Accuracy of Magnetic Resonance Imaging in Detecting Depth of Invasion of Oral Squamous Cell Carcinoma

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ABSTRACT

INTRODUCTION: Depth of Invasion (DOI) is a key prognostic factor for Oral Squamous Cell Carcinoma (OSCC), impacting surgical decisions. The research aims to evaluate the accuracy of Magnetic resonance imaging (MRI) in assessing DOI, comparing it with histopathological findings and also to determine the MRI-determined DOI cut-off value for predicting neck lymph node metastasis.

MATERIALS AND METHODS: It is a hospital based cross sectional study conducted over 18 months at Sri Manakula Vinayagar Medical College, Puducherry. The depth of invasion was measured in 70 patients who underwent MRI for preoperative evaluation of oral cavity cancers and was correlated with postoperative histopathological findings. The MRI-derived DOI was compared to the postoperative histopathological DOI to assess accuracy. The study also examined the relationship between MRI-derived DOI and cervical lymph node metastasis using a receiver operating characteristic (ROC) curve, with data analysis performed in SPSS 24.

RESULTS: The mean age of presentation was found to be around 57 years of age with male predominance. The most common site of involvement was buccal mucosa. Tumour's DOI was well correlated between MRI measurement and pathology with correlation coefficients of 0.94. MRI-derived DOI was 1.41 mm (10.7%) larger than pathology. The accuracy of MRI in deciding pathological DOI was 67.9%. The cut-off value of MRI-derived DOI was 8mm for predicting lymph node metastasis.

CONCLUSION: Utilizing MRI for preoperative DOI estimation enhances staging accuracy in oral cavity cancers, showing strong correlation with pathology. Despite MRI measuring DOI 10.7% larger than pathology, it's essential for preoperative staging.

***KEYWORDS*:** Depth of invasion (DOI); Magnetic resonance imaging (MRI); Oral squamous cell carcinoma; Lymph node metastasis; Preoperative cancer staging.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) ranks as the sixth most prevalent cancer globally and represents the primary location for malignancy within the head and neck region.[1] It is primary treated through surgical resection, often accompanied by neck dissection.[1] Decision regarding adjuvant radiotherapy are based on histopathologic characteristics like primary tumor size, margin status, lymph node involvement.[2,3]

Depth of invasion (DOI) of the tumor has emerged as a critical prognostic factor, strongly indicating the likelihood of lymph node metastasis and has been incorporated into the latest 8th edition of the Union for International Cancer Control (UICC) TNM Classification for Malignant Tumors for OSCC.[4] DOI measurements are taken perpendicular to the

deepest invasion point from the basal membrane of the normal mucosa.[5] DOI represents a pathological measurement, indicating the depth of tumor infiltration beneath the basal membrane while tumor thickness refers to the entire mass of the tumor at its thickest point. [4,6]

Generally, oral cancer assessment depends on cross-sectional imaging techniques, mainly using computed tomography (CT) and magnetic resonance imaging (MRI).[7] Previous studies have indicated a relatively strong correlation between radiological and histopathological measurements for tumor thickness.[8,9] However, only a limited number of radiological studies have investigated the correlation between imaging DOI and histopathological DOI.[10–13]

CT and MRI have been observed to overestimate DOI by approximately 20–30%.[4,7,10,14] While certain studies have indicated better accuracy of CT compared to MRI,[15] detailed reporting on measurement variations specific to each modality has been limited.[10,16] Therefore, an accurate method for assessing DOI in the preoperative imaging setting still requires definition.[17] With this background this study has been done to evaluate the precision of MRI in estimating DOI compared to the histopathological DOI of the tumor and to determine the cut-off value of MRI-determined DOI for predicting neck lymph node metastasis.

MATERIALS AND METHODS

This study was a hospital based Cross sectional study conducted in the Radiodiagnosis Department at Sri Manakula Vinayagar Medical College and Hospital (SMVMCH) in Kalitheerthalkuppam, Puducherry, India which is located in a village 25km west of Puducherry, for 18 months (From September 2022 to February 2024). Considering the positive predictive value of 89% for MRI in assessing pathological depth of invasion in a study by Alsaffar HA et al.,[10] the sample size of the present study was calculated to be 67 and rounded off to 70 at 95% confidence interval and 7.5% absolute precision.

