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Concordance of intraoperative frozen section diagnosis with routine histopathological diagnosis

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Abstract
Introduction: Intra-operative frozen section plays an important role in the management of surgical patients and yet it must be used prudently to avoid the indiscriminate usage of this important technique as it is subject to many limitations in comparison to the routine paraffin embedded tissue sections. In this study we have attempted to look at the concordance between the intraoperative frozen section diagnosis versus the regular histopathological diagnosis in our patients.
Aim of the study: To correlate the diagnosis given on Frozen section with Histopathological diagnosis.
Materials and Methods: This was a prospective study carried over a period of six months, from January 2019 to June 2019. Intraoperative Frozen sections were compared with routine regular paraffin embedded histopathology diagnosis in 51 patients. Detailed clinical history like age, gender, site, duration of lesions were noted.
Results: Various specimen types were received for Frozen sections during the time frame of this study, which included bone, soft tissue, genitourinary, skin, brain, and gastrointestinal tract tissue samples. Frozen section requests included asking for a diagnosis of a lesion (72.5%), margin status of a resected specimen containing malignancy (3.92%), lymph node status for the presence of metastatic tumor (23.5%). All the 51 cases (100%) of frozen section impressions were concordant with routine histopathological diagnosis.
Conclusion: The Intra-operative consultation using Frozen section is a very useful tool and guides the surgeon to intraoperatively modify the surgical approach. However, regular histopathological analysis is the gold standard for diagnosis.

Keywords: Intraoperative frozen section, cryostat, concordance of frozen versus routine histopathology

Introduction

Intra-operative frozen section (FS) helps in rapid diagnosis [1]. It was first applied clinically by William Welch in 1891 at Johns Hopkins Hospital [2]. It is used commonly during surgical procedures to detect malignancy so that modifications of surgery can be decided at the time of surgery on the table. Following the introduction of the cryostat in 1960, the intra operative frozen section examination was established as a highly reliable procedure for the rapid histological evaluation of tissue specimens during surgery [3]. Frozen section is also performed for evaluation of surgical margins and detection of lymph node metastasis. It can be applied to detect any unknown pathological process [4].

We conducted a comparative cross-sectional study on permanent histopathological sections in comparison to accuracy of frozen section. Histopathology is the gold standard method of diagnosing pathological processes. The objective of this type of study was to compare the diagnostic accuracy of frozen section with permanent histopathological sections and also to find its concordance and discordance rate with the final histopathological report.

The pathologist has to arrive at a correct decision in a shorter duration under pressure based on his experience, judgement and the knowledge of his specialty and clinical medicine. He should also have a keen awareness of the limitations of the method as the patient's life is often dramatically influenced by this report.

Both the surgeon and pathologist should be fully aware of the indications for FS. This will allow the appropriate request to be attended to. Only those requests that will definitely influence the intra-operative management should be addressed by FS.

Aim of the study

To correlate the diagnosis given on frozen section with histo-pathological diagnosis.

Materials and Methods

This was a prospective study carried out in the department of Pathology at Kamineni Academy of Medical Sciences and Research Centre, Hyderabad, India, over a period of six months from January 2019 to June 2019.

A total of 51 tissue specimens were received for intraoperative Frozen section. As per the surgeon's test request form, the indication for frozen section was noted. Representative tissue bits were submitted and cut in the cryostat. Rapid hematoxylin and eosin staining was done and the tissue sections were examined under light microscope and report was informed immediately to the surgeon telephonically and a typed report was also sent to the operation theatre. Later, after adequate fixation in 10% buffered neutral formalin, the tissue was submitted to routine histopathology processing and diagnosis was given on the regular sections. Both the frozen section and regular histopathology reports were compared in all the 51 cases for any discrepancies or additional findings. Patient details such as age, gender, clinical diagnosis, site of lesion, type of surgical procedure, were noted for all the patients.

For all cases, both frozen sections and routine sections were reviewed by two pathologists for diagnosis.

Observation and Results

Table 1: Types of specimen submitted for frozen section

Specimen	No. of cases	Percent (%)
Breast	18	35.2%
Gynaecology specimens	13	25.4%
Thyroid	5	9.8%
Kidney	4	7.8%
Gastro intestinal tract	3	5.8%
Others	8	15.6%
Total	51	100%

Most of the specimens were from breast for modified radical mastectomies for margin status.

