

Visualization of nasopharyngeal carcinoma with Tl-201 chloride and a three-head rotating gamma camera SPECT system

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Tl-201 SPECT was performed on 12 patients with Nasopharyngeal carcinoma (NPC) by means of a three-head rotating gamma camera to evaluate whether or not Tl-201 SPECT was useful and reliable for assessing the tumor viability of NPC. Tl-201 clearly accumulated in the tumor in 3 patients before radiation treatment and increased Tl-201 uptake by the lesion ceased after the treatment. Three of 9 patients who were followed up after radiotherapy developed apparent local recurrence and Tl-201 SPECT clearly visualized these recurrent lesions. Tl-201 SPECT was very useful for assessing the tumor response to irradiation and for detecting local recurrent tumor. A High resolution SPECT system employing Tl-201 chloride is a new reliable and accurate diagnostic tool for the assessment of NPC.

Key words: nasopharyngeal carcinoma, Tl-201 chloride, SPECT

INTRODUCTION

NASOPHARYNGEAL CARCINOMA (NPC) is a disease with a poor prognosis which often develops local recurrence after radiation therapy. The presence of local recurrent disease has been confirmed mainly by macroscopic examination or by CT, but conventional mirror examination and flexible fibroscope are of no use in detecting submucosal recurrent lesions.¹ It is also difficult to evaluate whether the lesion is viable only from the findings based on CT. Nowadays, Magnetic Resonance Imaging (MRI) provides accurate information concerning the extent of NPC, but it is still difficult to distinguish recurrent lesions from others when and if adequate enhancement with gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) cannot be obtained to separate recurrent lesions from normal tissues.²

Generally, head and neck cancers are easily observed macroscopically and the palpation is an

accurate way to detect cervical lymph node metastasis. Therefore, nuclear medical imaging is not regarded as important and is not as frequently used as other diagnostic methods in head and neck cancer including NPC. However, Yui, et al. reported that single photon emission computed tomography (SPECT) study of bone and gallium scintigraphies provides more reliable information than morphological imaging such as CT, and also emphasized the usefulness of SPECT study especially in head and neck cancer.^{3,4}

A three-head rotating SPECT system has excellent resolution compared to a dual-head or single head rotating system. And the use of a fan-beam collimator for scanning the head enabled FWHM to be 7 mm and provided superior SPECT images.⁵ In this study, we performed Tl-201 SPECT on the patients with NPC and evaluated its usefulness for the assessment of tumor viability. This study is based on the fact that the fan-beam collimator is suitable for low energy radionuclides including Tl-201 and also that Tl-201 reflected tumor viability more accurately than Ga-67 did in brain tumor⁶ and in VX-2 cancer.⁷ Therefore, we attempted a pilot study to ascertain whether Tl-201 SPECT is a new accurate and useful diagnostic tool for the assessment of NPC.

Received July 24, 1992, revision accepted November 8, 1992.

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MATERIALS AND METHODS

Twelve patients, 8 males and 4 females aged 28 to 71 yrs (mean 51 yrs), with NPC histologically proven were entered in this study. Twenty-two Tl-201 SPECT studies were performed for the follow-up study after radiation therapy in 9 of 12 patients and for the assessment of tumor extent before treatment in the remaining 3 patients. Data acquisition was started 5 min after the intravenous injection of 111 MBq (3 mCi) of Tl-201 chloride with a three-head rotating gamma camera (Toshiba GCA 9300A). After the rotation of each gamma camera with a 6° step angle, one step in 60 seconds, and with an acquisition matrix of 128 × 128, projection data from 60 steps were acquired in 20 minutes. Then the fan-beam projection data acquired with a 128 × 128 matrix were converted to parallel-beam projection data in a 64 × 64 matrix, and transaxial images with a 1.7 mm slice were reconstructed by means of Butterworth and Ramp filters for preprocessing and back-projection, respectively. In 8 of 12 patients, a Ga-67 SPECT study was also performed. Immediately after the Tl-201 SPECT study, 111 MBq (3 mCi) of Ga-67 citrate was intravenously injected and Ga-67 SPECT was started 72 hr after the injection. Fan-beam projection data were also converted to parallel-beam projection data as in the Tl-201 SPECT study, and a medium filter, which cuts out high frequency components and is an intermediate filter between Shep & Logan and Cesler filters, was used for the reconstruction of the Ga-67 SPECT image. The energy peak and window level were set at 80 KeV ± 20% for Tl-201, and at 93 KeV ± 20% and 184 KeV ± 20% for Ga-67. Attenuation correction was not performed in reconstructing Tl-201 and Ga-67 SPECT images.

