Functional Image of Dynamic Computed Tomography for the Evaluation of Cerebral Hemodynamics

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We report the usefulness of functional image of dynamic computed tomography as a technique for evaluating cerebral hemodynamics. Although the technique itself has been reported, the advance of computer technology has made it possible to obtain high-resolution functional images within only a few minutes. We conducted 70 examinations on 57 patients with cerebral ischemia and correlated the findings with clinical outcome. Those patients whose abnormalities were detected on all corrected mean transit time, time to peak, and peak value images developed massive cortical infarcts. On the other hand, patients with abnormalities detected only on the corrected mean transit time image had only partial low-density lesions on follow-up computed tomograms. Patients with abnormalities detected only on the time to peak image suffered repeated transient ischemic attacks, but follow-up computed tomograms showed no low-density lesion in most cases. Single-photon emission computed tomography with N-isopropyl-\(\text{\textsuperscript{123}}\)iodoamphetamine performed at the time of functional image of dynamic computed tomography showed a high concordance of the findings in many cases, especially those with hyperacute-stage cerebral ischemia, in which the concordance rate was 90.5% (19 of 21). Comparing images constructed from different parameters, functional image of dynamic computed tomography can delineate other than hemodynamic factors, such as extent of the vascular bed or the degree of collateral circulation. Thus, functional image of dynamic computed tomography is a potentially important and useful technique for the further analysis of cerebral hemodynamics. 

In treating cerebral ischemia, it is important to determine the exact extent and severity of the ischemia before lesions appear on computed tomograms (CT scans). Although some authors have recently reported the usefulness of magnetic resonance imaging (MRI) in treating acute-stage cerebral ischemia,\(^1,2\) morphologic changes such as those in water content cannot be seen until hours after onset. Positron emission tomography (PET) and single-photon emission computed tomography (SPECT) have made it possible to determine the extent of an ischemic focus based on metabolic changes.\(^3-5\) However, PET and SPECT require special and expensive equipment such as a cyclotron or a gamma camera and may be inappropriate for the prompt diagnosis of early cerebral ischemia in ordinary hospitals. As reported by many authors,\(^6-11\) dynamic CT has the potential to detect the extent of focal cerebral ischemia during the acute stage. However, it is difficult to detect the exact extent of an ischemic focus using dynamic CT because the manual determination of a region of interest (ROI) is required for the comparison of time–density curves. In 1981, Berninger et al\(^12\) reported obtaining the image of an ischemic area using dynamic CT, applying functional parameters calculated from the time–density curve to each pixel. This technique is called functional imaging. Although this early functional image required a lot of calculation time and was impaired by many artifacts, recent advances in CT technology have made it possible to create functional images of markedly high quality rapidly. New software developed by the Yokogawa Medical System Co., Ltd. (Tokyo, Japan) enabled us to obtain quickly information on a variety of cerebral hemodynamic variables in markedly high-quality images comparable to those obtained by xenon-enhanced CT or SPECT. We used this software with dynamic CT on 57 patients with cerebral ischemia and call the method functional image of dynamic CT (FID CT). The main purpose of this article is to explain the principle of FID CT and to show its usefulness.
Subjects and Methods

Since December 1987, we have performed 70 FID CT analyses in 57 patients treated in our hospital for cerebral ischemia. These 70 analyses included 29 cases of so-called hyperacute-stage cerebral infarction ≤6 hours after onset in which no ischemic changes had appeared on CT, 13 cases of symptomatic cerebral vasospasm after subarachnoid hemorrhage, 13 cases of chronic-stage cerebral infarction >1 week after onset, six cases during follow-up after superficial temporal-middle cerebral artery anastomosis, five cases with symptoms of cerebral ischemia after surgery for arteriovenous malformations (AVMs) or cerebrovascular moyamoya disease, and four cases of late convulsive seizures that seemed to be caused by cerebral ischemia.

