La classificazione WHO 2022 dei tumori tiroidei: cosa cambia?

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

Dott. Biagio Paolini

SC Anatomia Patologica 1

Fondazione IRCCS Istituto Nazionale dei Tumori – Milano

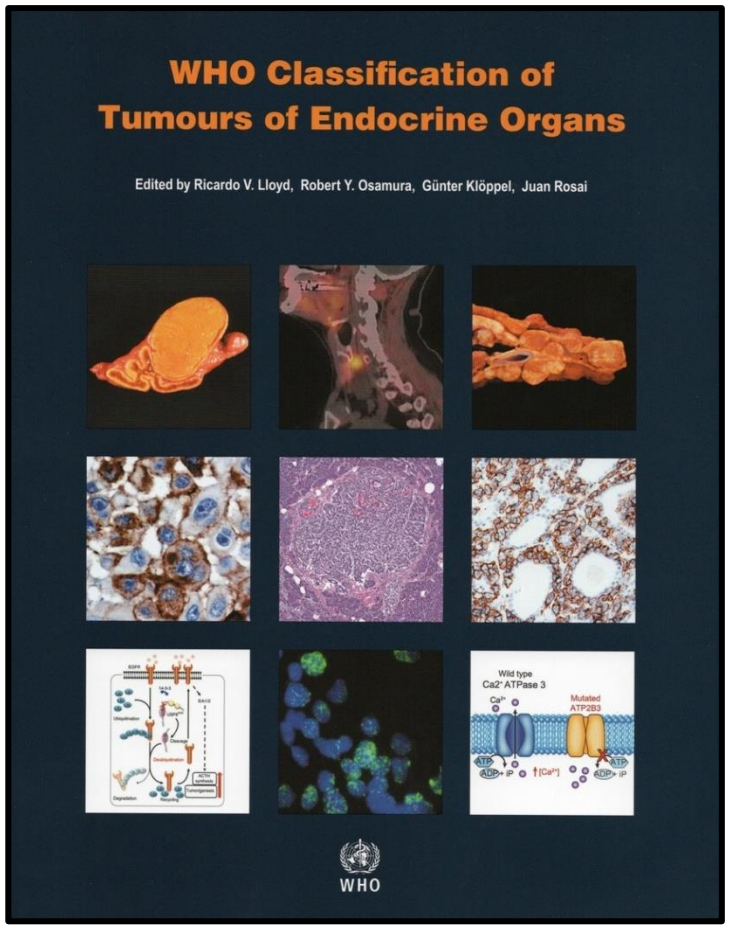
GENERAL PERSPECTIVE

-Most common endocrine tumors

-Largest chapter in the new WHO classification

-Remarkable genotype-morphology correlations

-Pathological-driven approach to therapy



Endocrine Pathology (2022) 33:27–63
https://doi.org/10.1007/s12022-022-09707-3

Overview of the 2022 WHO Classification of Thyroid Neoplasms

Zubair W. Baloch[1] · Sylvia L. Asa[2] · Justine A. Barletta[3] · Ronald A. Ghossein[4] · C. Christofer Juhlin[5,6] · Chan Kwon Jung[7] · Virginia A. LiVolsi[1] · Mauro G. Papotti[8] · Manuel Sobrinho-Simões[9] · Giovanni Tallini[10,11] · Ozgur Mete[12]

THE BIG RIP?

GENERAL PERSPECTIVE

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-Huge volume of benign disease

-Very rare highly aggressive malignancy

-Wide spectrum of intermediate lesions

-stepwise progression, accumulation of additional genetic events

-Still many barriers to a logical Linnaean classification of thyroid tumors

GENERAL PERSPECTIVE

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-Importance of molecular biology in thyroid pathology
    -revolutionized the discipline
    -proven the inherent value of classical histopathology

-Different patterns reflect specific molecular alterations

-Molecular tools enhanced our ability to predict:
    -prognosis
    -clinical behavior
    -efficacy of targeted therapies

GENERAL PERSPECTIVE

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Divides thyroid neoplasms into several new categories and allows for a clearer understanding

-Cell of origin (and type)

-Pathologic features

-Molecular profile

-Clinical course

Endocrine-Related Cancer | C Juhlin *et al.* | 30:2 | e220293

REVIEW

The 2022 WHO classification of thyroid tumors: novel concepts in nomenclature and grading

C Christofer Juhlin[1,2], Ozgur Mete[3,4,5] and Zubair W Baloch[6]

Endocrine Pathology (2022) 33:228–230
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The Next Steps for Endocrine Pathology

Sylvia L. Asa[1] · Lori A. Erickson[2] · Ozgur Mete[3]

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Overview of the 2022 WHO Classification of Thyroid Neoplasms

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Main diagnostic groups of the 2022 WHO Classification of Thyroid Neoplasms

Benign Lesions	Low-risk Neoplasms	Malignant Thyroid Neoplasms
Thyroid follicular nodular disease	Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)	**Follicular thyroid carcinoma (FTC)**: mi / eai / wi
Follicular thyroid adenoma	Follicular thyroid tumor of uncertain malignant potential (FT-UMP)	**Invasive encapsulated follicular variant papillary thyroid carcinoma (IEFV-PTC)**: mi / eai / wi
Follicular thyroid adenoma with papillary architecture	Well-differentiated thyroid tumor of uncertain malignant potential (WD-UMP)	**Oncocytic carcinoma of the thyroid (OCA)**: mi / eai / wi
Oncocytic adenoma	Hyalinizing trabecular thyroid tumor (HTT)	**Papillary thyroid carcinoma (PTC)** *Subtypes*: Infiltrative follicular; Tall cell; Columnar cell; Hobnail; Solid; Diffuse sclerosing; Warthin-like; Oncocytic
		Differentiated high-grade thyroid carcinoma (DHGTC): Papillary, follicular or solid growth; Invasive features; Any nuclear cytology; At least one of: -Mitotic count ≥5/2 mm^2 -Necrosis
		Poorly differentiated thyroid carcinoma (PDTC): Solid, trabecular or insular growth; Invasive features; No PTC nuclear features; At least one of: -Mitotic count ≥3/2 mm^2 -Necrosis -Convoluted nuclei
		Anaplastic thyroid carcinoma (ACA): Anaplastic features; Undifferentiated phenotype

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms

-Clinical Significance of PTC Subtypes

-“High-Grade” follicular cell-derived carcinomas

-The term “Hürthle”, end of a misnomer

-What’s New in the Understanding of ATC?

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms

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-What’s New in the Understanding of ATC?

FOLLICULAR NODULAR DISEASE

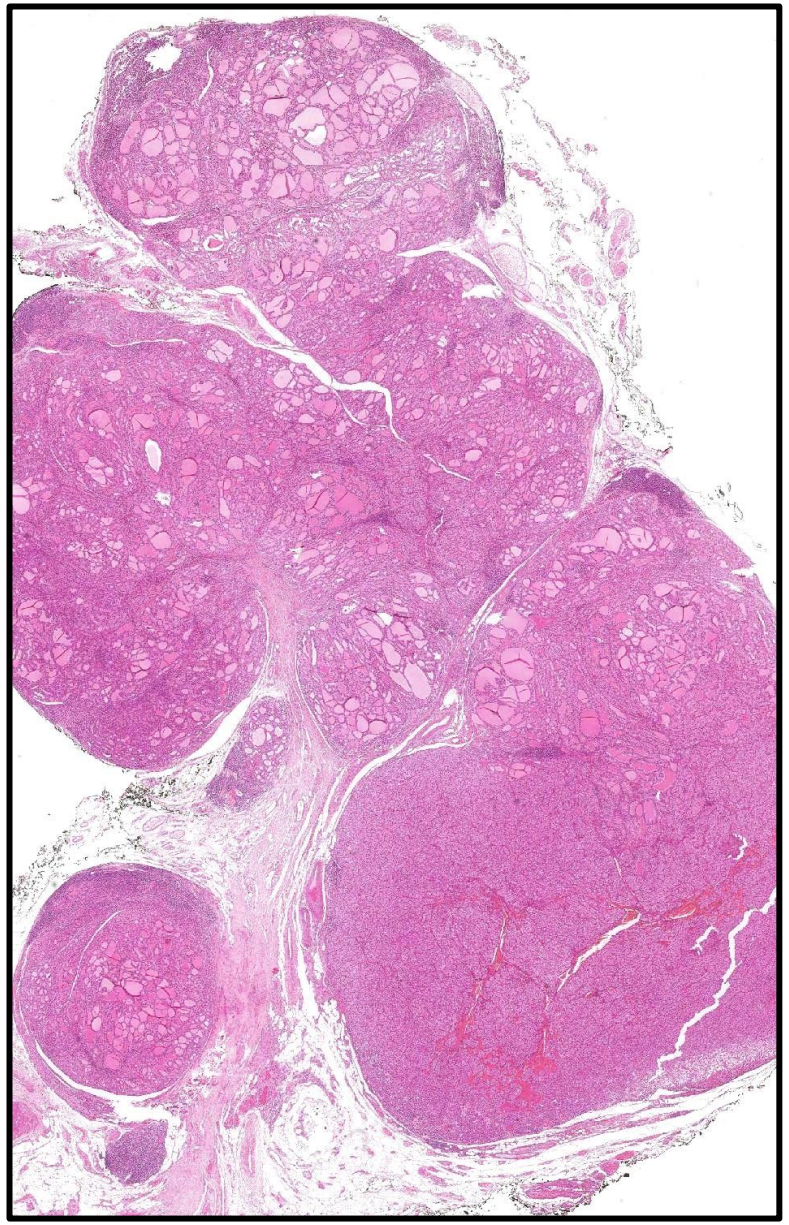
-The term “multinodular goiter” has been used for > 200 yr.

-It is inappropriate, avoids defining a lesion as hyperplastic
  -many lesions can give rise to a thyroid enlargement

-Studies have shown that these can be clonal – neoplasms

-Many genes involved
  -thyroid hormone pathway
  -TG, TPO, sodium-iodide symporter NIS
  -dual oxidase (DUOX2), XB130, and TSHR

-Familial and early-onset associated with DICER1 syndrome



FOLLICULAR DERIVED NEOPLASMS – LOW RISK

-Borderline tumors intermediate between benign and malignant tumors
-morphologically and clinically

-Extremely low potential to develop metastasis

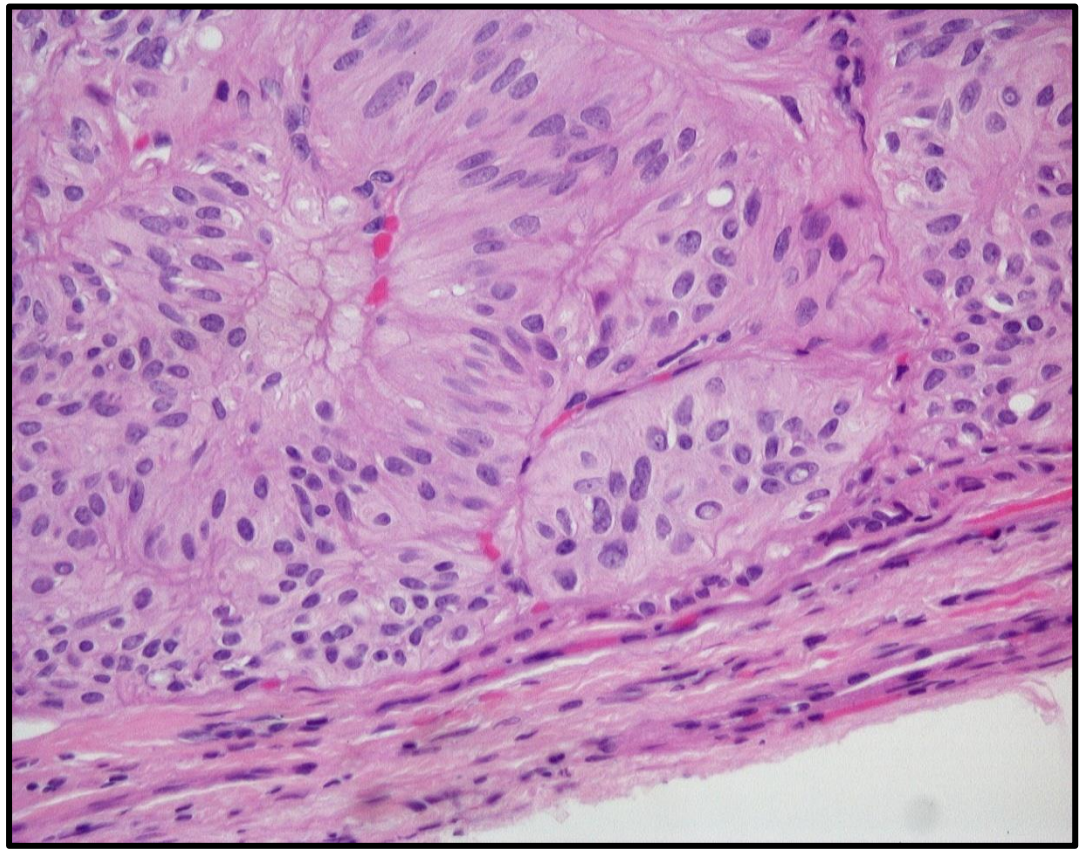
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

Thyroid tumors of uncertain malignant potential (TTUMP)

Hyalinizing trabecular tumor (HTT)

HYALINIZING TRABECULAR TUMOR - HTT

-Well demarcated, PTC-like nuclei
-Trabecular architecture
-Prominent hyaline material
    -secretion of basal membrane type protein
-Peculiar membrane staining of MIB1



-Specific molecular alteration
-Lack *BRAF* and *RAS* mutations
-*GLIS* gene rearrangements
    -not been identified in other thyroid tumors
PAX8::*GLIS3* and *PAX8*::*GLIS1*

No patients with *GLIS*-rearranged thyroid neoplasms have developed tumor recurrence or metastasis

NON-INVASIVE FOLLICULAR THYROID NEOPLASM WITH PAPILLARY-LIKE NUCLEAR FEATURES (NIFTP)

-Formerly known as "noninvasive encapsulated follicular variant of PTC"

-Renamed to NIFTP based on consensus study showing evidence for:
- -indolent biological behavior
- -lack of metastasis or recurrence

-Prevalence is 9.1% of all papillary thyroid cancers worldwide

-Diagnosis of NIFTP is possible only on surgical samples

NON-INVASIVE FOLLICULAR THYROID NEOPLASM WITH PAPILLARY-LIKE NUCLEAR FEATURES (NIFTP)

-Exclusion criteria:
- -Any capsular / vascular invasion
  - -whole capsule must be examined thoroughly
  - -if not, then the default diagnosis is still noninvasive encapsulated FVPTC
- -True papillary structures, psammoma bodies, infiltrative border
- -Tumor necrosis (not associated with FNA), increased mitoses (>3/10 HPF)
- -Cell morphology of PTC subtypes or oncocytic cytology (?)

