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Computer Simulations of Hoffman Brain Phantom:Sensitivity Measurements and Optimization of Data Analysis of [Tc-99m] ECD SPECT Before and After Acftazolamide Administraton

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Abstract

Consecutive brain [Tc-99m]ECD SPECT studies before and after acetazolamide (Diamox) administration have been performed with patients for the evaluation of cerebrovascular hemodynamic reserve. However, the quantitaitve potential of SPECT Diamox imaging is limited as a result of degrading fractors such as finite detector resolution, attenuation, scatter, poor counting statistics, and methods of data analysis. Making physical measurements in phantoms filled with known amounts of radioactivity can help characterize and potentially quantify the sensitivities. However, it is often very difficult to make a realistic phantom simulating patients in clinical situations.

By computer simulation, we studied the sensitivities of ECD SPECT before and after Diamox administration. The sensitivity is defined as$(\Delta N/N)/(\Delta S/S)\times 100\%$, where ΔN denotes the differences in mean counts between post-and pre-Diamox in the measured data, N denotes the mean counts befor Diamox in the measure data, ΔS denotes the differences in mean counts between post-and pre-Diamox in the model, and S denotes the mean counts before Diamox in the model. In clinical Diamox studies, the percentage changes of radioactivity could be determined to measure changes in radioactivity concentration by Diamox after subtracting pre-from post-Diamox data. However, the optimal amount of subtraction for 100% sensitivity is not known since this requires a thorough sensitivity analysis by computer simulation.

For consecutive brain SPECT imaging model before and after Diamox, when 30% increased radioactivity concentrations were assingned for Diamox effect in model, the sensitivities were measured as 51.03, 73.4, 94.00, 130.74% for 0, 100, 150, 200% subtraction, respectively. Sensitivity analysis indicated that the partial voluming effects due to finite detector resolution and statistical noise result in a significant underestimation of radioactivity measurements and the amount of underestimation depends on the % increase of radioactivity concentration and % subtraction of pre-from post-Diamox data. The 150% subtraction appears to be optimal in clinical situations where we expect approximately 30% changes in radioactivity concentration. The computer simulation may be a powerful technique to study sensitivities of ECD SPECT before and after Diamox administration.

Computer Simulations of Hoffman Brain Phantom:Sensitivity Measurements and Optimization of Data Analysis of (Tc-99m)ECD SPECT Before and After Acftazolamide Administraton

1. INTRODUCTION

Single photon emission computed tomography (SPECT) can be used to study regional cerebral perfusion in human brains with commercially available traces auch as [99mTc]HMPAO or [99mTc]ECD, and multi-hedaded SPECT camera.[1-3] At Asan medical center, consecutive brain [Tc-99m]ECD SPECT studies before and after acetazolamide (Diamox) admininstration have recently been performed with patients for the evaluation of cerebrovascular hemodynamic reserve(Fig. 1). It has previously been reported that consecutive brain [Tc-99m]HMPAO SPECT technique seemed to be of practical use for the evaluation of brain perfusion reserve and for the improvement of the sensitivity of detecting pathologic areas.[4] However, the quantitative potential of SPECT imaging is limited as a result of degrading factors cuch as finite detector resolution, attenuation, scatter, poor counting statistics, and methods of data analysis. Making physical measurements in phantoms filled with known amounts of radioactivity can help characterize and potentially quantify the effects of these degrading factors on SPECT images. However, it is often very diffecult to make a realistic phantom simulating patientsin clinical situations.

In recent clinical Diamox studies, the percentage changes of radioactivity were determined to measure changes in radioactivity concentration by Diamox after subtracting pre-from post-Diamox data. However, the optimal amount of subtraction for 100% sensitivity is not known since this requires a thorough sensitivity analysis by computer simulation. The advantage of a computer simulation. The advantage of a computer simulation approach is the ability to study individually and collectively the various factors which would not be separble in any physical measurements. By computer simulation, we studied the effects of finite detector resolution and statistical noise on measuring the sensitivities of ECD SPECT before and after Diamox administration. A sensitivtiy anslysis would give us some of the insights of clinical Diamox studies and predict an optimal amount of subtraction when the percentage changes of radioactivity need to be determined to measure change in radioactivity concentration by Diamo after subtracting pre- from post-Diamox data.

