



The Use of Frozen Sections in Buccal Mucosa Squamous Cell Carcinomas.

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ABSTRACT:

Introduction

Oral squamous cell carcinomas are highly prevalent in India, making them one of the most common types of cancer. The primary approach for treating oral squamous cell carcinomas is surgical excision, with complete surgical resection being the most reliable predictor of successful outcomes. In the final histopathology report, a margin of at least 5mm is considered negative. This study aimed to evaluate the diagnostic accuracy of intraoperative frozen section analysis in assessing tumour bed margins in patients with buccal mucosal squamous cell carcinoma.

Methods

A cross-sectional study was conducted at a tertiary care hospital in Jaipur, India. Between January 2021 and October 2022, a total of 127 patients with pure buccal mucosal squamous cell carcinoma were included in the study, and a total of 482 tumour margins were assessed.

Results

Among the 127 patients with pure buccal mucosa included in the study, 113 (89.0%) were males and 14 (11.0%) were females. The majority of these patients were classified as stage T2 (41; 32.3%) and T4 (44; 34.6%). Lymphovascular invasion was observed in 15 patients (11.8%), and perineural invasion was present in 8 patients (6.3%). Patients with worst patterns invasion 1, 2, 3 were 73 (57.5%) and 4,5 were 54 (42.5%) individuals, respectively. Metastatic lymph nodes were found in 54 (42.5%) of the patients, and 75 (59.1%) had a depth of invasion exceeding 7.50 mm. The frozen section revealed a positive predictive value of 75% and a negative predictive value of 99.3%. In comparison to the permanent section, the sensitivity of the frozen section was 50%, while the specificity was determined to be 99.79%.

Conclusion

The use of frozen section analysis is highly valuable in evaluating tumour margins. Although it demonstrates good diagnostic accuracy, strong clinical correlation is necessary to ensure optimal results.



Introduction:

The global incidence of oral cavity squamous cell carcinoma (OSCC) is increasing, particularly in southeast Asian countries where chewing tobacco is a common habit. According to GLOBACON 2020, OSCC is the 17th most common cancer in the world, accounting for 377,713 cases (2%) in 2020. In India, OSCC accounts for 135,929 cases (35%) in 2020, making it the second most common cancer and the third leading cause of death. Among males in India, OSCC is the most common cancer according to GLOBACON 2020. India bears a significant burden of oral cavity cancer globally, representing one-third of all cases(1). The high incidence of OSCC in India can be attributed to factors such as exposure to risk factors, lack of awareness, and delayed reporting, particularly among low-income groups(2,3). Oral squamous cell carcinoma (OSCC) accounts for about 84-97% of all oral cancer cases. Treatment for OSCC typically involves surgical excision, with complete removal of the primary tumor being a crucial prognostic factor for favorable outcomes(4,5). In the existing literature, a resection margin of 5 mm on the final histopathology report is considered adequate(6). However, frozen section does not guarantee disease-free resection on the final histopathology report(7). Studies have shown discrepancies between frozen section results and final histopathology reports, with positive margins found on the latter even when the frozen section reported negative(8,9). We conducted a study in our setting to determine how accurately is frozen sections in determining margins in compared to permanent sections in buccal mucosa squamous cell carcinoma patients. The findings from this study will assist head and neck surgeons in developing protocols and guidelines for the use of frozen sections in the management of oral squamous cell carcinomas.

Methodology:

In this study, we included patients who met the following inclusion criteria: biopsy-proven invasive squamous cell carcinoma with the epicenter in the buccal mucosa, at any stage without distant metastasis. We excluded patients with ulceration over the buccal

mucosa but negative biopsy for malignancy, non-squamous cell carcinoma of the buccal mucosa or other sub sites, distant metastatic disease of the oral cavity, prior oral or neck surgery, previous radiation or chemotherapy in the loco regional site, and co-existing malignancies.

This prospective study was conducted at a tertiary care hospital in Jaipur, India. Approval from the institutional ethical review committee was obtained, and data collection was done prospectively. A total of 127 patients presenting between January 2021 and October 2022 were included in the study. All the surgery was done by 5 surgical oncologist or trainee under their supervision and the decision to send frozen sections was based on clinical judgment during surgery. The buccal mucosa area was defined according to the AJCC 8th edition. A total of 482 frozen sections were sent for analysis in the treatment of these 127 patients.

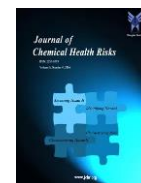
During surgery, frozen sections were reported by same pathologist who reports the final histopathology report. Subsequently, the outcomes of the frozen sections were compared to those of the permanent sections in order to ascertain the sensitivity, specificity, as well as the positive and negative predictive values.

