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^{18}F-FDG PET is superior to ^{67}Ga SPECT in the staging of non-Hodgkin's lymphoma

Fumiyasu YAMAMOTO,*,** Eriko TSUKAMOTO,** Kunihiro NAKADA,** Toshiki TAKEI,** Songji ZHAO,** Masahiro ASAKA* and Nagara TAMAKI**

**Third Department of Internal Medicine and **Department of Nuclear Medicine, Hokkaido University Graduate School of Medicine*

Objective: Our study aims to compare diagnostic accuracy between ^{18}F-FDG PET and ^{67}Ga SPECT in the staging of non-Hodgkin's lymphoma. ***Methods:*** Twenty-eight patients with non-Hodgkin's lymphoma, underwent ^{18}F-FDG PET, ^{67}Ga SPECT and CT for the pretreatment staging of malignant lymphoma between August 1999 and March 2002. ^{18}F-FDG PET imaging was obtained 60 minutes after the intravenous administration of 185 MBq of ^{18}F-FDG. ^{67}Ga SPECT imaging was obtained 2 days after the intravenous administration of 148 MBq of ^{67}Ga. ^{18}F-FDG PET and ^{67}Ga SPECT were performed within one month. Both imagings were performed on the area from the neck to the pelvis. The ^{18}F-FDG PET and ^{67}Ga SPECT findings were compared with the CT findings and the clinical course. ***Results:*** Sixty-six nodal lesions were clinically confirmed. Of these, 32 were identified by both ^{18}F-FDG PET and ^{67}Ga SPECT. The remaining 34 lesions were identified only by ^{18}F-FDG PET. The mean (± SD) sizes of the nodes were 34.7 ± 32.4 mm for ^{18}F-FDG-positive and ^{67}Ga-positive lesions and 15.7 ± 8.3 mm for ^{18}F-FDG-positive and ^{67}Ga-negative lesions ($p < 0.001$). Of the 23 extranodal lesions, 12 were identified by both ^{18}F-FDG PET and ^{67}Ga SPECT, whereas 6 lesions were identified by only ^{18}F-FDG PET. Five lesions were not identified by either technique. No ^{18}F-FDG-negative but ^{67}Ga-positive nodal or extranodal lesions were observed. The difference in findings between the two studies is related to the difference in the size but not in the histology or site of the lesions. ***Conclusion:*** ^{18}F-FDG PET detected significantly more lesions particularly small lesions than ^{67}Ga SPECT. Thus, ^{18}F-FDG PET is considered to be superior to ^{67}Ga SPECT in the staging of non-Hodgkin's lymphoma.

Key words: ^{18}F-FDG, ^{67}Ga citrate, emission computed tomography, non-Hodgkin's lymphoma

INTRODUCTION

ACCURATE STAGING is important in deciding the appropriate treatment for patients with non-Hodgkin's lymphoma.[1] Positron emission tomography (PET) can provide metabolic information useful in the staging of malignant lymphoma. 2-[^{18}F]-fluoro-2-deoxy-D-glucose (^{18}F-FDG) uptake by tumors is proportional to the glycolytic metabolic rate of viable tumor cells, reflecting the increased metabolic demand for glucose.[2] An important role of ^{18}F-FDG as a tumor-seeking agent has been established for various malignant tumors.[3,4] The glucose analog ^{18}F-FDG is transported, phosphorylated, and metabolically trapped in malignant cells. Malignant lymphoma enhances ^{18}F-FDG uptake, indicating a high metabolic activity. The staging of malignant lymphoma utilizing ^{18}F-FDG PET has been reported to be reliable in terms of accuracy, correlation with proliferative activity, and cost effectiveness, as compared with conventional imaging techniques.[5–18]

^{67}Ga imaging has been used for the staging of Hodgkin's disease and high-grade non-Hodgkin's lymphoma, however, it suffers from a low spatial resolution, lack of

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For reprint contact: Fumiyasu Yamamoto, M.D., Department of Nuclear Medicine, Hokkaido University Graduate School of Medicine, Kita 15 Nishi 7, Kita-ku, Sapporo 060–8638, JAPAN.

