Squash Cytology versus Frozen Section for Intraoperative Diagnosis of Lesions of Central Nervous System: A Cross-sectional Study

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Original Article

ABSTRACT

Introduction: Intraoperative assessment of neurosurgical specimens using squash cytology and frozen sections is helpful to plan extent of surgery and determine adequacy of representative tissue. Combination of these techniques has been shown to increase diagnostic accuracy and rate of concordance with final diagnosis.

Aim: To assess usefulness of squash preparation and cryostat sections in making intraoperative diagnosis and to compare accuracy of squash cytology and frozen sections with respect to the final histopathological diagnosis.

Materials and Methods: In this cross-sectional study conducted at a tertiary care hospital in Maharashtra, India, 110 neurosurgical specimens received for intraoperative consultation were assessed over the period of two years (January 2016- December 2017). The squash smears and frozen section diagnoses were compared with the final histopathological diagnosis and their diagnostic accuracy was determined. Sensitivity, specificity, positive predictive value and negative predictive value were calculated using appropriate statistical method.

Results: Predominant age group in this study was 41-50 years (n=31, 28.1%) with male to female ratio of 2.23:1. Gliomas were most frequently encountered tumours (n=48) with Glioblastoma forming the commonest subgroup (n=19). The diagnostic accuracy, sensitivity and specificity of squash cytology were 90.72%, 93.50% and 80.01%, respectively. The diagnostic accuracy, sensitivity and specificity of frozen section were 95.87%, 97.40% and 90.01%, respectively.

Conclusion: The diagnostic accuracy, sensitivity and specificity were better for frozen section than squash cytology. A more accurate intraoperative diagnosis was achieved by combining the methods.

Keywords: Brain, Gliomas, Meningiomas, Spinal cord, Squash smears

INTRODUCTION

Despite the significant advances in neuroimaging, squash cytology and frozen section remains an important tool for the neurosurgeons which can influence the course of management of the patient during intraoperative period as they can help to plan the extent of surgery. These techniques can also be of great help in defining the margin of the lesion with adjacent brain parenchyma and safeguarding the surgeon against sampling a non representative tissue [1]. In the setting of stereotactic biopsies, primary goal of frozen section evaluation is assessment for adequacy and availability of representative tissue to make a final diagnosis. Intraoperative assessment also facilitates availability of material for ancillary studies such as the electron microscopy, microbiological cultures, frozen tissue storage, molecular pathology etc. In the molecular era, many Central Nervous System (CNS) tumour require molecular studies for accurate typing and grading. Intraoperative assessment can ensure that the tissue is adequate and representative for these analyses.

The ideal intraoperative method used for assessment should be accurate, rapid and should allow preservation of tissue for paraffin section study.

Frozen section method is preferred especially when tissue is of firm consistency. However, as the brain tissue is predisposed to show ice crystal artefacts, its frozen section interpretation may prove difficult and so squash smears are made. The advantage of squash smears over frozen sections is that it is easy to smear CNS tissue with soft texture, can be done even when the sample is limited and rapid intraoperative diagnosis can be obtained within short time [2,3]. It is especially beneficial in centers where the cryostat is unavailable, in case of a power breakdown, or if there is a lack of trained technical personnel [4]. These techniques can be used in isolation but their combination was shown to increase the diagnostic accuracy with a high rate of concordance with the final diagnosis [5-7]. The purpose of intraoperative assessment is not to diagnose and grade every case definitively but is to provide preliminary information to the operating surgeon and in fact one of the major sources of error is the pathologist succumbing to the pressure to diagnose and grade the tumour [4]. The World Health Organisation (WHO) classification 2016 has adopted the integrated diagnosis which combines histology with genetic information [8]. This affects the specificity of intraoperative diagnosis for some tumours such as gliomas hence there should be little need to further subclassify these tumours and to provide accurate WHO grading during intraoperative consultation.

