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research article

The 3-Dimensional Dynamic PET/CT System with 13N-Ammonia was used to assess normal values of myocardial blood flow and reserve.

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Abstract

Purpose : For quantitation of cardiac muscle blood flow (MBF), 2-dimensional (2D) 13N-ammonia PET has been used. However, most of recent PET systems operate solely three-d (3D) mode, and there are not any reports concerning traditional worth of MBF measured by 3D PET/CT system. during this study, we have a tendency to evaluated traditional values of MBF and cardiac muscle flow reserve (MFR) with 13N-ammonia by exploitation 3D PET/CT system. Comparisons of values between the current study and antecedently reports with 2nd PET systems were dole out. **Materials and methods :** 9 traditional volunteers were listed. MBF of dipyridamole stress and rest were measured by 3D PET/CT with 13N-ammonia. MBF was measured by 2-compartmet model analysis, and MFR make up my mind because the quantitative relation of dipyridamole/rest MBF. Finally, we have a tendency to assessed regional (three coronary territories) and world MBF and MFR. **Results :** Average MBF at dipyridamole/rest were LAD:3.42 ± 0.73/1.26 ± 0.22, LCX:4.23 ± 1.17/1.20 ± 0.22, RCA:3.68 ± 0.89/1.35 ± 0.82, global:3.69 ± 0.83/1.26 ± 0.31 (mL/min/g), severally. Average MFR was LAD: two.74 ± 0.43, LCX:3.54 ± 0.72, RCA:3.20 ± 1.22, global:2.98 ± 0.59, severally. Those results were virtually similar with previous reports with 2nd 13N-ammonia PET. However, higher rest MBF and nonuniformity of congestion MBF were discovered. **Conclusions :** traditional values of MBF and MFR with 3D 13N-ammonia PET were virtually comparable the values evaluated by typical 2nd PET. However, it desires more concerns to enhance nonuniformity of congestion MBF and better rest MBF.

Introduction

For quantitative measure of heart muscle blood flow (MBF) and heart muscle flow reserve (MFR), 2-dimensional (2D) dynamic PET with 13N-ammonia has been well established [1- 4]. And this noninvasive approach has been used for the assessment of severity of artery unwellness [5-8] and alternative heart diseases [9-11], and it's conjointly been applied for the analysis of pharmacological intervention [12], epithelial tissue functions of artery [13,14], and also the standing of heart muscle microcirculation [15,16].
However, most of recent PET and PET/CT systems operate solely three-dimensional (3D) mode for the reduction of radiation dose and also the improvement of sensitivity and image quality. In clinical settings, the employment of 3D PET has incontestible blessings for brain imaging [17,18] and medicine [19]. On the opposite hand, improvement of

count rate within the 3D acquisition influences the rise of scatter, random events and dead time, compared with standard second acquisition. Consequently, viscus applications are less clear, particularly within the measuring of MBF. Moreover, there has been no report revealing regarding the traditional values of MBF and MFR measured by 3D PET/CT system with 13N-ammonia. {and the|and therefore the|and conjointly the} comparison reports with antecedently according results evaluated by standard second PET system haven't also been revealed.

In this study, we tend to measured the traditional values of MBF and MFR with 13N-ammonia by mistreatment 3D PET/CT system, and investigated feasibleness of 3D PET for 13N-ammonia study compared with antecedently according traditional values evaluated by standard second dynamic PET.

MATERIALS AND WAYS

Study Population

Nine healthy volunteers (mean age: thirty.3±8.7 years, four men) with an occasional chance of artery unwellness were registered during this study. All subjects eluded alkaloid intake twenty four hours before this PET study. This study protocol was approved by moral committee of our university, and every one subjects gave written consent.

PET Scanner

Image knowledge were obtained with Associate in Nursing integrated PET/CT system (Gemini GXL, Philips co.). This PET/CT system combines the 16-slice CT scanner and a multiring metallic element oxyorthosilicate metallic element (GSO-Zr) detector system and may acquire knowledge in precisely 3D mode. the scale of GSO crystals area unit 4mm (transaxial) ×6mm (axial) ×30mm (radial). This PET/CT system has 420 photomultipliers and people detectors area unit organized with PIXELAR system, not the standard block system, for the development of uniformity. It covers Associate in Nursing axial field of read (FOV) of 18cm and a transversal FOV of 57cm, and also the energy window was set to 419-590 keV, and coincidence time window was set to seven.5 ns. The axial special resolution was five.3 metric linear unit with full-width at half- most at one cm radius from the middle, and also the sensitivity was eight.0 cps/kBq at 10cm radius from the middle. The higher limit of radiation concentration for this camera, because the index of the count-rate characteristic, was 17.6 kBq/mL. careful National Electrical makers Association alphabetic character 2-2001 performance of this PET/CT system was according antecedently by Sathiakumar C, et al. [20]

