Neurol Med Chir (Tokyo) 44, 105 ~ 111, 2004

Supratentorial Dynamic Computed Tomography for the Diagnosis of Vertebrobasilar Ischemic Stroke

Takeshi NAGAHORI, Yutaka HIRASHIMA*, Kimiko UMEMURA, Michiharu NISHIJIMA**, Naoya KUWAYAMA*, Michiya KUBO*, and Shunro ENDO*

Department of Neurosurgery of Takaoka Social Insurance Hospital, Takaoka, Toyama;
**Department of Neurosurgery of Toyama Medical and Pharmaceutical University, Toyama;*
***Department of Neurosurgery of Aomori Center Hospital, Aomori*

Abstract

Dynamic computed tomography (CT) is an established method for the evaluation of perfusion in acute ischemic stroke, but is not frequently used to assess infratentorial ischemia. Eleven patients with vertebrobasilar ischemia underwent dynamic CT on admission and/or during the follow-up period. The time of appearance (TA) and time to peak (TTP) were mapped and differences in TA (ΔTA) and TTP (ΔTTP) between the bilateral middle cerebral artery and posterior cerebral artery (PCA) territories were calculated. Conventional angiography and brain imaging including CT and magnetic resonance imaging were also performed. The TA and TTP maps obtained within 48 hours after onset exhibited time delay in eight of nine patients in the bilateral PCA territories. ΔTA and ΔTTP were greater in patients with stenosis or occlusion of the bilateral vertebral arteries or the basilar artery, and in patients without collateral circulation via the posterior communicating arteries than in control subjects. Furthermore, TA and TTP normalized dramatically in patients with recanalization of the arteries. ΔTA and ΔTTP were also normalized. ΔTA and ΔTTP were negatively correlated with the time from onset to examination. Dynamic CT can provide important information in patients with vertebrobasilar ischemic stroke, and may allow the diagnosis of acute ischemia and monitoring of the course.

Key words: dynamic computed tomography, vertebrobasilar ischemic stroke, basilar artery occlusion, collateral circulation

Introduction

Planning of treatment for acute cerebral ischemia requires accurate determination of the extent and severity of the ischemia. Transcranial duplex sonography,[8] digital subtraction angiography,[15] computed tomography (CT) angiography,[15] xenon-enhanced CT,[9] positron emission tomography,[6,10] single-photon emission CT,[1,3] and various magnetic resonance (MR) imaging techniques[2,4,7] are all established methods for evaluating acute stroke. However, use of these methods is limited in ordinary hospitals because special and expensive equipment is required and examinations are usually time-consuming. CT is usually performed to exclude hemorrhage and definitive irreversible cerebral infarction in patients suspected of having acute stroke.

Received April 9, 2003; Accepted October 15, 2003

Dynamic CT with contrast medium can acquire and evaluate perfusion scans rapidly and economically.[11,12] However, dynamic CT is not often applied to vertebrobasilar ischemia because of bone artifacts and the difficulty in selecting regions of interest (ROIs).[5,13,14]

The present study performed supratentorial dynamic CT in patients with vertebrobasilar ischemic stroke to evaluate whether functional maps and parameters of dynamic CT are useful for the diagnosis and monitoring of treatment.

Materials and Methods

Eleven patients with vertebrobasilar ischemic stroke, five males and six females aged 63 to 85 years (mean 75.1 years), were admitted to the Department of Neurosurgery, Takaoka Social Insurance Hospital, between February 1998 and January 2000 (Table 1). Symptoms included disorder of conscious-

Table 1 Summary of characteristics of patients with vertebrobasilar ischemic stroke

Case No.	Age/ Sex	Symptoms	Cerebral angiography		Lesions on MR imaging	Outcome
			VA or BA	PComA		
1	78/F	T	no union of lt VA, rt VA occl. (recanal.)	+	none	GR
2	71/M	CN, V, T	no union of lt VA, rt VA occl.	+	cerebellum	MD
3	65/M	H, V	bil VA sten.	+	pons	GR
4	79/F	C, H	bil VA occl.	−	pons	SD
5	73/F	C, T	n.e.	n.e.	pons, cerebellum	D
6	63/F	C	BA occl. (recanal.)	+	pons	GR
7	85/F	C, H	BA occl.	−	occipital lobe	MD
8	82/M	C	BA occl. (recanal.)	−	pons, occipital lobe	D
9	74/M	V, CN, C, T	BA occl.	−	pons	D
10	78/M	H	bil VA steno.	+	none	GR
11	78/F	H	bil VA steno.	+	pons	GR

