A Brief Overview about Possible Imaging Modalities of Stroke

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Abstract
Background: NCCT is the main imaging modality for the initial evaluation of patients with suspected stroke, allowing clinicians to identify hemorrhage, which produces a good contrast between the "bright", high attenuating clot, and the "dark" low attenuating cerebrospinal fluid . This is crit- ical in selecting patients for intravenous thrombolysis (IVT) via tissue plasminogen activator (t-PA) within 4.5 hours since hem- orrhage is an absolute contraindication and must be excluded . Moreover, the presence of various early ischemic changes (EIC), including parenchymal hypoattenuation, cortical sulcal effacement , and loss of grey-white matter differentiation may be visualized up to 6 hours from symptom onset and inform treatment decisions. CT angiography (CTA) is a bolus contrast tracking technique that can be used to visualize the macrovasculature from the aortic arch to the cranial vertex within 15 s . Spatial resolution is excellent and in fact superior to most clinical magnetic resonance angiography sequences. In conventional CTA, an optimal intravenous contrast bolus profile consists of a rapid rise, plateau of peak enhancement, followed by a rapid fall. Scan acquisition is triggered by contrast bolus-arrival in the aortic arch, which is designed to capture images at the peak arterial enhancement phase . Multiphase CT angiography (mCTA) was developed in an attempt to obtain temporal information by tracking the bolus beyond the peak arterial phase . By repeating the CT acquisition in 1 mm slice increments following a delay of 7–8 s and another 7–8 s, images of the vasculature in the late arterial and venous phases can be obtained.
Keywords: vasculature, acquisition, hypoattenuation, attenuating

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Introduction
NCCT is the main imaging modality for the initial evaluation of patients with suspected stroke, allowing clinicians to identify hemorrhage, which produces a good contrast between the "bright", high attenuating clot, and the "dark" low attenuating cerebrospinal fluid . This is crit- ical in selecting patients for intravenous thrombolysis (IVT) via tissue plasminogen activator (t-PA) within 4.5 hours since hem- orrhage is an absolute contraindication and must be excluded . Moreover, the presence of various early ischemic changes (EIC), including parenchymal

hypoattenuation, cortical sulcal effacement , and loss of grey-white matter differentiation may be visualized up to 6 hours from symptom onset and inform treatment decisions(1).

Furthermore, a “hyperdense vessel” sign may be visualized on NCCT, providing evi- dence of a possible intraluminal thrombus indicative of a large-vessel occlusion (LVO). However, this hyperdense sign has limited clinical use because its diagnostic capability varies by location, often with high specificity but poor to moderate sensitivity **(2).**

NCCT is used to detect haemorrhage and is considered a reliable method for distinguishing haemorrhagic from ischaemic cases in the acute phase .However, the early infarct core is not detectable by NCCT. It can only be used to detect the infarct core in the late stage of stroke when a hypodensity is clearly visible **(3).** NCCT imaging of the brain parenchyma is fundamental to the selection of patients for all acute stroke therapies. In addition to ruling out intracranial hemorrhage, NCCT can also be used to estimate the extent of early ischemic injury.

Early NCCT signs of ischemia include sulcal effacement and decreased x- ray attenuation resulting in loss of gray-white matter differentiation. Isolated sulcal effacement reflects venous dilation and elevated cerebral blood volume, which is not always associat- ed with irreversible injury. In contrast, the loss of gray- white matter tissue differentiation indicates cytotoxic edema that results from a failure of ATP-dependent processes within neurons/glia and subsequent cell death. This ultimately results in fluid shifts from the intravascular compartment into the brain parenchyma, reducing tissue density and therefore x- ray attenuation. The rate of this process is highly vari- able, but always lags the changes seen on diffusion- weighted MRI. Nonetheless, NCCT remains the stan- dard initial diagnostic investigation in most stroke centers worldwide due to ease of access and shorter acquisition time **(4).**

FIG. 1 : NCCT scan showing infarct core (red border) in the right hemisphere (left in the image) one week after the stroke(3).

CT-angiography

CT angiography (CTA) is a bolus contrast tracking technique that can be used to visualize the macrovasculature from the aortic arch to the cranial vertex within 15 s . Spatial resolution is excellent and in fact superior to most clinical magnetic resonance angiography sequences.