Dynamic scan acquisition protocol

Regional MBF at rest and through medicine stress were measured as shown in Figure one. In every MBF measure, once CT scan for attenuation correction (120KV, 50-100mAs; automobile exposure control), 185 MBq of 13N-ammonia was administered with endovenous bolus injection, and now followed by total 12-min dynamic emission scan with list mode. The list knowledge were sorted to following sequence of frames: ten sec. ×12 frames + 600 sec. × 1 frame. The last frame of information was used for static imaging of heart muscle distribution of 13N-ammonia. supported the estimation of count-rate characteristic, the dose of 13N-ammonia: 185MBq was indiscriminately set for the adequate count acquisition beneath the higher limit of count-rate characteristic. we tend to took hour for the allowance of the decay of 13N-ammonia between rest and medicine stress acquisitions. because the medicine stress to achieve congestion state, dipyridamole (0.16mg/kg) was administrated for four minutes, and three minutes once the termination of dipyridamle infusion, 13N-ammonia injection and knowledge acquisition were started, as represented higher than.

During the dipyridamole stress and through quarter-hour of recovery, pressure and vital sign were recorded each two minutes. ECG (ECG) was monitored unceasingly throughout the dipyridamole stress, and a 12-lead cardiogram was recorded at baseline and each minute. At the tip of PET study, 60mg of bronchodilator was administrated for the reverse of dipyridamole result.

Image reconstruction

The data were corrected for random coincidences, geometry, normalization, dead-time losses, scatter, and attenuation. The attenuation correction was performed using the attenuation map generated from CT data acquired prior to the emission scan. Scatter correction was included in the reconstruction process using "single scatter simulation method" implemented by manufacturer. The 3D emission data was reconstructed by use of line of response (LOR) algorithm without converting into 2D data set [21]. Reconstructed image had a matrix size of 128×128×52 with 4mm cubic voxel.

Data analysis

All images were transferred to an off-line personal computer (Endeavor MT8800, EPSON co. Operating system: Windows XP professional), and measurement of MBF was processed semi automatically with PMOD software package (version 2.95, PMOD Technologies Ltd.), based on the 2-compartmet model

analysis as previously reported [22-24]. Regions of interest (ROI) were drawn semi automatically by use of a center-line within the myocardium in the projection of three dimensions (short-axis, vertical long, horizontal-long). According to the recommendation of American heart Association (AHA), 17-myocardial segment model was adopted for this analysis. For the input function, ROI was drawn in left ventricular blood pool, and for the septal spillover correction, ROI was drawn in right ventricular blood pool using summed data of first 0-120 seconds frames. MBF was estimated by model fitting of the myocardial time-activity curves [25]. Partial volume and spillover were corrected with the method which was developed and validated by Hutchins et al. [1,26] MFR was determined as the ratio of MBF during dipyridamole stress to that at rest. Finally, we assessed regional (LAD, LCX, and RCA territories) and global MBF and MFR.

Statistical analysis

Statistical analysis was performed with StatView statistical package (SAS Institute, Cary, NC). All data were expressed as the mean ± standard deviation. We adopted a paired t test for the comparison of hemodynamic findings at rest and those on dipyridamole stress, and adopted one factor repeated measures analysis of variance (ANOVA) for the analysis of MBF and MFR between three coronary territories, followed by Scheffe test if significant differences were observed. A value of $p<0.05$ was considered significant.

RESULTS

Characteristics of study subjects

Subjects' characteristics are shown in Table 1. Average age was 30.3 ± 8.7 years, average BMI was 22.2 ± 3.4. Three subjects had risk factors, two had familial history of coronary artery disease (CAD) and the other had hyperlipidemia (no need for medical therapy).

Hemodynamic changes during pharmacological stress

Hemodynamic findings such as blood pressure (systolic, diastolic, and mean pressure), heart rate, rate pressure product (RPP), were shown in Table 2. Significant increase of RPP which was observed during pharmacological stress implied that adequate vasodilation and hyperemia was achieved by dipyridamole.

