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Evaluation of CT Functional Imaging in Patients with Cerebral Ischemia

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ABSTRACT

CT functional imaging makes it possible to demonstrate the time course of contrast enhancement as visual images by assigning a shade of gray to each pixel within a scan plane depending on the value of the selected transit parameter at the pixel. In order to assess the clinical usefulness of this method, CT functional images were created from dynamic CT scans of 14 patients with ischemic cerebrovascular diseases who showed negative or equivocal findings on the first conventional CT examination. Diagnostic abilities of CT functional images, especially of the first moment (M1-functional images), were tested by the prospective analysis of clinical course and subsequent CT studies, and were compared with those of conventional and dynamic CT scans.

Conventional CT scans could only suggest the existence of abnormality in one of the 14 cases. Visual inspection of dynamic CT images and analysis of time-density curves were helpful in detecting the abnormal blood flow in 3 of the 14 cases. M1-functional images could reveal the existence and the extent of ischemic lesions responsible for symptoms in 12 of the 14 cases. CT functional imaging was found to be a useful technique for the detection of cerebral ischemia and for the early diagnosis of cerebral infarction.

Advances in computed tomography (CT) technology have made it possible to follow the flow dynamics of contrast material through an organ with rapid sequence CT scanning immediately after the administration of a bolus of contrast material. This diagnostic technique is called "dynamic CT" and provides functional information of the organ in the form of serial CT images with different degrees of contrast enhancement and also in the form of time-density curves. Interpretation of dynamic CT involves visual inspection of the serial images and analysis of time-density curves which reflect the dynamics of contrast material in regions of interest (ROI's). This method, when applied to intracranial lesions, has contributed to the studies of the hemodynamics of various tumorous and vascular diseases.

Recent improvements in software components have brought about a better data analytic modality called "functional imaging". This new method makes it possible to demonstrate the time course of contrast enhancement as visual images by grey-scale presentation of the values of a certain transit parameter for all the pixels within a scan plane. Functional imaging techniques were initially developed for nuclear medicine[7] and were first applied to analysis of dynamic CT data by Berninger and his coworkers[2,9]. Although there have been several reports in the literature dealing with applications of this method[4,8,10], its clinical values are not well established because of limited experiences.

In order to assess the usefulness of this method, we created CT functional images from dynamic CT scans of 14 patients with cerebral ischemia and negative or equivocal findings on the initial conventional CT examination. Diagnostic abilities of CT functional images were tested by the prospective analysis of clinical courses and the subsequent CT studies, and were compared with those of conventional and dynamic CT scans.

MATERIALS AND METHODS

The materials include 14 patients with ischemic cerebrovascular syndromes who showed negative or equivocal findings on the first conventional CT examination. Dynamic CT scans were carried out on a GE CT/T 8800 scanner and CT functional images were constructed by utilizing a special research software program "GEDIS 6.22".

Dynamic CT The optimum scan plane of a section for a dynamic CT scan was selected based on the clinical neurological symptoms of the patient. Immediately after the rapid intravenous administration of contrast material, six consecutive scans were taken from the brain. The scanning sequence was composed of a 4.8-second clockwise scan followed by an interscan delay of 1.4 seconds, then a 4.8-second counterclockwise scan. This sequence was repeated for a total of six scans covering a period of 35 seconds. The contrast material, 40—60 ml (0.8 ml/kg of body weight) of 60% Urografin, was injected within the antecubital vein by hand as rapidly as possible. ROI's for the analysis of time-density curves were routinely placed over each territory of the three major arteries (anterior, middle and posterior cerebral artery) and the data of densities over time within each ROI were smoothed by fitting them to a gamma variate function.

CT functional imaging CT functional images were created from the intrinsic data obtained during dynamic CT scans. Actual procedures of CT functional imaging are: 1) The numerical data obtained from each full 360° scan were separated into two consecutive but overlapping 212° segments, each of which was processed using standard reconstruction methods (segmentation). 2) Among the 12 images obtained by the segmentation, those with poor quality were discarded and excellent ones were reregistered for the CT functional imaging. 3) Each reregistered image was smoothed by averaging the CT number of each pixel with its immediate neighbors in order to reduce the effects of noise. 4) For each set of spatially corresponding pixels, a gamma variate curve was fitted to the change in CT number relative to the initial baseline values in order to derive the transit parameters (Fig. 1). This procedure also includes a recirculation correction. 5) The calculated values of a certain parameter were displayed as a CT functional image by assigning a shade of gray to each pixel depending on the value of the selected parameter at the pixel. The procedures from 3) to 5) were accomplished semiautomatically.

