Whole-Body Hybrid PET with ^{18}F-FDG in the Staging of Non-Hodgkin's Lymphoma

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PET with a double-head gamma camera (hybrid PET) is a new approach to tumor imaging with ^{18}F-FDG. This study was conducted to clarify the feasibility of whole-body FDG hybrid PET in the staging of non-Hodgkin's lymphoma (NHL) in comparison with PET with a dedicated camera (dedicated PET) and to compare the results of both FDG studies with those of CT and ^{67}Ga scanning as conventional imaging studies (CIS). **Methods:** Thirty patients with NHL were prospectively evaluated. The results of the imaging studies regarding detection of the sites involved and staging were compared with each other and with those of the reference standard based on the final overall clinical evaluation. **Results:** Of the total of 206 sites, whole-body FDG hybrid PET and dedicated PET detected 159 sites (77.2%) and 179 sites (86.9%), respectively. Eighteen of the 20 sites missed by hybrid PET alone consisted of lesions $<$ 1.5 cm. Both FDG studies provided concordant staging results in all but 2 patients. CIS, on the other hand, detected 164 (79.6%) of the 206 sites, 137 of which were also detected by hybrid PET. Hybrid PET detected an additional 22 sites not found by CIS, whereas CIS detected 27 additional sites. Hybrid PET and CIS provided concordant staging results in 19 patients. Hybrid PET correctly staged NHL in 5 additional patients, whereas CIS correctly staged NHL in only 1 additional patient. **Conclusion:** Whole-body FDG hybrid PET appeared to be an accurate method of staging NHL. Despite its poorer image quality compared with dedicated PET, hybrid PET provided NHL staging results comparable with those of dedicated PET. Hybrid PET also yielded results comparable with those of CIS. However, whole-body FDG hybrid PET is currently inadequate as a single modality for staging NHL and is complementary to CT.

Key Words: FDG; hybrid PET; dedicated PET; CT; non-Hodgkin's lymphoma

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Non-Hodgkin's lymphoma (NHL) is one of the few malignancies that is potentially curable with existing treatment modalities, even in advanced or recurrent disease. The overall mortality rate has decreased significantly in the past 25 y, and the 5-y survival rate is more than 40% even for stage IV disease (*1*). However, for unknown reasons, the incidence of NHL is increasing (*2*).

Accurate staging is important for the proper selection of therapy in NHL as well as other malignant tumors. In addition to the clinical history and physical examination, CT and ^{67}Ga scanning, and sometimes MRI, are currently used as conventional methods of staging. Although providing significant anatomic and morphologic information, CT has certain limitations, including a limited ability to distinguish between malignant and benign lymph nodes. Nodal staging with CT is largely based on lymph node size, which correlates with the frequency of nodal involvement; however, even small nodes may harbor involvement, whereas large nodes may be benign (*3*). ^{67}Ga scanning also has some limitations in the staging of lymphoma, such as low spatial resolution and rather low sensitivity in the abdomen and pelvis because of hepatic uptake and intestinal excretion (*4*). MRI is currently performed only as part of the staging process because of difficulty in routinely obtaining whole-body images.

PET with a glucose analog, ^{18}F-FDG, is being increasingly recognized as a promising new method in the field of oncology (*5–8*). FDG PET allows detection of the increased glucose uptake characteristic of malignant cells (*9,10*), and several studies have shown the usefulness of FDG PET with a dedicated camera in the staging of lymphoma (*11–16*). This finding suggests that the whole-body acquisition method might allow accurate staging in a single imaging study.

More recently, hybrid PET has emerged as a new FDG imaging technique. It uses a double-head gamma camera equipped with a coincidence detection system for ^{18}F. Such a system is relatively inexpensive compared with a dedicated PET camera and is now expected to provide a good alternative to FDG dedicated PET in oncologic diagnosis (*17,18*). Several investigators, including us, have shown FDG hybrid PET to have high sensitivity in detecting malignant tumors $>$ 1.5 cm (*19–23*). However, to our knowledge, no reports have been published as to the validity of whole-body FDG hybrid PET in the staging of lymphoma.

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The purposes of this study were, first, to clarify the feasibility of whole-body FDG hybrid PET in the staging of NHL in comparison with dedicated PET and, second, to compare the results of hybrid and dedicated PET with those of CT and ^{67}Ga scanning as conventional imaging studies (CIS).

MATERIALS AND METHODS

Patients

Thirty patients (16 men, 14 women; mean age, 57 y) (Table 1) with untreated or recurrent NHL confirmed by biopsy were prospectively recruited into this study. Although 5 patients with recurrent disease were included, they were patients who had obtained a complete remission without any evidence of residual mass. According to the revised European-American classification of lymphoid neoplasms and its clinical grouping schema (*24*,*25*), 13 patients had indolent lymphomas (low risk), 15 had aggressive lymphomas (intermediate risk), and 2 had very aggressive lymphomas (high risk). Biopsy was performed both of the enlarged lymph node and of the iliac crest bone marrow in every patient. Written informed consent was obtained from all patients, and the study protocol was approved by the ethics committee of Osaka University Graduate School of Medicine.

