

## Recent Topics of Thyroid Cytopathology: Reporting Systems & Ancillary Studies

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No potential COI to disclose

## Kuma Hospital is the center for excellence in thyroid care

<b>Bed</b> (including 4 RI therapy rooms)	58
<b>Doctors</b> (Full-time)	33
Surgeon	9
ENT	4
Physician	16
Anesthesiologist	2
Pathologist	2
Cytotechnologist	5



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Cytotechnologist

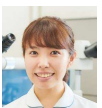
5



Dr. T Hayashi



M Higuchi



A Suzuki



A Tanaka



R Kanematsu



N Yamao

## Kuma Hospital is the center for excellence in thyroid care

Outpatients /year  
**181,405**  
初診患者数 13,239人 入院患者数 2,028人

Outpatients /day  
**664**

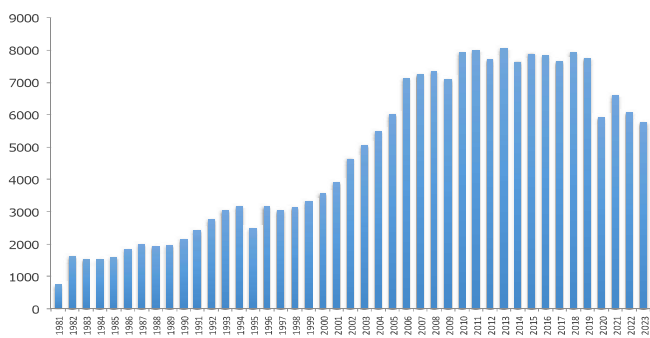
Surgery cases /year  
**1,937**

Graves Disease 143件 Parathyroid 128件  
Benign 503件 Malignant 1053件 Others 110件

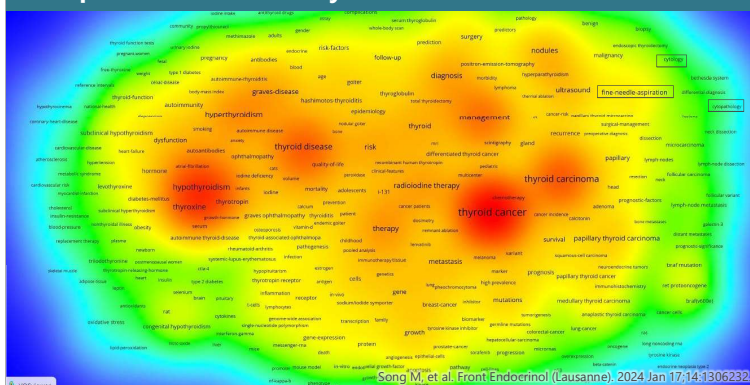
Academic presentations /year  
**27**  
in English

Academic articles /year  
**31**  
in English

## Trend of thyroid FNA cases in Kuma Hospital (1981-2023)



## Hot spots in the field of thyroid disease research



## The Bethesda System is globally used for thyroid FNA

1st

NCI Thyroid FNA  
Conference,  
Bethesda  
2007

2nd

International  
Cytology Congress,  
Yokohama  
2016

3rd

International  
Cytology Congress,  
Baltimore  
2022



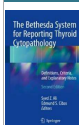
## Main 8 revisions in 3rd edition of TBSRTC

1. Diagnostic categories were unified under a single term
2. ROMs were revised
3. AUS was subcategorized into AUS with nuclear atypia and AUS-other
4. FN included mild or focal nuclear alterations associated with PTC
5. Data from the pediatric population were included
6. Differentiated high-grade thyroid carcinomas were included
7. Images were updated
8. Chapters covering clinical perspectives, imaging studies, molecular testing, and ancillary tests were added

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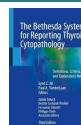
## 1. Diagnostic categories were unified under a single term



2nd edition	3rd edition
I Nondiagnostic/Unsatisfactory	Nondiagnostic
II Benign	Benign
III Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS)	Atypia of Undetermined Significance (AUS)
IV Follicular Neoplasm/Suspicious For a Follicular Neoplasm (FN/SFN)	Follicular Neoplasm (FN)
V Suspicious for Malignancy	Suspicious for Malignancy
VI Malignant	Malignant

Three categories had two terms

A single term is used for each category



2. ROMs were revised based on the recent reports

3. AUS was subcategorized

Category	2 <sup>nd</sup> edition %	3 <sup>rd</sup> edition % (mean)
Nondiagnostic	5–10	5–20 (13)
Benign	0–3	2–7 (4)
AUS	~10–30	13–30 (22)
Follicular Neoplasm	25–40	23–34 (30) ↓
Suspicious for Malignancy	50–75	67–83 (74) ↑
Malignant	97–99	97–100 (97)

AUS with nuclear atypia

- Focal nuclear atypia
- Extensive but mild nuclear atypia
- Atypical cyst lining cells
- “Histiocytoid” cells
- Nuclear & architectural atypia

AUS –Other

- Architectural atypia
- Oncocytic/Oncocyte atypia
- Atypia, NOS
  - Nuclear changes not suggestive of PTC
  - Psammoma bodies
- Atypical lymphoid cells, r/o lymphoma

Ali SZ, et al. *Thyroid* 2023;33:1039–1044.

3. AUS was subcategorized

AUS with nuclear atypia

- Focal nuclear atypia
  - Extensive but mild nuclear atypia
  - Atypical cyst lining cells
  - “Histiocytoid” cells
  - Nuclear & architectural atypia
- Architectural atypia
  - Oncocytic/Oncocyte atypia
  - Atypia, NOS
    - Nuclear changes not suggestive of PTC
    - Psammoma bodies
  - Atypical lymphoid cells, r/o lymphoma

ROM=59%

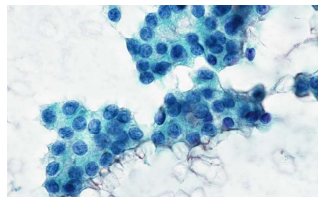
ROM=6.5%

Ali SZ, et al. *Thyroid* 2023;33:1039–1044.

4. NIFTP-suspected cases are classified into FN category

Previous term : Non-invasive, encapsulated, follicular subtype PTC  
Current term : Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

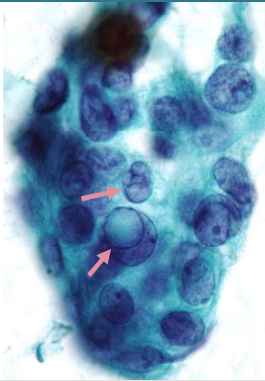
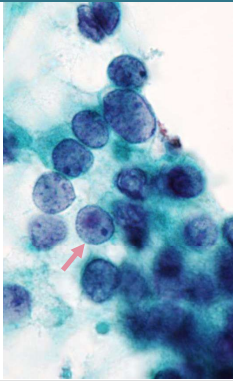
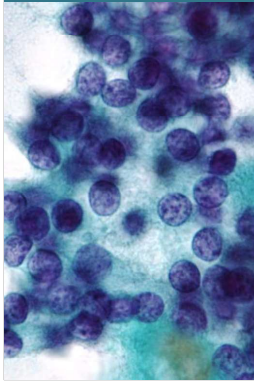
- NIFTP is **histological** diagnostic term
- Cytological diagnosis of NIFTP is **impossible**
- FN included mild or focal nuclear alterations associated with PTC



FN (FA/FTC)

FN (NIFTP)

Malignant (FV-PTC)



Impact of NIFTP

ROM of intermediate categories was decreased

Diagnostic category	Estimated ROM if including NIFTP Mean %	Decrease in ROM if excluding NIFTP Mean %	Estimated final ROM if excluding NIFTP Mean %
Nondiagnostic	13	1.3	12
Benign	4	2.4	2
AUS	22	6.4	16
Follicular Neoplasm	30	7.1	23
Suspicious for Malignancy	74	9.1	65
Malignant	97	2.6	94

Ali SZ, et al. *Thyroid* 2023;33:1039–1044.

