

DIAGNOSTIC UTILITY, ERRORS AND LIMITATIONS OF FROZEN SECTION IN SURGICAL PATHOLOGY

Sonal Amit¹, Lubna Khan², Shrijeet Chakraborty³, Muktha R Pai⁴, Ramadas Naik⁵

¹Associate Professor, Department of Pathology, Autonomous State Medical College, Kanpur Dehat, India

²Professor, Department of Pathology, GSVM Medical College, Kanpur, India

³Specialist Registrar, The Walton Centre, Fazakerly, Liverpool, United Kingdom

⁴Professor, Pathology Department, Mangalore Institute of Oncology, Mangalore, India

⁵Professor, Pathology Department, Yenepoya Medical College, Mangalore, India

Received : 27/02/2024
Received in revised form : 28/03/2024
Accepted : 07/04/2024

Keywords:

Frozen section, Diagnostic accuracy, Intraoperative consultation, Limitations, Errors.

Corresponding Author:

Dr. Sonal Amit,
Email: drsonalamit@gmail.com

DOI: 10.47009/jamp.2024.6.2.153

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 742-747



Abstract

Background: Frozen section is an indispensable tool for intraoperative consultation in modern surgical practice, which guides therapeutic decisions and patient management. It is imperative to have a high diagnostic accuracy and deep understanding of challenges and limitations, if this technique is to offer maximum service. Skilled technical staff and experienced pathologist aware of pitfalls and limitations of technique are cornerstones of successful frozen section diagnosis. The present study was undertaken with the aim to ascertain the diagnostic accuracy of frozen sections in various tissues of the body and to understand the diagnostic pitfalls. **Materials and Methods:** Sixty-five unfixed tissues from various organs were subjected to frozen section and frozen section diagnosis was compared with paraffin section diagnosis on the same tissue and after further gross sampling. Assessment of specimen quality and diagnostic accuracy was made along with an attempt to understand technical artifacts and identify causes of error/ limitations in discordant and deferred cases. **Result:** The most common indication for frozen section was determination of diagnosis with breast as the most frequent site. Excellent preparation quality of frozen section was achieved in 93.8% cases. Out of 65 cases in the study, frozen section diagnosis was comparable to paraffin section in 61 (93.8%) cases including a deferral rate of 1.5%. Diagnostic discrepancy was observed in 4 (6.2%) cases. The most common cause of error was gross sampling followed by interpretation error. The sensitivity and specificity of frozen were 94.1% and 93.6% respectively. **Conclusion:** Frozen section diagnosis is a valuable tool for intra-operative consultation with high diagnostic accuracy. Thorough sampling, awareness of diagnostic pitfalls and technical artifacts, along with effective communication between surgeon and pathologist are cornerstones of successful frozen section consultation.

INTRODUCTION

Since its first usage for intra-operative consultation by eminent pathologist Welch and subsequent development by Wilson, the frozen section technique has acquired the status of an indispensable element of intra-operative consultation in modern surgical pathology.^[1,2] Largely employed for diagnosis and to guide therapeutic decision in the its nascent years, the realm of frozen section has now expanded to various other indications like evaluation of surgical margins, determining adequacy of resection, identify unknown tissue and various ancillary techniques.^[2,3] Because the intra-operative diagnosis offered by the pathologist poses

serious consequences for the patient,^[4] it is imperative to understand the utility as well as limitations of this technique in order to improve quality of intra-operative consultations.^[5]

MATERIALS AND METHODS

The study was performed on 65 cases, received as fresh tissue, without fixative. After a detailed gross examination, representative tissues were submitted for cryostat sectioning. The temperature varied between -18°C to -25°C, depending upon the tissue. The sections were cut at 5-8 micron, picked on albumin coated slides. Rapid H & Estaining of the sections were done as per standard protocol. The

tissue remaining after cryo-sectioning was subsequently processed by paraffin-embedding technique, so as to compare the diagnosis of frozen section with permanent sections on the same tissue. The frozen section diagnosis was also compared with paraffin section diagnosis after submitting more sections from final resected specimen, so as to evaluate sampling error, if any. Each case was analyzed in the light of clinical and radiological details provided.

