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Intraoperative Evaluation Of Resected Bony Margins Using Frozen Section Analysis And Trephine Drill Extraction Technique-A Systematic Review

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Abstract-
Introduction:
In Oral & Maxillofacial Surgery, achieving precise and accurate intraoperative assessment of bone margins is paramount for successful outcomes. This systematic review aims to comprehensively evaluate the utility and effectiveness of two commonly employed techniques for this purpose: frozen section analysis and the trephine drill extraction method.
Methods:
A systematic review of literature was done across a wide array of databases, including Cochrane Library, Embase, and PubMed from inception to the present. Studies focusing on the assessment of intraoperative bony margins in Oral & Maxillofacial Surgery utilizing frozen section analysis and the trephine drill extraction method were included. Quality assessment was performed using established criteria, and relevant data were extracted for synthesis.
Frozen Section Analysis:
Frozen section analysis has emerged as a widely used method for intraoperative assessment of bone margins. The literature suggests that this technique offers real-time evaluation, allowing surgeons to make immediate decisions regarding the extent of resection. Our review includes studies investigating the diagnostic accuracy, sensitivity, and specificity of frozen section analysis in various oral and maxillofacial surgical procedures. We discuss the implications of its use in achieving tumor-free margins and the impact on patient outcomes.
Trephine Drill Extraction Method:
The trephine drill extraction method is another approach gaining attention in the assessment of bone margins. This technique involves the use of a trephine drill to extract a core sample for histopathological analysis. We present findings from studies exploring the feasibility and reliability of the trephine drill extraction method, considering its potential advantages over traditional methods. Insights into its application in different surgical scenarios, such as tumor resections and osteotomies, are discussed.
Comparative Analysis:
A critical aspect of our review involves a comparative analysis of the two techniques. We evaluate their respective strengths, limitations, and applicability in different clinical contexts. Factors such as turnaround time, cost-effectiveness, and ease of integration into routine practice are considered. The goal is to provide clinicians with evidence-based guidance on selecting the most appropriate method for intraoperative bone margin assessment in specific scenarios.
Clinical Implications:
The synthesis of available evidence in this review accords to a deeper understanding of the limitations and strengths of frozen section analysis and the trephine drill extraction method. Clinicians can use this information to make informed decisions regarding intraoperative bone margin assessment, ultimately optimizing surgical precision and patient outcomes in Oral & Maxillofacial Surgery.
Conclusion:
This systematic review offers a comprehensive analysis by the assessment of intraoperative bony margins using analysis of the frozen section and the trephine drill extraction method in Oral & Maxillofacial Surgery. By synthesizing current evidence, we provide valuable insights into the diagnostic accuracy, feasibility, and

comparative effectiveness of these techniques. This knowledge aims to guide clinicians in enhancing the precision of bone margin assessment, ultimately contributing to improved patient outcomes in diverse surgical scenarios.
Keywords- *Frozen section analysis, Trephine drill extraction, intraoperative evaluation, bony margin*

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I. Introduction

Intraoperative evaluation of bony margins refers to the assessment and examination of surgical bone margins during a surgical procedure. [1] This evaluation is typically performed to ensure complete resection of a tumour or to assess the adequacy of bone removal in procedures such as orthopaedic surgeries or tumour excisions.

Visual inspection is the initial step in evaluating bony margins during surgery. Surgeons visually examine the bone surfaces to assess for any visible tumor tissue or irregularities. This can be done using direct visualization or with the assistance of surgical magnification devices, such as surgical loupes or microscopes. Palpation involves using tactile feedback to assess the bone margins. Surgeons use their sense of touch to feel for any irregularities or abnormal tissue. Palpation can help identify subtle changes in bone texture or detect any remaining tumor or abnormal growth.[2]

A method of real-time imaging technique that uses X-rays to create dynamic images of surgical site is known as fluoroscopy.[3] It can be used to assess bony margins during orthopedic procedures, allowing surgeons to visualize the bone anatomy, alignment, and resection margins in real-time. In some cases, intraoperative techniques of imaging such as intraoperative CT (computed tomography) or intraoperative MRI (magnetic resonance imaging) may be used to obtain detailed images of the bone and surrounding tissues. These imaging modalities can provide high-resolution images to assess the bone margins and ensures resection of the tumour completely.[3]

Analysis of the frozen section involves the rapid freezing and subsequent microscopic examination of a tissue sample obtained during surgery. It provides quick histopathological information about the presence of tumor cells at the margin. The surgeon can receive preliminary results during the surgery, which can guide further decisions on the extent of bone resection. Specimen radiography involves obtaining X-ray images of the excised bone specimen. This technique allows surgeons to evaluate the margins of the excised bone outside the patient's body. Radiographs can help confirm if the tumor has been completely removed or if additional resection is necessary.[4]

The choice of intraoperative evaluation method depends on the surgical procedure, the nature of the pathology, and the available resources. These techniques aim to ensure complete tumor resection, minimize the risk of recurrence, and preserve healthy bone tissue. Intraoperative assessment of bony margins is crucial to optimize surgical outcomes and provide the best possible patient care.

