

## PREOPERATIVE MEASUREMENT OF TUMOR THICKNESS OF ORAL TONGUE CARCINOMA WITH INTRAORAL ULTRASONOGRAPHY

Anthony Po-Wing Yuen, FHKAM(ORL), Raymond Wai-Man Ng, FHKAM(Plastic), Paul Kin-Yip Lam, FHKAM(ORL), Ambrose Ho, MBBS

Department of Surgery, The University of Hong Kong Medical Centre, Queen Mary Hospital, Hong Kong. E-mail: pwyuen@hkucc.hku.hk

Accepted 27 March 2007

Published online 31 August 2007 in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/hed.20678

**Abstract:** *Background.* Tumor thickness of oral tongue carcinoma is an important independent prognostic factor for local recurrence, subclinical nodal metastasis, and survival. An accurate preoperative assessment of tumor thickness is therefore essential in optimizing treatment algorithm. The present study aims at evaluating the accuracy of intraoral ultrasonography in preoperative measurement of tumor thickness.

*Methods.* Forty-five patients with oral tongue carcinoma had intraoral ultrasonography to document tumor thickness using a 7.5 MHz right angle probe. The ultrasonic tumor thickness was correlated with the fresh unpreserved surgical specimen pathologic tumor thickness.

*Results.* Ultrasonic tumor thickness had significant correlation with pathologic tumor thickness. The accuracies of ultrasonic measurement of tumor thickness in staging of tumor thickness at cutoff values between 3 and 15 mm were above 91%.

*Conclusion.* Intraoral ultrasonography had satisfactory accuracy in the measurement of tumor thickness and is a useful adjunct in assisting pretreatment staging and prognosis evaluation of oral tongue carcinoma. ©2007 Wiley Periodicals, Inc. *Head Neck* 30: 230–234, 2008

**Keywords:** tongue; thickness; depth; carcinoma; ultrasound

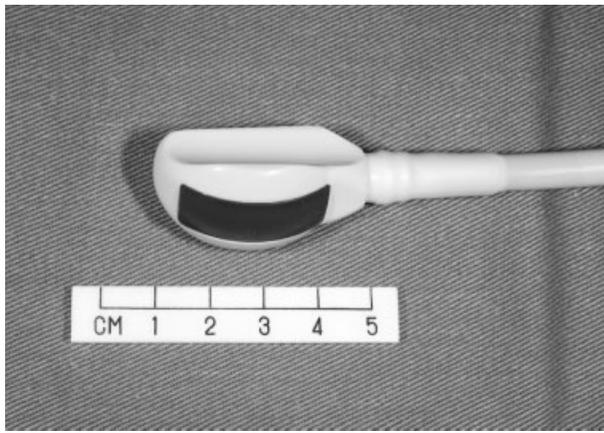
The largest tumor diameter has been used for many years in staging T1-3 oral tongue carcinoma

in the American Joint Committee on Cancer (AJCC) and Union Internationale Contre le Cancer (UICC) TNM staging systems. The largest diameter of oral tongue carcinoma is either the tumor length or width. Tumor thickness is almost never the largest diameter of oral tongue carcinoma and therefore has no contribution to the current AJCC and UICC prognostic staging.<sup>1,2</sup> We and many other authors have shown that tumor thickness, but not the largest dimension, is a significant independent prognostic factor in predicting subclinical nodal metastasis, local recurrence, and survival of patients with oral tongue carcinoma.<sup>1–7</sup> It is, however, still unresolved as to the best cutoff thickness value for staging purpose despite the unequivocal evidence that the thicker the tumor, the higher would be the risk of local recurrence, subclinical nodal metastasis, and treatment failure. The proposed cutoff thickness values for prognosis or staging by various studies vary between 3 and 9 mm.<sup>1–7</sup>

Oral tongue carcinoma is an aggressive cancer, and prevention of treatment failure by optimal primary treatment is always preferred.<sup>8–13</sup> A more aggressive treatment algorithm including

Correspondence to: A. P.-W. Yuen

© 2007 Wiley Periodicals, Inc.



