

# Intraoral Ultrasonographic Features of Tongue Cancer and the Incidence of Cervical Lymph Node Metastasis



Masaru Konishi, DDS, PhD,\* Minoru Fujita, DDS, PhD,† Kiichi Shimabukuro, DDS,‡  
Pongsapak Wongratwanich, DDS,§  
Rinus Gerardus Verdonschot, PhD,|| and Naoya Kakimoto, DDS, PhD¶

**Purpose:** The purpose of this study was to investigate the relationship between the visual characteristics of tongue lesion images obtained through intraoral ultrasonographic examination and the occurrence of late cervical lymph node metastasis in patients with tongue cancer.

**Patients and Methods:** This study investigated patients with primary tongue cancer who were examined using intraoral ultrasonography at Hiroshima University Hospital between January 2014 and December 2017. The inclusion criteria were squamous cell carcinoma, curative treatment administration, lateral side of tongue, surgery or brachytherapy alone, no cervical lymph node or distant metastasis as primary treatment, and treatment in our hospital. The exclusion criteria were carcinoma in situ, palliative treatment, dorsum of tongue, and multiple primary cancers. The follow-up period was more than 1 year. The primary endpoint was the occurrence of late cervical lymph node metastasis, and the primary predictor variables were age, gender, longest diameter, thickness, margin or border shapes of the lesion, and treatment methods. The relationship between the occurrence of late cervical lymph node metastasis and the longest diameter, thickness, margin types, and border types as evaluated through intraoral ultrasonography were assessed. The data were collected through a retrospective chart review.

**Results:** Fifty-four patients were included in this study. The analysis indicated that irregular lesion margins were significantly associated with the occurrence of late cervical lymph node metastasis ( $P < .0001$ ). The cutoff value for late cervical lymph node metastasis was 21.2 mm for the longest diameter and 3.9 mm for the thickness.

**Conclusions:** The results of this study indicates that the irregular lesion margin assessed using intraoral ultrasonography may serve as an effective predictor of late cervical lymph node metastasis in N0 cases.

© 2020 American Association of Oral and Maxillofacial Surgeons

*J Oral Maxillofac Surg* 79:932-939, 2021

Cervical lymph node metastasis associates with poor prognosis in patients with tongue cancer; thus, it is important to control its initiation.<sup>1</sup> The treatment of

stage I and II tongue cancer usually requires local surgery or brachytherapy.<sup>2,3</sup> The occult metastasis rates to the cervical lymph node are reported between 8.2

\*Assistant Professor, Department of Oral and Maxillofacial Radiology, Hiroshima University Hospital, Hiroshima, Japan.

†Former Associate Professor, Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.

‡Graduate Student, Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.

§Graduate Student, Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.

||Assistant Professor, Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.

¶Professor and Chair, Department of Oral and Maxillofacial Radiology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan.

Conflict of Interest Disclosures: None of the authors have any relevant financial relationship(s) with a commercial interest.

Address correspondence and reprint requests to Dr Konishi: Department of Oral and Maxillofacial Radiology, Hiroshima University Hospital, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8553, Japan; e-mail: [mkonishi@hiroshima-u.ac.jp](mailto:mkonishi@hiroshima-u.ac.jp)

Received August 5 2020

Accepted September 2 2020

© 2020 American Association of Oral and Maxillofacial Surgeons

0278-2391/20/31123-X

<https://doi.org/10.1016/j.joms.2020.09.006>

and 46.3% in patients with stage I or II oral tongue squamous cell carcinoma.<sup>4</sup> However, these patients are locally treated with surgery or brachytherapy alone, and prophylactic neck dissection for N0 patients remains controversial.<sup>2</sup>

The potential value of intraoral ultrasonographic (IUS) examination for management of tongue cancer has been described previously.<sup>5</sup> The correlation of IUS and histopathologic findings has also been statistically confirmed.<sup>6,7</sup> Furthermore, the association between IUS-assisted tongue cancer findings and the occurrence of cervical lymph node metastasis has been reported. The IUS features, such as thickness,<sup>8-10</sup> depth of invasion,<sup>11</sup> margin shape,<sup>12</sup> and tumor vascularity by color Doppler ultrasonography,<sup>13</sup> have been shown to predict the incidence of cervical lymph node metastasis in patients with tongue cancer.

Furthermore, the presence of multiple lymph node metastases<sup>14</sup> or extranodal invasion<sup>15,16</sup> has been described as poor prognostic factors for late cervical lymph node metastasis. Moreover, prophylactic neck dissection may improve the prognoses in such cases.

Here, we have studied the relationship between the IUS features and incidence of late cervical lymph node metastasis in patients with tongue cancer. Moreover, we have investigated whether the IUS findings can predict association of irregular lesion margin with extranodal invasion. The study objectives included investigating the relationship of age, gender, treatment, longest diameter, lesion thickness, border type, and margin type of the primary tongue lesion as measured with IUS in the presence of delayed metastases with the incidence of cervical lymph nodes and time frame of metastasis. The null hypothesis stated that there was no statistically significant difference in these parameters between patients with and without late metastases or in the duration of the incidence of metastases.