A semi-quantitative score based on study by Mair et al,^[6] was employed, to assess preparation quality with a score 0 for poor quality preparation, 1 for compromised diagnosis due to tissue distortion and 2 for minimal tissue distortion. The frozen and paraffin section diagnosis was compared and diagnostic accuracy was scored; score 0 indicating incorrect diagnosis with regard to benign/ malignant process; 1 for correct regarding benign/ malignant process but incorrect specific diagnosis or, deferred diagnosis; and 2 for correct and specific diagnosis. The discrepant and deferred cases were analyzed and errors were classified based on Rogers et al,^[7] as sampling error, interpretation error and failure of communication. Technical errors and inadequate tissue were also included as potential sources of error. Sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of frozen section technique were calculated. To elucidate the associations and comparisons between different parameters, Pearson Chi-square value (χ^2) with one degree of freedom was applied wherever appropriate, with a significance level (P value) of less than 0.001.

RESULTS

Out of 65 cases in present study, frozen section was employed for determination of diagnosis in 61 (93.8%) followed by margin assessment in 3 (4.6%) and ancillary study in 1 (1.5%) cases. An excellent preparation quality was achieved in 93.8% (SQS3) cases. Tissue distortion compromising ease of diagnosis was observed in 4.6% (SQS1) and it was suboptimal in 1.5% (SQS0) cases. [Figure 1]

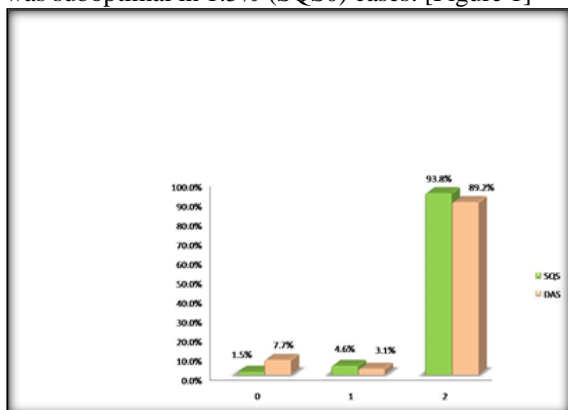


Figure 1: Assessment of Specimen Quality assessment score (SQS) and Diagnostic Accuracy score (DAS) in the study

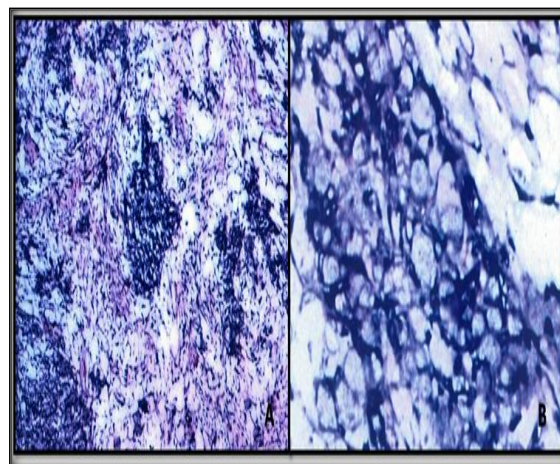


Figure 2: Kruckenberg tumor of ovary. (A) showing nests of signet ring cells embedded in edematous stroma (Frozen H&E, x100); (B) High power view showing signet ring cells with hyperchromatic nuclei (Frozen H&E, x400)

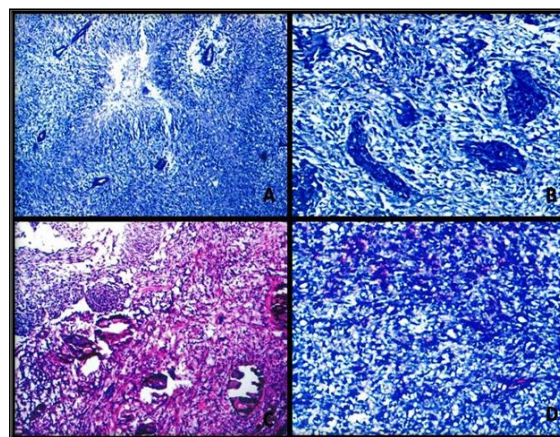


Figure 3: Frozen section of CNS neoplasms. (A) Glioblastoma showing wreath like necrosis (Frozen H&E, x100); (B) same case showing and microvascular proliferation (Frozen H&E, x100); (C) Psammomatous meningioma with whorls of meningothelial cells and numerous psammoma bodies (Frozen H&E, x100); (D) Glioblastoma undergraded as Anaplastic Astrocytoma based on high cellularity and pleomorphism as necrosis or microvascular proliferation were not discerned (Frozen H&E, x400);

