

## Original Article

## Diagnostic accuracy of intraoperative consultation of central nervous system specimens in Thammasat University Hospital

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### Abstract

**Introduction:** To determine diagnostic accuracy of intraoperative consultation of central nervous system specimens at Thammasat University Hospital.

**Method:** Descriptive retrospective study of 56 cases that had intraoperative consultation and surgery during January 2012 to June 2017. Discordant cases were reviewed for diagnosis and cause. The diagnoses were analyzed by 2x2 contingency table

**Result:** 56 cases were included in this study. The diagnostic accuracy was 89.3%

**Conclusion:** The accuracy of this research is good when comparing to other studies in Thailand (83.33 - 89%).

**Key words:** diagnostic accuracy, intraoperative consultation, central nervous system and spinal cord

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## Introduction

The intraoperative consultation is an important tool for surgical management during operations, especially in neurosurgery. Nowadays the patients with neurologic conditions that required surgery in Thammasat University Hospital (TUH) are increasing. Hence the evaluation of accuracy, deferral cases and factors that associated to deferral diagnosis are essential for further intraoperative consultation for central nervous system and spinal cord specimen development in Thammasat university hospital.

## Method

This descriptive retrospective study was approved by Ethics committee of faculty of medicine, Thammasat University Hospital.

All cases of intraoperative consultation for central nervous system and spinal cord specimen with corresponding final surgical specimens from Pathology Unit at TUH from 1<sup>st</sup> January 2012 to 30<sup>th</sup> June 2017 were collected. The cases with absence of glass slides and paraffin blocks and cases with faded intraoperative consultation slides were excluded from this research. All included cases were to compare the diagnosis of intraoperative and final surgical specimen from own first pathologist and categorized to concordant group and discordant/deferral case group. Discordant/deferral group were reviewed by an experienced pathologist (second author and second pathologist) together with a resident (first author) to determine diagnoses, factors that associated to discordant/deferred diagnosis. Gender, age and intraoperative consultation specimen size were collected.

The data were analyzed via STATA and 2x2 contingency table. Intraoperative consultation specimens that were diagnosed as lymphoma and high grade neoplasm were classified as "Positive group." Intraoperative consultation specimens that were diagnosed as normal tissue and low grade neoplasm were classified as "Negative group." Final surgical specimens that were diagnosed as morphology code /2 /3 of World Health Organization (WHO) Classification of tumors of the Central Nervous system 2016<sup>11</sup> and World Health Organization (WHO) Classification of tumors of the Hematopoietic and Lymphoid tissues 2017<sup>12</sup> were classified as "Positive group." Final surgical specimens that were diagnosed as morphology code /0 /1 of World Health Organization (WHO) Classification of tumors of the Central Nervous system 2016<sup>11</sup> and World Health Organization (WHO) Classification of tumors of the Hematopoietic and Lymphoid tissues 2017<sup>12</sup> were classified as "Negative group." The cases that could not be definitely diagnosed and the differential diagnoses were reported instead were categorized as "deferral case," the deferral cases were excluded from statistical calculation. Demographic data were presented as average value.

Immunohistochemistry and additional slide section were performed in the cases that required further information to diagnose.

## Result

Fifty-seven cases were collected. One case was excluded from the research due to absence of intraoperative consultation slides. Fifty-six cases were divided into concordant group (N = 47) and discordant/deferral group (N = 9) (Figure 1).