Prevalence of NIFTP among PTCs and FTAs in Japan

PTC

<<<

FTA

Site	PTC → NIFTP	
	n	%
Japan, Kobe	50	0.5%
Japan, Fukuoka	12	3.1%
South Korea, Seoul	95	1.5%
South Korea, Seoul	5	0.2%
China, Shandong	16	0.3%
China, Wuxi	6	0.3%
Taiwan, Taipei	18	4.7%
Thailand, Bangkok	4	2.5%
Vietnam, Ho Chi Minh City	0	0%
	206	0.8%

Institution (in Japan)	FTA → NIFTP
A (29)	8 (27.6%)
B (21)	5 (23.8%)
C (17)	6 (35.3%)
D (26)	6 (23.1%)
E (11)	1 (9.1%)
F (46)	19 (41.3%)
Total (145)	45 (31.0%)

Hirokawa M, et al. *Pathol Int.* 2024 ;74:26–32.

Bychkov A, et al. *Thyroid* 2017;27:983–

Impact of NIFTP on ROM in Kuma Hospital

	ND	Benign	AUS	FN	SFM	Malignant
NIFTP= Malignant	1,287 (12.4%)	6,910 (66.4%)	421 (4.0%)	330 (3.2%)	172 (1.7%)	1,279 (12.3%)
NIFTP≠ malignant	1,287 (12.4%)	6,910 (66.4%)	365 (3.5%)	410 (3.9%)	156 (1.5%)	1,271 (12.2%)
Change in ROM	0%	0%	-0.5%	+0.7	-0.2%	-0.1%

Higuchi M, et al. *Endocr J.* 2018;65:1193–1198.

5. Data from the pediatric population were included

Dx category	Adults ROM Mean% (range)	Pediatrics ROM Mean% (range)	Adults Usual management	Pediatrics Possible management recommendations
Nondiagnostic	13 (5–20)	14 (0–33)	Repeat FNA with US guidance	Repeat FNA with US guidance
Benign	4 (2–7)	6 (0–27)	Clinical & US follow-up	Clinical & US follow-up
AUS	22 (13–30)	28 (11–54)	Repeat FNA, <b>molecular testing</b> , diagnostic lobectomy, or surveillance	Repeat FNA or <b>surgical resection</b>
Follicular Neoplasm	30 (23–34)	50 (28–100)	<b>Molecular testing</b> , diagnostic lobectomy	<b>Surgical resection</b>
SFM	74 (67–83)	81 (40–100)	<b>Molecular testing</b> , lobectomy or near-total thyroidectomy	<b>Surgical resection</b>
Malignant	97 (97–100)	98 (86–100)	Lobectomy or near-total thyroidectomy	<b>Surgical resection</b>

6. Differentiated high-grade thyroid carcinomas were included

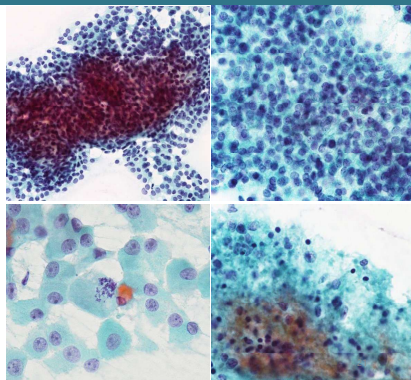
2nd

3rd

8 Papillary Thyroid Carcinoma and Variants.....	91	8 Papillary Thyroid Carcinoma, Subtypes, and Related Tumors.....	135
9 Medullary Thyroid Carcinoma.....	117	9 Medullary Thyroid Carcinoma.....	177
10 Poorly Differentiated Thyroid Carcinoma.....	129	10 High-Grade Follicular Cell-Derived Non-Anaplastic Thyroid Carcinoma.....	197
11 Undifferentiated (Anaplastic) Carcinoma and Squamous Cell Carcinoma of the Thyroid.....	139	11 Undifferentiated (Anaplastic) Thyroid Carcinoma.....	213
12 Metastatic Tumors and Lymphomas.....	153	12 Metastatic Tumors, Lymphomas, and Rare Tumors of the Thyroid.....	227
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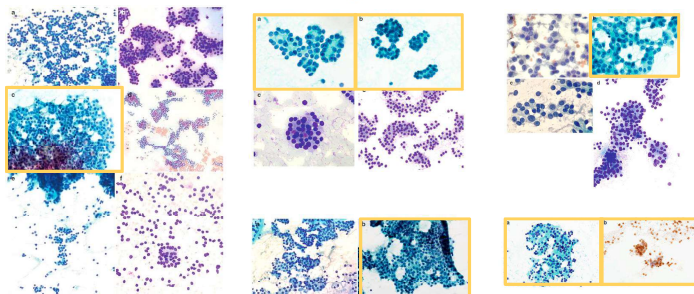
- Hypercellularity
- Insular, solid cluster, trabecular arrangement**
- Monotonous population  
Plasmacytoid, Oncocytic,  
Microfollicular cluster
- High N/C ratio
- No or little colloid
- Apoptosis, **Mitosis**
- Necrotic materials**



## Images updated in follicular neoplasm

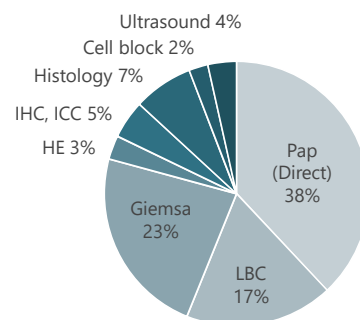
## 5 Follicular Neoplasm ..... 81

Manon Auger, Fabiano Callegari, Guido Fadda,  
Mitsuyoshi Hirokawa, and Lisa Rooper



## 7. Images were updated

1<sup>st</sup> : 240 photos  
↓  
2<sup>nd</sup> : 361 photos  
↓  
3<sup>rd</sup> : 404 photos



## 8. Two chapters were added

## 2nd

## 3rd

9 Medullary Thyroid Carcinoma.....	117	9 Medullary Thyroid Carcinoma.....	177
Martha B. Pitman, Yolanda C. Oertel, and Kim R. Geisinger		David Poller, Darcy Kerr, Maria Lozano, and Philippe Vielh	
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		Michiya Nishino, Paul VanderLaan, Giancarlo Trossone, Claudio Bellevicine, N. Paul Ober, and Camille Buffet	
		Index.....	285

