

# Does diagnostic accuracy of surgeon's perception outweigh frozen section analysis in determining intraoperative clear mucosal surgical margins in oral squamous cell carcinoma patients?

## ABSTRACT

**Introduction:** The lucrativeness of the frozen section for intraoperative margin assessment in head and neck squamous cell carcinoma is debatable till date. The purpose of this study was to evaluate whether surgeon's perception by gross examination (GE) of margin is an alternative to frozen section.

**Aim:** The aim was to compare the diagnostic accuracy (DA) of surgeon's perception of tumor-free mucosal and soft-tissue surgical margins intraoperatively assessed by GE and frozen section analysis (FSA).

**Methodology:** A prospective, observational study was conducted on 59 histologically proven cases of oral squamous cell carcinoma. Two hundred and thirty-six mucosal margins were assessed by an experienced surgeon (ES) and thereafter subjected subsequently to FSA. These results were compared with the gold standard histopathology (HPE). The sensitivity (SS), specificity (SP), positive predictor value (PPV), negative predictor value (NPV), and DA of surgeon's perception by GE were calculated and subsequently compared with FSA and HPE using descriptive and inferential statistics.

**Results:** The SS, SP, PPV, NPV, and DA of ES by GE were 80%, 99.12%, 80%, 99.12%, and 98.30%, respectively when compared to HPE, and the SS of 90%, SP of 98.32%, PPV, NPV, and DA were 69.23%, 99.57%, and 97.98%, respectively when compared with HPE. The results of the surgeon's perception by GE were comparable to the results of FSA.

**Conclusion:** The study concludes that surgeon's perception by GE is upfront reliable alternative intraoperative method to FSA in places where FS is not available.

**Keywords:** Frozen section, gross examination, oral squamous cell carcinoma, surgical margin

## INTRODUCTION

The mainstay for oncological curative treatment is the primary surgery with or without adjuvant radio or chemotherapy or both when needed.<sup>[1]</sup> The primary surgery involves resection of tumor without residual tumor mass along with a rim of healthy tissue.<sup>[2]</sup> Owing to anatomical restrictions, it is difficult intraoperatively to assess adequate margin at all sites of the tumor.<sup>[3,4]</sup>

The overall outcome of the disease is governed by certain prognostic factors such as biological and molecular factors

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which include histopathologic grading of the tumor, depth of tumor invasion, tumor, node, metastasis stage, extracapsular spread, completeness of resection, and perineural and perivascular spread.<sup>[5]</sup> Of the above, the status of the resection margin has been reported as an independent prognostic indicator for DSA (disease-specific survival).<sup>[4]</sup> The presence of positive margin doubles the risk of local recurrence compared to negative margin.<sup>[6]</sup>

The completeness of surgery requires pathologically negative margin (R0 resection) around the exposed tumor. In literature, there are conflicting views regarding the overwhelming oncological clearance.<sup>[7]</sup> The clearance margin has ranged from 1 mm to 7 mm.<sup>[8]</sup> Intraoperative margin assessment is routinely done by frozen section analysis (FSA) since ages. The inherent drawbacks of FSA are that it has a minimal detection rate of only 25%–34%. The other drawbacks are that it is technique sensitive, low cost–benefit ratio, requirement of additional trained personnel, and its unavailability in growing countries.<sup>[9,10]</sup>

In resource-limited areas, intraoperative gross examination (GE) of surgical specimen by surgeon's perception remains the widely used method for assessment of surgical margins.<sup>[11]</sup> To validate the diagnostic accuracy (DA) of surgeon's perception as a reliable alternative against the intraoperative FSA, we conducted an observational, comparative study with a hypothesis that a DA of surgeons perception in achieving intraoperative clear mucosal margins by GE can be used as a reliable alternative to FSA.<sup>[12]</sup>

## METHODOLOGY

The current prospective, observational, comparative study consisted of 59 primary resectable, histopathologically proven cases of oral squamous cell carcinoma (OSCC), which underwent surgical resection of the tumor with a curative intent between August 2017 and June 2019. It was conducted in the department of oral and maxillofacial surgery. The study conforms with the Helsinki declaration and its later amendments or comparable ethical standards and institutional ethical guidelines prescribed by the central ethics committee on human research at Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra. (ref. no.-DMIMS [DU]/IEC/2017–2018/6693). Informed consent was obtained from all patients who were included in the study.

