

Comparison of gallium-67 citrate and technetium-99m tetrofosmin scan to detect Hodgkin's disease

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Objective: The purpose of this study was to compare the usefulness of gallium-67 citrate (^{67}Ga) and technetium-99m tetrofosmin (Tc-TF) scan to detect Hodgkin's disease (HD). **Methods:** In this study, 24 patients with HD underwent ^{67}Ga and Tc-TF scan before receiving any therapy. **Results:** ^{67}Ga scan could detect HD in all 24 (100%) patients. Tc-TF scan could detect HD in 22/24 (91.6%) patients, but it was false-negative in one case of infradiaphragmatic HD and in another case with chemotherapy resistance. There was no significant difference in detection sensitivity between ^{67}Ga and Tc-TF scan. **Conclusions:** We conclude that Tc-TF scan can not replace conventional ^{67}Ga scan to detect HD.

Key words: gallium-67 citrate, technetium-99m tetrofosmin, Hodgkin's disease

INTRODUCTION

A WHOLE BODY SCAN for the initial staging of Hodgkin's disease (HD) is necessary for two purposes: localization of active disease and assessment of the systemic spread of the disease. Whole body fluorine-18-deoxyglucose (FDG-PET) is the most sensitive tool to detect non-Hodgkin's lymphoma.¹ However, it is often not available and is expensive. In 1968, Gallium-67 citrate (^{67}Ga) was used for the first time to demonstrate the presence of HD.² It seems to behave as an analogue of the ferric ion, accumulating within the tumor cell by simple diffusion and possible penetration via the calcium channels. Many studies have demonstrated the value of ^{67}Ga scan to detect HD.^{3,4} However, ^{67}Ga does have several disadvantages including physical properties poorly adapted to the gamma

camera, an osteotropic nature, dose-dependent sensitivity, higher irradiation, and intestinal elimination.^{5,6} Technetium-99m tetrofosmin (Tc-TF) scan has been tried successfully to detect HD.^{7,8} However, the utility of ^{67}Ga and Tc-TF scans to detect HD has not been compared. This prompted us to compare ^{67}Ga and Tc-TF scans to detect HD before treatment.

PATIENTS AND METHODS

Patients

Before receiving any therapy, 24 patients (14 men, 10 women; aged: 28 to 62 years) with biopsy proven and untreated HD underwent ^{67}Ga and Tc-TF scans (Table 1). Classification of HD at diagnosis was based on Lukes and Butler system for HD.⁹ Positive ^{67}Ga or Tc-TF scan results were confirmed by CT scan and proven by biopsy findings.

^{67}Ga scan

Patients received a laxative (bisacodyl) the day before ^{67}Ga scan. The equipment consisted of a large

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Table 1 Detailed data of patients in this study

Case No.	Sex	Age (years)	Tumor stage	B symptoms	Scan results	
					Tc-TF	⁶⁷ Ga
1	F	28	II	Yes	Positive	Positive
2	F	30	II	Yes	Positive	Positive
3	F	35	II	Yes	Negative	Positive
4	F	36	III	Yes	Negative	Positive
5	F	38	II	Yes	Positive	Positive
6	F	40	II	Yes	Positive	Positive
7	F	40	II	Yes	Positive	Positive
8	F	43	II	Yes	Positive	Positive
9	F	53	III	Yes	Positive	Positive
10	F	60	III	Yes	Positive	Positive
11	M	33	IV	No	Positive	Positive
12	M	35	IV	No	Positive	Positive
13	M	45	IV	No	Positive	Positive
14	M	47	IV	No	Positive	Positive
15	M	51	I	Yes	Positive	Positive
16	M	53	IV	Yes	Positive	Positive
17	M	55	I	Yes	Positive	Positive
18	M	55	IV	Yes	Positive	Positive
19	M	56	IV	No	Positive	Positive
20	M	59	IV	No	Positive	Positive
21	M	60	IV	No	Positive	Positive
22	M	61	IV	No	Positive	Positive
23	M	62	IV	No	Positive	Positive
24	M	62	IV	No	Positive	Positive

F: female, M: male, Tc-TF: technetium-99m tetrofosmin, ⁶⁷Ga: gallium-67 citrate

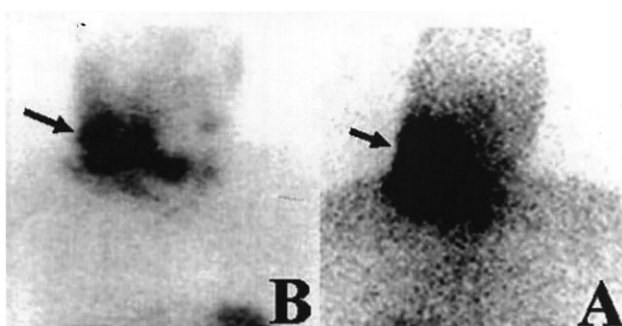


Fig. 1 (A) The ⁶⁷Ga and (B) Tc-TF scans show abnormal one large mass in the right neck (*arrow*).