**FIGURE 1.** A right angle 7.5 MHz ultrasound probe.

elective neck dissection and postoperative radiotherapy should therefore be considered in thick tumors.<sup>8,10</sup> On the other hand, thin tumors have low risk of local recurrence and subclinical nodal metastasis, simple glossectomy alone is adequate.<sup>1,2,9</sup> If the staging and management algorithm are based on tumor thickness, an accurate preoperative assessment of tumor thickness is necessary. Clinical assessment of tumor thickness with palpation using our fingers is insufficient to reach millimeter-resolution accuracy. We have shown that MRI can accurately measure tumor thickness.<sup>13</sup> Ultrasonography has been used in our outpatient clinic in the assessment and follow-up of head and neck cancer, particularly in the evaluation of neck mass and screening of subclinical nodal metastasis. It has advantages of being noninvasive, lacking radioactive hazard, simple, repeatable, readily available in an outpatient office facility, and less expensive compared with MRI. The present prospective study aims at evaluating the correlation between ultrasonic and pathologic tumor thickness in helping to stage the tumor thickness of oral tongue carcinoma preoperatively.

#### **MATERIALS AND METHODS**

The study was conducted between September 2001 and June 2006 in the Department of Surgery, Queen Mary Hospital, Hong Kong. All patients had squamous cell carcinoma of the oral tongue classified as T1-3. The intraoral ultrasound in this study was performed in the operating room by the operating surgeon immediately before glossectomy to avoid the discrepancy of ultrasonic and pathologic results due to tumor growth during the time period between the 2 measurements.

Patients with carcinoma of the tongue base, floor of mouth, other subsites of the oral cavity, or T4 oral tongue carcinoma were excluded. Patients with excision biopsy prior to definitive glossectomy, local recurrence after prior glossectomy, prior radiotherapy, and chemotherapy were also excluded. A total of 45 consecutive patients were recruited in the present study, including 28 men and 17 women, with a median age of 59 years (range, 22–90 years). The preoperative clinical AJCC TNM stages were 18 cT1N0M0, 21 cT2 (20 N0, 1 N1) M0 and 6 cT3 (5 N0, 1N2) M0. There were 18 well-differentiated, 20 moderately differentiated, and 7 poorly differentiated carcinomas.

All patients were examined with a 7.5 MHz right angled probe of the Aloka Ultrasonic system (model SSD-1700, Japan) immediately before glossectomy in the operation theater (Figure 1). A dark hypoechoic acoustic shadow can be seen clearly distinct from the surrounding normal echoic tongue tissue as seen in Figure 2. The probe was moved around the tumor surface until the acoustic shadow with deepest tumor invasion was located. The picture was frozen in the monitor, and the tumor thickness was measured by the ultrasonic machine along a perpendicular line from a point on the surface of the tumor to the point of deepest tumor projection as shown in Figure 2. The measurement had resolution of 0.1 mm. The procedure was repeated 3 times to ensure consistent results of maximum tumor thickness. To avoid the distortion and shrinkage of tumor tissue by subsequent procedures of histologic processing, the fresh glossectomy specimen was immediately cut open in the operation theater before fixation in formalin. The tumor was cut in multiple coronal and sagittal planes for assessment of pathologic



**FIGURE 2.** Ultrasonic image of tumor is shown as hypoechoic shadow.

thickness using a measuring caliper as shown in Figure 3. Tumor tissue could be visualized clearly as whitish hard tumor mass distinctly different from the surrounding uninvolved reddish soft tongue muscles. The tumor tissue in the deepest invasive front was sampled for histologic examination for confirmation of presence of tumor.

