Fractal Dimension-Based Cortical Dysplasia Detection Using MR Images for Children with Epilepsy

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Abstract - *About 80% of paediatric intractable epilepsy patients have accompanying cortical dysplasia. However, there are no established methods for noninvasive detection of cortical dysplasia. This paper proposes a novel method for automatically detecting cortical dysplasia using paediatric MR images. In order to evaluate cortical dysplasia in MR images, texture features and fractal dimension were extracted with an automated method and support vectors were used to evaluate the degree of cortical dysplasia. The proposed method was applied to three paediatric epilepsy patients. The automated method identified the cortical dysplasia lesion with a sensitivity of 94%, a mean specificity of 85%, and a mean efficiency of 87%.*

Keywords: Cortical Dysplasia, Epilepsy, Paediatric, MR images, Support Vector Machine, Brain

1 Introduction

Epilepsy patients have symptoms such as sudden convulsions, stroke, and absence seizures. Today, epilepsy patients comprise about 1% of the population [1]. Epilepsy seizures can be suppressed with antiepileptic medication in many but not all patients: about 20% of epilepsy patients cannot be treated with current antiepileptic medications. These patients are said to have intractable epilepsy.

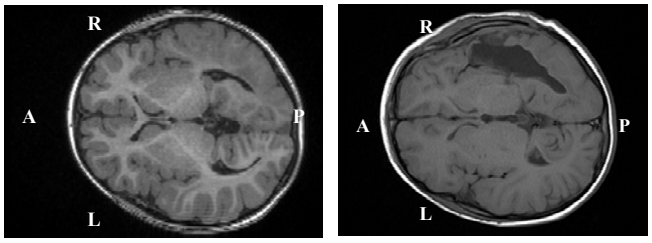
Cortical dysplasia is one origin of intractable epilepsy [2]. In the case of paediatric patients, about 80% of intractable epilepsy patients have accompanying cortical dysplasia [3]. Cortical dysplasia is a congenital anomaly of the cerebral cortex resulting from abnormal neuronal migration. It appears as an indistinct boundary between white matter (WM) and gray matter (GM) on magnetic resonance (MR) images. The area and degree of cortical dysplasia lesions are different between patients. When a cortical dysplasia lesion is localized, treatment may be possible. In order to suppress the epileptic seizures, the focal cortical dysplasia lesion is surgically excised [4].

Although intractable epilepsy with cortical dysplasia can be treated surgically, many patients are not treated because there are only few methods that can be used to non-invasively locate cortical dysplasia. The current gold-standard for detection of focal cortical dysplasia is based on electrocorticography (ECoG). With ECoG, the cerebral surface is exposed and electrodes are directly attached to the cerebral surface for a number of weeks. Because ECoG is very invasive, it is not appropriate for use as a screening tool. A noninvasive screening method for patients with suspected intractable epilepsy patients is needed. If cortical dysplasia could be discovered during childhood, the quality of life of such patients would improve.

An imaging technique that could be used for identification of cortical dysplasia is magnetic resonance (MR) imaging. An MR image can noninvasively acquire sectional images with a high soft-tissue contrast. However, the accuracy of manual detection of cortical dysplasia lesions from MR images largely depends on the observer's skill and experience. In addition, there is both large intra- and inter-observer variability. Therefore, an automated method for detection of cortical dysplasia lesions from brain MR images could be of clinical use.

It is especially important to detect cortical dysplasia lesions in the paediatric brain, because many patients with epilepsy experience onset of symptoms in childhood. Optimal treatment in childhood may suppress epileptic seizures, facilitate development and improve outcomes. However, few studies have reported on detection of cortical dysplasia with MR images of the paediatric brain.

A few conventional methods can be used for detection of cortical dysplasia in adult brain MR images. Colliot *et al*. has proposed a detection method that uses a pattern classifier that is learned by features extracted from MR images [5]. One important feature used in their method is cortical thickness. However, it is difficult to apply their method to children because there is currently no way to calculate cortical thickness for the paediatric brain. Colliot *et al*. [6] and Srivastava *et al*. [7] have proposed imaging methods based on voxel-based morphometry (VBM). VBM normalizes the cerebrum of subjects into a standardized



(a) Pre-operation. (b) Post-operation.