Inclusion Criteria:

All patients of either sex with clinically diagnosed oral cavity cancer who were referred to Radio diagnosis department for cross sectional imaging were included in the study.

Exclusion Criteria:

Patients who were ineligible for MRI examination (claustrophobic/anxiety disorder patients, patients with metallic implants/pacemaker) and those who had recurrent disease or prior treatment or neurosurgical tumors or primary malignancy elsewhere were excluded.

Brief procedure:

After obtaining the history, the patient was subjected to T1 weighted, T2 weighted and STIR sequences of Magnetic Resonance Imaging. MRI was performed on 1.5 Tesla PHILIPS whole body MR systems using standard imaging head coil. TSE sequences were used to obtain T1WI (3500- 4500/90 [TR msec/TE msec]; axial, coronal), T2WI (3500-4500/90; axial, coronal) and STIR (1500/60/230 [TR msec/TE msec/TI msec]; axial, coronal). All imaging parameters had 250 mm FOV, 512 matrix, 3 mm thickness, and 0.5 mm slice gap.

The depth of invasion was measured by drawing a **radiological plumb line** along the "interpreted mucosal plane" (basement membrane) across intact surface of the normal mucosa and measuring the deepest point of tumor invasion from this line. (Figure 1A and 1B)

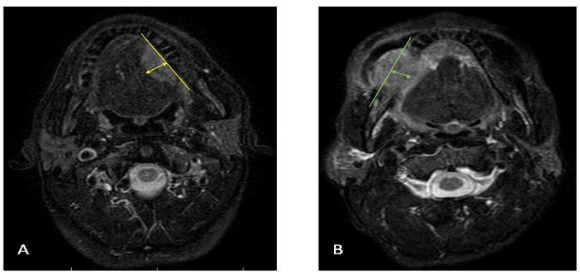

Figure 1A: Axial STIR MRI section of Tongue squamous cell carcinoma showing DOI measurement. Solid yellow line represents the radiological plumb line. MRI measured DOI in shown in yellow arrows.

Figure 1B: Axial STIR MRI section of Right alveolar squamous cell carcinoma showing DOI measurement. Solid green line represents the Radiological plumb line. MRI measured DOI in shown in green arrows.

The depth of invasion was determined by two radiologists independently, and a mean of the two readings was used for analysis. The radiologists were blinded to each other's results and any other patient information to maintain objectivity. Measurements were predominantly done on T2 weighted and STIR sequences in axial plane. In cases where coronal plane was found to better estimate DOI, it was used for measurement. Finally, the MRI findings were correlated with the postoperative Histopathological Reports to verify and validate the imaging results.

Statistical analysis:

Data was entered into mastersheet and then analyzed with SPSS version 24.

Categorical data were depicted through frequencies and percentages, while continuous data were illustrated using the mean and standard deviation. The categorical variables were analyzed using Chi-square test and continuous variables using independent t test. P value < 0.05 was considered as statistically significant at 95% CI. Pearson's correlation coefficient was used to find correlation. Interobserver agreement was assessed using the kappa statistic. The receiver operating curve (ROC) was plotted for mean DOI by MRI to derive the optimum cut-off for nodal metastasis.

Ethical considerations:

Institutional ethics committee approval was obtained (**IEC no. EC/64/2022**) and the study was conducted according to STARD checklist. Informed consent was obtained from participants in their native language.

RESULTS

Seventy patients were included in the study (mean (SD) age 56.89 (11.52) years). The age range of the study participants was 24 - 78 years. There were 42 (60%) males and 26 (37.1%) females and 2 (2.9 %) Transgender with a male : female ratio of 1.6:1. The most common site of involvement was buccal mucosa in 29 patients (41.4%). The tumour characteristics of the patients in the study group are given in **Table 1.**

Table 1: Tumour Characteristics of Patients (N = 70)

Patient Characteristics	No. (percentage)
Diagnosis Site	
Buccal Mucosa	29 (41.4%)
Tongue	17 (24.3%)
Lip	5 (7.1%)
Others (Alveolus, Maxilla, Hard palate, Retromolar trigone)	19 (27.2%)
T stage:	
T1/2	18 (25.7%)
T3/4	52 (74.3 %)
Nodal Metastasis	
Node Negative	46 (65.7 %)
Node Positive	24 (34.3 %)
Mean DOI on MRI (mm):	
Radiologist 1	14.55
Radiologist 2	14.62
Average	14.58
Mean histological DOI (mm):	13.17

Mean DOI (n = 70 patients)

The mean depth of invasion by observer 1 was 14.55 ± 7.2 and by observer 2 was 14.62 ± 7.0.