BA: basilar artery, C: disorder of consciousness, CN: cranial nerve involvement, D: death, GR: good recovery, H: hemiparesis, MD: moderate disability, n.e.: not examined, occl.: occlusion, PComA: posterior communicating artery, recanal.: recanalization, SD: severe disability, sten.: stenosis, T: tetraparesis, V: vertigo, VA: vertebral artery.

ness in six patients, hemiparesis in five, tetraparesis in four, vertigo in three, and cranial nerve involvement in two. Transient ischemic attacks preceding stroke were recorded in three patients.

Conventional angiography was performed except for one patient (Case 5) who exhibited severe disorder of consciousness on admission. Follow-up angiography was performed in five patients (Cases 1, 2, 4, 6, and 8). Brain diffusion MR imaging approximately 7 days after onset demonstrated lesions in the following structures: pons in seven patients, cerebellum in two, and occipital lobe in two. However, two patients (Cases 1 and 10) had no lesions. Urokinase was administered intravenously if the diagnosis was established within 6 hours after onset.

Five control subjects who underwent examinations including dynamic CT to detect asymptomatic brain disease were also included in this study. Their sex and age matched those of the patients. Informed consent was obtained from each patient or family.

Initial dynamic CT was performed in nine patients (Cases 1 to 9) within 48 hours after onset and in two patients (Cases 10 and 11) later than 48 hours. Repeat dynamic CT was performed in four patients (Cases 1 to 4) between the acute and chronic stages (7 to 60 days after onset). A slip-ring CT scanner was used (Quantex; GE-YMS, Tokyo). After baseline CT examination without contrast enhancement, dynamic scanning began at 5 seconds after bolus injection (8 ml/sec) of non-ionic contrast medium (40 ml of Iopamidol 300; Schering, Tokyo) via the right antecubital vein. Six continuous scans with scan time of 2 seconds and scan interval of 2 seconds, and two continuous scans with scan time of 2 seconds and scan interval of 5 seconds were obtained for each procedure. The CT slice included the splenium of the corpus callosum parallel to the orbitomeatal line. ROIs were placed symmetrically as circles of 3 cm diameter at the centers of the middle cerebral artery (MCA) and posterior cerebral artery (PCA) territories (Fig. 1). No patient exhibited adverse reactions to contrast medium. Raw data from dynamic CT ROIs were processed with a gamma-variate function, and time-density curves were

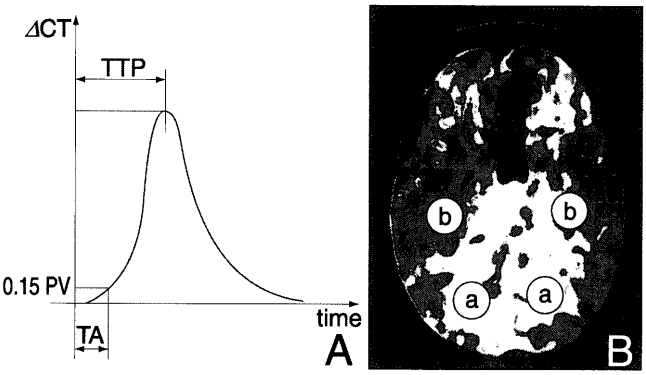

Fig. 1 A: Schematic representation of the parameters of dynamic computed tomography (CT) obtained from time-density curves. ΔCT: optical density, PV: peak value, TA: time of appearance, TTP: time to peak. B: Dynamic CT scan showing the regions of interest in the territories of the posterior cerebral artery (a) and middle cerebral artery (b).

prepared. The time of appearance (TA) and time to peak (TTP) were extracted (Fig. 1). The mean differences of TA and TTP between the bilateral MCA and PCA territories (ΔTA and ΔTTP) were calculated from the time-density curves. Functional maps of TA and TTP were drawn from the resulting dynamically-enhanced scans. TA is a parameter related to the extent of the development of collateral circulation in the presence of occlusive lesions in the main arteries. TTP may be related to cerebral blood flow.