## Imaging study (ACR-TI-RADS)

Indication for cytology is determined based on **US findings & tumor size**

Composition (choose 1)	Echogenicity (choose 1)	Shape (choose 1)	Margin (choose 1)	Echogenic foci (choose all that apply)	Category	Descriptor	Point value	FNA
Cystic/ mostly cystic	0 Anechoic	0 Wider-than-tall	0 Smooth	0 None	TR1	Benign	0 points*	N.I.
Spongiform	0 Hyperechoic/ isoechoic	1 Taller-than-wide	3 Ill-defined	0 Comet-tail artifacts	TR2	Not suspicious	2 points	N.I.
Mixed cystic/solid	1 Hypoechoic	2	2 Lobulated/ irregular	2 Macrocalcifications	TR3	Mildly suspicious	3 points	If >2.5 cm
Solid/ mostly solid	2 Very hypoechoic	3	3 Extra-thyroid extension	3 Peripheral ("rim") calcifications	TR4	Moderately suspicious	4-6 points	If >1.5 cm
				3 Pan-nodule echogenic foci	TR5	Highly suspicious	7+ points	If >1.0 cm

Abbreviations: N.I., not indicated; N.A., not applicable; cm, cm  
\*A total score of 1 point is not possible

ACR: American College of Radiology  
TI-RADS: Thyroid Imaging Reporting and Data System

## Comparison of three molecular tests

	ThyroSeq v3	ThyGenX / ThyraMIR1	Afirma GSC
<b>Oncogenic mutations &amp; gene fusion</b>	112 genes (12,135 variants), >120 gene fusion	10genes (42 variants), 28 gene fusion	346 genes (761 variants), 130 gene fusion
<b>Gene expression analysis</b>	19 genes	4 housekeeping genes for quality control	1,115 genes
<b>MicroRNA expression analysis</b>	No	10 microRNAs	No
<b>Chromosomal copy number alterations</b>	10 chromosomal region	No	LOH analysis
<b>For follicular cell</b>	Yes	Yes	Yes
<b>For parathyroid</b>	Yes	Yes	Yes
<b>For C cell</b>	Yes	Yes	Yes
<b>For NIFTP</b>	RAS/RAS-like	RAS/RAS-like	GSC-S
<b>For high-grade</b>	TERT, TP53	TERT	TP53 mutation

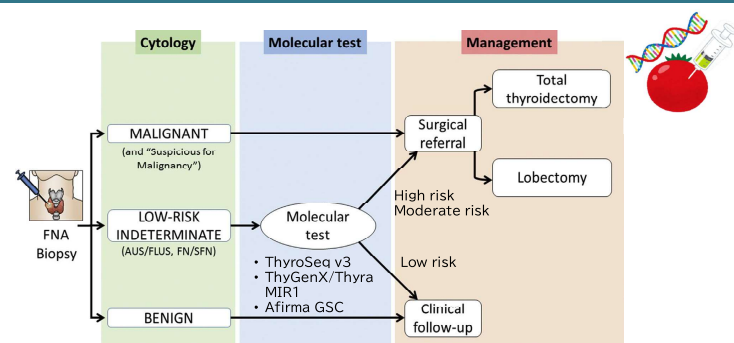
Nishino M, Krane JF. Acta Cytol. 2020;64:40-51.

## Accuracies of three molecular tests

	ThyroSeq v3	ThyGenX / ThyraMIR1	Afirma GSC
Cases, n	247	109	190
Malignant	28%	32%	24%
Benign	61%	61%	54%
Sensitivity	94%	89%	91%
Specificity	82%	85%	68%
<b>NPV</b>	<b>97%</b>	<b>94%</b>	<b>96%</b>
<b>PPV</b>	<b>66%</b>	<b>74%</b>	<b>47%</b>

Nishino M, Krane JF. Acta Cytol. 2020;64:40-51.

## Clinical management using molecular testing



Nishino, M., Krane, J. F. 2018;11;467-487.

## Molecular testing using aspirated materials

Not performed in Japan because...



- NO insurance coverage
- Extremely expensive
- NOT cost-effective

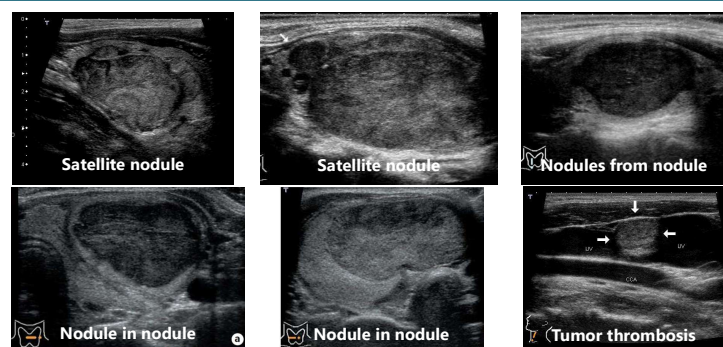
Hirokawa M, et al. Cancer Cytopathol. 2023;131:415-420.

## ROM &amp; clinical managements

Categories	Bethesda System		Japan (Data from 7 institutions)	
	ROM	clinical management	ROM	clinical management
<b>Nondiagnostic</b>	13% (5-20%)	Repeat FNA with US guidance	6.3% (3.1-10.9%)	Re-aspiration, follow-up for benign US findings
<b>Cyst fluid</b>	2%	Repeat FNA or Follow up	1.3% (0-5.0%)	Follow-up, re-aspiration for malignant US findings
<b>Benign</b>	1-2%	Clinical and US follow-up	0.8% (0.3-1.4%)	
<b>AUS</b>	22% (13-30%)	Repeat FNA, <b>molecular testing</b> , diagnostic lobectomy, or surveillance	19.3% (9.7-39.1%)	<b>Re-aspiration or follow-up based on US findings</b> , ancillary study
nuclear atypia	36-44%		29.8% (13.9-42.6%)	
others	15-23%		8.1% (5.7-14.6%)	
<b>FN</b>	30% (23-34%)	<b>Molecular testing</b> , diagnostic lobectomy	12.6% (6.6-17.8%)	<b>Resection or follow-up based on other clinical findings</b>
<b>SFM</b>	74% (67-83%)	<b>Molecular testing</b> , lobectomy or near-total thyroidectomy	91.9% (78.6-100%)	Resection, surveillance for low-risk micro PTC
<b>Malignant</b>	97% (97-100%)	Lobectomy or near-total thyroidectomy	99.5% (99.2-100%)	

## US features indicating malignancy

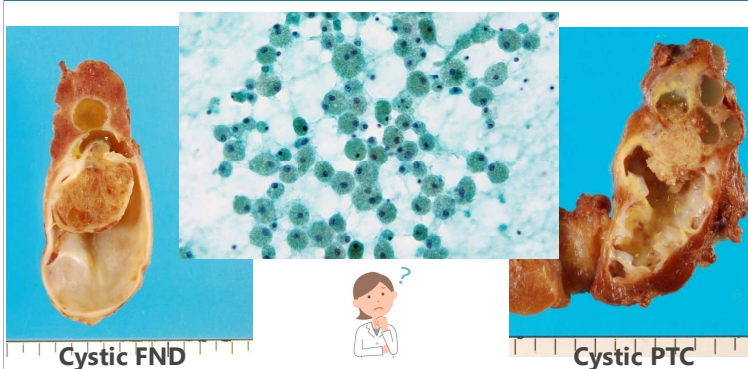
31



Kobayashi K, et al. Eur Thyroid J. 2017; PMID: 28589092 Kobayashi K, et al. Med Ultrason. 2016;18:25-9.

