



Original Research Article

Accuracy of intraoperative frozen section in assessing margins in oral cancers: A tertiary care hospital based study

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ABSTRACT

Introduction: To study the accuracy of intraoperative frozen section diagnosis in assessing margins in oral cancer resection. But reliability of frozen sections in predicting the ultimate final margin status is unknown. We compared frozen and permanent reads to identify risk factors for overall discrepancies between intraoperative and final margin status.

Aims and Objective: To evaluate the role of frozen section diagnosis as a guide in resection of oral cancer lesions.

Material and Methods: Pathology reports of 284 surgical resections specimens between 2018 and 2020 were retrospectively reviewed. A total of 104 cases (470 margins) met inclusion criteria. The reports of frozen sections are compared with the results of histologic findings obtained by routine paraffin embedded Haematoxylin and Eosin method.

Result: The comparison of the section from margins i.e. anterior, posterior, medial, lateral and deep, altogether 470 margins from 104 patients showed concordance in 437 margins, i.e. 446 margins were negative in both frozen section and Paraffin method and 16 margins were positive in both frozen section and Paraffin method. 22 margins were positive in paraffin method. 18 margins were positive in frozen section. The eight margins showed disagreement in frozen section and paraffin embedded Haematoxylin and Eosin method.

Conclusion: Individual frozen section reads are highly accurate. However, negative intraoperative margins do not guarantee margin-negative resections. The process of selecting representative margins for intraoperative analysis should be refined. The surgeon and the pathologist must understand the limitations of frozen sections.

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1. Introduction

Frozen section evaluation is a key technique used by the pathologists during the intraoperative consultation.¹ It plays a very important role in the surgical management of patients with neoplastic disease and it is an essential component for a surgical theatre complex. The modern frozen section as practiced today was developed by Dr. Louis B Wilson in 1905.² It is routinely used by the surgeons of various specialties for rapid assessment of presence of tumor in tissues, the most common being the surgical margins.³

Intraoperative frozen section assessment of surgical margins is a widely used practice in head and neck surgery.⁴ The best chance of surgical cure in oral cancer is complete removal of all malignant cells. Unfortunately, it is not possible to identify the microscopic extent of the tumor invasion by inspection and palpation.⁵

The ability to surgically remove cancers with negative margins has significant impact on local tumor recurrence and overall survival for patients with head and neck squamous cell carcinomas.^{5,6}

The use of frozen section is varied. Frozen section help in the rapid diagnosis of the lesions and in intraoperative histological evaluation of tumor resection borders and in determining the adequacy of the surgical margins. They

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are also useful in determining whether a tumor is benign or malignant, so that the extent of the resection can be decided.⁷

Further, the decision to perform a radical surgery of lymph nodes is entirely dependent on the frozen section. This is done without prolonging the surgery and thus acts as a guide to the surgeon in making a therapeutic decision, while the patient is still on the operating table.⁸

Errors in diagnosis are most often due to difficulty in recognition of certain types of lesions, inadequate sampling, technical problems or the lack of communication between the surgeon and pathologist.⁹

As the diagnosis made by pathologist from frozen section may have serious consequences for the treatment of the patient, a high degree of accuracy is mandatory. Considering the above factors, this study was performed to evaluate the accuracy of intraoperative frozen section microscopy in assessing the margins in oral cancer.

2. Material and Methods

A retrospective study was conducted to evaluate the efficacy and accuracy of a frozen section in oral cancer involving 104 cases (470 margins). Data was collected from the records of the frozen section reports of oral cancer patients who underwent resections which had intraoperative consultations involving frozen sections were considered, during the period from January 2018 to December 2019 at Shri Ram Murti Smarak Institute of Medical Sciences Bareilly.

2.1. Inclusion criteria

Patients with small biopsy-proven oral carcinoma prior to the frozen section, of all age groups with no sex predilection were included in the study.

2.2. Exclusion criteria

Patients with prior history of oral cancers, prior treatment (such as excision biopsy, nodal biopsy, radiotherapy) and lack of positive histopathology were not included in the study.

