

Evidence-Base Medicine Conference

April 1, 2013

Department of Pathology

Yen-Chang Clark Lai, MD

Clinical Senario

- A 77-year-old woman had the history of renal pelvic urothelial carcinoma status post nephroureterectomy on 2007. She received regular follow-up in our out-patient department(OPD).
- A neck mass was noted in recent one week. She came to our OPD for help.
- The results of thyroid function test were within normal range.
- Fine needle aspiration of the thyroid nodule showed **degenerated atypical follicular cells**.
- Neck CT revealed a heterogenous enhanced mass about 4.7x3.5x3.2 cm.

Clinical Senario

- Surgical intervention with intraoperative frozen section examination were performed.
- The frozen section diagnosis was “benign”.
- The patient received bilateral subtotal thyroidectomy.
- The final pathological diagnosis is follicular adenoma in the right thyroid and nodular goiter in the left thyroid.

EBM五大步驟

- Asking (提出臨床問題)
 - Background questions
 - Foreground questions
- Acquire
- Appraisal
- Apply
- Audit

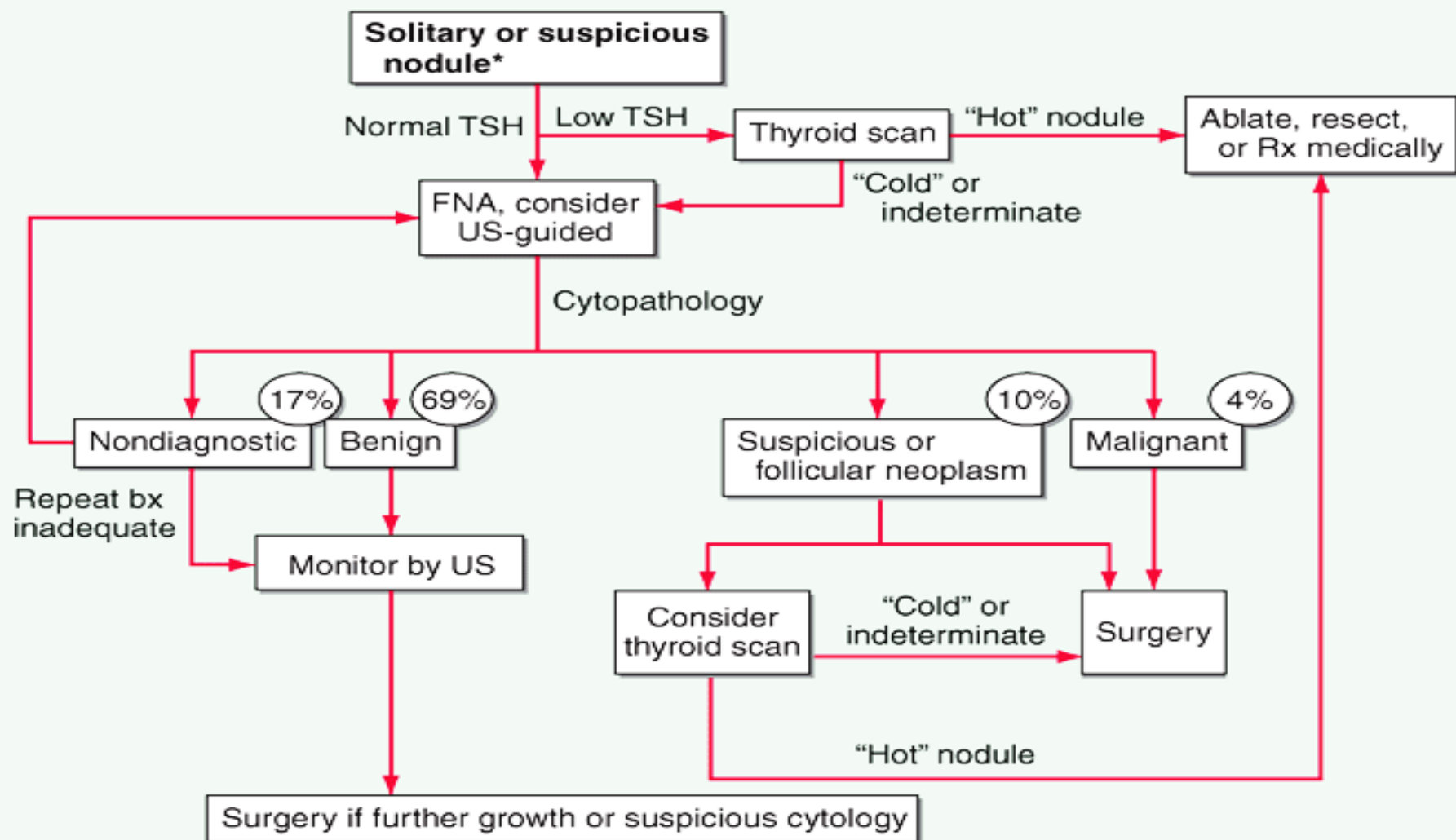
Background Questions

- Q1: What is the purpose of frozen section during thyroidectomy?
- Q2: Is there any benefit during intraoperation?

Q1: What is the purpose of frozen section during thyroidectomy?

- Frozen section analysis during thyroid surgery should only be employed when it will have an impact on surgical decision making .
- In general, frozen section analysis can be helpful for confirmation of thyroid malignancy intraoperatively when the preoperative cytology was atypical or suspicious for papillary carcinoma.