The mean depth of invasion by MRI was 14.58 ± 7.3 and by HPE was 13.17 ± 6.09. The difference between mean DOI by MRI and HPE was 1.41 mm. The percentage of overestimation of depth of invasion by MRI was 10.70%.

The Kappa coefficient between two observers was 0.639 which shows good strength of agreement between observers which was statistically significant. (p value = 0.001*)

Comparison of Depth of invasion by MRI and HPE among the study participants:

For the entire cohort, when MR-DOI was graded into 3 categories: ≤5 mm, 5–10 mm and >10 mm, **(Table 2)** which is one criteria of the of T-stage classification. The accuracy of MRI was found to be 72.8% compared to pathology. Accuracy was noted to be lower in superficial tumors (DOI < 5mm) in our study.

Table 2. Comparison of Depth of invasion by MRI and HPE among the study participants (N = 70)

MRI DOI	HPE- DOI			
	< 5 mm	5 to 10 mm	> 10 mm	Total
< 5 mm	2	0	0	2
5 to 10 mm	5	12	2	19
> 10 mm	1	11	37	49
Total	8	23	39	70

Correlation of MRI DOI AND HPE DOI among the study participants:

The depth of invasion by MRI had a strong positive correlation (0.94) with Depth of invasion by HPE which was statistically significant by Pearsons correlation coefficient.

ROC curve analysis for DOI cutoff in predicting lymph node metastasis among the study participants:

The Receiver Operating Characteristic (ROC) curve analysis (**Figure 2**) of mean depth of invasion by MRI showed cut-off threshold value as 8mm (95% CI = 5.32 to 14.00), with a sensitivity of 95.6%, and a specificity of 80.9%. The area under the curve (AUC) was 0.722 (95% C.I = 0.462 to 0.803) with a statistically significant p value (p = 0.002).

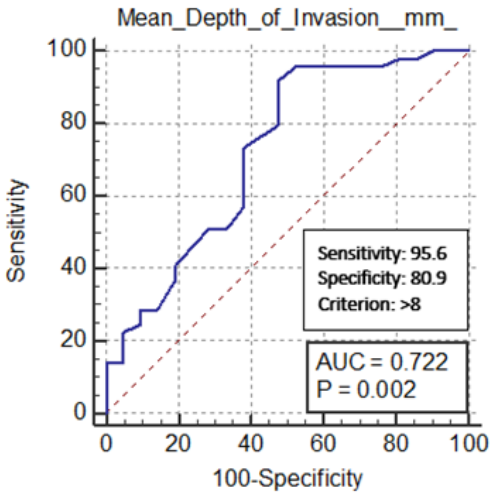

Figure 2. ROC curve analysis for DOI cutoff in predicting lymph node metastasis among the study participants (N = 70)

DISCUSSION

The eight edition of American Joint Committee on Cancer (AJCC) staging system incorporates tumor depth of invasion into the T stage of oral cancer,[18] raising questions about the accuracy of preoperative staging compared to pathology. This study evaluated the accuracy of MRI in measuring the depth of invasion in oral squamous cell carcinoma,

highlighting MRI's excellent soft-tissue resolution and reproducibility.

A pivotal finding in this study was the significant correlation between MRI-estimated DOI and histological DOI. Consistent with numerous previous studies comparing MRI-derived depth of invasion to pathology, our findings align well. **Park et al.**[19] and **Vidiri et al.**[20] similarly concluded that preoperative MRI accurately measures tumor invasion depth, as they both observed significant correlations between MRI and pathology results. Interestingly, **Goel et al.**[11] and **Alsaffar et al.**[10] likewise identified significant correlations between MRI-derived DOI and pathological DOI. However, **Goel et al.** did not explore the reproducibility of DOI measurements on MR images, and **Alsaffar et al.** omitted details regarding the MR sequences utilized for DOI assessment, highlighting only a moderate inter-reader radiologic correlation.