## RESULTS

Of all 45 tumors, the median pathologic tumor thickness was 8.5 mm (mean, 11.0 mm; range, 3.0–35.0 mm). There was a statistically significant correlation between pathologic and ultrasonic thickness (Pearson's correlation coefficient = 0.940,  $p < .005$ ). The scatter plot of the ultrasonic versus pathologic tumor thickness is shown in Figure 4. The diagonal line in Figure 4 represents the linear regression equation (pathologic thickness =  $0.36 + 0.97 \times$  ultrasonic thickness). Most of the scatter points were close to this linear regression line.

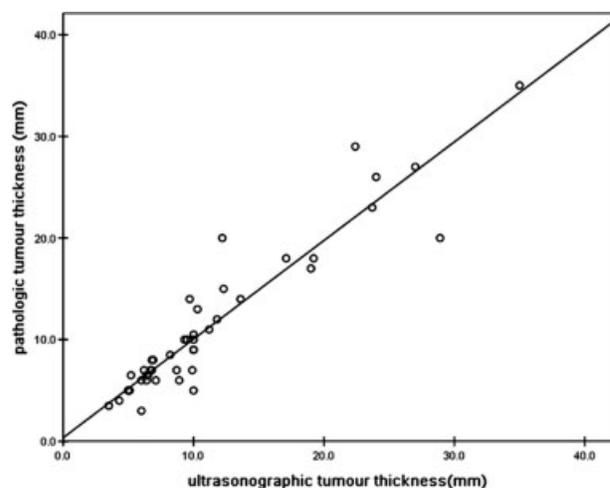
Since it is still unresolved as to the best cutoff thickness for staging purpose, the accuracies of ultrasonic staging of tumor thickness at cutoff values between 3 and 15 mm were analyzed as shown in Table 1. The accuracies were at or above 91% for various cut-off thicknesses being used. The accuracies of staging for thickness cutoff values between 16 and 35 mm were all at or above 93% (details are not included in Table 1).

## DISCUSSION

Local and nodal relapses account for the majority of treatment failures of oral tongue carcinoma.<sup>8,10,12</sup> Subclinical nodal metastasis has been reported in 30% to 45% T1-2 clinically node-nega-



**FIGURE 3.** Pathologic tumor thickness of fresh unpreserved glossectomy specimen.



**FIGURE 4.** Scatterplot of ultrasonic and pathologic tumor thickness.

tive patients.<sup>1-7</sup> These subclinical micrometastases are too small to be detected by any available radiologic investigations.<sup>14</sup> There is, however, little difference between T1 and T2 for prediction of subclinical nodal metastasis, local recurrence, and long-term survival.<sup>1,2</sup> There are many studies showing that tumor thickness, rather than its largest diameter, is a more significant prognostic factor for prediction of subclinical nodal metastasis, local recurrence, and survival of oral tongue carcinoma.<sup>1-7</sup> Although many researchers have recommended use of tumor thickness in the clinical and pathologic staging of oral tongue carcinoma in the last 20 years, this has not been adopted in either AJCC or UICC staging system. One of the important reasons why tumor thickness is not included in AJCC and UICC staging systems is the difficulty of clinical palpation to assess the tumor thickness down to 1 mm resolution. This is a major issue, particularly for those doctors who use radiotherapy or laser evaporation of the tumor as primary treatment. There is no en bloc surgical specimen for accurate documentation of pathologic tumor thickness after these treatments. It will be almost impossible for these centers to report treatment results if the staging system is totally replaced by tumor thickness.

For tumor thickness to be used in clinical T staging and treatment planning, it has to be measured accurately by clinical methods before treatment. Intraoral ultrasonography has been previously shown by Shintani et al to be useful in the assessment of tumor thickness of oral carcinoma.<sup>15</sup> Our study has again demonstrated that noninvasive intraoral ultrasonography

