



Review

Brain ischemia: CT and MRI techniques in acute ischemic stroke

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ABSTRACT

Imaging plays a central role for intravenous and intra-arterial arterial ischemic stroke treatment patient selection.

Computed tomography (CT) / CT angiography or magnetic resonance (MR) / MR angiography imaging are used to exclude stroke mimics and haemorrhage, to determine the cause and mechanism of stroke, to define the extension of brain infarct and to identify the arterial occlusion. Imaging may identify the patients that will benefit more from revascularization therapies independently of the conventional therapeutic time window allowing individualized treatment decisions and improving individual patient outcome. Multiparametric CT/MR imaging may be used to identify the extension of potential viable brain tissue (penumbra) and of irreversible brain lesion (core) using CT perfusion and/or diffusion weighted and perfusion weighted MR imaging. The status of the arterial collateral circulation and the type and extension of the clot may be assessed by imaging.

The accuracy and the clinical significance for treatment and patient clinical outcome of different imaging techniques are reviewed.

1. Introduction

Stroke is one of the most frequent causes of death and disability in developed countries, having an estimated overall adult prevalence of 2.5%, which rises with increasing age, being estimated to be 45% for age group of more than 85 years if silent infarcts are also taken into consideration [1]. Arterial ischemic stroke (AIS) is one the three leading causes of death in developed countries; with one death caused by stroke for each 15–18 total deaths [1]. Stroke represents also a tremendous social burden, not only by the associate mortality but also by the morbidity associated with this disease. As a consequence of the population ageing it is expected that the health costs with stroke will continue to rise exponentially over the next decades.

Most of the strokes are ischemic, more than 80% of cases, being thromboembolic due to large artery atherosclerosis, cardio-embolic, and small vessel occlusion the commonest causes of AIS [1]. The other causes of stroke include intracerebral haemorrhage (~12%) and sub-arachnoid haemorrhage, accounting for approximately ~9% and 3%, respectively [1].

The mortality rates associated with stroke have been decreasing over the last years due to better general clinical care and specific stroke treatment. The current available AIS treatments include intravenous thrombolysis with tissue plasminogen activator during the first 4.5 h after clinical onset and intra-arterial (endovascular) mechanical

revascularization, either by stent clot retrieval and/or clot aspiration, during the first 6–8 h after symptom onset [2,3]. The objective of these treatments is to promote the rapid revascularization of the brain tissue, impeding the evolution of the viable (reversible) ischemic brain tissue (penumbra) into death (irreversible) brain tissue (core).

Imaging is the cornerstone for the diagnosis of ischemic stroke, not only for the AIS but also subacute and chronic ischemic brain lesions. In AIS, it is also crucial for treatment patient selection. Therefore, not surprisingly, over the last years, the major focus of imaging research has been the AIS evaluation, aiming better and faster diagnosis and optimized individual patient selection for treatment, selecting those patients with a potential good outcome after treatment and excluding the poor candidates for treatment.

“Time is brain” is a central concept that underlies the importance of the prompt AIS diagnosis and treatment. It is estimated that there is a loss of about 1.9 million neurons per minute in an acute middle cerebral artery (MCA) occlusion [4]. The benefit of the treatment diminishes significantly and is lost after 4.5 for IV treatment and after 6–8 h for IA treatment [2,3]. There may be some exceptions, such as posterior circulation strokes and patients with good arterial collateral circulation, which may have a longer time window for IA treatment. As an example, the number of patients needed to treat (NNT) for IV thrombolysis is 4–5 if the treatment is initiated before 90 min; 9 if the treatment is initiated before in-between 90 and 180 min; and 14 if the treatment is initiated

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Table 1
Acute ischemic stroke imaging assessment.

Essential imaging evaluation		
P	Parenchyma	Exclusion of haemorrhage and stroke mimics Arterial ischemic stroke detection
P	Pipe (vascular)	Arterial occlusion detection
Additional imaging evaluation		
C	Collaterals	Collateral circulation status assessment
C	Core	Core/Penumbra size estimation
C	Clot	Clot assessment

Essential imaging evaluation.

P – parenchyma: Exclusion haemorrhage and stroke mimics.

Parenchymal evaluation (AIS detection).

P – pipe: Vascular evaluation (arterial occlusion detection).

Additional imaging evaluation.

C – collaterals: Collateral circulation assessment.

C – core: Penumbra/core assessment.

C – clot: Clot assessment.

in-between 180 and 270 min, representing a decay of approximately 10% chance of good outcome (mRS 0–2) for each 30 min of treatment delay [5].

Every single patient will have a different stroke time evolution depending on several factors, the most important being their own (arterial) collateral brain circulation that may keep the penumbra area viable for a longer period of time. Therefore, relevant imaging information should include the extension of the core (or penumbra) and the individual collateral circulation, which may allow the individual AIS treatment strategies.

We review the imaging protocol for AIS and review future aspects of a precision medicine approach for the diagnosis of stroke using advanced CT and MRI protocols (Table 1).

2. Essential imaging evaluation

Neuroimaging is essential for stroke assessment. Computed tomography (CT) and magnetic resonance imaging (MRI) protocols provide excellent tools for the evaluation of acute ischemic stroke [6]. The major objectives of AIS imaging are to rule out haemorrhage and stroke mimics and to select the best candidates for IV or IA treatments based on the extension of established infarct (core) and the arterial occlusion site. For this, computed tomography (CT) and magnetic resonance (MR) imaging have been extensively assessed [7,8].

AIS are medical emergencies and the treatment decision (conservative approach; IV thrombolysis and/or mechanical revascularization) is based on the time window and two major imaging features: parenchymal lesion and arterial occlusion site.

Parenchymal imaging establishing the diagnosis and extent of ischemia and vascular imaging determining the arterial occlusion location, by CT/CTA or MRI/MRA, are mandatory for the AIS evaluation. Additional information regarding the collateral flow, penumbra and core extension may have added value for individual treatment decision.

The imaging modality chosen for initial AIS evaluation is mostly driven by the 24 h × 7 days immediate equipment availability and by the possibility to provide the critical information required for the different possible treatments. As a result of the wider availability, CT is the most commonly worldwide used imaging technique employed for acute stroke [7–9].

2.1. Parenchymal evaluation

2.1.1. Exclusion of brain haemorrhage and stroke mimics

For the initial assessment of AIS, the imaging methods should be able to exclude the presence of brain haemorrhage, stroke mimics and other causes of stroke.

In the acute phase, both CT and MRI (using T2*WI and/or susceptibility imaging) have high accuracy for haemorrhage detection, with sensitivities and specificities of approximately 100% [7,8,10,11]. MRI has better accuracy for identification of the intraluminal thrombus, small petechial haemorrhagic transformation and previous chronic lobar hematomas and/or microbleeds.