E-mail: fumiyasu@xb4.so-net.ne.jp

Table 1 Patients' characteristics and imaging results

Patient No.	Age (y)	Sex	Region of nodal lesions	Region of extranodal lesions	FDG-PET finding	SUV	Ga finding	CT size (mm)	Final diagnosis	Grade	Stage		
											Ga	FDG-PET	Final diagnosis
1	48	F	Para-aorta		+		+	120	+	Low	I	I	I
2	58	F		Ileum	–		–		+	Low	0	0	I
3	58	M	Lt/Rt subclavia		+	6.2	+	18/21	+	High	III	III	III
			Lt/Rt axilla		+	3.8	+	22/21	+				
			Para-aorta		+	9.2	+	28	+				
			Left inguen		+	6.2	+	27	+				
			Left neck		+	3.7	–	21	+				
			Mediastinum		+	3.8	–	10	+				
			Left hilus		+	6.9	–	16	+				
			Right inguen		+	6.2	–	17	+				
				Lung	+	6.5	+		+				
				Spleen	+		+		+				
4	48	M	Waldeyer		+	4.7	–	20	+	High	I	IV	IV
			Lt/Rt neck		+	1.7/2.8	–	12/11	+				
				Lung	+	4.9	+	8	+				
				Liver	+	2.7	–	11	+				
5	71	F	Right neck		+	6.4	+	30	+	High	I	III	III
			Left neck		+	6.4	–	19	+				
			Right axilla		+	2.5	–	12	+				
			Lt/Rt inguen		+	3.1	–	13	+				
6	56	M	Waldeyer		+	17.5	+	20	+	Intermediate	II	II	II
			Left neck		+	17	+	21	+				
7	69	M		Stomach	+	12.4	+		+	Intermediate	I	I	I
8	64	M	Left neck		+		+	142	+	High	II	II	II
9	57	F		Colon	–		–		+	High	0	0	IV
10	63	M	Left subclavia		+	6.9	+	53	+	High	III	III	III
			Para-aorta		+	5.6	+	39	+				
11	61	F		Stomach	–		–		+	Low	0	0	I
12	65	F	Waldeyer		+	3.8	+	13	+	Low	II	II	II
			Lt/Rt neck		+	4.2/9.3	+	15/21	+				
			Right axilla		+	4.2	+	17	+				
13	73	F	Lt/Rt subclavia		+	1.6/1.3	+	6/5	+	Low	II	III	III
			Right axilla		+	3.9	+	85	+				
			Left axilla		+	2.5	–	50	+				
				Bone	+	2.9	+		+				
				Orbit	+	2	+		+				
				Stomach	+	3.9	–		+				
14	43	M	Right neck		+	1.7	–	17	+	Low	0	II	II
			Right subclavia		+	1.7	–	15	+				
15	72	M		Stomach	–		–		+	Low	0	0	I
16	53	F	Right neck		+	3.6	+	16	+	Low	I	III	III
			Left neck		+	2.4	–	8	+				
			Para-aorta		+	3	–	14	+				
17	55	M	Para-aorta		+		+	71	+	Intermediate	III	III	III
			Right mesentery		+		+	87	+				
				Bone	+		+		+				

18	36	M	Para-aorta		+	6.6	+	47	+	Low	I	IV	IV
			Lt/Rt neck		+		–	14/21	+				
			Lt/Rt subclavia		+		–	12/10	+				
			Lt/Rt axilla		+		–	6/10	+				
			Lt/Rt mesentery		+		–	10/36	+				
			Lt/Rt inguen		+		–	19/14	+				
				Bone	+		–		+				
				Spleen	+		–		+				
19	17	M	Left neck		+	1.7	–	8	+	Intermediate	0	I	I
20	54	F		Stomach	–		–		+	Low	0	0	I
21	21	M	Para-aorta		+	4.6	+	18	+	High	II	IV	IV
			Lt/Rt mesentery		+	4.6	+	11/14	+				
			Mediastinum		+		–	18	+				
				Bone	+	1.7	–		+				
22	80	F		Thyroid	+	2.5	+	45	+	Low	I	I	I
23	79	F	Waldeyer		+	4.3	+	30	+	Intermediate	I	I	I
24	60	F		Lung	+	2.5	+	17	+	Low	I	I	I
25	74	F	Para-aorta		+	3.9	–	12	+	Intermediate	0	II	II
				Stomach	+	5.7	–		+				
26	49	M		Stomach	+	8.8	+		+	Intermediate	I	I	I
27	64	M	Mediastinum		+		–	20	+	Low	II	II	II
				Thyroid	+		+	56	+				
				Lung	+		+	61	+				
28	60	F	Lt/Rt hilus		+	7/6.3	+	25/32	+	Intermediate	III	III	III
			Para-aorta		+	4.7	+	17	+				
			Left inguen		+	1.4	+	18	+				
			Lt/Rt neck		+	1.4/5.6	–	5/15	+				
			Mediastinum		+	10.8	–	17	+				
			Left mesentery		+	2	–	18	+				

specificity and difficulty in objective assessment of its uptake. Furthermore, its sensitivity is low for infradiaphragmatic disease owing to the physiological uptake in the abdomen, and lack of ^{67}Ga accumulation in low-grade lymphoma.[19] Single photon emission tomography (SPECT) considerably increases the accuracy of ^{67}Ga imaging in the staging of malignant lymphoma.[20–23] However, only limited data are available for direct comparison of ^{18}F-FDG PET with ^{67}Ga whole-body SPECT in the staging of malignant lymphoma.

Our study aims to compare the diagnostic accuracy between ^{18}F-FDG PET and ^{67}Ga whole-body SPECT in the staging of non-Hodgkin's lymphoma.

MATERIALS AND METHODS

Patients

This study focused on 28 patients with non-Hodgkin's lymphoma (NHL) (14 men, 14 women; age range, 17–80 y; mean age, 57.4 ± 15.1 y). The clinical staging showed stage I lymphoma in 11 patients, stage II lymphoma in 6 patients, stage III lymphoma in 7 patients, and stage IV lymphoma in 4 patients. By histological studies, we classified the 28 patients with NHL into three groups: low-grade NHL, 13; intermediate-grade NHL, 8; and high-grade NHL, 7. They all underwent ^{18}F-FDG PET, ^{67}Ga SPECT and CT for the pretreatment staging of malignant lymphoma between August 1999 and March 2002. Informed consent was obtained from all the patients participating in the study.