## Patients and Methods

This study investigated patients with primary tongue cancer who were examined using intraoral ultrasonography at Hiroshima University Hospital between January 2014 and December 2017. The inclusion criteria were squamous cell carcinoma, curative treatment administration, lateral side of tongue, surgery or brachytherapy alone, no cervical lymph node or distant metastasis as primary treatment, and treatment in our hospital. The exclusion criteria were carcinoma in situ, palliative treatment, dorsum of tongue, and multiple primary cancers. This study followed the Declaration of Helsinki on medical protocol and ethics, and the regional Ethical Review Board

of Hiroshima University approved the study. In accordance with the guidelines by the local institutional ethics committee, informed consent was obtained in the form of opt out.

The ProSound alpha 7 system (Hitachi-Aloka Medical, Japan) with 7.5 MHz/38-mm linear probe was used for all the examinations. A 10-mm thick acoustic coupling material was placed on the surface of the probe and was covered with a rubber probe cover filled with water. The probe was placed in contact with the surface of the tongue lesion, and a cross section measuring the maximum thickness and the longest diameter was visualized. Two dentists (M.F. and M.K.), engaged in the ultrasonographic examination with 35 (M.F.) and 15 (M.K.) years of experience, performed the investigations. The longest diameter and lesion thickness were measured, and the margin and border types were assessed by 1 examiner (M.K.).

The observation period for late lymph node metastasis was extended at least for 1 year after the initial treatment. Late lymph node metastasis was defined as the occurrence of metastasis after the surgery or radiotherapy for primary tongue lesion and histopathologic diagnosis performed after the neck dissection. The longest diameter, thickness, margin types, and border types were examined using IUS. The lesion margin types were classified as being smooth or irregular. Furthermore, the lesion border types were classified into *clear* or *unclear* patterns. The method of measuring the longest diameter and thickness of lesion as well as the criteria for the margin and border types have been represented in [Figures 1 and 2](#). The relationship between the longest diameter, thickness, margin and border types, and the occurrence of late cervical lymph node metastasis were examined. The differences in the patient age, gender, longest diameter, thickness, margin type, and border type between the surgery and brachytherapy were investigated in the nonmetastasis and metastasis groups. Furthermore, in patients with late cervical lymph node metastasis, we evaluated the association of the longest diameter, thickness, margin types, and border types with the duration until occurrence of metastasis and extranodal invasion. The data were collected through a retrospective chart review.

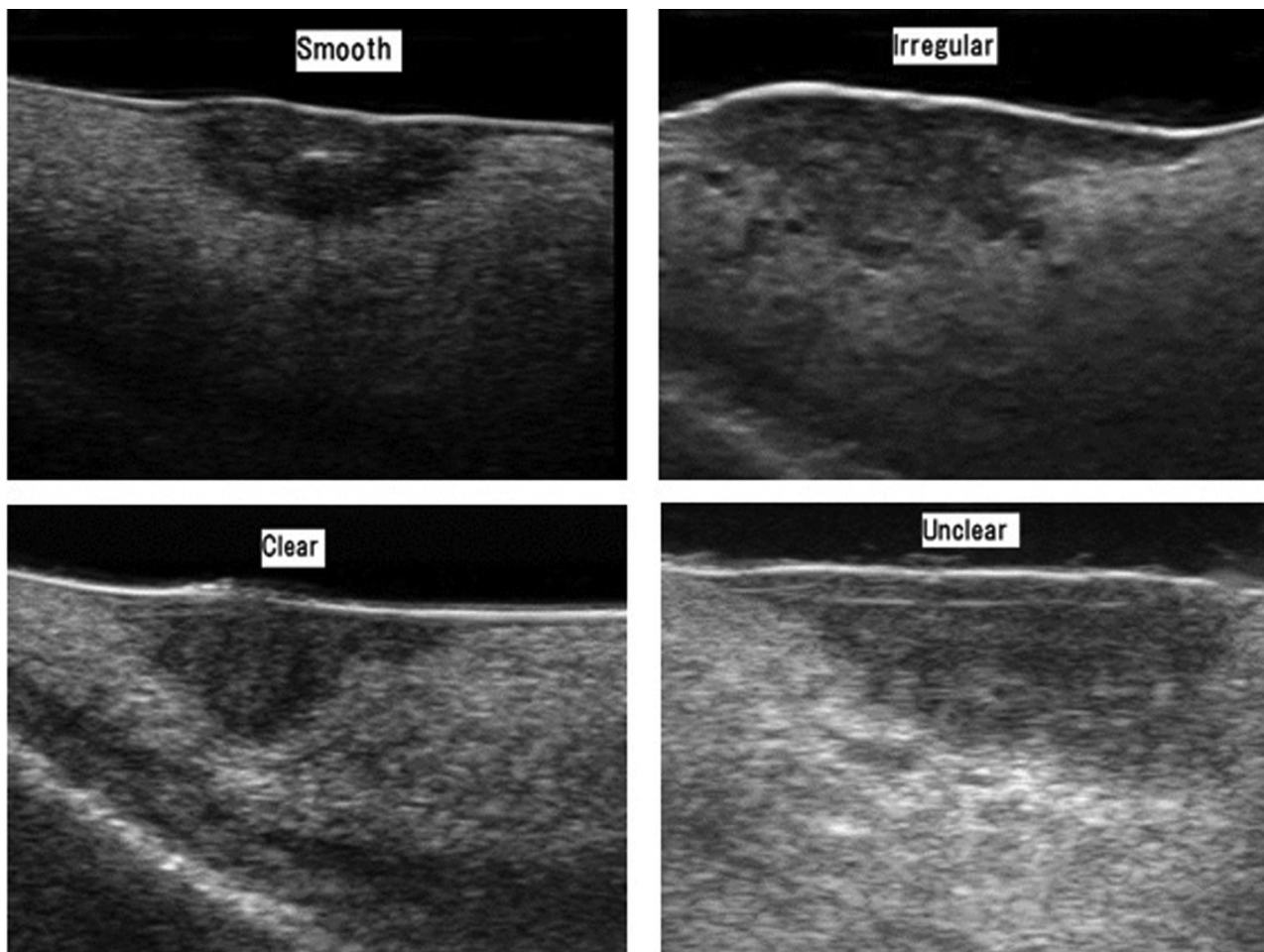
The primary endpoint was the occurrence of late cervical lymph node metastasis, and the primary predictor variables were age, gender, longest diameter, thickness, margin or border shapes of the lesion, and treatment methods. The Wilcoxon rank sum test and Fisher exact test were performed for the univariate and multivariate analyses of the variables between cervical lymph node metastasis and nonmetastasis groups. The longest diameter and thickness were