Skull and ventricles were excluded from the calculation for CT functional imaging and were displayed as black.

$$C(t) = K \cdot (t-AT)^{\alpha} \cdot e^{-(t-AT)/\beta}$$

C(t) = increment of CT numbers
t = time after start of scan
K = constant scale factor
α , β = fitting coefficients
AT = arrival time of contrast

Fig. 1. Gamma variate function used as the fitting equation.
Alpha and beta are determined by the least square method to best fit the change in time-density value at each pixel. For each pixel, the value of a selected parameter is calculated from the two coefficients (alpha, beta) and displayed by the grey scale.

Transit parameters Two coefficients (α, β) were obtained by fitting a gamma variate curve to the time-density change during dynamic CT scanning. Transit parameters were derived from them, and include rise time [$\alpha\beta$], peak time [$AT+\alpha\beta$], decay time [β], area under curve [$K \cdot \beta^{(\alpha+1)} \cdot \Gamma(\alpha+1)$], inflection points [$AT+\beta(\alpha \pm \sqrt{\alpha})$], first moment [$AT+\beta(\alpha+1)$; abbreviated as M1] and corrected first moment [$\beta\ (\alpha+1)$].

In this study, we focused our attention on the CT functional images of M1, which appear to be most useful for evaluating the dynamics of contrast material. The value of this transit parameter provides a measure of the mean transit time through the compartment and it reflects regional relative intravascular blood flow[1]. In CT functional images of M1, brightness of pixels is proportional to the value of M1, i.e., a brighter region has a larger value of M1 (longer transit time and slower transit) than a darker region.

RESULTS

Conventional CT scans could only detect the existence of abnormality in one of the 14 cases by demonstrating obscured sulci and minimal decrease in density in the region where poor perfusion was clinically expected to be. Visual examination of dynamic CT images and analysis of time-density curves were helpful in detecting the abnormal blood flow in 3 of the 14 cases, although the extent of each lesion was not exactly determined by them. On the other hand, CT functional images of M1 (M1-functional image) could reveal the existence and the extent of ischemic lesions responsible for symptoms in 12 of the 14 cases. The usefulness of CT functional imaging in the diagnosis of cerebrovascular ischemia can be appreciated from the following clinical examples.