We identified a notable level of interobserver reliability in detecting depth DOI between two radiologists. It is worth highlighting that the agreement tends to be better between experienced readers.[20]

Our results show that MR-DOI tends to be greater than P-DOI by 10.7 %, which is in line with the findings of the majority of earlier studies.[21–24] However, the specific magnitude of the variance wasn't uniform across the studies. The differences between mean MRI DOI and HPE DOI observed in our study and various other studies is presented in **Table 3.**

Table 3: Overall difference between mean MRI DOI and HPE DOI in our study and other studies

Studies	**Place & Year of study**	**Difference between mean MRI DOI and HPE DOI**	**Percentage of Overestimation**
Our study	**India, 2022-24**	**1.41 mm**	**10.7 %**
Mao MH et al (21)	China, 2015-17	2.32 mm	24.6 %
Ravikanth R et al (22)	India, 2017-19	1.9 mm	13.3 %
Alharbi et al (23)	Saudi Arabia, 2017-22	1.72 mm	11 %
Mair M et al (24)	United Kingdom, 2017-19	1.25 mm	10 %

The overestimation of MRI-derived DOI may be due to specimen shrinkage and distortion during pathological evaluation, which can reduce tumor and margin dimensions by up to 30%.[25,26] Peritumoral edema or inflammation, especially after a biopsy, can also lead to larger MRI-derived DOI. Extended MRI durations and artifacts from tongue movement, swallowing, and dental hardware further affect measurement accuracy.[27] Performing MRI before biopsy and minimizing the time between formalin immersion and pathological examination are recommended to improve accuracy.

For the entire sample, when MR-DOI was categorized into three groups: ≤5 mm, 5–10 mm, and >10 mm, matching a T-stage classification criterion. The accuracy of MRI in comparison to pathology was found to be 72.8%. These results align with those reported by **Fu Y et al.,**[28] who found an MRI accuracy rate of 67.9%.Accuracy was noted to be lower in superficial tumors (DOI < 5mm) in our study. Consistent with our findings, **Alsaffar et al.**[10] noted that in cases with tumors measuring less than 5 mm in P-DOI, MR-DOI and P-DOI did not correlate well.

In our study, we observed that a ROC cut-off of 8mm on MRI predicted lymph node metastasis with a sensitivity of 95.6% and a specificity of 80.9%.The MR-DOI threshold for identifying lymph node metastasis varies among different studies. As an illustration, **Mao et al.**[21] found that an MR-DOI of 8 mm was able to effectively anticipate nodal metastasis, a conclusion that closely parallels our own results. In contrast, **Park et al.**[19] advocated for a higher threshold of 9.5 mm to detect positive lymph nodes in tongue cancer, while **Mair et al**.[24] concluded that a significantly lower threshold of 4.5 mm was ample for identifying lymph node metastasis. Therefore, elective neck dissection is warranted for DOIs exceeding 8 mm, based on our study.

The study's limitations include a small sample size and being a single-center study. Exclusion of previously operated, chemotherapy, and radiotherapy cases prevented evaluating MRI accuracy in recurrent or post-treatment scenarios. MRI also struggles with accurately distinguishing small or superficial tumors from adjacent tissues, hence integrating intraoral ultrasound and diffusion-weighted imaging (DWI) can improve accuracy. To confirm the reliability of MRI-measured DOI across various T stages, extensive large-scale, multi-center prospective studies with integrated volumetric imaging are recommended.

CONCLUSION

The study concludes that MRI is a valuable tool for preoperative DOI estimation in oral squamous cell carcinomas, improving staging accuracy compared to postoperative pathological staging. MRI-derived DOI correlates strongly with pathology-derived DOI, though MR-DOI is slightly larger. MRI measurements show minimal variation between radiologists, with an 8 mm MR-DOI cutoff predicting cervical lymph node metastasis. Overall, it plays a crucial role in guiding surgical treatment and management decisions, including the extent of elective neck dissection.

ABBREVIATIONS

AJCC	American Joint Committee on Cancer
CT	Computed Tomography
DWI	Diffusion Weighted Image
DOI	Depth of Invasion
MRI	Magnetic Resonance Imaging
OSCC	Oral Squamous Cell Carcinoma
ROC	Receiver Operator Curve
UICC	Union for International Cancer Control

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