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Computer-aided evaluation method of white matter hyperintensities related to subcortical vascular dementia based on magnetic resonance imaging

Yasuo Kawata [a,1], Hidetaka Arimura [b,*], Yasuo Yamashita [a], Taiki Magome [a], Masafumi Ohki [b], Fukai Toyofuku [b], Yoshiharu Higashida [b], Kazuhiro Tsuchiya [c]

[a] *Graduate School of Medical Science, Kyushu University, Fukuoka 812-8582, Japan*
[b] *Faculty of Medical Science, Kyushu University, Fukuoka 812-8582, Japan*
[c] *Department of Radiology, Kyorin University, Mitaka, Tokyo 181-8611, Japan*

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ABSTRACT

It has been reported that the severity of subcortical vascular dementia (VaD) correlated with an area ratio of white matter hyperintensity (WMH) regions to the brain parenchyma (WMH area ratio). The purpose of this study was to develop a computer-aided evaluation method of WMH regions for diagnosis of subcortical VaD based on magnetic resonance (MR) images. A brain parenchymal region was segmented based on the histogram analysis of a T1-weigthed image. The WMH regions were segmented on the subtraction image between a T1-weighted and fluid-attenuated inversion-recovery (FLAIR) images using two segmentation methods, i.e., a region-growing technique and a level-set method, which were automatically and adaptively selected on each WMH region based on its image features by using a support vector machine. We applied the proposed method to 33 slices of the three types of MR images with 245 lesions, which were acquired from 10 patients (age range: 64–90 years, mean: 78) with a diagnosis of VaD on a 1.5-T MR imaging scanner. The average similarity index between regions determined by a manual method and the proposed method was 93.5 ± 2.0% for brain parenchymal regions and 78.2 ± 11.0% for WMH regions. The WMH area ratio obtained by the proposed method correlated with that determined by two neuroradiologists with a correlation coefficient of 0.992. The results presented in this study suggest that the proposed method could assist neuroradiologists in the evaluation of WMH regions related to the subcortical VaD.

1. Introduction

Subcortical vascular dementia (VaD) is a neurodegenerative disorder that leads to a progressive decline in memory and cognitive function, and is considered the second most common cause of dementia in Japan. The prevalence of VaD in demented patients older than 70 years in Japan is around 27% including a mixed type of dementia of Alzheimer's disease and VaD [1]. Although VaD is caused by various types of cerebrovascular diseases (e.g., ischemia or hemorrhage), we focus on the subcortical ischemic VaD in this study. Ischemic lesions show hyperintensity in the cerebral white matter, i.e., periventricular hyperintense (PVH) regions and white matter hyperintense (WMH) regions, on fluid-attenuated inversion-recovery (FLAIR) images or T2-weighted images at MR imaging. It has been reported that the degree of the symptom of VaD correlated with an area ratio of WMH regions to the whole brain parenchyma (WMH area ratio) [2–7], which could provide diagnostic information for the treatment of VaD. Gootjes et al. reported that the severity of dementia correlated with the WMH area ratio in VaD patients, but not in patients with Alzheimer's disease (AD) and control subjects [7]. Thus, it is imperative to estimate the WMH area ratio for evaluation of the degree of VaD or differentiation of VaD from AD. However, since neuroradiologists have to manually evaluate both WMH regions and brain parenchymal regions [2–7], it is very time-consuming and difficult in routine clinical practice. Although several investigators have reported a number of methods for detection of WMH regions using MR images [8–11], further studies to determine the WMH area ratios should be needed for assisting neuroradiologists in the evaluation of the degree of VaD. Therefore, the purpose of this study was to develop a computer-aided evaluation method of the WMH regions within the brain parenchymal region for diagnosis of subcortical vascular dementia based on three types of magnetic resonance (MR) images including T1-weighted, T2-weighted, and FLAIR images.

* Corresponding author at: Department of Health Science, Faculty of Medical Science, Kyushu University 3-1-1, Maidashi, Higashi-ku, Fukuoka 812-8582, Japan. Tel.: +81 92 642 6719; fax: +81 92 642 6719.
E-mail address: arimura@shs.kyushu-u.ac.jp (H. Arimura).
[1] Current address: Hitachi Medical Corporation, Kashiwa 277-0804, Japan.

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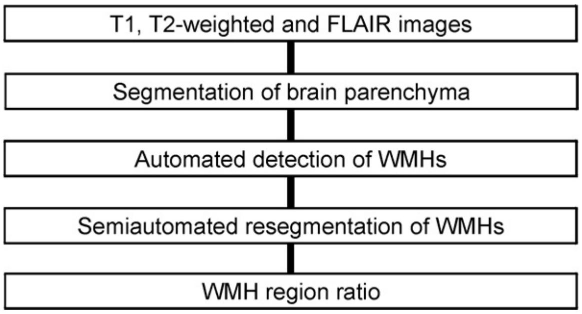

Fig. 1. Overall scheme of a proposed method for determination of a WMH area ratio using MR images.