**FIGURE 1.** Measurement method for the longest diameter and thickness. The thickness of lesion has been measured from the tongue surface to the deepest level of hypoechoic area. The longest diameter of the lesion meant the maximal length of hypoechoic area.

Konishi et al. *Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg* 2021.

analyzed using the receiver operating characteristic (ROC) analysis (which is a graphical illustration of the diagnostic capacity of binary classification system through systematic variation of discrimination threshold) and by establishing the area under the curve (AUC) (0.9 to 1.0, 0.9 to 0.7, and 0.7 to 0.5 for high, moderate, and low accuracy, respectively) cutoff values. The cutoff values were defined as the maximum of (sensitivity + specificity – 1) values using the Youden's index. The correlation of longest diameter or thickness and the period to late cervical lymph node metastasis was analyzed using the Spearman's rank correlation coefficient analysis. The correlation of the margin or border types with the duration for late cervical lymph node metastasis was analyzed using the Wilcoxon rank sum test. The relationship of the longest diameter or thickness with the presence or the absence of extranodal invasion was also analyzed using the Wilcoxon rank sum test. Moreover, the relationship between the margin or border types and the incidence of extranodal invasion was analyzed using the Fisher exact test. The JMP Pro, version 14.0



**FIGURE 2.** Classification of margin and border types. The examples of smooth or irregular margin types and the clear or unclear border types are shown.

Konishi et al. *Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg* 2021.

(SAS Institute, Cary, NC) was used for all the statistical analysis. A  $P$  value  $<.05$  was considered to be statistically significant.

## Results

Seventy patients with primary tongue cancer were examined using IUS at Hiroshima University Hospital between January 2014 and December 2017. Within this sample, the exclusion criteria were patients who were palliative and not curative ( $n = 3$ ), patients who underwent both surgery and radiation therapy ( $n = 1$ ), patients who had cervical lymph node metastases at the time of primary treatment ( $n = 2$ ), patients who underwent treatment at another hospital ( $n = 2$ ), patients who had lesions on the dorsum of tongue ( $n = 1$ ), patients who were previously treated for cancer of the buccal mucosa ( $n = 1$ ), and patients who had carcinoma in situ on histopathology ( $n = 6$ ). These patients ( $n = 16$ ) were excluded from the study. Fifty-four patients were therefore ultimately included in this study.

The patient characteristics are shown in [Table 1](#). The 54 patients consisted of 32 males and 22 females and had a mean age of 63.1 years (range, 26 to 91). The T-factors were classified into T1 ( $n = 16$ ), T2 ( $n = 35$ ), and T3 ( $n = 3$ ). Patients were either treated with surgery alone ( $n = 27$ ) or brachytherapy alone ( $n = 27$ ). Late cervical lymph node metastasis was observed in 20 patients (37.0%). The median duration for occurrence of cervical lymph node metastasis was 5 months (range, 2 to 26) after treatment of the primary lesion. The clinicopathologic features according to surgery or brachytherapy in the nonmetastasis and metastasis groups are shown in [Table 2](#). The differences in values of the longest diameter and thickness