Stroke mimics are those nonvascular conditions that present with stroke like symptoms, such as acute neurologic deficits. The most common stroke mimics are psychogenic disorders (conversion), seizures (ictal and postictal phases), migraine, and metabolic conditions, such as hypoglycemia, hyperglycemia. There are also other vascular diseases such as brain hypertensive encephalopathy, posterior reversible encephalopathy syndrome (PRES), reversible cerebral vasoconstriction syndrome (RCVS), venous thrombosis, which may present with acute neurological deficits and should be distinguished from the typical AIS [2].

2.1.2. Parenchymal evaluation (AIS detection)

Diffusion-weighted imaging (DWI) and the corresponding apparent diffusion coefficient (ADC) maps is the most sensitive imaging modality to depict brain ischemia, with a sensitivity up to 73–92% in the first 3 h and up to 95–100% in the first 6 h [3,6–8].

In AIS, the ADC values show an early decrease (from minutes to less than 1 h) due to cell depolarization and cytotoxic oedema, when CT and T2 WI imaging are still normal. The initial decrease in the ADC values is followed by a “pseudonormalization” due to a progressive increase in the extracellular water content (vasogenic edema) and finally, after 7–15 days, there is a clear increase in the ADC values due to cell lysis and necrosis.

CT has a significantly lower sensitivity, compared to MR, to depict AIS, with an overall sensitivity of 57–71% in the first 24 h, and only 12% in the first 3 h [3,6–8]. CT sensitivity is very low in posterior fossa and deep infarcts [3,6–8]. CT specificity is very high approaching the 100%, in the presence of the correct clinical setting and with the *de novo* appearance of the (later mentioned in the text) parenchymal changes [3,6–8].

Although CT is not as sensitive for detection of ischemia as MRI with diffusion-weighted imaging (DWI), it is an widespread, efficient, readily available, diagnostic tool for emergency situations, having been used in all of the major therapeutic trials using intravenous tissue plasminogen activator (TPA) therapy and/or mechanical thrombectomy, as the main imaging modality.

A directed review of the native non-contrast CT in acute stroke glean key diagnostic information in less than a minute. The classical CT imaging findings in AIS, are present in less than 50% of AIS cases, and include the: loss of grey-white matter distinction, which includes the insular ribbon sign (representing the loss of the grey-white interface at the insular cortex), obscuration of the lenticular nucleus (basal ganglia loss of the grey-white interface), gyral swelling and sulci effacement, and parenchymal hypoattenuation. Parenchymal hypoattenuation results from the presence of cytotoxic (intracellular) oedema and is a sign of irreversible tissue damage (Fig. 1).

For TPA and endovascular treatment decisions, patients with haemorrhage or signs of large cortical ischemia are excluded from thrombolytic and/or thrombectomy treatments, since the involvement of more than one third of the MCA territory on CT is associated with a higher risk for haemorrhagic transformation. The ASPECT score (Alberta Stroke Program Emergency CT) provides an easy, reproducible and structured method for acute stroke CT reading and treatment triage. This divides the middle cerebral territory into 10 areas (6 cortical and 4 deep), encompassing slices from the basal nuclei to the top of the ventricles. (Fig. 2) The reader takes a point off for each region showing ischemic changes and tallies the result. A normal score is therefore 10 and complete territorial infarction is an ASPECTs = 0. When scans from several large trial databases were scored using ASPECTs, scores of 7 and below were found to correlate with poor

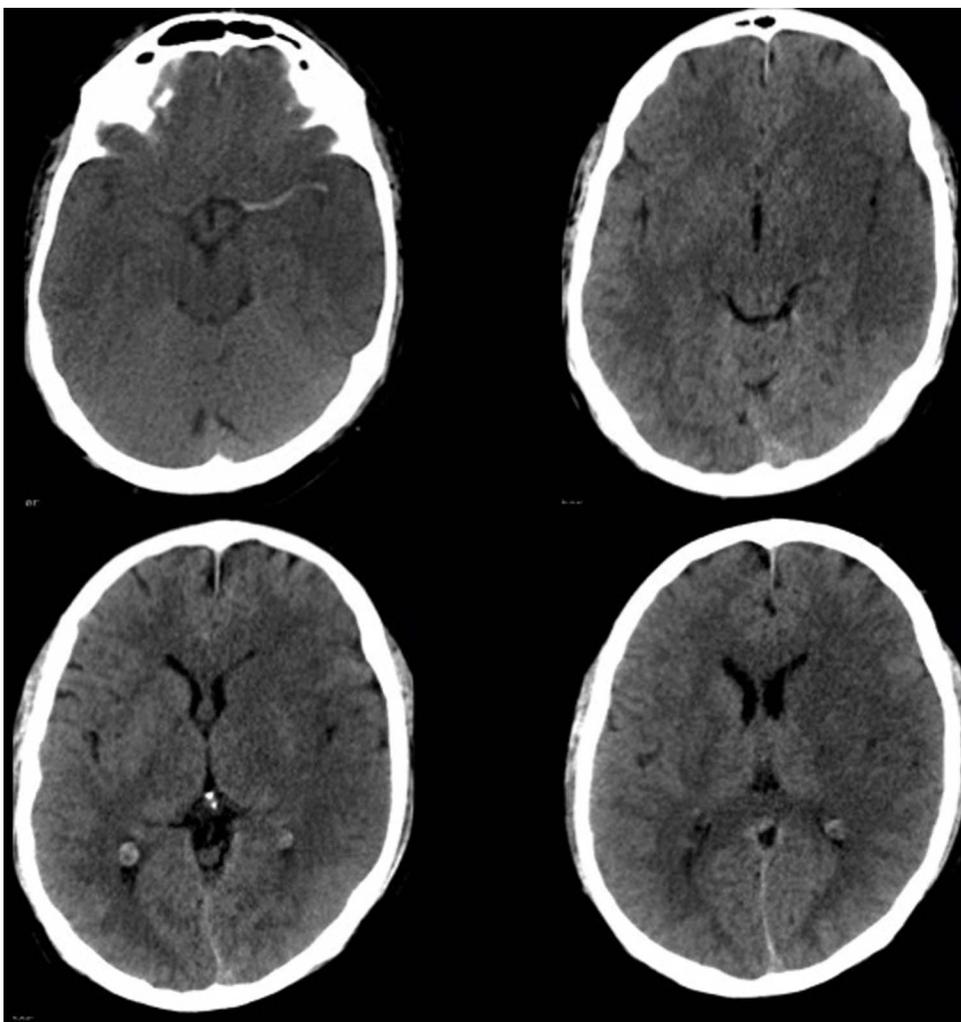


Fig. 1. Computed tomography axial of a patient with acute left middle cerebral ischemic stroke. The images show signs of acute ischemic stroke with lenticular nucleus, internal capsule, frontal, temporal and insular hypodensity and sulci effacement. There is associated hyperdense middle cerebral artery.

outcome, either with or without subsequent therapy, and higher rate of haemorrhagic transformation [12]. Similar target ASPECTs selection criteria were used in the recent successful endovascular trials, since when large infarcts were present at the baseline CT, patients are unlikely to do well with therapy. ASPECTs also provides excellent shorthand for communication amongst the stroke team members during urgent triage. The state of the parenchyma needs to be carefully evaluated as acute treatment decisions are weighed, since treatment of patients with large infarct lesions is not only fruitless but also potentially dangerous. A similar scale (pcASPECTS) has been proposed for the posterior circulation AIS with similar advantages for predicting the patient outcome [13,14].

