Thyroid Follicular Cell Carcinomas in WHO classification and our new proposal

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The 7th ADPC 北京, 2008/10/25

甲状腺癌病理組織分類
（WHO2004　and Williams' classification）

Papillary carcinoma
Follicular carcinoma
Poorly differentiated carcinoma
Undifferentiated carcinoma
Squamous cell carcinoma
Mucoepidermoid carcinoma
Sclerosing mucoepidermoid carcinoma with eosinophilia
Mucinous carcinoma
Medullary thyroid carcinoma
Mixed medullary and follicular cell carcinoma
etc

Williams ED: Guest Editorial: Two proposal regarding the terminology of thyroid tumours. Int J Surg Pathol 8: 181-183, 2000.

1 Follicular Adenoma
2 Follicular Carcinoma
3 Papillary Carcinoma
4 WDC-NOS
(Well differentiated Carcinoma, not otherwise specified)
5 WDT-UMP and FT-UMP
(Well differentiated tumor and follicular tumor of uncertain malignant potential)

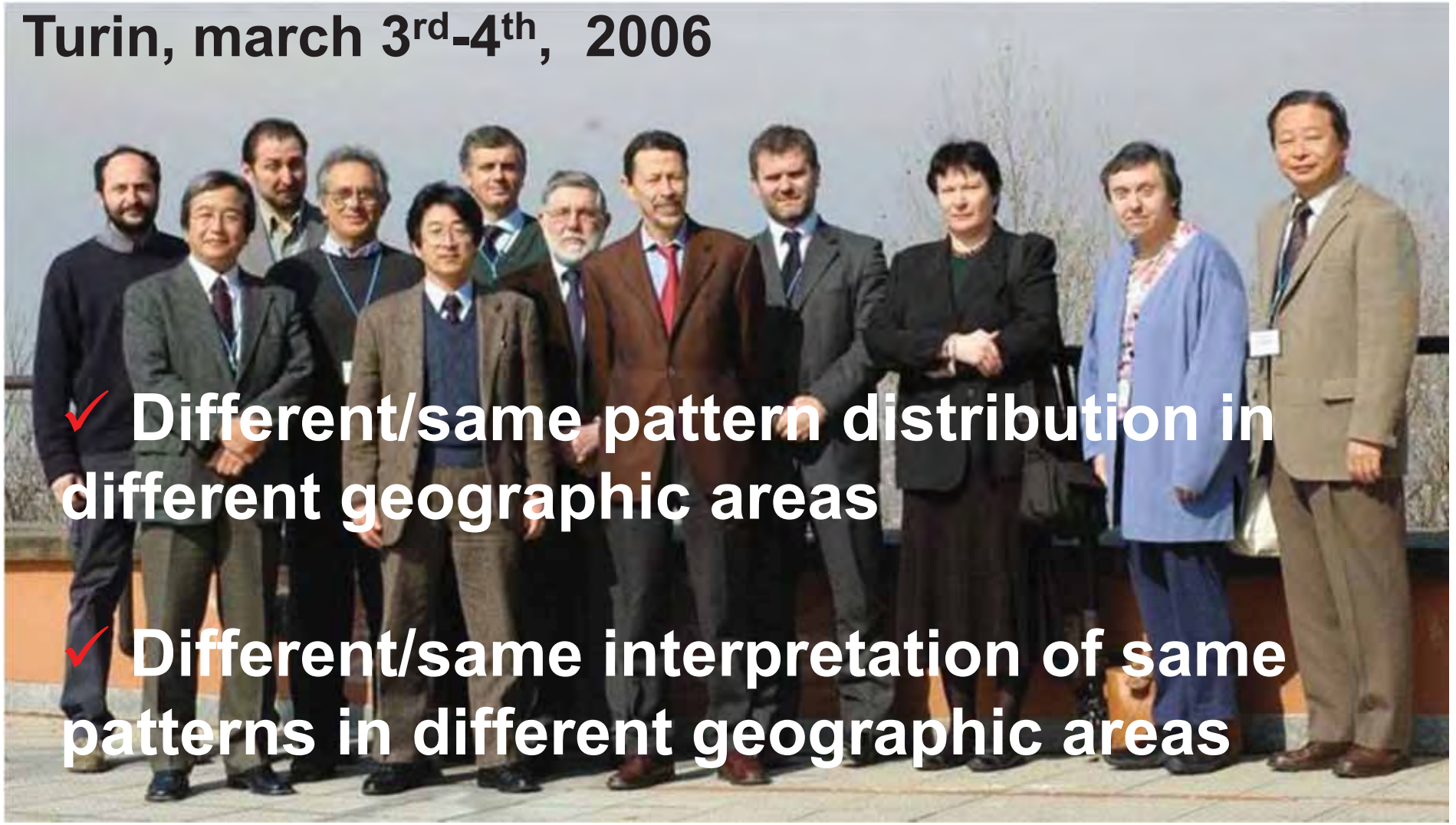
Definition of PDC in WHO Classification is not pure morphological or histopathologic.

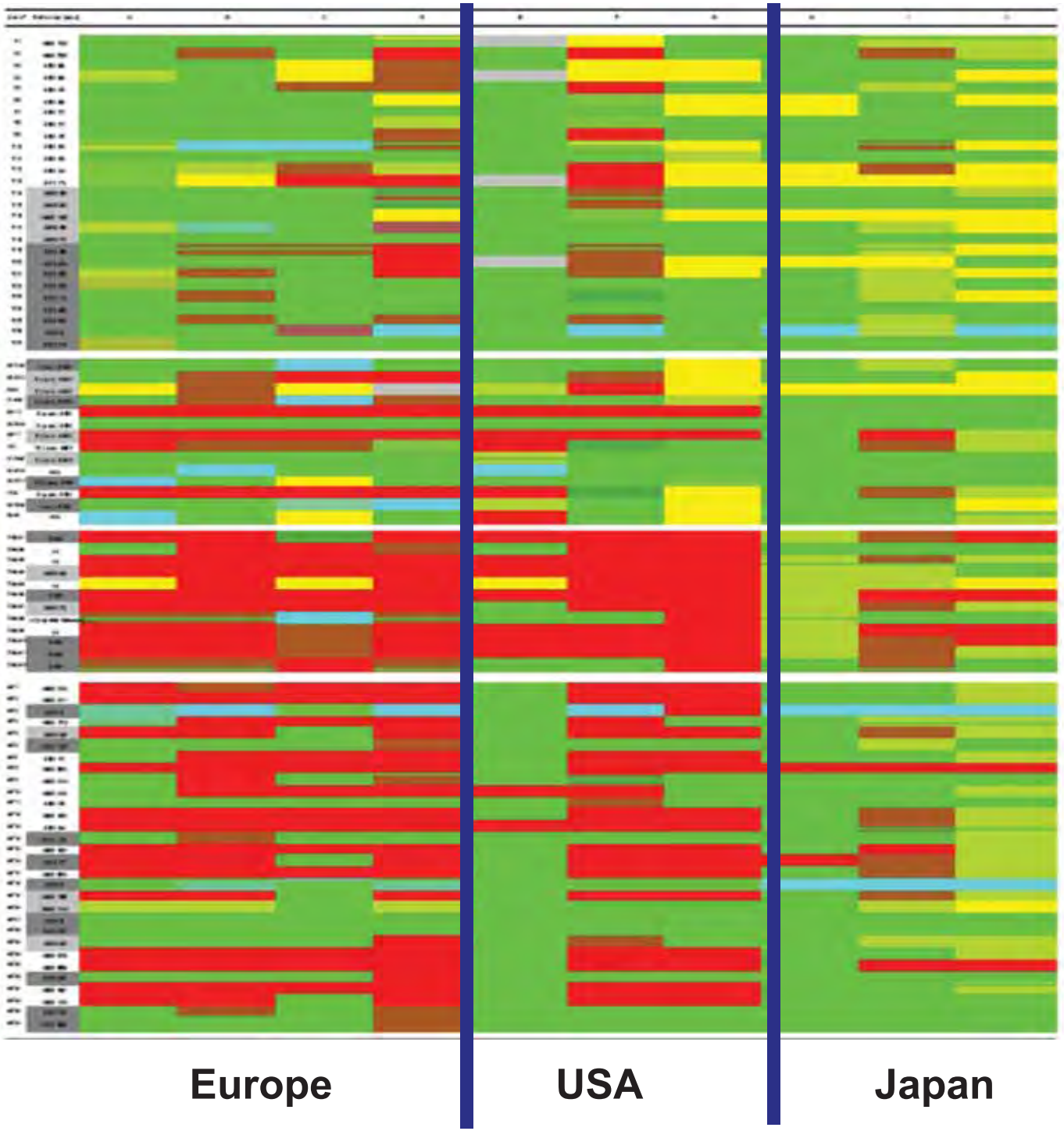
Follicular-cell neoplasms that show limited evidence of structural follicular cell differentiation and occupy both morphologically and behaviourally an intermediate position between differentiated and undifferentiated carcinoma.

