Perfusion imaging in brain disease

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\textbf{Abstract} Perfusion CT or MRI have been extensively developed over the last years and are accessible on most imaging machines. Perfusion CT has taken a major place in the assessment of a stroke. Its role has to be specified for the diagnosis and treatment of the vasospasm, complicating a subarachnoid hemorrhage. Perfusion MRI should be included in the assessment of any brain tumor, both at the time of the diagnosis as well as in the post-treatment monitoring. It is included in the multimodal approach required for the optimum treatment of this disease. The applications in epilepsy and the neurodegenerative diseases are in the evaluation process.

The exploration of the brain by radiology can’t be summed up by the acquisition of morphological information. It should include metabolic data (1H MR spectroscopy), microstructural data (diffusion), vascular data (perfusion angiography) and functional data (activation imaging).

Since the beginning of the year 2000, first pass brain perfusion MRI has taken off and has become unavoidable for the characterization and monitoring of neoplastic processes [1–3].

Secondly, with the appearance of MDCT scanners enabling the acquisition of several slices in less than 1 s, the perfusion CT-scan has also developed. Quickly and easily available, this technique has widely imposed itself in emergencies, in particular for the care of stroke victims [4,5]. It is also a pertinent tool to assess the vasospasm complicating subarachnoid hemorrhages, thereby enabling the application of the best therapeutic strategy.

We will detail the value of perfusion imaging in the different clinical applications.

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Acute brain ischemia

The first cause of disability in the adult in developed countries and the third leading cause of mortality, the stroke or cerebrovascular accident (CVA) is a public health problem receiving optimum care by neurological critical care units (NCCU). Imaging in standard slices with angiographic sequences associated with diffusion MRI (with or without perfusion) and the perfusion CT-scan are the different means available. Used to advantage, they should quickly, and without delaying the therapeutic care of the patient, indicate a diagnosis of brain ischemia while specifying the extent of the lesion, define the extent of the perfusion anomalies and assess their reversibility, search for the cause of the ischemia by indicating the level of the arterial occlusion. The severe functional prognosis perceived, several years ago, as an inexorable fatality, has improved considerably with the arrival of intravenous or intra-arterial thrombolysis and the emergency care of CVA, fairly close to that of infarction of the myocardium. In a study carried out in 1999, only 3% of the patients, who should have been treated within the first three hours, were able to benefit from thrombolysis. Although the time before arrival at a NCCU has been reduced, due to improved organization of care and the increased awareness of the medical and paramedical team as to CVA, it’s still interesting to try and extend this time, without harming the patient, so as to allow him to benefit from the greatest number of adapted treatments [6], and possibly consider arterial recanalization.

Once the arterial occlusion has been assessed, the definition of the penumbra (that is, the hypoperfused tissue with a risk of necrosis, but whose damage is potentially reversible) is the cornerstone of therapeutic care. Treatment by alteplase leads to arterial recanalization and regression of the neurological deficiency as a function of the extent of the penumbra. Studies have shown the value of intravenous thrombolysis carried out within 4 1/2 h after the onset of the neurological deficiency [7]. Symptomatic intracranial hemorrhages due to the alteplase occur at a rate similar to that observed when the delay is less than 3 h [8]. An MRI study, including diffusion and perfusion parameters, has demonstrated the efficacy of intravenous thrombolysis with 6 h [9]. The real challenge is to identify and define the profile of the patients that may benefit from thrombolysis according to the time before treatment with respect to the onset of the clinical deficiency. The difficulty is to recognize the penumbra and differentiate it from a benign oligemia. Dani et al. [10] and Mishra et al. [11] point out, in their analyses of the literature, the different definitions in CT-scan and MRI, of the infarcted zones, of the tissue at risk and the tissue without a risk of ischemia. The parameters used and the thresholds chosen vary a great deal according to the team. Even if it’s possible to lengthen the time before thrombolysis, the precocity of the care remains the best guarantee of a good functional recovery.

