Z-score Mapping Method for Extracting Hypoattenuation Areas of Hyperacute Stroke in Unenhanced CT

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Rationale and Objectives: The purpose of this study was to develop a *z*-score mapping method on the basis of a voxel-by-voxel analysis to visualize hypoattenuation areas of hyperacute stroke on unenhanced computed tomographic (CT) images.

Materials and Methods: The algorithm of the developed method consisted of five main steps: anatomic standardization, the construction of a normal reference database, calculation of the *z* scores, the elimination of false-positive areas, and the extraction of hypoattenuation areas. The obtained *z*-score map was then superimposed on the original CT images for identifying hypoattenuation areas of hyperacute stroke on the unenhanced CT images. The method was applied to 21 patients with infarctions of the middle cerebral artery territory <3 hours after symptom onset. The performance of the method was evaluated using receiver-operating characteristic analysis.

Results: Hypoattenuation regions could be significantly distinguished from normal regions by *z*-score values ($P < .0001$). The area under the receiver-operating characteristic curve for distinction between 68 hypoattenuation regions and 142 normal regions was 0.834.

Conclusions: The developed method has the potential to accurately indicate high–signal intensity areas corresponding to hypoattenua-tion areas on CT images in the hyperacute stage of stroke.

Key Words: Acute ischemic stroke; hypoattenuation; *z* score; voxel-by-voxel analysis.

Currently, unenhanced computed tomographic (CT) imaging still serves as an initial neuroimaging examination in the diagnosis of acute ischemic stroke because of its accessibility and speed, although diffusion-weighted magnetic resonance (MR) imaging in acute ischemic stroke has been supported (1,2). Identifying hypoattenuation of ischemic brain parenchyma is important in the interpretation of acute stroke on CT images. Hypoattenuation is a subtle attenuation change (in Hounsfield units [HU]) of ischemic brain tissue. In recent years, tissue plasminogen activator thrombolysis has been approved by the US Food and Drug Administration as an effective treatment for acute stroke <3 hours after symptom onset. Patients with large areas of ischemic lesions would incur a high risk for fatal hemorrhagic complications after thrombolysis. To avoid the risk, unenhanced CT imaging plays an important role in rapidly selecting patients. Thus, quantifying the extent of areas of ischemic lesions is mandatory to select patients for thrombolysis with low risk for hemorrhage. A quantitative CT scoring system, the Alberta Stroke Program Early CT Score (ASPECTS) (3), is often used to help interpreters in quantifying the extent of ischemic lesions of acute stroke in the territory of the middle cerebral artery (MCA). When evaluating the extent of ischemic areas using the ASPECTS method, the extent of the regions of ischemic lesions (hypoattenuation or brain swelling) is quantified by counting the number of lesions among 10 predefined regions. However, the sensitivity for the detection of acute stroke was <50% on unenhanced CT images (4), even when the ASPECTS system was used.

The presence of hypoattenuation is an important CT finding of acute ischemic stroke. The detectability of hypoattenuation within a few hours of symptom onset largely depends on the skill and experiences of the reader, because of difficulty in the detection of subtle attenuation changes of ischemic brain tissue (5,6). Therefore, improvement in the detection of parenchymal hypoattenuation on unenhanced CT images would be desirable. To cope with this issue, we have developed an adaptive smoothing filter to reduce image

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noise (7,8). The results showed that the proposed filter had potential usefulness in the improvement of detection (9). However, the method was effective for detecting only the presence of hypoattenuation. The extent of hypoattenuation was difficult to identify with this method. Maldjian et al (10) reported an automated segmentation method for identifying hypoattenuation of acute ischemia. In their report, histograms of voxel density distributions in the lentiform nucleus and insula were in comparison to those of the contralateral side on the brain image. The method, however, was limited to analyzing only two of the 10 regions in ASPECTS (ie, the lentiform nucleus and insula).

Recently, voxel-by-voxel (VBV) analysis has been used in positron emission tomographic (PET) imaging and single-photon emission computed tomography (11,12) for identifying the extent of areas of slightly decreased signal values in three-dimensional brain data. The VBV analysis consists of the following steps: anatomic standardization, the generation of a normal reference database, calculation of the *z* score for an individual's data set, the elimination of false-positive areas, and the extraction of lesions. Some work has shown that the *z*-score maps obtained from VBV analysis are effective in the diagnosis of early Alzheimer's disease (11,12). However, to the best of our knowledge, so far no work has focused on applying VBV analysis to unenhanced CT images for extracting areas of hypoattenuation of acute ischemic stroke. We hypothesized that if VBV analysis is applied to unenhanced CT images, a high–*z* score area corresponding to the decreased attenuation area in ischemic brain tissue might be obtained.