Multiparametric magnetic resonance imaging (MRI) AIS protocols, with very short acquisition times, combining conventional MR sequences such as diffusion weighted images (DWI), fluid attenuated inversion recovery (FLAIR), MR angiography (MRA) and additional perfusion weighted MRI (PWI), and have been used in several high volume stroke centers worldwide. Short acquisition times reduce motion artefacts and enable the study of acute stroke patients with moderate cooperation. Fast image reconstruction makes the results of MRA or PWI available within a few minutes, optimally including maps to operationally estimate the size of the ischemic core and putative penumbra [15]. Similar quantification methods, as the ASPECTS score, or even quantitative evaluation of the ischemic tissue volume may be applied. The major advantage of MRI in stroke is the availability of DWI, which is the most sensitive technique to depict infarct and the best infarct core predictor. (Fig. 3) Other MRI advantages include the characterization of

the lesion extension, the presence of previous haemorrhages and the assessment of the stroke mechanism.

It is widely accepted that diffusion abnormalities, with ADC reduced values, demonstrating the presence of cytotoxic (intracellular) oedema are a sign of irreversible lesion, and represent the best image marker for the infarct core. Therefore, it is generally accepted that DWI-visible ischemia (confirmed by low ADC) measuring more than 70 ml, or a DWI-ASPECTs of less than 7, indicates a large core volume, a threshold beyond which intervention may be fruitless [16]. The major non-diffusion effect contributing to hyperintensity in DWI is the “T2 shine through” effect, due to the “contamination” of DW images by T2 signal hyperintensity, resulting from lesions with T2 prolongation (i.e. vasogenic oedema). Since T2 contamination does not influence quantitative maps of the ADC, the quantitative ADC maps should be used to confirm the presence of cytotoxic oedema and to estimate the extension and the age of an ischemic lesion.

There are some exceptions to the DWI-irreversibility concept. DWI brain abnormalities may be, at least, partially reversible, if early and effective (spontaneous or therapeutic) reperfusion is achieved, specially in less than 3 h after arterial occlusion [17–20]. No association of an ADC threshold with irreversible injury could certainly established and even with severe ADC changes may be reversible, as demonstrated in brain regions with more than 50% decreased ADC-values, compared with the mean contralateral value [17–20]. In human stroke, the degree of ADC-decreases is correlated with the ischemic impairment but does not predict the fate of the tissue after potential reperfusion. This complicates the ability to predict which DWI-positive regions represent true

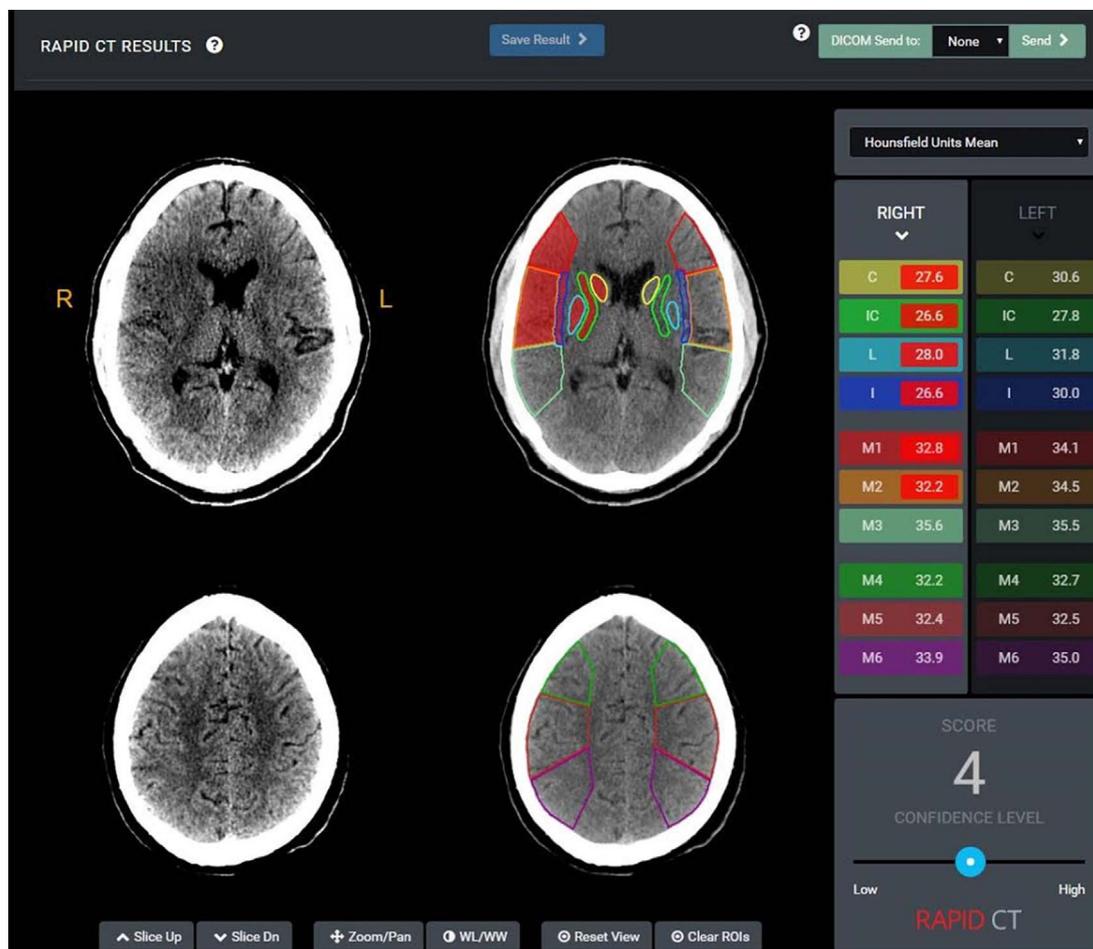


Fig. 2. Automated ASPECTS in acute MCA ischemia. Images are first automatically aligned, then thresholded Hounsfield units are used to detect regions of hypodensity. Hypodense areas are filled with color overlay (red fill, right images) within areas of suspected ischemia, and results are routed to PACS. The ASPECT system scores 4 deep structures and 6 cortical sectors highlighted on the overlaid grid (normal = 10, when no points are subtracted). Results are summarized by region in the table; ASPECTS here = 4. The user is also able to add or subtract suspicious areas based on manual inspection to arrive at a final score. (Images courtesy of Jeff Kleck, iSchemaView, RAPID software).

