



Is preoperative ultrasonography accurate in measuring tumor thickness and predicting the incidence of cervical metastasis in oral cancer? ☆

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SUMMARY

The need for elective neck dissection in patients with early stage oral cancer is controversial. A preoperative predictor of the risk of subclinical nodal metastasis would be useful. Studies have shown a strong correlation between histological tumor depth and the risk of nodal metastasis.

To determine if preoperative ultrasonography is an accurate measure of tumor depth in oral carcinoma. To assess if preoperatively measured tumor depth predicts an increased risk of subclinical metastatic neck disease and thus the need for elective neck dissection.

Twenty one consecutive patients with biopsy proven squamous cell carcinoma of the tongue/floor of mouth were analyzed prospectively. Each patient received a preoperative ultrasonography to assess tumor depth which was compared to histological measures. Univariate analysis was used to correlate tumor thickness and T stage with neck metastasis.

There was a significant correlation between the preoperative ultrasonography and histological measures of tumor depth (correlation coefficient 0.981, $P < 0.001$). The overall rate of lymph node metastasis was 52%. The rate of metastasis was 33% in N0 necks. In the group with tumors <5 mm in depth, the neck metastatic rate was 0%, as compared with 65% in the group ≥ 5 mm. Using univariate analysis tumor depth and T stage were significant predictors of cervical metastasis ($p = 0.0351$ and $p = 0.0300$, respectively).

Preoperative ultrasonography is an accurate measure of tumor depth in oral carcinoma. Tumor thickness is a significant predictor of nodal metastasis and elective neck dissection should be considered when this thickness is ≥ 5 mm.

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Introduction

A major determinant of the prognosis of oral carcinoma is the risk of cervical metastasis. While it is widely accepted that more advanced oral tumors be treated with elective neck dissection, management of stage I disease remains controversial. In the absence of clinical neck disease, stage I oral cancers are often treated with primary tumor resection and clinical follow up of the neck. However, studies have shown the incidence of occult neck metastasis in Stage I/II disease to be as high as 42%.¹ Thus, a predictor of the risk of subclinical nodal metastasis in oral cancer would be of

significant benefit in determining who requires elective neck dissection or adjuvant therapy.

Several factors have been evaluated for their ability to predict cervical metastasis. These include tumor stage, shape, thickness, grade, as well as the extent of vascular, lymphatic, and perineural invasion.^{2–5} Numerous studies have focused on tumor thickness and have shown a positive correlation between it and the risk of occult cervical metastasis.^{6–9} Recently, Yuen et al. reported tumor thickness to be the only factor with significant predictive value for subclinical nodal metastasis.¹⁰

The problem with this association is that these studies assess tumor depth histopathologically, which provides information that is not available preoperatively when treatment decisions are made. A preoperative measure of tumor thickness, and its validation, is hence imperative.

Shintani et al. assessed the thickness of tongue carcinomas preoperatively using ultrasonography.¹¹ These measurements were compared with those from histological sections after resection of

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the primary tumor. Their study showed significant correlation between the two measures.

This study aims to confirm that preoperative ultrasonography is an accurate measure of tumor thickness in oral carcinoma and thus a predictor of occult cervical metastasis. Ultrasonography measurements were compared to the incidence of neck metastasis in an attempt to develop a recommendation for elective neck dissection in cases of early stage oral carcinoma.

Materials and methods

This is a prospective study of 21 consecutive patients with oral carcinoma, presenting to two participating Head and Neck Surgical Oncologists (SMT, JT). All patients had biopsy proven squamous cell carcinoma of the tongue or floor of mouth. Each patient received the usual standard of care including investigations, treatment and follow up as per the QEII Health Science Centre Head and Neck Oncology Team. In addition, each patient received a pre-operative ultrasonography of the oral cancer to assess maximal tumor thickness.