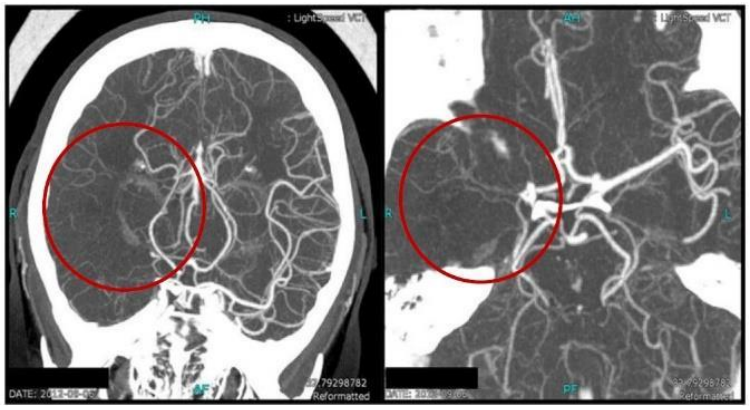

Fig.2: A CTA scan showing absence of the middle cerebral artery (MCA) (red circle) on the right hemisphere (left in the image). Image courtesy to (5).

Extracranial Vascular Imaging:

Extracranial CTA provides important stroke etiological information, including potential proximal embolic sources such as atheromatous lesions, arterial dissection, aneurysms, and thrombi anywhere from the aortic arch to the base of the skull. It has become the de facto standard of care for imaging the carotid bifurcation, as it allows visualization of extracranial atherosclerotic plaques, demonstrated as luminal irregularity/filling de- fects, stenosis, or occlusion **(6)** Two-dimensional maximum intensity projection (MIP) and three- dimensional multiplanar reconstructed images provide high-resolution angiographic images of the vascular tree that can be useful in determining the need for surgical intervention for carotid disease .

Intracranial Vascular Imaging :

CTA can be performed immediately following a NCCT and adds minimal time to imaging procedures, permitting efficient imaging of the cerebral vasculature. Identification of an intra-cranial arterial occlusion on CTA, in the presence of acute focal neurological deficits, generally confirms the diagnosis of acute ischemic stroke. This is a significant improvement over NCCT, as early ischemic changes are not always present, making a normal scan non-diagnostic. Identification of a large vessel occlusion (LVO) is particularly important, given the dramatic treatment effect of endovascular thrombectomy (EVT) in this patient population **(7)**

The extent of collateral cerebral blood flow can also be inferred from CT angiographic images. Opacification of smaller vessels distal to but in the territory of the affected artery can often be seen in LVO cases. Although sometimes incorrectly referred to as “collateral vessels,” these are in fact smaller branches of the affected cerebral artery, which are being filled by leptomeningeal anastomoses, or pial collateral vessels, which are themselves below the resolution of the CTA **(8).**

The exception to this is collateral flow at the level of the Circle of Willis in the case of distal internal carotid artery occlusions, which are readily visible on CTA. Pial collateral vessels may be anastomotic channels between the smallest branches of adjacent cerebral arteries, i.e., the anterior and middle cerebral artery. They may also represent anastomotic connections between terminal branches of the extracranial and intracranial circulation, i.e., ophthalmic and middle

cerebral artery. Collateral flow maintains tissue viability and is the physiological basis for the ischemic penumbra. The presence of collateral flow on CTA is predictive of outcome and response to reperfusion therapy **(9).**

Regions where blood vessels do not opacify on CTA source images are severely hypoperfused and generally go on to infarct irrespective of treatment. These regions can, therefore, be used to approximate the ischemic core. Delayed filling of vessels occurs in regions that are viable and potentially salvageable (the ischemic penumbra). Assessment of the extent of delay is made difficult by the fact that conventional CTA images are acquired by simultaneous tracking of the contrast bolus temporally and spatially (in an inferior to superior direction). This provides a "snapshot" of vessel filling at one time point, rather than a complete assessment of the dynamic process.

