Evaluation of mandibular invasion by head and neck cancers using ^{99m}Tc-methylene diphosphonate or ^{99m}Tc-hydroxymethylene diphosphonate and ^{201}Tl chloride dual isotope single photon emission computed tomography

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Whether a patient with head and neck cancer has mandibular invasion or not is important in determining the method of resection surgery. But, no modality is adequately reliable when used alone in the evaluation of mandibular invasion. Therefore, to more accurately diagnose mandibular invasion in head and neck cancer, we used a new modality, namely, ^{99m}Tc methylene diphosphonate (MDP) or ^{99m}Tc hydroxymethylene diphosphonate (HMDP) and ^{201}Tl chloride dual isotope single photon emission computed tomography (Tc/Tl SPECT). The aim of this study is to disclose the usefulness of Tc/Tl SPECT in the assessment of mandibular invasion by head and neck cancers. ^{99m}Tc-MDP or -HMDP SPECT (Tc SPECT)s and ^{201}Tl chloride SPECT (Tl SPECT)s were performed in 34 patients with suspected mandibular involvement of head and neck cancer. Thirty of 34 cases underwent both Tc/Tl SPECT and CT examination. Tc/Tl SPECT fusion images were obtained using the Automatic Registration Tool (ART, TOSHIBA, Japan) system. In the diagnosis of mandibular invasion on Tc/Tl SPECT fusion images, a problem was that the range of Tc and Tl uptake was changed by the condition of display used in the reconstruction and expression of the images. Then, prior to clinical evaluation, to reveal the most appropriate upper window level for display, a phantom study was performed. In a clinical study, the upper window level was set at 40 or 50%, which were verified to be the proper values in the preliminary study. The diagnostic accuracy obtained using Tc SPECT, Tc/Tl SPECT and CT was compared with the histopathological findings. Tc/Tl SPECT at 40 and 50% upper window level had higher specificity, accuracy, and positive predictive value (73.3%, 85.3%, 81.8%) than Tc SPECT alone (21.4%, 67.6%, 64.5%) and higher sensitivity and negative predictive value (94.7%, 91.7%) than CT (70.6%, 72.2%) for detecting mandibular invasion. Tc/Tl SPECT was a useful diagnostic procedure for the assessment of mandibular invasion by head and neck cancers.

Key words: mandibular invasion, head and neck tumor, ^{201}Tl chloride, SPECT, fusion image

INTRODUCTION

ALTHOUGH RADICAL RESECTION is recommended as a treatment to ablate head and neck cancers completely, it often causes aesthetic and functional disabilities. Head and neck cancers have a poor prognosis because of their high rate of locoregional recurrence. One of the reasons why head and neck cancers are thought to recur is insufficient

excision of the tumor.[1] Thus it is important to investigate the extent of the tumor as accurately as possible. Patients suspected of having mandibular invasion have been investigated by orthopantomography (OPG), computed tomography (CT),[2–7] magnetic resonance imaging (MRI),[8] perioperative periosteal stripping with direct inspection,[9] and bone scintigraphy including ^{99m}Tc-methylene diphosphonate (MDP) or ^{99m}Tc-hydroxymethylene diphosphonate (HMDP) single photon emission computed tomography (Tc SPECT).[10–14] However, there is no modality that is adequately reliable when used alone.[1,7,15,16] At present, CT and OPG take precedence over the other modalities. Some studies[10,11,13] have concluded that bone scintigraphy has high sensitivity but low specificity.

In our study, 34 patients with head and neck cancer underwent ^{99m}Tc-MDP or HMDP and ^{201}Tl chloride dual isotope SPECT (Tc/Tl SPECT). It is not always accurate to investigate mandibular involvement using Tc SPECT alone, because ^{99m}Tc-MDP or HMDP (Tc) uptake is caused not only by tumor activity, but also by inflammation or reactive change of the periosteum. ^{201}Tl chloride (Tl) uptake is thought to be a good reflection of tumor viability. In order to reveal uptake by tumor activity, we used Tc/Tl SPECT fusion imaging, a modified method regarding which only one report[17] has revealed its usefulness. We obtained Tc/Tl SPECT fusion image using the Automatic Registration Tool (ART, TOSHIBA, Japan) system. The objective of this study was to evaluate the usefulness of Tc/Tl SPECT for assessing mandibular invasion by head and neck cancer, as compared with Tc SPECT alone and CT.