APPROACH TO PT WITH THYROID NODULE



Q2: Is there any benefit during intraoperation?

- Papillary thyroid lesions – Fine needle aspiration (FNA) has high diagnostic accuracy for papillary lesions .
 - The use of frozen section analysis is rarely required for intraoperative assessment of lesions that are confirmed as papillary thyroid cancer by preoperative FNA.
- Frozen section analysis can be useful in the diagnosis of papillary thyroid cancer in lesions in which the preoperative FNA was suspicious or indeterminate, as the diagnosis may rely on nuclear features alone.

Foreground Questions

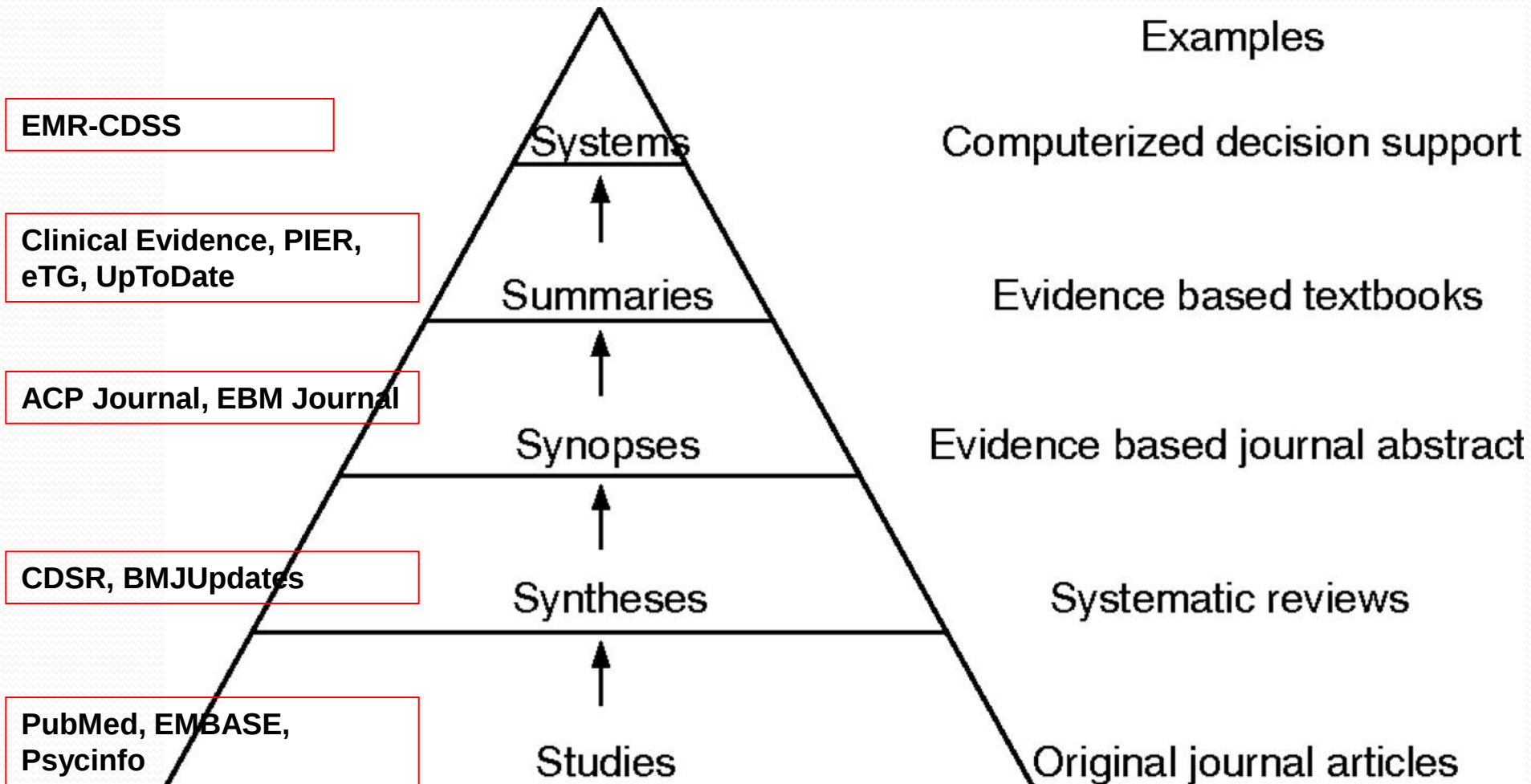
- Clarifying the problem using PICO model

術中冰凍切片能否有效改善甲狀腺結節/腫瘤之治療?	
<u>P</u> atient	With thyroid nodule/tumor
<u>I</u> ntervention	Frozen section to determine benign or malignant origin
<u>C</u> omparison	Without frozen section diagnosis
<u>O</u> utcome	Treatment

EBM五大步驟

- Asking
- Acquire (搜尋最有用的資料)
 - Search strategy: 5S model
- Appraisal
- Apply
- Audit

The "5S" Levels of Organization of Evidence



Search Strategy

- Finding out the correct keywords
 - Use MeSH to help identify terms
 - Thyroid gland
 - Frozen section
 - Intraoperative

Summaries



- Key words:
 - MeSH search
 - Thyroid gland
 - Frozen section
 - Intraoperative

Initial and reoperative thyroidectomy

TOPIC OUTLINE

SUMMARY & RECOMMENDATIONS

INTRODUCTION

INDICATIONS

PREOPERATIVE EVALUATION AND PREPARATION

INTRAOPERATIVE NEUROMONITORING

- Technique of nerve monitoring
- Efficacy of nerve monitoring

ANESTHESIA

- General anesthesia
- Cervical block

OPERATIVE MANAGEMENT

- Positioning
- Incision
- Exposure

hematogenously and there is little role for cervical lymphadenectomy. (See ["Surgical treatment of differentiated thyroid cancer", section on 'Approach to neck dissection'](#) and ["Medullary thyroid cancer: Treatment and prognosis"](#).)