-Additional exclusion criteria
- -No *BRAF*^{V600E} and *TERT* promoter mutations
- -No distant metastasis

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms ☑

-Clinical Significance of PTC Subtypes

-“High-Grade” follicular cell-derived carcinomas

-The term “Hürthle”, end of a misnomer

-What’s New in the Understanding of ATC?

Clinical Significance of the Subtypes of PTC

-Most common follicular cell-derived neoplasm

-PTC commonly occurs as a sporadic tumor
    -familial forms
    -pediatric cases

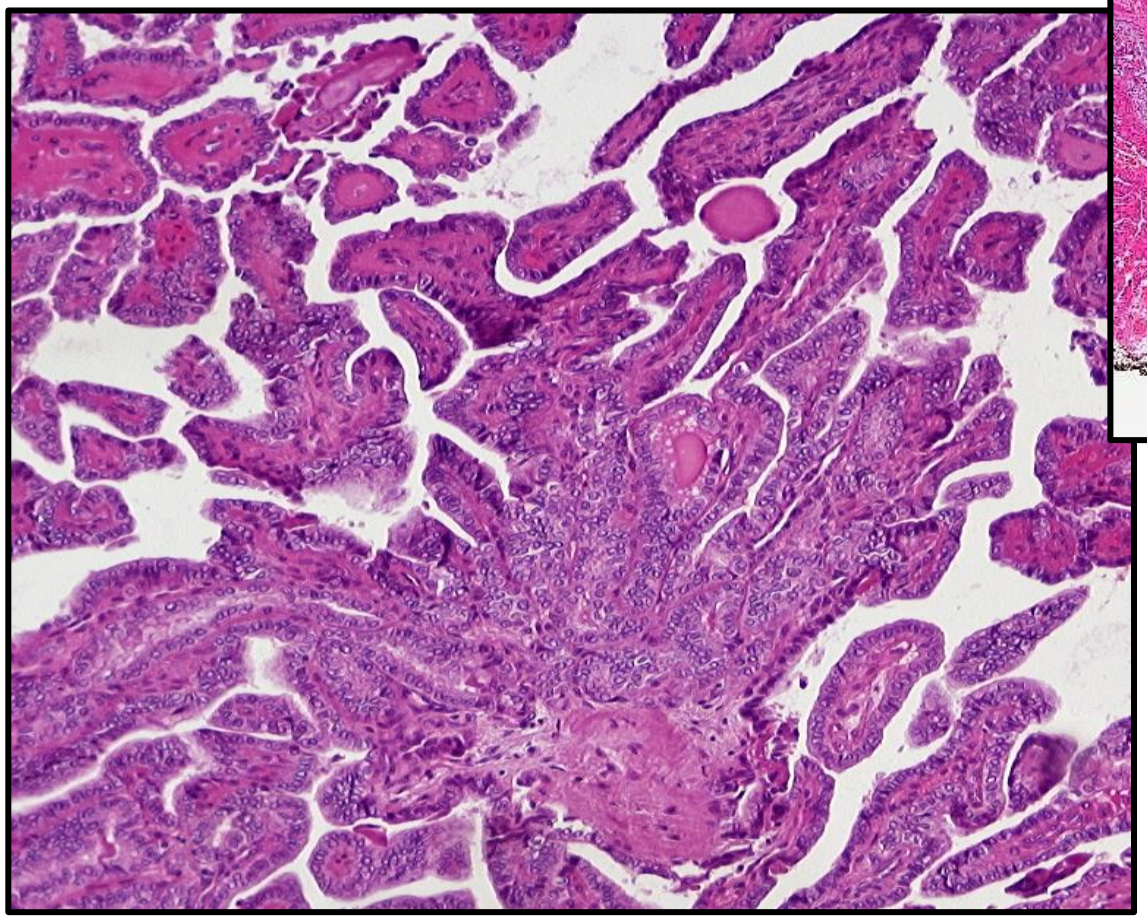
-Until the 2017 PTC was diagnosed based on nuclear cytology

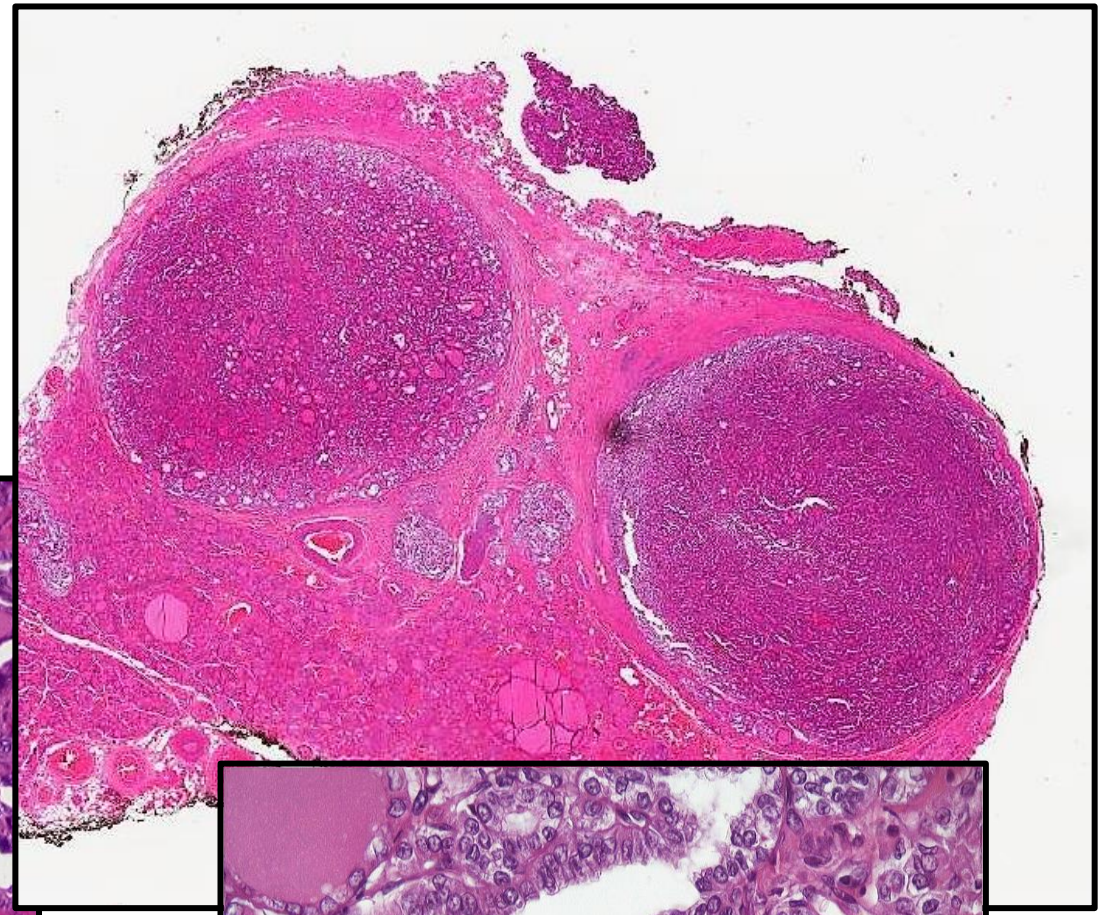
-This changed with the introduction of the NIFTP
    -either papillary growth / invasion was added

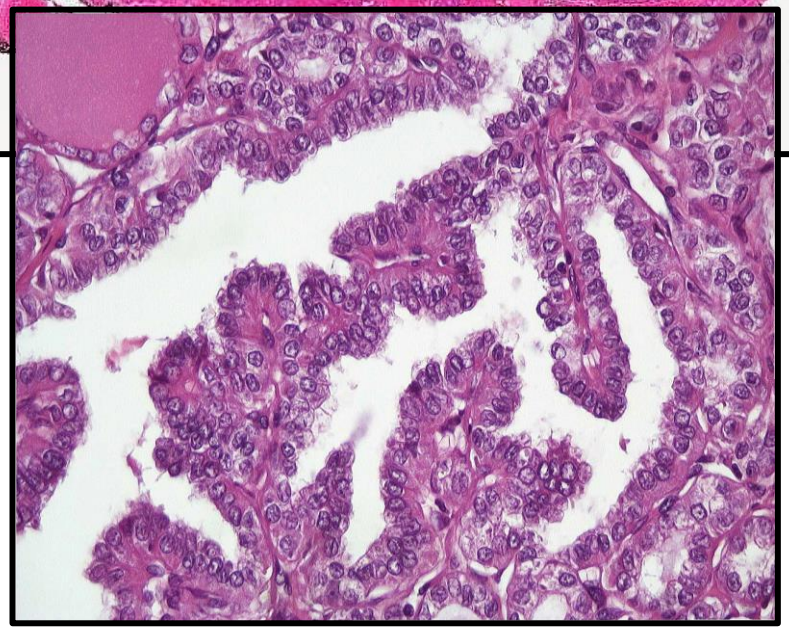
Clinical Significance of the Subtypes of PTC

Classic PTC is the paradigm for all PTC subtypes:

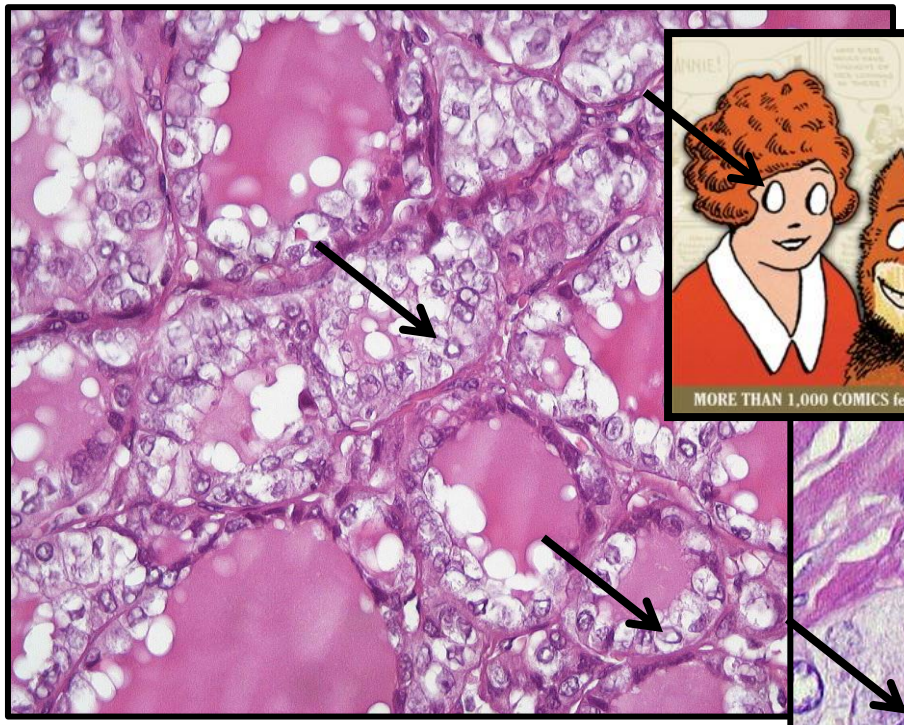
-well-formed papillae lined by tumor cells
-lymphatic permeation is the cause of LN mets
-specific set of nuclear features

