Neuroimaging applications of multislice CT perfusion

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Summary

- In acute stroke, very early cranial CT may be normal. Perfusion CT shows great promise in refining the selection of patients suitable for thrombolysis, as it can accurately determine infarct core from potentially salvageable ischaemic penumbra.
- In patients with acute subarachnoid haemorrhage, perfusion abnormalities are evident early on and can predict subsequent vasospasm. These can be detected by CT perfusion, which may enable more aggressive medical management of vasospasm.
- Some cerebral tumours are associated with angiogenesis and a breakdown of the blood-brain barrier. Angiogenesis can be detected as an increase in flow and volume parameters, and blood-brain barrier breakdown can be quantified as contrast accumulates in the interstitial space. Such aggressive features can distinguish malignant from benign tumours when standard imaging may not.
- CT perfusion is a very promising tool, and new advances in the technique are overcoming some of the initial shortcomings, leading to increased coverage, reduced processing time, and reduced volume and rate of contrast utilized.

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Abstract. *CT perfusion is an evolving technology that assesses the behaviour of intravenous contrast in cerebral tissue and provides quantitative information on cerebral blood flow parameters. It has been validated in many clinical situations against established techniques and is being increasingly applied in clinical situations to provide physiological information to direct medical therapies. This article reviews the evolution of perfusion measurements by CT, the principles of CT perfusion calculation and, with illustrated case histories, examines the clinical utility of this technique.*

Until recently, cranial CT was limited to display of anatomical information. Functional information was the domain of nuclear medicine studies and MRI. Attempts to gain perfusion information were initiated in the 1970s with the discovery of the effect of xenon gas on X-ray attenuation values. However, due to relatively long scanning time and requirement of a separate device for inhalation of xenon, this technique has not spread widely beyond its enthusiasts. CT perfusion with iodinated contrast medium has been increasing in popularity, particularly with the advent of spiral and multislice technology, and improvements in computing power.

This paper will briefly review the evolution of the technology, current technique and its applications with particular reference to stroke assessment.

History

The late 1970s and early 1980s saw the birth of perfusion CT. There was a greater understanding of the behaviour of iodinated contrast medium and xenon gas in biological tissue and an interest in how perfusion information could be extracted. Initial techniques were non or semi-quantitative, requiring long scan times (5–6 s per slice) and limited coverage [1, 2]. Advances in processing speed led to the development of colour perfusion maps, which remain the standard method of presenting overall perfusion information visually [3]. The advent of slip-ring and multislice technology increased the coverage available for analysis as well as reducing imaging time, opening up possibilities for dynamic perfusion imaging [4].

As either iodinated contrast media or xenon enter the imaging volume, the density of the tissue increases linearly. The early rise in density (maximal slope) is strongly correlated with the amount of contrast material delivered to the tissue and is therefore dependant on blood flow. By standardizing variables such as contrast medium concentration, utilising substances that remain in the vascular space, and high injection rates (10–20 ml s^{-1}, to reduce venous contamination before peak of arterial inflow is reached [5, 6]) a calculation of blood flow (CBF) is possible:

$$\mathrm{CBF} = \frac{\text{Maximal slope of tissue time density curve}}{\text{Peak arterial enhancement}}$$

Lower rates of contrast medium injection tends to underestimate CBF [5]. A more complex form of calculation (deconvolution) allows lower injection rates but makes a number of assumptions regarding material

behaviour and blood flow. This will be discussed below under theoretical aspects.

Non-dynamic perfused cerebral blood volume (pCBV)

An earlier method of calculating perfusion utilized a simple idea: subtracting a non-contrast cranial CT from one obtained after contrast medium administration. The remaining image is directly related to contrast density and therefore is proportional to the (theoretically known) contrast medium concentration and volume of blood at that time within the brain (pCBV [7]). The anatomy of the circle of Willis may also be derived from the same study. This method has been shown to improve accuracy in infarct localization [8]. There is, however, no dynamic information, which may be important in triaging patients for thrombolysis (see below). However, the whole brain is included in the analysis.

Other perfusion techniques

MR diffusion-weighted and perfusion imaging

Diffusion-weighted imaging (DWI) is a very sensitive MR technique to diagnose hyperacute stroke and can detect an ischaemic event only a few minutes old [9]. DWI provides information on the impact of ischaemia at cellular level, not on the perfusion disruption that caused it. DWI therefore defines non-salvageable ischaemic tissue. Contrast-enhanced MR perfusion (PMRI) is a semi-quantitative method to delineate areas of reduced perfusion based upon the effect of gadolinium. This technique requires an intact blood–brain barrier and is subject to susceptibility artefact. Matched areas on DWI and PMRI are thought to represent the irreversibly injured tissue (infarct core). A mismatch, with a larger hypoperfused area on PMRI than DWI abnormality, is thought to represent the reversible but ischaemic penumbra [10]. However, a portion of the DWI core may be potentially salvageable and the PMRI hypoperfused boundary may represent ''benign oligaemia'' (*i.e.* hypoperfused tissue which is not at risk of infarction) [11]. Nevertheless, it provides a good indication of the presence of salvageable penumbral tissue [12–14].

The MR environment, however, is inhospitable for acutely ill patients and contraindications (including pacemakers, previous clipping, intraocular foreign body) need to be excluded prior to imaging. This information may not be easily obtained in an emergency setting. MR compatible monitoring equipment is also required for such patients. Additionally, few centres within the UK provide 24 h access to MRI at present.