Histopathologic characteristics:

1) insular, trabecular and solid
2) infiltrative growth, necrosis, vascular invasion

Multi-continental study on poorly differentiated thyroid carcinoma (PDC)




PDC
WDC, follicular type
PTC, any variant
UC, others
Europe
USA
Japan

Problems in PDC diagnosis(1)

1：Low concordance rate in diagnosis.

2：High incidence(3-15%) in EU and USA,
but low in Asia(less than 1% in Japan).

3：Diagnostic criteria should include followings.

1）tumor area
minimal（Sakamoto），>10%（Nishida），>50%（WHO）

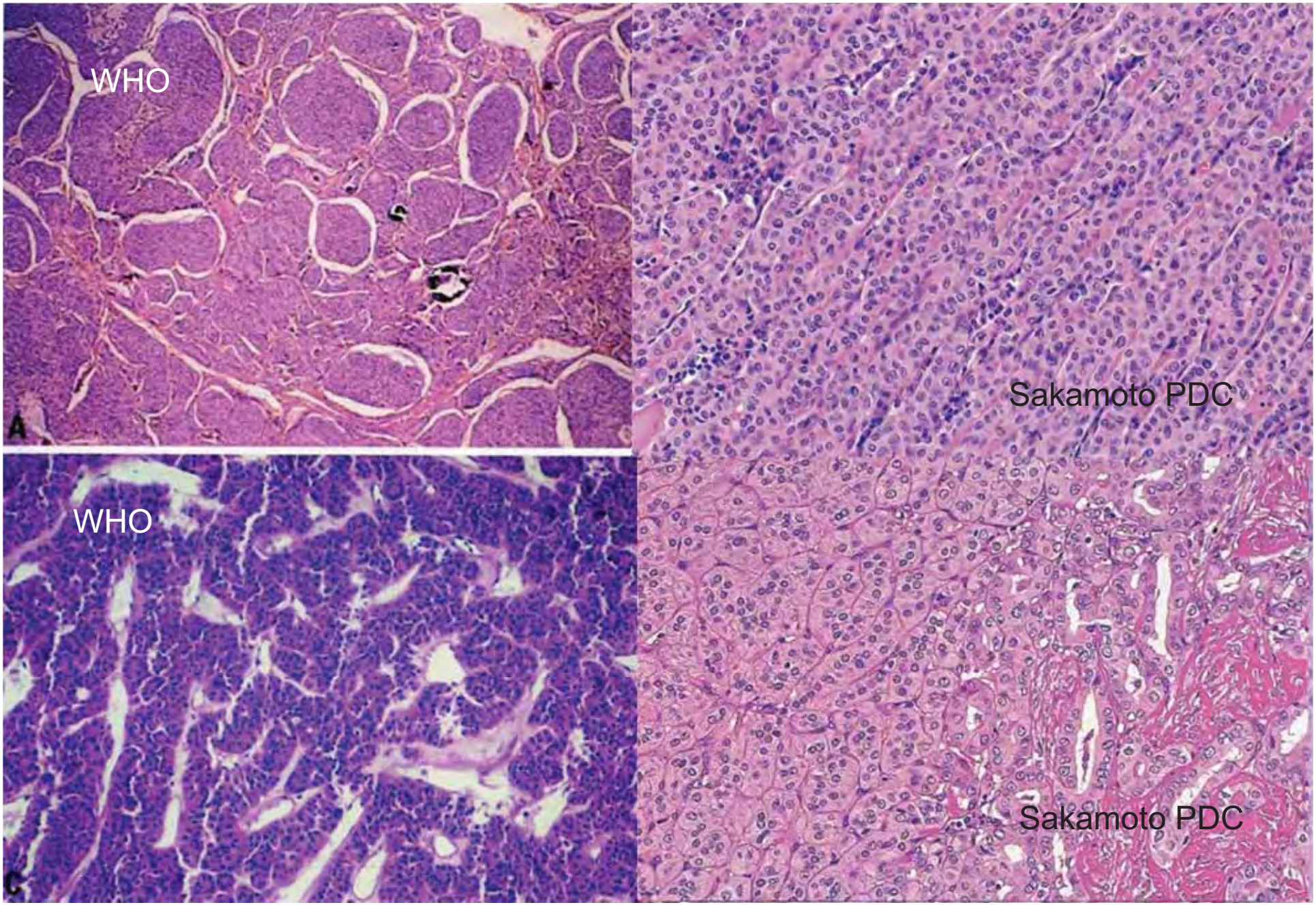
2）primary tumor or recurrent or metastatic tumor？

3）No clear border between UC and PDC.

4：New molecular markers are necessary.

5：It is not based on pure grade classification.

6：It is seen in advanced stage tumor, but
no evidence in early stage, yet.



低分化癌(PDC)　Are they the same tumors?

Poorly differentiated carcinoma (PDC)

common and different criteria

1）Sakamoto's Definition(Cancer,1983)

solid, trabecular or scirrhous

（regardless Histological Grade）

予後：5年生存率60-80%

頻度：日本10-15%?

2）WHO classification（Carcangiu & Rosai,1984）

poorly differentiated("Insular") carcinoma

solid, trabecular or insular+necrosis or mitoses

予後：5年生存率50%

頻度：日本1%,USA3%,Italy10%,中国?%

PTC, solid variant, may be included in PDC of Sakamoto's definition, but not in WHO classification.

Nikiforov YE et al., Solid variant of papillary thyroid carcinoma: incidence, clinical-pathologic characteristics, molecular analysis, and biologic behaviour. **Am J Surg Pathol 25:1478-1484, 2001.**

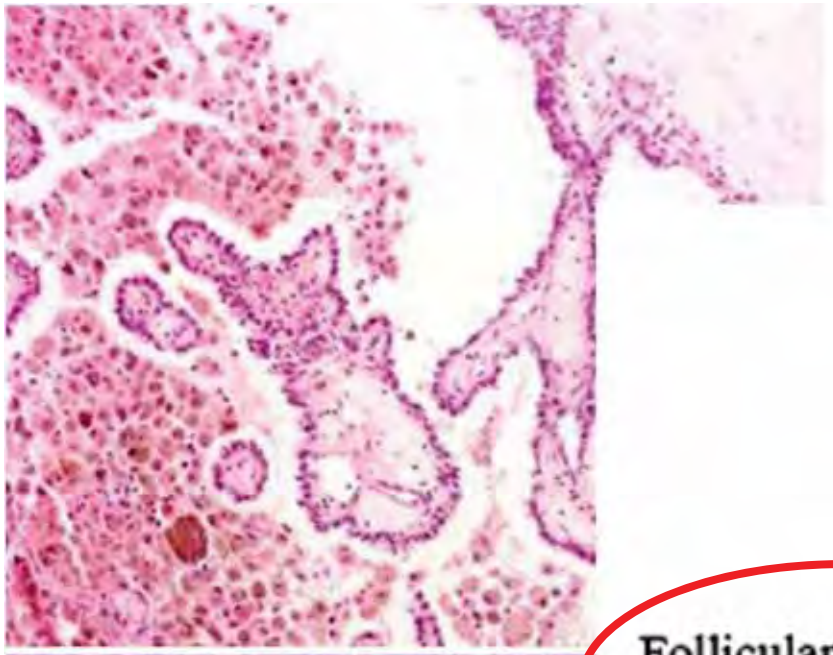
Mayo Clinic had experienced 20(2.6%) cases in 756 PTCs.

