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Original Research Article

Qualitative Comparison of Frozen Section with Routine Histopathological Section - Our Institutional Experience

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Abstract:

Introduction: Intraoperative frozen section is a vital tool for making a quick diagnosis for the surgeon. It is also an integral part of quality assurance in surgical pathology laboratories when compared with the paraffin section reports.

Aims and Objectives: 1) To analyze the discrepancies and deferrals in frozen section reporting when compared with the formalin fixed paraffin embedded sections. 2) Average turn over time.

Materials and Methods: A retrospective study was undertaken of all frozen sections reported in our institute, MS Ramaiah Hospital, from 1st June 2016 to 31st July 2018. The records of frozen section reports were reviewed and correlated with its paraffin section reports for concordance.

Results: A total of 257 frozen section reports were evaluated. 247 cases (96.10%) correlated and 10 cases (3.89%) were discordant. The overall sensitivity, specificity, positive predictive value and negative predictive value of the frozen section as compared to paraffin sections were 100%, 50%. 96.1% and 100% respectively. The average turnover time was 20 minutes.

Conclusion: Frozen section is an accurate and a valuable tool for intra operative surgical management. Errors in some subspecialties were higher than in others. The overall goal is to reduce errors, the number of deferrals and improve frozen section diagnosis turnaround times, which will have a great impact on patient care and surgical decision making.

Keywords: Frozen section, routine histopathological section, paraffin section reports.

Introduction

Lang first employed the use of freezing to harden tissues in the nineteenth century. De Riemer in 1818 made the pioneering effort of using frozen section technique for histopathological diagnosis. It was first used for intra operative consultation by William H Welch from John Hopkins Hospital in 1891. It was further developed by Wilson and Mccarty in 1905 at Mayo Clinic. The development of a cryomicrotome or popularly known as cryostat in 1959, has revolutionized the frozen section technique. [1]

Intra operative consultation provides immediate surgical management to establish the nature and type of lesion, confirm the presence of malignancy, status of surgical margins and ensuring the sufficient sampling of lesional tissue. The indications and limitations of frozen section diagnosis varies depending on the different organ systems. The pathologist has to arrive at a correct decision in a short duration under pressure bases on his experience, judgment and the knowledge of his speciality. [1]

He has to have a keen awareness of the limitations of the method as the patient's treatment is influenced by his report. Errors can be divided into technical errors, sampling and interpretation errors.

These include initial selection of tissue by the surgeon, the sampling of the tissue by the pathologist, the technical expertise required to make sections on the cryostat and preparation of the slides and errors in interpretation. [2]

Thus, careful evaluation at every step of the process makes a difference in providing the best possible treatment and care to the patient.

Material and Methods

A retrospective study was conducted in our institute, Ramaiah Medical College and Hospitals, from 1st of June 2016 to 31st of July 2018. All the frozen

section cases that were received during that period of time were taken into the study.

Fresh tissue samples were sent in clean plastic containers without any fixative or saline. This avoids the problem of fixation artefacts. This is accompanied with the requisition form with all the patient details and a brief clinical history and the indication for frozen section.

Detailed gross examination was done and documented and sections were submitted from representative areas. Frozen sectioning was done using the Lieca 1510 cryostat. OCT (optimal cutting temperature) compound (Lieca Company), used as the freezing medium, was poured over the metal chucks over which the sections were placed. The freezing temperature ranges from -15 degrees to -23 degrees depending on the type of tissue. After the tissue was frozen, the chuck was clamped onto the specimen head. Sections were cut were cut at 6-8 microns thickness and immediately fixed in 95% isopropyl alcohol. Rapid hematoxylin and eosin staining (H&E) was performed.

The microscopic examination and diagnosis were made on the consensus of two pathologists, including one senior pathologist. The report was then immediately conveyed to the operating surgeon through the intercom. The remaining tissue that was sent for frozen section was then fixed in 10% buffered formalin solution. After appropriate fixation, grossing was done and further samples were submitted for paraffin sections.