Nuclear medicine

This is a well-established and validated technique. A radioisotope, such as technetium-99m, is attached to a delivery compound (usually HMPAO – hexamethylpropylamine oxime) with a commercially available kit (taking 20–30 min to prepare). Upon injection, HMPAO-$^{99}Tc^{m}$ passes through the blood–brain barrier and is fixed in the cerebral tissues within 1 min. Uptake is proportional to CBF. Detection of fixed activity is performed with a 360° detector array to provide rudimentary anatomical information. This is performed during the next few hours [15]. The analysis is semi-quantitative comparing regions of interest (ROIs) of the affected and unaffected side, and a ratio calculated. In one multicentre blinded trial, the sensitivity for hypoperfusion in acute stroke was 86% with a sensitivity of 56% in lacunar infarcts [16]. The disadvantages in this method in the acute setting are: limited availability; low spatial resolution; and the semi-quantitative nature of the study, which assumes that the CBF in the comparison ROI is normal [17].

Xenon CT perfusion

In use since the late 1970s [18], this technique utilizes the properties of a highly lipid-soluble noble gas, with a high atomic number that increases the X-ray attenuation when it penetrates brain parenchyma through the blood–brain barrier. Its rate of tissue saturation is a slow process taking between 2 min and 15 min depending on blood flow. The rate of build up or washout can then be used to calculate local tissue blood flow [19]. CBF measured by Xe CT correlates well with proven experimental studies in animal models [5, 20, 21]. Multiple sections can be assessed with this technique. This method, however, is time consuming and requires the patient to inhale xenon for 4.5 min, which can be uncomfortable for acutely ill patients [22]. Xenon itself has a vasodilator effect and may increase CBF (up to 100%), in an unpredictable fashion with considerable inter- and intra-individual variation [22–24].

Theoretical aspects of CT perfusion

The desire for an accurate, reproducible technique to measure tissue perfusion *in vivo* that can be applied in a real clinical setting led to the development of CT perfusion. Iodinated contrast medium satisfies several important criteria for use as a perfusion agent: X-ray attenuation is proportional to tissue concentration [25]; the pharmacodynamics and toxicology are well understood (it remains in the vascular pool); it is cheap and widely available.

As contrast medium is infused through cerebral tissue, the density of this tissue increases over time, plateaus and then declines to a higher baseline (owing to recirculation). This ''time density curve'' is fundamental to calculating cerebral blood flow parameters (CBV and CBF).

Commercially available software (CT Perfusion, GE) based on the Windows operating system (Advantage Windows, GE) is utilized for CBF and CBV calculation. Small ROIs are placed over an unaffected vessel in the axial plane (usually the anterior cerebral artery) and another over the posterior aspect of the superior sagittal sinus. These arterial input and venous outflow functions, respectively, are required for the deconvolution analysis. This method enables contrast to be administered at rates of as low as 1.5 ml s^{-1} [26].

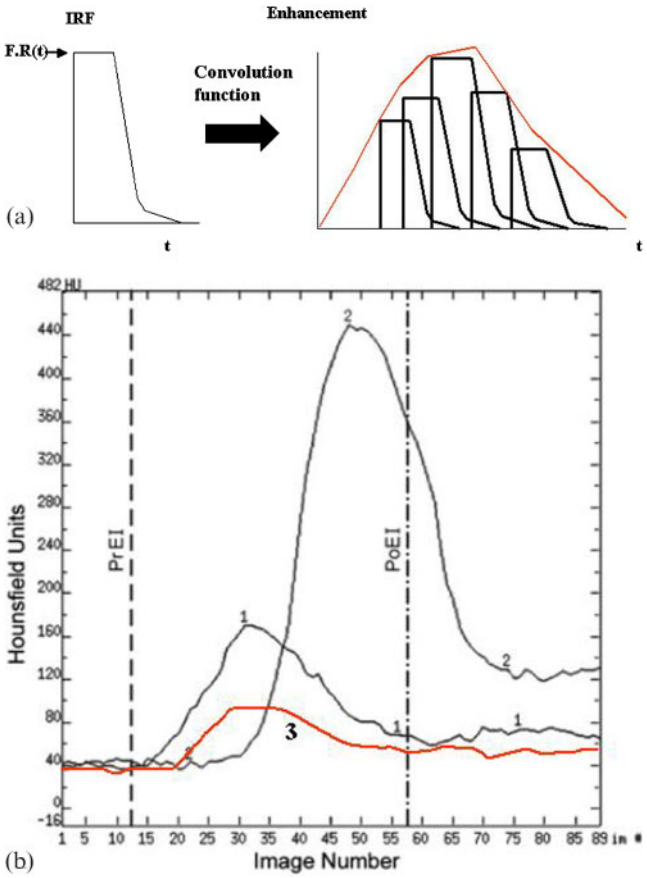


Figure 1. (a) The graph on the left is a representation of the impulse residue function (IRF). An instantaneous arrival of contrast bolus at the arterial input passes through the tissue. The length of the plateau represents the minimum transit time (MIT). The total area under the curve is the mean transit time. As contrast leaves the tissue there is decay in enhancement. The graph on the right illustrates the process of convolution. A general arterial input can be represented by multiple copies of the IRF, scaled according to differing concentrations at the arterial input and blood flow. The overall enhancement therefore is a summation of these IRFs time-shifted in accordance with the times of the bolus injection. (b) This is an image from a CT perfusion study showing the time density curves for the input artery, vein and region of interest placed over grey matter. Line 1 is the arterial input function. This provides the function: $C_a t$. Line 2 is the concentration of contrast medium in the superior sagittal sinus. This is required for the calculation of perfusion parameters. Line 3 is the time density curve of a region of interest and provides a measurement of Q(t).