Intraoral ultrasound examination was performed with a 10–12 MHz intracavitary probe. Gel was applied to the transducer tip and the probe covered with a latex sheath. The probe was then placed directly on the lesion and tumor thickness was measured in a vertical plane from the surface to the point of maximal depth. Measurements were to the nearest millimetre, all by a single radiologist.

Patients with T1 N0 lesions were treated with resection of the primary tumor without elective neck dissection. These patients were followed clinically and those who had no evidence of recurrence or cervical metastasis after 12 months were included in the group with pathologically negative nodes. Those patients with T2 or greater lesions were treated with resection of the primary tumor along with ipsilateral selective neck dissection.

Histological sections from each specimen were reviewed by a single pathologist, who was blinded as to the ultrasound results. Thickness was measured from the tumor surface to the point of maximal depth using an ocular micrometer. Specimens from patients undergoing neck dissection were then reviewed for any evidence of nodal disease.

Measurements of tumor thickness from histological specimens and those by ultrasonography were analyzed using the Pearson product moment correlation to determine the correlation coefficient between them. Tumor thickness was divided into two groups based on the associated incidence of nodal metastasis. One group included oral tumors up to 5 mm in the depth and the other in-

Table 1
TNM stage.

T stage	N0	N1	N2	N3	Totals
T1	4	1		0	5
T2	5	0	1	0	6
T3	4	1	1	0	6
T4	2	0	2	0	4
Totals	15	2	4	0	21

All the above tumors were M0.

cluded those greater than or equal to 5 mm. Univariate analysis using the Fisher exact test was used to assess the relationship of tumor thickness, as well as T stage, to the risk of cervical metastasis.

Results

Twenty one patients were enrolled in this study, of which 12 were male and 9 were female. Their ages ranged from 48 to 78 years, with an average age of 65. The TNM staging breakdown for all patients is shown (Table 1).

The measurements of tumor thickness from histological sections and by ultrasonography for each patient are shown in Fig. 1. When the two measures were compared there was a significant correlation between them as displayed in the scatter plot in

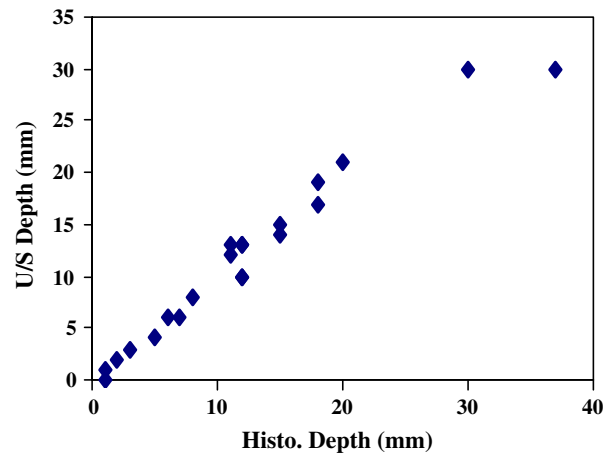


Figure 2 Scatter Plot of Ultrasound versus Histological measurements. The Pearson product moment correlation coefficient was 0.981 ($P < 0.001$).

