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Original Research Article

Correlation of intraoperative frozen section report and histopathological diagnosis: a two-year retrospective study

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ABSTRACT

Background: Frozen section is an intraoperative pathological technique which has very important role to play in diagnostics and also it plays important role in further surgical management as specially in oncology setup. The present study was undertaken to assess the degree of diagnostic accuracy of frozen section examination of various anatomical sites, overall accuracy, sensitivity and specificity of frozen section technique.
Methods: During the study period from 1st May 2021 to 30th April 2023, a total of 70 patients underwent surgery with intraoperative pathologic consultation for various malignant and non-malignant conditions were reviewed. For frozen section, fresh tissue was sent from the operation theatre to Pathology department and the gross specimens were inspected, dissected and blocks were cut on the cryostat (Leica CM 1950) using Optimal cooling temperature (OCT) compound as embedding medium followed by rapid Haematoxylin-Eosin staining.
Results: The most common indications for frozen section encountered in our institute were Sentinel/Locoregional lymph node (57%). Highest number cases were from lymph node (40) followed by thyroid (12), breast tissue (6) etc. Overall diagnostic accuracy of frozen section was 95.7% (67/70 cases). Concordance rate was 95.7% (67 cases), sensitivity 93.9% and specificity 97.2% with positive predictive value 96.7% and negative predictive value 94.7%.
Conclusions: Frozen section is the mainstay of rapid diagnosis in histopathology. It is an accurate and reliable method when it is used for suspicious malignancies, tumor resection margin, metastasis of lymph nodes and identification of tissue. It is chiefly performed to determine whether tissue being sampled is malignant or benign.

Keywords: Benign, Diagnostic accuracy, Frozen section, Haematoxylin eosin staining, Histopathology, Malignant

INTRODUCTION

Tissue specimen taken from a patient by doing a biopsy or an operation is usually assessed by the pathologist on the following day after the specimen is adequately fixed in formalin. However, occasionally surgeons need pathologic information more urgently thus, they will request for an intraoperative consultation on the tissue that is being taken out.[1] The beginning of this new era in intraoperative diagnosis was first introduced by William H. Welch, from Johns hopkins hospital in 1891.[2] Tissue obtained from a surgical specimen is frozen in a cryostat machine and then cut with a microtome. Slices of 5-6 um are obtained and stained (usually rapid haematoxylin and eosin). Using this method, a specimen can be ready for examination under the microscope in a short duration and thus can yield rapid information. However, the intraoperative frozen section method is a means of intraoperative consultation, the main purpose of which is to provide rapid gross or microscopic diagnoses that can guide surgeon to make best therapeutic decision during the operation or peri-operative management of a patient, including identification of an unknown pathologic process, evaluation of adequacy of margins, identification of lymph nodes metastases and identification of tissue.[3] Diagnostic accuracy of intra-operative frozen section depends largely on quality of

tissue sections backed by good clinical communication and experience of reporting pathologist.[4]

Periodic review of the correlation between frozen section diagnosis and final diagnosis is useful to identify the potential causes of errors and thus measures can be implemented to help prevent similar occurrences. Long term monitoring of frozen-permanent section correlation is associated with sustained improvement in performance.[5] The present study was undertaken to assess the degree of diagnostic accuracy of frozen section examination of various anatomical sites, overall accuracy, sensitivity and specificity of frozen section technique.

METHODS

A retrospective study was carried out in the histopathology section of Department of Pathology, Government Cancer hospital, Aurangabad, Maharashtra in which all the consequent intra-operative FS reported from 1st May 2021 till 30th April 2023, were analysed along with the corresponding formalin fixed paraffin embedded (FFPE) tissue sections and their final histopathological examination (HPE) reports. During this study period, a total of 70 patients underwent surgery with intraoperative pathologic consultation for various malignant and non-malignant conditions.

All the fresh tissue samples sent from the operation theatre to Pathology department in a clean plastic container containing normal saline without any fixative were considered. Samples send in any fixative were excluded. The gross specimens were inspected, dissected and blocks were cut on the cryostat (Leica CM 1950) using Optimal cooling temperature (OCT) compound as embedding medium followed by rapid Haematoxylin-Eosin staining.

Subsequently, for the permanent paraffin section, counterparts of frozen section specimens were fixed in 10% formalin, grossed and adequate representative sections were taken. The paraffin sections were then evaluated in H&E stain. The frozen section diagnoses were correlated with the final histological diagnosis to assess the accuracy of the technique. The number and type of discordant cases were compared; the cause for deferred diagnosis and the discordance were analysed. The data was obtained from the compiled manual records and stored sections on glass slides were retrieved for the study.

