

## Original Research Article

# Analysis of frozen section in correlation with surgical pathology diagnosis

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**Received:** 30 March 2019

**Accepted:** 04 May 2019

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### ABSTRACT

**Background:** Frozen section (FS) is a rapid diagnostic procedure performed on tissues obtained intraoperatively. This method serves useful purposes, such as determining the malignancy or benignancy of a suspected lesion, determining the adequacy of a biopsy of a suspected lesion, confirming the presence or absence of metastasis, and identifying small structures. But it bears many disadvantages and limitations, the most of which is the danger of incorrect diagnosis. Therefore, it is critical to determine efficiency of frozen section performance periodically. This study was performed to determine accuracy of frozen section by correlating the intra-operative frozen section diagnosis with final diagnosis on permanent sections.

**Methods:** In this retrospective study, authors compared the results of frozen section with their final permanent section diagnosis in Government Medical College and Hospital, Aurangabad, Maharashtra, India during January 2017 to December 2018.

**Results:** Study comprises 83 patients, of which 73 were female and 10 were male. Out of 83 cases, the diagnosis of 76 cases was concordant with conventional histopathology diagnosis while seven were discordant. This gave overall accuracy rate of 91.57% and discordant rate of 8.43%. The overall sensitivity was 85.71% and specificity was 97.92%. The positive predictive and negative predictive value was 96.77% and 90.38% respectively.

**Conclusions:** The accuracy, sensitivity, specificity of frozen section diagnosis in this study are comparable with most international quality control statistics for frozen sections. The results suggest that the correlation of intra-operative frozen section diagnosis with the final histopathological diagnosis on permanent sections forms an integral part of quality assurance activities in the surgical pathology laboratory and specific measures should be taken to reduce the number of discrepancies.

**Keywords:** Accuracy, Conventional histopathology, Frozen section, Intra-operative consultation,

### INTRODUCTION

The rapid frozen section method is a means of intraoperative pathological diagnosis, first introduced by Welch in 1891 and developed as a diagnostic tool by Cullen, Wilson, MacCarty et al.<sup>1</sup>

Tissue specimen taken from a patient by doing 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 intra-operative consultation on the tissue that is being taken out. The examination is made while the patient is under anesthesia on the operating table. The examination report will then be conveyed as soon as possible to the operating surgeon via telephone or

intercoms and the result will greatly influence the surgeon's intra-operational decision.<sup>2</sup>

Even though FS provides rapid gross or microscopic diagnoses that can guide intra- or peri-operative management of a patient, it is not the replacement for paraffin embedded tissue technique. Comparatively, FS is still inferior to the later due to its limitations. The sampling of specimen is limited and there are technical difficulties of getting good quality sections and staining of tissue; which will all influence the interpretation of the section by the pathologist.<sup>2</sup>

Periodic review of the frozen section diagnosis by correlating its diagnosis with the 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.<sup>3</sup>

This study aims are carried out to assess the degree of diagnostic accuracy of frozen section examination of various anatomical sites, the overall accuracy, sensitivity and specificity of the frozen section technique.

## METHODS

Present study was carried out in the Frozen Section and Histopathology Department of Pathology, Government Medical College and Hospital, Aurangabad, Maharashtra, India from 1<sup>st</sup> January 2017 to 31<sup>st</sup> December 2018. During this study period, a total of 83 patients underwent surgery with intra-operative pathologic consultation for various malignant and non-malignant conditions.

For frozen section, fresh tissue was sent in normal saline from the operation theater to the frozen section room and the gross specimens were inspected, dissected and sections were taken. Blocks were cut on the cryostat (Leica CM 3050 S) using Optimal Cooling Temperature (OCT) compound as embedding medium followed by rapid Hematoxylin-Eosin staining.

Surgeons were immediately informed of frozen section diagnosis through the interphone.

Frozen tissue as well as any remaining non frozen tissue were then fixed in 10% formalin solution and sent to Histopathology section where they were processed for routine paraffin section and followed by conventional Hematoxylin-Eosin staining on next day as per standard protocols and further reporting was done.

The impression of the pathologist as given to the surgeon at the time of surgery was compared to the final histopathology report of the permanent sections. The accuracy rate, sensitivity and specificity of the frozen section reporting was determined in comparison to the routine histopathology reporting.