Table 2: Indication for Requests for frozen section by surgeon

Indication	No. of cases	Percent (%)
Diagnosis of a lesion	37	72.5%
Lymph node status	12	23.5%
Margin status	2	3.92%
Total	51	100%

Most common indication for FS request was for the preliminary diagnosis as to its benign or malignant nature.

Table 3: Overall concordance rate of frozen section with histopathological reports

Correlation of diagnosis	No. of cases	Percent (%)
Concordant diagnosis	51	100%
Discordant diagnosis	0	-

All 51 cases (100%) showed positive correlation between the FS and routine section diagnosis.

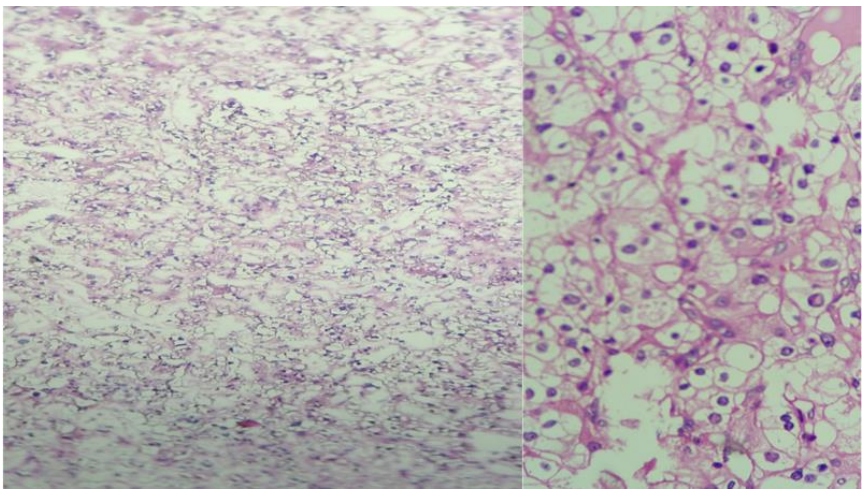

Fig 1: Clear cell carcinoma of kidney on frozen 10X (H&E) and routine histopathology 40X (H&E)

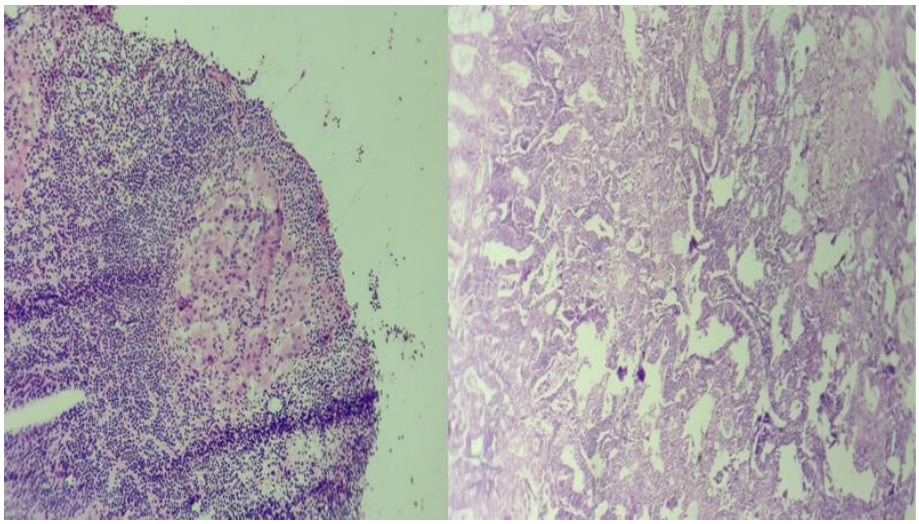

Fig 2: Metastasis from Endometrioid carcinoma in pelvic lymph node on frozen (H&E, 10X) and from uterus on routine histopathology 10X (H&E)

