

A COMPARATIVE STUDY OF FROZEN SECTION DIAGNOSIS WITH HISTOPATHOLOGY IN A TERTIARY HEALTH CARE CENTRE

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Received : 03/03/2025
Received in revised form : 09/05/2025
Accepted : 26/05/2025

Keywords:

Frozen section, Histopathology, H&E.

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DOI: 10.47009/jamp.2025.7.3.151

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (3); 778-781



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ABSTRACT

Background: Frozen section technique was first used by William H Welch from John Hopkins Hospital in 1891 for intra-operative consultation. This practice has since then evolved especially after development of cryostat in 1959. The classic indication for frozen section examination is the need for an immediate decision during a surgical procedure in differentiating between benign and malignant neoplasms to guide intra or perioperative patient management. This study aims to highlight the qualitative morphological comparison between both the techniques and to establish diagnostic accuracy of frozen sections. **Materials and Methods:** The present study included all the Frozen section received in the Department of pathology at JNUIMSRC, JAIPUR from 01 June 2022 to 30 November 2023. Fresh tissue was sent in a clean plastic container in saline without any fixative. Gross examination was done, specimen dissected and sections were taken from representative areas. Frozen sectioning was done on Leica CM 1520 cryostat set at a range between -250C to - 300C. Sections were cut at a thickness of 4- 5µ and were immediately stained with Rapid hematoxylin and eosin (H&E) staining. Frozen section diagnosis was made and it was immediately conveyed to the operating surgeon. Subsequently, for the permanent section, specimens were fixed in 10% formalin, grossed and adequate representative sections were taken. The frozen section diagnoses were compared to that of the H&E sections, to assess the accuracy of the technique. The frozen section results in comparison to final diagnoses were then categorized into four groups: Positive, Negative, false positives and false-negatives. Sensitivity, specificity, positive predictive value & negative predictive value were calculated. **Result:** Out of total 112 cases, Maximum 54(48.21%) Were in age group of 41-60 yrs followed by 38 cases (33.93%) in 21-40 yrs. of age group. Out of total 112cases,85(75.90%) were females while 27 (24.10%) were males. Out of 112 frozen,50(44.64%) Benign, 37(33.03%) malignant, Inflammatory 3(2.67%), Tubercular 4 (3.57%) & (18) 16.07% where margins were reported. Out of 112 tissue samples 41 cases were positive for malignancies by histopathology as well as on frozen section hence frozen section diagnosis is correlated well with histopathology diagnosis 100%. The positive predictive value and negative predictive value and accuracy were also 100% in our study. There was 100% concordance. **Conclusion:** The overall accuracy of our frozen section diagnoses is higher than that reported in the literature. No diagnostic discrepancy was reported in our study. We also believe that determining the presence or absence of malignancy without subtyping, it can be an option to decrease the discrepancies of frozen section diagnoses.

INTRODUCTION

Frozen section technique was first used by William H Welch from John Hopkins Hospital in 1891 for intra-operative consultation. This practice has since then evolved especially after development of cryostat in 1959.^[1,2] The correlation of intraoperative frozen section diagnosis with final diagnosis on routine histopathological section is an integral part of quality assurance in surgical pathology. The classic indication for frozen section examination is the need for an immediate decision during a surgical procedure in differentiating between benign and malignant neoplasms to guide intra or perioperative patient management. Other indications of frozen section are identification of tissue and unknown pathological processes, evaluation of margins, identification of lymph node metastasis, and confirmation of presence of representative samples for paraffin section diagnosis and to determine the nature of a lesion.^[3,4] The indications and limitations of frozen section diagnosis vary in different organs. Diagnostic discrepancies between frozen and H&E section are commonly observed in tissue from skin, breast, uterine cervix and thyroid.^[5-8] This study aims to highlight the qualitative morphological comparison between both the techniques and to establish diagnostic accuracy of frozen sections in various anatomical sites.

MATERIALS AND METHODS

The present study included all the Frozen section received in the Department of pathology at Jaipur national university institute for medical science and research center from 01 June 2022 to 30 November 2023. All the frozen section sent to pathology department were included in this study. Fresh tissue was sent in a clean plastic container in saline without any fixative along with requisition form with complete clinical details from the operation theater. Gross examination was done, specimen dissected and sections were taken from representative areas. Frozen sectioning was done on Leica CM 1520 cryostat. The cryostat was set at a range between -250C to -300C depending upon the nature of the tissue. Sections were cut at a thickness of 4-5 μ and were immediately stained with Rapid hematoxylin and eosin (H&E) staining. Frozen section diagnosis was made and it was immediately conveyed to the operating surgeon through intercom. The turnaround time of entire procedure from receipt of specimen to delivery of report was recorded. Subsequently, for the permanent section, specimens were fixed in 10% formalin, grossed and adequate representative sections were taken according to the standard guidelines. The sections were then evaluated in H&E stain. The frozen

section diagnoses were compared to that of the H&E sections, to assess the accuracy of the technique. The frozen section results in comparison to final diagnoses were then categorized into four groups: Positive, Negative, false positives and false-negatives. Sensitivity, specificity, positive predictive value & negative predictive value were calculated.

