DIAGNOSTIC ACCURACY AND PITFALLS OF FROZEN SECTION EXAMINATION IN A TERTIARY CARE CANCER HOSPITAL - A CASE SERIES ANALYSIS OF 531 CASES

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Abstract

INTRODUCTION: Frozen section (FS) analysis is an integral part of daily work-up of the surgical pathology department which require teamwork of pathologists, residents and technical staff. The aim of the study was to evaluate the accuracy and determinants of FS diagnosis, compared with the final histological diagnosis.

METHODS: The study included FS requisitions received in the Pathology department, from March 2020 to March 2022. Intraoperatively, tissue samples were processed and reported as per the standard FS protocol. Definitive histopathological diagnosis was made by examining sections of formalin fixed paraffin embedded (FFPE) block prepared from the remaining tissue after FS examination. The results of FS diagnosis were then compared with the final histopathological diagnosis.

RESULTS: Total 531 requisitions of FS analysis were received. Maximum requisitions came from surgeries of head and neck (41.05%) followed by genitourinary (17.89%) and others. The FS and FFPE histology were concordant in 519 (97.7%) cases while 5 (0.9%) cases were deferred. Overall specificity, sensitivity, PPV and NPV of FS examination as compared to final histopathology were 97.82%, 99.79%, 97.82% and 99.79%.

CONCLUSION: Pathologists should be well aware of the procedure, errors, troubleshooting and should be competent enough to arrive at the most conclusive diagnosis as early as possible which will have definite consequences on patient management. Periodic review of the correlation between frozen section (FS) diagnosis and final diagnosis is very useful and can serve as a measure of an institutional quality of service.

Keywords- frozen section (FS), concordance, formalin fixed paraffin embedded (FFPE), deference

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INTRODUCTION

Frozen section (FS) analysis has been an integral part of daily work-up of the surgical pathology department. To perform this task accurately and on time, teamwork of pathologists, residents and technical staff is required. The process is a quick step in the bigger picture of immediate surgical care to the patient, assessing the continuation or closure of the procedure.

Discrepancies between FS and formalin fixed paraffin embedded (FFPE) histology is expected owing to the limited tissue sampled and the technicalities involved during FS. The literature reports discordance rates between frozen section diagnoses and final histopathological diagnosis ranging from 1.4% to 12.9%. About 75% of studies report a discordance rate below 5%, with an overall median of 2.9%.[1] A study has stated FS errors affect the intra-operative patient management, that is in 0.1% of FS performed. [2]

FS examination is an integral part of surgical pathology and we receive 3-4 FS requisitions per day on an average. Therefore, the aim of the present study was to evaluate the accuracy and determinants of FS diagnosis, compared with the final histopathological diagnosis and also to identify the problems in cases of discrepancies.

PATIENTS AND METHODS

The present study was conducted in the Pathology department of Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan from March 2020 to March 2022. All FS requests received in the department were identified in the database. All the details related to intra-operative FS diagnosis and final FFPE diagnosis were collected and discordances were noted and analysed. The departments requesting for FS examination include General surgery, surgical oncology, Gynecology, Urology, Orthopaedics and Hepatopancreatobiliary.

Intraoperatively, tissue samples were processed as per the standard protocol. The fresh tissue specimens were received with proper identification and their duly filled requisition forms. All the relevant clinical and radiological data of the patient was taken beforehand. The specimens were examined properly macroscopically and were sampled depending on the indication of frozen section and also on the gross suspicion of the pathologist. The tissue was frozen in the cryostat and 4-5 um sections were cut and stained by rapid hematoxylin and eosin stain.

In cases of thyroid and lymphoid tissue, imprints were also prepared. The slides were examined by experienced pathologists. The reports of FS examination were given within 20-30 minutes of receiving requisition. For definitive histopathological diagnosis, the remaining tissue was formalin fixed, analysed grossly and sectioned. Paraffin blocks prepared from the tissue were cut and hematoxylin and eosin stained sections were prepared. The results of frozen section (FS) diagnosis were then compared with the final histology diagnosis. The result where FFPE diagnosis was similar to FS diagnosis was labelled concordant and the mismatched cases were labelled discordant. The discordant cases were further analysed and the parameters potentially influencing the FS accuracy were scrutinized.

RESULTS

Total 531 requisitions of FS analysis were received in 2 year period. Their case series analysis showed that maximum requisitions came from surgeries of head and neck (41.05%) followed by genitourinary (17.89%), endocrine (9.03%) and hepatopancreatobiliary system (7.90%) as shown in the graph (Table 1).

Table 1 Overview of concordant and discordant cases for Frozen Section and Fresh Frozen Paraffin Embedded Section (FFPE) as per site.

Specimen	Total number of cases	Concordant cases	Discordant cases	Deferred cases
Head and neck	218	211	2	2
Genitourinary system	95	93	1	1
Endocrine system	48	47	0	0
Hepatopancreatobiliary system	42	42	0	0
Gastrointestinal system	39	39	0	0
Breast	38	37	1	1
Lymph node	23	23	0	0
Bone and soft tissue	22	21	3	1
Bone marrow	6	6	0	0
TOTAL	531	519	7	5

The indications of FS were categorised into (i) requests to comment upon margin status, (ii) to provide probable diagnosis and (iii) comment on the nodal status, status of omental tissue, peritoneal tissue or mesentery. Maximum number of FS requests received were to know about the status of margins in 309 cases (58.19%). Also, requests were received to get the probable diagnosis in 182 (34.27%) and the nodal status in 40 (7.53%) cases respectively. (Table 2)

Table 2. Details of concordant and discordant cases as per indication of frozen section (FS) examination.

