

# Subclinical Neck Nodes in early stages of Oral Tongue Cancer: Evaluation and Comparison with HPE

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**Abstract-** Oral tongue cancers are very aggressive, known for skip metastasis, high recurrence rates and poor salvage results. Strong et al<sup>[3]</sup> stated that 60% of patients died of neck recurrence when they were managed by only resection of primary and observation of neck<sup>[3]</sup>. SOHND [Supra omohyoid neck dissection] is not adequate enough for complete pathological evaluation of all neck nodes at risk for patients of oral tongue malignancy.<sup>[2]</sup>

**Index Terms-** Oral; tongue; metastasis; cancer; MRI

## I. INTRODUCTION

The best evaluation method to detect occult neck nodes is very challenging. Management of subclinical cervical nodes in cancers of anterior  $2/3^{\text{rd}}$  of tongue remains to be controversial. Doing SOHND (Supra omohyoid neck dissection) N0 Neck is not sufficient due to the occurrence of skip metastasis.<sup>[1, 2]</sup> Results of salvage neck dissection after appearance of neck nodes are not very appealing<sup>[3]</sup>. Elective MND-III (modified neck dissection – Type III) in N<sub>0</sub> neck does not improve the survival<sup>[4]</sup>

A prospective study was conducted to know the best pre-operative evaluation method in comparison of HPE (Histo-Pathology Examination) of specimen of tongue excision and neck dissection to predict the subclinical neck nodes in early stage of oral tongue cancer.

### 1) Abstract

**Aims and objectives:** To evaluate the efficacy of prevailing methods of investigations to know the occurrence of subclinical neck nodes in early lesions of oral tongue malignancy.

**Study Design:** Prospective case series

**Protocol:** Early lesions of oral tongue cancer were evaluated by clinical examination, MRI [Magnetic resonance imaging] of oral cavity and neck, USG [Ultra Sonography] of neck. They were compared with histopathology with regards to neck nodes, cell differentiation, and depth of tumor invasion as all underwent wide excision of primary with type III MND [Modified neck dissection].

**Results:** USG has high sensitivity, specificity, positive and negative predictive value for neck nodes. MRI is a good tool to predict depth of tumor invasion which is a significant factor for local and cervical control, Differentiation of cell and depth of tumor invasion on HPE are a significant predictor of neck nodes

### 2) Introduction

Oral tongue cancers are very aggressive, known for skip metastasis, high recurrence rates and poor salvage results. Strong et al<sup>[3]</sup> stated that 60% of patients died of neck recurrence when they were managed by only resection of primary and observation of neck<sup>[3]</sup>. SOHND [Supra omohyoid neck dissection] is not adequate enough for complete pathological evaluation of all neck nodes at risk for patients of oral tongue malignancy.<sup>[2]</sup>

### 3) Research Elaborations

**Study Design:** Prospective case study

**Materials and methods:** A prospective study of 30 cases of carcinoma of oral tongue was carried out from July 2009 to December 2011 at Department of E.N.T. and Head and Neck, Govt. Medical College & New Civil Hospital, Surat. India.

**Inclusion Criteria:** All patients having T<sub>1</sub>, T<sub>2</sub> lesions of carcinoma of tongue arising from anterior <sup>2</sup>/<sub>3</sub><sup>rd</sup> of tongue were included.

**Exclusion Criteria:**

1. The patients previously treated and those who refused to give consent for study.
2. Patients not willing for regular follow up or did not turn up for regular follow up.
3. All patients with distant metastasis and major general debilitating disease.

**Prerequisite:**

1. The study design was thoroughly scrutinized and passed by Ethical committee of our institute.
2. All patients were informed, explained in detail about the study & only those patients were included in the study who gave written consent for the same.

**Protocol:** Each patient, included in the study was admitted in the ward, detailed history was taken, thorough local, general and systemic examination was performed. Pathological diagnosis was established by biopsy. Ultra sonography and MRI (Magnetic resonance imaging) of neck for neck nodes were done; FNAC (Fine Needle aspiration cytology) was done for palpable nodes and USG (Ultra Sonography) guided FNAC was done for impalpable nodes. TNM staging was done based on MRI which was done 5 to 7 days before final management.

All the patients underwent curative surgery as primary treatment in the form of wide excision of tongue with 2cm safety margins for primary. Modified type 3 neck dissection was done (for N + neck i.e. more than 1cm neck node on MRI and/or when the depth of tumor invasion was more than 3mm on MRI). Surgical specimen was sent for HPE after proper labeling of all margins and final staging was done based on HPE. Post-operative full dose radiotherapy was advised when indicated. Follow up at regular interval was carried out monthly for 6 months and 3 monthly thereafter. Local & Regional recurrence if any was treated appropriately.