In the molecular era, triaging of tissue is often required to provide a complete diagnosis. Knowing pros and cons of these techniques can guide the decision making during intraoperative consultation regarding how much time and tissue should be allotted to a particular technique. This is particularly important when the tissue is scanty.

The present study aimed to assess usefulness of the two methods of intraoperative assessment viz., squash preparation and frozen sections in making diagnosis of central nervous system lesions and attempted to identify the entities where one technique is more helpful than the other. It also compared the accuracy of squash cytology and frozen sections with respect to the final histopathological diagnosis and tried to assess the causes of discrepancies.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Pathology of a tertiary care hospital in Mumbai, Maharashtra, India. The study was conducted for the duration of two years (January 2016- December 2017) after obtaining approval from the Institution's Ethics Committee (file number EC210/2016). One hundred and ten cases of neuropathological specimens received for intraoperative consultation during the period of study were assessed.

Inclusion and exclusion criteria: Patients with space occupying lesions of brain or spinal cord and its coverings were included in the study. Bony lesions and samples inadequate for frozen section processing were excluded.

Study Procedure

Squash smear preparation: Small fragments of tissue about 0.5-1 mm² in size were spread on a slide and rapidly fixed in ether alcohol mixture for five minutes. The smear was then stained with rapid haematoxylin and eosin stain.

Frozen sections preparation: Tissue was cut in a cryostat at the temperature of -15°C and stained with haematoxylin and eosin stain.

The squash smears and frozen section diagnoses were compared with the final histopathological diagnosis and their diagnostic accuracy was judged. The WHO 2016 classification was followed for classification of tumours of the CNS [8].

STATISTICAL ANALYSIS

Sensitivity, specificity, positive predictive value and negative predictive value were calculated using standard definitions and formulae [9].

RESULTS

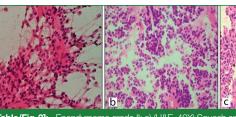
Intraoperative consultation was asked in 110 cases out of total 2088 CNS biopsies received during the study period. Majority of the patients in this study were in the age group 41-50 years (n=31, 28.1%) followed by 31-40 years (n=19, 17.2%), 21-30 years (n=16, 14.5%), 11-20 years (n=13, 11.8%), 0-10 years (n=12, 10.9%), 61-70 years (n=11, 10%), 51-60 years (n=7, 6.3%) and 71-80 years (n=1, 0.9%). There was a male preponderance with male to female ratio of 2.23:1 (76 males, 34 females).A total of 73 cases out of 110 were intra-axial (66.36%) with 37 cases being extra-axial (33.64%). Among intra-axial lesions, majority were supratentorial (n=62, 56.3%) with frontal lobe being the commonest site (n=19, 30.6%), followed by the temporal lobe (n=15, 24.1%), parietal lobe (n=10, 16.12%), ventricles (n=8, 12.9%), occipital lobe (n=2, 3.22%), pineal gland (n=2, 3.22%), thalamus (n=2, 3.22%), midbrain (n=2, 3.22%) and corpus callosum (n=2, 3.22%). Among extra-axial lesions of brain, more tumours were from supratentorial compartment (n=20) as compared to infratentotial (n=10). Among spinal lesions, more tumours were extra-medullary (n=7) than intra-medullary (n=4).

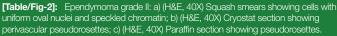
Of the total 110 cases, 97 cases were neoplastic and 13 cases were non neoplastic. Distribution of cases as per their diagnosis on squash cytology, frozen section and final paraffin block section was as follows. [Table/Fig-1], [Table/Fig-2]- Ependymoma Grade II, [Table/Fig-3]- Central Neurocytoma: WHO Grade II, [Table/ Fig-4]-Meningioma:WHO Grade I, [Table/Fig-5]- Tuberculoma. Gliomas were the most frequently encountered tumours (n=48) with Glioblastoma (n=19); [Table/Fig-6]- Glioblastoma: WHO Grade IV forming commonest subgroup. Cases were diagnosed as intermediate and high-grade glial neoplasm in which it was difficult to ascertain tumour morphology as astrocytic or oligodendroglial on intraoperative assessment. As per WHO 2016 classification, immunohistochemistry and molecular studies are required for definite diagnosis in these cases [8]. Inconclusive cases on squash and frozen were the cases in which the diagnosis could not be opined upon during intraoperative assessment and the diagnosis was given on paraffin sections of additional tissue received.