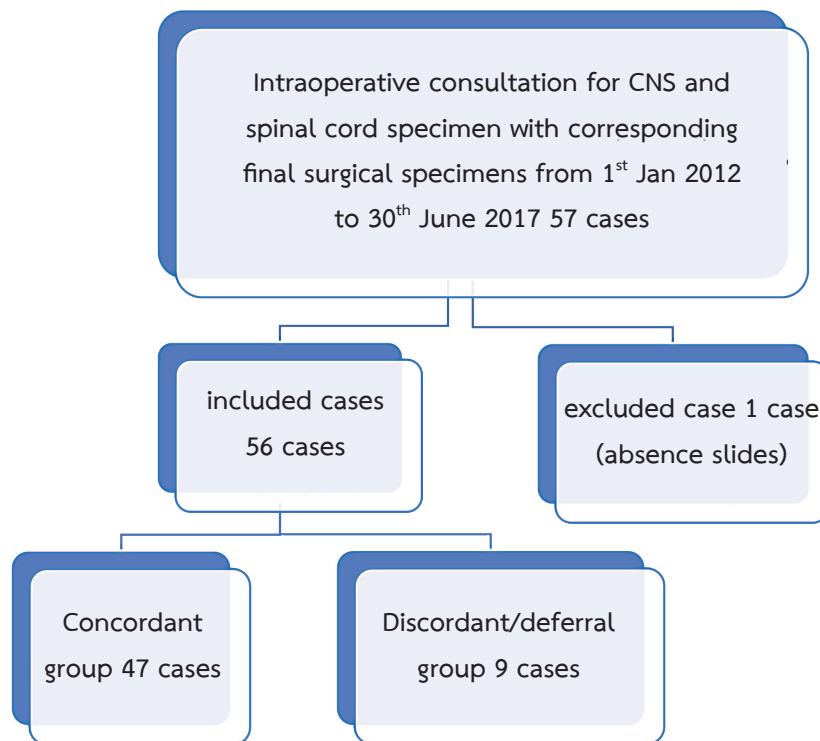


Figure 1 study flow chart

The concordant group consisted of 24 male patients and 23 female patients. The average age was 51.37 years. Age range was between 13 to 84 years old. The average intraoperative consultation specimen size was 6.7 mm. The range of intraoperative consultation specimen size was between 2 to 35 mm.

The discordant/deferral group consisted of 5 male patients and 4 female patients. The average age was 64.13 years. Age range was between 37 to 76 years old. The average intraoperative consultation specimen size was 6.4 mm. The range of intraoperative consultation specimen size was between 2 to 15 mm. (Table 1)

Table 1 Demographic data

Variable	Concordant group	Discordant/deferral group
Patients (N = 56)	47	9
Male/Female	24/23	5/4
Age (mean)	13 - 84 (51.37)	37 - 76 (64.13)
Size of specimen from intraoperative consultation (mean)	2 - 35 (6.7) mm.	2 - 15 (6.4) mm.

Diagnostic accuracy rate of intraoperative consultation for central nervous system and spinal cord specimen was 83.9%. Sensitivity and specificity of intraoperative consultation for central nervous

system and spinal cord specimen were 88% and 100%, respectively. Positive predictive value and negative predictive value were 100% and 89.6%, respectively. (Table 2)

**Table 2** 2x2 contingency table of concordant and discordant groups

Intraoperative diagnosis	Final surgical diagnosis		Total
	Positive	Negative	
Positive	22	0	22
Negative	3	26	29
Total	25	26	51

\* Five deferral cases were excluded from Table 2 and analyzed in separated section due to uncategorized into positive or negative case.

The most frequency factor was histomorphology overlapping of deferral case that consisted of round cell neoplasm (4 cases) and spindle cell neoplasm (1 case). The final surgical specimens were two cases hematologic malignancy, one case of carcinoma, one case of benign meningothelial tumor and one case of benign neuronal tumor.

The other factor was sampling error due to the main diagnostic tissue was not sampled that leading discordant diagnosis. Three cases were malignancy. Lesion was not found in intraoperative consultation specimen in 2/3 cases. Different tumor grade between intraoperative consultation specimen and corresponding final surgical specimens was occurred in 1/3 cases. (Table 3)

**Table 3** Cause of discordant/deferral group

Case	Intraoperative diagnosis	Review of Intraoperative diagnosis	Final surgical specimen diagnosis	Review of final surgical specimen diagnosis	Cause
1	Round cell tumor, most likely lymphoma or leukemia	Round blue cell neoplasm, differential diagnosis (DDX): lymphoma, metastatic carcinoma, and metastatic neuro-endocrine tumor	Metastatic small cell carcinoma of lung	Metastatic small cell carcinoma of lung	Deferral case
2	Round cell neoplasm, DDX: lymphoma and metastatic small cell carcinoma	Round cell neoplasm, DDX: lymphoma and metastatic small cell carcinoma	Extraventricular neurocytoma	Extraventricular neurocytoma	Deferral case
3	Low grade glioma	Low grade glioma with gemistocytic predominant	glioblastoma	glioblastoma	Sampling error

