CT perfusion of the brain – what is its role today and expectancies for tomorrow?

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Abstract

Computed tomography (CT) perfusion imaging delivers the information about regional differences of cerebral haemodynamics and can give additional information in different cerebral pathologies. Together with CT technology it has recently undergone significant progress by expansion of multidetector CTs (four to 320 detector-rows) and enlargement of detector width. The aim of this review is to provide an overview of the newest perfusion CT possibilities in imaging of different brain pathologies and to discuss the future development directions of perfusion CT.

Keywords: perfusion, CT, brain, stroke

Streszczenie

Perfuzja tomografii komputerowej (CTP) dostarcza dodatkowych informacji o miejscowych parametrach hemodynamicznych mózgu w różnych chorobach OUN. Równolegle z rozwijającą się technologią tomografii komputerowej, obserwuje się intensywny rozwój perfuzji TK, związany z ekspansją tomografów wielorzędowych (cztery do 320-rzędów) oraz zwiększeniem szerokości detektorów. Celem tej pracy jest omówienie najnowszych możliwości perfuzji tomografii komputerowej w obrazowaniu różnych chorób mózgu oraz dyskusja nad kierunkami rozwoju perfuzji TK w przyszłości.

Słowa kluczowe: perfuzja, TK, głowa, udar

Introduction

Computed tomography (CT) is a widely available and time-saving brain imaging method. It has a well established role as an examination of choice for imaging in an emergency setting. Over the last two decades computed tomography (CT) technology has undergone significant progress starting with multisection/spiral scanning and followed by expansion of multidetector CT (four to 128 detector-rows). These advances allowed quicker and more precise, three-dimensional (3D) acquisition, 3D CT angiography (CTA) and cerebral perfusion studies [1,2].

Perfusion imaging delivers the information about regional differences of cerebral haemodynamics and can give additional information in different cerebral pathologies. The main values measured include cerebral blood volume (CBV), blood flow (CBF), and mean transit time (MTT), the distribution of which can be presented visually as perfusion maps (Fig. 1 a, b).

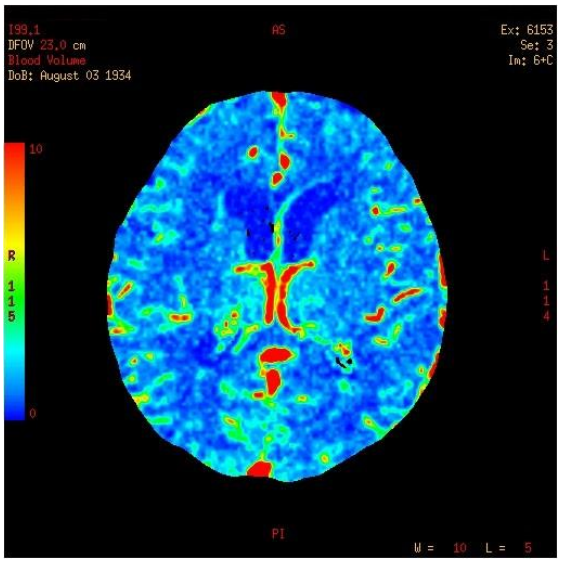
Until recently, perfusion CT systems remained limited in whole-brain coverage (z-axis). With standard (16- or 64-row) CT, acquisition of perfusion data is limited by the detector width, which is between 2 and 4 cm in most cases. With these techniques, lesions may be detected incompletely and small lesions may be even missed entirely if they are outside the perfusion ROI.

One approach to overcoming this limitation is the table toggling technique described by Roberts et al [3]. This technique alternates axial scan in two table positions and enables to double detector-width coverage, therefore providing coverage of 80 mm in the z-axis. Unfortunately, the results achieved with table toggling techniques have been limited by difficulty in standardizing calibration of the toggling technology and this technique cannot facilitate whole-brain perfusion imaging in a rapid scan time [1].

