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Optimization of Correction Factor for Linearization with Tc-99m HM PAO and Tc-99m ECD Brain SPECT

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Tc-99m HMPAO와 Tc-99m ECD 뇌SPECT의 뇌혈류량 정량화에 사용되는 Linearization Algorithm의 Correction Factor 조사

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- 초 록 -

연구목적: ^{99m}Tc *d,l*-hexamethylpropyleneamine oxime(HMPAO)와 ^{99m}Tc ethyl cysteinate dimer (ECD)의 뇌세포에 의한 섭취는 뇌혈류량에 비례를 한다. 그러나 뇌혈류량이 아주 높은 경우에는 뇌세포에 의한 섭취가 그 만큼 증가를 하지 않기 때문에 뇌혈류량이 과소평가 될 수 있다. 이를 보안하기 위하여 Lassen이 linearization algorithm을 만들었다. 그러나 이 방정식은 뇌의 상태에 따라 사용되는 알파값으로 표현되는 변수가 변할 수 있다. 저자들은 뇌경색이 있는 10명의 환자를 대상으로 가장 적절한 α값을 구하고자 하였다.

재료 및 방법: 10명의 환자들은 모두 0.1에서 10까지의 알파값을 이용하여 교정한 ^{99m}Tc-HMPAO와 ^{99m}Tc-ECD 뇌관류 단일광자방출 단층촬영(single photon emission computed tomography: SPECT) 영상을 구하고, 양전자방출단층촬영술로 뇌혈류영상을 구하였다. 그리고 상호정보의 최대화에 의한 multi-modal volume registration을 이용하는 컴퓨터프로그램으로 양전자방출단층촬영술로 구한 뇌혈류와 SPECT 영상에서 다양한 알파값을 대입하여 Lassen의 linearization algorithm으로 구한 뇌혈류값을 픽셀단위로 서로 비교하였다.

결과: Lassen의 linearization algorithm을 이용하여 구한 ^{99m}TC-HMPAO와 ^{99m}TC-ECD 뇌관류 SPECT의 국소 뇌혈류량은 알파값이 각각 1.4와 2.1일때 양전자방출전산화단층촬영술로 구한 뇌혈류량과의 상관관계가 가장 높았다.

결론: Lassen의 linearization algorithm을 이용하여 뇌혈류량을 정량화하는 경우에는 ^{99m}TC-HMPAO의 경우는 1.4, ^{99m}TC-ECD의 경우는 2.1을 사용할 때 뇌혈류량을 가장 잘 반영할 것으로 생각된다.

중심단어: ^{99m}Tc-HMPAO, ^{99m}Tc-ECD, Lassen's linearization algorithm, SPECT, PET, Cerebral blood flow

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Introduction

^{99m}Tc *d,l*-hexamethylpropyleneamine oxime (HMPAO) and ^{99m}Tc ethyl cysteinate dimer (ECD) were developed as retained-type brain perfusion tracers for single photon emission computed tomography(SPECT). They have been widely applied in the evaluation of regional cerebral blood flow(rCBF) (Podreka, et al., 1987 ; Leveille, et al., 1989; Walovitch, et al., 1989) However, the rCBF by both perfusion tracers at a high blood flow range was under estimated. To correct this, Lassen's linearization algorithm has been applied(Andersen, et al., 1988; Inugami, et al., 1988; Langen, et al., 1988 ; Lassen, et al., 1988; Lear, 1988; Yonekura, et al., 1988; Friberg, et al., 1994, Lassen, et al., 1994)

In Lassen's linearization algorithm, the correction factor(α value) was determined as the lipophilic to hydrophilic conversion rate constant divided by clearance rate via the blood brain barrier(back diffusion). Lassen(1988) and Friberg(1994) proposed 1.5 and 2.6 as the average α values for ^{99m}Tc-HMPAO and ^{99m}Tc-ECD, respectively, from the retained fraction and extraction derived from the residue curves generated by an intracarotid injection of these tracers in normal brains.

In this study, we got the optimal α value in both ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain SPECT images by pixel-by-pixel comparison with rCBF obtained by positron emission tomography(PET-rCBF).

Materials and Methods

Patients

We obtained informed consents from 10 patients(8 males and 2 females) with cerebrovascular disease ranging in age from 58 to 69 years(average, 62 years). All of them had chronic cerebral infarction.

The ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain SPECT and PET were performed within two weeks on each patient.