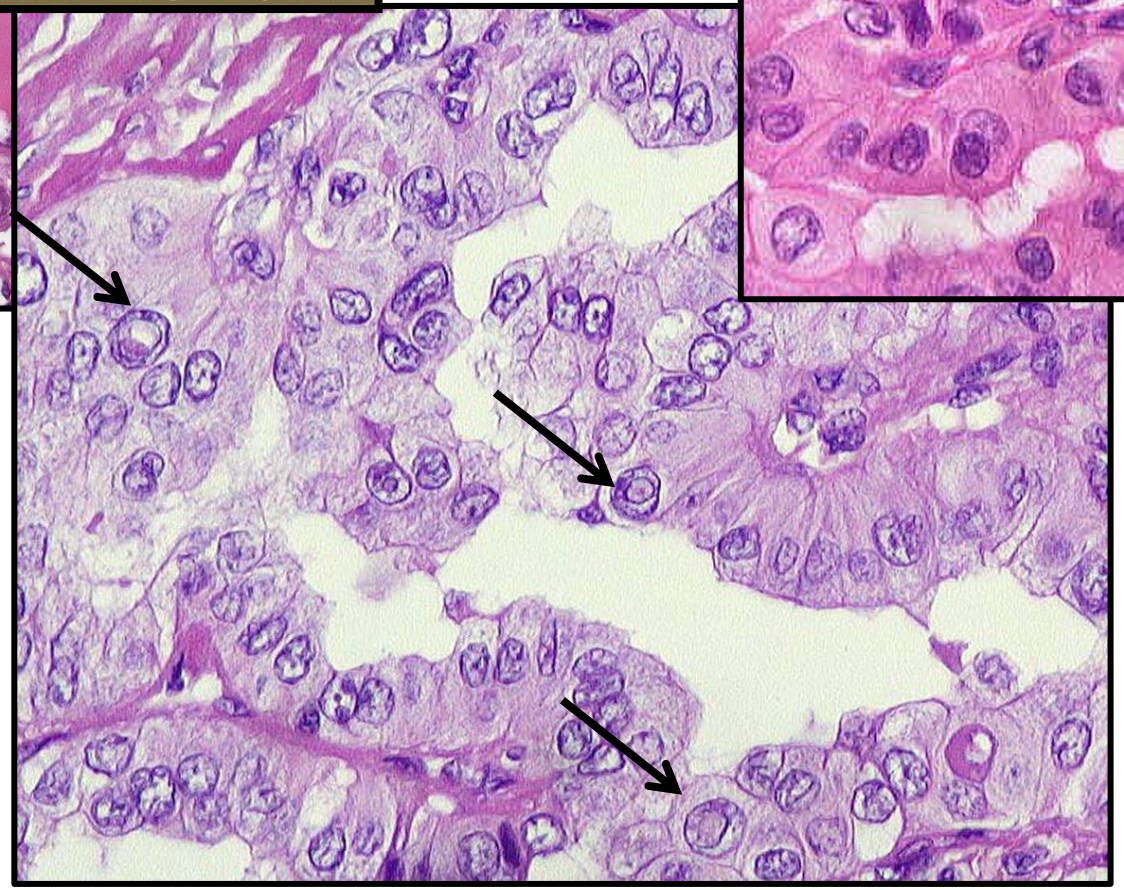


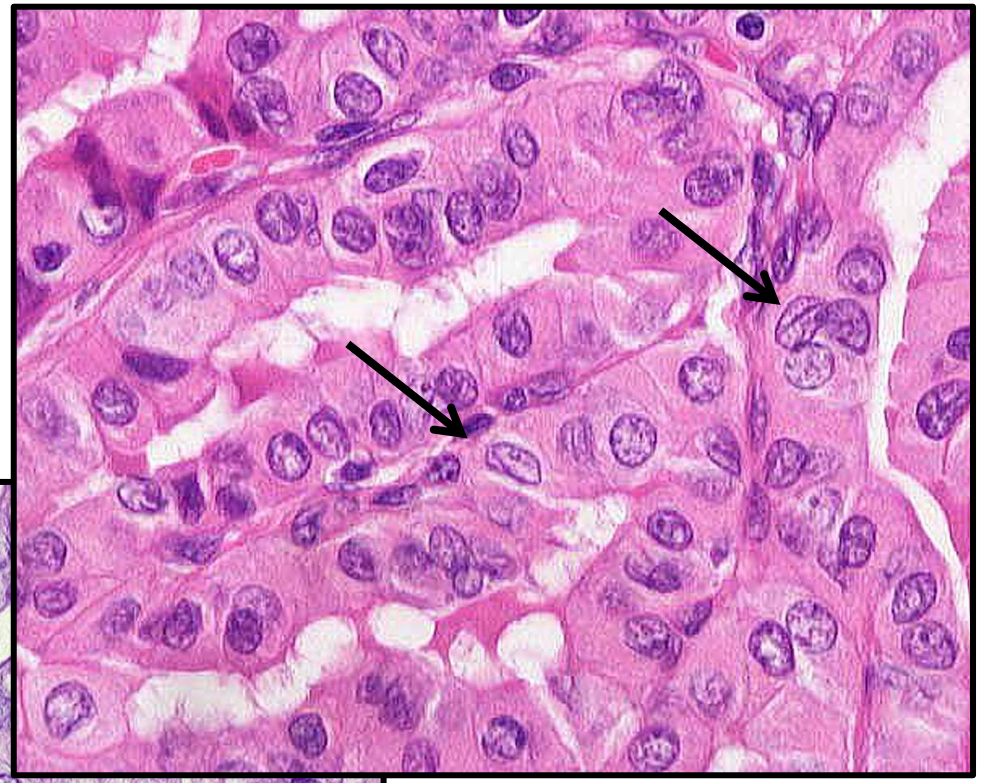




Clinical Significance of the Subtypes of PTC







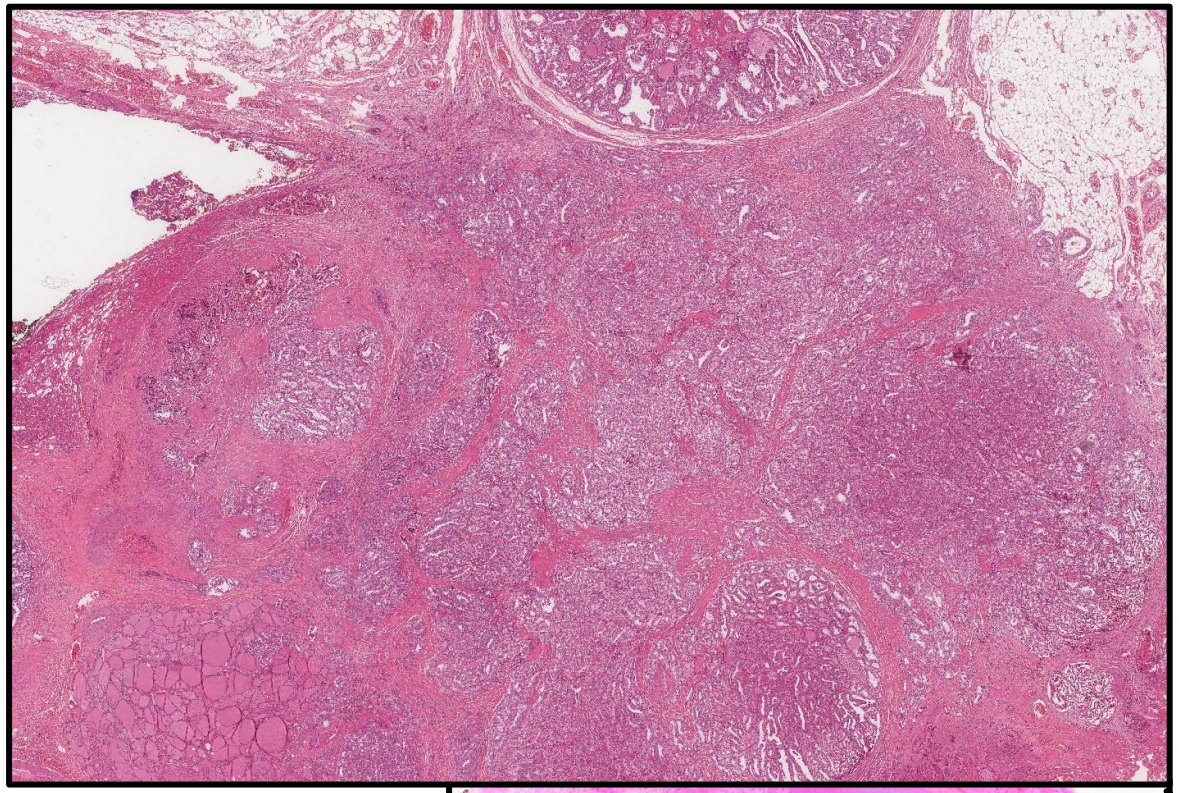
- **Size and shape**
- **Nuclear membrane irregularities**
- **Chromatin characteristics**

Clinical Significance of the Subtypes of PTC

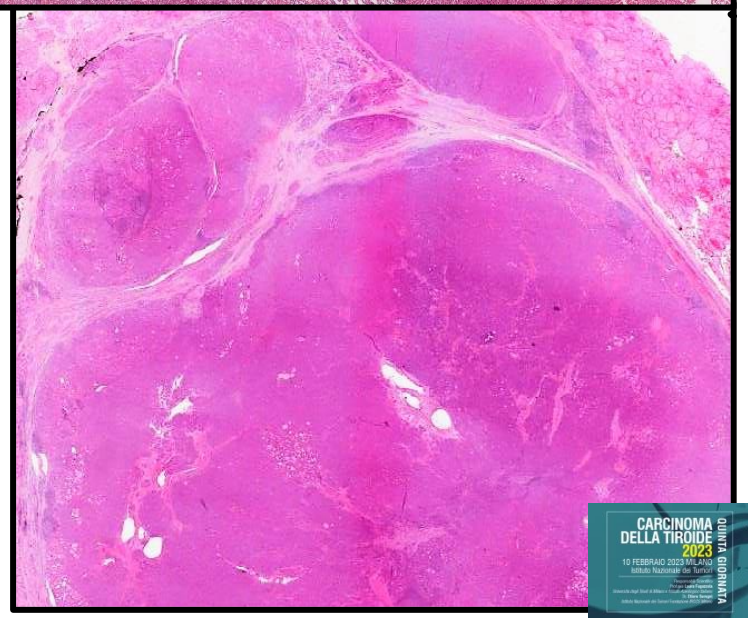
-Encapsulated form, excellent clinical prognosis

-partially infiltrated (variant)
-infiltrating (subtypes)

-Infiltrative Follicular PTC is a *BRAF*-like tumor (like a classic PTC)



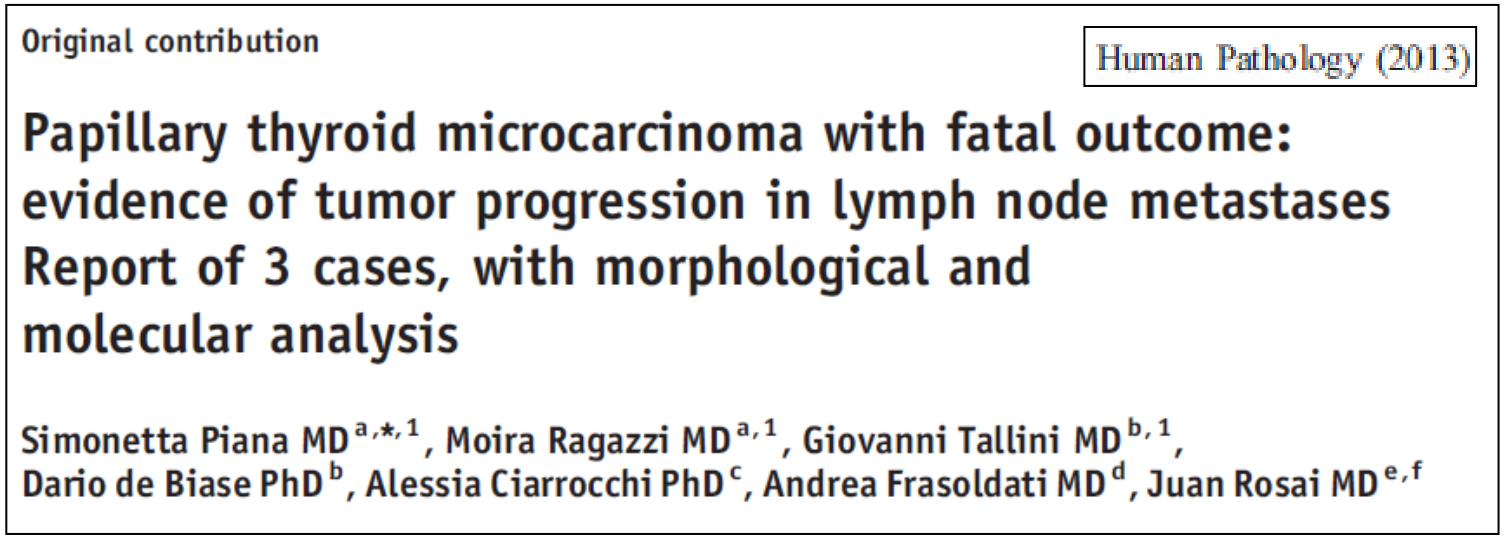
-Invasive encapsulated variant (IEFV-PTC) is a *RAS*-like tumor (like a FTC)



Clinical Significance of the Subtypes of PTC

-New WHO classification, the term “variant” replaced by “subtype”
-to align with other WHO tumor classifications
-to avoid confusion term "genetic variant(s)"

“PTC-microcarcinoma” should not be considered as a distinct subtype



Original contribution

Human Pathology (2013)

Papillary thyroid microcarcinoma with fatal outcome: evidence of tumor progression in lymph node metastases Report of 3 cases, with morphological and molecular analysis

Simonetta Piana MD[a,*,1], Moira Ragazzi MD[a,1], Giovanni Tallini MD[b,1], Dario de Biase PhD[b], Alessia Ciarrocchi PhD[c], Andrea Frasoldati MD[d], Juan Rosai MD[e,f]

-Cyclin D1 +

-BRAF negative

-p53 negative

-KRAS, HRAS, NRAS, PI3KC wt

Massive LN metastases with evidence of “tumor progression”
(tall cell, poorly differentiated areas, and high-grade cytology)

Clinical Significance of the Subtypes of PTC

-Tall cell, columnar cell and hobnail subtypes
- **-peculiar morphology or phenotype**
- **-aggressive clinicopathologic entity**
- **-intermediate risk of recurrence by ATA guidelines**


Review

Aggressive variants of follicular cell derived thyroid carcinoma; the so called 'Real Thyroid Carcinomas'

Zubair Baloch,[1] Virginia A LiVolsi,[2] Rashmi Tondon[2]