**Table 1.** Accuracy of ultrasonic staging of tumor thickness.

Pathologic thickness staging cutoff value	No. of patients (%)		
	Ultrasonic correct staging	Ultrasonic over-staging	Ultrasonic under-staging
≤3 mm > 3 mm	44 (98)	1 (2)	0
≤4 mm > 4 mm	43 (96)	2 (4)	0
≤5 mm > 5 mm	43 (96)	2 (4)	0
≤6 mm > 6 mm	41 (91)	3 (7)	1 (2)
≤7 mm > 7 mm	41 (91)	4 (9)	0
≤8 mm > 8 mm	42 (93)	3 (7)	0
≤9 mm > 9 mm	42 (93)	3 (7)	0
≤10 mm > 10 mm	45 (100)	0	0
≤11 mm > 11 mm	43 (96)	0	2 (4)
≤12 mm > 12 mm	43 (96)	0	2 (4)
≤13 mm > 13 mm	42 (93)	0	3 (7)
≤14 mm > 14 mm	43 (96)	0	2 (4)
≤15 mm > 15 mm	44 (98)	0	1 (2)

using 7.5 MHz probe could be used for accurate preoperative measurement of tumor thickness. It has high correlation (correlation coefficient of 0.97) with the pathologic thickness in fresh undistorted glossectomy surgical specimens. In addition, we have demonstrated that intraoral ultrasonography is over 90% accurate for staging the thickness on a wide range of cutoff values proposed by various authors.

Although thickness undoubtedly has prognostic value, it is unfortunate that different researchers use different thickness cutoff values for prognosis evaluation and treatment planning. The controversy of thickness cutoff point is due to multiple factors.<sup>16</sup> There are studies that used tumor depth instead of tumor thickness.<sup>3-7</sup> The cutoff value of depth and thickness would be different. Intraoral ultrasound can be used to measure tumor thickness, but not depth. There are many studies that have included tumors of other subsites of the oral cavity or even the oropharynx.<sup>16-21</sup> There may be different thickness cutoff values of other subsites compared with carcinoma of the oral tongue. There are studies that have included heterogeneous treatments including radiotherapy and chemotherapy, and the different treatments may produce different results.<sup>16</sup> There are also studies that have included clinical nodal metastasis in addition to subclinical nodal metastasis for evaluation of risk of nodal metastasis in relation to tumor thickness. The risk of nodal metastasis would be much higher if both clinical and subclinical nodal metastasis is included in these studies.<sup>16,21</sup> There is also unresolved opinion on the criteria to define the meaning of good and bad

prognosis. Those studies using higher rates of nodal metastasis, recurrence, and tumor-related mortality in the definition of poor prognosis will recommend higher cutoff values. Despite all these controversies and unresolved arguments on the optimal cutoff thickness, the results in this study demonstrate that intraoral ultrasonography can be used accurately for a wide range of thickness cutoff values for pretreatment prognosis and staging evaluation.

In addition to intraoral ultrasound, the other alternative tumor thickness assessment method is MRI. We have previously demonstrated that preoperative MRI of both T1- and T2-weighted images can accurately measure oral tongue carcinoma thickness.<sup>13</sup> Intraoral ultrasound can be used for accurate clinical assessment of tumor thickness comparable with MRI. Irrespective of the diversities of opinion on criteria of tumor thickness for staging, both MRI and intraoral ultrasound would be helpful preoperative assessment modalities for measurement of oral tongue carcinoma thickness for the planning of optimal treatment. Compared with MRI, ultrasound is inexpensive, simple, equally accurate, and readily available by the operating surgeon everyday. We can now circumvent the problem of long delays in obtaining an MRI appointment in the busy public hospital of the authors.

In conclusion, intraoral ultrasonography is an accurate assessment modality for thickness of oral tongue carcinoma. It is an acceptable alternative clinical assessment of tumor thickness in addition to MRI to assist pretreatment staging and prognosis evaluation.