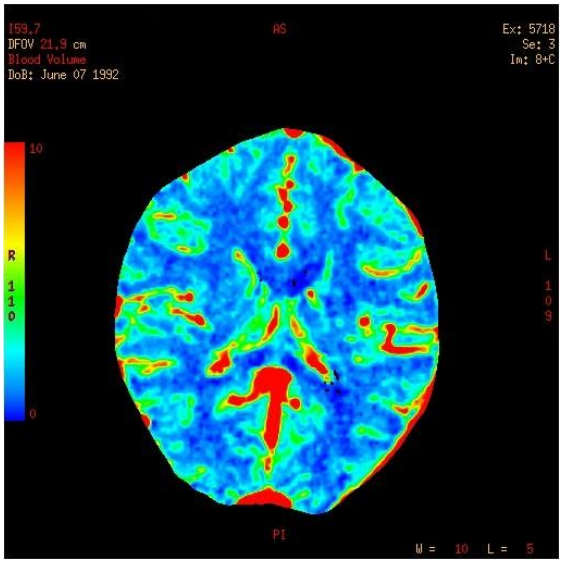
However, 256- and 320-slice CT providing a detector width of up to 16 cm have been recently introduced into clinical practice [4–6]. 160 mm of z-axis coverage has allowed for whole-brain evaluation with a single gantry rotation and enabled temporal uniformity with imaging of the entire brain during each volume acquisition following contrast medium administration. Whole-brain field of view gives hopes to detect smaller and/or additional lesions, which may be missed with less coverage and to include a better definition of the infarct core and the penumbra in ischaemic brain pathologies. First experience using multi-slice detectors for acute stroke imaging is promising [4-6]. However, more clinical data are needed to prove the advantage of this new technique, particularly in terms of the potentially increased radiation dose that may be required with higher z-coverage.

Fig 1. a) CBV map of a 72-year-old male with the diagnosis of mild AD, CT perfusion at the level of the basal ganglia. Marked diffuse cortex hypoperfusion, especially in the frontal lobes and right parietal lobe. Enlargement of frontal horns of lateral ventricles. b) Normal CBV map of a 18-year-old female.

a)



b)



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Acute ischaemic brain stroke

Stroke is one of the major diseases resulting in death or permanent disability worldwide. In Western countries, the age adjusted incidence rate is about 180 per 100,000 per year [7,8]. Most strokes are caused by acute ischaemia because of occlusion of a cerebral artery. There are different therapeutic possibilities for the management of acute stroke, including intravenous thrombolysis and endovascular techniques such as intra-arterial lysis, mechanical thrombectomy and stent angioplasty. In order to choose the best therapy for each individual case, evaluation of the haemodynamic situation must be done. It is important to exactly assess the so-called 'tissue-at-risk' or 'penumbra' which is defined as the cerebral tissue that is still salvageable despite reduced perfusion. This penumbra is also the target of re-canalising methods of stroke treatment.

Thrombolysis has been approved for use in acute stroke where the onset is less than 3 hours and the vascular territory involved is one third or less. Re-perfusion by thrombolytic therapy has proven beneficial in patients with early cerebral ischaemic stroke, and early induction of thrombolysis reduces the risk of intracranial haemorrhage and increases therapeutic efficacy. This stresses again the necessity of good patient selection for thrombolytic therapy [9].

CT perfusion shows benefit in acute stroke imaging and assessing the brain haemodynamics and, together with CT angiography (CTA), is part of a detailed stroke protocol in many hospitals today [2,10,11]. The new methodology of whole-brain perfusion scanning provides for extremely rapid and well available access to four important aspects of neurovascular disease assessment: (1) unenhanced whole-brain CT, (2) contrast-enhanced whole-brain CT, (3) real-time 3D dynamic CTA, and (4) whole-brain CT perfusion (CTP). This enables to see all aspects of steno-occlusive artery disease at one, large, brain imaging examination: places of artery clotting on CTA, ischaemic changes on unenhanced and enhanced whole-brain CT, and perfusion changes in the brain tissue surrounding the ischaemia. CT perfusion maps provided by computer software identify matched defects (both, matched decrease of CBF and CBV) which denote infarct core and mismatched defects (a reduction in CBF with maintained or even elevated CBV) which denote ischaemic tissue or penumbra. Mismatched defects in penumbra are probably due to a vasodilatation of precapillary arterioles and engorgement of veins. MTT is the parameter with highest sensitivity for early ischaemic lesion because it increases in any stage of ischaemic disease. However, it is less specific for acute stroke, as long MTT characterizes areas of ischaemia that include both chronic and acute stroke with reversible and irreversible tissue damage. [2, 10,12].

