

## **Correlation of Intraoperative Ultrasonographic Oral Tongue Shape and Border and Risk of Close Margins**

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## **Abstract**

Intraoperative ultrasound (IOUS) is a potentially useful adjunct to the resection of oral tongue cancers (OTC). IOUS images of the tumor-normal tissue interface show different patterns of invasion. In this retrospective series of 29 patients treated for OTC, we evaluated if there was a correlation between IOUS findings of patterns of invasion and final histology and assessed if there was any associated risk of increased incidence of positive or close margins with different patterns of invasion as seen on ultrasound. Although we found no significant correlation between ultrasound patterns of invasion and histological evaluation, we did find that an infiltrative pattern of invasion on IOUS did result in a significant risk of a close margin. Further exploration of these findings in a larger prospective study could provide definitive information on the efficacy of this modality in OTC resections.

## **Introduction**

Resection margin status is a key prognostic factor in oral tongue cancer (OTC) resection.<sup>1-3</sup> This need for better margin clearance has led to the investigation of real-time intraoperative imaging, such as intraoperative ultrasonography (IOUS), in assessing tumor extent<sup>4-8</sup> as currently there is no widely applied modality that allows a real time image guidance of intraoral soft tissue resections. In addition to tumor deep extent, various ultrasonographic appearances of OTC, including patterns of tumor margins and tumor borders, have also been studied.<sup>9-11</sup>

In this study, we aim to compare the infiltrative nature of tumor shape (TS) and the sharpness of tumor border (TB) on US and examined whether the sonographic TS and TB would have an impact on radial margin clearance. We also looked for a correlation between histologic and ultrasonographic patterns of invasion.

## **Materials and Methods**

### *Patients*

This study (2019P000381) was approved by the Institutional Review Board at Mass General Brigham. Twenty-nine consecutive patients with OTC who underwent tumor resection by a single surgeon with IOUS between August 2016 and September 2021 were retrospectively identified. A total of 23 of the 29 included patients were from a previously reported series.<sup>8,12</sup> A comprehensive chart review of key demographic and pathologic factors and oncologic outcomes was performed.

### *Surgical approach*

Tumor resections were done transorally as previously described.<sup>13</sup> Steps included using a ultrasound transducer initially, at resection mid-point and conclusion to identify the extent of the tumor including its deepest extent and depth of invasion (DOI), to maintain at least a 5 mm margin of tissue. Any modifications of the resection real time based on IOUS were related to the deep tumor extent.

### *Sonographic examination*

Two neuroradiologists, blinded to the histologic findings, analyzed the recorded ultrasound images. The characteristics considered were TS (noninfiltrative vs infiltrative) and TB (sharp vs ill-defined) (Figure 1). Infiltrative TS was defined as angular borders with parts that protruded deep in certain areas along the deep surface of tumors, while nodular, circular, or oval TS were characterized as noninfiltrative. TB was defined as follows: tumors with thin zones of transition and clear outlines that can be delineated using a sharp-tipped pen were designated as sharp TB, whereas tumors with wide zones of transition that can only be delineated with a wider brush were designated as ill-defined TB. The neuroradiologists completed their evaluations independently, and then collaborated on a consensus interpretation blinded to the histological findings.

### *Histological examination*

Two dedicated head and neck pathologists, blinded to the US findings, assessed histologic TS (non-infiltrative vs. infiltrative) and TB (sharp vs. ill-defined, and then reconciled them to produce consensus results.

## *Statistical Methods*

Patient characteristics were presented as numbers (percentages). Percent agreement and correlation coefficient (Cohen's  $\kappa$ ) were calculated to assess variability between pairs of evaluators within each specialty. Correlation analysis was performed using Fisher's exact test and Pearson's chi-square test for categorical data. Logistic regression was performed for univariable and multivariable analysis. Abiding the 1 in 10 rules, only 1 additional variable, other than the variable of interest (sonographic TS or TB), was included in the multivariable analysis. The selection of the additional variable was based on clinical relevance. Odds ratios and 95% confidence intervals were calculated for univariable and multivariable analyses. The significance level was 5%. Analyses of the data were performed using Stata/BE 17.0.

## **Results**

Our final cohort included 29 patients. Overall clear margins (defined as  $\geq 5$  mm) were achieved in a total of 18 patients (62%). Deep margin clearance ( $\geq 5$  mm) was achieved in 21 patients (72%). The evaluations of both sonographic TS and TB by 2 neuroradiologists showed substantial agreement (86.2%) with a Cohen's  $\kappa$  value of 0.73 ( $p < .001$ ). Ultrasonographic TS and TB did not significantly correlate with 1 another ( $p > .05$ ).

### **Ultrasonographic Prediction of Prognostic Factors**

Ultrasonographic TS significantly correlated with resection margin status only ( $p = .027$ ) (Table 1). On univariable analysis for margin status, only sonographic infiltrative TS was found to be a risk factor (odds ratio [OR] 6.9, 95% CI 1.3-37,  $p = .024$ ). There was no statistical significance between margin status and DOI. In a multivariable analysis controlling for T stage, infiltrative

TS on US remained a significant risk factor for margins less than 5mm with an odds ratio of 11.3 (95% CI: 1.42-90.4).

## **Discussion**

In this series of patients undergoing OTC resection with IOUS guidance, we found that ultrasonographic TS significantly correlates with the outcome of the surgical margins on multivariable analysis and has the potential to be the imaging correlate of the histopathological “worse pattern of invasion.” We did not however find a correlation between the ultrasonographic and histological findings. Other imaging modalities in evaluating the extent of oral cavity cancer have been studied. Depth of invasion assessment on magnetic resonance imaging (MRI) has been found to correlate with histologic DOI in tumors  $\geq 5$  mm only and IOUS has been found to outperform both computed tomography and MRI in estimating DOI for lesions  $< 5$  mm.<sup>12,14-16</sup> There are limitations to our study, including single surgeon participation, retrospective nature of the study, small sample size, and our selection of tumor descriptors from previous studies in the literature.

## **Conclusion**

Intraoperative US is an evolving technology in the surgical management of oral tongue cancer. This preliminary study correlated a series of US findings to determine that an infiltrative TS on ultrasound predicted a greater risk for resection margin  $< 5$ mm. Additional studies are necessary to validate these findings in order to determine if IOUS may play a more substantial role in improving surgical outcomes.

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Figure 1. Ultrasonographic border and shape. Examples of infiltrative (Fig 1A) and oval (non-infiltrative) TS (Fig 1B). Sharp TB with thin zones of transition (Fig 1C) is compared with an ill-defined border with wider zone of transition (Fig 1D).

Table 1. Correlation of tumor prognostic factors and ultrasonographic features.

	Ultrasonographic Tumor Shape	Ultrasonographic Tumor Border
Prognostic factors	p-value	p-value
pT stage		
T1		
T2	0.258	0.169
T3	-	-
pN stage		
N0		
N+	0.192	0.682
LVI		
Negative		
Positive	1.000	0.222
PNI		
Negative		
Positive	0.714	<b>0.021</b>
DOI		
<4mm		
≥4mm	0.249	0.128
ENE		
Negative		
Positive	0.078	0.598

Overall margin status		
$\geq 5\text{mm}$		
$< 5\text{mm}$	<b>0.027</b>	0.812