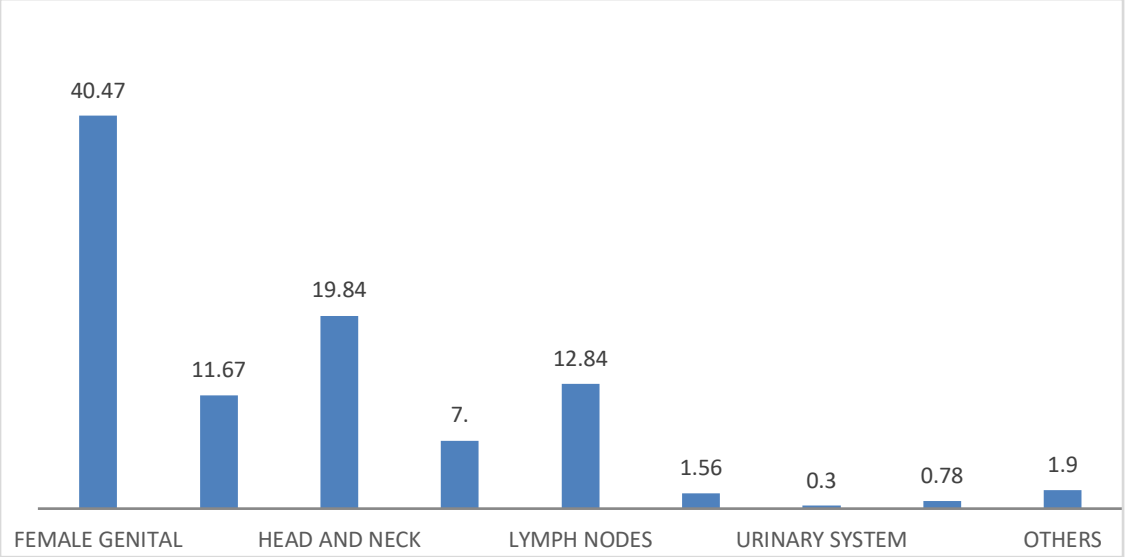
Conventional automated histoprocessing was done. The paraffin embedded sections were cut at 4-5 micron thickness stained with routine H&E staining technique. These slides were then reviewed by the pathologist. The frozen section and the respective paraffin section reports were entered in a separate register and documented for correlation.

Figure 1: Leica 1510 Cryostat Machine

Results

A total of 257 frozen section reports were evaluated. The table below (fig 1) enumerates the distribution of cases received from different organ systems.

As plotted, 40.47% of the frozen sections were received from the female genital system, sent from Departments of OBG and Surgical oncology. The cases were predominantly ovarian cysts, out of which most of them were diagnosed as benign, few as borderline and malignant. At times when peritoneal deposits were suspected, peritoneal wash was also sent for cytological examination. The second most common system was Head and neck, which represented 19.84% of the total samples sent, of which majority of them were sent for squash cytology. This was followed by lymph nodes (12.84%) for evaluation of metastasis and gastrointestinal system (11.67%) for the evaluation of surgical margins.



Graph 1: Distribution of cases (in %)

In the study, the most common pathological processes in frozen section diagnosis was verification and categorization of neoplasm (65.36%), followed by assessment of tumor margins (17.12%), and followed by lymph node metastasis (13.61%).

Out of 257 cases, 247 cases showed concordance with its respective paraffin section reports and 10 cases were discordant. No cases were deferred. The average turnaround time for all the cases was 20 minutes.

The distribution of the cases from different organ systems along with the number of concordant and discordant cases and accuracy percentage has been listed out in the table below.

Table 1: Distribution of cases within the different organ systems

Sr. No	Organ System	Total Cases	Concordant	Discordant	Accuracy (%)
1.	Female Genital System	106	104	02	98.11
2.	Hepatobiliary And Stomach	31	30	01	96.77
3.	Breast	20	18	02	90.00
4.	Thyroid	02	02	00	100.0
5.	Lungs And Mediastinum	04	04	00	100.0
6.	Head And Neck	52	51	01	98.07
7.	Kub	01	00	01	0
8.	Lymph Nodes	35	33	02	94.2
9.	Others (Skin And Soft Tissues Tumours)	06	05	01	83.33

The overall concordance rate was 96.1% and discordance rate was 3.89%.

Maximum concordance was seen in verification and categorization of neoplasm especially in gynecological oncology (predominantly ovarian neoplasm), where there was 100% concordance.

Discordancy was observed in assessment of surgical margins for tumor excision (9.09%) followed by lymph node metastasis (5.7%). The discordance was attributed to misinterpretations errors (1.6%) and sampling errors (1.82%).

The overall sensitivity, specificity, positive predictive value and negative predictive value of frozen section was calculated as 100%, 50%, 96.1% and 100% respectively.

Discussion

Frozen section plays a pivotal role in the surgical management of patients with both neoplastic and non-neoplastic diseases.