2. MATERIALS AND METHODS

2.1. Detector response characteristics

For three-headed SPECT camera equipped with a parallel-hole collimators(Trionix, Twinsburg, OH), the point spread function (PSF) was experimentally measured using a line source:polyethylene tubing(lmm i.d., 28 cm length) was filled a Tc-99m solutin (15 mCi (555 MBq)in 0.2ml)and the ends of the tubing thermally sealed. The tubing was secured on top of a flat surface as a straight line source. The camera face was positioned at several distances from the source, zero to eight Plexiglas sheets(1.3×23×23 cm) were positioned between the line source and the detector, and the source was imaged for 2min

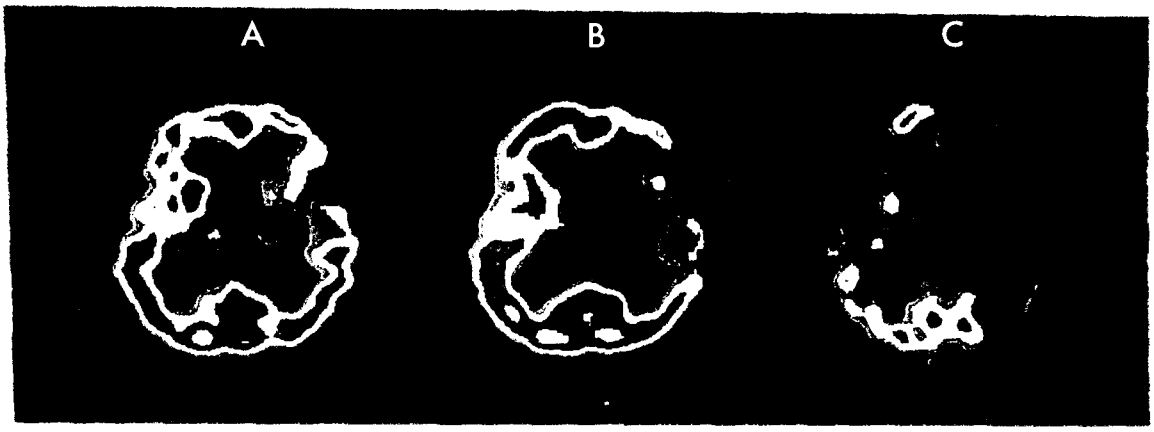

Fig. 1. An example of consecutive clinical brain〔Tc-99m〕SPECT reconstructed images pre-(A), post-(B) Diamox, and 150% subtracton (C)of pre- from post-Diamox administration. *Data acquisiton parameters* were 128×128matrix, 1.4 magnification factor, 3.2 mm pixel size, 90 angular views, and 20%〔Tc-99m〕energy windows. Filtered back projection with a Hamming filter at a cutoff frequency of 0.09 cycles/mm was used for the reconstruction.