In 21 of the 29 cases of hyperacute-stage cerebral infarction, 11 of 13 cases of symptomatic cerebral vasospasm after subarachnoid hemorrhage, and 11 of 13 cases of chronic-stage cerebral infarction N-isopropyl-p-(123I)iodoamphetamine (IMP) SPECT was carried out ≤24 hours after FID CT, and the extent of the ischemic focus was investigated and analyzed for concordance between the two imaging techniques. In cases in which we obtained definite findings, digital subtraction angiography was performed immediately after SPECT and the relations of findings from the three techniques were analyzed. One month after the initial examinations, follow-up CT was carried out in all cases and the extent of the low-density areas was examined.

A Yokogawa CT-9200 CT scanner was used. Before FID CT, ordinary axial scanning was used to determine the slice adequate for the examination. Forty milliliters of iopamidol was rapidly injected into an antecubital vein over 5 seconds through an 18-gauge needle. A slice was usually taken at the level of the basal ganglia because such a slice includes many vital structures, such as the thalamus and internal capsule, that are often insulted by an ischemic attack. Since the volume of contrast material was only 40 ml, two or three more slices could be examined. Following a baseline scan at a given interval, seven consecutive 5-second serial scans were performed with 1.5-second intervals between scans. Three segmented 212° images were made from each 5-second scan, resulting in 21 images.

The principle of FID CT is as follows. In conventional dynamic CT, the ROI is manually set and changes in optical density over the entire range are represented as a time–density curve. In FID CT, the ROI is minimized, that is, a time–density curve is prepared for each pixel. From these curves a variety of functional parameters are calculated, and the parameters are indicated for each pixel. This obtained image is an FID CT. To reduce artifacts, practical procedures include a preliminary smoothing process for each image before preparing the time–density curve, followed by γ-function approximation. Both the improvement of hardware and the development of high-performance software have made it possible to obtain a functional image in a short time. It takes 1.5 minutes for the smoothing process and approximately 2 minutes to calculate the functional images; therefore, all functional images can be obtained in only approximately 4 minutes. Considering the time for transferring the patient, it can be said that a virtually real-time image is available. It is a significant feature of FID CT that the technique allows immediate management of emergency patients.

The following eight functional parameter images can be obtained with the software (Figure 1): 1) time to peak, time from the start of the injection of contrast material to its peak concentration; 2) time of appearance, time from the start of the injection of contrast material to the point of elevation of the time–density curve; 3) mean transit time, time from the start of the injection of contrast material to the center of gravity of the time–density curve; 4) corrected mean transit time, (mean transit time)−(time of appearance); 5) peak value, maximum height of the time–density curve; 6) area, area under the time–density curve; 7) inflected width, duration between the steepest portions of the time–density curve; and 8) relative blood flow=1+(corrected mean transit time). Mean transit time, corrected mean transit time, inflected width, and relative blood flow reflect local cerebral blood flow, and peak value and area reflect the cerebral vascular bed or blood volume. Time to peak depends on involvement of the collateral circulation. We report the local cerebral...
hemodynamics mainly analyzed using the corrected mean transit time image as an index of local cerebral blood flow, the time to peak image as an index of collateral circulation, and the peak value image as an index of cerebral blood volume.

Results

The appearance of FID CT in a normal subject is presented in Figure 2. On the corrected mean transit time image, white matter, which is less perfused than gray matter, is shown as bright areas. Since the postero-temporal cortex is a watershed area, these bilateral areas are also shown as bright areas, indicating relatively low blood flow. On the time to peak image, contrast material is delayed in arriving in watershed areas, leading to their bright appearances. On the peak value image, cortical sulci and the cerebrospinal fluid cisterns are shown as bright areas because the vascular volumes there are relatively great.

Of 29 cases of hyperacute-stage cerebral infarction, the ischemic foci delineated by FID CT were detected as corresponding low-density areas on follow-up CT in nine cases; abnormalities had appeared on all corrected mean transit time, time to peak, and peak value images. In 12 cases an abnormality was detected on only the corrected mean transit time images; follow-up CT showed low-density areas corresponding only in part to the FID CT foci, and some low-density areas were thought to be lacunar infarcts. The remaining eight cases had abnormalities on only the time to peak images, indicating a delay of blood flow caused by an obstructed mainstem artery with abundant collateral circulation; repeated transient ischemic attacks were observed in these cases, but in most follow-up CT showed no low-density lesions.