Intraoperative frozen section – Frozen section analysis during thyroid surgery should only be employed when it will have an impact on surgical decision making [49]. In general, frozen section analysis can be helpful for confirmation of parathyroid tissue or thyroid malignancy intraoperatively when the preoperative cytology was atypical or suspicious.

- Parathyroid tissue – If a parathyroid gland is devascularized or resected during thyroidectomy, a frozen section should be obtained before autotransplantation to ensure that the specimen is indeed parathyroid tissue and not a metastatic lymph node or a portion of thyroid tissues. If the parathyroid is involved with tumor, it should be sacrificed. (See ["Identification of parathyroid glands"](#) above.)
- Papillary thyroid lesions – Fine needle aspiration (FNA) has high diagnostic accuracy for papillary lesions [49]. The use of frozen section analysis is rarely required for intraoperative assessment of lesions that are confirmed as papillary thyroid cancer by preoperative FNA. However, frozen section analysis can be useful in the diagnosis of papillary thyroid cancer in lesions in which the preoperative FNA was suspicious or indeterminate, as the diagnosis may rely on nuclear features alone. (See ["Overview of papillary thyroid cancer"](#).)
- Follicular thyroid lesions – Follicular neoplasms include nonpapillary follicular lesions, such as adenomatoid nodules, follicular adenomas, and follicular cancers that give rise to the same cytologic picture and are therefore indeterminate follicular lesions. Only about 20 percent of cases will be malignant on histologic examination [50]. Preoperative FNA is an accurate means of detecting papillary and medullary thyroid carcinomas, but it cannot distinguish between benign and malignant nonpapillary follicular lesions due to the inability to determine the presence of capsular and/or vascular invasion. A notable exception is follicular variant papillary thyroid cancer which is difficult to diagnose on both FNA and frozen section. (See ["Overview of follicular thyroid cancer"](#).)

Suggestive Management

- Follicular thyroid lesions –Preoperative FNA cannot distinguish between benign and malignant nonpapillary follicular lesions due to the inability to determine the presence of capsular and/or vascular invasion.
- The use of routine frozen section analysis to guide the intraoperative management of **follicular thyroid lesions** is controversial. Multiple sections of the tumor capsule are needed for definitive diagnosis of follicular lesions, making definitive diagnosis by intraoperative frozen section analysis **impractical and unreliable** at most institutions.

Synopses



- Key words:
 - MeSH search
 - Thyroid gland
 - Frozen section
 - Intraoperative

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Summaries



- Key words:
 - MeSH search
 - Thyroid gland
 - Frozen section
 - Intraoperative

thyroid gland frozen section intraoperative

Search



Result List 1 of 4

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Collapse All

A A A

Search Within Text



Thyroid nodule

Updated 2012 Aug 30 09:16:00 AM: gene-expression classifier may help rule out cancer in thyroid nodules with indeterminate cytology (N Engl J Med 2012 Aug 23) [view update](#) | [Show more updates](#)

Related Summaries:

- [Multinodular goiter](#)
- [Goiter](#) for list of related thyroid topics
- [Thyroid cancer](#) for list of thyroid cancer topics
- [Thyroid surgery considerations](#)

Overview:

- thyroid nodules may be caused by both benign and malignant disorders⁽¹⁾
- goal of evaluation is exclusion of malignant lesions^(1, 2)
- initial evaluation should include
 - identifying [risk factors for malignancy](#) including
 - head and neck irradiation in childhood
 - total body irradiation for bone marrow transplantation
 - family history of thyroid disease and thyroid carcinoma or thyroid cancer

Top

+ Related Summaries

Overview

+ General Information

Differential Diagnosis

+ Risk Factors

+ History and Physical

+ Diagnostic approach

Risk Factors for Malignancy

Management

+ Treatment of Benign Nodules

Prognosis

+ Prevention and Screening

Management Overview

Frozen section may not be sufficiently more useful than FNA in most cases to warrant increased operating time and expense

based on retrospective cohort study
outcomes for 231 patients having thyroidectomy compared to results of FNA, frozen section, or both
47 patients had final diagnosis of malignancy
comparing FNA vs. frozen section
sensitivity 50% vs. 50%
specificity 99% vs. 100%

Reference - *Am J Surg* 2002, 184(6):510; *Am Fam Physician* 2003, 15;67(8):1807

Syntheses



The Cochrane Library

Evidence for healthcare decision-making

- Key words:
 - MeSH search
 - Thyroid gland
 - Frozen section
 - intraoperative



THE COCHRANE LIBRARY

Independent high-quality evidence for health care decision making

from [The Cochrane Collaboration](#)