The patients with oral nonepithelial malignancies, recurrence cases, history of prior treatment of radio/chemotherapy, multiple primary tumors, areas of field cancerization, patients with residual, recurrent disease, and second primary tumor were excluded from the study.

The excision of tumor was done by trainee surgeon with a rim of 1–1.5 cm healthy tissue based on GE and palpation. The specimens were labeled with orientation stitches and measured the distance from tumor to clearance margin at all four directions. The inking of specimen was done at 5 mm from the tumor, as it is considered a safe margin according to the National Comprehensive Cancer Network (NCCN) guidelines.<sup>[2]</sup> This labeled resected specimen was handed over to the experienced surgeon (ES) to assess the resected tumor margin for adequacy and inadequacy. If according to ES assessment margins were adequate then, the margins were directly sent for FSA, whereas if margins were inadequate, it was revised and sent for FSA.

A total of 236 macroscopic margins evaluated by ES were subjected to FSA intraoperatively. Among these, 12 margins were microscopically reported as positive. Hence, these were subsequently revised and evaluated by FSA till it came out as negative. The pathologists were blinded to the results of trainee surgeon, and slides made intraoperatively were evaluated only by single pathologist to avoid bias. However, the results of FSA were timely reported to ES, intraoperatively to aid in decision-making.

After assessment by the frozen section, all these specimens were sent for permanent section. At the time of permanent sectioning, tumor was assessed sequentially at 1 mm apart, starting from the inked margin up to 10 mm from all four oriented sites of the resected surgical specimen. All four peripheral macroscopic mucosal margins checked by frozen section were never sampled again at the time of permanent section. However, the slides made from those margins which were analyzed during the frozen section were rechecked at the permanent section. Thus, the results of FSA and GE by ES were recorded as true positive, false positive, true negative, and false negative. Statistical analysis was done using descriptive and inferential statistics using sensitivity (SS), specificity (SP), positive predictor value (PPV), and negative predictor value (NPV), and software used in the analysis was SPSS (Statistical Package for Social Sciences) Version 24.0 (IBM Corporation®, Chicago, USA) 2016, and  $P < 0.05$  was considered as the level of significance.

## RESULTS

Among 248 (including revised margins), nine margins were positive and 239 were negative on histopathological analysis. These results were considered as the gold standard for comparing the results of ES and FSA.

In our study, SS, SP, PPV, NPV, and accuracy of ES as compared to histopathological examination (HPE) used as the gold

standard were 80%, 99.12%, 80%, 99.12%, and 98.30%, respectively [Graph 1].

SS, SP, PPV, NPV, and of FSA as compared to HPE were 90%, 98.32%, 69.23%, 99.57%, and 97.98%, respectively [Graph 2].

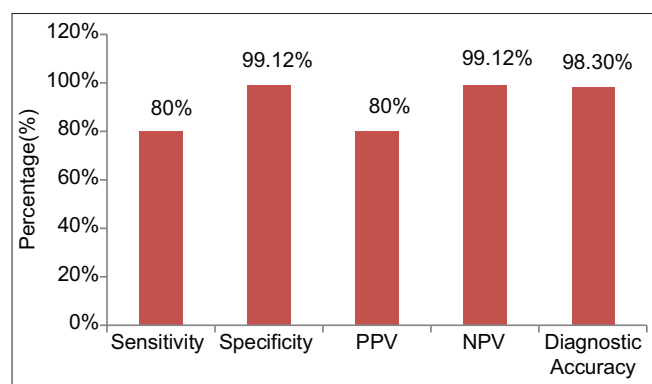
Therefore, the results suggested that the SP and accuracy of ES and FSA were found to be comparable. As SP of ES and FSA were 99.12% and 98.32%, respectively. The accuracy of surgeon's perception ES and FS was 98.30% and 97.98%, respectively.