Collateral Grading :

The extent of collateral vessel filling on CTA can be assessed qualitatively, i.e., "good" or "poor." As with all subjective assessments, inter-rater variability is significant and varies with experience. A number of rating systems have been developed in an effort to standardize CTA assessment of collateral flow and improve the selection of patients for treatment. Rating or scoring is based on the presence of vessel contrast opacification within the affected cerebral arterial territory. Regional rating of collateral flow, based on an adaption of the ASPECT score, has also been proposed **(10).**

Multiphase CTA:

In conventional CTA, an optimal intravenous contrast bolus profile consists of a rapid rise, plateau of peak enhancement, followed by a rapid fall. Scan acquisition is triggered by contrast bolus-arrival in the aortic arch, which is designed to capture images at the peak arterial enhancement phase . Multiphase CT angiography (mCTA) was developed in an attempt to obtain temporal information by tracking the bolus beyond the peak arterial phase. By repeating the CT acquisition in 1 mm slice increments following a delay of 7–8 s and another 7–8 s, images of the vasculature in the late arterial and venous phases can be obtained **(11).**

mCTA in theory assists in the differentiation of the ischemic core and penumbra. In the peak arterial phase, all hypoperfused territory will demonstrate lack of vessel opacification. Regions in which perfusion is delayed due to supply via collateral vessels will demonstrate vessel opacification in the later phases only. Thus, collateral flow can be more accurately demonstrated with mCTA. Collateral grade scoring systems have become increasingly complex **(12).**

The most recent iteration has gone beyond grading of simple opacification of vessels to in- clude regional delay of filling between phases, the extent of filling, and the delay of contrast washout in the late phases. Interestingly, the investigation of regional grading indicates that delayed washout in the late CTA phase is associated with poor outcome, which contrasts with other rating systems where persisting vessel opacification is considered to be consistent with a good collateral

flow pattern. These variables have been hypothesized to correspond to changes in local perfusion pressure and provide information that is similar to that obtained with CT perfusion (CTP) **(13)**

There are limited data supporting the use of multiphase CTA as a selection tool for reperfusion therapies. In the ESCAPE trial, 195/314 (62%) of patients were assessed with mCTA. In all other reper- fusion therapy trials, single-phase CTA was used to guide pa- tient selection. Comparative studies also suggest that mCTA may not appreciably change outcome or treatment selection over conventional CTA **(14).** The most significant limitation of mCTA, however, is that it allows assessment only of the macrovascular vessels. In order to demonstrate changes at the tissue level, an assessment of the microcirculation is required.

