LESION SIZE EVALUATION BY STATISTICAL PARAMETRIC MAPPING PROGRAM IN SIMULATED EPILEPTIC BRAIN.

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ABSTRACT

Several simulations of SPECT ictal and inter-ictal studies were performed in order to test the ability of SPM program for detection of brain lesion size and to determine the effect of site for size detection. Three cylindrical artificial lesions of diameters and length of 14x7 mm., 9x5 mm., and 4x5 mm. were positioned in 3 different regions [anterior cingulate cortex, posterior cingulate cortex, deep gray matter (basal ganglia)] in the brain phantom. Triple-headed SPECT acquisition of simulated ictal and inter-ictal states were carried out. All data were transferred to SPM2 program, which detected cluster volumes for each size and site were compared to actual lesion volumes. SPM could detect 14 mm lesion sizes at all sites. The 9 mm lesions were detected at anterior and basal ganglia sites. The 4 mm lesion was only detected at the anterior and basal ganglia site and the volume detected by SPM is larger than the true volume. In conclusion, size detected by SPM is much larger than the actual size. Sites of lesions may affect size detection.

INTRODUCTION

Nowadays Single Photon Emission Computed Tomography (SPECT) imaging is widely accepted as a study to confirm epileptogenic focus in intractable epilepsy. Traditional side by side visual interpretation of ictal and inter-ictal SPECT scan may sometimes be difficult in identifying the epileptogenic focus, particularly in patients with extratemporal or otherwise unlocalized intractable epilepsy by MRI.

Computer-aided subtraction ictal SPECT co-registration to MRI (SISCOM) was known to be more sensitive than visual analysis. Furthermore, concordance between SISCOM localization (site and size) and site of surgery is predictive of postoperative seizure outcome irrespective of MRI finding.[1] Thus, accuracy of size detection is a major concerned if SISCOM-guided surgery is to be performed. Statistical parametric mapping (SPM) is a software program that is increasingly used as an objective whole-brain analysis technique for functional neuroimaging. SPM was designed mainly to visualize the statistically significant region on data sets obtained from PET or SPECT during various kinds of activation. It has the capability of co-registration by mutual informations, re-aligments, spatial transformations into a template space, and contrast define giving a result of voxel values constituted a statistical parametric map of t-test. A few studies had been

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performed to validate the size detection by SPM.[2,3,4] Those studies simulated on neuroactivated brain compared to normal baseline of brain study. Therefore the studies cannot properly be applied in epilepsy patients who have hypoperfusion at the lesion interictally. Accuracy of size detection by SPM is important to identify the actual activation zone, in order to aid to define the surgical margin. In this study, we performed several simulations of SPECT ictal and interictal studies in order to test the ability of SPM2 for detection of brain lesion of various sizes and to determine the effect of site on size detection.

MATERIAL AND METHOD

Brain phantom

Brain phantom used in this study is locally made in elliptical shape (figure 1). The brain dimension is 2.5 cm thick, 13 cm wide and 18 cm high. The inner volume is 300 cc. It simulates the ^{99m}Tc-ECD activity distribution in the human brain. The ratio of count density of the gray matter, white matter and ventricles is 4: 1: 0 , respectively.

