Original Article

Evaluation of Tumor Thickness in Three Dimensions on Magnetic Resonance Imaging and its Comparison with Final Histopathology in Squamous Cell Carcinoma of the Tongue

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Abstract

Context: Tongue is a three dimensional structure and assessment of accurate tumor extent is important for surgical planning. Various imaging modalities are used to assess the dimensions and depth of tumor like MRI, CECT, and clinical examination with doubtful accuracy. **Aim:** To evaluate tumor thickness in three dimensions on MRI and whether it correlates well with final histopathology so as to assess its reliability in staging and planning treatment. **Material and Methods:** Fifty patients with biopsy proven squamous cell carcinoma of the tongue who were planned for surgery and willing to participate in the study were included. These patients underwent MRI to analyse tumor thickness and extent of tumor spread in three planes and it is correlated with final histopathology to assess the reliability of MRI in preoperative assessment. **Setting and Design:** This is a prospective study, conducted at a tertiary care hospital and research centre. Correlation and linear regression analysis were used to study the relationship between tumor dimensions in MRI and correlated with the results on final histopathology. **Result:** In this prospective study, we studied fifty cases of carcinoma tongue of which 38 were males and 12 were females. Mean age was 49 years. The tumor thickness on MRI correlated well with final histopathology and most values fell below the 1:1 (x=y) line of agreement. Also, depth of invasion on histopathology was correlated with MRI which also related well to the histopathology taking into account the shrinkage. **Conclusion:** There was a significant correlation between the MRI T staging and final histopathology and it is found that MRI findings and depth correlated well with final histopathology taking into account the shrinkage factor.

Keywords: *Carcinoma tongue, depth of invasion, magnetic resonance imaging, tumor thickness*

Introduction

Oral cancer is the 18th-most common cancer globally.[1] Squamous cell carcinoma (SCC) of the lower gingivobuccal complex and tongue is common in the Indian subcontinent, of which later has a relatively poor prognosis compared to other sites.[1,2] This is attributed to its complex three-dimensional (3D) muscular structure with little mucosa, increased mobility, its proximity to other intraoral structures, and rich lymphovascular supply.[3] With current inclusion of depth of tumor in staging and its role as a prognostic factor, there is a need of imaging which can accurately assess the pretreatment stage of tumor.[4,5] Out of all imaging modalities, magnetic resonance imaging (MRI) delineates soft-tissue involvement better and is considered the most accurate imaging for assessing tumor extent in tongue carcinoma.[6] As tumor has 3D anatomy, the definition of tumor thickness (TT) should be considered not only in terms of the lengths but also in the anterior-posterior, superior-inferior, and medial-lateral directions. This better represents the extent of invasion of oral tongue (OT) SCC and will be an important factor in deciding the surgery and predicting prognosis. Many reports demonstrated the limitations of the conventional tumor node metastasis staging system (7th edition) to determine the prognosis, and thus, various clinicopathological parameters such as TT and depth of invasion (DOI) are introduced for better prediction of patient survival in current American Joint Committee on Cancer (AJCC) 8th edition.[3,7] Different studies focused on the proper definitions of TT and DOI. TT refers to the thickness of the entire tumor mass. DOI refers to the extent of tumor beneath an epithelial

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surface. Comparing the two parameters, DOI predicts the risk of lymphatic and hematogenous spread more accurately.[8] Therefore, proper assessment of tumor extent on imaging is important for appropriate treatment planning.

Aim of the study

In this study, we estimated the thickness and direction of primary tumor spread using MRI in axial, coronal, and sagittal plane and correlated with final histopathology to evaluate the potential clinical significance of using a 3D measurement of TT in patients with OTSCC. In addition, DOI was measured in the axial plane, and this is correlated with final histopathology to see whether MRI findings correlate well with depth on final histopathology.