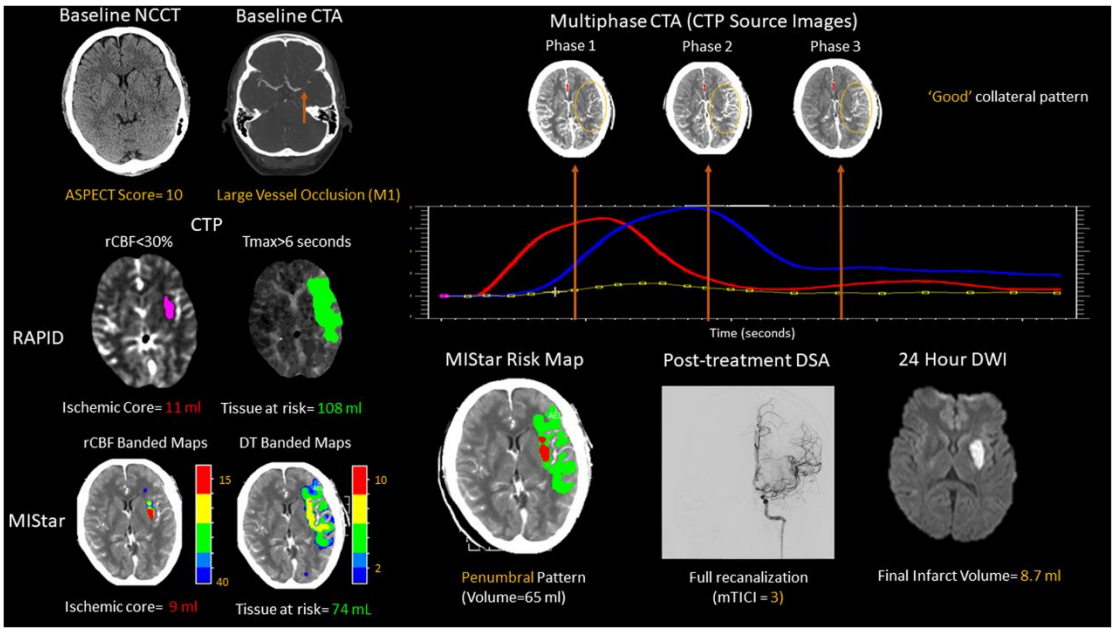

Fig. 3: Multimodal CT obtained in a 74-year-old male at 7.5 h after stroke onset. The NCCT shows no evidence of parenchymal early ischemic change (Alberta Stroke Program Early CT Score, ASPECTS = 10). Occlusion of the M1 segment of the left middle-cerebral artery (MCA) is demonstrated on the CT Angiogram (CTA). Multiphase CTA obtained from CTP source images suggests good collateral flow, although delayed late phase washout has been associated with poor outcome (see text). CT perfusion (CTP) images were post-processed using both the MIStar and RAPID software. Both programs utilize a double threshold approach schemic core definition, based on a relative cerebral blood flow (rCBF) of < 30%, within an area at risk defined by contrast delay. The larger penumbral volume reported with RAPID (108–11 = 97 ml) than MIStar is related to differences in deconvolution algorithms and the time domain parameter utilized to define tissue at risk (delay time (DT) = 74.0 ml (MISTAR) cf. Tmax = 108 ml (RAPID)). Successful recanalization (thrombolysis in cerebral infarction; TICI grade 3) was associated with a 24 h infarct volume and topography comparable to the ischemic core predicted by both RAPID and MIStar (4).

Magnetic Resonance Imaging

Advantages of MR-Based Stroke Imaging:

Currently, CT is accepted as the most effective imaging modality for evaluating patients with an acute ischemic stroke because of its distinctive advantages over MRI, such as its widespread availability, cost effectiveness, and rapid acquisition time . However, radiation hazards are inevitable in CT, because the dose of radiation during a comprehensive CT protocol for stroke is approximately six times that of an unenhanced head CT.Moreover, as a parenchymal imaging modality, CT is not sensitive in detecting small infarcts. In addition, a post-processing program is required to calculate the core infarct volume in CT perfusion imaging. In contrast, MRI-based stroke imaging has several characteristic advantages over CT.

First, DWI has the highest sensitivity for detecting acute ischemia, even if it is small and located in the posterior circulation. For the measurement of the infarct volume, which is important for excluding extensive infarction and calculating the volume of salvageable tissue in the later time window, DWI is the most accurate sequence for delineating the core infarct volume without a specific post-processing program . Moreover, selecting patients for mechanical thrombectomy based on the calculated core infarct volume (< 70 mL in the early time window) using DWI has been associated with favorable outcomes **(15).**

