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ORIGINAL ARTICLE

Usefulness of intra-oral ultrasonography to predict neck metastasis in patients with tongue carcinoma

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OBJECTIVE: To assess tissue characterization relating with neck metastasis of invasive tongue cancer, we investigate the usefulness of intra-oral ultrasonography (US).

MATERIALS AND METHODS: The patients with squamous cell carcinoma of the tongue (n = 110) were preoperatively evaluated with intra-oral US. The US images were compared with histological sections. The histological and ultrasonographic parameters were evaluated for their correlation with neck metastasis.

RESULTS AND CONCLUSION: High-quality ultrasonic images were obtained, and all lesions over 1 mm thickness by histology were detected. There was a significant correlation (P < 0.0001) between measurements of tumor thickness by US and histology. Univariate analysis showed that the histological parameters influencing neck metastasis were mode of invasion (P = 0.0006), muscular invasion (P < 0.0001), stromal reaction (P = 0.0002), and tumor thickness (P = 0.0004). Of the ultrasonographic parameters, shape of margin (P = 0.019), pattern of margin (P = 0.033), internal echo signal (P = 0.035), and tumor thickness (P < 0.0001) showed a significant correlation with neck metastasis. Ultrasound images of oral tongue cancer reflected the histological structures. Tumors with diffuse invasive mode shows an irregular and unclear tumor margins on US image. Thickness of 8 mm by ultrasound is useful as a cut-off point of predicting risk of neck metastasis of tongue cancer. Intra-oral US is a reliable tool in objectively predicting subclinical neck metastasis in tongue cancer.

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Keywords: tongue cancer; neck metastasis; intra-oral ultrasonography; tumor thickness; mode of invasion; pattern of border

Introduction

Squamous cell carcinoma (SCC) of the tongue is characterized by a high degree of aggression and a great propensity to metastasize to cervical lymph nodes. Because the development of lymph node metastasis directly affects the prognosis of the patients (Snow *et al*, 1982; Franceschi *et al*, 1993), tongue carcinoma should be graded as to its metastatic potential preoperatively to help decide on necessity for neck dissection.

Various clinical, pathological, and imaging parameters and molecular markers have been investigated for their value as predictors of neck metastasis and/or prognosis in oral cancer (Jacobsson *et al*, 1973; Spiro *et al*, 1986; Stuckensen *et al*, 2000; de Vicente *et al*, 2005; Keum *et al*, 2006; Massano *et al*, 2006). Among them, tumor thickness (the depth of invasion) and the mode of invasion at the tumor-host borderline are reported as an important prognostic factor in oral cancers, especially as a predictor of cervical lymph node metastasis. To obtain such information preoperatively, digital palpation, CT and MR imaging, and histopahtological examination by biopsy are routinely performed.

Because digital examination needs mastery of skills, it is inferior from the point of view ensuring consistent accuracy and objectivity. CT and MR imaging cannot often evaluate a tumor thickness and its extent precisely such as in the case of a small lesion or metal artifact by dental restoration. Histopathological examination by biopsy is a useful method not only to confirm diagnosis but also to estimate the malignant potential of tumor. For grading of malignancy, sampling of tumor tissue from advancing front of cancer would be necessary; however, it is not easy to make an accurate grading of tumor invasion by biopsy because of limited sampling from a part of tumor tissue.

Ultrasonography (US) is a non-invasive, rapid, easily repeatable, and economical examination. Intra-oral scanning on the tongue will compensate for those disadvantages of digital palpation, CT/MR imaging and pathological examinations. However, it is not clear how much US examination can give us precise information regarding the invasive front of tongue

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cancer to predict neck metastasis, especially clinically negative neck. The present study was undertaken for evaluating the usefulness of intra-oral US as a tool to predict neck metastasis and delineating the extent of tumor, particularly thickness and invasion pattern of tongue carcinomas.

Patients and methods

Patients

The present study is based upon a series of 110 patients with previously untreated invasive squamous cell carcinoma of the tongue who were preoperatively evaluated with intra-oral US. Table 1 shows the distribution of patients according to the Union Internationale Coutre le Cancer (UICC) classification (2002). Of the 110 patients, 40 (36.4%) had T1 lesions, 57 (51.8%) had T2 lesions, six (5.5%) had T3 lesions, and seven (6.4%) had T4 lesions. Neck status was routinely evaluated with cervical US, enhanced CT and MR image. Ninety-one patients (82.7%) were classified as N0, and 19 (17.3%) patients had clinically positive nodes. None of them had evidence of distant metastasis at the time of initial examination.

Tumor size was measured at the maximum diameter, and distributed from 5.0 to 50.0 mm in size (mean ± s.d. = 25.4 ± 10.7 mm).