Since its introduction in the late 20th century, the utilization of frozen section has seen a remarkable surge. It furnishes the surgeon with crucial pathological information while the patient is undergoing surgery. There exist numerous indications for performing frozen section, such as determining the nature and extent of a lesion, evaluating surgical margins, and ascertaining the adequacy of tissue for accurate diagnosis.

However, the primary objective of frozen section is to provide real-time guidance to the surgeon, enabling immediate decisions regarding the necessary extent and adequacy of the surgical procedure. Consequently, this judicious utilization of frozen

section significantly reduces the likelihood of requiring reoperation. [3,4,5] In a study done at university of Michigan Hospitals, Ann Arbor, USA on frozen section requests of 914 cases, it was noted that 95% were performed for appropriate reasons, which included evaluation margins (46%), establishing a primary diagnosis (43%) and determining adequacy or viability of tissue (3%) [6,7].

In our study, the most common pathological processes in frozen section diagnosis were verification and categorization of neoplasm (65.36%), followed by assessment of tumor margins (17.12%), and followed by lymph node metastasis (13.61%). Most centers reported an accuracy rate of frozen sections 92% to 98% depending on type of cases studied. [8] A large center like Mayo clinic Rochester, USA reported an overall accuracy of 97.8% on reviewing 24,880 frozen cases in a year. [4] In the study conducted by Jaafar H, a comparative overall accuracy of 97.56% was noted at a general hospital in Malaysia involving 215 frozen section specimens over 4 years duration. [1]

In our study of 257 frozen section cases, the overall accuracy rate is 96.1%, which can be interpreted as comparable with most internationally published standards. Other reported cases included accuracy rates of 98.1% in gynaecology, 98.03% in central nervous system, 96.7% in hepatobiliary and gastric system, 94.2% in lymph node metastasis, and 90% for assessing surgical margins in breast tumors.

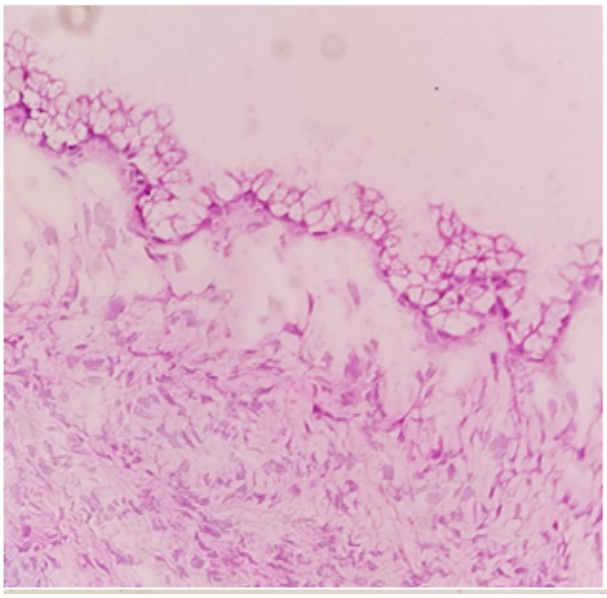


Figure 2a: Photomicrograph of the frozen section –mucinous cystadenoma. (H&E stain; 40x magnification)

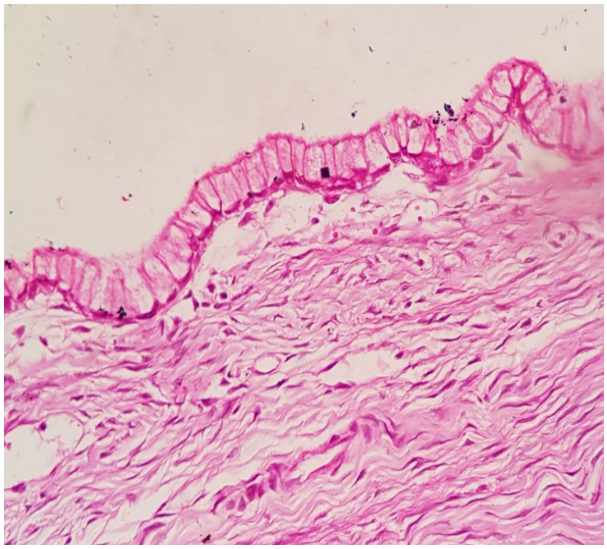


Figure 2b: Photomicrograph of the paraffin section – mucinous cystadenoma – correlates with the frozen section diagnosis. (H&E stain; 40x magnification)