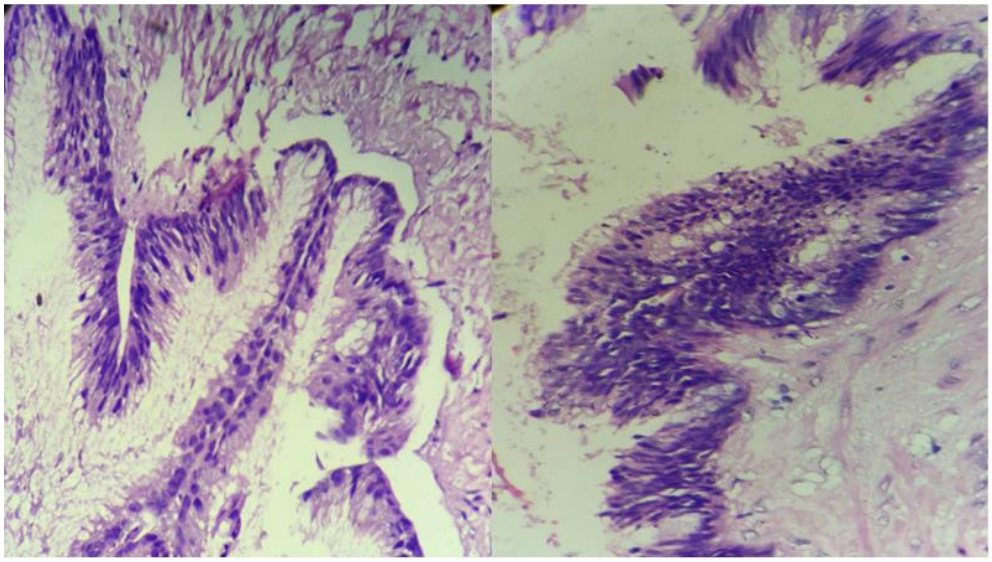

Fig 3: Mucinous cystadenoma of appendix on frozen 40X (H&E) and routine histopathology 40X (H&E)

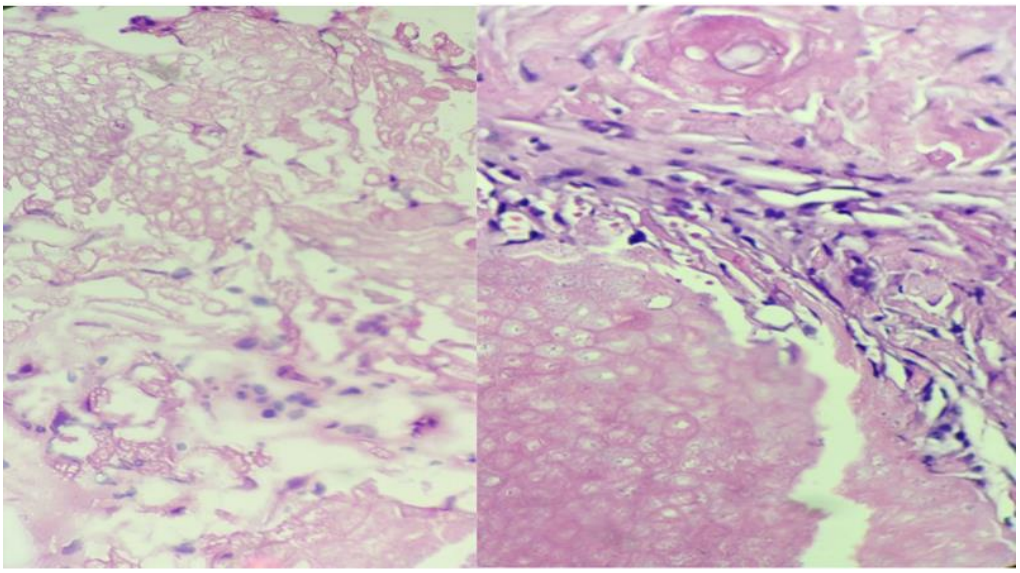

Fig 4: Pilomatricoma on frozen 40X (H&E) and routine histopathology 40X (H&E)

Discussion

There are various applications of frozen section study as follows: [5]

To establish the nature of lesion: To establish whether a lesion that needs resection is benign or malignant is very important to the operating surgeon, as this will decide the type of operative procedure or further sampling that he has to make.