Recent studies indicate that CT can provide accurate information not only on supratentorial perfusion disturbances but on infratentorial perfusion disturbances as well [13].

Kazufumi et al studied 58 patients with cerebral stroke to investigate the utility of CT perfusion with 64-row multi-detector row CT (MDCT) to overcome the limitations of CTP and the expense and long duration of MR examination. He concluded that combination of plain CT, CT angiography, and CTP with 64-row MDCT could demonstrate all segmental acute ischaemic lesions that caused severe neurological deficiency and required thrombolytic therapy to avoid irreversible damage. Furthermore, most segmental irreversible infarction can also be diagnosed and at the same time aortic dissection that may contraindicate thrombolytic therapy can be excluded. [14]. New 256 and 320-row CT machines give another advantage of simultaneous acquisition of CTP and whole-brain CTA in a single rotation and therefore draw back the major problem of CT perfusion performed with conventional CT which was a limited anatomical coverage of the brain [2,4,5].

Compromised cerebral venous outflow

Abnormal venous outflow affects brain perfusion and leads to elevated intracranial intravenous pressure. This pressure is not routinely measured in clinical practice but can lead to venous infarction, increased intracranial pressure, decreased cerebral perfusion pressure, and subarachnoid haemorrhage. Indirect evidence of increased venous pressure is reflected in the size change of the cerebral sinuses and the presence of venous infarctions. Clearance of the contrast from the brain venous circulation is directly reflected in changes in the venous time–density curves. Recently, Darwish and Amiridze studied the role of brain perfusion venous time–density curves in the diagnosis of cerebral venous hypertension [15]. They analysed 4 cases of different aetiology and found that the abnormal venous time–density curves correlated with clinically increased intravenous pressure and normalized after treating the underlying pathology.

The effects of this phenomenon on brain perfusion cannot be quantified at this point and there is a need to correlate these findings in the future to find algorithms by which the venous pressure and flow can be measured noninvasively. This future direction of brain perfusion CT findings may help to diagnose and provide further understanding of the effect of venous outflow compromise on brain perfusion in patients with congenital heart disease, pulmonary and hepatic venous hypertension, compartment syndromes who have severe traumatic brain injury. It may also help in the evaluation of the pathophysiology of SAH in perimesencephalic syndrome.

CT perfusion in cerebral vasospasm

Delayed cerebral vasospasm remains the most serious cause of morbidity and mortality in patients with aneurysmal subarachnoid haemorrhage (A-SAH). It appears in more than half of population with A-SAH and its complications may include permanent neurological deficits, stroke and even death. Patients with vasospasm are at high risk for poor clinical outcomes with long-term disability and death. Vasospasm typically develops 4 to 9 days following aneurysm rupture and is linked with cerebral perfusion abnormalities [16,17]. Clinical management is focused on early diagnosis to initiate treatment of vasospasm and preventative measures for its possible complications such as permanent neurological deficits, stroke and death. Sanelli et al evaluated the use of CT perfusion at an early stage, during admission baseline period (within 0-3 days) post A-SAH. They analysed 75 patients and concluded that A-SAH patients who develop vasospasm demonstrated early alterations in cerebral perfusion, with statistically significant CBF reduction and MTT prolongation. CT perfusion turned out to be of high specificity for development of vasospasm and may be used to identify patients with high risk of developing vasospasm in order to prevent them from future neurological complications [16].

