

Preoperative ultrasonography for tumor thickness evaluation in guiding management in patients with early oral tongue squamous cell carcinoma

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Abstract

Objectives: (1) To assess the statistical correlation between the tumor thickness (TT) by ultrasonography (USG) and microscopic measurement in cases of early oral tongue squamous cell carcinoma (OTSCC). (2) To assess the predictive capacity of TT by ultrasound in detecting nodal metastasis. **Materials and Methods:** Prospective analysis was performed in 24 patients for a period of 2 years from 2012 to 2013. Nodal status and TT measurement was done preoperatively by neck and intraoral USG respectively in cases of early (pT1 & T2, clinically N0) OTSCC. As per the institution protocol after histopathological confirmation of malignancy, all patients underwent resection of primary lesion and ipsilateral elective neck dissection (Level - I to IV). Measurement of TT was obtained intraoperatively from fresh glossectomy specimen and postoperatively from histopathological paraffin section examination. The statistical correlation between TT measured by USG and histopathology was assessed by Pearson's correlation coefficient. Chi-square test was used to find the association of pathological T stage, TT with pathological nodal status. **Results:** Significant statistical correlation was seen between TT by USG and microscopic measures. Between the two, TT measurements were within 1 mm in 37.5% (9/24) of cases, within 2 mm in 29.16% (7/24), and was greater than 2 mm in 8 cases. The Pearson's correlation r is 0.678 ($P < 0.001$) and ICC (interclass correlation coefficient) is 0.808. The average difference between microscopic and US thickness (Bias) is -0.14637 and the limits of agreement is (4.717, -4.863) with 95% limits of agreement. The rate of occult nodal metastasis was 16.6% and TT of <4 mm had no incidence of nodal metastasis. **Conclusion:** Ultrasonographic evaluation is reliable and cost-effective tool to measure the TT preoperatively, which will be of help in deciding the management in early OTSCC. TT of 4 mm and above was predictor of occult cervical nodal metastasis.

Key words: Ultrasound tongue; oral tongue cancer; squamous cell cancer

Introduction

Intraoral ultrasonography (USG) is a useful modality to evaluate the extend of tumor involvement of tongue

cancer and to ascertain its tumor thickness (TT).^[1-4] There exist several studies proving the statistical correlation between ultrasound TT and histopathological gross TT^[2,5-7]

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postsurgical resection, making ultrasound an essential modality in ascertaining the TT as well as to ascertain the regional lymph nodal metastasis.^[8-10]

Several studies have proved that the TT is an important factor to predict occult nodal metastasis. In literature review by Pentenero *et al.*,^[11] showed the TT cut off ranged from 2 mm to 10 mm, as prognostic factor. Other important prognostic predictive parameters include age, sex, tobacco intake, TNM (tumor, node, and metastasis) status, histopathological parameters like tumor border, infiltration, perineural, or vascular invasions.^[11-13]

When considering OTSCC, the risk of occult metastasis is 50% in clinically N0 neck.^[14,15] Thus in cases of early N0-OTSCC, it is prudent on the surgical team to decide on to whether to undertake an elective neck dissection or not.

The studies have used magnetic resonance imaging (MRI),^[16] ultrasound^[7] in preoperative assessment of TT with histopathology being the gold standard. Sonographic evaluation has the advantage of being rapid, less costly over MRI, although both modalities are noninvasive.

Materials and Methods

The study was carried out in the Department of Radiodiagnosis and Interventional Radiology from January 2012 to December 2013. 24 patients were included in the study. The ethics committee approved this prospective cross-sectional study. An informed consent was taken from all the patients undergoing study.

TT measured by macroscopic technique and intraoral ultrasound compared to the gold standard microscopic thickness statistically using: 1) Pearson correlation coefficient; 2) Interclass correlation; 3) Bland-Altman plot –95% confidence interval (CI). Chi-square test was used to find the association of pathological T stage and TT with pathological nodal status.

