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Diagnostic Accuracy of Frozen Sections in Central Nervous System Lesions

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Abstract: ***Introduction: Frozen section (FS) is a critical intraoperative diagnostic tool in the management of central nervous system (CNS) lesions, providing rapid histological assessment that guides surgical decision-making. Despite challenges in interpretation and tumor grading, FS remains indispensable for distinguishing neoplastic from non-neoplastic lesions and ensuring adequate tissue sampling. This study evaluates the accuracy and utility of FS in CNS lesion diagnosis, highlighting its role in optimizing neurosurgical outcomes. Aims: To evaluate the diagnostic accuracy of frozen section analysis by comparing intraoperative frozen section findings with final paraffin-embedded histopathology results. Material and methods: A retrospective study of 71 specimens of intra operative FS were carried out in histopathology section of B.J. Medical College, Ahmedabad. The diagnosis given on frozen section were compared with the final diagnosis given on permanent paraffin sections. The results were categorized into concordant and discordant. Results: The diagnostic accuracy of frozen section was found to be 90.14%. Discordant rate is 9.85%. Discordant rate or false negative diagnosis was because of technical, sampling and interpretative error. Conclusion: Frozen section is a rapid and reliable intraoperative diagnostic tool for CNS lesions, with accuracy rates typically between 85- 95%. Despite limitations in tumor grading and heterogeneous lesions, its strong concordance with paraffin histopathology makes it indispensable for guiding neurosurgical decision- making and improving patient outcomes.***

Keywords: Frozen section, CNS lesions, intraoperative diagnosis, histopathology accuracy, neurosurgical decision

1. Introduction

Intraoperative "frozen section" (FS) is an investigation which helps in guiding the surgeons to plan for further management at the time of operation [1, 2]. FS enables quick assessment of tissue architecture, helping distinguish neoplastic from non-neoplastic processes. [10]

The technique was first used by William H Welch in 1891 for intra operative consultation.

The major criteria's for requesting an intraoperative diagnosis include the following:

a) If intraoperative management will be influenced by the diagnosis.
b) If an unexpected lesion is seen at surgery which is different from what was suspected clinically
c) To assess margins if radical excision is planned [3, 4, 5]
d) Enzyme histochemistry, immunohistochemistry and immunofluorescence [4].

Intraoperative FS diagnosis can be done by use of cryostat equipment and other methods such as squash smear cytology and imprint cytology. [1]Studies have shown that combining FS with squash cytology enhances diagnostic yield, with concordance rates exceeding 90% in many series.[11]

- In our center, we use a combination of squash smear cytology and cryostat equipment technique.
- The diagnostic accuracy of FS in CNS lesions has been reported to be high, typically ranging between 85% and 95% when compared with permanent paraffin sections[13]. Its utility is particularly evident in differentiating broad tumor categories such as high and low grade gliomas, meningiomas, and metastatic tumors. However, limitations exist: freezing artifacts, sampling errors, and tumor heterogeneity- especially in diffuse gliomas- can complicate interpretation and occasionally lead to discrepancies between intraoperative and final diagnoses.[3]
- Recent advances, such as robot-assisted stereotactic biopsy, have further improved tissue sampling and diagnostic yield, reinforcing the relevance of FS in contemporary neuro-oncology.[5]
- Despite its limitations, FS continues to play a pivotal role in intraoperative diagnosis of CNS lesions. Its rapid turnaround, high accuracy, and ability to guide surgical management make it indispensable in neurosurgical practice. Evaluating FS accuracy is essential not only for validating its continued use but also for identifying areas where complementary techniques and technological innovations can further enhance patient outcomes.[6]

2. Aims and Objectives

To analyze the frozen section results and compare it with final paraffin sections and evaluate the diagnostic accuracy.

3. Material and Method

- This was a retrospective study conducted over a period of 11 months (Jan 2025 – Nov 2025). During this period, we received 71CNS cases and examined in Histopathology Section of Pathology Department of B.J Medical College and Civil Hospital Ahmedabad, Gujrat, India.
- Fresh tissues were received in a clean container along with requisition form with complete clinical details from the surgical departments.
- Gross examination of the specimen was done, then squash smears were prepared and then tissue sent to
- cryostat.
- Cryostat was set at a temperature between -20 to -28 ^{0}C. Sections were frozen and cut by cryostat machine using tissue freezing medium as embedding medium (OCT-optimum cutting temperature medium).
- Sections were cut at a thickness of 4-5µm and were immediately fixed in 95% isopropyl alcohol.
- After that rapid hematoxylin and eosin staining was done.
- Frozen section diagnosis was done under light microscope and immediately conveyed to the operating surgeon over phone.
- After frozen sectioning, remaining of the tissue bits are sent for routine paraffin embedding and labelled with RF.
- The diagnosis given on frozen section were compared with the final diagnosis given on paraffin
- sections, as indicated on the frozen section and final pathology report.