## Bethesda system: "Cyst Fluid Only" is included in "Nondiagnostic"

32



## Handling of cyst fluid in reporting systems

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Japan JSTS (2023)	US+Canada BSRTC (2023)	UK RCPath (2024)	Italy ICCRTC (2014)
I Unsatisfactory	I Nondiagnostic (cyst fluid only)	Thy1: ND for cytological diagnosis Thy1C: ND for cytological diagnosis-cystic lesion	TIR1: ND TIR1C: ND/cystic
II Cyst fluid			

## ROM of Nondiagnostic, CFO, and Benign

34

	Nondiagnostic excluding CFO	Cyst fluid only	Benign
	Takada, et al. (Endocr J. 2017)	Kanematsu, et al (Diagn Cytopathol. 2018)	Suzuki, et al. (J Jpn Soc Cytol 2014)
Prevalence (/all thyroid FNA)	7.6% (766/10036)	4.8% (469/9767)	67.8% (7007/10333)
Resected ROM (/resected nodules)	41.7% (43/103)	7.1% (1/14)	13.9% (79/577)
Overall ROM (/all nodules)	5.6% (43/766)	0.2% (1/469)	1.1% (79/7007)

p<0.001

## Reporting system (Japanese vs Bethesda)

35

Japanese system	Bethesda system
Unsatisfactory	Nondiagnostic (including Cyst fluid only)
Cyst fluid	
Benign	Benign
Undetermined Significance	Atypia of Undetermined Significance
Follicular neoplasm	Follicular neoplasm
Suspicious for malignancy	Suspicious for malignancy
Malignant	Malignant

Kamma H, et al. Endocr J 2022;69:139-154.

Ali SZ, et al. Thyroid 2023;33:1039-1044.

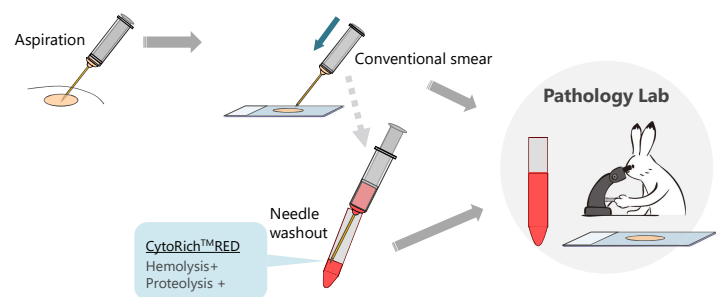
## Ancillary techniques on Thyroid FNA

36

1. Liquid-based cytology (LBC)
2. Immunocytochemistry
3. Biochemical measurement
4. Flow cytometry
5. Molecular testing
6. Artificial intelligence

## LBC sample are obtained from needle washout fluid

37



Hirokawa M, et al. Thyroid Fine-Needle Aspiration and Smearing Techniques. VidenaEndocrinology <https://doi.org/10.1089/ve.2018.0119>

## Advantages and disadvantages of LBC method

38

### Advantages

- Reduction of inadequate specimens
- Higher cell collection rate
- Fewer fields of view to be examined
- Disappearance of red blood cells and colloid
- Excellent preservation of cellular morphology
- Unique diagnostic clues
- Avoiding degeneration by smearing
- Capable of preparing several specimens for immunocytochemistry

### Disadvantages

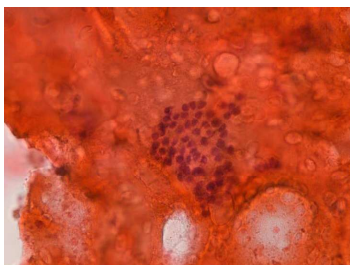
- More complicated preparation method
- Higher cost
- Cytological findings different from direct preparation
- Obscure diagnostic clue observed in direct smears

Suzuki A et al. Diagn Cytopathol 2014; 43: 108-113  
Suzuki A et al. Diagn Cytopathol 2016; 44: 659-664  
Suzuki A et al. Acta Cytol 2018;62:93-98

## Follicular nodular disease

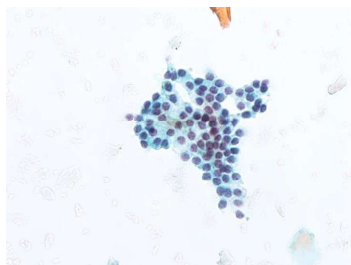
39

### Direct



- Embedded within blood components

### LBC

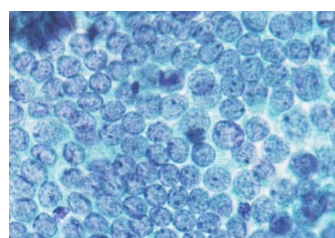


- No blood components

## Papillary thyroid carcinoma

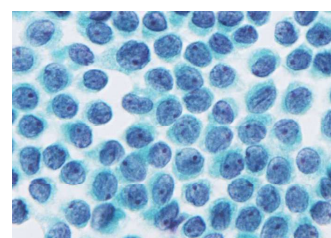
40

### Direct



- Nuclear overlapping

### LBC

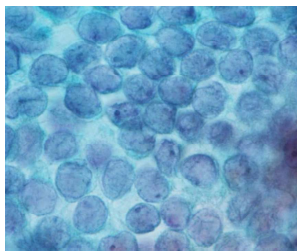


- Windows between carcinoma cells

Suzuki A et al. Diagn Cytopathol 2014; 43: 108-113

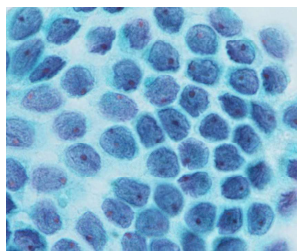


Direct



- Gland glass appearance
- Nuclear overlapping

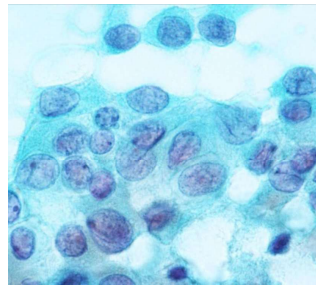
LBC



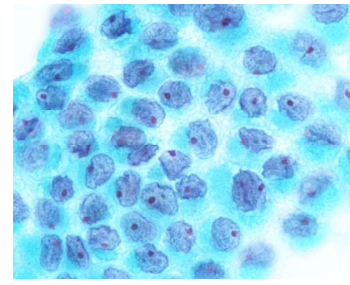
- No gland glass appearance
- No nuclear overlapping

