# Cortical Deformation Zone in Neocortical Epilepsy: 3D Surface-Projection Rendering of Brain MRI

신피질 간질에서 뇌 자기공명영상의 삼차원 Surface-Projection Rendering 기법을 이용한 피질변형영역에 관한 연구

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#### 국문 초록

목 적: 부분성 간질 환자를 치료함에 있어서 간질을 일으키는 뇌병변을 찾는 것은 매우 중요하다. MRI 기법의 발전으로 뇌의 구조적인 분석이 많이 향상되었지만 아직도 많은 신피질 간질(neocortical epilepsy)을 갖고 있는 환자들에서 기존의 2차원적인 MRI영상으로 간질병변을 찾을 수 없다. 이러한 환자들에서 surface-projection rendering (SPR)을 이용한 MRI의 3차원 분석이 얼마나 도움이 되는지 알아보기 위하여 이 연구를 시행하였다. 방 법: 20명의 정상인과 24명의 신피질 간질 환자들에서 기존의 2차원 MRI 분석(T1, T2, FLAIR, thin slice SPGR)과 3차원 SPR을 시행하였다. 정상인들의 sulco-gyral 형태를 기본으로 하여서 환자들의 뇌에서 피질의 변형(cortical deformation)을 임상정보 없이 진단하였다. 간질 수술과 침습적 뇌파감시 결과에 의하여 간질발생영역(epileptogenic zone), 발작시작영역(ictal onset zone) 및 흥분 영역(irritative zone)을 결정하였다. 결과: 2차원 MRI 분석은 신피질 축두엽 간질 10명중 5명(50%)에서, 그리고, 축두엽외 간질 14명중 5명(35,7%)에서 간질병면을 발견하였다. 반면, 3차원 SPR 분석은 신피질 축두엽 간질 10명중 9명(90%)에서, 축두엽외 간질 14명중 9명(64.3%)에서 간질병면을 진단할 수 있었다. 3차원 SPR에 의하여 발견된 피질변형영역은 10명에서 발작시작영역과 6명에서 흥분영역의 전체를 포함하고 있었고, 7명에서 발작시작영역과 11명에서 흥분영역과 겹쳐 있었으며, 각각 1명에서는 발작시작영역과 흥분영역에 접하여 있었다. 결론: 3차원 SPR 분석은 2차원 MRI 영상에서 찾을 수 없는 신피질 간질의 간질병면을 진단하는데 많은 도움이 되었다. (대한간질학회지 4:3-11, 2000)

중심 단어: 신피질 간질·피질변형·3차원 surface-projection rendering·Sulco-gyral 형태

# Introduction

Although the patterns of sulcal and gyral formations in <sup>1</sup>성균관대학교 의과대학 삼성서울병원 신경과학교실, <sup>3</sup>신경외과학교실, <sup>2</sup>뇌영상연구실

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the human brain are variable, brains of normal subjects show typical and similar cortical morphology in size, orientation, topology, and geometric complexity of sulcogyral patterns. The detection of the underlying structural abnormality in the cerebral cortex is very important in the treatment of patients with intractable partial epilepsy. Magnetic resonance imaging (MRI) has greatly improved the detection rate of brain lesion in epilepsy patients. In patients with mesial temporal lobe epilepsy (TLE), MRI finds hippocampal sclerosis frequently. However, neocortical TLE and extratemporal lobe epilepsy (extra-TLE) show a low detection rate of epileptogenic lesion on a conventional MRI. This should not be surprising. The cerebral cortex is a convoluted three-dimensional (3D) structure. Therefore, abnormalities in

its surface gyration that represent the underlying pathologic cortical architecture<sup>6</sup> may not be appreciated in two-dimensional (2D) MRI slices. Conventional 2D brain MRI images have many limitations in the evaluation of cortical morphology. The morphology of many sulci and fissures of various direction, length and depth can not be assessed adequately in cross-sectional 2D MRI images. The thickness of gyri may be over- or underestimated depending upon the angle of MRI scanning. During brain MRI scanning, the vertical or horizontal rotation of the patient's brain may produce a false asymmetry of cortical morphology such as gyral volume and sulcogyral patterns. The tangential cutting of winding sulcal gyral end may look like heterotopic gray matter in cross-sectional images. The lower sensitivity, false negative and false positive findings of conventional 2D MRI interpretation are ascribed to these problems. Sulco-gyral abnormalities may only be seen when the cerebral hemispheres are viewed as uncut 3D structures. Therefore, several methods have been developed to inspect the 3D cortical morphology. The goals of our study were to test the sensitivity and value of 3D surface projection rendering (SPR) in localizing epileptogenic zone and know the topical relationship between cortical deformation zones and brain regions with ictal or interictal EEG discharges.