SPECT study

The patients in the nuclear medicine suite at the National Cardiovascular Center were intravenously injected with 740MBq of ^{99m}Tc-HMPAO or ^{99m}Tc-ECD while resting in a supine with their eyes covered in a dimly lit room. The post-injection intervals were 10 minutes.

SPECT studies was performed using a ring-type gamma camera(Headtome SET-070; Shimadzu, Kyoto, Japan) with a 7.2-mm FWHM. Image data from a 30-min acquisition were collected into a 128 x 128 matrix using a high resolution collimator. All data were corrected for attenuation of 0.11 cm^{-1}, and the tomographic data were reconstructed using a filtered backprojection algorithm. Hence, 5-mm thick transaxial slices were obtained.

PET study

Regional CBFs were measured with a Headtome IV PET scanner(Shimadzu, Kyoto, Japan) at a spatial resolution of 4.5mm at FWHM and an inhalation of ^{15}O-labeled gas(Frackowiak, et al., 1980, Lammertsma, et al., 1981). An emission scan was corrected for the effect of tissue attenuation by corresponding transmission scans with an external ^{68}Ge-^{68}Ga ring source. The emission scan was performed while the patient lay supine with eyes closed. The scan was performed during continuous inhalation of ^{15}O-labeled carbon dioxide($C^{15}O_2$), while serial blood samples were obtained through a fine gauge brachial artery catheter to measure arterial isotope activity, arterial oxygen content(O_2con), and arterial PCO_2. We obtained 6 mm thick transaxial slices.

Correction of ^{99m}Tc-HMPAO and ^{99m}Tc-ECD SPECT images:

The corrected ^{99m}Tc-HMPAO and ^{99m}Tc-ECD SPECT images were made from raw images by using Lassen's linearization algorithm with various α values(Lassen, et al.,1988).

The following equation is the Lassen's lineariza tion algorithm.

$$F/Fr = [(C/Cr)\alpha] / [1 + \alpha - (C/Cr)]$$

(where C is the count rate; and F is the flow value per pixel of the brain region studied: Cr is the count rate; and Fr is the flow value of the reference region)

The cerebellar hemisphere ipsilateral to the diseased cerebral hemisphere was selected as the reference region to avoid possible effect of crossed cerebellar diaschisis. We used α values from 0.1 to 3 with an interval of 0.1 and from 3 to 5 with an interval of 0.5 and 10 to identify the closest agreement between the corrected ^{99m}Tc-HMPAO brain uptake and PET-rCBF and between the corrected ^{99m}Tc-ECD brain uptake and PET-rCBF.

Registration procedure

We registered the corrected SPECT and PET-rCBF images, which were archived by the adjustment of the relative position and orientation, until the mutual information between the images was maximized by using the software that incorporated the mutual information technique on a Unix computer(Sun Sparc 2) (Wells, et al., 1996). The corrected SPECT images were resliced with 14 tomographic planes to match with PET-rCBF images. And then, the 4 x 4 pixel-by-pixel(8 x 8mm) comparison of the ^{99m}Tc-HMPAO or ^{99m}Tc-ECD brain uptake with rCBF measured by PET was done.