**Table 3** Cause of discordant/deferral group

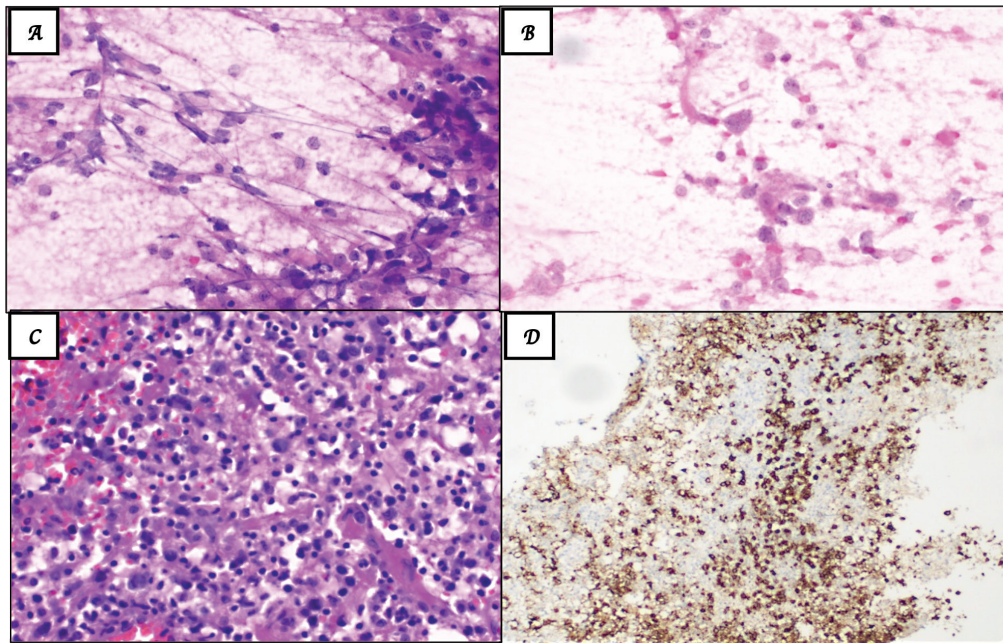
Case	Intraoperative diagnosis	Review of Intraoperative diagnosis	Final surgical specimen diagnosis	Review of final surgical specimen diagnosis	Cause
4	Atypical round cells lesion, DDX: glioma, pituitary adenoma, inflammatory process, and lymphoma	Lymphohistiocytic lesion, lymphoma cannot be excluded	Suspicious of small B cell lymphoid neoplasm	Suspicious of small B cell lymphoid neoplasm	Deferral case
5	Benign respiratory mucosa	Thick collagen with respiratory mucosa	Plasma cell neoplasm	Plasma cell neoplasm	Sampling error
6	Fragments of bone	Fragments of bone	Diffuse large B cell lymphoma	Diffuse large B cell lymphoma	Sampling error
7	Atypical round cell neoplasm, DDX: high grade glioma, lymphoma	High grade malignancy, defer to permanent	Diffuse large B cell lymphoma	Diffuse large B cell lymphoma	Deferral case
8	Spindle cell neoplasm with palisading and whirling formation, suggestive of mesenchymal tumor	Spindle cell neoplasm, differential diagnosis: meningioma, solitary fibrous tumor	Atypical meningioma	Atypical meningioma	Deferral case

No technical error, interpretation error, communicating error or others were associated with deferral diagnosis in this research.

### Discussion

Diagnostic accuracy rate of intraoperative consultation for central nervous system and spinal cord specimen in this research was 83.9% (47/56 cases). Percentage of discordant cases was 7.1% (4/56 cases). The cause of all four discordant cases was sampling error.

Percentage of deferral cases was 9.0% (5/56 cases). Three cases were partially concordant and the result of treatment was not changed (4<sup>th</sup>, 8<sup>th</sup> and 9<sup>th</sup> case from table 3). Two from five deferral



**Figure 2** 72-year-old female patient with periventricular mass in brain (8<sup>th</sup> case from Table 3). A) cytological preparation from intraoperative consultation specimen showed atypical round cells in fibrillary background (magnification 40x). B) single cells of atypical round cells were found in other areas (magnification 40x). C) dyscohesive round cells with nuclear atypia were identified in corresponding final surgical specimens (magnification 40x). D) immunostaining of CD 20 was positive, consistent with B-cell lymphoma.

Cases were absolutely discordant (1<sup>st</sup> and 2<sup>nd</sup> case from table 3). If partially concordant cases were included in concordant cases, the diagnostic accuracy will become to 89.3% (50/56 cases).