core tissue at baseline assessment. However, normalization of MR-parameters (ADC, T2WI) does not necessarily indicate true tissue salvage. Within normal appearing T2WI regions in postischemic MRI scans, a partial neuronal necrosis can be observed. [21]. Remarkably with shorter occlusion times the average lesion size in T2WI at 7 days, which is thought to represent the vasogenic edema, can be strikingly smaller than the histologically determined infarct size. [21]. Even after 10 min of vessel occlusion, a partial neuronal necrosis was observed in the absence of any T2WI lesion in the chronic stage [21].

FLAIR and/or T2 WI will become positive later than DWI, within the first 3–8 h after acute arterial occlusion. The MRI signs include brain increased signal intensity, swollen cortical gyri and increased signal intensity in the lumen of vessels, due to vessel occlusion, severe stenosis, vasculitic pattern or collateral leptomeningeal circulation. There is also a FLAIR/T2 signal pseudonormalization, occurring between 1 and 4 weeks (peak 2–3 weeks) due to the infiltration of inflammatory cells in the core area reducing the T2 hypersignal. FLAIR/T2 WI may also provide additional important information regarding the time of arterial occlusion, in cases of unknown time of stroke onset, such as wake-up strokes. The specificity of a FLAIR/DWI mismatch, in which T2 FLAIR images are negative and DWI positive, is approximately 78–93% for strokes with less than 3–4.5 h of evolution [22].

2.2. AIS imaging evaluation: vascular assessment

Vessel imaging is mandatory to define the site of occlusion and select patients for intra-arterial treatment. The presence of arterial

proximal occlusion should prompt the consideration of endovascular revascularization.

Patients with proximal clot (ICA or M1 segment MCA) and extensive clot burden (e.g. clot length > 5–8 mm) are unlikely to recanalize with intravenous TPA (18). The clot/occlusion arterial location predicts the recanalization rate for intravenous thrombolysis, with low recanalization rates for proximal occlusions, namely ICA-T (4.4%); M1 (32.3%), M2 (30.8%) and basilar (4%) segments/arteries [22,23].

The hyperdense artery sign on CT (hyperdense middle cerebral artery – HDMCA) (Figs. 1 and 6) and the corresponding T2*/SWI clot sign on MRI represent the thrombotic event location and are highly specific for artery occlusion [21]. The HDMCA sign is present in 31–67% of patients, having a high specificity but a low sensitivity (31–79%) [21]. The false positives include mostly vessel calcification and high haematocrit. [21]. The non-contrast CT done at 5 mm increments is only about 1/3 sensitive for detection of the hyperdense MCA sign, but thin sections and multiplanar reconstructions will double the HDMCA detection rate, and also helping to distinguish clot from mural atherosclerosis [21].

Both CTA, with sensitivity and specificity of up to 98% and MRA, with sensitivity of up to 87% and specificity of up to 98%, [24], have been shown to be highly accurate for the detection of arterial occlusion, with some CTA accuracy advantage compared with MRA [25,26].

CTA/MRA can directly show not only the location of vascular occlusion, but also more proximal (and treatable) clot sources such as atherosclerosis of the carotid bifurcation or cervicocephalic dissection and the collateral circulation, through the circle of Willis and/or more importantly through leptomeningeal arterial collaterals.

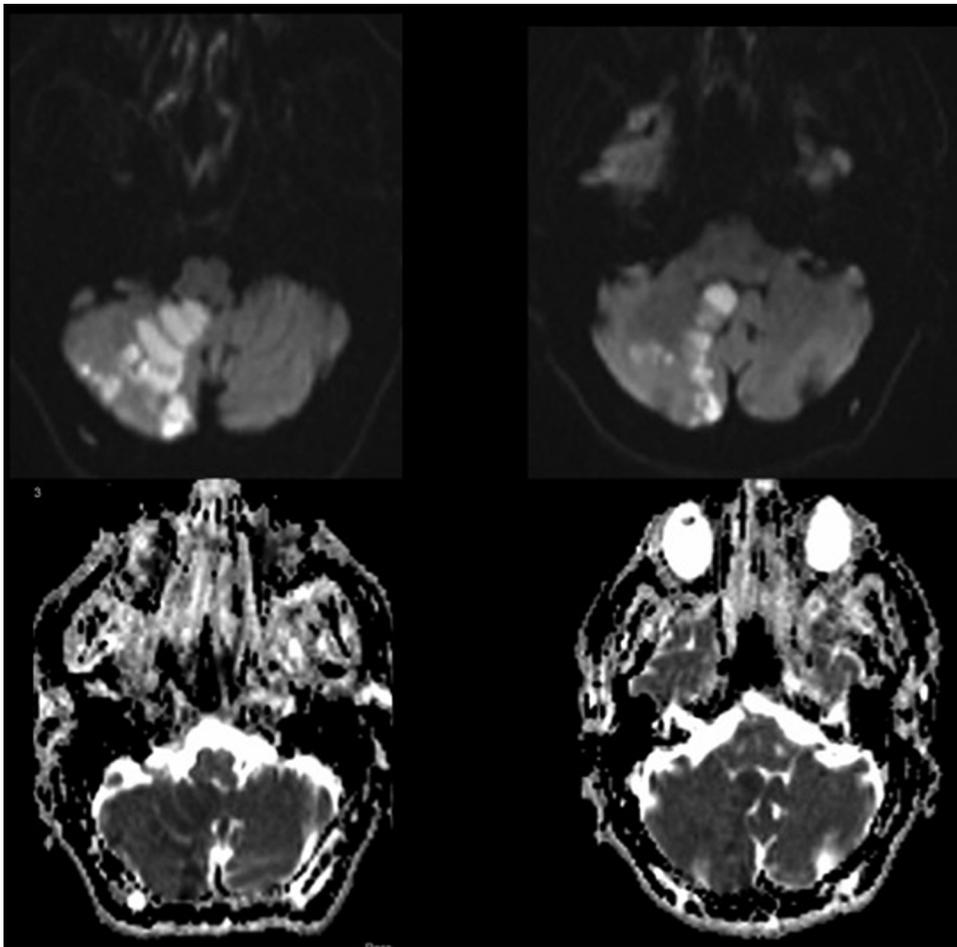


Fig. 3. Diffusion-weighted images and the corresponding ADC maps showing an acute right posterior inferior cerebellar artery infarct with the corresponding high signal on DWI and low signal (representing diffusion restriction) on the ADC maps.