Clinical Significance of the Subtypes of PTC

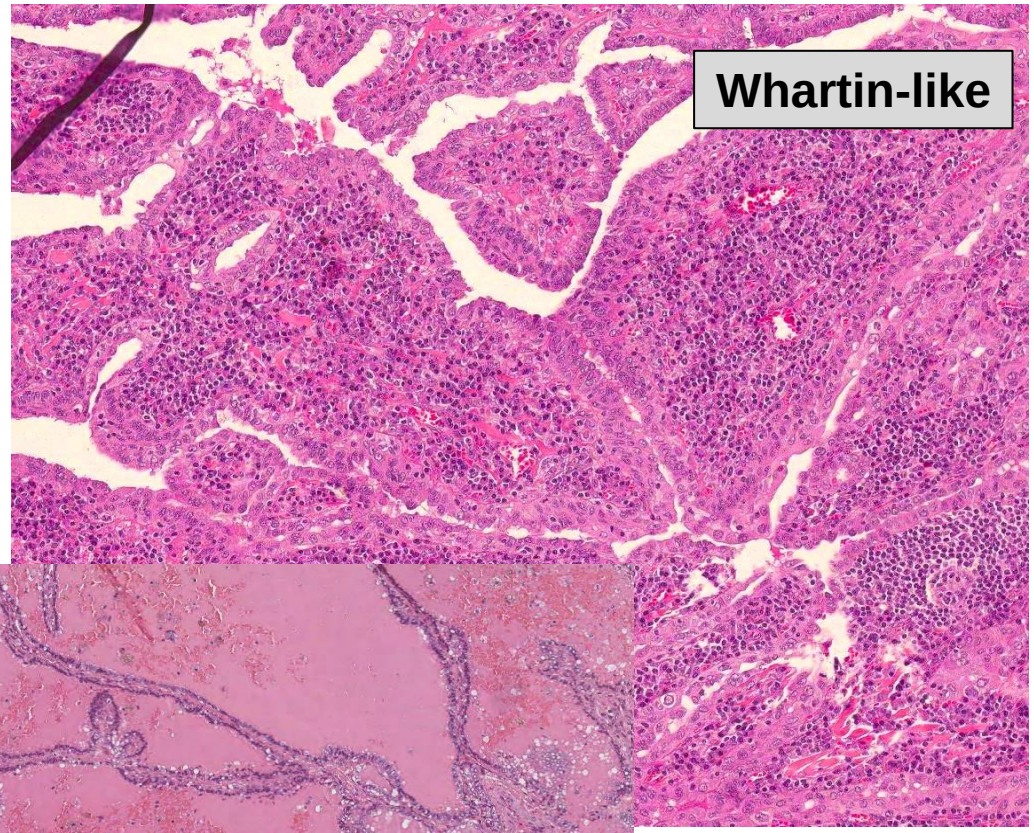
- -FOLLICULAR
- -MACROFOLLICULAR
- -ONCOCYTIC
- -WHARTIN-LIKE
- -CRIBRIFORM/MORULAR

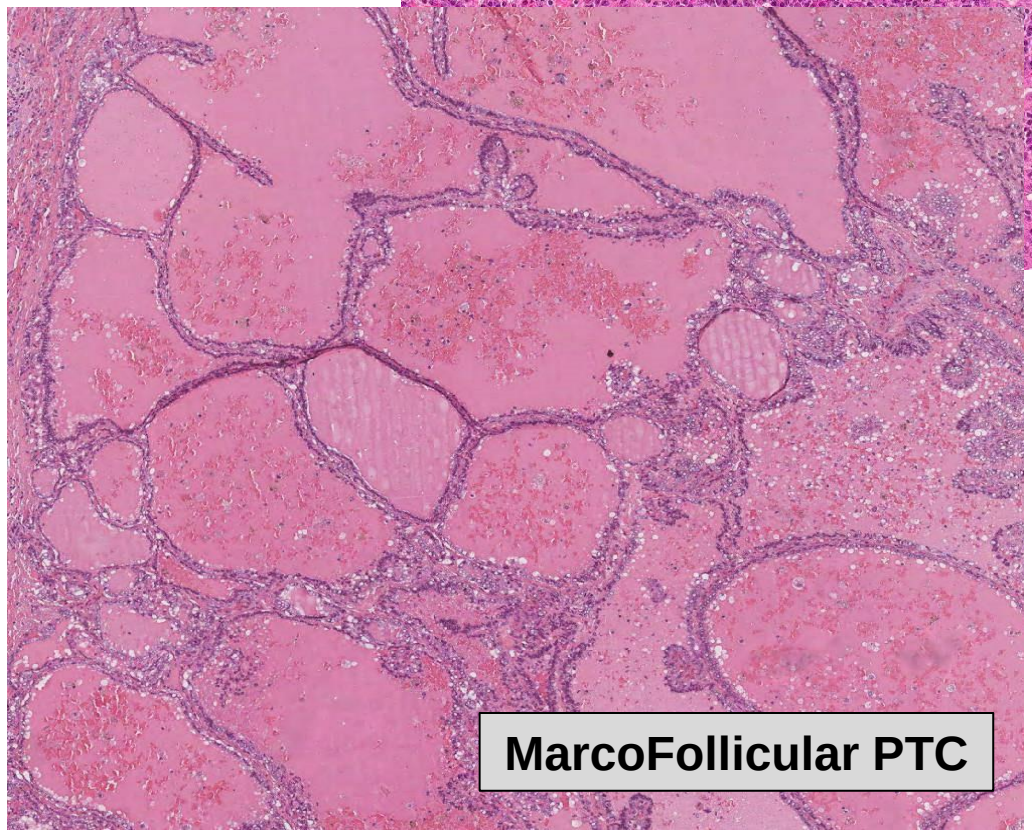
- -COLUMNAR CELL
- -TALL CELL
- -DIFFUSE SCLEROSING
- -SOLID
- -HOBNAIL

Clinical Significance of the Subtypes of PTC

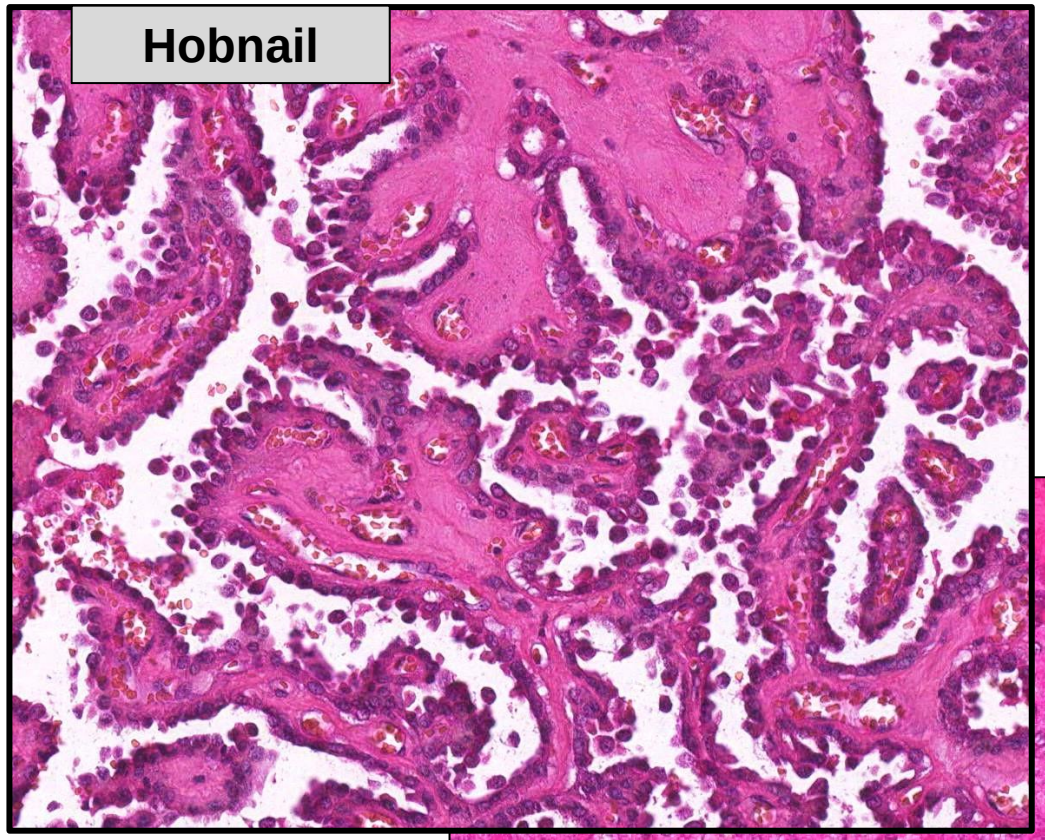
- -FOLLICULAR
- -MACROFOLLICULAR
- -ONCOCYTIC
- -WHARTIN-LIKE
- -CRIBRIFORM/MORULAR

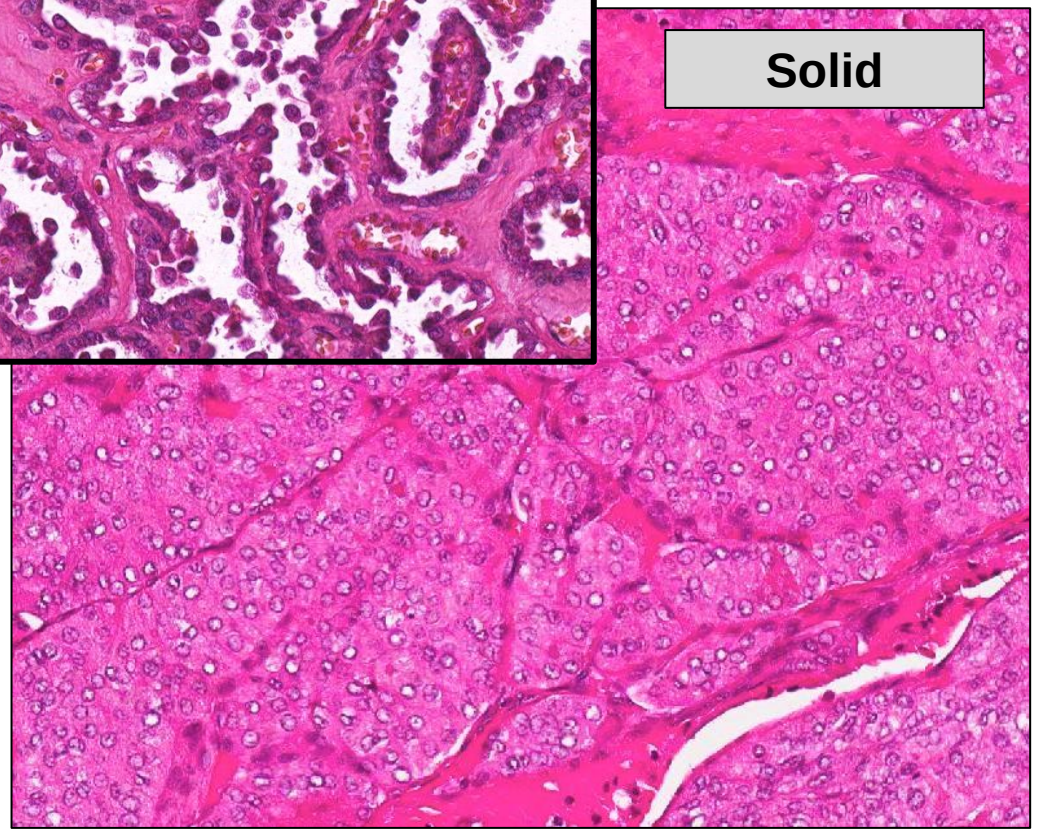
RAS mutation
PAX8/PPARγ
CCTNB1 mutation
BRAF mutation





Clinical Significance of the Subtypes of PTC





-COLUMNAR CELL

-TALL CELL

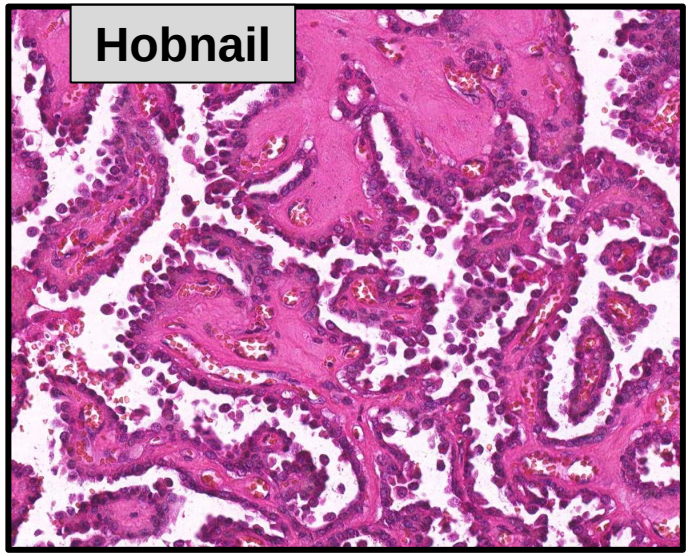
-DIFFUSE SCLEROSING

-SOLID

-HOBNAIL

BRAF mutation
RET/PTC
TERT mutation
p53 and PIK3CA

Clinical Significance of the Subtypes of PTC



Am J Surg Pathol • Volume 34, Number 1, January 2010

Papillary Thyroid Carcinoma With Prominent Hobnail Features: A New Aggressive Variant of Moderately Differentiated Papillary Carcinoma. A Clinicopathologic, Immunohistochemical, and Molecular Study of Eight Cases

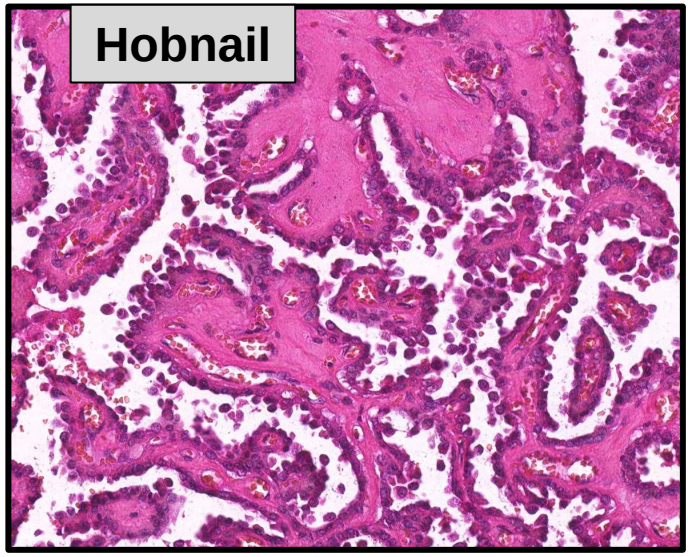
Sofia Asioli, MD,† Lori A. Erickson, MD,* Thomas J. Sebo, MD,* Jun Zhang, MD,* Long Jin, MD,* Geoffrey B. Thompson, MD,‡ and Ricardo V. Lloyd, MD, PhD**

TABLE 1. Clinicopathologic Features of Eight Cases of Papillary Thyroid Carcinoma With Prominent Hobnail Feature

Case	Age/ Sex	Size	Vascular Invasion	Nuclear Atypia	Mitoses (Atypical Mitoses)	% Hobnail Features	Post Surgical RT	Recur-rence	Lymph Nodes MTS	Distant MTS (Sites)	pTNM	BRAF Stautus	FU (mo)
1	51/F	2.0	Yes	Severe	9 (1)	75	Yes*	No	NA	Liver, lung, bone, brain, spinal cord	T1 (m) Nx M1	WT	DOD (6)
2	78/F	4.0	Yes	Moderate	4	100	Yes†	Yes	Yes	No	T3 (m) N1 M0	NA	DOD (10)
3	63/F	1.0	Yes	Moderate	3	60	No	No	Yes	Lung	T1 N1 M1	MUT	DOD (31)
4	28/F	1.2	No	Moderate	3	30	Yes	Yes	Yes	No	T3 (m) N0 M0	WT	AND (120)
5	58/M	1.8	Yes	Moderate	4	75	Yes	Yes	Yes	Shoulder, Lung, bone, muscle, pancreas	T3 (m) N1 M1	MUT	AWD (87)
6	53/F	3.5	Yes	Severe	5 (1)	75	Yes	No	No	No	T2 N0 M0	MUT	AND (236)
7	65/F	2.8	Yes	Moderate	6	50	Yes†	No	Yes	Brain, lung	T3 (m) N1 M1	MUT	DOD (124)
8	65/M	4.0	Yes	Severe	3	75	Yes*†	No	Yes	Epiglottis, larynx, nasopharynx, base of tounge, tonsils	T3 (m) N1 M1	WT	AWD (4)

*Patients underwent also to chemotherapy.
†Patients underwent also to external bean radiation therapy, case 2 at metiastinum, and sopraclavicular areas and case 7 at brain, respectively.
(m) indicates multifocal tumor; AND, alive no disease; AWD, alive with disease; DOD, dead of disease; F, female; FU, follow-up; M, male; MTS, metastasis; MUT, mutated; NA, not available; RT, radiotherapy; WT, wild type.