Suzuki A et al. *Diagn Cytopathol* 2014; 43: 108-113

Direct



LBC

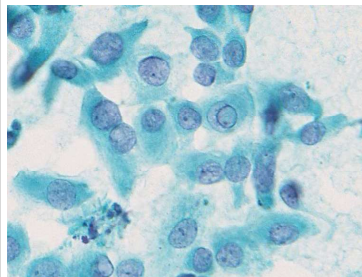


- Convoluted nuclei

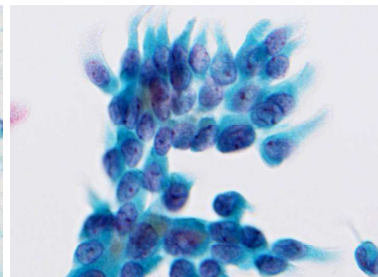
Suzuki A et al. *Diagn Cytopathol* 2014; 43: 108-113

## Tall cell subtype of papillary thyroid carcinoma

Direct



LBC



- Prominent cellular elongation

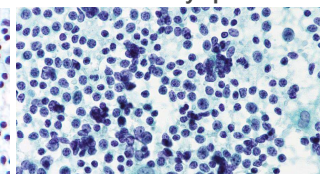
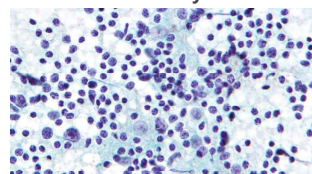
Suzuki A et al. *Diagn Cytopathol* 2014; 43: 108-113

## Hashimoto thyroiditis vs MALT lymphoma

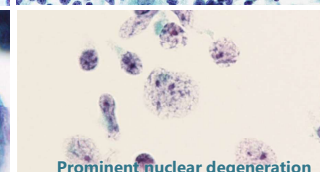
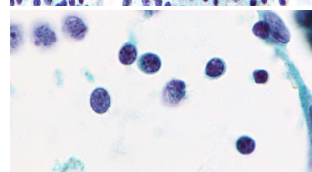
Hashimoto thyroiditis

MALT lymphoma

Direct



LBC



Prominent nuclear degeneration

Suzuki A et al. *Acta Cytol* 2018;62:93-98

## Thyroid FNA Cytology: Differential Diagnoses and Pitfalls

Kakudo K, Liu Z, Jung CK, Hirokawa M, Bychkov A, Lai CR

Springer; 3rd Edition, 2024

## Diagnostic Clues for Thyroid Aspiration Cytology

Aki Tanaka, Ayana Suzuki, and Mitsuyoshi Hirokawa

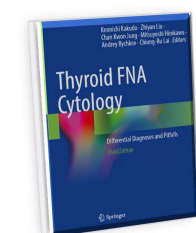
## 29.1 Introduction

Concerning a diagnosis of thyroid fine needle aspiration (FNA) cytology, we should understand that there are many characteristic findings, but no pathognomonic finding. For instance, intranuclear cytoplasmic inclusions are frequently seen in papillary thyroid carcinoma (PTC) cases and are characteristic of the tumor, but they are also observed in other thyroid conditions, such as hyalinizing trabecular (HTT), medullary thyroid carcinoma (MTC), anaplastic carcinoma (ATC), and so on (see Chap. 3). Therefore, they are not pathognomonic for PTC but are diagnostic. In this chapter, many diagnostic clues in thyroidology are described. The clues can be a shortcut aid in differential diagnosis, but it is not always possible to give too much importance to any one clue. The diagnosis should be based on a combination of multiple clues.

## 29.2.2 Watery Colloid

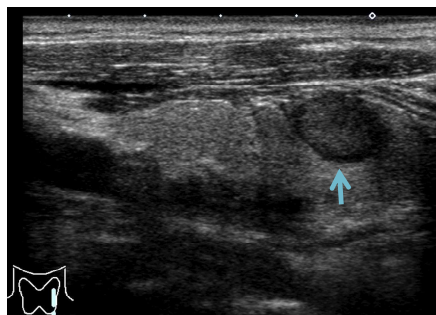
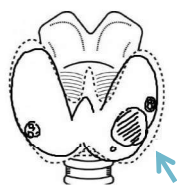
Watery colloid spreads as an acellular and homogeneous film on the glass slide (Fig. 29.1). It is cyanophilic to eosinophilic and thin to thick. It may look like plastic wrap or parched earth with cracks. In Giemsa stain, it tends to crack or spread unevenly on the slide glass, resulting in geometric pattern stained-glass appearance, spider web-like appearance, chicken wire pattern (Fig. 29.2) [2]. The abundant watery colloid indicates benign conditions. In liquid-based cytology (LBC) specimens, watery colloid disappears due to the lytic ability of the fixative, but may remain as subcellular (Fig. 29.3) or tissue paperlike colloid [3, 4].

## 29.2.3 Dense Colloid

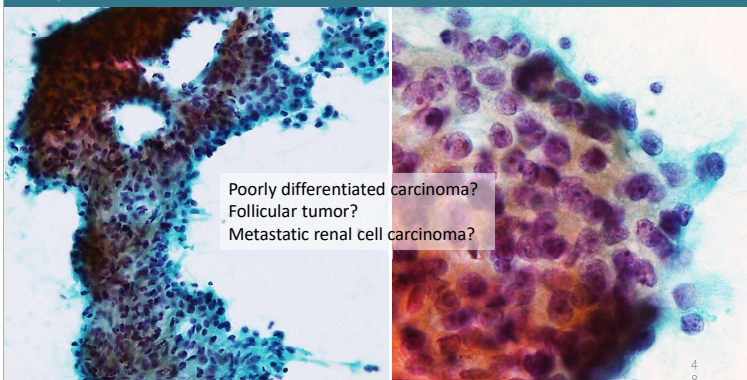


## 80-year-old, Male

- Past history of renal cell carcinoma resected 22 years ago



## 80-year-old, Male



## Three methods for Immunocytochemistry

- LBC method
- Cell block method
- Cell transfer method

can be performed after observing Pap-stained specimens



Hirokawa M, Suzuki A. *Acta Cytol*. 2024 Jul 22:1-9.

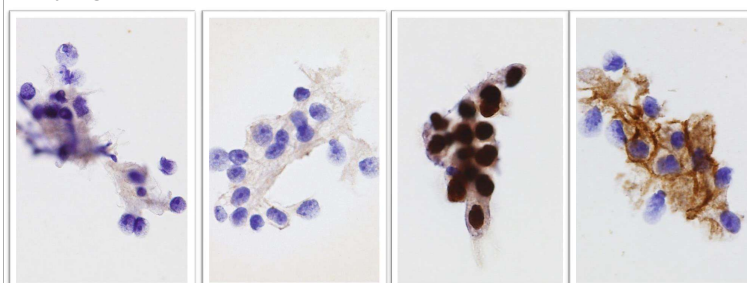
## Immunocytochemical results

Thyroglobulin

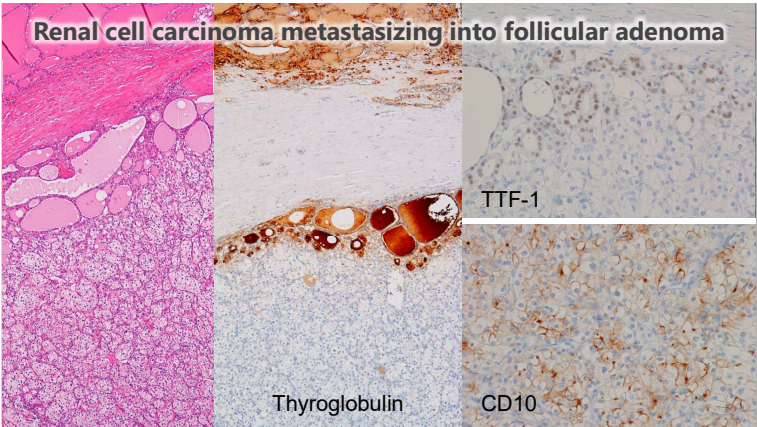
TTF-1

PAX8

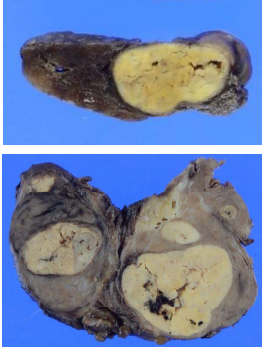
CD10







### Metastatic renal cell carcinoma



Solitary	85.7%
Multiple	14.7%
Within adenoma	42.9%
Post-nephrectomy time > 10 years	50.0%

Tanaka A, et al. Pathol Int. 2023;73:351-357.

