



## ASSESSMENT OF DEPTH OF INVASION, PATTERN OF INVASION, PERINEURAL INVASION AND LOCAL HOST RESPONSE(INVASIVE TUMOUR FRONT) IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF TONGUE.

### Histopathology

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### ABSTRACT

**Background:** Oral cancer is the 8th most common cancer in the world and accounts for 3% of all malignant neoplasms. It is a significant world health problem in India and account for 30% of all cancers in the country leading to a major cause of morbidity and mortality. 50% of Tongue Squamous Cell Carcinomas (TSCC) have neck metastasis at the time of diagnosis. Cervical lymph node metastasis is an important prognostic factor in oral Squamous Cell Carcinomas (OSCC). **Materials and Methods:** This is observational study performed in tertiary care cancer hospital, during year 2020-22. In this study 200 diagnosed cases of TSCC(all stages) who underwent primary tumour resection and neck dissection were analysed for Depth of invasion (DOI), pattern of invasion(POI), local host response(LHR) and perineural invasion(PNI) at invasive tumour front and these findings were correlated with lymph node(LN) metastasis to determine optimal treatment for TSCC. **Results:** 90 (45%) out of 200 cases had cervical LN metastasis on histopathological examination. DOI has significant correlation ( $p=0.001$ ) with LN metastasis. Worst pattern of invasion 4 (69%), moderate LHR (51.12%), PNI(52.11%) was most commonly seen among node metastatic cases. **Conclusion:** PNI, POI and LHR though excluded in AJCC staging, should be included in standard reporting which are important in predicting risk of metastasis in TSCC.

### KEYWORDS

Squamous cell carcinoma, Pattern of invasion, lymph node.

### INTRODUCTION:

Oral cavity is significantly more prone to an enormous number of environmental insults because of its exposure to the external environment and making it common site for many tumour and tumour like lesions, SCC is single most common malignant lesion of this region.<sup>1</sup>. Approximately 70,000 new cases and more than 48,000 oral cancer-related deaths occur yearly<sup>2</sup>.

14.09% of OSCC involves the tongue, and the lateral border of the tongue is more commonly involved<sup>3</sup>. Lymph node(LN) metastasis is the most significant parameter affecting overall survival in patients of OSCC. Cases of OSCC with cervical LN metastasis show 50% decrease in survival and a higher incidence of distant metastasis<sup>4</sup>. In the early stages of TSCC, the cervical LN are usually neither clinically palpable, nor seen upon radiologic examination. Still, these early-stage TSCC may harbour micro-metastasis in the LN<sup>5,6</sup>. There is a lot of controversy concerning the best way to approach such a neck disease in early-stage TSCC. Hence, the present study was conducted to analyse morphological features of malignancy at invasive tumour front which is the most representative area of the tumour<sup>7,11</sup> and compare these features between cervical node metastatic and non-metastatic TSCC which consists of:

- Depth of Invasion(DOI) measured from the basement membrane of adjacent normal squamous mucosa to the deepest point of invasion of tumour<sup>8</sup>.
- Pattern of invasion(POI): According to Brandwein-Gensler et al, there are two entities, predominant pattern of invasion(PPOI) and worst pattern of invasion(WPOI). POI was determined by measuring POI at the tumour interface of each slide of the resection specimen. PPOI is the most common POI found; the WPOI is the highest score present, no matter how focal<sup>9</sup>.
- Perineural Invasion(PNI): According to Batsaki et al.<sup>105,108</sup> PNI was defined as tumour cell invasion in, around and through the nerves<sup>10</sup>.
- Local Host Response(LHR): was classified as Dense when a continuous and dense rim of lymphoplasmacytic infiltration was present; Moderate when patches of lymphocytic infiltrates were present but discontinuous along the tumour stromal interface; and Mild to minimal when limited or no lymphocytic response seen<sup>9</sup>.

### AIMS AND OBJECTIVES:

#### AIM:

To analyse individual morphological patterns of malignancy at invasive tumour front in metastatic and non-metastatic TSCC.

### OBJECTIVES:

Compare these histomorphological patterns of malignancy between non-metastatic and metastatic TSCC which contribute to identification of parameters associated with cervical metastasis that could indicate aggressiveness of the tumour and determine optimal treatment for TSCC.

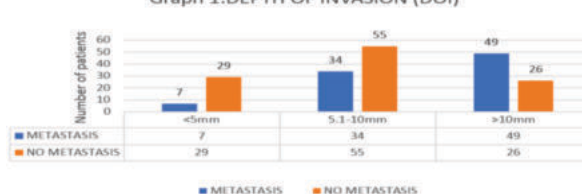
### MATERIALS AND METHODS:

This is observational study performed in tertiary care cancer hospital, during year 2020-22. In this study 200 diagnosed cases of TSCC(all stages) who underwent primary tumour resection and neck dissection were analysed for DOI, POI, LHR, PNI at invasive tumour front. Cases with recurrence of SCC, those with prior history of chemotherapy and radiation therapy, non-squamous malignancies of tongue and those having multiple tumours were excluded from study. Statistical univariate analysis with Fisher exact test and chi square test were used to assess the parameters in predicting lymph node metastasis.