Perfusion CT in epilepsy

CT perfusion can be a useful tool to differentiate stroke and stroke-mimicking conditions in the acute setting. Lie et al described a patient with no history of epilepsy who presented with subacute onset of aphasia and right-sided hemiparesis [18]. Ischaemic episode was supposed and brain CT, together with CTA and CT perfusion were performed to assess whether thrombolytic therapy could be administered. CTP, however, revealed regional hyperperfusion, with elevated CBF and CBV in the left parietal lobe, while MTT was not significantly altered when comparing both hemispheres. Such hyperperfusion have been described already in SPECT studies of epilepsy [19]. CTA did not show significant differences in the diameter between the right and left posterior cerebral artery. Further diagnostic means supported an epileptic origin of symptoms [18].

CT perfusion in differentiating intra-axial tumours

PCT can also reliably classify gliomas and lymphomas based on quantitative measurements of CBV and permeability value. Schramm et al analysed 43 patients with brain tumours (low-grade gliomas, glioblastomas and lymphomas) and found that in comparison with normal parenchyma, low-grade gliomas showed no significant difference of perfusion parameters, whereas high-grade gliomas demonstrated significantly higher values for permeability value, CBV and CBF. Lymphomas displayed significantly increased mean

permeability values compared with unaffected cerebral parenchyma but no elevation of CBV. High-grade gliomas showed significant higher CBV values than lymphomas [20]. PCT turns out to be useful in the preoperative differential diagnosis of intra-axial brain tumours and can provide a non-invasive mean of quantifying and classifying the characteristics of cerebral gliomas and lymphomas according to their regional perfusion parameters.

CT perfusion in dementias

Because perfusion imaging delivers the information about regional differences of cerebral perfusion, it may be helpful in the assessment of severity of dementia and eliciting different types of dementia. Perfusion imaging may be performed to demonstrate areas of reduced CBV and CBF in vascular dementia where CBF reductions are usually multifocal and subcortical. Zimny et al evaluated the usefulness of perfusion CT (pCT) in differentiating Alzheimer's disease (AD) from vascular dementia (VaD) and mixed dementia (MixD). They calculated regional perfusion parameters (rCBF, rCBV, and rMTT) from 31 ROIs in the grey and white matter of the frontal and temporal lobes, basal ganglia, and internal capsules bilaterally in 41 patients with different types of dementia. On the basis of these studies they concluded that perfusion CT may be a valuable method of distinguishing between AD and VaD but it seems to be of little significance in differentiating MixD from VaD and of no usefulness in distinguishing between AD and MixD [21].

Although CT scanning is still widely used because of its better accessibility over MRI, MRI with its various options is currently the modality of choice for assessing abnormalities in neurodegenerative syndromes.

Conclusions

CT perfusion imaging with both structural and functional neuroimaging techniques has the growing potential to provide clinicians with more precise information in different cerebral pathologies. Because CT scanning is still much more easily available in most clinical facilities and much cheaper than MR imaging, its role is more and more linked with emergency cases.

CTP plays important role in assessing vascular diseases like stroke, venous hypertension or arterial vasospam. CT perfusion imaging in acute stroke aids in safe thrombolytic therapy. Its use reduces the number of patients inappropriately thrombolysed. Furthermore it allows for widening of the potential therapeutic window of thrombolytic therapy. With newest options of whole-brain scanning in one gantry rotation, CTP offers direct and quick assessment of cerebral haemodynamics in an acute setting. MRI perfusion and diffusion, also very reliable methods to assess cerebral haemodynamics, are often difficult to perform in clinical emergencies, and MR imaging cannot be performed in patients with pacemakers or other implanted devices. In addition, use of gadolinium enhancement for MR perfusion analysis risks nephrogenic systemic fibrosis in patients with renal deficiency.

CT perfusion is also useful in other common pathologies like epilepsy, brain tumours or dementias, but here its role is often mostly overwhelmed by MR imaging and CTP reserves its place in differentiating clinically acute cases.

