Original article

Diagnostic accuracy of frozen section: experience at Fatima Jinnah Medical University, Lahore

Rabia Basharat[1], Madiha Iqbal[2], Huma Aslam[1], Munazza Iqbal[3], Farrukh Kamal[3]
[1]Assistant Professor, [2]Demonstrator, [3]Professor Pathology, Fatima Jinnah Medical University, Lahore, Pakistan
Correspondence to: Rabia Basharat E-mail: drrabiabasharat@yahoo.com

ABSTRACT

Background: The surgical approach and management depends on frozen section examination results and is variable for different frozen section results. Frozen section examination is a quick and reliable preliminary diagnostic intraoperative technique that allows surgeons to take immediate correct decisions at the operating table. In this study, the diagnostic accuracy of frozen section examination was determined at Fatima Jinnah Medical University, Lahore.

Patients and methods: Frozen section database from 1st January 2016 to 31st December 2017 was retrospectively reviewed and compared with permanent sections to determine the diagnostic accuracy, sensitivity and specificity of frozen section technique. The study included 103 cases. The cases were divided into concordant and discordant cases. The diagnostic disagreements were analyzed to determine the cause of discrepancy.

Results: Total 103 frozen section specimens were evaluated. The anatomical site was primarily the ovary, axillary lymph node, breast, skin, thyroid, uterus and kidney. Among them 102 (99.03%) cases were concordant and 1 (0.97%) case was discordant. The discordant case was false negative and the specific site was the ovary. There was no false positive result. The overall sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of frozen section examination compared to permanent section were 97.6%, 100%, 99%, 100% and 98.4% respectively. For individual anatomic locations, the diagnostic accuracy ranged from 97.9% to 100%. The diagnostic discrepancy was due to sampling error.

Conclusion: Frozen section is a highly accurate, valuable and reliable technique for making rapid preliminary intraoperative diagnosis, thus enabling surgeons in taking correct immediate decisions regarding appropriate surgical approach and further management at the operating table.

Keywords:
Frozen section; permanent section; accuracy

INTRODUCTION

Intraoperative frozen section analysis which was introduced by Dr. Louis B Wilson in 1905 is now being widely used for evaluating surgical specimens, thus guiding surgeons per-operatively.[1] With the advent of intraoperative frozen section, the pathologists started playing an important role in numerous surgeries by guiding surgeons in deciding the best surgical approach, thereby avoiding unnecessary repeat surgeries.[2-6] Frozen section provides rapid preliminary diagnosis, thus allowing the surgeon to take prompt decision at the operating table regarding appropriate surgical approach and further management.[7] Intra-operative frozen section is a reliable productive diagnostic technique for neoplastic as well as non-neoplastic lesions. It effectively allows organ identification, differentiation of benign and malignant neoplasms, and determination of disease extent and margin status per-operatively.[8] The pathologist should be aware of clinical history, preoperative findings, pathological entities and limitations of frozen section for accurate intra-operative diagnosis. Clear, concise, and skillful communication is critical to avoid possible significant mismanagement of the case.[9]

Frozen section should be highly accurate because false diagnoses can lead to harmful consequences for patients particularly in case of false positive results.[10] Therefore, analysis of accuracy of such an essential diagnostic technique is extremely important so that unnecessary or inadequate surgical procedures can be minimized.[5,11-15] False negative results cause the most frequent discordant results on comparison of frozen sections with permanent section results.[11,13,14,16] The rationale of performing this study was to assess the

Competing interest: The authors have declared no competing interests exist.

Citation: Basharat R, Iqbal M, Aslam H, Iqbal M, Kamal F. Diagnostic accuracy of frozen section: experience at Fatima Jinnah Medical University, Lahore. J Fatima Jinnah Med Univ 2018; 12(4):156-160.

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diagnostic accuracy of frozen section examination so as to use it as an essential rapid preliminary diagnostic intraoperative technique in taking immediate intraoperative decisions regarding best surgical approach and further management thus avoiding unnecessary repeat surgeries in our setting. Intraoperative frozen section data of previous two years was reviewed in this study to determine diagnostic accuracy of frozen section examinations.

PATIENTS AND METHODS

This was a comparative cross-sectional study of all histological specimens received from the gynecological and surgical units of Sir Ganga Ram Hospital, Lahore for intraoperative frozen section from 1st January 2016 to 31st December 2017 in the Department of Pathology, Fatima Jinnah Medical University, Lahore which is affiliated with a tertiary care hospital, Sir Ganga Ram Hospital, Lahore. The sampling technique was non-probability purposive sampling. Specimens of patients of all ages and both genders received from the gynecological and surgical units of Sir Ganga Ram Hospital, Lahore were included in the study. The cases in which clinical history and preoperative investigations were not available were excluded from the study. From the database, frozen section results and subsequent permanent section results of each specimen were selected for comparison. A total of 103 cases were included in the study.