Our inclusion criteria included patient population of any age or sex with, 1) Biopsy proven T1N0 or T2N0 primary squamous cell carcinoma of tongue; 2) Tumors located on lateral tongue in anterior two-third.

Our exclusion criteria included: 1) Tumor of tongue crossing the midline or involving the tip of tongue; 2) Tumor of lateral surface of anterior two-third of tongue infiltrating into surrounding structures; 3) Irradiated tumor of anterior two-third of tongue; 4) Recurrent tumor of anterior two-third of tongue; 5) Tumor of other subsites of oral cavity.

TT measurement was done as a part of preoperative assessment by intraoral ultrasound. All patients underwent resection of primary lesion and ipsilateral elective neck

dissection, i.e. supraomohyoid neck dissection (Level I to IV). Measurement of TT was obtained intraoperatively from fresh glossectomy specimen and postoperatively from histopathological paraffin section examination.

Ultrasound measurement was done using 17 or 9 MHz conventional linear probe with sterile cover. Tongue protruded, held gently with gauze and probe placed directly on tumor surface such that deformation of tumor was not caused [Figure 1]. TT measured from tumor surface to deepest point of invasion was used in protruding lesions; and for ulcerative lesions an imaginary line was drawn over the ulcerated area joining the normal mucosa on both ends and the deepest point of invasion was measured [Figure 2 and Figure 3a,b]. Neck ultrasound screening was done using 17 MHz linear conventional probe in all patients to assess suspicious nodes. There were no suspicious nodes that were detected in our sample size that included T1/T2, N0 early OTSCC.

After resection, specimen was placed in saline, and immediately shifted to the Department of Pathology for sectioning. To avoid shrinkage and distortion error, the specimen was not treated with formalin. Specimen measurements, tumor measurements (except for thickness), and clear margins (except deep clear margins) were noted before sectioning.

Specimen was later cut into approximately 2–3 mm thick transverse slices. Tumor tissue was visualized as whitish hard tumor mass from surrounding reddish uninvolved tongue muscle. Cut sections were examined for TT. Tissue section in which mucosa adjacent to the tumor was observed and which was considered to have greatest infiltration into the underlying tissue was noted in both ulcerated and exophytic lesion, disregarding any superficial keratin or inflammatory infiltrate that existed. Macroscopic TT measurements were obtained using hand held lens and Vernier caliper. This macroscopic TT was verified and confirmed by two other pathologist.

Microscopically lesion staged as per sixth edition of American Joint Committee on Cancer system (AJCC 2010).

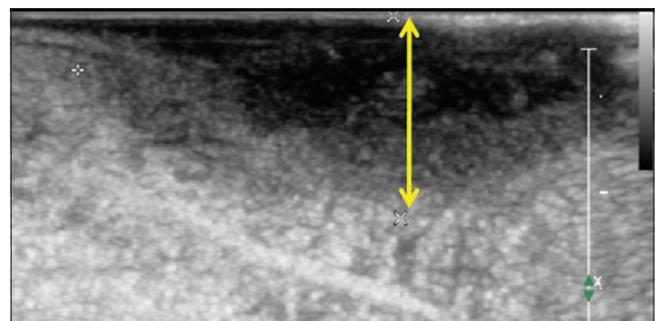


Figure 1: TT measurement from the lesion surface to the greatest depth of lesion

Histological measurements obtained using an ocular micrometer. Maximum thickness recorded from imaginary line reconstructing the intact mucosa to deepest point of invasion into underlying tissue, in both ulcerated and exophytic lesion, disregarding any superficial keratin or inflammatory infiltrates [Figure 4].

Slides were examined for lymphovascular invasion. Lymph node sections stained by hematoxylin-eosin (H and E). Serial sections of the same were stained using immunohistochemical marker PAN CK and observed under ocular microscope to record metastatic status by pathologist.