Imaging

^{18}F-FDG PET and ^{67}Ga SPECT were performed within one month. ^{18}F-FDG PET was performed using ECAT EXACT 47 or HR+ (Siemens; Knocksville, TN). After fasting for at least 6 hours, and about 60 minutes after ^{18}F-FDG administration, a whole-body emission scan and a transmission scan for attenuation correction were obtained with 128 × 128 matrices in the area covering the neck, thorax, abdomen and pelvis. The average ^{18}F-FDG injection dose was 185 MBq. These images were reconstructed by OSEM. The total acquisition time was about 30 minutes.[24,25]

^{67}Ga SPECT imaging was performed within one month before or after ^{18}F-FDG PET imaging. Planar and SPECT images were obtained using ECAM (Siemens;

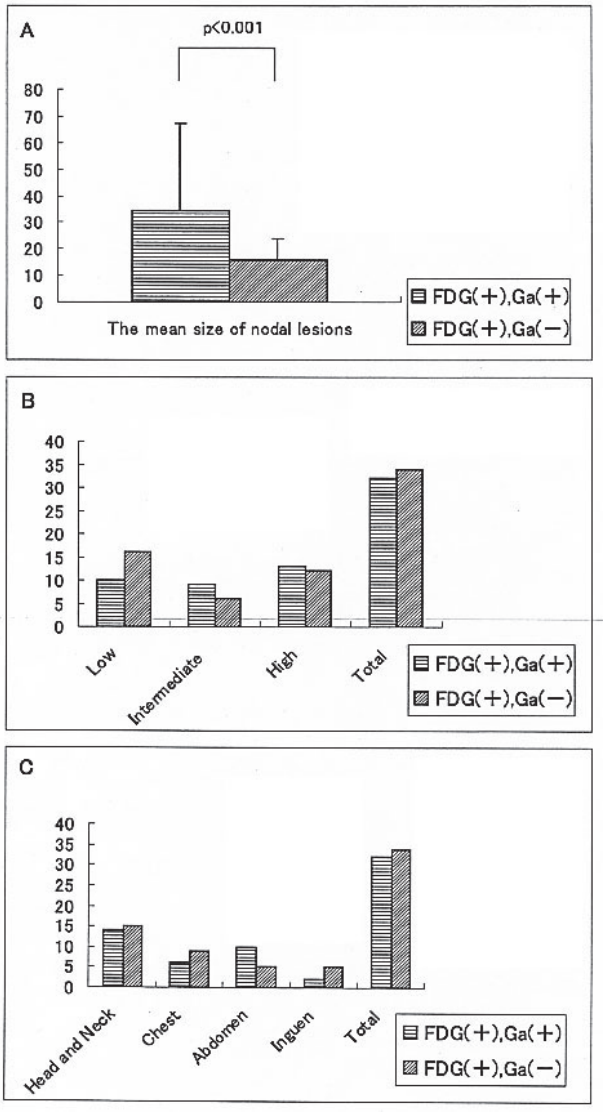

Fig. 1 Mean size of nodal lesions (A); classification according to the histologic type (nodal lesions) (B); classification according to the area of nodal lesions (C).

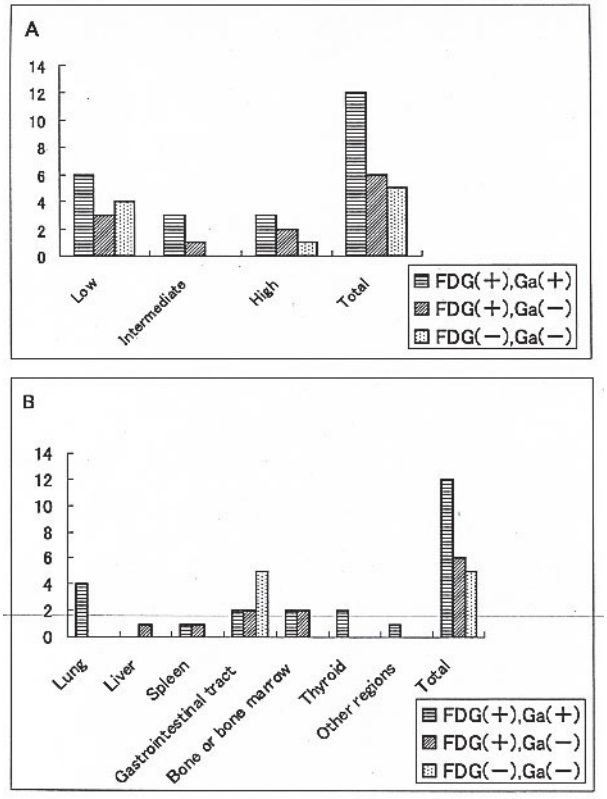

Fig. 2 Classification according to the histologic type (extranodal lesions) (A); classification according to the area of extranodal lesions (B).