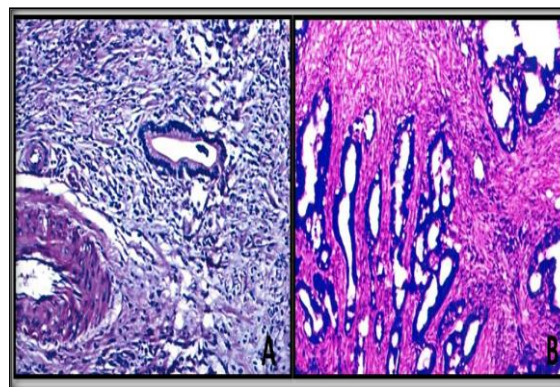


Figure 4: (A) Pancreatic lesion which was rendered a false negative diagnosis of chronic pancreatitis (Frozen H&E, x100); (B) Further sampling revealed well differentiated Adenocarcinoma (Paraffin H&E, x100)

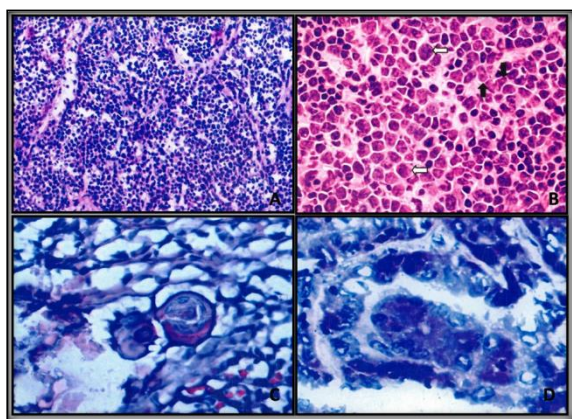


Figure 5: (A) Non-Hodgkin Lymphoma of lymph node with effaced architecture, atypical lymphoid and plasmacytoid cells (Frozen H&E, x100); (B) Another case of Non-Hodgkin lymphoma with diffuse pattern and atypical centroblasts (white arrow) and centrocytes (black arrow) like cells (Frozen H&E, x400); (C) Thyroid lesion with psammoma body suggesting Papillary carcinoma (Frozen H&E; x400); (D) confirmation of the diagnosis in the same case with identification of true papillae, the most reliable feature on frozen section as optically clear nuclei are absent (Frozen H&E; x400)

With respect to identification of benign/ malignant process the overall diagnostic accuracy in the present study was 93.8% (DAS1,2) including deferral rate of 1.5%. Discrepancy in diagnosis was reported in 6.2% cases. The sensitivity and specificity of frozen section was 94.1% and 93.6% respectively. Chi-square value was derived with a P-value <0.001, indicating good correlation between the technique of frozen section and permanent section. Breast (13/65) and female genital tract

(8/65) were the most common sites for frozen section in the study. [Table 1]

The accuracy of frozen section analysis varied with the organs studied. A diagnostic accuracy of 100% was achieved in CNS, bone, lymph node, genitourinary and soft tissue lesions. The diagnostic accuracy for breast and FGT specimens was 92.3% and 87.5% respectively with regard to correct identification of pathological process. Head and neck region, comprising thyroid, parotid, oral cavity growth and margin clearance tissues, resulted in diagnostic accuracy of 90.9%. Respiratory tract lesions comprised four cases with complete concordance in diagnosis in all 3 cases submitted for diagnosis determination. However, in 1 post-mortem case of suspected fat embolism, confirmation of same could not be achieved due to suboptimal Sudan III staining resulting in deferred diagnosis.

The discordance in diagnosis was observed in four cases (6.2%) in this study, with equal frequency of false positive and false negative errors (3.1% each) and deferral in one case (1.5%). False positive cases included phyllodes tumor misinterpreted as invasive carcinoma, and endometriotic cyst mistaken for borderline serous cystadenoma due to sampling error. A diagnosis of malignancy was missed in one case each of parotid and pancreatic lesion due to gross sampling error. Though diagnostic accuracy of intracranial tumors was excellent, tumor undergrading was observed in one case each of glioblastoma and anaplastic astrocytoma which were categorized as anaplastic astrocytoma and diffuse astrocytoma respectively on frozen sections.