Table 1: Age group distribution

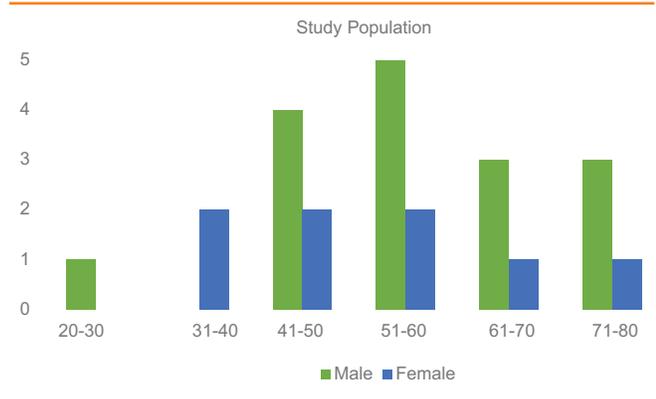


Table 2: Case distribution of tumor stage T1 and T2

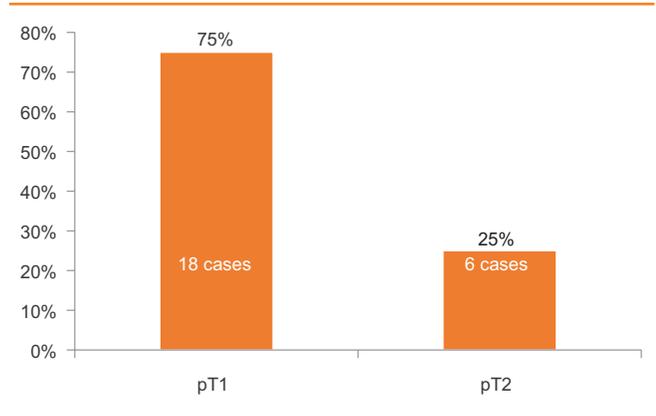
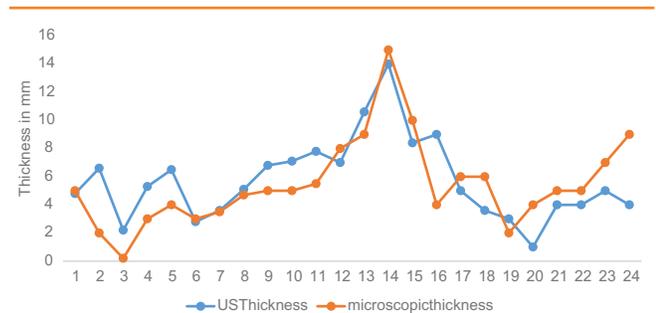


Table 3: Graphical representation of USG vs microscopic thickness distribution



Results

Twenty four patients with biopsy proven OTSCC were included in our study. Age group ranged from 22 years to 76 years (mean age 55) with 16 males (66.7%) and 8 females [Table 1]. Eighteen cases (75%) were pT1 and 6 cases (25%) were pT2 [Table 2].

Ultrasound TT vs. microscopic thickness [Table 3] was within 1 mm in 37.5% (9/24) of cases, within 2 mm in 29.16% (7/24), and

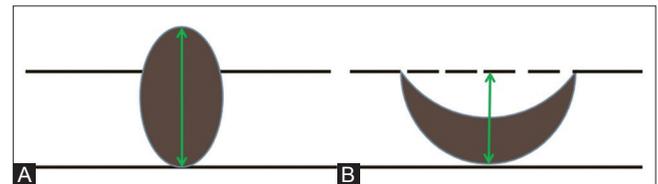


Figure 2 (A and B): (A) TT measurement in exophytic lesion; (B) showing TT measurements in ulcerative lesion