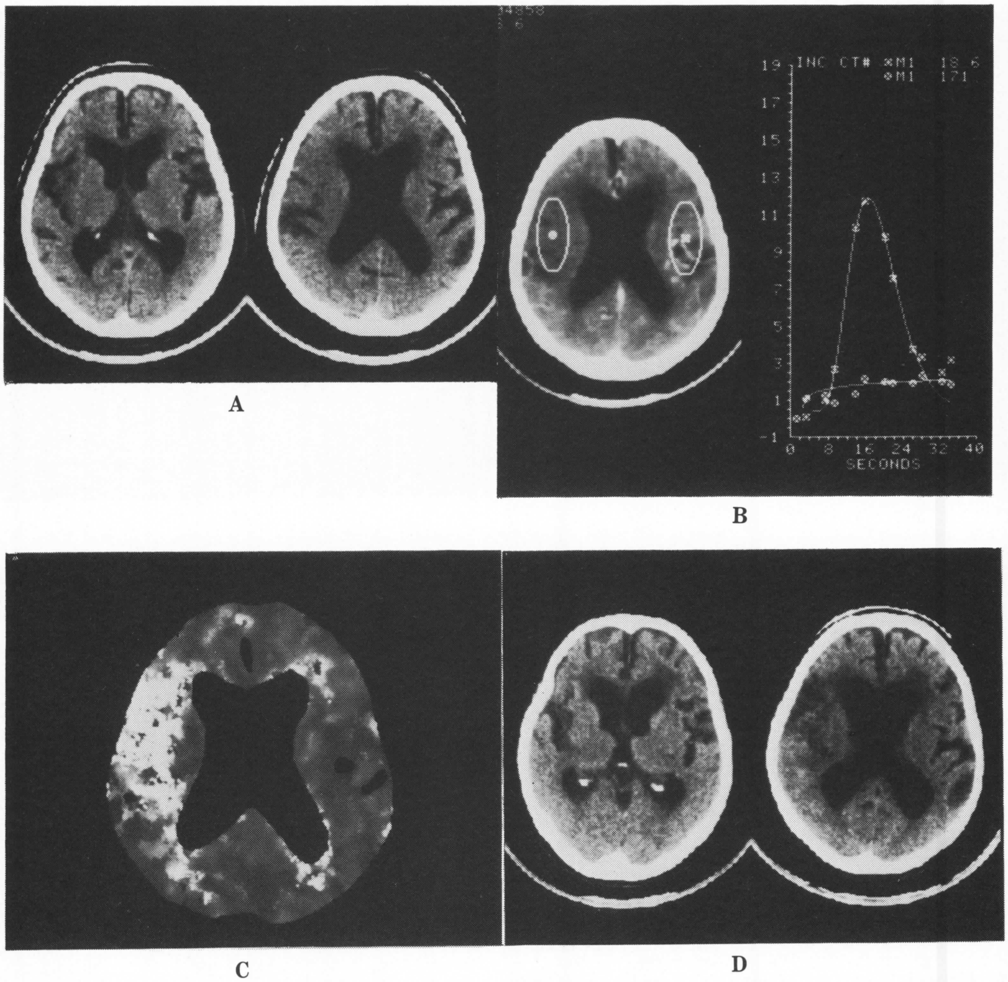

Fig. 2. Case 1, 84-year-old woman with numbness and left hemiplegia.
A: Conventional CT scans are equivocal, showing obscured sulci and decreased density in the right operculum. **B:** Analysis of time-density curves indicates no perfusion in the same area. **C:** The M1-functional image distinctively demonstrates the existence and the extent of impaired perfusion. **D:** CT scans performed four weeks later show dissolution of the right operculum.

Case 1. A 84-year-old woman was referred to our hospital for numbness and left hemiplegia which started about six hours prior to admission. Results of conventional CT scans were equivocal and revealed obscured sulci and decreased density in the right parietal region (Fig. 2A). A dynamic CT scan showed poor visualization of the opercular portion of the right middle cerebral artery and decrease in density in the corresponding area. The time-density curve obtained from the right parietal region showed no significant rise, indicating obliteration of blood flow (Fig. 2B). In the M1-functional image, the right operculum was recognized as the brightest area and the extent of the lesion was clearly demonstrated (Fig. 2C). A follow-up CT examination performed four weeks after the ictus showed a distinctive hypodense area in the right parietal region, which represented dissolution of the ischemic lesion (Fig. 2D).

Case 2. A 78-year-old man with known general arteriosclerotic disease was admitted because of mild left hemiparesis and dysarthria of seven hours duration. Conventional CT scans showed a small low dense spot in the right putamen, which was considered to be an old infarct and unrelated to the recent symptoms (Fig. 3A).