Based on surgeon's close inspection and digital palpation at the primary site, clinical growth pattern was classified into three types of superficial, exophytic and endophytic type (Kusukawa *et al*, 1998). Superficial tumor is an erythroplakic or leukoplakic lesion lacking deep induration. Exophytic tumor is a papillary or granular lesion with a little deep induration. Endophytic tumor is an ulcerative or indurative lesion with extensive deep part induration. Thus tumors were classified in 28 (25.5%) of superficial type, 23 (20.9%) of exophytic type, and 59 (53.6%) of endophytic type.

All patients were treated by surgery, and 64 (58.2%) of them had received chemotherapy prior to surgery with oral administration of 80–120 mg per body per day of TS-1® (Taiho Pharmaceutical Co., LTD., Tokyo, Japan) consisting of 2 weeks' administration including 5-day administration and 2-day termination following 1 week rest. Neck dissection was indicated in patients with clinically positive nodes. For the clinically N0 neck, the "wait and see" policy was employed, excepting patients who required cervical skin incision in facilitation for eventual glossectomy. Follow-up to detect lymph node metastasis in the neck consisted of a physical examination, enhanced CT examination, and cervical US examination. All patients were followed up every 2 weeks for the first 6 months, every month for the next 6 months, and every 2–3 months for at least 3 years after initial treatment. The minimum and mean follow-up period was 24 months and 50.8 months, respectively. Eighty-four patients (76.4%) were followed up for 60 months or more.

Thus 32 patients were treated for neck metastasis at the time of primary surgery, and 23 of them had histologically proven lymph node metastasis. Delayed neck metastasis had developed in 24 patients within 18 months after primary operation. Thus, these 47 (42.7%) patients were classified as the positive neck (N+) group, remaining 63 (57.3%) were classified as the negative neck (N−) group. There was no significant difference in incidence of neck metastasis and survival rate with adjuvant chemotherapy. Cause-specific 5-year cumulative survival rate of all cases was 88.9%.

Table 1 TNM classification (UICC, 2002) of 110 patients

N category	*T category*				*Total*
	T1	*T2*	*T3*	*T4*	
N0	37	47	5	2	91
N1	1	5	1	0	7
N2	2	5	0	4	11
N3	0	0	0	1	1
Total	40	57	6	7	110

All were M0.

Intra-oral ultrasonography and MRI

The B-mode intra-oral US scanning was done using gray scale imaging system SSD1200CV (ALOKA Co., LTD., Tokyo, Japan) attached with 7.5 MHz I-shaped or T-shaped linear transducers. The aperture of the transducer had a length of 5 cm and width of 1 cm. The lingual lesion was directly scanned on the surface laterally with I-shaped probe and from dorsum with T-shaped probe. Only light pressure was applied while holding the probe onto the tumor surface so as not to compress the tissues. Contralateral side of the tongue was scanned in similar manner as a control. Intra-oral US probed with respect to the shape of tumor margins, the pattern of tumor margins, the internal echo signal, and the tumor thickness of greatest depth, respectively. To keep objectivity, all intra-oral US examinations were performed by the same operator.

The shape of tumor margins was classified into two types: regular and irregular. The pattern of tumor margins was divided into three categories: with well-circumscribed margin (W type), with moderately clear margin (M type), and with diffuse and unclear margin (D type). According to the pattern of internal echo signals, the lesion was classified into the homogeneous or heterogeneous type respectively. Tumor thickness measured by US (usT) was compared with the measurements made by histological sections. MR images on Gd-diethyltriaminepentaacetic acid (DTPA) enhanced T1-weighted images were also examined with respect to the tumor thickness. Intra-oral US examination and MR imaging were performed before commencement of any treatment. Overall rates of cancer detection were 88.2% by intra-oral US and 72.0% by MR imaging, respectively.

Histopathological examinations

Cancer tissue specimens surgically obtained from these 110 patients were examined microscopically with hematoxylin-eosin (HE) staining. The microscopic slides were reviewed conforming to the following criteria: (i)

histological grades determined on the basis of classification proposed by the World Health Organization (Wahi *et al*, 1971), [well differentiated carcinoma (Grade I), moderately differentiated (Grade II), poorly differentiated (Grade III)]; (ii) mode of invasion at the tumor-host borderline was classified into three types (W, M, and D) as described previously (Umeda *et al*, 1992) (type W had a well-defined borderline, type M exhibited groups of tumor cells and had no distinct borderline, and type D spread in small aggregates with finger-like projections or invaded diffusely without forming nests of tumor cells); (iii) inflammatory cell infiltration classified into three groups [minimal lymphoplasmacytic infiltration with very few or small groups of lymphocytes at the periphery (Grade 1), moderate lymphoplasmacytic infiltration with multiple but scattered foci at the edge and beneath the tumor nest (Grade 2), marked lymphoplasmacytic infiltration occasionally forming band-like confluence (Grade 3)]; (iv) stromal reaction determined according to the fibrous tissue as medullary type, moderate type and scirrhous type; (v) histological tumor thickness (pT) was measured in each section using an ocular micrometer. The thickness measurement was obtained by the vertical measurement starting from surface of both the exophytic as well as endophytic tumor, up to the maximum point of the invasion (Yuen *et al*, 2000; Gonzalez-Moles *et al*, 2002; Kurokawa *et al*, 2002).