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Search

Search Manager

Medical Terms (MeSH)

Browse

To search an exact word(s) use quotation marks, e.g. "hospital" finds hospital; hospital (no quotation marks) finds hospital and hospitals; pay finds paid, pays, paying, payed)

[Add to top](#)

-	Edit	+	#1	thyroid	TH	2943
-	Edit	+	#2	frozen section	TH	350
-	Edit	+	#3	intraoperative	TH	9458
-	Edit	+	#4	#1 and #2 and #3	TH	7
-	+		#5		m TH	N/A

[View tips for Search Manager](#)

☐ Highlight orphan lines

[Save strategy](#)



The Cochrane Library

Evidence for healthcare decision-making

Search

Search Manager

Medical Terms (MeSH)

Browse



Title, Abstract, Keywords



thyroid frozen section intraoperative

Go

Save

[Search Limits](#)

View search tips (Word variations have been searched)

[Add to Search Manager](#)

All Results (3)

Cochrane Central Register of Controlled Trials : Issue 2 of 12, February 2013

There is **1** result from **683114** records for your search on 'thyroid frozen section intraoperative in title abstract keywords in Trials'

☐ Cochrane Reviews (0)

☒ All

☐ Review

☐ Protocol

☐ Other Reviews (0)

☒ Trials (1)

☐ Methods Studies (0)

☐ Technology Assessments (0)

☐ Economic Evaluations (2)

☐ Cochrane Groups (0)

Sort by Relevance

[Select all](#) | [Export all](#) | [Export selected](#)

- ☐ Randomized prospective evaluation of **frozen -section** analysis for follicular neoplasms of the **thyroid** .
Udelsman R , Westra WH , Donovan PI , Sohn TA and Cameron JL
Annals of surgery, 2001, 233(5), 716

[Export selected](#)

☒ All

☐ Current Issue

Me Methodology

Dg Diagnostic

Ov Overview

Abstract

- **OBJECTIVE:** To evaluate the clinical utility of frozen section in patients with follicular neoplasms of the thyroid in a randomized prospective trial.
- **SUMMARY BACKGROUND DATA:** The finding of a follicular neoplasm on fine-needle aspiration prompts many surgeons to perform intraoperative frozen section during thyroid lobectomy. However, the focal distribution of key diagnostic features of malignancy contributes to a high rate of noninformative frozen sections.
- **METHODS:** The series comprised 68 consecutive patients with a solitary thyroid nodule in whom fine-needle aspiration showed a follicular neoplasm. Patients were excluded for bilateral or nodal disease, extrathyroidal extension, or a definitive fine-needle aspiration diagnosis. Final pathologic findings were compared with frozen sections, and cost analyses were performed.

Abstract

- RESULTS: There were no significant differences between the groups in surgical time or total hospital charges; however, the charge per informative frozen section was approximately \$12,470.
- CONCLUSIONS: For the vast majority of patients (96.4%) with follicular neoplasms of the thyroid, frozen section is neither informative nor cost-effective

EBM五大步驟

- Asking
- Acquire
- Appraisal (嚴格評讀文獻)
 - 對找到的文章進行critical appraisal
- Apply
- Audit

Studies

PubMed Advanced Search Builder

[YouTube](#) [Tutorial](#)

((thyroid gland) AND frozen section) AND intraoperative

[Edit](#)

[Clear](#)

Builder

	All Fields	thyroid gland	-	Show index list
AND	All Fields	frozen section	-	Show index list
AND	All Fields	intraoperative	-	Show index list
AND	All Fields		- +	Show index list

[Search](#) or [Add to history](#)

History

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Search	Add to builder	Query	Items found	Time
#2	Add	Search thyroid gland frozen section intraoperative	85	23:14:02
#1	Add	Search thyroid frozen section intraoperative	210	23:13:43

Current Practices in Performing Frozen Sections for Thyroid and Parathyroid Pathology