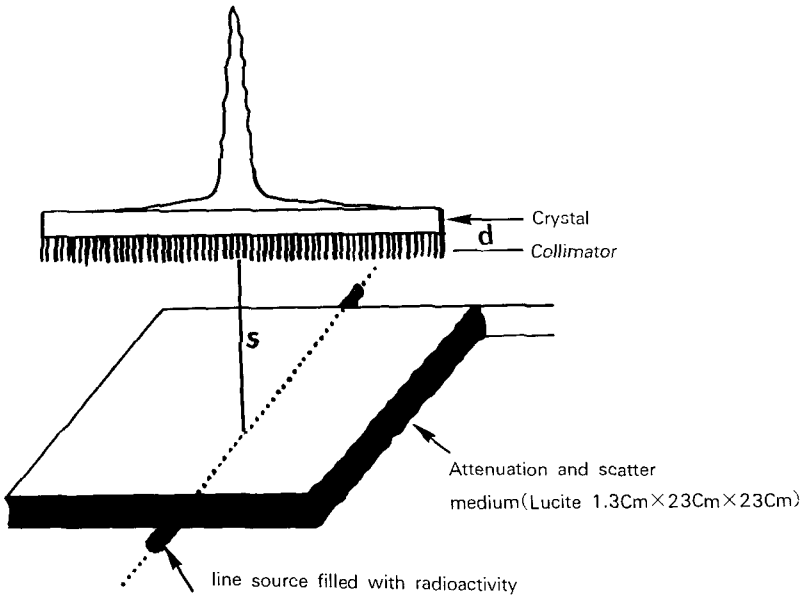

Fig. 2. A schematic diagram of experimental set-up to measure a line spread function.

(Fig.2). The line source was imaged using the Triad SPECT system. The acquisition parameters were:15% energy window, 128×128 array with 1. 11 mm/pixel for the projection data. The acquied data were decay-and dttenuation-corrected. The averaged profile profile perpendicular to the line source (Fig. 3) was analyzed as the sum of three Gaussians using an iterative nonlinear curve fitting procedure in order to fit adequately the low amplitude tails.

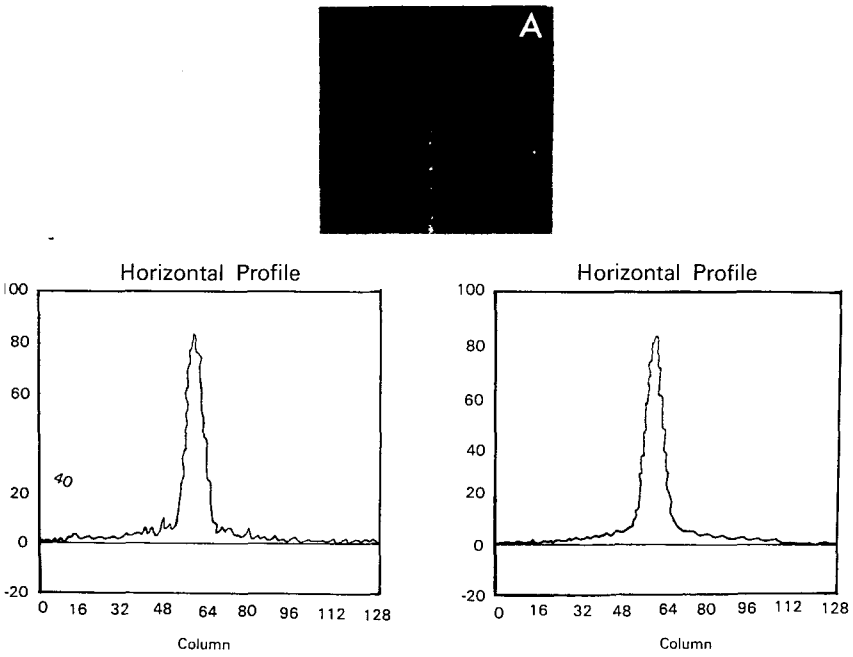

Fig. 3. An example of a line source image at 13cm distance from detector and 10.4cm depth of scatter medium (A), a normalized single horizontal profile to suppress the statistical noise (B), and normalized averaged horizontal profile to suppress the statistical noise (C).

2.2 Mathematical brain model

A brain slice at the level of the basal ganglia from the mathematical three dimensional Hoffman brain model was chosen for the simulation studes.[5] A small defect at right posterior parietal cortex (RPPC) was introduced and assigned to 10, 20, 30, 80, 160% increased radioactivity concentrations for the simulation(Fig. 4).