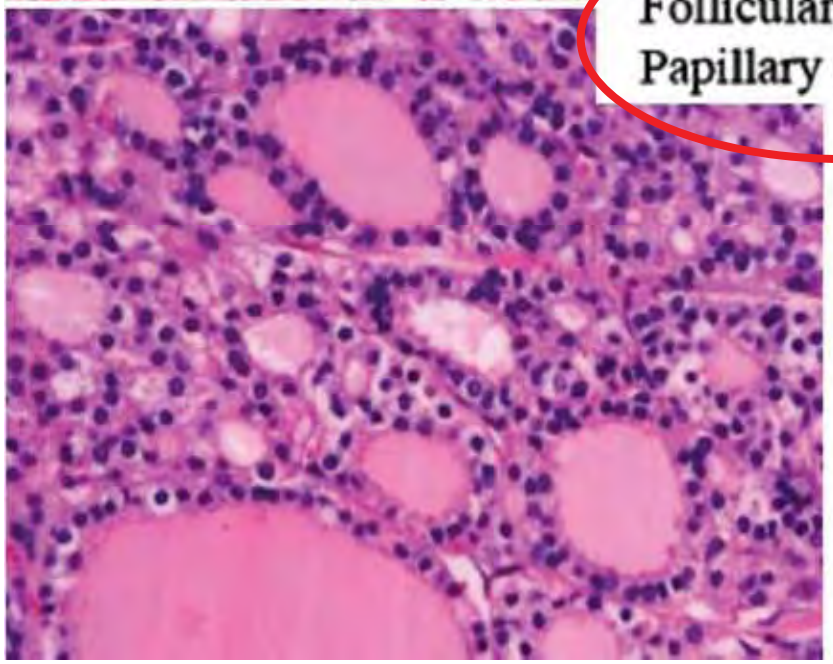
Diagnostic criteria: predominance (solid area>70%) and absence of tumor necrosis,

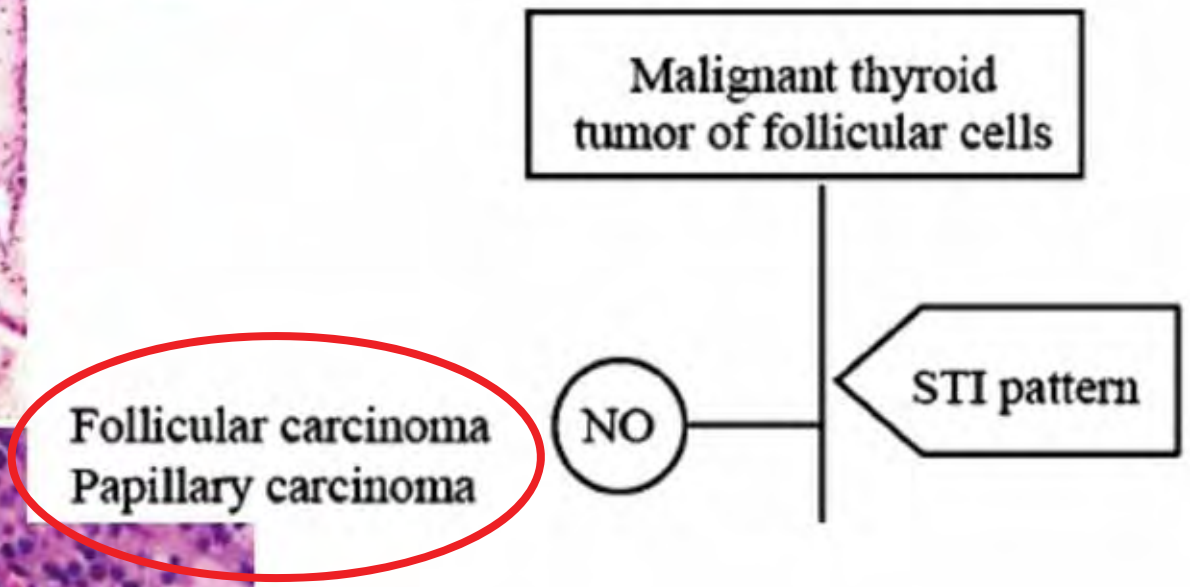
Over all survival rate of 20 SV PTCs was **90%**

Conclusion: **it should be distinguished from PDC.**

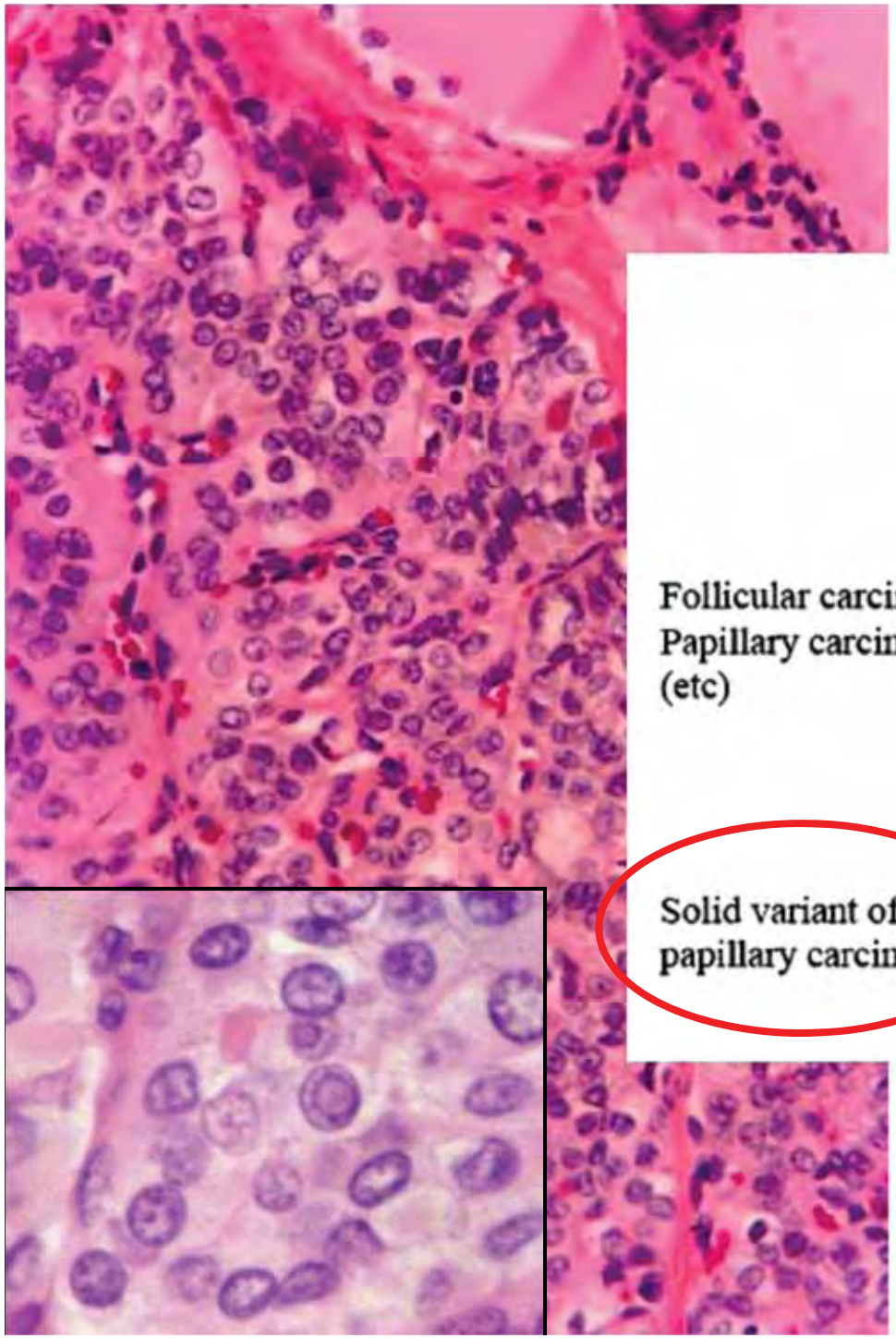
This conclusion was accepted in the consensus.