## DISCUSSION

The precept for head and neck squamous cell carcinoma aims toward the radical resection of tumor without leaving behind any neoplastic tissue. Having said that, negative margins are achieved in only 50%–80% of the patients. Positive tumor margin is associated with locoregional recurrence, overall survival, and disease-specific survival. It is also an indicator of poor prognosis. The presence of positive margin doubled the risk of local recurrence as compared to negative margin.<sup>[6]</sup>

The resection of tumor with adequate margins was performed by surgeon based on clinical palpation and experience, subsequently compared intraoperatively with FSA, since ages.<sup>[13]</sup> In literature, varied range of accuracy of FSA has been described from as low as 25% to 34% to as high as 96% to 99.5%.<sup>[11,14,15]</sup> There are certain inherent drawbacks of FSA such as poor cost–benefit ratio, requisite of additional proficient personnel, space requirement, and unavailability in growing countries rendering them inaccessible to most surgeons in their clinical practices.<sup>[15]</sup>

To overcome the shortcomings of FSA, we hypothesized a study comparing the DA of surgeon's perception by



Graph 1: The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of an experienced surgeon by gross examination versus histopathology

GE of surgical specimen against FSA as an alternative method in achieving clear mucosal and soft-tissue margins intraoperatively.

We assessed 236 macroscopic mucosal margins based on GE by surgeon's perception of tumor obtained from 59 histologically proven cases of OSCC. These 236 margins were subjected to FSA intraoperatively, and revision of 12 margins was performed according to FSA reporting.

In the present study, we found that the SS of surgeon's perception by GE was 80%, SP 99.12%, and DA 98.30%. A similar study carried out by Mair *et al.*<sup>[12]</sup> found that SP of the surgeon's perception by GE was 88.32%, and the study conducted by Chaturvedi *et al.*<sup>[11]</sup> showed higher SS rate up to 88.9% [Graph 1].

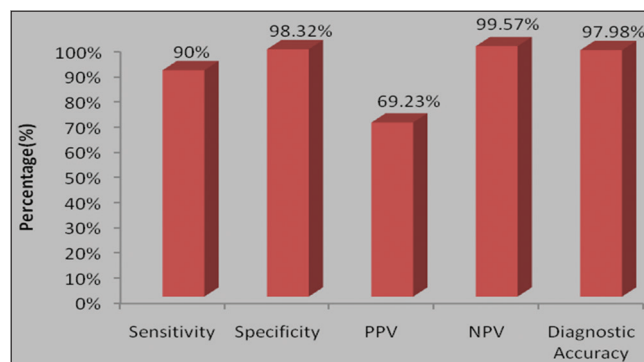
In the present study, the SS, SP, and accuracy of FSA were 90%, 98.32%, and 97.98, respectively. The similar results of SP 98.8% were shown by the study by Mair *et al.*<sup>[12]</sup> and similar accuracy of 96.74% shown by the study carried out by Sharma *et al.*<sup>[16]</sup> Although there is a wide range of accuracy of FSA cited in the literature, the study conducted by Chaturvedi *et al.*<sup>[11]</sup> showed SP and accuracy of FSA up to 100% [Graph 2].

With the SP of 99.12% and accuracy of 98.30% of surgeon's perception by GE, the surgeon can correctly identify the inadequate surgical margins without the need of FSA in resource-delimited domains.

To find the adequacy of margin beyond 5 mm, we performed cut serial sectioning of the margin from 5 mm up till 10 mm.<sup>[17]</sup> We found that 11/59 (18%) having involved or close margin at 6 mm whereas, in the rest of the patients, 48/59 (81.35%) having clear margin at and above 7 mm.

## CONCLUSION

Thus, we can conclude that the DA of an ES is comparable



Graph 2: The sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of frozen versus histopathology

to that of FSA and improves after 7 mm clearance margins of the tumor. Hence, this can be used as an alternative tool in achieving clear mucosal surgical margins intraoperatively against conventional sophisticated FSA technique.