were statistically significant between patients who underwent surgery and brachytherapy in both the nonmetastasis and metastasis groups. Moreover, these parameters were more prominent in the brachytherapy group than that in the surgery group. The analysis of the patient characteristics in the nonmetastasis and metastasis groups is shown in [Table 3](#) and [Figure 3](#). The mean values of the longest diameter in the nonmetastatic and metastatic groups were 20.8 and 28.5 mm, respectively, and these differences were significant in the univariate analysis (Wilcoxon rank sum test,  $P = .0058$ ). The AUC value was 0.73, and the cutoff value was 21.2 mm in the ROC analysis. Furthermore, the mean values of thickness in the nonmetastatic and metastatic groups were 4.8 and 7.5 mm, respectively, and a significant difference between the 2 groups was observed in the univariate analysis (Wilcoxon rank sum test,  $P = .0084$ ). The AUC value was 0.72, and the cutoff value was 3.9 mm in the ROC analysis. The nonmetastatic group showed 29 smooth and 5 irregular margins and 27 clear and 10 unclear borders, whereas the metastatic group showed 5 smooth and 15 irregular margins and 7 clear and 10 unclear borders, respectively. The univariate analyses indicated statistically significant differences between 2 groups ( $P < .0001$ ;  $P = .0352$ ). In addition, the rate of occurrence of late cervical lymph node metastasis was significantly higher in patients in the brachytherapy group than in the surgery group ( $P = .0473$ ). Furthermore, the multivariate analysis for the longest diameter, thickness, margin, border types, and treatment variables indicated the margin type of lesion to be significantly associated with the occurrence of cervical lymph node metastasis ( $P = .0006$ ).

The correlations between the longest diameter or thickness and period to cervical lymph node metastasis after treatment are shown in [Figure 4](#). The correlations between the longest diameter or thickness and period to cervical lymph node metastasis were not significant ( $P = .68$ ;  $P = .18$ ). The duration for occurrence of cervical lymph node metastasis after treatment ranged between 3 and 26 months (3, 7, 8, 15, and 26 months; median, 8 months) for smooth margins and 2 to 19 months (2, 3, 4, 5, 6, 9, 12, and 19 months; median, 4 months) for irregular margins ([Fig 5](#)). Furthermore, the duration for occurrence of cervical lymph node metastasis after treatment ranged between 3 and 26 months (3, 4, 8, 9, 15, 19, and 26 months; median, 6 months) for clear borders and 2 to 12 months (2, 3, 5, 6, 7, and 12 months; median, 5 months) for unclear borders ([Fig 5](#)). The differences between the duration of occurrence and the margin or border types were not statistically significant, although the irregular margin and unclear border types tended to have shorter duration before occurrence of cervical lymph node metastasis ( $P = .071$  and  $P = .22$ , respectively).

**Table 1. PATIENT CHARACTERISTICS**

Number of patients (n)	n = 54
Gender	Male: 32; female: 22
Age, yr; mean $\pm$ SD (median)	63.1 $\pm$ 17.2 (66.5)
Distribution of clinical T-factors	T1: 16; T2: 35; T3: 3
Treatment for primary lesion	Surgery: 27; brachytherapy: 27
Number of late lymph node metastasis	20
Period of late lymph node metastasis after initial treatment (median; minimum-maximum)	5 mo (range, 2-26)

Abbreviation: SD, standard deviation.

Konishi et al. Intraoral Ultrasonographic Features of Tongue Cancer. *J Oral Maxillofac Surg* 2021.

**Table 2. COMPARISONS BETWEEN THE SURGERY AND BRACHYTHERAPY IN THE NONMETASTASIS AND METASTASIS GROUPS**

Variable	Nonmetastasis (n = 34)			Metastasis (n = 20)		
	Surgery (n = 21)	Brachytherapy (n = 13)	P	Surgery (n = 6)	Brachytherapy (n = 14)	P
Age, yrs; mean ± SD (median)	66.2 ± 19.0 (72.0)	62.1 ± 16.5 (61.0)	NS	61.2 ± 17.1 (63.0)	60.1 ± 16.1 (63.5)	NS
Gender, M/F	12/9	8/5	NS	2/4	10/4	NS
Longest diameter, mm; mean ± SD (median)	17.7 ± 6.5 (16.7)	25.8 ± 6.1 (27.3)	.0016*	21.1 ± 7.2 (19.6)	31.8 ± 8.4 (29.6)	.0260*
Thickness, mm; mean ± SD (median)	3.8 ± 2.3 (2.9)	6.4 ± 3.6 (6.4)	.0144*	4.0 ± 0.9 (4.5)	8.9 ± 3.5 (9.3)	.0050*
Margin						
Smooth	17	12	NS	2	3	NS
Irregular	4	1		4	11	
Border						
Clear	17	10	NS	3	7	NS
Unclear	4	3		3	7	

Abbreviations: F, female; M, male; NS, nonsignificant; SD, standard deviation.

\* Statistically significant difference.

Konishi et al. *Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg* 2021.

The mean value of the longest diameter of the tongue lesion was 28.6 and 28.1 mm without and with extranodal invasion, respectively. The mean thickness of the tongue lesion was 8.5 and 7.1 mm without and with extranodal invasion, respectively. Neither parameter showed statistically significant differences between the groups with and without extranodal invasion ( $P = .92$  and  $P = .54$ , respectively).

