

# Interobserver Audit of Surgical Margins in Patients with Recurrence of Oral Squamous Cell Carcinoma – A Retrospective Study

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## ABSTRACT

**Introduction:** The fundamental aim of surgery in management of oral cancer is to provide adequate clearance of the tumour by complete removal of microscopic or subclinical foci of malignancy. Intraoperative frozen section diagnosis guides the surgeon to revise the surgical margins on table in real time and obtain clear surgical margins. Intraoperative frozen section diagnosis can be done by both general and oral pathologists. However, there can be interobserver variability in the evaluation of surgical margins among them. Hence, the aim of this study was to evaluate the archival intraoperative surgical margins in patients with recurrence of Oral Squamous Cell Carcinoma (OSCC) and to assess the interobserver variability among general and oral pathologists in reporting the archival intraoperative surgical margins.

**Materials and Methods:** Thirty-two patients with recurrence of OSCC were included in the study. A total of 200 archival intraoperative surgical margins of their previous surgery were assessed by two double blinded general pathologists and the scoring was done based on the presence/ absence of dysplasia and/or invasion and grade of dysplasia. The gradings provided were compared to the previous intraoperative frozen section diagnosis signed out by the oral and maxillofacial pathologist and the interobserver variability was assessed.

**Results:** A total of 200 archival intraoperative surgical margins were obtained from thirty two previously operated OSCC patients, who reported with recurrence. All the sections were assessed by two blinded General Pathologists. There was only slight disparity between the diagnosis of frank invasion cases between the General Pathologists and Oral and Maxillofacial Pathologists.

**Conclusion:** All the dental institutions should have a frozen section diagnostic facility. All the surgical margins must be completely processed and their histological and molecular evaluation must be done to minimize the chances of recurrence. Extensive training of oral pathologists must be conducted in collaboration with the general pathologists for accurate evaluation of margins.

**Keywords:** Surgical margins, Oral Squamous Cell Carcinoma, Recurrence, Interobserver variability, Intraoperative frozen section

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## INTRODUCTION

Surgery is the main treatment modality in management of oral cancer.<sup>1</sup> The fundamental aim of surgery is to provide adequate clearance of the tumour by complete removal of microscopic or subclinical foci of malignancy.<sup>2,3</sup> Hinni et al have defined surgical margin as any tissue plane where the surgeon's knife meets the patient.<sup>4</sup> It is highly subjective and mainly depends on surgeons on-table judgement, radiographic interpretations and preoperative planning. However, as per the guidelines issued by The UK Royal College of Pathologists, a margin which is at a distance of 5 mm or more from the invasive tumour cells is defined as a clear margin. Similarly, a margin at a distance of 1–5 mm is considered a close margin and <1 mm is considered to denote the involved margin.<sup>5</sup>

The safety margins of the resected primary lesion are confirmed during surgery by palpation and from intraoperative frozen section histological analysis.<sup>6</sup>

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Intraoperative frozen section diagnosis guides the surgeon to revise the surgical margins on table in real time and obtain clear surgical margins. Intraoperative frozen section diagnosis can be done by both general and oral pathologists. However, majority of the cases are reported by general pathologists. This could be due to the lack of frozen section facilities in majority of the dental colleges in India.<sup>7</sup>

Also, there can be interobserver variability in the evaluation of surgical margins among general and oral pathologists due to difference in experience, increased number of cases and type of grading system used. Major disagreements in the diagnosis of head and neck cancers have been reported previously, with the extent of discordance ranging from 7% to 16.3%, which can lead to serious consequences in management and prognosis of

**Table 1:** Margin assessment by General Pathologists and Oral and Maxillofacial Pathologists

Criteria	General Pathologist		Oral and Maxillofacial Pathologist	
	n	%	n	%
No Dysplasia	152	76	128	64
Mild Dysplasia	0	0	16	8
Moderate Dysplasia	8	4	24	12
Severe Dysplasia	0	0	0	0
Invasion	40	20	32	16

such patients.<sup>8</sup>

Hence, the aim of this study was to assess the interobserver variability among general and oral pathologists in reporting of archival intraoperative surgical margins in patients with recurrence of OSCC.

**MATERIALS AND METHODS**

Thirty-two patients with histopathologically confirmed recurrence of OSCC were included in the study. The archival intraoperative frozen sections of these patients were retrieved. The previous intraoperative surgical margins of the cases were collected from the archives of the Department of Oral and Maxillofacial Pathology. The slides were assessed by two blinded general pathologists and the scoring was done based on presence/ absence of dysplasia and/or invasion and grade of dysplasia. The grading provided by the general pathologists was compared to the previous intraoperative frozen section diagnosis signed out by the oral and maxillofacial pathologists. The results obtained were tabulated.

Cohen’s Kappa Statistics was used to assess the interobserver variability between the general pathologist and oral and maxillofacial pathologist using IBM SPSS software version 20.

