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Semi-quantitative assessment of oral cavity squamous cell carcinoma using ^{201}Tl SPECT for evaluating effectiveness of preoperative radiotherapy

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The aim of this study is to reveal the usefulness of semi-quantitative assessment using ^{201}Tl chloride (Tl) single photon emission computed tomography (SPECT) (Tl SPECT) to evaluate the effectiveness of radiotherapy in 15 patients with oral cavity squamous cell carcinma (SCC). Fifteen patients were diagnosed with SCC by biopsy. All 15 patients enrolled in this study were planned to undergo preoperative radiotherapy with or without chemotherapy using carboplatin (CBDCA) and received reduction operation. Tl SPECTs were performed 15 minutes after intravenous administration of 111 MBq ^{201}Tl chloride. Regions of Interest (ROI) were set up around tumor (T), and non-lesion (N) at the part of contralateral scalp at the height of the cerebellum. The ratios of mean counts in ROI of the tumor to those in non-lesion were measured as pre- and post-treatment T/N ratios (pre T/N, post T/N). Furthermore, reduction rate (RR) was obtained by calculating [(pre T/N – post T/N)/(pre T/N)] × 100%. Each parameter (pre T/N, post T/N, and RR) was compared to histopathological grade of surgical specimen based on the Oboshi and Shimosato classification (grade I–IV). RR showed significantly higher values in grade III and IV than in grade I and II ($p = 0.0008$). In conclusion, semi-quantitative assessment using Tl SPECT, especially calculating RR, is useful to evaluate the effectiveness of preoperative radiotherapy.

Key words: ^{201}Tl SPECT, radiotherapy, semi-quantitative evaluation, oral cavity squamous cell carcinoma

INTRODUCTION

ORAL CAVITY SQUAMOUS CELL CARCINOMA (SCC) has been generally treated with combined surgery and radiation therapy with or without chemotherapy (CHT), or either modality alone. Radical surgical treatment alone results in functional and esthetic defects, while reduction-operation after preoperative radiotherapy may result in a smaller defect. If irradiated tumor could be diagnosed to have no viable cells before surgery, reduction-operation could be selected as treatment. Furthermore, with respect to preoperative concurrent chemotherapy plus radical surgery, there is a report suggesting that patients who achieved good responses histopathologically had superior survival rates in comparison with patients having extensive residual tumor in surgically resected specimens of advanced oral cancer.[1] So, to determine how much to resect and predict the prognosis, it is important to evaluate the effectiveness of radiotherapy. In evaluating the effectiveness of preoperative radiotherapy for oral cavity SCC, histopathological examination has often been used, while Valentino et al.[2] reported that interval pathologic assessment might be misleading in patients diagnosed to have head and neck cancer treated with concurrent hyperfractinated radiation therapy and intraarterial

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Table 1 Characteristics of patients with HNSCC enrolled in this study

	Stage	Site of tumor	Differentiation	RT dose (Gy)	CHT*	IRTO (days)	Histological grade**	Clinical evaluation
Case 1	IVA	FOM	P/D	41.6	—	35	Grade IIb	PR
Case 2	IVA	Mandibular gingiva	W/D	41.6	260 mg	28	Grade IIa	NC
Case 3	IVA	RMT	W/D	41.6	—	55	Grade IIb	PR
Case 4	II	Buccal mocosa	W/D	38.4	252 mg	36	Grade IIb	NC
Case 5	IVA	Mandibular gingiva	M/D	41.6	—	44	Grade IIa	PR
Case 6	IVA	FOM	M/D	41.6	336 mg	33	Grade IIa	NC
Case 7	II	FOM	M/D	41.6	—	34	Grade IV	CR
Case 8	III	FOM	W/D	41.6	—	43	Grade IIb	NC
Case 9	IVA	Mandibular gingiva	M/D	41.6	378 mg	42	Grade IVc	PR
Case 10	II	Buccal mucosa	M/D	41.6	—	50	Grade IVc	CR
Case 11	IVA	Mandibular gingival	W/D	41.6	299 mg	36	Grade IIa	PR
Case 12	II	Mandibular gingiva	M/D	41.6	—	30	Grade IVb–c	PR
Case 13	II	Mandibular gingiva	W/D	41.6	—	52	Grade III	CR
Case 14	IVA	Maxillary gingiva	W/D	41.6	390 mg	31	Grade IVb	NC
Case 15	IVA	Maxillary gingiva	W/D	41.6	276 mg	29	Grade IVb	NC

RT = radiotherapy, CHT = chemotherapy, IRTO = intervals between the end of the radiotherapy and surgical operation, FOM = floor of the mouth, RMT = retromolar trigone, W, M, and P/D = well, moderately, and poorly differentiated

*When a case did not undergo CHT, — was indicated. When a case underwent CHT with CBDCA, the dose administered was shown.