2.3 Imaging simulation studies

A typical example of study protocol for consecutive clinical brain [Tc-99m]ECD SPECT studies before and after Diamox administration could be described as follows:the first projection data is acquired for 10 minutes starting from 10 minutes after 555 MBq (15 mCi) of [Tc-99m]ECD iniection and 1 g of Diamox is administered immediately after starting the first projection data acquisition. With no changes in the subject's head position, the scecond projection data is acquired for 10 minutes starting from 10minutes after and additional of 1110 MBq (30 mCi) of [Tc99m] ECD injection.[4] In simulation studies, radioactivity concentrations in a brain slice at the levelof the basal ganglia were assigened to 1 for gray matter and 0.25 for white matter, and 2 for gray matter and 0.5 for white

matter for pre-and post-Diamox simulations, respectively, except 10, 20, 30, 80, and 160% increased radioactivity concentrations over RPPC for post-Diamox to simulate the Diamox effects.

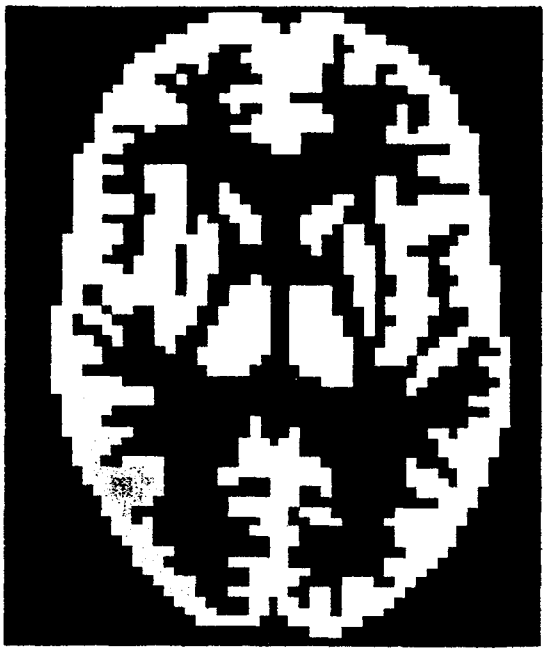

Fig. 4. Digitized mathematical brain model at the level of basal ganglia chosen from the three dimensional Hoffman brain model. The model was derived from MRI images, anatomy atlases, and the knowledge of anatomy and FDG distributions in the brain.

The simulated projection data built up as the successive summation of projection data for each nonzero voxel: for each nonzero voxel, the measured PSF was mulitplied by the voxel value, translated according to the voxel position, and summed into an array containing the accumulated according to the voxel position, and summed into an array containing the accumulated simulated projection data.[6,8] Four to one ratio between gray and white matter was used to simulate a realistic brain perfusion studies in clinical situations. The simulation parameters were 128 bins projection, 90 projection angles, pixel size of 3mm, and 15% energy window for Tc-99m. When noise was included in simulation, the projection data were scaled to the desired number of counts similar to the counts in clinical studies, and Poisson noise was computed using the rejetion method.[7,8] Filtered back projection with a Hamming filter at a cutoff frequency of 0.12 cycles/mm was used for the reconstruction.

2.4 Data analysis

Region of interest (ROI) was drawn over RPPC using the theoretical of gray matter and overlaid with the simulated reconstructed images. The mean counts/pixel were then obtained.