On a pixel-by-pixel basis, the time-density curve of cerebral tissue is analysed against that of the input and outflow function and this information is fed into the deconvolution program (Figure 1).

When iodinated contrast media is injected into a peripheral vein, the rate of delivery to cerebral tissue can be calculated: $F \times C_a t$ where F = cerebral blood flow and $C_a t$ = contrast medium concentration at the arterial input.

Assuming F is constant (non-pulsatile) over time, and if the mass of contrast medium is linear with respect to the arterial concentration, then the following equation can be calculated: $Q(t) = F \times C_a t * R(t)$ where Q(t) is the tissue concentration of contrast medium (the ''tissue residue function''). This gives rise to the increase in density in tissues on CT. R(t) is the impulse residue function (a theoretical concept) and is the impulse (or bolus) of contrast medium remaining in the tissue over time. * is the convolution operator. This is a summation of multiple time-shifted copies of R(t) multiplied by the concentration of contrast medium at that time (Figure 1a). $C_a t$ and Q(t) can be measured on CT (Figure 1b). The deconvolution operation is used to calculate $F \times R(t)$.

The initial height of $F \times R(t)$ curve provides CBF (Figure 1a). CBV is the area under the curve, or can be calculated as: (area under Q(t))/(area under $C_a t$).

The central volume principle interrelates the main perfusion parameters that can be readily measured [27]. It applies to tracers that are non-diffusible and remain in the vascular compartment (provided the blood–brain barrier is intact):

$$\mathrm{CBF} = \frac{\mathrm{CBV}}{\mathrm{MTT}}$$

CBF is measured in ml 100g tissue^{-1} min^{-1}; CBV is measured in ml 100g tissue^{-1}; and mean transit time (MTT) is measured in seconds.

The transit time of blood to traverse the cerebral capillary network, from the arterial inlet to the venous outlet varies in a given ROI as there are different path lengths, and so an average of the distribution of transit times is obtained, hence the term mean transit time [28]. The cerebral blood flow can be calculated from the central volume equation [29, 30]. The deconvolution method has been validated in a number of studies by the microsphere technique [31–33].

Technique

A 50 ml bolus of iodinated contrast medium, *e.g.* Niopam 300 mg dl^{-1} (Iopamidol) (Bracco UK Ltd, High Wycombe, UK) is injected at a rate of 3 ml s^{-1}. For non-tumour studies, imaging is started 5 s later; for tumour studies, imaging is started immediately to capture the early rise in parenychmal enhancement. 5 mm slices are obtained in cine mode every half second for a total of 50 s giving a high temporal resolution. On a four-slice unit, a 2 cm z-axis volume can be imaged (four slices of 5 mm thickness). The area studied is usually at the basal ganglia, which includes all three major arterial territories, perforator supply and the lower watershed areas. Alternatively, the imaging can be centred over a known abnormality (*e.g.* tumour or a more peripherally-sited infarct).

A 25 cm field of view and a matrix of 512×512 pixels are utilized. A sampling interval of up to 3 s may be allowed to reduce the number of images and dose. However, longer intervals lead to inaccuracies with overestimation of CBV, CBF, TTP (time to peak) and underestimation of MTT [34].

Clinical applications

Stroke

Plain CT of the head remains the standard first line imaging for patients with an acute ischaemic intracranial event. It can exclude an acute intracranial haemorrhage.

However, it has a relatively low sensitivity of 61–73% for detecting hyperacute stroke within the first 3–6 h [35, 36], when thrombolysis may salvage cerebral tissue [37, 38]. Also, the numerous stroke mimics (seizures, systemic infections, positional vertigo, hyponatraemia, encephalitis, demyelination, myasthenia gravis, parkinsonism [39]) may not demonstrate any abnormality on a plain CT.

The selection of patients for thrombolysis involves confirmation of the diagnosis, demonstration of the infarct extent and salvageable tissue, exclusion of haemorrhage and stroke mimics (Figure 2). Perfusion CT can be performed immediately after plain CT, takes only a few extra minutes to perform and obviates the need to transfer the patient to a different scanner thus minimizing any delay. Additionally, CT perfusion for stroke can be combined with a CT angiographic study (Figure 3) to provide a full early imaging assessment and determination of treatment and prognosis.

Validation of PCT

The rationale for perfusion CT is to identify the penumbral ''tissue at risk'', which is broadly defined as brain tissue which has reduced blood flow causing ischaemic injury and is fundamentally reversible if blood flow can be restored [40], and thus distinguish patients who would benefit from thrombolytic treatment from those who have developed predominantly infarcted tissue [6, 29, 41, 42].