CT perfusion

The first definitions of the penumbra and infarction rely on measurement of the cerebral blood flow (CBF). The CBF of a normally perfused area is greater than 40 mL/100 g/min, the CBF of a zone of oligemia is between 20 and 40 mL/100 g/min, the CBF of a zone of penumbra is between 10 and 20 mL/100 g/min, the CBF of an ischemic zone is under 10 mL/100 g/min. This measurement did not seem to be robust, since the CBF varies according to the age of the patient and is three times as high in the grey matter (GM) than in the white matter (WM), leading to a quantification that varies according to the percentage of GM and WM involved by the delimitation of the region of interest (ROI). Wintermark et al. [4] described the obvious superiority of perfusion CT over that of CT without injection for the detection of CVA and showed that the mean transit time (MTT) mapping is most sensitive and those of the cerebral blood volume (CBV) and the CBF the most specific. They also noted the importance of cerebral vascular autoregulation. In infarction, the vascular autoregulation is lost, there is a reduction in the CBF and CB. In the penumbra, there is a reduction in the CBF although the CBV tries to be maintained by vasodilatation and recruitment of the collateral pathways. In case of inappropriate perfusion, they observed an increase in the CBV and CB, an extension of the MTT and TTP (time to peak or time until the peak value). In 2006 [5], they proposed thresholds that are currently used as of two brains perfusion parameters:

- a 145% increase in the MTT with respect to the healthy contralateral tissue is the threshold value to define tissue at risk. It predicts the final size of the infarction without recanalization on the monitoring MRI. The MTT is time that does not vary much between the WM and GM (5 to 6 s) and its calculation is taken into account in the arterial input function. With a contralateral lesion not allowing for a reliable contralateral measurement, an absolute value of 7 s may be used;
- a CBV under 2 mL/100 g defines an infarcted zone with, as a reference, diffusion imaging acquired at the time of the patient’s admission.

The zone of penumbra is therefore defined as a tissue in which the MTT has increased by 145% from which the zone of ischemia is subtracted where the CBV is < 2 mL/100 g. These values are included in certain post-treatment software (Philips scanners, for example) that directly provides color mapping of these two parameters (Fig. 1).

Finally, very recent studies [12] emphasize other parameters and thresholds, by referring to control by diffusion MRI at 24 h and clinical scores after 24 h and 90. A relative delay (time close to the T_max used in MRI [see infra], but free of the arterial input function) greater than 2 s and a CBF under 40% that of the contralateral tissue would be the optimum parameters to define the tissue at risk and infarction, respectively. These research tools have to be perfected before they can be clinically used.

In parallel, the hemodynamic consequences of acute or chronic stenosis are assessed by perfusion CT, as are the phenomena of revascularization after surgery.

It’s still difficult with CT to study the posterior cerebral fossa and detect small lesions. This isn’t the case with MRI.

We propose a perfusion CT protocol (Appendix I).

Perfusion MRI

The diffusion sequence directly visualizes the ischemic necrosis in the form of a cytotoxic edema. The reduction
in the ADC beyond a certain threshold attests to an "irreversible" necrosis. It is therefore logical to look for the parameters and thresholds defining the tissue at risk in the MRI diffusion/perfusion association, as well as in the CT [13] (Fig. 2). An absolute quantification isn't always possible in perfusion MRI and it is necessary to avoid confusing mismatch and penumbra. Two studies have tried to describe the MRI profiles of patients who could benefit from intravenous thrombolysis. The DEFUSE study [14] compiled 74 patients all of whom benefited from an injection of tPA within 3 to 6 h after the onset of the neurological deficiency, regardless of the MRI data associating diffusion and perfusion. The main result that supports the initial hypothesis is that only patients presenting a mismatch benefited from a better neurological recovery with early reperfusion. The mismatch criteria are: a defined lesion on the perfusion series using the mapping of $T_{max}$ over 2 s, and size at least 20% greater than that measured from the diffusion sequence. The $T_{max}$ may be defined as the time before the gadolinium concentration peak is reached compared with the arrival of the gadolinium in the cerebral arteries. The perfusion is defined as a 30%-reduction in the volume of the hypoperfused zone in the control MRI carried out 6 h after the thrombolysis. The EPITHET study [15] tested the hypothesis that the presence of a mismatch predicts a response to the thrombolysis. This randomized study, compared a group of 52 patients receiving alteplase with a group of 49 patients receiving a placebo for a CVA occurring within 3 to 6 h, after an assessment by diffusion and perfusion MRI and independent of the results obtained. Control MRI was carried out three to five days after the initial assessment and then 90 days later. Reperfusion was defined as a 90% reduction in he volume of the hypoperfused zone on the control MRI carried out within five days of the thrombolysis. The clinical state was assessed using an NIHSS score. In this study, the tPA does not provide a significant reduction in the growth of the CVA in a first analysis,