Frozen Section Analysis Procedure

During a surgical procedure, the surgeon collects a tissue sample from the patient. The sample may be obtained from a suspicious lesion, tumor, or other specific sites of interest. The tissue is carefully handled to preserve its integrity and prevent any damage or contamination. The tissue sample is immediately transferred to the pathology laboratory and prepared for freezing. To ensure optimal preservation of tissue morphology, the sample is typically embedded in optimal cutting temperature (OCT) compound or immersed in a cryoprotectant solution. These measures help protect the tissue during the freezing process.[5]

The cryostat is a specialized instrument used for the freezing and sectioning of tissue samples. It is set to a low temperature, often around -20 to -30 degrees Celsius, and stabilized before use. The cryostat may utilize liquid nitrogen or other cooling methods to achieve the desired temperature. Once the cryostat is ready, the tissue sample is firmly secured onto a specimen holder or chuck. The frozen tissue block is mounted onto the microtome within the cryostat. The microtome enables controlled slicing of the tissue into thin sections. The sections are typically cut at a thickness of 5 to 10 micrometers, although this can be adjusted as needed. [4,5]

The freshly cut tissue sections are placed on glass slides, which are then subjected to various staining techniques. The most common stain used in frozen section analysis is haematoxylin and eosin (H&E). H&E staining provides contrast, highlighting cellular details and tissue structures. Additional specialized stains or immunohistochemical stains may be used for specific diagnostic purposes, depending on the suspected pathology. After staining, a pathologist analyses the slides under a microscope. The pathologist observes the cellular architecture, morphology, and any abnormalities present in the tissue sections. They assess cellular features, such as cell size, shape, nuclear characteristics, and the presence of any pathology. The pathologist makes a preliminary diagnosis based on the observed findings.[5]

The pathologist communicates the preliminary findings of the frozen section analysis to the surgical team, including the surgeon. The immediate results aid the surgeon in making real-time decisions during the ongoing surgical procedure. The pathologist may provide information regarding tumor margins, the presence of malignancy, or other relevant factors to guide the surgical intervention. The findings of the frozen section analysis are documented in the patient's medical records. If necessary, the remaining tissue sample can be processed for permanent histopathological analysis by formalin-fixation and paraffin embedding. This allows for a more comprehensive examination and final diagnosis.

It is important to note that frozen section analysis provides rapid results that aid in intraoperative decision-making. However, it is considered a preliminary assessment, and the final diagnosis may be confirmed or modified based on additional analyses performed on, paraffin-embedded, formalin-fixed tissue sections.

The frozen section analysis process requires skilled personnel, specialized equipment, and proper handling of the tissue samples to ensure accurate and reliable results.

Trephine Drill Extraction Technique

The patient is prepared for the procedure, which may involve general anaesthesia , conscious sedation, or local anaesthesia depending on the patient's needs and the complexity of the extraction. The surgical site is sterilized, and the surrounding area is draped to maintain a sterile field. An appropriate incision is made at the surgical site to access the bone or tissue that requires extraction. The incision size and location depend on the specific procedure and the anatomical site. Soft tissue flaps may be created and retracted to gain better access to the underlying bone or tissue. The trephine drill size is chosen based on the desired diameter of the extracted specimen. The trephine drill typically consists of a hollow cylindrical cutting instrument with a sharp outer edge and an inner core.

The trephine drill is carefully positioned and aligned perpendicular to the surface of the bone or tissue. The surgeon applies gentle pressure while rotating the drill to initiate the cutting process. The drill is gradually advanced into the bone or tissue until the desired depth is reached. As the trephine drill rotates, its sharp cutting edge creates a circular incision in the bone or tissue. The drill gradually removes the central circular section, called the trephine core or specimen. The extracted specimen is carefully lifted out using forceps or other appropriate instruments. Great care is taken to avoid damage to the surrounding structures.

Any bleeding from the extraction site is controlled using various haemostatic techniques, such as cauterization, pressure, or the use of haemostatic agents. The surgeon inspects the extraction site to ensure complete removal of the specimen and assesses the surrounding bone or tissue for any remaining fragments or irregularities. Depending on the procedure and the incision size, the wound may be closed with sutures, adhesive strips, or other closure techniques. The wound is dressed with appropriate dressings, and postoperative care instructions are provided to the patient, including pain management and wound care.

The extracted specimen is carefully handled and preserved according to the specific requirements of the procedure. It is usually sent to the pathology laboratory for further analysis, such as histopathological examination, which helps in diagnosing and determining the appropriate treatment or management plan. It is important to note that the trephine drill extraction technique may vary in details depending on the specific surgical procedure, such as bone grafting, biopsy, or implant placement, as well as the anatomical site and the surgeon's preferences and expertise. [7]

BACKGROUND

Objective

Intraoperative assessment of bone margins using analysis of the frozen section and extraction via trephine drill method.

