10F)**.

the information from the CT, which can better exclude hemorrhage and demonstrate vascular calcifications, and from the MRI, which has an inherently higher contrast to demonstrate small cortical lesions that will explain the patient's status.

Magnetic resonance is also mandatory for follow-up examinations: not only does it allow one to determine exact lesion extent, but it will also help determine prognosis based on this finding. Indeed, it has been demonstrated that both acute and late ischemic lesion volumes do correlate with clinical status and outcome [25].

The progresses and improvements in imaging that have been made in the last two decades have been enormous and have allowed us not just to improve diagnostic quality but also to gain insights into the disease processes that are ongoing so that therapy can be planned optimally and the follow-up can be as precise as possible. Thus, any stroke service should not rely on only CT or only MRI but use both in an optimized and optimal way in order to improve patient outcomes and safety.

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