Statistical analysis

Correlation analyses were made between neck metastasis and the variables studied by the chi-squared test and by Student's *t*-test for parametric data, respectively. Linear regression analysis was performed and scatter plots were generated for the imaging measurements *vs* the pathology measurements. The variables were also analyzed in relation to neck metastasis and survival by the Kaplan–Meier method and the log-rank test. The prognostic significance of ultrasonographic and pathological parameters for neck metastasis or overall survival was assessed by Cox's multivariate proportional regression analysis. Values of $P < 0.05$ were considered statistically significant. Cut-off point of tumor thickness associated with neck metastasis was determined by receiver operating characteristic (ROC) curve.

Results

High-quality ultrasonic images were obtained, and the method being that the lesion was detected as a hypoechoic image compared with the peripheral muscular tissues and the contralateral tongue (Figure 1). Ninety-seven of 110 (88.2%) lesions were detected as sonolucent lesions, and remaining 13 (11.8%) lesions were undetectable by US. On the other hand, 28.0% of the lesions were undetectable on MR image due to small size or metal artifact. According to the T-category, detection rate of T1 lesions was 72.5% by US and 45.2% by MR imaging, respectively. In T2 tumors, detection rate was 96.5% by US and 80.4% by MR imaging, respectively. All T3 and T4 tumors were detectable by both MRI and US. According to the clinical growth pattern, detection rates of superficial type, exophytic type, and endophytic type were 57.1, 95.7 and 100% respectively by US, and 10.0, 72.7 and 93.1% respectively by MR imaging. Thus overall detection rate of the primary lesion was 88.2% by intra-oral US in comparison to 72.0% by MR imaging.

All lesions over 1 mm in tumor thickness on histological section were detectable on intra-oral US image. MR imaging, on the other hand, could not identify most tumors less than 5.0 mm in thickness. A scatter plot of tumor thickness measurements by ultrasound and by pathology shows the reliability of ultrasound for evaluation of tumor thickness against histological measurement. There were significant correlations ($P < 0.001$, $R^2 = 0.74$) between the measurements of tumor thickness by ultrasonography (usT) and by pathology (pT). The correlation formula by linear regression analysis was as follows: usT (mm) = $0.93 + 1.13 \times$ pT (mm). According to the correlation formula, tumor thickness on US was measured with an over-assessment of 13% than that measured by actual surgical section.

According to the clinical growth pattern, neck metastasis developed 8.9% (4/28) in superficial tumors, 13.3% (6/23) in exophytic tumors, and 62.7% (37/59) in endophytic tumors, respectively. The clinical growth pattern was a significant value to predict neck metastasis ($P < 0.0001$). Tumor thickness by US was 1.9 ± 2.4 mm in superficial tumors, 8.0 ± 6.0 mm in exophytic tumors, and 10.7 ± 5.3 mm in endophytic tumors, respectively. 96.4% of superficial tumors were < 5 mm in tumor thickness regardless of tumor size. In endophytic tumors, there was a significant correlation ($P = 0.01$, $R^2 = 0.37$) between measurements of tumor thickness by ultrasound and tumor size.

Mean ± s.d. of usT of the N− group and the N+ group were 6.1 ± 5.3 mm and 10.4 ± 6.2 mm, respectively ($P < 0.0001$). Tumor thickness was the most reliable parameter to predict neck metastasis. According to the ROC curve, a cut-off point of tumor thickness predicting neck metastasis was determined as 8 mm (Figure 2). Three-year cumulative incidence of neck metastasis was 60.9% in tumors over 8.0 mm in usT *vs* 27.2% in those of 8.0 mm or less in usT ($P < 0.0001$). Thus tumors over 8.0 mm in thickness measured by US developed cervical lymph node metastasis in significantly high-incidence compared with those of 8.0 mm or less in thickness ($P = 0.040$ by multivariate analysis).