RESULTS

Total cases studied were 70 of them 10 were male and 60 were female. The age ranged was wide and varied from 10 years to 85 years. The most common indications for frozen section encountered in our institute were sentinel/ locoregional LN (57%) as depicted in Figure 1.

The maximum number of samples received for frozen section was from lymph node (40) followed by thyroid (12), breast tissue (6) etc. as shown in Figure 2.

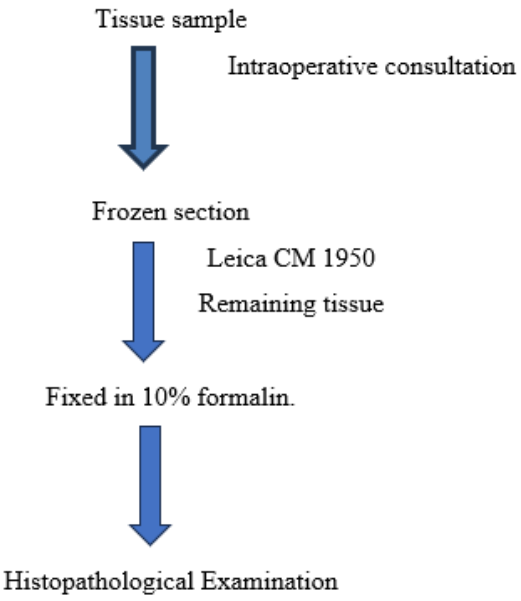

Figure 1: Tissue processing workflow.

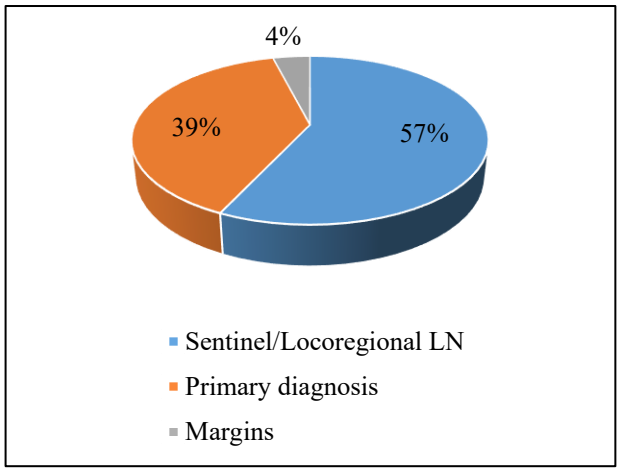

Figure 2: Indications for frozen section.

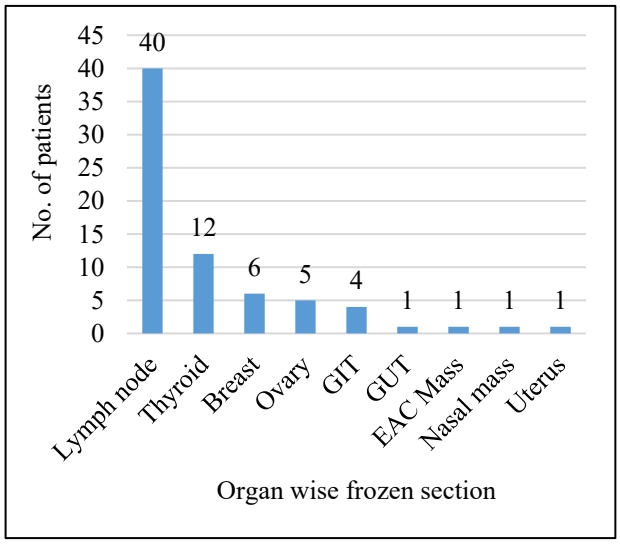

Figure 3: Organs submitted for frozen sections.

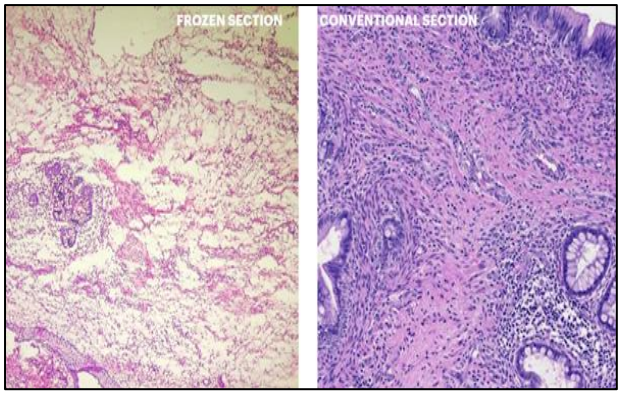

Figure 4: H&E-stained slide 400X view teratoma of ovary.