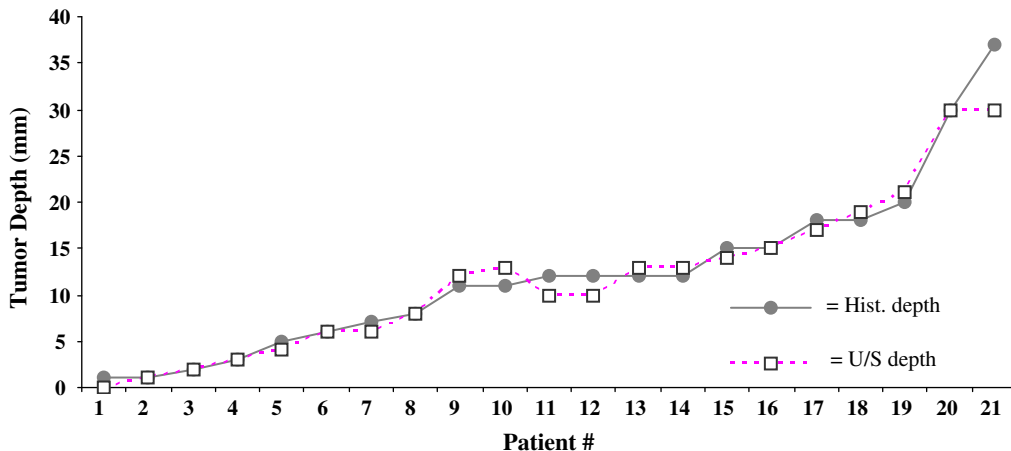


Figure 1 Ultrasound versus Histological measurements of tumor thickness. There was a significant correlation between the two measurements.

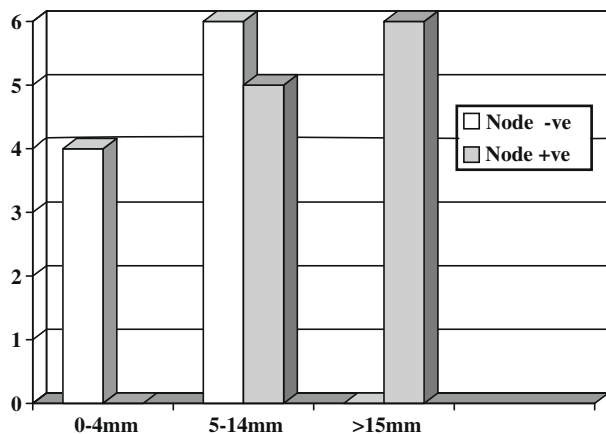


Figure 3 The relation of tumor thickness to the incidence of cervical nodal metastasis. Y axis represents number of cases.

Fig. 2. The Pearson product moment correlation coefficient was 0.981 ($P < 0.001$). Tumor thickness on ultrasonography ranged from 0 to 30 mm with an average of 11.1 mm. In patients with positive lymph node metastasis the average thickness increased to 15.6 mm. In the negative lymph node group, the average thickness decreased to 7.6 mm. The relation of tumor thickness to cervical metastasis is shown in Fig. 3.

The correlation of T stage to the risk of cervical metastasis was examined (Table 2). In the lymph node negative group, 8 of the 10 patients (80%) had T1 or T2 disease. This compared to only 3 of 11 (27%) in the lymph node positive group. As expected, cervical metastasis was more common in clinically advanced tumors. The result was statistically significant ($P = 0.03$) when T1/T2 tumors were compared to T3/T4 tumors.

All patients, with the exception of those with T1N0 tumors, received elective neck dissections. The four patients who did not have treatment of the neck were followed clinically for locoregional recurrence. Of the four, 3 had clinically negative necks after 12 months and were included in the lymph node negative group. One patient had regional neck recurrence and was included in the lymph node positive group. Overall, the rate of lymph node metastasis was 52% (11/21). When the N0 necks were considered alone, the subclinical nodal metastatic rate was 33% (5/15).

The smallest ultrasound measured thickness at which cervical nodal metastasis was found was 5 mm. As a result, tumors in this series were divided into two groups, those < 5 mm and those ≥ 5 mm (Table 3). In the < 5 mm group there were no patients with positive lymph node metastasis (0/4). In contrast, 65% (11/17) of patients in the ≥ 5 mm group had positive lymph nodes. About 35% (6/17) of patients with tumors ≥ 5 mm in thickness on ultrasonography did not develop neck disease. The difference was statistically significant ($P = 0.0351$). As stated, 33% (5/15) of patients with N0 necks had subclinical nodal metastasis. All 5 had tumors with maximal thickness ≥ 5 mm. Six patients were

Table 2
Correlation of T stage to cervical metastasis.

T Stage	-ve Lymph node mets	+ve Lymph node mets	% With nodal mets
T1	3	2	40
T2	5	1	17
T3	2	4	67
T4	0	4	100

When T1/T2 were compared to T3/T4 the difference in cervical metastasis was statistically significant; $P = 0.0300$ via Fisher exact test.