RESULTS

Table 1 summarizes the results of the Tl-201 SPECT

study of 12 patients with NPC. Case 10, a pretreatment case in a T₁N₂M₀ clinical stage, had increased uptake by the posterior wall of the nasopharynx, but Tl-201 uptake by the lesion disappeared after the radiation therapy. Cases 11 and 12 who were in a pretreatment state and in a T₄N₂M₀ clinical stage also had increased uptake by the lesion. Cases 2, 4, and 9 had apparent local recurrent disease and their recurrent lesions were clearly visualized by Tl-201 SPECT. Finally in 6 of 12 cases, three in a pretreatment state and the other three with local recurrent disease, positive findings were obtained by Tl-201 SPECT. All 6 cases with no abnormality in Tl-201 SPECT studies performed from 3 to 59 months (mean 21 months) after radiotherapy had no clinical signs or symptoms suggesting local recurrence. Tl-201 SPECT was compared with Ga-67 SPECT in 8 patients examined by both Tl-201 and Ga-67. In 4 of 8 patients, 2 pretreatment and 2 local recurrence, the lesions were positively delineated by both Tl-201 and Ga-67 SPECTs, so that between Tl-201 and Ga-67 SPECTs there was no difference in the positive rate for visualizing lesions.

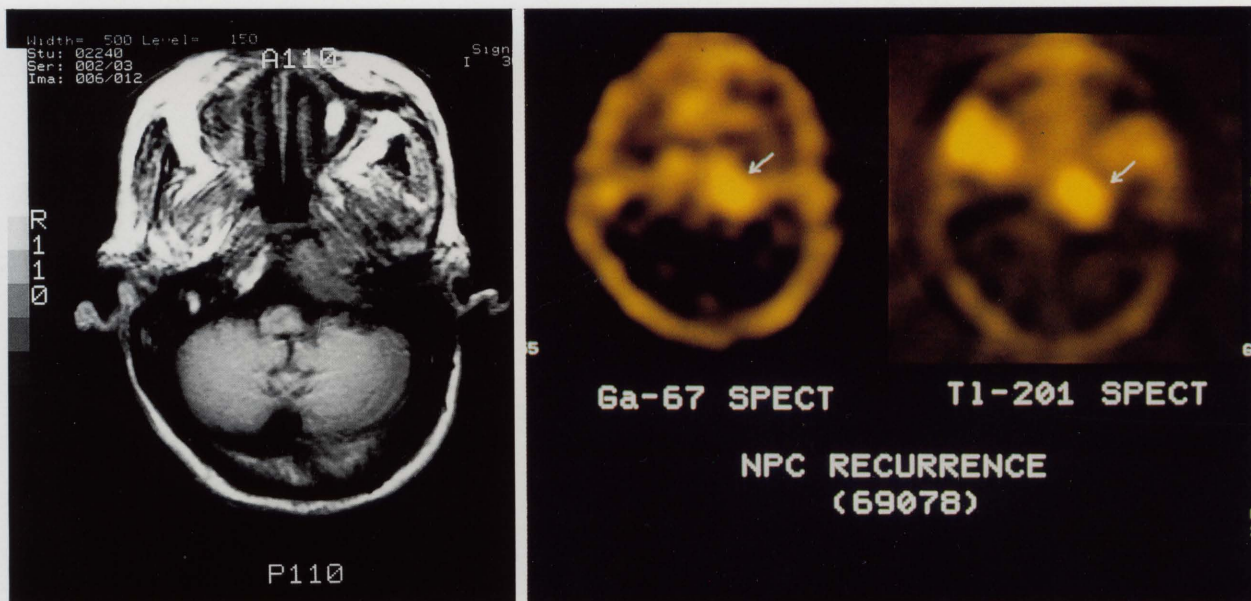
CASE PRESENTATION

Case 4 in Table 1: A 70-year-old male with NPC, T₄N₃M₀

This patient received 70 Gy radiation therapy for NPC and cervical lymph node metastases in September, 1990. Figure 1, A is a T1-weighted transaxial Magnetic Resonance (MR) image taken in September, 1991, just one year after the radiation treatment (Fig. 1A) and it shows a low intensity lesion spreading widely from the retropharyngeal space to the skull base. A Tl-201 SPECT taken at almost the same time clearly shows increased uptake by the low intensity lesion detected in an MR image (Fig. 1B). Although this Tl-201 SPECT image definitely delineated the lesion, no abnormality was seen in Tl-201