Fig. 1. Pre- and post-operative MR images of a cortical dysplasia lesion (Subject 1). A; anterior, P; posterior, R; right, and L; left.

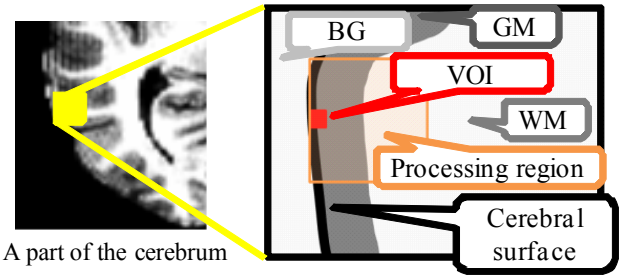


Fig. 2. Processing region. BG; background, GM; gray matter, WM; white matter, and VOI; voxel of interest.

cerebrum, and compares GM density with that of the normal brain [8]. These conventional methods cannot be applied to the paediatric brain because a standardized paediatric cerebrum does not yet exist. In addition, the conventional methods evaluate each voxel through extraction of image features from each voxel. The basic hypothesis behind the current method is straightforward: because cortical dysplasia is due to an anomaly of the cerebral cortex, then cortical dysplasia could be examined by extracting features of the cerebral cortex.

The present paper proposes a method for detecting cortical dysplasia lesions in paediatric brain using MR images. The proposed method evaluates the cerebral cortex by extracting texture features and fractal dimensions from regions perpendicular to the cerebral surface. The cortical dysplasia degree (CDD) of the perpendicular region was estimated by using a support vector machine (SVM) [8][9].

This paper is organized as follows. Section 2 introduces subjects and materials used in this study. Section 3 proposes a method for extraction of features of cortical dysplasia along with a CDD estimation method using SVM. Section 4 describes experimental results.

2 Subjects and Materials

To assess the proposed method, this study recruited 3 paediatric volunteers (Subjects 1, 2, and 3) with focal cortical dysplasia in the left or right lateral hemisphere. Subjects 1 and 2 were boys (6 years old and 10 months old) and Subject 3 was a girl (3 years old). Their cortical dysplasia lesions were determined using ECoG, and the excised lesions were pathologically confirmed. Parental informed consent was obtained in all cases. Axial T1-weighted MR images were acquired before the operation using a 1.5 Tesla MRI scanner (GE Medical Systems, WI, USA). Acquisition parameters for Subjects 1, 2 and 3 were repetition times of 8.46, 8.71 and 550 ms, echo times of 1.81, 1.82 and 9.00 ms, slice thicknesses of 1.30 mm, 1.40 mm, and 5.00 mm, and spatial resolutions of 0.86, 0.86 and 0.78, respectively. Matrix size was 256 by 256.

Figure 1 shows pre- and post-operative MR images of Subject 1. In this case, the cortical dysplasia lesion was found on the right hemisphere. In the lesion, the boundary between the cerebral cortex and WM tended to become indistinct as shown in Fig. 1(a). After surgical excision of the cortical dysplasia lesion, the MR signal of the excised area became hypointense (Fig. 1(b)).

In preliminary processing, bias of the MR signal was eliminated using FMRIB Software Library (FSL) [11][12] and the cerebral region was extracted by applying a previously developed method [13]. Then, the intensity of the extracted cerebral region was lineally normalized by using upper and lower thresholds. The thresholds were determined by using p-tile method. Also, the images were linearly converted into isovoxels.

3 Proposed Analysis Method

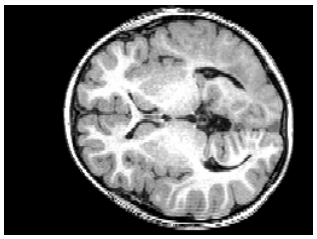
3.1 Overview

Cortical dysplasia is a brain dysplasia that is accompanied by morphological aberration of a nerve cell and a glia cell. The abnormal cerebral cortex is constructed from such abnormal nerve cells of various sizes. The six laminar structures of the cerebral cortex become irregular in appearance because of these abnormal nerve cells [10].