field-of-view gamma camera fitted with a high-resolution medium-energy collimator. Whole-body scan with ⁶⁷Ga was obtained 72 h after injection of 185 MBq (5 mCi) of ⁶⁷Ga, on the three peaks of Ga-67 (93 keV, 184 keV and 300 keV). Evaluation of ⁶⁷Ga scan was based on visual analysis by at least two of three nuclear medicine physicians blinded to the patients' clinical data. ⁶⁷Ga uptake \geq soft-tissue background was considered as a positive ⁶⁷Ga scan result (Figs. 1–3); otherwise it was considered as a negative result.¹⁰ For the patient with multiple lesions, the scan result was considered as positive if at least

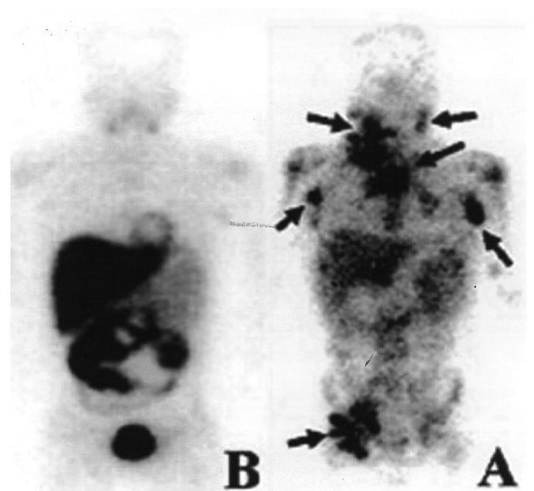


Fig. 2 (A) The ⁶⁷Ga scan shows multiple masses in the bilateral necks, bilateral axillary regions, mediastinum, and the right inguinal regions (*arrows*). (B) The Tc-TF scan shows no definitely abnormal tracer uptake.

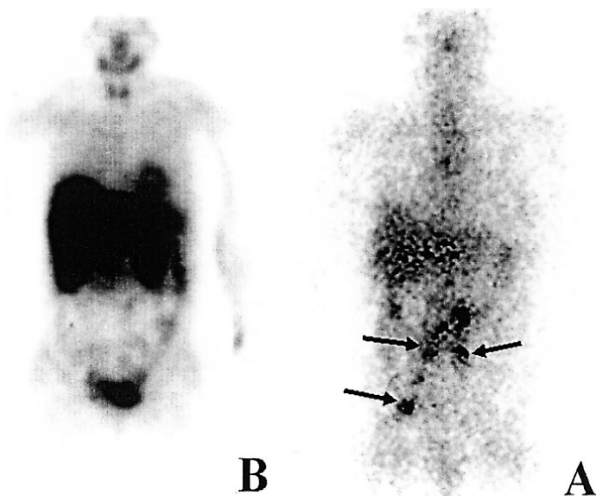


Fig. 3 (A) The ⁶⁷Ga scan reveals multiple masses in the paraaortic and the right inguinal regions (*arrows*). (B) The Tc-TF scan shows no definitely abnormal tracer uptake.

one lesion was detected, and considered to be negative if none of the lesions were detected.

^{99m}Tc tetrofosmin scan

There was a delay of 30 min from the time of oral intake of 500 mg perchlorate to the start of the imaging procedure to prevent abnormal uptake of free ^{99m}Tc pertechnetate. A commercial tetrofosmin preparation was obtained from Amersham International plc (Myoview). The labeling and quality control procedures were carried out according to the manufacturer's instructions. The radiochemical purity of ^{99m}Tc-TF used in the present study was consistently higher than 95%. Each patient was

Table 2 Distributions of age, tumor stage and B symptoms related to Tc-TF scan results

Tc-TF scan results	Sex		p value	Age		p value	Tumor stage			B symptoms		
	Female	Male		≤ 40 years	> 40 years		I–II	III–IV	p value	Yes	No	p value
Positive	8	14		7	15		8	14		12	10	
Negative	2	0	> 0.05	2	0	> 0.05	1	1	> 0.05	2	0	> 0.05

Tc-TF: technetium-99m tetrofosmin

positioned supine on the imaging table with the chest strapped to prevent motion. Ten minutes after intravenous injection of 740 MBq (20 mCi) Tc-TF, whole body images were obtained in the anterior and posterior projections. The equipment consisted of a large field-of-view gamma camera fitted with a low-energy, high-resolution collimator. A single 20% energy window was set at 140 keV, and 500 k counts were obtained for each static image. Evaluation of Tc-TF scan was based on visual analysis by at least two of three nuclear medicine physicians blinded to the patients' clinical data. Tc-TF uptake \geq soft-tissue background was considered as a positive Tc-TF scan result (Fig. 1); otherwise it was considered as a negative result (Figs. 2 and 3).⁸ For the patient with multiple lesions, the scan result was considered as positive if at least one lesion was detected, and negative if none of the lesions were detected.