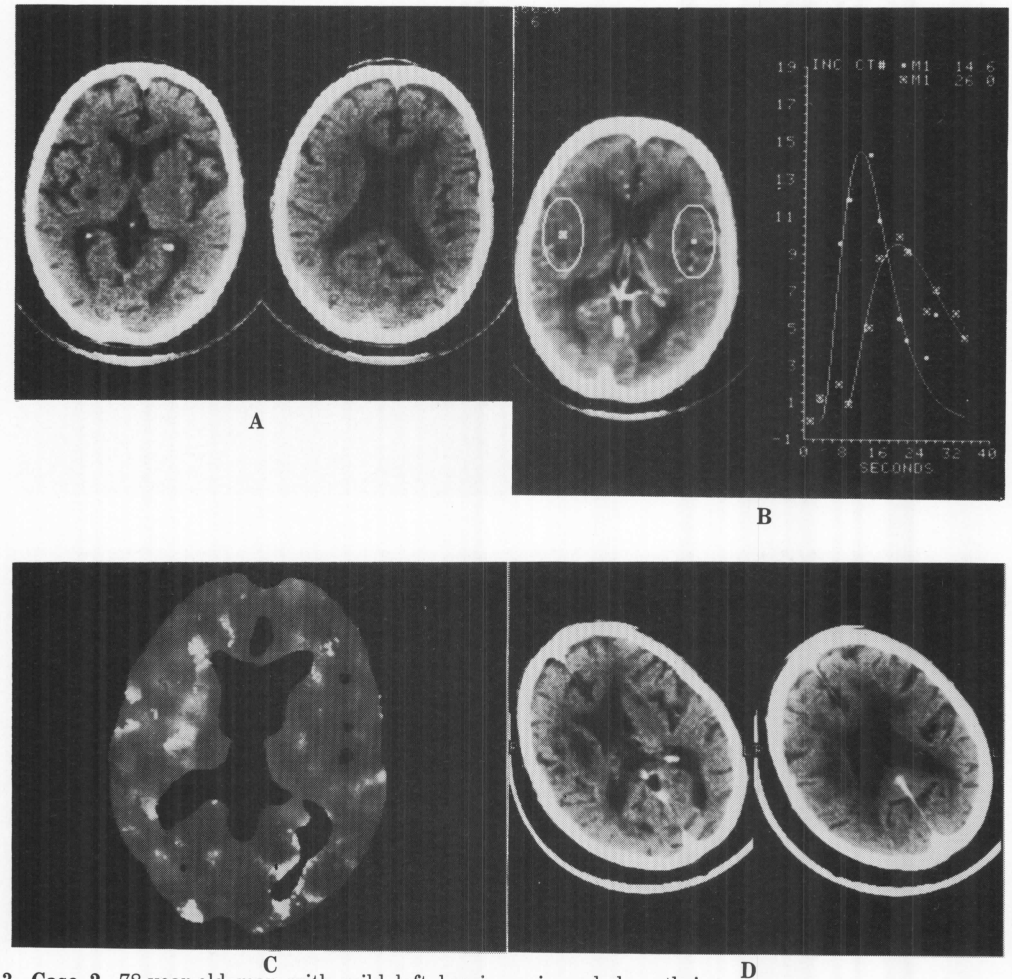

Fig. 3. Case 2, 78-year-old man with mild left hemiparesis and dysarthria.
A: Conventional CT scans do not reveal definitive findings responsible for the symptoms. **B:** Analysis of time-density curves shows a 11.4 second difference in mean transit time (M1) between the two hemispheres, the right more prolonged than the left. **C:** The M1-functional image reveals delayed circulation in the right hemisphere and absence of perfusion in the right putamen. **D:** Follow-up CT scans performed six days later demonstrate dissolution of the right putamen.

Visual inspection of the dynamic CT images showed contrast material appearing earlier in the left sylvian vessels than in the right. Analysis of time-density curves showed a remarkable difference in mean transit time (M1) between the two hemispheres, the right being more prolonged than the left (Fig. 3B). In the M1-functional image, the right hemisphere was expressed as a brighter area than the left and the right putamen was depicted by the brightest pixels (Fig. 3C). This suggested that the perfusion of the right hemispheric grey matter was delayed but barely retained while the putamen had no blood flow. In spite of anticoagulant therapy, the patient showed progressive neurologic deficits and the repeated CT examination performed six days later demonstrated dissolution of the right putamen (Fig. 3D).

Case 3. A 58-year-old man, who had a history of transient ischemic attack in the previous year, was admitted for left hemiplegia which started seven hours prior to admission. Conventional CT scans revealed no abnormalities (Fig. 4A). Visual inspection of dynamic CT images could not detect the causative lesions. Comparison of mean transit time (M1) in the two hemispheres showed a 4.7 second difference be-

