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The Diagnostic Accuracy of Intraoperative Frozen Section to Routine Paraffin Section: A Comparative Study

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ABSTRACT

Intraoperative frozen section plays an important role in the management of surgical patients with neoplastic and non-neoplastic diseases as it guides the surgeon to make decisions on the extent and/or adequacy of surgical procedures, thus decreasing the need for re operation. This study evaluates the diagnostic accuracy of intraoperative frozen section in comparison to the gold standard routine paraffin section. The objective of this study was to assess the diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of frozen section diagnosis in various anatomical sites. This retrospective study was conducted at the Department of Pathology, Vydehi Institute of Medical Sciences and Research Centre. A total of 190 cases from various anatomical sites sent for frozen section analysis between January 2018 and December 2019 were considered. The frozen section and paraffin section diagnoses were concordant in 187 (98.4%) and discordant in 3 (1.6%) cases. The discordant cases reported were due to misinterpretation. The diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of frozen sections in comparison with routine paraffin sections were 98.4%, 95.5% %, 99.3%, 97.7% and 98.6%, respectively. These values suggest a high level of reliability and accuracy in using frozen section diagnosis for identifying various pathologies. The intraoperative frozen section is accurate with high sensitivity and specificity. It should always be used when the preoperative diagnosis is not definite, as it provides reliable rapid intraoperative diagnosis, which will guide the surgeon in determining the type and extent of surgery to avoid undertreatment or over treatment of the patient. By avoiding technical errors in sectioning and staining and with better communication between pathologist and surgeon, the rate of discordant cases can be reduced.

INTRODUCTION

Frozen section analysis is an essential technique employed by the pathologists during intraoperative consultation. In 1891, William H. Welch of Johns Hopkins Hospital performed the first intraoperative consultation using the frozen section technique. Wilson and McCarty modified it further in 1905 at the Mayo Clinic. With the advent of the cryostat in 1960, the intraoperative frozen section examination became a very reliable method for the rapid histological assessment of tissue samples obtained during surgery[1,2]. Intraoperative frozen section plays an important role in the management of surgical patients with neoplastic and non-neoplastic diseases as it guides the surgeon to make decisions on the extent and/or adequacy of surgical procedures, thus decreasing the need for re operation[3,4]. The most common causes of errors in frozen section diagnosis are inadequate sampling, certain types of lesions, a lack of communication between the surgeon and pathologist and technical problems[5]. Although frozen section offers a rapid diagnosis, it should not be considered a replacement of the paraffin section, as frozen section is still inferior to paraffin section due to its various limitations, like pressure to diagnose immediately, lack of ancillary tests and frozen section artifacts[5-7]. This study was performed to evaluate the accuracy, sensitivity, specificity and predictive values of intraoperative frozen section analysis in comparison with routine paraffin section in various anatomical sites.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Pathology at Vydehi Institute of Medical Sciences and Research Centre to assess the diagnostic accuracy of intraoperative frozen sections in various anatomical sites involving 190 tissues from 190 surgical cases between January 2018 and December 2019. The relevant details were collected from the medical records. During intraoperative consultation, fresh tissue was sent in a clean plastic container from the operation theater without any fixative, along with a requisition form with complete clinical details. After a gross examination of the specimen, the representative areas were chosen for further analysis. The selected tissue samples were frozen using a cryostat machine at a temperature range of -20°C to -28°C depending on the nature of the tissue. The sections were cut in a cryostat to 5-6 µm thickness and stained with rapid Haematoxylon and eosin (HandE). These stained slides were examined under a light microscope by one or more pathologists. Results were informed immediately to the surgeon. After reporting, specimens were processed routinely for paraffin sections, stained with Haematoxylon and eosin and examined. The results of frozen sections and paraffin sections were compared and the accuracy of the frozen section, concordant and discordant rates, were

determined. The sensitivity, specificity, positive predictive value and negative predictive value were calculated to compare the results.

