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Application of Tc-99m-tetrofosmin as a tumor imaging agent: Comparison with Tl-201

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Tc-99m-tetrofosmin SPECT was performed on 6 occasions in 4 patients with hypopharyngeal carcinoma, lung carcinoma, esophageal carcinoma and maxillary plasmocytoma and compared with Tl-201 SPECT. All lesions accumulated both Tc-99m-tetrofosmin and Tl-201. Early uptake ratios of Tc-99m-tetrofosmin were about 2 but those of Tl-201 were much higher (more than 3). Washout rates of Tc-99m-tetrofosmin were higher than those of Tl-201. There was a good positive correlation between the early uptake ratio of Tc-99m-tetrofosmin and that of Tl-201. The delayed uptake ratio and washout rate showed poor correlation. In conclusion, early uptakes of both the agents were similar but their retention patterns were different. Tc-99m-tetrofosmin may be used for tumor imaging though more studies are required to evaluate diagnostic accuracy and the significance of delayed images.

Key words: tumor, Tc-99m-tetrofosmin, Tl-201, dual isotopes, SPECT

INTRODUCTION

TECHNETIUM-99m-tetrofosmin (Tc-99m-tetrofosmin), a lipophilic monovalent cation, has been developed for myocardial perfusion imaging.[1] Its accuracy in diagnosing myocardial ischemia is reported to be similar to thallium-201 chloride (Tl-201).[2,3] Because Tl-201 has shown potentiality in detecting various tumors,[4–6] Tc-99m-tetrofosmin is expected to be a tumor imaging agent. In this preliminary study, malignant tumors of various organs were imaged by Tc-99m-tetrofosmin and the results were compared with the findings of Tl-201 scans.

MATERIALS AND METHODS

On a total of 6 occasions in 4 patients (shown in Table 1), both early and delayed Tc-99m-tetrofosmin studies were performed. On 4 occasions dual isotope acquisition of Tc-99m-tetrofosmin and Tl-201 in the triple energy window mode (TEW) was done with a Toshiba, Japan GCA 9300A/DI triple head gamma camera. About 5–10 minutes after injecting 740 MBq of Tc-99m-tetrofosmin and 111 MBq of Tl-201, early single photon emission computed tomography (SPECT) was obtained in a 128 × 128 matrix by continuous acquisition (5 rotations, 4 minutes/rotation by 4° step). Delayed SPECT was obtained 2–3 hours after injection in the same acquisition mode. On one occasion, Tc-99m-tetrofosmin and only delayed Tl-201 SPECT were performed on separate days (3 days apart). After uniformity correction, reconstruction was performed with Butterworth and Ramp filters at different cut-off levels according to the counts in the projection images. In the same patients, however, reconstruction of both early and delayed images were performed by the same cut-off level to minimize the factors affected by different cut-off levels in the region of interest (ROI) counts. After selecting an appropriate axial image, a small square ROI was drawn over the highest activity in the lesion. For background activity, a large ROI was drawn over the surrounding normal tissue or opposite normal lung (in the case of lung and esophageal tumors). Average counts were taken as lesions or background activity for the following calculation. Uptake ratios for both early and delayed images (EUR or DUR) were calculated as follows:

$$\text{EUR or DUR} = \frac{\text{counts in ROI over the lesion}}{\text{counts in ROI over the background}}$$

The washout rate (WR) was calculated as follows:

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$$WR = \frac{\text{counts in ROI on early image} - \text{decay corrected counts in ROI on delayed image}}{\text{counts in ROI on early image}} \times 100$$

In the case of dual isotope acquisition, the ROI was drawn on the same slice and region of both Tc-99m-tetrofosmin and Tl-201 images. In the case of acquisition on different days, matching slices were taken for drawing the ROIs.