Focused Pico Question

POPULATION (P): Patients suffering with oral cancer.
INTERVENTION (I): Patients who underwent bony frozen section analysis.
COMPARISON (C): Patients who underwent bony excisional histopathological analysis.
OUTCOME (O): The main outcome of this study was effectiveness in evaluating tumor infiltration of bony margin intraoperatively

Protocol And Registration

This systematic review is registered in PROSPERO

Need For The Study

The evaluation of bone margin infiltration is a critical aspect in surgical procedures involving bone, such as tumor resections, orthopedic surgeries, and bone grafting. It is very essential to assess if tumor cells are present or absent near the surgical margins, for determining the adequacy of the surgery and guiding further treatment decisions. Both frozen section analysis and histopathological analysis play important roles in this evaluation, and understanding their effectiveness is essential. In summary, frozen section analysis provides rapid, real-time results for evaluating bone margin infiltration during surgery, allowing immediate decision-making. However, it has limitations such as limited sample size, potential artifacts, and interpretation challenges. Histopathological analysis, on the other hand, offers a comprehensive assessment of the tissue sample with high-quality staining but requires additional processing time and lacks real-time guidance. Both techniques are complementary and have their roles in the evaluation of bone margin infiltration, with the final diagnosis and treatment decisions often relying on the comprehensive analysis provided by histopathological examination. Hence, the aim of the present study is to compare the efficacy of frozen section analysis vs histopathological analysis in the English literature that has already been published.

II. Materials And Methods

Study Protocol and Registration

This systematic review was conducted in compliance with the PRISMA guidelines.

Articles had been obtained from internet-based sources on September 19, 2022. This review was registered in PROSPERO under the registration number CRD42023479444.

Research Questions

What is the effectiveness of frozen section analysis vs histopathological analysis in evaluating tumor infiltration of bony margin intraoperatively?

Search Strategy

A complete search of the data was performed across various internet databases for research articles in full text published till December 2022 using the keywords issued. Table 1 shows the total number of studies collected from each database. Using the Medical Subject Heading keywords, research articles in full text were carried out online in three journal databases. The articles assessed were from the Web of Science, PubMed and Scopus.

((((((((oral cancer) OR (oral carcinoma)) OR (oral squamous cell carcinoma)) OR (cancer of oral cavity)) OR (mouth cancer)) OR (tumor of oral cavity)) OR (oral neoplasm)) AND (((((((frozen section) OR (bony frozen section analysis)) OR (bony margin)) OR (alveolar margin)) OR (bony resection margin)) OR (bony surgical margin)) OR ((trephine drill) OR (trephine)) OR (drill) OR (trephination) OR (drilling))) AND (((((((microscopic study)) OR (histopathological study)) OR (microscopic analysis)) OR (histopathological analysis)) OR (microscopic evaluation)) OR (histopathological evaluation))) AND ((((((tumor infiltration) OR (tumor invasion)) OR (tumor positive margin)) OR (cancer positive margin)) OR (tumor penetration)) OR (tumor seeding))

Selection Criteria

The following were the selection criteria:
1. published peer-reviewed works that are included in the Scopus, PubMed, or Web of Science indexes.
2. Research papers published in English.

The criteria used for elimination include:
1. manuscripts that are yet to be released.
2. Research not comparing conventional neck dissection with endoscopic or robot-assisted neck dissection
3. A publication not published in English.