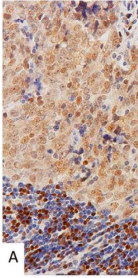
### Immunocytochemical panels used at Kuma Hospital

Target lesions	Antibodies
Follicular cell-derived lesion	PAX8(+), TTF-1(+), Thyroglobulin(+)
Medullary carcinoma	Calcitonin(+), CEA(+), Chromogranin A(+), TTF-1 (+), PAX8(-), Thyroglobulin(-)
Hyalinizing trabecular tumor	MIB-1 (cell membrane), Type IV collagen (hyaline materials), Cytokeratin 19(-)
Cribiform morular carcinoma	βcatenin(nuclei, cytoplasm), Estrogen receptor(+), Progesterone receptor(+)
Intrathyroidal thymic carcinoma	CD5 (+), p63(+), CD117(+), PAX8(-), TTF-1(-), Thyroglobulin(-)
Parathyroid adenoma	PTH(+), GATA-3(+), Chromogranin A(+), PAX8(-), TTF-1(-), Thyroglobulin(-)
Renal cell carcinoma	CD10(+), PAX8(+), TTF-1(-), Thyroglobulin(-)
Lung cancer	TTF-1(+), Thyroglobulin(-), PAX8(-)
Squamous cell carcinoma	PAX8(-)

Hirokawa M, Suzuki A. Acta Cytol. 2024 Jul 22:1-9.

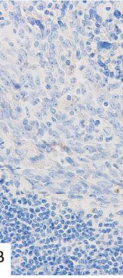
### Intrathyroidal thymic carcinoma

Polyclonal PAX8



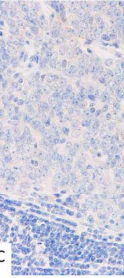
A

Monoclonal PAX8



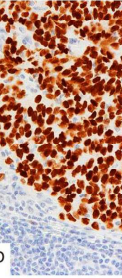
B

TTF-1



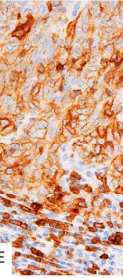
C

p63



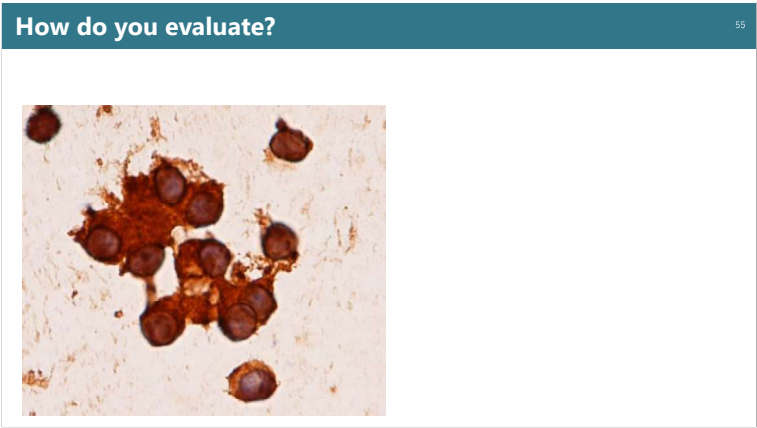
D

CD5



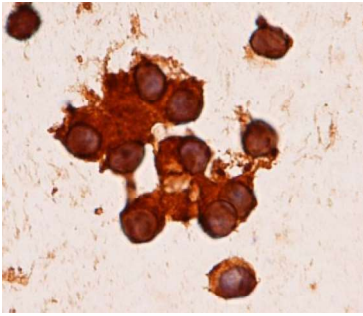
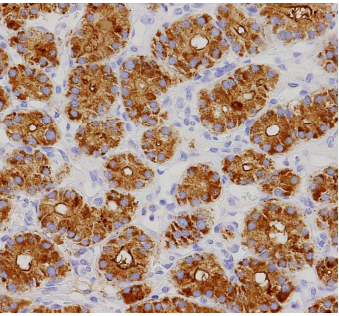
E

Suzuki A, et al. Endocr J. 2018;65:1171-1175.



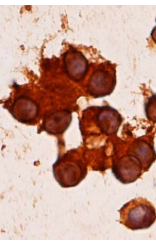
### How do you evaluate?


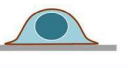
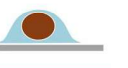



Thyroglobulin

### Pitfall in observing immunocytochemical specimens

Strong cytoplasmic immunoreactivity cause **pseudo**-nuclear positivity

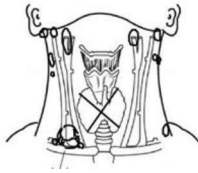



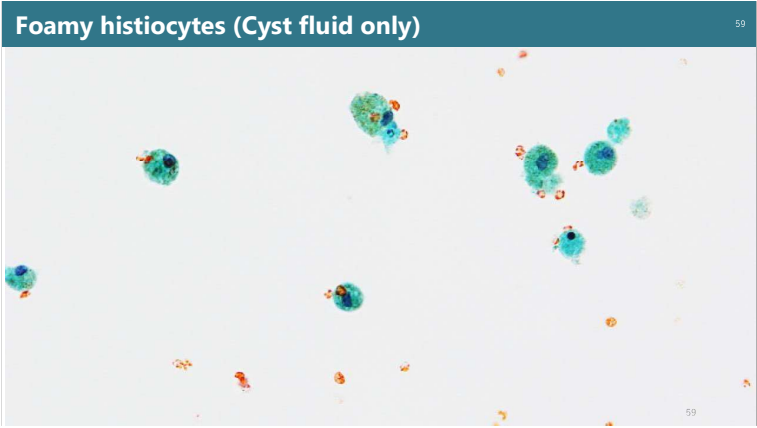
	Cytoplasm	Cell membrane	Nucleus
Lateral view from cut surface			
View under the microscope			

Hirokawa M, Suzuki A. Acta Cytol. 2024 Jul 22:1-9.