The statistical analysis was performed using SPSS software (version 26, SPSS Inc., Chicago, IL). To evaluate the accuracy of frozen sections in determining tumor-free margins, the sensitivity, specificity, positive predictive value, and negative predictive value were analyzed.

Result - In the study population of 127 individuals, 113 (89.0%) were males and 14 (11.0%) were females. The majority of patients were classified as stage T2 (41, 32.3%) or T4 (44, 34.6%). Lymphovascular invasion was observed in 15 (11.8%) patients, while perineural invasion was present in 8 (6.3%) patients. Patients with invasion patterns 1, 2, and 3 accounted for 73 (57.5%) individuals, while patterns 4 and 5 had 54 (42.5%) cases. Among the study population, 54 (42.5%) patients had metastatic lymph nodes, and 75 (59.1%) patients had a depth of invasion greater than 7.50 mm, well differentiated grade were 71(55.9%)

Table 1. Descriptive statistics for clinical parameters measured for the patients.

Variables		Number (%)
Gender	Male	113 (89.0%)
	Female	14 (11.0%)
Size of the tumour (T)	T1	16 (12.6%)
	T2	41(32.3%)
	T3	26 (20.5%)
	T4	44 (34.6%)
Lymphovascular Invasion	Not Seen	112 (88.2%)
	Seen	15 (11.8%)
Perineural Invasion	Not Seen	119 (93.7%)
	Seen	8 (6.3%)
Worst Pattern of Invasion	I, II, III	73 (57.5%)
	IV &V	54 (42.5%)



Metastatic Lymph node	No Nodes	73 (57.5%)
	Metastatic Lymph node	54 (42.5%)
Depth of Invasion (mm)	< 7.50 mm	(40.9%)
	> 7.50 mm	75 (59.1%)
Grades of tumour	Well	71(55.9%)
	Moderately, poor	56(54.1%)

The surgical resection continues until a negative margin is attained during the frozen section. Among the four positive margins identified in the frozen section, one was reported as negative in the permanent paraffin-

embedded sections. Conversely, out of the 478 negative margins identified during the frozen section, three were determined to be positive in the permanent paraffin-embedded sections.

sensitivity	50%
specificity	99.79%
positive predictive values	75%
negative predictive values	99.3%
diagnostic accuracy	99%

Frozen section	Permanent section			Total
	Positive	Negative	Total	
Positive	3	1	4	
Negative	3	475	478	
Total	6	476	482	

Table 2 - 2x2 table showing the comparison between permanent section and frozen section

Discussion -

Surgery serves as the primary treatment buccal mucosa squamous cell cancers, with the aim of achieving clear margins. However, identifying clear margins solely based on the surgeon's judgment during the operation may be fallible due to the presence of microscopic disease that can be easily missed. Even with adjuvant therapy close margin or positive margin has a high risk of local recurrence and poor overall survival. A study by Datta et al. revealed that 8.6% of patients exhibited microscopic spread beyond the gross disease margins [10]. Thus, frozen sections play a significant role in assessing margins in detail and providing timely information to surgeons during the operation. In Gerber et al. Study, the five-year overall survival in clear margin was 60% compared to 52% for involved resection margins. Similarly, the rate of recurrence was double (36%) in patients with positive tumor margins compared to those with negative tumor margins [11].

The accuracy of determining tumor-free margins through frozen sections in the resection of oral cavity cancers ranges from 96% to 98%. In our study, we found that the sensitivity of frozen sections compared to permanent sections was 50%, while the specificity was 99.79%. The positive predictive value was 75%, and the negative predictive value was 99.3%. The overall accuracy of the diagnosis was reported to be 99%, which is consistent with existing literature [7,8,12]. However, the low sensitivity may be attributed to only six samples testing positive in the final histopathology analysis.

Out of the positive margin cases, three patients were correctly identified using frozen sections and underwent further tissue removal. However, one patient was incorrectly identified as having positive margins, leading to unnecessary excision of excess tissue. Additionally, three patients had false-negative results on frozen sections but were found to have severe dysplasia on analysis of paraffin-embedded sections, causing the histopathologist to label them as positive margins. Margin shrinkage during the resection of oral cavity cancers is often overlooked. Tumor margins can undergo shrinkage, resulting in a close resection margin on the final histopathology report. Their recommendation was to ensure the resection of at least 8-10 mm of healthy tissue to negative more than 5 mm [13,14].

In conclusion, frozen sections are highly valuable in evaluating tumor margins and aiding surgeons in determining the adequacy of resection in oral cavity squamous cell carcinomas. Although frozen section has a high specificity, its sensitivity is low when compared to final histopathological report. This could be attributed to the low rate of positive final tumour margins overall and the intrinsic incapacity of tumour bed frozen margin analysis to appropriately account for the 3-dimensional association of tumour margins with the specimen's periphery.

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