RESULTS

Table 2 shows a summary of the scan results. In two patients, a Tc-99m-tetrofosmin study was performed before and after radiotherapy. Both Tc-99m-tetrofosmin and Tl-201 were accumulated in all lesions including the lesions after radiotherapy. Uptake ratios were always higher and washout rates were lower in the Tl-201 study. The highest uptake ratio was observed in a case of plasmocytoma in the maxillary sinus by both Tc-99m-tetrofosmin and Tl-201. Figure 1 shows the correlation of the quantitative results for Tc-99m-tetrofosmin and Tl-201. Though data were few, the early uptake ratio of Tc-99m-tetrofosmin and that of Tl-201 showed a positive correlation. There was also a positive correlation even after omitting the highest point. The delayed uptake ratio and washout rate showed poor correlation.

Figure 2 shows a case of plasmocytoma in the right maxillary sinus. Both Tc-99m-tetrofosmin and Tl-201 showed similar uptake intensity. Figure 3 shows a case of esophageal carcinoma with mediastinal lymph nodes metastasis. There was no definite demarcation of the tumor or lymph nodes after radiotherapy in CT images due to reactive inflammation in surrounding tissue but both Tc-99m-tetrofosmin and Tl-201 showed tumor and lymph nodes separately. Nevertheless, Tc-99m-tetrofosmin showed better resolution than Tl-201. In this case, both the tumor and the lymph node were resistant to radiotherapy.

DISCUSSION

The usefulness of Tl-201 imaging for various malignant tumors is well established.[4-6] Tetrofosmin, a newly developed myocardial perfusion imaging agent, has been shown to behave like Tl-201[3] even though the exact mechanism of uptake is not yet known, but preliminary results showed that uptake of Tc-99m-tetrofosmin might be related to cell membrane and mitochondrial potential.[7,8] Bosoglu et al. showed uptake of Tc-99m-tetrofosmin in lung tumors.[9] In this preliminary study, several tumors were imaged with Tc-99m-tetrofosmin and the results were compared with concurrent results of a Tl-201 study to evaluate the usefulness of Tc-99m-tetrofosmin in tumor imaging.