Knocksville, TN) 2 days after the intravenous administration of 148 MBq of ^{67}Ga citrate. Immediately after the planar imaging, SPECT images were also obtained by collecting 64 views for 20 seconds in each field of view with 64 × 64 matrices. Three SPECT images of the area covering the neck, thorax, abdomen, and pelvis were obtained. The SPECT was reconstructed by filtered back projection without attenuation correction. The total acquisition time was about 80–90 minutes.

Whole-body CT was performed using Aquillion (Toshiba; Tochigi) or Somatom Plus 4 (Siemens; Erlangen).

Analysis

^{18}F-FDG PET and ^{67}Ga SPECT images were visually interpreted by at least two experienced nuclear physicians by consensus and correlated carefully with the CT images at the same time. The lesions were considered positive if a definite localized area of higher uptake than that in the surrounding normal tissue was present, except for the physiologic uptake. The regions of nodal lesions were divided into 15 areas: Waldeyer, left and right neck, left and right subclavicles, left and right axillae, mediastinum, left and right hili, para-aorta, left and right mesenteries, left and right inguina. They were grouped into four areas: head and neck (Waldeyer, left and right neck, left and right subclavicles), chest (left and right axillae, mediastinum, left and right hili), abdomen (para-aorta, left and right mesenteries), and inguen (left and right inguina). The regions of extranodal lesions were divided into seven areas: lung, liver, spleen, gastrointestinal tract, bone or bone marrow, thyroid and other regions. Multiple lesions in one area were defined as a single lesion. The size of the largest nodal or extranodal lesions in each area was defined as maximal diameter determined by CT images. The ^{18}F-FDG PET and ^{67}Ga SPECT findings were compared with the CT findings, histological findings, and clinical course. We considered the lesions to be negative when the lesion size did not change for six months in cases in which histological confirmation was available.

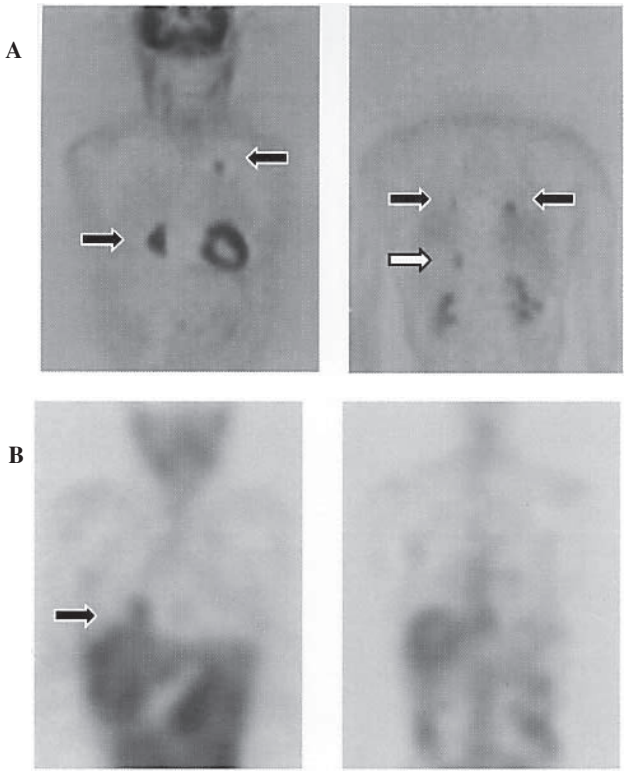

Fig. 3 A 48-year-old man with Stage IV NHL (Patient 4). ^{18}F-FDG PET images reveal intense accumulation of ^{18}F-FDG in multiple lung lesions (*black arrow*) and a liver lesion (A). ^{67}Ga SPECT images reveal accumulation of ^{67}Ga limited to a single lung (*black arrow*) (B). This case was understaged by ^{67}Ga SPECT compared with ^{18}F-FDG PET (Stage I to IV).

