Improvement of Detection of Hypoattenuation in Acute Ischemic Stroke in Unenhanced Computed Tomography Using an Adaptive Smoothing Filter

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Background: Much attention has been directed toward identifying early signs of cerebral ischemia on computed tomography (CT) images. Hypoattenuation of ischemic brain parenchyma has been found to be the most frequent early sign.

Purpose: To evaluate the effect of a previously proposed adaptive smoothing filter for improving detection of parenchymal hypoattenuation of acute ischemic stroke on unenhanced CT images.

Material and Methods: Twenty-six patients with parenchymal hypoattenuation and 49 control subjects without hypoattenuation were retrospectively selected in this study. The adaptive partial median filter (APMF) designed for improving detectability of hypoattenuation areas on unenhanced CT images was applied. Seven radiologists, including four certified radiologists and three radiology residents, indicated their confidence level regarding the presence (or absence) of hypoattenuation on CT images, first without and then with the APMF processed images. Their performances without and with the APMF processed images were evaluated by receiver operating characteristic (ROC) analysis.

Results: The mean areas under the ROC curves (AUC) for all observers increased from 0.875 to 0.929 (P = 0.002) when the radiologists observed with the APMF processed images. The mean sensitivity in the detection of hypoattenuation significantly improved, from 69% (126 of 182 observations) to 89% (151 of 182 observations), when employing the APMF (P = 0.012). The specificity, however, was unaffected by the APMF (P = 0.41).

Conclusion: The APMF has the potential to improve the detection of parenchymal hypoattenuation of acute ischemic stroke on unenhanced CT images.

Key words: CT; detection; diagnosis; infarction; ischemia

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Unenhanced computed tomography (CT) still serves as an initial neuroimaging examination in the diagnosis of acute stroke at most institutions because it is widely accessible and convenient, although diffusion-weighted magnetic resonance (MR) imaging in acute stroke is beginning to be supported (1, 2). Over the last decade, much attention has been directed toward identifying the early signs of cerebral ischemia on CT images (3–12).

The presence of early signs involving more than one-third of the middle cerebral artery (MCA) territory has been used as an exclusion criterion for thrombolysis (13, 14). Hypoattenuation of ischemic brain parenchyma, which is seen as gray matter becoming isodense to adjacent white matter,
or loss of gray–white matter interface, has been found to be the most frequent early sign (5, 6). However, the detectability of subtle hypoattenuation areas in acute stroke is mostly dependent on the skill and experience of the interpreters (15, 16). Therefore, it has been advised that low interobserver agreement for the detection of hypoattenuation should be improved (17). Previous studies have attempted to improve the detectability of hypoattenuation using image analyses (18, 19).

We have previously reported on a noise reduction filter, an adaptive partial smoothing filter (APSF), for improving the detectability of low-contrast objects (20–22). The results of these studies indicated that the APSF was able to greatly reduce image noise, resulting in visually enhanced parenchymal hypoattenuation of acute stroke on CT images. We have recently developed an adaptive partial median filter (APMF) based on the APSF (23). Our simulation studies using simulated CT images with gray–white matter interface have shown that the performance of the APMF was better than that of the APSF (23). The APMF has also been applied to four clinical images without performing any clinical evaluation (24).

The purpose of this study was to evaluate the effect of the APMF for the detection of parenchymal hypoattenuation of acute stroke on unenhanced CT images using receiver operating characteristic (ROC) analysis.

Material and Methods

The study protocol was approved by our institutional review board. Patients’ informed consent was not required.

Data selection
One board-certified neuroradiologist (K.I.) retrospectively selected the CT images of 26 patients with parenchymal hypoattenuation and those of 49 randomly selected control patients presenting for workup of headache, without any neurological deficits suggesting stroke and without parenchymal hypoattenuation, from the CT files of Sendai City Hospital, Sendai, Japan. The files were dated between June 2000 and March 2005. For the purpose of ROC analysis, the CT images of 26 patients with various degrees of difficulty in detecting parenchymal hypoattenuation on CT images were selected. Hypoattenuation was defined as a region of abnormally low density of the brain structure relative to attenuation of the contralateral hemisphere. The mean ages of the patients with and without hypoattenuation were 70 years (age range 41–90 years) and 75 years (age range 38–94 years), respectively. The patients with hypoattenuation consisted of 13 men and 13 women; the control subjects without hypoattenuation comprised 22 men and 27 women. The mean interval between onset of stroke and first imaging was 2 hours 38 min (range 1–5 hours).