Among histopathological parameters, mode of invasion ($P = 0.0006$), muscular invasion ($P < 0.0001$), stromal reaction ($P = 0.0002$) and tumor thickness ($P = 0.0004$) were predictive for neck metastasis by univariate analysis (Table 2). Mutivariate analysis showed that muscular invasion was the only significant parameter associated with neck metastasis ($P = 0.014$). There was a significant correlation between mode of invasion and stromal reaction ($P < 0.0001$). Regarding the clinical growth pattern, 76.5% of tumors with diffuse invasive mode (D-type) in histology showed endophytic growth pattern clinically. For the other variables analyzed such as histological grade and

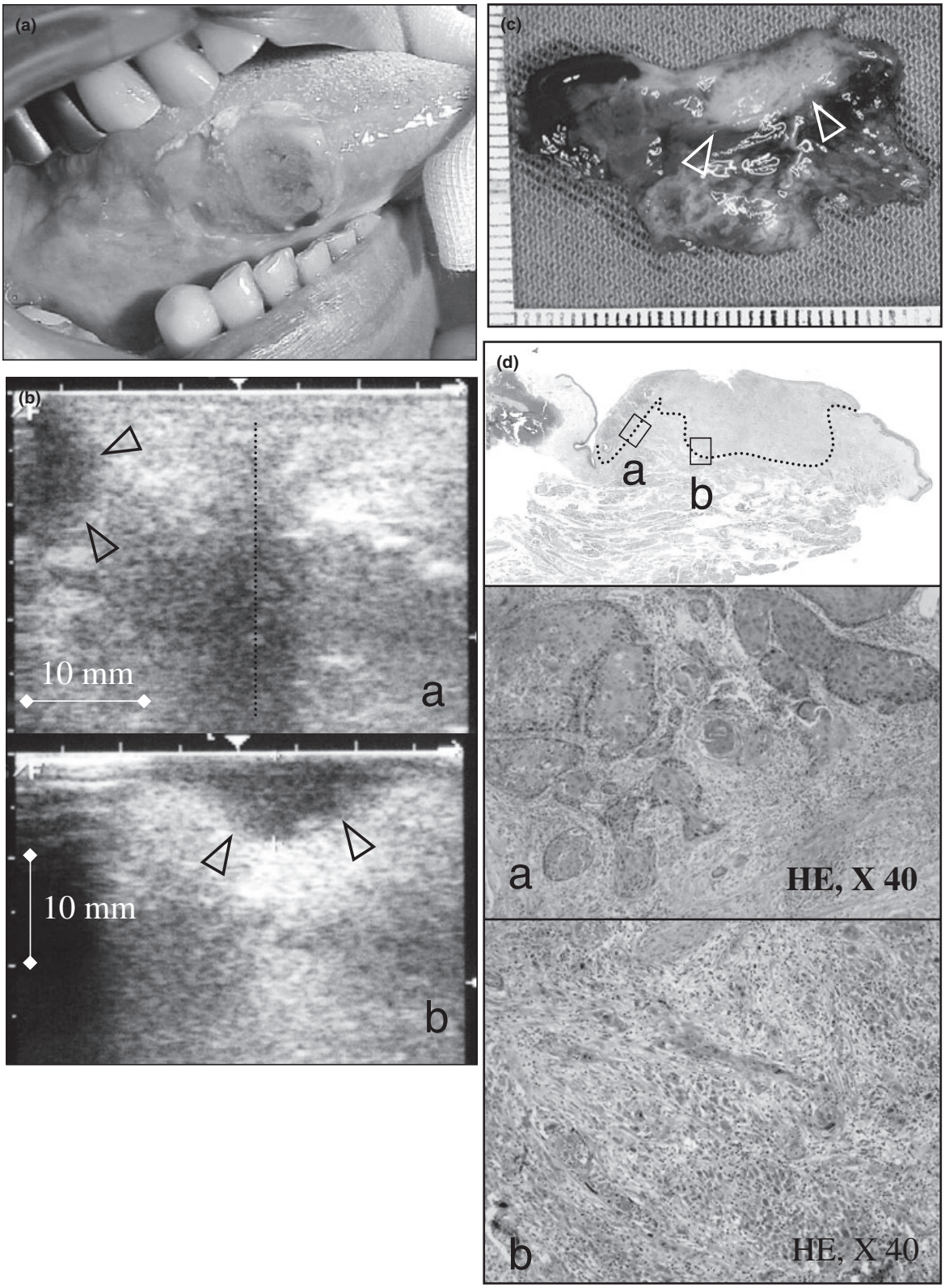

Figure 1 (**a**) T2N0 endophytic tumor of the marginal tongue. (**b**) Intra-oral ultrasound images. The lesion was preoperatively scanned from dorsum of the tongue (1, upper side shows dorsum surface and dotted line shows lingual septum) and from lateral marginal tongue (2, upper side shows lateral surface). Tumor was detected as a homogenous hypoechoic lesion with regular but unclear border (arrowheads). (**c**) Macroscopic view of cut surface of resected tongue specimen. (**d**) Pathological images of the tongue specimen. Tumor outline in the section (dotted line) matches well that in ultrasound image. Pathologic mode of invasion at the tumor-host borderline varied from part to part. Part (1) shows M-type of invasive mode exhibited groups of tumor cells with no distinct borderline (middle). While, part (2) shows D-type invasive mode spread diffusely without forming nests of tumor cells