Robert Y. Osamura & Jennifer L. Hunt

Virchows Arch (2008) 453:433–440

DOI 10.1007/s00428-008-0674-x

Abstract

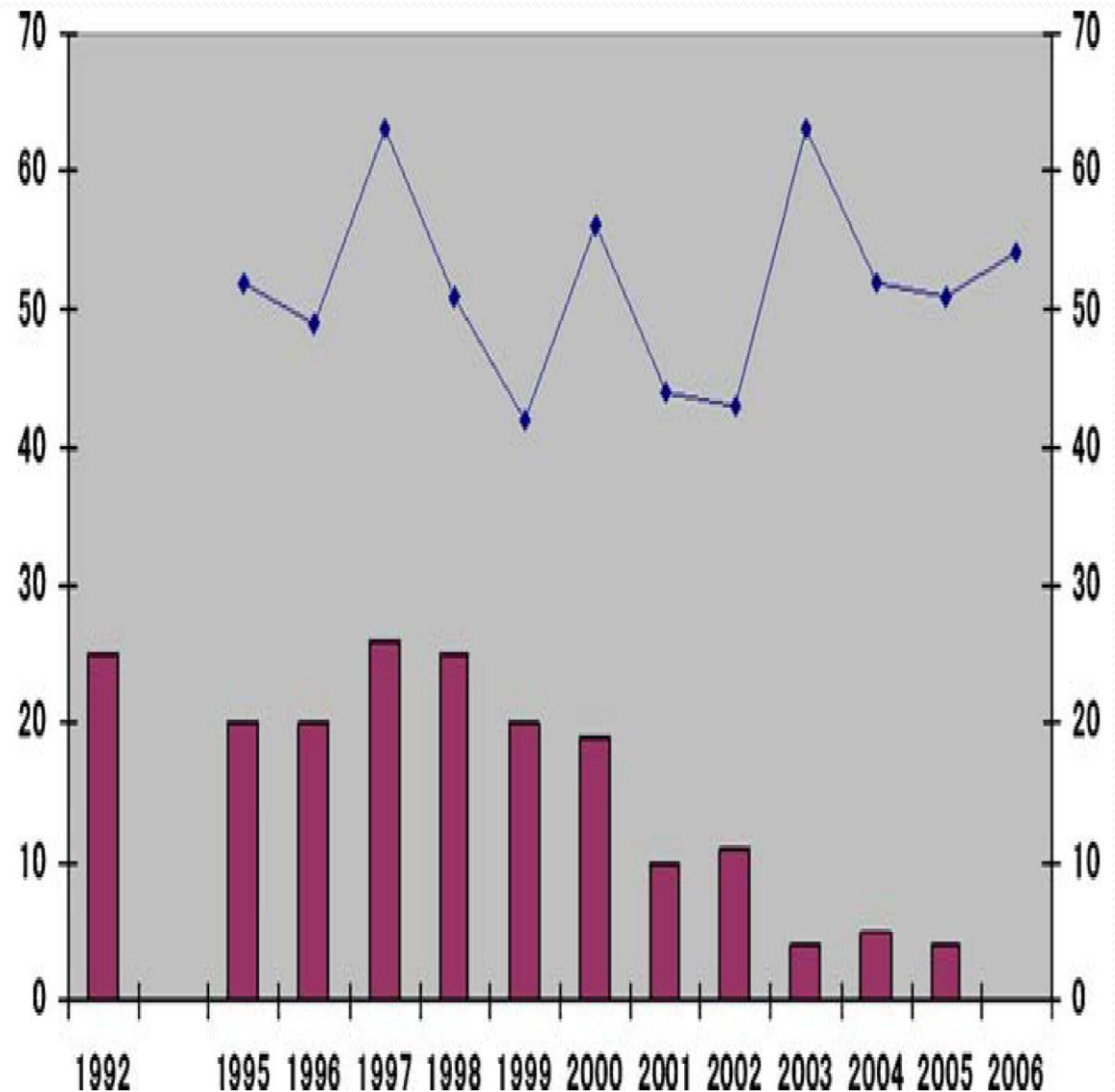
In this review article, current trends in thyroid and parathyroid frozen sections are discussed.

The decline in the number of thyroid frozen sections has been attributed to two major factors: **highly diagnostic preoperative fine needle aspiration** for papillary carcinomas, the most frequent type of thyroid cancers, and the acknowledgment in the literature of the **disadvantageous frozen sections for follicular tumors**.

Several authors have argued that the frozen section of thyroid nodules should be limited only to cases that have a preoperative cytology diagnosis as **“atypical” or “suspicious”**.

It is concluded that thyroid and parathyroid frozen section examination is restricted to selected situations.

Fig. 1 Trend over 14-year period for the use of frozen section diagnosis for thyroid surgeries at Tokai University Hospital. The *red bars* demonstrate the number of frozen sections performed for thyroids each year, and the *blue line* indicates the number of surgeries performed for thyroid disease in each year. The number of frozen sections decreased dramatically, while the number of overall thyroid surgeries remained relatively constant