**Patients were diagnosed referring to the Oboshi and Shimosato classification for histological grade.

supradose cisplatin. Evaluation of effectiveness of radiotherapy using ^{201}Tl chloride (Tl) single photon emission computed tomography (SPECT) (Tl SPECT) has been performed in brain tumor,[3–6] lung cancer,[7–10] bone and soft tissue sarcoma,[11] and esophageal cancer.[12] With respect to head and neck region, there are a few reports on nasopharyngeal carcinoma (NPC).[13–15] Omura et al.[16] reported that it was useful to evaluate the effectiveness of preoperative radiotherapy using Tl SPECT in SCC of maxilla, and Tl uptake at pre- and post-radiotherapy tended to correlate with the histopathological diagnosis. Nagamachi et al.[17] conducted the assessment using pretreatment Tl SPECT in head and neck cancer and revealed that the delayed and retention indices were useful parameters. In this study, we compared the semi-quantitative parameters of Tl SPECT with histopathological grade after preoperative radiotherapy and evaluated whether or not these parameters are useful for assessing the effectiveness of radiotherapy.

MATERIALS AND METHODS

Materials

Characteristics of all 15 patients were exhibited in Table 1. All 15 patients admitted into our institution from 1997 November to 2000 May, were diagnosed to have SCC in oral cavity by biopsy, and enrolled in this study. Patients consisted of 9 males and 6 females, aged from 47 to 76 years (mean 62 years). None of the 15 patients had undergone any treatment before admission. Tumor, node and metastasis (TNM) classification was applied according to the 1987 guidelines of the Union Internationale Contre le Cancer (UICC). Five of 15 patients were classified as T2, 1 as T3, and 9 as T4, and 10 of 15 were classified as N0, 2 as N1, and 3 as N2. Six of 15 cases had tumors in mandibular gingiva, 4 in the floor of the mouth (FOM), 2 in buccal mucosa, 2 in maxillary gingiva, and 1 in retromolar trigone (RMT). All patient provided informed consent for the investigation, and this study followed the ethical standards of the committee on human experimentation of our institution. All patients were followed for 5 to 66 months (mo) (mean 32 mo) from the first admission. Clinial parameters were defined by referring to the report of Spector et al.[18] However, in our study we classified patients with metastasis, locoregional recurrent disease, delayed regional metastasis, and distant metastasis into the group with recurrence. Furthermore, tumor death meant to die as a result of the tumor or tumor-related post-therapeutic causes.

Tl SPECT imaging

Pre-treatment Tl SPECTs were performed in 14 of 15 cases 1 to 30 days (mean 9 days) before the initiation of radiotherapy and in 1 case 1 day after the beginning of radiation. All patients underwent post-treatment Tl SPECT 17 to 51 days (mean 33 days) after the completion of radiotherapy. At 15 minutes post intravenous injection of 111 MBq ^{201}Tl chloride, SPECT was taken using a triple head rotating gamma camera (GCA9300, Toshiba Medical System Co., Tokyo, Japan), equipped with a low-energy parallel-hole collimator. The photopeak was set for 71 keV and a 40% symmetric window was used. Image data were obtained for 30 min in 120° rotation in a 128 × 128 matrix (3.2 mm per a pixel). The reconstructed

Table 2 The Oboshi and Shimosato classification

Grade I	There is injury to tumor cells but no disruption of cancer nests.
Grade IIa	There are viable tumor cells in large area.
Grade IIb	There are viable tumor cells in small area.
Grade III	There are only non-viable tumor cells.
Grade IVa	Specimen has no tumor cells with large necrotic area.
Grade IVb	Specimen has no tumor cells, consisting of granular tissue.
Grade IVc	Specimen has no tumor cells, consisting of scar tissue.

Table 3 Comparison between diagnosis for effectiveness of preoperative radiotherapy based on clinical findings and histopathological classification

Clinical findings	Grade I & II	Grade III & IV	total
CR	0	3	3
PR	4	2	6
NC	4	2	6

CR = complete response, PR = partial response, NC = no change

images were obtained with a Ramp filter following the ordered subsets expectation maximization (OSEM) algorithm using Butterworth filter. Scatter and attenuation correction was not performed. Region of Interest (ROI) was set around the tumor, and the part of scalp on the contralateral side was selected as non-lesion. In the post-treatment study, we selected the same ROI as in the pre-treatment study to avoid mistaking the region with Tl uptake by radiation mucosistis for the region with Tl uptake by tumor. In the pre- and post-treatment studies, the ratios of mean counts in the region of the tumor (T) to those in the non-lesion (N) were measured as T/N ratios (pre T/N, post T/N). Furthermore, the rates of reduction from pre-treatment to post-treatment (RR) were calculated as follow:

$$[(\text{pre T/N} - \text{post T/N})/(\text{pre T/N})] \times 100\%$$

CT imaging

Before the initiation of preoperative radiotherapy CT examinations were performed in 13 of 15 cases 0 to 8 days (mean 3 days) after Tl SPECT. Of 13 studies, 9 CE-CT scans and 4 CT scans were obtained. On the other hand, 22 to 51 days (mean 33 days) after the completion of radiotherapy, 11 cases underwent CT examinations. In 7 of 11 cases, CT imagings were performed 3 to 5 days (mean 3 days) before Tl SPECT. The remaining 4 patients underwent CT scans 0 to 6 days (mean 2 days) after the radioisotope studies. Of 11 examinations, 10 CE-CT scans and 1 CT scan were taken. CT images were taken in 5 mm thick contiguous sections from the skull base to the thoracic inlet in a 512 × 512 matrix, using High Speed Advantage (GE Yokogawa System, Japan).

Radiotherapy

The radiation dose of all 15 cases ranged from 38.4 to 41.6 Gy (mean 41.4 Gy). All patients underwent external accelerated hyperfractionated radiotherapy (AHF), and 1.6 Gy per fraction was administered twice a day. Concurrent CHT with administration of 249 to 390 mg carboplatin (CBDCA) (mean 306 mg) was performed in 7 of 15 cases.

Clinical diagnosis for effectiveness by radiotherapy was made according to General Rules for Clinical Studies on Head and Neck Cancer advocated by the Japan Society for Head and Neck Cancer. That is, Complete Response (CR): whole lesion disappeared, Partial Response (PR): volume of the lesion reduced more than 50%, and No Change (NC): volume of the lesion reduced less than 50% or increased less than 25%. Four of 15 patients were classified according to the clinical finding for lack of pre- or post-treatment morphological study. In 2 of the remaining 11 patients, it was difficult to reveal the tumor sizes in pre- and post-CT scans. Thus, 9 cases, including one undergoing MRI examination 4 days after the initiation of radiotherapy, were diagnosed using morphological investigations. In these 9 cases, post-treatment CT examinations were performed 22 to 51 days (mean 33 days) after the completion of radiotherapy.

Pathological diagnosis

Radical operations were performed in all 15 cases 28 to 55 days after the completion of treatment (mean 39 days). The specimens were stored in formalin and then sectioned and stained with hematoxylin and eosin. Four experienced pathologists investigated the resected tumors. Considering histopathological diagnosis of effectiveness of radiotherapy, the Oboshi and Shimosato classification[9] was applied to all cases (grade I–IV Table 2). We regarded grade I & II (8 cases) as the non-effective group and grade III & IV (7 cases) as the effective group. Semi-quantitative parameters (pre T/N, post T/N, and RR) were compared in these two groups.

Statistical analysis

The data analysis was done with Stat view software package (Version 5.0; Abacus Concepts, Inc., Barkeley, CA). Student's t-test was applied to test for independence between semi-quantitative parameters and histopathological classifications. When the p value was <0.05, the statistical difference was considered significant.

RESULTS

There was a significant difference in RR between grade I & II (32.13 ± 11.34%) and grade III & IV (54.14 ± 7.47%) ($p = 0.0008$ Fig. 1a). Namely, the higher the RR, the fewer viable cells were shown. In evaluating the effectiveness of