4. Results

- In this retrospective study, total 71 cases were received for intraoperative consultation (frozen section) in 11 months.
- In all cases, cryostat sections (FS) plus squash smears were prepared.
- The ages of the patients ranged from 2 to 71 years.
- Out of 71 cases, 42 were males and 29 were females.
- Our results showed a reasonably good percentage of accuracy.
- Out of 71 cases, (64) cases were concordant, 7 (9.85%) cases were discrepant with diagnostic
- accuracy of 90.14%.
- Here the reason of discrepancy is mainly interpretation and technical error.
- In the present study overall diagnostic accuracy of frozen section was 90.14% which is comparable to other studies shown in the table no.1 [7, 8, 9, 10]

Table 1: Comparison of diagnostic accuracy of different studies

Authors (Studies)	Diagnostic Accuracy
Win Tta (2019) [10]	89.4%
Shah AB (1998)[5]	90.4%
Saumya Mishra *et al*. (2016)[7]	96.2%
Patil P *et al*. (2016)[8]	96.9%
Present study (2025)	90.14%

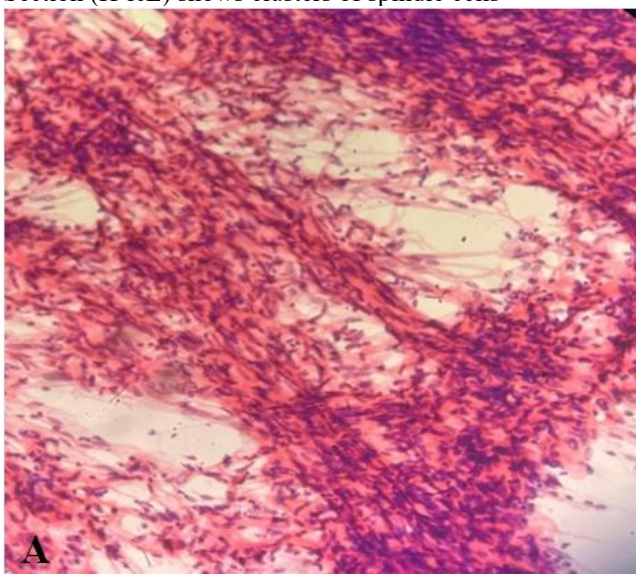
Table 2: Summary of diagnosis given at frozen section

Diagnosis	No. of Cases	Percentage
Astrocytoma low grade and High grade	17	23.90%
Meningioma	11	15.50%
Glioblastoma	6	8.45%
Schwannoma	3	4.22%
Medulloblastoma	3	4.22%
Pituitary Adenoma	5	7.04%
Metastatic Carcinoma with neuroendocrine features	1	1.40%
Ependymoma	4	5.63%
Tuberculosis	1	1.40%
Low Grade Glioma	9	12.68%
papillary lesion -Possibility of Metastasis	1	1.40%
CNS Embryonal tumor with rhabdoid feature	1	1.40%
Hemangioblastoma	2	2.82%
Pleomorphic Xanthoastrocytoma	5	7.04%
Ganglioglioma	1	1.40%
Pineal parenchymal tumor	1	1.40%
Total	71	

Table 3: Comparison of discrepant cases with Biopsy diagnosis.
Histological discrepant cases in our study (Total-7)-9.9%

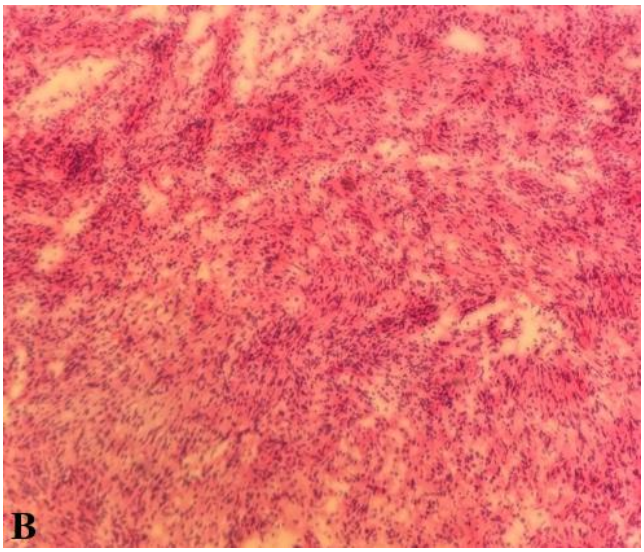
Frozen Diagnosis	Final diagnosis	No. of cases
Low grade glioma	Glioblastoma (WHO Grade IV)	1
Pleomorphic xanthoastrocytoma	Glioblastoma	1
Ependymoma	Gangliocytoma	1
Astrocytoma	Ependymoma	1
Astrocytoma	Glioblastoma	1
Hemangioblastoma (WHO Grade I)	Pleomorphic xanthoastrocytoma	1
Gangliogangliomа	Pleomorphic xanthoastrocytoma	1
TOTAL		7 (9.9%)