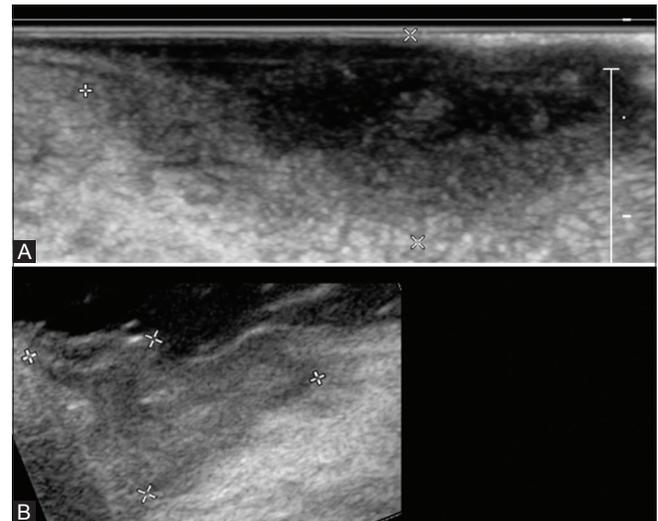


Figure 3 (A and B): (A) Exophytic lesion in ultrasound; (B) ulcerative lesion in ultrasound

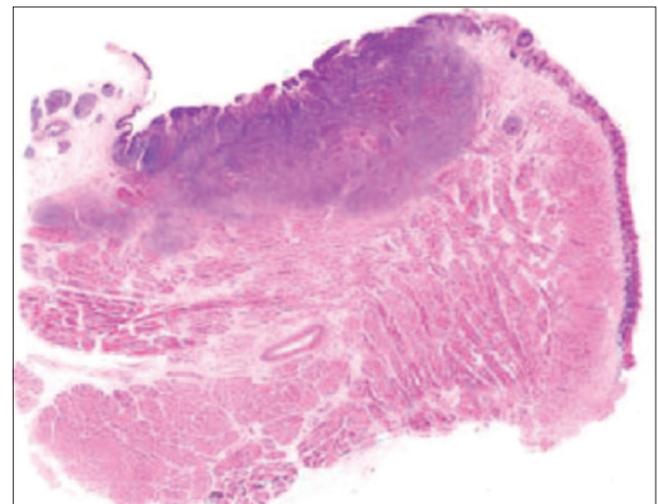


Figure 4: Microscopic section of tongue with infiltrating carcinoma

Table 4: Bland-Altman and interclass correlation of USG vs microscopic thickness distribution

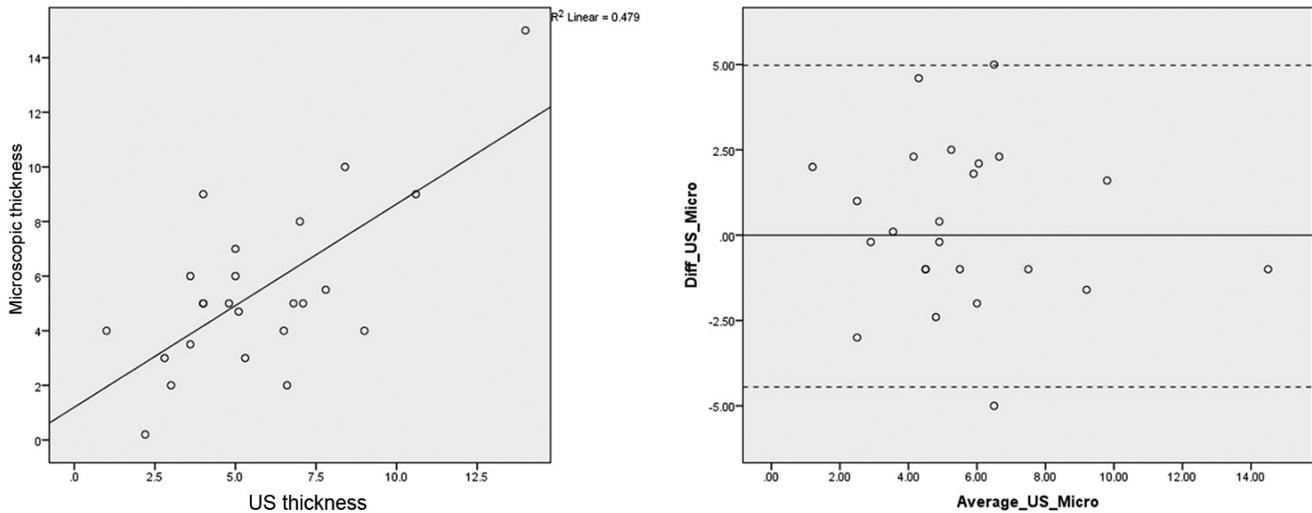
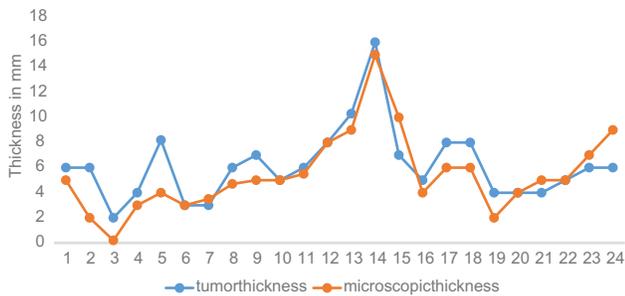