Brain parenchymal viability is dependant on its blood flow (CBF) [40, 43]. Normal CBF values are up to 50 ml 100 g^{-1} min^{-1} for grey matter, 30–40 ml 100 g^{-1} min^{-1} for white matter. CBF values below about 20 ml 100 g^{-1} min^{-1} lead to neuronal dysfunction, which may be reversible if flow is restored. Values below 10–12 ml 100 g^{-1} min^{-1} that are sustained for a few minutes to hours, causes the sodium–potassium adenosine triphosphate (ATP)-dependant pump to become irreversibly impaired, leading to calcium and water influx, cell death and cytotoxic oedema [40, 44–46]. CBF below 10 ml 100 g^{-1} min^{-1} will lead to rapid and irreversible infarction [47–50].

Acute vessel occlusion leads to an ischaemic ''penumbra'', which is initially reversible. This tissue may remain viable for only a few hours [51, 52]. Eventually, irreversible infarction occurs, which starts centrally and may grow to progressively replace the penumbra [40, 53]. Infarction on CT is demonstrated as a reduction in density (indicating an increase in cell water content and cytotoxic oedema). Regardless of time from ictus, any tissue that is of low attenuation on the presenting CT will progress to infarction.

The various parameters used in perfusion imaging will be considered separately in the assessment of stroke.

Cerebral blood flow

Sensitivity for ischaemia

There is a balance to be struck between thresholds for blood flow measurements and sensitivity to cerebral infarction. Specificity can be increased with very low blood flow criteria. In a study by Koenig et al [25], CBF on perfusion CT using a single axial slice at the level of the basal ganglia had a sensitivity for hyperacute stroke (within 6 h) of 89%. The three false negatives occurred because the infarcts were outside the scanning level.

In a study by Kloska et al [53], perfusion CT was performed using multislice CT with the imaging centred at the basal ganglia and two 10 mm slices were reconstructed. Looking at three parameters CBF, CBV and TTP they demonstrated a sensitivity of 79%. However, five of the nine false negatives were, again, outside the scanning range and the remaining four had a mean infarct size of only 1.59 cm^2. There were no false positive results in either study.

Mayer et al [6] used between one and three levels to determine CBF. The first level was at the basal ganglia and, if it was negative, a rostral level or, in patients with motor aphasia, a dorsal level was obtained. CBF studies detected 100% of infarcts >10 ml. Sensitivity for infarction >1.5 ml was 94%. Specificity was 87% using moderate decreases in CBF as the cut-off (<60%). These were relative values obtained by comparing with the assumed normal side.

Infarct size

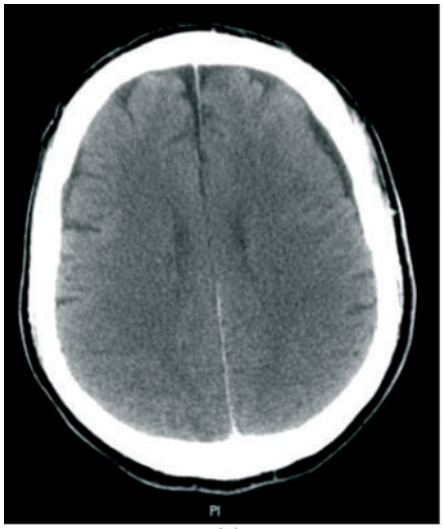
A threshold of <10 ml 100 g^{-1} min^{-1} is accurate in predicting the final size of the infarct and therefore the irreversibly ischaemic core [49]. In a study by Wintermark et al [40], a threshold for CBF reduction to <66% of the contralateral (normal) hemisphere in patients with persistent arterial occlusion correlated well with the DWI abnormality on MRI performed 3 days later.

Further studies have shown that of all the perfusion parameters, CBF reduction shows the best correlation with the final size of infarct in patients with or without thrombolysis [25, 54]. One small study of 20 patients demonstrated that, using a CBF threshold of 12 ml 100 g^{-1} min^{-1}, the correlation with final infarct size was better than with acute DWI [55]. There is also good correlation with single photon emission computerized tomography (SPECT) with respect to the size of the ischaemic area [25].

Cerebral blood volume

Although CBV has been used to detect ischaemic tissue non-dynamically [56, 57], it is its purported ability to differentiate the penumbra from core infarct when used in conjunction with CBF that appears most promising. The ischaemic but reversible penumbra will have reduced CBF, but CBV may be increased due to vascular dilatation in an attempt to maintain oxygen delivery (autoregulation). Autoregulatory ability is lost in infarcted tissue and vasodilatation therefore does not occur. In the core, both CBV and CBF will be reduced [5, 58]. Increased total CBV in the ischaemic penumbra has also been demonstrated on MR perfusion studies [10, 59].