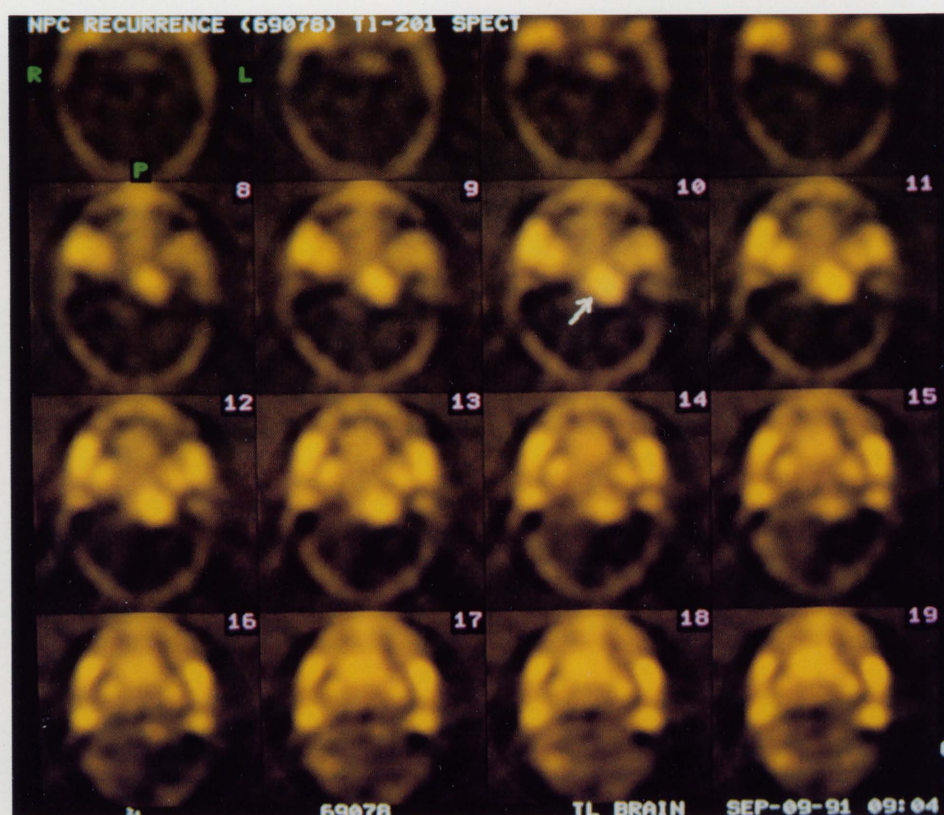
Table 1 Summary of Tl-201 SPECT of nasopharyngeal carcinoma

Case	Age	Sex	TNM	State	Tl-201 uptake	Ga-67 uptake
1	37	M	T ₁ N ₃ M ₀	Follow-up	(-)	(-)
2	58	F	T ₄ N ₃ M ₁	Recurrence	(+)	Not done
3	71	M	T ₄ N ₃ M ₀	Follow-up	(-)	Not done
4	70	M	T ₄ N ₃ M ₀	Recurrence	(+)	(+)
5	33	M	T ₄ N ₂ M ₀	Follow-up	(-)	(-)
6	44	M	T ₄ N ₃ M ₀	Follow-up	(-)	Not done
7	47	F	T ₁ N ₂ M ₀	Follow-up	(-)	(-)
8	45	M	T ₄ N ₃ M ₀	Follow-up	(-)	(-)
9	67	M	T ₄ N ₂ M ₀	Recurrence	(+)	(+)
10	37	F	T ₁ N ₂ M ₀	Pretreatment	(+)	(+)
11	41	M	T ₄ N ₂ M ₀	Pretreatment	(+)	(+)
12	28	F	T ₄ N ₂ M ₀	Pretreatment	(+)	Not done