Furthermore, the lesions showed smooth ( $n = 1$ ) and irregular ( $n = 3$ ) margins without extranodal invasion and smooth ( $n = 4$ ) and irregular ( $n = 10$ ) margins with extranodal invasion, although no significant differences were observed for these parameters between the groups with and without extranodal invasion ( $P = .89$ ). Furthermore, the lesions showed clear ( $n = 2$ ) and irregular ( $n = 2$ ) margins in the group

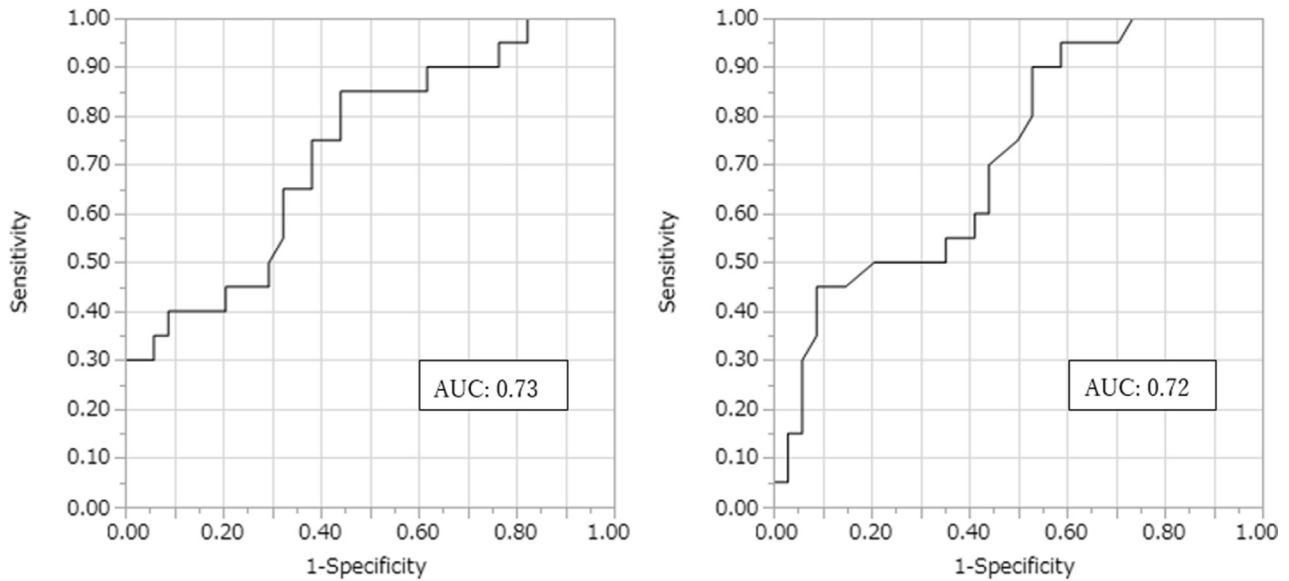
**Table 3. UNIVARIATE AND MULTIVARIATE ANALYSIS COMPARING DIFFERENT PARAMETERS BETWEEN THE NON-METASTASIS AND METASTASIS GROUPS**

	Nonmetastasis (n = 34)	Metastasis (n = 20)	Univariate	Multivariate
			P	
Age, yr; mean ± SD (median)	64.6 ± 17.9 (70.5)	60.4 ± 15.9 (63.0)	.2031	—
Gender, M/F	20/12	14/8	.9323	—
Longest diameter, mm; mean ± SD (median)	20.8 ± 7.5 (19.8)	28.5 ± 9.3 (26.6)	.0058*	.74697
Thickness, mm; mean ± SD (median)	4.8 ± 3.1 (4.5)	7.5 ± 3.7 (6.4)	.0084*	.92096
Margin				
Smooth	29	5	<.0001*	.00064*
Irregular	5	15		
Border				
Clear	27	7	.0352*	.74159
Unclear	10	10		
Treatment				
Surgery	21	6	.0473*	.22983
Brachytherapy	13	14		

Abbreviations: F, female; M, male; SD, standard deviation.

\* Statistically significant difference.

Konishi et al. *Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg* 2021.



**FIGURE 3.** Receiver operating characteristic (ROC) analysis for the longest diameter (*left*) and thickness (*right*) in the nonmetastatic and metastatic groups. The AUC value was 0.73, and the cutoff value was 21.2 mm in the ROC analysis of longest diameter by Youden’s index. The AUC value was 0.72, and the cutoff value was 3.9 mm in the ROC analysis of thickness by Youden’s index. Abbreviations: AUC, area under the curve.