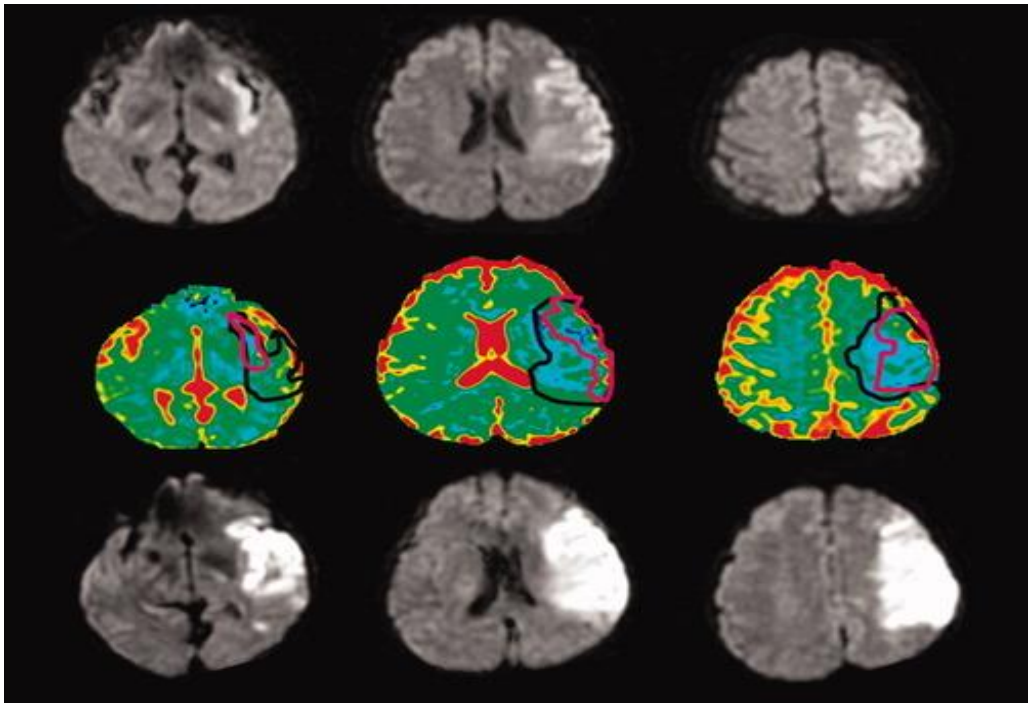

Fig. 4: Using Diffusion MRI to estimate clinical ischemic penumbra. Top row, DWI obtained ~3 h after stroke onset. Middle row, pseudocolor images with outlines of initial DWI lesion (red line) and prediction of final infarct (black line) . Bottom row, follow-up DWI obtained ~24 h after stroke in this patient who was not recanalized(Images provided by Y. Samson.)(16).

MRI Acceleration Techniques :

The recent advances in MRI technology largely aim to speed up acquisition. The current improvements in multicoil technology and the commercialization of stronger magnetic fields enable several newly developed fast-imaging tools to be applied in daily practice while maintaining sufficient imaging quality. In the following paragraphs, we briefly discuss the principles, key elements, advantages, and disadvantages of MRI acceleration techniques for stroke imaging.

Echo-Planar Imaging (EPI):

EPI is the classic fast-imaging technique, wherein the entire k-space is filled with a radiofrequency (RF) pulse (single-shot EPI) . The rapid gradient switching enables each MR slice to be acquired within 50-100 ms . Currently, the techniques that fill the entire k-space with a few RF pulses are also classified as EPI sequences (multi- shot EPI). The echo train length (ETL), also referred to as the EPI factor by Siemens and Philips, is defined as the number of k-space lines encoded in a single shot **(15).**

Thus, in single-shot EPI, the number of phase-encoding steps is equal to the ETL, and in multi-shot EPI, the ETL is a key parameter for determining the acquisition speed. The main strength of single-shot EPI is that it can be done with most MR scanners regardless of their type or vendor. However, geometric distortion and susceptibility artifacts are the limitations of the EPI technique. Fortunately, the combination of EPI and parallel imaging can partially solve these issues **(15).**

The main sequences that apply this technique are diffusion, perfusion, and functional MRI. For stroke imaging, EPI has been applied in DWI, gradient- echo (GRE), FLAIR, and MR perfusion imaging (dynamic susceptibility contrast MRI) . FLAIR-like echo-planar images can also be obtained using inversion(pulses **(17).**

Parallel Imaging :

The EPI technique enables fast imaging, but the rapid gradient change can cause problems, such as high-level acoustic noise and magnetic burden. Parallel imaging can solve these problems, because it was developed to target a reconstruction step **(15.)**.In this technique, rapid acquisition is achieved by means of k-space undersampling in the phase-encoding direction, and the problem caused by undersampling (aliasing artifacts) is solved by means of creative reconstruction that uses positional information derived from a multichannel phased-array coil . Originally, multiple small receiver coils were developed to reduce noise and increase the signal-to-noise ratio (SNR). Several overlapping small coils can cover the volume of one large coil; when information from all the small coils is summed, the noise decreases, and the SNR increases.

However, in parallel imaging, positional information from the multichannel phased-array coil is used to supplement the insufficient k-space information. For example, if several coils are placed around the head, the strength of the signal from a specific location depends on its proximity to the coil. By considering the coil position and estimating the location of the signal, one can create a

position map, that is, a coil sensitivity map in image domain reconstruction and autocalibration signal data in k-space domain reconstruction **(15).**

There are two different reconstruction methods in parallel imaging . The first is image domain reconstruction, which generates unfolded images using a coil-sensitivity map from the aliased image derived from the undersampled k-space (reconstruct and then correct). The other is k-space domain reconstruction, wherein the undersampled k-space is filled using autocalibration signal data before Fourier transformation (correct and then reconstruct). The former provides a slightly higher SNR and is more appropriate for small homogeneous body regions, such as the brain, whereas the latter is more advantageous for combination with the EPI technique. Presently, both methods are actively applied in neuroimaging **(15).**

