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Lesion detectability of a gamma camera based coincidence system with FDG in patients with malignant tumors: A comparison with dedicated positron emission tomography

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Objective: The aim of this study was to investigate the lesion detectability of a gamma camera based coincidence detector system (c-PET system) in comparison to the dedicated PET system (d-PET system), and thereby clarify the feasibility of the clinical application of this system and also describe any factors influencing the lesion detectability of the c-PET system. ***Methods:*** We examined 74 patients including 19 with malignant lymphoma, 16 with lung cancer, 9 with primary malignant bone tumor, 7 with esophageal cancer, 6 with malignant melanoma, 3 with hepatocelluar carcinoma, 3 with primary unknown cancer, 2 with breast cancer, 2 with colon cancer, and 7 with others. d-PET images were obtained using ECAT EXACT HR$^+$ at 60 min, followed by c-PET imaging using ECAM at 120 min after the injection of 185 MBq of FDG. Each image was reconstructed without any attenuation correction. In the image interpretation, the whole body was classified into 16 regions (5 superficial regions and 11 deep regions). The FDG accumulation of the lesions was evaluated by visual grading based on the consensus of three nuclear medicine physicians, and the findings were classified into three grades; (++), (+), and (−). The lesions were also classified into 3 groups according to their size: large group ($\geq$ 2 cm), middle group (1 $\leq$ $<$ 2 cm) and small group ($<$ 1 cm). ***Results:*** In 627 regions, the abnormal FDG uptake was detected in 109 regions by the d-PET system. Out of 109 regions, the c-PET system could detect the lesions in 91 regions and was false positive in 1 region. Therefore, the sensitivity, specificity, and accuracy of the c-PET system were 83.5%, 99.8% and 97.0%, respectively. Lesion detectability of the small group (54.5%) was significantly lower than that of the large group (97.9%) ($p < 0.001$) and that of the middle group (93.1%) ($p < 0.001$); however, the difference in lesion detectability between the large and middle groups was not significant. Neither the degree of FDG accumulation nor the location of the lesion markedly influenced the lesion detectability of the c-PET system. However, when we focused on the large and middle size lesions, the detectability of deep lesions tended to be lower than that of superficial lesions. ***Conclusion:*** In conclusion, the lesion detectability of the c-PET system was inferior to that of the d-PET system, especially in the case of small lesions. Further examination is required to assess the clinical usefulness of the c-PET system.

Key words: FDG, coincidence PET, dedicated PET

INTRODUCTION

POSITRON EMISSION TOMOGRAPHY (PET) using 2-deoxy-2-[^{18}F]-fluoro-D-glucose (FDG) is currently employed for tumor detection, prognostic stratification, planning and monitoring of tumor therapy, and early detection of tumor recurrence.[1] A classical PET device constructed with a full-ring detector system with bisthmuth germanate (BGO)

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crystals is able to sensitively detect the annihilation radiation and is referred to as dedicated PET (d-PET system). However, the d-PET system is expensive and thus has only a limited availability.

Recently, a gamma camera based coincidence detector system (c-PET system) has been developed.[2,3] The system has a coincidence detection mode added to a standard dual-head gamma camera with sodium-iodine detectors, and thus detects two annihilation radiations in the coincidence mode simultaneously. This novel system, which is less expensive than the d-PET system, can be used for both SPECT and PET at both specialist institutions and general hospitals. The basic performance characteristics of the c-PET system, such as the spatial resolution, have been reported to be comparable to those of the d-PET system,[4] and early reports demonstrated the usefulness of the c-PET system to detect the tumor FDG uptake.[5–9] However, the c-PET system is relatively less sensitive for the detection of annihilation radiation and also has both low sensitivity and low count rate characteristics.[10,11] These limitations of the c-PET system may cause a lower detectability of tumor FDG accumulation in comparison with the d-PET system.

The aim of this study is to evaluate the lesion detectability using the c-PET system compared with d-PET system in the clinical use of FDG, and to clarify the factors influencing detectabiliy of the c-PET system from the viewpoint of lesion characteristics.

