

## Usefulness of Ga-67 brain SPECT in patients with CNS malignant lymphoma

Hirofumi FUJII,\* Shigeru KOSUDA,\* Kenzo SUZUKI,\* Hachiro YORINO,\* Sakiko AKITA,\* Hitoshi NEGISHI,\* Osamu NAKAMURA,\*\* Nobuyuki SHITARA\*\* and Atsushi KUBO\*\*\*

*\*Department of Radiology, \*\*Department of Neurosurgery, Tokyo Metropolitan Komagome Hospital*

*\*\*\*Department of Radiology, School of Medicine, Keio University*

The efficacy of Ga-67 SPECT imaging of CNS malignant lymphoma was investigated in 14 studies of 11 patients. As compared with planar images, the SPECT imaging improved the detectability of the focus of CNS malignant lymphoma. All untreated cases showed L/N ratios higher than 3.0. And the L/N ratios also changed according to remission or relapse of CNS malignant lymphoma.

**Key words:** malignant lymphoma, gallium-67, brain tumor, SPECT

### INTRODUCTION

IT IS WELL KNOWN that gallium-67 (Ga-67) often exhibits a high affinity for the focus of malignant lymphoma.<sup>1</sup> The test with this radionuclide is also effective for evaluating therapeutic efficacy in this disease entity.<sup>2-4</sup>

Although SPECT studies with Ga-67 have rarely been performed due to the physical properties of Ga-67, which are poorer than those of technetium-99m (Tc-99m),<sup>5</sup> some more recent reports have shown that SPECT imaging with Ga-67 is associated with higher sensitivity and specificity than conventional planar Ga-67 imaging in the diagnosis of malignant lymphoma involving the extracranial region.<sup>5-7</sup>

It has also already been reported that Ga-67 has an affinity for intracranial malignant lymphoma comparable to that observed at the extracranial site on planar images,<sup>8</sup> but there have been only a few reports on SPECT imaging of malignant lymphomas of the central nervous system (CNS).<sup>9</sup>

In recent years, the number of patients suffering from CNS malignant lymphoma has been increasing.<sup>10,11</sup> As malignant lymphoma is the second most common lesion to form intracranial masses after toxoplasmosis in AIDS patients, this disease entity has been attracting increasing attention.<sup>12,13</sup>

In the present study, we examined Ga-67 SPECT imaging for CNS malignant lymphoma to determine the usefulness of this radionuclide strategy.

### MATERIALS AND METHODS

#### *Patients*

Ga-67 studies were conducted between October, 1991 and April, 1994 on 11 patients (7 males and 4 females, ages ranging from 38 to 81 years, with a mean of 58.2 years) with CNS malignant lymphoma. Fourteen brain SPECT images of these 11 patients were obtained.

Among 11, 9 had primary CNS lymphoma and 2 had lymphoma metastasizing to the CNS. Pathological examinations proved that 9 had non-Hodgkin's lymphoma. The other 2 were diagnosed as having lymphoma because of their rapid response to steroid medication and radiotherapy. Ten were examined before the initiation of the treatment. One case (No. 5) was examined after the initial treatment. Three patients underwent repeat studies. Two (No. 1 and No. 10) were examined for the second time immediately after the treatment, whereas the other (No. 5) was examined after an 18 month interval, as she had exacerbated symptoms. The results of these repeat studies were used to compare the clinical symptoms and other imagings to evaluate the change in the disease during the interval. Planar images of 7 patients were examined. Three were also subjected to thallium-201 (Tl-201) brain SPECT studies to compare with the efficacy of Ga SPECT. The studies with both Ga-67 and Tl-201 were performed within a short interval without treatment. L/N ratios of

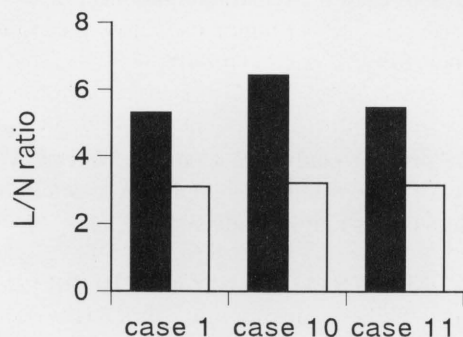
Received January 8, 1996, revision accepted August 5, 1996.