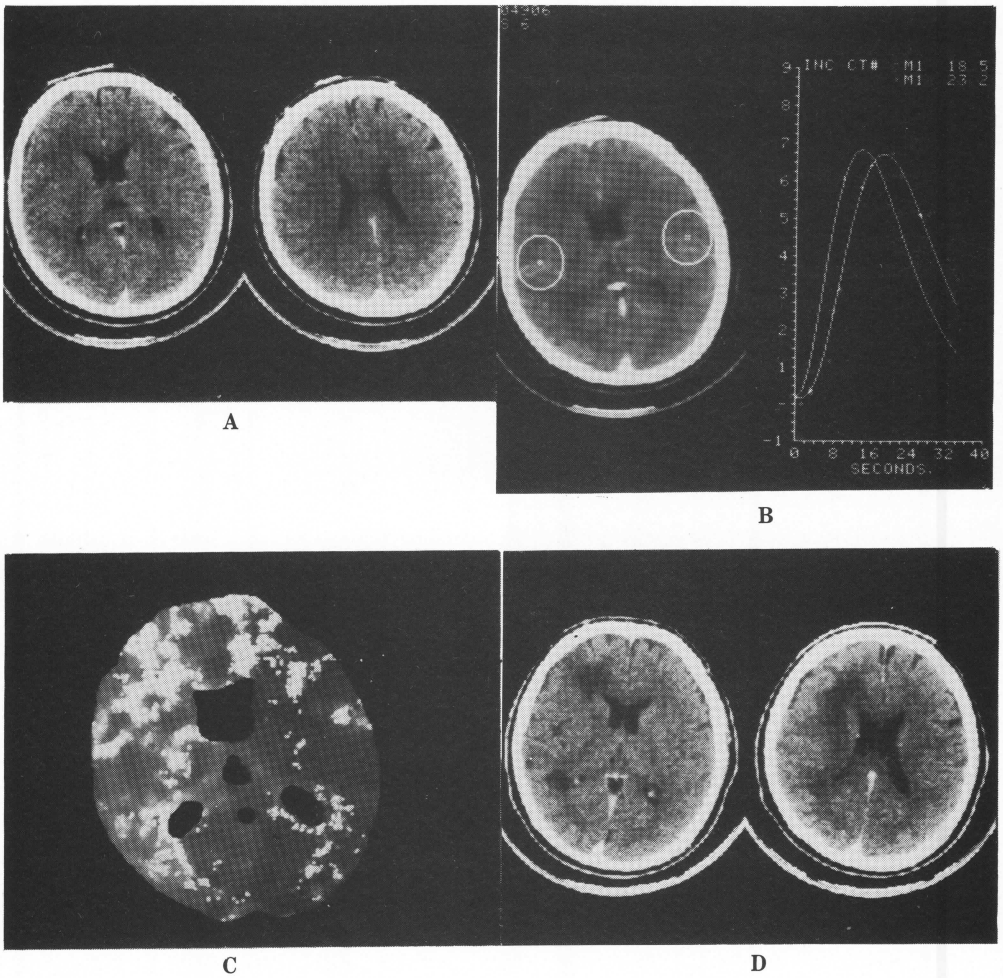

Fig. 4. Case 3, 58-year-old man with left hemiplegia.
A: Conventional CT scans reveal no abnormalities. **B:** Comparison of mean transit time in the two hemispheres shows a 4.7 second difference between the right and left, the right being slightly longer. **C:** The M1-functional image suggests an occlusive disease of the right cervical or intracranial major artery. **D:** Follow-up CT scans performed nine days later show extensive watershed infarction in the right hemisphere.

tween the right and left, the right being slightly slower (Fig. 4B). In the M1-functional image, the right hemisphere was depicted by brighter pixels than the left, and this suggested an occlusive disease of the ipsilateral cervical or intracranial major artery (Fig. 4C). Angiographic examinations were rejected and the patient was administered anticoagulant therapy. CT scans performed nine days after the ictus revealed extensive watershed infarction involving the right anterior frontal white matter and the white matter adjacent to the right lateral ventricle (Fig. 4D).

Case 4. A 72-year-old man with diabetes mellitus was admitted for left hemiparesis and dysarthria which started four hours prior to admission. Neither conventional CT scans nor visual inspection of dynamic CT images could disclose the lesion responsible for the episode (Fig. 5A). Routine analysis of time-density curves failed to reveal significant difference in blood flow between the two hemispheres. The M1-functional image showed a small bright area in the right putamen, representing decreased perfusion in the right lenticulostriate artery territory (Fig. 5B). Fig. 5C shows time-density curves obtained by placing ROI's exactly over