# Methods

Twenty-four patients with neocortical epilepsy and 20 age-matched normal controls were included in this study. Ten patients had neocortical TLE and 14 had extra-TLE. Epileptogenic zones of all subjects were confirmed by intracranial EEG monitoring and resective surgery. All patients and normal controls had MRI studies. T1, T2 axial, T2, FLAIR thin slice coronal images, and 1.5 mm thick SPGR of the whole brain were obtained.

## 1. MRI

#### 1) Conventional MRI interpretation

A neuroradiologist read all MRI images of the patients without clinical information and determined the presence of localized lesion including cortical abnormality. The only lesions which were located at or near the epileptic focus were included in calculating the sensitivity of detecting epileptogenic lesion.

#### 2) 3D Surface-Projection Rendering

One neurologist and one neuroimage analyst interpreted the results of 3D SPR of the brain MRIs in comparison with those of normal controls. 3D SPR was performed with Analyze 7.5 version software (Biomedical Image Resource, Mayo Foundation, Rochester, Minn) as the following steps.

Brain MRI was performed with Signa 1.5-Tesla unit (GE Medical Systems, Milwaukee). Fast SPGR (SPoiled Gradient Recalled Acquisition in the Steady State, contiguous coronal 124 slices, 1.5 mm thin section, repetition time[TR]: 11.2 milliseconds[msec], echo time[TE]: 2.1 milliseconds[msec], field of view[FOV]: 22 cm, number of excitation[NEX]: 1, flip angle: 20°) and SPGR (contiguous coronal 124 slices, 1.6 mm thin section, TR: 30 msec, TE: 7 msec, FOV 22 cm, 1 NEX, flip angle: 45°) MRI images were obtained and transported to Sun Ultra 1 Creator workstation (Sun Microsystems, Mountain View, Calif.). The cortical surface was segmented by intensity-based automatic boundary tracing method and manual editing in 124 MRI slices of each subject. The segmented MRI slices were reconstructed by SPR technique to display 3D cortical surface (Fig. 1). Because this 3D image shows only one side of the brain, cortical surfaces of the right and left hemispheres cannot be compared side by side. We stretched out the outer surface of the 3D brain MRI image on 2D plane by using radial surface rendering technique (Fig. 1). Gross pattern analysis was performed by visual inspection in the radial surface rendering pictures. If abnormality was suspicious, those regions of the brain were re-inspected in 3D SPR images by rotating the spherical 3D brain. The shape, volume, complexity and direction of gyri and sulci were analyzed. The cortical patterns of 20 normal brains were considered as a gold standard. One neurologist (Chung SC) and one neuroimage analyst (Tae WS) interpreted the results of 3D SPR of brains with epilepsy, in comparison with the sulco-gyral patterns of normal brains. Both of them were blind to clinical information and determined the presence

and location of cortical deformation by agreement of two. The localizations of cortical abnormality determined by the conventional method and 3D SPR technique were related to the epileptogenic zone confirmed by an epilepsy surgery.

# The localization of ictal onset zone (IOZ) and irritative zone (IRZ)

Ictal onset zone (where ictal discharges started) and irritative zone (where interictal spikes occurred) were determined by intracranial EEG recording and were localized on 3D MRI brain surface of individual patient by 3D MRI reconstruction and overlay of subdural grids on 3D MRI by MRI-CT co-registration. Then, the anatomical relationship of IOZ and IRZ to cortical deformation zone (CDZ) were determined. If CDZ included the whole area of IOZ or IRZ, this CDZ was categorized as "included". When CDZ overlapped partly with IOZ or IRZ, then the CDZ was categorized as "overlapped". If CDZ was placed by the side of IOZ or IRZ without an intervening brain tissue, the CDZ was termed as "connec-ted". When CDZ was near IOZ or IRZ with some intervening space, the CDZ was decided as "adjacent".

#### 3. Statistical analysis

Inter-observer agreement between the first two reviewers was determined by Cohen's Kappa ( $\kappa$ ) scores using generalized kappa-type statistics. Agreement was considered poor when was <0.4, good when was 0.4 to 0.

75, and excellent when was > 0.75.8

# Results

The ages of the 20 normal controls ranged from 18 to 36 years (mean = 27.7). The number of patients was 24 and their ages were 6-46 years (mean = 21.7). The subtypes of extra-TLE were 9 frontal lobe and 4 frontoparietal lobe, and 1 parietal lobe epilepsies.