MATERIALS AND METHODS

Patients

We examined 74 cases (male/female = 48/26, age range, 12–87 years; mean age, 53.7 years) including 19 cases with malignant lymphoma, 16 with lung cancer, 9 with primary malignant bone tumor, 7 with esophageal cancer, 6 with malignant melanoma, 3 with hepatocellular carcinoma, 3 with primary unknown cancer, 2 with breast cancer, 2 with colon cancer, and 7 with others. All patients were fasted for at least 4 hours before the examination. The blood glucose level was 103.8 ± 7.4 (mean ± S.D.) mg/d*l* at the FDG administration. This study was approved by the Committee for the Clinical Application of Cyclotron-Produced Radionuclides in Kyushu University Hospital, and written informed consent was obtained from all patients before the initiation of the study.

FDG-PET

The d-PET examination was performed using ECAT EXACT HR$^+$ (Siemens, Knoxville, USA) equipped with BGO crystals. Intrinsic spatial resolution was 4.6 mm full width at half maximum (FWHM) at the center, and the sensitivity of the device was 46.5 cps/Bq/m*l*. The data acquisition was started 60 minutes after the intravenous administration of 185 MBq FDG. Emission scans were obtained in a 3-dimensional mode from the head to the thigh by 9 bed positions with an acquisition time of 2 minutes each. The images were reconstructed with a filtered back projection using the Hanning filter (cutoff = 0.4 cycle/pixel) without attenuation correction. FWHM on the reconstructed image was 7.2 mm. No attenuation correction was performed.

Following the d-PET examination on the same day, the c-PET examination was performed at 120 min after FDG administration using E.CAM (Siemens, Knoxville, USA) with a dual-head gamma camera equipped with a coincidence detection system, using a 5/8-inch-thick NaI(Tl) crystal. The intrinsic spatial resolution was 5.6 mm FWHM at the center, and the sensitivity of the device was 0.6 cps/Bq/m*l*. Emission scans were obtained in a 3-dimensional mode with an acquisition time of 10 minutes for each bed position with total 1–3 bed positions. The images were reconstructed with ordered-subset expectation maximization (OS-EM) algorithm (2 iterations with 6 ordered subsets). The FWHM on the reconstructed image was 13.1 mm. No attenuation correction was performed.

Data analysis

We examined the lesion detectability of the c-PET system based on the abnormal FDG accumulation detected by the d-PET system. To interpret both the d-PET and c-PET images, we categorized the whole body into the following 16 regions: 2 regions in head and neck area (superficial and deep regions), 5 in chest area (axillar and paraclavicular region, chest wall, lung fields, hilar & mediastinal regions, and others), 7 in the abdominal area (abdominal wall, liver, other parenchymal organs, gastrointestinal tracts, lymph nodes, bone, and others), and 2 in the extremities (soft tissue and bone). All 16 of these regions were classified into 2 groups namely superficial (superficial region of head and neck, axillar and paraclavicular region of chest and chest wall, abdominal wall, and soft tissue of the extremities) and deep regions (deep region of head and neck, lung field, mediastinal, hilar region, and others of the chest, liver, parenchymal organs, gastrointestinal tract, lymph nodes, bones, and others of the abdomen, and bone of the extremities) according to the location.

The lesion characteristics with d-PET positive were analyzed according to the following three points: size, location, and degree of FDG accumulation. The lesions were classified into 3 groups according to size: large group consisted of lesions measuring 2 cm or more in

Table 1 Detectability of the c-PET system in comparison to the d-PET system

		d-PET	
		Positive	Negative
c-PET	Positive	91	1
	Negative	18	517
	Total	109	518

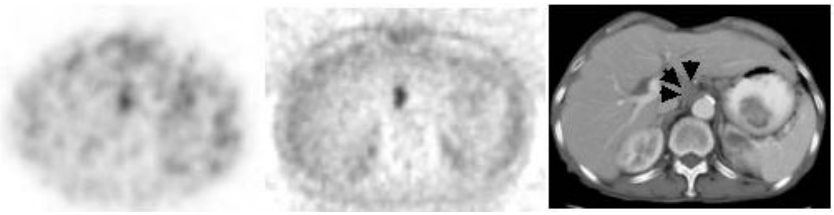

Fig. 1 An 87-year-old male with esophageal cancer and lymph node metastasis of the gastroduodenal ligament. Both c-PET (*left*) and d-PET (*middle*) showed an abnormal FDG accumulation in the upper abdominal region. Abdominal CT (*right*) showed a lymph node with an 8.5 mm diameter in the short axis in the gastroduodenal ligament (*arrow*).

