Original Article

DOI: 10.7860/JCDR/2022/56453.16393

Pathology Section

A Retrospective Study on Turnaround Time for Frozen Sections- A Tertiary Care Centre Experience from Southern India

S RIMA[1], A SANTHOSH[2], SANJEET ROY[3]

ABSTRACT

Introduction: Intraoperative consultation by frozen sections is an integral and essential part of surgical pathology to provide critical real-time information and guide in further intraoperative management. Diagnostic accuracy and Turnaround Time (TAT) have been considered as essential parameters which decide its effectiveness. Although diagnostic accuracy has been studied extensively, very few studies have assessed TAT of frozen sections.

Aim: To assess the TAT for frozen sections in a tertiary centre and identifying the various practical factors determining it.

Materials and Methods: This retrospective study was conducted in Department of General Pathology at Christian Medical college, Vellore, Tamil Nadu, India, on 615 frozen section samples obtained during the time period of June 2020 to June 2021. The TAT was defined as the time interval between receipt of sample and the time at which report was conveyed to the surgeon. The TAT for frozen sections should not exceed 30 minutes as per the criteria proposed by National Accreditation Board for Testing and Calibration Laboratories (NABL). Further details such as number of sites per frozen, number of pathologists involved, number of tissue blocks and slides made, requirement of deeper sections and special stains were documented and the factors influencing TAT were analysed based upon their subspeciality.

Results: A total of 35,175 specimens were received during the study period, of which 615 cases had frozen sections. Out of 615, 16.9% had TAT of more than 30 minutes, however when only one tissue block was submitted (n=221), 90% were within TAT. The delay in TAT was likely to occur when more than two pathologists participated in the FS diagnosis, more number of sections/tissue blocks were required, the pathologist had to retrieve and review previous case material during the FS procedure, simultaneously receiving additional specimens and requirement of special stains.

Conclusion: Turnaround time for frozen sections depends on several preanalytical and analytical reasons. An overall TAT that includes these factors cannot be taken as a standalone quality indicator of the laboratory. Therefore, a checklist that includes specimen receiving time, slide receiving time and time at which the diagnosis was conveyed to the surgeon needs to be documented to help understand where the delay happens. A periodic assessment of intraoperative frozen section TAT should be an integral part of an ongoing quality assurance program.

Keywords: Intraoperative consultation, Quality control, Surgical pathology

INTRODUCTION

Intraoperative consultation is an integral and essential part of surgical pathology and patient care, which helps in providing critical real-time information and guiding intraoperative clinical decision making [1]. Successful accomplishment of intraoperative consultation requires knowledge of relevant clinical history, familiarity with the surgical procedure technique, a keen knowledge of gross and microscopic pathology and a perfect work of the lab. The two main quality indicators of a frozen section are diagnostic accuracy and Turnaround Time (TAT) [2]. Turnaround time is defined as the time from which pathologists received Frozen Section (FS) specimens to the time they communicated FS results to the surgeon [3]. TAT of frozen sections is of vital significance and is one of the main quality indicators in surgical pathology. The TAT is dependent on several preanalytical and analytical factors. Although diagnostic accuracy of frozen section has been studied extensively, very few studies have assessed TAT of frozen sections and the various preanalytical and analytical factors influencing it in each of the sub-specialities of surgical pathology.

The aim of the study was to assess the TAT for frozen sections in a tertiary centre over a year and identifying the various practical factors determining it.

MATERIALS AND METHODS

This retrospective study was conducted in Department of General Pathology at Christian Medical college, Vellore, Tamil Nadu, India, on 615 frozen section samples obtained during the time period of June 2020 to June 2021. The data was analysed over a period of 6 months (September 2021 to February 2022). This study received ethical clearance by the Institutional Review Board (IRB number:15415; Dated on 23rd February, 2022). All frozen section samples sent during the period of June 2020 to June 2021.

Study Procedure

Two pathologists including a junior and senior pathologist were usually involved in the frozen section duty on any day. This mix of individuals fairly represents the spread of experience at the academic institution.