TABLE 1
Summary of Patient Data

Patient no.	Age (y)	Sex	Clinical group*	Stage†
1	48	F	Indolent	II
2	41	F	Indolent	III
3	49	F	Indolent	III
4	49	F	Indolent	III
5	64	M	Indolent	III
6	31	F	Indolent	IV
7	37	M	Indolent	IV
8	39	F	Indolent	IV
9	54	M	Indolent	IV
10	54	F	Indolent	IV
11	55	F	Indolent	IV
12	66	M	Indolent	IV
13	73	M	Indolent	IV
14	64	M	Aggressive	I
15	79	M	Aggressive	I
16	79	F	Aggressive	I
17	45	F	Aggressive	II
18	70	M	Aggressive	II
19	71	M	Aggressive	II
20	75	M	Aggressive	II
21	82	M	Aggressive	II
22	62	M	Aggressive	III
23	63	M	Aggressive	III
24	66	F	Aggressive	IV
25	66	F	Aggressive	IV
26	69	M	Aggressive	IV
27	72	F	Aggressive	IV
28	75	F	Aggressive	IV
29	14	M	Very aggressive	IV
30	20	M	Very aggressive	IV

*Indolent lymphoma is low risk, aggressive lymphoma is intermediate risk, and very aggressive lymphoma is high risk.
†Stage is based on reference standard.

FDG Studies

Whole-body FDG dedicated PET was performed with a Headtome V/SET 2400W (Shimadzu Co., Kyoto, Japan), which can simultaneously acquire 63 contiguous 3.1-mm-thick sections (20 cm total thickness) in one bed position. Intrinsic resolution was 3.7 mm full width at half maximum at the center, and the sensitivity of the device was 7,300 cps/kBq. All patients fasted for at least 4 h before the examination. Simultaneous emission–transmission scans were obtained 1 h after injection of 370 MBq FDG in two-dimensional mode from the neck to the symphysis and, if warranted by clinical suspicion, of the head and the lower extremities. This scan required three to four bed positions with an acquisition time of 10 min each, resulting in a total scanning time of 30–40 min. Images were reconstructed with an ordered-subset expectation maximization (OS-EM) algorithm (one iteration with 12 ordered subsets).

On the same day as the dedicated PET examination, whole-body FDG hybrid PET was performed with a double-head gamma camera equipped with a coincidence detection system for ^{18}F (E.CAM+; Siemens Medical Systems, Inc., Hoffman Estates, IL). The axial field of view was 38 cm, and the slice thickness was approximately 5 mm. The intrinsic resolution was 4.9 mm full width at half maximum at the center, and sensitivity was 270 cps/kBq. Data acquisition was begun approximately 2 h after FDG administration. Sixty projections were acquired, 15 s per view, in one bed position. Two or three bed positions were used to cover the same axial field of view as for the dedicated PET, and thus the total scanning time was more than 30 min or 45 min, respectively. Data were acquired in two-dimensional mode without attenuation correction. Each dataset was rebinned by single-slice rebinning and reconstructed with an OS-EM algorithm (two iterations with six ordered subsets).

All patients examined with FDG were randomized and the findings qualitatively interpreted in an independent and blinded manner by two nuclear medicine physicians. The hybrid PET images were read before the dedicated PET images, with a few weeks between interpretations. Transaxial and coronal images were reviewed on a high-resolution display. Areas of FDG uptake were classified according to location, intensity, size, shape, and lateral asymmetry. Any foci of FDG uptake that were increased relative to background and not located in areas of physiologically increased uptake were considered suggestive of lymphoma. The final diagnosis was determined by consensus between the two observers.

CIS

All patients underwent CT of the neck, chest, and abdomen/pelvis and ^{67}Ga scanning as CIS. CT scans were obtained within 2 wk of the FDG studies with a HiSpeed Advantage unit (General Electric Medical Systems, Milwaukee, WI). Studies of the neck, chest, and abdomen/pelvis were performed separately. Neck studies were performed with 5-mm-thick contiguous axial sections using the incremental technique. For the chest studies, contiguous 5-mm-thick sections were obtained in the mediastinum and hilum, and 7-mm-thick sections in the remaining area were obtained by helical scanning. Abdominal/pelvic studies were performed with 7-mm-thick contiguous axial sections using the incremental technique. All studies except for those of two patients were performed with 90 mL intravenous nonionic contrast material (iohexol [Om-

nipaque 300 Syringe; Daiichi Pharmaceutical, Tokyo, Japan]), which was administered at a rate of 1.5 mL/s with a power injector. Cervical and thoracic lymph nodes > 1.0 cm in diameter were considered pathologic; lymph nodes in other regions were evaluated according to the standard size criteria for the individual node group (*26*,*27*). Lymph nodes were also considered pathologic if other signs of malignancy, such as high number, central necrosis, or abnormal contrast material enhancement, were encountered. Extranodal involvement was evaluated according to the standard CT criterion, such as unexplained infiltrates or focal abnormalities in normal-sized organs, massively enlarged organs, or enlarged organs with infiltrates.