The tissue was taken as samples from the margins of the resected specimen marked by surgeons for suspicion of invasion. So we sampled either three or more margins either anterior, posterior, medial, lateral or deep, from patients who are undergoing surgical resection for malignancies. Each of the samples obtained were evaluated by both the frozen sections and routine paraffin sections and compared.

The apparatus used was THERMO FSE 1508. The section selected for frozen section study was placed on the embedding media which was poured on dry surface of the chucks. The chuck with tissue and embedding media were kept in cryostat cabinet. The cryostat cabinet was adjusted to a temperature OF -30°C. The microtome apparatus in the

cryostat is of rotary type, where the head part containing the tissue is mobile, while the knife part remains stationary. With the help of anti-roll guide, unfolded frozen sections of 6 microns thickness were obtained and the sections were placed on glass slides. The sections get attached to the glass slide due to difference in temperature. Haematoxylin and eosin staining procedure for frozen sections were done.

Similarly, Haematoxyline and Eosin staining procedure for paraffin sections were also done. The frozen sections were prepared immediately and examined by pathologist. The results of these sections were compared with the results of histologic findings obtained by routine paraffin embedded heamatoxylin and eosin method.

Details of the frozen section reports were collected along with age, gender and diagnosis. Reports of Frozen section were analyzed for tumor, surgical margins and lymph node metastasis. For all cases reported as positive margin, re-resections were done and all specimens were sent for routine margin analysis. Permanent section diagnosis is widely considered to be the datum in this diagnosis area.¹⁰ Reports were cross checked with the corresponding paraffin sections and analyzed for any mismatches.

We classify the margins on frozen section as "positive" when margin showed tumor deposits either in form of invasive carcinoma or carcinoma in situ, "close" when distance of tumor from resected margin was less than 5 mm and "negative" when distance of tumor from resected margin was either 5mm or more than 5 mm.

When frozen sections were diagnosed as moderate dysplasia or more advanced lesions, pathologists recommended the additional removal of surgical margins.

The statistical analysis for sensitivity, specificity, false positivity, false negativity, predictive value of positive test, predictive value of negative test and accuracy have all been determined.

3. Results and Observation

The evaluation and comparison of frozen sections with that of paraffin sections in assessing margins of oral squamous cell carcinoma of 104 patients were done and 470 sections analyzed.

Out of the 104 patients, 59 (56.4%) were males, and 45 (43.6%) were females. A slight male preponderance with a male to female ratio of 1.17:1 was noted [Figure 1]. The age of the patients varied from 27 year to 91 years. The maximum incidences of cases were seen in the age range of 51-60 years [Figure 2].

The comparison of the section from margins i.e. anterior, posterior, medial, lateral and deep, altogether 470 margins from 104 patients showed concordance in 462 margins, i.e 446 margins were negative in both frozen section and Paraffin method and 16 margins were positive in both frozen section and Paraffin method. 22 margins were positive in paraffin method. 18 margins were positive in frozen section.