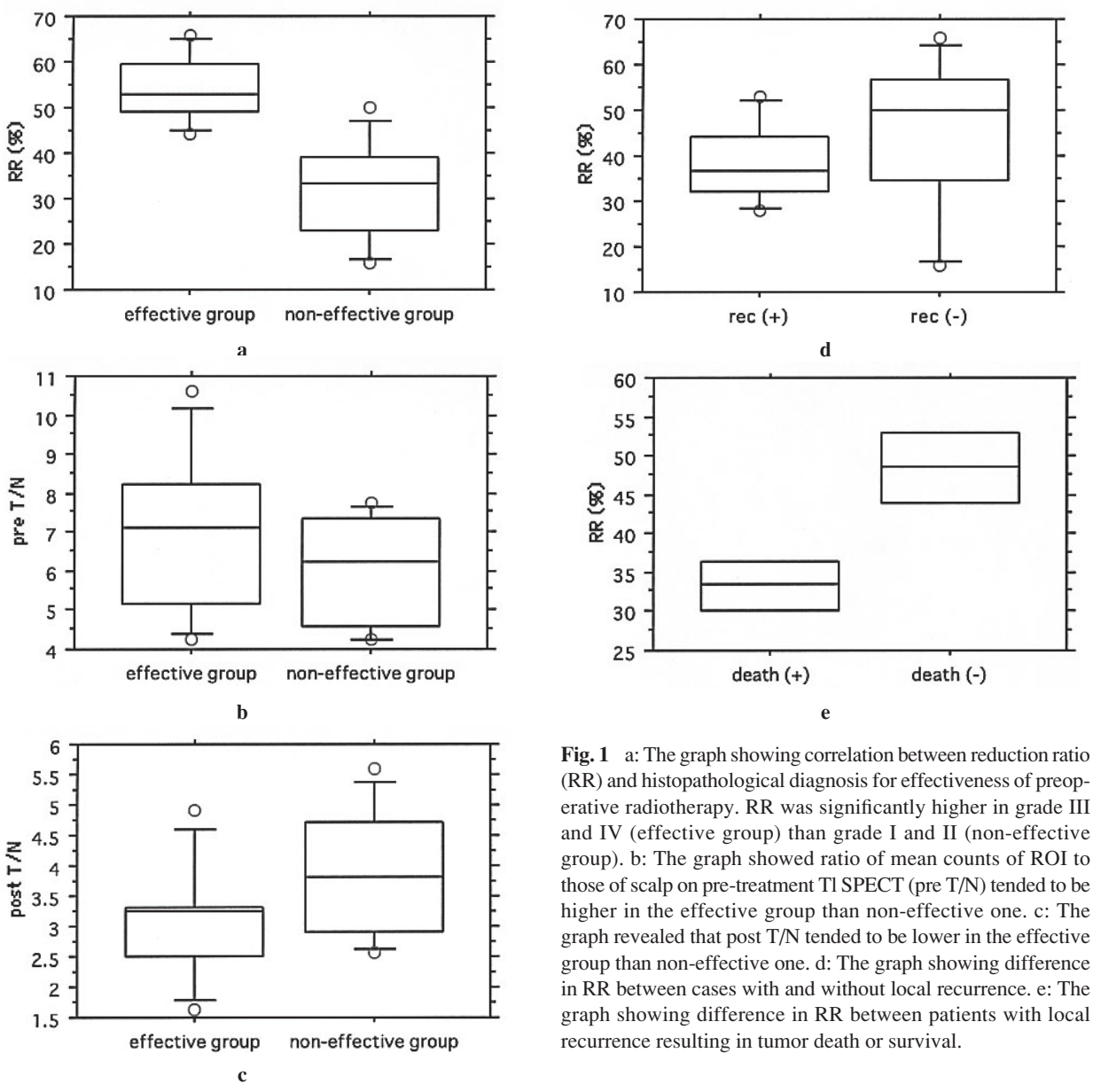
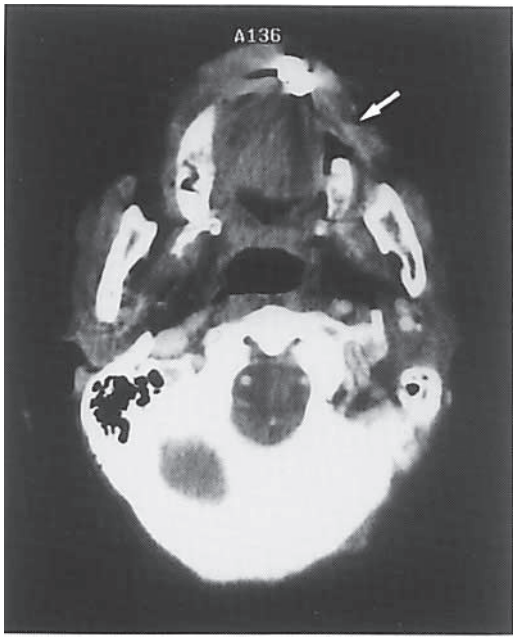


Fig. 1 a: The graph showing correlation between reduction ratio (RR) and histopathological diagnosis for effectiveness of preoperative radiotherapy. RR was significantly higher in grade III and IV (effective group) than grade I and II (non-effective group). b: The graph showed ratio of mean counts of ROI to those of scalp on pre-treatment Tl SPECT (pre T/N) tended to be higher in the effective group than non-effective one. c: The graph revealed that post T/N tended to be lower in the effective group than non-effective one. d: The graph showing difference in RR between cases with and without local recurrence. e: The graph showing difference in RR between patients with local recurrence resulting in tumor death or survival.