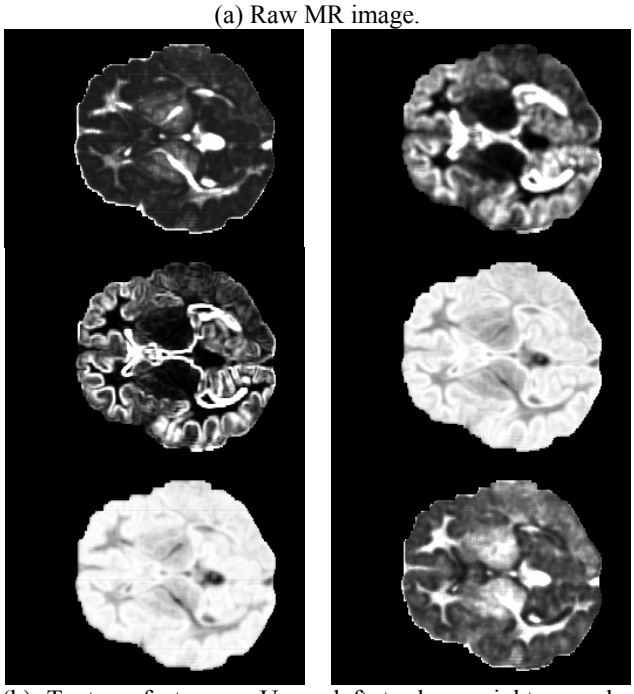
To assess the six laminar structures, the proposed method evaluates cerebral surface voxels and extracts features from both the voxel of interest (VOI) and also the surrounding voxels (together called the processing region). From the processing region, the method extracts two types of features: one evaluating the spatial distribution of the MR signal, and the other evaluating the shape of the cerebral contour. Using the extracted features, CDD is estimated by means of a pattern classification technique.

In summary, the proposed method consists of the following steps described in detail below.

For each cerebral surface voxel:
[Step 1] Construct a processing region,
[Step 2] Extract two types of features, and
[Step 3] Estimate CDD using SVM.



(a) Raw MR image.



(b) Texture features. Upper-left to lower-right: angular second moment, (2) contrast, (3) variance, (4) sum entropy, (5) entropy, and (6) differential variance.

Fig. 3. Texture feature extraction.

3.2 Processing region

To extract the smooth surface of the cerebrum, mathematical morphology operators are applied to the surface of the segmented cerebral region. VOIs used in the proposed method to assign CDDs were on the smooth cerebral surface.

For each VOI, a processing region is constructed as shown in Fig. 2. The processing region is formed by a square whose size is L [voxels] × L [voxels] perpendicular to the cerebral surface, and the VOI is located at the center of the outer vertex.

3.3 Feature extraction

To evaluate the anomaly of cerebral cortex layer, two types of features are extracted from the processing region. The first feature evaluates the spatial distribution of the MR signal because cortical dysplasia appears as irregular order of the MR signal. The second feature evaluates the shape of the cerebral surface because the cortical dysplasia will deform the cerebral surface, called polymicrogyria, which shows an excessive number of small gyri on the cerebral surface [17].

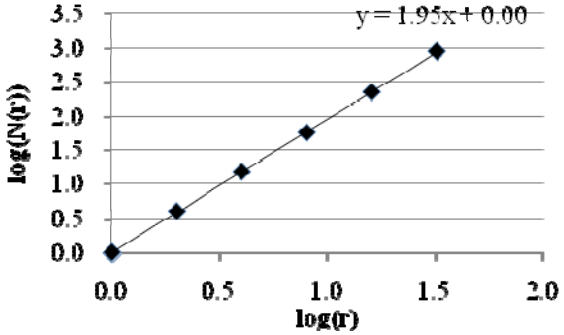


Fig. 4. Fractal dimension with the box-counting method.

The first feature is evaluated using texture features. They are calculated using gray level co-occurrence matrix (GLCM) [14][15]. In order to reduce processing time of calculating GLCM, the normalization images are converted into 32 gray levels where 0 represents the minimum MR signal of the cerebrum, and 31 represents the maximum. Texture features are calculated using parameters; (d, θ, φ) = (3.0, 0.0, 45.0). The following seven features are calculated as texture features (1) angular second moment, (2) contrast, (3) variance, (4) sum entropy, (5) entropy, (6) differential variance, and (7) fractal dimension. The texture features are defined previously [14], and examples are shown in Fig. 3.