## RESULTS

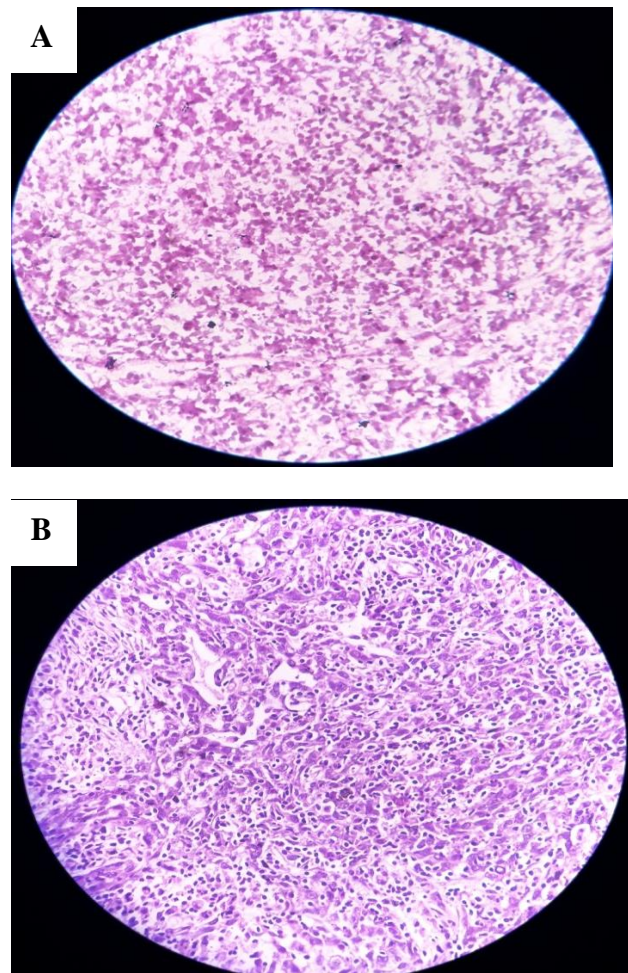
Study comprises 83 patients, of which 73 were female and 10 were male. The age range was wide and varied from 02 years to 77 years.

Indications for frozen section encountered in authors' institute were:

- Primary diagnosis and verification and categorization of neoplasm (92.8%),
- Assessment of nodal status (7.2%) mostly in breast and git malignancies.

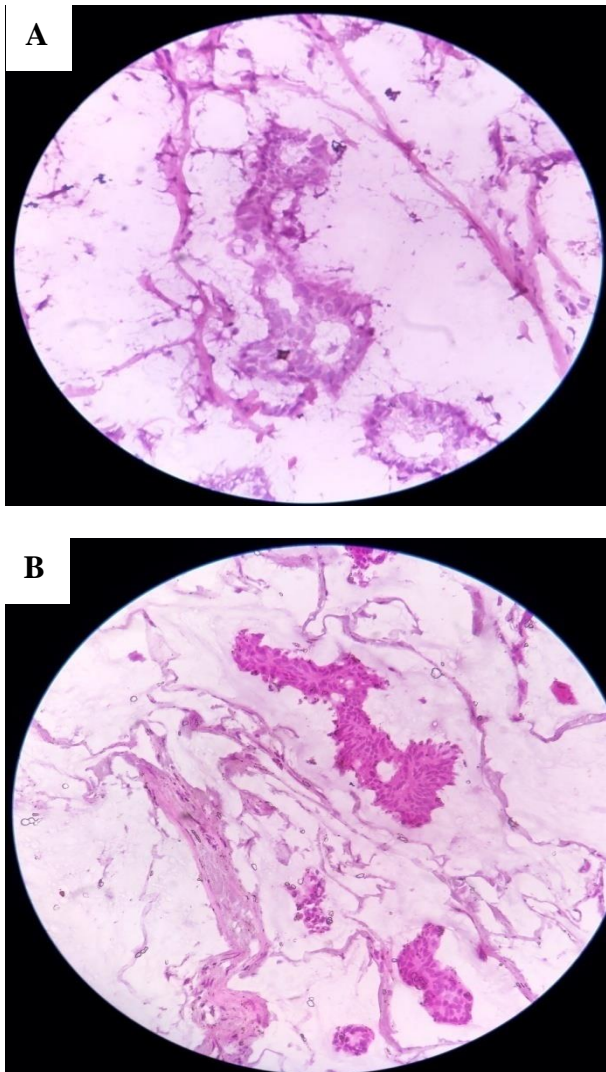
Sample sent for frozen section include tissue from breast 50 (60.24%), GIT 9 (10.84%), thyroid 6 (7.22%), lymph node 6 (7.22%), ovary 6 (7.22%), testis 2 (2.40%), penile skin 2 (2.40%), soft tissue 1(1.20%) and adrenal gland 1 (1.20%).