RESULTS AND DISCUSSIONS

In the present study, frozen sections of 190 tissues were studied from 190 surgical cases and correlated with routine paraffin sections. The submitted tissues for frozen section analysis were primarily from ovary, lymph node, uterus with cervix, gall bladder, thyroid, breast, ear, testis and other tissues (liver, ureter, kidney, pancreas, buccal mucosa, intestine, stomach and tongue). Indications for frozen section were verification and categorization of neoplasms, evaluation of margins, determination of the organ of origin and identification of the presence of metastatic disease. The routine paraffin section diagnosis was taken as gold standard for evaluating the accuracy of intraoperative frozen section. The frozen section and paraffin section diagnoses were concordant in 187 (98.4%) and discordant in 3 (1.6%) cases (Table 1). Among discordant cases, two were ovarian tissue and one was uterine tissue. The reason for the discrepancy was also assessed by reviewing frozen section slides. Three discordant cases reported were due to misinterpretation (Table 2). The diagnostic accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of intraoperative frozen sections in comparison with routine paraffin sections were 98.4%, 95.5 %, 99.3%, 97.7% and 98.6% respectively (Table 3). These values suggest a high level of reliability and accuracy in using frozen section diagnosis.

Table 1: Frequency of Concordant and Discordant Cases

Tissue	No. of Cases	Concordant Cases	Discordant Cases
Ovary	71	69	2
Lymph node	38	38	0
Uterus with cervix	28	27	1
Gall bladder	10	10	0
Thyroid	8	8	0
Breast	8	8	0
Ear	4	4	0
Testis	3	3	0
Others	20	20	0
Total (%)	190	187 (98.4%)	3 (1.6%)

Table 2: Discordant Cases

Tissue	Frozen Section Diagnosis	Paraffin Section Diagnosis	Reason for Discrepancy
Uterus	Atypical Leiomyoma	Adenosarcoma	Misinterpretation
Ovary	Serous Borderline Tumor with Xanthogranulomatous Inflammation	Serous Cystadenoma with Xanthogranulomatous Inflammation	Misinterpretation
Ovary	Mucinous Cystadenoma	Mucinous Borderline Tumor	Misinterpretation

Table 3: Comparative Statistical Analysis of Intraoperative Frozen Section with Routine Paraffin Section in 190 Cases

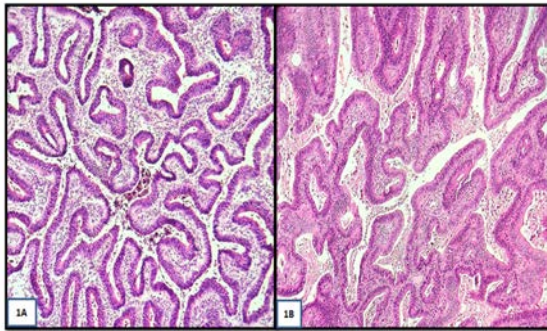| Parameter	Value (%)
Diagnostic Accuracy	98.4 %
Sensitivity	95.5 %
Specificity	99.3%
Positive Predictive Value	97.7%
Negative Predictive Value	98.6%

Fig. 1: Microphotograph of Mucinous Cystadenocarcinoma of Ovary-Frozen Section, 10x (1A) and Routine Paraffin Section, H and E ,10x (1B)
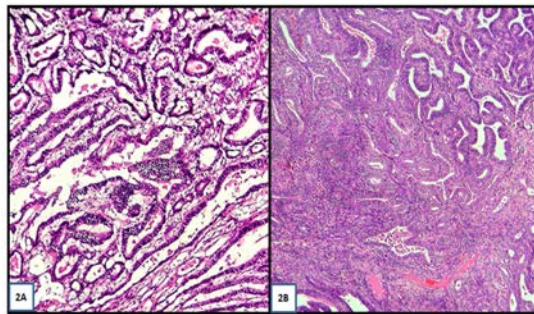

Fig. 2: Microphotograph of Serous Cystadenocarcinoma of Ovary-Frozen Section, 10x (2A) and Routine Paraffin Section, H and E, 10x (2B)
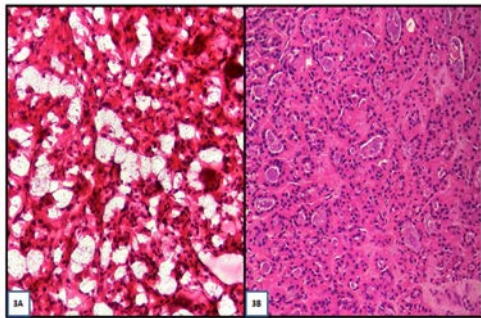

Fig. 3: Microphotograph of Hurthle Cell Adenoma of Thyroid-Frozen Section, 10x (3A) and Routine Paraffin Section, H and E, 10x (3B)
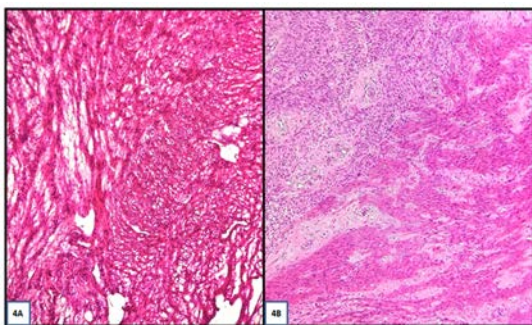