Clinical Significance of the Subtypes of PTC



Hobnail Variant of Papillary Thyroid Carcinoma

Clinicopathologic and Molecular Evidence of Progression to Undifferentiated Carcinoma in 2 Cases

José M. Cameselle-Teijeiro, MD, PhD,† Irene Rodríguez-Pérez, MD,‡ Ricardo Celestino, PhD,§‖ Catarina Eloy, MD, PhD,§‖ Magalí Piso-Neira, BSc,* Ihab Abdulkader-Nallib, MD, PhD,* Paula Soares, PhD,§‖¶ and Manuel Sobrinho-Simões, MD, PhD§‖¶#*

Am J Surg Pathol • Volume 41, Number 6, June 2017

TABLE 2. Main Immunohistochemical and Molecular Findings in the 2 Cases of HV of PTC With Progression to UC

Case/sample	TTF1	TG	CT	Ki-67 (%)	p53	*BRAF*	*TERT*	*NRAS*	*HRAS*	*KRAS*	*RET/PTC1*	*RET/PTC3*	*PAX8/PPARγ*
1/Primary	+	+	–	4.6	+	V600E	C228T	wt	wt	wt	wt	wt	wt
1/Liver metastasis*	+ (WD)	+ (WD)	– (WD)	NA	NA	V600E (WD)	NA	NA	NA	NA	NA	NA	NA
	+ (UD)	– (UD)	– (UD)			V600E (UD)							
2/Primary	+	+	–	5	+	wt	wt	wt	wt	wt	NA	NA	NA
2/Recurrence†	+ (WD)	+ (WD)	– (WD)	30 (WD)	+ WD	wt (WD)	wt (WD)	wt (WD)	wt (WD)	wt (WD)	NA	NA	NA
	– (UD)	– (UD)	– (UD)	80 (UD)	+ UD	wt (UD)	wt (UD)	wt (UD)	wt (UD)	wt (UD)	NA	NA	NA

*Liver metastasis 10 years after thyroidectomy showed a tumor with WD and UD components.
†Tumor neck recurrence 6 years after thyroidectomy showed a tumor with WD and UD components.
CT indicates calcitonin; NA, not available; UD, undifferentiated; WD, well differentiated; wt, wild type.

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms ☑

-Clinical Significance of PTC Subtypes ☑

-“High-Grade” follicular cell-derived carcinomas

-The term “Hürthle”, end of a misnomer

-What’s New in the Understanding of ATC?

“High-Grade” follicular cell-derived carcinomas

THE TWEENER TUMOR

-Intermediate clinical behavior between WDTC and ATC

-Intermediate molecular landscape between WDTC and ATC

-High grade or poorly differentiated carcinoma?

-Topic debated for decades

“High-Grade” follicular cell-derived carcinomas

-1907, Theodor Langhans from Brema described a *wuchernde Struma* (proliferating struma)

-1974, OERTC classification, moderately differentiated form of thyroid carcinoma

-1983, Sakamoto = PDTC

-1984, Carcangiu = PDTC, insular type

"Poorly" sounds like "grade"

-2004, WHO included PDTC in classification of thyroid tumors

-2006, MSKCC criteria for diagnosis

-2007, Turin criteria for diagnosis

“High-Grade” follicular cell-derived carcinomas

-1907, Theodor Langhans from Brema described a *wuchernde Struma* (proliferating struma)

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"Poorly" sounds like "histotype"

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-2007, Turin criteria for diagnosis

“High-Grade” follicular cell-derived carcinomas

New WHO classification recognizes two groups of high-grade non-anaplastic follicular cell–derived carcinomas

-PDTC

-DHGTC

	PDTC (Turin criteria)	DHGTC
Growth pattern	Required: solid/trabecular/insular	Papillary, follicular, solid*
Nuclear Cytology	Required: no features of PTC	Any
Other features: tumor necrosis, mitosis and convoluted nuclei	Minimum requirement: one of the following three features: Mitotic count $\geq 3/2$ mm^2 Tumor necrosis Convoluted nuclei	Minimum requirement: one of the following two features: Mitotic count $\geq 5/2$ mm^2 Tumor necrosis
Anaplastic features	Absent	Absent

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 • Volume 31, Number 8, August 2007

Poorly Differentiated Thyroid Carcinomas Defined on the Basis of Mitosis and Necrosis

A Clinicopathologic Study of 58 Patients

David Hiltzik, M.D.[1]
Diane L. Carlson, M.D.[2]
R. Michael Tuttle, M.D.[3]
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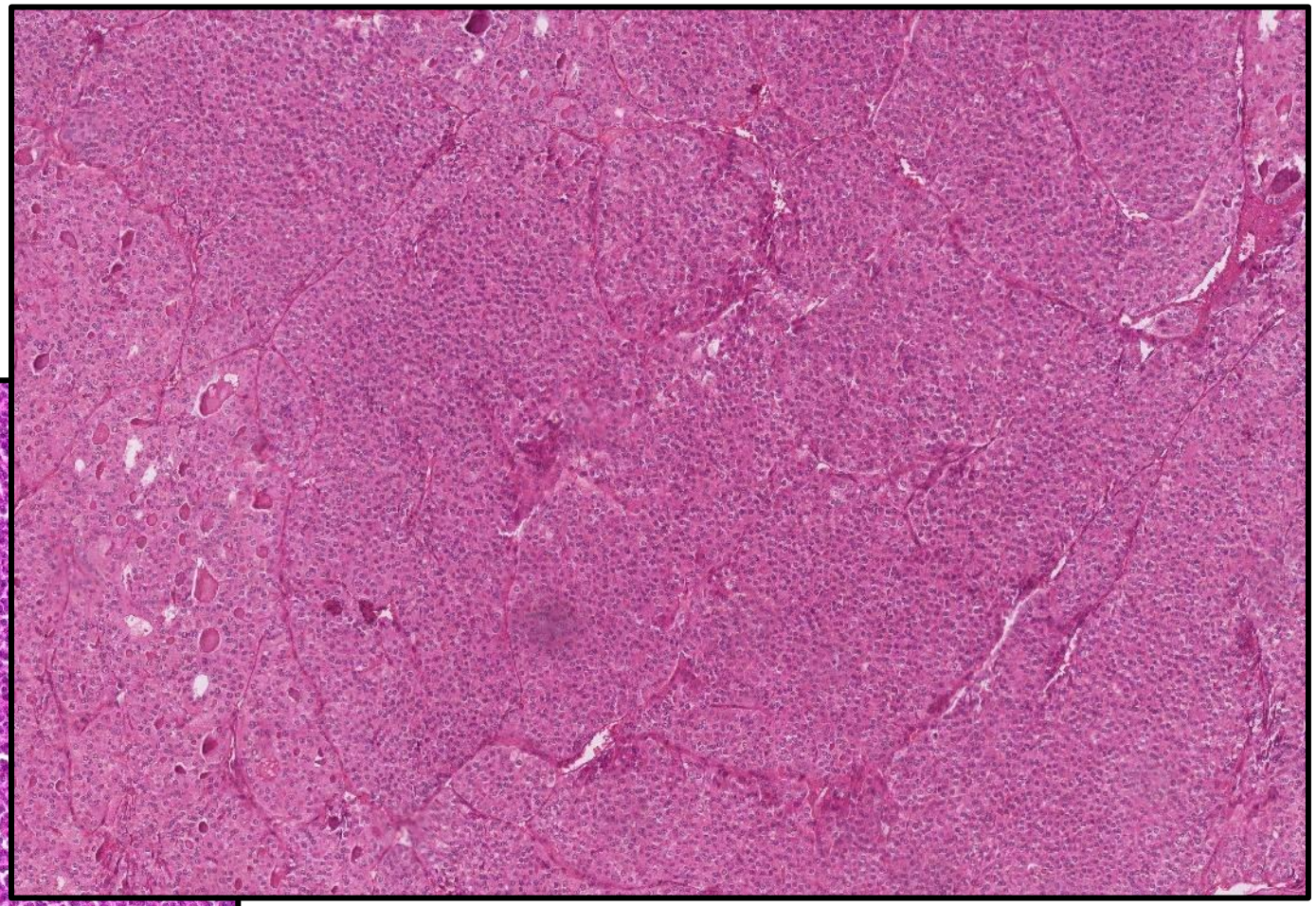
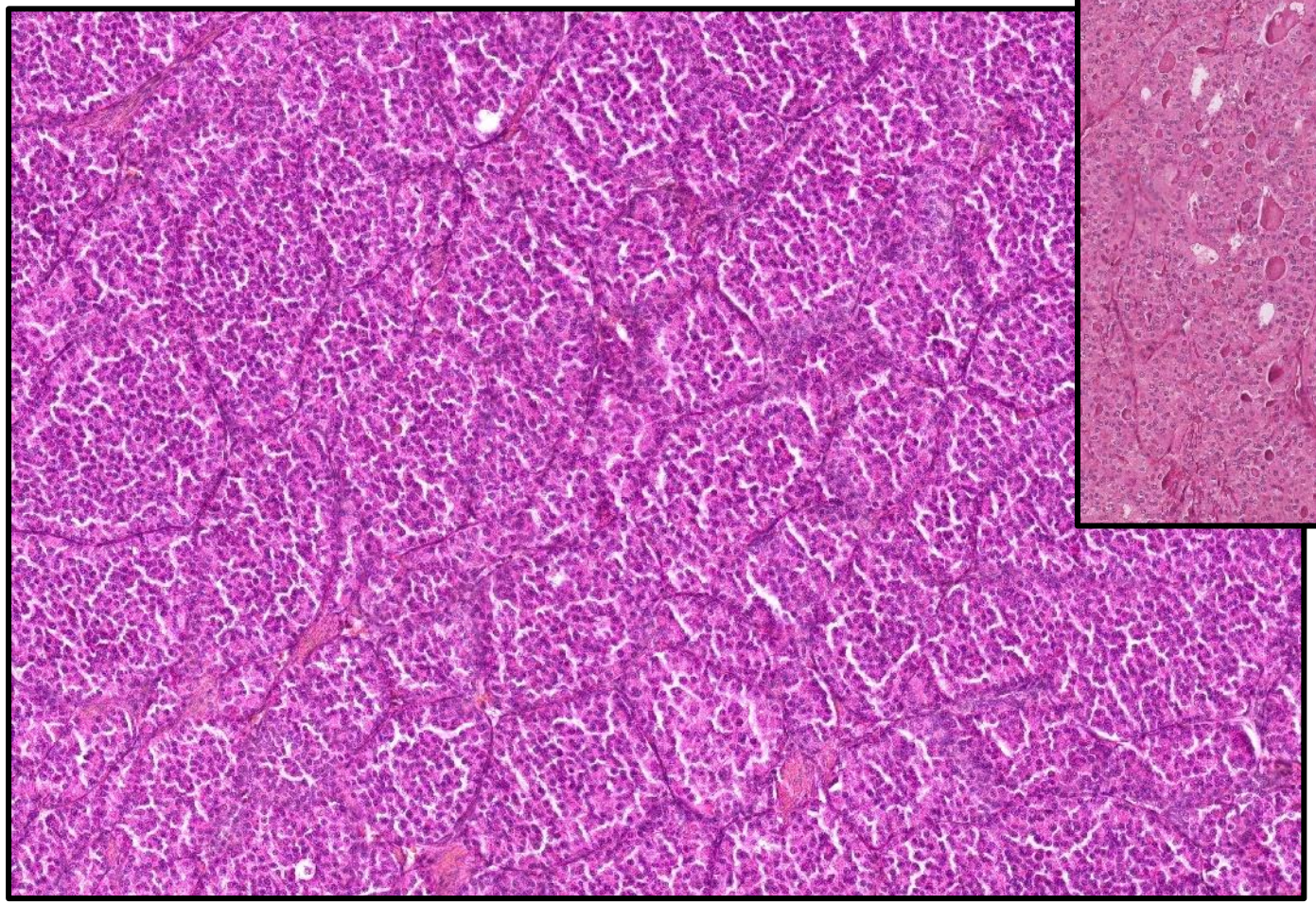
Buvanesh Singh, M.D., Ph.D.[5]
Ronald A. Ghossein, M.D.[2]