Image analysis of myocardial perfusion

Visual evaluation and polar map analysis of the myocardial 13N-ammonia distribution at rest and during dipyridamole hyperemia showed homogeneous uptake in all study subjects. These results suggested that all subjects were free from significant coronary artery disease. Figure 2 showed representative data in this study subjects.

Myocardial blood flow

Myocardial blood flow (MBF; mL/g/min) at rest and during dipyridamole stress of each study subject is shown in table 3. Average resting MBF was 1.26±0.22 (range: 0.88-1.56) on LAD, 1.20±0.22 (range: 0.88-1.50) on LCX, 1.35±0.82 (range: 0.76-3.39) on RCA regions, and 1.26±0.31 (range: 0.97-1.90) as global MBF. In the resting MBF, no significant difference was observed between MBF in three coronary territories. On the other hand, average blood flow on pharmacological stress was 3.42±0.73 SBP: Systolic blood pressure; DBP: diastolic blood pressure; mBP: mean blood pressure; HR: heart rate; Bpm: beats per minute; RPP: rate pressure product. #P<0.001, *P<0.0001 vs. Rest (range: 2.49-4.28) on LAD, 4.23±1.17 (range: 2.97-6.22) on LCX, 3.68±0.89 (range: 2.34-4.92) on RCA regions, and 3.69±0.83 (range: 2.56-5.12) as global MBF. In MBF during dipyridamole stress, LCX region showed significant higher MBF than LAD region (P<0.01).

Myocardial flow reserve

Myocardial flow reserve (MFR) of each study subject, which was defined as a ratio of MBF during pharmacological stress to flow at rest, was shown in table 4. Since MBF of LCX region on dipyridamole stress was significantly higher, MFR of LCX was tending to be higher than other coronary territories; however, there was not statistical significance.

Comparison with previously reported values of MBF and MFR obtained by 2D PET systems (Table 5) Some previous studies quantifying MBF and MFR in normal volunteers, which was evaluated by conventional 2-dimension acquisition with 13N-ammonia PET (2D ammonia PET), have been reported [1,6,13-16,27,28]. Although mean global MBF at pharmacological stress was within the range of previously reported values, mean MBF at resting state showed higher trend compared to that obtained by 2D ammonia PET. Calculated MFR showed lower trend compared to the reported values.

DISCUSSION

We performed quantitative analysis of myocardial perfusion in nine healthy volunteers with 13N-ammonia by using 3D PET/CT system. For the calculation of MBF, we adopted 2-compartment model analysis and utilized PMOD software. Most of the values of MBF and MFR evaluated by 3D mode were almost similar with those which were previously reported with conventional 2D mode. Some reports revealed the equivalence between 2D and

3D acquisition for the quantification of MBF with 3D/2D hybrid PET system [29-33]. Schepis T, et al. reported the comparability of 3D and 2D acquisition of 13N-ammonia PET in the patients with known or suspected CAD evaluated by 3D/2D hybrid PET/CT system, for the detection of coronary artery disease with advantage of reduction for radiation exposure [33]. However, normal values of MBF absolutely quantitated with 3D PET/CT system have not been reported. Schepis T, et al. showed good agreements between MBF values obtained by 3D acquisition and 2D acquisition. There are discrepancies between our results and theirs. For examples, the average MBF values at rest and those on stress of this study were higher, and MFR was lower. These discrepancies might be due to different study conditions:

1. physical differences of PET/CT systems (numbers of rings and crystals of PET detectors),
2. Reconstruction methods (2D-FBP/3D-FORE-FBP/3D-FORE-OSEM/3D-RIP vs. 3D-LOR),
3. Study subjects (suspected or known coronary artery diseases vs. normal healthy subjects),
4. Analyzed time duration of dynamic data (20-min vs. 2-min). For example, since each PET system has different numbers of rings and materials of detectors, the influences of scatter, random event, and dead time were different, MBF measurement by 3D PET/CT system has not been generally authorized for quantitative accuracy. In this study, since our PET/

CT system has only availability of 3D data acquisition and was unable to make direct comparison between 2D and 3D data in the same system, we surveyed the previously reported data obtained by 2D acquisition data and compared with the present results. Although MBF at pharmacological stress matched with that by 2D acquisition data, higher MBF at rest and regional heterogeneity in MBF on pharmacological stress were observed, which were different from data previously reported.