Fig. 4: Microphotograph of Leiomyoma of Uterus -Frozen Section, 10x (4A) and Routine Paraffin Section, H and E, 10x (4B)
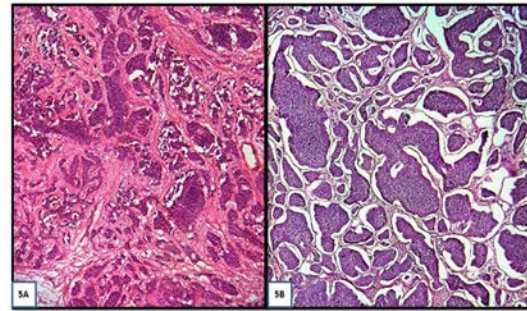

Fig. 5: Microphotograph of Neuroendocrine Tumor of Ileum-Frozen Section, 10x (5A) and Routine Paraffin Section, H and E, 10x (5B)

The intraoperative frozen diagnosis of malignancy is crucial as it determines the extent of surgery to avoid undertreatment or over treatment of the patient[8]. This is especially helpful in young patients, those with metastatic tumors, borderline tumors, or situations where it is difficult to distinguish a benign tumor from a malignant one, it also gives an immediate and accurate diagnosis and permits tissue preservation for paraffin embedding. For an adequate section, it requires technical equipment (a cryostat), technical expertise in the field and an experienced histopathologist for interpretation. Thus, in order to regard frozen section examination as a reliable diagnostic tool, its accuracy needs to be assessed[4,6,9]. By comparing intraoperative frozen sections with routine paraffin sections we also tried to evaluate the diagnostic accuracy of frozen section in the institution. A total of 190 cases were included in this study., other similar studies such as Shrestha[12], Patil[10], Phulgirkar[4] and Adhikari[11] included 404, 100, 72 and 41 cases, respectively. In the present study, the total number of concordant and discordant cases was 187 (98.4%) and 3 (1.6%), respectively. Among the three discordant cases, one case of adenosarcoma of the uterus was misinterpreted as atypical leiomyoma on frozen sections., it was mainly due to inadequate preoperative information and freezing artifacts. Two cases were of the ovary., out of the two, one case of serous cystadenoma with xanthogranulomatous inflammation was over diagnosed as a serous borderline tumor with xanthogranulomatous inflammation and the other case of mucinous borderline tumor was under diagnosed as mucinous cystadenoma on frozen sections. These discrepancies were mainly due to the interpretation error. As shown by earlier studies, ovarian epithelial tumors represent one of the most challenging areas on frozen sections and contribute significantly to the low diagnostic accuracy and sensitivity rates for ovarian neoplasms that have been observed due to tumor heterogeneity and sampling limitations in frozen sections[16]. Patil[10] had similar results of three discordant cases., out of three discordant diagnoses, one was false positive,

where choroid plexus papilloma was diagnosed as choroid plexus carcinoma on frozen sections and two were false negative, where in one case of breast, malignant phyllodes was diagnosed as benign phyllodes on frozen section and in the other case of ovary, a serous cystadenocarcinoma was reported as serous cystadenoma on frozen section. Diagnostic accuracy in the present study was 98.4%, which is comparable to other studies done by Shrestha[12] (94.3%), Adhikari[11] (97%) and Phulgirkar[4] (90.7%). According to this study, the sensitivity, specificity, positive predictive value and negative predictive value of frozen sections were 95.5%, 99.3%, 97.7% and 98.6% respectively and results were comparable with other studies done by Hatami[3], Preeti[9], Bharadwaj[6]. (Table 4).

Table 4: Comparison of Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value with Various Other Studies

	Present Study	Hatami[3]	Preeti[9]	Bharadwaj[6]
Sensitivity	95.5%	92.9%	75.0%	89.5%
Specificity	99.3%	99.5%	97.5%	98.5%
Positive Predictive Value	97.7%	98.5%	90.9%	96.7%
Negative Predictive Value	98.6%	97.8%	94.0%	94.9%

The diagnostic errors associated with intraoperative consultation can be categorized as follows: interpretation error, sampling error and poor interdepartmental communication. Errors in interpretation might arise due to several factors, such as freezing procedure artifacts, lesion rarity, or pathologists' inexperience[11,12,14,15]. In order to reduce error, studies have mentioned using imprint or crush cytological techniques along the frozen section[13,12].