Although the use of $[^{123}]$IMP SPECT in stroke is not well-defined, this technique may give some adjunctive information about cerebral hemodynamics. We compared the results of FID CT with those of SPECT in 21 cases of hyperacute-stage cerebral infarction. The ischemic sites determined by FID CT ≤6 hours after onset coincided with those obtained by SPECT in 19 (90.5%). There was one (4.8%) false-negative case, in which an abnormality was detected by SPECT but not FID CT, and one (4.8%) false-positive case, in which an abnormality was detected by FID CT but not SPECT. FID CT and SPECT findings agreed in eight (72.7%) of 11 cases of symptomatic cerebral vasospasm after subarachnoid hemorrhage; there were three false-negatives (27.3%). FID CT and SPECT findings concurred in six (54.5%) of 11 cases of chronic-stage cerebral infarction; there were three (27.3%) false-negatives and two (18.2%) false-positives.

Case Reports

We describe four cases, two with hyperacute-stage cerebral infarction, one with an AVM, and one with a brain tumor.

Case 1. This 75-year-old woman was brought to our hospital because of the sudden onset of left hemiparesis. CT 2 hours after onset showed no abnormalities (Figure 3, left upper). However, FID CT performed immediately afterwards clearly revealed a low-perfusion area in the right frontotemporal region (Figure 3, left middle). The same area was demonstrated as an ischemic lesion by $[^{123}]$IMP SPECT 1 day after admission (Figure 3, right middle). Digital subtraction angiography showed complete occlusion of the right internal carotid artery (Figure 3, right upper). The detected lesion had become a low-density area by the time of follow-up CT 1 week later (Figure 3, lower).

Case 2. This 62-year-old man, in whom megadolichobasilaris had been pointed out, visited our hosp-
FIGURE 3. Case 1. Left upper: Computed tomogram (CT scan) on admission. Left middle: Functional image of dynamic computed tomography (FID CT) (corrected mean transit time image). Ischemic lesion in right frontotemporal cortical area is clearly demonstrated. Right upper: Digital subtraction angiogram revealed occlusion of right internal carotid artery. Right middle: Single-photon emission computed tomogram showed hypoperfused area quite similar to that detected by FID CT. Lower: Follow-up CT scan 1 week after admission showed low-density area in right frontotemporal area that had been detected by FID CT on admission.

tal with the chief complaint of sudden motor aphasia. He had a history of repeated paralysis of the right upper limb during the previous 2 months. CT on admission did not show any abnormality, but angiography revealed occlusion at the trifurcation of the left middle cerebral artery and delineated only one branch, the frontal branch (Figure 4, top). The ischemic area was perfused by abundant cortical anastomoses from the anterior cerebral artery. FID CT indicated, slightly on the corrected mean transit time image and clearly on the time to peak image, an abnormality in the area of the middle cerebral artery (Figure 4, bottom). Apparently this patient's recent repeated neurologic disorders were caused by retarded circulation.

Case 3. This 40-year-old man visited our department for examination of a delayed convulsive seizure. CT on admission displayed a low-density area with a relatively definite boundary, deep in the temporal lobe (Figure 5, left); there was no enhancement of the site. By CT findings it was difficult to distinguish an infarcted focus from tumors such as low-grade astrocytoma. By FID CT (Figure 5, bottom), the abnormality was not detected on either the corrected mean transit time or the time to peak images, but it was detected on the peak value image. The vascular bed was increased in the region, but there was little change in blood flow. This strongly indicated a tumorous lesion. CT 1 month later showed an enlargement of this abnormal region, part of which had become a high-density area (Figure 5, right). At surgery the patient was found to have a low-grade astrocytoma.

Case 4. This 24-year-old woman visited our depart- ment for close examination of a convulsive seizure. A huge AVM in the right temporal lobe was diagnosed based on the findings of cerebral angiography and contrast-enhanced CT (Figure 6, top). FID CT showed no marked change on the corrected mean transit time and the time to peak images, but the peak value image showed an abnormality in the region (Figure 6, bottom). Apparently this patient had a relatively small hemodynamic abnormality despite marked enlargement of the vascular bed. FID CT succeeded in detecting hemodynamics at and around the nidus of an AVM.