Table 2 Comparison of lesion detection between the d-PET system and c-PET system based on differences in the type of disease

Disease	d-PET: positive c-PET: positive	d-PET: positive c-PET: negative	d-PET: negative c-PET: positive	d-PET: negative c-PET: negative	total	rates of concordance
Malignant lymphoma	20	5	1	164	190	96.8%
Lung cancer	28	5	0	74	107	95.3%
Malignant bone tumor	8	1	0	40	49	98.0%
Esophageal cancer	14	1	0	49	64	98.4%
Malignant melanoma	5	2	0	50	57	96.5%
Hepatocellular carcinoma	0	0	0	36	36	100%
Primary unknown cancer	3	2	0	21	26	92.3%
Breast cancer	4	0	0	24	28	100%
Colon cancer	1	0	0	20	21	100%
Others	8	2	0	40	50	96.0%

Table 3 Relationship between the detectability of the c-PET system and the characteristics of the lesions

Location:	superficial:	73.3%	(22/30)	N.S.	
	deep:	87.3%	(69/79)		
Size:	≥ 2 cm:	97.9%	(46/47)	N.S.	*
	1–2 cm:	93.1%	(27/29)	*	
	< 1 cm:	54.5%	(18/33)		
Degree of FDG accumulation:	(++):	86.5%	(77/89)	N.S.	
	(+):	70.0%	(14/20)		

*: $p < 0.001$ (χ^2-test)

diameter, middle group of lesions measuring less than 2 cm and 1 cm or more, and small group measuring less than 1 cm based on other morphological examinations such as CT or conventional radiographs. The FDG uptake was qualitatively evaluated by visual grading into three degrees; intensely positive (++), positive (+), and negative (–). d-PET and c-PET images were interpreted independently based mainly on the coronal images, referring to the transaxial and sagittal images if needed but without use of MPR images. The results were determined based on the consensus of three nuclear medicine physicians with experience in FDG-PET image interpretation for twenty years (Y.K.), fifteen years (M.S.), and three years (H.K.). Finally, 627 regions in 74 patients were evaluated by both the c-PET and d-PET system. When at least 1 lesion was not detected by the c-PET in a region, that region was considered to be negative even if other lesions could be detected by the c-PET system.

The statistical analysis calculations of sensitivity, specificity, and accuracy were derived using a standard formula. The chi square test was used to analyze the influence of lesion characteristics on detectability.

RESULTS

Detectability of the c-PET system compared with the d-PET system

Out of a total of 627 regions, 109 regions were determined to be positive by the d-PET system. The detectability of the c-PET system was summarized in Table 1. The c-PET system detected 91 of 109 regions (Figs. 1 and 2). Of 527 regions that were d-PET negative, c-PET system showed one false positive region. The sensitivity, specificity, and accuracy were 83.5%, 99.8% and 97.0%, respectively. Differences in the lesion detection according to the type of disease were shown in Table 2. The rates of concordance

Table 4 Lesion detectability according to three factors: location, size, and intensity of FDG accumulation

		Size ≥ 2 cm		2–1 cm		< 1 cm	
		location		location		location	
		superficial	deep	superficial	deep	superficial	deep
degree	++	100% (3/3)	100% (38/38)	100% (8/8)	87.5% (14/16)	50.0% (5/10)	64.3% (9/14)
	+	100% (1/1)	80.0% (4/5)	100% (1/1)	100% (4/4)	57.1% (4/7)	0% (0/2)
		100% (4/4)	97.7% (42/43)	100% (9/9)	90.0% (18/20)	52.9% (9/17)	56.3% (9/16)

