30th Annual International IEEE EMBS Conference
Vancouver, British Columbia, Canada, August 20-24, 2008

Computer-Aided Diagnosis Scheme for Classification of Lacunar Infarcts and Enlarged Virchow-Robin Spaces in Brain MR Images

Yoshikazu Uchiyama, Takuya Kunieda, Takahiko Asano, Hiroki Kato, Takeshi Hara, Masayuki Kanematsu, Toru Iwama, Hiroaki Hoshi, Yasutomi Kinosada, Hiroshi Fujita

Abstract—**The detection of asymptomatic lacunar infarcts on magnetic resonance (MR) images is important because their presence indicates an increased risk of severe cerebral infarction. However, accurate identification of lacunar infarcts on MR images is often hard for radiologists because of the difficulty in distinguishing lacunar infarcts and enlarged Virchow-Robin spaces. Therefore, we developed a computer-aided diagnosis (CAD) scheme for the classification of lacunar infarcts and enlarged Virchow-Robin spaces. Our database consisted of T1- and T2- weighted images obtained from 109 patients. The locations of lacunar infarcts and enlarged Virchow-Robin spaces were determined by an experienced neuroradiologist. It included 89 lacunar infarcts and 20 enlarged Virchow-Robin spaces. We first enhanced the lesions in T2-weighted image by using the white top-hat transformation. A gray-level thresholding was then applied to the enhanced image for the segmentation of lesions. From the segmented lesions, we determined image features, such as size, shape, location, and signal intensities in T1- and T2- weighted images. A neural network was then employed for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. Our computerized method was evaluated by using a leave-one-out method. The result indicated that the area under the ROC curve was 0.945. Therefore, our CAD scheme would be useful in assisting radiologists for diagnosis of silent cerebral infarctions in MR images.**

Keywords: Lacunar infarcts, Virchow-Robin spaces, Magnetic resonance imaging (MRI), Computer-Aided Diagnosis, Classification

I. INTRODUCTION

CEREBROVASCULAR diseases are the third leading cause of death in Japan [1]. Therefore, a screening system for early detection of asymptomatic brain diseases, called *Brain Dock* or *Brain Check-up*, is widely performed. Because of the recent progress of magnetic resonance (MR) imaging, various types of asymptomatic cerebral diseases are detected in this screening system. Therefore, we developed computer-aided diagnosis (CAD) schemes for the detection of lacunar infarcts [2-4], unruptured aneurysms [5], occlusion [6], and leukoaraiosis [7], in order to assist radiologists in image interpretation by using the computer output as a guide.

The detection of asymptomatic lacunar infarcts in the screening system of brain diseases is important because their presence indicates an increased risk of severe infarction [8]. However, to our knowledge, no reports have been published on CAD scheme for the detection of lacunar infarcts. Therefore, we developed a CAD scheme for the detection of lacunar infarcts in T1- and T2-weighted images [2-4]. The current level of the performance of our CAD scheme for the detection of lacunar infarcts is 96.8% in sensitivity with a number of false positive (FP) of 0.3 per slice [4]. With the use of the output of CAD scheme, the radiologists' confidence in detecting lacunar infarcts might be increased because our CAD scheme can detect almost all the lacunar infarcts accurately. However, a problem is that relatively large number of FPs was also detected together by using this method.

It is important for any CAD scheme to reduce the number of FPs as much as possible. However, the majority of FPs detected by computer might be different from those detected by radiologists, and thus radiologists might be disregard these obvious FPs identified by computer. Therefore, one important question regarding the output value of our CAD scheme whether radiologists can really improve their performance if the computer output is given to them. Thus, we conducted an observer study in order to investigate the effect of our CAD scheme on radiologists' performance for the detection of lacunar infarcts on T1- and T2-weighted images [9]. Nine radiologists participated in the observer study. The radiologists interpreted T1- and T2- weighted image and indicated their confidence level regarding the presence (or absence) of lacunar infarct on each MR scan first without and then with use of the computer output. The observer performance without and with the computer output was evaluated with receiver operating characteristic (ROC) analysis [10]. For all nine radiologists, the mean area under the ROC curves without and with computer output were 0.891 and 0.937, respectively. The detection performance of radiologists was improved significantly when they used the computer output (p=.032).