#### 1. Conventional 2D MRI interpretation (Table 1)

Twenty normal subjects showed normal 2D brain MRI images. The conventional MRI reading could identify epileptogenic lesions in five of the 10 neocortical TLE (50%) and five of the 14 extra-TLE (35.7%). The 2D MRI di-

**Table 1.** The detection rate of cortical deformation in patients with neocortical epilepsy (conventional 2D MRf vs. 3D surface-projection rendering)

		Conventional 2D MI	RI 3D SPR
Neocortical TLE	Cortical Abn. (+)	5	9
	Contical Abn. (-)	5	1
	Sensitivity	50%	90%
Extra-TLE	Cortical Abn. (+)	5	9
	Cortical Abn. (-)	9	5
	Sensitivity	35.7%	64.3%
Total number of detection		. 10	18*
Total mean sensitivity		41.7%	75%

Abn.: abnormality

TLE: temporal lobe epilepsy

SPR : surface-projection rendering

\*: p=0.008 (McNemar test, two-tailed)

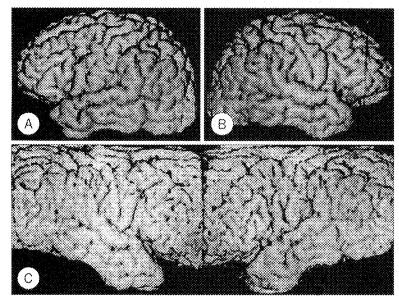


Fig. 1. 3D surface-projection rendering showing left and right hemispheres (A, B). Spherical 3D surface rendering of brain MRI were stretched out on 2D plane (C: radial surface rendering) and symmetry of sulco-gyral patterns in both hemispheres can be compared side by side.

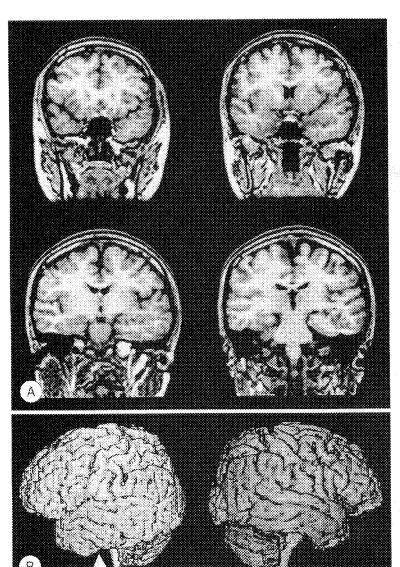


Fig. 2. This patient had malformation in left mesial temporal region on 2D MRI (Fig-A). 3D rendering showed suicogyral anomaly (vertical complex gyral pattern in Fig-B) in left lateral temporal region which was not visualized in 2D MRI. Epileptogenic focurer found in both mesial and lateral temporal regions by invasive monitoring and epilepsy surgery.

agnoses of lesions were four focal encephalomalacia, five cortical malformation (cortical thickening, heterotopic gray matter, pachygyria), and 1 dysembryoblastic neuroepithelial tumor.

# MRI interpretation by 3D surface-projection rendering (SPR) technique (Table 1)

3D SPR found a mild atrophy of the left superior temporal gyrus in one of the 20 normal subjects. Otherwise normal subjects showed well formed dense gyri, parallel superior, middle and inferior temporal sulco-gyral patterns, regular gyral thickness, and relatively regular, symmetric sulci and fissures as shown in Fig. 1. However, 3D SPR of epileptic brains revealed diffuse gyral atrophy,

focal gyral thickening, volume reduction, ill-defined gyral margins, loss or distortion of normal sulcal patterns, increased complexity of superior, middle or/and inferior temporal gyral patterns, and vertical-dominant sulco-gyral pattern in temporal lobe (Fig. 2, 3). 3D SPR technique detected cortical deformations in nine of the 10 neocortical TLE (90%) and nine of the 14 extra-TLE (64.3%). In patients who had no lesion in conventional 2D images, 3D SPR revealed additional four cortical abnormalities of the five (80%) neocortical TLE and four of the nine (44.4%) extra-TLE. Most of the cortical deformation zones were larger than the sizes of the lesions found in conventional 2D MRI.

