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ACCURACY OF MRI IN MEASUREMENT OF DEPTH OF INVASION IN ORAL CANCER AND ITS HISTOPATHOLOGICAL CORRELATION

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Abstract:
AIM: To evaluate accuracy of MRI in measurement of Depth of Invasion and Bone involvement in Oral cancer and its histopathological correlation.
Material & methods: 70 patients with biopsy proven oral cancer with clinical stage at or below T4a were included in this hospital based descriptive type of observational study. All patients underwent preoperative MRI examination. MRI was performed on PHILIPS INGENIA 3 TESLA MRI. Images were interpreted for Depth of invasion and Bone involvement. All patients underwent surgery and the final diagnosis was made by histopathology. Statistical analysis was applied to find out the Sensitivity, Specificity, Accuracy, PPV and NPV of MRI. Correlation was inferred by Pearson's Correlation coefficient. P-value < 0.05 was taken as significant.
Results: Average Depth of invasion calculated on MRI was 8.48mm and by histopathology was 6.90mm.Pearsons correlation coefficient was 0.988. Shrinkage factor was 0.81. Sensitivity, specificity, accuracy, PPV and NPV of MRI in predicting Bone invasion was 92.3%, 90.90%, 91.42%, 85.71% and 95.23% respectively.
Conclusion: Depth of invasion in oral malignancies can be measured reliably on MRI which helps in predicting cervical lymph nodal metastasis which can be used as an important supportive tool in deciding type of neck dissection and prognosis of patient.
Keywords: Depth of invasion, MRI, Oral Cancer.

INTRODUCTION:

Oral cancer is the 12th most common cancer globally and the 8th most common in developing countries.[1]The incidence of oral cancer in Indian males is 13% of all malignancies and is the third most common cancer in Indian females.[2] Squamous cell carcinomas amount to more than 90% of malignant tumours of the oral cavity. Squamous cell carcinoma of lower gingivo buccal complex and tongue are the most common cancer in the Indian sub-continent due to tobacco chewing and alcohol abuse and have been described as Indian oral cancer.[3] Increased incidence of oral squamous cell carcinoma in Indian population is rampant because of habit like use of tobacco, tobacco with lime, or tobacco with betel-nut and alcohol.[4]

The prognosis of carcinoma of the oral cavity is influenced by variety of factors such as degree of cellular differentiation, size, location, presence of infiltration into the bony tissue, immune response, age, gender, patients, socio economic status and the presence of cervical lymph node metastasis, the latter being considered the most important factor when determining the prognosis.[5-7] The overall five-year survival rates for cancers of the tongue and oral cavity are around 50%.

The value of imaging in the evaluating Depth of invasion of oral squamous cell carcinoma (OSCC) is in judging operability, assessment of the prognostic characteristics the presence of cervical lymph node metastasis, detection of bone infiltration.[8] Surgical planning depends on tumor invasion: the surgeon needs to know the extent of tumor invasion to achieve adequate surgical clearance.

Owing to superior soft tissue contrast capability and non-involvement of any biological risk to the patient, MRI is the imaging modality of choice in local assessment of oral cavity.[9-11]The choice of appropriate treatment for patients with oral cancer depends largely on accurate pre-treatment evaluation of Depth of invasion. Magnetic resonance imaging (MRI) can produce excellent-quality images and direct multi planar formats without ionizing radiation.

This study evaluated the squamous cell carcinomas of the oral cavity (oral tongue and gingivo-buccal complex) on the basis of their depth of tumor invasion and bone involvement assuming histopathology as gold standard.

MATERIAL AND METHODS:

This Hospital based Descriptive type of Observational Study was conducted in the Department of Radio-diagnosis and Modern imaging of S.M.S. Medical College, Jaipur from March 2017 to February 2018 after approval from institutional Research Review Board.

Sample size of 70 patients with biopsy proven oral cancer at or below clinical stage T4a according to TNM staging classification were included in study following appropriate consent.

INCLUSION CRITERIA:

1. All biopsy proven patients (in patients or out patients) of oral cancer at or below clinical stage T4a referred to the department of Radio-diagnosis for MRI examination.
2. Both male and female patients.
3. Patients who gave appropriate informed and written consent for MRI, Neck Dissection and Histopathological examination.