Table 1: Site distribution with Diagnostic accuracy and cause of error (n=65)

Site	Number of cases	Diagnostic accuracy	Error	Cause of error	Remarks (if any)
Breast	13	92.30%	False Positive	Interpretation	Phyllodes tumor misinterpreted as Invasive carcinoma
Female genital tract	8	87.50%	False Positive	Gross sampling error	Endometriotic cyst diagnosed as Borderline serous cystadenoma on Frozen section
Head & Neck	11	90.90%	False Negative	Gross sampling error	Mucoepidermoid carcinoma missed on frozen section
Central Nervous System	6	100%	None	NA	Tumor undergrading was observed
Gastrointestinal tract	6	83.30%	False Negative	Gross sampling error	Adenocarcinoma missed on frozen section
Genitourinary tract	5	100%	None	NA	-
Respiratory tract	4	75%	None	NA	Unsatisfactory Sudan III stain resulting in deferral in a case of fat embolism
Bone	4	100%	None	NA	-
Lymph node	3	100%	None	NA	-
Miscellaneous	5	100%	None	NA	-

DISCUSSION

The frozen section technique is an invaluable tool to assist the surgeon with intraoperative diagnosis. The

indications for frozen section in this study were comparable to other studies in literature.^[8,9] The specimen preparation quality in the present study were significantly superior to that of Mair et al,^[6]

who achieved SQS of 2, 1 and 0 in 68%, 31.6% and 0.5% respectively in 206 cases included in their study. On the contrary, in their study DAS 2, 1 and zero in 96.1%, 2.9% and 1% cases respectively was better than the present study^[6]

The accuracy rate of 93.8% in the present study is comparable with most studies in literature reporting accuracy rate between 94.2% to 99%.^[3,4,7,10,11] The sensitivity (94.1%), positive (94.1%) and negative (93.6%) predictive value of the study was higher than that reported by Agarwal et al,^[4] and Vahini et al,^[12] though the specificity (93.6%) was lower compared to Agarwal et al.^[4] The diagnostic accuracy in the study with respect to indications is similar to Sawady et al,^[9] who achieved 100% accuracy in evaluation of surgical margins. However, contrary to the successful use of frozen section for special studies by Oneson et al,^[8] Sudan III staining for fat embolism in this study was not successful. This was the sole case where frozen section was used for special purpose and the failure could be due to infrequent usage of this staining method in our setup.

The discordance in diagnosis was observed in four cases (6.2%) in this study, contributed equally by false positive and false negative errors (3.1% each) and deferral in one case (1.5%). This is congruent with the study of Ahmad et al^[13] reporting equal false positive and false negative rate. However, in contrast to their study where the major source of error was interpretation, in the present study faulty gross sampling and interpretation contributed to erroneous diagnosis in 3 and 1 case respectively [Table 1]. Interpretation errors were compounded by lack of communication of clinical history in one case. Assessment of errors was similar to other studies^[8,9,10,11]

Ackerman et al believe that the errors can be minimized if clinical data is available and high quality technique is employed. Inflammatory cells trapped in dense scar tissue may result in false positive diagnosis of malignancy^[3] which was also the experience in this study. Pathologist needs to be alert to other mimickers of malignancy also like proliferating mesothelial pseudoacini, endometrial glands within lymph nodes and heterotopic pancreatic ducts coursing through muscles^[3] According to Horn et al, who reported false negative and false positive rate of 1.9% and 0.6% respectively, the incorrect diagnosis of malignancy is far more ominous than incorrect diagnosis of benignity as the former may subject the patient to needless mutilating surgery.^[14]

Breast, the largest group in the study had a diagnostic accuracy of 92.3%, lower than other studies^[3,10,15] Though most authors^[3,10,15] have cited higher false negativity rate owing to sampling errors in breast, the experience in this study was similar to Sawady et al,^[9] with a higher false positive (7.6%) and lower false negative (0.0%) which could be attributed to small sample size and misinterpretation. Papillary intraductal lesions,

sclerotic lesion with florid epithelial proliferation and entrapped inflammatory cells, can be over diagnosed as malignancy^[3,10,15]. Kagali et al reported deferral rate of 5% due to histological dilemma or too small sample size.^[16] According to Silva et al, differentiating insitu from invasive carcinoma becomes significant only in cases with small focus of invasive disease, as both extensive insitu disease and invasive tumors, are treated by radical mastectomy. The differentiation of lobular carcinoma insitu from cancerization of lobules is also not important in frozen sections, as this may influence the treatment of opposite breast, but not the immediate management of ipsilateral breast.^[17]