Data are presented as mean ± standard deviation. Comparisons of data between two groups were performed using Student's t test, and between three groups or more using one-way analyses of variance followed by Fisher's protected least-squares difference test. Correlations between ΔTA and ΔTTP and the duration between onset and examination of dynamic CT or clinical outcome at 3 months were analyzed by determination of Spearman's rank correlation. P values < 0.05 were considered significant.

Results

Initial cerebral angiography revealed stenosis of the bilateral vertebral arteries in one patient (Case 3), complete occlusion of the bilateral vertebral arteries in one (Case 4), complete occlusion of one vertebral artery with non-union of the contralateral vertebral artery in two (Cases 1 and 2), and occlusion of the basilar artery in four (Cases 6, 7, 8, and 9).

Functional maps of TA and TTP exhibited time delay in the bilateral PCA territories in eight of nine patients (Cases 1 to 9) who underwent dynamic CT within 48 hours after onset (Table 2). ΔTA and ΔTTP were compared between patients with obstructive lesions of the bilateral vertebral arteries or basilar artery, and the control subjects (Table 3). Both ΔTA and ΔTTP were significantly greater in patients with obstructive lesions than in the control subjects. ΔTA and ΔTTP were also compared between the control subjects and patients without collateral circulation via the bilateral posterior communicating arteries (PComAs) or patients with collateral circulation via at least one PComA

Table 2 ΔTTP and ΔTA measured at various stages

Case No.	Acute stage (≦48 hrs)		Subacute or chronic stage		
	ΔTTP (sec)	ΔTA (sec)	Day	ΔTTP (sec)	ΔTA (sec)
1	1.8	1.6	30	0.8	0.1
2	2.3	1.1	7	1.1	0.2
3	0.9	0.2	60	0.6	0.1
4	2.2	2.5	30	1	0
5	2.2	1.2		n.e.	
6	1	0.5		n.e.	
7	2.6	2.4		n.e.	
8	3.4	1.5		n.e.	
9	2.0	0.5		n.e.	
10	n.e.		30	0.4	0.1
11	n.e.		60	0.8	1.2

ΔTA: difference of time of appearance between the bilateral middle cerebral and posterior cerebral artery territories, ΔTTP: difference of time to peak between the bilateral middle cerebral and posterior cerebral artery territories, n.e.: not examined.

Table 3 Comparison of mean ΔTA and ΔTTP in various patient groups

	ΔTA (sec)	ΔTTP (sec)
Control subjects (n = 5)	0.24 ± 0.152	0.780 ± 0.335
Stenosis/occlusion (n = 8)	1.29 ± 0.871	2.03 ± 0.819
	(p = 0.0237 vs. control)	(p = 0.0085 vs. control)
Collateral circulation via PComA		
with (n = 4)	0.850 ± 0.624	1.50 ± 0.668
without (n = 4)	1.73 ± 0.932	2.55 ± 0.619
	(p = 0.0052 vs. control)	(p = 0.0007 vs. control, p = 0.0208 vs. with circulation)
Repeat dynamic CT		
≦14 days (n = 10)	1.17 ± 0.841	1.95 ± 0.784
	(p = 0.0202 vs. control, p = 0.0284 vs. ≧15 days)	(p = 0.0062 vs. control, p = 0.0007 vs. ≧15 days)
≧15 days (n = 5)	0.300 ± 0.505	0.400 ± 0.707

CT: computed tomography, PComA: posterior communicating artery, ΔTA: difference of time of appearance between the bilateral middle cerebral and posterior cerebral artery territories, ΔTTP: difference of time to peak between the bilateral middle cerebral and posterior cerebral artery territories.