The main advantage of parallel imaging is that it speeds up image acquisition. The parameter for speed is the parallel imaging acceleration factor (the amount of k-space data required for a fully sampled image/amount of k-space data actually acquired). The most common commercially available acceleration factor range is 1.5 to 4 . Another advantage of parallel imaging is its wide applicability. Theoretically, parallel imaging can be applied to all types of pulse sequences and can be easily combined with other fast-imaging methods **(18.).**

SMS Imaging

The technical principle of SMS imaging is multi-section excitation in a single repetition time using multiband RF pulses. Accelerated imaging can be achieved by means of the simultaneous acquisition of signals from such slices. The speed parameter in SMS imaging is the section acceleration factor, that is, the number of simultaneously acquired slices. The commercially used acceleration factors range from 2 to 8. Currently, acceleration factors of 2 to 4 can be achieved without SNR loss. The major sequences that use this method are DWI, diffusion tensor imaging, and functional MRI **(18.).**

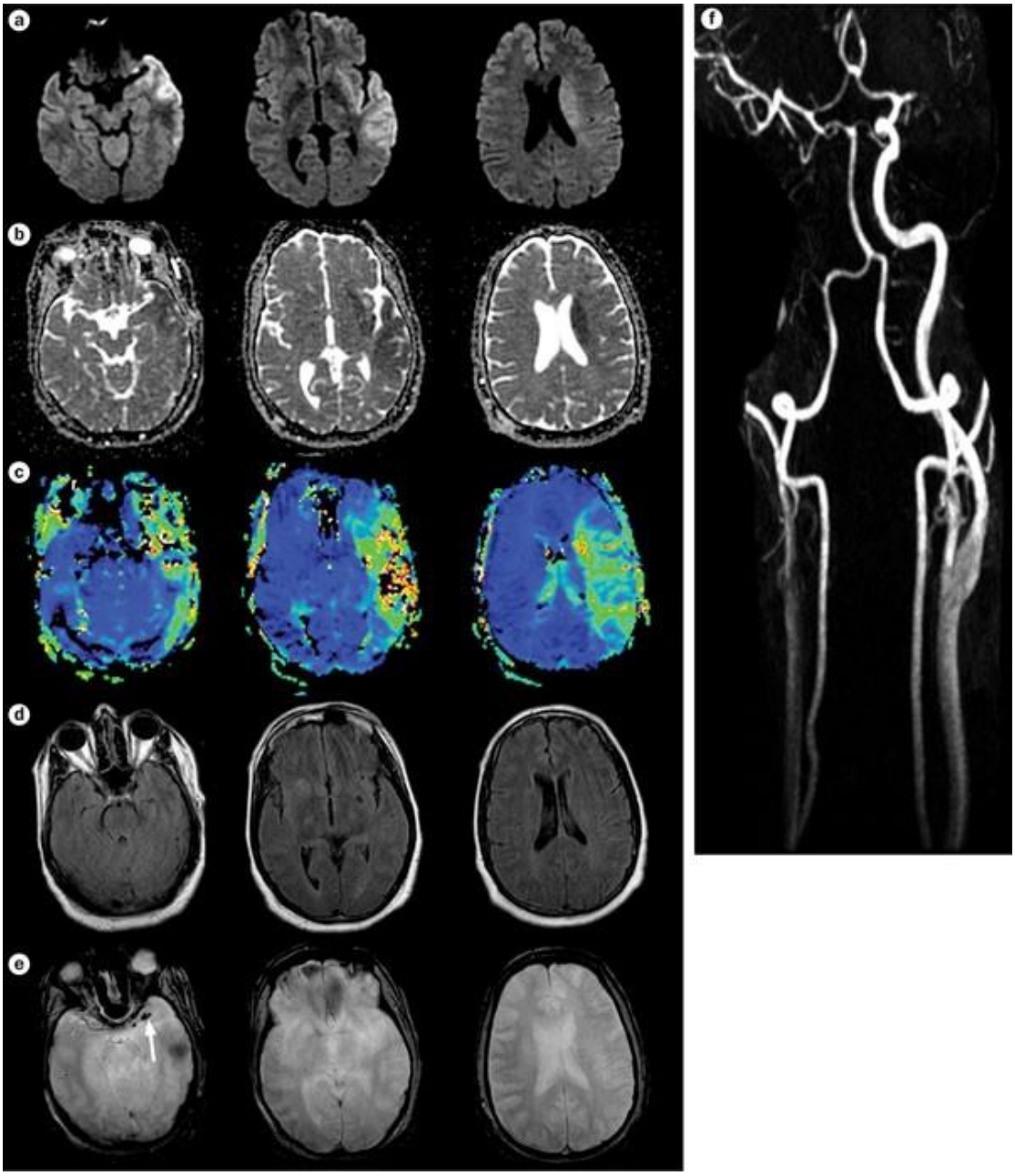