preoperative radiotherapy, comparing histopathological classifications to the treatment effectiveness based on the clinical findings, of 8 cases classified as grade I & II, 4 cases belonged to PR (50.0%). On the other hand, of 7 cases classified as grade III & IV, 3, 2, and 2 cases (42.9%, 28.6%, 28.6%) belonged to CR PR, and NC, respectively (Table 3). That is to say, the decision for the effectiveness of preoperative radiotherapy based on the clinical findings was not always consistent with that based on the histopathological findings. Pre T/N and post T/N were not significantly differentiated between grade I & II and grade III & IV ($p = 0.4004$, Fig. 1b, $p = 0.1640$, Fig. 1c, respectively). Pre T/N of the effective group tended to be higher (6.887 ± 2.220) than that of the non-effective one (6.049 ± 1.491). In contrast, post T/N of the effective group had a tendency to be lower (3.066 ± 1.107) as compared to the non-effective one (3.880 ± 1.107). In this study, 6 of 15 patients had recurrence, 4 of whom died. These 4 patients died from 5 to 15 mo (mean 8.5 mo) after operation. Their recurrences were found from 3 to 13 mo (mean 6.5 mo) after the end of treatment. On the other hand, 2 of 6 cases with recurrence showed recurrent disease from 38 to 49 mo (mean 43.5 mo) after surgery. With respect to histopathological grade, 3 of 4 cases with tumor death were classified as grade IIa, and 1 as grade IIb. One each of the remaining 2 cases with recurrence was classified as grade III and grade IV. No significant difference in RR was obtained between cases with ($38.33 \pm 9.00\%$) and without recurrence ($45.11 \pm 17.59\%$) ($p = 0.4033$, Fig. 1d). However, there was a significant difference in RR between patients who died of primary disease ($33.250 \pm 4.272\%$) and the ones alive but having recur-



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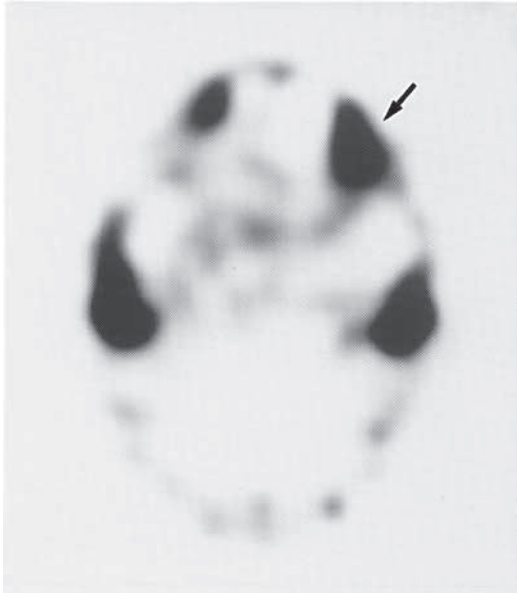

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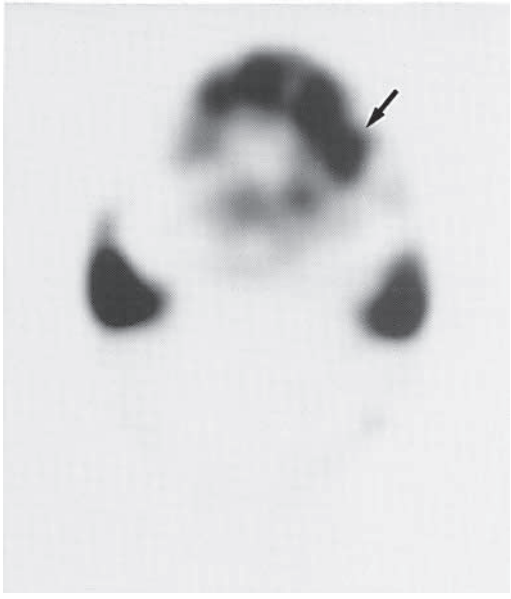

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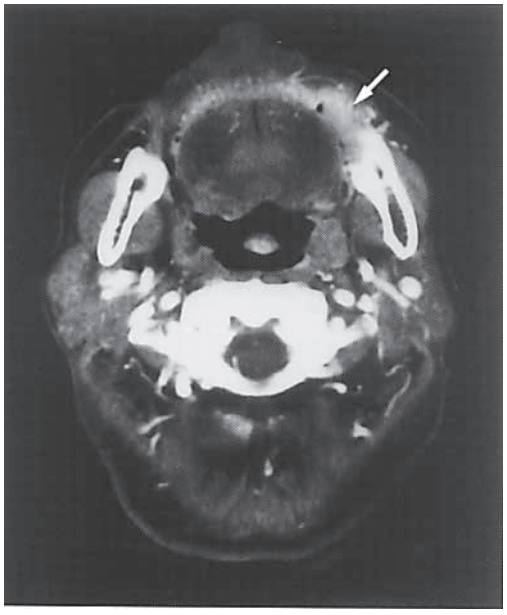
Fig. 2 a: CT at pre-treatment showed tumor in the left side of buccal mucosa (*arrow*). b: On pre-treatment Tl SPECT, intense uptake in the lesion corresponding to the tumor was identified (*arrow*). c: Tl SPECT at post-treatment showed slightly diminished uptake by the lesion corresponding to the tumor (*arrow*). Uptakes by the lesions adjacent to the uptake by the tumor were caused by mucositis.

rence (48.500 ± 6.364%) (p = 0.0226, Fig. 1e).