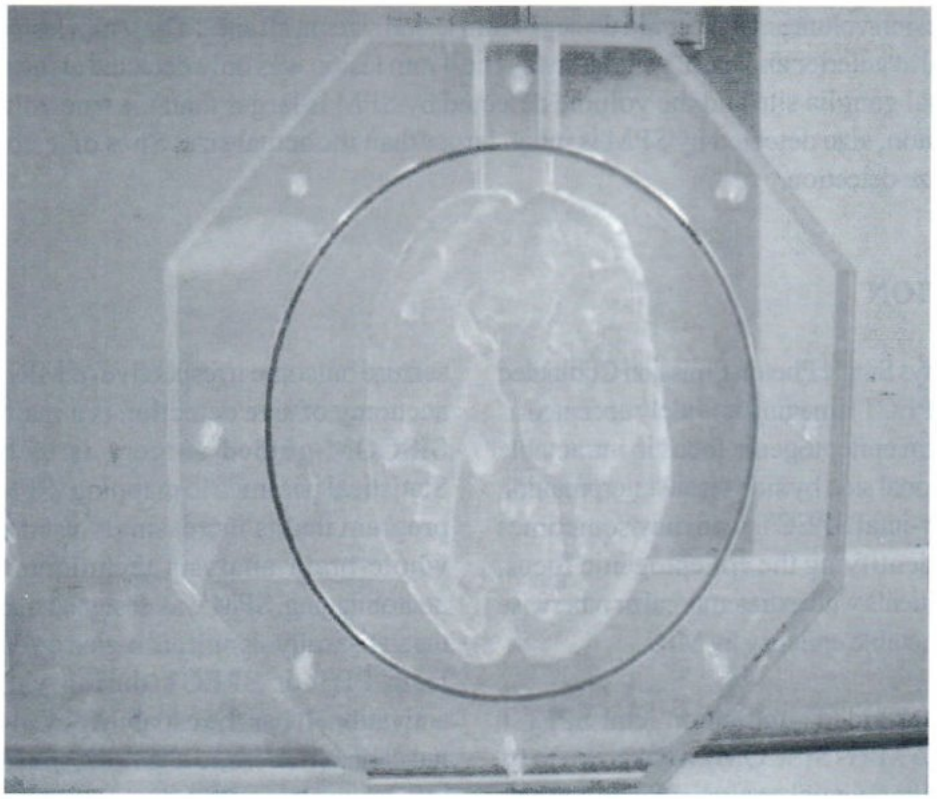

Fig.1 brain phantom

Artificial lesions

There were three sizes of cylindrical-shaped lesions used in this study. (figure 2)

1. Large size : diameter 14 mm., length 7 mm., volume1.5 cc
2. Medium size : diameter 9 mm., length 5 mm., volume 0.4 cc
3. Small size : diameter 4 mm., length 5 mm., volume 0.1 cc

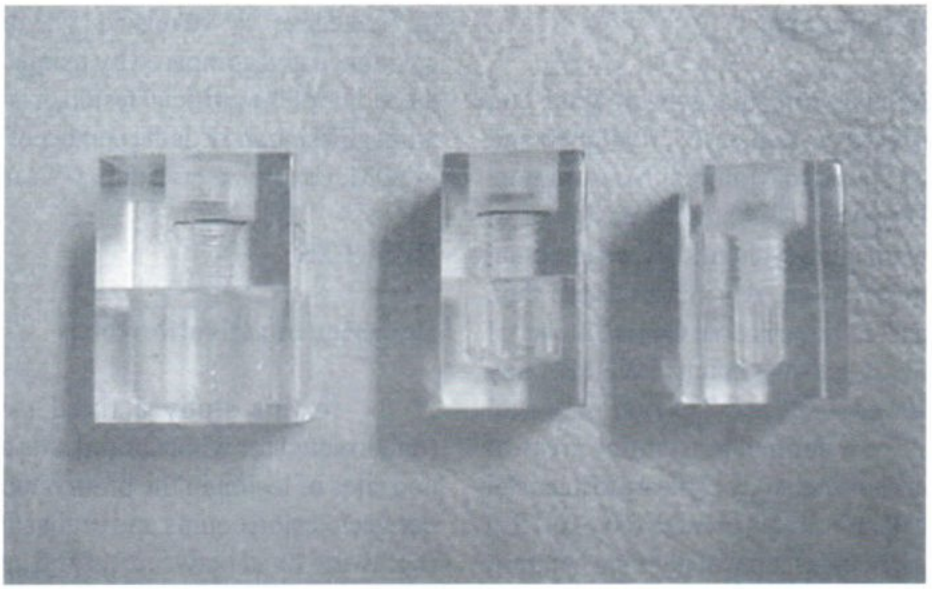

Fig.2 Artificial lesions

Data Collection

Three artificial lesions of three diameters (14 mm, 9 mm, 4 mm) were positioned in 3 different regions [anterior cingulate cortex and posterior cingulate cortex , deep gray matter (basal ganglia) in the brain phantom.