3. Additional imaging evaluation

Arterial ischemic stroke should be seen as a continuous and dynamic process, in which time has a significant influence. The imaging assessment represents only a “snapshot” in time, and multiple parameters (penumbra, core, collaterals) will vary over time for the same patient.

Getting beyond the basic CT or MRI assessment, with evaluation of the collateral vascular and perfusion imaging, it is possible to more accurately establish the diagnosis, the prognosis, and the underlying cause of stroke. This may be used to personalize the treatment decision accordingly to the individual patient hemodynamic status. Other important use of core/penumbra imaging includes the identification of stroke mimics avoiding unnecessary treatments.

Perfusion imaging can also assist in identifying small distal occlusions, which in turn helps in the interpretation of MRA and CTA exams. In patients with TIA, perfusion maps can objectively show a referable defect in up to a quarter of patients with otherwise normal MRI-MRA protocols.

Whether to include perfusion routinely in clinical practice, and the exact method to use, is still controversial [27,28] and will require more trials before a definitive answer is established. Overall, an imaging AIS favourable pattern would include patients with a small core, large penumbra-core mismatch and good arterial collaterals [29].

3.1. Arterial collateral circulation status assessment

Brain arterial collateral circulation represents an important factor for the AIS clinical outcome. Good collateral status, either through the circle of Willis or, more importantly, through leptomeningeal anastomosis, is an easy and reliable predictor of good outcome. Patients with

good collateral circulation, have more favourable outcomes [30–32]. The presence of good collaterals decreases the penumbra size, prolongs the therapeutic time window and reduces the infarct progression rate [33,34].

The collateral arterial circulation has a high interindividual variability, in respect to the number, size, distribution of collaterals and respective compensatory capacity. The collaterogenesis is genetic mediated, being proposed that chromosome 7 (Dce1 locus – previous named Canq1) regulates the extension of collateral arteries [35] and the genes responsible for vascular endothelial growth factor (VEGFa) and chloride intracellular channel 4 (CLIC4) expression also plays a role [36,37]. The development of collateral circulation occurs early on the embryonic development with up to 70% of arterial collaterals develop between the 13 and 14 weeks of gestation [38]. Over the years, several acquired factors have shown some influence on the individual collateral status, namely factors that decrease the number and diameter of collaterals, such as ageing, chronic hypertension, metabolic syndrome, hyperuricemia, among others, and factors that may potentiate the increase in number and diameter of collaterals, such as chronic hypoperfusion, consequent to chronic arterial stenosis/occlusion [33,34,39].

Arterial collateral circulation may be assessed by CTA, MRA or DSA. There is a multiplicity of scales grading the collateral circulation [40,41]. Independently of the grading scale, all of them evaluate: – the extension of the collateral circulation (structural evaluation) assessing the anatomical extension and diameter of the arterial collaterals, and for DSA also the capillary blush area; – the hemodynamics (functional evaluation) assessing the presence and distinction between antegrade and retrograde filling; – and the timing of retrograde arterial filling and/or venous filling. The most common collateral grading scales are the Qureshi collateral score (5-point scale), the Capillary Index Score (CSI),

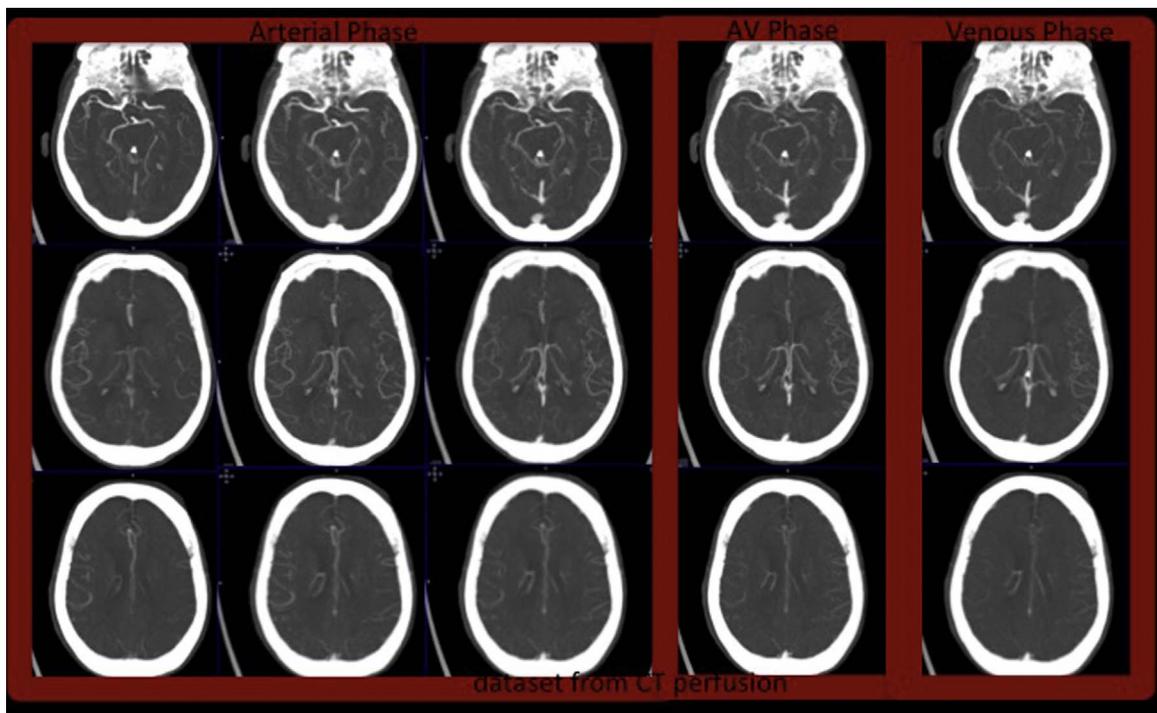


Fig. 4. Arterial collateral assessment using CT Perfusion dataset of a patient with left middle cerebral artery occlusion. There is a good arterial collateral pattern, with the presence of collaterals in a region greater than 50% of the left MCA territory, filling slightly later than the contralateral side.

the American Society of Interventional & Therapeutic Neuroradiology (ASITN)/Society of Neurointerventional Surgery (SNIS) Collateral Grading (ACG) System, Miteff score, Kim Score (DSA), Tan Score (CTA), and finally the ASPECT Score: Collateral Scoring on mCTA [40,41]. It is important to have late phase angiographic images for correct collateral status estimation, which may be accomplished by using the perfusion datasets (Fig. 4) or multiphase CTA [42]. The description of all grading scales is beyond the scope of this review, but it should be mentioned that a highly reproducible and easy classification has been used in the ESCAPE trial, comparing the collateral arterial filling with the contralateral brain on multiphase CTA, dichotomizing in two major groups: good collaterals (presence of collaterals in a region greater than 50% of the MCA territory) and bad collaterals (no or minimal collaterals in a region greater than 50% of the MCA territory) [3,43] (Fig. 5).