^{67}Ga scanning was performed within 2 wk of the FDG examination, 48 h after intravenous injection of 74 MBq ^{67}Ga citrate (Nihon Medi-Physics Co., Ltd., Hyogo, Japan). Images were acquired with a double-head large-field-of-view gamma camera (E. CAM+) equipped with medium-energy general-purpose collimators, and three energy peaks of 92, 185, and 300 keV (20%, 15%, and 20% windows, respectively) were used. Whole-body images in anterior and posterior views were obtained (scan speed, 10 cm/min) and supplemented with appropriate SPECT images. SPECT was performed by collecting 32 projections in 180° of rotation at a rate of 50 s per projection. Abnormal ^{67}Ga uptake was defined as any focal or diffuse area of increased activity in a location incompatible with normal anatomy. Although high-dose ^{67}Ga scanning is recommended for detection of lymphoma (*28*), low-dose ^{67}Ga scanning is currently used in Japan. Therefore, only the complementary role of ^{67}Ga scanning to CT was analyzed in this study.

The CIS images were evaluated by two radiologists without knowing the results of the FDG studies other than the diagnosis of NHL. The final diagnosis was also determined by consensus between the two radiologists.

Data Analysis

The true clinical stage of disease (the reference standard) was constructed on the basis of the final overall clinical evaluation, which included all available data (physical examinations, biopsies, FDG studies, and CIS) and all follow-up examinations and studies.

Lesion detectability was analyzed by comparing the findings of the FDG studies and CIS on the basis of the reference standard at the following anatomic sites: supradiaphragmatic region (left and right cervical, left and right supraclavicular, left and right axillary, and mediastinal and hilar), infradiaphragmatic region (para-aortic, abdominal [e.g., mesenteric], left and right iliac, and left and right inguinal), and extranodal region (splenic, bone and bone marrow, and other extranodal sites). Every discrete lesion in the disease site was not counted. The imaging findings were directly compared to determine concordance at the anatomic sites by the two observers. In cases of discordance because of mislocation of the positive site at the border of the anatomic region on FDG images, the findings of the FDG studies were corrected on the basis of CT findings unless the disease stage was changed. Staging accuracy was analyzed by comparing the results of the FDG studies and CIS with each other and with the reference standard.

RESULTS

Representative FDG hybrid PET and dedicated PET images in a patient with multiple NHL lesions (patient 10) are shown in Figure 1. A total of 206 disease sites (100 supradiaphragmatic, 78 infradiaphragmatic, and 28 extranodal) were discovered on the basis of biopsy findings ($n = 60$) or follow-up clinical assessment ($n = 146$). The distribution of these sites obtained by both FDG studies, CIS, and the reference standard is shown in Table 2. Three patients had