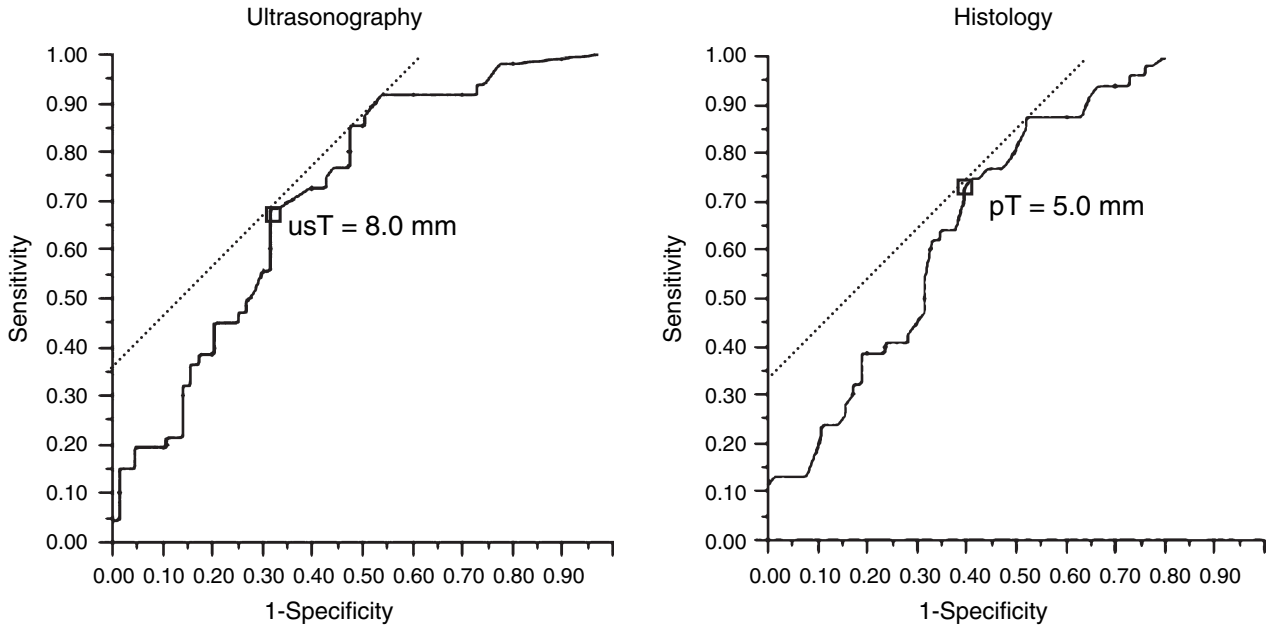

Figure 2 Receiver operating characteristic curve according to tumor thickness and neck metastasis

Table 2 Correlation between clinicopathologic parameters and neck metastasis

	Neck metastasis							
	N−group (*n* = 63)		*N*+*group* (*n* = 47)		*Total* (*n* = 110)			
Pathologic parameters	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*Univariate P-value*	*Multivariate P-value*
Histological grade								
Grade I	36	(57.1)	35	(74.5)	71	(64.5)	NS	NS
Grade II	25	(39.7)	12	(25.5)	37	(33.6)		
Grade III	2	(3.2)	0	(0.0)	2	(1.8)		
Mode of invasion								
W-type	17	(27.0)	2	(4.3)	19	(17.3)	< 0.001	NS
M-type	25	(39.7)	15	(31.9)	40	(36.4)		
D-type	21	(31.3)	30	(63.8)	51	(46.4)		
Muscular invasion								
Absent	31	(49.2)	4	(8.5)	35	(31.8)	< 0.001	0.014
Present	32	(50.8)	43	(91.5)	75	(68.2)		
Inflammatory cell infiltration								
Grade 1	14	(22.2)	14	(29.8)	28	(25.5)	NS	NS
Grade 2	26	(41.3)	21	(44.7)	45	(42.7)		
Grade 3	23	(36.5)	12	(26.7)	35	(31.8)		
Stromal reaction								
Medurally	32	(50.8)	10	(21.3)	42	(38.2)	< 0.001	NS
Intermediate	25	(36.8)	19	(40.4)	44	(40.0)		
Scirrhous	6	(9.5)	18	(38.3)	24	(21.8)		
Tumour thickness (pT)								
< 5.0 mm	37	(58.7)	12	(25.5)	49	(44.5)	< 0.001	NS
≥ 5.0 mm	26	(41.3)	35	(74.5)	61	(55.5)		

NS, not significant.

inflammatory cell infiltration, no statistically significant correlations with neck metastasis were found.