One of the axial CT images through the basal ganglia region was selected from each of the 26 patients and 49 control subjects. Twenty-six images with hypoattenuation showed varying extent of hypoattenuation of brain tissue on CT images. Four of the images, in particular, showed slight hypoattenuation at the lentiform nucleus. The details of hypoattenuation of the 26 patients are summarized in Table 1. The diagnosis of stroke was confirmed by diffusion-weighted MR imaging or follow-up CT 1–7 days after the onset of symptoms.

The CT examinations were performed using Pro-Seed Accell (GE Yokogawa Medical Systems, Tokyo, Japan) in sequential mode. The images were reconstructed with a standard-version reconstruction algorithm routinely set in our institution. The technical parameters for the slices selected in this study included the following: tube voltage 120 kV, tube current–time product 400 mAs, matrix size 512 × 512, slice thickness 10 mm, and field of view 250 mm.

APMF
The APMF is a median filter with variable filter shape and size determined according to the distribution of pixel values of anatomical structure contours or edges in the region of interest. For example, if pixels of edges (i.e., the interface of gray–white matter) are included in a region of interest, a filter having a small size is used as a weak low-pass filter to preserve the edge of the structure. If none of the edges is included in a region of interest, a filter having a larger size is used as a powerful low-pass filter to smooth noisy images.

The APMF is applied to reconstruct CT images obtained from a workstation. The execution time required for image data transfer implementation, image processing, and image display with a personal computer was less than 1 min.

Details of the APMF algorithm and parameter values of the APMF used in this study are described in the Appendix.
The selected images were retrieved from our picture archiving and communication system (PACS) workstation (PathSpeed; GE Yokogawa Medical Systems, Tokyo, Japan). The image data in Digital Imaging and Communications in Medicine (DICOM) version 3.0 format were transferred to a personal computer (n9030; HP, Tokyo, Japan).

The APMF was applied to the 26 images with hypoattenuation and the 49 images without hypoattenuation. This resulted in a total of 150 images obtained in the present study: 75 unprocessed and 75 APMF processed images.

Observer test
Seven radiologists, including three neuroradiologists (years of experience 5–20; including T.K. and H.T.), one general radiologist (years of experience 18), and three radiology residents (years of experience 1–4), evaluated the effect of the APMF in the detection of parenchymal hypoattenuation. The neuroradiologist who selected the images did not serve as an observer. The observers were asked to indicate their confidence level regarding the presence (or absence) of a parenchymal hypoattenuation, with attention to the gray–white matter interface, by using a continuous rating scale (25). The observers were blinded to all clinical features. The continuous rating scale was displayed on a 20-inch color monitor (Multiscan G500; SONY, Tokyo, Japan) with a 100-point scale, the left, right, and center of which indicated “definitely absent,” “definitely present,” and “ambiguous,” respectively. The sequential observer test was performed (26) in this study. The observers indicated their confidence level with an indicator on a bar in the display. First, each observer viewed an original CT image only and gave an initial rating. The APMF processed image was then displayed next to the original image. The observers then viewed both the original and the APMF processed images, and gave a second rating. For the second rating, the observer was asked to shift more than 20 points from a point first determined on a bar, if he or she had strong confidence in the presence or absence of parenchymal hypoattenuation using the APMF processed images. The indicator was originally set at a point of 50 before the initial rating. A 20-HU window width was preset to accentuate gray–white matter on the monitor when the observers started to view images. The observers were allowed to adjust window.

Table 1. Summary of patients

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age, years</th>
<th>Sex</th>
<th>Side</th>
<th>Time to CT, hours</th>
<th>Location of early CT signs</th>
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<tr>
<td>1</td>
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<td>M</td>
<td>L</td>
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<td>L</td>
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<tr>
<td>2</td>
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<td>3</td>
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<td>R</td>
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<td>I, M1, M2, M3</td>
</tr>
<tr>
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<td>F</td>
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<tr>
<td>5</td>
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<td>F</td>
<td>L</td>
<td>1.5</td>
<td>L, I, M1, M2</td>
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<tr>
<td>6</td>
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<td>M</td>
<td>L</td>
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<tr>
<td>7</td>
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<td>L</td>
<td>2.3</td>
<td>L, I, C</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
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<td>I, M2</td>
</tr>
<tr>
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<td>L</td>
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<td>M</td>
<td>L</td>
<td>2.8</td>
<td>L, I, M1</td>
</tr>
</tbody>
</table>

L: lentiform; I: insular ribbon; C: caudate; M1: anterior middle cerebral artery (MCA) cortex; M2: MCA cortex lateral to insular ribbon; M3: posterior MCA cortex.
widths and center level settings as necessary. Reading time was not limited in this study.