#### 4) Results or Finding

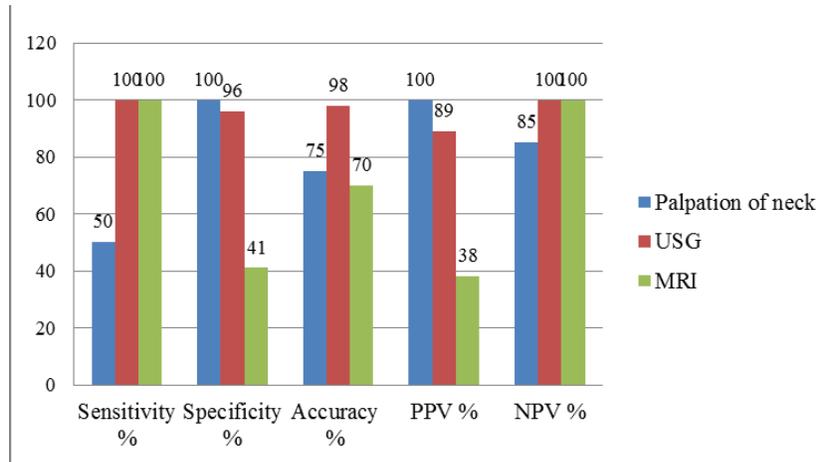
Our study comprised of 17 males and 13 females, with male to female ratio of 1.3 : 1, in the age group of 21-80 years, with mean age of presentation being 50 years. In this study, only 3 patients were without any additions. 27 patients were addicted to tobacco and in addition, two of them were consuming alcohol. The most common site of lesion was lateral margin of tongue in 96.66% patients, whereas only one patient had growth on ventral surface of tongue (3.33%).

In this study we observed that 76.66% of lesions were ulcerative, 16.66% were endophytic and only 6.66% were exophytic.

*Table 1: N staging based on different investigations:*

N Stage	N <sub>0</sub>	N <sub>1</sub>	N <sub>2</sub>
Palpation of neck	26	04	0
USG Neck	21	09	0
MRI Neck	9	19	02
FNAC	Not Possible	Inconclusive	Inclusive
HPE	22	06	02

In our study we found the following statistical value for each method of evaluation of neck node as mentioned in Graph 1



Graph 1: Statistical value of different investigations for neck nodes

Chi Square = 26.26  
 DF (Degree of Freedom) = 6  
 P (Probability) = 0.0002  
 (PPV = Positive Predictive Value, NPV = Negative Predictive Value)

Out of 26 patients of N<sub>0</sub> stage, 5 were upgraded to N<sub>1</sub> on USG and 17 were upgraded to N<sub>1</sub> on MRI Neck. This is indicative of USG as more sensitive to pick up impalpable neck nodes with sensitivity of 100% and specificity of 96% compared to MRI.

On MRI of neck, we found 9 patients with N<sub>0</sub> and 21 with positive neck node. For neck node positivity standard criteria were taken into consideration. We found sensitivity and specificity of MRI to be 100% and 41 % respectively.

Table 2: T staging based on different investigations:

	T <sub>1</sub> Stage	T <sub>2</sub> Stage	T <sub>3</sub> Stage (4.1 cm)
Clinical Examination	21	09	0
MRI	14	14	02
HPE	05	22	03

Chi Square = 18.18  
 DF = 4  
 P = 0.0011

When different evaluation methods were compared with T staging the P = 0.001 which was highly significant.

Above table shows that clinical examination underestimates the tumor which on MRI gets upgraded. 8 patients of RT<sub>1</sub> (Radiological) on MRI were upgraded to pT<sub>2</sub> (pathological) and one patient of RT<sub>2</sub> was upgraded to pT<sub>3</sub> on HPE.

Table 3: Comparison of T stage with N staging on HPE

	N <sub>0</sub> (MRI/HPE)	N <sub>1</sub> (MRI/HPE)	N <sub>2</sub> (MRI/HPE)
T <sub>1</sub>	7/2	6/2	1/1
T <sub>2</sub>	2/19	11/2	1/1
T <sub>3</sub>	0/1	2/2	0/0

Chi-square = 9.18  
 DF = 4

P = 0.057

but on MRI,  
 Chi-square = 5.63  
 DF = 4  
 P = 0.229

For MRI above data are indicative that size of the tumor is directly proportional to neck node metastasis as both patients with T<sub>3</sub> came as positive neck node on microscopic examination. Correlation of T stage with N stage is significant on HPE as P value is 0.057 but MRI does not correlate the same significantly as P value is 0.229.