For reprint contact: Hirofumi Fujii, M.D., Department of Radiology, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, JAPAN.

**Table 1** Results of 11 patients

No.	age, sex	pathology	location/size (cm)	planar	L/N (Ga)	L/N (Tl)
1.	81F	P/ML	rtF/ 4 × 3	+	3.3	
1-2.	81F		rtF/ 3 × 2	+	5.3	3.1
2.	75M	M/NH	rtT/ 2 × 2		4.7	
3.	53M	M/NH	ltF/ 2 × 2	+	3.3	
4.	44M	P/NH	rtF/ 3 × 3		3.6	
5.	38F	P/NH	rtF/ 1 × 1		1.6	
5-2.	39F		rtF/ 4 × 2		3.3	
6.	61M	P/NH	rtPa/ 8 × 5	++	5.7	
7.	44M	P/NH	rtPa/ 4 × 1		3.9	
8.	63F	P/ML	ltB/ 2 × 2	-	3.0	
9.	58M	P/NH	ltO/ 3 × 3		7.2	
10.	70M	P/NH	ltF/ 2 × 2	+	6.4	3.2
10-2.	71M		ltF/0.5 × 0.5		1.3	
11.	53F	P/NH	rtPa/ 3 × 3		5.5	3.2

- 2: the second study, P: primary, M: metastasis, ML: unclassified malignant lymphoma, NH: non-Hodgkin lymphoma, F: frontal, T: temporal, Pa: parietal, O: occipital, B: brain stem



**Fig. 1** L/N ratios of Ga-67 and Tl-201 SPECTs. black column: Ga-67, white column: Tl-201.

both isopotes were compared. Two patients (No. 4 and No. 7) were HIV positive.

#### SPECT imaging

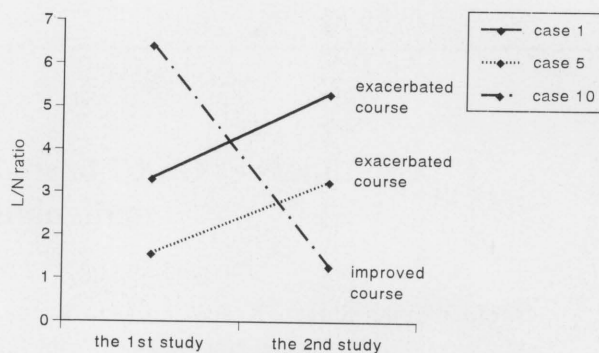
Three mCi (111 MBq) of Ga-67 citrate was injected intravenously 48 to 72 hours before the imaging procedure.

Three mCi (111 MBq) of Tl-201 chloride was injected intravenously. Early SPECT imagings were examined 10 min later.

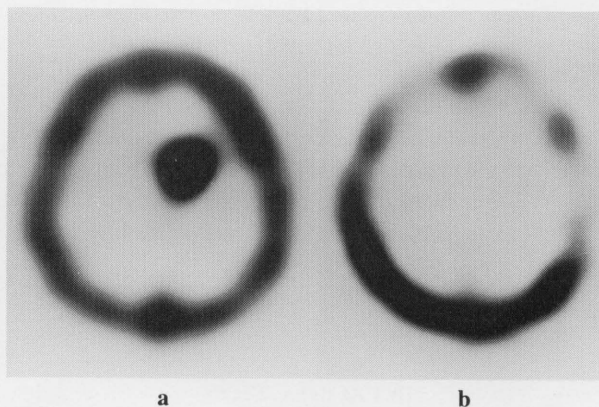
SPECT was obtained with a dual head rotating camera (TOSHIBA GCA 90A, Tokyo). A computer (TOSHIBA GMS 55U, Tokyo) was employed for image processing.

Sixty projections were acquired during a 360° rotation, with each projection lasting 30 seconds. A 64 × 64 matrix was used to acquire the raw projections. The data collected were reconstructed by means of a filtered back-projection technique, with a Butterworth filter and Chesler algorithm. Neither tissue attenuation correction nor scatter subtraction was performed. The thickness of each slice was 10.6 mm.