CONCLUSION

The intraoperative frozen section is accurate with high sensitivity and specificity. It also provides reliable and cost-effective details necessary for rapid diagnosis. It should always be used when the preoperative diagnosis is not definite, as it guides the surgeon in determining the type and extent of surgery to avoid undertreatment or over treatment of the patient. By avoiding technical errors in sectioning and staining and with better communication between pathologist and surgeon, the rate of discordant cases can be reduced. Re-evaluation of the interpretations by a second pathologist in uncertainty is also helpful in reducing discordant cases.

REFERENCES

1. Vahini, G., B.A. Ramakrishna, S. Kaza and M.R. Murthy., 2017. Intraoperative Frozen Section -A Golden Tool for Diagnosis of Surgical Biopsies. Int. Clin. Pathol. J., 4: 22-26.

2. Mishra, S., M. Gupta, V. Bharat and R. Bansal., 2016. Qualitative comparative study of frozen section with routine histological technique. National journal of laboratory medicine., 5: 44-50.

3. Hatami, H., Z. Mohsenifar and S.N. Alavi., 2015. The diagnostic accuracy of frozen section compared to permanent section: a single center study in Iran. Iran J Pathol., 10: 295-299.

4. Phulgirkar, P.P. and S.D. Dakhure., 2018. The Diagnostic accuracy of frozen section compared to routine histological technique-A comparative study. Int J Sci Healthcare Res., 3: 88-92.

5. Jaafar, H., 2006. Intra-operative frozen section consultation: concepts, applications and limitations. Malays J Med Sci., 13: 4-12.

6. Bharadwaj, B.S., M. Deka, M. Salvi, B.K. Das and B.C. Goswami, 2022. Frozen Section Versus Permanent Section in Cancer Diagnosis: A Single Centre Study. Asian Pac. J. Cancer Care, 7: 247-251.

7. Namdar, Z.M., N. Omidifar, P. Arasteh, M. Akrami and S. Tahmasebi et al., 2021. How accurate is frozen section pathology compared to permanent pathology in detecting involved margins and lymph nodes in breast cancer? World J. Surg. Oncol., 19: 1-7.

8. Maheshwari, A., S. Gupta, S. Kane, Y. Kulkarni, L.C.B.K. Goyal and H.B. Tongaonkar, 2006. Accuracy of intraoperative frozen section in the diagnosis of ovarian neoplasms: Experience at a tertiary oncology center. World J. Surg. Oncol., 4: 1-4.

9. Preeti, A., G. Sameer, S. Kulranjan, S.A. Abhinav, R. Preeti and Y. Sunita, et al., 2016. Intra-operative frozen sections: experience at a tertiary care centre. Asian Pac J Cancer Prev., 17: 5057-5061.

10. Patil, P., S. Shukla, A. Bhake and K. Hiwale, 2015. Accuracy of frozen section analysis in correlation with surgical pathology diagnosis. Int. J. Res. Med. Sci., 3: 399-404.

11. Adhikari, P., P. Upadhyaya, S. Karki, C.S. Agrawal, S.T. Chhetri and A. Agrawal, 2018. Accuracy of Frozen Section with Histopathological Report in an Institute. J. Nepal Med. Assoc., 56: 572-577.

12. Shrestha, S., R. Basyal, T.S.S. Pathak, M. Lee, H. Dhakal and C. Pun, et al., 2009. Comparative Study of Frozen Section Diagnoses with Histopathology. Post Graduate Medical of NAMS., 9: 1-5.

13. Khoo, J.J., 2004. An audit of intraoperative frozen section in Johor. Med J Malaysia., 59: 50-55.

14. Pandey, S., S. Bhamra and A. Singh, 2020. Accuracy of intraoperative frozen section in assessing margins in oral cancers: A tertiary care hospital based study. Indian J. Pathol. Oncol., 7: 415-419.

15. Abbasi, F., Z. Yekta and A. Aryan., 2012. Accuracy of Frozen Sections. Iran. J. Pathol., 7: 3-8.

16. Buza, N., 2019. Frozen Section Diagnosis of Ovarian Epithelial Tumors: Diagnostic Pearls and Pitfalls. Arch. Pathol. & Lab. Med., 143: 47-64.