Fig. 5: The patient arrived at the emergency room 45 min after symptom onset. MRI was started 20 min later, and the patient was treated with intravenous tissue plasminogen activator 55 min after arrival. a | DWI sequence showed an area of hyperintensity in the right temporal, insular and frontal lobes. b | Apparent diffusion coefficient map showed a matching area of hypointensity, confirming that the DWI lesion was due to acute ischemia. c | Mean transit time maps showed an area of hypoperfused tissue larger than the DWI abnormality; the difference represented the penumbra. d | Fluid-attenuated inversion recovery showed no matching hyperintensity, indicating that the DWI lesion was <6 h old. e | The gradient-recalled echo sequence showed no evidence of acute or chronic hemorrhage, but a clot was seen in the right MCA (arrow). f | Contrast-enhanced MRA of the neck and brain revealed a chronic asymptomatic right carotid occlusion, although the patient had good collateral flow through the anterior communicating artery, and his right

carotid artery was normal. The proximal right MCA abruptly terminated in the proximal portion, as confirmed by axial MRA. Abbreviations: DWI, diffusion-weighted imaging; MCA, middle cerebral artery; MRA, magnetic resonance angiography. (19)

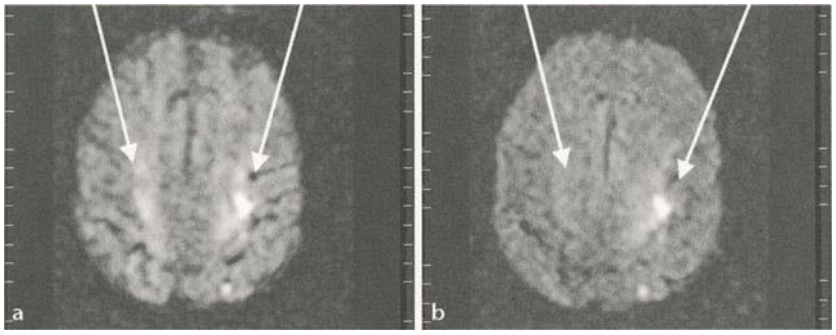

Fig. 6:Anisotropic (a) and isotropic DWI (b). There is a definite lesion in the left parietal lobe of the MCA territory seen on both DWI (arrows). The lesion in the right parietal lobe seen in a is physiological diffusion in the corona radiata which cannot be depicted anymore in b (arrows).