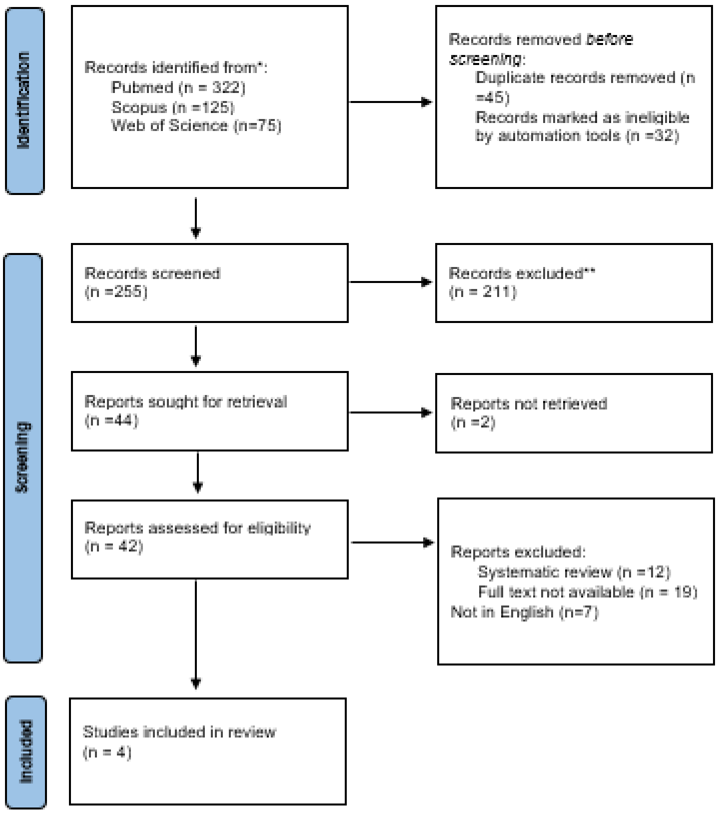
Type of Studies Included

All Randomized Clinical trials and retrospective study pertaining to oral cancer categorized into two groups, one with frozen section analysis and another with histopathological analysis were performed.

Data Extraction (Selection and Coding)

The primary review authors (S.N.) independently screened the titles and abstracts of the literature search result together with an assigned co-screener (S.P.L) provided supervisory oversight and validated the selection process. Disagreements were resolved through discussions, and the final decision was made by S.P.L. The full-text articles were then independently screened for inclusion and further processing. As needed, corresponding authors were contacted to provide the missing information. A distinctively customized Excel sheet was fabricated to register the data obtained from the studies.

Data Extraction And Analysis
Prisma
PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only



Data Extraction

Authors	Type of study	Study duration	Sample	Diagnosis	Population	Lymph nodes examined	Lymph nodes affected	Depth of invasion	Perineural invasion	lymphovascular invasion	WPOI	Resection technique
Berat Demir [5]	retrospective	January 2018 and 2019.	181	squamous cell carcinoma	118 (65.2%) were males, 63 (34.8%) females, and the mean (+SD) age was 57.4 + 16.1years	27.8 + 22.4	3.0 + 2.2	11.9 + 8.5	88 (48.6%),	43 (23.8%)	11 (6.1%)	
Markus Nieberler [17]		2010 and 2013		squamous cell carcinoma	73; there were 50 men and 23 women with a mean age of							

					56 years							
Andreas Wysluch [18]	2010	2006 to 2007,		squamous cell carcinoma	20 consecutive patients (age, 39–88 years; mean age, 67 years; 13 women, 7 men)							Floor of mouth- 25% Retromolar- 75%
Kyle J. Chambers, [19]	Retrospective	2010 and 2013	41	squamous cell carcinoma	Thirty-one (75.6%) were male and 10 (24.4%) were female				14 (73.7) 5 (26.3	7 (63.6) 4 (36.4)		

Interpretation Of Risk Of Bias Analysis-

The present systematic review evaluated the following attributes of the included studies: study design, sample size, and period of follow-up. Formal risk of bias assessment tools, using the ‘Newcastle–Ottawa’ scale for evaluation of potential biases. The studies will be evaluated by two independent reviewers, with a third reviewer being consulted, if there are any disagreements which shall be resolved with a proper discussion. The systematic evaluation of study characteristics and risk of bias will ensure the reliability and validity of the review's findings.

Using the tool, each study is assessed according to eight criteria that are categorized into the following: selecting the study groups, evaluating the comparability of the groups, and identifying the exposure or result of interest for cohort or case-control or studies, respectively. Each quality item is given a star, which acts as a rapid visual evaluation. The best calibre research receives up to nine stars in the star system. The University of Newcastle in Australia and the University of Ottawa in Canada collaborated to develop the approach, which defined variables for data extraction through a Delphi process. After then, the scale was improved and tested using systematic reviews. Additionally, it has been modified for ubiquity. The maximum score of 6 was by one study and score of 5 was by three studies. The studies were of fair quality.

III. Results

Demir et al. reported a mean age of 57.4 ± 16.1 years among 181 patients who had surgery for oral malignancies; 118 (65.2%) were males and 63 (34.8%) were females in the study by Berat Demir. Most commonly occurring sites for oral cancers were the tongue (n = 71, 39.2%), palatal mucosa (n = 18, 10%), the lower gingivobuccal sulcus (n = 15, 8.3%), mucosa ofthe floor of the mouth (n = 18, 10%), retromolar trigone (n = 16, 8.8%), and the upper gingivobuccal sulcus (n = 9, 4.9%). The mean (±SD) quantity of lymph nodes was assessed and it showed that the nodes impacted were 27.8 ± 22.4 and 3.0 ± 2.2, in that order. Mean of Depth of invasion was found to be 11.9 ± 8.5 (range 1-40) mm (±SD). On the whole, grades of 1, 2, 3, and 22 (12.2%), 37 (20.4%), 72 (39.8%), and 50 (27.6%) individuals were obtained. Of the patients, 6 (3.1%) had discrepancies. Out of the six individuals who have been identified to have a positive result following a permanent pathological investigation three had false negative results. In two patients, the discrepancy was caused by a sample error; however, in the other patient, the study of the permanent sections revealed an interpretation error. Even though 2 (1.1%) of the patients had frozen sections diagnosed with malignancies, the malignancies were found to be negative in the permanent pathology.[5]