“High-Grade” follicular cell-derived carcinomas

PDTC

Insular pattern

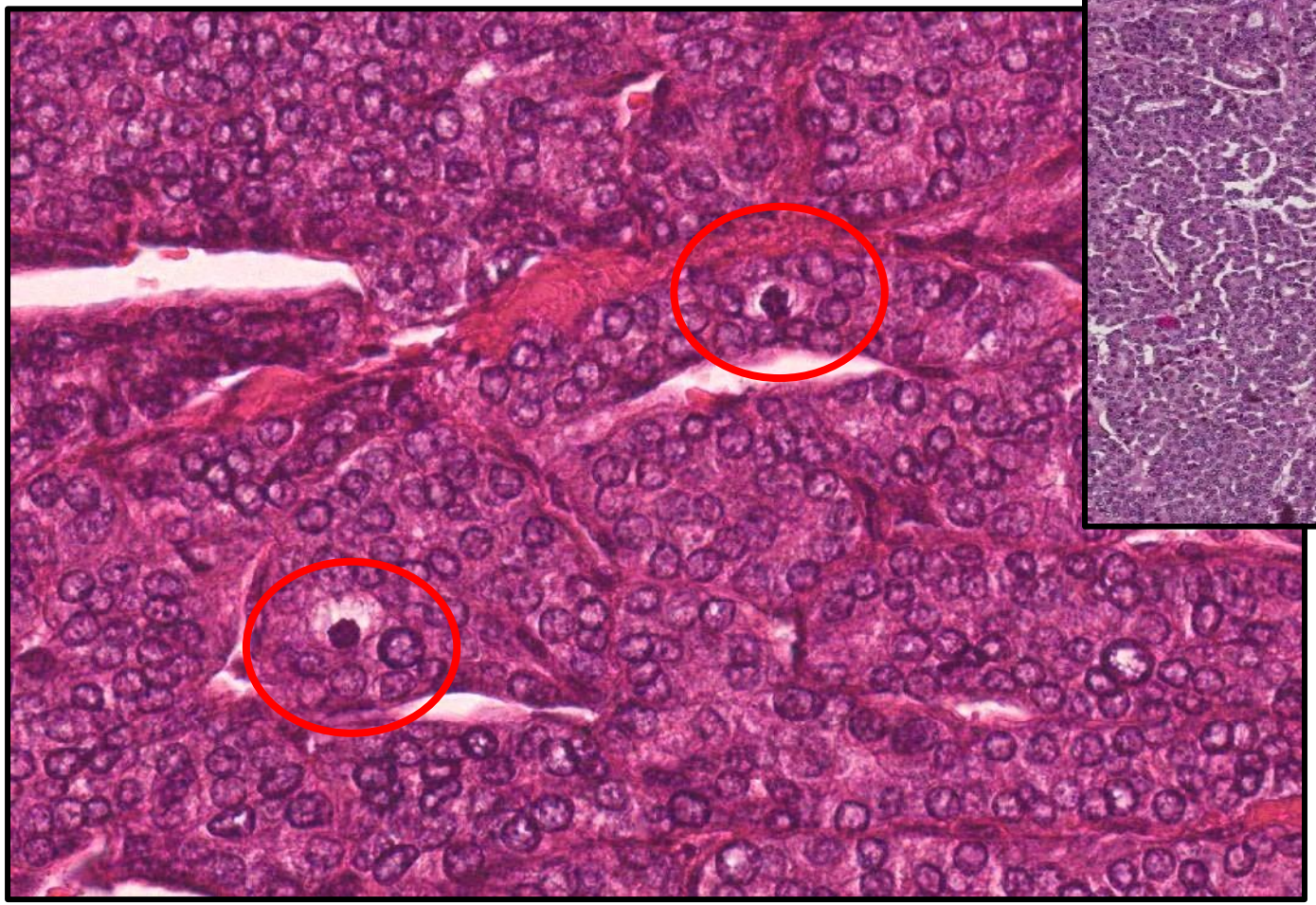


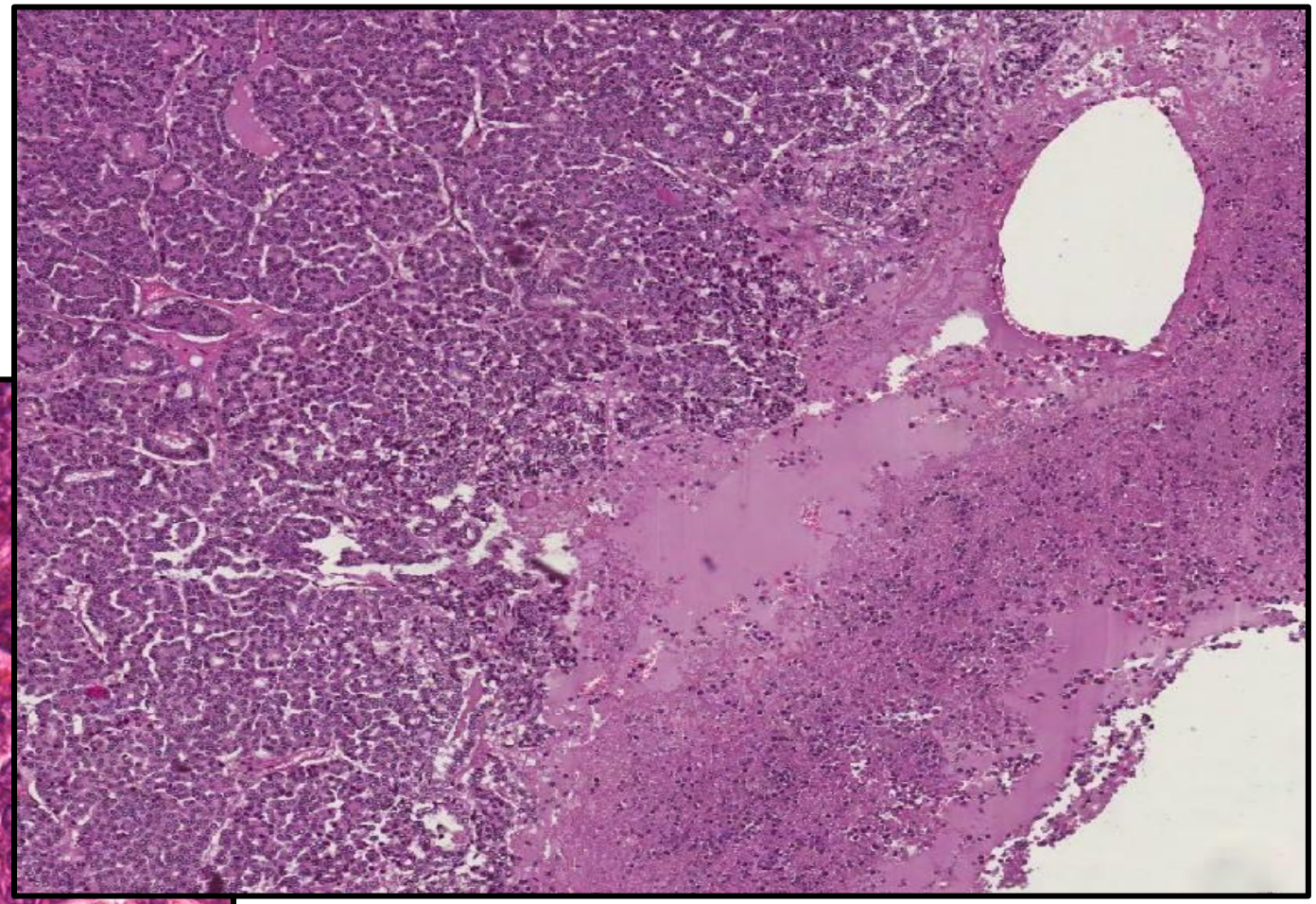


“High-Grade” follicular cell-derived carcinomas

DHGTC

Mitosis





Necrosis

BEWARE OF THE WHAFFT!

“High-Grade” follicular cell-derived carcinomas

-PDTC 10-year OS of 46% and a 60% DSS 10 years

-DHGTC have an approximately similar DSS (56% at 10 years)

-Memorial vs Turin definitions:
- -RAI-refractory PET+ thyroid cancer
- -fatal non-anaplastic thyroid cancer

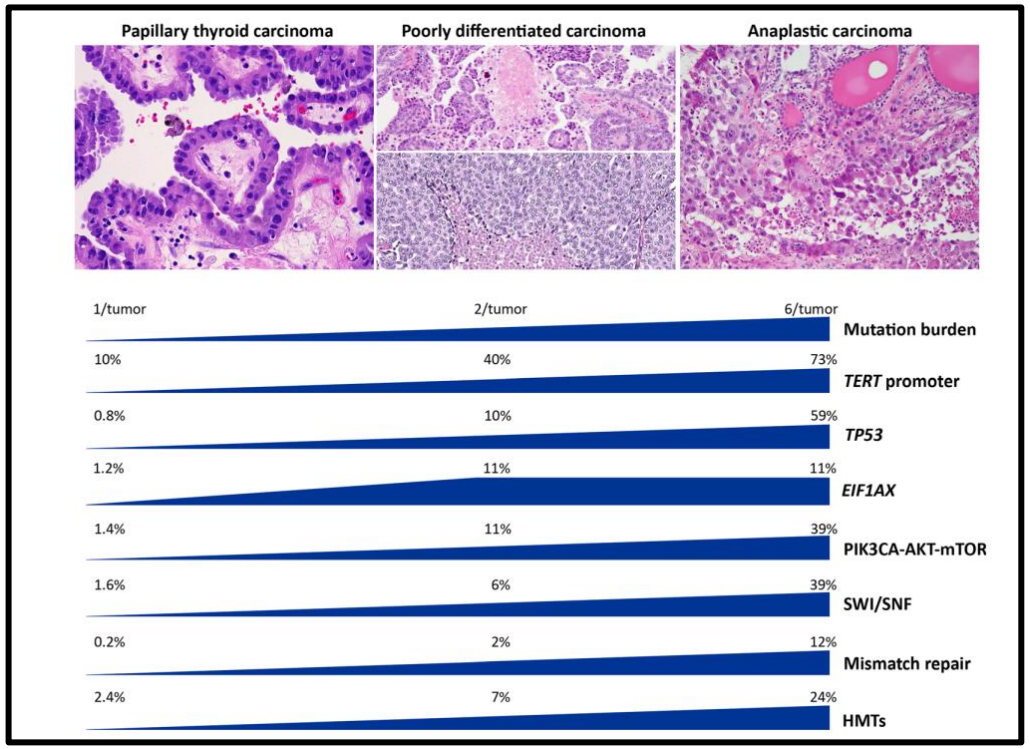
-All patients who died from non-ATC had $\geq$ 1 of the following features:
- -gross ETE
- -extensive vascular invasion
- -PDTC component in either primary, local mets or distant mets
- -at least 10% PD component

“High-Grade” follicular cell-derived carcinomas

Endocr Pathol (2016) 27:205–212
DOI 10.1007/s12022-016-9445-4

Genomic Landscape of poorly Differentiated and Anaplastic Thyroid Carcinoma

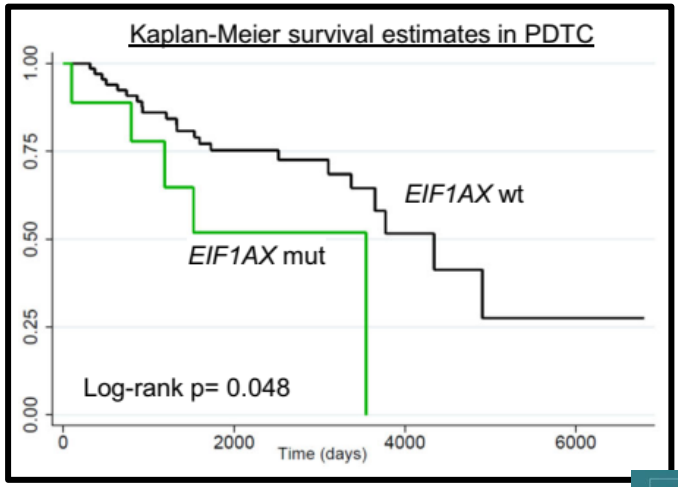
Bin Xu[1] · Ronald Ghossein[1]



-RAS and BRAF mutations common and mutually exclusive
  -BRAF-mut PDTC >>> lower than WDTC, regional met
  -RAS-mut PDTC >>> distant mets

-Increasing mutational burden PTC >>> PDTC >>> ATC

-MB is associated with older age, higher stage, descresed OS



-Frequent mutations (TERT, EIF1AX, MED12, PIK3C) in fatal *VS* nonfatal PDTC

“High-Grade” follicular cell-derived carcinomas

Endocr Pathol (2016) 27:205–212
DOI 10.1007/s12022-016-9445-4

Genomic Landscape of poorly Differentiated and Anaplastic Thyroid Carcinoma

Bin Xu [1] · Ronald Ghossein [1]

-TERT promoter mutation most common mutation in PDTC (40%)

-TP53 most common tumor suppressor mutation in PDTC (16%)

-Chromosomal rearrangements 14% (RET/PTC, PAX8/PPARγ, ALK fusions)

-Copy number alterations 1q gain, 22q loss

“High-Grade” follicular cell-derived carcinomas

-Evidences from NSG can help in choosing new therapeutic strategies

-Targeting Pathways

prevent TKI resistance

simoultaneous targeting MAPK,

PI3K/AKT or PI3K/mTOR inhibition plus paclitaxel)

-TERT based immunotherapy (+/- checkpoint inibithors)

-Blocking NF-kb (bortezomib) or HIF1α and VEGFR pathways (cabozantinib)

-MED12 can be targeted by sorafenib and Senexin A

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms ☑

-Clinical Significance of PTC Subtypes ☑

-“High-Grade” follicular cell-derived carcinomas ☑

-The term “Hürthle”, end of a misnomer

-What’s New in the Understanding of ATC?