### Cystic lesion in the lateral neck

- Past history of total thyroidectomy for PTC

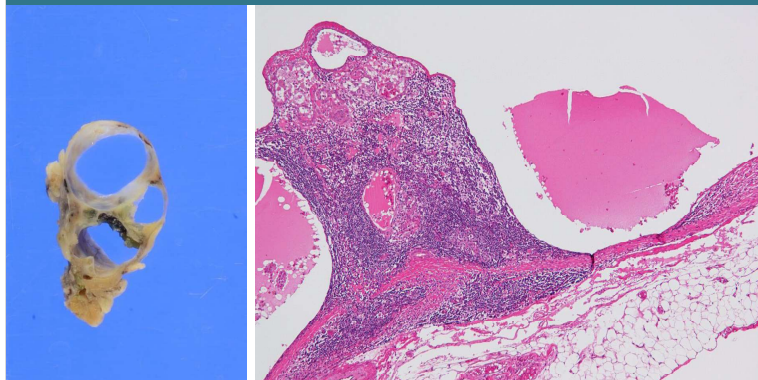





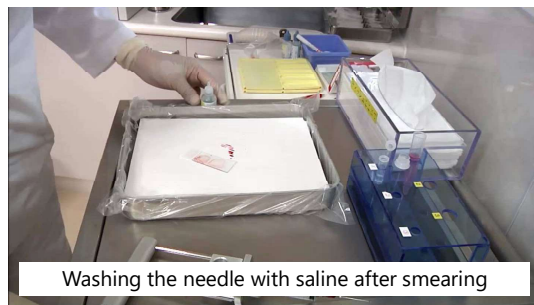
### Foamy histiocytes (Cyst fluid only)

Do you report "Benign"?

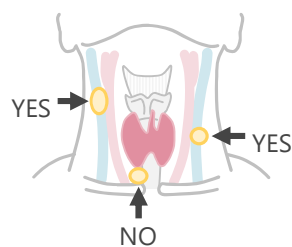




項目名称	検査結果
検体情報1	*****
Tg <sup>+</sup> ンク1	1353.0
Tg <sup>+</sup> ンク2	>8000



Washing the needle with saline after smearing

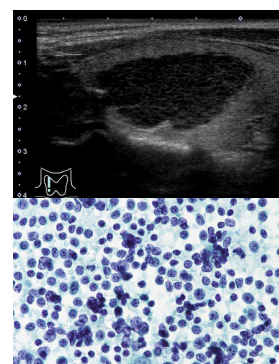
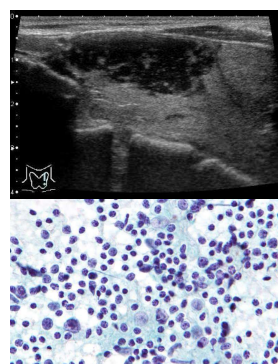
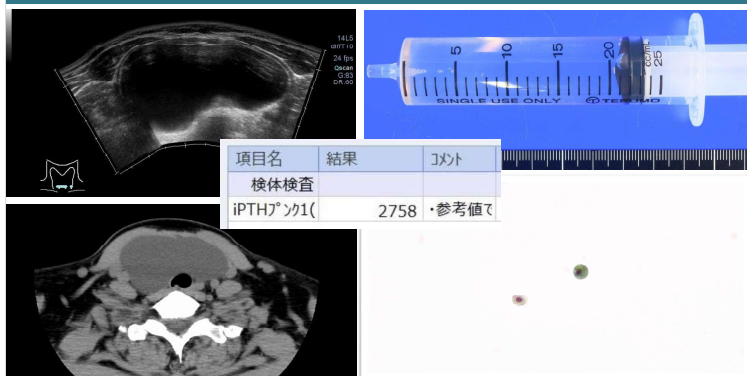
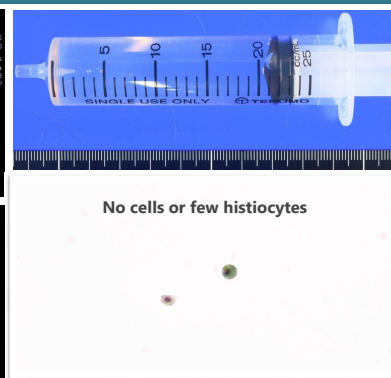
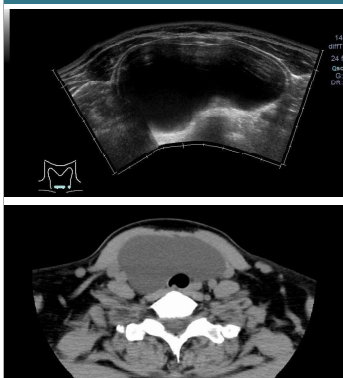


**NOT** recommended for **central lymph nodes**  
because thyroid tissue may be present on the route

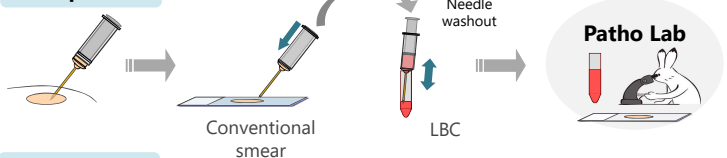
Hirokawa M, Suzuki A. J Pathol Transl Med. 2025;59:214-224.



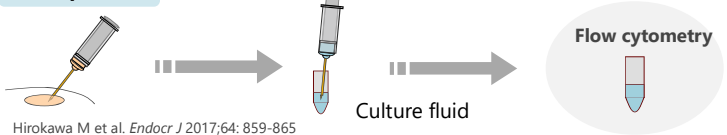
**Tg** for metastatic thyroid carcinoma  
**Calcitonin** for medullary carcinoma  
**PTH** for parathyroid lesions

Hirokawa M, et al. Thyroid Fine-Needle Aspiration and Smearing Techniques. VideoEndocrinology <https://doi.org/10.1089/ve.2018.0119>

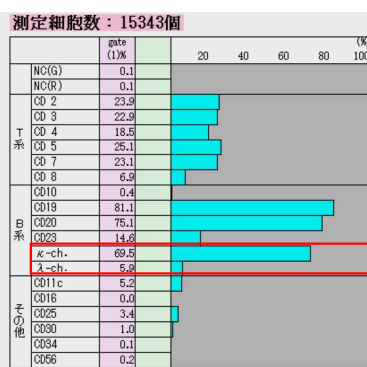
## 1st Aspiration



## 2nd Aspiration



Hirokawa M et al. Endocr J 2017;64: 859-865



- Almost all primary thyroid lymphomas are **B-cell type**
- The monoclonality is demonstrated by **Light-chain restriction**

Definition of light chain restriction

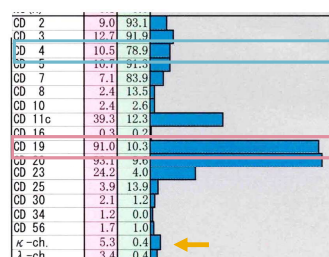
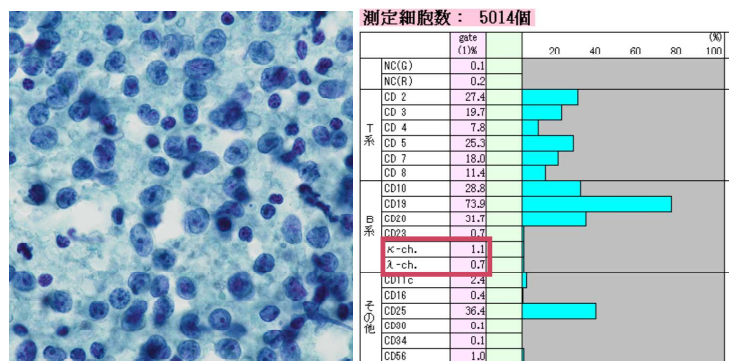
**κ/λ ratio > 3.0**Hirokawa M et al. Endocr J 2017;64: 859-865  
Suzuki A, et al. Endocr J 2019; 66: 1083-1091