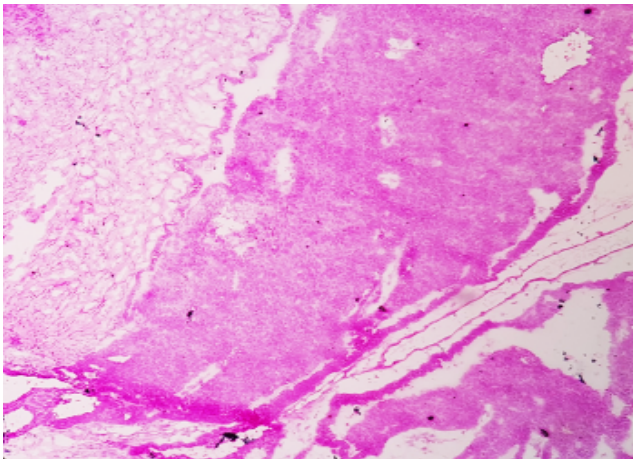


Figure 3a: Photomicrograph of frozen section- borderline mucinous tumour ovary (H& E stain; 40 X magnifications)

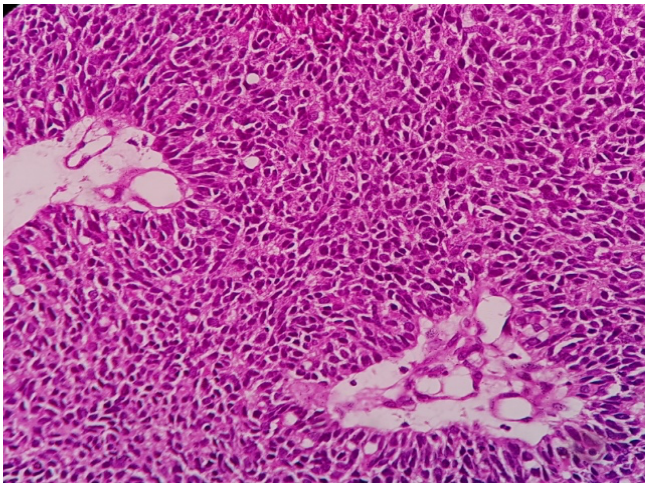


Figure 3b: Photomicrograph of the corresponding paraffin section report- Borderline mucinous tumour ovary. (H&E stain; 40x magnification)

There are various reasons for discordance amongst the frozen and paraffin sections, the main reasons being, sampling errors, sectioning/staining errors and interpretation errors.

In one case, frozen section was sent for the evaluation of tumor invasion into the ureter from a diagnosed case of urothelial bladder carcinoma. The frozen section report was dispatched as negative but on reviewing the paraffin section report, it was observed there was metastasis. The reason for this discordance can be attributed to the limitations we face in providing deeper sections during the frozen section procedure.

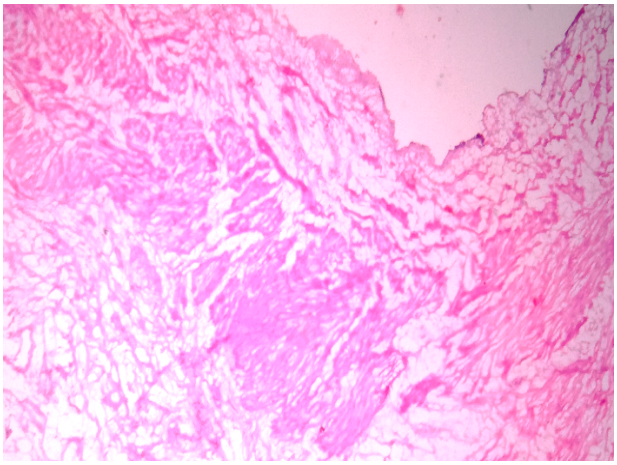


Figure 4a: Photomicrograph of the frozen section of the ureteric biopsy: showed no evidence of tumour. (H&E stain; 40x magnification)

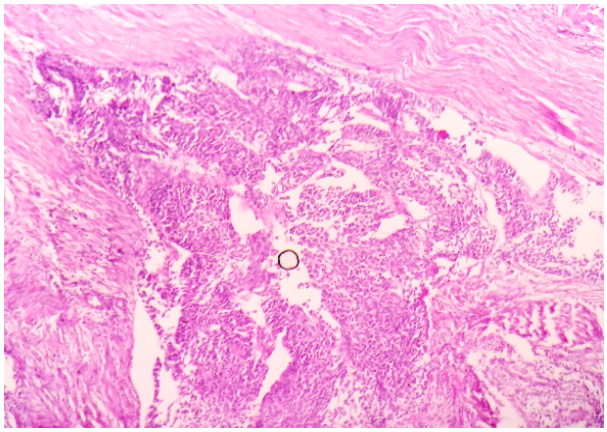


Figure 4b: Photomicrograph of the paraffin section: showed evidence of metastatic urothelial carcinoma. (H&E stain; 40x magnification)