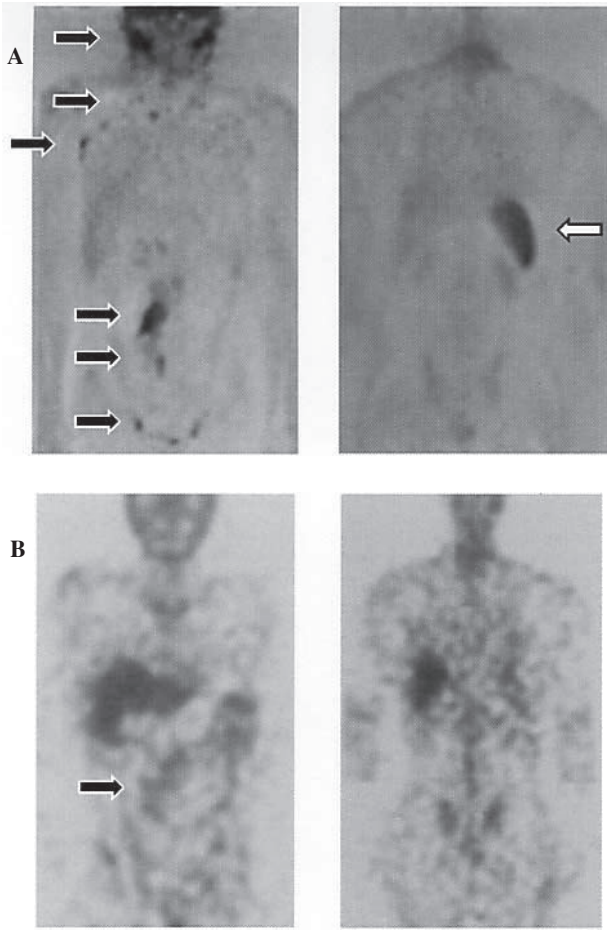

Fig. 4 A 36-year-old man with Stage IV NHL (Patient 18). ^{18}F-FDG PET images reveal intense accumulation of ^{18}F-FDG in the neck, subclavia, axilla, para-aorta, mesentery, inguen (*black arrow*), and spleen (*white arrow*) (A). ^{67}Ga SPECT images only show accumulation of ^{67}Ga in the para-aorta (*black arrow*) (B). This case was understaged by ^{67}Ga SPECT compared with ^{18}F-FDG PET (Stage I to IV).

Statistical analysis

Lesion size was shown as mean ± SD value. The ^{18}F-FDG PET and ^{67}Ga SPECT findings were compared using 2-tailed Student's t test for unpaired data. A p value less than 0.05 was considered to be statistically significant.

RESULTS

Sixty-six nodal lesions were clinically confirmed (Table 1). Of these, 32 were identified by both ^{18}F-FDG PET and ^{67}Ga SPECT. The remaining 34 lesions were identified only by ^{18}F-FDG PET. On the other hand, there were no ^{18}F-FDG negative but ^{67}Ga positive lesions. The mean nodal size of the ^{18}F-FDG-positive and ^{67}Ga-positive lesions was 34.7 ± 32.4 mm while the ^{18}F-FDG-positive and ^{67}Ga-negative lesions were significantly smaller (15.7 ± 8.3 mm) ($p < 0.001$) (Fig. 1A).

The histological analyses confirmed 26 low-grade NHL, 15 intermediate-grade NHL, and 25 high-grade NHL. The 32 ^{18}F-FDG-positive and ^{67}Ga-positive nodal lesions consisted of 10 low-grade NHL (38%), 9 intermediate-grade NHL (60%), and 13 high-grade NHL (52%). The remaining 34 ^{18}F-FDG-positive and ^{67}Ga-negative nodal lesions consisted of 16 low-grade NHL (62%), 6 intermediate-grade NHL (40%), and 12 high-grade NHL (48%) (Fig. 1B). Thus, ^{18}F-FDG PET or ^{67}Ga SPECT findings are not related to the histologic type of nodal lesion.

The 32 ^{18}F-FDG-positive and ^{67}Ga-positive nodal lesions were distributed as follows: 14 in the head and neck areas, 6 in the chest area, 10 in the abdominal area, and 2 in the inguinal area. The remaining 34 ^{18}F-FDG-positive and ^{67}Ga-negative nodal lesions were distributed as follows: 15 in the head and neck areas, 9 in the chest area, 5 in the abdominal area, and 5 in the inguinal area (Fig. 1C). Thus, ^{18}F-FDG PET or ^{67}Ga SPECT findings are not related to the sites of nodal lesions.

Twenty-three extranodal lesions were clinically confirmed. Of these, twelve were identified by both ^{18}F-FDG PET and ^{67}Ga SPECT. Six of the remaining 11 lesions were identified only by ^{18}F-FDG PET, but five lesions

were not identified by either technique. The lesion size was obtained only in 6 lesions by CT. The mean extranodal size of the ^{18}F-FDG-positive and ^{67}Ga-positive lesions was 37.8 ± 28.5 mm (n = 5), whereas the size of ^{18}F-FDG-positive and ^{67}Ga-negative lesions was small (11 mm: n = 1). Three of these five lesions were in the stomach, another was in the colon and the other was in the ileum. No ^{18}F-FDG-negative but ^{67}Ga-positive lesions were observed.

In the histological analyses, the 12 ^{18}F-FDG-positive and ^{67}Ga-positive extranodal lesions consisted of six low-grade NHL, three intermediate-grade NHL, and three high-grade NHL. The six ^{18}F-FDG-positive but ^{67}Ga-negative extranodal lesions consisted of three low-grade NHL, one intermediate-grade NHL, and two high-grade NHL. The five lesions which were not identified by either technique consisted of four low-grade NHL and one high-grade NHL lesions (Fig. 2A). These five lesions were histologically confirmed by endoscopic examination. Thus, ^{18}F-FDG PET or ^{67}Ga SPECT findings were not related to the histologic type of extranodal lesions.

The 12 ^{18}F-FDG-positive and ^{67}Ga-positive extranodal lesions were distributed as follows: four in the lungs, one in the spleen, two in the gastrointestinal tract, two in the bones or bone marrow, two in the thyroid, and one in other regions. The six ^{18}F-FDG-positive but ^{67}Ga-negative extranodal lesions were distributed as follows: one in the liver, one in the spleen, two in the gastrointestinal tract, and two in the bones or bone marrow (Fig. 2B). Most lesions in the liver, spleen, gastrointestinal tract, and bone or bone marrow were identified only by ^{18}F-FDG PET.