The ICAB depicted a sensitivity of 95.3% and a specificity of 96% in the initial patient population in the study by Nieberlel et al. The findings showed a 95.7% accuracy rate, a substantial correlation between the histology and cytological data, and correspondingly high and low predictive values of 93.8% and 96.9%. ICAB showed 80% sensitivity, 98.9% specificity, and 98% accuracy in the validation cohort. The cytological and histological results showed a substantial correlation (κ, 0.91; P <.001), with 80% and 98% for the positive and negative predictive values, respectively. At bone margins, ICAB might predict the status of final resection with a sensitivity of 80% and a specificity of 97.5%. At the bone margins, there is substantial correlation between the histological and cytological resection status.[17]

20 patients' worth of 84 trephine specimens were examined using the frozen section and decalcification techniques in the study by Andreas Wysluch. Nineteen out of the eighty-four specimens had tumour infiltration of the bone according to the final evaluation (decalcified standard processing). Out of 84 samples, 5 (6%) had a mismatch between the usual decalcification of bony boundaries and the results of intraoperative frozen-section examination. It was determined that four patients (4.8%) lacked tumour invasion. Nevertheless, during the decalcification procedure, they demonstrated bone degradation caused by the tumour. A single case (2.4%) was determined to have a tumour, however a routine decalcification revealed no invasion. Overall, there was a 94% concordance between the decalcification analysis and the intraoperative frozen-section analysis.78.9% sensitivity and 98.5% specificity were assessed for frozen-section analysis.[18]

The findings for specificity and sensitivity by patient (n = 20) and bony margin (n = 35 resected margins) were further examined. It might be computed to have a sensitivity of 77% versus 80% and a specificity of 90% versus 95%. Nine individuals underwent segment resections in total. In two cases (22%), the invasion by cancer was confirmed by histopathology. Seventy-six percent of the specimens showed evidence of tumour infiltration, whereas 89% of them were compatible with the conclusive histologic result. In frozen-section analysis, twenty-four percent did not exhibit a discernible histologic tumour infiltrate. Five of the specimens listed above were misdiagnosed in the segment resection group. [18]

Margin resections were performed on seven individuals, or 35 percent. Standard decalcification processing indicated no histological tumor infiltration in six (86%) of them. There were no tumours found in 94% of the excised bone specimens.

Based on the database, Chamber et al found 41 cases in total. There were 31 men (75.6%) and 10 women (24.4%). 43 to 85 years old was the age range, with 74.1 years being the mean. Referrals for recurrent cutaneous SCC came from twenty-two cases (53.7%). Initially, micrographic surgery was used in a total of 9 patients (40.9%), extensive excision locally was done in 4 patients (18.2%), and a modality of unknown excision was done in 9 patients (40.9%) of the patients who were referred due to recurrent disease. Most tumours were found on the cheek (26.8%) or scalp (43.9%). Additionally, tumours were discovered on the eyelid (2.4%), nose (4.9%), lip (4.9%), and ear (17.1%). The average size of the tumour defect was 5.1 cm (62.9 cm), and after processing the 2-mm surrounding tissue was excised as a margin, there were an average of 6.0 frozen specimens per patient. A lymphovascular invasion was found in 11 instances (26.7%). In 19 (46.3%) of the cases, perineural invasion was found.[19]

In the study by Chambers et al. 10 of the 247 (4.0%) frozen-section specimens and in 8 of the forty-one cases (19.5%) discrepancies were found between margins of the frozen section margins and that of the permanent. There was a disparity between the permanent section & frozen section and in four cases of cheek tumours (36.4% of all tumours) and four cases of scalp tumours (22.1% of all tumours). The false-negative rate for tumours that had priorly undergone Mohs resection was 44.4%, while the false-negative rate for recurrent tumours that were resected using a different method was 17.3%. A false-negative rate of 8.7% was linked to tumour defect larger than 4 cm, which was less than the 35.3% false-negative rate for a tumour defect less than four centimeters. [19]

In summary, the tongue was the most frequently found tumour subsite. The postoperative pathological malignancy and the frozen, positive malignancy intraoperatively were in agreement. There was no discernible difference between the negative intraoperative malignancy, the frozen, and the postoperative safe surgical margin. Of the 84 specimens, sixty-eight (81%) had no tumour infiltration, while 16 (19%) had positive results from frozen section examination. While 4 specimens (4.8%) were found to be free of tumour invasion, they did exhibit tumor-induced bone degradation upon decalcification. Despite the fact that one specimen (2.4%) tested positive, routine decalcification revealed no invasion. Between the two methods, there was an overall 94% (79) consistency with 79% sensitivity and 98% specificity.In 61.3%, 34.5%, and 17.1% of patients, respectively, poorly differentiated carcinoma, lymphovascular invasion and perineural invasion were found. Eight cases (19.5%) had differences between the permanent and frozen section boundaries. For poorly differentiated cancer, lymphovascular invasion, and perineural invasion, the corresponding false-negative rates were 14%, 36%, and 26%. In predicting the difference between frozen and permanent margins, poorly differentiated carcinoma, perineural invasion and lymphovascular invasion had negative and positive predictive values of 80% and 14%, 84% and 36%, and 92% and 26%, respectively.