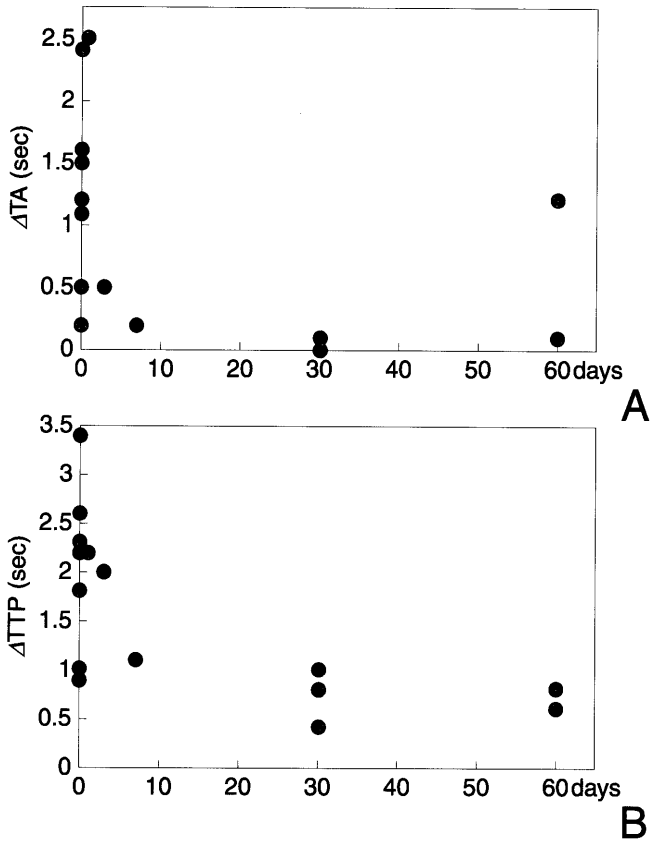

Fig. 2 Relationship between number of days from onset to examination and difference in time of appearance (ΔTA) (A) and time to peak (ΔTTP) (B) between the regions of interest of the posterior cerebral artery and middle cerebral artery. There were significant correlations between ΔTA (p = 0.045) and ΔTTP (p = 0.013) and number of days (Spearman's rank correlation).

(Table 3). ΔTA was significantly greater in the patients without collateral circulation than in the control subjects. ΔTTP was also significantly greater in the patients without collateral circulation compared to both patients with collateral circulation and the control subjects. ΔTA and ΔTTP were compared within 14 days after onset, at least 15 days after onset, and with the control subjects (Table 3). ΔTA and ΔTTP measured within 14 days after onset were significantly greater than those measured at least 15 days after onset and in the control subjects.

Furthermore, significant correlations were observed between the time from onset to examination and ΔTA (p = 0.045) and ΔTTP (p = 0.013) (Fig. 2). Three of these four patients underwent follow-up angiography. Time delay of the functional maps of TA and TTP in the PCA territories were improved in all cases on follow-up dynamic CT. The follow-up functional maps of TA and TTP normalized dramatically in Case 1 who showed recanalization of an artery with good outcome (Fig. 3).

Discussion

The present study performed dynamic CT in the supratentorial region of patients with vertebrobasilar ischemic stroke. The technique may affect the dynamics of the anterior circulation in cases of vertebrobasilar ischemia, but elongation of TA and TTP due to the disease must be greater than any change induced by dynamic CT. Eight of nine patients with vertebrobasilar ischemic stroke exhibited TA and TTP time delay in the bilateral PCA territories on functional maps within 48 hours after onset. The parameters of time-density curves of dynamic CT should be compared between four groups according to stenosis or occlusion of vertebral arteries or basilar artery and the presence of collateral circulation via the PComAs. However, we compared these factors separately due to the small sample size. ΔTA and ΔTTP within 48 hours after onset were significantly greater in patients with obstructive lesions than in control subjects, and significantly greater in patients without collateral circulation than in control subjects. Follow-up functional maps exhibited recovery of TA and TTP in the PCA territories in all examined patients. Furthermore, significant correlations between the time from onset to examination and the ΔTA or ΔTTP were observed. These findings may reflect the recovery of the brain circulation with the natural course of disease and treatment. The main vessel occlusion is important to determine to initiate treatment such as fibrinolysis in patients with acute ischemic stroke. Clinical signs and symptoms may allow the identification of main vessel occlusion. However, patients with vertebrobasilar infarction tend to show only vertigo or relatively mild neurological deficits in the acute stage of infarction, because of the progressive infarction. Therefore, an objective diagnosis method is more necessary for vertebrobasilar infarction than for anterior circulation.