Figures 2 and 3 show representative cases with non-effective and effective tumor resulting in histological grade IIb and IVc, respectively. Figure 2a showed a pre-treatment CT of a 76-year-old-female who had SCC in the left side of the buccal mucosa (Case 4). Tl SPECT at pre-treatment exhibited intense uptake by the lesion corresponding to the tumor on CT, and pre T/N was 7.42 (Fig. 2b). The patient received preoperative radiotherapy of 38.4 Gy with administration of 252 mg CBDCA. Tl SPECT after therapy indicated slightly diminished uptake by the tumor and post T/N was 4.91 (Fig. 2c). RR was 18% and histological grade was grade IIb. From the clinical point of view, she was classified as NC. Figure 3a indicated CE-CT of a 71-year-old-male diagnosed with SCC on the left side of the buccal gingiva (Case 10). Pre-treatment Tl SPECT exhibited abnormal uptake of Tl by the lesion corresponding to tumor on CE-CT and pre T/N was 7.46 (Fig. 3b). The patient underwent radiotherapy of 41.6 Gy without CHT. In post-treatment Tl SPECT, abnormal uptake of Tl was markedly diminished, and post T/N was 3.30 (Fig. 3c). RR was 48% and he was histopathologically diagnosed as grade IVc. From the clinical findings, his result of treatment was CR.

DISCUSSION

Oral cavity SCC has generally been treated with combined surgery and radiation therapy with or without chemotherapy or either modality alone. In determining treatment, there is a report by Pericot et al.[20] that survival was significantly associated with the type of treatment in SCC of the oral cavity and oropharynx. Mohr et al.[21] reported that the percentages were higher after radical surgery alone for locoregional recurrence and for death than combined preoperative radiotherapy followed by radical surgery in SCC of the oral cavity and oropharynx. Furthermore, unfortunately, radical surgical treatment alone often leads to functional and esthetic defects. Compared with surgery alone, radiation treatment with or without



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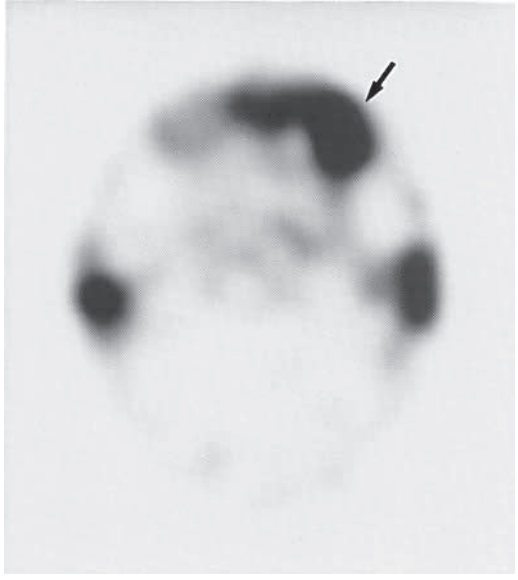

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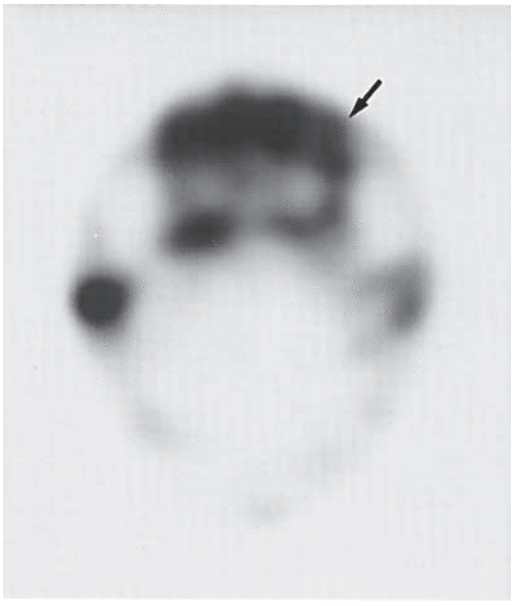

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Fig. 3 a: On contrast enhanced CT (CE-CT), there was tumor in the left side of buccal mucosa (*arrow*). b: There was intense uptake in the lesion corresponding to the tumor on Tl SPECT at pre-treatment (*arrow*). c: Tl SPECT at post-radiotherapy exhibited markedly diminished uptake by the tumor (*arrow*). Uptakes by the lesions adjacent to the uptake by the tumor were caused by mucositis.