## REFERENCES

1. Yuen APW, Lam KY, Wei WI, et al. A comparison of prognostic significance of tumor diameter, length, width, thickness, area, volume and clinicopathological features of oral tongue carcinoma. *Am J Surg* 2000;180:139–143.
2. 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* 2002;24:513–520.
3. Veness MJ, Morgan GJ, Sathiyaseelan Y, GebSKI V. Anterior tongue cancer and the incidence of cervical lymph node metastasis with increasing tumor thickness: should elective treatment to the neck be standard practice in all patients? *ANZ J Surg* 2005;75:101–105.
4. O-Charoenrat P, Pillai G, Patel S, et al. Tumor thickness predicts cervical nodal metastasis and survival in early oral tongue carcinoma. *Oral Oncol* 2003;39:386–390.
5. Lim SC, Zhang S, Ishii G, et al. Predictive markers for late cervical metastasis in stage I and II invasive squamous cell carcinoma of the oral tongue. *Clin Cancer Res* 2004;10:166–172.
6. Kurokawa H, Yamashita Y, Takeda S, et al. Risk factors for late cervical lymph node metastasis in patients with stage I or II carcinoma of the tongue. *Head Neck* 2002;24:731–736.
7. Sparano A, Weinstein G, Challan A, Yodul M, Weber R. Multivariate predictors of occult neck metastasis in early oral tongue cancer. *Otolaryngol Head Neck Surg* 2004;131:472–476.
8. Yuen APW, Wei WI, Wong YM, Tang KC. Elective neck dissection versus observation in the surgical treatment of early oral tongue carcinoma. *Head Neck* 1997;19:583–588.
9. Yuen APW, Wong BYH. Ultrasonic glossectomy—simple and bloodless. *Head Neck* 2005;27:690–695.
10. Yuen APW, Wei WI, Wong YM, Tang KC. Comprehensive analysis of results of surgical treatment of oral tongue carcinoma in Hong Kong. *Chinese Med J* 1997;110:859–864.
11. Yuen APW, Lam KY, Chan ACL, Wei WI, Lam LK. Clinicopathological analysis of local spread of carcinoma of tongue. *Am J Surg* 1998;175:242–244.
12. Yuen APW, Wei WI, Wong SHW, Ng RWM. Local recurrence of carcinoma of tongue: patient prognosis. *Ear Nose Throat J* 1998;77:181–184.
13. Lam P, Au-Yeung KM, Cheng PW, et al. Correlating MRI and histologic tumor thickness in the assessment of oral tongue cancer. *Am J Roentgenol* 2004;182:803–808.
14. Yuen APW, Lam KY, Chan CLA, Wei WI, Lam LK, Ho CM. Clinicopathological analysis of elective neck dissection for N0 neck of early oral tongue carcinoma. *Am J Surg* 1999;177:90–92.
15. Shintani S, Nakayama B, Matsuura H, et al. Intraoral ultrasonography is useful to evaluate tumor thickness in tongue carcinoma. *Am J Surg* 1997;173:345–347.
16. Pentenero M, Gandolfo S, Carrozzo M. Importance of tumor thickness and depth of invasion in nodal involvement and prognosis of oral squamous cell carcinoma: a review of the literature. *Head Neck* 2005;27:1080–1091.
17. Spiro RH, Huvos AG, Wong GY, et al. Predictive value of tumor thickness in squamous carcinoma confined to the tongue and floor of mouth. *Am J Surg* 1986;152:345–350.
18. Shingaki S, Suzuki I, Nakajima T, Kawasaki T. Evaluation of histopathological parameters in predicting cervical lymph node metastasis of oral and oropharyngeal carcinomas. *Oral Surg Oral Med Oral Pathol* 1988;66:683–688.
19. Martinez-Gimeno C, Rodriguez EM, Vila CN, Varela CL. Squamous cell carcinoma of the oral cavity: a clinicopathologic scoring system for evaluating risk of cervical lymph node metastasis. *Laryngoscope* 1995;105:728–733.
20. Woolgar JA, Scott J. Prediction of cervical lymph node metastasis in squamous cell carcinoma of the tongue/floor of mouth. *Head Neck* 1995;17:463–472.
21. O'Brien CJ, Lauer CS, Fredericks S, et al. Tumor thickness influences prognosis of T1 and T2 oral cavity cancer—but what thickness? *Head Neck* 2003;25:937–945.