Preliminary study
In evaluating mandibular invasion using ART, we made a fusion display consisting of Tl SPECT in red and Tc SPECT in white. Intensity of the uptake of Tc and Tl of the composed image can be changed by arranging the upper window level for display. Condition of intensity of Tc SPECT or Tl SPECT could not be changed independently. When we diagnose mandibular invasion on Tc/Tl SPECT fusion images a problem is that the extent of Tc or Tl uptake changes according to the condition of the
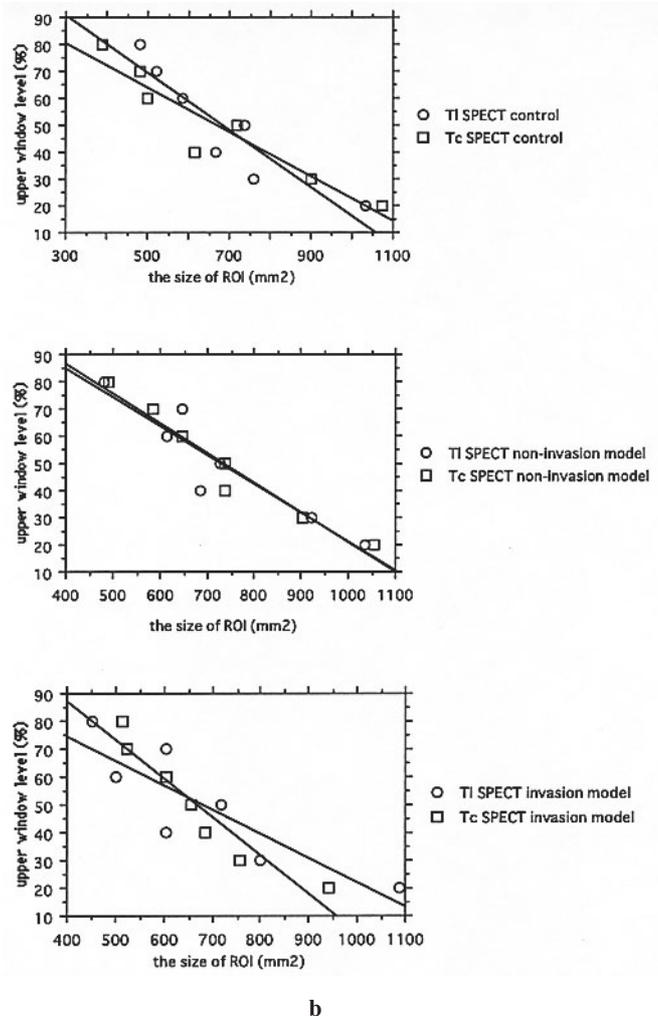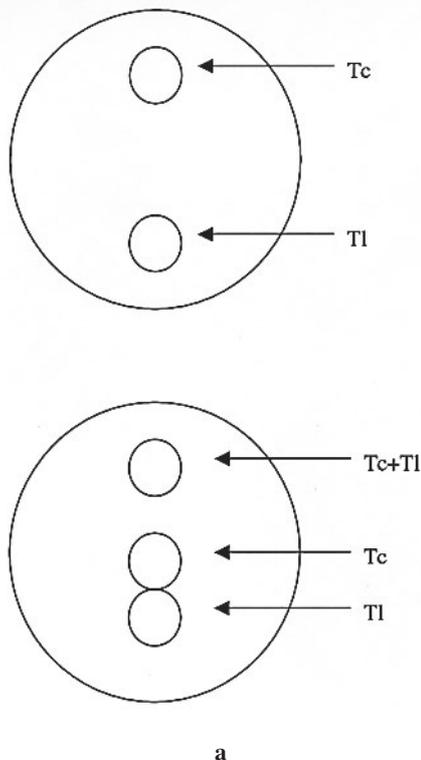

Fig. 1 a: Seen from the top of the 6,500 m*l* pillar, the pillar with Tl was set on the contralateral side of the one with Tc in the phantom study for control (*upper figure*). For the second phantom study, two pillar were filled with Tc and Tl close to each other and one pillar was filled with a mixture of Tc and Tl (*lower figure*). b: From the top of the figures to the bottom, graphs showed inverse correlations between size of ROI in Tl (r = 0.915, 0.935, 0.862) or Tc SPECT (r = 0.941, 0.974, 0.954) and upper window level in the control model, non-invasion model, and invasion model, respectively.

Table 1 Sites of head and neck cancer

Site	Number of cases
Mandible	14
Floor of the mouth	9
Tongue	5
Retromolar trigone	2
Buccal mucosa	2
Lower lip	1
Submandibular gland	1

Table 2 Diagnostic basis of mandibular invasion using Tc/Tl SPECT

Tc SPECT	Tl SPECT	Diagnosis
Positive	Positive	Mandibular invasion
Positive	Negative	Inflammation or tooth disease
Negative	Positive	No mandibular invasion
Negative	Negative	Normal

Positive and negative means increased uptake and no increased uptake respectively by the lesion.