In the observer study [9], we realized that the majority of FPs are different from those detected by radiologists, and thus radiologists can disregard these obvious FPs identified by

Manuscript received April 13, 2008. This work was supported in part by a grant for the "Knowledge Cluster Creation Project (Project leader: H. Fujita)" from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

Y. Uchiyama and Y. Kinosada are with Dept. of Biomedical Informatics, Graduate School of Medicine, Gifu University, Yanagido 1-1, Gifu, 501-1194, Japan

T. Kunieda, T. Hara and H. Fujita are with Dept. of Intelligent Image Information, Graduate School of Medicine, Gifu University, Japan

T. Asano, H. Kato, M. Kanematsu, H. Hoshi are with Dept. of Radiology, Graduate School of Medicine, Gifu University, Japan.

T. Iwama is with Dept. of Neurosurgery, Graduate School of Medicine, Gifu University, Japan.

computer. However, it is of interest to note that some FPs due to enlarged Virchow-Robin spaces detected by computer were difficult for radiologists to distinguish from lacunar infarcts. These are the main cause of detrimental effects of our CAD scheme. If radiologists are strongly influenced by these FPs due to enlarged Virchow-Robin spaces, the patient might have unnecessary medical treatment. Virchow-Robin space is a normal change caused from the atrophy of brain tissue related with age. It has small focal hyperintensity in T2-weighted image. Clinical literature also reported that it is important to distinguish between lacunar infarcts and enlarged Virchow-Robin spaces [11]. Therefore, in this study, we developed a computerized method for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces.

II. MATERIAL

Our database consisted of T1- and T2- weighted images obtained from 109 patients. These images were acquired using a 1.5 T MR scanner (Signa Excite Twin Speed 1.5 T; GE Medical Systems) at the Gifu University Hospital (Gifu, Japan). The T1- and T2- weighted images were obtained using the fast spin-echo method with an effective echo time (TE) of 8 – 12 ms and 96 – 105 ms, respectively, and a repetition time (TR) of 300 – 500 ms and 3000 – 3500 ms, respectively. The matrix size of the axial image was 512×512, with a spatial resolution of 0.47 mm per pixel. The slice thickness was 5 mm and the slice gap was 2 mm. The locations of lacunar infarct and enlarged Virchow-Robin space were determined by an experienced neuroradiologist. It included 89 lacunar infarcts and 20 enlarged Virchow-Robin spaces. Figure 1 shows examples of a lacunar infarct and an enlarged Virchow-Robin space. They have low signal intensity in T1- weighted image and high signal intensity in T2- weighted image. It is often difficult for radiologists to distinguish between lacunar infarcts and enlarged Virchow-Robin spaces.

III. METHOD

A. Segmentation of the lesion

Both lacunar infarct and Virchow-Robin space are small focal hyperintensity lesions in T2-weighted image. We first enhanced these lesions in T2-weighetd image by using morphological "white" top-hat transformation. The morphological white top-hat transform is defined by the subtraction of the opening of an original image from the original image. This operation corresponds to extract "white" patterns smaller than structure element used. The structure element was a 15×15 square, so that the lesions could be extracted. The lacunar infarcts were classified into two types based on their location: the isolated lacunar infarcts and lacunar infarcts adjacent to the cerebral ventricle. The former can be easily extracted using a simple threshold technique. However, it is difficult to extract the latter because the adjacent cerebral ventricle also has a high intensity value and its pixel value is similar to that of the lacunar infarcts. By using white top-hat transformation, both the isolated lacunar infarct and the lacunar infarct adjacent to the cerebral ventricle were enhanced. Thus, extraction of the lacunar infarcts adjacent to the cerebral ventricle is rendered easy using a thresholding technique. In order to segment the lesions, we then applied gray-level thresholding technique to the morphological white top-hat transformed image.