CHT before surgery is a more conservative method and makes reduction-operation possible, when radiotherapy may bring a good result. With respect to preoperative concurrent chemotherapy plus radical surgery, there is a report suggesting that patients who achieved good responses histopathologically had superior survival rates in comparison with patients having extensive residual tumor in surgically resected specimen of advanced oral cancer.[1] Another study[22] indicated that phosphorylated Akt (P-Akt) which induced radiation resistance was variable as predictor of local failure in head and neck cancer. Therefore, for the purpose of defining the extent of resection and predicting the prognosis, it is important to assess the effectiveness of preoperative radiotherapy.

To assess the response to treatment in head and neck cancers, some morphological modalities such as CT and MRI have been mainly used.[23,24] But, in fact, it is often difficult to do accurate assessment using these modalities. In our study, on 2 of 11 CT scans obtained after treatment, identifying the lesion was difficult. When CR diagnosed using CT scans was classified as the response group, and PR and NC the non-response group, only 2 CR cases and 2 NC cases coincided with the effective group (grade III & IV) and non-effective group (grade I & II). Nakahara et al.[12] reported that in the assessment of the effect of preoperative chemoradiotherapy in advanced esophageal squamous cell carcinoma, a statistically significant difference was evident for reduction ratio obtained by Tl SPECT, in contrast to no significant difference in the reduction ratio calculated using CT or barium swallow. Furthermore, Togawa et al.[13] revealed that Tl SPECT had potential in the early assessment of the response to treatment of patients with NPC when compared with MRI. To the best of our knowledge, no report has focused on diagnostic accuracy in assessing the effectiveness of radiotherapy in oral cavity cancer using CT/MRI. In a prior report, changes after radiotherapy in larynx and pharynx were often difficult to differentiate from tumor itself,[23] just as in oral cancers. So, we compared RR obtained by Tl SPECT with the histopathological classi-

fication and morphological imaging, regarding cases with SCC in the oral cavity.

In our study, we used the Oboshi and Shimosato classification for evaluation of the effectiveness of preoperative radiotherapy. For histopathological classification of head and neck cancer, Valentino et al.[2] divided patients into groups having no cancer and residual cancer. Brun et al. classified patients into 4 group according to the proportion of viable tumor cells; grade I: 0% viable cells, grade II: 5%, grade III: 5–50%, and grade IV: more than 50%. They showed a statistically significant higher survival rate in regression grade I and II. Although Kirita et al. used the same classification as us, they compared patients with extensive residual tumor (grade IIa) to those with good responses (grade IIb, III, IV), and reported that patients belonging to grade IIb, III, IV had superior survival rates in comparison with those belonging to grade IIa in surgical resected specimens.[1] However, the aim of our study is to reveal the usefulness of semi-quantitative value of Tl SPECT for assessing the effectiveness of preoperative radiotherapy, and so we compared each parameter with the histopathological classification. Tl is said to accumulate in viable tumor cells[28,29]; therefore, for the purpose of reflecting the peculiarity of this functional imaging in the result, it is the best way to classify patients into groups with (grade I & II) or without (grade III & IV) viable tumor cells.

Tl SPECT has been used in evaluating viability of untreated tumors including brain tumors,[4,28,29] lung cancer[30,31] and head and neck cancer.[32] In evaluating the effectiveness of radiotherapy, some kinds of semi-quantitative values such as early and delayed ratios of mean counts in ROI to those in non-lesion, retention indexes at pre- and post-treatment, and reduction rate have been used. For example, Moustafa et al.[3] reported that astrocytoma recurrent cases showed marked differences in early and delayed Tl uptake and retention index at post-treatment compared with postradiation gliosis. Lorberboym et al.[5] showed that Tl SPECT using post-therapy early image, was more accurate than CT scans in a prospective evaluation of brain tumors. Another author[7] revealed that pre- and post-treatment Tl SPECTs and early uptake ratio were very useful to evaluate the treatment response. Yoshimura et al.[10] used a new semi-quantitative value, functional image after radiotherapy and showed its usefulness in the diagnosis of recurrence. Regarding bone and soft tissue sarcomas, there is a report by Kostakoglu et al.,[11] indicating that early Tl uptake after treatment was more accurate than other modalities in differentiating residual recurrent tumor from post-therapy changes. In head and neck region, same authors[14] showed that Tl SPECT after radiotherapy had higher specificity than CT/MRI in differentiating residual/recurrence disease from post-therapy changes in patients with nasopharyngeal carcinoma. However, there is only a single report in which authors tried to distinguish radiosensitive tumors from radioresistant ones by evaluating early and delayed ratios, and retention index before radiotherapy in head and neck cancers.[17] In the present study, we assessed the effectiveness of radiotherapy using RR. RR showed a significant correlation with the histopathological findings.