Discussion

In 1981 Berninger et al. first reported the visualization of a focus of cerebral ischemia from dynamic CT scans using functional image formation, which had been proposed in nuclear medicine by Kaihara et al. The same software was used in 1983 and 1984 to display the hemodynamics of an AVM, those after extracranial–intracranial artery bypass surgery, and those of a cerebral tumor. However, imaging required considerable time for calculation and the obtained images contained many artifacts. Simultaneously, new imaging techniques such as PET, SPECT, and xenon-enhanced CT had been developed rapidly. Therefore, functional imaging by dynamic CT has gradually fallen into disuse.

In 1987, the Yokogawa Medical System Co., Ltd. developed epoch-making new software. Owing to the introduction of a high-performance computer processor and the improvement of software, we can obtain within a few minutes high-resolution images that are not at all inferior to those given by xenon-enhanced CT. We describe the characteristics of this procedure, FID CT.
The greatest feature of FID CT is that cerebral hemodynamics can be detected without any special machines; only a CT scanner and iodinated contrast material are required. FID CT makes examination possible even in ordinary hospitals lacking high-grade machines. Because most patients with cerebrovascular disorders are treated in ordinary hospitals having no special equipment except a CT scanner, the generalized use of FID CT will be of great benefit.

Second, high-resolution images can be obtained, as we demonstrate. Examination requires only a short time, approximately 4 minutes. FID CT provides information on the hemodynamics of an emergency patient in the same time as that required for contrast-enhanced CT. Thus, the information is available before the patient is brought to the ward, so that rapid and adequate treatment can be started.

Third, the reliability of information given by FID CT was found to be very high, particularly in cases of hyperacute-stage cerebral infarction, as shown by comparisons of FID CT and SPECT. In cases of chronic-stage cerebral infarction, there were some discrepancies between the findings of FID CT and SPECT. This can be partially explained by differ-
FIGURE 5. Case 3. Left: Unenhanced computed tomogram (CT scan) on admission. Low-density area was seen in deep temporal area. Bottom: Functional images of dynamic computed tomography. cMTT, corrected mean transit time image; TP, time to peak image; PV, peak value image. Lesion is illustrated only on PV; both cMTT and TP are normal. This finding shows increase of local blood volume in detected area. Right: CT scan 1 month later showed enlargement of lesion, with abnormal enhancement. Lesion was found to be astrocytoma by surgical exposure.

ences in the detection principles; FID CT shows only relative, not quantitative, blood flow whereas SPECT theoretically represents the latter. Some other factors such as collateral blood flow, recirculation, and reactive hyperemia in cases of chronic ischemia may also play roles in the discrepancies found. Further study is under way to clarify the usefulness of FID CT in patients with chronic cerebral ischemia.

Finally, FID CT can delineate factors other than cerebral hemodynamics. By using different parameters, the time for blood to arrive in an area, the extent of the cerebral vascular bed, etc., can be delineated. FID CT easily detects a condition in which there is little change in local cerebral blood flow despite an enlargement of the cerebral vascular bed, such as is seen in patients with a certain AVM or a cerebral tumor, as demonstrated above.

Although attention is likely to be paid to techniques using expensive equipment such as MRI and PET, ordinary x-ray CT with processing refinements
FIGURE 6. Case 4. Top: Contrast-enhanced computed tomograms. Huge arteriovenous malformation in right temporal lobe is noted. Bottom: Functional images of dynamic computed tomography clearly showed hemodynamics of lesion. cMTT, corrected mean transit time image; TP, time to peak image; PV, peak value image. Brighter area of PV indicated increase in local vascular bed. Local cerebral blood flow and circulation time around nidus are almost normal.
can afford a great deal of information. Because of its ease of use and the high quality of its images, FID CT may become the first-choice technique for examining patients with early cerebral ischemia.

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