A

C

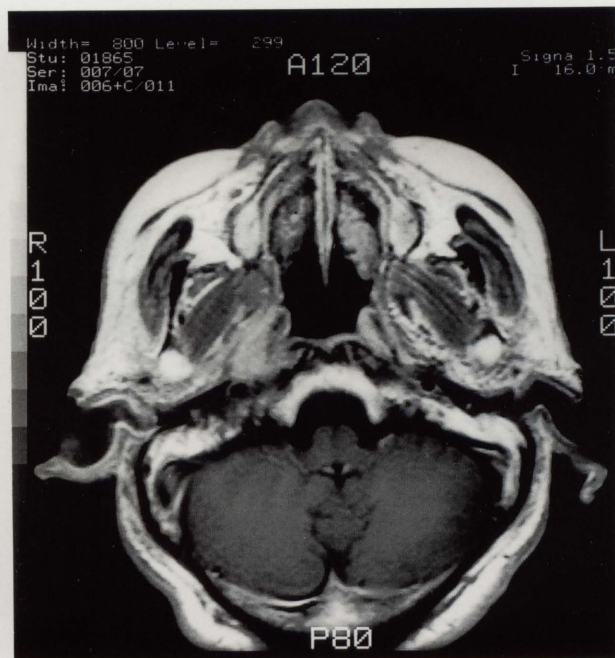


B

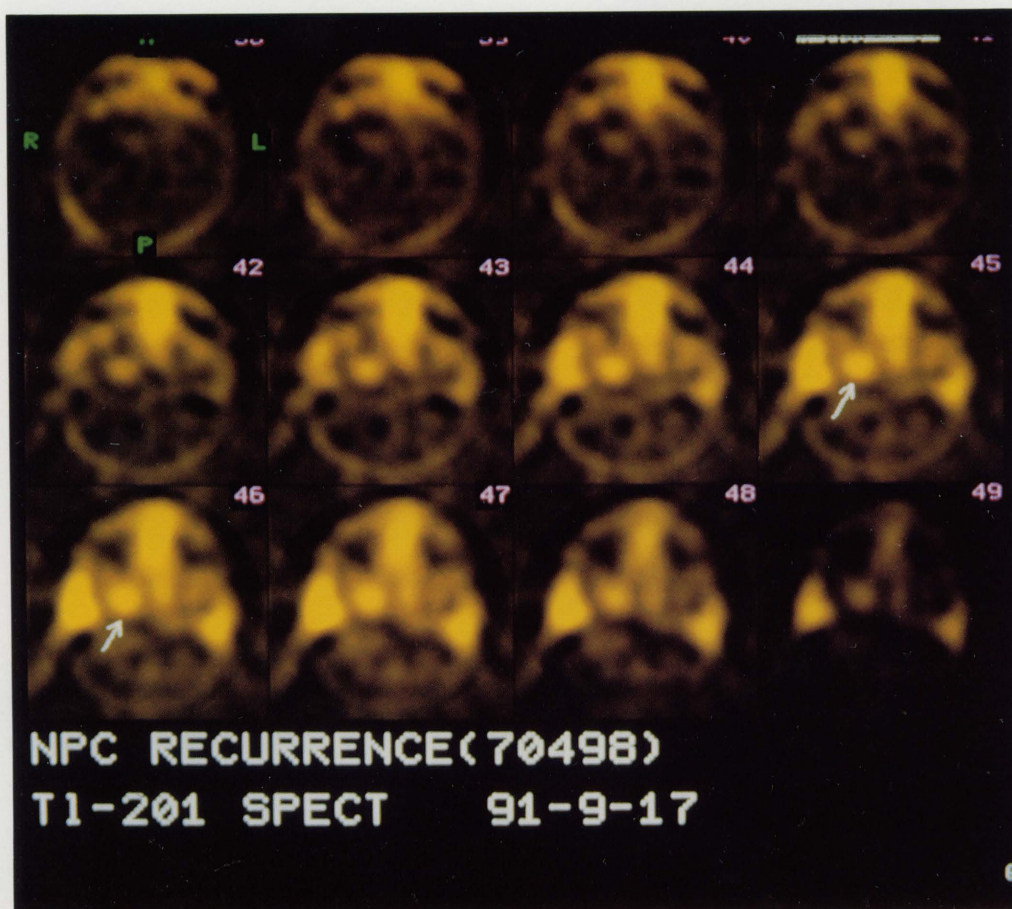
Fig. 1 A-C. Case 4 in Table 1, A 70-year-old male with NPC. A. T1-weighted transaxial MR image showing a low intensity lesion spreading from retropharyngeal space to skull base. B. Tl-201 SPECT clearly indicates increased uptake by the recurrent lesion detected by MR image. C. Comparison between Ga-67 and Tl-201 SPECT images. Tl-201 delineates the recurrent lesion more definitively than Ga-67.