These results suggest that functional mapping of TA and TTP or calculation of ΔTA and ΔTTP by early dynamic CT can predict the presence of occlusion or severe stenosis in the bilateral vertebral arteries or basilar artery, especially in patients without collateral circulation via the PComAs. Further studies are required to assess the efficacy of dynamic CT for the diagnosis and monitoring of the course of disease in patients with vertebrobasilar ischemic stroke.

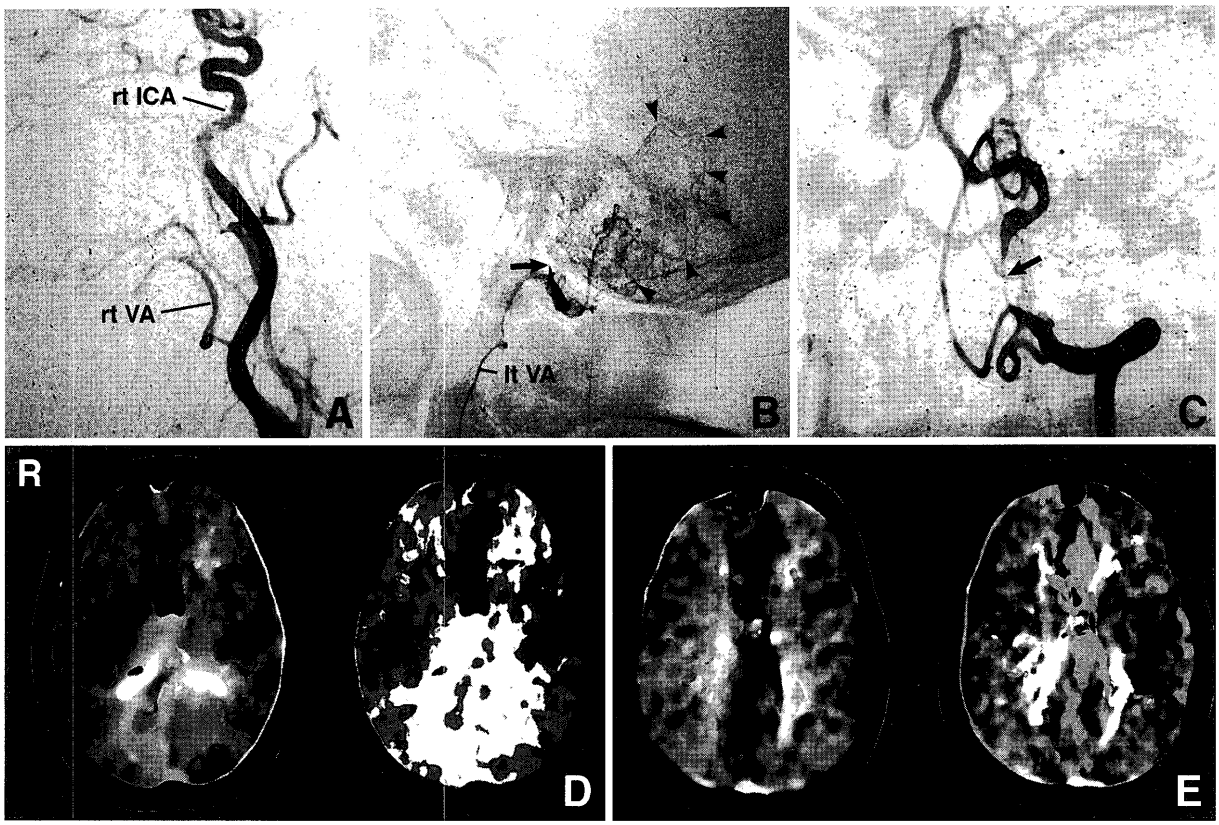

Fig. 3 Case 1. Vertebral angiograms on admission showing no flow in the right vertebral artery (VA) distal to the posterior inferior cerebellar artery (A) and occlusion (*arrow*) of the left VA with leptomeningeal anastomosis via the posterior inferior cerebellar artery (*arrowheads*) (B), and recanalization (*arrow*) of the left VA on day 7 (C). Dynamic computed tomography scans on admission showing time delay in the time of appearance (*right*) and time to peak (*left*) in the bilateral posterior cerebral artery territories (D), and normal findings on day 30 (E). ICA: internal carotid artery.

Acknowledgments

The authors thank Mr. Yasuo Nakayama and Ms. Tomomi Kiyohara for preparing the manuscript.