The sensitivity is defined as:

$$(\Delta N/N)/(\Delta S/S)\times 100\% \qquad (2-1)$$

where ΔN denotes the differences in mean counts between post-and pre-Diamox in the measured data, N denotes the mean counts before Diamox in the measured data, ΔS denotes the differences in mean counts between post-and pre-Diamox in the model, and S denotes the mean counts before Diamox in the model. Ink clinical Diamox studies, the percentage changes of radioactivity were determined to measure changes in radioactivity concentration by Diamox as[4]:

$$\%\ \text{change of radioactivity} = 100\times(C_{postDiamox} - C_{preDiamox\ corr.})/C_{preDiamox\ corr.} \qquad (2-2)$$

$$C_{preDiamox\ corr.} = (T_{preDiamox}/T_{postDiamox})\times(D_{postDiamox}/T_{preDiamox}) \qquad (2-3)$$

where $C_{postDiamox}$ and $C_{preDiamox}$ are the mean reconstructed counts for each ROI in the pre-Diamox and post-Diamox images, respectively, and $T_{preDiamox}$ and $T_{postDiamox}$are the scanning time for the SPECT data acquisition in the pre-Diamox and post-Diamox images, respectively, and $D_{postDiamox}$ and $T_{preDiamox}$ are the administered radioactivity dose of [Tc-99m]ECD in the pre-Diamox and post-Diamox images, respectively. $C_{preDiamox\ corr.}$ represents the $C_{preDiamox}$ corrected for the differences in data acquisition time and radioactivity dose between the pre-and post- studies. However, the accuracy of % change of radioactivity may ont repersent the true values due to detector response, attenuation, scatter, and statistical noise. It is often measured ratios between left and right regions after 100% subtraction of pre-Diamox from post-Diamox studies to increase the lesion detectability. In simulated reconstructed images, it would be possible to study various kinds of data analysis including above methods. The sensitivity$(\Delta N/N)/(\Delta S/S)\times 100\%$ were measued for 100, 150, 200% subtractions of pre-Diamox from post-Diamox data to study the effects of subtraction techniques on measurements of sensitivities.

3. RESULTS

3.1 Detector response charateristics

The parameters to be fit were the amplitude (A), sigma (σ), and center of each Gaussian. The first Gaussian represented the geometric detector response, and the second and third Gaussians represented the components due to scatter within the plexiglas, and septal penetration(Fig. 5). A and σ for all three Gaussians could be modeled as functions of the distance between the line source and the detector face and the depth of the Plexiglas scattering medium. Only the first Gaussian, which represented the geometric detector response, is used in the simulations presented here, and A and σ for this component could be modeled as a function of the distance(D)between the line source and the detector face and the depth (d) of the line source within the scattering medium (A=2,094counts-4.957counts/mm D;for $0\text{mm}\leq d<39$ mm,$\sigma=1.407\text{mm}+0.01298\ D+d(-9.667\times10^{-4}+4.312\times10^{-5}D)$, and for $39\text{mm}\leq d<250$, $\sigma=1.$ the source and from the point source would theoreticlly be the same;however A for the point