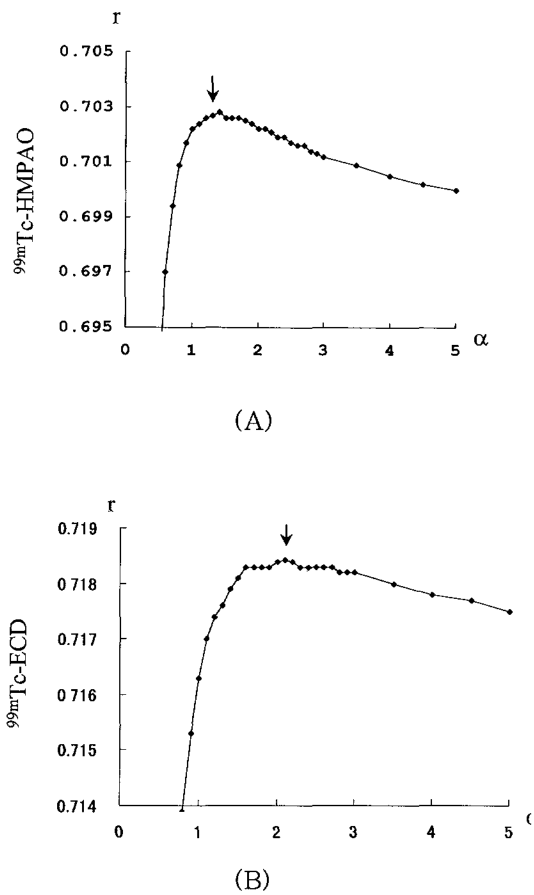
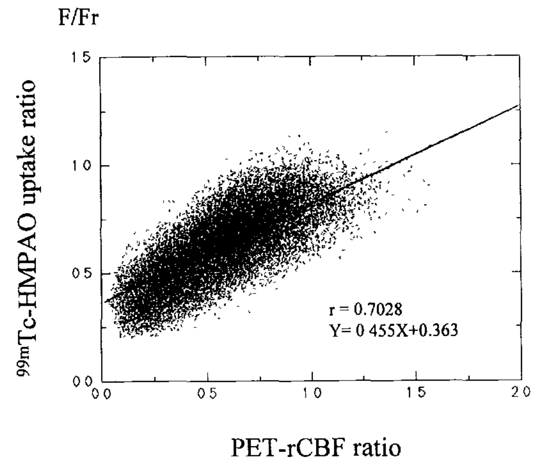
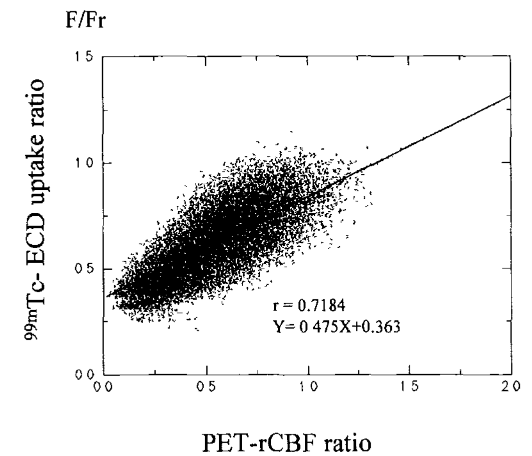


Fig. 1. The scattergram of the correlation coefficients(PET-rCBF vs. corrected ^{99m}Tc-HMPAO uptake(A) and PET-rCBF vs. corrected ^{99m}Tc-ECD uptake(B)) as a function of the α value of Lassen's linearization algorithm. The highest correlation coefficient in ^{99m}Tc-HMPAO and ^{99m}Tc-ECD was obtained with α values of 1.4 and 2.1(arrows), respectively.



(A)



(B)

Fig. 2. The scattergrams of the corrected(α=1.4) ^{99m}Tc-HMPAO brain uptake vs. PET-rCBF (A) and the corrected(α=2.1) ^{99m}Tc-ECD brain uptake and PET-rCBF(B).

Statistical analysis

The relationship between the corrected ^{99m}Tc-HMPAO brain uptake and PET-rCBF and between the corrected ^{99m}Tc-ECD brain uptake and PET-rCBF were examined by using linear regression analysis. The ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain uptakes with all 10 patients were plotted with PET-rCBF in the scattergrams and the correlation coefficients and slopes of the linear regression lines between ^{99m}Tc-HMPAO brain uptake and PET-rCBF and between ^{99m}Tc-ECD brain uptake and PET-rCBF were obtained. This sequence of analysis was repeated by using different α values.

Results

The correlation coefficients of the scattergrams were calculated as a function of α for ^{99m}Tc-HMPAO and ^{99m}Tc-ECD. The correction factor was highest when the values of ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain SPECT were 1.4 and 2.1, respectively(Fig. 1). The relationship between PET-rCBF and the corrected ^{99m}Tc-HMPAO(α=1.4) and between PET-rCBF and the corrected ^{99m}Tc-ECD(α=2.1) are shown in Fig. 2. The values of correlation coefficients of ^{99m}Tc-HMPAO and ^{99m}Tc-ECD