Table 3
Correlation of tumor thickness to cervical metastasis.

	Negative lymph node mets	Positive lymph node mets	Totals
Tumor thickness < 5 mm	4	0	4
Tumor thickness > 5 mm	6	11	17
Totals	10	11	21

The difference between the two groups was statistically significant; $P = 0.0351$ via Fisher exact test.

clinically staged with node positive neck disease. All six patients had tumors with maximal thickness ≥ 5 mm.

There were four patients with Stage I disease (T1N0). The average tumor thickness in this subgroup was 2.25 mm. One of these patients developed regional neck recurrence. Tumor thickness for that patient was 6 mm.

Discussion

It has been well documented that there is a strong association between the thickness of oral cancers and the risk of cervical nodal metastasis.^{6–10} However, these associations are based on pathological measurements which do not provide information for operative planning. Shintani et al. showed that preoperative ultrasound is an accurate measure of tumor thickness in tongue cancer. No study to date has correlated tumor thickness, as measured by ultrasonography, to the risk of nodal metastasis.

In this series we confirmed that ultrasonography is indeed an accurate measure of tumor thickness when compared to histological measurements. Ultrasonography versus histological measures were within 1 mm in 81% (17/21) of cases, within 2 mm in 93% (20/21), and was greater than 2 mm in only one case. In that single case, the tumor was 3.7 cm thick and the U/S transducer used could only assess depth up to 3 cm. If this case is excluded due to this technical shortfall, then all cases were measured within 2 mm.

Other radiological techniques, including CT and MRI, have been assessed for their ability to measure tumor depth. However, for lesions less than 5 mm these modalities have difficulty delineating a density difference from normal tissue. This makes accurate measurements of depth difficult.¹²

The correlation of T stage to the risk of cervical metastasis was examined. In univariate analysis, the difference between T1/T2 tumors and T3/T4 tumors was significant. As expected, risk increases with more advanced tumors. This association has not been consistently reported in the literature. Spiro et al.⁸ and Mohit-Tabatabai et al.⁹ noted similar findings, while Ragson et al.⁷ noted T stage did not correlate with nodal metastasis. Thus, T stage alone should not be used to predict subclinical nodal disease.

Our study supports the previously reported correlation between tumor thickness and nodal metastasis. In this instance, the correlation is to a preoperative measure of thickness (ultrasonography) as opposed to that from histological sections. There are varying reports as to what thickness level should necessitate elective neck dissection. In this series, the lowest depth at which there was cervical metastasis was 5 mm. As a result, patients were broken down into two groups: < 5 mm and ≥ 5 mm. Other papers have also reported 5 mm as being the critical depth after which there is increased metastatic risk.^{6,7} Of the patients in the < 5 mm group, none (0/4) had nodal metastasis. In the ≥ 5 mm group, 65% (11/17) had positive nodal disease. A univariate analysis between the two groups showed a statistically significant difference.

Most of the controversy regarding elective neck dissection in oral carcinoma pertains to stage I disease. The risk of cervical metastasis versus that of unnecessary neck dissection must be considered. In this series there were 4 patients with stage I disease.

Only one of these developed cervical metastasis, and interestingly that patient had a tumor with a depth greater than 5 mm (6 mm).

Conclusion

In oral cancer, tumor thickness is a significant predictor of cervical nodal metastasis. Our findings support preoperative ultrasonography as an accurate measure of maximal tumor thickness. In cases where this measure is equal to or greater than 5 mm, we would suggest the surgeon should strongly consider performing an elective neck dissection.

The authors have no conflict of interest to disclose. The first author (SMT) is to receive a cash prize of 500.00 as the paper was selected as the “Best Clinical Paper” at the 2nd International Academy of Oral Oncology Meeting in Toronto, Ontario.

Conflicts of Interest Statement

None declared.

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