The term “Hürthle”, end of a misnomer

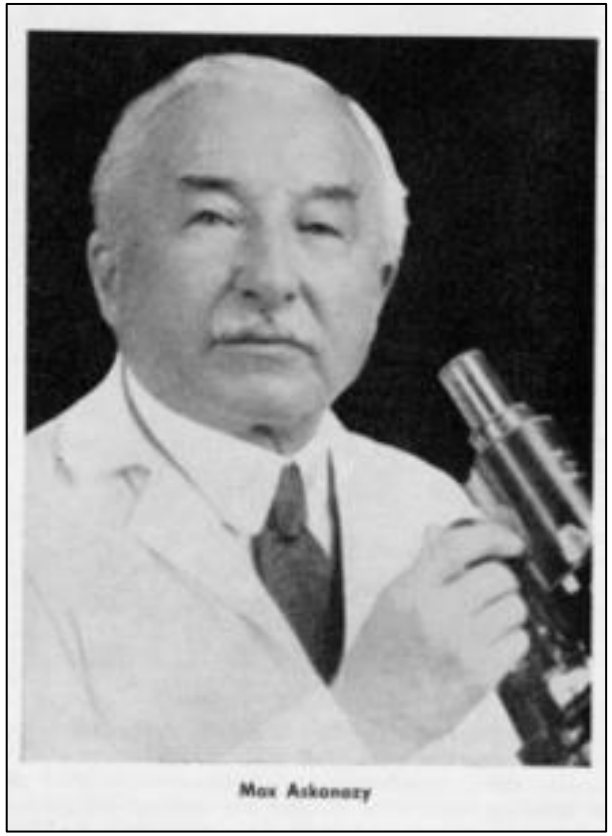
From 4th ed. of the WHO guidelines, oncocytic thyroid carcinoma (OCA) was listed as a separate entity due to its histology, molecular profile and patient prognosis

In the 5th ed. nomenclature ‘Hürthle’ is discouraged, as it derives from Karl Hürthle, a German histologist who described parafollicular C-cell rather than oncocyte cells

Beiträge zur Kenntniss des Secretionsvorgangs in der Schilddrüse.

Von

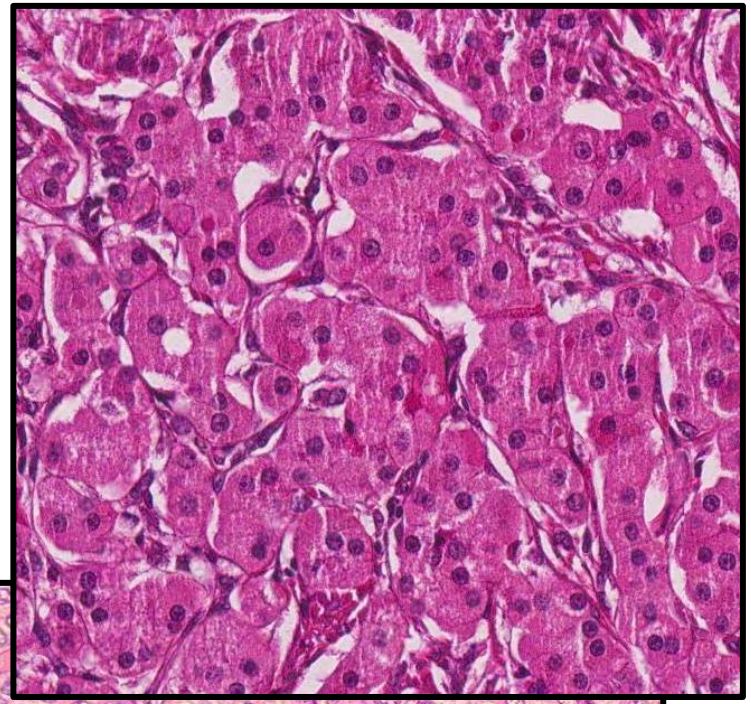
Dr. **K. Hürthle,**
Privatdocent und Assistent des Instituts.

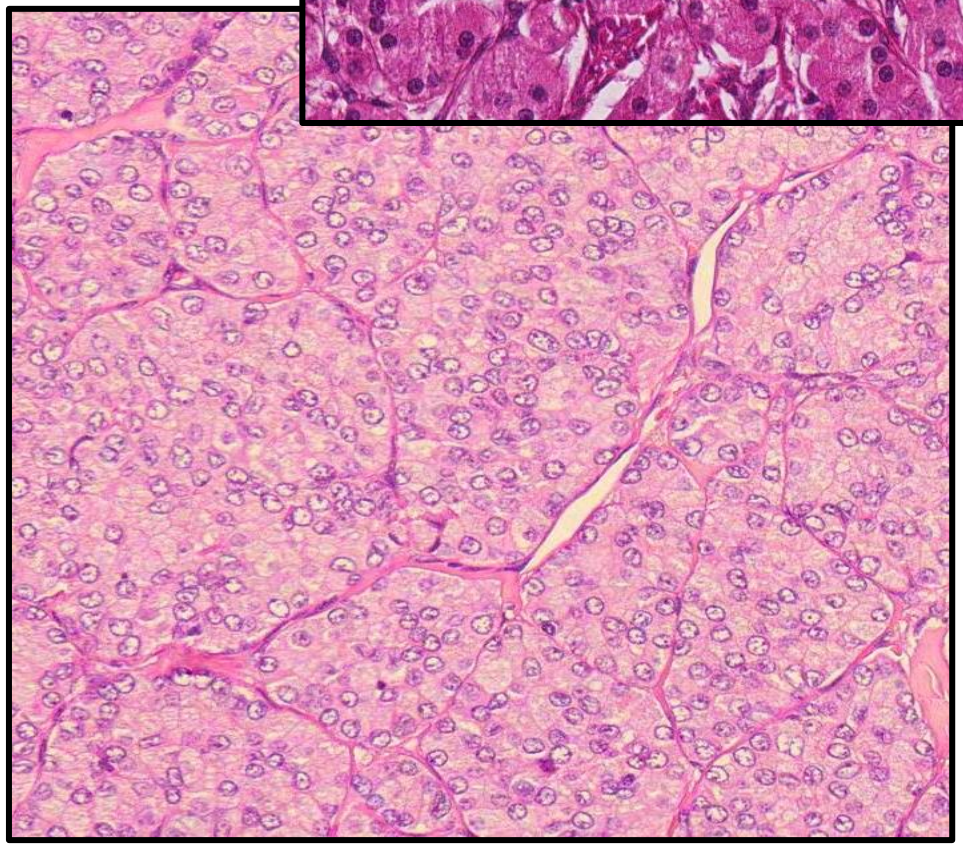


The real discoverer…

The term “Hürthle”, end of a misnomer

-Oncocytic cells
- -larger than normal thyrocyte
- -abundant granular eosinophilic cytoplasm
- -marked accumulation of dysfunctional mitochondria





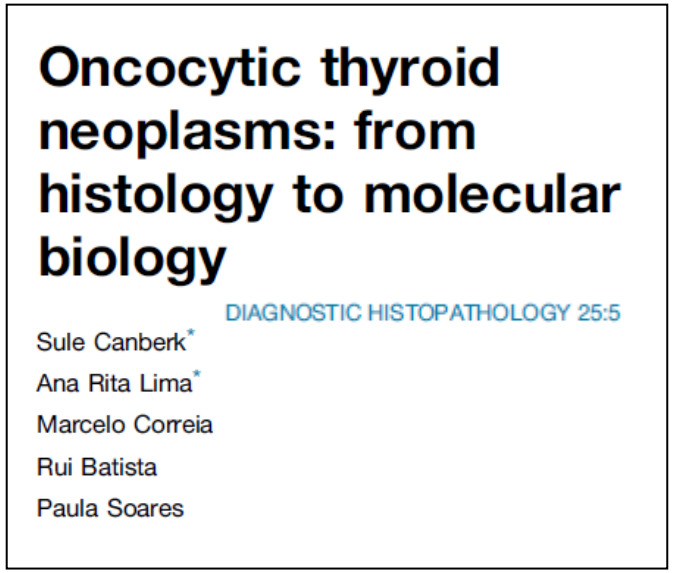
-OCA requires histological evidence of malignancy
- -capsular and/or vascular invasion
- -absence of high-grade features
- -pathologic stratification similar to FTC

The term “Hürthle”, end of a misnomer

-Homoplasmic or highly heteroplasmic (>70%) mtDNA mutations
-complex I subunit genes of the electron transport chain

-Widespread chromosome losses
-near-genome-wide haploidization with or without genome endoreduplication

-*RAS* mutations (lower rate than FTC), *EIF1AX*, *TERT*, *TP53*, *NF1*, and *CDKN1A*



The term “Hürthle”, end of a misnomer

-Wide controversy regarding prognosis of OCA
    -locoregional LN involvement is more frequent
    -general consensus of OCA as a more aggressive form of FTC

-It is hard to conclude that OCA have a poorer prognosis than non-OCA

-OCA carry a similar prognosis to non-OCA
    -particularly if we take into consideration tumor size and gender

-Patients with OCA should be treated as equivalent FTC regarding stage
    -less prone to concentrating ^{131}I ?

TO DISCUSS

-Benign and low-risk follicular cell-derived neoplasms ☑

-Clinical Significance of PTC Subtypes ☑

-“High-Grade” follicular cell-derived carcinomas ☑

-The term “Hürthle”, end of a misnomer ☑

-What’s New in the Understanding of ATC?

What's New in the Understanding of ATC?