3.2. Core/penumbra assessment

AIS is associated with a decrease in the cerebral blood flow (CBF) distal to the arterial occlusion, which may be partially compensated by the hemodynamic reserve with vasodilatation, arterial recruitment and collateral circulation. There is a consequent increase in the circulation times, measured as arterial arrival times or transit times, (such as mean transit time – MTT; first moment transit time – FMT; time to peak of the deconvolved tissue residue function Tmax; or time to peak – TTP) and a preserved or even increased total volume of blood (CBV – Cerebral Blood Volume) [21,44]. Below the normal CBF threshold of approximately 55 ml/100 gm tissue/minute, the autoregulatory mechanisms may achieve a maintenance (or elevation) of blood volumes keeping the neuronal cells viable (penumbra area). Over time, as the critical ischemic CBF threshold (approximately 15–20 ml/100gm/min) is exceeded, the brain becomes ischemic, the clinical deficits appear, and there is progressive evolution to infarction (core) unless arterial flow is quickly restored [21,44]. The rate of progression is highly dependent on the individual arterial collateral status [21,44].

The “core” represents a central area in the brain arterial territory that has unviable tissue with irreversible lesion, even if the recanalization of the occluded artery is early achieved. The “penumbra”

area, surrounds the core, is composed of viable brain tissue with loss of electric activity (metabolic and ionic dysfunction), but the cellular structural integrity is maintained, and there is a potential recovery after timely recanalization of the occluded artery [6]. Surrounding penumbra is the oligemia area in which the CBF is decreased but not to the extent for infarction risk and both normal neural function and integrity are maintained.

Penumbra is the target of the revascularization therapeutic approaches. The penumbra evaluation is important to exclude patients without salvageable tissue from treatment avoiding potentially futile or even harmful revascularization treatments or to include patients that being beyond the therapeutic time window would still benefit for revascularization [44–46]. AIS with baseline larger core infarcts are associated with worse clinical outcome, even with intra-arterial treatment and despite the recanalization rate, with larger final infarct areas and increased risk for symptomatic intracranial haemorrhage. [15,47–51] The presence of “malignant profile” characterized by a volume equal or exceeding 70 ml of DWI abnormalities, and/or a volume equal or superior to 100 ml of perfusion changes, such as Tmax > 8 s, is associated with adverse outcome independently of the revascularization [15,52].

Several CT and MR imaging parameters have been suggested for the assessment of core and penumbra [22,50,52–56]. This includes DWI-MRI for core assessment and several CT and MR perfusion parametric maps, such as: circulation times (mean transit time – MTT, first moment transit time – FMT, Tmax, or time to peak – TTP) measured in seconds; the total amount of blood in the vascular bed measured in ml/100gm (cerebral blood volume – CBV); and the overall rate of blood delivery per unit of time (cerebral blood flow – CBF) measured in ml/100gm/min (CBV = CBF*MTT) [21]. However, there is no fully validated clinical perfusion parameter nor perfusion threshold to distinguish core, penumbra and benign oligemia [22,50,52–56].

DWI-MRI is the best method to evaluate the infarct core with both high sensitivity (91–100%) and specificity (86–100%) [57]. As mentioned before, there are exceptions and DWI lesion reversibility, which may occur in 8–44% of cases, depending on the duration of the stroke, earliness of reperfusion, and baseline ADC decrease magnitude