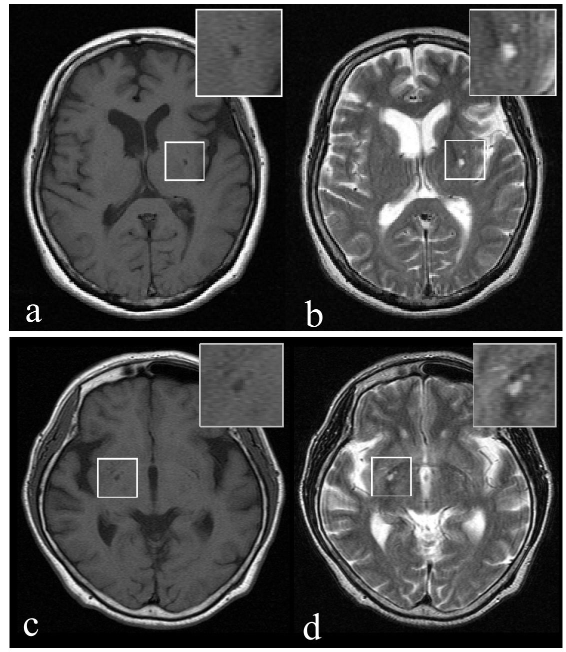

Figure 1. Example of lacunr infarct in (a) T1-weighted image and (b) T2-weighted image. Example of enlarged Virchow-Robin space in (c) T1-weigthed image and (d) T2-weighted image.

B. Determination of image features

For clarifying the characteristic of lacunar infarcts and enlarged Virchow-Robin spaces in T1- and T2-weighted images, we determined six features from the segmented region by using the method described in the previous section. These features included the location x and y, size, the degree of irregularity, and signal intensity differences in the T1- and T2-weighted images.

Location.- The location x and y were defined based on the centroid in the segmented region. The location is often useful information for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces.

Size and degree of irregularity. - The size was defined by the number of pixels in the segmented region. The degree of irregularity was given as 1-C/L, where C is the length of circumference of the circle having the same area as the segmented region. The L is boundary length of the segmented region.

Signal intensity difference. - The signal intensity difference in the T1- and T2-weighted images were also important features for distinguishing between lacunar infarcts

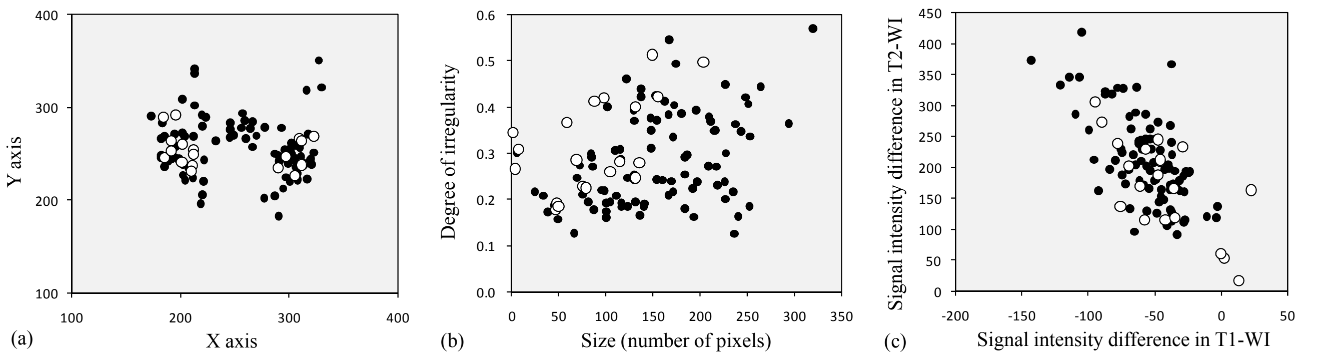

Figure 2. Distribution of six features obtained from lacunar infarcts and enlarged Virchow-Robin spaces. (a) Relation between locations x and y as features for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. The black and the white circles indicate lacunar infarcts and enlarged Virchow-Robin spaces, respectively. (b) Relation between size and degree of irregularity. (c) Relation between signal intensity difference in T1-weighted image (WI) and signal intensity difference in T2-weighted image.

and enlarged Virchow-Robin spaces. They were defined by the difference in the value between the average pixel value of the segmented region and the average pixel value of the peripheral region. The peripheral region was given as the differential region between the binary image of the segmented region and its expanded region. The expanded region was calculated by applying the dilation process to the binarized region of the segmented region three times in succession.

C. *Classification of lacunar infarcts and enlarged Virchow-Robin spaces*

A neural network with six features was employed for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. A three-layer neural network, which consisted of 6 input units, 2 hidden units, and 1 output unit, was used in this study. The number of hidden units was determined empirically. The input data for the neural network were six features determined in the previous section. The neural network generates a decision boundary that optimally partitions the feature space into the two classes, i.e., class A for lacunar infarcts and class B for enlarged Virchow-Robin spaces. The output value of the neural network indicates the likelihood of the occurrence of lacunar infarct. For training and testing of the neural network, the leave-one-out method was employed. By changing the threshold level of the output value, we can determine the classification performance using our computerized scheme.