2. Materials and methods

2.1. Clinical cases and MR imaging

Ten patients (age range: 64–90 years, mean: 78, $M = 4$, $F = 6$), who were given a diagnosis of VaD in a university hospital, were scanned on a 1.5-T MRI scanner (Excelart; Toshiba Medical Systems, Tochigi, Japan) by using T1-weighted (TR [repetition time]/TE [echo time]: 496/12 ms), T2-weighted (TR/TE: 4280/105 ms) and FLAIR (TR/TE/TI [inversion time]: 8000/105/2300 ms) sequences with a slice thickness of 5 mm and a slice gap of 1.5 mm. This study was performed under the protocol approved by the institutional review board of the university hospital. Each MR image consisted of 320×320–512×512 pixels at a pixel size of 0.43 mm, and the gray levels were 10 bits. To develop a robust computer-aided diagnosis system for detection of WMH regions, we needed to apply the proposed method to various sorts of WMH regions as much as possible as a validation test. Therefore, 33 slices with 245 WMH regions (7.4 lesions per slice) were selected by an experienced neuroradiologist and an experienced medical physicist from 10 cases, considering slice location, WMH region location, size, shape and contrast. Nine out of the 33 slices were used for the determination of parameters in the proposed method.

2.2. Overall scheme of propose method

An overall scheme of a proposed method for the determination of the WMH area ratio is shown in Fig. 1. The proposed method consisted of four steps, i.e., (1) segmentation of the brain parenchyma, (2) the automated detection step for initial WMH regions, (3) the subsequent semiautomated resegmentation step for the WMH regions, and (4) determination of the WMH area ratio.

2.3. Segmentation of brain parenchyma

A brain parenchymal region was segmented by analyzing a histogram of a T1-weigthed image and determining step by step three threshold values for reducing the background, cerebrospinal fluid (CSF) and fat regions, respectively. Fig. 2 shows an example of a histogram of an original T1-weighted image. The histogram of the T1-weigthed image can be divided into three peaks and one part, which correspond to the background (the first largest peak), CSF (the third largest peak), brain parenchyma (the second largest peak) and fat regions. The three threshold values, T_{BG}, T_{CSF} and T_{FAT}, for reducing the background, CSF and fat regions, respectively, are shown in Fig. 2. The threshold value, T_{BG}, for the background region was determined by $T_{BG} = M_{BG} + k_{BG}SD_{BG}$, where M_{BG} and SD_{BG} are the mean value and the standard deviation (SD), respectively, determined from the first largest peak with more than a certain number of pixels, which was empirically set as 10,000 pixels in this study, k_{BG} is the constant, which was empirically set as 10. The threshold value, $T_{CSF,}$ for the CSF regions was obtained by an automated thresholding technique based on a linear discriminant analysis [12] for the histogram of the T1-weighted image. By using a similar method to the background, the threshold value for reducing the fat region, T_{FAT}, was determined by $T_{FAT} = M_{BP} + k_{BP}SD_{BP}$, where M_{BP} and SD_{BP} are the mean value and the standard deviation, respectively, determined from the second largest peak with more than a certain number of pixels, which was empirically set as 700 pixels in this study, k_{BP} is the constant, which was empirically set as 4. We believe that in general, the effective diameters of the brain parenchymal regions in 2D slices may be larger than 12.8 mm (a very small region), which corresponds to 700 pixels (129.43 mm^2). However, the final results depend on the set of parameters. If the threshold value for reducing the fat regions was extremely small or large, the final results would be deteriorated. For investigating the usefulness of the set of parameters, we performed a validation test of the segmentation method for brain parenchymal region by using 24 slices in the 10 cases, which were not used for determination of the set of parameters.

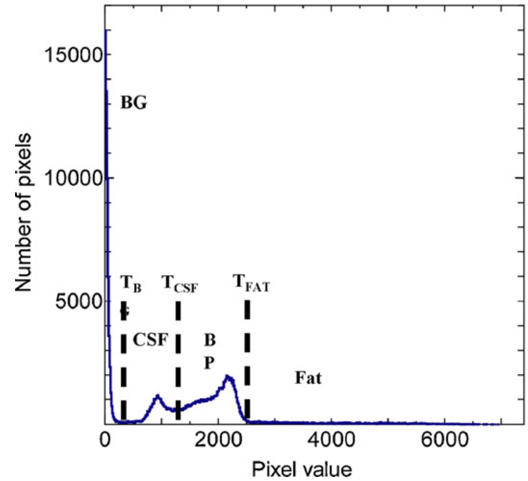

Fig. 2. A histogram of an original T1-weighted image, which has three peaks and one part corresponding to the back ground, CSF, brain parenchyma and fat regions, respectively. T_{BG}, T_{CSF} and T_{FAT} are the threshold values for reducing the background, CSF and fat regions, respectively.

After reducing the fat region, small holes with a zero pixel could occur within the brain parenchymal region, because a number of pixels in the brain parenchymal region are similar to those in the fat regions. Therefore, the holes were filled in by putting a rough brain parenchymal region without holes to the brain parenchymal region after reducing the fat region. The rough brain parenchymal region without holes was obtained by applying a circular morphological erosion kernel to the brain parenchymal region after reducing the background.

2.4. Automated detection of WMH regions

We employed an automated method for the detection of WMH regions, which was developed in a previous study [13]. First, WMH regions were enhanced by subtraction of a T1-weighted image from a FLAIR image. For the subtraction, the T1-weighted image and FLAIR image were automatically aligned using a cross-correlation coefficient between the two images. Second, initial WMH candidates were identified by applying a multiple gray-level thresholding technique to the FLAIR-T1 subtraction image. Third, WMH candidate regions were segmented by a region-growing technique from seed points detected by the multiple gray-level thresholding technique. Many false positives (FPs) were removed based on the output of an artificial neural network (ANN), which