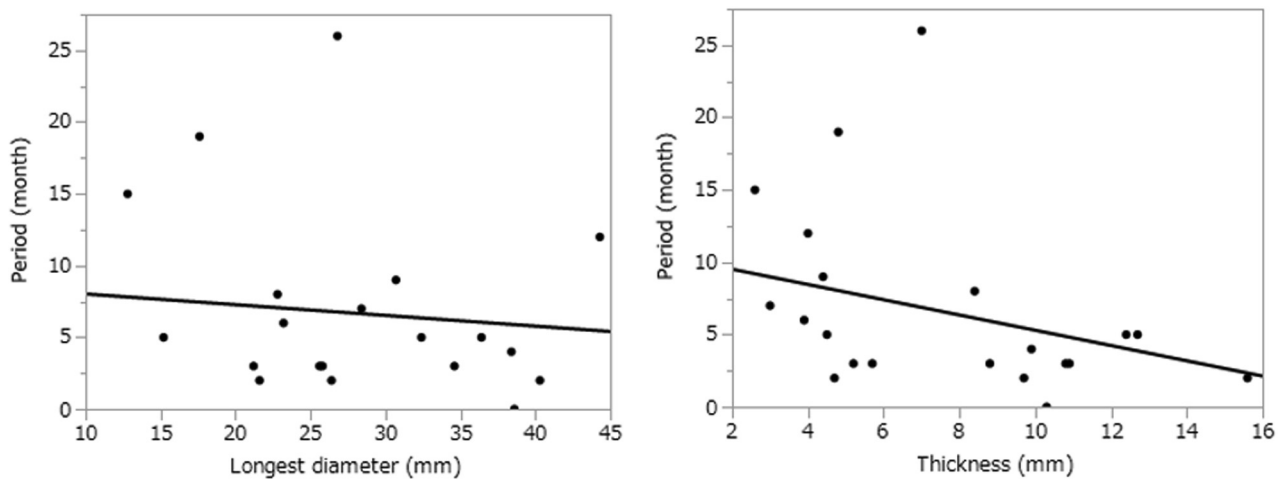
*Konishi et al. Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg 2021.*

without extranodal invasion and clear (n = 6) and unclear (n = 8) margins in the group with extranodal invasion, but the differences were not significant (P = .80). In addition, the other parameters, such as longest diameter, thickness, margin types, and border types showed no statistically significant differences between the groups with or without extranodal invasion.

**Discussion**

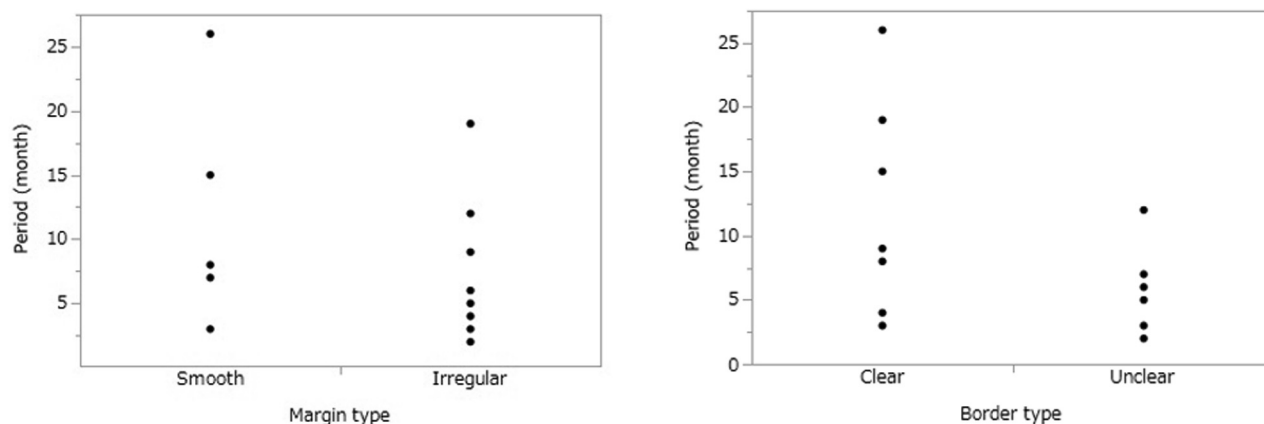
The development of cervical lymph node metastasis is considered as a poor prognostic factor in patients

with tongue cancer and reduces the overall survival rate.<sup>17</sup> Tongue cancer is likely to metastasize as the cervical lymph node metastasis, and there is a high incidence rate of occult metastasis (20.1 to 40.0%) in patients with stage I or II oral tongue cancer.<sup>18-22</sup> Therefore, it is essential to predict or detect the cervical lymph node metastasis as soon as possible to improve the treatment outcome. This study investigated the association between ultrasonographic features and the occurrence of cervical lymph node metastasis after treatment of patients with primary tongue lesion. The longest diameter, thickness, margin



**FIGURE 4.** Relationship between either the length or the thickness and duration of cervical lymph node metastasis after treatment. The correlations between either the longest diameter or the thickness and a period to cervical lymph node metastasis were not statistically significant.

*Konishi et al. Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg 2021.*



**FIGURE 5.** Association of duration of cervical lymph node metastasis after treatment with either margin or border types. The correlation between the duration of metastasis and either margin or border types was not statistically significant, except for irregular margin.

