Original Article

The Efficiency of The Cytological Method in Intra-operative Diagnosis

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Abstract:

Background: *In the intra-operative diagnosis, cytological examination has been performed accompanying the frozen section technique, which is the standard technique, because it renders more details of nuclear chromatin with less artifacts. Given that the cytological method requires no expensive instruments, it might be suitable for small hospitals where the frozen section is not available.* ***Objective:*** *This diagnostic study therefore aimed to determine sensitivity and specificity of the cytological technique for intra-operative diagnosis.* ***Design:*** *The diagnostic study was done. Of 628 cases requested for frozen section during the study period, 540 had slides available for review, and the cytological technique was performed in 362 cases.* ***Results:*** *Sensitivity and specificity of the cytological technique in diagnosing malignant lesions were 87.0% and 96.4%; whereas those of the frozen section technique were 91.1% and 99.4%, respectively, using final diagnoses from permanent sections as a gold standard. A McNemar test revealed no difference in the efficiency of these two methods, with areas under ROC curves 0.917 and 0.952, respectively.* ***Conclusion:*** *This study confirms the cytological technique as a helpful auxiliary procedure to be performed along with the standard frozen section technique. Furthermore, it may also be a helpful standalone intra-operative technique in the hospitals where frozen section is not available.*

Keywords: ● *Intra-operative consultation* ● *Frozen section* ● *Cytology*

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นิพนธ์ต้นฉบับ

การวินิจฉัยระหว่างทำการผ่าตัดด้วยวิธีเซลล์พยาธิวิทยา

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บทคัดย่อ

ความเป็นมา *ในการวินิจฉัยระหว่างทำการผ่าตัด ได้มีการตรวจด้วยวิธีทางเซลล์พยาธิวิทยาร่วมกับวิธีแช่แข็งซึ่งเป็นวิธีมาตรฐาน เนื่องจากวิธีทางเซลล์พยาธิวิทยาให้รายละเอียดของโครมาตินชัดเจนกว่า และมีการผิดรูปของเซลล์จากกระบวนการเตรียมสไลด์น้อยกว่า นอกจากนี้ วิธีทางเซลล์พยาธิวิทยาไม่ต้องอาศัยเครื่องมือราคาแพง จึงอาจเหมาะสมสำหรับโรงพยาบาลขนาดเล็ก ด้วยเหตุนี้* ***วัตถุประสงค์*** *เพื่อศึกษาความไวและความจำเพาะของการตรวจด้วยวิธีทางเซลล์พยาธิวิทยาในการวินิจฉัยระหว่างทำการผ่าตัด* ***วิธีการ*** *การศึกษาวิธีการวินิจฉัยในผู้ป่วย 628 ราย มีสไลด์ 540 สไลด์ที่สามารถอ่านได้ และการตรวจทางเซลล์พยาธิวิทยาจำนวน 362 ราย ความไวและความจำเพาะ ร้อยละ 87.0 และ 96.0 และวิธีแช่แข็ง ร้อยละ 91.1 และ 99.4 ตามลำดับ ซึ่งการทดสอบ McNemar พบว่า ทั้งสองวิธีมีประสิทธิภาพในการวินิจฉัยมะเร็งไม่แตกต่างกัน พื้นที่ใต้กราฟ ROC คือ 0.917 และ 0.952 ตามลำดับ การศึกษานี้ยืนยันว่า วิธีทางเซลล์พยาธิวิทยามีประโยชน์ ควรทำร่วมกับวิธีแช่แข็ง และอาจเป็นวิธีที่สามารถใช้ได้ในโรงพยาบาลซึ่งไม่มีเครื่องมือสำหรับการตรวจด้วยวิธีแช่แข็ง*

คำสำคัญ: ● *การวินิจฉัยระหว่างทำการผ่าตัด* ● *วิธีแช่แข็ง* ● *วิธีทางเซลล์พยาธิวิทยา*

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Introduction

The frozen section technique is a standard procedure to examine fresh specimens intraoperatively. In this technique, received specimens are put in the cryostat at -25 to -30 °C, and stained with Hematoxylin and Eosin. This technique is useful in intraoperative consultation for determining the nature of a lesion with an uncertain diagnosis, examining the margin status[1,2], and evaluating the lymph node involvement by a tumor[3]. The information is helpful for consulting surgeons to make a proper therapeutic decision.

Recently, the cytological technique has been used in examining fresh specimens as an auxiliary procedure. Advantages of this technique include easy accessibility, inexpensiveness, fastness, absence of artifacts commonly found in the frozen section technique (ice artifact, crush artifact), no requirement of an expensive cryostat machine, and a low risk of contamination. A combination of this technique and the frozen section technique, along with the availability of clinical history, and careful gross examination, helps improve the accuracy of the diagnosis[4]. This study aimed to determine the accuracy of the cytological technique in the intra-operative diagnosis.

Materials and Methods

Slides and request forms of the 540 cases that were submitted for intra-operative diagnosis within January 2005 to December 2006 were retrieved. Only cases with uncertain diagnoses were selected. Cases sent for determining the margin status were excluded. Slides from both frozen section and cytological techniques with some information about organs or sites of lesions were provided to 2 pathologists with a time limit of 5 minutes to reproduce to real situations of intra-operative consultations. Results of each slide from frozen section and cytological techniques were classified as positive (malignant), negative (benign), suspicious (criteria of malignancy not fulfilled), and unsatisfactory (diagnosis cannot be done due to limitation of received specimens, sampling errors of examiners, or the inadequate number of specimens). Data were recorded in SPSS program and analyzed using a McNemar test. An ROC curve was created for comparing sensitivity and specificity in diagnosis of the malignancy status between the frozen section technique and the cytological technique. Results from formalin-fixed paraffin-embedded tissue were defined as the gold standard.

