

The Diagnostic Accuracy of Frozen Section Compared to Routine Histological Technique - A Comparative Study

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ABSTRACT

Introduction: Intraoperative consultation by frozen section technique is an invaluable tool for immediate diagnosis. Its accuracy and limitations vary with different anatomical sites.

Aim: Qualitative morphological comparison between frozen section and routine formalin fixed paraffin embedded sections and determine the diagnostic accuracy in various anatomical sites.

Materials and Methods: 75 tissue specimens from 72 cases were studied over a period of 20 months. Diagnostic accuracy of frozen section and its morphological quality and reliability in comparison to histopathology was evaluated for overall morphology. The turnaround time and limitations in section preparation and problems encountered were assessed.

Results: Diagnostic accuracy of frozen section was 90.7% with, false negative rate of 4% and 5.3% of inconsistent diagnosis. The nuclear details, cellular outline and overall morphological quality of frozen section was slightly inferior to that of routine histopathology section, however, staining and cytoplasmic details were comparable. Most common limitation was freezing artifact. The average turnaround time was within 30 minutes in 76% cases.

Conclusion: Intra-operative frozen section diagnosis is very useful and highly accurate procedure but one needs to be aware of its indications and limitations. Avoiding technical errors in sectioning and staining, intimal cooperation with surgeon can avoid certain limitations and provide rapid, reliable, cost effective information necessary for optimum patient care.

Key Words: Frozen section, Diagnosis and Indications.

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 permanent 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

This was a retrospective study from a computerized database of all frozen sections conducted over a period of 20

months (June 2016 to May 2018) on 75 tissue specimens from 72 consecutive cases received from Surgical Departments for intra-operative consultation. 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 3050S cryostat. The cryostat was set at a range between -18°C to -24°C 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 permanent sections, to assess the accuracy of the technique. The frozen section results in comparison to final diagnoses were then categorized into four groups: consistent, inconsistent, false-positives and false-negatives.

RESULTS

Frozen section was performed on 75 tissues from 72 consecutive cases, and its diagnosis was compared with final conventional histopathology diagnosis in terms of qualitative morphology, diagnostic accuracy. The nuclear details, cellular outline and overall morphological quality of frozen section was slightly inferior to that of routine histopathology section, however, staining and cytoplasmic details were comparable. Clinical-frozen section diagnosis was concordant in 62% cases. While diagnostic accuracy of frozen section was 90.7% (68/75 cases) when compared with permanent section. [Table 1] None of the case was reported false positive. Sampling error was the main reason for the false negative diagnosis. In 5.3% of cases, diagnosis was inconsistent to permanent section mainly due to lack of adequate clinical information and inadequate material. Most common limitation was freezing artifact. The average turnaround time was within 30 minutes in 76% cases.

Table 1 Frozen section diagnosis in 75 cases

Accuracy	90.7%
Inconsistent	5.3%
False Positive	-
False Negative	4%

The primary indication was presence/typing of neoplasm in 60 cases, and to determine presence of ganglion cells in four cases of Hirschsprung's disease and for nodal status in six cases. Remaining 5 cases were indicated mainly to establish the diagnosis [Table 2].

Table 2

Sr No	Site	Non-neoplastic	Neoplastic		Total
			Benign	Malignant	
1.	Breast	06	19	19	44
2.	Ovary	00	04	00	04
3.	Male genital system	03	00	02	05
4.	Thyroid	04	01	00	05
5.	Liver\Gall bladder	01	00	01	02
6.	Gastrointestinal system	04	00	04	08
7.	Lymph node	04	00	02	06
8.	Adrenal gland	00	00	01	01
	Total	22	24	29	75

Breast was the commonest tissue received for frozen section with 44

specimens, all were for presence/typing of neoplasm, clinical-frozen concordance was

50%. Among 44 breast cases, invasive ductal carcinoma (17) was the most common followed by, one case of mucinous carcinoma and one case of papillary carcinoma. The benign (19) cases include 17 cases of fibroadenoma (Figure 1) and 2 cases of phyllodes tumor. The remaining 6 cases were Non-neoplastic, which include Fibrocystic disease (3) and Inflammatory lesions (3). Gastrointestinal tract (GIT) comprised of 8 cases where 1 case from stomach and 3 cases were from small and large bowel for presence of neoplasm and other 4 cases to determine presence of ganglion cells in Hirschsprung's disease. One case of liver and one case of Gall bladder, each for metastatic deposits. Six cases of lymph node include 4 cases of reactive lymph node and two cases of metastatic deposits. There were four cases from ovary that include each case of simple cyst, dermoid cyst, cystadenofibroma and Borderline serous cystadenoma.

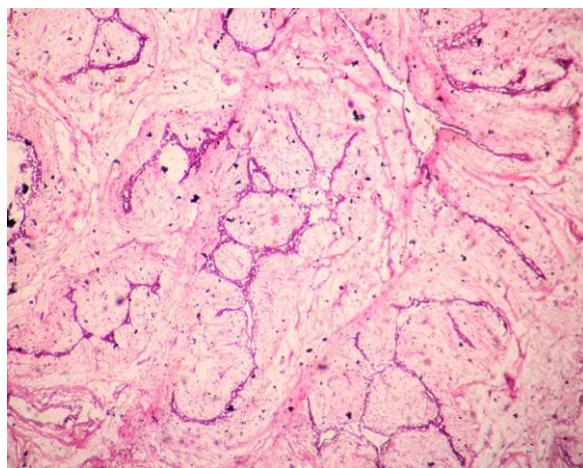


Figure 1: Fibroadenoma Breast

We received 5 cases of Male genital system, 4 cases from testis and one case from penile growth to see for presence of neoplasm. In these cases, 3 cases were negative, one case was reported as

embryonal carcinoma of testis and one case of Squamous cell carcinoma Penis. (Figure 2) All cases of Thyroid (4) were Non-neoplastic which include 3 cases of colloid goitre and one case of Hashimoto's thyroiditis. One case of parathyroid adenoma (Figure 3) was also reported.