IV. Discussion

In the realm of oncological surgical procedures, the attainment of pristine surgical margins holds paramount significance. Surgeons aspire to affirm the absence of microscopic surgical margins conducive to malignancy, even following the macroscopic excision of the tumor. In clinical practice, the predominant modality for appraising surgical margins involves the employment of frozen section examination. Notably, Mannelli et al. observed that aside from the escalation in human resource utilization, temporal considerations, and financial implications associated with oversampling, there exists a concomitant risk of overlooking a positive surgical margin.[20]

Conversely, our study's findings concerning the frozen assessment of surgical margins, encompassing both affirmative and negative outcomes, were discovered to align seamlessly with subsequent postoperative pathological analyses. As per the insights provided by Due et al., it was discerned that a discernible percentage, ranging from two percent to ten percent of frozen section results, initially categorized as negative during intraoperative evaluations, could be positively identified.[21] The veracity of our results was substantiated by confirming a high degree of congruence with recent literature, demonstrating consistent outcomes between frozen section analyses reported as negative during intraoperative assessments and the meticulous scrutiny of postoperative pathology.[20,21]

The observed concordance exhibited a proportional augmentation with the escalation in the quantity of conducted frozen examinations. Due et al. advocated an enhancement in the precision of intraoperative frozen evaluation through a refined definition of surgical bed sampling.[20] While this option entails a potential reduction in the pathologist's misdiagnosis rate, it is noteworthy that the benefits of an increased frequency of frozen examinations outweigh the associated drawbacks.

Despite the inherent disadvantages of conducting additional frozen sections, such as prolonging the duration of the operation and augmenting the expenses incurred in the frozen examination process, these drawbacks are eclipsed by the consequential advantages when considering postoperative surgical margin positivity and the need for subsequent treatment. Notably, the assessments of the frozen sections revealed a remarkable 99% sensitivity and a commendable 96% specificity, as reported by Due et al. [22,23] These outcomes, though somewhat optimistic when juxtaposed with earlier publications, exhibit a commendable consistency with select studies from the existing body of literature.[24]

The sampling strategy employed, especially the location of the sample collection, may have an influence on our findings; this is a crucial consideration for frozen data. There are three recognised methods for sampling: tumor-bed, specimen-driven, or a mix of the two. When comparing the frozen result to the specimen technique, the specimen-driven approach results in a greater surgical defect and shows that the resection is complete. Since the frozen sections are obtained by the surgeon from the side of the tumor bed that is deeper, this procedure, however, leads to erroneous results. This illusion results from the withdrawal of the deep soft tissue retraction, particularly in large-scale defects like T2-4 oral squamous cell cancer.The superiority of the specimen-driven technique over the tumour bed technique is highlighted by recent investigations. Since we employed the specimen-driven method, we think that this contributed to the high degree of compliance.

One of the most difficult aspects of frozen assessment, regardless of technique, is the lack of a precise definition for the ideal distance for clean surgical margins. [25,26] A recent study highlights that the absence of safe surgical margin delineation is the true cause of concerns regarding frozen examinations. This ambiguity is exacerbated by the shrinkage of oral cavity biopsies. Szewczyk and colleagues took a distinct tack when addressing the frozen examination. According to what they reported, even in cases where the definitive pathology following excision is negative, a positive surgical margin is a factor that indicates the aggressive course of the tumour in the biopsies sent by the surgeon from the surgical bed. This condition should be taken into account when administering adjuvant therapy.[27]

In the study conducted by Nieberler et al., they undertook the formidable challenge of addressing the persistent and unresolved concern of ensuring adequate resection at the bone edges. The primary issue stemmed from the inherent inaccuracies in radiographic and clinical assessments performed both before and during surgery to determine the presence and extent of carcinoma infiltration into the bone. Consequently, the risk of inadequate bone resection margins loomed over every surgical approach devised for therapeutic purposes. To tackle this challenge effectively, the study advocated for the routine intraoperative measurement of bone resection margins as the most accurate approach.[28] Numerous methods have been proposed in the past to offer a resolution to this predicament. Forrest et al. conducted an evaluation of bone margins intraoperatively by curetting the proximal 1 cm of cancellous bone from mandibular resection sites in 29 patients. The comparison of frozen portions of the cancellous bone to the final pathologic surgical margin revealed the prediction of adequate resection in 97% of 33 margins.[29] A subsequent investigation, encompassing a larger sample size and a broader spectrum of diseases, demonstrated a sensitivity of 88.9% and a specificity of 100%.[30] It is worth noting that these investigations were confined to cancellous bone tissue, as cortical bone necessitates decalcification before histological examination, limiting the scope of such studies. In addressing this limitation, Oxford et al. employed a curved osteotome to meticulously cut small, transparent cortical bone slices from the edges of the resection, providing an innovative solution to the challenge at hand.[32]