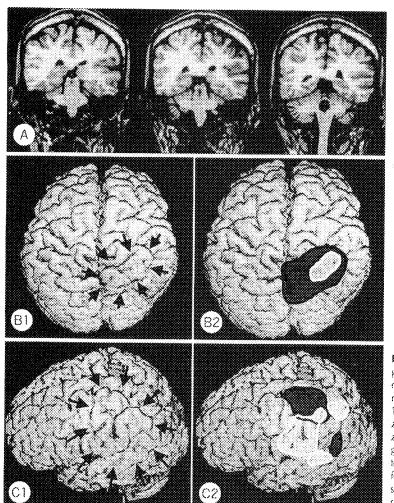


Fig. 3. Upper row: 2D MRI of patient-A showed no gyral abnormality. Middle row: However, 3D rendering of this patient showed thick gyri with loss of normal sulco-gyral pattern on a right parietal lobe (B-1: cortical deformation zone). B-2 shows irritative zone (interictal spikes: black circle) and ictal onset zone (white circle) on the brain region with sulco-gyral anomaly. Lower row: Distorted sulco-gyral patterns in left pericentral region (C-1: cortical deformation zone). C-2 shows irritative zone (interictal spikes: black circle) and ictal onset zone (white circle) on the brain region with sulco-gyral anomaly.

# 3. False localization of 3D surface-projection rendering technique

3D SPR revealed one false localization (10%) in neo-cortical TLE and two false localization (14.3%) in extra-TLE. A diffuse temporal lobe atrophy was found on the contralateral side of the epileptic focus in neocortical TLE. Left temporal lobe atrophy (right frontal lobe epilepsy) and left temporoparietal atrophy (right frontal lobe epilepsy) were detected by 3D SPR in extra-TLE. These findings were reproduced by repeated segmentation and 3D rendering. Therefore, it is unlikely that these atrophies in false location are artifacts related to 3D SPR technique.

# 4. The interobserver reliability between two interpreters

The concordance rates between two interpreters of 3D SPR were 90% in neocordical TLE and 85.7% in extra-

TLE. The mean concordance rate was 87.5% in all subjects. The interobserver agreement was excellent (k=0, 78,  $p \le 0.05$ , kappa statistics).

 The topical relationships between cortical deformation zones, ictal onset zones and irritative zones (Fig. 3).

The CDZ included the whole areas of IOZ in nine (52, 9%) and IRZ in six (35.3%), overlapped with IOZ in seven (41.2%) and IRZ in 10 (58.8%), were connected to IOZ in one (5.9%) and IRZ in one (5.9%).

#### 6. Pathology and surgical outcome

The pathological diagnoses of resected brain tissues were eight cortical dysplasia, one cortical dysplasia with numor and one cortical dysplasia with nuberous sclerosis in patients with neocortical TLE, and 12 cortical dysplasia and two gliosis in patients with extra-TLE. The

postsurgical outcomes of all patients were evaluated according to the Engel's classification.\* Sixteen patients (66.7%) were seizure free (class 1). Five patients (20.8%) were almost seizure-free except for rare disabling seizures since surgery (class 11). Three patients (12.5%) had worthwhile reduction of seizures (class 111). The postsurgical follow-up periods of all patients were more than 2 years.

## Discussion

Inspection of cerebral cortex is very important for the diagnosis of neurological disorders. To analyze a brain cortex precisely, the rendering image of brain MRI must closely represent in vivo brain cortex. However, some technical problems in 3D rendering could produce false positive or false negative results. The factors related to the technical problems are MRI quality, segmentation method, and rendering method.

To obtain MRI image of good quality, motion artifact should be avoided. The motion artifact may produce partial volume effect and loss of normal sulco-gyral pattern in 3D images. The MRI image with high signal-to-noise ratio (SNR) was more adequate for segmentation. Fast-SPGR (Fast SPoiled Gradient Recalled Acquisition in the Steady State) MRI showed a diffuse boundary intensity of gray matter poorly separated from the cerebrospinal fluid (CSF) due to low SNR. So, the segmentation of border will become inaccurate and the thickness of the segmented gray matter may be inconsistent in the

semi-automated method. 3D rendering of cerebral cortex from this segmentation might present false positive results such as focal atrophy and irregular gyration (Fig. 4A & B). For the best visualization of cortical surface, MRI should have thin inter-slice thickness, high spatial resolution, high signal to noise ratio and minimum or no motion artifact.