RESULTS

The present study was carried out in the Department of Pathology, Jaipur National University Institute for Medical Sciences & Research Centre, Jaipur. A total number of 112 various biopsies were received for Frozen sections from the patients attending JNUIMSRC Hospital Jaipur.

Out of total 112 cases, Maximum 54(48.21%) Were in age group of 41-60 yrs followed by 38 cases(33.93%) in 21-40 yrs. of age group. Out of total 112 cases, 85(75.90%) were females while 27 (24.10%) were males [Table1]. That was due to maximum frozen section were received from Obstetrics and gynaecology Department followed by General Surgery. Out of 112 frozen, 50(44.64%) Benign, 37(33.03%) malignant, Inflammatory 3(2.67%), Tubercular 4 (3.57%) & (18) 16.07% where margins were reported [Table2]. It was observed that maximum biopsy tissues were received 41 (36.6%) from Ovary, excision followed by 20 (17.85%) Adnexa & 13 (11.6%) brain tissue. it was observed that maximum biopsy tissues were received from obstetrics and gynecology Department 61(54.46%) followed by 27 (24.10%) from General Surgery, 12 (10.71%) from Onco-Surgery and others. In the present study it was observed that Maximum number of the malignant cases were found 13 (11.61%) each from obstetrics and gynecology & General Surgery while 3(2.38%) inflammatory cases were received only from General Surgery, 4(3.57%) Tubercular cases were received from obstetrics and gynecology, General Surgery & Neuro Surgery. In the present study total 18 margins were evaluated out of which 14 (77.78%) was found negative while 4 (22.22%) margins were found Positive for malignancies and respective extended revised margins were also received and found negative. In the present study total 112 cases were enrolled for the comparative study of frozen section and histopathological examination. There was 100% concordance. Out of 112 tissue samples 41 cases were positive for malignancies by histopathology as well as on frozen section hence frozen section diagnosis is correlated well with FFPE histopathology diagnosis [Table3]. showing frozen section is as good as histopathological examination test found 100% sensitive and 100% specific test. The positive predictive value and negative predictive value and accuracy were also 100% in our study [Table4].

Table 1: Age & Sex Wise Distribution of Cases as Received for Frozen Section

Age	Male	Percentage Male	Female	Percentage Female
<20 Yrs	0	0.00%	02	1.78%
21-40 Yrs	6	5.35%	32	28.57%
41-60 Yrs	15	13.39%	39	34.82%
>60 Yrs	6	5.35%	12	10.71%
Total	27	24.10%	85	75.90%

Table 2: Comparison of Frozen Sections and Histopathological Examination.

Diagnosed Category	Diagnosed under frozen section	Diagnosed under histopathological section	Concordance
Inflammatory	3	3	100%
Tubercular	4	4	100%
Benign	50	50	100%
Malignant	37	37	100%
Margins	18	18	100%
Total	112	112	100%

Table3: Comparison of Frozen Section with Histopathology

Test	Histopathology Positive n=41		Histopathology Negative n=71	
	Positive(A)	Negative(C)	Positive(B)	Negative(D)
Frozen section	41	0	0	71

Table4: Performance of Frozen Section Methods Tested in a Comparison withHistopathological Examination

Test	Sensitivity (%)	Specificity (%)	Positive Predictive value(%)	Negative Predictive Value(%)	Accuracy (%)
Frozen section	100%	100%	100%	100%	100%
Histopathology	100%	100%	100%	100%	100%