Konisbi et al. *Intraoral Ultrasonographic Features of Tongue Cancer. J Oral Maxillofac Surg* 2021.

type, border type, and treatment were found to be significantly associated with the late cervical lymph node metastasis in the univariate analysis, although only the margin type was significantly associated with the metastasis in the multivariate analysis. In addition, the longest diameter and thickness were observed to be causally correlated with high rate of late cervical lymph node metastasis in the brachytherapy group compared with that in the surgery group. The results showed that the irregular margin of tongue lesions in IUS images was significantly associated with the occurrence of the late cervical lymph node metastasis. The cutoff values in our study relative to the cervical lymph node metastasis were 21.2 mm for longest diameter and 3.9 mm for thickness. Previous studies observed a significant increase in the incidence of cervical lymph node metastasis with a cutoff value of 4 to 18 mm for tongue cancer thickness measured using IUS.<sup>7-9,23-28</sup> Whereas, the meta-analysis showed that the cutoff value for tumor thickness in oral cancer and cervical lymph node metastasis was 4 mm.<sup>29</sup> Thus, the thickness cutoff value of 3.9 mm is consistent with that obtained in the meta-analysis. The diverse cutoff values (3 to 18 mm) can be attributed to the variability in IUS imaging, such as the ultrasonography equipment and types of probe used. Moreover, the direction in which the probe is applied to the lesion, deformation of the lesion because of probe handling by the examiner, and settings of the invasion tip by the examiner may influence the cutoff values. Taylor et al<sup>9</sup> suggested that an elective neck dissection can be indicated in cases with tumor thickness of 5 mm and/or greater. Natori et al<sup>23</sup> suggested that patients with tumor thickness of 8 mm and/or greater, along with irregular and diffuse margins in the IUS images, should be treated by elective neck surgery. Furthermore, Matsuura et al<sup>26</sup> suggested that because patients with maximum tumor thickness of 8 mm and/or greater are prone to initiation of late

neck lymph node metastasis, the risk of subsequent cervical lymph node metastases can be reduced using prophylactic 30 Gy external beam radiotherapy. Although the relationship between the longest diameter and late cervical lymph node metastasis has not been reported previously, the present study reports the cutoff value of 21.2 mm (AUC = 0.73, moderate accuracy) to be associated with late cervical lymph node metastasis. Therefore, patients with T2 classification tumors should be considered to be prone to developing late cervical lymph node metastasis.

Previous studies have proposed the existence of relationship between the border types, margin types, and occurrence of cervical lymph node metastasis. Arijji et al<sup>13</sup> reported that the invasive margin was significantly correlated with cervical lymph node metastasis. Furthermore, Mattalitti et al<sup>12</sup> also described that permeated margin shapes showed high rate of nodal metastasis (50%) and low overall survival rate (65%). In addition, no significant differences between the clear or unclear border types and occurrence of cervical lymph node metastasis have been reported.<sup>22</sup> Conversely, the rate of cervical lymph node metastasis was 63.8% in the unclear border group, which constitutes a significantly higher rate than that in the other types in univariate analysis, although there were no significant differences in multivariate analysis.<sup>17</sup> This report corroborates our results.

Next, although patients having an irregular margin and unclear border types tended to have shorter duration of occurrence of cervical lymph node metastasis, the differences were not statistically significant. Thus, patients having tongue lesions with irregular margins or unclear borders, longest diameter of greater than 21.2 mm, and thickness of 3.9 mm should be followed closely to ensure early detection of late cervical lymph node metastasis until about 1-year post-treatment.

There are several limitations in this study. First, because the study was performed by a single evaluator at a single institution, the results were limited by the small sample size. Second, as 50% of the patients received brachytherapy, they could be diagnosed only using biopsy specimens. This hampered the comparative analysis between IUS and histopathologic images. Thus, to overcome this, in future, we will only study the patients with tongue cancer who underwent surgical treatment. Finally, the criteria for determining the margin or border types were relatively subjective and possibly varied depending on the evaluator. Therefore, it would be necessary to include more evaluators or develop an objective image analysis method that is less prone to subjective influences, such as the use of deep learning networks.

In conclusion, this study with the IUS findings showed that irregular margin of the lesion was associated with occurrence of late cervical lymph node metastasis. The occurrence of late cervical lymph node metastasis was associated with longest diameter and thickness at cutoff values of 21.2 and 3.9 mm, respectively. The analysis indicated the margin of the IUS findings to be an effective predictor of cervical lymph node metastasis in patients with N0 tumors. Thus, in patients with clinically negative neck examinations, prediction of occult cervical lymph node metastases through the use of IUS will permit the performance of elective neck dissection, thereby improving the patient treatment outcomes.

### Acknowledgments

We would like to thank Editage (<http://www.editage.jp>) for English language editing.