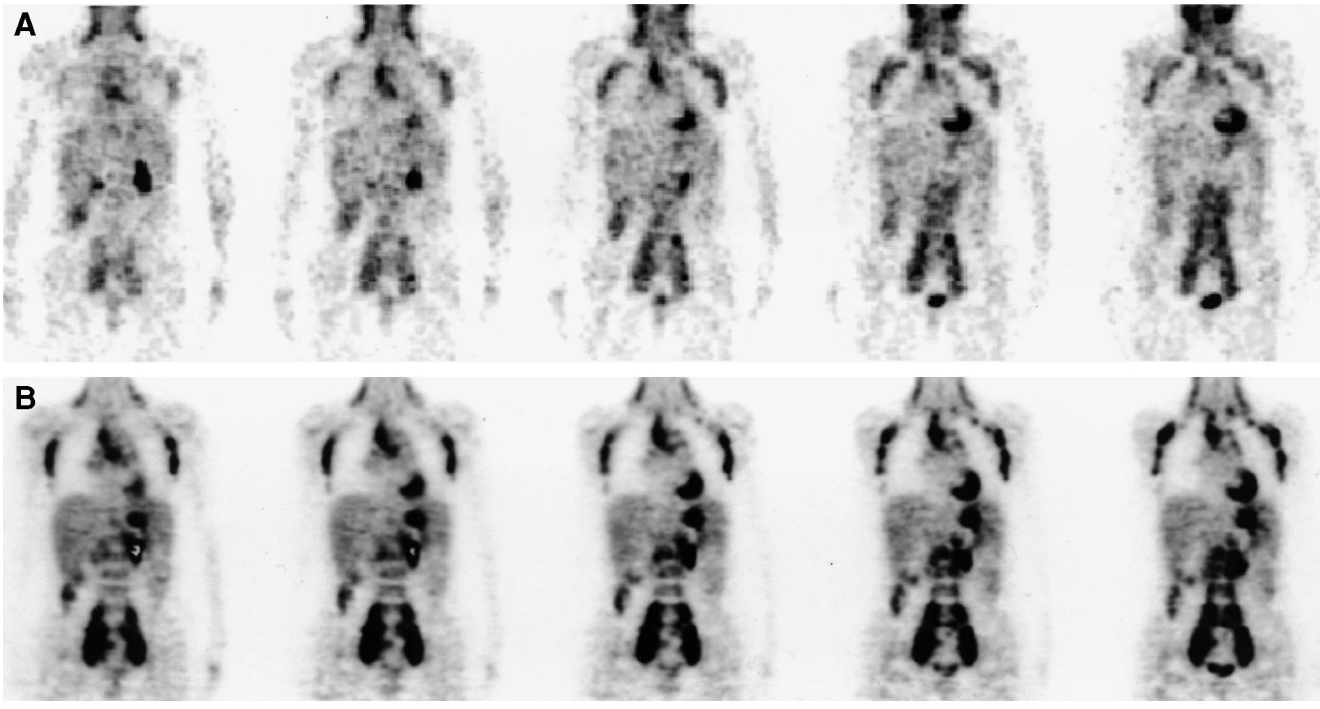

FIGURE 1. Patient 10. Coronal images obtained by FDG hybrid PET (A) and dedicated PET (B). Bilateral cervical to axillary, mediastinal, and para-aortic to bilateral iliac sites are detected on both sets of images. Clearer images and higher lesion-to-background contrast are achieved with dedicated PET than with hybrid PET.

TABLE 2
Distribution of True-Positive Disease Sites Based on FDG Hybrid PET and Dedicated PET, CIS, and Reference Standard

Site	Hybrid PET	Dedicated PET	CIS	Reference standard
Cervical	26	29	28	33
Supraclavicular	23	27	22	29
Axillary	15	18	20	22
Mediastinal and hilar	12	14	13	16
Subtotal: supradiaphragmatic	76	88	83	100
Para-aortic	13	14	13	15
Abdominal	9	9	11	11
Iliac	21	25	20	28
Inguinal	19	20	22	24
Subtotal: infradiaphragmatic	62	68	66	78
Splenic	4	4	3	4
Bone and bone marrow	7	7	1	12
Other extranodal	10	12	11	12
Subtotal: extranodal	21	23	15	28
Total	159	179	164	206

stage I disease, 6 had stage II, 6 had stage III, and 15 had stage IV. Disease stage based on the imaging modalities and the reference standard are compared in Table 3.

Comparison Between FDG Hybrid PET and Dedicated PET

Of the 206 disease sites, whole-body FDG hybrid PET and dedicated PET detected 159 sites (77.2%) and 179 sites (86.9%), respectively: 76 (76.0%) and 88 (88.0%) of the 100 supradiaphragmatic sites, 62 (79.5%) and 68 (87.2%) of the 78 infradiaphragmatic sites, and 21 (75.0%) and 23 (82.1%) of the 28 extranodal sites. Hybrid PET detected 88.8% of the sites found by dedicated PET: 86.4% of the supradiaphragmatic sites, 91.2% of the infradiaphragmatic sites, and 91.3% of the extranodal sites. All sites detected by hybrid PET were the same as those detected by dedicated PET. Dedicated PET detected an additional 20 true-positive sites not detected by hybrid PET: 3 cervical, 4 supraclavicular, 3 axillary, 2 mediastinal, 1 para-aortic, 4 iliac, 1 inguinal, 1 hepatic, and 1 soft-tissue. Of these, 1 supraclavicular site (patient 4; Fig. 2) and 1 liver site were the only sites consisting of lesions $>$ 1.5 cm. Twenty-seven sites were not detected by either FDG study compared with the reference standard. Of these sites, 12 consisted of superficial nodes that were small (approximately 1 cm) but palpable on physical examination. Five cases of bone marrow involvement were also not detected by either FDG study. Dedicated PET showed false-positive findings in patient 3, whose dense beltlike FDG uptake along the splenic flexure of the colon had been diagnosed as positive for NHL but was shown to be negative by endoscopy and biopsy.

In all but 2 patients, concordant staging results were obtained by both FDG studies. In patient 22, with stage III disease, an axillary lesion detected by dedicated PET was missed by hybrid PET, and as a result the NHL was understaged as stage II. Another discordant case was in patient 3, in whom the NHL was overstaged as stage IV by dedicated PET. Compared with the reference standard, both FDG studies understaged 5 stage IV cases because of inability to detect bone marrow involvement. However, hybrid and dedicated PET correctly staged 24 (80.0%) and 24 (80.0%), respectively, of the 30 cases of NHL.