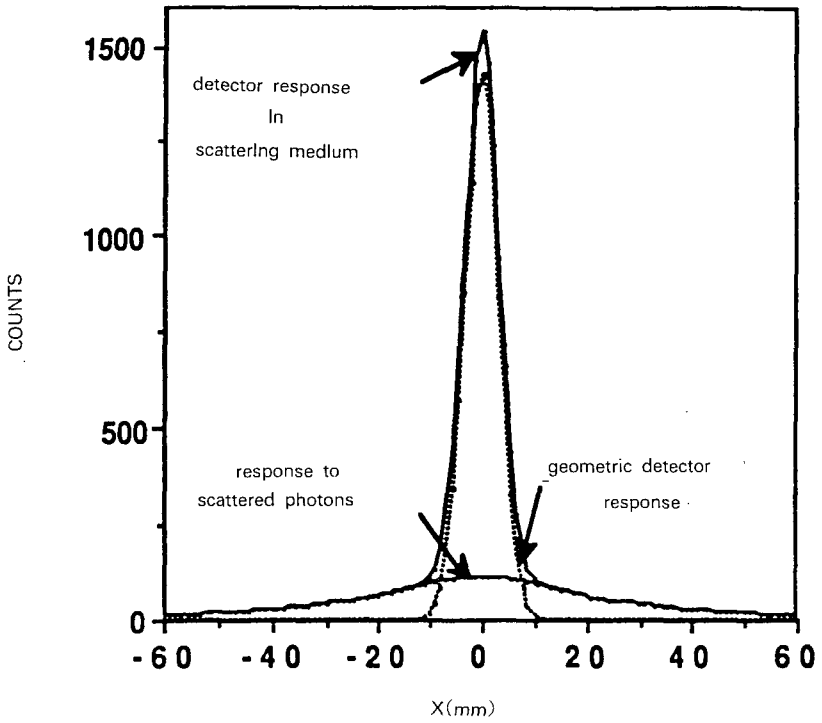

Fig. 5. Line source response function modeled as the sum of three Gaussians at 13cm distance from the detector and at 10.4cm depth of scatter medium.

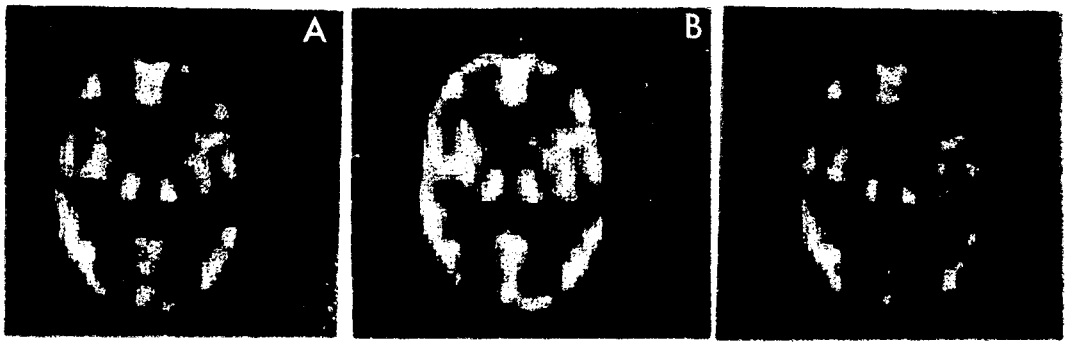

Fig. 6. Simulated rectonstructed SPECT images for pre-(A)and post-(B) Diamox, and 150% subtraction (C)of pre-from post-Diamox model. For post-Diamox model, 30% increased radioactivity concentration over RPPC was assigned and the noise was included at the level of clinical situation(400,000 and 1,200,000counts per slice for pre- and post-Diamox, respectively). For the purpose of display, images were normalized to the individual slice.