Table 3

Diagnosis for mandibular invasion using Tc SPECT alone

	TP	TN	FP	FN	Total
Tc SPECT	20	3	11	0	34

TP = true positive, TN = true negative
FP = false positive, FN = false negative

Accuracy of Tc SPECT alone

	Sensitivity	Specificity	Accuracy	PPV	NPV
Tc SPECT	100.0%	21.4%	67.6%	64.5%	100.0%

PPV = Positive predictive value
NPV = Negative predictive value

display; upper window level. For example, the higher the upper window level is set, the smaller becomes the lesion. In order to delineate the most proper condition of display for Tc/Tl SPECT fusion image using the ART system, we performed a phantom study. At the beginning of the study, for control image, Tc and Tl SPECTs were taken using a 20 ml pillar (30 mm in diameter) with 4.61×10^5 Bq/g ^{99m}Tc-MDP and one with 1.03×10^5 Bq/g ^{201}Tl chloride in the 6,500 ml pillar (200 mm in diameter) filled with water. Second, for the non-invasion model, these two 20 ml pillars were set up close to each other. On the other hand, for the invasion model, a 20 ml pillar filled with 8.87×10^5 Bq/g ^{99m}Tc-MDP, and 6.42×10^4 Bq/g ^{201}Tl chloride was fixed on the contralateral side (Fig. 1a). The study was performed using a triple head rotating gamma camera (GCA9300, TOSHIBA, Japan) equipped with low-energy parallel-hole collimator. Photopeaks were set

at 140 keV for Tc and 71 keV for Tl. Acquisition time was 30 min in a matrix and pixel of 128×128 and 3.2 mm, respectively. Scattered correction was done using triple energy window (TEW) method[18,19]; main windows were 20% for Tc and 40% for Tl, lower and upper sub windows were 7% for both Tc and Tl. Reconstruction was performed using ordered-subsets expectation maximization (OSEM) algorithm with Butterworth and Ramp filters. Finally, fusion image was made by using the ART system. Planar images were taken for 20 min in a 512×512 matrix. In semi-quantitative assessment, mean counts and number of pixels of region of interest (ROI) were obtained under 20%, 30%, 40%, 50%, 60%, 70%, and 80% upper window levels. In all models, sizes of ROI for pillar phantom were calculated by the following formula; size = number of pixels $\times 3.2 \times 3.2$ (mm^2), and compared with the actual cross section area of the pillar phantom (706.5 mm^2). The data analysis was done with Stat view software package (Version 5.0; Abacus Concepts, Inc., Berkeley, CA).

Results were shown in Figure 1b; in the phantom study of the control model, the sizes of ROIs in Tl and Tc SPECT were inversely correlated with the upper window level (r = 0.915, 0.941). When the size was 706.5 mm^2, the upper window levels of Tl and Tc SPECT were within the range of 40 to 50% (47.545%, 47.105%). With respect to the experiment for the non-invasion model, sizes of ROIs in Tl and Tc SPECT were also inversely correlated with upper window level (r = 0.934, 0.974). The upper window levels of Tc and Tl SPECT were within the range of 50 to 60% at the size of 706.5 mm^2 (52.4275%, 53.083%). Regarding the experiment for the invasion model, size of ROIs in Tl and Tc SPECT were also inversely correlated with upper window level (r = 0.862, 0.954). When the size was 706.5 mm^2, the upper window levels of Tl and Tc SPECT were within the range from 40 to 50% (47.6445%, 44.93%).

MATERIALS AND METHODS

Patients

Thirty-four patients with suspected mandibular invasion by head and neck cancer based on clinical findings such as tumor location, tumor size, and tumor adhesion to the mandible, who were treated at Chiba Cancer Center, Chiba, Japan between July 1997 and July 2002, were enrolled in this prospective study. They consisted of 23 males and 11 females, aged 39 to 85 (mean 63) years. Table 1 shows the sites of the cancers. Sizes of tumor were measured by the average value between length and width on CT images of 25 cases, when recognition of tumor location was possible. In the remaining 9 cases, in one evaluation was done on MRI, and in 8 the length and width were actually measured. The average values were 15 to 75 mm (mean; 34.5 mm). The specimens were stored in formalin, then sectioned and stained with hematoxylin

Table 4

Diagnosis for mandibular invasion using Tc/Tl SPECT at 3 upper window levels

Upper window level	TP	TN	FP	FN	Total
40%	18	11	4	1	34
50%	18	11	4	1	34
60%	16	11	4	3	34