Comparison Between FDG Studies and CIS

Of the 206 disease sites, CT and ^{67}Ga scanning as CIS detected 164 sites (79.6%): 83 (83.0%) of the 100 supradiaphragmatic sites, 66 (84.6%) of the 78 infradiaphragmatic sites, and 15 (53.6%) of the 28 extranodal sites. FDG hybrid PET and CIS yielded concordant results at 137 sites (68 supradiaphragmatic, 55 infradiaphragmatic, and 14 extranodal), but FDG hybrid PET detected an additional 22 sites not detected by CIS: 2 cervical, 4 supraclavicular, 2 mediastinal, 1 para-aortic, 6 iliac, 1 splenic (patient 24; Fig. 3), and 6 bone marrow. Among these 22 sites, 10 of the 15 nodal sites were seen on CT but diagnosed as negative for NHL because of the size criteria (patient 1; Fig. 4). On the other hand, CIS found 27 other sites not detected by FDG hybrid PET: 3 cervical, 3 supraclavicular, 5 axillary, 3 mediastinal, 1 para-aortic, 2 abdominal, 5 iliac, 4 inguinal, and 1 hepatic. One supraclavicular, 1 mediastinal, 1 abdominal, 1 iliac, 2 inguinal, and 1 hepatic site composed lesions $>$ 1.5 cm.

The results of FDG dedicated PET and CIS were concordant at 147 sites (75 supradiaphragmatic, 57 infradiaphragmatic, and 15 extranodal). FDG dedicated PET found 32 other sites not detected by CIS: 3 cervical, 5 supraclavicular, 2 axillary, 3 mediastinal, 2 para-aortic, 8 iliac, 1 inguinal, 1 splenic (patient 24: Fig. 3), 6 bone marrow, and 1 soft-tissue. Among these, 16 of 24 nodal sites were seen on CT but diagnosed as negative for NHL because of the size criteria (patient 1; Fig. 4). CIS, on the other hand, detected an additional 17 sites: 2 cervical, 4 axillary, 2 mediastinal, 1 para-aortic, 2 abdominal, 3 iliac, and 3 inguinal. One abdominal, 1 iliac, and 2 inguinal sites composed lesions $>$ 1.5 cm.

TABLE 3
Comparison of Disease Stage Based on FDG Hybrid PET and Dedicated PET, CIS, and Reference Standard

Stage	Hybrid PET	Dedicated PET	CIS	Reference standard
I	4 (3)	4 (3)	4 (3)	3
II	7 (6)	6 (6)	6 (6)	6
III	9 (5)	9 (5)	15 (6)	6
IV	10 (10)	11 (10)	5 (5)	15

Numbers in parentheses are numbers concordant with reference standard.

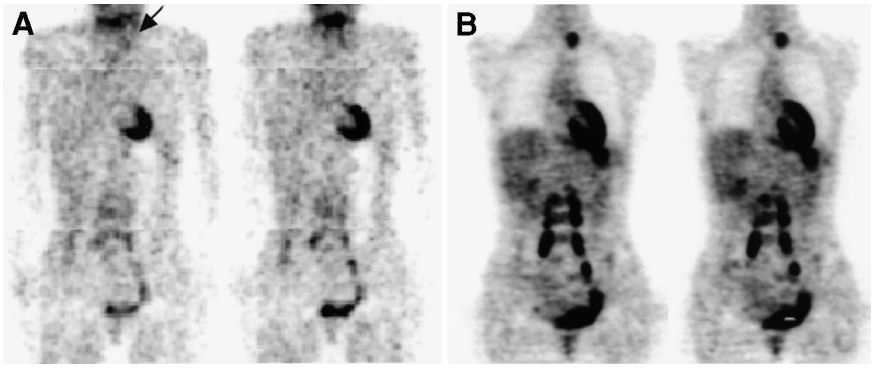

FIGURE 2. Patient 4. Coronal images obtained by FDG hybrid PET (A) and dedicated PET (B). Left supraclavicular site is clearly depicted by dedicated PET. Hybrid PET, on other hand, shows only faint uptake at corresponding site (arrow), which is not considered pathologic.

Except in 1 patient, no differences were seen between the detection of sites of indolent, aggressive, or very aggressive lymphoma by the two FDG studies. In patient 12, who had lymphoplasmacytic lymphoma (indolent lymphoma, low risk), CT detected numerous bulky lesions from the cervical to the inguinal sites. However, both FDG images showed no or only faint uptake by these lesions (Fig. 5).

Even without the results of ^{67}Ga scanning, CT alone detected as many as 161 sites (82 supradiaphragmatic, 66 infradiaphragmatic, and 13 extranodal). All sites detected by ^{67}Ga scanning were also detected by both FDG studies.

Compared with the reference standard, CIS allowed correct staging in 20 (66.7%) of the 30 patients. Staging in 19 of the 20 patients was also correct by both FDG studies. In spite of concordant staging results by both FDG studies and CIS, misdiagnosis occurred in 5 patients because of inability to detect bone marrow involvement, and CIS understaged stage IV disease in an additional 5 patients.