Table 4: Pathological cell differentiation and Correlation with N stage.

N Stage	N <sub>0</sub>	N <sub>1</sub>	N <sub>2</sub>
Well differentiated	18	0	0
Moderately differentiated	02	02	01
Poorly Differentiated	02	04	01

This shows significant correlation between grade of differentiation and neck node involvement with;  
 Chi square = 17  
 DF = 4  
 P = 0.002

Table 5: Comparison of depth of tumor invasion with T stage on MRI/HPE

	T <sub>1</sub> (MRI/HPE)	T <sub>2</sub> (MRI/HPE)	T <sub>3</sub> (MRI/HPE)
< 3mm	0/0	0/0	0/0
3 to 9mm	7/5	0/8	0
> 9mm	7/0	14/14	2/3

For MRI;  
 Chi-square = 10.4  
 DF = 2  
 P = 0.005

and for HPE  
 Chi-square = 9.27  
 DF = 2  
 P = 0.010

The above table shows that as the size of lesion increases the depth of invasion to deeper structure of tongue also increases. When depth of tumor invasion was compared with T staging for MRI, P = 0.005 and for HPE, P = 0.01 both are highly significant.

As none of our patients had depth of tumor invasion < 3mm on MRI all were posted for MND type 3, 22 came as negative for metastasis on HPE and 08 came as positive for metastasis indicating that MRI over estimates the nodes.

Table 6: Comparison of depth of tumor invasion with N stage on MRI/HPE

	N <sub>0</sub> (MRI/HPE)	N <sub>1</sub> (MRI/HPE)	N <sub>2</sub> (MRI/HPE)
< 3mm	0/0	0/0	0/0
3 to 9mm	5/22	1/2	0/0
> 9mm	4/0	18/4	2/2

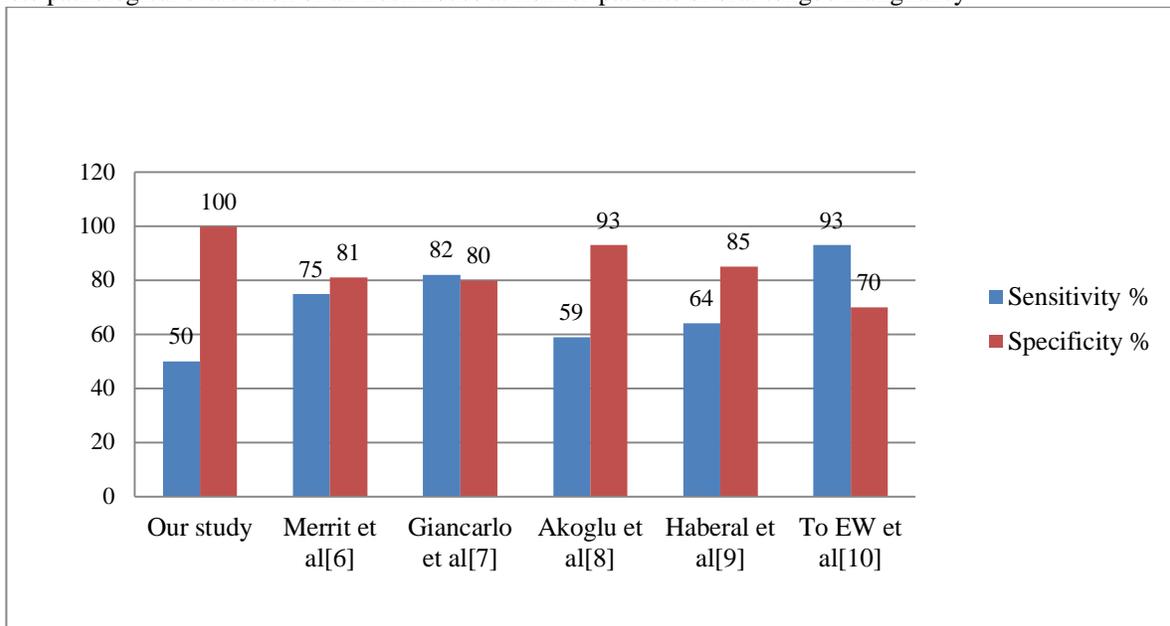
MRI;  
Chi-square = 10.2  
DF= 2  
P= 0.006

and HPE  
Chi-square = 21.7  
DF= 2  
P = 0.000

This suggests that depth of invasion is good indicator of possibility of neck metastasis on MRI as well as HPE. For tumor thickness 3 to 9mm,  $\frac{1}{6}$  (16%) on MRI and  $\frac{2}{24}$  (8%) on HPE were found to have neck nodes. For tumor thickness > 9mm,  $\frac{20}{24}$  (83%) on MRI and  $\frac{6}{6}$  (100%) were found to be neck node positive on HPE.