Materials and Methods

This prospective study was conducted in the Department of Surgical Oncology, DR.RMLIMS, Lucknow, a tertiary care hospital and research center. Fifty patients with biopsy proven SCC of the tongue who were planned for surgery and willing to participate were included in the study. Patients with a history of previous head-and-neck cancer, prior surgery, or radiotherapy to the neck were excluded from the study. The data were collected and analyzed over 1½ year. Detailed history, clinical examination, routine hematological, and biochemical investigations were made. Patients included in the study underwent MRI (3T GE Signa MRI) with 4-mm sequences. Routine T1WI (axial and coronal spin-echo T1W [TR, 500–600 ms; TE, 7–10 ms]), T2WI (axial, coronal, and sagittal fast-spin echo T2W [TR, 3000–4000 ms; TE, 90–100 ms]), coronal short-tau inversion recovery (STIR) (inversion time, 150 ms) sequences, and postcontrast axial T1W sequence were performed. The thickness of tumor in three dimensions and DOI were noted. The TT on MRI was measured was as follows: a reference line was drawn as the longest tumor diameter anteroposteriorly on the axial view, mediolaterally on the coronal view, and superoinferiorly on the sagittal view, respectively. TT was obtained from the summation of the distance of the perpendicular line from the reference line to the deepest infiltration point and to the most projecting point of tumor. Therefore, TT demonstrates the extent of infiltration of tumor mediolaterally on the axial view [Figure 1a], anteroposteriorly [Figure 1b] on the sagittal view, and superoinferiorly on the coronal view [Figure 1c], respectively.

Estimation of depth of tumor

Axial gadolinium-enhanced T2-weighted sequence was used to measure DOI in the tongue where tumor lie vertically and hence reflected in a medial-to-lateral dimension. A horizontal line joining the two tumor-mucosa junctions was drawn as a reference line [Figure 2a and b]. DOI was measured by drawing perpendicular lines from the reference line to the point of maximal tumor projection, and tumor thickness was calculated by adding these two parameters. If the tumor was ulcerative, the reference line was determined in the same way and considered as original surface level, exophytic lesions were ignored and length measurement was simplified to represent invasion.

All patients were then treated with wide excision of the primary tumor with 1–1.5 cm resection margins and neck dissection. Patients without clinical nodal metastasis underwent extended supraomohyoid lymph node (LN) dissection (levels I–IV) and patients with metastatic LN underwent modified radical (levels I–V). TT in all three dimensions and DOI were noted in final histopathology, including other characteristics, such as lymph nodal status, lymphovascular invasion, and perineural invasion. Pathologically, DOI was measured from the level of the basement membrane of the closest adjacent normal mucosa. A "plumb line" is dropped from this plane to the deepest point of tumor invasion which corresponds to the depth [Figures 3-5]. MRI findings were then correlated with final histopathology using correlation and regression analysis.

Statistical analysis

Correlation and linear regression analysis were used to investigate the relation between TT in MRI and DOI on

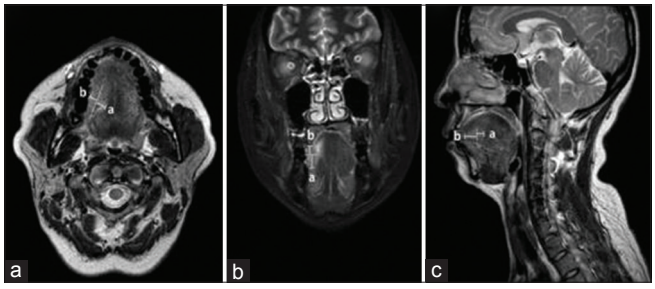

Figure 1: Measurement of tumor thickness on magnetic resonance imaging. The reference line was defined as the longest tumor diameter anteroposteriorly on the axial view (a), mediolaterally on the coronal view (b), and superoinferiorly on the sagittal view (c), respectively. Tumor thickness was obtained from the summation of the distance of the perpendicular line from the reference line to the deepest infiltration point (a) and to the most projecting point of tumor (b)

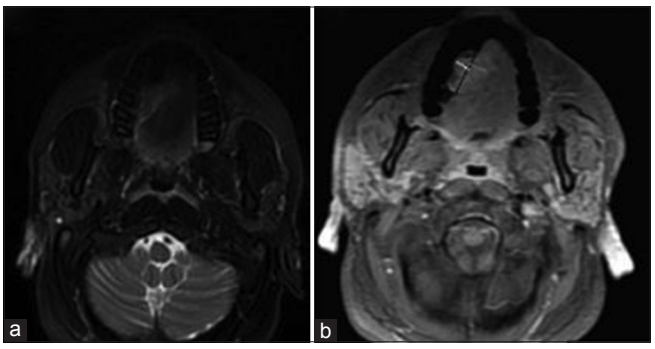

Figure 2: (a) T2-weighted MR image heterogeneously hyperintense lesion-right lateral aspect of the tongue. (b) Calculating the depth of invasion (red line) in the right lateral border of carcinoma tongue after drawing the reference line (black line). The white line represents exophytic mass which is ignored

histopathology reports. A "shrinkage factor" was defined as the slope of the best-fitting line constrained to fit through the origin. Pearson's correlation coefficient was also calculated to quantify the strength of linear correlation between the two measures of thickness. $P < 0.05$ was considered as statistically significant.