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#### Conflicts of interest

There are no conflicts of interest.

#### REFERENCES

- Hingnikar P, Bhola N, Jadhav A, Wankhade A, Mishra A, Agrawal A. Evaluation of safe surgical mucosal margins with and without intra-operative vital staining with toluidine blue in cases of oral squamous cell carcinoma – A comparative study. *BAOJ Cancer Res Ther* 2018;4:59.
- Anderson CR, Sisson K, Moncrieff M. A meta-analysis of margin size and local recurrence in oral squamous cell carcinoma. *Oral Oncol* 2015;51:464-9.
- Mitchell DA, Kanatas A, Murphy C, Chengot P, Smith AB, Ong TK. Margins and survival in oral cancer. *Br J Oral Maxillofac Surg* 2018;56:820-9.
- Wong LS, McMahan J, Devine J, McLellan D, Thompson E, Farrow A, *et al.* Influence of close resection margins on local recurrence and disease-specific survival in oral and oropharyngeal carcinoma. *Br J Oral Maxillofac Surg* 2012;50:102-8.
- Németh Z, Velich N, Bogdan S, Ujjál M, Szabó G, Suba ZS. The prognostic role of clinical, morphological and molecular markers in oral squamous cell tumors. *Neoplasma* 2005;52:95-102.
- Loree TR, Strong EW. Significance of positive margins in oral cavity squamous carcinoma. *Am J Surg* 1990;160:410-4.
- Upile T, Fisher C, Jerjes W, El Maaytah M, Searle A, Archer D, *et al.* The uncertainty of the surgical margin in the treatment of head and neck cancer. *Oral Oncol* 2007;43:321-6.
- Zanoni DK, Migliacci JC, Xu B, Katabi N, Montero PH, Ganly I, *et al.* A proposal to redefine close surgical margins in squamous cell carcinoma of the oral tongue. *JAMA Otolaryngol Head Neck Surg* 2017;143:555-60.
- Yadav GS, Donoghue M, Tauro DP, Yadav A, Agarwal S. Intraoperative imprint evaluation of surgical margins in oral squamous cell carcinoma. *Acta Cytol* 2013;57:75-83.
- Agarwal A, Bhola N, Kambala R, Borle RM. Touch imprint cytology: Can it serve as an alternative to frozen section in intraoperative assessment of cervical metastasis in oral squamous cell carcinoma? *J Oral Maxillofac Surg* 2019;77:994-9.
- Chaturvedi P, Datta S, Nair S, Nair D, Pawar P, Vaishampayan S, *et al.* Gross examination by the surgeon as an alternative to frozen section for assessment of adequacy of surgical margin in head and neck squamous cell carcinoma. *Head Neck* 2014;36:557-63.
- Mair M, Nair D, Nair S, Dutta S, Garg A, Malik A, *et al.* Intraoperative gross examination vs frozen section for achievement of adequate margin in oral cancer surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2017;123:544-9.
- Byers RM, Bland KI, Borlase B, Luna M. The prognostic and therapeutic value of frozen section determinations in the surgical treatment of squamous carcinoma of the head and neck. *Am J Surg* 1978;136:525-8.
- Ord RA, Aisner S. Accuracy of frozen sections in assessing margins in oral cancer resection. *J Oral Maxillofac Surg* 1997;55:663-9.
- DiNardo LJ, Lin J, Karageorge LS, Powers CN. Accuracy, utility, and cost of frozen section margins in head and neck cancer surgery. *Laryngoscope* 2000;110:1773-6.
- Sharma SM, Prasad BR, Pushparaj S, Poojary D. Accuracy of intraoperative frozen section in assessing margins in oral cancer resection. *J Maxillofac Oral Surg* 2009;8:357-61.
- Pathak KA, Nason RW, Penner C, Viallet NR, Sutherland D, Kerr PD. Impact of use of frozen section assessment of operative margins on survival in oral cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:235-9.