### Breast



**Figure 1: IDC breast. (A): 4X view of rapid H&E stained slide of frozen section shows infiltrating ductal carcinoma of breast, (B): 4X view of routine H&E stained slide of conventional -histopathology section shows infiltrating ductal carcinoma of breast.**

Most common sample received for frozen section was breast lump biopsy 50 (60.24%). It includes Infiltrating ductal carcinoma (19 cases, Figure 1), fibroadenoma (17 cases), chronic mastitis (7 cases), fibrocystic disease(3 cases), benign phylloid (2 cases), intracystic papillary carcinoma (1 case) and mucinous adenocarcinoma (1 case, Figure 2).



**Figure 2: Mucinous adenocarcinoma of breast. (A): 4X view of rapid H&E stained slide of frozen section shows mucinous adenocarcinoma of breast, (B): 4X view of routine H&E stained slide of conventional - histopathology section shows mucinous adenocarcinoma of breast.**

Infiltrating ductal carcinoma was the most common diagnosis on frozen section). There were two cases of proliferative breast disease on frozen section of which one turned out to be chronic granulomatous mastitis and other case turned out to be intracystic papillary carcinoma on conventional histopathology.

In other two cases, the diagnosis of benign breast disease on frozen section turned out to be Infiltrating ductal

carcinoma on conventional histopathology. These cases comprised false negative diagnosis on frozen section. The accuracy of frozen section diagnosis for breast was found to be 92%.

### **GIT**

Gastrointestinal tract comprised nine cases; four from rectum, two each from colon and stomach and one from liver. There were five cases of adenocarcinoma. Out of five cases two cases were reported as negative for malignancy on frozen section. There were three cases which were negative for malignancy both on frozen and conventional histopathology.

One case for ganglion cell status, shows presence of ganglion cells on both procedures. The accuracy of frozen section diagnosis for breast was found to be 77.78%.

### **Thyroid**

It comprised six cases of all frozen sections. Goiter was diagnosed in five cases and hashimoto thyroiditis in one case. All the six cases from thyroid showed concordance with conventional histopathology diagnosis. This gave an accuracy rate of 100%.

### **Lymph node**

Authors received six lymph node biopsies for frozen section. Out of six lymph nodes, five were to assess the nodal status in cases of malignancy. There was 100% concordance between frozen section and conventional histopathology diagnosis in these five cases. There was a case of tuberculous lymphadenitis, which is not correctly diagnosed on frozen section.

### **Ovary**

It comprised six cases of all frozen sections. The most common diagnosis was serous cystadenoma (2 cases), luteal cyst (2 cases) and one case each of mucinous cystadenoma and dermoid cyst. All the six cases from ovary showed concordance with conventional histopathology diagnosis. This gave an accuracy rate of 100%.

### **Testis**

There were 2 cases of partial testicular atrophy, which were correctly diagnosed on frozen section. This gave an accuracy rate of 100%.

### **Penis**

There were two cases of squamous cell carcinoma. Both the cases showed concordance with conventional histopathology diagnosis.



**Soft tissue**

There was one case of fibroma, which is correctly diagnosed on frozen section. This gave an accuracy rate of 100%.

**Adrenal gland**

There was one case of adrenocortical carcinoma, which is correctly diagnosed on frozen section. This gave an accuracy rate of 100%.

Out of 83 cases, the diagnosis of 76 cases was concordant with conventional histopathology diagnosis while seven were discordant. This gave overall accuracy rate of 91.57% and discordant rate of 8.43%. The overall sensitivity was 85.71% and specificity was 97.92%. The positive predictive and negative predictive value was 96.77% and 90.38% respectively.

Most common causes of discordant diagnosis are sampling error (71.43%) and interpretative error (28.57%). Authors also evaluated the accuracy of frozen section according to the anatomic site, which is shown in Table 1.

**Table 1: Organ wise accuracy of frozen section.**

Anatomical site	No. of cases	Concordant cases	Discordant cases	Accuracy (%)
Breast	50	46	4	92
GIT	9	7	2	77.78
Thyroid	6	6	-	100
Lymph node	6	5	1	83.66
Ovary	6	6	-	100
Testis	2	2	-	100
Penis	2	2	-	100
Soft tissue	1	1	-	100
Adrenal gland	1	1	-	100
Total	83	76	7	91.57

**DISCUSSION**

At times during performance of surgical procedures, it is sometimes necessary to get a rapid diagnosis of a pathologic process. This can be accomplished through use of a FS.<sup>2</sup>

FS provides rapid gross or microscopic diagnosis that can guide intra- or peri-operative management of a patient. Even though FS provides rapid diagnosis, it should not be used to replace paraffin embedded tissue technique. Comparatively, FS is still inferior to the later due to its limitations. The sampling of specimen is limited and

there are technical difficulties of getting good quality sections and staining of tissue; which will all influence the interpretation of the section by the pathologist.