The US images of primary tumors well reflected histological findings, such as mode of invasion and stromal reaction. There were significant correlations between histological mode of invasion and shape of tumor margins, pattern of tumor margins and internal echo signal by US. There was a significant correlation between mode of invasion by section and pattern of tumor margins by ultrasound (Table 3). Desmoplastic tumor tissues showed irregular shape with unclear margins and heterogeneous pattern of internal echo signal on US image. On the other hand, US echo signal had no relation to the degree of keratinization and inflammatory cell infiltration. Thus, shape of tumor margins ($P = 0.019$), pattern of tumor margins

Table 3 Correlation between mode of invasion by pathology and pattern of border by ultrasound

	Pattern of border by ultrasound						
	W-type (n = 36)		*M-type (n = 32)*		*D-type (n = 29)*		
Mode of invasion by pathology	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*P-value*
W-type (n = 13)	8	(22.2)	5	(15.6)	0	(0.0)	0.007
M-type (n = 36)	16	(44.4)	10	(31.3)	10	(34.5)	
D-type (n = 48)	12	(33.3)	17	(53.1)	19	(65.5)	

W-type, well-circumscribed margin; M-type, moderately clear margin; D-type, diffuse and unclear margin.

(P = 0.033) and internal echo signal (P = 0.035) of the intra-oral US image were also significant parameters to predict neck metastasis (Table 4).

In the analysis limited to the early stage tumors (T1 and T2), clinical growth pattern (P < 0.0001) and tumor thickness on US (P = 0.007) were significant parameters to predict risk of neck metastasis.

Cause-specific 5-year cumulative survival of the N−group and the N+ group was 100 and 74.4%, respectively (P < 0.0001) (Figure 3). In ultrasonographic parameters, pattern of margin was the only significant factor affecting survival (P = 0.026); however, there was no significant difference between survival and shape of margin, internal echo signal and tumor thickness (Figure 4).

Discussion

Cervical lymph nodes metastasis is well known to be an indicator of poor prognosis in patients with tongue cancer (Prince and Bailey, 1999). Neck dissection is a standard treatment for N+ neck, while elective treatment of clinically negative necks is still controversial. Incidence of neck metastasis of tongue SCC was relatively high with 37–53% (Fukano *et al*, 1997; Woolgar, 1999; Yuen *et al*, 2000), and with 42.7% as a whole in the present study. To avoid unnecessary surgical intervention for N0 patients, many investigators have examined factors that may be used as an index for neck metastasis. Significant variation in aggressiveness of individual tumors is noticed and many parameters for grading malignancy based on a histological investigation of the primary tumor tissue had been reported (Broders, 1920; Arthur and Fenner, 1966; Jacobsson *et al*, 1973; Lund *et al*, 1975; Willen *et al*, 1975; Holm *et al*, 1982; Yamamoto *et al*, 1984). We found a significant correlation between neck metastasis and histological parameters, such as mode of invasion, muscular invasion, stromal reaction, and tumor thickness. Among them, muscular invasion is the most important histological parameter to predict neck metastasis. Pimenta Amaral *et al* (2004) reported that muscular invasion is a significant predictive factor of occult metastasis in lymph nodes. Some reports (Ho *et al*, 1992; Byers *et al*, 1998) suggested that depth of muscular invasion is strongly associated with the risk of occult metastasis.

There are many reports that tumor thickness is a valuable predictor of cervical lymph node metastasis (Mohit-Tabatabai *et al*, 1986; Moore *et al*, 1986; Spiro *et al*, 1986; Urist *et al*, 1987; Brown *et al*, 1989; Rasgon *et al*, 1989; Woolgar, 1996; Hiratsuka *et al*, 1997; Asakage *et al*, 1998; Myers *et al*, 2000; Kane *et al*, 2006). Spiro *et al* (1986) suggested that the increase in thickness was associated with the presence of occult metastasis. Our study has shown that tumor thickness of 5 mm by histology and of 8 mm by US is a cut-off point of predicting risk of neck metastasis of tongue cancer (Figure 2). Unlike histology, US is unaffected by shrinkage of tissue following excision, formalin fixation and slide preparation. Accordingly, US images reflect actual tumor thickness more precisely than that by histological sections.