EXCLUSION CRITERIA:

1. Claustrophobic patients.
2. Patients with metallic implants, pacemakers.
3. Patients of oral cancer with clinical staging greater than T4a.
4. Malignancies other than tongue and gingivo-buccal in location.
5. Patients who were not willing to have MRI, Neck Dissection and Histopathological examination.

METHOD OF DATA COLLECTION:

All patients underwent preoperative MRI examination. All patients underwent surgery and the final diagnosis was made by histopathology.

MRI PROTOCOL:

MRI Machine – PHILIPS INGENIA 3 TESLA was used. Position of Patient – supine on the MRI table and head coil was applied. Routine T1WI (Axial and coronal spin echo T1W), T2WI (Axial, coronal and sagittal fast spin echo T2W), Short Tau Inversion Recovery (STIR) sequences followed by post contrast axial T1W sequences were taken.

DEPTH OF INVASION:

Axial gadolinium-enhanced T1-weighted sequence was used to measure depth of invasion for tongue and buccal sub-sites where tumours lie vertically and hence reflected in a medial to lateral dimension.

A horizontal line joining the two tumour–mucosa junctions was drawn as a reference line. We measured the depth of invasion by drawing perpendicular lines from the reference line to the point of maximal tumour projection and invasion.

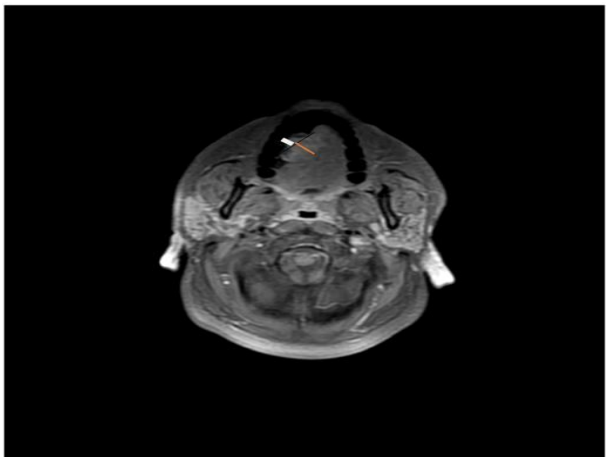


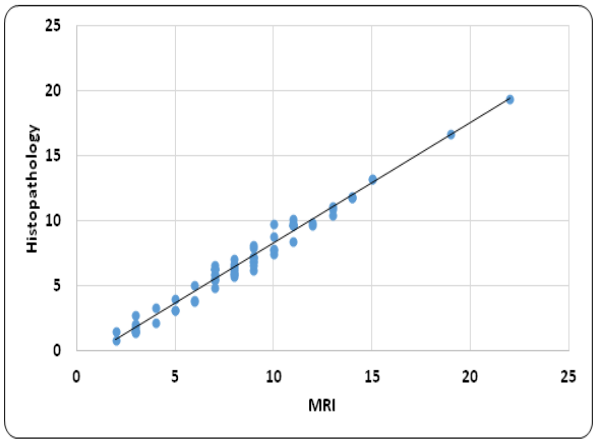
Figure 1: Calculating depth of invasion (red line) in right lateral border of carcinoma tongue after drawing reference line(black line).White line represents exophytic mass which is ignored

BONE INVASION

MRI diagnostic criteria we used for the evaluation of the infiltration of mandibular bone were :- (1) Lack of the typical hypo intense signal of cortical bone on T1 which is replaced by the signal intensity of the tumour, useful to determinate the cortical invasion. (2) Presence of enhancement after Gd- DTPA administration, in order to demonstrate the marrow involvement.