Results

In this prospective study, we studied 50 cases of carcinoma tongue, of which 38 were male and 12 were female, with a mean age of 49 years.

Correlation of tumor thickness in anteroposterior plane

When comparing the TT on MRI with the pathology reports, most values fell below the 1:1 ($x = y$) line of agreement, i.e., TT measured on MRI was greater than that of pathological TT. This diminution of thickness between imaging and histology is calculated as a "shrinkage factor" represented graphically by the slope of the best-fitting regression line constrained to pass through the origin [Figure 6]. In this study, shrinkage factor of 0.9 mm was recorded on MRI in anteroposterior. Hence, tumor measured on MRI as 10 mm typically translates to 9 mm on the pathology report. However, some amount of shrinkage will be there due to effects of electrocautery and formalin. TT in anteroposterior plane in MRI correlated significantly ($r = 0.851$, $P < 0.001$).

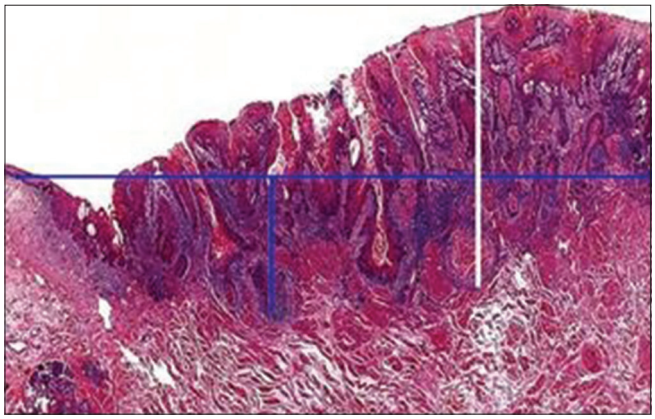

Figure 3: The terms "Depth of Invasion" and "Tumor Thickness" have been used interchangeably, which is incorrect. The white bar represents maximum tumor thickness, which here is greater than the depth of invasion (blue bar)

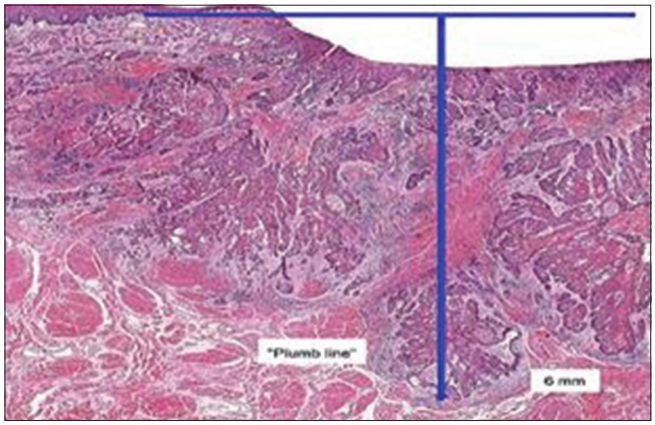

Figure 5: Depth of invasion in an ulcerated carcinoma. Notice how "tumor thickness" would be deceptively thinner than depth of invasion

Correlation of tumor thickness in craniocaudal plane

When comparing the TT reported on MRI with the pathology reports, most values fell below the 1:1 ($x = y$) line of agreement, i.e., TT measured in MRI was greater than that of pathological tumor thickness [Figure 7]. As explained previously above, the shrinkage factor of 0.9 mm was recorded in MRI craniocaudal plane. Figure 7 shows correlation of TT in craniocaudal plane in MRI with histopathology report. The best-fitting slope line is shown in curve along with P values in table. TT