Gender distribution

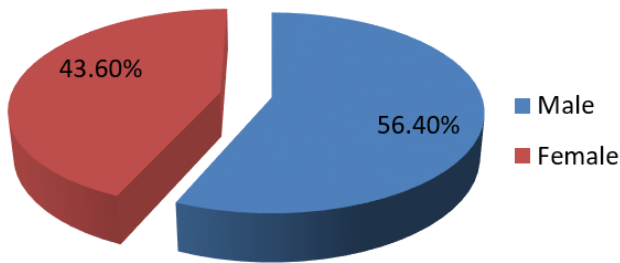


Fig. 1: Gender distribution

Age wise distribution

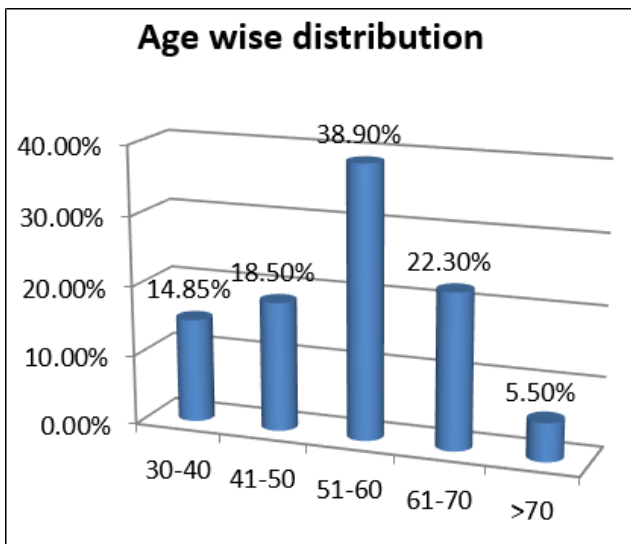


Fig. 2: Age wise distribution

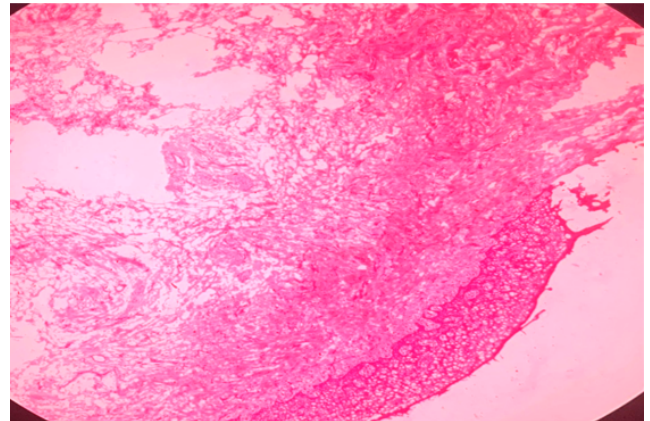


Fig. 3: Negative Margin. Frozen section (H&E) (4x)

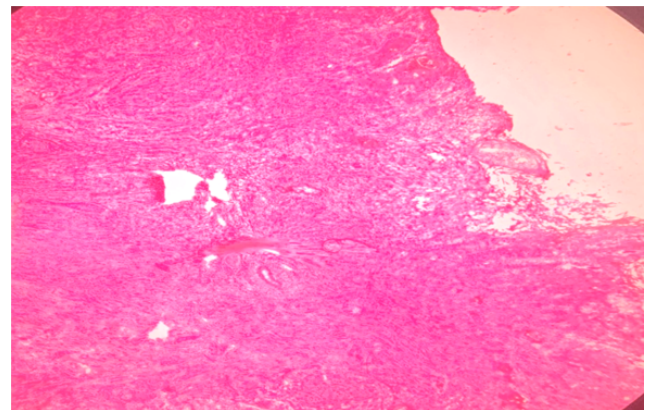


Fig. 4: Positive margin frozen section (H&E) (4x)

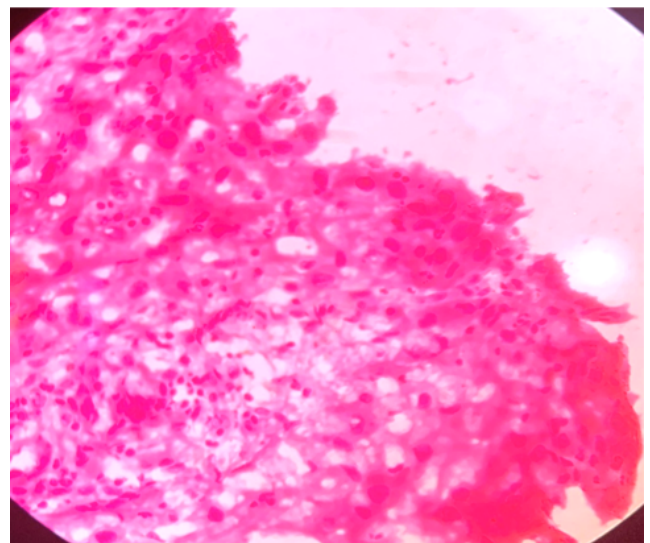


Fig. 5: Positivemargin frozen section (H&E) (40x)

The eight margins showed disagreement in frozen section and paraffin embedded Haematoxylin and Eosin method [Table 1].