Presence of lesion: FS is sometimes utilized to confirm the presence of a lesion or skip lesion in surgically suspicious tissue area.

To confirm the presence of a benign lesion: This is especially important in the case of a bony lesion. A benign lesion needs to be confirmed for curettage and packing. Malignant bone lesion is usually diagnosed using preoperative biopsy.

Sufficient tissue is present for the diagnosis or not: FS is sometimes utilized to check whether the representative site or enough material is obtained before the tissue is sent for histopathological diagnosis.

To grade the lesion: Grading of a malignant tumour is best done after the tumour is removed. However, sometimes it may be necessary to do so intraoperatively to guide the surgical procedure e.g. during evaluation for the presence or absence of endometrial carcinoma, or presence of another lesion spotted unexpectedly during an operation can also be subjected to FS.

To determine the adequacy of the margins- Determining the organ of origin using FS during surgery should not replace surgeon's skill in gross anatomy. However, this procedure is important when dealing with tissue such as parathyroid glands that are too small and difficult to recognize.

To establish the evidence of invasion: Adequacy of surgical margins is very important on large resections in a case of malignancy. In a complicated operating site such as the head and neck, margin clearance of a malignant lesion is very crucial as tumour recurrence can be very aggressive and difficult to treat. FS also has a role in assessing the extension of bone tumour in the marrow to help surgeon in deciding the operative maneuver. In case of an infiltrative tumour such as desmoid tumour, FS plays a very important role in getting margin clearance. Surgical margins for skin tumors such as basal cell carcinoma and squamous cell carcinoma sometimes need to be assessed for best cosmetic results.

To establish evidence of invasion: FS is used to establish the presence of tumour invasion to the lymph nodes and nerves. It is also sometimes used to ascertain metastasis at distant organs.

To determine the presence of infection: This is basically to look for the presence of tissue inflammation, granuloma and any fungal elements.

To acquire fresh tissue for special studies: Fresh tissue sometimes is required for special studies such as electron microscopy, genetic and molecular studies as well as for microbiological studies.

FS also has some limitations: 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. These limitations can be divided into three main categories namely sampling error, technical problem and interpretative error. [6, 7]

Poor sampling of the tissue/ limitation of the surgeon: This is a very obvious limitation for the pathologist since he has to interpret whatever tissue is sent by the surgeon. Sometimes the pathologist and even the radiologist may be required to go into the operating theater (OT) to evaluate the representative tissue taken.

Poor selection of appropriate tissue after grossing: Tissue sample sent to the laboratory for FS is sometimes large and therefore the pathologist must use his discretion to sample the most representative tissue areas. This may greatly influence his interpretation. Sometimes the orientation of the tissue sent is not clear and communication with the surgeon in the OT is thus important.

Extensive tumor degeneration or necrosis: Sampling a large tumour is sometimes difficult. The surgeon must choose a viable area and avoid necrotic one. Recognizing areas of tissue reaction to tumour such as edema and fibrosis are also important as sampling of these areas sometimes leave the pathologist with no diagnostic material.

Poor assessment of capsular or vascular invasion: Assessment of capsular or vascular invasion is very difficult in FS and subjected to sampling errors. Therefore, assessing such a condition in endocrine neoplasms especially follicular carcinoma of the thyroid is controversial and requires good communication between both parties.

Malignant component in ovarian teratoma cannot be ascertained: Searching for immature component in an ovarian teratoma is rather time consuming in FS and subjected to sampling error. It is not possible for all the tumors to be sampled either intraoperatively or in the pathology laboratory for FS. Therefore, a report of benign teratoma does not totally rule out a malignant one until the tumour is adequately sampled later.

Technical problems [5]

Freezing artifacts/Xylene artifacts: Freezing artifacts cause much damage to the tissue structure of the FS. Inadequate xylene treatment and improper cover slipping of slides cause drying artifacts, whereas any water present in xylene solution contributes to cloudy sections. All these can greatly jeopardize the reading of the slides.

Poor quality section: Frozen tissue section is not easy to cut compared to paraffin embedded sections. The section is usually thick and occasionally folded. Air bubbles may easily get into the tissue sections. A thick section may render it difficult to visualize clearly the nuclear details for

example in cases of lymphomas; and the cytoplasmic details of histiocytes, oncocytes and tumour cells. In addition, soft tissue such as brain and fatty tissue are difficult to cut and may cause numerous incomplete cutting and folding nicks which may affect the interpretation of the slides.