2A



2B



2C

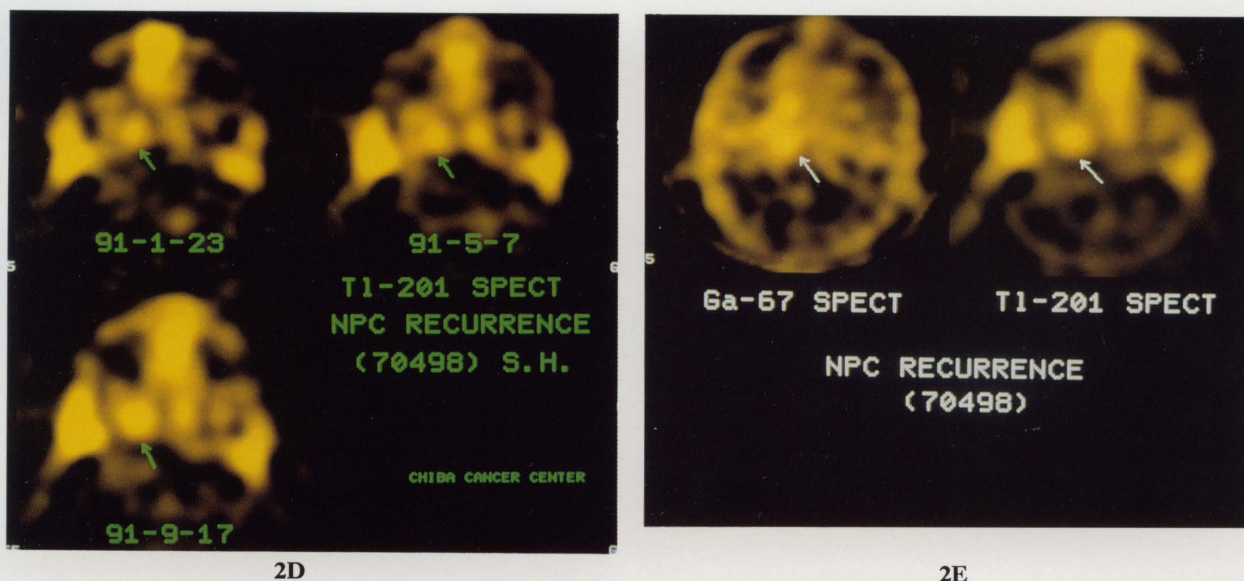


Fig. 2 A-E. Case 9 in Table 1, A 67-year-old male with NPC. A. Tl-weighted MR image showing a low intensity lesion of the right parapharyngeal space. B. Tl-weighted MR image after the administration of Gd-DTPA shows diffuse enhancement of the lesion. C. Tl-201 SPECT positively delineates the lesion at right parapharyngeal space. D. Tl-201 SPECTs serially taken in January, May, and September, 1991. A small increased uptake by the right parapharyngeal lesion is already shown in January, 1991 (arrow). E. Comparison between Ga-67 and Tl-201 SPECT images. The lesion detected by Tl-201 SPECT well corresponds to the lesion enhanced on MR image than Ga-67 SPECT.

SPECT studies previously performed 2 and 5 months after treatment. Not only the recurrent lesion but also the pterygoid and masticatory muscles and the parotid gland physiologically took up Tl-201. Figure 1C further compares the Ga-67 SPECT image with the Tl-201 SPECT image in almost the same transaxial slice. Although Ga-67 could visualize the lesion, Tl-201 delineated the lesion more definitely than Ga-67.