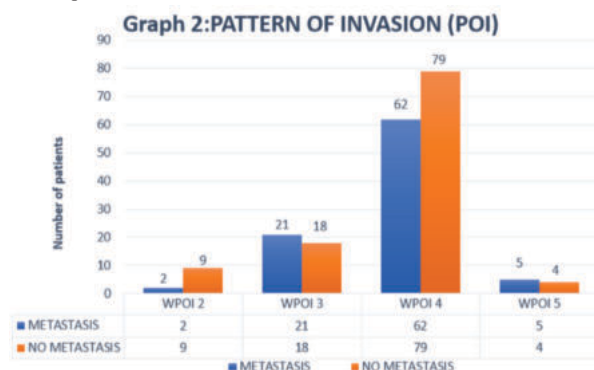
### OBSERVATIONS AND RESULTS:

1. Of all the cases studied 74.50 % were male and 25.50% were female in this study corresponding to male preponderance.
2. Majority, 61 cases (30.50%) belonged to age group 41-50 years, followed by 44 (22%) cases in age group 31-40 years. Most cases occurring in 5<sup>th</sup> decade of life.
3. In our study percentage of cases with node metastasis (Graph 1), with DOI <5mm is 7.78%, with DOI 5.1-10mm is 37.77% and with DOI >10mm is 54.45%. This shows DOI >10mm increases the risk of node metastasis.

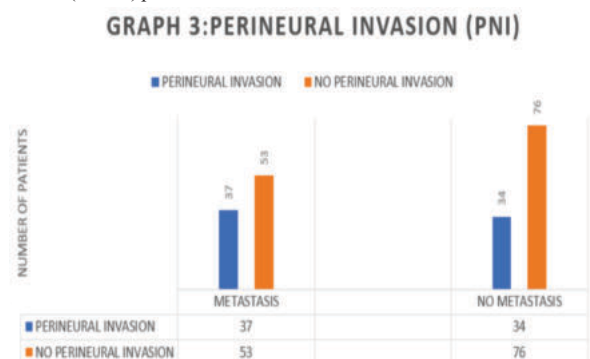
Graph 1: DEPTH OF INVASION (DOI)



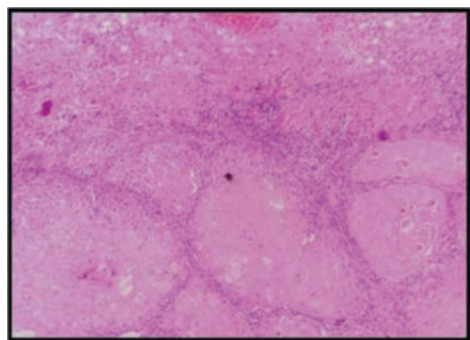
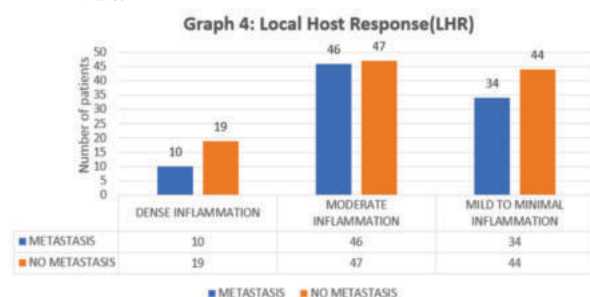
4. Worst pattern of invasion(WPOI) 1 was not seen in any of the patients, there were 11 patients with WPOI 2 (Graph 2, Fig. 1.a) amongst which 2 (2%) patients had cervical node metastasis, there were 39 patients with WPOI 3 (Fig 1b) amongst which 21(23.45%) patients had cervical node metastasis, there were 141 patients with WPOI 4 (Fig.1.c) amongst which 62(69%) patients had cervical node metastasis, there were 9 patients with WPOI 5 (Fig.1.d), amongst which 5 (5.55%) patients had cervical node metastasis. This shows WPOI 4 ,the most common POI amongst all patterns.



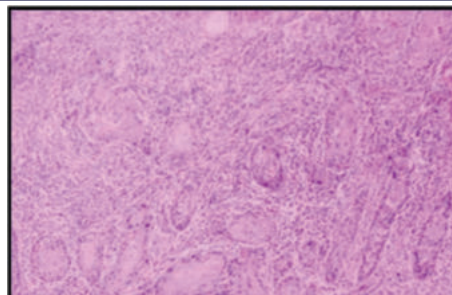
5. PNI(Graph 3, Fig 2) was seen in 71 patients, amongst which 37(35.5%)patients had cervical node metastasis.