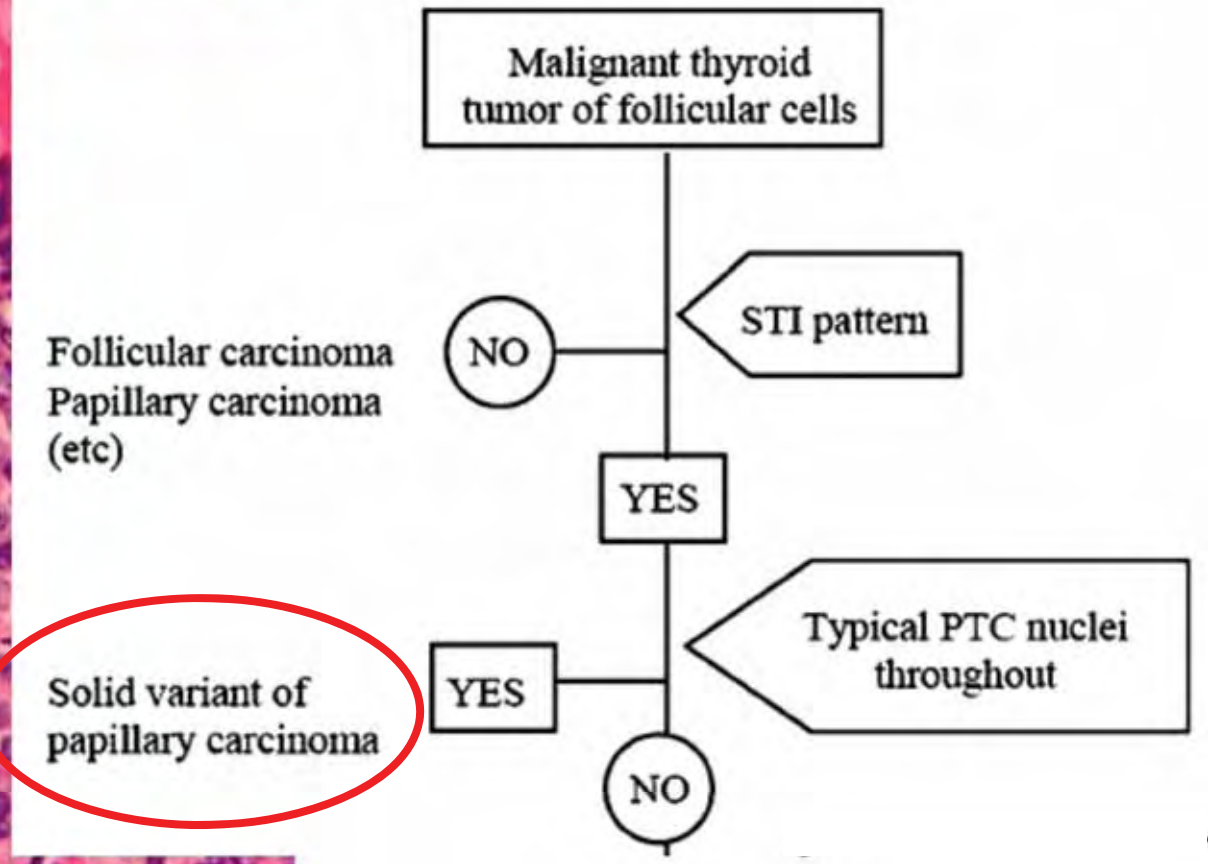




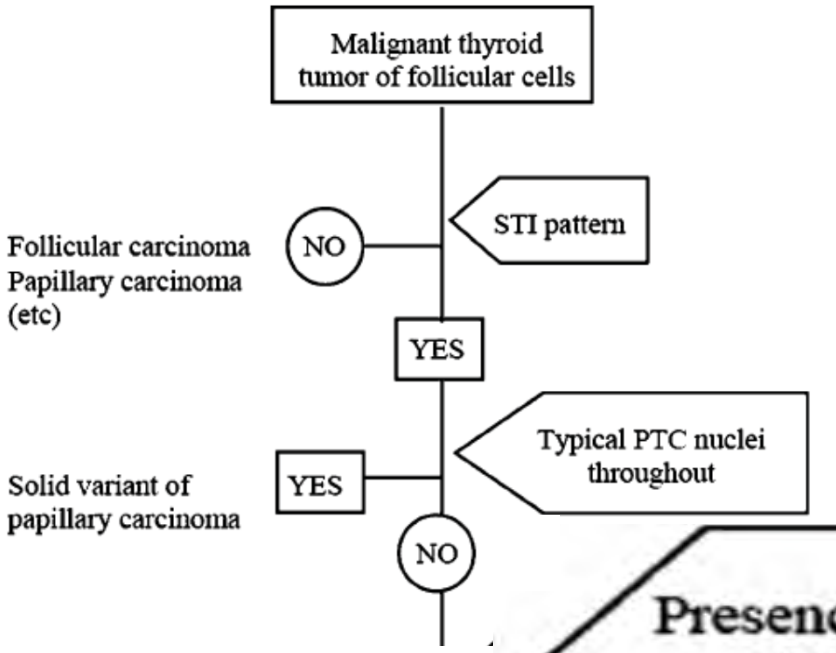


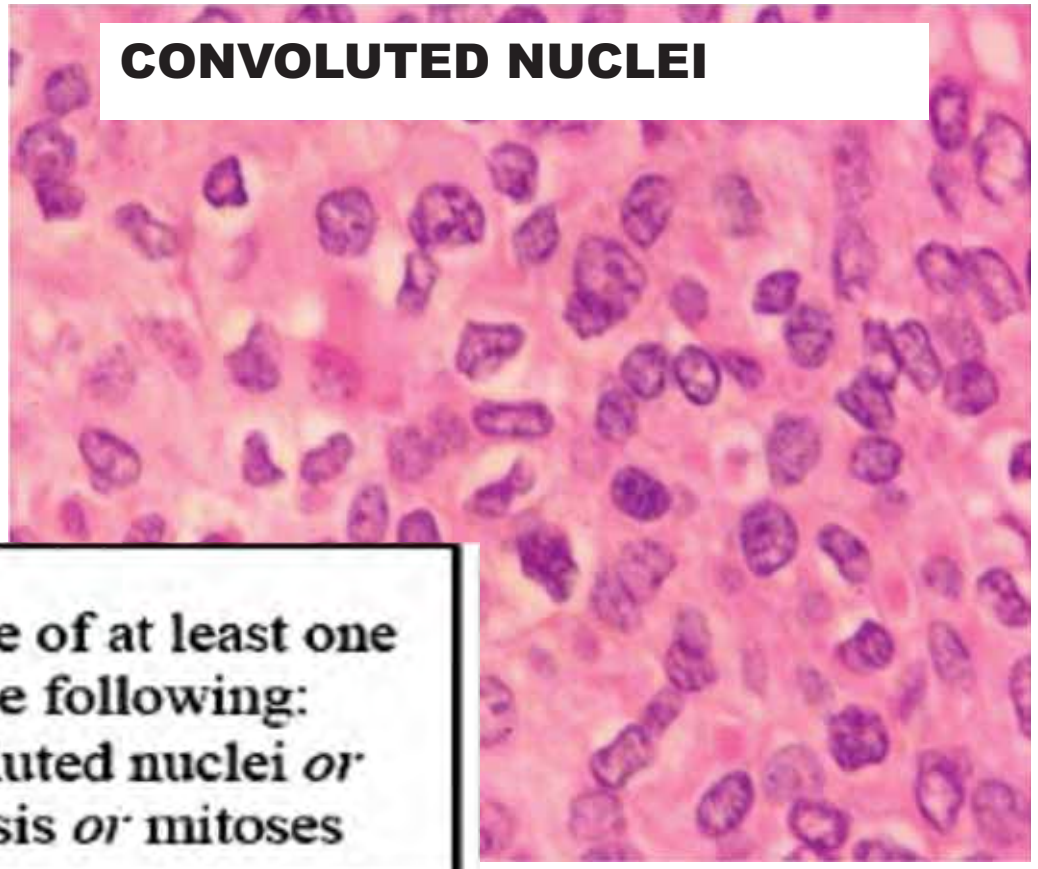
PDC must have solid/trabecular/insular growth pattern