DISCUSSION

FDG dedicated PET has been reported to be of great use in the evaluation of various kinds of tumors, including malignant lymphoma (*5–8*). However, clinical application of FDG dedicated PET is currently limited because of the need for expensive equipment, that is, an in-house cyclotron and a dedicated PET camera. In 1995, the double-head gamma camera with coincidence detection (hybrid PET camera) was first introduced as a new method for FDG imaging; the hybrid PET camera was intended as an alternative to the dedicated PET camera (*29*). Since then, the performance of the hybrid PET camera has been improved dramatically, and the number of devices in use has been increasing rapidly. In their preliminary study, Shreve et al. (*19*) showed that FDG hybrid PET could detect many of the lesions detected by dedicated PET, particularly in the lungs, but that hybrid PET showed poor sensitivity for lesions in the abdomen and lesions < 1.5 cm at all locations outside the lungs. Another group also showed the high sensitivity of FDG hybrid PET for lesions > 1.5 cm, especially in the lungs (*20*). However, to our knowledge, no reports have been published on the validity of whole-body FDG hybrid PET in the staging of malignant lymphoma, and only a few of the FDG PET studies on lymphoma have used whole-body imaging (*14–16*).

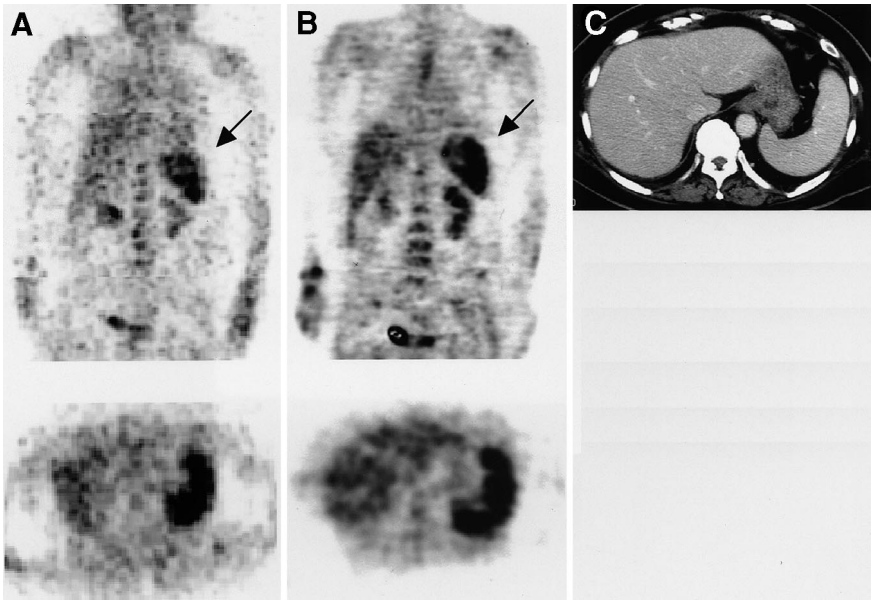

FIGURE 3. Patient 24. Diffuse spleen involvement (arrows) is detected by both FDG hybrid PET (A) and dedicated PET (B) (top: coronal; bottom: axial). (C) CT fails to detect involvement, showing only splenomegaly.