TP = true positive, TN = true negative
FP = false positive, FN = false negative

Accuracy of Tc/Tl SPECT at 3 upper window levels

Upper window level	Sensitivity	Specificity	Accuracy	PPV	NPV
40%	94.7%	73.3%	85.3%	81.8%	91.7%
50%	94.7%	73.3%	85.3%	81.8%	91.7%
60%	84.2%	73.3%	79.4%	80.0%	78.6%

PPV = Positive predictive value
NPV = Negative predictive value

Table 5

Diagnoses of mandibular invasion using CT

TP	TN	FP	FN	Total
12	13	0	5	30

TP = true positive, TN = true negative
FP = false positive, FN = false negative

Accuracy of CT

Sensitivity	Specificity	Accuracy	PPV	NPV
70.6%	100.0%	83.3%	100.0%	72.2%

PPV = Positive predictive value
NPV = Negative predictive value

and eosin. Histopathologically, 29 of 34 cases were diagnosed as squamous cell carcinoma (SCC). Among the remaining five cases, two were classified as verrucous carcinoma and the three others as adenosquamous carcinoma, osteosarcoma, and malignant fibrous histiocytoma, respectively. Five of all patients had undergone radiotherapy 9 to 78 months prior to the Tc/Tl SPECT examination (mean 40 months), and the radiation dose was 50–75.26 Gy (mean 60.9 Gy). For 30 of the 34 patients, CT scans were taken. Their radionuclide examinations and CT investigations were performed one to 83 days (median 34 days) and one to 80 days (median 30 days) before operation, respectively. With respect to the primary site, after Tc/Tl SPECT examination, 14 patients were treated by preoperative radiotherapy. All patients provided informed consent for the investigation with Tc SPECT and Tl SPECT. This study followed the ethical standards of

the committee on human experimentation of our institution.

Tc SPECT and Tc/Tl SPECT imaging
Whole-body bone scintigraphy was performed two to three hours after the intravenous injection of 740 MBq of ^{99m}Tc-MDP or -HMDP. After taking a bone scan, 111 MBq of ^{201}Tl chloride was also given intravenously. Tc/Tl SPECT was taken at 15 minutes postinjection of the ^{201}Tl chloride. Dual isotope SPECT was taken using a triple head rotating gamma camera (GCA9300), equipped with a low-energy parallel-hole collimator. The photopeak was set at 140 keV and 71 keV for Tc and Tl SPECT, respectively. A 20% and 40% symmetric window was used for Tc SPECT and Tl SPECT, respectively. The images were acquired in a 128×128 matrix. The slices were reconstructed using the OSEM algorithm with Ramp and Butterworth filters. We then obtained a Tc/Tl SPECT fusion image using the ART system.

Imaging analyses of Tc SPECT and Tc/Tl SPECT
For Tc SPECT alone, mandibular invasion was considered as positive when Tc uptake was shown in the region corresponding to the mandible or abutting the tumor in the axial slice that had the highest abnormal uptake of Tc. When it was difficult to judge mandibular invasion from the axial slice, we diagnosed it from the coronal one. For Tc/Tl SPECT, using the fusion image, at 40, 50, 60% upper window, we diagnosed mandibular invasion to be positive when the lesion with abnormal Tl uptake overlapped that with abnormal Tc uptake in the axial slice with the highest Tl uptake by the tumor (Table 2). From the result of the preliminary study, it was diagnosed as negative when the lesion with Tl uptake only bordered that with Tc uptake. A single interpreter read the scans without knowledge of the histopathological findings. Whether there was bone involvement or not was finally verified by histopathological assessment of the surgical specimen, and the results of both SPECTs were compared with the histological diagnosis.