When non-lesion is set up on radioisotope SPECT at post radiotherapy, it is necessary to take the effect of irradiation into account. Regarding ^{99m}Tc-MDP uptake, a previous report[33] revealed that the irradiated bone showed a significant decrease in bone metabolism at 2–18 mo after irradiation. Considering Tl uptake, in an *in vitro* study using a human papillary thyroid carcinoma cell line by Staudenherz and colleagues,[34] it was concluded that Tl uptake was significantly higher after radiation at continuous incubation. There is a report that the perivertical space was selected but variation of soft tissue activity could not be completely eliminated.[17] In this study, we set up non-lesion at the part of contralateral scalp to avoid including the inflammatory area around the tumor by irradiation within the non-lesion. The scalp at the height of the cerebellum was out of the extent of irradiation, thereby avoiding decrease of Tl uptake by irradiation.

Interestingly, although the mean counts of ROI at post-radiotherapy tended to be higher in the effective group than non-effective one ($p = 0.1586$, effective group: 11.839 ± 15.597, non-effective group: 3.617 ± 0.980), the former had a tendency to show lower post T/N than the latter ($p = 0.1640$, effective group: 3.066 ± 1.017, non-effective group: 3.880 ± 1.107). This result may be attributable to the fact that non-lesion set up at scalp could avoid the effect of irradiation. Post T/N has a possibility to be lower than expected when non-lesion involved the region of mucositis in the oral cavity. In contrast, the value has a possibility to be higher than expected when non-lesion involved the scalp on the same slice where the tumor was present, because the scalp might be involved within the range of irradiation. Tl uptake by the tumoral lesion irradiated was often said to diminish compared to that at the pre-treatment. However, in this study the correlation between the mean counts of ROI and T/N at post-treatment seem to disclose the possibility of non-lesion set up at scalp to exclude the effect by radiotherapy.

To know effectiveness of preoperative radiotherapy, no modality with adequate confidence is available. Interval pathologic assessment can be misleading.[2] Although some authors recommended to use 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG)[35–39] or [^{11}C]methionine[40] positron emission tomography (PET) to predict the outcome of radiotherapy in head and neck tumors, PET is not popularized. Therefore, in evaluating the effectiveness of radiotherapy for patients with SCC in the oral cavity, it is recommended to use Tl SPECT, because Tl SPECT is more popular than PET and semi-quantitative parameter, RR is useful to evaluate the effectiveness of radiotherapy.

On the other hand, in this study, although the cases with recurrence showed lower RR compared to those without

recurrence, there was no significant difference in RR between them. Therefore, it may be difficult to predict whether recurrence will occur or not using RR. Stages of 6 cases with recurrence were IVA in 4 patients (66.7%) whose outcome was tumor death, and II in 2 (33.3%) who still survive. Significant difference in RR could be obtained between cases with local failure resulting in death from disease and those surviving (Fig. 1e). On the other hand, stages of 9 cases without recurrence were IVA in 5 patients (55.6%), III in 1 (11.1%), and II in 3 (33.3%). In the head and neck region, there are some reports suggesting stage,[41] T stage,[42,43] and tumor size[44] as prognostic predictors. Vicente et al.[4] noted that patients with oral SCC treated by surgery with or without postoperative adjuvant radiotherapy in stage III and IV showed a statistically significant lower survival rate than those in stage II. Referring to the study by Cano et al.,[48] it is suggested that local control was significantly predicted by T stage, and independently significant factors predicting tumor-specific survival included stage. Furthermore, T stage was demonstrated to be the most significant factor affecting local control in the study by Nathu et al.[43] Overgaard and colleagues indicated tumor size as a significantly important parameter related to both probability of local control and survival.[44] Although we could not specify factors associated with death, our result showed that RR and stage had the possibility to affect survival. To the best of our knowledge, only one report revealed that higher value of Tl index showed a tendency for shorter survival in cerebral tumors.[45] In our study, although there was no significant difference between cases with RR of more than and less than 43% (mean 43%) ($p = 0.2926$), cases with higher RR tended to show a higher survival rate. But the number of patients enrolled in this study was small and thus larger numbers of subjects must be studied before any firm conclusion can be reached.

CONCLUSION

Semi-quantitative study using Tl SPECT was useful in evaluating the effectiveness of pre-operative radiotherapy for SCC in the oral cavity.

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