Wintermark et al studied the cerebral blood volume within the ischaemic area (defined as a reduction in CBF of 35% compared with the normal side) [40]. Pixels corresponding to values higher or lower than 2.5 ml 100 g^{-1} were defined as ischaemic penumbra or infarct,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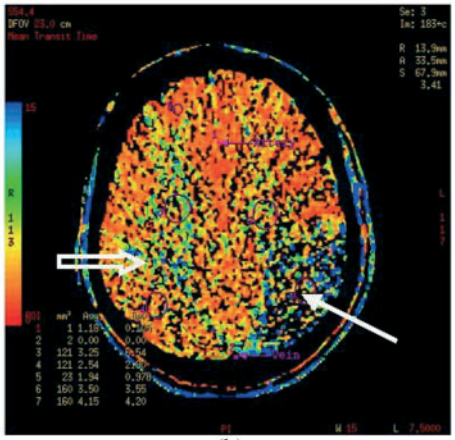
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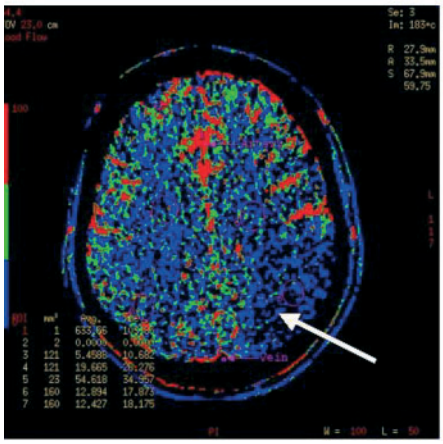
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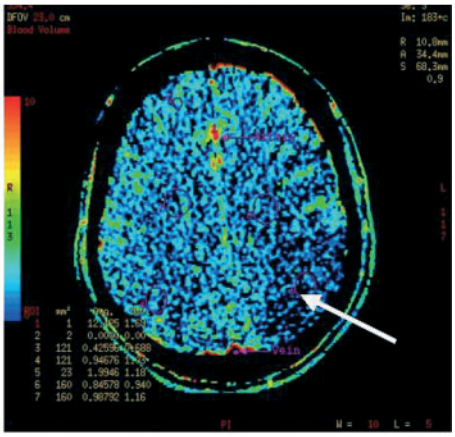
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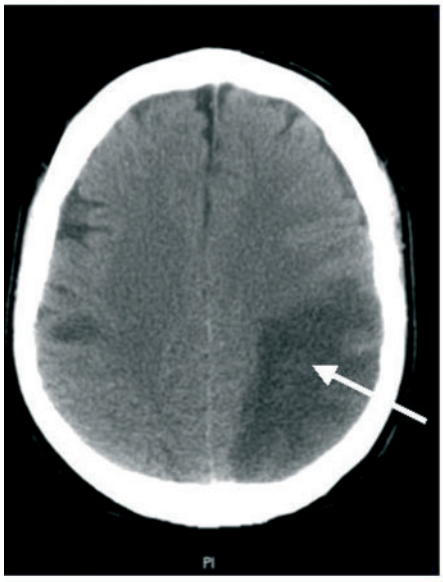

(e)

Figure 2. (a–e) Early stroke: case study. A 60-year-old male undergoing coronary angiography for investigation of angina. The procedure itself was technically uncomplicated. In recovery, he developed left hemiparesis followed by right hemiparesis and dysphasia. CT head and CT perfusion was requested as a prelude to intravenous thrombolysis. (a) Initial cranial CT 1.5 h after symptom onset shows no apparent abnormality. (b) CT perfusion image. Mean transit time (MTT) map. There is a well-circumscribed area of slightly prolonged MTT of over 4 s in the left parietal lobe (arrow). In the subcortical right parietal lobe is a more subtle area of prolonged MTT (hollow arrow). (c) There is a significant reduction in blood flow in the same area below 15 ml 100 g^{-1} tissue. (d) Cerebral blood volume (CBV) map shows a significant reduction in volume below 1.5 ml 100 g^{-1} min^{-1}. Interpretation CT perfusion (CTP) was performed within 1.5 h of first symptom onset. The blood volume and blood flow parameters are already below the threshold for cell survival. The area of reduced MTT, CBV and cerebral blood flow (CBF) are equal, indicating that there is no ischaemic penumbra and the patient is not likely to benefit from thrombolysis. However, clinically, and on CT criteria (no large established early infarct and no haemorrhage), the patient was suitable for intravenous thrombolysis and this was administered 2.5 h after symptom onset. (e) The patient failed to improve after thrombolysis. Cranial CT performed the following day to exclude haemorrhage shows an infarct that was predicted very accurately by the CTP study. A small contralateral right parietal infarct is also shown.

respectively. This value was chosen because cerebral parenchyma below this value is unlikely to survive. In patients who had recanalization of the occluded artery either spontaneously or after thrombolysis, the final infarct size (as defined by DWI) was underestimated by CBV measurements below 2.5 ml 100 g^{-1} and overestimated by CBV over 2.5 ml 100 g^{-1} [41]. In other words, infarction occurs at CBV volumes above 2.5 ml 100 g^{-1} and CBV is not the sole predictor of ischaemic tissue's fate.

Mean transit time

This is the most sensitive but least specific indicator for stroke [60]. The apparent abnormal area in stroke patients is larger than that of CBF and CBV [61]. This may represent attempts at collateralization and areas of prolonged MTT will include salvageable tissue. MTT may be very useful in the setting of vasospasm (see below) and may be influenced by significant proximal stenoses.

Time to peak

This is defined as the time delay between the first arrival of the contrast bolus within major arteries in the imaged section and the bolus peak in the brain tissue [62]. Harrigan et al assessed cerebral ischaemia in patients with subarachnoid haemorrhage (SAH) and found colour coded TTP maps demonstrated regions of ischaemia more readily than CBF or CBV maps [62].