Results

There were 628 cases requested for frozen section during the study period, with 540 cases having slides available for review and 362 cases for which the cytological technique was performed. Diagnoses could be made in 292 cases using a combination of cytological and frozen section techniques. The results from these techniques are shown in Table 1, using final diagnoses from permanent sections of the remaining tissue as the gold standard

Accuracy, sensitivity, specificity, positive predictive value, and negative predictive value of the cytological technique were 92.5%, 87.0%, 96.4%, 94.7%, and 91.1%; whereas those of the frozen section technique were 95.9%, 91.1%, 99.4%, 99.1% and 93.9%, respectively. The McNemar test revealed a statistical correlation of numbers of positive cases when using the cytological technique with the final results ($p = 0.52$) and with the frozen section technique ($p = 1.00$). This relationship was not detected between the frozen section technique and the final diagnosis ($p = 0.006$). However, a Kappa test revealed a stronger relationship between the frozen section results and the final diagnoses (0.915) than

Table 1 Results from cytological and frozen section techniques compared with results from permanent sections of formalin-fixed paraffin-embedded tissue

Technique		Results from Permanent Sections		Sum (%)
		Positive (%)	Negative (%)	
Cytology	Positive	107 (87.0)	6 (3.6)	113 (38.7)
	Negative	16 (13.0)	163 (96.4)	179 (61.3)
	Sum	**123 (42.1)**	**169 (57.9)**	**292 (100)**
Frozen section	Positive	112 (91.1)	1 (0.6)	113 (38.7)
	Negative	11 (8.9)	168 (99.4)	179 (61.3)
	Sum	**123 (42.1)**	**169 (57.9)**	**292 (100)**

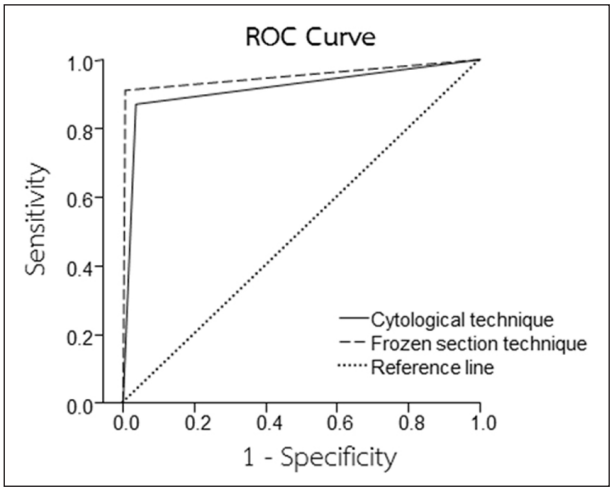

Figure 1 Receiver Operating Characteristic (ROC) curves of the cytological technique and the frozen section technique, using final reports as the reference line

between the cytological technique results and the final diagnoses (0.844). Furthermore, there are 4 false-negative cases from the frozen section technique that could be detected as malignant using the cytological technique. Receiver Operating Characteristic (ROC) curves of the cytological technique and the frozen section technique, using final reports as the reference line, reveals that areas under the curves for these techniques were 0.917 and 0.952, respectively (Figure 1). Additionally, 14 out of 18 cases that were suspicious for malignancy from cytology were actually malignant; 2 and 5 of which were reported as suspicious for malignancy and benign when using the frozen section technique, respectively.

Discussion

The cytological technique has been studied to determine its usefulness and accuracy for primary examination of intraoperative diagnosis 5, including this study, revealing that it has 90.5-97.7% accuracy, 80.0-100.0% sensitivity, and 95.0-100.0% specificity 6-10. However, this procedure has not been performed in some institutes because of the lack of well-experienced cytopathologists or negligibility of its usefulness.

Our study showed that the frozen section technique had a better correlation with final diagnoses than the cytological technique. However, the results from these two techniques were well correlated to each other. Noteworthy, 4 cases in which no malignancy was detected using the frozen section technique were cytologically detected as malignant lesions. This study suggested that the cytological technique is a helpful and beneficial auxiliary procedure to be performed along with the standard frozen section technique. Despite a higher rate of false positive and false negative results when using the cytological technique, this technique was able to help suggest malignancy in 2 cases, which were reported as suspicious for malignancy using the frozen section technique. Moreover, malignancy was detected using the cytological technique in 5 cases that were falsely reported as negative using the frozen section technique. These beneficial effects of the cytol-

ogy technique emphasize its importance in intra-operative diagnosis.

Most false diagnoses were caused by unfamiliarity of the reading pathologists with lesions of many organs that were not routinely examined in cytological practice at the institute, such as the brain, eye, stomach, liver, ovary, and bone. In some of these organs, the criteria for discernment between benign and malignant lesions were different from other organs. Another possible factor is the sampling error when smears were taken from non-neoplastic areas in specimens. These factors could be improved by more proficiency of cytopathologists who examine the slides. This may be achieved by more experience in examining cytological slides from various organs and more use of the cytological technique in intra-operative consultation. Noteworthy, in some cases, false diagnoses were caused by extremely well differentiation of malignant neoplasms. In these cases, the diagnosis of malignancy might be helped by the presence of stromal invasion, which could only be seen histologically.

In conclusion, the cytological technique has been shown to be beneficial in an intra-operative diagnosis. Potentially, this technique may also be utilized as a standalone technique for intra-operative consultation in hospitals where frozen section facilities are not available. However, the technique is still limited by its inability to determine the margin status and its requirement of well-experienced cytopathologists.

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