In the present study of breast lesions, there were two cases of proliferative breast disease on frozen section of which one turned out to be chronic granulomatous mastitis and other case turned out to be intracystic papillary carcinoma on conventional histopathology. This discordance in both the cases is due to interpretation error. In other two cases, the diagnosis of Benign breast disease on frozen section turned out to be Infiltrating ductal carcinoma on conventional histopathology. This discordance in both the cases is due to sampling error.

**Table 2: 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
Junn-Liang et al <sup>4</sup>	China	01 year	1084	97.7%	96.16%	99.43%
Farah-Klibi F et al <sup>5</sup>	France	03 year	1207	97.5%	84.6%	99.8%
Shrestha S et al <sup>6</sup>	India	05 year	404	94.6%	94.56%	94.55%
Fariba Abbasi et al <sup>7</sup>	Iran	0 7 year	200	96.5%	93.1%	97.7%
Peter JH et al <sup>8</sup>	North America	01 year	1952	96.5%	-	-
Chandramouleeswari K et al <sup>9</sup>	India	01 year	51	92%	-	-
Patil P et al <sup>10</sup>	India	02 year	100	96.96%	97.23%	96.30%
Present study	India	02 year	83	91.57%	85.71%	97.92%

In GIT, two cases of adenocarcinoma, reported as negative malignancy. It is due to sampling error. There was a case of tuberculous lymphadenitis, which is not correctly diagnosed on frozen section due sampling error.

The overall accuracy of frozen section diagnosis reported in the literature varies from 92% to 97.98%.<sup>4-10</sup> Present study shows an accuracy rate of 91.57%. This is near the range reported. The sensitivity of frozen section reported in various studies ranges from 84.6% to 97.98%.<sup>5-7</sup> Authors observed sensitivity of 85.71%, which is within the range. The reported specificity of frozen section in literature ranges from 94.55% to 100%.<sup>5-7,10</sup> Authors reported the specificity of 97.92%, which is also within the range (Table 2). Limitations of FS can be divided into three main categories namely sampling error, technical problem and interpretative error.<sup>11,12</sup>

Sampling errors include poor sampling of tissue/limitation of the surgeons, Poor selection of appropriate tissue after grossing, extensive tumour degeneration or necrosis, poor assessment of capsular or vascular invasion. Searching for immature component in an ovarian teratoma is rather time consuming in FS and subjected to sampling error.

Technical problems include freezing artifacts, Poor quality section, bloated cell morphology and Poorly stained section.

Interpretative errors include tumours that mimic the normal tissue are difficult to diagnose e.g., signet ring cells in diffuse gastric carcinoma. There is difficulty in assessment of chronic pancreatitis versus pancreatic carcinoma and difficulty in assessing ganglion cells and hypertrophied nerve bundles in Hirschsprung disease. FS should not be treated as an emergency procedure due to the difficulty of the procedure and the availability of the technician.<sup>2</sup> Close cooperation between the surgeon and the pathologist is required if a meaningful frozen report is to be achieved. Preferably, the case should be discussed beforehand between the surgeon and the pathologist.<sup>2</sup>

Most common causes of discordant diagnosis in the present study are sampling error (71.43%) and interpretative error (28.57%). Which is also seen Zarbo, et al, Novis et al, and Ahmad Z et al.<sup>13-15</sup>

These limitations of FS need to be taken into consideration when requesting for this procedure, in order to avoid grave mistakes that will be detrimental to the patient's management.

## CONCLUSION

The accuracy, Sensitivity, Specificity of frozen section diagnosis in this study are comparable with most international quality control statistics for frozen sections. The results suggest that the correlation of intra-operative

frozen section diagnosis with the final histopathological diagnosis on permanent sections forms an integral part of quality assurance activities in the surgical pathology laboratory and specific measures should be taken to reduce the number of discrepancies.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Tangde A, Shrivastava V, Joshi A. Analysis of frozen section in correlation with surgical pathology diagnosis. *Int J Res Med Sci* 2019;7:2312-7.