In the interictal state, the lesions in the phantom were not filled with radioactivity, while the surrounding brain was filled with 20 μCi/ml of $^{99m}TcO^{4-}$. For ictal study, the lesions were filled with radioactivity about 70-150 μCi in each lesions. The three sizes of lesions were placed in 3 regions of the brain phantom. For each data set, acquisition were performed 3 times by a triple head SPECT (Trionix Research lab, Model Triad 20T Twinsberg OH, USA), which two sites (anterior, posterior) of the same size were performed simultaneously and basal ganglia separately. Identical acquisition parameters were used for all interictal and ictal images which were as followed; LEUR (low energy ultra high resolution) collimators, matrix size 128x128, zoom 1.6, pixel size 2.8 mm., acquisition time 40 sec/view in 40 views.

Data Analysis

The acquisition data were reconstructed and activation ratio of lesion to normal brain in reconstructed images of each lesion size were collected. The reconstruction of data sets followed the protocol commonly used in our section for brain scanning with cut-off frequency 0.7, order 5 and Butterworth filter. Four-points attenuation

compensation were applied.

After reconstruction, the images of all sites and sizes were displayed on screen in order to assure that all lesions were visualized. The data were then exported to interfile format within the SUN workstation. The interfile files were transferred to personnel computer, and converted to Analyze Format by MRIcro program.

By SPM program, the data of ictal and interictal states were co-registered, realigned and transformed into standard Montreal Neurological Institute (MNI) space. This step is designed to co-register a series of image volumes of the same brain to a single representative. All images were then smoothed with a three-dimensional Gaussian filter of 16 mm. full-width-at-half-maximum (FWHM). Gray matter threshold were fixed at 0.8.[4] Contrast of ictal minus interictal were defined to examine areas of higher tracer uptake in ictal study compare to interictal study. The result demonstrated number of voxels (k_e) in activated focus. For each time of defining contrast, parameter of height threshold which is *p*-value uncorrected for whole brain were adjusted to find the best cut-off level at each size and site of experiment. This type of *p*-value was used because this is a study in a phantom which the lesions location were already known.

The true volume of artificial lesions ($V = \pi r^2 h$) and the volume of voxels detected by SPM (k_e*voxelsize_x* voxelsize_y* voxelsize_z) were calculated and compared by using t-test. Where r is the radius of the artificial lesion, h is the length of the artificial lesion and k_e is the number of voxels presented in SPM, voxel size x = 2 mm, y = 2 m, z = 2 mm.

RESULTS

Detection of activation focus

In this study a fixed p-value = 0.001 (uncorrected for whole brain) was used for all sizes and sites of lesion in the brain phantom. The ratios between lesion counts and brain soft tissues counts (bg.) were fixed between 1.4 and 2.6 (Table 1). The reconstructed SPECT images are shown in figure 3.

Table 1 SPM visualization of lesion at various sites and sizes (p=0.001)

Lesion site/size	Lesion : bg ratio	Visualization by SPM
Anterior cortex		
4 mm	1.4	None
9 mm	2.4	Cluster
14 mm	2.6	Cluster
Posterior cortex		
4 mm	1.4	None
9 mm	1.7	None
14 mm	1.8	Cluster
Basal ganglia		
4 mm	2.4	Cluster
9 mm	2.2	Cluster
14 mm	1.8	Cluster

All lesions of ictal and inter-ictal simulated SPECT images of all sizes can be visualized clearly. (Figure 3)

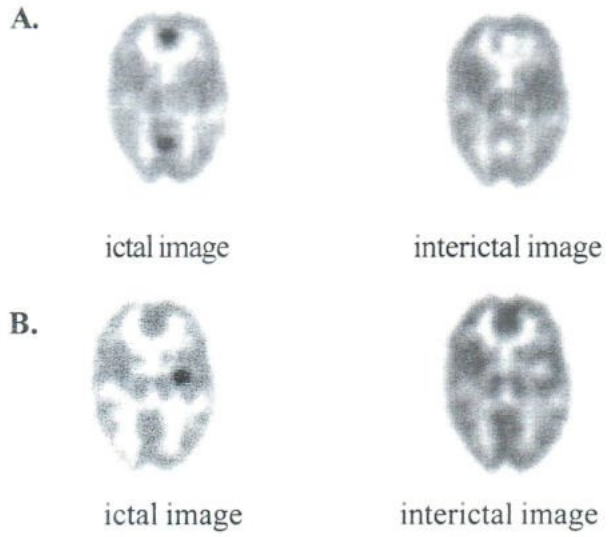

Fig.3 A. Reconstructed SPECT brain image with lesions placed at anterior and posterior cingulate cortex., B. Lesion placed at basal ganglia

By SPM program, the activation foci were detected in some sites and sizes. Projecting on the glass brain as shown in figure 4 shows the lesions detected by SPM.