References

1) Alexandrov AV, Black SE, Ehrlich LE, Bladin CF, Smurawska LT, Pirisi A, Caldwell CB: Simple visual analysis of brain perfusion on HMPAO SPECT predicts early outcome in acute stroke. *Stroke* 27: 1537–1542, 1996
2) Arenillas JF, Rovira A, Molina CA, Grive E, Montaner J, Alvarez-Sabin J: Prediction of early neurological deterioration using diffusion- and perfusion-weighted imaging in hyperacute middle cerebral artery ischemic stroke. *Stroke* 33: 2197–2205, 2002
3) Berrouschot J, Barthel H, von Kummer R, Knapp WH, Hesse S, Schneider D: 99mTechnetium-ethyl-cysteinate-dimer single-photon emission CT can predict fatal ischemic brain edema. *Stroke* 29: 2556–2562, 1998
4) Fiebach J, Jansen O, Schellinger P, Knauth M, Hartmann M, Heiland S, Ryssel H, Pohlers O, Hacke W, Sartor K: Comparison of CT with diffusion-weighted MRI in patients with hyperacute stroke. *Neuroradiology* 43: 628–632, 2001
5) Goto Y, Arakawa Y, Ishii A, Nishizaki J, Ueno Y, Kikuta K, Yoshizumi H, Yamagata S: [Analysis of dynamic CT functional imaging parameters in patients with acute basilar artery occlusion]. *No To Shinkei* 51: 419–424, 1999 (Jpn, with Eng abstract)
6) Heiss WD, Grond M, Thiel A, von Stockhausen HM, Rudolf J, Ghaemi M, Lottgen J, Stenzel C, Pawlik G: Tissue at risk of infarction rescued by early reperfusion: a positron emission tomography study in systemic recombinant tissue plasminogen activator thrombolysis of acute stroke. *J Cereb Blood Flow Metab* 18: 1298–1307, 1998
7) Jaillard A, Hommel M, Baird AE, Linfante I, Llinas RH, Caplan LR, Edelman RR, Warach S: Significance of early CT signs in acute stroke: a CT scan-diffusion

MRI study. *Cerebrovasc Dis* 13: 47–56, 2002
8) Kaps M, Link A: Transcranial sonographic monitoring during thrombolytic therapy. *AJNR Am J Neuroradiol* 19: 758–760, 1998
9) Levy EI, Scarrow AM, Kanal E, Rubin G, Yonas H, Kirby L: Reversible ischemia determined by xenon-enhanced CT after 90 minutes of complete basilar artery occlusion. *AJNR Am J Neuroradiol* 19: 1943–1946, 1998
10) Marchal G, Furlan M, Beaudouin V, Rioux P, Hauttement JL, Serrati C, dela Sayette V, LeDoze F, Viader F, Derlon JM, Baron JC: Early spontaneous hyperperfusion after stroke. A marker of favourable tissue outcome? *Brain* 119: 409–419, 1996
11) Mayer TE, Hamann GH, Baranczyk J, Rosengarten B, Klotz E, Wiesmann M, Missler U, Schulte-Altedorneburg G, Brueckmann HJ: Dynamic CT perfusion image of acute stroke. *AJNR Am J Neuroradiol* 21: 1441–1449, 2000
12) Rother J, Jonetz-Mentzel L, Fiala A, Reichenbach JR, Herzau M, Kaiser WA, Weiller C: Hemodynamic assessment of acute stroke using dynamic single-slice computed tomographic perfusion image. *Arch Neurol* 57: 1161–1166, 2000
13) Valvassori GE, Dobben GD: Hindbrain circulation and its evaluation by dynamic computed tomography. *Ann Otol Rhinol Laryngol* 91: 506–509, 1982
14) Vonofakos D, March H, Hacker H: CT diagnosis of basilar artery occlusion. *AJNR Am J Neuroradiol* 4: 525–528, 1983
15) Wildermuth S, Knauth M, Brandt T, Winter R, Sartir K, Hacke W: Role of CT angiography in patient selection for thrombolytic therapy in acute hemispheric stroke. *Stroke* 29: 935–938, 1998

Address reprint requests to: Y. Hirashima, M.D., Department of Neurosurgery, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan.
e-mail: yhira@ms.toyama-mpu.ac.jp

Commentary

In this study dynamic CT scanning after contrast, now available in most centers, was used in patients with vertebrobasilar ischemic strokes, comparing the times of appearance and peak contrast in the posterior cerebral and middle cerebral territories. Significant delays were found in both these times, especially in patients with little angiographic evidence of collateral supply by the posterior communicating arteries. As pointed out, clinical deficits may be only minor in the early stages, and a test that shows major vessel occlusion at this time may be very useful.