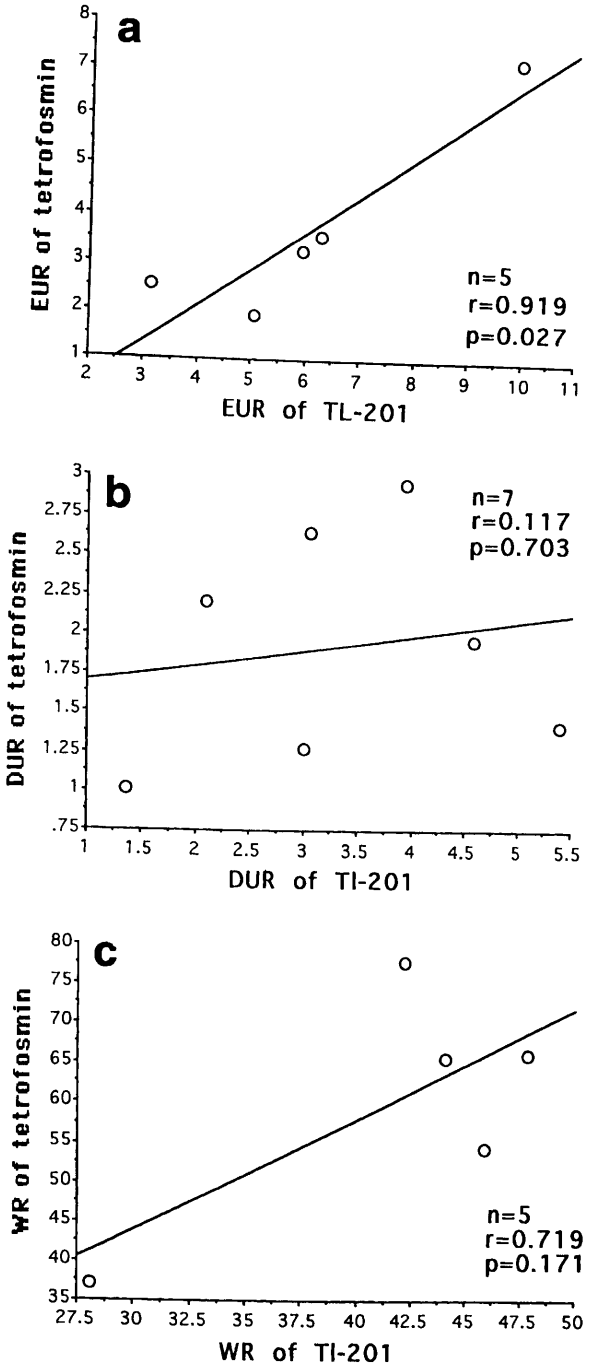

Fig. 1 The statistical analysis of the results of Tc-99m-tetrofosmin and Tl-201. (a) Early uptake ratio (EUR) showed good correlation though (b) delayed uptake ratio (DUR) and (c) washout rate (WR) had poor correlation.

Our protocol was to perform a dual isotope SPECT study to minimize the chances of misplacement of ROI over lesions as far as possible. In our department, a phantom SPECT study with Tc-99m and Tl-201 with a TEW mode showed very little cross talk of Tc-99m activity on Tl-201 images (8.2%) and there was almost none on Tc-99m images from Tl-201 (2.2%). All the lesions showed positive uptake for both Tc-99m-

Table 1 Summary of the patients and diagnosis

Pts. no.	Age	Sex	Site of tumor	Histopathology	Time of studies
1	45	M	Hypopharynx	SCC	Before and after radiotherapy
2	62	M	Esophagus and LN	Mod. Diff. SCC	Before and after radiotherapy
3	70	F	Maxillary Sinus	Plasmocytoma	Before radiotherapy
4	65	M	Lung and LN	Adenocarcinoma	After 1 course of chemotherapy

F: female, M: male, SCC: squamous cell carcinoma, LN: lymph node metastasis, Mod. Diff.: moderately differentiated

Table 2 Summary of scan results

Pts. no.	Comments	Lesions	Tc-99m-tetrofosmin			Tl-201		
			EUR	DUR	WR	EUR	DUR	WR
1	BR	Tumor	1.93	1.27	37.19	5.05	3.00	28.06
	AR	Tumor	2.52	1.01	65.46	3.12	1.35	44.04
2	BR	Tumor	2.08	1.43	57.21	—	—	—
		LN	1.97	1.97	41.42	—	—	—
	AR	Tumor	3.57	1.41	77.64	6.29	5.29	42.18
		LN	3.25	1.95	65.91	5.94	4.59	47.89
3	BR	Tumor	7.15	2.94	54.28	9.95	3.94	45.90
4	CT	Tumor	2.54	2.63	50.80		3.05	
		LN	1.68	2.20	48.95		2.09	

EUR: early uptake ratio, DUR: delayed uptake ratio, WR: washout rate, BR: before radiotherapy, AR: after radiotherapy, CT: after 1 course of chemotherapy

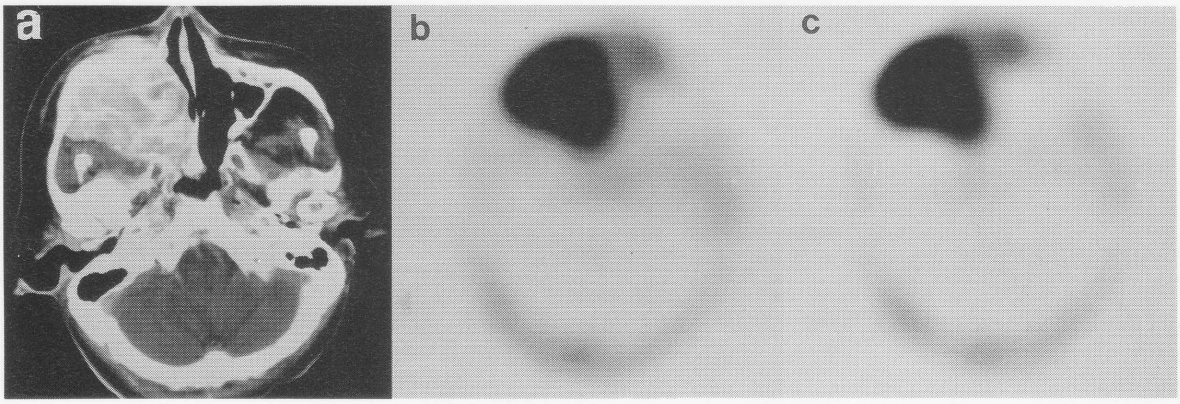

Fig. 2 A case of plasmocytoma in right maxillary sinus. (a) Enhanced CT shows enhancement of the mass with feature of bony destruction. Dual isotope early SPECT of (b) Tc-99m-tetrofosmin and (c) Tl-201 shows intense activity at the corresponding site of the mass.