Figure 1. Right hemiplegia occurring 3½ h before: a: the CT-scan shows early signs of CVA; b: the perfusion CT shows an extensive seat of Ischemia of the left sylvian territory with mismatch. The red ROI corresponds to the necrosis (CBV < 2 mmL/100 g, reduction in CBF), the green ROI verte corresponds to the penumra (reduction in CBF, preservation of CBV and over 300% extension of the MTT); c and d: the CT-angiography shows thrombosis of the left middle cerebral artery (c) and dissection of the inner carotid (d).
Right hemiplegia and aphasia occurring 2 to 3 h before, noted upon waking up: a: the cytotoxic edema is not very extensive in the diffusion series; b: the ischemia is still not FLAIR visible; c–f: mismatch between the perfusion data (mapping of CBV: c: T₀; d: Tc; e: MTT; f: the diffusion data; g: corresponding perfusion curves; h: thrombosis of the left inner carotid.
but significantly increases the reperfusion in patients with mismatch, itself associated with a better clinical recovery.

Therefore, the patients with a lesion defined in perfusion by $T_{\text{max}}$ mapping superior to 2 s with a volume superior to 120% of the lesion in diffusion may benefit from treatment with tPA beyond a period of 3 h, that is between 3 and 6 h.

The perfusion/diffusion MRI also helps identify and eliminate poor candidates for thrombolysis. These patients with a high risk of hemorrhage present an ischemic seat exceeding 100 mL in diffusion and/or perfusion anomalies defined by a $T_{\text{max}}$ superior to 8 s in a volume of 100 mL and more [14].

The quantifications obtained from the DEFUSE and EPI-THET studies have been refined. Studies carried out in 2009 show that part of the lesions initially visible in diffusion are reversible [16] and retain a $T_{\text{max}}$ superior to 4 s to predict the final size of the infarction in case of non reperfusion and a $T_{\text{max}}$ between 4 and 6 s to best estimate the penumbra [17].

Lansberg et al. [18] proposed an automated and fast post-treatment to differentiate three groups of patients with new threshold values:

• patients with a mismatch (ratio of the damaged volume in perfusion with a $T_{\text{max}}$ superior to 6 s and the volume defined from the diffusion hypersignal superior to 1.2) benefit from reperfusion by presenting a better clinical evolution and a reduction in the extension of the infarction. The value of 6 s for the $T_{\text{max}}$ is very close to that of 5.5 proposed in a study correlating positron emission tomography and perfusion MRI for the definition of the penumbra [19];

• patients without mismatch who did not present a clinical response or a reduction in the extension of the infarction after reperfusion;

• patients with a malignant profile (volume damaged over 100 mL in the diffusion data or with a $T_{\text{max}} > 8$ s in the perfusion data) who do not benefit from reperfusion.

These criteria may be of use in the care of the wake-up CVA [20]. Recently, Campbell et al. [21] confirmed that rare cases of regressive lesions in diffusion do not alter the calculation of the mismatch.

To simplify and shorten these analyses, teams apply the ASPECTS scores initially intended to assess the topography of the extension of the ischemia in CT with diffusion and perfusion data ($T_{\text{max}}$) leading to a mismatch score [22].

We propose a perfusion MRI protocol (Appendix II).