The specimens received for frozen sections at the receiving counter in the laboratory were checked and time stamped on a request form that contains the patient identification number, name, clinical speciality and clinical details of the patient. Infective and universal precautions were taken for all the specimens. As the number of biopsies from patients with Coronavirus Disease 2019 (COVID-19) increased during this time period, all samples from such patients were asked to be marked as "COVID-19 positive". All the specimens were examined grossly and details such as type of specimen, number of specimens, three dimensional measurements, colour, consistency, margin status (if needed) were documented.

A laboratory technologist assigned on frozen duty performed the cryostat sections, slide staining and cover slipping. Usually, two slides containing two sections were made from a tissue block for Haematoxylin and Eosin (H&E) stain. Left over tissue if any was processed for permanent sections. Two cryostats (Leica CM 1520

and Leica CM 1860 UV) were utilised for frozen sections during the study period. The latter model of cryostat (Leica CM 1860 UV) was used in biohazard samples. Because of the increase in fungal infection in this COVID-19 era, Periodic Acid Schiff (PAS) stain and multiple deeper sections were also requested when required. The slides were then handed over to the duty pathologist(s) and a diagnosis was made, taking into consideration the clinical, radiological and gross features. If further consultation was needed, a surgical pathologist with expertise in that area was consulted for the final diagnosis. The sample receiving time and time at which the diagnosis was conveyed to the operating surgeon was documented. This paper assessed the TAT regardless of number of frozen section blocks required for final diagnosis. All the details were documented in the pathology database as well as in a separate register for frozen sections, according to the National Accreditation Board for Testing and Calibration Laboratories (NABL) requirements.

To make analysis process more manageable for data interpretation on a large scale, authors categorised the specimens into 11 categories based upon their sub-speciality: Head and neck, Gynaecology, Endocrine, Gastrointestinal, Central nervous system, Bone and soft tissue, Haemato-lymphoid, Dermatology, Pulmonary, Hepatopancreaticobiliary and Urology. The details such as indication for frozen section, number of specimens/sites per frozen, total number of pathologists involved, number of tissue blocks and slides made, requirement of deeper sections and special stains were documented and the factors influencing TAT in each case were analysed.

According to the specific criteria for accreditation of medical laboratories proposed by NABL, the TAT for frozen sections should not exceed 30 minutes and was taken as the cut-off for this study.

STATISTICAL ANALYSIS

Data was entered using Microsoft excel and screened for outliers and extreme values. Descriptive statistics for continuous variables were measured using mean±SD, median, Interquartile ratio. All categorical variables were represented as numbers and percentage.

RESULTS

The total number of specimens received in the Department of General Pathology during the period of the study was 35,175 of which 615 cases had frozen sections for intraoperative diagnosis [Table/Fig-1].

The indications for frozen sections in this study were the following:

- Presence or absence of lesion/malignancy (310 cases, 50.4%)
- Subtyping/categorisation of tumour (34 cases, 5.5%)
- Margin status (43 cases, 7%)
- Identification of fungal elements (178 cases, 28.9%)
- Identification of ganglion cells (35 cases, 5.7%)
- Others (15 cases; 2.5%)

Speciality	Number of cases (n=615)	Turnaround Time (TAT)	
		Within TAT	Outside TAT
Head and neck	228 (37.1%)	191 (83.8%)	37 (16.2%)
Gynaecology	135 (21.9%)	103 (76.3%)	32 (23.7%)
Hepatobiliary	82 (13.3%)	69 (84.1%)	13 (15.9%)
Central nervous system	64 (10.4%)	63 (98.4%)	1 (1.6%)
Gastrointestinal	46 (7.5%)	32 (69.6%)	14 (30.4%)
Bone and soft tissue	23 (3.6%)	21 (91.3%)	2 (8.7%)
Lymph node	17 (2.7%)	14 (82.4%)	3 (17.6%)
Endocrine	9 (1.4%)	8 (88.9%)	1 (11.1%)
Urology	7 (1.1%)	6 (85.8%)	1 (14.2%)
Dermatology	3 (0.5%)	3	-
Pulmonary	1 (0.1%)	1	-

[Table/Fig-1]: Speciality-wise distribution of cases and their TAT.

Among 615 cases, 529 cases (86%) had specimens sent from a single site while the remaining 86 cases (14%) had specimens from multiple sites (ranging from two to six sites) to be evaluated.