tetrofosmin and Tl-201. Early uptake ratios in the tumor were about 2 for Tc-99m-tetrofosmin and more than 3 for Tl-201. In one case (patient 2) the early uptake ratio became higher after radiotherapy though there was no change in the delayed uptake ratio. Radiotherapy was ineffective for the patient and higher uptake might be due to growth of the tumor as well as a reactive inflammatory change causing hyperemia. In the other case (patient 1) though Tc-99m-tetrofosmin had a higher early uptake ratio at the tumor after radiotherapy the delayed uptake ratio was lower than before. This might have been due to reactive inflammatory change because tumor size was decreased after radiotherapy but it might not have been completely cured. In both the cases for Tl-201 there were higher early uptake ratios than those for Tc-99m-tetrofosmin.

With this small amount of data, the early uptake ratios of Tc-99m-tetrofosmin and Tl-201 positively correlated even though there was no correlation found with the delayed uptake ratios. These findings may indicate that both Tc-99m-tetrofosmin and Tl-201 accumulate primarily inside the tumor in the same mechanism. Early uptake is more likely to be dependent on the blood flow even though the retention mechanisms of the two agents may be different, which was indicated by a higher washout rate for Tc-99m-tetrofosmin.

In this study, because all lesions were detected by Tc-99m-tetrofosmin, Tc-99m-tetrofosmin as well as Tl-201

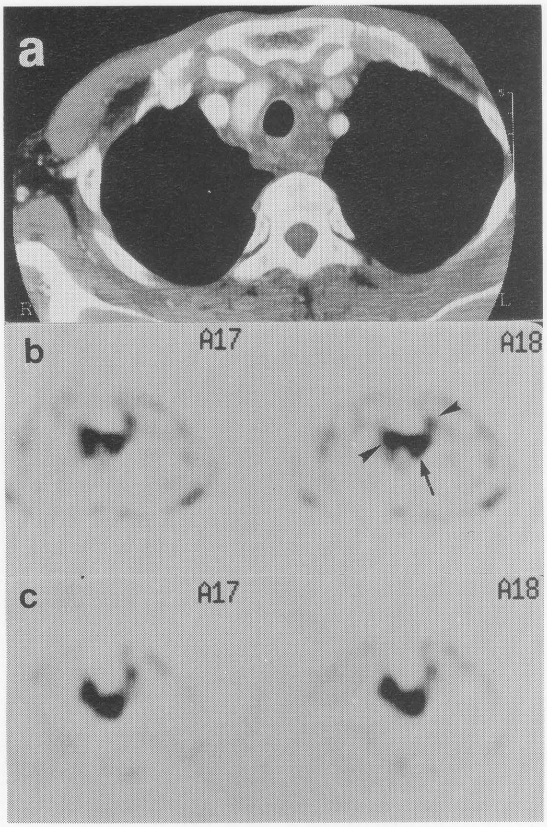

Fig. 3 A case of esophageal carcinoma with mediastinal lymph nodes metastasis. (a) Enhanced CT shows diffuse enhancement at the soft tissue density mass around esophagus and lymph nodes. Note there was no definite demarcation between tumor and surrounding structures due to inflammatory change following radiotherapy. Both (b) Tc-99m-tetrofosmin and (c) Tl-201 early SPECT showed the tumor (arrow) and lymph nodes (arrow heads) separately. Note Tc-99m-tetrofosmin showed better resolution than Tl-201.

may be useful in detecting malignant tumors. Tc-99m-tetrofosmin may also be used to assess tumor viability both before and after radiotherapy. But more study is required to draw a conclusion regarding the diagnostic accuracy and significance of delayed images.

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