Before the test, each observer was shown 14 training images so that they could become familiar with the characteristics of the APMF processed images and the test procedure. The training images were not included in the images used in the observer test.

Statistical analysis
The effect of the APMF on the detection of parenchymal hypoattenuation was analyzed by using ROC analysis. A computer program (ROCKIT 0.9B; C. E. Metz, University of Chicago, Ill., USA) was used for obtaining binormal ROC curves from the continuous rating data (25). The statistical significance of the difference in the areas under these curves (AUC) obtained without and with the APMF processed images was tested by use of the jackknife method, which included both reader variation and case sample variation, by means of an analysis of variance approach (27). A computer program (LABMRMC; C. E. Metz, University of Chicago, Ill., USA) was used for the test.

We assumed that a “clinically relevant change” in confidence levels occurred only when the difference was higher than 20 points between the first and the second ratings on a 100-point confidence rating scale. The justification for use of this limit of 20 points was based on a report by Hirai et al. (28). In cases with hypoattenuation, a shift of more than 20 points to the right implied that it was detrimental. Inversely, in cases without hypoattenuation, a shift of more than 20 points to the left implied that the APMF was beneficial, and a similar shift to the right implied that the APMF was detrimental. In cases with hypoattenuation, a change from a negative finding to a positive finding implied that the APMF was beneficial, and a change from a positive finding to a negative finding implied that it was detrimental. Inversely, in cases without hypoattenuation, a change from a positive finding to a negative finding implied that the APMF was beneficial, and a change from a negative finding to a positive finding implied that it was detrimental. We calculated the number of images that the APMF made observers perform a “clinically reversed action” among the images in which clinically relevant changes occurred. The differences between the average numbers of the two clinically reversed actions for the seven observers were calculated by using the Student’s paired t test.

Average sensitivity and specificity in the detection of parenchymal hypoattenuation were calculated without and with the APMF processed images. The statistically significant differences in sensitivity and specificity without and with the APMF processed images were evaluated by using the Student’s paired t test. When $P < 0.05$, it was considered significantly different.

Results
Two examples of unenhanced CT images of acute stroke after applying the APMF are shown in Figs. 1 and 2.

The ROC curves for the detection of parenchymal hypoattenuation obtained from all observers without and with the APMF processed images are shown in Fig. 3. The average AUC value improved from 0.875 to 0.929 when the observers viewed the original CT images together with the APMF processed images, and this difference was statistically significant ($P = 0.002$). Fig. 4 shows the AUC values for the seven observers without and with the APMF processed images. Note that all observers had improved performance when the APMF processed images were shown.

The results of the clinically relevant change in confidence levels are shown in Fig. 5. In cases with hypoattenuation, the average number of images affected beneficially by using the APMF processed images was significantly larger than that of images affected detrimentally ($P < 0.05$). In cases without hypoattenuation, no significant difference was found between the numbers of images affected beneficially and detrimentally ($P = 0.13$).

The results of clinically reversed action in image findings are shown in Fig. 6. In cases with clinically relevant changes occurring in the images with
hypoattenuation, the average number of images in which a finding was reversed beneficially was larger than that reversed detrimentally ($P < 0.05$). In cases without hypoattenuation, no significant difference was observed between the numbers of images in which findings were reversed beneficially and detrimentally ($P = 0.22$).

The average sensitivity in the detection of hypoattenuation improved significantly, from 69% (126 of 182 observations) to 89% (151 of 182 observations), by using the APMF ($P = 0.012$). The average specificity was 84% (306 of 343 observations) and 92% (315 of 343 observations), respectively, for the images without and with the APMF. No significant difference in the specificities between images without and with the APMF was found ($P = 0.41$).

**Discussion**

Recognizing the presence of hypoattenuation in order to diagnose acute stroke is crucially important in initial CT scans (8, 9). However, interobserver agreement for detecting parenchymal hypoattenuation on CT images of acute stroke patients is poor. It has been reported that $k$ values for parenchymal

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**Fig. 1.** An 88-year-old-woman with right hemiplegia at 1.5 hours after stroke onset (Table 1, patient 17). The use of the APMF prevented four observers from missing hypoattenuation regions. A. The original image with the standard window width of 80 HU shows that parenchymal hypoattenuation is inconspicuous, although effacement of sulci in the left parieto-occipital area is identified. B. The original image with a narrow window width of 20 HU shows that parenchymal hypoattenuation is subtly detectable at the left lentiform nucleus. C. The APMF processed image viewed with a window width of 20 HU shows that the hypoattenuation at the left lentiform nucleus is clearly detectable (arrows). D. Follow-up unenhanced CT image taken 4 days after ictus reveals hypodense areas in the left MCA and PCA distributions.
hypoattenuation are low, ranging from 0.30 to 0.53 (16). One of the reasons for these low k values may be the subtle change of attenuation in Hounsfield units in ischemic brain tissue. Kucinski et al. reported a decrease of 1.3 HU at 2.5 hours after the onset of acute ischemic stroke (29). This subtle change may be buried in image noise on the CT images. In order to solve the issue of poor interobserver agreement, reducing the image noise may be an effective method. Thus, we applied the APMF to unenhanced CT images in order to achieve this purpose.