The critical aspect in the growth of a tongue tumor is probably the deep invasion into the tongue musculature, in which the vascular invasion and metastatic spread are

Table 4 Correlation between ultrasound parameters and neck metastasis

	Neck metastasis							
	N− group[a] *(n = 51)*		*N+ group*[a] *(n = 46)*		*Total*[a] *(n = 97)*			
Ultrasound parameters	*No.*	*(%)*	*No.*	*(%)*	*No.*	*(%)*	*Univariate P-value*	*Multi- variate P-value*
Shape of border								
Regular	38	(74.5)	23	(50.0)	61	(59.1)	0.012	NS
Irregular	13	(25.5)	23	(50.0)	36	40.9)		
Pattern of border								
W-type	25	(49.0)	11	(23.9)	36	(37.1)	0.017	NS
M-type	16	(31.4)	16	(34.8)	32	(33.0)		
D-type	10	(19.6)	19	(41.3)	29	(44.3)		
Internal echo signal								
Homogenous	39	(76.5)	25	(54.4)	50	(59.1)	0.021	NS
Heterogenous	12	(23.5)	21	(45.7)	33	(40.9)		
Tumor thickness (usT)								
< 8.0 mm	31	(60.8)	15	(32.6)	46	(47.4)	< 0.001	0.040
≥8.0 mm	20	(39.2)	31	(67.4)	51	(52.6)		

[a]Thirteen cases not detected on US were excluded from the analysis.

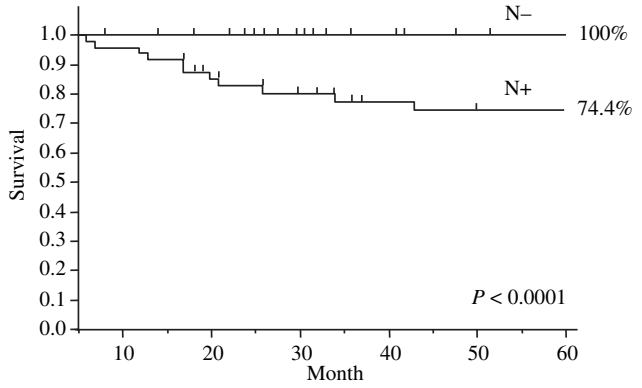

Figure 3 Cause-specific cumulative survival curves according to neck metastasis

likely to occur, and not the exophytic growth. However, thickness is the measurement of the vertical bulk of the tumor and includes exophytic as well as endophytic portion of the tumor. Bulky exophytic carcinomas with little invasion, oncologically behave as superficial tumors. Particularly, endophytic lesions are expected to infiltrate more deeply than exophytic ones, even if an equal tumor thickness (Kane *et al*, 2006). Therefore, measuring the depth of invasion from the level of the normal mucosal surface provides more accurate measure on the depth of tumor infiltration in the tongue tissue for prognostic consideration than tumor thickness measured from the surface of the tumor (Brown *et al*, 1989). It is necessary to consider that the measurement of tumor thickness overestimates the depth of invasion of an exophytic tumor and possibly underestimates the depth of invasion of an endophytic, ulcerative tumor.

Many reports have shown that mode of invasion at tumor-host borderline is a reliable predictive parameter for malignant potential of oral cancer (Jacobsson *et al*, 1973; Yamamoto *et al*, 1983a,b; Yamamoto *et al*, 1984; Bryne *et al*, 1992; Umeda *et al*, 1992; Bryne, 1998; Spiro *et al*, 1999). For an accurate grading of mode of invasion, an incisional tissue sampling of advancing front of cancer is recommended (Yamamoto *et al*, 1983a,b). However, Dedivitis (2003) suggested that various types of grades of invasion in the same specimen and the initial biopsy possibly would not be able to determine the exact grade of the complete specimen. High detectability (especially 100% in endophytic tumors) for tongue cancer by intra-oral US is of great significance to grade the malignancy. Therefore, it is possible to make an accurate grading of invasive mode according to the entire tumor image by intra-oral US. For improved prediction of neck metastasis, particularly in early tongue cancer with clinically N0 neck, intra-oral US is a useful tool for accurate evaluation of mode of invasion as well as tumor thickness (Heppt and Issing, 1992; Shintani *et al*, 1997, 2001).