Table 1: Comparison of depth of tumor invasion on MRI and Histopathology Pearson's Correlation Coefficient

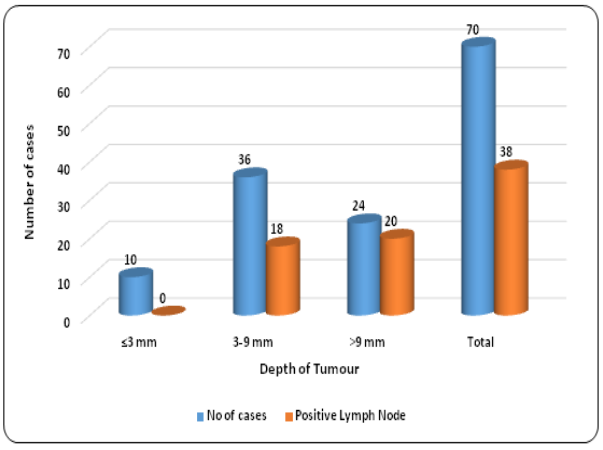
	Mean	Std. Deviation	N	Correlation R	p-value
MRI	8.48	3.91	70	0.988	0.00001 (S), p<0.05
Histopathology	6.90	3.66	70		
Shrinkage Factor	0.81				



Graph 1: Comparison of depth of tumor invasion on of MRI and Histopathology Pearson's Correlation Coefficient

Table 2: Percentage of cases positive for cervical malignant metastatic lymph nodes according to depth of tumor invasion

Depth of tumor (Range)	No of cases	Positive Lymph Node
≤3 mm	10	-
3-9 mm	36	18 (50%)
>9 mm	24	20 (83.33%)
Total	70	38 (54.28%)



Graph 2: Percentage of cases positive for cervical malignant metastatic lymph nodes according to depth of tumor invasion

Table 3: Binary Classification of bone involvement on MRI versus Histopathology

		Histopathology		
		Positive	Negative	Total
MRI	Positive	24	4	28
	Negative	2	40	42
Total		26	44	70

STATISTICAL ANALYSIS

Statistical analysis was applied to find out the Sensitivity, Specificity, Accuracy, PPV and NPV of MRI. Correlation was inferred by Pearson's Correlation coefficient. P-value < 0.05 was taken as significant.

RESULTS

Average depth of invasion calculated on MRI was 8.48mm and by histopathology was 6.90mm. Pearsons correlation coefficient was 0.988. Shrinkage factor was 0.81 in the present study.

83.33% of patients with depth of invasion greater than 9mm showed evidence of cervical lymph nodal metastasis at one or another levels while 50% cases with depth of invasion greater than 3mm but less than 9mm showed cervical lymph nodal metastasis. No evidence of cervical lymph nodal metastasis in cases in which depth of invasion was less than 3mm was noted.

Sensitivity, specificity, accuracy, PPV and NPV of MRI in predicting bone invasion was 92.3%, 90.90%, 91.42%,85.71% and 95.23% respectively when compared histopathologically.

DISCUSSION

The oral squamous cell carcinoma (OSCC) is one of the rapidly growing oral cancers in the literature of oncology and it is the 6th most common cancer in the world. Tobacco and heavy alcohol is the predominant cause of oral cancers. Tobacco alone covers 90% of all oral cancers. The five year survival rate of oral cancer is 68% in early stage and 27% in the late stage.[12]

The Indian subcontinent has one of the highest incidences of oral cancer in the world; mainly due to the high prevalence of chewing a combination of smokeless tobacco and areca nut[13]

Literature reveals that, of all the prognostic parameters that have been evaluated, tumor thickness and depth of invasion have emerged as the best predictors for cervical nodal metastasis. As stated by Moore et al[14]depth of invasion and tumor thickness are not the same, and a distinction has to be made, even though many authors use these two terms synonymously. ''Depth of invasion'' means the extent of cancer growth into the tissue beneath an epithelial surface. Cases in which the epithelium is destroyed, some investigators reconstruct a surface line and measure from this line. However, the depth

of invasion is sometimes expressed by referring to the microscopic, anatomic deep structures that are reached, rather than by referring to objective micrometre measurements in millimetres. On the other hand, thickness concerns the entire tumor mass; an objective parameter is needed, and it can be obtained using an ocular micrometre. The proximity to blood vessels and lymphatics is what determines an increased risk of nodal metastases developing in as much as it facilitates the tumour's ability to expand. Therefore, it might be better to take into consideration the actual mass that is present beneath the theoretical reconstruction of a basement membrane (depth of invasion) rather than the thickness of the entire tumor.