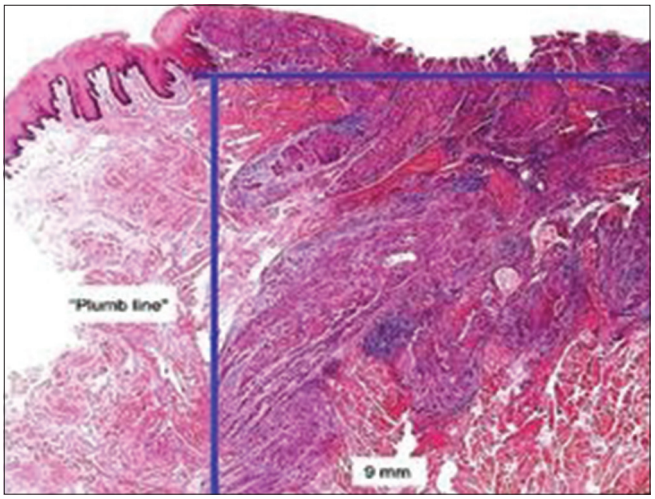

Figure 4: To measure the depth of invasion, establish the horizon that is at the level of the basement membrane relative to the closest intact squamous mucosa. The greatest invasion is measured by dropping a "plumb line" from the horizon

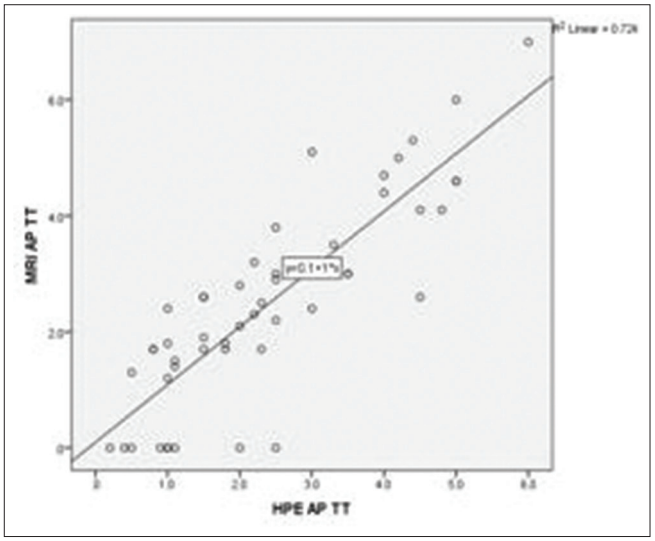

Figure 6: Correlation and regression analysis between tumor thickness in magnetic resonance imaging (anteroposterior) and histopathology

in anteroposterior plane in MRI correlated significantly with pathology (r = 0.795, P < 0.001) [Table 1].

Correlation of tumor thickness in the axial plane [Table 1]

TT in the axial plane in MRI correlated well (r = 0.736, P < 0.001) with final histopathology with shrinkage factor being 1.0001 [Figure 8]. When comparing the TT reported on MRI with the pathology reports, most values fell around the 1:1 (x = y) line of agreement, i.e., TT measured in MRI was nearly equal that of pathological TT. There is minimum shrinkage in the axial plane. The minimum shrinkage may be due to varying amount of edema and fibrotic tissue in vicinity of tumor, as a larger amount of lesions were located on the lateral border and are probably exophytic**.**

Correlation of depth of invasion in axial plane in magnetic resonance imaging versus final histopathology [Table 1]

When DOI reported on MRI was correlated with the pathology reports, most values fell below the 1:1 (x = y) line of agreement, that is, TT measured in MRI was greater than that of pathological TT [Figure 9]. DOI in MRI (r = 0.900; P < 0.001) correlated well with pathological DOI. Using regression analysis, shrinkage factor obtained was 0.78. Maximum shrinkage factor was seen in this category which in fact may be due shrinkage of muscle mass by electrocautery and formalin.

Difference in staging due to depth of invasion involvement category (American Joint Committee on Cancer 7th vs. American Joint Committee on Cancer 8th)

DOI is now included in AJCC 8th edition for T staging. T staging was done according to AJCC 7th and AJCC 8th and it was seen that maximum variation is seen in T1 and T3 stage after involving DOI criteria. Twenty-four lesions were T1 that were reduced to only 12 according to new AJCC 8th staging [Table 2]. Hence, DOI should be assessed preoperatively for proper treatment planning.