Meningioma on Squash smear
Section (H &E) shows clusters of spindle cells

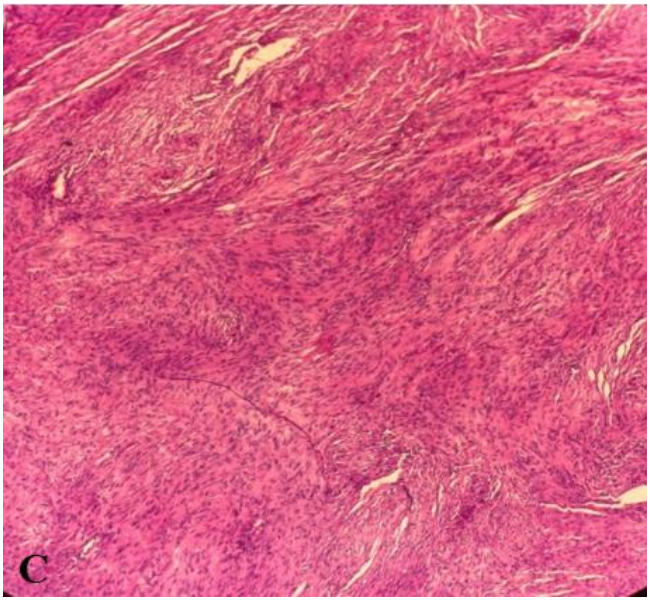


Meningioma on Frozen section
Section (H &E) shows markedly cellular tumor tissue showing plump spindle shaped tumor cells with mild to moderate cellular atypia, arranged in small group and sheets

with hylinized and collagenous stromal matrix



Meningioma on Routine section
Section (H &E) shows spindle to polygonal meningothelial cells arranged in whorls with interlacing fascicles



5. Discussion

Intraoperative frozen section continues to play a pivotal role in neurosurgical practice, providing rapid guidance on the presence and nature of central nervous system (CNS) lesions. However, its diagnostic accuracy is limited by technical artifacts, sampling error, and tumor heterogeneity. In our study, **7 cases (9.85%)** demonstrated discrepancies between frozen section and final histopathological diagnosis. This rate of discordance aligns with published literature, where accuracy ranges from **83–97% for intracranial tumors.**

Astrocytic Tumors
Astrocytic tumors were a frequent source of frozen section misdiagnosis. As outlined in the WHO Classification of Tumours of the Central Nervous System, necrosis and microvascular proliferation may be focal and absent in limited frozen samples, resulting in undergrading, while Rosai and Ackerman emphasize that marked pleomorphism, particularly in pleomorphic xanthoastrocytoma, may lead to overgrading as glioblastoma.[15] These limitations underscore the inherent challenges of intraoperative grading of astrocytic tumors.

Astrocytoma vs Ependymoma
Differentiating infiltrative astrocytomas from circumscribed ependymomas is particularly challenging in spinal cord tumors. One astrocytoma was misdiagnosed as ependymoma, and conversely, one ependymoma was reported as gangliocytoma. Examination of paraffin-embedded sections provides improved preservation of tissue architecture and cytologic detail, allowing reliable identification of defining histologic features and definitive diagnosis [15].

Rare Entities
Rare tumors such as PXA, ganglioglioma, and hemangioblastoma contributed to additional discrepancies. Their histological heterogeneity and overlapping features with glial or neuronal tumors make them prone to misclassification.

Causes of Misdiagnosis
The underlying causes of misdiagnosis can be attributed to:

- **Technical error**: Freezing distorts nuclear detail and obscures diagnostic structures.
- **Sampling error**: Diagnostic features such as necrosis or pseudorosettes may be absent in small fragments.
- **Tumor heterogeneity**: CNS tumors often contain mixed histological patterns, leading to misinterpretation.
- Rare tumor types may not be readily recognized because of turn around time of frozen section (within 30 mins).

Implications
While frozen section remains invaluable for **intraoperative guidance**, its role is primarily to confirm **neoplastic vs non-neoplastic tissue** and provide a **broad categorization** (glial vs non-glial, high-grade vs low-grade).

Definitive diagnosis and grading require **permanent sections with immunohistochemistry and molecular testing**. Awareness of common pitfalls- especially in distinguishing astrocytoma, glioblastoma, and ependymoma—can improve diagnostic accuracy and surgical decision-making.

6. Conclusion

Frozen section remains an indispensable adjunct in the intraoperative management of CNS tumors, providing rapid guidance to surgeons regarding the presence and general nature of neoplastic tissue. However, our study demonstrates that **9.85% of cases showed diagnostic discrepancies**, reflecting the limitations of frozen section in accurately classifying and grading tumors. The most frequent pitfalls involved **astrocytic tumors**, where sampling error and tumor heterogeneity led to under- or over-grading, and **ependymomas**, where pseudorosettes were obscured or missed. Rare entities such as pleomorphic xanthoastrocytoma, ganglioglioma, and hemangioblastoma further contributed to misdiagnosis due to overlapping

histological features.

These findings reinforce that frozen section should be interpreted with caution, serving primarily to distinguish **neoplastic from non-neoplastic tissue** and to provide **broad categorization** rather than definitive diagnosis. Permanent sections, immunohistochemistry, and molecular testing remain essential for accurate classification and grading. Greater awareness of common pitfalls, combined with complementary techniques such as intraoperative smear cytology, can enhance diagnostic accuracy. Ultimately, careful interpretation of frozen section findings with clinical, radiological, and final histopathological data ensures optimal patient management.

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