IV. Results

Quantitative analysis. – Figure 2 shows the distribution of six features obtained from 89 lacunar infarcts and 20 enlarged Virchow-Robin spaces. The black circles and the white circles indicate lacunar infarcts and enlarged Virchow-Robin spaces, respectively. Figure 2(a) shows the relationship between location x and location y. These values were defined by the centroid in the lesions. As shown in this figure, we can distinguish some lacunar infarcts from enlarged Virchow-Robin spaces by using the location information. Figure 2(b) shows the relationship between size and degree of irregularity. The sizes for enlarged Virchow-Robin spaces appear to be smaller than those for lacunar infarcts. Figure 2(c) shows the relationship between signal intensity difference in T1-weighted image and signal intensity difference in T2-weighted image. The signal density differences in T2-weighted image for enlarged Virchow-Robin spaces appear to be smaller than those for lacunar infarcts.

Table 1 shows the results of tests for univariate equality of group means. Wilk's lambda [12] is defined as the ratio of within –group variance to the total variance and indicates the degree of discrimination between lacunar infarcts and enlarged Virchow-Robin spaces; for the size, this value was less than that for any other feature. The *F*-value [12] for the size was also higher than that for any other feature. This result indicates that the size greatly contributes in distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. The location features contributed some extent in distinguishing them. However, as shown in Figure 2(a), location features are useful for distinguishing lacunar infarcts located at the periphery of the lateral ventricle from enlarged Virchow-Robin spaces. Thus we successfully used the location features as a parameter in this study.

Classification performance. – To investigate the usefulness of the six features, we employed a neural network with six features for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. To evaluate the classification performance, ROC analysis was used. The ROC curve was obtained by changing the threshold value in the output value of neural network. The LABROC4 [13], which is a software developed by University of Chicago Kurt Rossmann Laboratory, was used for calculating ROC curve. Figure 3 shows ROC curve obtained from our CAD scheme for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. The AUC value (area under the ROC curve) was 0.945. The sensitivity and specificity for the detection of lacunar infarcts were 93.3% (83/89) and 75.0% (15/20), respectively. The results indicate that our computerized method is useful for classification of lacunar

Table 1 Test for univariate equality of group means in distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces.

Feature	Wilks' lambda	*F* value	*P* value
Location x	0.998	0.258	.613
Location y	0.997	0.360	.550
Size	0.853	18.458	<.001
Degree of irregularity	0.987	1.418	.236
Intensity difference T1	0.967	3.659	.058
Intensity difference T2	0.954	5.210	.024

infarcts and enlarged Virchow-Robin spaces in T1- and T2-weighted images.

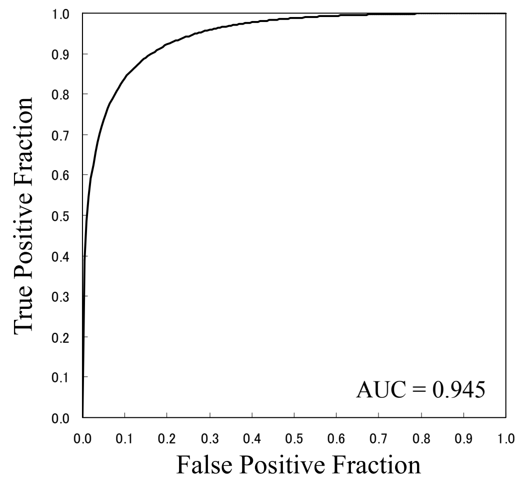

Figure 3. ROC curve for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces, which was obtained from the output values of neural network.

V. Discussion

As the result, our computerized method achieved high classification performance. However, the image database used was selected from only one hospital. The cases might have been influenced by the quality of scanner and acquisition parameters such as the echo time and repetition time. Thus in the future, we need to expand our database by collecting images from various scanners from several hospitals, and then evaluate our method by using independent databases.

Our CAD scheme can output results of quantitative analysis of the lesion and the likelihood of lacunar infarcts. Therefore, our computerized scheme might be useful in assisting radiologists for distinguishing between lacunar infarcts and enlarged Virchow-Robin spaces. To investigate the usefulness of our CAD scheme, it is imperative to perform an observer study without and with the aid of the CAD output.