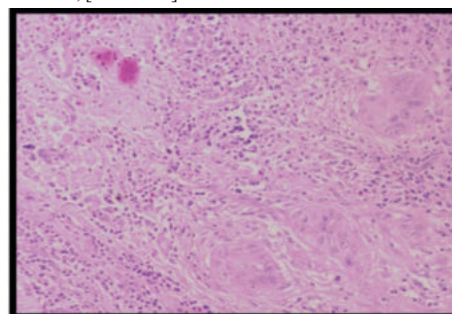
6. In our study percentage of cases with node metastasis (Graph 4) with Dense inflammation (Fig.3) is 11.11%, with Moderate inflammation 51.12%, with Mild to minimal inflammation is 37.77% . This shows Moderate lymphoplasmacytic infiltrate was most commonly seen followed by mild lymphoplasmacytic infiltrate.



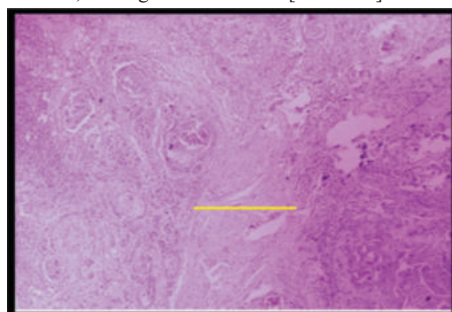
**Figure 1. a:** 40x: Tumour With Broad Pushing "Fingers" [WPOI-II]



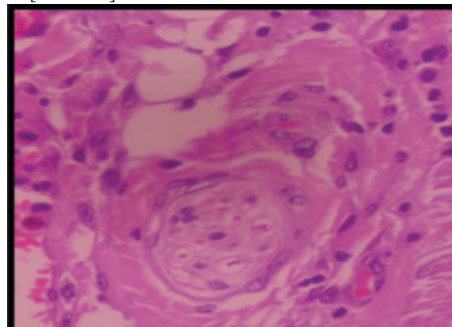
**Figure 1.b :** 40X :Tumour With Invading Islands With More Than 15 Cells Per Island; [WPOI III].



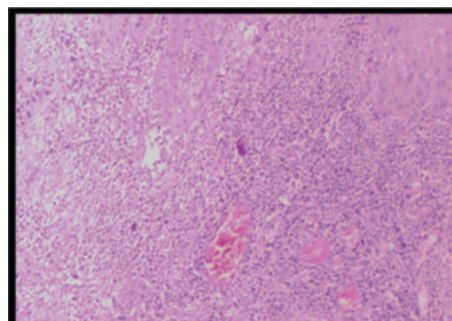
**Figure 1.c :** 40 X :Tumour With Invading Islands With Fewer Than 15 Cells Per Island, Or Single Cell Invasion [WPOI IV].



**Figure 1.d:** 40X :Tumour Satellites Of Any Size With A 1mm Distance Of Intervening Normal Tissue (Yellow line) At The Tumour-Host Interface. [WPOI V]



**Figure 2:** 40X: Above figure shows encirclement of nerve by tumour cells.



**Figure 3. :** 40 X :Dense LHR : Above figure shows a continuous and dense rim of lymphoplasmacytic infiltration.

**DISCUSSION:**

TSCC are one of the most common cancers among oral cancers. Histopathological grading system for invasive tumour front was firstly introduced by Bryne et al<sup>11</sup> for oral cancer. Invasive tumour front assessment can be easily done as a part of routine histopathological examination. Many studies have shown that these histopathological features can predict LN metastasis in OSCC.

**Depth Of Invasion:**

Kane et al<sup>12</sup>, Almangush et al<sup>13</sup>, Aditi-Nuzhat et al<sup>14</sup> found a significant correlation between DOI and node metastasis in OSCC, concordant with our study (p value of 0.001).

**Worst Pattern Of Invasion:**

Studies on OSCC by Lundqvist et al<sup>15</sup>, Kane et al<sup>12</sup> and Yeun et al.<sup>16</sup> did not find any correlation of POI with LN metastasis, similar to our observation (p value of 0.17).

**Perineural Invasion:**

Kane et al<sup>12</sup>, Lim et al.<sup>4</sup>, Yeun et al.<sup>16</sup> did not find correlation of PNI with LN metastasis in patients with early OSCC. Our study also did not find significant correlation of LN metastasis with PNI (p value of 0.06).

**Local Host Response:**

Martinez-Gimeno et al.<sup>17</sup>, Yeun et al.<sup>16</sup> and Kane et al.<sup>12</sup> found no significant correlation with inflammatory infiltrates and cervical node metastasis when the degree of inflammatory reaction was divided into light, moderate, and intense, similar to our study (p value-0.34)

**CONCLUSION:**

DOI is the most reliable predictor for nodal metastasis in surgical management of TSCC. WPOI, PNI, LHR although not included in AJCC should be included in standard reporting, which will help in predicting morbidity and mortality.

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