In female genital lesions, discrepancy in diagnosis was observed in one (12.5%) case wherein erroneous sampling of fallopian tube from a tubo-ovarian mass mimicked papillae of borderline ovarian tumor. This false positivity rate was congruent with Ahmad et al and Houck et al.^[13,19] Houck emphasized the importance of accurately diagnosing borderline lesions since it provides the patients with benefit of fertility preservation.^[19] False negative diagnosis may occur due to faulty sampling, interpretation error and incorrect histological type.^[9,19] Insufficient tissue and minimal areas of malignancy in deceptively encapsulated tumors, ascertained only after studying multiple paraffin sections pose other challenges.^[18] Some authors have reported high accuracy with no errors but, significant deferral rate.^[7,8,9,18] Though Krukenberg tumor in the present study did not pose any difficulty [Figure 2], it has the potential to mimic mesenchymal neoplasm due to plump stromal cells masking the signet ring cells especially, when latter are sparse.^[20]

Diagnostic accuracy in Head and neck lesions was 85.8% in the present study, which is lower than that reported in other studies.^[3,7,13,21,22] Faulty gross sampling and interpretation error similarly was responsible for false negative diagnoses in this study as was the experience of other authors.^[21,22] According to Remson et al,^[21] both surgeon and pathologist may be responsible for sampling errors, as multicentric lesions may be missed when only one frozen section is performed on a specimen due to time constraints. Necrotizing sialometaplasia and odontogenic residue may mimic malignancy and can be mistaken for positive margins in juxtaoral organs.^[23]

The usefulness of frozen section in thyroid is quite controversial. Optically clear nuclei, a unique fixation artifact and one of the most reliable feature on paraffin section for papillary carcinoma, is absent in frozen section.^[3] Most errors reported by Nakazawa et al,^[10] were the result of faulty sampling of multicentric tumors while others were attributed to microcarcinomas harbored in glands, otherwise having features of goitre. In many cases, correct diagnosis could be rendered only after examining multiple paraffin sections.^[10,15] Colloid rich thyroid lesions which crumble on cryotomy

resulting in unsatisfactory preparations may also result in missed diagnosis of malignancy.^[6]

In CNS tumors, diagnostic accuracy of 100% was obtained with minor grading errors [Figure 3], which was superior to other studies.^[7,15] Holaday et al,^[15] and Plesec et al,^[24] reported 1.1% and 7% grading discrepancies, respectively. The latter believe that most gliomas are morphologically heterogeneous, sampling dependent lesions and inaccuracies due to sampling error are an unavoidable trade off in satisfying surgeon's need for a rapid consultation. Differentiation of reactive gliosis from low grade astrocytoma, schwannoma from meningioma, and astrocytoma from oligodendroglioma along with erroneous interpretation were the major causes of diagnostic inaccuracies.^[15,24,25]

A diagnostic accuracy of more than 96% was seen in gastrointestinal tract specimens.^[3,7,15] with false negative results being the major discrepancy due to interpretive errors.^[3,15] In pancreatectomy specimens, 80% of the errors reported by various authors occurred due to pronounced chronic pancreatitis with excessive fibrosis and minimal carcinomatous foci.^[3,10,26] In the present study, false negative diagnosis of chronic pancreatitis was rendered in one case which was attributed to sampling error [Figure 4]. The diagnosis of pancreatic malignancy was arrived at only after submitting multiple sections for paraffin section diagnosis and which undoubtedly had florid chronic pancreatitis.

With respect to genitor-urinary and bone lesions, 100% diagnostic accuracy was achieved in this study comparable to most other studies. However, Krishnan et al reported 20.8% discordance in renal lesions, owing to faulty sampling and interpretation errors most of which were seen in cystic lesions.^[27] The diagnosis of bony lesions on frozen sections poses serious therapeutic implications like loss of limb and radical procedures based on cryostat diagnosis alone should be discouraged. It is possible to offer many correct diagnoses, if a pathologist is willing to be conservative and not render a positive diagnosis unless he can do so with assurance.^[14,15] Withholding pertinent information from the pathologist, gross sampling error, misinterpretation and challenge posed by giant cell containing osseous lesions having a wide array of differential diagnosis, are also reasons for errors.^[7,15]