Case 9 in Table 1: A 67-year-old male with NPC, $T_4N_2M_0$

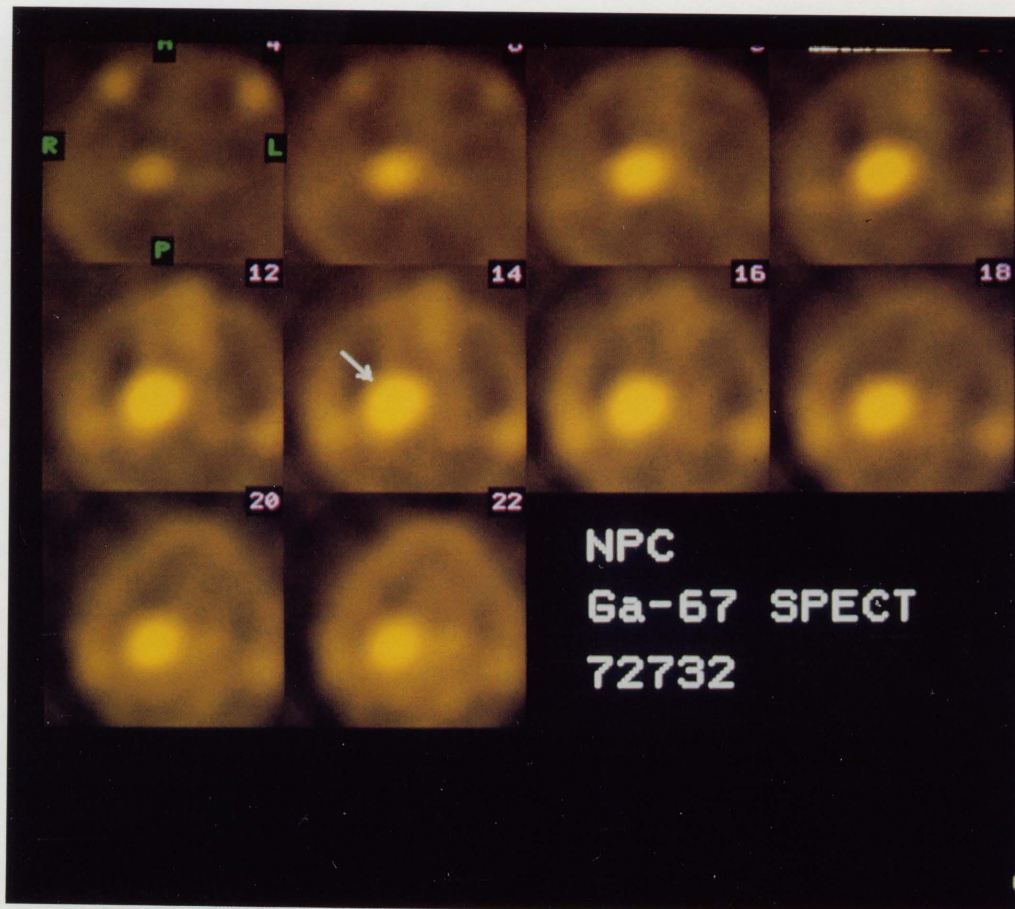
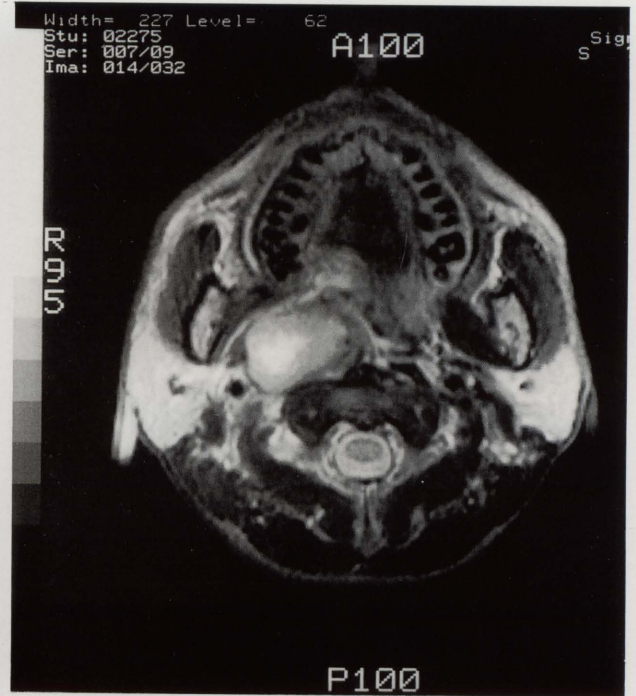
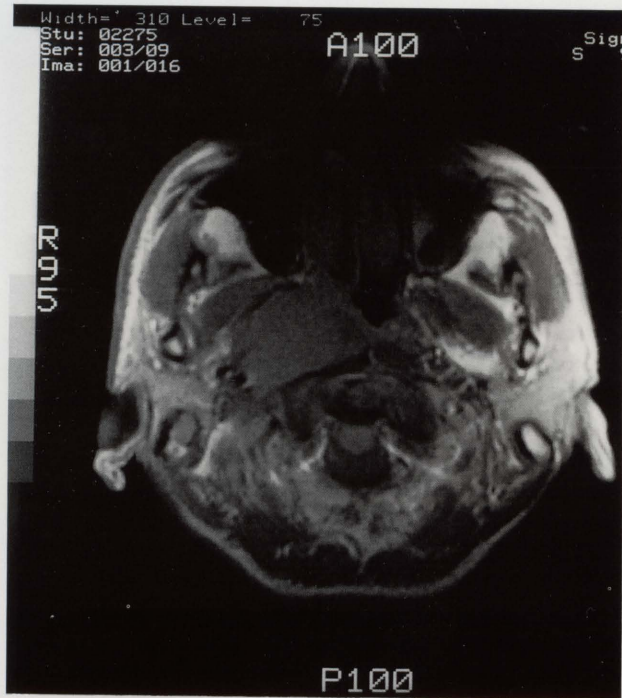
The patient received chemotherapy and radiation therapy for NPC with a total dose of 70 Gy from March to May, 1989, and noticed swelling of the right cervical lymph nodes at the end of December, 1990. Etoposide was given orally from February to July, 1991. Figure 2A is a Tl-weighted MR image taken in June, 1991, and it visualizes the low intensity lesion in the right parapharyngeal space. This lesion was diffusely enhanced by Gd-DTPA and was thought to be a local recurrent lesion (Fig. 2B).

Figure 2C is a Tl-201 SPECT image taken 3 months after the MR study and it clearly visualizes the right parapharyngeal lesion. When these Tl-201 SPECT images which were serially taken in January, May, and September, 1991 were compared, a small increased uptake by the right parapharyngeal space

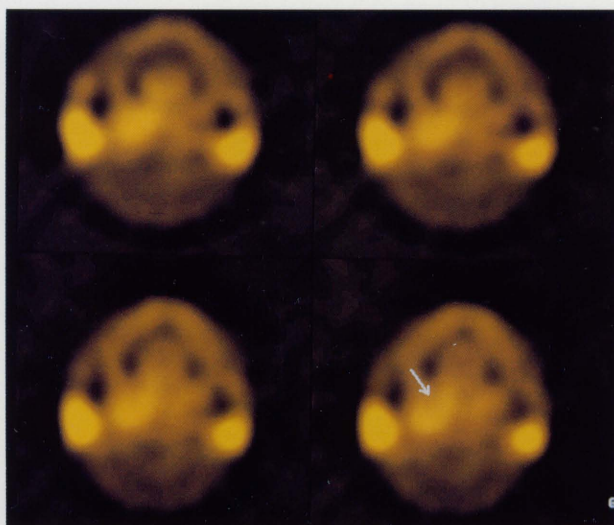
was already seen in January, 1991, and the uptake became more obvious with the passage of time (Fig. 2D). It was therefore thought that a small recurrent lesion already existed in the right parapharyngeal space at the time of swelling of right cervical lymph nodes. Figure 2E further compares Ga-67 SPECT with Tl-201 SPECT in almost the same transaxial slice and shows that the distribution of Ga-67 uptake is different from that of Tl-201 uptake. Tl-201 SPECT more clearly visualizes the lesion corresponding to the lesion enhanced on MR image than Ga-67 SPECT does.