In the segmentation of a brain from CSF space, the manual tracing method requires a lot of labor and time. Therefore, full or semi-automated segmentation method has been used. Segmentation should include all brain structures. In automated methods like mathematical morphology, region growing and intensity thresholding, is it is very difficult to correct the unexpected noise due to their full automation. The noise may resemble atrophy, irregular gyration, and loss of normal sulcal patterns (Fig. 4C & D).

The combined use of intensity based autotracing and anatomical boundary correction by an operator can make the brain cortex image closer to a real brain (Fig. 4B, 5). In our study, the segmentation of one brain took about 30-60 minutes by the combined method.

There are many rendering algorithms for medical image visualization. MIP (Maximum Intensity Projection) has been used for MR angiography. Woxel and surface rendering techniques are frequently used for object's shape visualization. Many studies have been performed using voxel based gradient-shading method or surface rendering with a shape description. However, to

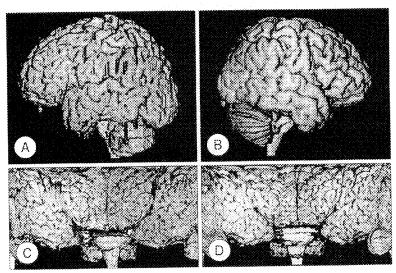


Fig. 4. Upper row: 3D surface rendering of brain with different pulse sequences. A. Poor visualization of a brain surface with irregular gyral thickness and sulcal widths in fast SPGR MRI (TR/TE: 11.2/2, flip angle: 20°), B. More realistic cortical surface was generated in SPGR MRI (TR/TE: 30/7, flip angle: 45°), Lower row: Two different results of radial-surface rendering of the same brain image of the fast SPGR MRI. Tight segmentation made brain cortex look like diffuse atrophy and loss of normal sulco-gyral patterns in left temporal lobe (C). However, the cortical image with an appropriate segmentation shows good sulco-gyral patterns (D).

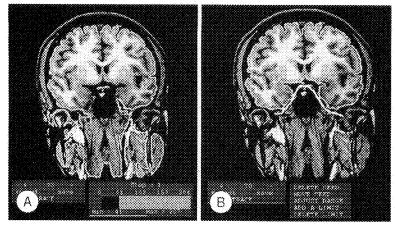


Fig. 5. Semi-automated segmentation: automatic segmentation (A) includes extra-cerebral structures which were manually excluded by adding a limiting line (B).

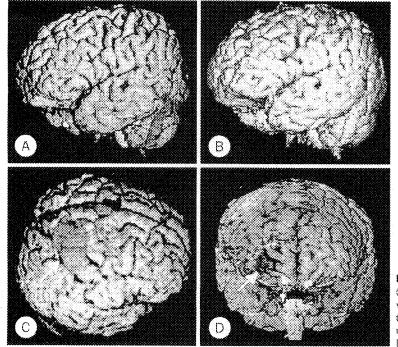


Fig. 6. Upper row: 3D surface-projection rendering (A) shows more precise sulco-gyral patterns than a voxel gradient rendering (B). Lower row: Subtle intensity difference on 3D surface-projection rendering reveals a undermining tumor (C) in a right parietal lobe and a focal atrophy (D) in a right frontal lobe.

illustrate the real sulco-gyral formation and the intensity change of cerebral cortex, surface-projection rendering algorithm is better for the localization of cortical lesion (Fig. 6A & B). Furthermore, SPR algorithm through reflecting image intensity<sup>16</sup> can detect the signal changes of cerebral cortex easily (Fig. 6C & D).

Our study used 3D SPR and radial surface rendering techniques to detect cortical deformation in the brains with epileptic patients. Radial surface rendering technique stretched out bilateral spherical cortical surfaces on the same 2D plane and made it possible to compare the lateral cortical surfaces of the right and teft hemispheres simultaneously (Fig. 1). This technique is convenient and

very helpful for screening subtle asymmetries of gyral and sulcal morphology in cerebral cortex. However, radial surface rendering of 3D brain produced some distortion of image such as elongation or flattening at the brain regions near the interhemispheric fissure. After visual screening of bilateral hemispheres in radial surface rendering, the brain regions with suspicious abnormality were re-inspected in spherical 3D SPR images. The quality of brain MRI in some of the patients was not as good as that of recent patient's MRI because fast SPGR scanning had been used in the earlier period. The higher the quality of brain MRI images and the accuracy of segmentation were, the cortical morphology of 3D SPR be-

came more realistic. If the quality of MRI image improves, the sensitivity of 3D SPR for identifying cortical deformation will increase significantly.