CT imaging
Of 34 patients, 30 underwent CT examinations. For 2 of 30, CT examinations were done at other institutions before attending our center, and one had not been evaluated under bone window. Of 28 studies, 25 studies were performed using High Speed Advantage and 3 using Light Speed Ultra (GE Yokogawa Medical System, Japan). CT studies were performed in the axial plane with 5-mm-thick contiguous sections from the skull base to the thoracic inlet. For bone condition, upper and lower windows were set at 1,500 to 2,000, and 150 to 250 CT value, respectively. On the other hand, 350 to 450 upper window and 60 to 85 lower one were adopted to soft tissue condition. Twenty contrast enhanced CT (CE-CT) images and 10 CT images were obtained in a 512×512
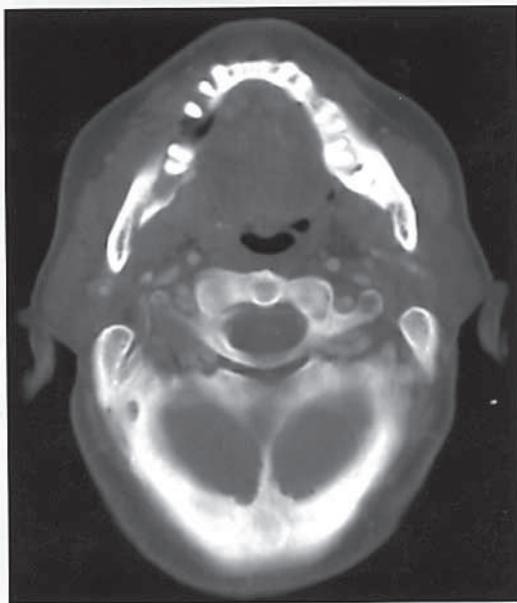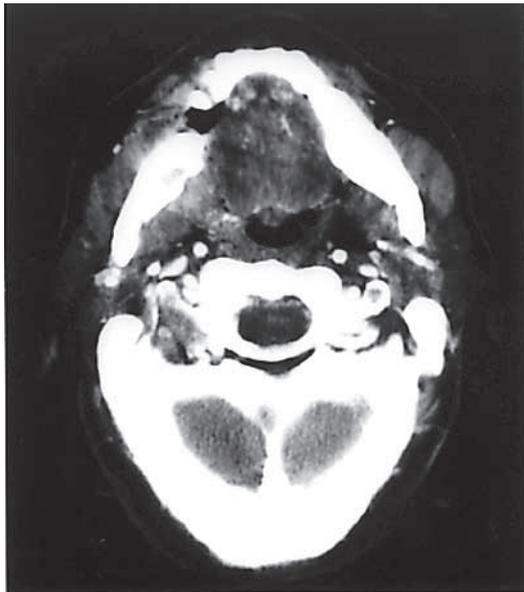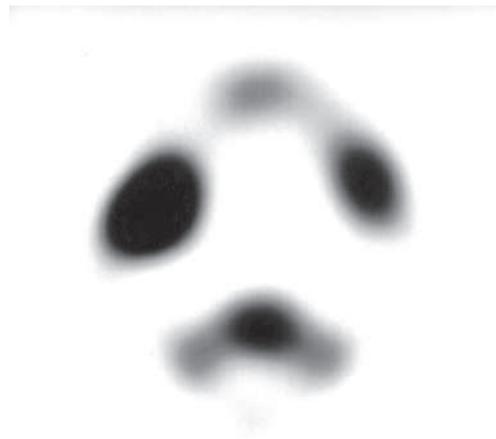
Fig. 2 a: The upper scan was contrast enhanced CT (CE-CT) under soft tissue window (wu: 342.25/wl: 85.06 CT value), and the lower one was under bone window (wu: 2005.84/wl: 255.69 CT value). Mandibular invasion was diagnosed as positive. b: In ^{99m}Tc-HMDP SPECT (Tc SPECT), the area appearing to abut the tumor on CE-CT showed abnormal Tc uptake. The diagnosis was positive. c: Under 50% upper window level, Tc/Tl SPECT revealed that Tl uptake overlapped most of the lesion with Tc uptake and the diagnosis was positive for mandibular invasion. From the top of the figure, Tc SPECT is presented in the first layer in white, Tl SPECT in the third in red, and the Tc/Tl SPECT fusion image in the second.