**RESULTS**

Thirty-two histopathologically confirmed recurrent OSCC patients were included in the study. A total of 200 archival intraoperative surgical margins were retrieved. These margins were assessed by two double blinded general pathologists. The general pathologists used the WHO system and graded 152 margins as no dysplasia (76%), 8 margin as moderate dysplasia (4%) and 40 margins having frank invasion (20%). The oral

**Table 2:** Inter-observer agreement between General Pathologists and Oral and Maxillofacial Pathologists

Count			Oral Pathologist					Total
			No dysplasia	Mild dysplasia	Moderate dysplasia	Severe dysplasia	Invasion	
			0	16	24	128	32	
General Pathologist	No dysplasia	0	1	0	0	0	0	1
	Mild dysplasia	0	1	1	0	0	0	2
	Moderate dysplasia	8	0	0	1	0	0	1
	Severe dysplasia	152	0	0	0	0	1	1
	Invasion	40	0	0	0	1	0	1
Total			2	1	1	1	1	6

Symmetric Measures

	Value	Asymp. Std. Error <sup>a</sup>	Approx. Tb	Approx. Sig.
Measurement of agreement Kappa	.130	.107	1.369	.171
N of valid cases	6			

- a. Not assuming the null hypothesis
- b. Using the asymptotic standard error assuming the null hypothesis
- OP – Oral Pathologists
- GP – General Pathologists



and maxillofacial pathologists also used the WHO system to sign out 128 margins as no dysplasia (64%), 16 margins as mild dysplasia (8%), 24 margins as moderate dysplasia (12%) and 32 margins having frank invasion into the underlying connective tissue (16%). [Table 1] In our study, the discrepancy among general pathologist and oral pathologists in reporting absence of dysplasia was 20%, mild and moderate dysplasia was 8% and frank invasion was 4%. None of the section demonstrated severe dysplasia.

Cohen's kappa statistics was run to determine the inter-observer reliability. There was only slight agreement (kappa value= 0.130) between the general pathologists and oral and maxillofacial pathologists. [Table 2]

## DISCUSSION

Inadequate resected margins result in increased chance of recurrence and poor survival rate in patients with OSCC. Hence, appropriate intraoperative clearance of surgical margins is of utmost importance to prevent recurrence and improve the prognosis. Intraoperative frozen section diagnosis can be done by both general and oral pathologists. However, this may result in interobserver variability which can hamper the intraoperative diagnosis of surgical margins. Thus, in the present study, we assessed the interobserver variability among general and oral pathologists in diagnosing intraoperative surgical margins.

In the present study, there was no evidence of dysplasia in 70% of the archival intraoperative margins that were examined by the general and oral pathologists. The presence of recurrence in histologically clear margins could be due to the concept of field cancerization, where the tissue harbours genetic alterations which may result in recurrence.<sup>9</sup> Studies have also found that 52% patients with negative margins expressed p53 mutations.<sup>10,11</sup> This suggests that post-operative processing and histopathological and immunohistochemical assessment of all the intraoperative margins should be done to prevent the overlooking of apparently 'clear' surgical margins.<sup>12</sup>

Mild and moderate dysplasia was seen in 8% of the archival intraoperative margins and frank invasion was seen in 18% of the margins evaluated by the general and oral pathologists. The presence of inadequate / positive surgical margins could be a reason for the recurrence in these patients.<sup>13,14</sup> Therefore, the surgical margins should be revised on table by the surgeon in case of inadequate margins during intraoperative diagnosis.<sup>15,16</sup>

There was only slight agreement (kappa value= 0.130) between the General and Oral Pathologists in grading the surgical margins. Two margins reported as adequate by oral pathologists were reclassified as invasive by the general pathologists. This could be due to the disparity in the number of cases reported by oral pathologists and general pathologists. General pathologists are exposed to increased number of cases and are trained in intraoperative frozen section diagnosis. Addition of intraoperative frozen sections, immunohistochemistry and advanced molecular techniques will add more arrows to the quiver in OSCC management.<sup>17</sup>

There was a slight disparity in identification of positive margins among general pathologists and oral pathologists. This could be due to larger volume of cases, and better experience.<sup>18</sup> Healthy case discussions with their general pathologist peers can aid the oral pathologists in arriving at an accurate

diagnosis. Frequent training programmes can be conducted in collaboration with general pathologists, and collaborative team reporting can be encouraged.<sup>19</sup>

In literature, there is no data reflecting upon the use of frozen section facilities in dental institutions for providing intraoperative histopathological clearance. Hence, all dental institutions should be equipped with a frozen section diagnosis facility and competent oral pathologists for reporting Oral Squamous Cell Carcinoma.<sup>20</sup> However, it should be followed by complete post-operative processing and histopathological and immunohistochemical evaluation of margins.

## CONCLUSION

All the dental institutions should have a frozen section diagnosis facility and competent oral pathologists to perform intraoperative histopathological evaluation of the surgical margin to ensure clearance of the margin. All the surgical margins must be completely processed and their histological and molecular evaluation must be done to minimize the chances of recurrence. Extensive training of oral pathologists must be conducted in collaboration with the general pathologists for accurate evaluation of margins.

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