Table 1: Tumour thickness in antero-posterior plane, cranio-caudal plane, axial plane in MRI correlated well (r=0.851, P<0.001), (r=0.795. P<0.001), (r=0.736, P<0.001) with final histopathology with shrinkage factor being 0.90, 0.91 respectively

Parameter assessed	Pearson correlation**	Significance (2 tailed P)
MRI AP TT	0.851	0.0000
HPE AP TT	0.851	0.0000
MRI CC TT	0.795	0.0000
HPE CC TT	0.795	0.0000
MRI AXIAL TT	0.736	0.0000
HPE AXIAL TT	0.736	0.0000
MRI DOI (mm)	0.903	0.0000
HPE DOI (mm)	0.903	0.0000

**Correlation is significant at the 0.01 level (two-tailed). TT: Tumor thickness, MRI: Magnetic resonance imaging, DOI: Depth of invasion, AP: Antero-posterior, CC: Cranio-caudal, HPE: histopathology

Discussion

Assessment of tumor dimensions is important in OT cancer to stage the disease and plan the surgery. Excellent

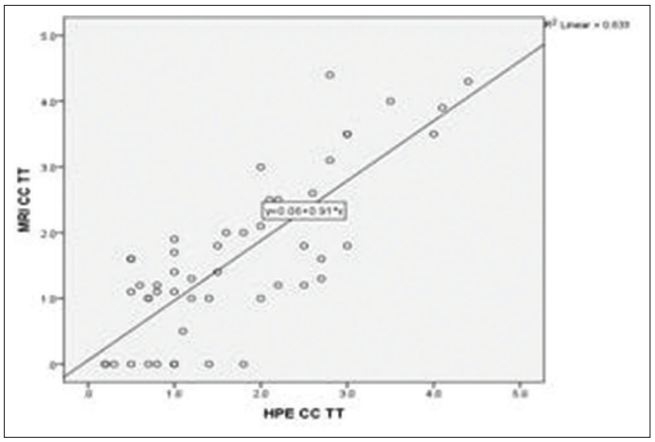

Figure 7: Correlation and regression analysis between tumor thickness in magnetic resonance imaging (craniocaudal) and histopathology

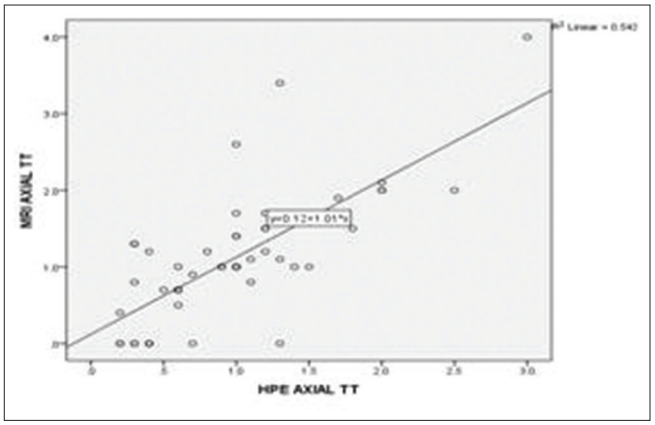

Figure 8: Correlation and regression analysis between tumor thickness in magnetic resonance imaging (axial) and histopathology

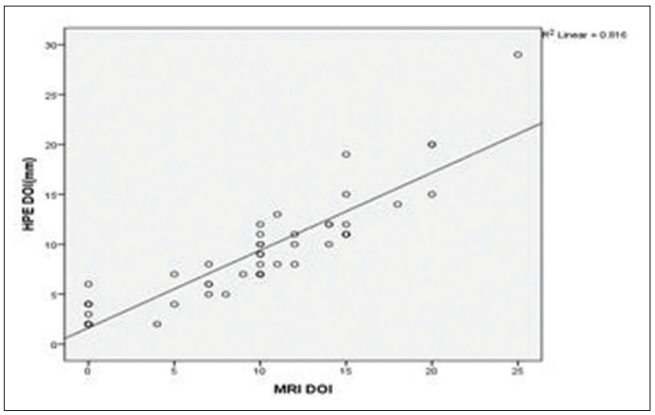

Figure 9: Correlation and regression analysis between the depth of invasion in magnetic resonance imaging and histopathology

soft-tissue discrimination of MRI readily reveals tumor invasion in the oral cavity and is used to assess the extent of locoregional spread, the DOI, and the extent of lymhadenopathy.[9] T2WI and STIR images instead of gadolinium-enhanced T1WI are used for TT measurement as inflammation, changes due to biopsy as well as tumor mass can be enhanced by contrast agent and tumor size may be overestimated on contrast-enhanced T1WI. In this study, MRI was adequate in determining DOI as with final pathology for tumors ≥4 mm in depth, but not for those <4 mm. 5 mm was used as a cutoff for depth at which the risk of nodal metastases increases.[10] There have been previous studies investigating the accuracy of MRI in predicting the DOI of OT SCC, but these studies were retrospective with small sample size and none compared extent of tongue cancer (extent in 3D, TT, DOI) in MRI with final histopathology.