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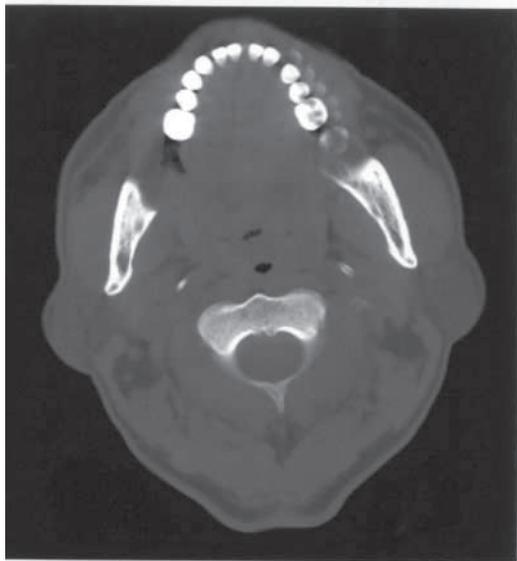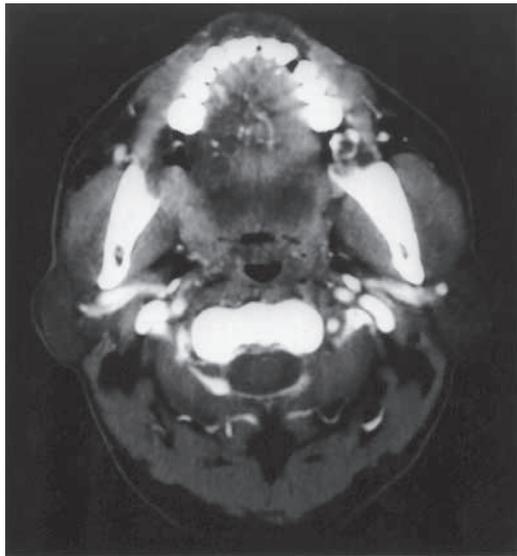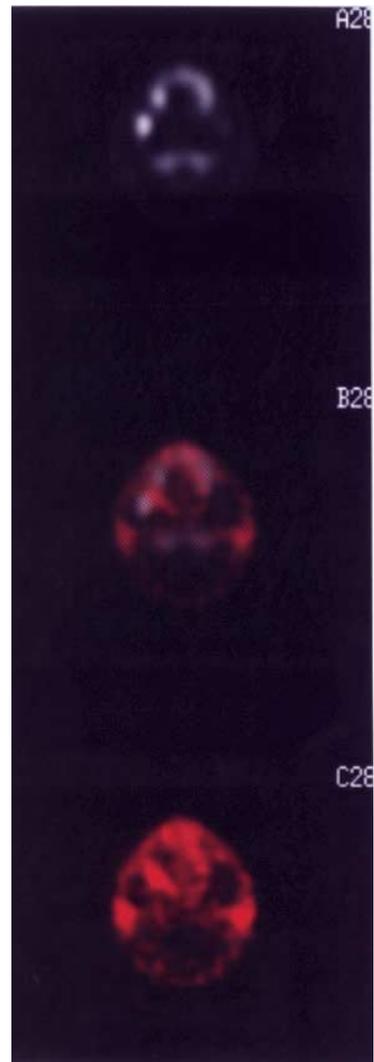
Fig. 3 a: The upper scan was contrast enhanced CT (CE-CT) under soft tissue window (wu: 342.25/wl: 85.06 CT value), and the lower one was under bone window (wu: 2005.84/wl: 255.69 CT value). Mandibular invasion was diagnosed as positive. b: Tc SPECT exhibited abnormal uptake in the lesion appearing to abut the tumor on CE-CT. The diagnosis was positive. c: Under 50% upper window level, Tc/Tl SPECT showed the area with Tl uptake only bordering on that with Tc uptake, and the diagnosis was negative. From the top of the figure, Tc SPECT is presented in the first layer in white, Tl SPECT in the third in red, and the Tc/Tl SPECT fusion image in the second.

matrix. The criterion of mandibular invasion was defect of the bone corresponding to the cortex adjacent to the tumoral mass. A single interpreter read the scans without knowledge of the histopathological findings, referring to both bone and soft tissue window scans.

RESULTS

The diagnostic accuracy of Tc SPECT and Tc/Tl SPECT is shown in Tables 3 and 4. All Tc/Tl SPECT had higher specificity, accuracy, and positive predictive value (PPV) (at 40%, 50%, 60% upper window level; 73.3%, 73.3%, 73.3% for specificity, 85.3%, 85.3%, 79.4% for accuracy, and 81.8%, 81.8%, 80.0% for PPV) than Tc SPECT used alone (21.4%, 67.6%, 64.5%). Regarding the upper window level, all diagnostic values at 40 and 50% were superior to those at 60%. Table 5 showed the result using CT. Among these 3 modalities, specificity and PPV were highest using CT. From the histopathological point of view, to determine whether Tl correctly accumulated to the tumorous side or not, Tl uptake on fusion images at 50% upper window level, which specimens could be three-dimensionally reconstructed, was compared with the pathological findings in 12 cases. In 10 of 12 cases, the area with Tl uptake corresponded to the area identified to have tumor tissue in the specimen. In contrast, in the remaining 2 cases, the lesion with Tl uptake partly coincided with tumor tissue. One case, diagnosed to have SCC of the lower lip, had no Tl uptake in the lesion showing only perineural invasion of the mandible. In the other patient with SCC of the mandible there was no Tl uptake in the area, which exhibited tumor invasion within the epithelium. Figure 2a shows contrast enhanced CT (CE-CT) of a typical case of a 71-year-old male with SCC of the right side of the mandibular gingiva. Both Tc (Fig. 2b) and Tc/Tl SPECT (Fig. 2c) showed true positives (TP). Compared with the histopathological finding, the lesion with Tl uptake largely coincided with that verified to have tumor tissue. On the other hand, Figure 3a exhibits CE-CT of a typical case of a 63-year-old male with SCC of the right side of the retromolar trigone. Tc SPECT (Fig. 3b) showed false positive (FP) whereas Tc/Tl SPECT (Fig. 3c) showed true negative (TN). The area where Tl uptake was present largely corresponded to that exhibiting tumor tissue.