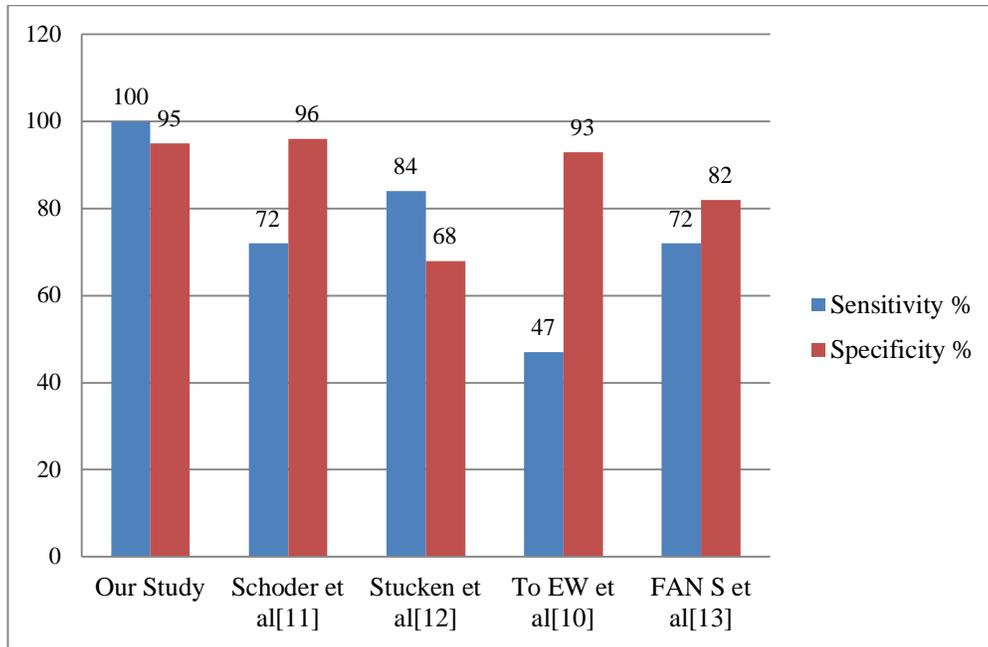
**Discussion:**

Cancer of tongue comprises of 35 % of all oral cavity cancers. <sup>[16]</sup> In our study it was 31%. These lesions are very aggressive, known for skip metastasis, high recurrence rates and poor salvage results. Strong et al <sup>[3]</sup> stated that 60% of patients died of neck recurrence when they were managed by only resection of primary and observation of neck .Primary aggressive intervention yields better results keeping in mind the functional morbidity of tongue excision and neck dissection <sup>[3]</sup>. SOHND is not adequate enough for complete pathological evaluation of all neck nodes at risk for patients of oral tongue malignancy <sup>[11]</sup>.



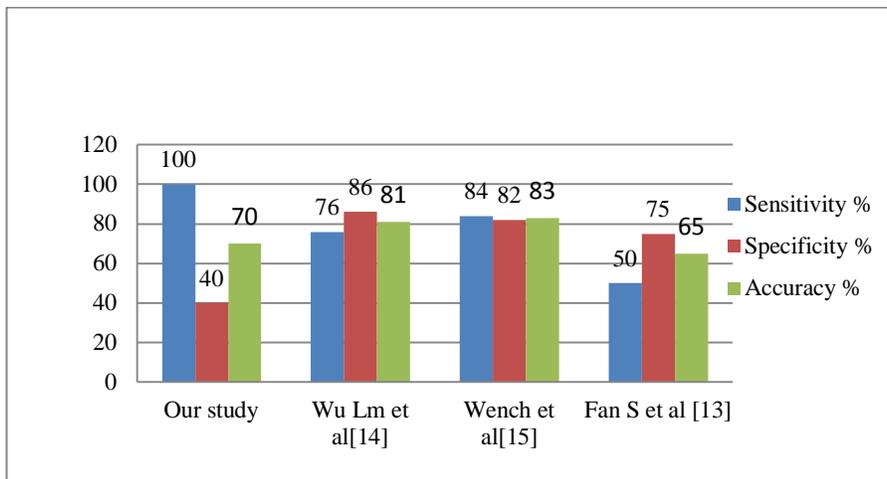
Graph 2: Comparison of statistical values with other studies on palpation of neck