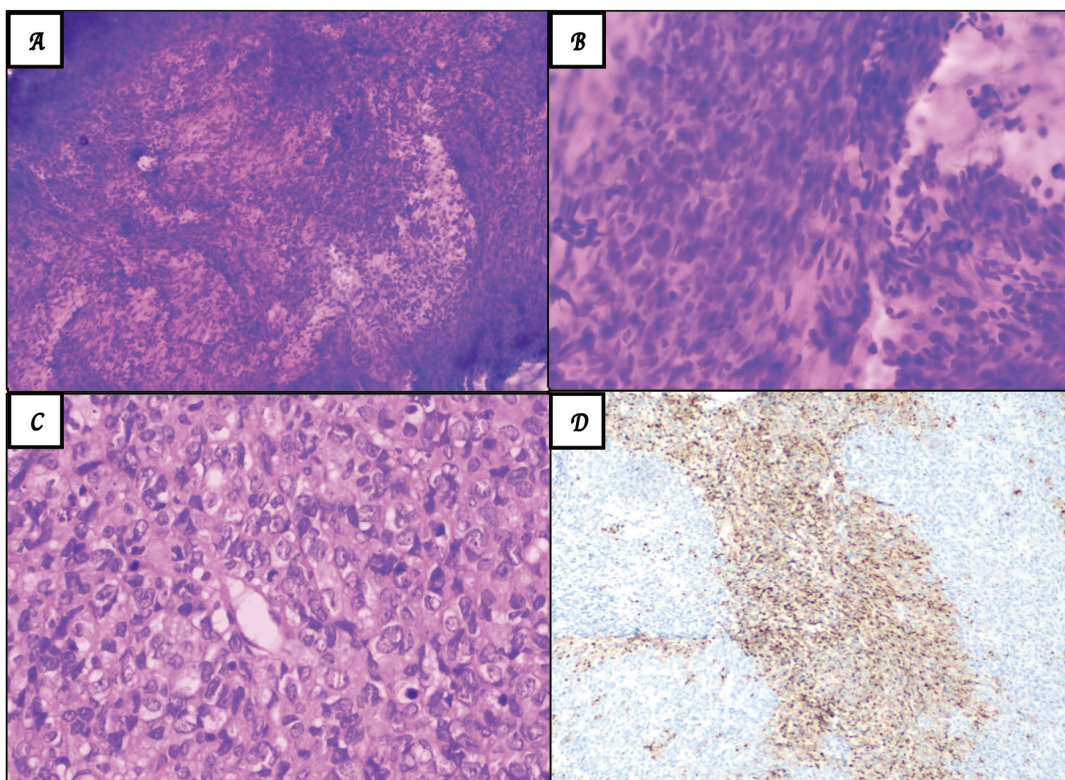
Form the literature review, there were two studies about diagnostic accuracy of intraoperative consultation for central nervous system and spinal cord specimen compares to corresponding final surgical specimens in Thailand. Diagnostic accuracy

of study at Siriraj Hospital and Thammasat University Hospital were 89% and 83.33%, respectively. Hence the diagnostic accuracy in this was indifferent from the previous two studies.

The factors that associated with discordant diagnosis were histomorphology overlapping of deferral cases (the most common) and sampling error (the second most common).

Wannissorn N. and Himakoun W. studied about the accuracy of intraoperative consultation in Thammasat University hospital from 2006 to 2010. The discordant cases were 83.33%. The discordant case was the specimen from brain that was differentially diagnosed between diffuse large B-cell lymphoma and glioblastoma. The pathologist diagnosed the intraoperative consultation specimen as high-grade glial tumor because there were inflammatory cells with increased number of astrocytes. Atypical lymphocyte from freezing artifact or perivascular infiltration that were characteristic in lymphoma was not present. Permanent sections showed infiltrating atypical lymphocytes. The diagnosis was diffuse large B-cell lymphoma after confirmed by immunostaining.

The cause of discordance in this study was technical error. The technical error was freezing artifact. The limitation was small size of specimen.<sup>10</sup> When compared to this study, the most common cause of discordance was histomorphology overlapping of deferral cases (0.09%) (5/56 cases) and the second most common was sampling error (0.07%) (4/56 cases). Technical error was not the cause of this study. Four cases of deferral group were round cell tumor. They were composed of two cases of hematologic malignancy, one case of carcinoma, one case of neuronal tumor and one case of spindle cell neoplasm that became meningothelial tumor (Figure 3). Four cases of sampling



**Figure 3** 76-year-old female patient with loss of sensation at right of body with parasagittal mass (9<sup>th</sup> case from Table 3). A) cytological preparation from intraoperative consultation specimen showed hypercellular lesion, arranged in fascicles (magnification 10x). B) The character of cell was spindle cell with same size and shape (magnification 40x). C) Corresponding final surgical specimen, the tumor cells were atypia. Mitotic count was 14/10 HPF (arrow) (magnification 40x). D) immunostaining of EMA was positive, consistent with atypical meningioma (magnification 10x).