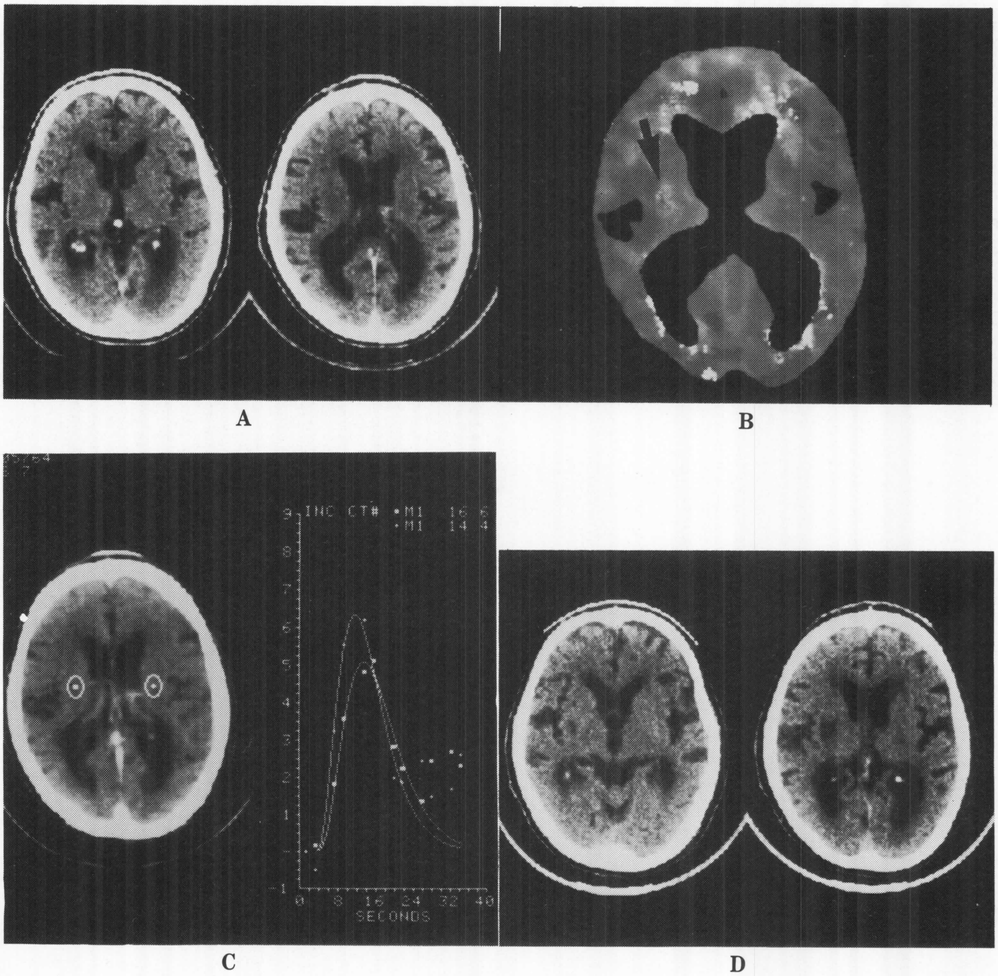

Fig. 5. Case 4, 72-year-old man with left hemiparesis and dysarthria.
A: Conventional CT scans show no abnormalities. **B:** The M1-functional image reveals decreased perfusion in the right putamen. **C:** Analysis of time-density curves shows a 2.2 second difference in mean transit time between the left and right putamen. The position and the range of each ROI are determined with reference to the M1-functional image. **D:** CT scans performed five days later show hypodense infarct involving the right putamen.

the lesion disclosed by the M1-functional image and the symmetrical area in the left hemisphere. Mean transit time derived from the two ROI's differed by only 2.2 seconds, the right being slower than the left. Follow-up CT scans performed five days later showed hypodense infarct involving the right putamen (Fig. 5D).

DISCUSSION

Dynamic CT of the brain has been widely used because of its technical simplicity. This technique has been applied to a variety of studies including evaluation of hemodynamics in the brain with ischemia, tumors and arteriovenous malformations[3,5,6,11-13]. In these studies, analysis of time-density curves has played an important role by providing useful parameters closely related to the blood flow. But the results are largely dependent upon manual settings of ROI's, making the objective or optimal evaluations sometimes unfeasible. In small lesions, it is frequently difficult to determine the position and the range of ROI's unless visual inspection of dynamic CT images gives definitive findings. A prior knowledge of the patient's clinical history may influence the operator's choice of area and be reflected in the subsequent results.