Case 11 in Table 1: A 41-year-old male with NPC, $T_4N_2M_0$

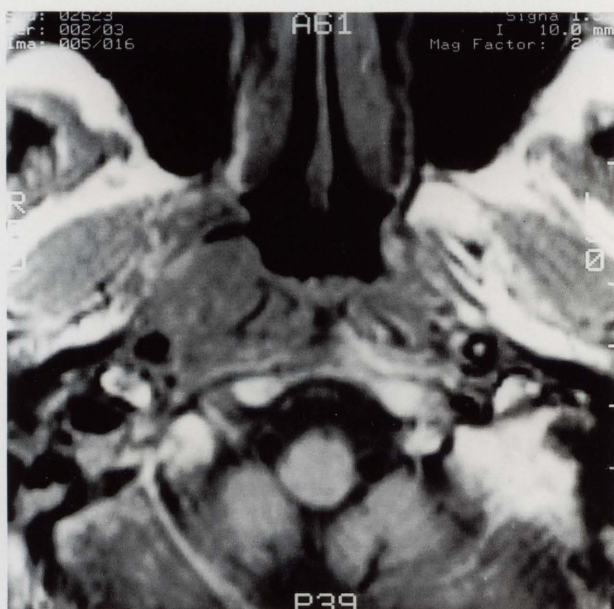
This patient visited our hospital in September, 1991 complaining of a sore throat. The Tl-weighted transaxial MR image shows a huge low intensity tumor originating in the right parapharyngeal space and extending to the posterior wall of the nasopharynx (Fig. 3A). At a slice of 14 mm below, the T2-weighted MR image indicates that the tumor has spread to the mesopharynx and there is a high intensity lesion, probably central necrosis, in the central region of the tumor (Fig. 3B). Ga-67 SPECT indicated a great accumulation of Ga-67 corresponding to the tumor detected in the MR image, but the central necrotic lesion was not delineated as a cold



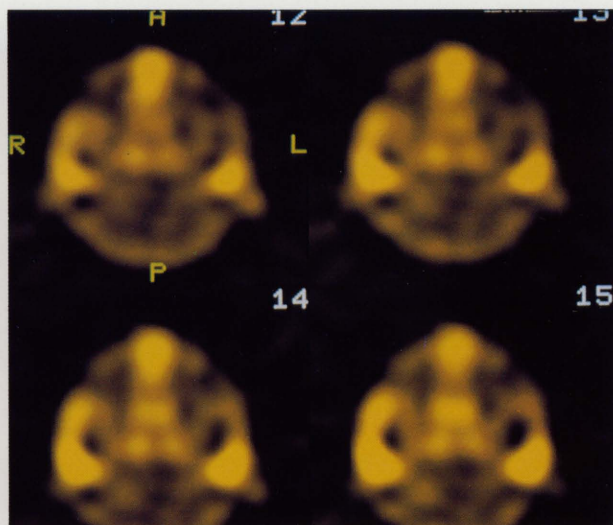
3C



3D



3F



3E

Fig. 3 A-F. Case 11 in Table 1, A 41-year-old male with NPC. A. T1-weighted transaxial MR image showing a huge low intensity tumor. B. T2-weighted MR image indicates the tumor spreading to mesopharynx with a high intensity lesion in the central region of the tumor suggesting central necrosis. C. Ga-67 SPECT indicates a high accumulation in the tumor. D. Tl-201 SPECT also clearly demonstrates the tumor with central defectiveness (arrow). E. Tl-201 SPECT after irradiation shows a slight increased uptake by the right parapharyngeal region. F. T1-weighted transaxial MR image after irradiation shows a marked tumor reduction but also the slight swelling of the right parapharyngeal space.

defect (Fig. 3C). Tl-201 SPECT also clearly demonstrated the tumor. Although Tl-201 uptake by the tumor was not so great as Ga-67 uptake, Tl-201 showed a defect in the central necrotic lesion, and closely corresponded with MR image finding (Fig. 3D). Figure 3E is a Tl-201 SPECT after radiation therapy with a dose of 62 Gy and shows a remarkable decrease in Tl-201 uptake in the right parapharyngeal region, but there is still slight uptake. In the Tl-weighted MR transaxial image just after radiotherapy there is marked reduction in the size of the tumor but also slight swelling of the right parapharyngeal space (Fig. 3F).