Table 5: Graphical representation of macroscopic vs. microscopic thickness distribution



greater than 2 mm in 33.34% (8/24) of cases. Very thin lesions (as thin as 1 mm included in the study) could be detected with ultrasound. Pearson correlation for ultrasound and microscopic thickness was $r = 0.692$ ($P < 0.001$) and interclass correlation for ultrasound and microscopic thickness, (interclass correlation coefficient) ICC = 0.821 [Table 4].

Macroscopic vs. microscopic thickness [Table 5] was within 1 mm in 37.5% (9/24) of cases, within 2 mm in 25% (6/24), greater than 2 mm in 16.6% (4/24) of cases, no difference or exactly same in 20.8% (5/24) of cases. Macroscopic vs. microscopic thickness was within 1 mm in 37.5% (9/24) of cases, within 2 mm in 25% (6/24), greater than 2 mm in 16.6% (4/24) of cases, no difference or exactly same in 20.8% (5/24) of cases. The Pearson correlation for macroscopic and microscopic thickness $r = 0.834$ ($P < 0.001$) and interclass correlation for macroscopic and microscopic thickness, ICC = 0.898 [Table 6].

There is significant correlation between macroscopic vs. microscopic measures of TT (correlation coefficient 0.834, $P < 0.001$) as well as between USG and microscopic

thickness (correlation coefficient 0.692, $P < 0.001$). Among the two techniques, macroscopic measurement showed better agreement to microscopic thickness. Average difference between microscopic thickness and US thickness (Bias) is -0.14637 with 95% limits of agreement.

TT of 4 mm and above is an indicator of cervical lymph node metastasis. Overall rate of occult lymph node metastasis was 16.6% [Table 7].

Discussion

Oral tongue squamous cell carcinoma (OTSCC) is the most prevalent malignant neoplasm of oral cavity with worst survival rates.^[17] Various preoperative techniques have been described for TT evaluation of OTSCC by ultrasound, computed tomography (CT) and MRI with variable results and the gold standard being histopathological evaluation. There are studies that point towards the superiority of ultrasound in TT assessment over CT and MRI.^[18,19] Intraoperative assessment technique by frozen section have also been described.

In our study, there was significant correlation between microscopic vs. macroscopic and USG vs. microscopic measurements. Between the two, macroscopic measurements showed better agreement to microscopic thickness than to ultrasound.

Cervical nodal metastasis is the most important prognosticator of survival in OTSCC. The risk of occult cervical nodal metastasis in early OTSCC varies from 6% to 46%.^[10] The regional rate of recurrence in clinically untreated N0 neck varies from 30% to 47%^[20,21] for early OTSCC (T1 & T2). Controversies exist onto whether to treat early N0-OTSCC with elective neck node dissection. The TT cut

Table 6: Bland-Altman and interclass correlation of macroscopic vs. microscopic thickness distribution