DISCUSSION

There is a report indicating that the factors that determine disease control in the surgical management of oral cancer are tumor size, nodal status, and completeness of resection. One of the treatments for head and neck cancer is surgery consisting of marginal and segmental resection. Lately, studies about routes of tumor entry into the mandible have been published,[20] leading to acceptance of the view of marginal resection. There are some reports regarding the mandibular-preserving–procedure.[21,22] For the purpose of preserving mandibular continuation and preventing functional and esthetic disability, marginal resection is recommended in appropriate cases. Politi et al. suggested that the cases most suitable for marginal resection are those with no bone invasion, but requiring bone removal to ensure good tumor margins because of the proximity of the cancer to the jaw.[15] Totsuka et al. revealed that marginal resection was effective in controlling lower gingival cancers with and without apparent bone involvement. When either erosive bone defects that did not extend beyond the inferior alveolar canal, or invasive bone defects confined to a superficial area of the alveolar bone were detected radiologically,[23] they stated that marginal resection was thought effective. Therefore, pre-operative diagnosis of mandibular invasion is a most important issue.

Although patients suspected of having mandibular involvement of head and neck cancer have been investigated using OPG, CT,[24] MRI,[8] periosteal stripping,[9] planar bone scintigraphy and Tc SPECT,[10–14] no single modality has the ability to accurately assess bone invasion by itself.[1,7,15,16] Some investigators recommend using two or more modalities that can complement each other, for example, CT and MRI. In our study, Tc/Tl dual isotope SPECT was performed to evaluate mandibular invasion by head and neck cancer. Its specificity, accuracy, and PPV were higher than those of Tc SPECT alone. Imola et al.[11] demonstrated 95% sensitivity and 72% specificity using Tc SPECT. In a previous study using the same modality, Curran et al. showed 100% sensitivity and 29% specificity,[10] and Zieron et al. demonstrated 95% and 48% using Tc SPECT.[12] Acton et al. reported 60% and 67% for the corresponding values by using quantification ratios of Tc SPECT.[13] Our results showed 100.0% sensitivity and 21.4% specificity with Tc SPECT but 94.7% sensitivity and 73.3% specificity using Tc/Tl SPECT at 40 or 50% upper window level. The specificity of Tc/Tl SPECT was higher than that of Tc SPECT, because Tc SPECT has low PPV, and we could not distinguish what caused the high uptake of Tc corresponding to the mandible or adjacent to the tumor among bone involvement, reactive changes of the periosteum caused by the tumor, inflammation, or dental disease.

Although in a previous report using semi-quantitative values of Tc SPECT,[14] Chan et al. suggested that lesion to spine ratio and lesion to non-lesion ratio in mandibular invasion cases were significantly higher than in those with normal mandible or dental disease, in fact, the mechanism of skeletal tracer uptake seems to be too complicated[23] to differentiate the cause, for example, between Tc uptake by tumor and by reactive changes of the periosteum. Therefore, by making use of the merit of the superimposing technique lately being used, it may be possible to obtain a superior result.

Tl uptake is thought to reflect tumor activity, and so

mandibular invasion could be diagnosed as positive when Tl accumulation was present in a lesion localized to the mandible. However, using Tl SPECT alone is an inadequate method to evaluate bone involvement because it could not visualize normal bone including mandible. Therefore, Tc/Tl SPECT is needed to disclose the increased uptake of Tc caused by tumor invasion. Tl SPECT has been frequently used for differentiating brain tumors[25,26] and for evaluating the effectiveness of treatments for recurrent brain tumors from necrosis.[27] Regarding head and neck cancers, Tl SPECT has been used for evaluating primary lesion[28] and the effectiveness of radiotherapy.[29–32] The first study using ^{99m}Tc-HMDP and ^{201}Tl dual isotope SPECT evaluated skull-base invasion by head and neck tumors.[33] There has been only one report demonstrating the usefulness of dual-isotope SPECT using ^{99m}Tc-HMDP and ^{201}Tl-chloride to assess mandibular invasion; that study described 39 patients with intraoral squamous cell carcinoma.[17] In this previous study, the sensitivity, specificity, and accuracy of the dual-isotope SPECT were 100%, 88.5%, and 92.3%, respectively. They compared between early and delayed Tc/Tl SPECT obtained at 10 min and 2 hr post-injection of Tl respectively, and obtained the same diagnostic values. We performed only early examination, and made use of early image of Tl SPECT for Tc/Tl SPECT. In making Tc/Tl SPECT fusion image using the ART system, a problem is that the larger the area overlapping between Tc and Tl becomes, the lower becomes the upper window level of Tl SPECT image for reconstruction. The two previous studies using Tc/Tl SPECT did not refer to this point. Therefore, for the purpose of establishing the proper value, we performed the phantom study. The result was that in all 3 kinds of model the sizes of ROI in Tl and Tc SPECT and those of the actual cross section area of the phantom pillars were closest within the range of 40 to 60% upper window level. In the clinical study, 2 of 34 cases showed no abnormal Tc uptake at 60% level, while the accuracy obtained under 40 and 50% level was the same and fairly high.