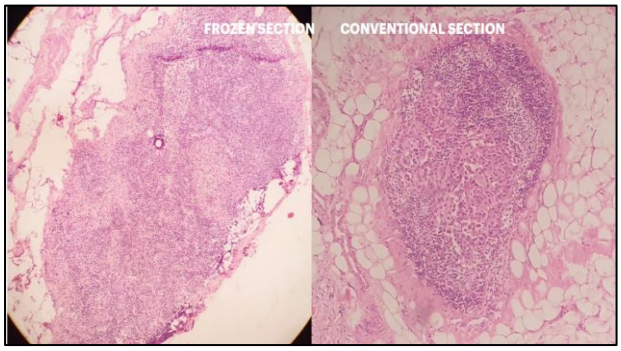

Figure 5: H&E-stained slide 400X view, metastatic deposits in lymph node.

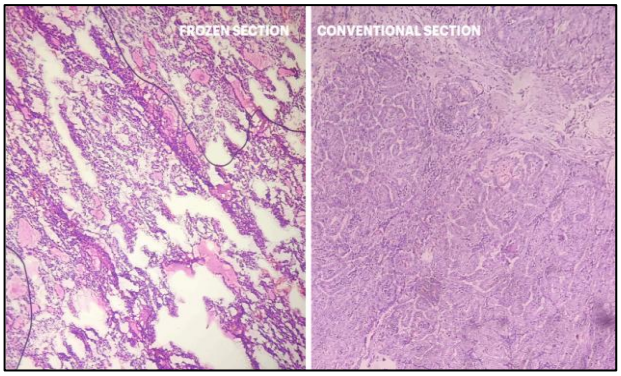

Figure 6: H&E-stained slide 400X view papillary thyroid cancer.

Organ wise correlation of frozen and permanent section diagnosis revealed an accuracy of 95.7% (67/70) (Table 1). Lymph node 40 discordant 2 and concordant 38. Thyroid 12 cases- discordant 1, thyroiditis 1, follicular neoplasm 3, PTC 3, goitre 4. Breast 6 cases- mucinous carcinoma 1, benign phyllodes 1, fibroadenoma 2, IDC 3. Ovary 5 cases- discordant 1, teratoma 1, mucinous neoplasm 3. GIT 3 Cases- FOT SMA 1, adenocarcinoma (rectum and hepatic duct) 2. GUT 1- RCC. Nasal mass 1- malignant round cell tumor. Uterus 1-leiomyoma. EAC mass 1- spindle cell lesion. Overall diagnostic accuracy of frozen section was 95.7% (67/70 cases). Concordance rate was 95.7% (67 cases), sensitivity 93.9% and specificity 97.2% with positive predictive value 96.7% and negative predictive value 94.7% as shown in Table 2.

Table 1: Demographic distribution of cases.

Age range (in years)	Male	Female	Total
10-19	1	8	9
20-29	2	9	11
30-39	1	10	11
40-49	1	9	10
50-59	1	7	8
60-69	2	6	8
70-79	1	6	7
80-85	1	5	6
Total	10	60	70

Table 2: Organ wise accuracy of frozen section.

Anatomical site/ Origin	Number of cases	Concordant cases	Discordant cases	Accuracy
Sentinel LN/LN	40	38	02	95%
Thyroid	12	11	01	91.6%
Breast	06	06	00	100%
Ovary	05	05	00	100%
GIT/GUT	04	04	00	100%
Uterus	01	01	00	100%
Nasal mass	01	01	00	100%
EAC mass	01	01	00	100%
Total	70	67	03	95.7%

Table 3: Results of the study.

Concordant cases out of 70 cases	67
Discordant cases	03
Overall Accuracy	95.7
Sensitivity	93.9
Specificity	97.2
Positive predictive value	96.7
Negative predictive value	94.7
False positive	1.40
False negative	2.85

DISCUSSION

Frozen section provides rapid gross and microscopic diagnosis to assist the surgeon in guiding best therapeutic approach for the patient during surgery itself. It requires good correlation of clinical, radiological and histopathological data. A general diagnosis rather than an exact diagnosis should be given to assist surgeon to proceed in choosing best therapeutic approach for the patient.[6] Frozen section is a multistep process involving surgical resection, intraoperative preparation of slides and their microscopic examination, communicating FS diagnosis to surgeon and processing remaining tissue for further workup.