A total of 582 cases (94.6%) were reported by two pathologists while the remaining (5.4%) were reported with the help of a third senior pathologist who was experienced in that sub-speciality. A total of 104 cases (16.9%) fell outside of the recommended TAT.

Detailed analysis of the most common specialities which had delayed TAT were as follows. The preanalytical factors are shown in [Table/Fig-2].

Preanalytical factors	Analytical factors
Total number of sections submitted	Varying skillset and experience of pathologist on frozen duty
Requirement of deeper sections	
Requirement of special stains	Requirement of further expert consult
Simultaneous multiple frozen sections	
Technical quality	

[Table/Fig-2]: Possible factors influencing TAT.

Gynaecological specimens: The common indications for frozen section in gynaecological pathology was to identify the presence or absence of lesion/malignancy followed by characterisation of the tumour. Among the cases that fell out of TAT, 32 cases (30.4%) were gynaecological specimens, with an average TAT of 36 minutes (range from 31 mins to 45 mins). Six out of these 32 cases had samples from multiple sites, nine cases required consultation from a third senior pathologist for expert opinion. The number of blocks required in these 32 cases ranged from three to eight blocks with an average of four blocks per case. The number of slides including deeper sections required in these cases ranged from 6-20 slides with an average of nine slides per case. All these cases had concordance with final histopathological diagnosis.

Head and neck specimens: A total of 37 cases (35.2%) in head and neck speciality were out of recommended TAT, with an average of 38 minutes (range from 32 mins to 55 mins). The most common indication (67%) for frozen in these cases was to look for fungal infection. About 21 out of 37 cases (57%) and 29 out of 37 cases (78%) required deeper sections and PAS stain respectively to identify fungal organisms. There was discordance in the final histopathological report in four of these cases.

Gastrointestinal specimens: Among the total number of gastrointestinal specimens sent for frozen study, 14 out of 46 cases (30.4%) had a delayed TAT with an average time of 37 minutes (range from 31-45 minutes). Ten out of these 14 cases (71.4%) were sent with suspected Hirschsprung's disease as indication. The most common reasons for delay in these were due to specimens from multiple sites (n=8), requirement of deeper sections (n=10) and consultation with expert pathologist for difficult cases (n=5). Only one cases had discordance with final histopathological diagnosis.

Hepatobiliary specimens: The two most common indications for frozen sections in this sub-speciality were to identify the presence or absence of lesion/malignancy (77%) and to assess margin status (22%). A total of 13 out of 82 cases (15.9%) in this sub-speciality had delayed TAT with an average time of 40 minutes (range from 32-45 minutes). The various reasons for the delay in TAT were the requirement of multiple deeper sections, consult from a senior/third pathologist in difficult cases and when multiple samples were sent at different time intervals. The average number of blocks examined in each case was four. Only one case had discordance with final histological diagnosis.

Central nervous system: Squash smear cytology was done in 47 out of 64 cases (73.4%), while in the remaining cases both smear and frozen sections were done. Only one case had delayed TAT of 33 minutes. Most of the cases (87%) with squash smear cytology had a TAT within 15 minutes.

In this study, only 221 out of the total 615 cases (36%) had single block for diagnosis and these cases had an average TAT of 26 minutes (range from 15-40 minutes). Among these cases, only 20, 10% went out of the TAT as proposed by NABL (30 minutes). No significant association was identified between overall TAT and the accuracy of the frozen section diagnosis. [Table/Fig-3] presents the reasons for outside of TAT in the departments.

Subspeciality	Reason for outside of TAT
Head and neck	Use of special stain (PAS stain) to look for fungal organisms in COVID-19 era
Gynaecology	Requirement of multiple sections
Hepatobiliary	-Muliple samples/site, -Consult from a senior/third pathologist in difficult cases.
Gastrointestinal	Multiple sequential samples at different time intervals
Lymph node	Requirement of deeper sections
Central nervous system	Difficult diagnosis
Bone and soft tissue	Consultation with a senior pathologist
Endocrine	Consultation with a senior pathologist
Urology	Multiple sections

[Table/Fig-3]: Reasons for outside TAT in each speciality.