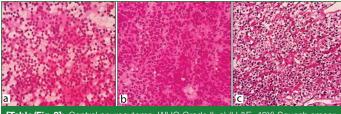
Frozen sections were more helpful than squash cytology for giving diagnosis in 39 cases out of 110 and in 44 cases, squash cytology and frozen section were both equally useful. There were five cases in which the diagnosis could be given only when squash and frozen section were taken together and one case was inconclusive even after studying both squash smears and frozen section together. This

Diagnosis	No. of cases on squash (n=110)	No. of cases on frozen (n=110)	No. of cases on paraffin (n=110)						
Astrocytoma	8	8	6						
Pilocytic astrocytoma	6	6	6						
Oligodendroglioma	4	4	4						
Intermediate grade glial neoplasm	3	3	4						
Anaplastic oligodendroglioma	2	2	2						
High-grade glial neoplasm	11	8	3						
Glioblastoma	7	12	19						
Ependymoma	4	4	4						
Reactive gliosis/edge of the lesion	4	4	4						
Central Neurocytoma	6	6	6						
DNET	1	1	1						
Malignant round cell tumour	1	1	-						
Medulloblastoma	3	3	3						
AT/RT	2	2	2						
Pineoblastoma	2	2	2						
Ewing's sarcoma	1	2	2						
Meningioma	11	11	10						
Schwannoma	4	5	5						
Haemangiopericytoma	1	1	1						
Chordoma	2	2	2						
Lymphoma	5	5	5						
Langerhans cell histiocytosis	1	1	1						
Metastasis	4	4	4						
Pituitary adenoma	4	4	4						
Demyelinating disease	1	1	1						
Inflammatory lesion	5	5	6						
Vascular malformation	-	-	1						
Cysts	1	2	2						
Inconclusive	6	1	-						
	[Table/Fig-1]: Diagnosis of squash and frozen section.								

DNET: Dysembryoplastic neuroepithelial tumour: AT/RT: Atypical tera



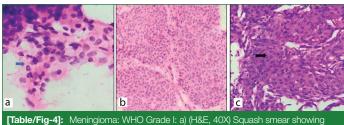




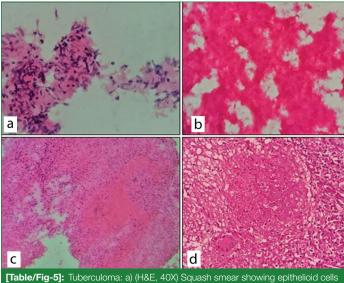
[Table/Fig-3]: Central neurocytoma: WHO Grade II: a) (H &E, 40X) Squash smear showing monomorphic cells with round nuclei and speckled chromatin; b) (H&E, 40X) Cryostat section showing sheets of monomorphic cells against delicate fibrillary background; c) (H&E, 40X) Paraffin section showing cells having perinuclear halos, separated by delicate vessels.

case of vascular malformation along with three discrepant cases was correctly diagnosed only on paraffin section [Table/Fig-7,8]. Among three discordant cases, first case was diagnosed intraoperatively as meningioma. Final diagnosis on paraffin section was metastatic carcinoma [Table/Fig-9]: Second case was diagnosed on frozen and squash as Metastatic Carcinoma which turned out to be

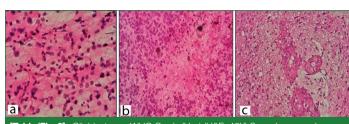
No of cases No of cases No of cases



plump cells with intranuclear clear inclusions (blue arrow); b) (H&E, 40X) Cryostat sections showing meningothelial cells arranged in nests; c) (H&E, 40X) Paraffin section showing whorls of meningothelial cells. Intranuclear clear inclusions seen (black arrow).



granuloma; b) (H&E, 40X) Squash smear showing caseous necrosis; c) (H&E, 40X) Cryostat section showing caseous necrosis with surrounding lymphocytes; d) (H&E, 40X) Paraffin section showing epithelioid cell granuloma with Langhans giant cell.