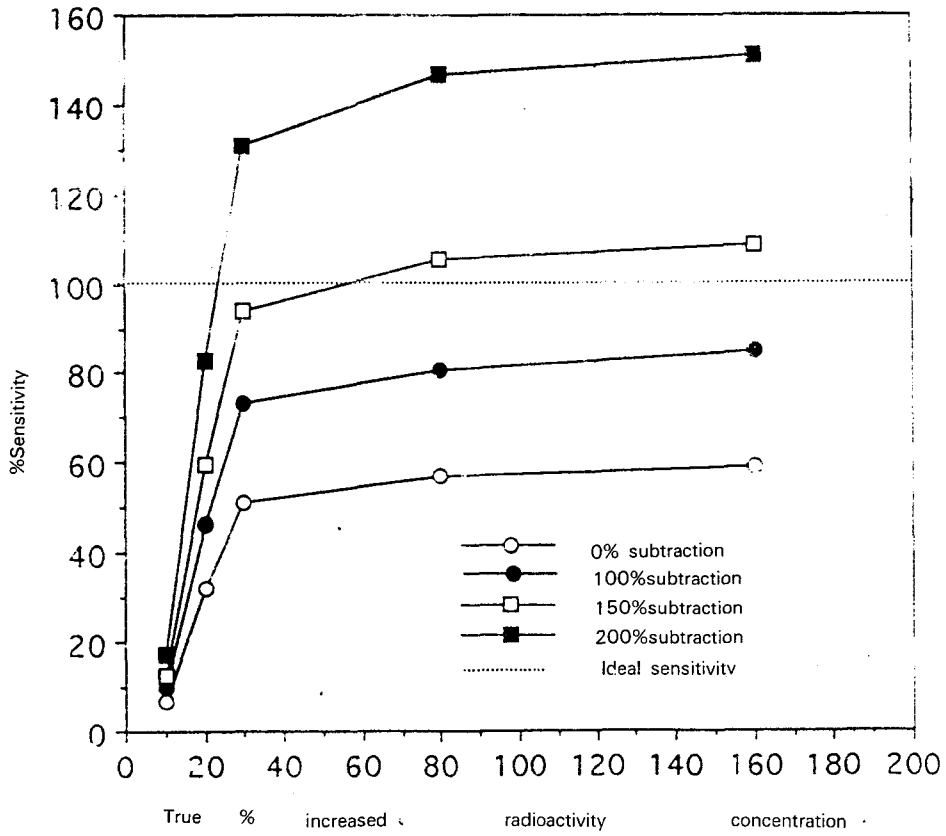

Fig. 7. Sensitivity plosts for 0, 100, 150, 200% subtraction of pre- from post-Diamox data when 10, 20, 30, 80, 160% increased radioactivity concentrations were assingned for Diamox effect in the model.

source must be computed from the formula[6]:

$$A_{PSF}=A_{LSF}/(\mathrm{sqrt}(2\pi)\sigma_{LSF}) \qquad (3-1)$$

3.2 Imaging simulation studies

Fig. 6 shows the simulated reconstructed images which are qualitaively similar to the reconstructed images of the physical phantom or brain SPECT studies. In the presence of noise, 10% increase of radioactivity concentration over RPPC was not distinguishable. However, 20 or 30% increase clearly shows apparent increased counts in reconstructed images. Fig. 7 shows the sensitivities for 0,100, 150, 200% subtracion of pre- from pot-Diamox administration, when 10, 20, 30, 80, 160% increased radioactivity concentrations were assigned in the model. For consecutive brain SPECT imaging model before and after Diamox, the sensitivities wer measured as (6.90, 32.41, 51.03, 57.24, 59.05%) for no subtraction, (9.92, 46.63, 73.4, 80.88, 84.95%)for

100% subtraction, (12.71, 59.72, 94.00, 105.46, 108.80)for 150% subtraction, (17.67, 83.04, 130.74, 146.64, 151.28%)for 200% subtraction when (10, 20, 30, 80, 160%) increased radioactivity concentrations were assigened for Diamox effect in the model, respectively. The sensitivity for 10% increas in the model was 6.9% which is a significant under es timation when subtraction was not applied. The sensitivity was somewhat increased when the subtraction was applied. However, the sensitivity was 17.67% even when the 200% subtraction was applied. This indicates that detecting 10% increased radioactivity concentration may be very difficult in this imaging situation. It's been assumed that there will be 30% changes in radioactivity concentration in many clinical situations. The sensitivity for 30% increase in the model was 51.03% which is still a significant underestimation when subtraction was not applied. When the 100 or 150% subtraction was applied, the sensitivity was 73.40 or 94%, respectively. However, the sensitivity was 130.74% when the 200% subtraction was applied. This indicates that subtraction techniques should be used with a caution.