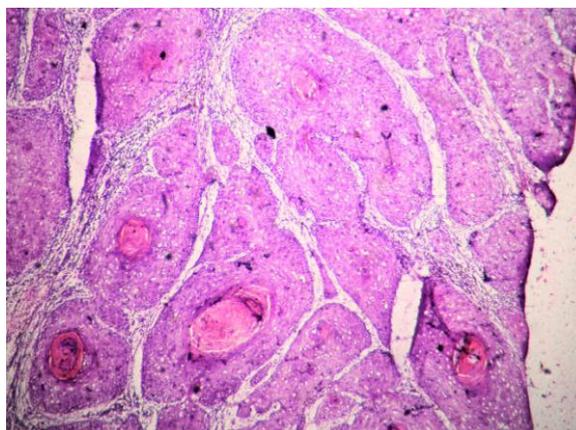


Figure 2: Squamous cell carcinoma Of Penis.

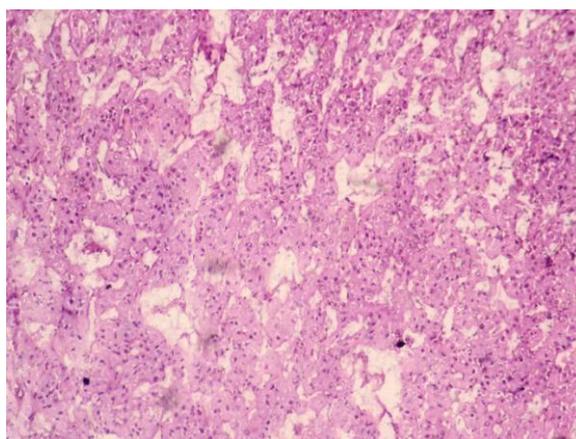


Figure 3: Parathyroid Adenoma.

One rare case of adrenocortical carcinoma was reported on frozen.

Sixty-eight cases showed diagnostic concordance among frozen and conventional histopathology, 3 cases were reported false negative and in 4 cases, diagnosis were inconsistent [Table 3].

Table 3 Comparison of Frozen & Final diagnosis in Inconsistent and False Negative cases

Site	Frozen	Final HP	False -ve	Inconsistent
Breast	No e/o Malignancy	IDC	01	-
	Benign Breast lesion	IDC	01	-
	Proliferative disorder of Breast	Papillary carcinoma	01	-
	Proliferative disorder of Breast	Granulomatous mastitis	-	01
	Inflammatory lesion	Granulomatous mastitis	-	01
	Ovary	No e/o Malignancy	Simple cyst	-
Lymph node	Reactive Lymphadenitis	Tuberculous lymphadenitis	-	01

DISCUSSION

Intraoperative diagnosis of malignancy by frozen section is very important as it aids in determining the extent of surgery. This is very valuable especially in young patients, in cases of borderline tumors, metastatic tumors or in certain cases which are hard to differentiate from malignancy. The accuracy of frozen section examination should therefore be evaluated in order to consider this diagnostic tool to be dependable. In our study, the overall accuracy rate was 90.7% which is comparable to previous studies which range from 94 to 98%. In our study, 7 cases were incorrectly diagnosed. Of these, 4 cases were under diagnosed and 3 were diagnosed with false negative rate of 4% comparable with 3 to 4.6% of deferred rate in the published results. However, the indication, accuracy and limitations of frozen section vary with different organ that have been discussed and published regularly. [9-12]

In the present study, 58.7% of biopsies for frozen section were from breast. Two cases of ductal carcinoma and one case of papillary carcinoma were under diagnosed as hyperplasia and benign breast lesion respectively. These discrepancies were mainly due to the interpretation error and partly due to lack of interdepartmental communication. Interpretation errors may result from artifacts of the freezing procedure and rarity of the lesion.

In other sites such as hepatobiliary, gastrointestinal and male genital system, Lymph node frozen sections were sent for primary diagnosis, margin assessment and nodal metastasis. Benign and malignant lesions were identified correctly in most of the cases, but, typing error was a frequent problem. This was due to loss of architectural pattern and freezing artifact. Many authors believe that determining the presence of malignancy without subtyping can be the best option to decrease the discrepancies. [13] Frozen section is not needed for the evaluation of inflammatory changes. In cases of suspected malignancy

arising in Inflammatory Bowel Disease, frozen section may be helpful.

At times, diagnostic accuracy of frozen section may be much higher than that of fine needle aspiration cytology. Frozen section can be considered only when the clinical suspicion of malignancy is significant and the fine needle aspiration cytology results are suspicious or unsatisfactory and in patients with unexpected findings during surgery.

CONCLUSION

The intra-operative consultation using frozen section is a very useful and highly accurate procedure but one needs to be aware of its indication and limitations. Gross inspection, sampling by pathologist, frozen complemented with cytological and histological review and communication between surgeon and pathologist can avoid certain limitations and provide rapid, reliable, cost effective information necessary for optimum patient care.

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