[Table/Fig-6]: Glioblastoma: WHO Grade IV: a) (H&E, 40X) Squash smear showing high cellularity and cells with large pleomorphic nuclei; b) (H&E, 40X) Cryostat section showing high cellularity, nuclear pleomorphism and palisaded necrosis; c) (H&E, 40X) Paraffin section showing microvascular proliferation.

Gliosarcoma on paraffin block [Table/Fig-10]. Last discordant case was of necrotising granulomatous inflammation which was diagnosed intraoperatively as malignant round cell tumour [Table/ Fig-11].

Sensitivity, specificity, positive predictive value, negative predictive value and overall diagnostic accuracy were all higher for frozen section as compared to the squash cytology. Their comparison is summarised in [Table/Fig-12].

DISCUSSION

The two principal techniques for establishing a rapid intraoperative diagnosis and to confirm or exclude the presence of a particular pathology are frozen section and squash smear examination.

In our institute, intraoperative consultation was asked in 5.26% of total cases received during the study period. It was asked only in those cases in which intraoperative diagnosis was necessary to decide the course of surgery or in cases in which intraoperatively there was a probable discrepancy with radiological impression.

Out of the total 110 cases, though the diagnosis could be made in most of the cases in both squash smear and frozen section, cytomorphological details were better preserved on squash smear in 18 cases as compared to frozen section, while frozen section showed better architectural details in 39 cases as compared to squash smear. The diagnosis could be equally given on squash cytology and frozen section in 44 cases. Diagnosis could be given in five cases only when squash cytology and frozen section were considered together.

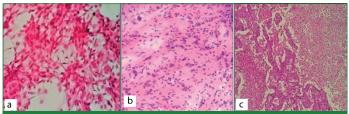
Architectural details were better preserved in frozen section than squash smear. Of the total 48 glial neoplasms, diagnosis was better made on frozen section in 13 cases as compared to squash smear and in 24 cases, diagnosis was given equally both on squash smears and frozen section. One case of gliosarcoma was discordant both on squash cytology and frozen section, on which it was called as metastatic carcinoma. Squash smear showed characteristic "copper-wire" fibrillary architecture in H & E stained smears, a feature that was not clearly apparent on frozen section. Nuclear details were also better appreciated in squash smear. Frozen section, however, was considered valuable for assessing architecture as in the diagnosis of glioblastoma exhibiting palisading necrosis. This characteristic necrosis was also helpful in differentiating glioblastoma from metastatic tumours [6].

Lesions	Squash better than frozen	Frozen better than squash	Both equally good	Diagnosis only when both interpreted together	Diagnosis made on paraffin	Total cases
Astrocytoma	2	2	2			6
Pilocytic astrocytoma	2	1	3			6
Oligodendroglioma	1	1	2			4
Intermediate grade glial neoplasm			4			4
Anaplastic oligodendroglioma	1		1			2
High-grade glial neoplasm	1		2			3
Glioblastoma	3	7	8	2	1	19
Ependymomas		2	2			4
Central neurocytoma	2	1	3			6
DNET		1				1
Medulloblastoma		1	2			3
AT/RT		2				2
Pineoblastoma		1	1			2
Ewing's sarcoma/PNET		1	1	1		2
Meningiomas	2	5	3			10
Schwannoma		2	2	1		5
Haemangiopericytoma		1				1
Chordoma	1	1				2