4. DISCUSSION AND CONCLUSION

SPECT and PET can be used to study regional cerebral perfusion in human brains. We have performed consecutive brain [Tc-99m]ECD SPECT studies before and after Diamox administration with patients for the evaluation of cerebrovascular hemodynamic reserve. However, the quantitive potential of SPECT imaging is limited as a result of degrading factors such as finite detector resolution, attenuation, scatter, poor counting statistics, and the methods of data analysis. In clinical Diamox studies, the percentage changes of radioactivity have been determined to measure changes in radioactivity concentration by Diamox. However, the methods have not been theoretically investigated. By computer simulation, we studied the effects of partial voluming effects and statistical noise on measuring the sensitivities of ECD SPECT before and after Diamox administration and optimize the subtraction methods. For example, the sensitivity for 30% changes in the model resulted in 51.03%. However, the sensitivity was dramaticlly improved when 150%subtraction method was applied.

The advantage of a computer simulation approach is the ability to study individually and collectively the various factors which would not be separable in any physical measurements. Sensitivity analysis indicated that the partial voluming effects due to finite detector resolution and statistical noise redulfin a significant underestimation of radioactivity measurements and the amount of underestimation depends on the % increase of radioactivity concentration and % subtraction of pre-from post-Diamox data. Making physical measurements in phantoms filled with known amounts of radioactivity can help characterize and potentially quantify the effects of these degrading factors on SPECT images. However, it is often very difficult to make a realistic phantom simulating patients in clinical situations.

The computer simulation may be a powerful technique to study and optimize the sensitivities of ECD SPECT before and after Diamox administration.

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Acetazolamide 사용전후〔Tc-99m〕EDC SPECT 데이타 분석 방법의 최적화 및 민감도 측정

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초 록

Acetazolamide (Diamox)사용전후 〔Tc-99m〕ECD SPECT를 이용한 연속 뇌촬영은 뇌혈관의 혈역학 예비를 평가하기 위하여 사용되고 있다. 그러나 SPECT Diamox 영상의 정량적 평가 가능성은 검출기의 해상도, 감쇄, 산란, 노이즈, 그리고 데이타 분석 방법들에 의해 제한되고 있다. 알고 있는 양의 방사능을 채운 팬텀을 측정함으로써 민감도를 측정하거나 또는 분석할 수도 있다. 그러나 임상환경에서 환자를 시뮬레이션하는 현실성 있는 팬텀을 만드는 것은 매우 어렵다.

Diamox 사용전후 ECD SPECT의 민감도가 컴퓨터 시뮬레이션에 의해 측정되었다. 민감도는 (△N/N)/(△S/S)×100%로 정의되고 △N은 측정된 데이타에서 Diamox 사용후와 사용전의 평균값 차이이고, N은 측정된 데이타에서 Diamox 사용전 평균값이고, △S는 모형에서 Diamox 사용후와 사용전의 평균값이고, S는 모형에서 Diamox사용전 평균값이었다. Diamox를 이용한 임상연구에서는 Diamox후에서 Diamox전 데이타를 감산한 후 Diamox에 의한 방사능 양의 변화를 측정함으로써 방사능의 변화율이 결정될 수 있다. 그러나 100% 민감도를 위한 최적의 감산 양은 알려져 있지 않고 이것은 컴퓨터 시뮬레이션을 이용 철저한 민감도 분석을 요한다.

Diamox 사용전후 연속 뇌 SPECT 영상 모형을 위하여 30% 증가된 방사능 양을 Diamox 영향으로 했을때 민감도는 0, 100, 150, 200% 감산에 대해 각각 51.03, 73.40, 94.00, 130.74%로 측정되었다.

민감도 분석은 검출기의 해상도에 의한 부분용적 효과와 통계적 노이즈는 방사능 측정의 과소 평가가 된다는 것을 보였고 과소 평가 되는 양은 방사능 양이 몇% 증가했는가 또는 Diamox후 데이타에서 Diamox전 데이타를 몇% 감산 했는가에 의존 된다는 것을 보였다.

임상에서 방사능 양의 변화가 약 30%라 기대했을때 150%의 감산이 최적인 것으로 나타났다. 컴퓨터 시뮬레이션은 Diamox 전후의 ECD SPECT 민감도를 연구하는데 매우 중한 기술로 생각된다.