In contrast to permanent decalcified sections, the assessment of slices from 25 patients employing regular frozen sections without decalcification revealed a commendable sensitivity of 89% and a specificity of 100%. Cylindrical bony samples, obtained from mandibular bony resected margins using a trephine drill, yielded a sensitivity of 80% & a specificity of 95% when subjected to cryostat sections, involving eighty-four trephine specimens from twenty individuals.[5]. In a more recent inquiry, the comparison involved final decalcified cross-sectional mandibular bone margins against bone marrow curetting and inferior alveolar nerve biopsies from forty-seven margins in twenty-seven patients, all analysed through frozen section assessments. Despite three cases presenting false-negative findings among six positive margins, the results demonstrated an impressive specificity of 100% and a sensitivity of 50%.

While earlier methodologies yielded satisfactory results, their integration into routine clinical practice was hindered by technological challenges. The inherent hardness and rigidity of calcified bone posed technical processing issues, particularly in the context of frozen sections, leading to significant artefactual distortion of specimens. The background often exhibited hemorrhagic elements and contamination with bone dust from drills or saws, necessitating specialized training for the assessment of frozen bone sections. The frequent use of intraoperative bone margin measurement could potentially impact the surgical process by diminishing quality, diagnostic value, and overall reliability, imposing important constraints. In response to these challenges, a proposal was made to expedite the decalcification process by pre-sectioning bone specimens in conjunction with microwave radiation. Conversely, a 3-hour protocol for intraoperative rapid decalcification involved multiple working phases, confining the technique to a conventional intraoperative diagnostic methodology due to its inherent limitations.

Mahmood and collaborators pursued an alternative strategy to circumvent the need for frozen sections by adopting intraoperative cytological assessment of bone marrow specimens extracted from the margins of mandibular bony resections.[35] Despite a modest sample size of thirty-five cancellous bone smear/touch preparations from seven patients, this study illuminated the viability of cytological evaluation for bony margins. The correlation between final histology results and all cytological findings underscored the method's simplicity, cost-effectiveness, and reliability for routine clinical application. Utilization of elastic scattering spectroscopy was articulated as a technically sophisticated approach for discerning positive bony margins. The study scrutinized 341 elastic scattering spectroscopy spectra obtained from mandibular specimens sourced from twenty-one patients, further contributing to the exploration of innovative methodologies in the field.

On the other hand, they developed and verified the ICAB to regularly evaluate specimens of cancellous bone, including soft tissue, including the inferior alveolar nerve. Furthermore, we discovered that cortical bone scraping specimens are suitable for cytology. Nevertheless, because there were only three cases, they were not included in the statistical analysis, and more research is required to determine their diagnostic usefulness. In comparison to the number of patients in the validation cohort, where we concentrated on the cytological outcome of the final resection ma, we collected multiple specimens from a single patient in the first patient cohort, which allowed us to focus over the viability of the cytological evaluation of bone and produce more samples and positive controls.

In the study conducted by O'Brien et al., it was revealed that only 16% of mandibular resections led to bone invasion, with marginal resections accounting for 7% of these cases.[36] Conversely, in nearly two-thirds of instances involving segmental resections, the anticipation of bone invasion becomes more pronounced. More specifically, evidence of bone infiltration was identified in 65% of segmental resections and 7% of marginal resections among the individuals examined. Hence, it becomes imperative to refine both preoperative and intraoperative diagnostic procedures in order to address this variability in bone invasion occurrences.

Jerjes et al. innovatively introduced advanced methodologies for intraoperative diagnosis of bone composition through the application of cutting-edge technology.[37] Their experimentation involved the utilization of elastic scattering spectroscopy (ESS), a pioneering technique designed to quantify the penetration of tumor cells into bone. The evaluation of formalin-fixed bone margins was juxtaposed with histopathologic diagnostic findings. ESS, known for its sensitivity to morphologic alterations at both cellular and subcellular levels, generates distinct spectral signatures based on the diverse ways in which normal and aberrant tissues scatter light.[9]

Within the mandibular specimens of 21 individuals, a total of 341 spectra were obtained. Among these, 231 spectra originated from histologically positive sites, while the remaining ones were derived from normal tissue. The achieved specificity and sensitivity rates were noteworthy, reaching 80% and 70%, respectively. These results suggest that ESS holds promise in detecting tumor involvement at resection margins. The demonstrated reliability of this formalin-fixed tissue investigation also carries the potential to significantly streamline pathology efforts. If these findings could be extended to in vivo applications, they might offer an immediate and precise method for evaluating margins in clinical practice. However, the incorporation of this methodology into clinical settings is currently a subject of ongoing discussion.