Errors may occur due to problem in any of steps.[7] It is costly and technically limited. Frozen section is also more difficult to interpret than examination of paraffin embedded sections. Interpretation error was the most common error in the study followed by gross sampling error. There was no clinically significant error due to sectioning, staining and technical imperfection in the study.[8] Previous studies also concluded that disagreements were mostly due to interpretive and gross sampling errors.[9,10]

Case from lymph nodes showing false negative result was due to sampling error. SLN were cut along long axis at 2-3 mm interval while for histopathological diagnosis cut at 100 um intervals. Therefore, small metastatic foci were missed. One case from thyroid showing false negative results, which turned out to be papillary thyroid cancer was a result of interpretation error. In this, the assessment was difficult due to cytologic artefact generated by freezing, resulting in crystal formation which generated nuclear clearing as well as intranuclear bubbles. PTC is diagnosis based on constellation of nuclear features (elongation, grooves, clearing), which was revealed on conventional histopathology. The present study confirmed that intraoperative frozen sections, regardless of the initial indications influence immediate patient care decisions, resulting in changed surgical procedures in almost 41% of all operative cases. Frozen section helps intraoperatively in determining the extent of the surgery, presence or absence of neoplasm is crucial and to determine type of operative procedure and in further management. Margin status of a malignant lesion is important to avoid further tumor recurrence. Achieving adequate margin especially in case of head and neck surgeries, lumpectomy or resected margin status is of utmost importance.

Conservative surgeries from the patient's view provides less stress and strain through therapeutic interventions, best provided by intraoperative frozen section diagnosis. Radical surgeries in case of lymph node dissection helps in reducing post op patient morbidity. In case of breast carcinomas, patient could undergo axillary staging at time of surgery, thereby sparing them a second surgical procedure. Axillary lymph node dissection remains the standard practice when residual carcinoma, regardless of size is identified in sentinel lymph node following neoadjuvant chemotherapy. In case of thyroid lesions, it has been used to aid further surgical decision making whether to perform Total thyroidectomy /hemithyroidectomy/lobectomy. In cases of unsatisfactory FNAC or suspicious for malignancy, intraoperative frozen section is useful. In case of ovarian lesions, patients with primary ovarian cancer need comprehensive staging surgery, in contrast, benign tumors can be treated with limited and fertility sparing surgery. Accurate frozen section diagnosis is critical in preventing both over and under treatment. Also critical in determining whether to perform omentectomy. In the present study, total number of concordant was 67 (95.7%) which was similar to study done by Bharadwaj et al, (95.5%), Hatami et al (97.96%).[6,11] Discordance was 3 (4.2%) which was comparable to other studies by Bharadwaj et al, Hatami et al and Mahe et al.[6,11,12] Diagnostic accuracy of frozen section was 95.7% (67/70 cases) in current study which is comparable to other studies like Bharadwaj et al (95.5%) and Preeti et al, (94.2%).[13] In the present study sensitivity was 93.9%, specificity 97.2%, positive predictive value 96.7% and negative predictive value was 94.9% which was comparable to study done by Bharadwaj et al, where the sensitivity was 89.5%, specificity 98.5%, positive predictive value 96.7% and negative predictive value was 94.9%.[7] Also, results were compatible to other studies as shown Table 4.

Table 4: Comparison of various studies with present study on overall accuracy, sensitivity and specificity.

Name of study	Country	Study period	No. of cases	Accuracy (%)	Sensitivity (%)	Specificity (%)
Patil et al[1]	India	2 years	100	96.96%	97.22%	96.30%
Adhikari et al[8]	Nepal	1 year	41	97%	94%	87%
Ayyagari et al[14]	India	2 years	66	98.48%	96.87%	100%
Nikhra et al[15]	India	2 years	197	96.4%	93.4%	99.04%
Dhakal et al[16]	Nepal	1 year	47	91.4%	85.18%	100%
Present study	India	2 years	70	95.7%	93.9%	97.2%

The study had limitations including small sample size of 70 patients. Also only small portion of the specimen is examined during intraoperative frozen section consultation. Rapid diagnosis required during surgery led to rushed interpretations.

CONCLUSION

Frozen section is the mainstay of rapid diagnosis in histopathology. It is an accurate and reliable method when it is used for suspicious malignancies, tumor resection margin, metastasis of lymph nodes and identification of tissue. It is chiefly performed to determine whether tissue being sampled is malignant or benign. Intraoperative consultation using frozen section is very useful, but one needs to be aware of its indication and limitations.

Complete patient history, imaging findings, gross inspection, accurate sampling, avoiding technical errors in sectioning and staining, frozen section complemented with histological review and close cooperation with surgeon can avoid certain limitations and provide rapid, reliable and cost-effective information necessary for optimum patient care. Continuous monitoring should be performed to reduce errors and thus improve quality of frozen section diagnosis for sustained improved performance.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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