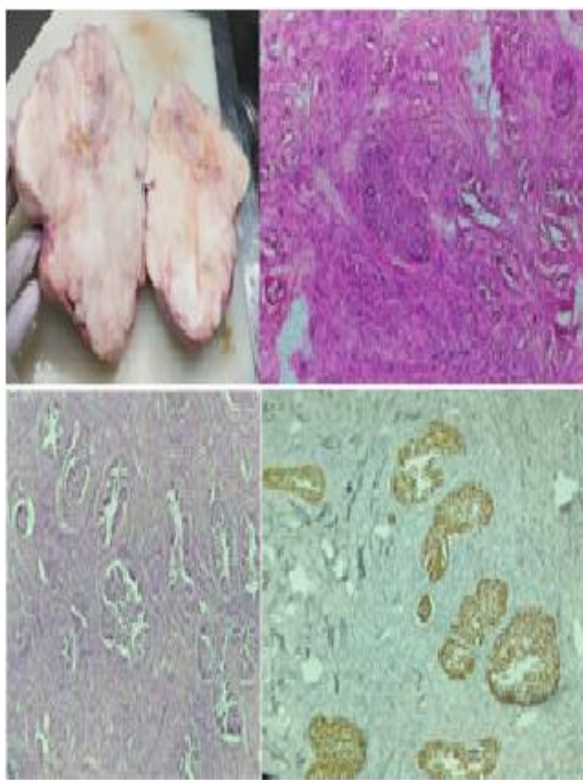


Figure1A- Gross image of ovarian mass diagnosed as Brenner tumour with calcification. **1B:** Frozen Photomicrograph of Brenner's tumor showing transitional epithelium embedded in fibromatous stroma (Rapid H & E staining 100 x magnification). **1C:** Histopathology Brenner's tumor showing transitional epithelium embedded in fibromatous stroma in (H & E staining 100 x magnification). **1D:** Immunohistochemistry p63 positivity in Brenner's tumor in 100 x magnification

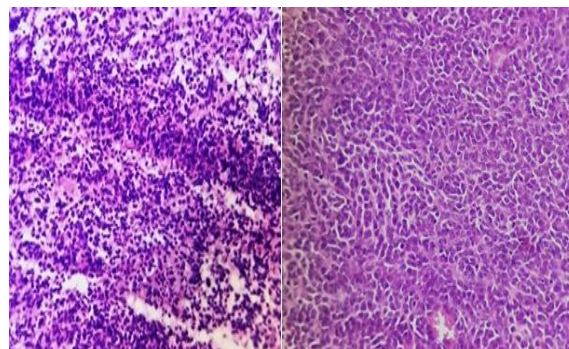


Figure 2A: Frozen photomicrograph of Small round blue cell tumor showing densely packed undifferentiated cells, medulloblastoma (100 x magnification in rapid H&E staining). **2B:** Histopathology image of Small round blue cell tumor showing Homer Wright rosettes (medulloblastoma) at (100x magnification, H&E staining)

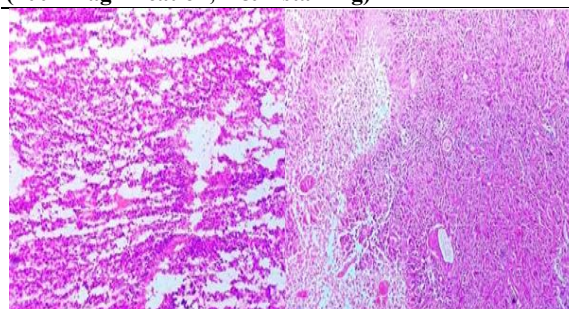


Figure 3A- Frozen photomicrograph of Glioblastoma Multiforme showing pseudo palisading with nuclear chromasia at 100 x magnification (H&E staining). **3B:** Histopathology image of Glioblastoma Multiforme showing pseudo palisading with neoplastic cells surrounding necrosis at (100 x magnification in H&E staining)

DISCUSSION

In our study, the total concordance rate between the histopathological reports and the frozen section was 100.00%. This is comparable to the accuracy of frozen sections reported in various studies, which ranges from 91.5 to 97.4%. In a study by FaribaAbbasi and colleagues in Iran, the concordant rate was 74.5%, which was lower than our result¹⁰. In a 2001 study of 243 ovarian tumors, Pinto PB found that the frozen section was accurate in 94% of the cases and inaccurate in 6% of the cases.^[11] Comparable findings were found in the current analysis of 112 individuals, where the diagnosis of a frozen section was correct in 100% of instances.

The 61 samples from the obstetrics and gynecology department that were used in this study were primarily ovarian and B/L adnexa; of these, 13 (11.60%) were found to be malignant and 45 (40.17%) to be benign, with 100% concordance with histopathological formalin-fixed paraffin embedded tissue section. Out of the 112 frozen sections that were obtained for diagnosis in the current investigation, 10 brain sections were determined to be malignant, with 8 (7.40%) of those cases finding 100% concordance with the histological diagnosis. Other research indicated accuracy for benign 92.8% -100% and for malignant 79.6% - 93%. A concordance rate of 98.3% was observed by Zarbo et al. (1991),^[12] 97.2% by Novis et al (1997),^[13] and 81.5% by Patel et al. (2017).^[9] Intraoperative frozen section inspection of margins is frequently helpful in achieving complete tumor excision. Clear margin reduce the chance of local control. Tumor-free margins at the time of surgery have been associated with lower local tumor recurrence rates and higher survival rates.