DISCUSSION

Due to the ongoing COVID-19 pandemic, the total number of routine surgical biopsies and frozen section specimens were in general low during the period of study. There were relatively more number of frozen sections requested from head and neck surgery when compared to other specialities due to the unforeseen rise in invasive fungal rhinosinusitis. Due to the nation-wide lockdown, the proportion of samples from other specialities were also relatively far lesser during this period [4]. Although there were several reasons identified for the overall increase in duration of TAT, each sub-speciality had its own unique causes.

Probable reasons for cases falling out of TAT in gynaecological specimens were the need for multiple sections/extensive sampling in cases of borderline mucinous and serous tumours, extensively infarcted/cystic lesions and others with difficult/rare diagnosis (ex: sex cord stromal tumours) [5-7]. In gynaecological specimens, the total number of sections examined and need for expert opinion were found to be the main factors in determining TAT rather than requirement of deeper sections and special stains.

Due to the rise in fungal infections during COVID-19 pandemic, [8,9] most of the head and neck subspeciality cases required deeper sections and PAS stain to help in identifying fungal organisms. The minimum time required for PAS stain is ~25 minutes and hence one of the main reasons for delay in TAT was due to the need for PAS stain and the other being requirement of multiple deeper sections [10].

Among the specialities, hepatobiliary had the lengthiest TAT (40 minutes), which could be attributed to the multiple sections taken and subsequent frozen specimens sent to assess the margin status if the initial margin status was found to be positive. The TAT for cases which had revision of margins were calculated from the receipt of the first frozen sample. In general, the rarity of the hepatobiliary specimens and their complexity increases the turnaround time when compared to other sub-specialities [11].

Compared to all other specialities, Gastro intestinal speciality had the most number of cases outside TAT (14, 30.4%), the reasons being samples sent from multiple sites simultaneously and requirement of multilevel deeper sections before rendering a diagnosis for suspected Hirschsprung's disease [12,13].

Therefore, it is advisable that the number of sections to be submitted needs to be judicious to avoid undue delay in the turnaround time. The use of digital pathology/telepathology would be essential in the era of increasing subspecialisation of pathology for rendering quick and accurate FS diagnoses [14]. In the present study, 16.9% of cases had TAT of more than 30 minutes and were more likely to occur when more than two pathologists participated in the FS diagnosis, more number of sections/tissue blocks were required, the pathologist had to retrieve and review previous case material during the FS procedure, the pathologist simultaneously received additional specimens from other/same FS cases and special stains were required to look for fungal organisms.

The study by Zarbo RJ et al., study which included nearly 80,000 cases of frozen section, found that the mean blocks examined per case was 1.5, however, in the present study the mean blocks examined per case was 2.3. The increase in the number of blocks per case could have resulted in delayed TAT as identified in this study [15].

In the present study, most of the cases required multiple blocks for diagnosis due to complexity of the cases seen in a tertiary centre, however of all the cases that had a single block (221, 36%), the average TAT was found to be 26 minutes. Among these cases, 90% fell within TAT as proposed by NABL. This is in concordance with a similar study done by Novis DA and Zarbo RJ, that was published in 1997, where they had surveyed many laboratories and suggested that 90% of the cases with a single block could be completed within 20 minutes [3].

As proposed by Laakman JM et al., establishing a single TAT for frozen sections in all sub-specialities may not be ideal as the variability of frozen section times is dependent on specimen type [16]. Similar findings were observed in this study where gynaecological and gastrointestinal subspecialities had a relatively longer turnaround time compared to other specialities.

Limitation(s)

The study was done amidst COVID-19 pandemic during which there were increased number of frozen sections from head and neck surgery which led to sampling bias. Since, the time taken from receipt of sample to handing over of the slide to the duty pathologist (slide receiving time) was not documented in most of the cases, the exact reason for the delay in TAT could not be assessed.

CONCLUSION(S)

The turnaround time is dependent on several preanalytical and analytical factors. An overall TAT that includes both these factors cannot be taken as a standalone quality indicator of the laboratory. Therefore, a checklist that includes specimen receiving time, slide receiving time and time at which the frozen section diagnosis was conveyed to the surgeon needs to be documented individually to help understand where the delay happens. Checklist implementation is a significant step that allows the laboratory leadership to reliably assess if the delay happened due to preanalytical or analytical factors, thereby helping in improving the overall quality management plan.