A soft-copy review with variable window width and center level settings has been performed in order to improve the detection of parenchymal hypoattenuation of ischemic stroke (30). Reviewing CT images with a narrow window width on a monitor for accentuating the contrast of gray–white matter leads to increased sensitivity for detecting parenchymal hypoattenuation. However, this operation visually increases image noise. For the APMF processed images, on the other hand, the contrast of gray–white matter was enhanced without accentuating image noise when using a narrow window width of 20 HU (Figs. 1 and 2).

In the present study, the number of images affected beneficially was increased by use of the APMF in cases with hypoattenuation. Our results may suggest that interpreters recognize parenchymal hypoattenuation of acute stroke with confidence in clinical practice. Moreover, in approximately 50%
of the beneficially affected images, the observer's interpretation of the CT images was reversed beneficially from negative findings to positive findings in the images with hypoattenuation by using the APMF processed images. In contrast, the number of detrimentally reversed actions was significantly smaller than that of the beneficially reversed actions. This result indicates that the use of the APMF can prevent observers from missing hypoattenuation regions.

In the observer test of the 49 cases without hypoattenuation, it was shown in eight cases that the clinically reversed action was changed detrimentally from a positive finding to a negative finding by three residents. However, in two cases, it was shown that the clinically reversed action was changed detrimentally by two radiologists. The visual information shown on the APMF processed images was considerably different from that shown on the original CT images. Therefore, interpreters might need to become accustomed to the application of the APMF. In clinical practice, interpreters should review the APMF processed images together with the standard CT images for interpretation when using the APMF.

In the present study, the sequential observer test was performed in such a way that the APMF images were always viewed after original images. Therefore, the test has an inherent bias, although it has been reported that the sequential test has no significant difference compared with an independent test (31, 32).

There was a difference between the observer test and clinical environment. No patients with an old cerebral infarction were included in this study, but patients with old cerebral infarctions are examined by emergency CT scans in a clinical setting. In patients with old cerebral infarctions, low-density areas of the old infarction might affect detection of new hypoattenuation areas of acute stroke on the APMF images. This might bias the results of the present study.

Several studies have reported that adaptive filters have the ability to reduce image noise without loss of image quality in many medical imaging modalities, including CT (33–36). The common purpose of these reports was to reduce exposure dose while maintaining image quality. One group showed that the use of an adaptive edge-preserving noise reduction filter had the potential to reduce the radiation dose by approximately 50% in CT of the liver (33), and another demonstrated that an adaptive filter accomplished a 68% reduction of radiation dose in CT perfusion (34). A noise reduction filter used to reduce abdominal CT image noise while preserving the qualitative appearance of the noise without a perceptible loss of anatomic structure delineation has been reported (35). Also, another study has shown that, by using an adaptive filter, noise reduction values of typically 30–60% can be achieved in noncylindrical body regions such as the shoulders, while maintaining image resolution (36). In contrast to these publications, in the present study, we applied the APMF for the purpose of improving the detectability of hypoattenuation of acute stroke. The APMF can reduce image noise
strongly, and is designed to enhance only low-contrast objects on CT images.

In this study, we have validated the effect of the APMF for improving the detection of hypoattenuation of acute ischemic stroke on unenhanced CT images obtained from a single-slice scanner. In future, we also need to validate the effect of the APMF on images obtained from new-generation multislice CT scanners.

Recently, we also proposed an algorithm for automated detection of hypoattenuation based on the comparison between CT-value histograms of the right and left cerebral hemispheres (37). In this work, we used the same patient data as that used in the present study. The results of this automated detection method showed that the sensitivity of detection of hypoattenuation was 92%, with approximately 0.16 false positives per image. The automated detection method had higher sensitivity than the APMF method in the observer test. However, the performance of these two methods cannot be directly compared, because the performance of the automated detection method was evaluated after optimal training on the dataset. Therefore, the result of the evaluation might be biased. Further studies on the performance evaluation of the automated detection method using an observer test are still needed.