In order to disclose accumulation of Tl caused by tumor tissue, we compared Tc/Tl SPECT fusion image with the histopathological findings, and found that in 10 of 12 cases the lesion with Tl uptake corresponded to tumor tissue. In the other 2 cases, the areas where tumor cells were present but which had no Tl uptake were those with perineural invasion and invasion within epithelium. For this reason, it is thought that the area had too small invasion to exhibit intense uptake due to the limited spatial resolution of the study using SPECT. To the best of our knowledge, there only two studies have reported comparison of Tl uptake on SPECT with the histopathological findings.[34,35] With respect to brain tumor, Yoshii et al. revealed that the delayed Tl uptake may be of value for estimating the viability and degree of malignancy of glial tumors, because of the relation of Tl accumulation to
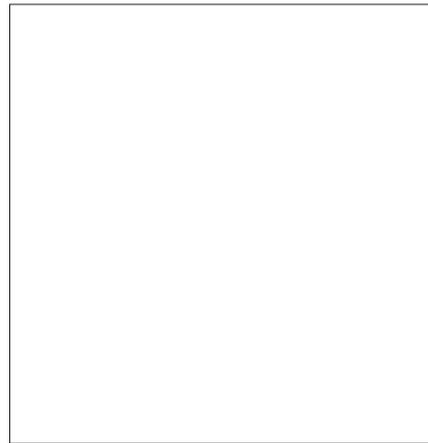
Fig. 4 The decision tree for mandibular invasion in 30 cases underwent both Tc/Tl SPECT and CT examination. Use of Tc/Tl SPECT and CT appears to be useful to diagnose mandibular invasion.

tumor cell density.[34] Our previous study indicated that Tl uptake on early image was reflected by its peculiar biochemical mechanisms.[35]

The reason why we obtained high specificity in Tc/Tl SPECT but low specificity in Tc SPECT is thought to be mainly based on the fact that seven of our 34 cases were diagnosed as FP in Tc SPECT but TN in Tc/Tl SPECT. None of them had undergone radiotherapy before attending our institution. Three of these seven cases underwent mandibulectomy after preoperative radiotherapy, and their histopathological findings were different from those before receiving radiotherapy. We confirmed the remaining four cases histologically. Two of 4 cases had insufficient surgical specimen for investigation, but the other two cases showed bone destruction caused not by tumor tissue.

We had 1 case diagnosed as TP by Tc SPECT but FN by Tc/Tl SPECT. The size of the tumor of this case was 35 mm × 19 mm (average value: 27 mm), and the value was not especially small in comparison with the others. Volume of tumor has been reported to affect uptake of Tl.[36] Then, there seems to be a possibility that the area with Tl uptake unreasonably evaluated smaller by small volume would have an effect on diagnosis using Tc/Tl SPECT. However, In our study, no significant difference in tumor volume was noted among the groups with FN, FP, TN, and TP.

Among the imaging modalities for mandibular invasion by head and neck tumor, CT is most often used. In this study, sensitivity and negative predictive value (NPV) were lower in CT than in Tc/Tl SPECT, while in contrast, specificity and PPV were higher. Referring to the previous reports, the ranges of sensitivity, specificity, PPV, NPV were 45.5% to 91.3%, 57% to 96.3%, 65% to 95.4% and 61.1% to 93% respectively. Sensitivity and NPV

obtained by us were within these ranges (70.6%, 72.2%), and specificity and PPV were superior (100%, 100%). Some authors have suggested a decision tree for mandibular invasion, using clinical findings and imaging modality, in oral[37] and oropharyngeal cancers.[38] In this study, regarding diagnosis of mandibular invasion, we could make the decision tree consisting of only imaging modalities. Figure 4 shows the decision tree composed of Tc/Tl SPECT and CT based on the actual results of 30 patients who underwent both Tc/Tl SPECT and CT. First, patients were classified according to diagnosis using CT (PPV = 100.0%, NPV = 70.6%). Second, patients diagnosed as negative underwent Tc/Tl SPECT, and higher NPV was obtained (90.9%).

In conclusion, Tc/Tl SPECT was a useful method to detect mandibular invasion by head and neck tumors.

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