In frozen section, after freezing tissue rapidly to –20°C, sections were cut on a cryomicrotome and stained. In this way, microscopic examination of tissues were made within 5 to 10 minutes of its excision. Frozen section was performed on a machine called a cryostat. Laboratory workers and doctors were informed about frozen section by surgeons beforehand, so that the cryostat temperature could be maintained at –20°C. Specimens without fixation were received and gross examination was performed. The pathologist took the representative sections. If any single fragment was received, the tissue was processed as such. The tissue was then placed on a metallic block and covered with an appropriate amount of OCT compound. The OCT compound along with tissue was frozen within 1 to 2 minutes. The block holder was placed over the freezing stage of the cryostat. The glass door of the cryostat was closed to maintain its temperature. The door of the cryostat was opened, the block holder transferred to its stage and fixed. The block was trimmed with a cutting machine and the sections were transferred to the slides which were then stained with rapid hematoxylin-eosin. Pathologists examined the prepared slides and printed the frozen test reports which were then delivered to the concerned doctors. The results were also entered into the database.

Fixation of remaining tissues in formalin was done followed by routine paraffin embedding. A manual microtome was used to cut the paraffin blocks. Slides were prepared, stained with hematoxylin-eosin and then examined by pathologists.[17] New reports were generated. The results were also entered into the same register where the previous results of frozen biopsies were documented.

The frozen section diagnoses were compared with permanent section results. The frozen section results were compared to final diagnoses and categorized into two groups: concordant and discordant. The examinations was considered concordant when the permanent and frozen section diagnosis was the same and discordant if there was mismatch between frozen section and permanent section diagnosis. Finally, discordant cases were analyzed and causes of disagreement were recorded. All frozen examinations were part of the study as they followed the same methodology described above.

All the data was analyzed with SPSS version 17. The variables included anatomical site, frozen section diagnosis and permanent section diagnosis. The data was qualitative. Frequencies and percentages were calculated for qualitative data i.e. anatomical site, and concordant and discordant cases. A 2x2 table was used to calculate sensitivity, specificity, positive predictive value, negative predictive value and accuracy of frozen section examination taking permanent section diagnosis as gold standard.

RESULTS

This study included intraoperative histological specimens of 103 patients referred from the gynecological and surgical units of Sir Ganga Ram Hospital, Lahore from 1st January 2016 to 31st December 2017. Out of the 103 histological specimens, the anatomical site was ovary in 48 patients (46.6%), axillary lymph node in 30 patients (29.1%), breast in 6 patients (5.8%), skin in 6 patients (5.8%), thyroid in 5 patients (4.9%), uterus in 5 patients (4.9%) and kidney in 3 patients (2.9%) (Figure 1).

There were 102 (99.03%) concordant cases and 1 (0.97%) discordant case in this study (Figure 2). The discordant case was an ovarian borderline serous tumour and the reason for discrepancy was sampling error. Out of the 103 histological specimens, 61

(59.23%) specimens were reported to be benign, 1

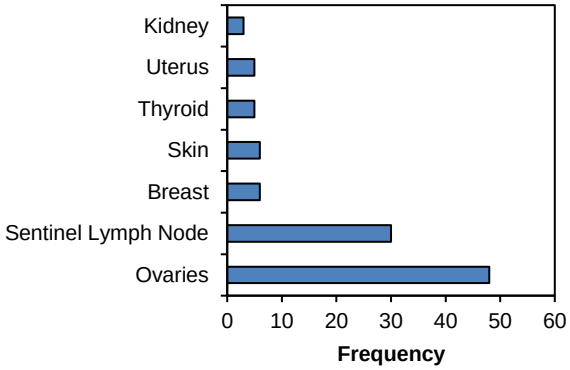

Figure 1. Frozen Section examination distribution by anatomical sites

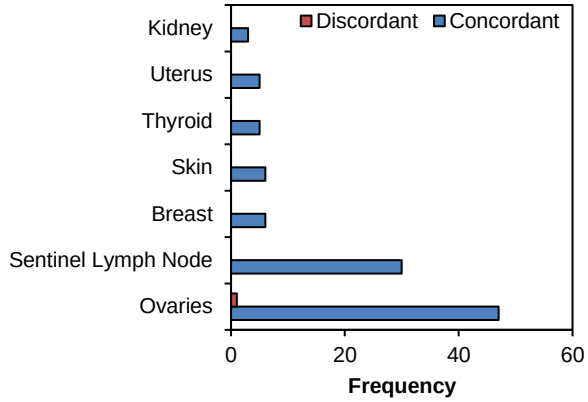

Figure 2. Frequency of concordant and discordant cases

(0.97%) specimen to be borderline and 41 (39.8%) specimens to be malignant on frozen section examination whereas 61 (59.2%) specimens were reported to be benign and 42 (40.8%) specimens to be malignant on subsequent permanent section examination. There was no deferred case in the study likely due to evaluation of each specimen by two senior consultant pathologists.

On comparison of results of frozen section examination with subsequent permanent section examination, the overall sensitivity of frozen section examination was 97.6%, specificity 100%, diagnostic accuracy 99%, positive predictive value 100% and negative predictive value 98.4% (Table 1).

The sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of frozen section examination for ovaries were 92.3%, 100%, 97.9%, 100% and 97.2% respectively whereas the sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value all were 100% for all other anatomical sites evaluated in this study (Table 1).

DISCUSSION

Frozen section pathological examination is a well-known procedure for prompt preliminary intraoperative diagnosis, thus helping surgeons in making therapeutic decisions regarding extent of resection. The accuracy of frozen section biopsy should be high for a surgeon to be confident in deciding the surgical approach to be used.[13] The overall diagnostic accuracy of frozen section examination compared with subsequent permanent section examination in our study was 99% in which 103 frozen section specimens were reviewed over a period of 2 years. The diagnostic accuracy of frozen section ranges from 87% to 97% according to different studies.[4,18-24] Some studies show even higher levels, ranging from 98.3% to 98.9%.[4,12,25] The accuracy reported by Mayo clinic Rochester, USA was 97.8%.[4]

The accuracy reported by a general hospital in Malaysia was 97.56% which studied 215 frozen section specimens over a duration of 4 years.[23] The diagnostic accuracy of frozen sections reported by Cerski and colleagues was 97.7%[16] and Pinto and colleagues was 97.08%.[21] Diagnostic accuracy of frozen section examination in studies by Junn-Liang et al.[26] in China, Farah-Klibi F. et al.[27] in France, Shrestha S. et al.[28] in India and Fariba Abbasi et al.[29] in Iran were 97.7%, 97.5%, 94.6% and 96.5% respectively which is comparable with this study.

The sensitivity of frozen section ranges from 84.6% to 97.9% according to literature.[27-29] The overall sensitivity of frozen section examination in this study was 97.6% which is in accordance to literature. The specificity of frozen section reported in various studies ranges from 94.55% to 100%.[27-29] In this study, the specificity was 100%, which is within the reported range.

The diagnostic accuracy ranged from 97.9% to 100.00% on analysis by specific anatomic site which is in accordance with the ranges reported by other authors.[13,14,16,30-32] The accuracy of frozen section examination is variable and depends on the anatomic location studied.[13,16,21,33] The most examined organ in this study was the ovary, with 48 (46.6%) samples.

There were 102 (99.03%) concordant cases and 1 (0.97%) discordant case in this study. The accuracy of frozen section was determined by Wendum and Flejou

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who studied 847 consecutive specimens in a teaching hospital.[34] Concordant and discordant rates were 92.6%

Table 1. Accuracy of frozen section examination

Anatomical site	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
Ovaries	92.3%	100%	100%	97.2%	97.9%
Sentinel LN	100%	100%	100%	100%	100%
Breast	100%	100%	100%	100%	100%
Skin	100%	100%	100%	100%	100%
Thyroid	100%	100%	100%	100%	100%
Uterus	100%	100%	100%	100%	100%
Kidney	100%	100%	100%	100%	100%
Overall	97.6%	100%	100%	98.4%	99.0%

and 1.7% respectively which is comparable with our study.

Diagnostic discrepancies are often due to false-negative results which range from 0.4% to 2.56%.[11,13,14] Certain diagnostic discrepancies cannot be avoided and may be related to distribution of the focal lesion which may be absent or deeply situated in the specimen sent to the pathologist, thus leading to discordant result. Other factors leading to diagnostic disagreements include technical limitations, insufficient material, sampling error, misinterpretation and lack of clinical information.[3,5,23,25,33-37] The discordant case in this study was due to sampling error. Well-differentiated malignant tumors that can be confused with proliferative lesions and malignant lesions with associated inflammatory processes are the causes which most often lead to discordant results.[38] In this study there was only one false-negative result that led to diagnostic discrepancy which was an ovarian borderline serous tumour.

There was no false-positive result in this study which is in accordance with other studies[30,31,39], although they may vary from 0.14% to 1.46%.[11,13,14,32] It is best to postpone the diagnosis when there is any uncertainty to decrease the frequency of false positive results as stated by Rosen.[35] In another study[11], it was suggested that conclusions from inconclusive interpretations should not be drawn by pathologists and management should be proceeded as if no test was performed.

A study[25] involving 461 institutions assessing more than 90,000 frozen sections concluded that the most common three sites of diagnostic disagreement were skin (17.1%), breast (16.7%) and female genital system (10.2%). In present study, the site of diagnostic discordance was the ovary.

Frozen section interpretation depends on experience. Interpretation of frozen section specimens by experienced pathologists leads to decreased error rate.[40-42] In our study, each specimen was evaluated by two senior consultant pathologists, thereby decreasing discordance rate and leading to a high diagnostic accuracy.

CONCLUSION

Frozen section examination due to its high diagnostic accuracy especially when evaluated by experienced consultant pathologists is doubtlessly the best rapid preliminary diagnostic intraoperative technique and plays an important role by providing rapid preliminary diagnosis intraoperatively thereby allowing surgeons to take immediate decisions at the operating table regarding best surgical approach and further management thus avoiding unnecessary repeat surgeries.

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