ROI was drawn over a lesion on the slice showing the



**Fig. 2** Interval change of L/N ratios.



**Fig. 3** 70M (No. 10). The activity of the lesion almost disappeared after the completion of the treatment regimen including chemotherapy and irradiation. L/N ratio decreased from 6.4 to 1.3. a: before treatment, b: after treatment.

greatest activity. The second ROI was determined on the contralateral side by performing a horizontal flip. But a ROI was created in the normal area adjacent to a lesion when the latter was located on the midline.

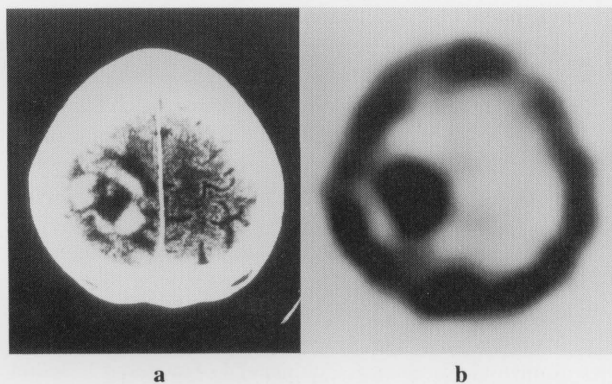
The activity of the first ROI covering the lesion was L (lesion); the second was N (normal); and the L/N ratio was calculated by dividing L by N (L/N).<sup>14</sup>

#### RESULTS

The results were summarized in Table 1.

SPECT and planar images of 7 patients were compared. In 6 of these, the foci of malignant lymphoma could be detected even on the planar images, and SPECT images were able to show the locations and extent of the foci in all 6, thus proving its superiority to planar images. Ten untreated patients showed high activity corresponding with the foci on the CT or MRI and all their L/N ratios exceeded 3.0. The other patient (No. 5), who underwent successful previous treatment, had a lower L/N ratio than 3.0.

The 3 patients who were also subjected to Tl-201 examinations had high activities in the lymphoma foci in both radionuclide studies; but their Ga-67 images showed a lesion with stronger contrast than in the Tl-201 images.



**Fig. 4** 44M (No. 4). AIDS patient. CT image (a) showed the central necrosis in the lesion. Ga-67 (b) was strongly accumulated into the focus with a L/N ratio of 3.6.

The means of the L/N ratios on their Ga-67 SPECT images and Tl-201 images were 5.7 and 3.2, respectively, with the former being about double the latter (Fig. 1).

For 3 patients who underwent repeat studies, the L/N ratio increased in 2 patients who experienced exacerbation, but a reduction was noted in this ratio in the other patient who showed a marked response to the therapy (Fig. 2 and Fig. 3). In the latter, a small enhanced area persisted on the CT image after treatment but his symptoms remained unchanged for one year. We believe that this enhanced area represented a necrotic change.

Two HIV-positive cases were included in this study. For both, central low density areas were noted on the CT and the L/N ratios exceeded 3.0 (Fig. 4).

## DISCUSSION

In recent years the number of patients suffering from malignant lymphoma of the CNS has increased.<sup>10,11,15</sup> With advances in diagnostic imaging techniques, opportunities to capture tomographic images of this lesion have increased. CNS lymphomas have been shown as iso- to hyper-dense lesions on precontrast CT images; and various degrees of enhancement were noted on the contrast-enhanced CT.<sup>16,17</sup> On MRI, CNS lymphoma shows iso- or slightly hyper-intense signal relative to the gray matter on T2-weighted images,<sup>10,18</sup> but these tomographic findings are not specific to CNS lymphoma and there are no established methods to evaluate these lesions with radionuclides. In this study, we conducted Ga-67 SPECT for this type of lymphoma and evaluated its usefulness.

In 7 patients whose planar images were also available for comparison, each SPECT image was found to visualize the foci more clearly. In one patient, the lesion was seen only on the SPECT image. In the others, the foci were readily recognized, even on planar images but SPECT facilitated the evaluation of the extent of the lesions. Recently, radionuclide images have often been compared with other tomographic images such as CT and MRI. In this respect, SPECT imaging has also been shown to have

an advantage over planar imaging. Although Ga-67 is considered to be unsuitable for SPECT imaging due to its physical properties, which are less desirable than those of Tc-99m,<sup>5</sup> we came to the conclusion, based on the present study, that Ga-67 can be used in SPECT imaging of the brain.