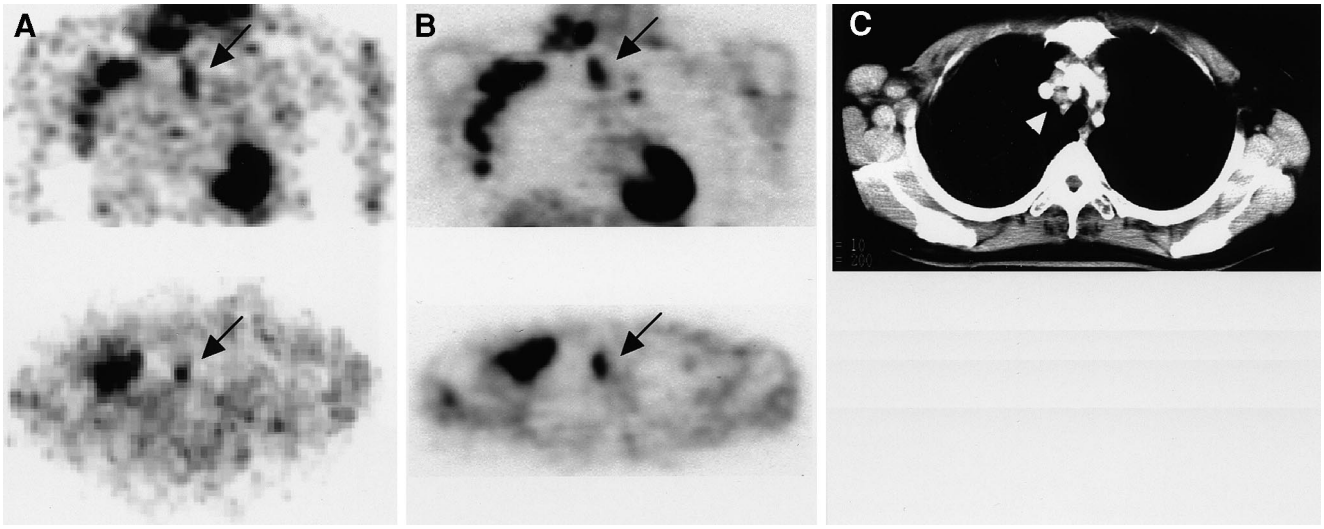

FIGURE 4. Patient 1. Images obtained by FDG hybrid PET (A) and dedicated PET (B) (top: coronal; bottom: axial) show hot uptake at mediastinal site (arrows). Eight-millimeter lesion is seen on CT (arrowhead) but was diagnosed as negative for NHL because of size criteria.

The first purpose of this study was to clarify the feasibility of whole-body FDG hybrid PET, in comparison with dedicated PET, in the staging of NHL. Of the total of 206 disease sites, hybrid and dedicated PET detected 159 and 179 sites, respectively. Hybrid PET failed to detect 20 sites in addition to the 27 sites missed by both FDG studies. As previous studies suggested (*19,20*), most of the lesions at these sites were $<$1.5 cm or were the lesions in the infradiaphragmatic region. However, FDG hybrid PET allowed detection of as many as 88.8% of the sites detected by dedicated PET. Hybrid PET also provided staging results concordant with those of dedicated PET in all but 2 patients and provided correct staging in 24 of 30 patients compared with the reference standard. The FDG dedicated PET images in this study were obtained with a modern, dedicated camera using the simultaneous emission–transmission data acquisition method and OS-EM reconstruction algorithm, and thus they are considered to represent the best quality current technology can provide. The results of FDG dedicated PET were almost completely consistent with those reported previously (*14–16*). FDG hybrid PET, on the other hand, was performed with some disadvantages for detection

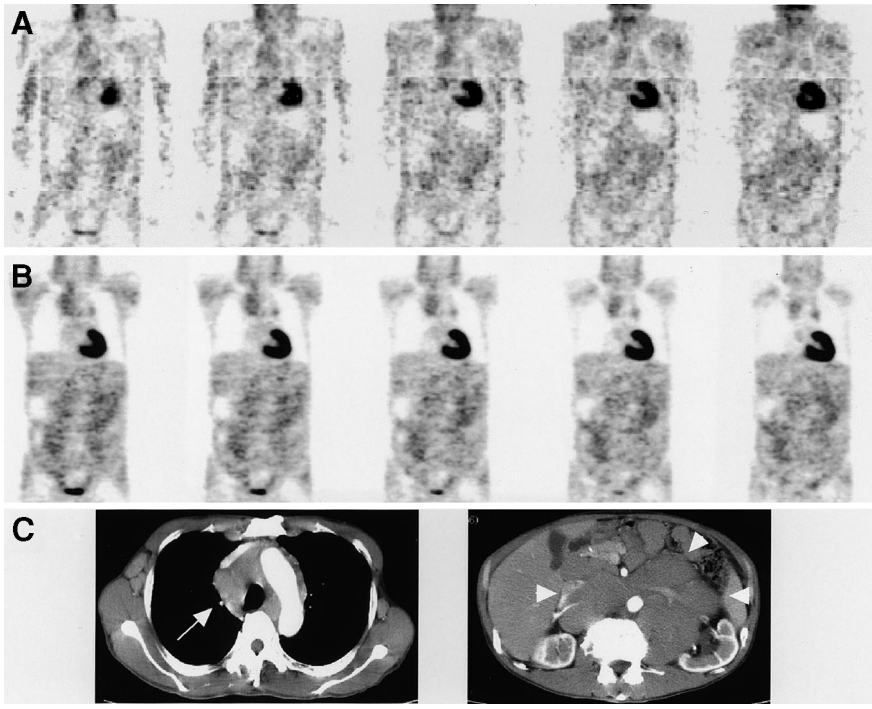

FIGURE 5. Patient 12, with indolent, low-risk lymphoplasmacytic lymphoma. Images obtained by both coronal FDG hybrid PET (A) and dedicated PET (B) show only faint uptake at sites that CT (C) shows to have numerous bulky lesions. Lesions extend from cervical to inguinal regions, including mediastinal (arrow) and para-aortic (arrowheads).