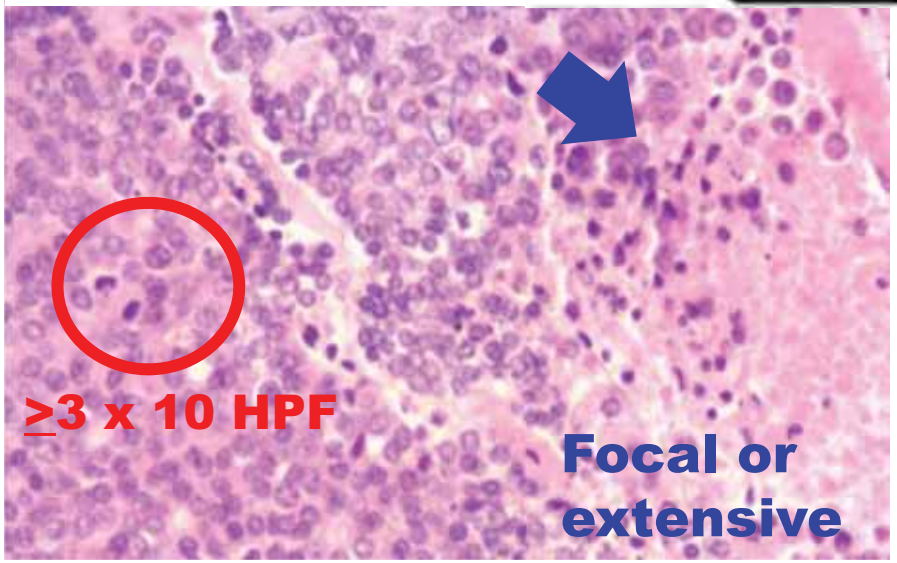


PTC, solid variant
should be excluded

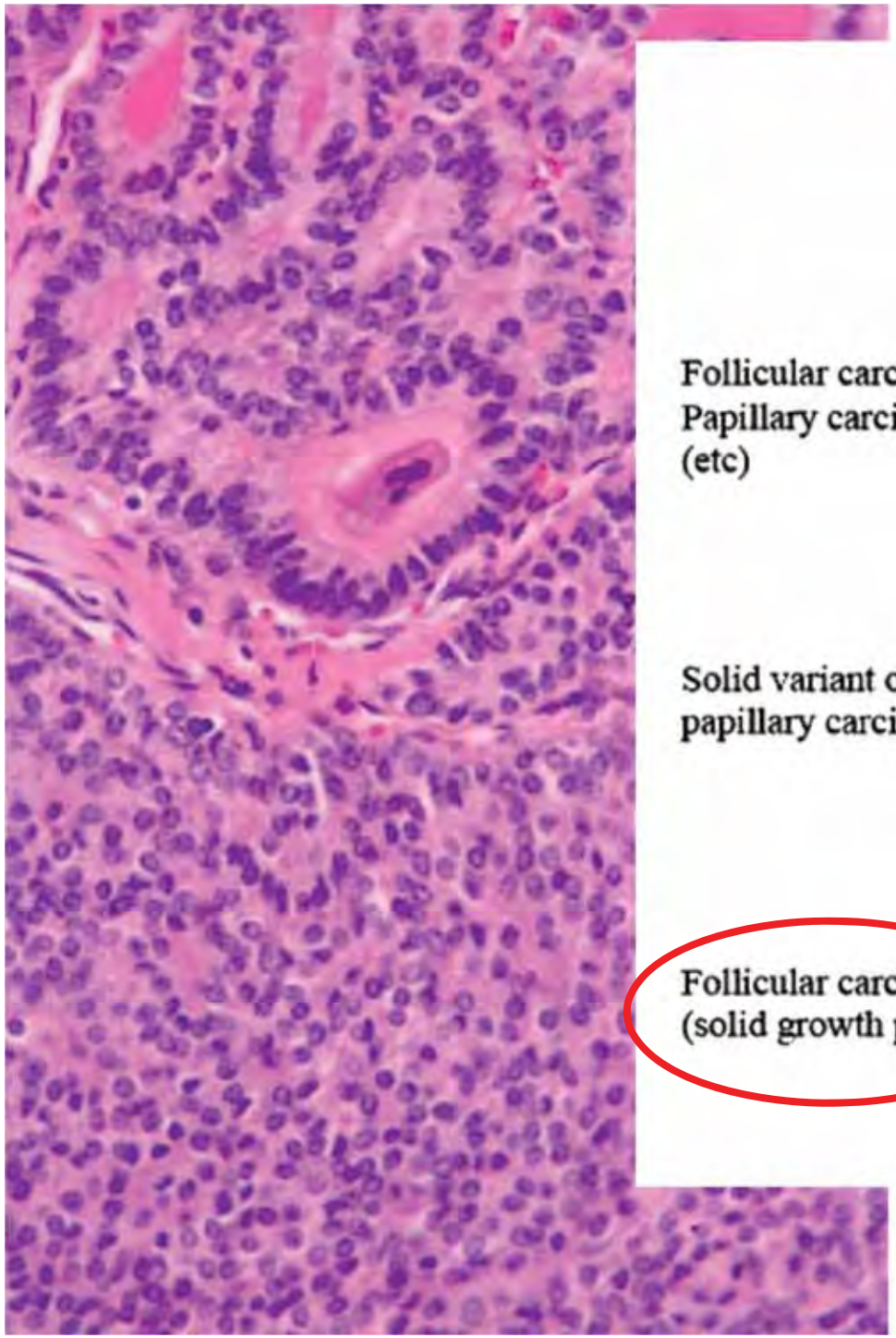




Presence of at least one of the following: convoluted nuclei *or* necrosis *or* mitoses



…..small round nuclei with irregular (“convoluted” or “raisin-like”) contours, slightly smaller and darker as compared to the typical nuclei of papillary carcinoma, with only occasional grooves and loss of ground-glass appearance and pseudo-inclusions.



Malignant thyroid tumor of follicular cells

STI pattern

NO

Follicular carcinoma
Papillary carcinoma
(etc)

YES

Typical PTC nuclei throughout

YES

Solid variant of papillary carcinoma

NO

Presence of at least one of the following: convoluted nuclei *or* necrosis *or* mitoses

NO

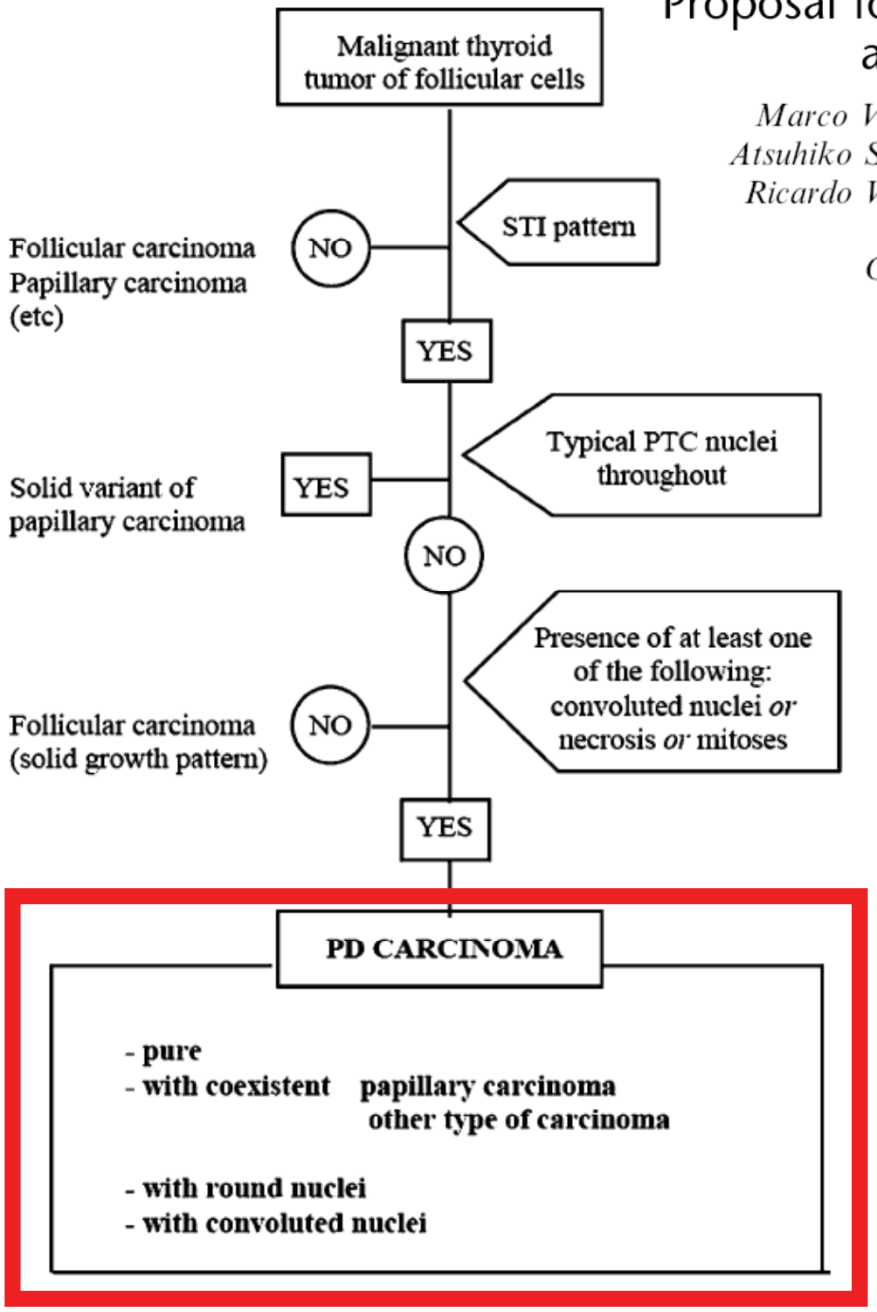
Follicular carcinoma (solid growth pattern)