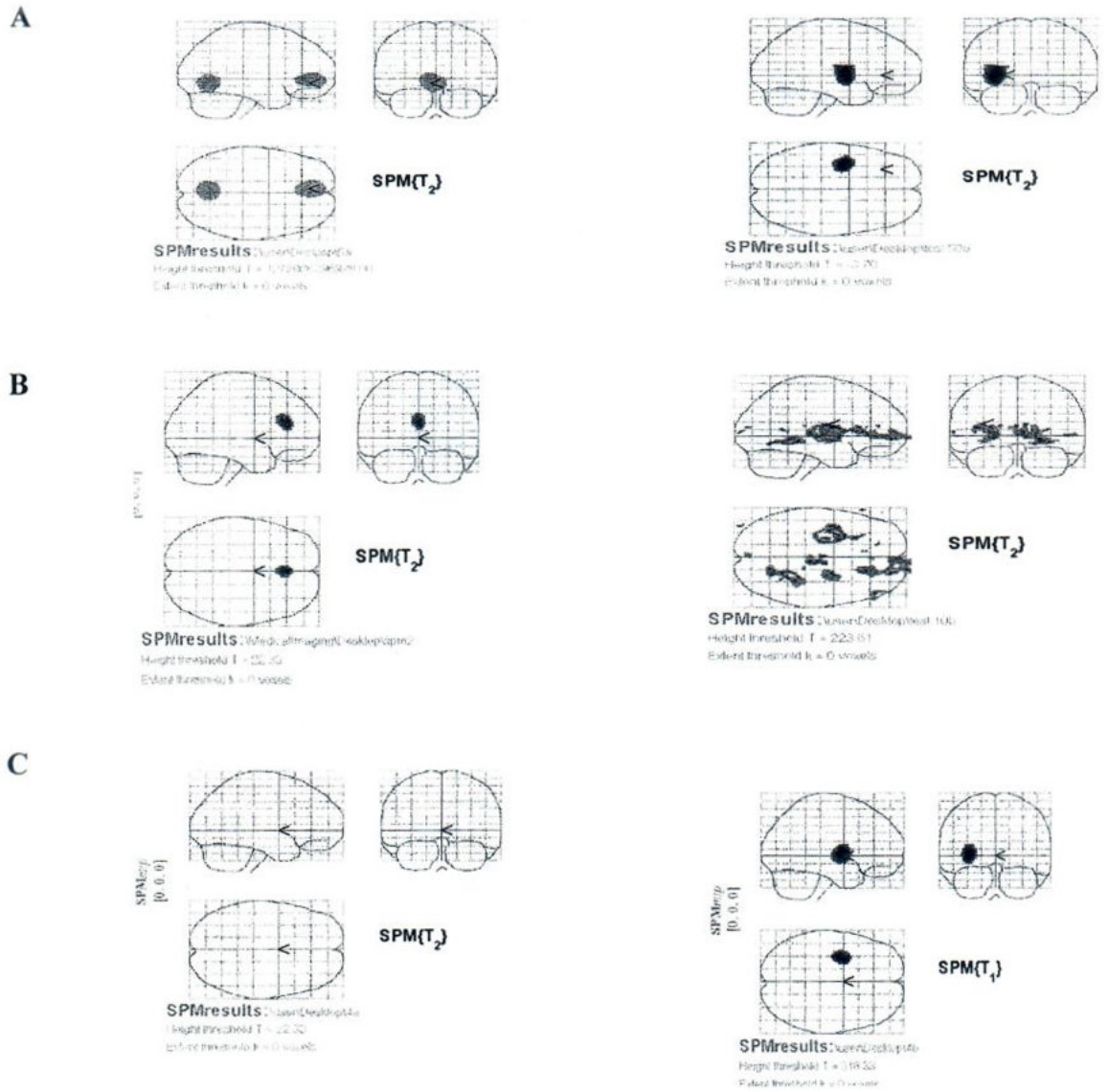

Fig.4 Activation foci detected by SPM; A. lesion size 14 mm. at anterior and posterior cingulate cortex (left), at basal ganglia (right) ; B. lesion size 9 mm. at anterior and posterior cingulate cortex (left), at basal ganglia (right) ; C. lesion size 4 mm. at anterior and posterior cingulate cortex (left), and at basal ganglia (right).