The second feature is fractal dimension. The fractal dimension is a statistical measure of how completely a fractal fills space in fractal geometry. There are several ways to define fractal dimension. One principal method is the box-counting method [18]. To apply this method, the contour line of the target object is needed. However, brain MR images are given as grayscale images, and it is difficult to extract the cerebral surface in detail from these images. Thus, the present paper modified the box-counting method for 2-dimensional grayscale images as follows.

The processing region (L × L voxels) is covered with a grid of square cells with cell size r *by* r voxels. The intensity of each cell is calculated by a linear interpolation. Instead of calculating the number of cells needed to cover the structure, the number of edge voxels in the grid of square cells, $N(r)$, is calculated. The edge voxels are extracted by applying the Sobel operator. Also, the number $N(r)$ is given by a power law:

$$N(r) = const \bullet r^{-D_B} . \qquad (1)$$

where D_B is the fractal dimension. Using this equation, the total area A covered by the squares of size r is calculated by:

$$A(r) = N(r) \bullet r^2 = const \bullet r^{-D_B} \bullet r^2 = const \bullet r^{2-D_B} . \qquad (2)$$

Thus, D_B is determined by:

$$D_B = 2 - \frac{\ln A(r)}{\ln r}. \qquad (3)$$

To calculate $\frac{\ln A(r)}{\ln r}$, the cell size r is changed from 1 to 32 by a power of 2, and the slope of the regression line is calculated by a least squares method. Figure 4 shows an example of calculating the fractal dimension with a box-counting method. In this case, the slope of the regression line is 1.95, and the fractal dimension is 0.05.

3.4 CDD estimation

CDD is estimated by using SVM, which is trained by using preoperative MR images of a subject with focal cortical dysplasia. To train the SVM, two classes of voxels are prepared. One is a cortical dysplasia class, and the other is a healthy class.

The cortical dysplasia class voxels are extracted by a physician by delineation of the cortical dysplasia lesion with respect to the surgically excised region, the post-operative MR images, and operation records.

Healthy class voxels are extracted from a longitudinal fissure-symmetric region in the contra-lateral hemisphere in order to obtain features of normal cortical layers at the same gyri as the cortical dysplasia region.

For each cortical dysplasia voxel and each healthy class voxel, the seven features described in the previous section are calculated. Using a set of the calculated feature values and