Statistical analysis was done. There was two false positive and six false negative cases [Table 2]. The percentage of sensitivity, specificity and accuracy were 78.57, 99.55, and 98.32 respectively. The predictive values of positive test and negative test were 91.66 & 98.67 [Table 3].

4. Discussion

Frozen section analysis during intraoperative consultation is an important tool in ensuring adequate margin clearance^{10,11} & to obtain a definite immediate diagnosis, on the basis of which surgical decision will be made.

Achievement of an adequate tumor free margin is the aim of head and neck squamous cell carcinoma surgery, as it is a well known predictor of local failure and distant failures.¹⁴ Considering that there may be shrinkage of surgical margin (31% to 46%) at the time of paraffin section,

Table 1: Findings of microscopic evaluation of margins

No. of cases	Number of margins evaluated	Presence of carcinoma in frozen section	Presence of carcinoma in paraffin section	Negative frozen section	Negative paraffin section
104	470	18	22	452	448

Table 2: Tabulation of true positive, true negative, false positive, false negative results

No of cases	Number of margins evaluated	True Positive	True Negative	False Positive	False Negative
104	470	22	448	01	04

Table 3: Comparative statistical analysis of frozen sections with paraffin sections

No. of cases	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Efficiency(Accuracy) (%)
104	84.61	99.77	95.65	98.67	98.32

Table 4: Comparison of concordance rates reported in different series

Authors	Accuracy (%)	Sensitivity (%)	Specificity (%)
DiNardo et al ¹² (2000)	98.3	86.8	98.9
Sharma SM et al ⁷ (2008)	96.74	2.0	99.41
DU et al (2016) ¹³	96.7	83.1	97.9
Present study	98.32	78.57	99.55

most surgeons aim at 8 to 10 mm of margins during surgery to achieve a 5 mm tumor free margin.⁴

Immediate diagnosis allows the surgeon to proceed with further therapy without any kind of delay. A definite immediate diagnosis is said to be dependent on the reliability of frozen sections.¹⁵ Many authors have carried out frozen section study on soft tissue tumors and margins evaluation in the different parts of body, with varying percentages of reliability.^{12,16}

Frozen sections have been used both in the diagnosis and to evaluate margins. In most publications, accuracy for such diagnosis is 96.8% to 98%.^{7,13,15,17} The diagnosis on lesions in different regions of the body were varied in their accuracy form 91.5% to 98%,¹⁰ and in head and neck neoplasm 96% to 99%.^{3,7,17}

There are essentially two main sources of frozen section errors. An error can be interpretive wherein the pathologist makes an incorrect histologic diagnosis. Distortion of the tissue architecture during the freezing process, uneven sectioning, or poor staining can all increase the likelihood of this form of error. When in doubt, the pathologist defers diagnosis. Although not as satisfying as a definitive diagnosis, it is preferable to an interpretive error.

Specimen processing adds further potential for sampling error because usually only a portion of the frozen section specimen is sectioned and embedded for immediate evaluation.

The limitation of present study was that there was small sample size and not too good collaboration between

surgeon & pathologist. Future improvements in the margin evaluation through the development of molecular tumor markers may further diminish errors.

5. Conclusion

Frozen section is a helpful tool in intraoperative decision making in indicated situations. The results are highly specific but only moderately sensitive compared with the final margins from the resections specimens. It is shown that frozen sections were beneficial in the present series as, patients who had positive results required revision of margins. The surgeon and pathologist must understand the limitations of frozen section and attempt to minimize the cost and sampling error. However, intraoperative molecular analysis of surgical margins may eventually be developed as the 'state of the art' method for cancer surgery.

6. Source of Funding

None.

7. Conflict of Interest

None.

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