### Delayed cerebral ischemia (DCI) due to a vasospasm

DCI is a serious complication of subarachnoid hemorrhages (SAH), most often due to the rupture of a brain aneurism (Fig. 3). The rate of morbi-mortality is high, since 46% of the surviving patients suffer from cognitive disorders [23]. The vasospasm, an inflammatory reaction of the vascular walls, occurs between D4 and D21 (with a maximum between D6 and D12), especially if the SAH is considerable (high Fisher grade). This reaction is observed in arteriography in 2/3 of the patients, although its clinical translation is more rare. The patients present the insidious onset of impaired consciousness and focal neurological deficiency, assigning a major role to the complementary examinations required to make an early diagnosis. While the Doppler is only pertinent in the exploration of the sylvian artery, the CT-angiography is little by little replacing the angiography in the detection of the vasospasm, which is classified as moderate (25 to 50% reduction in the diameter of the vessels) or severe (reduction exceeding 50% in the diameter of the vessels). Nevertheless, the absence of a vasospasm does not exclude the possibility of the occurrence of an ischemia and the presence of a vasospasm does not prove the ischemia. Only half of the patients with a severe vasospasm present a delayed ischemia. The reduction in cerebral perfusion due to the vasospasm is therefore not the only factor responsible for the ischemia [24]. This would explain why the vessels with the most severe vasospasm correspond to the less perfused region in only 2/3 of the cases. This is why it’s necessary to look for a technique providing arguments as soon as the onset of the clinical signs corroborate the ischemic hypothesis. Perfusion CT is routinely used in the

![Figure 3](image_url) Subarachnoid hemorrhage by rupture of an aneurism: a: appearance of a diffuse vasospasm of the sylvian arteries in the controls; b: over 6.5 s increase in the MTT in the sylvian and right anterior cerebral territories with the drop in the CBF.
diagnosis of acute ischemia. Its value in delayed ischemia has only been recently demonstrated. Thresholds on the perfusion CT have been proposed to corroborate the diagnosis of vasospasm. For Wintermark et al. [25], an increase in the MTT above 6.4 s reveals a high risk for DCI, and the arterial territory should be evaluated in CT-angiography to search for a reduction in the diameter of the arteries that will lead to an angiography for diagnostic and therapeutic purposes. According to Dankbaar et al. [26], the MTT threshold is 5.9 s or a 1.1 s difference with the contralateral ROI. A relative increase in the MTT (exceeding 146% in the reference region) has also been proposed [27].

The qualitative analysis [28] visually assessing the mapping of MTT, CBV and CBF would suffice to demonstrate the superiority of perfusion CT over CT-angiography (sensitivity of 0.84% versus 0.64, specificity 0.79% versus 0.5), the gold standard to make the diagnosis of delayed ischemia being the analysis of the entire clinical file by two experienced neurologists. This visual approach has already been proposed in comparison with angiography, with a very high sensitivity (92%) and specificity of the MTT (86%) [29].

In practice, the interpretation of the perfusion CT in the search for DCI is difficult. It’s first necessary to verify the dynamics of the arterial and venous curves. As opposed to acute ischemia, the pathology is diffuse. It’s necessary to avoid placing the measurement of the arterial input function used for the de-convolution in a pathological zone, as this would make any interpretation erroneous. It may be advisable to place a ROI in the territories of the lenticuostriate arteries, not very affected by the DCI.

**Tumor disease**

MRI dominates the exploration of brain tumors due to its great sensitivity, in particular via the T2-weighted/FLAIR sequences, to detect tumor infiltration at a distance from the main lesion. The morphological assessment of an expansive process includes T1-weighted sequences, T2-weighted/FLAIR sequences, T1-weighted sequences after the injection of gadolinium. An enhancement after injection only attests to a rupture of the blood-brain barrier (BBB) and not the presence of neo-vessels. However, the characterization of the vascularization of a tumor is fundamental to approach the histological diagnosis and assess the grade of evolution, in particular in case of glioma. The appearance of a neo-angiogenesis within a glioma is an evolutive and decisive turning point in the disease. These neo-vessels present an increase in their diameter, their permeability and their density, as well as endothelial proliferation. Only perfusion techniques give access to tumor microvascularization. First pass perfusion is the technique most often used in the diagnosis of the tumor. It can measure the relative cerebral blood volume in the tumor (ratio between the highest blood volume registered within the tumor and the blood volume registered in the healthy contralateral white matter), as well as the capillary permeability. These two parameters have to be assessed, or even quantified when possible with the post-treatment software.