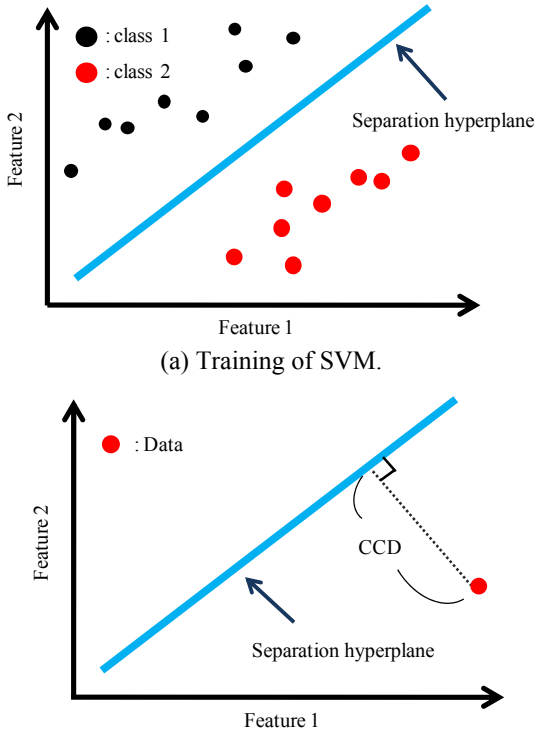
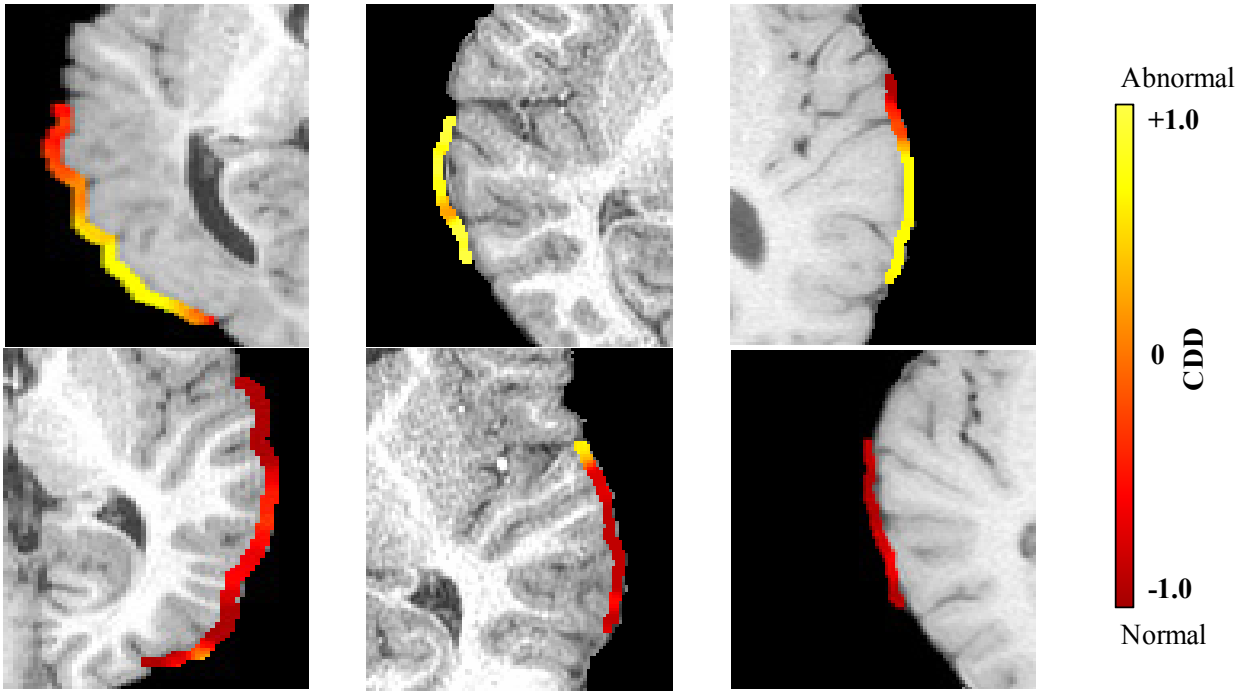


Fig. 5. Cortical dysplasia estimation using SVM.



(a) Subject 1 (b) Subject 2 (c) Subject 3

Fig. 6. Experimental results of the learning capability test. Upper images show the CDD map around the cortical dysplasia lesion, and lower images show the CDD map around the healthy region, superimposed on the raw MR images.

Table 1. Experimental results of the learning capability test.

Subject	Sensitivity	Specificity	Efficiency
#1	81.0%	97.2%	86.4%
#2	100.0%	85.7%	92.9%
#3	72.6%	100.0%	82.4%

Table 2. Experimental results of the generalization capability test. For each test, SVM was trained using the remaining subjects' data.

Subject	Sensitivity	Specificity	Efficiency
#1	84.2%	71.4%	77.5%
#2	92.9%	86.0%	89.8%
#3	88.4%	100.0%	93.9%

Table 3. Comparison with conventional methods.

Method	Learning capability test			Generalization test		
	Mean Sensitivity	Mean Specificity	Mean Efficiency	Mean Sensitivity	Mean Specificity	Mean Efficiency
Ref. [19]	72.8 %	80.6 %	77.1 %	50.2 %	46.9 %	48.2 %
Ref. [20]	90.9%	93.1%	92.0%	90.5%	54.7%	73.0%
Proposed method	84.5%	94.3%	87.2%	88.5%	85.8%	87.0%

the given class, SVM is trained. That is, a voxel corresponds to an object, feature values of the voxel correspond to a vector of variables, and the cortical dysplasia class and the healthy class correspond to classes (+1 or -1) of the objects.