For the lesions not detected by SPM (4 mm. at anterior and posterior, 9 mm at posterior), varying threshold was attempted first. There was no lesion detected by varying the threshold. Afterward varying the lesion:background ratio were tried ranging from 2.1-2.5. These could not generate the lesions visualization by SPM as well.

Numbers of voxels (k_e) detected by SPM program for each size were calculated to transfer to term of the volume detected by SPM (k_e* voxelsize_x* voxelsize_y* voxelsize_z) and compare it against the true volume of artificial lesions ($V = \pi r^2 h$). The comparison between two volumes is shown in Table 2.

Table 2 The volume of the brain lesion size 14, 9, 4 mm. determined by SPM compared to the actual volume at different sites.

Lesion site/size	No.of voxel (k_e)	SPM volume(mm^3) [(k_e). 2x2x2]	True volume(mm^3) ($\pi r^2 h$)	Volume ratio (SPM : True)
Anterior cortex				
14 mm	1144	9152	1077	8.4
9 mm	368	2944	317	9.2
4 mm	None	None	62.8	-
Posterior cortex				
14 mm	1052	8416	1077	7.8
9 mm	None	None	317	-
4 mm	None	None	62.8	-
Basal ganglia				
14 mm	978	7896	1077	7.2
9 mm	314	2512	317	7.9
4 mm	110	880	62.8	14.0

DISCUSSION AND CONCLUSION

In this study, several simulations of SPECT ictal and inter-ictal studies were performed in order to test ability of SPM program (version 2) for the detection of the size of brain lesion and to determine effect of site on size detection. The detection of activation focus was achieved for brain phantom with 14 mm lesion size at all 3 sites. The 9 mm lesions were detected at anterior and basal ganglia sites except at posterior cortex site and the 4 mm lesions were absolutely not detected at anterior and posterior sites, but only at the basal ganglia in the brain phantom. If compare to previous study by Stamatakis, et al,[4] the study was found that, for the smallest lesion they used (20 voxel = 160 ml), the intensity of lesion should be 30% or more than the brain background. In our study, we used smaller volume of lesion (63 ml), so the intensity should be more than 30% by theory. Increasing intensity of the lesion not previously visualized (anterior cingulate cortex of 4 mm lesion and posterior cingulate cortex of 4 mm and 9 mm lesions) up to 150% more than the brain background did not produce visualization. This might be the effect of SPM software itself, which new advanced version such as SPM5 may allow future studies in SPM analysis activation detectability.

We found that the sites also may affect the size detection; all lesions were detected more efficiently at the basal ganglia sites. Results are not in agreement with the previous publish studies.[1,3,4]

From the result of this study, the calculated volume detected by SPM was 7-14 times larger than the real volume. This can be assumed that SPM process resulted in error in size detection, which might be due to statistical variation in nuclear medicine imaging. All images are normally blurred and have less resolution compare with other modalities. Furthermore, the resulted image from SPM is a contrast between ictal simulated and inter-ictal simulated images. This might produce differences between images that is more than the real lesion boundary. Thus the apparent volume of activation in an SPM program does not represent the real volume of activated focus as stated before.[6] However, we did not take lesion intensity to count on the effect of intensity on size detection.

The limitations of this study are : 1.) The inability of SPM program to detect the exact volume of the lesion:bg count 1.4-2.6 and 2.) The small sample size, thus, only the trend of relation can be observed. Positive correlation of volume detected by SPM and true volume were found.

In conclusion SPM program is able to detect large hyperintensity size and might be helpful for further clinical use. However, the size detected by SPM is much larger than the actual size. Sites of the lesion may affect the sizes detection.

ACKNOWLEDGEMENT

The authors would like to thank Assoc. Prof. Dr. Anchali Krisanachinda for her kind advices. The study was financially supported by master research granted from Graduate school, Chulalongkorn University.

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