We are working on constructing a computer-aided diagnosis (CAD) system for detecting hypoattenuating areas in acute ischemic stroke in unenhanced CT. The APMF has been developed as a first step in the CAD system so as to enhance hypoattenuation visually. The CAD system for detecting hypoattenuation of acute ischemic stroke, consisting of both the automated detection method and the APMF method, will be constructed in the near future.

In conclusion, the sensitivity of the detection of hypoattenuating areas on unenhanced CT images may be enhanced by application of the APMF. Therefore, we believe that the APMF can help radiologists to improve the detection of parenchymal hypoattenuation areas of acute stroke on unenhanced CT images.

![Figure 5](image1.png)  
Fig. 5. Number of images in which interpretation was affected by APMF processed images in those with (A) and without (B) hypoattenuation.

![Figure 6](image2.png)  
Fig. 6. Number of images in which findings were reversed by use of the APMF processed images among the images in which clinically relevant changes occurred with (A) and without (B) hypoattenuation.
Acknowledgements

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References


Appendix

APMF algorithm

Fig. 7 shows the flow chart of the technique’s main steps, which are as follows:

1. After applying a \( M \times M \) averaging filter to the original image, each pixel \((i, j)\) of the image \( I \) is assigned an upper window \( W_{\text{max}} \times W_{\text{max}} \) centered on it, whose size is smaller than the original image, where \( W_{\text{max}} \) is an odd number.

2. Let \( T \) be a given threshold. Pixel \((k, l)\) within \( W_{\text{max}} \times W_{\text{max}} \) is assigned a binary mask value 1 if \(|I_k - I_l| \leq T\), else it is assigned a binary mask value 0. This results in constructing a binary image. Fig. 8 shows an example in the case of \( T = 5 \) and \( W = 9 \).

3. For each window size \( C \times C \) \( (C = 3, 5, \ldots, W_{\text{max}}) \), the percentage \( P_0 \) of zeros is computed over the region of the external area of the \( C \times C \) window. The actual window size (\( W \)) is determined when the percentage \( P_0 \) is not greater than \( \alpha \% \), and is closest to \( \alpha \% \). Fig. 8C shows three various external areas \( \{C = 3, 7, 9\} \) and the respective \( P_0 \) computed from each window. \( W = 7 \) was determined as the actual window size when \( \alpha \) was set at 60.

4. The processed image \( I' \) is obtained from \( I(i, j) = M(i, j) \), where \( M(i, j) \) is the median value in the image \( I \) of pixels labeled as the binary mask value 1 in the window \( W \times W \) around pixel \((i, j)\). Fig. 8D shows the final mask image obtained from Fig. 8B and C.

5. Steps 2–4 are iteratively performed at each pixel as the center pixel in the original image. The method used for determination of filter size and shape of the APMF is similar to that used for the adaptive neighborhood selection algorithm (38). However, these two methods are entirely different techniques. The adaptive neighborhood contrast enhancement is not a noise reduction filter, but a contrast enhancement technique.

APMF parameter

The performance of the APMF depends on four parameters: \( T \), \( \alpha \), \( W_{\text{max}} \), and \( M \). Of these parameters, \( T \) is the most important, since it determines a rough boundary of gray and white matter on a brain CT image. An APMF with parameters \( T = 3.0 \), \( \alpha = 60\% \), \( W_{\text{max}} = 13 \), and \( M = 5 \) was applied to the unenhanced CT images in this study. These parameters were obtained from our previous study (23) and were the same values as those used for the APSF (20, 21).
Fig. 8. Adaptive neighborhood selection with a threshold value of $T = 5$. A. An example of a window image ($I$) whose initial window size is $9 \times 9$ ($W_{max} = 9$). The pixel value of the central pixel in $I$ is 35 ($I(i, j) = 35$ (black)). B. Mask image generated from Fig. 8A in the case of $T = 5$. For example, the pixel value $I(i, j) = 31$ (gray; immediately above the central pixel) is assigned a binary mask value 1, because $|I(k, l) - I(i, j)| \leq T$ (i.e., $|31 - 35| \leq 5$). C. Determination of actual window size ($W$). The percentage of zeros ($P_0$) is computed over the region of the external area (gray) of the mask image with window size $C = 3, 7, 9$. The actual window size is assigned as $W = 7$, when $P_0$ is set at 60%. D. Final mask image obtained from Fig. 8B and C. The processed image $I'$ is obtained from $I'(i, j) = M(i, j)$, where $M(i, j)$ is the mean value in the image $I$ of pixels labeled as the binary mask value 1 in the window $W \times W$ around pixel $(i, j)$. 