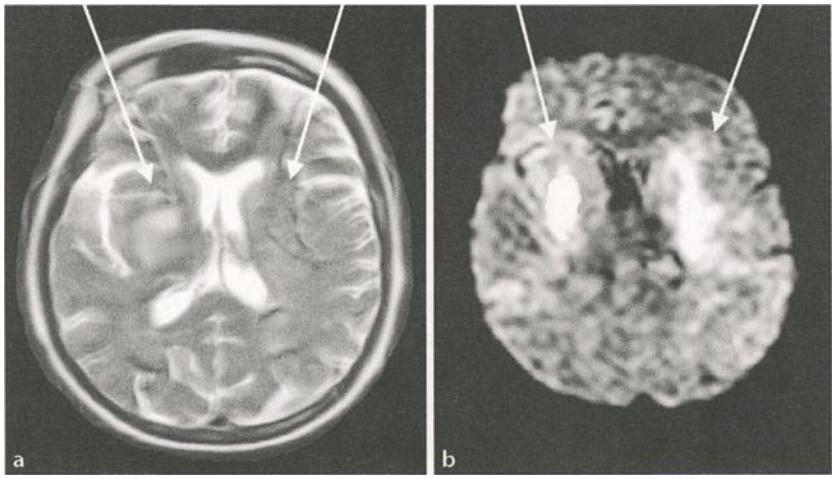

Fig.7 :T2-WI (a) and DWI (b) of a subacute ischemic in- farction on the right and a hyperacute ischemic infarction on the left, which is not shown on T2-WI but only on DWI. b The DWI shows a strong hyperintensity on the right, which is due to a loss of diffusion *and* a T2-effect of edema as seen in a (arrows). The lesion in the left MCA territory, seen only on the DWI (b) and not on T2-WI (a) is due to diffusion impairment only and depicts a hyperacute ischemic infarction (20)

Stroke severity:

The National Institutes of Health Stroke Scale (NIHSS) is a 15- item impairment scale used to measure stroke severity. It was originally developed in 1989 and is now a widely used outcome measure in the recombinant tissue plasminogen activator stroke trials. In the current National Stroke Foundation guidelines, the NIHSS is recommended as a valid tool to assess stroke severity in emergency departments (21)

The NIHSS includes the following domains: level of conscious- ness, eye movements, integrity of visual fields, facial movements, arm and leg muscle strength, sensation, coordination, language, speech and neglect. Each impairment is scored on an ordinal scale ranging from 0 to 2, 0 to 3, or 0 to 4. Item scores are summed to a total score ranging from 0 to 42 (the higher the score, the more severe the stroke). The original 15-item NIHSS remains the most widely accessible, although several versions have been developed (such as the 5-, 8- and 11-item modified NIHSS) and are avail- able in many languages **(21)**

The NIHSS' strong ability to predict outcomes after stroke helps clinicians provide accurate information to patients, set realistic goals for therapy and plan for discharge. The NIHSS captures both motor and non-motor impairments of stroke, and provides a good overview of people's deficits. The NIHSS may however be inade- quate in providing information to guide exercise prescription, as it does not measure specific muscle strength. Also, since the NIHSS only measures impairments, it does not provide information on activity limitations such as difficulties with bed mobility, sitting, standing, walking and upper limb function. However, the NIHSS could be used in conjunction with scales such as the Motor Assess- studied extensively **(21*).***

Table (1): National Inistitiute of Health Stroke Scale Stroke, NIHSS (aliem.com)

National Institutes of Health Stroke Scale score	
1a. Level of consciousness	0 = Alert; keenly responsive 1 = Not alert, but arousable by minor stimulation 2 = Not alert; requires repeated stimulation 3 = Unresponsive or responds only with reflex
1b. Level of consciousness questions: What is the month? What is your age?	0 = Answers two questions correctly 1 = Answers one question correctly 2 = Answers neither question correctly
1c. Level of consciousness commands: Open and close your eyes. Grip and release your hand.	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2. Best gaze	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation
3. Visual	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia
4. Facial palsy	0 = Normal symmetric movements 1 = Minor paralysis 2 = Partial paralysis 3 = Complete paralysis of one or both sides
5. Motor arm 5a. Left arm 5b. Right arm	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity; limb falls 4 = No movement
6. Motor leg 6a. Left leg 6b. Right leg	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement
7. Limb ataxia	0 = Absent 1 = Present in one limb 2 = Present in two limbs
8. Sensory	0 = Normal; no sensory loss 1 = Mild-to-moderate sensory loss 2 = Severe to total sensory loss
9. Best language	0 = No aphasia; normal 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute, global aphasia
10. Dysarthria	0 = Normal 1 = Mild to moderate dysarthria 2 = Severe dysarthria
11. Extinction and inattention	0 = No abnormality 1 = Visual, tactile, auditory, spatial, or personal inattention 2 = Profound hemi-inattention or extinction
Total score = 0–42.	

Table (2): The Glasgow Coma Scale (GCS)(researchgate.net).

Feature	Response	Score
Best eye response	Open spontaneously	4
	Open to verbal command	3
	Open to pain	2
	No eye opening	1
Best verbal response	Orientated	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No verbal response	1
Best motor response	Obeys commands	6
	Localising pain	5
	Withdrawal from pain	4
	Flexion to pain	3
	Extension to pain	2
	No motor response	1

Conflicts of Interest: The authors declare no conflict of interest.

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