**Glial tumors**

The presence or absence of enhancement is not enough to classify gliomas as low or high grade [30]. For many years now, the histological grade of gliomas has been correlated with the tumor blood volume. The greater the increase in volume, the higher the grade [1,31,32] (Fig. 4). Below a threshold of 1.5, it’s possible to exclude the possibility of a malignant glioma [33], whereas a threshold of 1.75 identifies high grade gliomas with a sensitivity, specificity, positive predictive value and negative predictive value of 95%, 57.5%, 87%, and 79.3% respectively [34]. The cerebral blood volume is often underestimated due to the increased permeability of tumor vessels and the T1-weighted effects induced. The injection of a bolus of contrast agent prior to the acquisition of the first pass perfusion series is recommended in order to correct them [35]. However, this pre-injection will mask the passage below the baseline, observed in case of lymphoma, for example, which is a pertinent diagnostic criterion. Independently of this histological criteria, the CBV has a predictive value in knowing the mean survival before progression: below 1.75, it’s 3585 days; above 1.75, it’s 265 days [36]. A higher prognostic value (2.2) is retained in case of oligodendrogloma [37]. The permeability, assessed by a parameter called Ktrans is also correlated with the histological grade, although less than the CBV [38]. With a low-grade glioma, the permeability and enhancement play an unfavorable prognostic role [39].

It should be noted that the CBV of oligodendroglomas is on the average higher than that of astrocytomas [40] and that certain oligodendrogliomas present seats of hypervascularization due to a rich capillary network, while remaining histologically benign [33].

In practice, the detection of a seat of neo-vascularization within a neoplastic process indicating a low-grade glioma should be the target of the biopsy, since it corresponds to a suspected highly malignant zone [41]. The appearance of a seat of neo-vascularization during the monitoring of a low-grade glioma suggests the evolution towards a high grade tumor (Fig. 5) and most often leads to a change or resumption of therapy.

During the monitoring of gliomas, it’s fundamental to always use the same acquisition protocol in order to obtain comparable explorations [42]. In particular, the controls should always be carried out on the same MRI machine when two machines with different fields are available.

Radiotherapy and chemotherapy induce post-therapeutic rearrangements and it’s difficult to interpret the morphological images according to MacDonald’s et al. criteria [43]. Pseudo-progression corresponds to an increase in the volume of the enhancement, whether or not associated with an increase in clinical deficiency. Radiotherapy, whose effects are potentiated by chemotherapy, provokes inflammatory phenomena, endothelial lesions, with an increase in capillary permeability and the presence of an edema. A reduction in the CBV indicates a pseudo-progression, whereas an increase suggests tumor evolution [44]. A threshold of two was proposed to differentiate tumor recurrence and post-therapeutic effects, such as radionecrosis, in a study that integrates spectroscopic data [45], opening the way to multimodal MRI. The pseudo-response is a reduction in the volume of the enhancement due to the use of an
antiangiogenic agent such as Bevacizumab that closes the blood-brain barrier and reduces neo-vascularization. The spectacular results observed in the first days of treatment are not necessarily correlated with a clinical improvement. The T2-weighted and FLAIR sequences are then fully useful along with the description of the RANO criteria [46].

Based on this data, we find that it’s obligatory to interpret the MRI with an exact understanding of the therapeutic treatment regimen.

Pilocytic astrocytoma (Fig. 6) is a specific grade 1 glioma according to the WHO, presenting a low CBV (close to 1) and a high permeability. These characteristics differentiate it from a hemangioblastoma that resembles it morphologically (cystic tumor with fleshy nodule of the posterior cerebral fossa) [47,48], but that presents a very distinct hypervascularization.