	Specificity	Sensitivity	PPV	NPV
<b>Ultrasound</b>	32.6% (14/43)	62.5% (20/32)	74.1% (20/27)	93.3% (14/15)
<b>FNA</b>	41.9% (18/43)	59.4% (19/32)	90.5% (19/21)	94.7% (18/19)
<b>Flow cytometry</b>	<b>88.4%</b> (38/43)	<b>75.0%</b> (24/32)	82.8% (24/29)	82.6% (38/46)

Hirokawa M et al. *Endocr J* 2017;64:859-865.

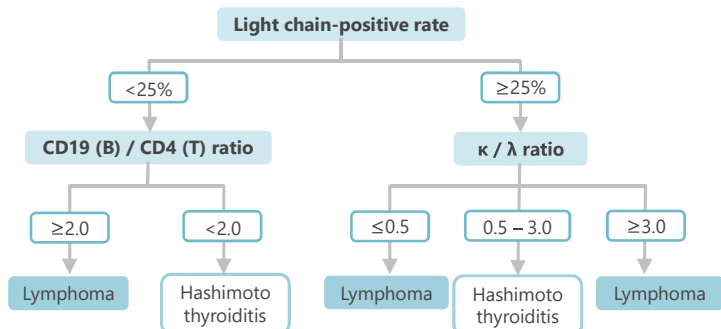
	Total	MALT	DLBCL	FL
Aspirated materials (n)	99	80	16	3
Light chain restriction	73 (73.7%)	60 (75.0%)	11 (68.8%)	2 (66.7%)
Resected materials (n)	104	86	16	2
Light chain restriction	72 (69.2%)	61 (70.9%)	9 (56.3%)	2 (100%)

MALT, mucosa-associated lymphoid tissue lymphoma; DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma

Suzuki A, et al. *Endocr J* 2019;66:1083-1091

**Light chain-positive rate <25%**  
**CD19 (B) / CD4 (T) >2.0**

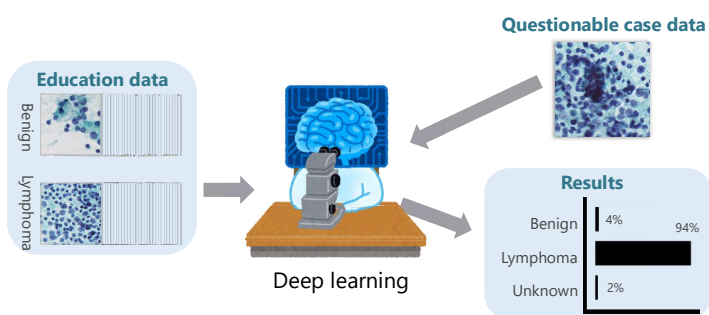
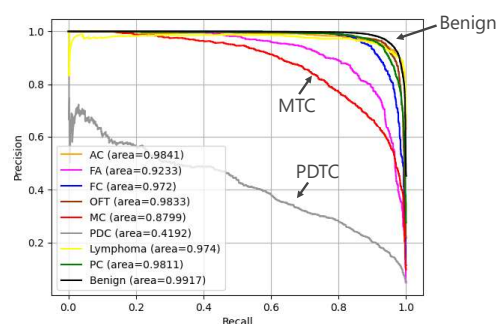
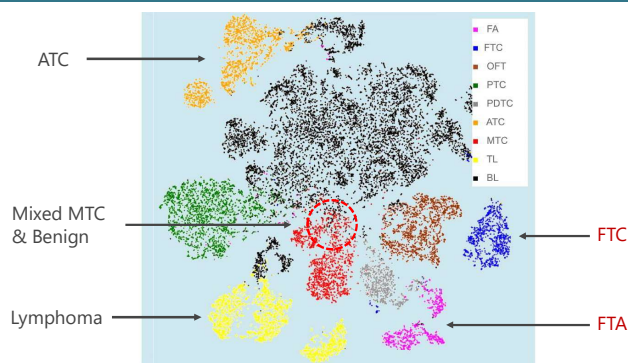
Sensitivity	88.9% (8/9)
Specificity	100% (3/3)
PPV	100% (8/8)
NPV	75.0% (3/4)

Suzuki A et al. *Endocr J* 2022;69:291-297.Suzuki A et al. *Endocr J* 2022;69:291-297.

Mitsuyoshi Hirokawa<sup>1)</sup>, Ayana Suzuki<sup>1)</sup>, Yuko Hashimoto<sup>2)</sup>, Shinya Satoh<sup>3)</sup>, Sule Canberk<sup>4),5)</sup>, Jie Yang Zhuang<sup>6)</sup>, Chan Kwon Jung<sup>7)</sup>, Nichthida Tangnuntachai<sup>8)</sup>, Bozidar Kovacevic<sup>9)</sup>, Yun Zhu<sup>10)</sup>, Shipra Agarwal<sup>11)</sup> and Kennichi Kakudo<sup>12)</sup>

	Often to Always*	Occasionally to Sometimes**	Never to Rarely***
Ultrasound	10	0	0
Cytology	9	1	0
Flow cytometry	1	4	5
Histological examinations			
Core needle biopsy	3	6	1
Open biopsy	1	6	3
Lobectomy	6	2	2
Thyroidectomy	3	3	2

\*: 60-100%; \*\*: 30-60%; \*\*\*: 0-30%

Hirokawa M, et al. *Endocr J* 2020;67:1085-1091Hirokawa M, et al. *Cancer Cytopathol* 2023;131:217-225.Hirokawa M, et al. *Cancer Cytopathol* 2023;131:217-225.Hirokawa M, et al. *Cancer Cytopathol* 2023;131:217-225.

Dx category	Adults Usual management	Pediatrics Possible management recommendations
Nondiagnostic	Repeat FNA with US guidance	Repeat FNA with US guidance
Benign	Clinical and US follow-up	Clinical and US follow-up
AUS	Repeat FNA, Molecular testing, diagnostic lobectomy, or Surveillance, (AI analysis)	Repeat FNA or surgical resection, (AI analysis)
Follicular Neoplasm	Molecular testing, diagnostic lobectomy, (AI analysis)	Surgical resection, (AI analysis)
SFM	Molecular testing, lobectomy or near-total thyroidectomy	Surgical resection
Malignant	Lobectomy or near-total thyroidectomy	Surgical resection



Just visit our website "Kobe Thyroid Cytology Club"  
and download the handouts of today's lecture.



Google

Kobe Thyroid Cytology

Google 検索

I'm Feeling Lucky



Scan me!

Thank you for your attention



Hotel Grand Tjokro Bandung, Aug 3<sup>rd</sup> 2019