In this article, we present a *z*-score mapping method based on VBV analysis to visualize areas of hypoattenuation of acute ischemic stroke on unenhanced CT images.

MATERIALS AND METHODS

Figure 1 is a flowchart of the algorithm of our proposed method for extracting hypoattenuation areas on unenhanced CT images. The basic approach of the algorithm is to use *z*-score mapping on the basis of VBV analysis. Preprocessing and postprocessing techniques are also performed to yield high accuracy of the proposed method. This algorithm is described in more detail in the following. The study protocol was approved by our institutional review board. Informed consent was not required.

Patient Database

Between April 2007 and December 2008, as a preselection, 34 consecutive patients with symptoms suggestive of MCA territory stroke were collected from the CT files of Sendai City Hospital, Sendai, Japan. From the 34 collected CT files, 21 patients were selected for this study using the following inclusion criteria: (1) the first CT scan was performed <3 hours after stroke onset, (2) no patients had evidence of old infarctions, and (3) no patients presented with leukoaraiosis. The 21 patients consisted of 14 men and seven women (age range, 46–92 years; mean age, 66.5 years). All patients underwent the first unenhanced CT scan <3 hours (mean, 1.86 hours; range, 0.67–3 hours) after the onset of stroke ictus.

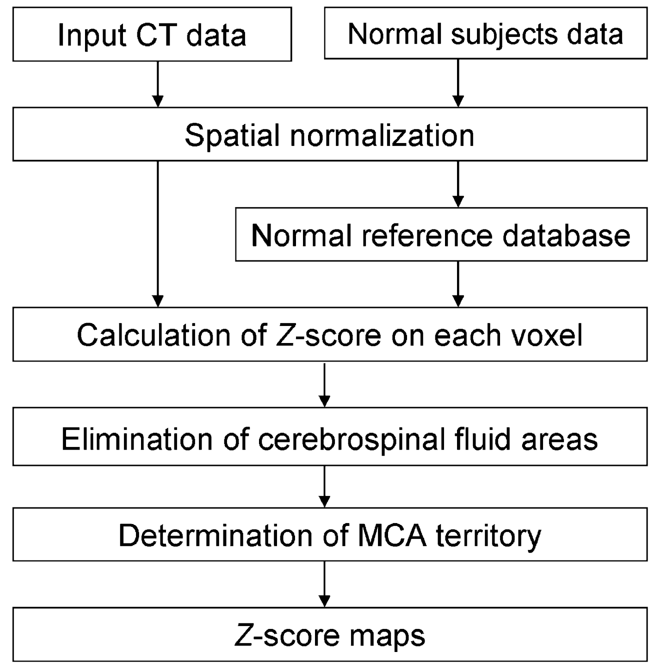

Figure 1. Flowchart illustrating the process of generating a *z*-score map for the extraction of hypoattenuation regions on unenhanced computed tomographic (CT) images. MCA, middle cerebral artery.

To constitute a normal reference database for the VBV analysis, 28 normal subjects were selected according to the following three inclusion criteria: (1) no calcification in the basal ganglia region, (2) no low-density area of old cerebral infarction, and (3) no dilation of the cerebral ventricles and sulcus. The mean age of the normal subjects was 54.2 years (range, 40–67 years), significantly lower than that of the selected patients. A detailed description is given in the "Discussion" section. All images were acquired using a 16-slice multidetector CT scanner (Emotion 16; Siemens Medical Solutions, Forchheim, Germany). At our institution, CT scans are routinely performed using a matrix size of 512 × 512 and a field of view of 230 mm, with 4.8-mm contiguous sections.

To constitute a "gold standard" of hypoattenuation for the selected patients, two neuroradiologists identified in consensus the existence of hypoattenuation in the MCA territory according to the ASPECTS method. Figure 2 shows the 10 regions of the ASPECTS (3) on unenhanced CT images. In the present study, according to the ASPECTS method, the MCA territory in the ischemic hemisphere was divided into 10 regions of interest. These regions included the lentiform nucleus (L), insula (I), caudate nucleus (C), internal capsule (IC), anterior inferior frontal lobe (M1), temporal lobe (M2), inferior parietal and posterior temporal lobe (M3), anterior superior frontal lobe (M4), precentral and superior frontal lobe (M5), and superior parietal lobe (M6). As a result, a total of 210 regions from the 21 patients were