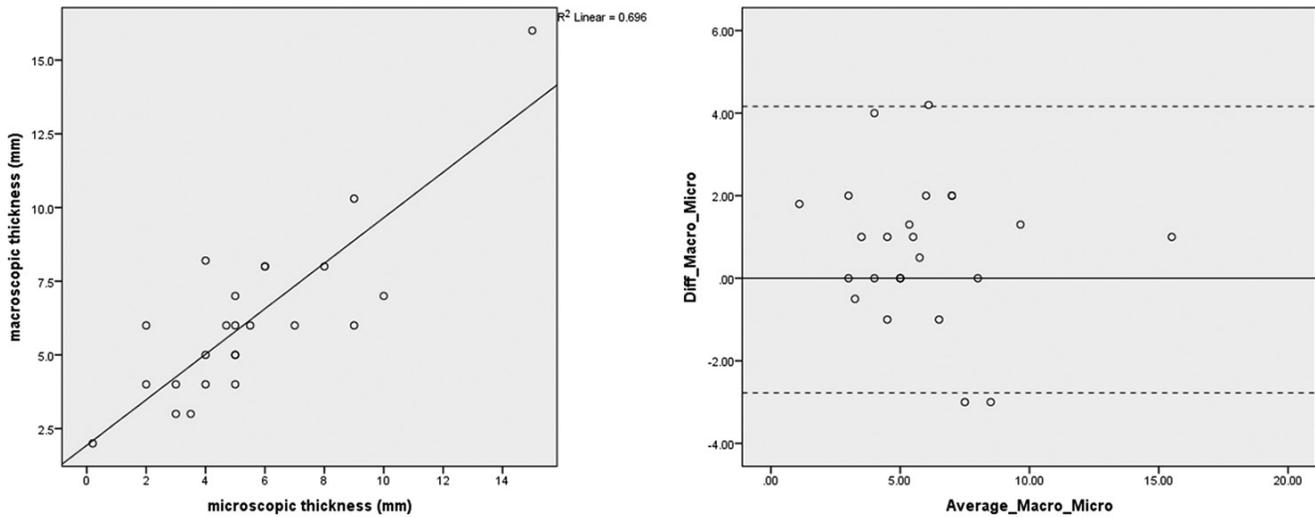


Table 7: Occult nodal metastasis distribution in relation to TT

| Pathological parameter | Total (24) | | Positive nodes | | Negative nodes | | P |
|------------------------|------------|----|----------------|------|----------------|------|-------|
| | n | % | n | % | n | % | |
| pT1 | 18 | 75 | 3 | 16.7 | 15 | 83.3 | 1 |
| pT2 | 6 | 25 | 1 | 16.7 | 5 | 83.3 | |
| TT <4 mm | 6 | 25 | 0 | 0 | 6 | 100 | 0.533 |
| TT ≥4 mm | 18 | 75 | 4 | 22.2 | 14 | 77.8 | |

off for deciding to treat the neck varies greatly in literature from 1.5 mm to 10 mm, being most often 4 mm.^[22,23]

In our study, the rate of occult metastasis was 16.6%. The incidence of occult nodal metastasis was zero when TT cut off was less than 4 mm.

Our study had few limitations:

- Discrepancy arising due to tumor shrinkage during the fixation process was not addressed in the study. The effect reported is variable ranging in literature from 4.1% to 30%.^[24] In our study, however, we tried to minimize the variability due to tumor shrinkage by fixation being done in less than 24 h
- Exophytic lesions, while being measured with USG probe over the lesion, may cause some pressure effect over the tumor, thus resulting in variations in TT and depth of involvement. However, we tried to reduce this effect by minimizing the pressure of application, by placing the probe over the tumor as gently as possible and with the same radiologist doing all the TT measurement
- Almost all studies depicting USG TT was done intraoperatively after anesthesia. However, we tried in this study to do an USG TT as a part of preoperative assessment and to confirm its statistical validity.

Conclusion

1. Ultrasound TT evaluation is a reliable and cost-effective tool to measure the TT preoperatively, which will be of help in deciding the management of N0 neck in early OTSCC
2. TT of 4 mm and above was predictor of occult cervical lymph node metastasis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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