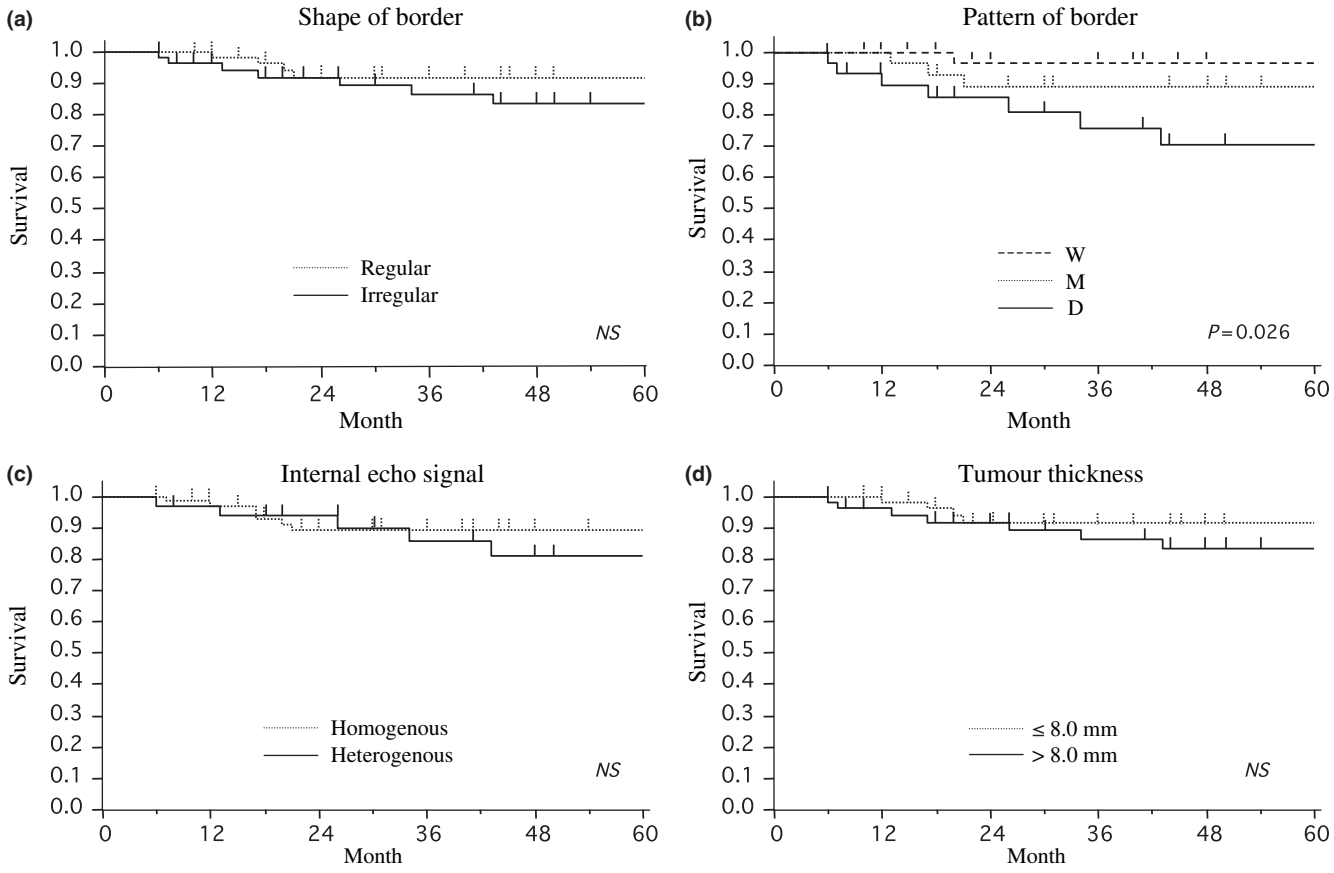

Figure 4 Cause-specific 5-year cumulative survival curves according to the ultrasonographic parameters

In the present study, we found that the shape and pattern of tumor margins on US image are important findings to grade the malignancy of tongue cancer. There was a significant correlation between mode of invasion by section and pattern of tumor margins by ultrasound. Namely, tumors with diffuse invasive mode shows irregular and unclear margins on US image. In particular, pattern of tumor margins is indicative of prognosis of patients with tongue cancer as well as neck involvement. We suggest that the neck of patients with endophytic tumor infiltrating 8.0 mm or more thickness with an irregular and diffuse tumor margins on US image should be treated electively. Matsuura *et al* (1998) also reported that patients with maximum tumor thickness ≥8 mm by US are more likely to fail in the neck region. Yamane *et al* (2006) demonstrated that intra-oral US in conjunction with the proposed computer-aided diagnosis system allows tissue characterization and prediction of subclinical cervical lymph node metastasis of T1N0 or T2N0 tongue carcinoma. Furthermore, tumors with diffuse margins by US should be excised taking into account the clearance at the deep margin. Ultrasound imaging applied intra-orally is a reliable tool in objectively assessing both the tumor thickness and the surgical margin clearance at the time of surgery (Songra *et al*, 2006).

In conclusion, intra-oral ultrasonographic assessment of the tumor thickness and the pattern of tumor margins would provide useful information to perform optimal treatment based on the grade of malignancy for patients with tongue cancer, particularly early stage tumor.

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