of small lesions. To avoid a long examination time, the acquisition time per bed position was shorter than adopted in published studies (*19*–*23*). The hybrid PET images were obtained without attenuation correction by transmission scanning, because transmission scan sources have yet to be permitted in Japan. However, despite the poorer image quality compared with dedicated PET, hybrid PET provided good results, comparable with those of dedicated PET, in this group of NHL patients. Although some authors have suggested that hybrid PET has a limited ability to detect lesions outside the lungs (*19*,*20*), this study found little difference in detection of sites in the supradiaphragmatic, infradiaphragmatic, and extranodal regions. This phenomenon has several possible reasons. One is that patients with lymphoma often present with swelling of multiple lymph nodes at the site involved. Another is that FDG uptake by lymphoma is reported to be higher than by other malignancies (*30*). A third possible reason is that this study focused on detection of the disease site, not every discrete lesion, and many of the infradiaphragmatic lesions in this study were massive and large. These favorable conditions for hybrid PET may have been responsible for the good results, even in the infradiaphragmatic region, where hybrid PET is considered less likely to detect lesions. Most of the patients in this study were middle-aged or elderly Japanese, who are generally smaller than Western people. This situation also may have favored hybrid PET without attenuation correction. In their phantom study, Coleman et al. (*31*) showed that FDG hybrid PET provided clearer images with attenuation correction than without it and that attenuation-corrected images allowed detection of smaller spheres than did non–attenuation-corrected images. Attenuation correction on hybrid PET is capable of reducing the artificially high apparent uptake in the lung or soft tissue, as seen in the attenuation-corrected dedicated PET images. Of the 20 sites not detected by hybrid PET alone in this study, 11 were in superficial lymph node areas. With attenuation correction, hybrid PET may have detected these sites by virtue of the lower soft-tissue background. Further clinical studies are required to clarify the usefulness of attenuation correction of hybrid PET in the staging of lymphoma.

The second purpose of this study was to compare the results of FDG hybrid PET and dedicated PET with those of CT and ^{67}Ga scanning as CIS. Of the total of 206 disease sites, CIS provided results concordant with those of hybrid PET at 137 sites and with those of dedicated PET at 147 sites. Hybrid PET and dedicated PET found an additional 22 sites and 32 sites, respectively, not detected by CIS. Many of them were seen on CT but were diagnosed as negative for NHL because of the size criteria. Both FDG studies correctly staged 5 cases that were understaged by CIS. CIS, on the other hand, found an additional 27 and 17 sites undetected by hybrid PET and dedicated PET, respectively. However, there was only one site missed by hybrid PET that caused a change in disease stage. These results suggest that both whole-body hybrid PET and dedicated PET are at least comparable with CIS in the staging of lymphoma. Especially noteworthy is that both FDG studies detected bone marrow involvement in 7 of the 12 cases, whereas CIS detected it in only one case, which presented as bone destruction. Moreover, both FDG studies depicted 4 cases of diffuse spleen involvement more clearly than did CIS. In their comparative study, Moog et al. (*32*) showed that FDG dedicated PET provided more information on extranodal lesions than did CT. The results obtained by hybrid PET or dedicated PET in this study were almost the same as in their study. However, in selected indolent lymphomas, such as that in patient 12, neither FDG hybrid PET nor dedicated PET allowed detection of many of the lesions identified by CT. This phenomenon has already been reported by some authors (*33*,*34*), and thus FDG hybrid PET and dedicated PET should be considered inadequate as a single modality for the staging of lymphoma and as complementary to CT instead. Because low-dose ^{67}Ga scanning is unsuitable for the staging of lymphoma (*28*), the complementary role of ^{67}Ga scanning to CT was analyzed in this study. However, ^{67}Ga scanning supplemented the information provided by CT in only 3 of the 30 cases, indicating that low-dose ^{67}Ga scanning plays only a limited complementary role to CT in the staging of lymphoma. In the future, when FDG is readily available, hybrid PET or dedicated PET, instead of ^{67}Ga scanning, will play an effective complementary role to CT in the staging of lymphoma.

This study has certain limitations. First, not all the presumed lesions were confirmed histopathologically. For ethical reasons, most of the discrepant results were discriminated by clinical or imaging follow-up instead of by biopsy. The reference standard, which was defined on the basis of the final overall clinical evaluation (physical examinations, biopsies, imaging studies, and follow-up), may therefore be imperfect. However, this is an inevitable problem inherent in lymphoma imaging in general. Second, a high percentage of patients in this study had stage IV disease. Although more than one third of NHL patients are reported to present with stage IV disease (*1*), the 50% in this study was rather high. The reason for this high percentage may be that this study was conducted at a university hospital, where patients with advanced stage disease tend to concentrate. Third, some of the patients in this study were examined for recurrent disease. However, they were patients who had obtained a complete remission without residual mass and therefore were considered similar to fresh cases except for the history of treatment.

CONCLUSION

Whole-body FDG hybrid PET appeared to be an accurate method of staging NHL. Despite the poorer image quality compared with dedicated PET, FDG hybrid PET yielded results comparable with those of dedicated PET in the staging of NHL. Hybrid PET not only detected most of the involved sites depicted by CIS but also revealed additional

sites not detected by CIS. However, not all sites found by CIS were detected by hybrid PET. Soon, whole-body FDG hybrid PET, instead of ^{67}Ga scanning, will play an effective complementary role to CT in the staging of lymphoma.

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