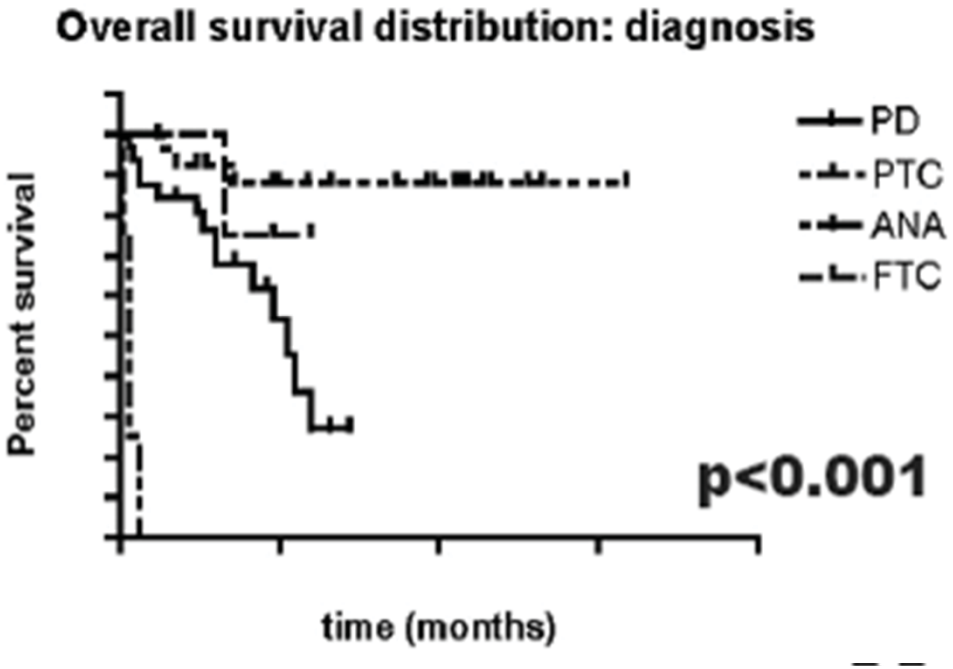
YES

Poorly Differentiated Thyroid Carcinoma: The Turin Proposal for the Use of Uniform Diagnostic Criteria and an Algorithmic Diagnostic Approach

Marco Volante, MD, Paola Collini, MD,† Yuri E. Nikiforov, MD, PhD,‡ Atsuhiko Sakamoto, MD,§ Kennichi Kakudo, MD, PhD,‖ Ryohei Katoh, MD,¶ Ricardo V. Lloyd, MD,# Virginia A. LiVolsi, MD,** Mauro Papotti, MD,* Manuel Sobrinho-Simoes, MD, PhD,†† Gianni Bussolati, MD, FRCPath,‡‡ and Juan Rosai, MD§§*

(*Am J Surg Pathol* 2007;31:1256–1264)





PTC, aggressive variants

Tall Cell Variant

(advanced stage, aged, poor prognosis)

Ostrowski ML et al: Tall cell varian of papillary thyroid carcinoma.
Am J Surg Pathol 20:964-974, 1996.

Columnar Cell Variant

(No coloid,TTF1/TG +, no nulear features of PTC)

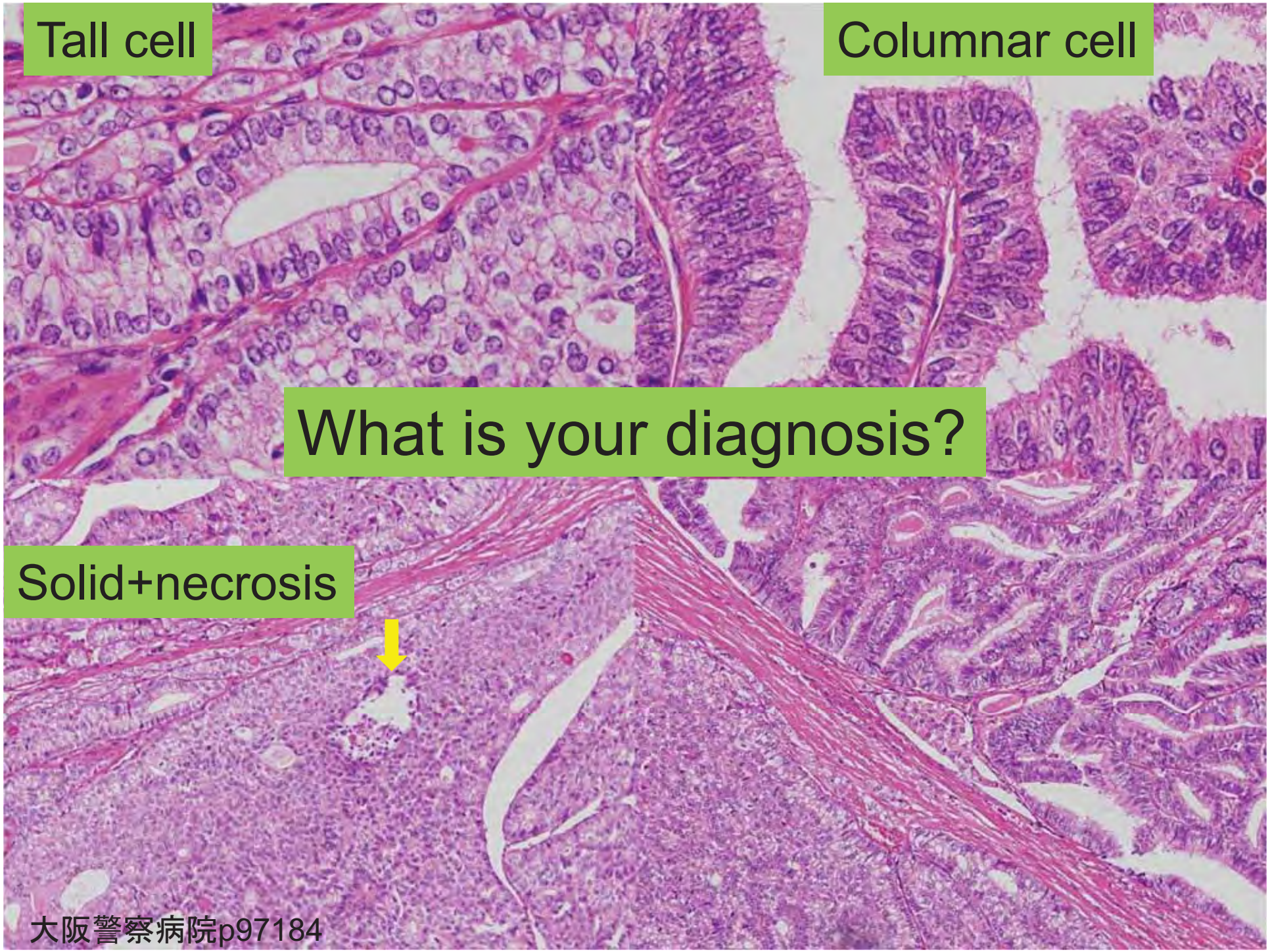
Wenig BM et al: Thyroid papillary carcinoma of columnar cell type.
Cancer 82:740-753, 1998.

Soild Variant

(more in children and radiation exposed)

Nikiforov YE et al: Solid variant of papillary thyroid carcinoma.
Am J Surg Pathol 25:1478-1484, 2001.

Many publications included them in PDC, but WHO classification excluded the above PTC, aggressive variants, from PDC.


Tall cell
Columnar cell
What is your diagnosis?
Solid+necrosis
大阪警察病院p97184

Problems in PDC diagnosis(2)

Tumors usually contain various histologic types in various proportions.

3：Diagnostic criteria should include followings.

1）**tumor area**

minimal（Sakamoto），

more than 10%（Nishida），

more than 50%（WHO)

2）Primary tumor, recurrent or metastatic tumor？

3）No clear border between UC and PDC.

Problems in classification of thyroid tumors

1) No borderline lesion between benign and malignant
2) No overlap lesion between PTC and FTC.
3) No invasive growth is necessary for PTC diagnosis but for FTC.

FTC: invasive growth: capsule, vascular or distant metastasis

Benign atypical adenoma, when none of the above, even with high grade histology.