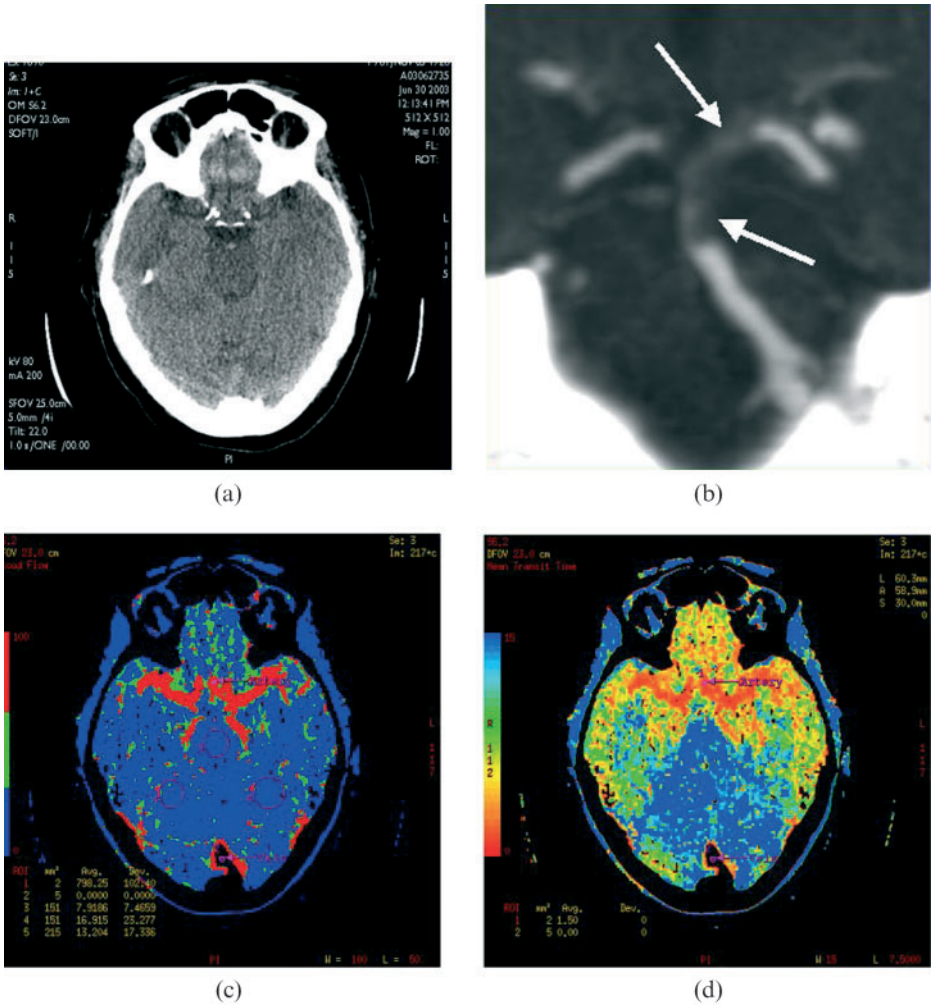


Figure 3. (a–d) Acute ischaemia. A 70-year-old woman collapsed at home and required immediate intubation, as she was not securing her airway. No relevant medical history was available. There was clinical evidence of brainstem dysfunction. The clinical diagnosis was of intracranial haemorrhage or catastrophic ischaemia. (a) Plain CT shows no haemorrhage. There is, however, general obscuration of the grey–white matter junction and subtle low density of the pons, as well as slightly increased density within the basilar artery. (b) Basilar artery thrombosis was suspected as the cause of these changes. CT angiography (2.5 mm coronal maximum intensity projection) shows a thrombus within the terminal basilar artery extending into the left posterior cerebral artery (arrows). (c) Cerebral blood flow (CBF) map. Low blood flow within the temporo-occipital regions and pons is demonstrated, with all areas being below 15 ml 100 g^{-1} min^{-1}. (d) Mean transit time (MTT) is significantly prolonged in the pons and vermis. Interpretation: basilar artery thrombosis is confirmed. In a large area, there is no salvageable tissue. The more focal nature of the MTT abnormality may reflect areas that are unable to receive collateral flow. The patient was not offered thrombolysis on the basis of this study and died a few hours later.

Subarachnoid haemorrhage

Perfusion CT is an extremely promising tool in determining prognosis in patients who present with aneurysmal subarachnoid haemorrhage. It may also increase the sensitivity for detection of cerebral vasospasm and direct appropriate management (Figure 4). After SAH, there is progressive decline in the CBF values until 10–20 days [63, 64]. Nabavi noted also an initial drop in CBF in days 1–3, which appeared more severe in patients who subsequently developed significant vasospasm despite an initially good clinical course [65].

Other authors have similarly found that patients with favourable outcome had significantly higher CBF values measured early in subarachnoid haemorrhage whatever the clinical state (excluding coma) of the patient [66].

Studies using other perfusion methods showed a strong correlation between a CBF below 12 ml 100 g^{-1} min^{-1} and subsequent cerebral infarction [67, 68]. Harrigan showed that patients who had ischaemia on CTP (defined as: CBF <20 ml 100 ml^{-1} min^{-1} or TTP >9 s) had appropriate areas of vasospasm on subsequent catheter angiography and underwent successful angioplasty. Two patients who had hyperaemia on CT perfusion (CTP) (increased CBF and CBV) had their hyperdynamic therapy adjusted, which resulted in clinical improvement.