Lymphoma

The incidence of malignant non-hodgkin lymphoma (NHL) is increasing. The diagnosis of lymphoma as of the MRI helps avoid starting corticotherapy, which may eliminate the lesion and render a biopsy impossible. The lymphoma presents characteristics in diffusion as well as in perfusion. In diffusion, there is a reduction in the ADC related to the very cellular nature of the tumor. In perfusion, the CBV is low, close to 1.5 [49,50] and the baseline very distinctly passes above its initial value (Fig. 7). This data is particularly useful in identifying the meningeal forms of the lymphomas that are thereby distinguished from meningiomas and meningeal metastases and to detect the multiple lymphomatous sites.

Besides the CBV, other parameters may be analyzed, such as the percentage signal recovery (PSR) that corresponds to the minimum difference in signal over the difference between the minimum signal and baseline [51]. The advantage of the PSR is that it integrates the idea of permeability attested to by the passage above the baseline of the perfusion curve. Lymphomas are characterized [52] by high PSR means and maximums.

Meningiomas

The World Health Organization classification of tumors lists 15 sub-types of meningiomas. It’s therefore difficult to describe the general criteria of vascularization for all of
these meningiomas. The CBV of angiomatous meningiomas is higher than that of meningiothelial meningiomas, itself higher than that of fibroblastic meningiomas [53]. A high CBV in a peri-lesional edema suggests an anaplastic meningioma [54].

In medical practice, a highly hypervascularized extra-axial tumor indicates a meningioma rather than a schwannoma [55] or a dural metastasis [56], although hypervascular metastases may induce an error. A highly hypervascularized intra-ventricular tumor indicates a meningioma rather than a neurocytoma or subependymoma (Fig. 8) [57].

**Metastases**

Very frequent, brain metastases are hypervascular. If they are alone and if a neoplastic antecedent is not known, the differential diagnosis with a malignant glial cell tumor is difficult. The PSR of metastases is statistically lower than that of malignant gliomas [52]. The study of the peritumoral environment helps differentiate the two diagnostic hypotheses. The CBV observed in a peri-tumoral zone with a metastasis is lower than that observed with a malignant glioma [58] due to the peri-lesional tumor infiltration observed with a glioma. This semiological sign, when it

![Figure 5](image-url)
exists, seems most reliable in clinical practice to distinguish the quantitative data of two tumor entities, even if it often overlaps.

**Pseudo-tumoral process**

**Abscess**

Rare, the brain abscess, from a clinical as well as a radiological viewpoint, suggests the possibility of a primary or secondary malignant tumor. The diffusion series, that shows a low ADC within the purulent necrosis, is the key to the diagnosis. The perfusion, by revealing a little vascularized, abscess capsule [59], rich in collagen fibers, is a complementary non-useable series in the case under discussion [60] (Fig. 9). This characteristic, like any semilogical sign, may be erroneous [61], thereby emphasizing the importance of multimodal approaches associating perfusion, diffusion and spectroscopy [62].

**Demyelinating lesions**

Extensive areas of demyelination may imitate a tumor [63]. When the pseudo-tumor is present during the first attack of multiple sclerosis or when this is a single episode (acute disseminated encephalomyelitis), the radiological diagnosis is difficult. The lesions appear as enhanced masses, often surrounded by an edema. However, the mean CBV of these lesions is under one [64], differing greatly from that of malignant brain tumors (Fig. 10).

Parallel to the quantitative perfusion data, the small veins along which demyelinating areas are visible through the effect of magnetic susceptibility on the native slices, then orient the diagnosis.

**Value of CT in tumor disease**

CT is less pertinent than MRI in the assessment of the extension of tumors. Nevertheless, it has several advantages [65]:

- the lineal relationship between the concentration of the contrast product and the attenuation of the X-rays provides more robust estimates of the CBV and the permeability;
- it isn’t sensitive to the effects of magnetic susceptibility related to post-therapeutic rearrangements that often perturb the interpretation of the MRI during the monitoring [66];
- with only one acquisition, it provides access to the usual parameters (CBV, CBF, MTT) as well as the permeability data.