In the clinical staging of the 28 patients, nine patients (32%) were upstaged by additionally performing ^{18}F-FDG PET, whereas none were downstaged when compared with ^{67}Ga SPECT (Table 1).

Case presentations

Figure 3 shows ^{18}F-FDG PET images (A) and ^{67}Ga SPECT images (B) of a 48-year-old man with Stage IV NHL (Patient 4). ^{18}F-FDG PET images reveal intense accumulation in multiple lung lesions and a liver lesion. ^{67}Ga SPECT images only reveal accumulation of ^{67}Ga in the single lung. This case was understaged by ^{67}Ga SPECT compared with ^{18}F-FDG PET (Stage I to IV).

Figure 4 shows ^{18}F-FDG PET images (A) and ^{67}Ga SPECT images (B) of a 36-year-old man with Stage IV NHL (Patient 18). ^{18}F-FDG PET reveals intense accumulation in the neck, subclavia, axilla, para-aorta, mesentery, inguen, and spleen. ^{67}Ga SPECT images show only accumulation in the para-aorta. This case was understaged by ^{67}Ga SPECT compared with ^{18}F-FDG PET (Stage I to II).

DISCUSSION

Our principal finding in this study is that ^{18}F-FDG PET enables the identification of more nodal and extranodal lesions than ^{67}Ga SPECT in the staging of non-Hodgkin's lymphoma. On the other hand, there were no lesions that were ^{18}F-FDG-negative but ^{67}Ga-positive. The difference in findings between the two studies were related to the differences in the size but not in the histology or site of the lesions. Thus, ^{18}F-FDG PET is considered to be superior to ^{67}Ga SPECT in the staging of non-Hodgkin's lymphoma.

^{67}Ga imaging can provide important diagnostic information for the evaluation of lymphoma patients. It is superior to morphologic imaging techniques because of its affinity to viable lymphoma cells. It provides additional information on previously unsuspected sites of the disease that are not detected by other imaging modalities.[26–28] Nevertheless, ^{67}Ga imaging has not achieved the expected wide acceptance, possibly because of the meticulous technique and expertise required for optimal interpretation of the findings.[29] The use of SPECT considerably increases the accuracy of ^{67}Ga imaging in the staging of malignant lymphoma.[20–23] However, ^{18}F-FDG PET, which provides images whose quality is superior to that of images obtained by ^{67}Ga SPECT, may have an impact on the current role of ^{67}Ga SPECT in the management of lymphoma patients. ^{18}F-FDG PET has several advantages over ^{67}Ga SPECT. PET does not require a collimator system and thus provides a higher sensitivity, and therefore, a shorter acquisition time with less statistical noise as compared with ^{67}Ga SPECT, which requires medium-energy collimators. In addition, PET provides much higher spatial resolution images (5–7 mm in FWHM) than ^{67}Ga SPECT (15–20 mm in FWHM). These physical advantages of the PET system over SPECT permit the realization of a higher target-to-background ratio, and thus, the detection of smaller lesions with more reliable interpretation of the images. ^{18}F-FDG PET reduces nonspecific abdominal uptake and acquisition time with higher sensitivity for lymphoma detection.[30–33] The current study confirmed a previous report showing that ^{18}F-FDG PET enables the detection of significantly smaller nodal lesions than those detected by ^{67}Ga images, even with use of SPECT. Another advantage of ^{18}F-FDG PET is that imaging can be performed only 60 minutes after tracer administration as compared with 48–72 hours in the study of ^{67}Ga imaging. Therefore, the imaging results can be obtained quickly. Such quick reports have clinical importance for the appropriate management of patients with malignant lymphoma.

The sensitivity of ^{67}Ga scan in the evaluation of lymphoma is highly dependent on cell type and the size and location of the lesion.[34,35] It is reported that the sensitivity of ^{67}Ga imaging for low-grade lymphoma is significantly less than that for HD and intermediate-or-high-grade

NHL since gallium avidity for low-grade lymphoma is low.[36] Leskinen-Kallio et al. assessed quantitative ^{18}F-FDG uptake in 14 untreated patients with lymphoma and found an increase in FDG uptake directly proportional to histological grading.[6] However, the present study showed no relationships between histologic type and the rate of nodal or extranodal lesion detection by ^{18}F-FDG PET or ^{67}Ga SPECT. These different results as compared to the previous reports may be attributed to slightly higher sensitivity for detecting low grade lymphoma by ^{67}Ga-SPECT. Further study is warranted to confirm the present results with greater numbers of patient. On the other hand, the present study showed that the lesions identified by both techniques were significantly larger than those identified only by ^{18}F-FDG PET.

It is also reported that the lymphoma site may affect the sensitivity of ^{67}Ga scan.[35] ^{67}Ga imaging has a high sensitivity and specificity for the detection of mediastinal diseases.[34] The sensitivity for the detection of abdominal diseases is low. However, the present study demonstrated that the area of nodal lesions was not related to the rate of nodal lesion detection by ^{18}F-FDG PET or ^{67}Ga SPECT. The detection of hepatic and/or splenic involvement using this imaging technique is difficult because of the physiological uptake of ^{67}Ga by these organs. The present study indicated that most lesions of the liver, spleen, gastrointestinal tract, and bone or bone marrow were identified only by ^{18}F-FDG PET. ^{18}F-FDG PET appears to be more sensitive and accurate for detecting nodal and extranodal lesions than ^{67}Ga SPECT.