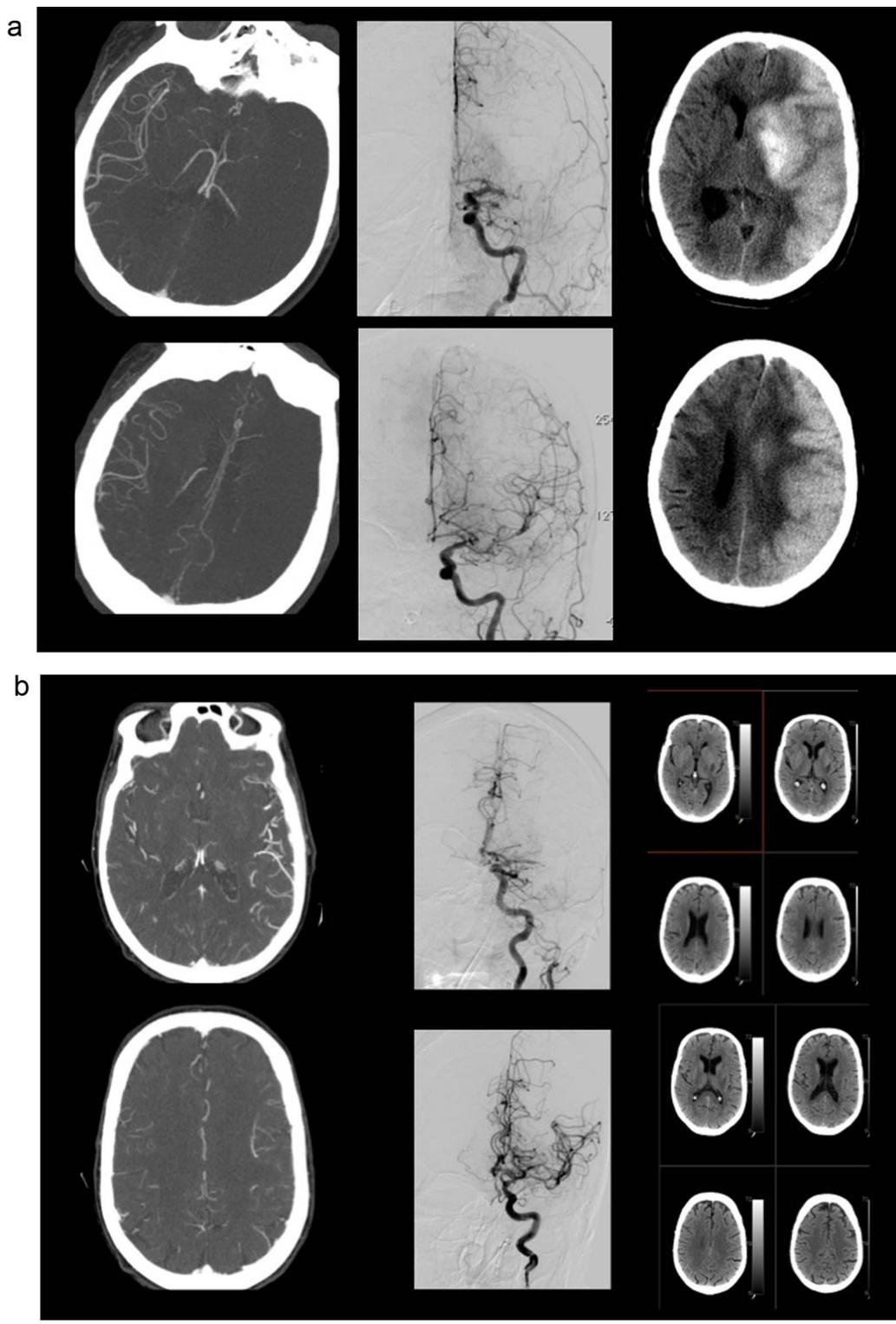


Fig. 5. Arterial collateral patterns. Two patients with acute AIS due left middle cerebral artery occlusion and M1 occlusions and distinct arterial collateral patterns. (1) Female 82 year-old at approximately 4 h after symptoms onset with poor/bad arterial collateral pattern. The thrombectomy was successful obtaining a complete revascularization (TICI 3) but with a dismal outcome with a massive infarct of the complete MCA territory. (2) Female 84 year-old at approximately 4.5 h after symptoms onset with good arterial collateral pattern. The thrombectomy was successful obtaining a complete revascularization (TICI 3), an excellent outcome with a small ischemic lenticular nucleus infarct.

[17–20]. However, this potential reversibility may not be consistently associated with improve clinical outcomes nor with changes in the treatment decision [20,58,59] and the real reversibility could be residual in both incidence and amount of tissue involved, as shown in the DEFUSE-EPITHET trial analysis (6.7% with a median volume of 2.3 cm³) [60].

Several CT perfusion parameters (Fig. 6) have also been used to define core, such as CBF decrease (rCBF reduction greater than 30–45% of the normal CBF) [61–63] CBV decrease (below 2–2.5 ml/100 g) [63,65] and MTT increase (above 8.3 s) [64] have been suggested.

There is still some debate regarding which is the best CTP parameter to define the infarct core, namely CBV or CBF decrease. It seems that CBF reduction (rCBF reduction greater than 30%) may correlate better with the DWI findings [7,66].

Regarding the penumbra, the most common perfusion parameters/thresholds suggested have been the increased Tmax (PWI-Tmax longer than 6.5 s and CTP-Tmax longer than 5.5 s) [67], the MTT increase (longer than 6 to 12–13 s or above of 145–249% rMTT of the contralateral) [61,64,68] and the decreased CBF (r CBF lower than 66% or CBF below ~28 ml/100 g/min) [61–63,66]

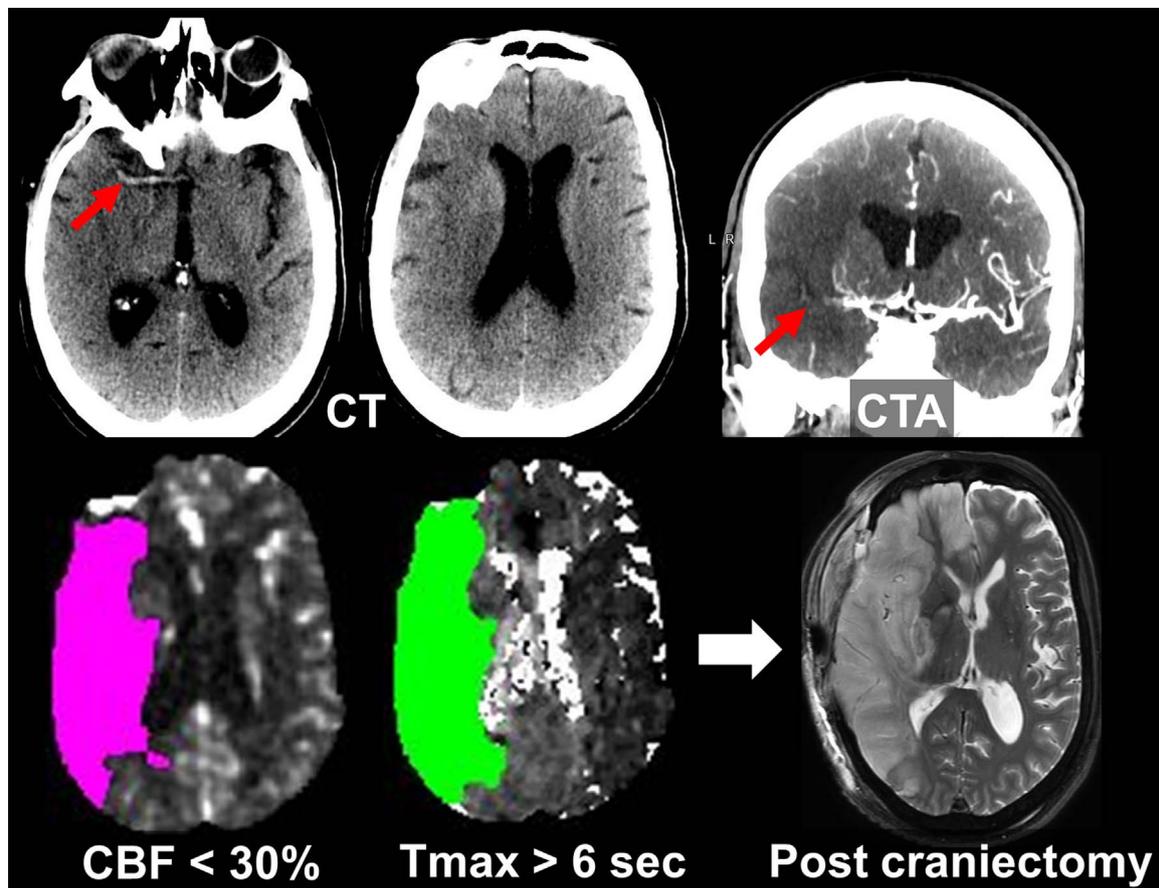


Fig. 6. Right MCA occlusion, multimodal CT triage. This patient presented with a proximal M1 occlusion (hyperdense artery sign and corresponding CTA cut-off, red arrows), poor distal collateral filling, and ASPECTS = 4. Thresholded CT perfusion images show a very large presumptive core (165 ml for CBF < 30% of normal) with only slight penumbra beyond (Tmax is largely matched; RAPID software, only 1 of 16 slices shown). Parenchymal, vascular, and CTP imaging features all predict poor outcome and futility for intervention. He was therefore treated with prophylactic craniectomy.