**Neurodegenerative disease**

The diagnosis of dementia, especially in Alzheimer’s disease, is based on the clinical data and the neuropsychological
tests. Morphological imaging (MRI) should be obtained in order to eliminate the tumoral or vascular causes and look for specific zones of atrophy. In atypical cases, it’s possible to use biological markers in the LCR (tau protein and abeta 42) and metabolic data derived from scintigraphy or positon emission tomography. These expensive examinations detect regions of hypo-metabolism that may be replaced by spin labeling MRI, not requiring an injection, and provide both a morphological and a functional study. For example, a high correlation has been found between positron emission tomography and spin labeling MRI, both showing angular gyrus impairment or the posterior part of the cingulated cortex in Alzheimer’s disease [67,68].

Figure 7. Lymphoma revealed by recent headache in a 65-year-old man: a: obstructive lesion of the interventricular foramen; b: the mass is massively enhanced; c: CBV ration slightly lower than one and major permeability of the neoplastic vessels (very pronounced passage above the baseline of the perfusion curve).
Figure 8. Meningioma developing in the 4th ventricle in a 72-year-old woman: a: the enhancement of the mass is homogenous; b: it is hypervascular on the CBV mapping; c: the CBV ratio equals 15.
Figure 9. Toxoplasmosis revealing HIV seropositivity in a 42-year-old man consulting for right hemibody sensory disorders: a: left thalamic lesion surrounded by an edema; b: this lesion is massively enhanced; c: it does not present hypervascularization; d: there is an increase in capillary permeability.
Figure 10. a: CT without injection; b: perfusion CT (CBF); c: angioscan; d: FLAIR; e: mapping of the ADC.
Conclusion

Perfusion CT and MRI are an integral part of a neuroradiological assessment. Ischemic and tumor disease are two major groups in which they play a preponderant role. Their role in epileptic and neurodegenerative disease is being studied.

TAKE-HOME MESSAGES

Acute ischemic disease:
- perfusion CT and MRI should assess the brain tissue at risk (penumbra) in case of acute CVA;
- quantitative values are recognized in perfusion CT: a CBV < 2 mL/100 g defines the infarcted zone, a 145% increase in the MTT defines the penumbra;
- MRI is used to identify the good candidates for thrombolysis (positive mismatch) and exclude the bad candidates with a high risk of hemorrhage;
- the quantitative data should be made more exact by perfusion MRI.

Delayed ischemia (vasospasm):
- perfusion CT and CT-angiography should replace angiography in the diagnosis of vasospasm. The MTT is the most important parameter to determine (thresholds need to be specified).

Tumor disease:
- the perfusion curves of lymphoma and pilocytic astrocytoma are similar. The CBV ratio is close to 1, the passage above the baseline is very distinct;
- the higher the grade of the glioma, the higher the CBV;
- the CBV of gliomas, independent of the histological grade, predicts the mean survival before progression;
- the appearance of neurovascularization within a low-grade glioma indicates tumoral evolutivity towards a higher grade;
- the threshold of two helps differentiate tumor recurrence from radionecrosis.

Clinical case

Six days ago, this 77-year-old woman benefited from right carotid endarterectomy for very tight bulbary and post-bulbar stenosis, revealed by paresthesia of the right hemibody. She consulted for seizures of the face and arm.

Questions

1. Does this case involve a post endarterectomy CVA?
2. What factors favor a brain reperfusion syndrome?
   a) Poorly controlled HBP
   b) Antecedents of CVA
   c) Tight arterial stenosis
   d) A deficient cerebral blood flow in transcranial Doppler before surgery
3. How do you account for the perfusion data (CBF)?
4. What is your diagnosis?