	Frozen section diagnosis	**Final diagnosis**	
Margins status (n=309)	Negative -300	Positive -0	Negative -300
	Positive- 9	Positive -5	Negative -4
Diagnosis(n=182)	Benign- 155	Benign- 152	Malignant-3
	Malignant- 27	Benign-0	Malignant- 27
Nodal status(n=40)	Positive- 10	Positive- 10	Negative -0
	Negative -30	Positive- 0	Negative -30

The FS and FFPE histology were concordant in 519 (97.7%) cases while 7 (1.3%) cases were discordant. The discordant cases included four requests for margin status (57.14%) and one case (14.28%) for diagnosis in ovary, breast and soft tissue each (Table 3).

Table 3: Reasons for discordance between frozen section (FS) and final histopathological diagnosis.

Discordant cases	**FS Request**	**Frozen section diagnosis**	**Final diagnosis**	**Reason for discordance**
Buccal mucosa	Margin	Positive	Negative	Sampling error
Forehead	Margin	Positive	Negative	Technical error
Ovary	Diagnostic	Mucinous cyst adenoma	Borderline mucinous tumor	Sampling error
Breast	Diagnostic	Phyllodes tumor	Malignant phyllodes tumor	Reporting error
Thigh mass	Margin	Positive	Negative	Sampling error
Abdominal mass	Margin	Positive	Negative	Sampling error
Retroperitoneal mass	Diagnostic	Small round blue cell tumor ?neuroendocrine	Round cell sarcoma	Reporting error

Out of the total 531 cases, the diagnosis of five cases (0.9%) was deferred (Table 4).

Table 4: Reason of deference in different cases.

Site	**Reason for deference**
Thyroid	Equivocal PAP diagnosis
Salivary gland	Mucoepidermoid carcinoma vs Plemorphic adenoma vs Squamous metaplasia
Breast	Phyllodes tumour with raised mitotic activity
Soft tissue (thigh)	Spindle cell with raised nuclear pleomorphism
Ovary	? Borderline mucinous tumor

Revised margins were resubmitted for FS examination in 9 positive margins cases which were then reported as negative.

Overall specificity, sensitivity, PPV and NPV of FS examination as compared to final histopathology were 97.82%, 99.79%, 97.82% and 99.79%. It showed excellent results in all FS indications except low positive predictive value (PPV) of margin status evaluation (55.56%) and slightly low sensitivity (90%) in diagnostic indication when all the indications were evaluated individually (Table 5).

Table 5: Specificity, sensitivity, positive predictive value and negative predictive value of frozen section (FS) case analysis.

Frozen section (FS) request	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
For diagnosis	90	100	100	98.1
For margin status	100	98.7	55.56	100
For nodal status	100	100	100	100
Overall	97.82%	99.79%	97.82%	99.79%

DISCUSSION

The most important role of FS is to provide rapid and definite diagnosis which will guide the operative management of a patient including evaluation of margin adequacy, identification of tissue adequacy, identification of lymph node metastasis and for diagnosing the pathology in difficult cases. [3]

Pre-analytical factors including clinical data, radiological findings and biochemical tests play important role in predicting the diagnosis in cases of FS with diagnostic requisition. Duly filled request form along with proper patient characteristics influence the accuracy of FS diagnosis.[4] Analytical factors like technical errors, sampling errors, suboptimal slide preparation are responsible for the wrong diagnosis in FS.[5] The inaccuracy of FS results has been attributed 90% to these factors.[6] These include not only sampling from the representative area which depicts the experience of the pathologist to identify correct gross features representative of the tumor characteristics like grossing of necrosed area, skipping the borders of a tumor (important diagnostic point in certain tumors), missing the small solid parts in a grossly cystic lesion etc. Also, suboptimal slide preparation including incomplete cuts due to improper embedding of the tissue, folds in the sections, serrations on the slide prepared, improper clearing and dehydration during staining procedure, ineffective staining particularly with hematoxylin, adds to the inaccuracy. The pathologist as well may affect the preparation of slides by giving improper guidance to the technical staff. [5] The accuracy of FS diagnosis also depends on the experience of the pathologists which is likely to be high with experienced pathologists. In a large study 914 ovarian FS performed, misdiagnosis was more frequent in the General Surgery department than in the specialist oncology department. [7]

The surgeon had gone ahead to revise the margins in 9 positive margins cases which were then reported as negative in FS of revised margins submission. So it helped both patient and surgeon to take extra margins at the same sitting, reducing the morbidity associated with next surgery.

Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the present study is comparable with the reported data. The above parametric value of frozen section in comparison with permanent section (as gold standard) were 85.18%, 100%, 100% and 83.33% respectively in a study conducted by Dhakal B et al. [8] and 92.95%, 99.55%, 98.50% and 97.80% respectively in a study by Hatami et al.[4]

There should be periodic review of the correlation between frozen section diagnosis and final diagnosis as a useful tool which can measure institution's quality of service. A team work between pathologists, trainee, technicians and surgeons will be fruitful to reduce the rates of discordance and provide better patient care.

CONCLUSION

The present study showed that frozen section examination is a very good tool with high accuracy rate (97.7%) in diagnosis which will help surgeon to make intraoperative decisions accurately and on time. Overall specificity, sensitivity, PPV and NPV of FS examination as compared to final histopathology were 97.82%, 99.79%, 97.82% and 99.79% respectively. Pathologists are the final authority to take decision on the frozen section inspite of all clinical and technical problems coming in the path. Hence, he should be well aware of the procedure, errors, troubleshooting and the knowledge to arrive at the most conclusive diagnosis as early as possible which will have definite consequences on patient management.

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