PTC: nuclear features of PTC

1) nuclear grooves,
2) cytoplasmic inclusions
3) ground glass nuclei

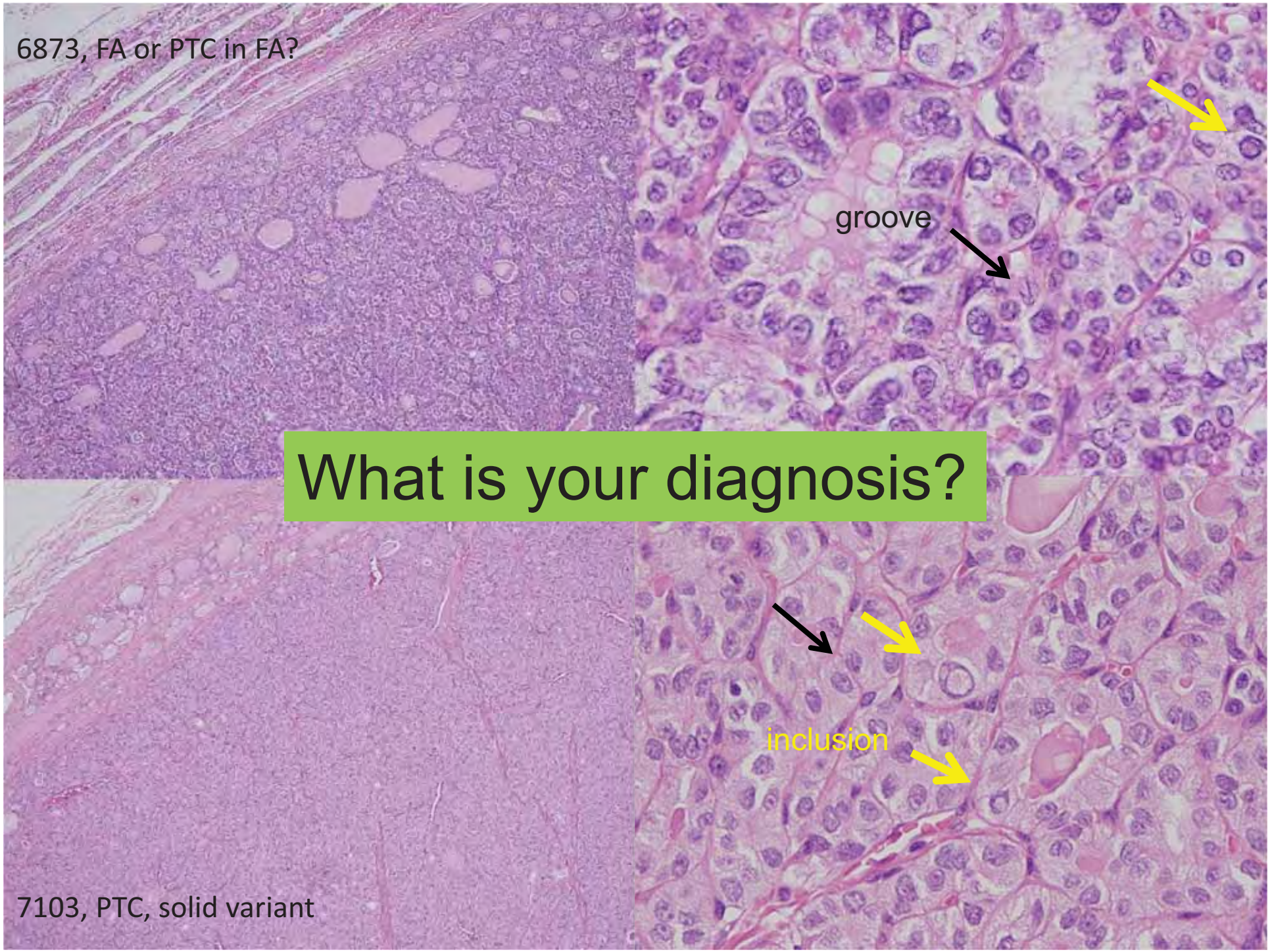

6873, FA or PTC in FA?
groove
What is your diagnosis?
inclusion
7103, PTC, solid variant

TABLE 1. Summary of Diagnoses by Reviewers*

Reviewer	FVPCA	FA	FCA	Other
1	100	0	0	0
2	74.7	12.6	0	12.6
3	85.1	13.8	1.1	0
4	77.0	20.7	1.1	1.1
5	91.9	4.7	0	3.5
6	100	0	0	0
7	91.9	1.1	0	6.9
8	98.9	0	1.1	0
9	46.0	37.9	12.6	3.5
10	60.9	11.5	1.2	26.4

FVPCA, follicular variant of papillary carcinoma; FA, follicular adenoma; FCA, follicular carcinoma.

*The percentage of 87 tumors.

Lloyd RV et al: Observer variation in the diagnosis of follicular variant of papillary thyroid carcinoma. Am J Surg Pathol. 28:1336-1340, 2004.

PTC: definite PTC nucleus vs minimal PTC nuclear change

Chan JK: Strict criteria should be applied in the diagnosis of encapsulated follicular variant of papillary thyroid carcinoma.

Am J Clin Pathol 117:16-18, 2002.

Is it OK for you to change your criteria?

It is the reason for low concordance.

Problems in classification of thyroid tumors

Distinction of PTC and FTC

is necessary because:

1) Difference in pattern of metastasis.
2) Difference in treatment
3) Difference in expected pattern of recurrence.

No overlap lesion between PTC and FTC?

Both are low grade carcinoma of same histogenesis.

Sometimes the distinction is not clear.

It is the reason for low concordance.

Williams ED: Guest Editorial:
Two proposal regarding the terminology of thyroid tumours.
Int J Surg Pathol 8: 181-183, 2000.

1 Follicular Adnoma

2 Follicular Carcinoma

3 Papillary Carcinoma

4 WDC-NOS

(Well differentiated Carcinoma, not otherwise specified)

5 WDT-UMP and FT-UMP

(Well differentiated tumor and follicular tumor
of uncertain malignant potential)

WDC-NOS (Well-Differentiated Carcinoma, not otherwise specified): An encapsulated tumor of well-differentiated follicular cells showing obvious capsular and/or blood vessel invasion and having questionable PTC-type nuclear changes.

WDT-UMP (Well-Differentiated tumor of uncertain malignant potential) : An encapsulated tumor composed of well-differentiated follicular cells with questionable PTC-type nuclear changes, no blood vessel invasion, and capsular invasion that is either absent or questionable.

FT-UMP (Follicular Tumor of uncertain malignant potential): An encapsulated tumor composed of well-differentiated follicular cells with questionable capsular invasion, no blood vessel invasion, and no PTC-type nuclear changes.

New Classification of Thyroid Follicular Cell Tumors, proposed by Williams 2000.