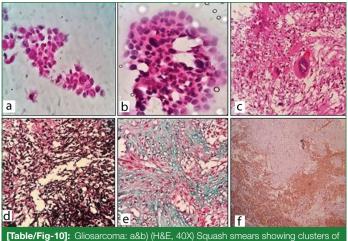
Lymphoma	1	2	2			5	
Langerhan's cell histiocytosis		1				1	
Metastasis		2	1		1	4	
Pituitary adenoma		1	3			4	
Edge of the lesion/ reactive gliosis		1	3			4	
Demyelinating disease		1				1	
Inflammatory lesion	2	3			1	6	
Vascular malformation					1	1	
Cysts		2		1		2	
Total	18	39	44	5	4	110	
[Table/Fig-7]: Comparison of squash smear and frozen section for diagnosis (n=110).							

DNET: Dysembryoolastic neuroepithelial tumour; AT/RT: Atvoical teratoid/Rhabdoid tumour; PNET: Primitive neuro-ectodem

Squash	Frozen	Paraffin					
Inconclusive	Malignant round cell tumour	Malignant round cell tumour- Ewing's sarcoma					
Inconclusive	Arachnoid cyst	Arachnoid cyst					
Inconclusive	Glioblastoma	Glioblastoma					
Inconclusive	Glioblastoma	Glioblastoma					
Inconclusive	Schwannoma	Schwannoma					
[Table/Fig-8]: Inconclusive cases on squash cytology correctly diagnosed on frozen section							



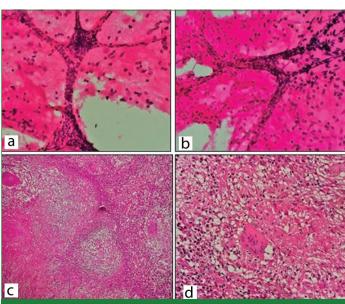
[Table/Fig-9]: Metastatic Carcinoma: a) squash smear (H&E, 40X); and b) Frozen section (H&E 40X): Lesion was reported as Meningioma due to spindly nature of the cells with plump nuclei. Firm nature of tissue resulted in poorly spread squash smears. c) (H&E, 40X): Lesion was diagnosed as metastatic carcinoma on final paraffin section.



[Table/Fig-10]: Gliosarcoma: a&b) (H&E, 40X) Squash smears showing clusters of abnormal epithelioid cells. It was reported as metastatic carcinoma; c) (H&E, 40X) High-grade glioma with sarcomatous appearance and bizarre cells; d) (Reticulin stain , 40X) Tumour showing rich reticulin positivity; e) (Mason's trichrome stain, 40X) highlighting collagen production by the tumour; f) (GFAP, 40X) GFAP positivity seen in glial areas whereas it was negative in sarcomatous areas.

In the study done by Savargaokar P and Farmer PM, frozen section was more helpful for diagnosing meningioma [6]. In this study, out of the 10 cases of meningioma, diagnosis could be more easily given on frozen section in five cases as compared to squash smears. In three cases, diagnosis was given equally on both squash smears and frozen section [Table/Fig-5].

Of the four cases of metastatic lesions, architectural details were better preserved on frozen section in two cases and were diagnosed better on frozen. In one case, diagnosis could be given only when



[Table/Fig-11]: Tuberculoma: a&b) (H&E, 40X) Squash smears showing a vascular lesion with infiltration by small round cells. Due to high cellularity and shrunken appearance of lymphocytes, it was misinterpreted as malignant round cell turmour. No granulomas or giant cells were seen. Frozen section was hard to interpret due to freezing artefacts; c&d) (H&E, 40X) Necrotising granulomatous lesion, as seen on final paraffin section.