There are a number of limitations in the current study. First, all the lesions were clinically confirmed by a follow-up study. Moreover, not all of the lesions were histologically confirmed. In practice, it is rather difficult to compare the radionuclide findings in all lesions with only histologic confirmation in the staging of malignant lymphoma. Second, most of the assessments required subjective interpretation. To minimize the error in the interpretations, each image was visually assessed by at least two experienced nuclear medicine physicians by consensus and correlated with the CT images at the same time. Also, the number of patients was quite limited. Although the current study showed significantly small lesions detected only by ^{18}F-FDG PET, this did not reveal the difference between the radionuclide findings and histology or site of the lesions. To verify this preliminary finding, more patient data may be required. Also ^{67}Ga imaging was acquired at 48 hours after tracer administration in order to obtain higher counts which may be more suitable for SPECT imaging. But this imaging protocol may cause higher background activity.

CONCLUSION

^{18}F-FDG PET detected significantly more lesions, particularly small lesions than ^{67}Ga SPECT during the staging of non-Hodgkin's lymphoma. The differences between the two imaging findings were related to the difference in the size but not in the histology or site of the lesions. Thus ^{18}F-FDG PET is considered to be superior to ^{67}Ga SPECT in the study of non-Hodgkin's lymphoma.

REFERRENCES

1. Schoder H, Meta J, Yap C, Ariannejad M, Rao J, Phelps ME, et al. Effect of whole-body (^{18})F-FDG PET imaging on clinical staging and management of patients with malignant lymphoma. *J Nucl Med* 2001; 42: 1139–1143.
2. Som P, Atkins HL, Bandoyphadhyay D, Fowler JS, MacGregor RR, Matsui K, et al. A fluorinated glucose analog, 2-fluoro-2-deoxy-D-glucose (F-18). *J Nucl Med* 1980; 21: 670–675.
3. Schiepers C, Hoh CK. Positron emission tomography as a diagnostic tool in oncology. *Eur Radiol* 1998; 8: 1481–1494.
4. Rigo P, Paulus P, Kaschten BJ, Hustinx R, Bury T, Jerusalem G, et al. Oncological applications of positron emission tomography with fluorine-18 fluorodeoxyglucose. *Eur J Nucl Med* 1996; 23: 1641–1674.
5. Newman JS, Francis IR, Kaminski MS, et al. Imaging of lymphoma with PET with 2-[^{18}F]fluoro-2-deoxy-D-glucose: correlation with CT. *Radiology* 1994; 190: 111–116.
6. Leskinen-Kallio S, Ruotsalainen U, Nagren K, Teras M, Joensuu H. Uptake of carbon-11-methionine and fluorodeoxyglucose in non-Hodgkin's lymphoma: a PET study. *J Nucl Med* 1991; 32: 1211–1218.
7. Jerusalem G, Warland V, Najjar F, Paulus P, Fassotte MF, Fillet G, et al. Whole- body ^{18}F-FDG PET for the evaluation of patients with Hodgkin's disease and non-Hodgkin's lymphoma. *Nucl Med Commun* 1999; 20: 13–20.
8. Hoh CK, Glaspy J, Rosen P, et al. Whole-body FDG-PET imaging for staging of Hodgkin's disease and lymphoma. *J Nucl Med* 1997; 38: 343–348.
9. Valk PE, Pounds TR, Wolkow HB, et al. PET-FDG whole-body imaging in staging Hodgkin's disease: comparison to conventional imaging. *J Nucl Med* 1995; 36: 199P.
10. Moog F, Bangerter M, Diederichs CG, et al. Lymphoma: Role of whole-body 2-deoxy-2[F-18]fluoro-D-glucose (FDG) PET in nodal staging. *Radiology* 1997; 203: 795–800.
11. Cremerius U, Fabry U, Neuerburg J, Zimny M, Osieka R, Buell U. Positron emission tomography with ^{18}F-FDG to detect residual disease after therapy for malignant lymphoma. *Nucl Med Commun* 1998; 19: 1055–1063.
12. Stumpe KD, Urbinelli M, Steinert HC, Glanzmann C, Buck A, von Schulthess GK. Whole-body positron emission tomography using fluorodeoxyglucose for staging of lymphoma: effectiveness and comparison with computed tomography. *Eur J Nucl Med* 1998; 25: 721–728.
13. Rodriguez M, Ahlstrom H, Sundin A, Rehn S, Sundstrom C, Hagberg H, et al. ^{18}F FDG PET in gastric non-Hodgkin's lymphoma. *Acta Oncol* 1997; 36: 577–584.
14. Moog F, Bangerter M, Diederichs CG, Guhlmann A, Merkle E, Frickhofen N, et al. Extranodal malignant lymphoma: detection with FDG PET versus CT. *Radiology* 1998; 206: 475–481.