Some reasons for higher MBF at rest are speculated. One is the lower dose of 13N-ammonia; 185 MBq than other studies. The lowest dose of 13N-ammonia in previous reports was 500 MBq [33]. In this study, based on the evaluation of count-rate characteristic of this PET/CT system, dose of 13N-ammonia: 185 MBq was determined. However, lower dose than previous studies might induce susceptibility to noises and image quality. Since the compartment analysis for 13N-ammonia utilizes image-driven arterial input function, the noises on both myocaridial tissue and input function cause bias in the estimated MBF value, especially in lower myocardial perfusion state like at rest. The other was that scatter correction in 3D mode might be insufficient for the quantitative analysis. In 3D mode, scatter event are typically 30% to 50% of the total collected counts [34]. Therefore, 3D acquisition needs appropriate correction method for scatter. In this PET/ CT system, single scatter simulation method was included in the reconstruction process, and this method reported to yield images with quantitative accuracy [35]. However, in theory, single scatter simulation cannot handle the multiple scatter and the scatter originating from outside the FOV of the scanner. Furthermore, since single scatter simulation is performed with extremely complicated algorithm, the cases which were included error data, such as misalignment of CT attenuation correction (CTAC) map and emission PET data, would be influenced by significant artifacts [34]. For these reasons, scatter correction with this method might be insufficient for the myocardial blood flow analysis, especially at rest state which showed lower blood flow and might be susceptible to scatters.

There were few reports describing about the uniformity of regional MBF in normal subjects evaluated by 2D ammonia PET. Nagamachi S, et al. reported the normal values of regional MBF at rest and during pharmacological stress: LAD (stress/rest) = 1.93±0.39/0.59±0.13, LCX (stress/rest) =1.95±0.43/0.65±0.21, RCA (stress/rest) =2.14±0.43/0.64±0.14 (mL/g/min), and they concluded that no heterogeneity was observed in MBF of three coronary territories in both rest and stress state [36]. And Hutshins GD, et al. also reported that there was no heterogeneity in MBF of each coronary arteries (values of MBF were not available in the text) [1]. However, this study showed different results from previous reports, that heterogeneity of MBF during pharmacological stress was observed: MBF during pharmacological stress on LCX was higher than that on LAD territory.

Misalignment between CTAC map and PET images was thought to be one of the factors for influencing to the heterogeneity in our study. Koepfli, et al. reported that CTAC was comparable to conventional transmission scan with a rotating Ge-68 source for the qualitative and quantitative assessment of MBF [37]. However, Alessio, et al. revealed that helical CT was insufficient for the attenuation correction of cardiac PET, because respiratory motion induced misalignment of the attenuation map and emission PET images. And they concluded that cine CT would offer an alternative to helical CT for compensating for respiratory motion in the attenuation correction [38]. Furthermore, Loghin, et al. demonstrated in conventional rest/stress PET studies, 21.7% of the studies

showed misalignment artifact typically in anterolateral or lateral segments of the left ventricle. Through manual corregistration of transmission and emission data, the artifacts could be removed [39]. In this study, helical CT was utilized as a tool for attenuation correction. We performed automatic coregistration between CT and PET image with manual adjustment. In a visual evaluation, it was difficult to detect major misalignment. However, minor misalignment which could not be detected by visual evaluation might be present and gave some influences to the heterogeneity. Moreover, as the other reason for these results, scatter correction in 3D mode, which was similar with the reason of higher MBF at rest described above, might be insufficient to eliminate the regional heterogeneity.

There were several limitations in this study. As previously described, direct comparison between values evaluated by 2D and 3D mode was impossible in this PET/CT system. Therefore, we could not conclude about the absolute equivalence of this PET/CT system and conventional 2D acquisition. Furthermore, since this study dealt with a small number of subjects, these results need to be confirmed in larger study for statistically certain analysis.

CONCLUSIONS

We performed quantitative measurement of normal value of MBF and MFR with 13N-ammonia by using 3D PET/CT system, and those results were almost comparable with the values measured by conventional 2D PET system. However, higher rest MBF and heterogeneity of hyperemic MBF was observed. Therefore, for more accurate evaluation of MBF and MFR by using 3D PET/CT system, the improvement of the alignment of CTAC map and PET images, scatter correction, and the consideration of dose of [13] N-ammonia administration might be necessary.

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