Trauma

Complex perfusion abnormalities may be seen after head injury which may not be all readily assessed by invasive cerebral perfusion monitoring. High regional variation, abnormal autoregulation and disturbed blood–brain barrier all co-exist. Despite this, CTP variables (CBF, CBV, MTT) have been found to correlate sig-

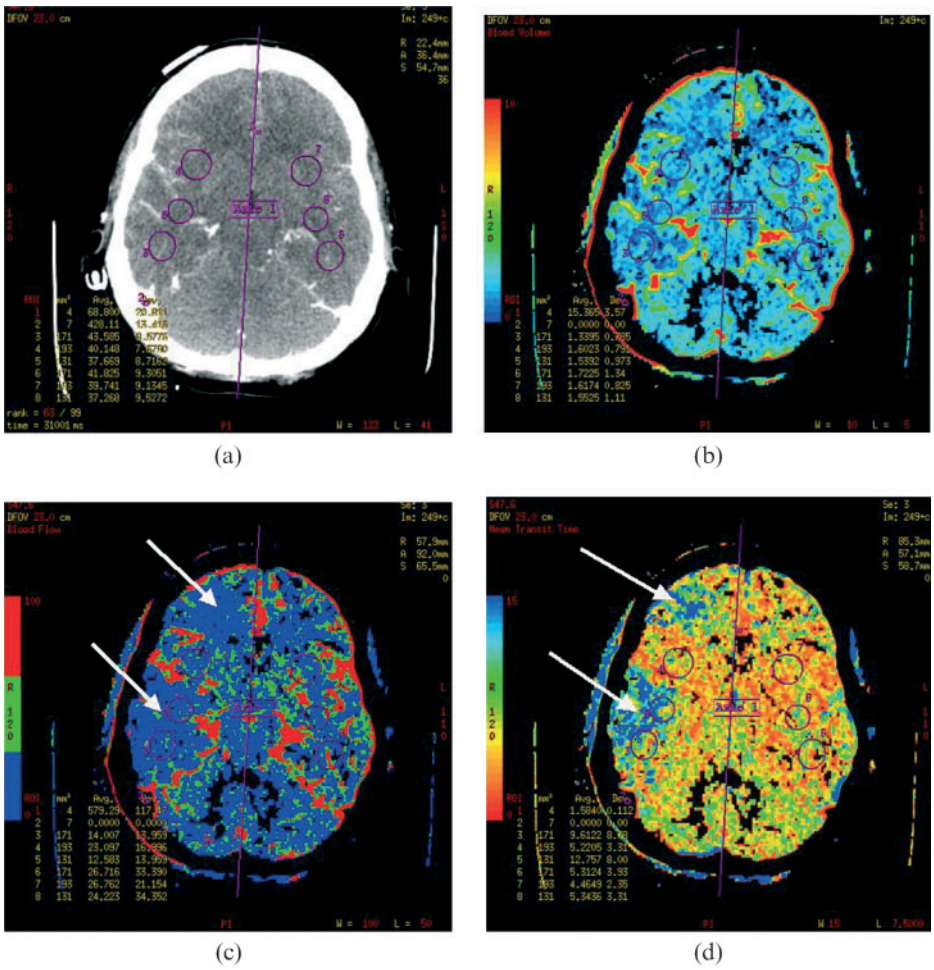
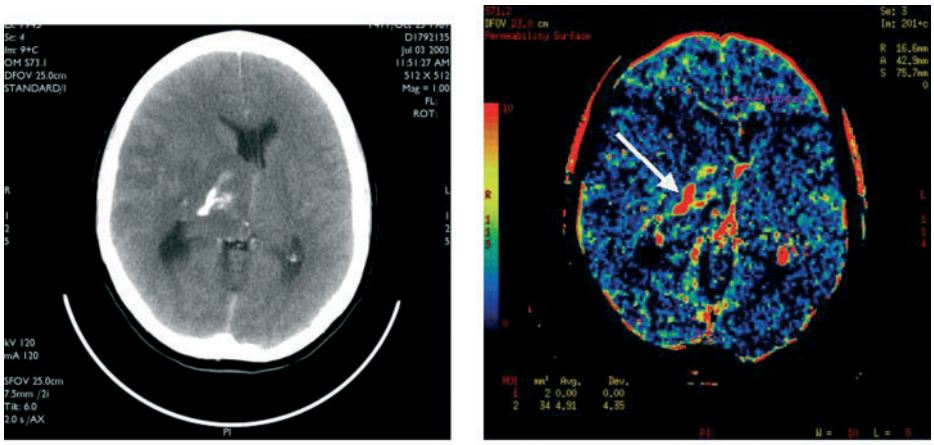


Figure 4. (a–d) Assessment of vasospasm. A previously fit and well female presented with acute subarachnoid haemorrhage. She was stable with no focal defect; at the time the causative right middle cerebral artery aneurysm was coiled endovascularly. Two days later she developed a left hemiparesis. The clinical diagnosis was of likely vasospasm but CT perfusion was requested to determine tissue viability. (a) CT from CT perfusion study with regions of interest in the affected and unaffected hemisphere for comparison. There was no evidence of ischaemia on plain CT. (b) Cerebral blood volume (CBV) map shows no deficit. (c) Cerebral blood flow (CBF) map shows a slight reduction in blood flow in the right frontal lobe and more severe reduction in the temporal lobe (arrows). (d) Mean transit time (MTT) map. There are reasonably well-circumscribed areas of prolonged MTT up to 12 s that conform to vascular territories of the right middle cerebral artery. Interpretation: the prolonged MTT, with normal blood volume and reduced blood flow (a function of time) is indicative of vasospasm. The CBF parameters show that cerebral tissue is not irreversibly ischaemic. However, parameters in the right temporal lobe suggest that unless the spasm is relieved and/or blood flow increased, infarction may ensue. The patient was aggressively treated with haemodilution, hyperhydration and hypertensive (HHH) therapy and eventually made a full recovery.