The frozen section specimens indicated an absence of disease, yet about 20% of samples examined in this study exhibited positive margins upon subsequent permanent pathology assessment. A seasoned head and neck pathologist meticulously evaluated the complete specimen margin in each case, employing the en face approach. Cases with a history of perineural invasion, lymphovascular invasion, and prior Mohs resection displayed a heightened incidence of false-negative results; however, these associations did not attain statistical significance. Moreover, a larger false-negative rate was observed in cases characterized by smaller defect sizes. In this series, the scalp and face emerged as the two predominant tumor sites, and interestingly, these locations exclusively harboured tumors that manifested disparities between the frozen and permanent sections, underscoring the intricacies involved in accurate pathological assessments within these specific anatomical regions.[22]

Analogous findings have been observed in alternative inquiries utilizing Frozen Section for the assessment of cutaneous Squamous Cell Carcinoma (SCC), wherein the incidence of false negative reports has displayed variability ranging from two percent% to 15%. [13-15]. However, there exists a paucity of information elucidating the methodologies employed for the collection and scrutiny of frozen section margins across these distinct series.

Given the elevated risk characteristics inherent to Squamous Cell Carcinoma, it is noteworthy that a substantial proportion of frozen section literature predominantly relies on data derived from basal cell carcinoma, a context that may not be entirely applicable to SCC. The population scrutinized in this study was notably high-risk, as evidenced by a pronounced perineural invasion rate of 46%, a figure markedly higher than the 4.6% reported in a prior comprehensive prospective study addressing the incidence of perineural invasion in cutaneous SCC.[16]

Regrettably, the current body of literature lacks more expansive research investigations specifically focusing on cutaneous Squamous Cell Carcinoma manifesting high-risk features, thereby underscoring a notable gap in our understanding of this clinical context.

V. Conclusion

The intraoperative examination of bone margins utilizing frozen section analysis and the trephine drill extraction method is a significant part of surgical operations, particularly in oncological surgeries where the complete removal of malignant tissue is essential. The intra-op assessment is a useful component contributing significantly to the precision and success of surgeries, particularly in the context of tumor resections. The combination of frozen section analysis and the trephine drill extraction technique offers a comprehensive and real-time approach to ensuring the adequacy of margin clearance.

The utilization of frozen section analysis allows for the quick evaluation of the tissue samples during surgery.. This real-time feedback aids surgeons in making informed decisions about the extent of tissue resection, minimizing the risk of leaving residual malignant tissue. The trephine drill extraction technique provides a precise method for obtaining bone samples for frozen section analysis. This ensures that the evaluation is representative of the actual surgical margins, enhancing the accuracy of intraoperative assessments.

In cancer surgeries, achieving negative margins is crucial for reducing the risk of local recurrence. The intraoperative evaluation of bony margins helps to confirm that the surgical resection has effectively removed all cancerous tissue, promoting better long-term outcomes for patients. By identifying inadequate margins intraoperatively, the surgeon can take immediate corrective actions, potentially reducing the need for reoperations and additional interventions. This not only saves time but also minimizes the physical and emotional burden on patients.

While frozen section analysis and the trephine drill extraction technique offer valuable insights, challenges such as sampling errors or limited sensitivity may exist. Surgeons should be mindful of the limitations and interpret results in conjunction with clinical judgment.

Intraoperative margin assessment involves close collaboration between surgeons, pathologists, and other relevant medical professionals. Effective communication and teamwork are essential for optimizing the use of these techniques and ensuring comprehensive patient care.

Some investigations found a moderate incidence of discrepancy between the permanent section analysis and frozen section analysis of the surgical margins from head and neck high-risk cutaneous squamous cell carcinomas. A higher rate of frozen section disagreement seems to be related to the existence or lack of specific histopathologic characteristics. When planning a definitive excision and reconstruction, assessment of such characteristics in a preoperative biopsy or staging excision may prove useful. Some studies found consistency in the postoperative pathology results of individuals with positive and negative surgical margins. Frozen section analysis may be used safely to assess perioperative surgical margins of squamous cell carcinoma of the oral cavity.

In conclusion, the integration of frozen section analysis and the trephine drill extraction method in intraoperative bony margin evaluation represents a significant advancement in surgical practice. This approach empowers surgeons to make real-time decisions, enhances the precision of tissue removal, and ultimately contributes to improved patient outcomes, particularly in the challenging context of oncological surgeries. Ongoing research and technological advancements will likely continue to refine and expand the capabilities of intraoperative margin assessment techniques.

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