There is a significant role of imaging in predicting depth of tumour invasion. Various studies showed role of MRI in predicting depth of tumour invasion. Tetsumura A et al (2001),[15] Iwai et al,[16] Paul Lam et al.[17] According to them the radiologic tumor thickness as measured on contrast-enhanced T1-weighted images had significant correlation with histologic tumor thickness. This study observed the similar findings with a mean radiological tumour thickness of 8.48mm and histological tumour thickness of 6.90mm.The Pearson's Correlation Coefficient(R) was calculated and its value came out to be 0.988 (p-value of 0.00001).Paul Lam et al [17] showed almost similar Pearson's Correlation Coefficient value (R)-0.938.

MRI showed slightly greater thickness when compared to histological thickness. The possible cause of the discrepancy between the histologic and radiologic thicknesses may be due to the shrinkage of specimen during formalin fixation despite the immediate stretching and pinning of specimen on a foam board. Shrinkage factor for the present study came out to be 0.81.

In the present study prediction of lymph nodal metastasis was done based on Depth of invasion calculated on contrast-enhanced T1-weighted images and then was compared with the Histopathological nodal status. These lymph nodal metastasis was divided according to proposed tumor Depth of invasion staging classifications. These included stage I (Depth of invasion </=3 mm), stage II (> 3 mm but <9mm) and stage III (> 9 mm). 38 patients out of 70 patients showed metastasis to the cervical lymph nodes according to Depth of invasion. A total of 10 cases showed depth of invasion </= 3mm (Stage I),out of which no patient showed metastatic cervical lymphadenopathy. 36 cases showed Depth of invasion between 3 and 9mm,out of which 18 patients (50%) were positive for metastasis to cervical lymph nodes. 24 cases showed Depth of invasion >9mm with a 20 patients (83%) were positive for metastatic lymphadenopathy. According to Anthony Po Wing Yuenet al[18] **,** tumor of up to 3 mm Depth of invasion had 10% nodal metastasis, Depth of invasion of more than 3 mm and upto 9 mm had 50% nodal metastasis, tumor of more than 9 mm had 65% nodal metastasis. However Paul Lam et al[17] uses similar Depth of invasion staging classification and found 9% for stage I,21% for stage II and 45% for stage III.

In the present study, the depth of invasion is directly proportional to the cervical lymph node metastasis. The statistically significant value is indicative of progressive increase in lymph node metastasis with increase in the depth of tumor invasion. The probable reason could be that the thick tumors, which invade more deeply, have access to wider lymphatics in which tumor emboli can form more readily than in the small-caliber lymphatics of superficial areas.

The evaluation of either the depth or the extension of the invasion of both the soft tissue and the bone adjacent to the lesion is necessary to well stage the oral-cavity tumours. Clinical assessment of mandibular invasion is possible by either evaluating clinical symptoms and signs or bimanually assessing the mobility of the tumour in relation to the mandible[19]. However, the clinical examination always requires an imaging correlation. Antonello Vidiri et al[20] and Maryam Koopaie et al[21] compared computed tomography and magnetic resonance imaging in the evaluation of the mandibular invasion by squamous cell carcinomas (SCC) of the oral cavity and showed better sensitivity ,specificity and accuracy of MRI in prediction of bone invasion by oral squamous cell malignancies. In the present study, we reported a total of 28 out of 70 cases positive for bone invasion considering the probable tumour invasion of either cortical and/or medullary components involvement. Post-operative histopathology reveals 24 cases positive for bone invasion. MRI had given false positive results in 4 cases and missed 2 cases that were positive for bone invasion giving a sensitivity of 92.3%, specificity of 90.90% and accuracy of

91.42%.PPV and NPV was 85.71% and 95.23% respectively

CONCLUSION

Depth of invasion in oral malignancies can be measured reliably on MRI which helps in predicting cervical lymph nodal metastasis which can be used as an important supportive tool in deciding type of neck dissection and prognosis of patient.

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