(a) (b)

Figure 5. (a, b) Assessment of tumour vascularity. A 30-year-old male patient with a deep seated right hemispheric low-grade astrocytoma. The tumour had been under observation for 10 years and had been relatively static in appearance and the patient had also been clinically stable. The patient presented with increased seizures and headache, and tumour growth and/or upgrading was suspected. (a) Axial post-contrast cranial CT through the tumour in the right thalamus. There is central calcification and localized mass effect. (b) Image from the CT perfusion (CTP) study. Mean transit time (MTT), cerebral blood volume (CBV), cerebral blood flow (CBF) were normal. There is increased permeability in the central aspect of the tumour (arrow), indicating either a breakdown in the blood–brain barrier or increased vascularity. Either of these changes indicates that the tumour has upgraded. This was confirmed on subsequent biopsy.

nificantly with local invasive cerebral perfusion pressure (CPP) monitoring in patients with closed head trauma [69].

Wintermark et al showed that admission perfusion CT had a much higher sensitivity for cerebral contusions (87.5%) compared with plain CT (39.6%), with a specificity of 93.9% [69]. Of the six scans with false negative results, one was diffusely oligaemic and the other five had contusions which were outside the perfusion sections. The CBF (mean 33.2 ml 100 g^{-1} min^{-1}) and CBV (mean 2.8 ml 100 g^{-1}) were significantly lower and the MTT (mean 8.5 s) was significantly raised within the cerebral contusions compared with controls (CBF 48.82 ml 100 g^{-1} min^{-1}, CBV 3.3 ml 100 g^{-1}, MTT 4.3 s).

Normal or hyperaemic perfusion (raised CBV, CBF) was associated with a favourable outcome with oligaemia predicting an unfavourable outcome. This is thought to be due to loss of autoregulation associated with more severe head trauma, and these findings have been correlated in perfusion studies using other modalities [71–73]. Perfusion CT has been proposed to help in determining patients who need early and aggressive treatment to prevent intracranial hypertension [70].

Tumour

Certain aggressive intracranial tumours stimulate angiogenesis to feed their rapid growth. These vessels are associated with an abnormal blood–brain barrier. When contrast medium arrives in a pathological vascular bed, some will transfer from the vascular to the extracellular space. Vascular contrast medium will tend to reduce in density over time, whereas interstitial contrast medium will not. The permeability surface area product (PS) is an additional parameter derived by computing the fraction of contrast medium accumulating in the extravascular space. Increase in PS in tumours reflects this abnormal angiogenesis [74]. A different deconvolution method to account for this contrast leakage provides CBF, CBV and PS measurements [31, 75].

CTP may provides a better delineation between benign peritumoural oedema (no increase in PS) and malignant infiltration (increased PS), compared with plain CT [74, 76]. CTP may also be used to assess tumour grade with increased heterogeneity and blood volume on CBV maps reflecting higher grade tumours [74, 77] (Figure 5). Regions of high CBV may then be targeted for biopsy. Conventional CT may suffer from sampling error in heterogeneous gliomas or tumour recurrence in radiation necrosis [74].

CTP has been applied to meningiomas to determine which lesions may benefit from pre-operative embolization. CTP parameters nave been correlated with angiographic vascularity and intraoperative blood loss [78].

Multimodality MRI, however, remains the investigation of choice in assessing intracranial tumours with increased contrast resolution, multiplanar capabilities, spectroscopy, perfusion and DWI. CT may have a role to play in patients where MRI is contraindicated, although more research is required.

Chronic ischaemia

CT perfusion has been applied to patients with chronic ischaemia in which a revascularization procedure is planned [79, 80]. A perfusion study (SPECT, CTP, Xe CT) is performed pre- and post-administration of acetazolamide (a carbonic anhydrase inhibitor), which acts as a cerebral vasodilator. A normal response is an increase in cerebral blood flow of up to 30% over baseline. A limited or no response signifies that, if the causative stenotic lesion progresses, the brain cannot compensate any further to a

reduction in flow (an impaired cerebrovascular reserve capacity). The cerebral tissue is said to be under haemodynamic stress and the patient may benefit from a procedure to increase cerebral blood flow [81]. There is a significant correlation between PET [80] and CT perfusion [81, 82] for decreased vascular reserve utilizing cerebral blood volume. CTP may be used *in lieu* of xenon CT and SPECT for the selection of patients requiring revascularization, including carotid endarterectomy, bypass surgery and endovascular angioplasty [82].

Conclusion

Perfusion CT is an evolving technique which has been used in a number of applications, notably in stroke. There are ongoing studies assessing its role in decision making for thrombolysis and in tumour assessment. Drawbacks include a relatively low spatial resolution and limited volume coverage.

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