Bloated cell morphology: Depending on how good and how fast the tissue freezing process is, and its water content, this step will determine whether the cell morphology is preserved or not. However, in most cases of FS, the cell morphology is inferior to that of the paraffin embedded section. FS tends to cause the cells to be larger and appear bloated and the pathologist must take this into consideration when examining the tissue sample.

Poorly stained section: Likewise, due to the problem of fixation by freezing, the staining quality of the sections is also affected. As pathologist depends on colors as well as morphology, studying cells and its surrounding tissues, this factor may affect his judgement. To obtain a better morphology and staining quality of the slide sections, some laboratories heat the tissue sample (s) in formalin for a brief period before subjecting it/them to freezing. However, this will increase the turn-around time of the procedure.

In the present study a total of 51 cases of frozen section diagnosis were compared with routine histopathological diagnosis. The total concordance rate of frozen section with histopathological reports in our study was 100% and the discordance rate was 0%.

In a similar study conducted by Fariba Abbasi *et al* [8] the concordant rate was 74.5% which is lower than our result and the discordant rate was 4% in their study which is higher than that of our study.

In a similar study conducted by Adhikari *et al* [9] the concordant rate was 90.2% which is lower than our result and the discordant rate was 9.8%.

In a similar study conducted by Shrestha S *et al* [10] the concordant rate was 90.7% which is lower than our result and the discordant rate was 4%.

Table 4: Comparison with other studies

Study	Sample size Sample	Concordant diagnosis	Discordant diagnosis
Fariba Abbasi *et al* [8]	200	74.5%	4%
Adhikari *et al* [9]	41	90.2%	9.8%
Shrestha S *et al* [10]	75	90.7%	4%
Present study	51	100%	0%

The status of frozen section as a cost effective tool in thyroid lesions has been debated because of increased operative time without true consensus. [11] Most surgeons perform frozen section in thyroid lesions to confirm diagnosis of neoplasia made by FNAC. [12] In a study conducted in USA, the sensitivity and specificity of frozen section were 76.9% and 67.9% respectively and the positive predictive value (PPV) and negative predictive value (NPV) were 27.8% and 94.8%. [13] In the present study, we received only five cases of thyroid. So, sensitivity and other parameters to determine the accuracy of frozen section in comparison to histopathology were not calculated.

Intra-operative frozen section analysis of margins is widely employed to assist in complete tumor extirpation.

Lower local tumor recurrence rates and improved survival have been reported when tumor-free margins are achieved at the time of surgery [14]. Failure to achieve clear margins reduces the chance of local control [15].

Our experience with the frozen section examination of tissue margins is that the evaluation of re-excision margins of the tumour sometimes becomes difficult because the large size of a tumour may distort the normal anatomy resulting in improper orientation of the tissue margins. In such cases comparing original margins for frozen section and final margins after re excision appears inappropriate. In such scenarios we recommend processing remains of the original tissue after frozen section with gold standard histopathological method and comparing it with the frozen section. The main indications for intra-operative consultation in the evaluation of gastrointestinal tract specimens were to evaluate the adequacy of resection (Margin check), diagnosis and to evaluate the extent of disease [16]. The overall accuracy of our frozen section diagnoses is similar to that reported in the literature.

We also believe that determining the presence or absence of malignancy without subtyping it can be an option to decrease the discrepancies of frozen section diagnoses.

Limitation of our study was the limited number of cases and the short duration of the study because of which we were unable to calculate the accuracy of frozen section in all the organ systems separately.

Conclusion

The role, value, and limitations of frozen section and gross consultation were variable in different sites. Frozen section aided the surgeon to choose the best therapeutic approach and in rapid diagnosis of a pathological process. It confirmed the diagnosis of carcinoma if the fine needle aspiration cytology or core needle biopsies were inconclusive prior to major radical surgery. It also provided an assessment of resection margins in carcinoma. Frozen section was also helpful when unexpected disease process was encountered that required a definite diagnosis to decide on further management.

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