REFERENCES

[1] Lechago J. The Frozen Section: Pathology in the Trenches. Arch Pathol Lab Med. 2005;129(12):1529-31.
[2] Nakhleh RE. What is quality in surgical pathology? J Clin Pathol. 2006;59(7):669-72.
[3] Novis DA, Zarbo RJ. Interinstitutional comparison of frozen section turnaround time. A College of American Pathologists Q-Probes study of 32868 frozen sections in 700 hospitals. Arch Pathol Lab Med. 1997;121(6):559-67.
[4] Ahmad Z, Rahim S, Ud Din N, Ahmed A. Practice of Academic Surgical Pathology During the COVID-19 Pandemic. Am J Clin Pathol. 2020;154(6):724-30.
[5] Acs G. Intraoperative consultation in gynecologic pathology. Semin Diagn Pathol. 2002;19(4):237-54.
[6] De Decker K, Jaroch KH, Edens MA, Bart J, Kooreman LFS, Kruitwagen RFPM, et al. Frozen section diagnosis of borderline ovarian tumors with suspicious features of invasive cancer is a devil's dilemma for the surgeon: A systematic review and meta-analysis. Acta Obstet Gynecol Scand. 2021;100(8):1369-76.
[7] Akrivos N, Thomakos N, Sotiropoulou M, Rodolakis A, Antsaklis A. Intraoperative Consultation in Ovarian Pathology. Gynecol Obstet Invest. 2010;70(3):193-99.
[8] Hofman V, Castillo L, Bétis F, Guevara N, Gari-Toussaint M, Hofman P. Usefulness of frozen section in rhinocerebral mucormycosis diagnosis and management. Pathology. 2003;35(3):212-16.

[9] Alkhateb R, Menon PD, Tariq H, Hackman S, Nazarullah A, Mais DD. Accuracy of Intraoperative Frozen Section in Detection of Acute Invasive Fungal Rhinosinusitis. Arch Pathol Lab Med. 2021;145(6):736-43.
[10] Bancroft JD, Gamble M. Theory and practice of histological technique. 6th ed. Elsevier: 2008.
[11] Lechago J. Frozen Section Examination of Liver, Gallbladder, and Pancreas. 2005;129(12):1610-18.
[12] Shayan K, Smith C, Langer JC. Reliability of intraoperative frozen sections in the management of Hirschsprung's disease. J Pediatr Surg. 2004;39(9):1345-48.
[13] Maia DM. The Reliability of Frozen-Section Diagnosis in the Pathologic Evaluation of Hirschsprung's Disease. Am J Surg Pathol. 2000;24(12):1675-77.
[14] Huang Y, Lei Y, Wang Q, Li D, Ma L, Guo L, et al. Telepathology consultation for frozen section diagnosis in China. Diagn Pathol. 2018;13(1):29.
[15] Zarbo RJ, Hoffman GG, Howanitz PJ. Interinstitutional comparison of frozen-section consultation. A College of American Pathologists Q-Probe study of 79,647 consultations in 297 North American institutions. Arch Pathol Lab Med. 1991;115(12):1187-94.
[16] Laakman JM, Chen SJ, Lake KS, Blau JL, Rajan DA, Samuelson MI, et al. Frozen Section Quality Assurance: Using Separate Frozen Section Slide Preparation Times and Interpretative Time Measurements to Improve Process. American Journal of Clinical Pathology. 2021;156(3):461-70.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of General Pathology, Christian Medical College, Vellore, Tamil Nadu, India.
2. Assistant Professor, Department of General Pathology, Christian Medical College, Vellore, Tamil Nadu, India.
3. Assistant Professor, Department of General Pathology, Christian Medical College, Vellore, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. A Santhosh,
Assistant Professor, Department of General Pathology, 4th Floor, ASHA Building, Vellore, Tamil Nadu, India.
E-mail: dr.immanuelraj@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 24, 2022
- Manual Googling: Mar 24, 2022
- iThenticate Software: Apr 04, 2022 (8%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 17, 2022**
Date of Peer Review: **Mar 25, 2022**
Date of Acceptance: **Apr 06, 2022**
Date of Publishing: **May 01, 2022**