Parameters	Squash smear	Frozen section					
Sensitivity	93.50%	97.40%					
Specificity	80.01%	90.01%					
Positive predictive value	94.73%	97.40%					
Negative predictive value	76.19%	90.01%					
Diagnostic accuracy	90.72%	95.87%					
[Table/Fig-12]: Diagnostic accuracy, sensitivity and specificity of squash and frozen section							

squash smears and frozen section were taken together. One case of metastasis was found to be discordant on both squash cytology and frozen section. Savargaonkar P and Farmer PM found that metastatic tumours showed a variety of results [6]. Many (6/11) cases were better recognised on frozen section due to preservation of the architecture.

Out of five cases of schwannoma, two cases was better diagnosed on frozen section. In two cases, diagnosis was given on both frozen section and squash smears taken together.

In a study done by Kleihues P et al., cytologic preparations were found to be superior to frozen section for diagnosis of lymphomas, though in our study frozen was better than squash in 2 out of 5 cases [10]. In two cases diagnosis was given equally on both squash smears and frozen section whereas squash smear was better in one case.

There was discrepancy in the squash smear and final diagnosis in three cases. The first case was metastatic poorly differentiated carcinoma which was diagnosed as fibroblastic meningioma on both squash smear and frozen section. This discrepancy was due to badly spread squash smear. This was probably the result of the firm texture of the tumour. Also, the tumour cells were spindly and this resulted in an incorrect diagnosis on frozen section.

The second case was of gliosarcoma which was diagnosed as metastatic carcinoma both on squash smear and frozen section. The reason for this was that spindle cell sarcomatous component was not seen in tissue received for frozen section. In gliosarcoma these areas may be focally seen in tissue received later for paraffin, as was seen in the case. The cells were epithelioid and malignant and were mistaken as metastatic carcinoma.

The third case was diagnosed as malignant round cell tumour both on squash smear and frozen section, but the final diagnosis on histopathology paraffin sections was given as necrotising granulomatous lesion. This discrepancy on squash cytology was because of thick smears. The areas of high cellularity seen were misinterpreted. Also, due to drying artefacts, the lymphocytes were shrunken and were interpreted as round tumour cells which were thought to be possibly neoplastic. There were freezing artefacts seen on frozen section, because of which the caseous necrotic areas were difficult to interpret as granulomas and also the nuclear details were not preserved.

In our study, there were three cases which were graded wrongly during intraoperative assessment. One case was diagnosed as low-grade glial neoplasm both on squash smears and frozen section but was diagnosed as intermediate grade glial neoplasm on paraffin sections. The second case was of an intermediate grade glial neoplasm which was diagnosed as astrocytoma grade II both on squash smears and frozen section. Third case was of a high-grade glial neoplasm on paraffin section which was diagnosed as intermediate grade glial neoplasm both on squash smears and frozen section. The discrepancies in all these three cases were due to limited sampling at the time of intraoperative assessment. Due to tumour heterogeneity which is often seen in gliomas, small amount of tissue sampled for intraoperative diagnosis may not be representative of the actual grade of the tumour. The areas suggesting higher grade like mitosis, necrosis or microvascular proliferation were missing in the tissue sent initially and the correct tumour grading could be given only after sampling areas from subsequent tissue received postoperatively.

In the study done by Cheunsuchon P in the neoplastic category, tumour type misclassification i.e, one tumour being classified as the other was the most common discrepancy (66.7%) followed by deviation of tumour grading (27%) and misdiagnosis of tumour to non tumour condition (6.3%) [11]. In the present study, the most common discrepancy was deviation of tumour grading (50%), followed by tumour type misclassification discrepancy (33.33%) and misdiagnosis of non tumour to tumour condition (16.66%). Plesec TP and Prayson RA found less than 3% of frozen section diagnoses were discrepant with the final diagnoses which corroborates with our study where we found less than 3% discrepant case on frozen section [12].