Statistical analyses

For ⁶⁷Ga and Tc-TF scans, the differences in incidences of positive and negative results between female versus male patients, patients aged >40 years versus patients aged \leq 40 years, stage I–II versus stage III–IV patients, and patients with versus without B symptoms (night sweats, fever $>38^{\circ}\text{C}$ for 3 consecutive days, and unexplained weight loss of $>10\%$ body weight) were assessed by Fisher exact p tests. If the p value was <0.05 , the difference was considered significant.

RESULTS

Patient characteristics, ⁶⁷Ga and Tc-TF scan results and results are summarized in Table 1. ⁶⁷Ga scan could detect HD in all 24 (100%) patients, and Tc-TF scan in 22/24 (91.7%) patients. One case with chemotherapy resistance (Fig. 2) and another case of infradiaphragmatic HD (Fig. 3) detected on ⁶⁷Ga scan were negative on Tc-TF scan. However, there were no significant differences in the incidences of positive and negative Tc-TF scan results between female versus male patients, patients aged >40 years versus patients aged \leq 40 years, stage I–II versus stage III–IV patients, or patients with versus without B symptoms (Table 2). There was no significant difference in detection sensitivity between ⁶⁷Ga and Tc-TF scan (p value > 0.05 by a Fisher exact p test).

DISCUSSION

⁶⁷Ga seems to behave as an analogue of the ferric ion, accumulating within the tumor cell by simple diffusion and possible penetration via the calcium channels. Many studies have demonstrated the usefulness of ⁶⁷Ga scan to detect HD.^{3,5} The tumor uptake mechanism of Tc-TF has been suggested to involve mitochondria and plasma membrane potentials of the tumor cell, as well as the cellular mitochondria content.^{11–13} On the other hand, the uptake may be caused by an indirect phenomenon, such as increased tumor blood flow or capillary permeability. Tc-TF scan has been used successfully to detect HD.^{7,8}

In the present study, ⁶⁷Ga scan could detect HD in all 24 (100%) patients. However, in our previous study of 50 patients with malignant lymphoma including HD or HDL,¹⁰ ⁶⁷Ga scan detected 45 (90%) patients, but was false-negative in 3 cases with low-grade NHL and in 2 cases of NHL with bone marrow involvement. However, there was no significance for ⁶⁷Ga scan to detect HD only and HD/HDL together (p value > 0.05 by a Fisher exact p test). In the present study, Tc-TF scan could detect HD in 22/24 (91.7%) patients. One case with chemotherapy resistance (Fig. 2) and another case of infradiaphragmatic HD (Fig. 3) detected on ⁶⁷Ga scan were negative on Tc-TF scan. In our previous study,¹⁰ Tc-TF scan detected 44 (88%) patients, but was also false-negative in 4 cases of infradiaphragmatic malignant lymphoma, and in 2 cases with chemotherapy resistance. In addition, there was no significance for Tc-TF scan to detect HD only and HD/HDL together (p value > 0.05 by a Fisher exact p test).

Tc-TF scan did not detect the other HD with chemotherapy resistance in our study (Fig. 2), which may reflect the relationship between negative Tc-TF scan results and relatively high expressions of Pgp or MRP. After reviewing our previous studies, all patients with good response had positive Tc-TF scan results but negative Tc-TF scan results but positive Pgp or MRP expression. All patients with poor response had negative Tc-TF scan results but positive Pgp or MRP expression.^{11–16} In addition, one case of infradiaphragmatic HD (Fig. 3) detected on ⁶⁷Ga scan was negative on Tc-TF scan. Therefore, the biliary-intestinal route of elimination of Tc-TF makes it difficult to use this compound in the investigation of infradiaphragmatic HD. We also found no significant differences in the incidences of positive and negative ⁶⁷Ga and Tc-TF scan results when compared with sex, age, tumor stage, or

presence/absence of B symptoms.

The results of this study showed that there is no significant difference in detection sensitivity between ^{67}Ga and Tc-TF scan (p value > 0.05 by a Fisher exact p test). We conclude that Tc-TF scan can not replace conventional ^{67}Ga scan to detect HD.

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