We received eighteen cases in all, including margins from suspected cases of cancer, for examination of the frozen section. Every edge in the frozen section was precisely evaluated in light of the final histopathology result. When the tumor's margins on the frozen slice proved negative, the surgeons were able to remove it as necessary. This restricted their excision field. Research from Virginia (DiNardo L J et al., 2000) shows that accuracy rates for frozen section margin interpretation for oral cancer can range from 71.3% to 97.5% in the USA with 100% accuracy, we had a higher rate.^[14] The reason for the increased prevalence of oral cancer in our area is the widespread usage of tobacco products like gutka and khaini. In a 2011 study, Olson et al. recommended three sections from the oral resection margins to reduce error caused by insufficient frozen sample (Olson et al., 2011).^[15]

Based on our experience with frozen section analysis of tissue margins, a large tumor may deform the normal anatomy, resulting in inappropriate orientation of the tissue margins, which can occasionally make the evaluation of the tumor's re- excision margins difficult. In these cases,

it seems inappropriate to compare the initial margins for the frozen area with the final margins after re-excision. In these cases, we recommend processing the remaining original tissue after freezing segment and comparing it with the frozen section using the gold standard histological approach. The main reasons for intra-operative consultation when evaluating gastrointestinal tract specimens are to diagnose the condition, ascertain the extent of illness (e.g., tumor dissemination), and evaluate the adequacy of resection (margin status).^[16]

Out of the gastrointestinal tract, we obtained ten instances in total. The purpose of the frozen section of these tissues was, in some circumstances, to evaluate the margins for the presence of a tumor and, in other situations, to identify unidentified disease processes. On the frozen slice, aberrant cells proliferated into glands and tubules in each sample. These individuals' adenocarcinomas in the affected organ(samples from the ileum, duodenum, stomach, and caecum) were discovered using histological investigation. Our study also revealed that the gastrointestinal tract was associated with fewer diagnostic discrepancies, which is in line with findings from other studies.^[17]

A single lymph node removed in order to look for stomach adenocarcinoma metastatic deposits on a frozen section produced true positive results. To select tissue for frozen section analysis, a thorough gross examination of the tumor is required for intraoperative frozen section diagnosis. Furthermore, the decision needs to be made within minutes; otherwise, the aim of the quick diagnosis procedure would be defeated. The final pathologic diagnosis has the advantage that many complete specimens were sampled, which increases the possibility of detecting microscopic foci of malignant epithelial alterations in a primarily benign mass.^[18]

In the present study, among all biopsy sections from various sites, gynecological specimens were in highest number followed by brain tissue which was similar to the study done by Purbesh Adhikari et al, 2014-15 & Parikshit Patil et al reported brain tissue was in highest number followed by breast and gynecological specimen.^[19,20] The concordance rate in the present study was 100% which was approximately equal to the study done by Prajapati et al,^[21] in which concordance rate was 94.93% while in the study of Vikram et al,^[22] and selvakumar et al,^[23] concordance rate were 95% and 94.7 % respectively.

The total accuracy rate of my research is 100%, which is higher than the study by Maurya et al.^[24] The positive predictive value of the present investigation was 100%, whereas that of the research by Pawan et al,^[25] was 98.8%. The current study's diagnostic accuracy rate for frozen sections was higher than that of the previous investigation. The short study period and small number of cases made it difficult to assess accuracy in each organ system independently. The current study's negative

predictive value was 100%, compared to 97-80% and 99.956%, respectively, for Hatami et al.^[26] and Prajapati et al.^[21]

CONCLUSION

Frozen section is as good as histopathological examination test found 100% sensitive and 100% specific test. The positive predictive value and negative predictive value and accuracy were also 100% in our study. To conclude, the overall accuracy of our frozen section diagnoses is higher than that reported in the literature. No diagnostic discrepancy was reported in our study. We also believe that determining the presence or absence of malignancy without subtyping it can be an option to decrease the discrepancies of frozen section diagnoses. Limitation of our study was the limited number of cases and the duration of the study because of which we were unable to calculate the accuracy of frozen section in all the organ systems separately.

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