Another discordant case was that of a lymph node excision that was sent from the department of surgical oncology. The primary tumour was from the head of pancreas. On frozen section microscopy, no tumour deposits were noted. On paraffin sections, it was positive for pancreatic adenocarcinoma. In this case due poor quality of the sections it was difficult to visualize the nuclear details. Both chronic pancreatitis and pancreatic carcinoma cause destruction of the normal pancreatic tissue and elicits marked fibroblastic reaction of the stroma.

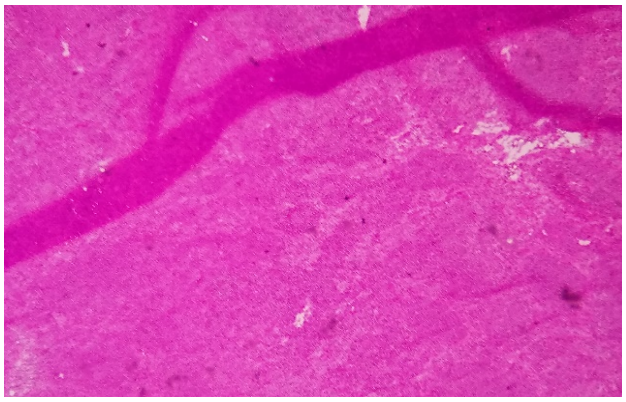


Figure 5a: Photomicrograph of the frozen section of the lymph node biopsy- no evidence of tumour metastasis. (H&E stain; 40x magnification)

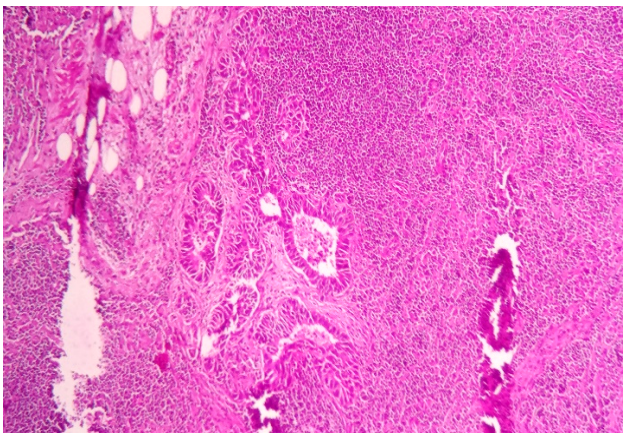


Figure 5b: Photomicrograph of the paraffin section of the same lymph node – positive for adenocarcinoma pancreas. (H&E stain; 40x magnification)

One more interesting case was received from the department of OBG. The tissue sent was from a fibroid uterus. The frozen section diagnosis was given as leiomyoma. On consequent evaluation of the paraffin sections, the diagnosis was given as symplastic leiomyoma. The reason for discordance here is the technical limitations that we face during frozen section microscopy that is the lack of diagnostic morphological features.

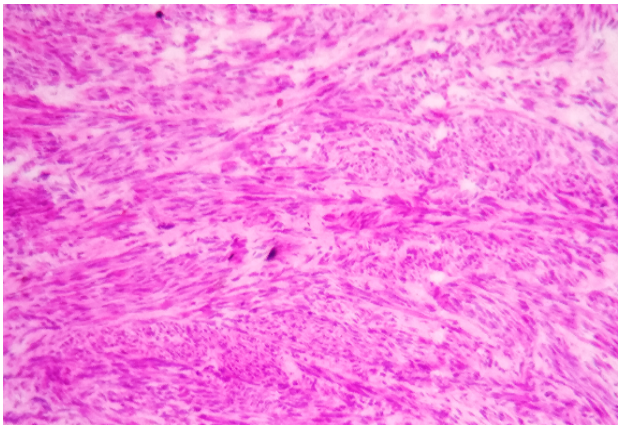


Figure 6a: Photomicrograph of the frozen section from fibroid- leiomyoma – smooth muscle cells arranged in interlacing bundles and fascicles. (H&E stain; 40x magnification)