In the category of four respiratory tract lesions in the present study, accurate diagnosis was achieved in 3/4 along with a deferral in 1/4 case owing to unsatisfactory Sudan III preparation. High diagnostic accuracy for lung frozen sections was reported by Ackerman et al,^[3] who believed that presence of inflammatory cells does not preclude a diagnosis of malignancy and, Holaday et al,^[15] who attributed error to gross sampling both by the surgeon and pathologist.^[15] Frozen section is recommended for every pulmonary surgery since sensitivity of this technique is far superior compared

to macroscopic examination performed by surgeons, with regard to malignant as well as benign lesions.^[28]

Only three lymph node specimens were subjected to frozen section in this study with 100% accuracy [Figure 5A&B]. This is superior to the 98.6% and 97.5% accuracy reported by Ackerman et al,^[3] and Holaday et al,^[12] respectively in their study on much larger sample size. Holaday et al studied 842 lymph node frozen sections and recommended submitting only a portion of lymph nodes for frozen sections since distortion induced by freezing may obviate a definitive diagnosis on permanent sections also.^[15] Oneson et al reported a high inconclusive rate of 11% stating that a higher deferral rate is acceptable in this group, as the prime reason for consultation is to verify that adequate tissue has been obtained for biopsy and for special studies.^[8] Although some authors do not recommend frozen section for soft tissue lesions^[29] the results of this study contradict this view, similar to studies by Ackerman and Sawady et al achieving a high accuracy. However, the limitation of small sample size in this study cannot be overruled.

While interpreting frozen sections, pathologist must not ignore subtle clues like psammoma bodies in thyroid lesion as emphasized by Ackerman et al,^[5] and Kraemer, warranting a hunt for papillary carcinoma. This was also the experience in this study where papillary carcinoma was correctly identified based on spotting psammoma body which prompted a search for true papillae on deeper sections [Figure 5C&D]. Contrarily, certain features like optically clear nuclei, a fixation artifact that is unique and one of the most reliable features on paraffin section, are absent in frozen section.^[5]

Pathologist also needs to be aware of technical artifacts. In the present study, the preparation quality was excellent in most cases. However, section folding artifact was seen in margin clearance tissues attributed to thin, linear, fat rich tissues. Extensive ice-crystal artifact was observed in a case of thyroid malignancy which compromised the ease of diagnosis. Uncommon ancillary studies may also end up in unsatisfactory preparations as was the case with Sudan III stain in suspected fat embolism, making the whole exercise non-contributory. Extensive crushing observed in a setup where cryogenic sections usually are of good quality should also alert one about the presence of monstrous lesions like neuroendocrine carcinoma or lymphoma, as was seen in bronchial growth diagnosed correctly as small cell carcinoma in this study. Careful search will usually reveal few intact cells with characteristic features.

CONCLUSION

As the decisions made on frozen sections may have serious consequences for the patient, it is imperative to have high diagnostic accuracy for it to be used as

tool of intraoperative consultation. Like any other technique, however, the frozen section is not without limitations. The importance of technical expertise, awareness and familiarity with artifacts, a thorough appraisal of clinical details and a meticulous gross examination of the tissue sent, cannot be underscored. Highest diagnostic accuracy is achievable when there is co-operation between a surgeon with interest in pathology and a pathologist with a clinical viewpoint.