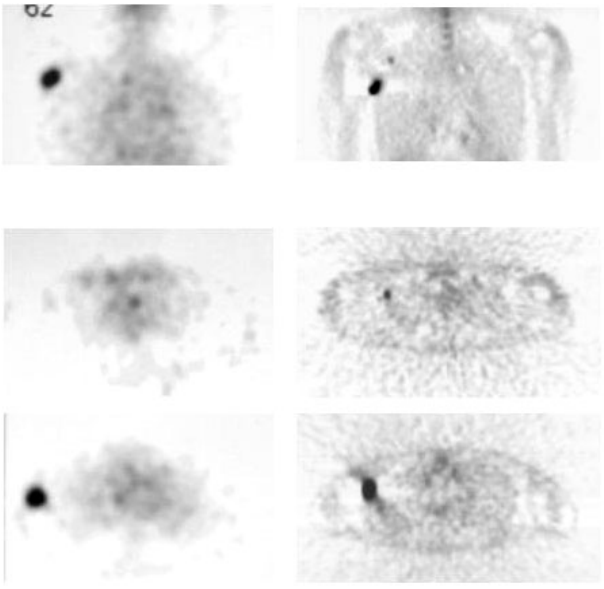

Fig. 2 A 35-year-old female with malignant melanoma. The d-PET image showed 2 abnormal FDG accumulations in the right axillar region (*right*). Although the c-PET images showed one abnormal accumulation, no other small lesion was detected (*left*).

between the detectability of the d-PET system and the c-PET system for each type of disease were more than 90%.

The factors influencing lesion detectability in the c-PET system

The detectability of the c-PET system according to the characteristics of lesions including location, size, and the FDG uptake in d-PET positive lesions is shown in Table 3. One hundred and nine lesions were classified into 2 groups according to their location as superficial regions (n = 30) and deep regions (n = 79). The detectability of the c-PET system in the superficial regions was 79.3% and was not significantly different from that in the deep regions (87.3%). When considering the lesion size, the detectability of the c-PET system in the large group (n = 47) was 97.9%, that in the middle group (n = 29) was 93.1%, and that in the small group (n = 33) was 54.5%. The difference in lesion detectability among the three groups was statistically significant ($p < 0.001$). Lesion detectability of the small group was significantly lower than that of the large and middle groups ($p < 0.001$); however, the difference in lesion detectability between the large and middle groups was not significant. According to the degree of FDG accumulation, the detectability of the c-PET system was not significantly different between the high uptake lesions (86.5%, n = 89) and low uptake lesions (70%, n = 20).

The additive effect of lesion characteristics on the detectability of the c-PET system is shown in Table 4. In the large and middle lesion groups, the detectability in the superficial group was higher than that in the deep group, though the difference was not significant. On the other hand, the location of the lesion did not influence the detectability in the small lesion group. In the small lesion group, neither the location nor the degree of FDG accumulation had any influence on the detectability of the c-PET system.

DISCUSSION

The usefulness of FDG-PET in oncology has already been established, though both the high cost of the d-PET system and difficulty of drug delivery are impediments to the diffusion of this technology. The development of the c-PET system provides the opportunity to implement FDG-PET studies in virtually any potential users.[12] We evaluated the lesion detectability of the c-PET system and factors influencing the lesion detectability in clinical practice.

In this study, the c-PET system showed a specificity of 99.8%, and sensitivity of 87.2%. This inferior sensitivity of the c-PET system compared with the d-PET system is consistent with previous reports.[7,11] Subsequently, we analyzed the factors influencing the lesion detectability in Tables 3 and 4. Lesion detectability of the c-PET system depended on the lesion size with statistical significance. The relatively low detectability of the c-PET system in small lesions was comparable to the findings of previous reports.[7,13,14] Boren et al. reported that most of the lesions missed by the c-PET system were smaller than 1.5 cm in size.[13] Zimny et al. also reported that the lesion detection rate of the c-PET system was 60% for lesions smaller than 2 cm.[14] In our result, the lesion detectability of the small group was significanly low, while that of the middle group

was comparable to that of the large group. Although the intrinsic spatial resolution of the c-PET system is comparable to that of the d-PET system, the total spatial resolution of the c-PET system under our practical conditions is lower than that of the d-PET system. An underestimation of the FDG accumulation in small lesions, due to the low spatial resolution of the c-PET system, could result in a lower lesion detectability. One other possibility is the limited efficacy of the c-PET system for the detection of the annihilation radiation which thus resulted in a low count rate.[10,11] The sensitivities of the c-PET system devices which we used in this study were 80 times lower than that in the d-PET system. The lower sensitivity of the c-PET system is considered to be due to the use of thin sodium iodine detectors and the limited angle of detection covered by the two detectors. Another possibility is the poor contrast of lesions to the surrounding normal tissue in the c-PET system. A relatively high frequency of non-true coincidences contributes to the higher background activity of the c-PET system.[9] This factor results in a poor contrast resolution of the c-PET system. The conjunction of a low count rate and a limited contrast resolution may provide a poorer image quality of the c-PET system than that of the d-PET system.