CT functional imaging can visualize the time course of contrast enhancement at all the pixels within the entire scan plane and allows an evaluation of regional dynamics of contrast material without the subjective maneuver of setting ROI's. In 11 of our cases, focal or diffuse decrease in perfusion was found by CT functional imaging in the locales where conventional CT scans failed to reveal structural abnormalities. The value of CT functional imaging in the detection of cerebral ischemia and in the early diagnosis of cerebral infarction appears evident. This diagnostic technique will be useful for determining a timely and appropriate therapy and for planning further examinations.

There are some limitations inherent in this technique. 1) CT functional images derived from dynamic CT scanning using iodinated contrast medium does not permit a direct estimation of flow rate. However, perfusion of the brain as revealed by CT functional imaging was strictly symmetrical in the healthy subjects, and the comparison of the right and left sides of the brain seems to be reliable in detecting the areas of abnormal perfusion. 2) Repeat injections of the contrast material are required for studying multiple scan planes because the CT functional imaging is limited to a single level at a time. 3) The technique may not be applicable to the lesions in the posterior fossa due to high spatial frequency artifact. 4) The intrinsic noise of the scanner gives invalid values to pixels in the regions with lower vascularity as found in watershed areas because of low signal-noise ratio. The resulting poor image may lead us to a wrong diagnosis.

Further technical improvements will, in the near future, diminish these limitations by a shorter scan time, a higher data density, a higher signal-noise ratio and an ability to perform dynamic CT scans at several levels simultaneously.

REFERENCES

1. **Axel, L.** 1980. Cerebral blood flow determination by rapid-sequence computed tomography: a theoretical analysis. Radiology **137**: 679—686.
2. **Berninger, W., Redington, R., Leue, W., Axel, L., Norman, D., Brundage, B., Carlsson, E., Herfkens, R. and Lipton, M.** 1981. Technical aspect and clinical applications of CT/X, a dynamic CT scanner. J. Comput. Assist. Tomogr. **5**: 206—215.
3. **Dobben, G.D., Valvassori, G.E., Mafee, M.F. and Berninger, W.H.** 1979. Evaluation of brain circulation by rapid rotational computed tomography. Radiology **133**: 105—111.
4. **Handa, J., Matsuda, M., Nakasu, Y., Nakasu, S. and Morioka, Y.** 1983. Dynamic computed tomography and functional imaging in cerebral vascular anomalies. Surg. Neurol. **19**: 497—507.
5. **Heinz, E.R., Dubois, P., Osborn, D., Drayer, B. and Barrett, W.** 1979. Dynamic computed tomography study of the brain. J. Comput. Assist. Tomogr. **3**: 641—649.
6. **Ikeda, Y. and Nakazawa, S.** 1984. Analysis of peritumoral edema — in special reference to the value of contrast enhanced CT scan and dynamic CT scan. Brain and Nerve **36**: 1055—1062.
7. **Kaihara, S., Natarajan, T.K., Maynard, C.D. and Wagner, H.N.** 1969. Construction of a functional image from spatially localized rate constants obtained from serial camera and rectilinear scanner data. Radiology **93**: 1345—1348.
8. **Nakagomi, T. and Takakura, K.** 1984. Dynamic computed tomography of brain tumor. Brain and Nerve **36**: 1031—1040.
9. **Norman, D., Axel, L., Berninger, W.H., Edwards, M.S., Cann, C.E., Redington, R.W. and**

Cox, L. 1981. Dynamic computed tomography of the brain: techniques, data analysis, and applications, A.J.N.R. **2**: 1—12.
10. **Takahashi, N., Kikuchi, H. and Karasawa, J.** 1983. Dynamic CT in patients with superficial temporal-middle cerebral artery anastomosis. A.J.N.R. **4**: 454—457.
11. **Traupe, H., Heiss, W.D., Hoeffken, W. and Zulch, K.J.** 1980. Perfusion patterns in CT transit studies. Neuroradiology **19**: 181—191.
12. **Wasenko, J.J., Cacayorin, E.D., Petro, G.R., Salibi, N.A., Hodge, C.H., Modesti, L.M. and King, R.B.** 1985. Dynamic computed tomography: intracranial applications. Neurosurgery **16**: 573—578.
13. **Wing, S.D., Anderson. R.E. and Osborn, A.G.** 1980. Dynamic cranial computed tomography: preliminary results. A.J.R. **134**: 941—945.