REFERENCES

- Gal AA: The centennial anniversary of the frozen section technique at Mayo clinic; *Arch Pathol Lab Med*; 2005: 129,1532-35.
- Lechago J: Frozen section: Pathology in trenches; *Arch Pathol Lab Med*; 2005:129, 1529-30
- Ackerman LV, Ramirez GA: The indications for and limitations of frozen section diagnosis; *Br J Surg*; 1959:46, 336-350
- Agarwal P et al: Intra-operative frozen sections: Experience at a tertiary care centre; *Asian Pac J Cancer Prev*; 17 (12), 5057-61
- Patil P, Shukla S, Bhake A, Hiwale K: Accuracy of frozen section analysis in correlation with surgical pathology diagnosis; *Int J Res Med Sci*; 2015: 3,399-404
- Mair S, Lash RH, Suskin D, Medelsohn G. Intraoperative surgical specimen evaluation: Frozen section analysis, Cytological examination, or Both? *Am J ClinPathol*; 1991: 96,8-14
- Rogers C, Klatt EC, Chandrasoma P. Accuracy of frozen section diagnosis in a teaching hospital. *Arch Pathol Lab Med*; 1987: 111, 514-518
- Oneson RH, Minke JA, Silverberg SG: Intraoperative pathologic Consultation. An audit of 1000 recent consecutive cases. *Am J Surg Pathol*;1989: 13(3): 237-243
- Sawady J, Berner JJ, Siegler EE. Accuracy of and reasons for frozen sections: A correlative, retrospective study. *Hum Pathol*; 1988: 19, 1019-1023
- Nakazawa H, Rosen P, Lane N, Lattes R. Frozen section experience in 3000 cases: Accuracy, Limitations and Value in residency training. *Am J ClinPathol*; 1968: 49(1), 41-52
- Lerman RI, Pitcock JA. Frozen section experience in 3249 specimens. *SurgGynObs*; 1972: 135, 930-932
- Vahini G, Ramakrishna BA, Kaza S et al. Intraoperative frozen section- a golden tool for diagnosis of surgical biopsies. *IntClinPathol J*; 2017: 4(1), 22-26
- Ahmad Z, Barakzai MA, Indrees R, Bhurji Y. Correlation of intraoperative frozen section consultation with the final diagnosis at a referral center in Karachi, Pakistan. *Indian J PatholMicrobiol*; 2008: 51(4), 469-473
- Horn RC. What can be expected of the surgical pathologist from frozen section examinations. *Surg clinics of North America*; 1962: 42, 443-454
- Holaday WJ and Assor D: Ten thousand consecutive frozen sections: A retrospective study focusing on Accuracy and quality control. *Am J Clin Path*; 1974: 61,769-777
- Kagali VA. The role and limitations of frozen section diagnosis of palpable mass in the breast. *SurgGynecolObstet*; 1983: 156, 168-70
- Silva EG. Breast. In: Silva EG, Kraemer BB eds. *Intraoperative Pathological Diagnosis. Frozen section and Other techniques*. Baltimore MD: Williams and Wilkins; 1987: 25-50
- Da Cunha BA, Salvatore CA, Faria RM: Frozen section biopsy of ovarian neoplasms. *Int J GynaecolObstet*; 1983: 21, 103-110
- Houck K, Mikrui N, Duska L, Chang Y, Fuller A F, Bell D, Goodman A: Borderline tumors of ovary: correlation of frozen and permanent histopathological diagnosis; *ObstetGynecol*; 2000 95(6)(1), 839-843
- Coffey D, Kaplan AL, Ramzy I: Intraoperative consultation in gynecologic pathology. *Arch Pathol Lab Med*; 2005:129, 1544-1557
- Remson KA, Lucente FE, Biller HF. Reliability of frozen section diagnosis in head and neck neoplasms. *Laryngoscope*; 1984: 94, 519-524.
- Gandour-Edwards RF, Donald PJ, Wiese DA. Accuracy of intraoperative frozen section diagnosis in head and neck surgery: Experience at a university medical centre. *Head and Neck*; 2006: 15(1), 33-38
- Batsakis JG. Head and Neck. In: Silva EG, Kraemer BB eds. *Intraoperative Pathological Diagnosis. Frozen section and Other techniques*. Baltimore MD: Williams and Wilkins; 1987: 71-102
- Plessec TP, Prayson RA: Frozen section Discrepancy in the evaluation of central tumors. *Arch Pathol Lab Med*; 2007:131, 1532-1540
- Shah AB, Muzumdar GA, Chitale AR, Bhagwati SN: Squash preparation and frozen section in intraoperative diagnosis of central nervous system tumors. *ActaCytologica*; 1998: 42,1149-1154.
- Garda L. Gastrointestinal tract, Pancreas and Liver. In: Silva EG, Kraemer BB eds. *Intraoperative Pathological Diagnosis. Frozen section and Other techniques*. Baltimore MD: Williams and Wilkins; 1987: 145-166
- Krishnan B, Lechago J, Ayala G, Truong L: Intraoperative consultation for renal lesions; *Am J ClinPathol*; 2003: 120, 528-535
- Nashef SAM, Kakadellis JG, Hasleton PS, Whitaker JS, Gregory CM, Jones MT. Histological examination of preoperative frozen sections in suspected lung cancer. *Thorax*; 1993:48, 388-389
- Stout AP. Frozen section diagnosis in surgery. *Surgical clinics of North America*. 1956;36: 335-344