Error occurred due to intraoperative consultation specimens were not corresponding to the lesions that leading to misdiagnosis.

From literature review, Thomas P, et al from the United States of America that had a lot of number of cases identified that the most common pathologic cause, leading to discordant diagnosis was spindle cell lesion. There was confusion between meningioma and other spindle cell neoplasms such as schwannoma, paraganglioma, and sarcoma. The other common cause was glial lesion, reactive Vs neoplastic lesion, CNS lymphoma and tumor overgrading. These causes increased difficulty of diagnosis because they had histomorphology overlapping that found in frozen section and cytologic study of intraoperative consultation. For example, frozen sections of spindle cell lesion can be challenging, particularly with limited submitted tissue or tissue distorted by crush artifact or cautery. Both meningiomas and schwannomas commonly arise in the cerebellopontine angle region. Although degenerative atypia ("ancient" change) is classically characteristic of schwannomas, meningiomas can demonstrate prominent nuclear pleomorphism at times. In addition, some meningiomas lack whorling, epithelioid syncytia, psammoma bodies, or uniform nuclei with blunted ends and intranuclear pseudoinclusions or cytoplasmic invaginations, features that are typically used in making the diagnosis. Useful histologic clues suggesting schwannoma are perivascular hemosiderin deposition, mixtures of loose (Antoni B) and compact (Antoni A) patterns, wavy with pointed ends of nuclei, and Verocay bodies. On occasion, the classic biphasic appearance of a schwannoma may not be evident in the sampled tissue. Freeze artifact can also induce changes in meningiomas that can mimic the Antoni B pattern of a schwannoma. In those instances in which the distinction cannot be made based on histology at

FS with certainty, rather than overinterpreting and succumbing to pressures of providing a diagnosis, a diagnosis of benign spindled cell tumor with a suggestion of what the differential diagnosis may include is reasonable.<sup>2</sup>

From this study, the patient's information, clinical data, radiologic finding, location of lesion and intraoperative finding are important to accurate intraoperative consultation. If the lesion is too difficult to give definite diagnosis, differential diagnosis should be performed instead to prevent therapeutic mistake.

The limitation of this study is lack of expert neuropathologist in Thammasat University Hospital. Then all cases in this study were reviewed by general pathologist that has experience in neuropathology.

### Acknowledgement

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### บทคัดย่อ

ความแม่นยำของการให้คำปรึกษาระหว่างผ่าตัดของสิ่งส่งตรวจระบบประสาทส่วนกลางในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

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**บทนำ:** เพื่อประเมินความแม่นยำในการวินิจฉัยด้วยวิธีการให้คำปรึกษาระหว่างผ่าตัดของสิ่งส่งตรวจระบบประสาทส่วนกลางในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

**วิธีการศึกษา:** การศึกษาแบบย้อนหลัง นับตั้งแต่วันที่ 1 มกราคม พ.ศ. 2555 ถึง 30 มิถุนายน พ.ศ. 2560 จากเคสทั้งหมดที่ได้รับการให้คำปรึกษาระหว่างผ่าตัดในระบบประสาทส่วนกลางและไขสันหลัง นำเคสที่มีผลทางพยาธิวิทยาไม่สอดคล้องกันมาตรวจซ้ำเพื่อตรวจวินิจฉัยและหาสาเหตุ วิเคราะห์ด้วย 2x2 contingency table

**ผลการศึกษา:** ผู้ป่วยทั้งหมด 56 ราย ความแม่นยำในการวินิจฉัย เท่ากับ 89.3%

**สรุปผลการศึกษา:** ความแม่นยำในการวินิจฉัย เทียบการศึกษาภายในประเทศอยู่ในเกณฑ์ดี (83.33 - 89%)

**คำสำคัญ:** ความแม่นยำ, การให้คำปรึกษาระหว่างผ่าตัด, ระบบประสาทและไขสันหลัง