VI. Conclusions

We developed CAD scheme for the classification of lacunar infarcts and enlarged Virchow-Robin spaces. The results clarified the quantitative characteristic of lacunar infarcts and enlarged Virchow-Robin spaces in MR images. In addition, our computerized method with these image features achieved high classification performance. Therefore, our CAD scheme might be useful in assisting radiologists for the detection of silent cerebral infarctions in MR images.

References

[1] Health and Welfare Statistics Association, "Vital Statistics of Japan 2005," Volume 1, 2005.

[2] R. Yokoyama, X. Zhang, Y. Uchiyama, H. Fujita, T. Hara, X. Zhou, M. Kanematsu, T. Asano, H. Kondo, S. Goshima, H. Hoshi, and T. Iwama, " Development of an automated method for detection of chronic lacunar infarct regions on brain MR images," IEICE Trans. Inf. & Syst., E90-D(6), 943-954, 2007.

[3] Y. Uchiyama, R. Yokoyama, H. Ando, T. Asano, H. Kato, H. Yamakawa, H. Yamakawa, T. Hara, T. Iwama, H. Hoshi, and H. Fujita, "Computer-aided diagnosis scheme for detection of lacunar infarcts in MR images," Academic Radiology, 14(12), 1554-1561, 2007.

[4] Y. Uchiyama, R. Yokoyama, H.Ando, T. Asano, H. Kato, H.Yamakawa, H. Yamakawa, T. Hara, T. Iwama, H. Hoshi, and H. Fujita, "Improvement of automated detection method of lacunar infarcts in brain MR images," Proc of IEEE Engineering in Medicine and Biology 29th Annual International Conference, Shanghai, China, 1599-1602, Lyon, France, 2007.

[5] Y. Uchiyama, H. Ando, R. Yokoyama, T. Hara, H. Fujita, and T. Iwama, "Computer-aided diagnosis scheme for detection of unruptured intracranial aneurysms in MR angiography," Proc of IEEE Engineering in Medicine and Biology 27th Annual International Conference, Shanghai, China, 3031-3034, 2005.

[6] M. Yamauchi, Y. Uchiyama, R. Yokoyama, T. Hara, H. Fujita, H. Ando, H. Yamakawa, T. Iwama, and H. Hoshi, "Computerized scheme for detection of arterial occlusion in brain MRA images," Proc of SPIE Medical Imaging : Computer-Aided Diagnosis, 6514, 65142C-1 - 65142C-9, 2007.

[7] Y. Uchiyama, T. Kunieda, T. Hara, H. Fujita, H. Ando, H. Yamakawa, T. Asano, H. Kato, T. Iwama, M. Kanematsu, and H. Hoshi, "Automated segmentation of different-sized leukoaraiosis regons in brain MR images," Proc. of SPIE Medical Imaging 2008, in press, 2008.

[8] S. Kobayashi, K. Okada, H. Koide, H. Bokura, and S. Yamaguchi, "Subcortical silent brain infarction as a risk factor for clinical stroke," Stroke, 28, 1932-1939, 1997.

[9] Y. Uchiyama, R. Yokoyama, T. Asano, H. Kato, H. Yamakawa, H. Ando, H. Yamakawa, T. Hara, T. Iwama, H. Hoshi, and H. Fujita, "Performance of computer-aided diagnosis for detection of lacunar infarcts on brain MR images: ROC analysis of radiologists' detection," International Journal of Computer Assisted Radiology and Surgery, Vol.2, Supplement 1, S395-S397, 2007.

[10] C. E. Metz, "ROC methodology in radiologic imaging," Invest. Radiol., 21, 720-733, 1986.

[11] H. Boukura, S. Kobayashi, and S. Yamaguchi, "Discrimination of silent lacunar infarction from enlarged Virchow-Robin spaces on brain magnetic resonance imaging and pathological study," Journal of Neurology, 245, 116-112, 1998.

[12] R. A. Johnson and D. W. Wicherm, "Applied multivariate statistical analysis," Prentice Hall, Englewood Cliffs, NJ, 2007.

[13] C. E. Mets, B.A. Herman, and J. H. Shen, "Maximum likelihood estimation of receiver operating characteristic (ROC) curves from continuously distributed data," Stat. Med. 17, 1033-1053, 1998.