Until recently, we have calculated L/N ratios for Tl-201 SPECT studies to evaluate the viability of brain tumor cells, mainly glioma, and reported the efficacy of this method.<sup>14</sup> In the present study, the L/N ratios from the Ga-67 SPECT examinations were also calculated by employing a similar method to determine the validity of this parameter as a quantitative index for the activity of CNS malignant lymphoma. In 10 patients with untreated lesions, except No. 5, who were suspected of having a viable tumor in the foci, all L/N ratios from Ga-67 SPECT exceeded 3.0. These data suggested that the L/N ratio may be a semi-quantitative index of the activity of CNS malignant lymphoma.

Nevertheless, the L/N ratio may be underestimated due to a partial volume effect when the size of the lesion is small. Then, if a small tumor has a low L/N ratio, we should evaluate the result carefully.

In 3 patients, Tl-201 SPECT was also conducted within a short interval without treatment. Although the number of patients in this category was very small, we found that all of the L/N ratios from the Ga-67 SPECT were about twice as high as those obtained with Tl-201. The finding was reversed in glioma, where the L/N ratio was higher for Tl-201 SPECT than for Ga-67 SPECT.<sup>19</sup> It has been reported that Ga-67 has a high affinity for metastatic tumors and abscesses in addition to lymphomas of intracranial mass lesions.<sup>20</sup> Metastatic lesions are suspected in a history of malignant disease and abscesses often manifest as inflammatory symptoms, but differentiating between lymphomas and gliomas remains an important issue. Because other tomographic images of malignant lymphomas of the CNS show non-specific findings, Ga-67 SPECT may be an effective method to use in detecting CNS lymphoma.

As for three patients whose changes on Ga-67 SPECT could be traced, all exhibited changes in their L/N ratios concomitant with the extent of exacerbation or remission of CNS lymphomas. This suggested that the L/N ratio may be used as an objective index for the evaluation of the therapeutic efficacy in CNS lymphoma and for the detection of relapsed lymphoma. One patient with a good response to the treatment (No. 10) manifested no exacerbation of clinical symptoms for one year. After remission, a small enhanced area remained on the CT images, whereas Ga-67 SPECT showed no active foci. Thus, like extracranial lesions,<sup>4</sup> Ga-67 SPECT could express the therapeutic effect of CNS lymphoma more precisely than enhanced CT.

With the number of AIDS patients mounting, the incidence of AIDS-related malignant lymphoma of the CNS

is also increasing.<sup>15</sup> It is known that half of the foci of AIDS-related malignant lymphoma of the CNS show a poorly enhanced area in the central portion on conventional tomographic images such as CT and MRI, a feature that distinguishes this clinical entity from non-AIDS lymphoma.<sup>13</sup> Our two patients with AIDS-related malignant lymphoma of the CNS also exhibited central low density, but their L/N ratios from Ga-67 SPECT, as well as those of non-AIDS patients, exceeded 3.0. Ga-67 SPECT showed similar results for detection of CNS malignant lymphoma even in AIDS patients as well as in non-AIDS cases, differing from the results on CT or MRI.

In conclusion, SPECT studies with Ga-67 contribute to improving the detectability of the focus for CNS malignant lymphomas, as compared with planar images. Untreated cases of CNS malignant lymphoma showed high L/N ratios and this index changed according to the status of the lymphoma.