Answers

1. There’s an increase in ADC, the lesion therefore correspond to a vasogenic and not cytotoxic edema.
2. a, b, c, d.
3. There’s an increase in CBF since there is a loss of cerebral vascular autoregulation.
4. Diagnosis: vasogenic edema by brain reperfusion syndrome.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Appendix I. Perfusion CT protocol

The last generation of scanners almost completely covers of the brain and brain perfusion isn’t limited to 2 cm as before. The positioning of the perfusion series is related to the clinical deficiency and most probable topography of the seat of the ischemia. After a series without injection, the next step consists of the acquisition of images in dynamic mode, at the rate of eight joint slices, each with a thickness of 5 mm, for 40 s (one image every two seconds) during the intravenous peripheral injection of a bolus of 40 mL of OMNIPAQUE 300 (iohexol 300 mgI/mL, GE Healthcare®) at 4 mL/sec in a peripheral vein (cathlon 20G), using an automatic injector (SWISS MEDICAL CARE). The injection lasts for 10 s. The acquisition begins 6 s after the beginning of the injection and lasts for 40 s. One hundred and sixty images are acquired during this period, that is, 20 images for each of the eight slice levels, at a rate of one image every 2 s. This protocol thereby provides eight CT brain slices, each 5 mm thick, or a volume of 40 mm. The mapping of the CBV, CBF, MTT and TTP is generated, giving quick access to a first qualitative analysis. ROI representing the arterial territories are positioned for the calculation of the quantitative data.

Appendix II. Perfusion MRI protocol

An echo gradient sequence is usually used (for example, at 1.5 T, a multishot sequence with RT = 507 ms, ET = 30 ms, angle = 40°, 12 slices 5.5 mm thick obtained every 1.5 s for one minute); the injection is carried out with the usual dosage (0.2 mL/kg or 0.1 mmol/kg) with a flow of 6 mL/s, concomitant to the dynamic acquisition. The same mapping as in the CT-scan is generated.

The ROI vary: in ischemic disease, the ROI describe the vascular territories, in tumor disease, a ROI is positioned in the zone where the CBV is highest, another in the contralateral white matter to form the $\frac{CBV_{tumor}}{CBV_{white \ matter}}$ ratio representative of the tumor.
References


[35] Boxerman JL, Schmida KM, Weisskoff RM. Relative cerebral blood volume maps corrected for contrast agent extrava-

[36] Law M, Young RJ, Babb JS, Peccerelli N, Chheang S, Gruber ML, et al. Gliomas: predicting time to progression or sur-

[37] Jiang Z, Le Bas JF, Grand S, Salon C, Pasteris C, Hoff-


[40] Chag S, Tihan T, Crawford F, Fischbein NJ, Chang S, Bollen A, et al. Differentiation of low-grade oligodendrogliomas from low-grade astrocytomas by using quantitative blood-


[42] Mauz N, Kraunik A, Tropes I, Lamalle L, Sellier E, Eker O, et al. Perfusion magnetic resonance imaging: Comparison of semio-


[46] Wen PY, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, Galanis E, et al. Updated response assessment criteria for high-


[48] Kumar VA, Knopp EA, Zaggag D. Magnetic resonance dynamic susceptibility-weighted contrast-enhanced perfusion imaging in the diagnosis of posterior fossa hemangioblastomas and pilo-


[51] Cha S, Lup JM, Chen MH, Lamberk KR, McDermott MW, Berger MS, et al. Differentiation of glioblastoma multiforme and single brain metastasis by peak height and percentage of signal inten-
sity recovery derived from dynamic susceptibility-weighted contrast-enhanced perfusion MR imaging. AJNR Am J Neuro-

centage signal recovery derived from MR dynamic susceptibility contrast imaging is useful to differentiate common enhanc-


[54] Zhang H, Rodiger LA, Shen T, Miao J, Oudkerk M. Preoperative subtyping of meningiomas by perfusion MR imaging. Neurora-

[55] Limy A, Sasiadek M. Contribution of perfusion-weighted mag-

[56] Kremer S, Grand S, Remy C, Pasquier B, Benabid AL, Brac-


[58] Law M, Cha S, Knopp EA, Johnson G, Arnett J, Litt AW. High-


[62] Chiang IC, Hsieh TJ, Chiu ML, Liu GC, Kuo YT, Lin WC. Distinc-


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