Preda *et al*. investigated 33 cases of OT SCC retrospectively and demonstrated that MRI thicknesses correlated strongly with histological tumor thicknesses (correlation coefficient = 0.68, $P < 0.0001$).[11] Park *et al*. evaluated 114 patients with oral cavity and oropharyngeal SCC, of which 49 patients had OTSCC. Relationship between MRI and histological DOI in OT was high with a correlation coefficient of 0.949.[12] In this study, the mean DOI on histology and MRI was 8.82 mm and 9.24 mm, respectively. As pointed by Lwin *et al*., there is tumor shrinkage after resection in all oral cavity subsites, including OT.[13] The tumor shrinkage factor for OT cancer had been reported to be 0.87, while in our study, shrinkage factor obtained was 0.78. Other studies also showed significant correlations between MRI versus histological DOI which correlated well with our results.[14,15] It is generally considered that DOI and prediction of risk of nodal metastases are based on pathologic assessment and not on clinical or radiographic assessment as they may under or overestimate DOI and did not have the same ability to predict nodal metastases. While MRI was shown to correlate well with pathological depth and is more sensitive and specific for depth measurements than clinical assessment; nevertheless, the palpation of tumor for assessment of depth is complementary and may be useful in situations where either MRI is unavailable or difficult to interpret due to artifacts. In a prospective study, Yuen *et al*. examined the correlation between ultrasound and pathologic TT in 45 OT carcinoma patients during general anesthesia and before commencing surgery.[16] There was a statistically significant correlation coefficient of 0.940 ($P < 0.005$). While this technique may be difficult to perform in clinic due to pain or trismus, its improved ability to measure TT does warrant further investigation.

TT or maximum tumor dimension is an independent prognostic parameter. As stated by Moore *et al*., DOI and TT are not the same, and a distinction has to be made, even though many authors use these two terms synonymously.[17] The concept of TT primarily originated from histological measurements.[18] However, preoperative imaging would be necessary to determine the surgical extent. Therefore, various techniques such as ultrasound, computed tomography, and MRI were used for preoperative evaluation of TT in oral cavity carcinoma.[19]

Previous studies about TT on MRI usually measured TT as the mediallateral length in an axial view.[20] However, the direction of tumor progression may be variable. Okura *et al*. reported that TT and the distance to the paralingual space (i.e., the space between the genioglossus and intrinsic tongue muscles) measured in the MRI coronal view had a predictable value for cervical LN metastasis in OTSCC.[20] The affected area is located under the intrinsic tongue muscles with plenty of lymphatics and neurovascular structures and henceforth is a crucial channel to the cervical space for tumor metastasis. Therefore, TT on MRI should be considered not only on an axial view but should also be evaluated three dimensionally as in our study. Kwon *et al*. also compared the TT in all the three planes and compared with various clinicopathological parameters.[21] TT showed significant correlations with final histopathology. The present study also showed significant correlations in MRI dimensions with final histopathology, with shrinkage factor being 0.9. Maximum shrinkage factor of approximately 1 cm was obtained in axial dimension; this may be due inflammatory, postbiopsy changes and exophytic nature of tumor mass as maximum tumors were located on lateral border of the tongue. Recently, DOI has been included in AJCC 8th staging for oral cavity cancers. However, depth is accurately determined on the postoperative histopathology reports. If determined preoperatively, it can determine the prognosis and appropriate planning of the treatment. MRI is the best imaging modality for TT and DOI, there are no standard guidelines regarding it and studies with larger

Table 2: Association between radiological and pathological T stage according to the American Joint Committee on Cancer 7th staging

Radiological T stage	HPE T stage			Total	Chi-square and Kappa analysis
	T1	T2	T3		
T1	19	2	0	21	P<0.001 Significant (P<0.05)
T2	5	13	1	19	
T3	0	3	7	10	
Total	24	18	8	50	

HPE: Histopathology

number of patients will be required in future to set up MRI protocols regarding accurate assessment of TT and DOI.

Conclusion

In the present study, comparing TT in three dimensions on MRI with final histopathology in SCC of the tongue; there is a significant correlation was observed between TT in MRI in anteroposterior, craniocaudal, and axial dimensions with final histopathology. There is also a significant correlation observed between the DOI in MRI with final histopathology. Shrinkage factor was seen in correspondence with the previous studies. There was a significant correlation between the MRI T staging and final histopathology. Further, MRI neither under stages or over stages the T staging.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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