DISCUSSION

Most NPC are histologically classified into undifferentiated squamous cell carcinomata.⁸ They grow diffusely and infiltrate, appearing like a granuloma.⁹ Therefore, the main treatment for NPC is radiotherapy, but it often recurs locally after irradiation and the prognosis of recurrent cases is very poor.¹⁰ The epipharynx is easily observed by posterior rhinoscopy, but adequate observation still requires a skilled hand. Nowadays, fiberoptic examination enables to get more precise findings than by conventional mirror examination, but these macroscopic examinations are ineffective for tumors infiltrating and growing in the submucosa. It is

difficult to clinically evaluate the presence and extent of these recurrent submucosal tumors. Local recurrence of NPC frequently occurs in the para- and retro-pharyngeal spaces or in the skull base, but it can not be histologically confirmed even by biopsy in fiberoptic observation if the mucosa of the epipharynx is normal and intact.

MRI has more excellent spacial resolution and provides more clear soft tissue contrast than CT, and has been recognized as useful in evaluating tumors of the head and neck.¹¹ In particular it is well known that Gd-DTPA can enhance the tumor outline and clarify the margin between the tumor and the pharyngeal mucosa.¹² However, inadequate enhancement of the tumor outline or the similar enhancement of the tumor and normal tissue makes the evaluation difficult.

Tl-201 is one of the most common tumor-seeking agents in clinical use, but it has been used only for imaging lung cancer or thyroid cancer.^{13,14} However, recently, the clinical usefulness of Tl-201 has been reevaluated. For instance, Tl-201 has been reported to reflect tumor viability and the grade of malignancy of brain tumors^{15,16} and to visualize cancer of the pancreas.¹⁷ Oriuchi, et al. in particular reported that Tl-201 accumulation in glioma was well correlated with the uptake of bromodeoxyuridine, a biological marker indicating a proliferative state in the tumor, and that Tl-201 correctly reflected the extent of a viable tumor which has the potential to grow.¹⁸ Schwartz, et al. also reported that Tl-201 SPECT was very useful in differentiating recurrent glioma after irradiation from radiation necrosis.¹⁹ Kaplan, et al. stated that Tl-201 offered the most accurate correlation with a viable tumor and Tl-201 scans more accurately reflected a viable tumor burden than other radionuclide studies of primary brain tumors.⁶ Tl-201 is therefore thought to be an excellent radionuclide for determining residual tumor burden and for detecting recurrent lesions.

The clinical usefulness of Tl-201 in head and neck cancer was reported in 1979 by Yui, et al.²⁰ and they reported that results with Tl-201 was almost the same as with Ga-67. However, to our knowledge, no Tl-201 study with SPECT has yet been performed for NPC. Ga-67 scintigraphy rather than Tl-201 scintigraphy is generally performed in head and neck cancer because many head and neck cancers are classified as squamous cell carcinomas which generally take up much more Ga-67 than Tl-201.¹³ Furthermore, single- or dual-head rotating SPECT systems usually used these days have spacial resolution very inferior to that of CT or MRI. Therefore, examination by means of SPECT has not been as frequently performed as CT or MRI.

The three-head rotating gamma camera we used

for this study has a special fan-beam collimator for brain perfusion studies and provides more excellent spacial resolution and clearer images than the usual SPECT system. This new SPECT system can visualize a tumor 10 mm in diameter positively with Tl-201 chloride.²¹ Although the effective field of this system is only 22×21 cm, it covers not only the brain but also the skull base and epipharynx. Furthermore, we can take an image with Tl-201 chloride because the fan-beam collimator is suitable for low energy radionuclides such as Tc-99m, I-123 and Tl-201.

Three patients who received Tl-201 SPECT before treatment had positive results with Tl-201, and Tl-201 uptake disappeared following the completion of irradiation. Therefore, Tl-201 SPECT was thought to be useful for assessing the tumor response after irradiation. Also, as shown in case 11, whereas Tl-201 SPECT visualized the necrotic lesion of the tumor as a defect, Ga-67 SPECT could not separate necrosis from a viable lesion. In other words, Tl-201 is considered to offer a more reliable image reflecting tumor viability than Ga-67. Ito, et al. stated that Tl-201 had greater affinity with viable tumor sites than with necrotic tumors and also showed that the viable to necrotic tumor ratios for Tl-201 and Ga-67 uptakes were 5.1 and 2.1, respectively.⁷

In this study, 2 of 3 patients diagnosed to have tumor relapse based on Tl-201 SPECT and the clinical course received biopsy but had negative histological results. It is therefore possible that Tl-201 SPECT can diagnose local recurrence which infiltrates the submucosa and cannot be histologically confirmed even by biopsy. However, not only Tl-201 but also Ga-67 uptake by the tumor is well correlated to the growth rate of the tumor.²² Generally, the growth and the viability of the tumor vary under the conditions from before to after treatment. Therefore, a further precise study is necessary to confirm which nuclide, Tl-201 or Ga-67, is available and whether both nuclides are necessary for assessing the growth rate and the viability of NPC.

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