By training the SVM using the prepared training datasets, an optimum separation hyperplane is obtained which is a linear classifier with a maximum margin for the training data as illustrated in Fig. 5(a). Using the trained SVM, CDD, here δ, is defined as a distance from test data vector of the processing region to the hyperplane. It is illustrated in Fig. 5(b), and calculated by:

$$\delta = \mathbf{w} \bullet \mathbf{x} - h \,. \qquad (4)$$

where $\mathbf{w}$ denotes a normal vector that is perpendicular to the optimum separation hyperplane, $h/\|\boldsymbol{\omega}\|$ denotes the offset of the hyperplane from the origin along the normal vector $\boldsymbol{\omega}$, and $\mathbf{x}$ is a feature vector of evaluated object. CDD takes a value between -1 and +1: positive values denote the degree of the layer of the abnormal layer with cortical dysplasia, and negative values denote the degree of the healthy layer.

4 Experimental results

To evaluate the proposed method, two experiments were conducted: a learning capability test and a generalization capability test. The learning capability test trained the SVM using MR images of each subject, and evaluated the CDD estimation performance using the same subject. The generalization capability test trained the SVM using MR images of two subjects, and evaluated the CDD estimation performance using the remaining subject according to the leave-one-out method. The analysis parameter used was the size of the processing region; L = 32 [voxel], and the same parameter was used for all subjects.

Figure 6 shows experimental results of the learning capability test for each subject. To evaluate the experimental results visually, a CDD map was generated in which the CDD was described by a yellow-red colour scale. As shown in these images, higher CDD values were assigned for almost all voxels in the cortical dysplasia lesion. Lower CDD values were assigned for almost all voxels in the healthy region.

The experimental results were quantitatively evaluated using sensitivity, specificity and efficiency as shown in Table 1. Metrics were calculated using ground truth data given by a physician. Every measure takes the higher value for better results. With the present three subjects, the mean sensitivity was 85%, mean specificity was 94%, and mean efficiency was 87%.

Experimental results of the generalization capability test were also quantitatively evaluated in the same manner. Table 2 tabulates the sensitivity, specificity and efficiency. In this table, “Subject” denotes the test subject, while the remaining 2 subjects were used to train the SVM. With the present three subjects, the mean sensitivity was 89%, the mean specificity was 86%, and the mean efficiency was 87%.

5 Discussion

Two methods for estimating CDD using MR images have been previously reported [19][20]. The first method constructs a processing region by forming a 3-dimensional triangular prism perpendicular to the cerebral surface, and extracts texture features [19]. The second method constructs a processing region in 2 dimensions by connecting a line from a VOI on the cerebral surface to the nearest voxel on the boundary between GM and WM, and calculates a signal change from the intensity profile on the line and texture features [20].

The mean sensitivity, specificity and efficiency of the learning capability and generalization tests with the two conventional methods and the proposed method are summarized in Table 3. Although both of the conventional methods showed better results for the learning capability test, the results worsened with the generalization test. The proposed method exhibited a similar performance for both

tests. These results indicate that texture features and signal changes vary from person to person. In contrast, the fractal dimension extracted a characteristic feature of polymicrogyri well.

6 Conclusions

In the present report, a novel system for noninvasively detecting cortical dysplasia lesions using MR images is proposed. Because the conventional method of detecting cortical dysplasia using ECoG is highly invasive, this approach could be a non-invasive breakthrough in diagnosis of childhood-onset epilepsy. The proposed method extracted fractal dimension and texture features from MR images. The fractal dimension represents the characteristic change of the cerebral shape called polymicrogyri, and the texture features represent the characteristic change of the MR signal. Using the extracted features, SVM assigns CDD for VOIs on the cerebral surface. Experimental results on three paediatric epilepsy patients showed that the mean sensitivity and efficiency were higher than 80% for both the learning capability and generalization tests.

The main limitation of the proposed method is that it is implemented in 2-dimensional space. However, the method will be easily extended into 3-dimensional space processing because the fractal dimension and texture features can be calculated in 3-dimensional space. Another limitation is that the study group consisted of only three subjects.

7 Acknowledgements

This work was supported in part by Grants-in-Aid for Scientific Research, Japan.

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