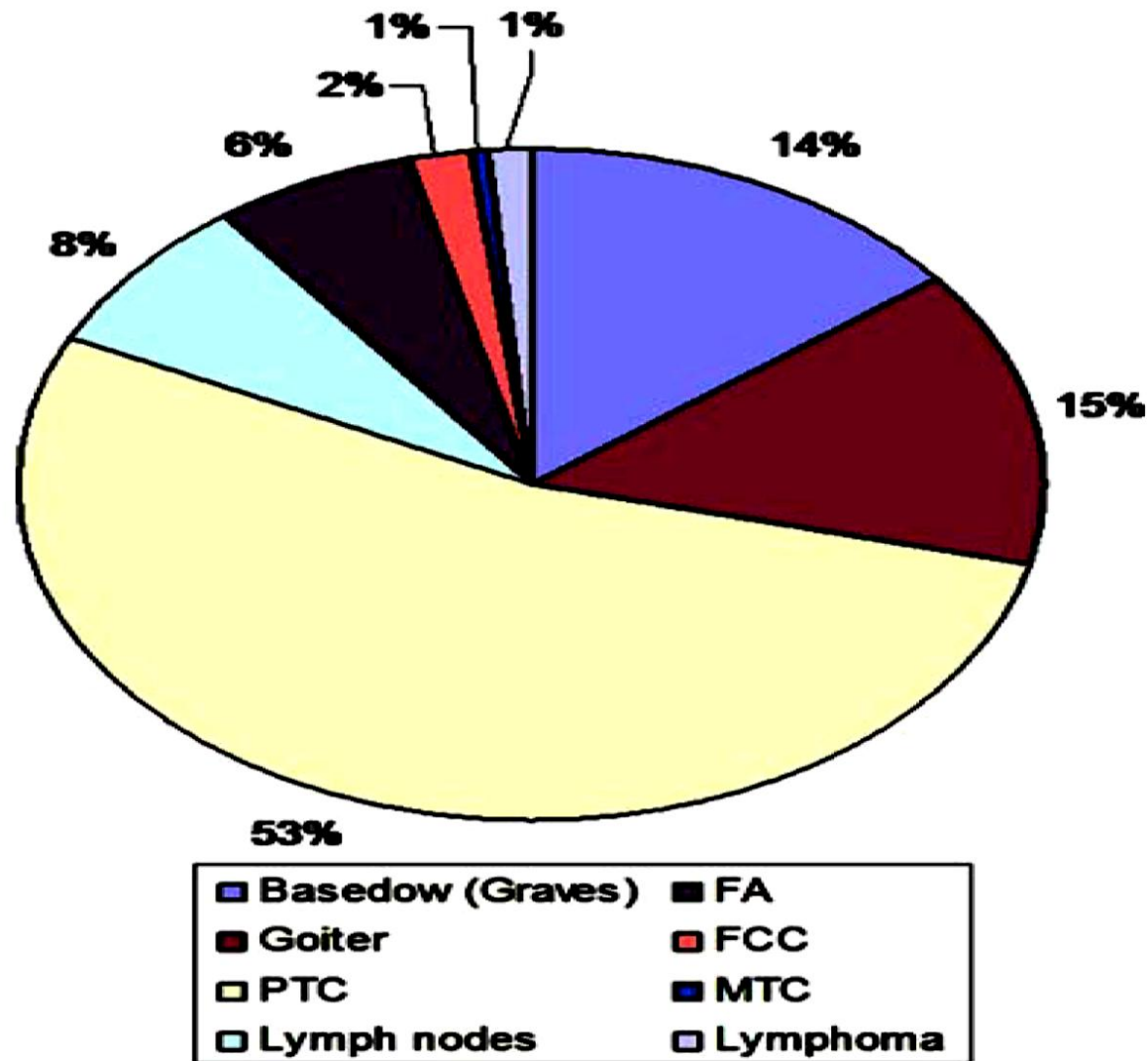


Fig. 2 Incidence of different diseases and diagnoses in surgical thyroid lesions at Itoh Hospital for Thyroid Diseases in 2006. None of these cases underwent frozen section