Merritt et al. <sup>[6]</sup> in a systematic review of studies comparing palpation with computed tomography (CT), found a sensitivity of 75% and 83% and a specificity of 81% and 83% for palpation and CT, respectively. Giancarlo et al. <sup>[7]</sup> comparing palpation with ultrasonography (US) found no differences between the methods, and palpation had a sensitivity of only 82% and specificity of 80%. Akoglu et al. <sup>[8]</sup> studied 23 patients and found a sensitivity for palpation of 59.2% and a specificity of 93%. Haberal et al <sup>[9]</sup> documented sensitivity of 64% and specificity of 85%. To EW et al <sup>[10]</sup> found sensitivity of 93% and specificity of 70%. We got 50 % sensitivity and 100% specificity on palpation of neck.



Graph 3: Comparison of statistical values with other studies on USG

On USG the sensitivity and specificity was found to be 100% and 95% in our study which was comparable with Akoglu et al<sup>[8]</sup> as 80 % and 59 % respectively., Haberal et al<sup>[9]</sup> documented the same as 72% and 96% respectively. The sensitivity, specificity and accuracy were found to be 47%, 93% and 70%, respectively in a study by To EW et al<sup>[10]</sup> Schoder et al<sup>[11]</sup> documented 72% sensitivity and 96% specificity by USG. The sensitivity and specificity for USG by Stuken et al<sup>[12]</sup> (84% & 68%), EMW et al<sup>[10]</sup> (47% & 93%) FAN et al<sup>[13]</sup> (72.5% & 82.1%) is documented in the literature.



Graph 4: Comparison of statistical values with other studies on MRI

Wu LM et al<sup>[14]</sup> found sensitivity of 76 % with specificity of 86 % for MRI. A Meta-analysis conducted by Wenche M Klerkx et al<sup>[15]</sup> found sensitivity of 0.84 (95% CI = 0.70 to 0.92), with a specificity of 0.82 (95% CI = 0.72 to 0.89) for the nine studies that incorporated contrast enhancement in their multiple malignancy criteria for MRI. Whereas Fan S et al<sup>[13]</sup> documented it to be 50 % and 75 % respectively for MRI.

Lam P et al<sup>[16]</sup> found significant accuracy for measurement of tumor thickness and staging on contrast enhanced T<sub>1</sub>-weighted and T<sub>2</sub> weighted MRI when compared with histology tumor thickness (R = 0.938 and 0.941, respectively).

Po wing et al found<sup>[17]</sup>, tumor of up to 3 mm thickness has 8% subclinical nodal metastasis, tumor thickness of more than 3mm and up to 9mm had 44% subclinical nodal metastasis, tumor of more than 9 mm had 53% subclinical nodal metastasis.

Fukano et al <sup>[18]</sup> found overall cervical metastatic rate to be 35.4% and depth of invasion was statistically significant predictors of regional metastasis  $p = 0.0003$  on HPE compared to our study where the same was 26% and  $P = 0.000$ , highly significant.

Morton RP et al <sup>[19]</sup> found no association between tumor thickness and nodal metastasis. Perineural infiltration was the only factor to approach statistical significance.

Veness M J et al <sup>[20]</sup> found tumor thickness  $\leq 5$  mm versus  $> 5$  mm the incidence of nodal metastases was 8% versus 51% ( $P = 0.007$ ).

In our study when depth of tumor invasion was compared with neck nodes MRI turned out to be a good indicator with  $P = 0.006$ .

## 5) Conclusion

- Preoperative USG of the neck is best investigation to predict subclinical neck node with sensitivity of 100% and specificity of 95%.
- T stage on MRI is not a significant criterion to predict cervical metastasis  $P = 0.229$ , but the same for HPE is  $P = 0.057$ .
- Cell differentiation on HPE correlates significantly with occurrence of neck node  $P = 0.002$ .
- Depth of tumor invasion on MRI correlates very well with T staging  $P = 0.005$ , the same for HPE,  $P = 0.01$  highly significant.
- Depth of tumor invasion on MRI is one of the significant criteria to predict sub clinical micro metastasis  $p = 0.006$ , the same for HPE,  $P = 0.00$  very significant.

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