### References

- Ferlito A, Rinaldo A, Robbins KT, et al: Changing concepts in the surgical management of the cervical node metastasis. *Oral Oncol* 39:429, 2003
- Hanai N, Asakage T, Kiyota N, et al: Controversies in relation to neck management in N0 early oral tongue cancer. *Jpn J Clin Oncol* 49:297, 2019
- Fujita M, Hirokawa Y, Kashiwado K, et al: An analysis of mandibular bone complications in radiotherapy for T1 and T2 carcinoma of the oral tongue. *Int J Radiat Oncol Biol Phys* 34:333, 1996
- Abu-Ghanem S, Yehuda M, Carmel NN, et al: Elective neck dissection vs observation in early-stage squamous cell carcinoma of the oral tongue with no clinically apparent lymph node metastasis in the neck: a systematic review and meta-analysis. *JAMA Otolaryngol - Head Neck Surg* 142:857, 2016
- Tarabichi O, Bulbul MG, Kanumuri VV, et al: Utility of intraoral ultrasound in managing oral tongue squamous cell carcinoma: Systematic review. *Laryngoscope* 129:662, 2019
- Shintani S, Yoshihama Y, Ueyama Y, et al: The usefulness of intraoral ultrasonography in the evaluation of oral cancer. *Int J Oral Maxillofac Surg* 30:139, 2001
- Kaneoya A, Hasegawa S, Tanaka Y, Omura K: Quantitative analysis of invasive front in tongue cancer using ultrasonography. *J Oral Maxillofac Surg* 67:40, 2009
- Hayashi T, Ito J, Taira S, Katsura K: The relationship of primary tumor thickness in carcinoma of the tongue to subsequent lymph node metastasis. *Dentomaxillofac Radiol* 30:242, 2001
- Mark Taylor S, Drover C, MacEachern R, et al: Is preoperative ultrasonography accurate in measuring tumor thickness and predicting the incidence of cervical metastasis in oral cancer? *Oral Oncol* 46:38, 2010
- Asakage T, Yokose T, Mukai K, et al: Tumor thickness predicts cervical metastasis in patients with Stage I/II carcinoma of the tongue. *Cancer* 82:1443, 1998
- Fukano H, Matsuura H, Hasegawa Y, Nakamura S: Depth of invasion as a predictive factor for cervical lymph node metastasis in tongue carcinoma. *Head Neck* 19:205, 1997
- Mattalitti SFO, Kawazu T, Kawano S, et al: Estimation of prognosis of tongue cancer using tumor depth and margin shape obtained from ultrasonography. *Oral Radiol* 33:101, 2017
- Ariji Y, Goto M, Fukano H, et al: Role of intraoral color Doppler sonography in predicting delayed cervical lymph node metastasis in patients with early-stage tongue cancer: A pilot study. *Oral Surg Oral Med Oral Pathol Oral Radiol* 119:246, 2015
- Cooper JS, Pajak TF, Forastiere AA, et al: Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *N Engl J Med* 350:1937, 2004
- Shingaki S, Nomura T, Takada M, et al: The impact of extranodal spread of lymph node metastases in patients with oral cancer. *Int J Oral Maxillofac Surg* 28:279, 1999
- Woolgar JA, Rogers SN, Lowe D, et al: Cervical lymph node metastasis in oral cancer: The importance of even microscopic extracapsular spread. *Oral Oncol* 39:130, 2003
- Kurokawa H, Yamashita Y, Takeda S, et al: Risk factors for late cervical lymph node metastases in patients with stage I or II carcinoma of the tongue. *Head Neck* 24:731, 2002
- D'Cruz AK, Siddachari RC, Walvekar RR, et al: Elective neck dissection for the management of the N0 neck in early cancer of the oral tongue: Need for a randomized controlled trial. *Head Neck* 31:618, 2009
- Yuen APW, Lam KY, Lam LK, et al: Prognostic factors of clinically stage I and II oral tongue carcinoma - a comparative study of stage, thickness, shape, growth pattern, invasive front malignancy grading, Martinez-Gimeno score, and pathologic features. *Head Neck* 24:513, 2002
- Goto M, Hasegawa Y, Terada A, et al: Prognostic significance of late cervical metastasis and distant failure in patients with stage I and II oral tongue cancers. *Oral Oncol* 41:62, 2005
- Tai SK, Li WY, Chu PY, et al: Risks and clinical implications of perineural invasion in T1-2 oral tongue squamous cell carcinoma. *Head Neck* 34:994, 2012
- Yii NW, Patel SG, Rhys-Evans PH, Breach NM: Management of the N0 neck in early cancer of the oral tongue. *Clin Otolaryngol Allied Sci* 24:757, 1999
- Natori T, Koga M, Anegawa E, et al: Usefulness of intra-oral ultrasonography to predict neck metastasis in patients with tongue carcinoma. *Oral Dis* 14:591, 2008
- Yesuratnam A, Wiesenfeld D, Tsui A, et al: Preoperative evaluation of oral tongue squamous cell carcinoma with intraoral ultrasound and magnetic resonance imaging - Comparison with histopathological tumour thickness and accuracy in guiding patient management. *Int J Oral Maxillofac Surg* 43:787, 2014
- Lodder WL, Teertstra HJ, Tan IB, et al: Tumour thickness in oral cancer using an intra-oral ultrasound probe. *Eur Radiol* 21:98, 2011
- Matsuura K, Hirokawa Y, Fujita M, et al: Treatment results of stage I and II oral tongue cancer with interstitial brachytherapy: Maximum tumor thickness is prognostic of nodal metastasis. *Int J Radiat Oncol Biol Phys* 40:535, 1998
- Chammas MC, MacEdo TAA, Moyses RA, et al: Relationship between the appearance of tongue carcinoma on intraoral ultrasonography and neck metastasis. *Oral Radiol* 27:1, 2011
- Shinozaki Y, Jinbu Y, Ito H, et al: Relationship between appearance of tongue carcinoma on intraoral ultrasonography and histopathologic findings. *Oral Surg Oral Med Oral Pathol Oral Radiol* 117:634, 2014
- Huang TY, Hsu LP, Wen YH, et al: Predictors of locoregional recurrence in early stage oral cavity cancer with free surgical margins. *Oral Oncol* 46:49, 2010