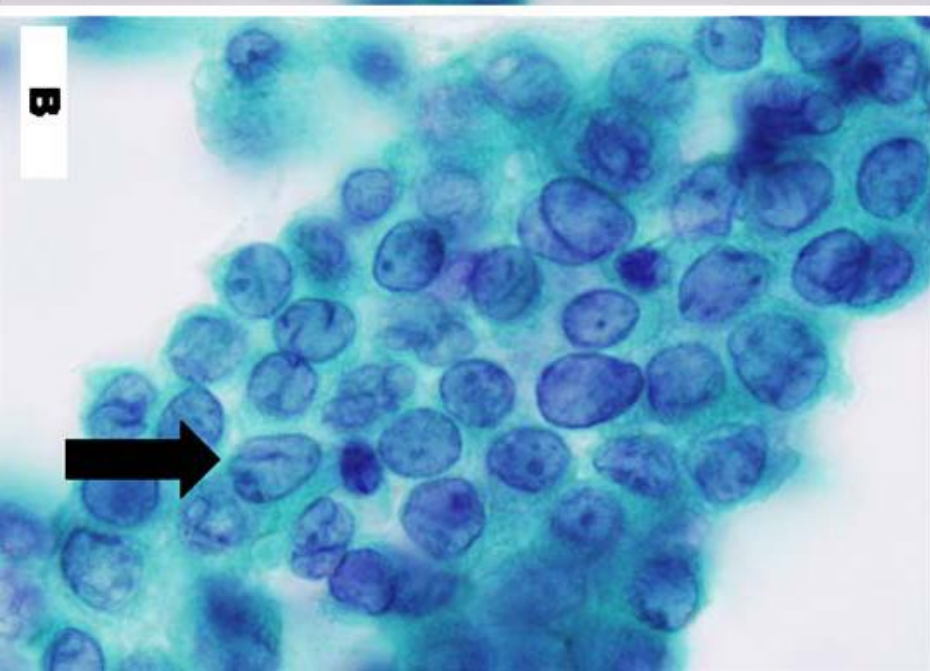
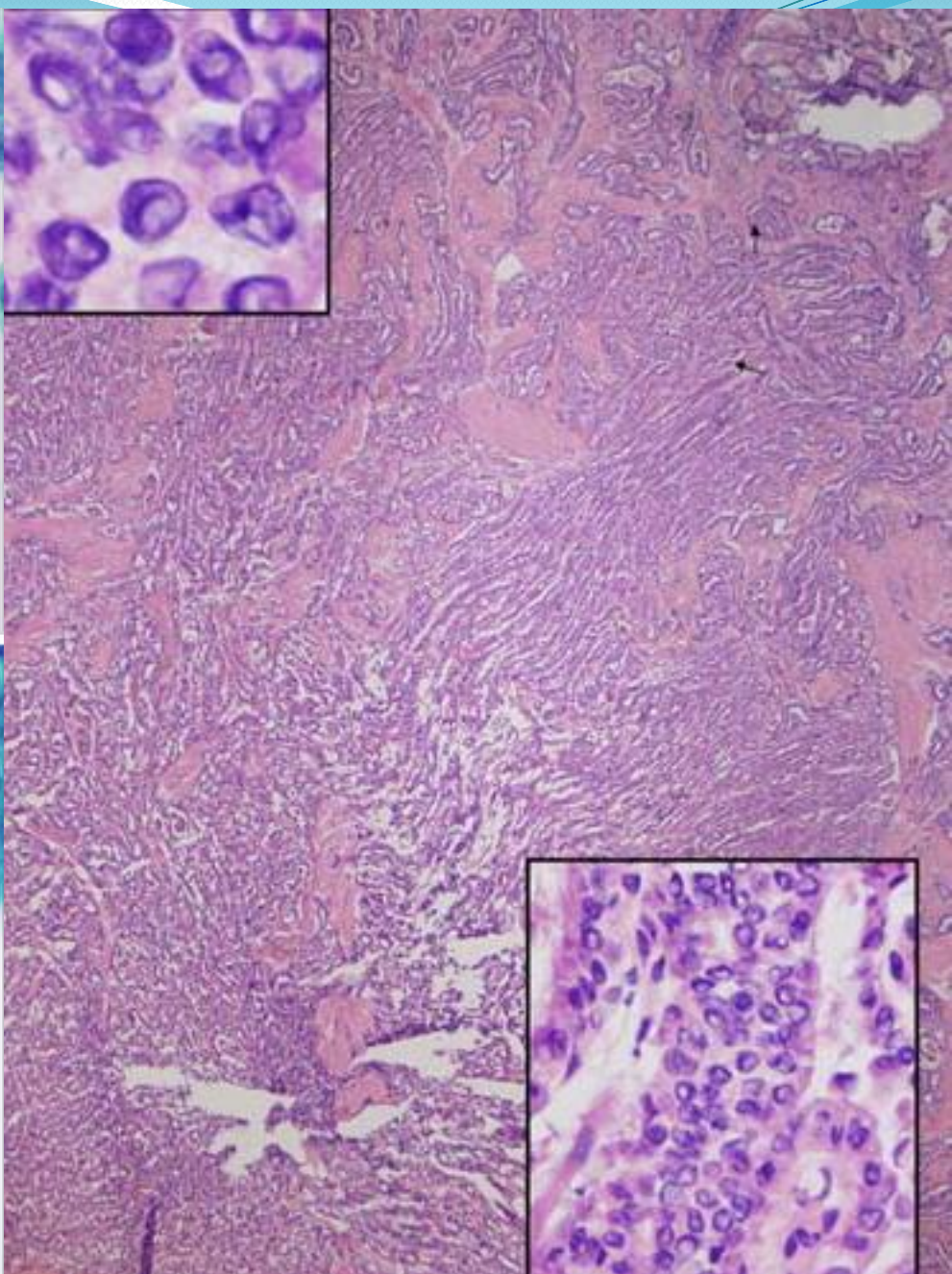
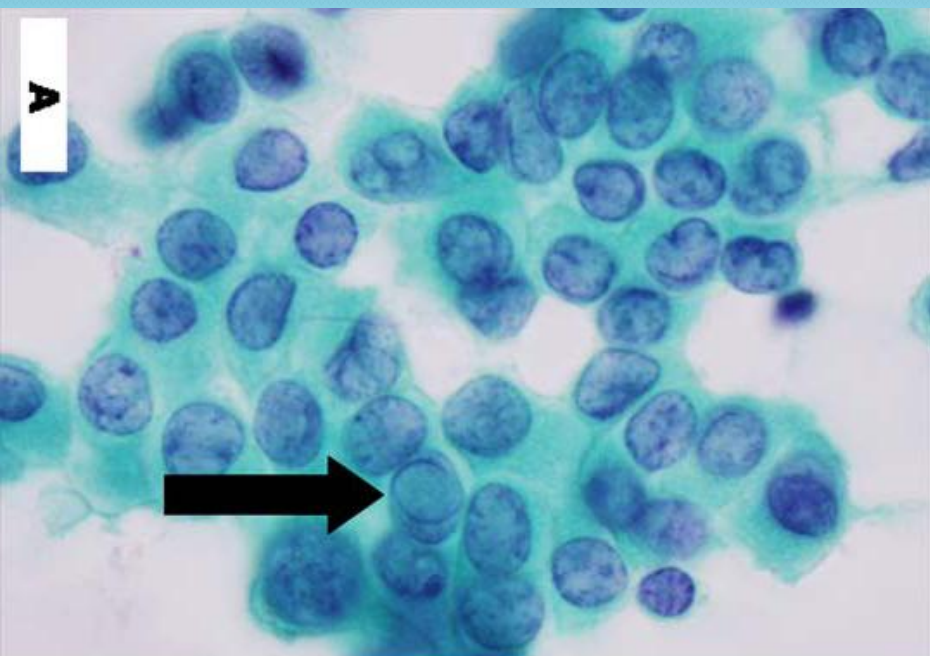


Table 1 Advantages and disadvantages of frozen section examination

Advantages

Diagnosis available for immediate decision making

Disadvantages

Tissue wasting secondary to sectioning

Preliminary nature of the diagnosis

Sampling errors

Conclusions

The number of cases of thyroid frozen sections has decreased remarkably in recent years. This is, on the one hand, due to the excellent results of the preoperative diagnosis by FNA cytology, and on the other hand, the recognition of the low sensitivity of frozen section examination in case of a follicular thyroid lesion. However, it is particularly important to note that thyroid frozen sections are recommended in the cases “suspicious” or “atypical” for PTC by FNA.