In all 110 cases, cytological and frozen section diagnoses were carried out and compared with paraffin sections. Out of 110 cases, squash smears were adequate in 104 cases and in six cases, smears were inconclusive, as they were badly spread due to firm texture of some tumours (schwannoma, cyst etc.,). Thus, cytological diagnosis could only be offered in 104 cases. There were 101 cases which were correctly diagnosed on squash hence the diagnostic accuracy on cytology was 90.72%. The sensitivity and specificity were 93.50% and 80.01%, respectively. The positive predictive value was 94.73%. Different studies carried out by Asha T et al., Pogady P et al., Imtiaz AQ et al., and Iqbal M et al., on squash cytology have shown a variable accuracy rate of 87%-95.35% which may also be due to differences in experience and exposure to squash cytology among pathologists [13-16].

Frozen section diagnosis could be offered in 109 cases. In one case, frozen section had only blood clot rendering it impossible for diagnosis. There were 106 cases in which the diagnosis was correctly made on frozen section, hence diagnostic accuracy on frozen section was 95.87%. The sensitivity and specificity were 97.40 % and 90.01%, respectively. The positive predictive value was 97.40%. Findings are compared with other studies in following table [Table/Fig-13] [17-19].

There were two cases in which frozen section was better than squash smear in making correct diagnosis. Both these cases were of Glioblastoma. These were diagnosed correctly on frozen section but were misdiagnosed on squash smear. The squash smears were inadequate to make diagnosis because only necrotic areas were sampled from the specimen received for frozen. Also, this discrepancy was due to the preparation of the smear from the area which lacked mitoses and microvascular proliferation. Correct diagnosis on frozen section was due to representative areas sampled for frozen section from other bits and also due to better preservation of architecture which helped in identifying features like palisaded necrosis and microvascular proliferation. Also, larger bit was used for frozen section than for squash. This may increase the diagnostic yield in some cases.

There were six cases on squash cytology in which diagnosis could not be made due to tissue being firm (one case of schwannoma, one of arachnoid cyst, one of Ewing's sarcoma and one being only blood clot) and due to presence of only necrotic material (two cases of glioblastoma). Out of these six cases, five were diagnosed correctly on frozen section. In such cases frozen section was observed to be better than squash smears.

The advantage of squash smear over frozen is that relatively little tissue is required to perform the procedure. This is of particular importance in small samples because it allows more tissue to be saved for further molecular testing. Also, the procedure is quicker and easier to perform because it does not require sectioning of tissue prior to staining.

Thus, limitations of one procedure can be compensated by the advantages of the other. A more accurate intraoperative consultation can be achieved by combining the methods for making the diagnosis during intraoperative consultation.

	Sensiti	tivity (%) Specificity (%)		Positive predictive value (%)		Negative predictive value (%)		Diagnostic accuracy (%)		
Study	Frozen	Squash	Frozen	Squash	Frozen	Squash	Frozen	Squash	Frozen	Squash
Chand P et al., (2016, India) [17]	96.8	95.5	100	100					95	91.25
Samal S et al., (2018, India) [18]	96.15	94.4	75	85.7	96.15	98.07	75	66.67	85.7	75
Biswal R et al., (2019, India) [19]	78.89	81.11	98.95	98.89	81.61	81.11	98.76	98.89	81.88	78.88
Present study	97.4	93.5	90.01	80.01	97.4	94.73	90.01	76.19	95.87	90.72

[Table/Fig-13]: Comparison of diagnostic accuracy, sensitivity and specificity of squash and frozen section with other studies [17-19]

Limitation(s)

The lab received tissue for intraoperative consultation from various organs hence the cryostat temperature was maintained at -20°C. This did occasionally lead to freezing artefacts as optimum temperature for brain was found to be around -10 to -15°C. 2) The sample received for intraoperative consultation varied in size and at times it was small and hence did not represent or reflect true grade or morphology resulting in discrepancy in diagnosis.

CONCLUSION(S)

The diagnostic accuracy, sensitivity and specificity were marginally better for frozen section than squash cytology. Frozen section was more accurate than squash smear in diagnosis owing to better preservation of architectural details. Limitations of one technique were compensated by the advantages of the other. Thus, a more accurate intraoperative diagnosis could be achieved by combining the methods.

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