## REFERENCES

1. Edwards CL, Hayes RL. Tumor scanning with <sup>67</sup>Ga-citrate. *J Nucl Med* 10: 103-105, 1969.
2. Turner DA, Fordham EW, Ali A, Slayton RE. Gallium-67 imaging in the management of Hodgkin's disease and other malignant lymphomas. *Seminars in Nuclear Medicine* 8: 205-218, 1978.
3. Israel O, Front D, Lam M, Ben-Haim S, Kleinhaus U, Ben-Shachar M, et al. Gallium 67 imaging in monitoring lymphoma response to treatment. *Cancer* 61: 2439-2443, 1988.
4. Nedellec G, Lioure B, Bussy E, Carlouz R, Gaillard JF, Auzanneau G. Evaluation of residual masses after lymphoma treatment: the contribution of gallium-67 tomoscintigraphy. *Nouvelle Revue Francaise d Hematologie* 32: 187-190, 1990.
5. Harwood SJ, Carroll RG, Anderson M, Friedman BI, Zangara LM, Brunette AK, et al. SPECT gallium scanning for lymphoma and infection. *Clin Nucl Med* 12: 694-702, 1987.
6. Tumeh SS, Rosenthal DS, Kaplan WD, English RJ, Holman BL. Lymphoma: evaluation with Ga-67 SPECT. *Radiology* 164: 111-114, 1987.
7. Fukunaga M, Mukai T, Fujita T, Shigeno C, Morita R, Torizuka K. Emission computed tomography, using rotating gamma camera, of tumor image with <sup>67</sup>Ga-citrate—detection of involved lesions in malignant lymphoma. *KAKU IGAKU (Jpn J Nucl Med)* 18: 1343-1351, 1981.
8. Zidar BL, Adatepe M, Hryschko F, Hartsock RJ, Kessler L, Lyons TA. Diagnosis of non-Hodgkin's lymphoma intracerebral mass lesions. Usefulness of Tc-99m pertechnetate and Ga-67 citrate brain scans. *Clin Nucl Med* 7: 497-501, 1982.
9. Kosuda S, Aoki S, Suzuki K, Nakamura H, Nakamura O, Shidara N. Primary malignant lymphoma of the central nervous system by Ga-67 and Tl-201 brain SPECT. *Clin Nucl Med* 17: 961-964, 1992.
10. Roman-Goldstein SM, Goldman DL, Howieson J, Belkin R, Neuwelt EA. MR of primary CNS lymphoma in immunologically normal patients. *AJNR* 13: 1207-1213, 1992.
11. Eby NL, Grufferman S, Flannelly CM, Schold SC, Vogel FS, Burger PC. Increasing incidence of primary brain lymphoma in the US. *Cancer* 62: 2461-2465, 1988.
12. Petito CK, Cho E-S, Lemann W, Navia BA, Price RW. Neuropathology of acquired immunodeficiency syndrome (AIDS): an autopsy review. *J Neuropathol Exp Neurol* 45: 635-646, 1986.
13. Lee Y-Y, Bruner JM, Tassel PV, Libshitz HI. Primary central nervous system lymphoma: CT and pathologic correlation. *AJR* 147: 747-752, 1986.
14. Kosuda S, Fujii H, Aoki S, Suzuki K, Tanaka Y, Nakamura O, et al. Reassessment of quantitative thallium-201 brain SPECT for miscellaneous brain tumors. *Ann Nucl Med* 7: 257-263, 1993.
15. Osborn AG. *Diagnostic Neuroradiology*. 1st ed. St. Louis: Mosby, 1994.
16. Palacios E, Gorelick PB, Gonzalez CF, Fine M. Malignant lymphoma of the nervous system. *J Comput Assist Tomogr* 6: 689-701, 1982.
17. Whelan MA, Kricheff II. Intracranial lymphoma. *Semin Roentgenol* 19: 91-99, 1984.
18. Schwaighofer BW, Hesselink JR, Press GA, Wolf RL, Healy ME, Berthoty DP. Primary intracranial CNS lymphoma: MR manifestations. *AJNR* 10: 725-729, 1989.
19. Kaplan WD, Takvorian T, Morris JH, Rumbaugh CL, Connolly BT, Atkins HL. Thallium-201 brain tumor imaging: a comparative study with pathologic correlation. *J Nucl Med* 28: 47-52, 1987.
20. Akisada M, Miyamae T. Combination technique with <sup>67</sup>Ga-citrate and <sup>99m</sup>TcO<sub>4</sub> in the brain scintigraphy by the conventional rectilinear scanner. *KAKU IGAKU (Jpn J Nucl Med)* 12: 221-233, 1975.