Level of Evidence

Level	Therapy/Prevention, Aetiology/Harm
1a	Systematic review (with homogeneity) of RCTs
1b	Individual RCT (with narrow Confidence Interval)
1c	All or none (ie all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality RCT; e.g., <80% follow-up)
2c	"Outcomes" Research or ecologic studies (studies of group changes)
3a	Systematic review (with homogeneity) of case-control studies
3b	Individual Case-Control Study
4	Case-series (and poor quality cohort and case-control studies)
5	Expert opinion or based on physiology, bench research or "first principles"

Item	<u>AAMPICOT</u> for therapy- Criteria	Comments
Answer	此文獻有沒有回答我的問題	有
Authors	作者群是這領域的專家嗎？	是
	有沒有利益衝突？	應該沒有 (無相關廠商支持記錄)
Method	本文獻研究設計是屬於以下那一類SR, RCT, Cohort, Case-control, Case series or report, Expert opinion	Systemic review
Population	取樣是否為隨機取樣？	是, 所選入之文獻全部皆為隨機取樣
	取的樣本是否具代表性？其特性是否接近我的病人	是
	分組是否是隨機分組？	是
	分組是否採用盲法？	否

Comparison	AAMPICOT for therapy- Criteria	Comments
Intervention	給予實驗組的處置是否描述清楚， 並且是臨床可行的？	有描述清楚(frozen section , final diagnosis), 而且是临床上可行的判別方式
Comparison	給予對照組的處置是否描述清楚，並且是臨床可行的？各種可能比較皆有了？	• 大部分的文獻都有描述清楚，並且也是临床上可進行的治療方式 • 比較 frozen section vs. without frozen section
Outcome	測量了那些結果？是否用客觀的方式測量？	• Incidence of thyroid gland frozen section • Percentage of types of thyroid glands
	這些結果是否有統計學上的重要性？	是
	這些結果是否有臨床上的重要性？	是
	是否呈現結果的「數值」，「p值」，「信賴區間」，「檢力」？	是
Time	測量結果的時間點是否合宜？	是，short/mid/long term都有考慮進去
	追蹤時間是否夠長？	Long term追蹤最長的則有追蹤至15年
	文獻發表時間？	2008

EBM五大步驟

- Asking
- Acquire
- Appraisal
- Apply (臨床應用)
 - 結合醫學倫理方法將文獻結果應用在病人身上
- Audit

Will the results help me in caring for my patients ?

- Is my patient so different to those in the study that the results cannot apply?
 - No
- Is the management feasible in my setting?
 - Yes
- Will the potential benefits of management outweigh the potential harms of treatment for my patient?
 - Need more data

醫療現況

冷凍切片檢查非必要性術中檢查要項

病人意願

經過上述文獻結果的解釋，病人有意願拒絕接受冷凍切片術中檢查

生活品質

延長手術以及麻醉所需時間
反覆手術而延長住院以及回復時間

社會脈絡

已納入健保給付之治療項目

EBM五大步驟

- Asking
- Acquire
- Appraisal
- Apply
- Audit (自我評估)

在「提出臨床問題」方面的自我評估

- 我提出的問題是否具有臨床重要性？是
- 我是否明確的陳述了我的問題？
 - 我的foreground question 是否可以清楚的寫成PICO？是
 - 我的background question是否包括what, when, how, who等字根？是
- 我是否清楚的知道自己問題的定位？（亦即可以定位自己的問題是屬於診斷上的、治療上的、預後上的或流行病學上的），並據以提出問題？是，屬於診斷範疇
- 對於無法立刻回答的問題，我是否有任何方式將問題紀錄起來以備將來有空時再找答案？是

在「搜尋最佳證據」方面的自我評估

- 我是否已盡全力搜尋？是
- 我是否知道我的問題的最佳證據來源？是
- 我是否從大量的資料庫來搜尋答案？是
- 我工作環境的軟硬體設備是否能支援我在遇到問題時進行立即的搜尋？是
- 我是否在搜尋上愈來愈熟練了？是
- 我會使用「斷字」、布林邏輯、同義詞、MeSH term，限制（limiters）等方法來搜尋？是
- 我的搜尋比起圖書館人員或其他對於提供病人最新最好醫療有熱情的同事如何？有進步空間

關於「嚴格評讀文獻」方面的自我評估

- 我是否盡全力做評讀了？是
- 我是否了解Number need to treat 的意義？大致了解
- 我是否了解Likelihood Ratios的意義？大致了解
- 我是否了解worksheet每一項的意義？大致了解
- 評讀後，我是否做出了結論？是

關於「應用到病人身上」的自我評估

- 我是否將搜尋到的最佳證據應用到我的臨床工作中？
是
- 我是否能將搜尋到的結論如NNT, LR用病人聽得懂的方式解釋給病人或臨床醫師聽？可以
- 當搜尋到的最佳證據與實際臨床作為不同時，我如何解釋？目前所搜尋到的文獻之結論為統計分析過後的結果是否定的，然臨床應用上需要進一步做為參考

Thank you for listening!