15. Bangerter M, Moog F, Buchmann I, Kotzerke J, Griesshammer M, Hafner M, et al. Whole-body 2-[^{18}F]-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) for accurate staging of Hodgkin's disease. *Ann Oncol* 1998; 9: 1117–1122.
16. Jerusalem G, Beguin Y, Fassotte MF, Najjar F, Paulus P, Rigo P, et al. Whole-body positron emission tomography using ^{18}F-fluorodeoxyglucose for posttreatment evaluation in Hodgkin's disease and non-Hodgkin's lymphoma has higher diagnostic and prognostic value than classical computed tomography scan imaging. *Blood* 1999; 94: 429–433.
17. Bangerter M, Kotzerke J, Griesshammer M, Elsner K, Reske SN, Bergmann L. Positron emission tomography with 18-fluorodeoxyglucose in the staging and follow up of lymphoma in the chest. *Acta Oncol* 1999; 38: 799–804.
18. Wiedmann E, Baican B, Hertel A, Baum RP, Chow KU, Knupp B, et al. Positron emission tomography (PET) for staging and evaluation of response to treatment in patients with Hodgkin's disease. *Leuk Lymphoma* 1999; 34: 545–551.
19. Kostakoglu L, Goldsmith SJ. Fluorine-18 fluorodeoxyglucose positron emission tomography in the staging and follow-up of lymphoma: is it time to shift gear? *Eur J Nucl Med* 2000; 27: 1564–1578.
20. Bekerman C, Hoffer PB, Bitran JD. The role of gallium-67 in the clinical evaluation of cancer. *Semin Nucl Med* 1985; 14: 296–323.
21. Anderson KC, Lew MA, Gorgone BC, Martel J, Leamy CB, Sullivan B. High-dose gallium imaging in lymphoma. *Am J Med* 1983; 75: 327–331.
22. Front D, Israel O, Epelbaum R, et al. Ga-67 SPECT before and after treatment of lymphoma. *Radiology* 1990; 175: 515–519.
23. Tumeh SS, Rosenthal DS, Kaplan WD, English RJ, Holman BL. Lymphoma: Evaluation with Ga-67 SPECT. *Radiology* 1987; 164: 111–114.
24. Shiga T, Tsukamoto E, Nakada K, Morita K, Kato T, et al. Comparison of ^{18}F-FDG, ^{131}I-Na, and ^{201}Tl in diagnosis of recurrent or metastatic thyroid carcinoma. *J Nucl Med* 2001; 42: 414–419.
25. Kato T, Tsukamoto E, Kuge Y, Katoh C, Nambu T, Nobuta A, et al. Clinical role of ^{18}F-FDG PET for initial staging of patients with extrahepatic bile duct cancer. *Eur J Nucl Med* 2002; 29: 1047–1054.
26. Seabold JE, Votaw ML, Keyes JW Jr, Foley WD, Balachandran S, Gill SP, et al. Gallium-67 citrate scanning. *Arch Intern Med* 1976; 136: 1370–1374.
27. Rudders RA, McCaffrey JA, Kahn PC. The relative roles of gallium-67-citrate scanning and lymphangiography in the current management of malignant lymphoma. *Cancer* 1977; 40: 1439–1443.
28. Longo DL, Schilsky RL, Blei L, Cano R, Johnston GS, Young RC. Gallium-67 scanning: Limited usefulness in staging patients with non-Hodgkin's lymphoma. *Am J Med* 1980; 68: 695–700.
29. Bar-Shalom R, Mor M, Yefremov N, Goldsmith SJ. The value of Ga-67 scintigraphy and F-18 fluorodeoxyglucose positron emission tomography in staging and monitoring the response of lymphoma to treatment. *Semin Nucl Med* 2001; 31: 177–190.
30. Morris J. The stage is set for the diffusion of positron emission tomography in oncology. *Med J Aust* 1999; 171: 527–528.
31. Willkomm P, Palmedo H, Grunwald F, Ruhlmann J, Biersack HJ. Functional imaging of Hodgkin's disease with FDG-PET and gallium-67. *Nuklearmedizin* 1998; 37: 251–253.
32. Paul R. Comparison of fluorine-18-2-fluorodeoxyglucose and gallium 67 citrate imaging for detection of lymphoma. *J Nucl Med* 1987; 28: 288–292.
33. Okada J, Yoshikawa K, Imazeki K, Minoshima S, Uno K, Itami J, et al. The use of FDG PET in the detection and management of malignant lymphomas: correlation of uptake with prognosis. *J Nucl Med* 1991; 32: 686–691.
34. Kostakoglu L, Yeh SDJ, Portlock C, Heelan R, Yao TJ, Niedzwiecki D, et al. Validation of gallium-67 citrate single photon emission tomography in biopsy-confirmed residual Hodgkin's disease in the mediastinum. *J Nucl Med* 1992; 33: 345–350.
35. Bartold SP, Donohue KJ, Fletcher JW, Haynie TP, Henkin RE, Silberstein EB, et al. Procedure guideline for gallium scintigraphy in the evaluation of malignant disease. *J Nucl Med* 1997; 38: 990–994.
36. Gallamini A, Biggi A, Fruttero A, Pugno F, Cavallero G, Pregno P, et al. Revisiting the prognostic role of gallium scintigraphy in low-grade non-Hodgkin's lymphoma. *Eur J Nucl Med* 1997; 24: 1499–1506.