References

1. Orrison W.W. Jr., Snyder K.V., Hopkins L.N. et al. Whole-brain dynamic CT angiography and perfusion imaging. Clin. Radiol., 2011; 66: 566-574.
2. Dorn F., Muenzel D., Meier R. et al. Brain perfusion CT for acute stroke using a 256-slice CT: improvement of diagnostic information by large volume coverage. Eur. Radiol. 2011; 21:1803–1810.
3. Roberts H.C., Roberts T.P., Smith W.S. et al. Multisection dynamic CT perfusion for acute cerebral ischemia: the "toggling-table" technique. AJNR Am. J. Neuroradiol. 2011; 22:1077–1080.
4. Murayama K., Katada K., Nakane M et al. Whole-brain perfusion CT performed with a prototype 256-detector row CT system: initial experience. Radiology; 2009; 250:202–211.
5. Siebert E., Bohner G., Dewey M. et al. 320-slice CT neuroimaging: initial clinical experience and image quality evaluation. Br. J. Radiol., 2009; 82:561–570.
6. Page M., Nandurkar D., Crossett M.P. et al. Comparison of 4 cm Z-axis and 16 cm Z-axis multidetector CT perfusion. Eur. Radiol., 2010; 20:1508–1514.
7. Rosamond W., Flegal K., Furie K. et al. Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation, 2008; 117:e25–e146.
8. Truelsen T., Piechowski-Jozwiak B., Bonita R. et al. Stroke incidence and prevalence in Europe: a review of available data. Eur. J. Neurol., 2006; 13: 581–598.
9. Schellinger P.D., Fiebach J.B., Mohr A. et al. Thrombolytic therapy for ischemic stroke–a review. Part I—Intravenous thrombolysis. Crit. Care Med., 2001; 29:1812–1818.
10. Wintermark M. Brain perfusion-CT in acute stroke patients. Eur. Radiol., 2005; 15 (Suppl. 4):D28–D31.
11. Lövblad K.O., Baird A.E. Computed tomography in acute ischemic stroke. Neuroradiology, 2010; 52:175–187.
12. Soares B.P., Dankbaar J.W., Bredno J. et al. Automated versus manual post-processing of perfusion-CT data in patients with acute cerebral ischemia: influence on interobserver variability. Neuroradiology, 2009; 51:445–451.
13. Silvernnoinen H.M., Hamberg L.M., Lindberg P.J. et al. CT Perfusion identifies increased salvage of tissue in patients receiving intravenous recombinant tissue plasminogen activator within 3 hours of stroke onset. AJNR Am. J. Neuroradiol., 2008; 29:1118–1123.
14. Kazufumi S., Satoru M., Ai M. et al. Utility of CT perfusion with 64-row multi-detector CT for acute ischemic brain stroke. Emerg. Radiol., 2011; 18:95–101.
15. Darwish R.S., Amiridze N.S. Brain perfusion abnormalities in patients with compromised venous outflow. J. Neurol., 2011; 258:1445–1450.

16. Sanelli P.C., Jou A., Gold R. et al. Using CT perfusion during the early baseline period in aneurysmal subarachnoid hemorrhage to assess for development of vasospasm. Neuroradiology, 2011; 53:425–434.
17. Nabavi D.G., LeBlanc L.M., Baxter B. et al. Monitoring cerebral perfusion after subarachnoid hemorrhage using CT. Neuroradiology, 2001; 43:7–16.
18. Lie C.H., Seifert M., Poggenborg J. et al. Perfusion computer tomography helps to differentiate seizure and stroke in acute setting. Clin. Neurol. and Neurosurgery, 2011; 113: 925–927.
19. Bussière M., Pelz D., Reid R.H., Young G.B. Prolonged deficits after focal inhibitory seizures. Neurocrit. Care, 2005; 2(1):29–37.
20. Schramm P., Xyda A., Klotz E. et al. Dynamic CT perfusion imaging of intra-axial brain tumours: differentiation of high-grade gliomas from primary CNS lymphomas. Eur. Radiol., 2010; 20: 2482–2490.
21. Zimny A., Sasiadek M., Leszek J. et al. Does perfusion CT enable differentiating Alzheimer's disease from vascular dementia and mixed dementia? A preliminary report. J. of the Neurol. Sci., 2007; 257: 114– 120.

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