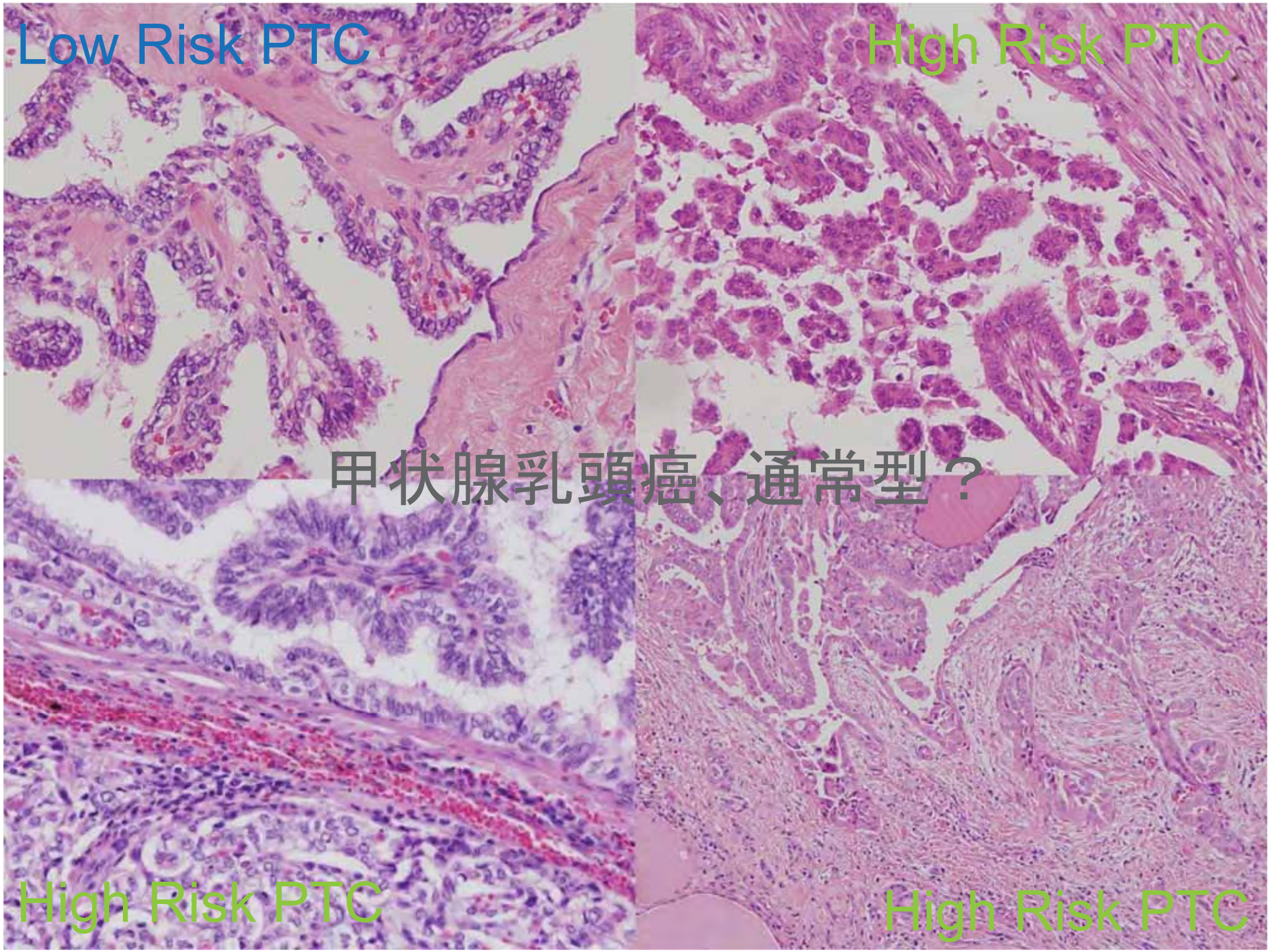
1) Benign: Follicular Adenoma
2) Borderline: WDT-UMP and FT-UMP
3) Malignant: Follicular Cell Carcinoma(PTC and FTC)
   A) Well Differentiated Adenocarcinoma
   B) Moderately Differentiated Adenocarcinoma
   C) Poorly Differentiated Carcinoma
   D) Undifferentiated Carcinoma

benign-borderline-low grade-high grade malignancy

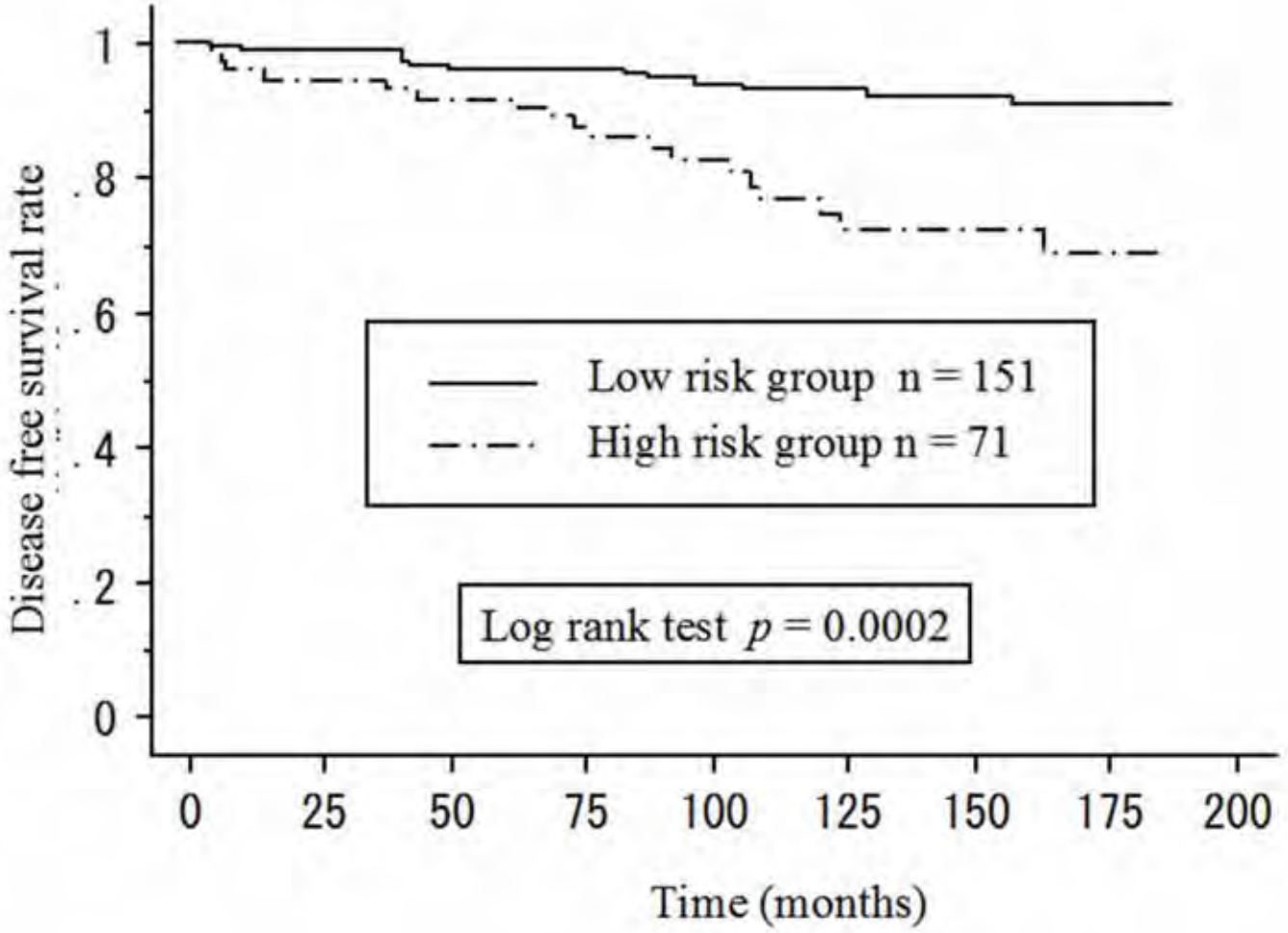
DFS (disease-free survival) and CSS (cause-specific survival) of thyroid carcinomas, currative surgery, Kuma Hosp, Kobe, Jap

	10-year DFS	10-year CSS
FTC		
Minimally invasive	86.3%	97.2%
Widely invasive	65.4%	97.4%
PTC		
Low risk	93.0~93.1%	100%
High risk	78.7~82.5%	91.5%
PDC (WHO)		
FTC type	43.0%	71.2%
PTC type	53.8%	80.0%

No difference in 10-year DFSs between FTC and PTC


Low Risk PTC
High Risk PTC
甲状腺乳頭癌、通常型？
High Risk PTC
High Risk PTC

Identification of high-risk group in common type of thyroid carcinoma. Bai et al, Cancer Science, 2008



Prognostic sublassification of common type PTCs

Prognostic stratification of PTC and FTC who were treated curatively proved that

1) No difference in 10-year CSS between minimally inv FTC and widely inv FTC.
2) More recurrence in widely inv FTC than minimally inv FTC.
3) FTC is not more aggressive than PTC in 10-year CSS.
4) PTC, non-solid type, can be subclassified in Low-risk and High-risk groups.

Therefore we combined PTC and FTC into one category as Follicular Cell Carcinoma.

New Classification of Thyroid Follicular Cell Tumors, proposed by Kakudo, 2008.

1) Follicular Adenoma
2) WDT-UMP and FT-UMP
3) Follicular Cell Carcinoma
   A) Well Differentiated Adenocarcinoma
   B) Moderately Differentiated Adenocarcinoma
   C) Poorly Differentiated Carcinoma
   D) Undifferentiated Carcinoma

Prognostic classification by histological parameters, growth pattern, cellular differentiation and histological grade. It covers all follicular cell carcinomas, PTC, FTC, PDC and etc.

The proposed new classification solves the problems in classification of thyroid tumors.

1) Minimize observer disagreements, because borderline lesions (WDT-UMP and FT-UMP by Williams) were set up.
2) Distinction between PTC and FTC become not essential, because they were combined into one diagnosis(Follicular Cell Carcinoma).
3) Prognostic classification of follicular cell carcinoma provide useful information for patient's care.