It seems that the major clinical outcome determinant is the size of the core and not the presence of the ischemic penumbra, as the later can be anticipated as the remaining arterial territory fed by the occluded artery [70–72]. Therefore, core-imaging is essential to select those patients that with a small core will have better prognosis, presumably independently of the time window [70].

There has been a relevant heterogeneity regarding the core/penumbra perfusion thresholds, with significant differences between studies reflecting a poor standardization with high variability among study protocols, regions of interested evaluated (generally combined grey/white matter which have distinct perfusions), algorithms post-processing techniques, with large sources of variability in parametric quantification, and with associated low interobserver reproducibility [27,55,61,69].

MRI perfusion (PWI) – diffusion (DWI) evaluation may also allow the characterization of the type and timing of stroke. (Fig. 7) Large vessel occlusion leads to target mismatch (PWI > DWI) and infarct growth is expected if no revascularization is achieved. No target mismatch (PWI = DWI) may be seen in large vessel strokes in which the stroke is established and the collateral circulation prevents further infarct growth. Inverse mismatch pattern (PWI < DWI) may be seen in early large vessel stroke reperfusion phase or in lacunar infarcts. Positive diffusion lesions without perfusion abnormalities may be seen in transient ischemic attacks and small distal (cortical or perforator) artery occlusion. Diffusion negative stroke-like presentations, with either perfusion abnormalities or normal perfusion maps may be seen in migraine, reversible vasoconstriction cerebral syndromes, posterior reversible encephalopathy syndrome, and transient ischemic attacks.

Diffusion positive lesions with increase perfusion (CBF or CBV) may be seen during the ictal/postictal seizure phase and the migraine aura.

3.3. Imaging of the clot

Additionally, both clot length and type have shown prognostic value. There are quantitative scores for evaluating the extension of the clot, such as the Clot burden Score. Clots with lengths over 8 mm and/or hypodense (fibrin-rich) compared to smaller and hyperdense (red blood cell-rich) thrombus, have lower recanalization with IV thrombolysis [73–77].

4. Conclusions

Imaging is essential for patient selection in AIS treatment. Parenchymal and vascular imaging is mandatory, either by CT/CTA and/or MRI/MRA depending on the immediate local availability.

Advanced stroke CT and MRI protocols, including arterial collateral status and core/penumbra mismatch, provide precise information about the individual stroke pathophysiology. The use individualized physiological imaging should allow better patient selection for treatment within and beyond the usual time therapeutic window. The presence of a small core and good collateral circulation are associated with good outcome. In opposition, the presence of malignant DWI profile, the absence of penumbra and the absence of collateral circulation are associated with bad outcome independently of the time from stroke onset and revascularization results.

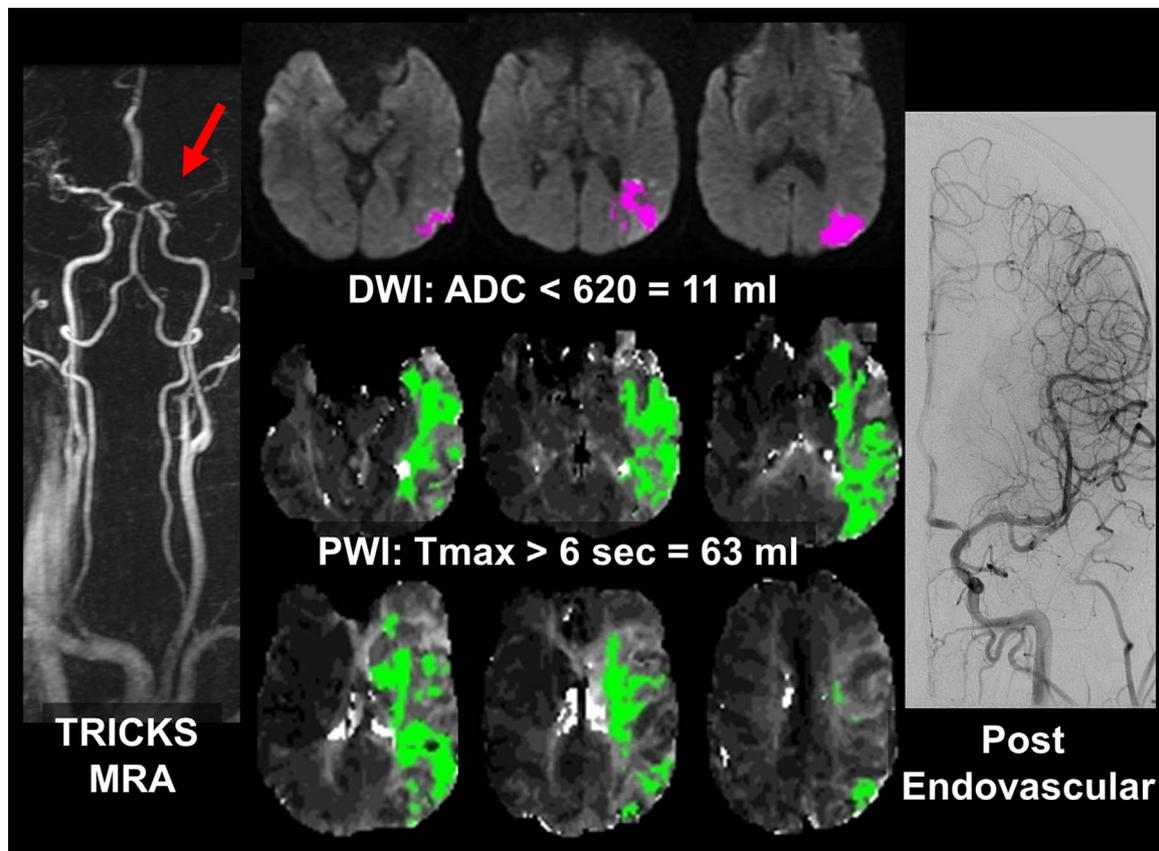


Fig. 7. Symptomatic left carotid terminus occlusion (arrow) at 4.5 h, perfusion-diffusion mismatch triage and selection. Thresholded ADCs (pink shading) show a small area of presumptive core ischemia, while prolonged perfusion transit times suggest a much larger area of putative penumbra (green shading, RAPID software). Full recanalization and complete recovery were achieved. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

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