Temporal lobe is limited superiorly and anteriorly by the Sylvian fissure and blends posteriorly with the parietal and occipital lobes. Two sulci and three gyri are seen on the lateral surface. The superior and inferior temporal sulci start 8 to 10 mm from the temporal pole and run parallel to the Sylvian fissure. The superior, middle and inferior temporal convolutions were separated by these two sulci. This well organized pattern of lateral temporal surface morphology was observed consistently in normal subjects. Nine of the ten neocortical TLE patients showed disruption or alteration of normal sulcogyral patterns such as focal atrophy or gyral thickening, irregular array of sulci and gyri, vertical arrangement of superior and inferior temporal sulci, and ill-defined gyral margins in 3D SPR. It was an interesting observation that the brain regions with sulco-gyral anomalies were concordant to the epileptogenic areas. Although small alteration of cortical morphology can be produced by various causes of brain damages, the changes of the whole cortical morphology such as vertical array of lateral temporal sulci or different gyral distribution and thickness appears to have formed in an intrauterine developmental period of the brain. However, when we looked into the onset ages of seizures and birth history of patients who had abnormal array of sulci and gyri with relatively normal gyral volumes, no significant differences were observed.

Similar alterations of lateral temporal sulci were observed in schizophrenia patients. Kikinis et al. (1994) studied sulco-gyral patterns of temporal and frontal cortices

in 15 schizophrenic patients. They reported that schizophrenics had a more vertical orientation to the sulci in the left temporal lobe, with an interrupted course of sulci due to gyri coursing across the sulci. These data suggest that some of the abnormalities observed in schizophrenia may have their origin in alterations occurring during the course of the neurodevelopment when the sulco-gyral pattern is determined. The pathology results of our study (most of sulco-gyral pattern anomalies were associated with cortical dysplasia) support that sulco-gyral malformation may occur during intrauterine neural development.

Sulco-gyral anomalies observed in extra-TLE patients were gyral atrophy, focal gyral thickening, volume reduction, ill-defined gyral margins, loss of normal sulcal patterns, and increased gyral complexity. Four of the nine patients with no lesion on conventional 2D MRI showed sulco-gyral abnormalities in 3D SPR images. Sisodiya et al. (1996) could find gyral abnormalities in seven of the 16 cryptogenic clinically extra-TLE patients. Gyral anomalies observed in their study were macrogyria and increased gyral complexity with altered disposition. But the epileptogenic foci of these patients were not confirmed by surgery and considered most frontal lobe on clinical grounds only (historical and scalp EEG findings).

We believe that further improvement of 3D rendering technique and combined use of FDG-PET co-registered with MRI will increase the in vivo detection rate of epileptogenic lesion in patients with partial epilepsy.

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#### **ABSTRACT**

*Purpose*: The detection of epileptogenic lesion plays an important role in the management of patients with partial epilepsy. Although the development of MRI improved the examination of cerebral hemispheres greatly, many patients with neocortical temporal lobe epilepsy (TLE) or extratemporal lobe epilepsy (extra-TLE) still show no lesion in conventional two-dimensional (2D) images. To increase the yield of MRI in those patients, we performed three-dimensional (3D) surface-projection rendering (SPR) of the cerebral hemispheres. *Methods*: Conventional 2D MRI (T1, T2, FLAIR, thin slice SPGR) and 3D SPR were performed in 24 patients with neocortical TLE and extra-TLE, and 20 normal subjects. Sulcogyral patterns were evaluated blindly to clinical information. The locations of the epileptogenic zone, ictal onset zone (IOZ) and irritative zone (IRZ) were determined by intracranial EEG monitoring and epilepsy surgery. *Results*: The 2D MRI identified epileptogenic lesions in five of the 10 neocortical TLE (50%) and five of the 14 extra-TLE (35.7%). 3D SPR revealed abnormal sulcogyral patterns in 9 of the 10 neocortical TLE (90%) and 9 of the 14 extra-TLE (64.3%). Cortical deformation zones with sulcogyral anomalies included the whole area of IOZ in 10 (55.5%) and IRZ in 6 (33.3%), overlapped with IOZ in 7 (38.9%) and IRZ in 11 (61.1%), were connected to IOZ in 1 (5.6%) and IRZ in 1 (5.6%). *Conclusion*: 3D SPR of volumetric MRI data can detect epileptogenic structural lesions of neocortical epilepsy that are not visible in the conventional 2D images. (J Korean Epilep Soc 4: 3-11, 2000)

KEY WORDS: Partial epilepsy · Cortical deformation · 3D surface-projection rendering · Sulcogyral anomaly.