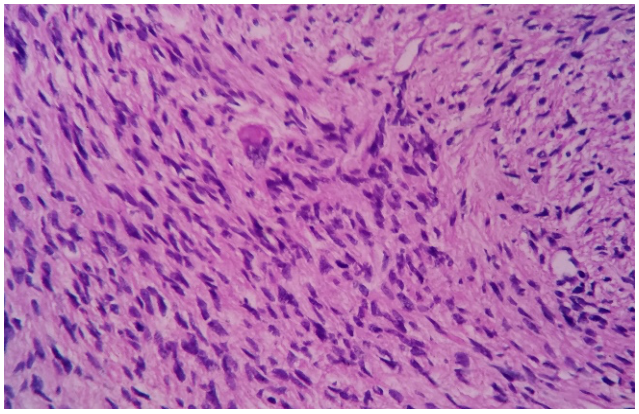


Figure 6b: Photomicrograph of the paraffin section – symplastic leiomyoma – atypical (H&E stain; 40x magnification

Intraoperative consultation in ovarian tumours is extremely important to determine the extent of surgery required, especially in women who wish to retain their fertility. Diagnostic difficulties are met especially in cases of endometriosis or borderline tumours which are hard to differentiate clinicoradiologically. In our study, there were no false positive reports. False negative reports (with respect to diagnosis of malignancy) were 9 cases (3.5%). The maximum correlation was seen in ovarian tumours.

Pinto et al in studying 243 frozen sections for ovarian tumours noted an accuracy rate of 98.5% for malignant tumors but only 78.6% for borderline tumours.9 Utilizing frozen section to determine tumour grade is also less sensitive with accuracy of only 88.6% in 260 endometrial cancers studied by Quinlivan JA et al. [10]

Sampling error is main reason for diagnostic discrepancy. This is because of remarkable heterogeneity of tumours from area to area within the same ovarian mass such as mucinous tumours and teratomas. 7% of ovarian tumours represent mestatasis from primary malignant neoplasms from other organs. [2]The frequency of performing breast frozen sections is 20% to 30% at MD Anderson in Houston, Texas, USA, where they have average 70 diagnostic frozen sections per day.4 In our study, we received a total of 20 frozen sections of breast tissue for surgical margins out of which 18 showed concordance with paraffin section reports(90% accuracy).

Least concordance was seen in skin and soft tissue tumours followed by lymph node biopsies. False negative results are often associated with diagnostic discrepancies, ranging from 0.4-2.56%. [11] Prevalence of certain diagnostic discrepancies are almost inevitable in frozen section and may be explained by the distribution of several focal lesions, which require several deeper cuts in paraffin sections. Problems and implicit technical limitations, insufficient material and lack of adequate clinical data also contribute to discordant results. [11]

The discordant rates of frozen section in different studies in literature ranges from 1.4 to 12.9%. [2] In the study conducted by Silva et al, the accuracy of frozen section pathological examinations was 93.30%. They attributed this to the differences in the anatomic sites studied. In their study, the most examined organ was the thyroid with 111 cases (25.65%) with most of them having inconclusive reports. Most studies have concluded that disagreements in frozen section diagnosis are mostly

due to interpretative and sampling errors, followed by sectioning, inadequate history, staining and labeling. [12]

Most frequent limitation in our study was observed in assessment of surgical margins for tumor excision (9.09%) followed by lymph node metastasis (5.7%). This is mainly attributed to interpretation errors resulting from technical artifacts due to freezing procedure or sectioning, which distorts the cellular details.

CAP specified the turnaround time (TAT) in frozen section reporting should be completed in 20 minutes in 90% of the cases or else analysis of outliners should be done. However, TAT does not include transport time prior to receipt of specimen, and also this standard allows exclusion of cases where multiple sequential studies were performed. [13] In our study, 70% of the cases were reported in less than 20 minutes. The reasons for delay in reporting in the remaining 30 % was attributed to technical issues such as availability of only one cryostat machine, limited number of skilled technicians, multiple tissues sent per case and many cases coming at once from different departments.

Conclusion

Frozen section is an intraoperative consultation with high reliability and accuracy. Frozen section, though having its various limitations, is still an extremely valuable tool for the operating surgeon to make a quick and reliable on table decision, having long standing impact on patient care.

Errors in some subspecialities were higher than others. It has its own limitations which we can try to overcome by taking specific measures to reduce the number of discrepancies such as improved technical staff, more accurate sectioning from the frozen section biopsy and delaying the diagnosis until accurate history and biopsy material is sent.

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