As one would perhaps expect, these delays became less with the passage of time since the stroke, suggesting a gradual recovery in posterior circulation flow. It would be very interesting to see if this was more marked in patients with spontaneous recanalization or after thrombolytic treatment, and this would be worth considering in a larger group of patients in a future study.

The numbers are small so far, but at least in the time to peak concentration there was very little overlap in values between the four patients with and the four without good posterior communicating collateral flow. I would certainly encourage the authors to continue with this study on larger groups as discussed, to see if the technique remains accurate and to determine whether it may have a place in guidance of therapy in this difficult patient group. Will it turn out that thrombolytic therapy is clinically useful only in those with large delays in contrast filling?

Nicholas W. C. Dorsch, M.D., F.R.C.S., F.R.A.C.S.
Department of Neurosurgery
Westmead Hospital
Sydney, Australia

Perfusion CT has a number of advantages over other perfusion imaging methods. It is fast and can offer a one-stop method for evaluation of an ischemic stroke. However, use of the perfusion CT for the posterior fossa has been limited due to artifacts caused by the bony structures. This article by Nagahori et al. is notable in that they were able to demonstrate significant delay in perfusion indices in the posterior cerebral artery (PCA) territory caused by vertebrobasilar ischemia. By comparing the differences of the perfusion indices between the middle cerebral artery and the PCA territories with the control group, the authors could show significant delay in the time of appearance (TA) and time to peak (TTP) in cases with stenosis or occlusion of the vertebrobasilar system, and in cases without collaterals from the posterior communicating artery. These indices reflect the circulatory status of the affected region from primary and secondary collaterals, and may have important implications regarding diagnosis, therapeutic planning and treatment outcome. The authors have successfully provided a method for predicting vertebrobasilar ischemia with perfusion CT. However, the authors acknowledge the possibility of compounding hemodynamic effects of the anterior circulation in the PCA territory through collaterals. The presence of the posterior communicating artery, its caliber, and also such secondary collaterals as leptomeningeal anastomoses, may be factors that could affect the

results of perfusion indices. This interesting study should be further scrutinized with a larger study group.

Dong Ik KIM, *M.D.**
and Kyu Chang LEE, *M.D.*
*Departments of Diagnostic Radiology**
and Neurosurgery
Yonsei University College of Medicine
Seoul, Republic of Korea

Nagahori and colleagues from Toyama present here a fascinating study designed to test their hypothesis that dynamic CT scanning will be of value in predicting posterior circulation occlusive lesions in stroke patients. The implication of their work is that early detection and screening of patients with mild symptoms, using a simple test (dynamic CT), can guide diagnostics (by angiography) and acute stage treatment (with urokinase or similar methods).

Consideration of the method shows that the experimental techniques are sound and reproducible. Eleven patients were studied with five controls. The study design was excellent and the patients were well-documented and well followed-up.

There are three major new findings from this excellent study. The first is that TA and TTP are prolonged with obstructive posterior circulation vascular lesions. The second is that these radiographic changes are significantly worse in the presence of inadequate collateral circulation, particularly with unilateral or bilateral absence of the PCoA. The third major finding is that there is improvement of TA and TTP values (shortening) over time as collaterals are recruited, and most interestingly that this improvement can be correlated with anatomical improvement, such as recanalization, in cases where serial angiography was available.

The study concept was fascinating and the study has been well-performed. The authors should be congratulated for documenting a simple test that will now have great application in predicting which patients, perhaps with only the mildest of symptoms, may have posterior circulation vascular lesions that would warrant rapid and aggressive treatment.

Christopher M. LOFTUS, *M.D., F.A.C.S.*
Department of Neurological Surgery
The University of Oklahoma College of Medicine
Oklahoma City, Oklahoma, U.S.A.