In this study, the detectability of the c-PET system for superficial lesions tended to be lower than that for deep lesions. This result seems to be different from that in a previous report which mentioned that the c-PET system tended to miss centrally located lesions.[13] In our study, the superficial group contained greater numbers of small lesions (less than 1 cm) than the deep group. This fact is thought to affect the detectability of superficial lesions, because the c-PET system showed a better detectability in superficial lesions than in deep lesions when we only examined large lesions. Although the low detectability of deep seated lesions is considered to be mainly due to attenuation effects, we could not perform attenuation correction for both d-PET and c-PET because of the following three reasons. First, transmission scan could not be performed in the c-PET system of our hospital. Second, post-injection transmission scan could not be obtained in d-PET system on earlier studies because of the limitations of the software. Third, it has been reported that FDG-PET studies without attenuation correction did not show inferior diagnostic ability in comparison with attenuation correction.[15–17] Another possibility is that the increased scatter effect in deep-seated lesions resulted in a decreased count rate and an increased non-true coincidence, leading to a deterioration in the image contrast and lesion detectability in deep-seated lesions. Thus the addition of attenuation correction to the c-PET system is expected to improve both the signal-to-noise ratio and the lesion detectability.[18]

Although the diagnostic ability of the c-PET system is inferior to that of the d-PET system, the validity of the c-PET system for clinical use should still be further discussed and compared to conventional morphological studies including CT, MRI, and US or gallium scanning. Tatsumi et al. reported the c-PET system to be useful for staging malignant lymphoma and also comparable to the d-PET system.[6] Furthermore, they also found that the c-PET system detected many additional lesions in comparison to conventional imaging studies including CT and ^{67}Ga scanning. Lin et al. reported that the c-PET system detected additional tumor sites compared with gallium scans for malignant lymphoma.[19] The c-PET system has also been reported to be useful for diagnosing both pulmonary nodules and lymph node metastasis.[7,8,19]

Some limitations of our study include the fact that the detectability of the c-PET system was examined based on the abnormal FDG accumulation detected by the d-PET system as a gold standard. Because the purpose of this study was to examine the basic ability of the c-PET system to detect FDG accumulation in clinical practice, we did not use the presence of tumors as a gold standard. It is possible that the time-dependent change of FDG distribution in patients may influence the lesion detectability, because data acquisition started at 1 hour in the d-PET system and at 2 hours in the c-PET system after FDG administration in our study. The images obtained at a delayed scan (almost 2 hrs after the FDG administration) have been reported to have an improved tumor-to-normal count ratio in comparison with those obtained at an early scan.[20,21] Because both the longer FDG uptake and longer clearance time might be advantageous for the c-PET system, the observed difference in the data acquisition start time between the d-PET system and c-PET system is thus not considered to be the cause of the inferior detectability of the c-PET system. Another factor which may influence the lesion detectability is the image reconstruction method. We used the OSEM method for the c-PET system and the FBP method for the d-PET system. Because the OSEM method is generally thought to improve the image contrast and decrease the noise,[22] the c-PET system is considered to be advantageous for image quality regarding the image reconstruction method. As a result, the lower lesion detectability of the c-PET system is not considered to be due to any difference in the image reconstruction method.

In conclusion, we investigated both the lesion detectability of the c-PET system in comparison to the d-PET system and the factors influencing lesion detectability. The major factor influencing the detectability of the c-PET system was the size of the lesions. The diagnosis of small lesions measuring less than 1 cm in size thus has to be made with caution. Furthermore, the location of lesions also tended to influence the lesion detectability. Although the detectability of the c-PET system is inferior to that of the d-PET system, further examinations to assess the influence of the c-PET system are still required before this system can become clinically available.

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