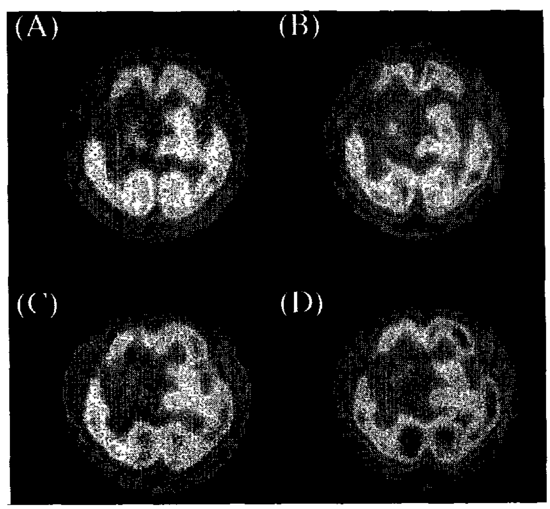


Fig. 3. Uncorrected(A) and corrected(a=1.4)(B) ^{99m}Tc -HMPAO images and uncorrected(C) and corrected(α=2.1)(D) ^{99m}Tc ECD images. Contrast in the corrected images is enhanced

brain SPECT using the optimal correction factors were 0.7028 and 0.7184, respectively.

Discussion

We corrected ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain images by Lassen's linearization algorithm using various α values and compared those with the PET-rCBF images. The optimal α values were 1.4 for ^{99m}Tc-HMPAO and 2.1 for ^{99m}Tc-ECD, respectively.

^{99m}Tc-HMPAO and ^{99m}Tc-ECD had some limitations quantifying brain perfusion and differed somewhat from the true rCBF because they had a back diffusion and low extraction. The differences between the uptake of these tracer and the rCBF revealed a curvilinear relationship with rCBF, suggesting flow-limited uptake at a high flow range(Andersen, et al., 1988; Inugami, et al., 1988; Langen, et al., 1988; Lassen, ct al., 1988; Lear, 1988; Yonekura, et al., 1988; Greenberg, et al., 1994; Tsuchida, et al., 1994). Lassen(1988) described a linearization algorithm for ^{99m}Tc-HMPAO for correcting the flow-limited uptake at high blood flow. Lassen's linearization algorithm used a three-compartment model and presented it with the ratio of the flow to the reference flow(F/Fr). In this algorithm, the α value was determined as the ratio of the conversion rate constant to the back diffusion in the reference region. Lassen (1988) calculated the average α value was 1.5 in 8 patients without cerebral lesions according to CT scans and angiograms. Anderson(1988) used α values of 1.2, 1.5, and 2.0 to find the best agreement with the corrected ^{99m}Tc-HMPAO image when compared with ^{133}Xe tomography and he also reported an optimal α value of 1.5.

The back diffusion and washout from the brain with ^{99m}Tc-ECD resulted in poor correlation at high blood flow(Greenberg, et al., 1994; Tsuchida, et al., 1994). Friberg(1994) also applied Lassen's linearization algorithm to ^{99m}Tc-ECD and calculated an average α value of 2.6 in 4 patients. In contrast, Shishido(1994) used 0.55 as the α value and reported improved linearization and correlation with rCBF after using Lassen's linearization algorithm in ^{99m}Tc-ECD brain SPECT.

The α value was different among individuals and diseased regions of the brain. We decided the optimal α vlue in ^{99m}TC-HMPAO and ^{99m}TC-ECD brain SPECT by pixel-by-pixel comparison with all tomographic images including gray matter and white matter in cerbrovascular disease patients. To decrease bias which may occur during drawing of the ROI, we adjusted the relative position and orientation between PET-rCBF and SPECT images by using multi-modal volume registration and by maximization of mutual information. The present study showed that the optimal α values were 1.4 in ^{99m}Tc-HMPAO and 2.1 in ^{99m}Tc-ECD brain SPECT, which were lower than those of Lassen(1988) and Friberg (1994).

Summary

We conducted this study to find the optimal correction factor(α) of Lassen's linearization algorithm which has been applied for correction of flow-limited uptake at a high

flow range in ^{99m}Tc *d,l*-hexamethylpropyleneamine oxime(HMPAO) and ^{99m}Tc ethyl cysteinate dimer(ECD). Ten patients with chronic cerebral infarction were involved in this study. We obtained the corrected ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain SPECT(single photon emission computed tomography) using the algorithm with *α* values that varied from 0.1 to 10 and compared the results with regional cerebral blood flow determined by positron emission tomography (PET-rCBF). The multi-modal volume registration by maximization of mutual information was used for matching between PET-rCBF and SPECT images. The highest correlation coefficient between ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain uptake and PET-rCBF was revealed at *α*: 1.4 and 2.1, respectively.

We concluded that the *α* values of Lassen's linearization algorithm for ^{99m}Tc-HMPAO and ^{99m}Tc-ECD brain SPECT images were 1.4 and 2.1, respectively to indicate cerebral blood flow with comparison of PET-rCBF.

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