-New (the old one) definition

-Anaplastic follicular cell-derived carcinoma

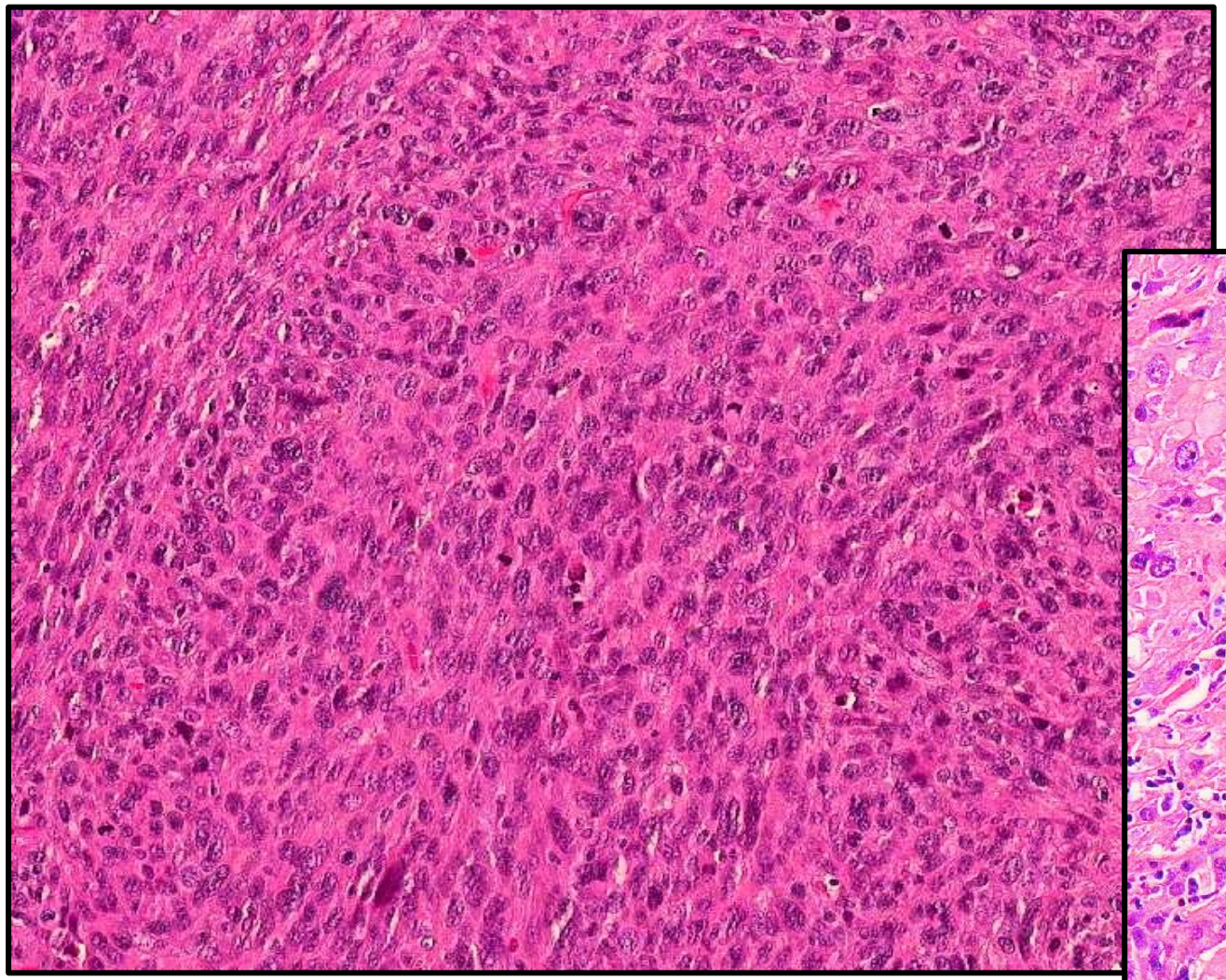
-Highly aggressive, dismal prognosis

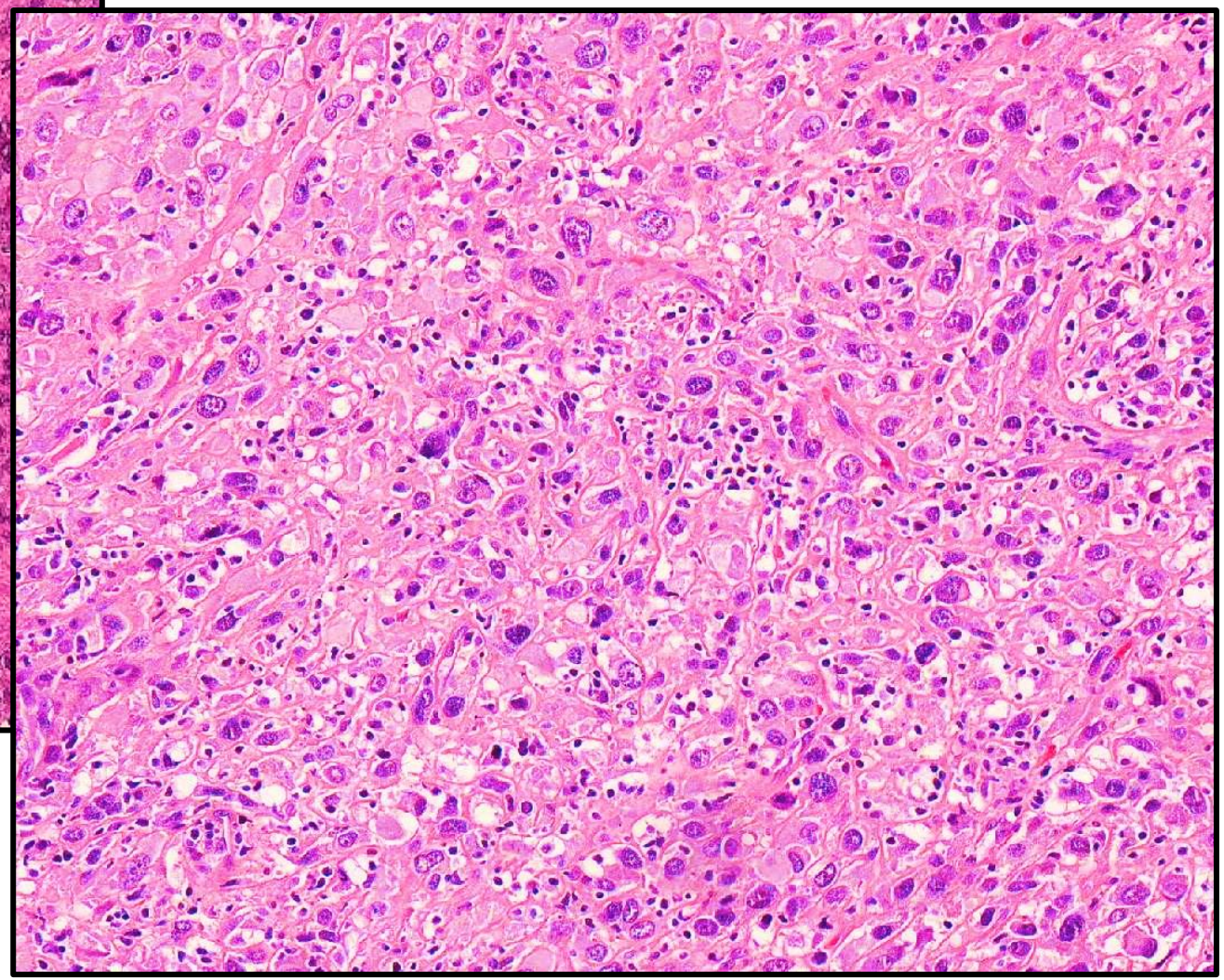
-Can be associated with a differentiated form

-Can be present an undifferentiated phenotype

-Variable morphology (beware of differential diagnosis!)
- -spindle
- -plemorphic
- -osteoclast-like giant cells
- -divergent differentiations (chondro, osteo…)
- -squamous / squamoid

What's New in the Understanding of ATC?





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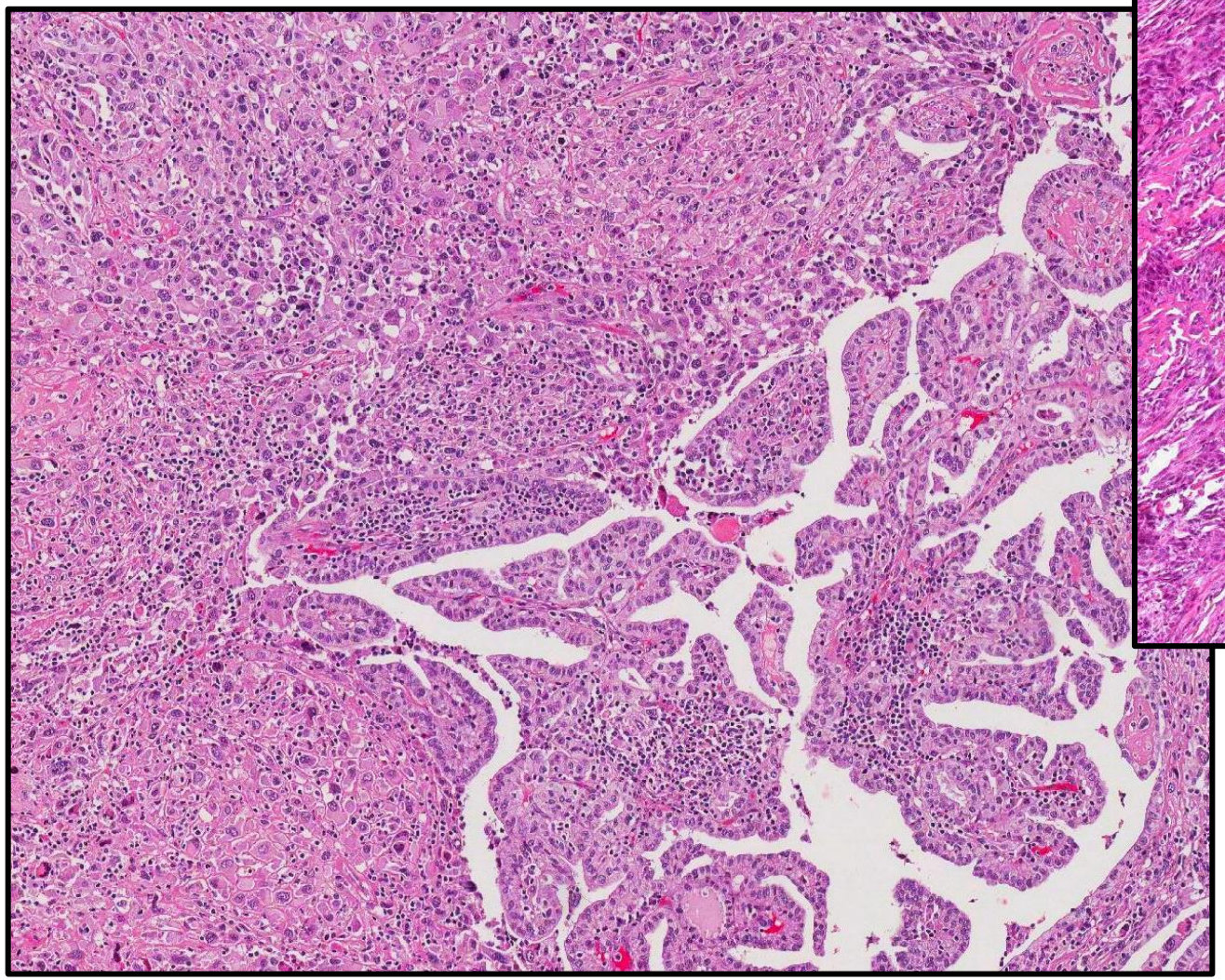

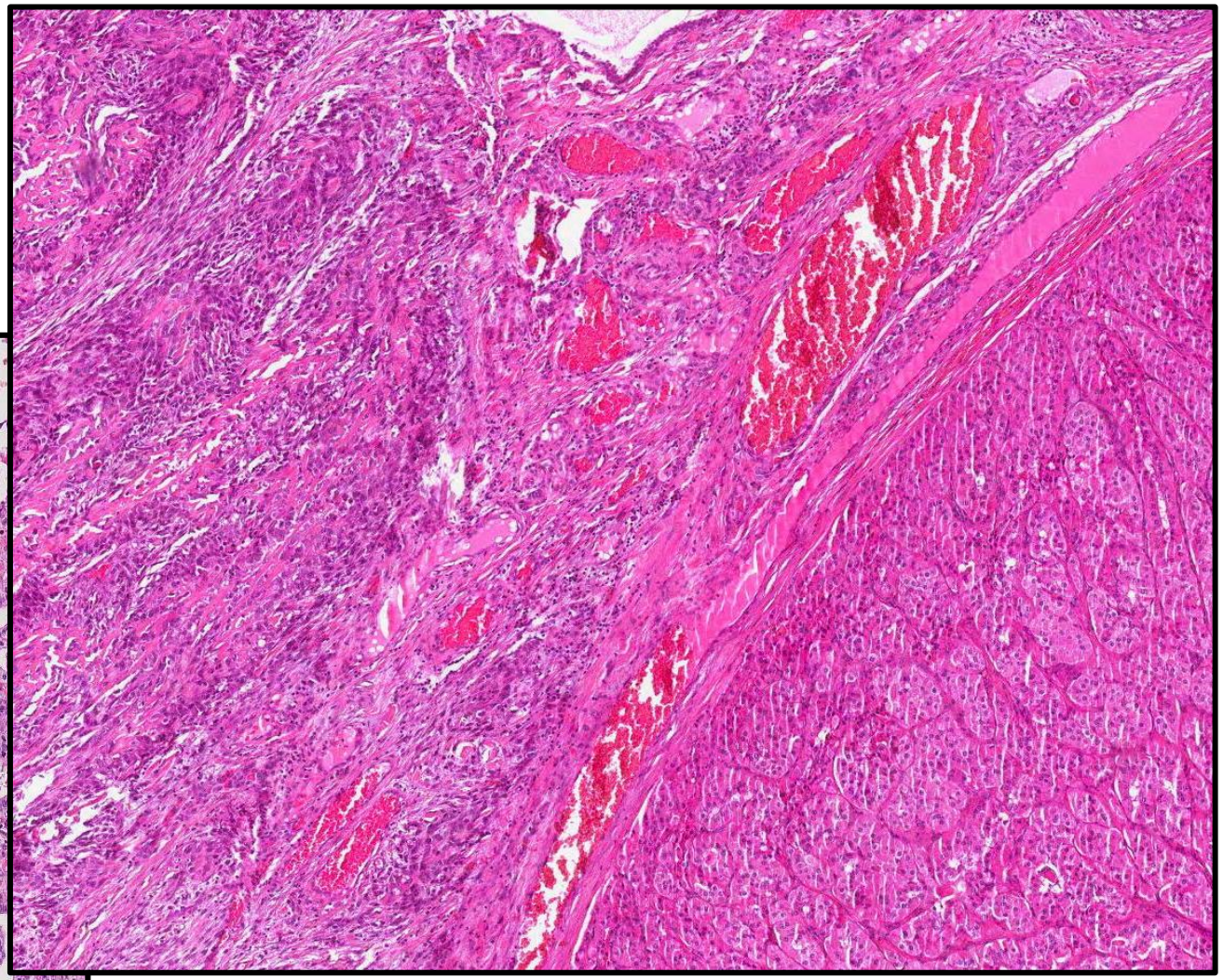

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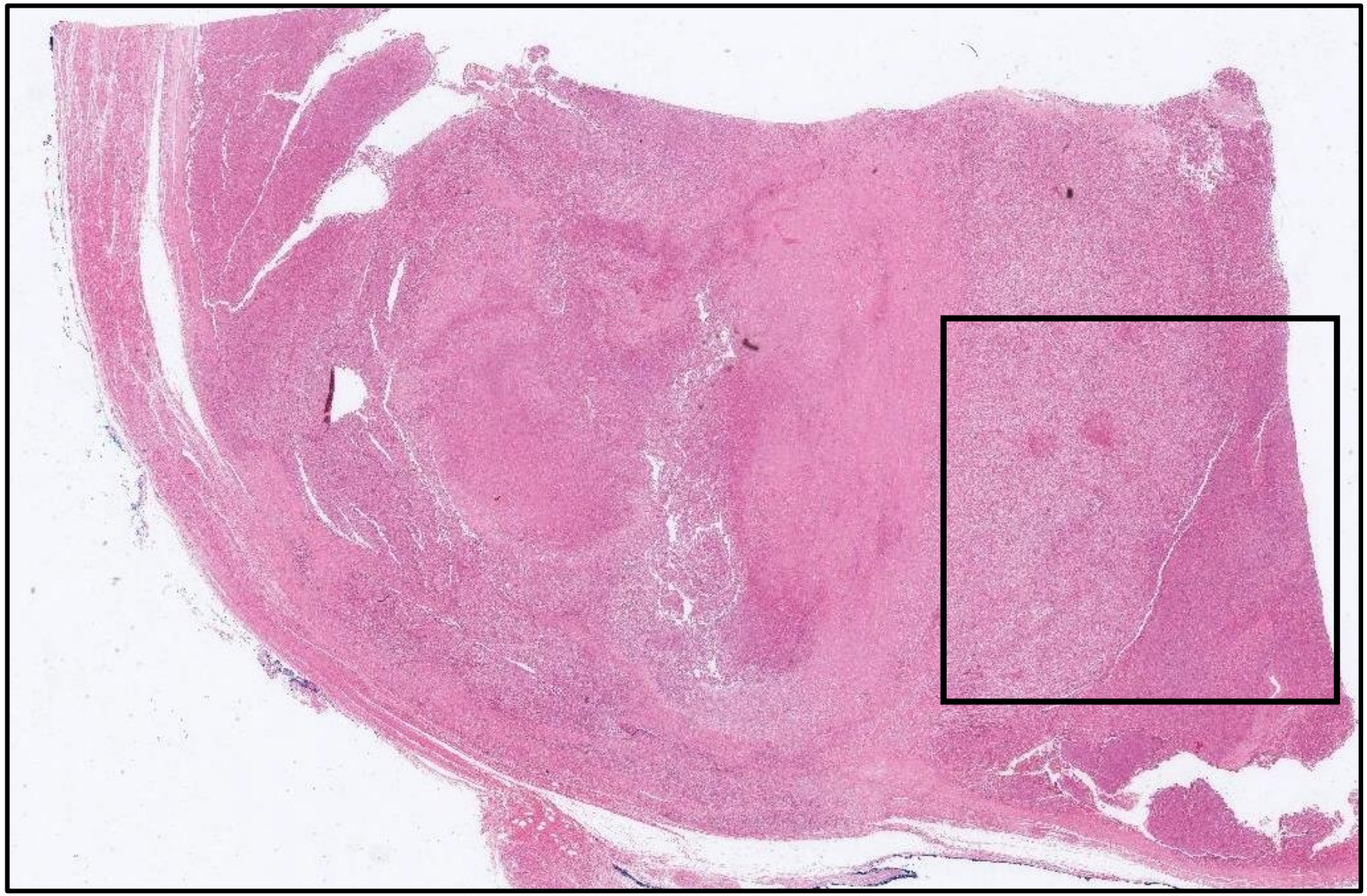

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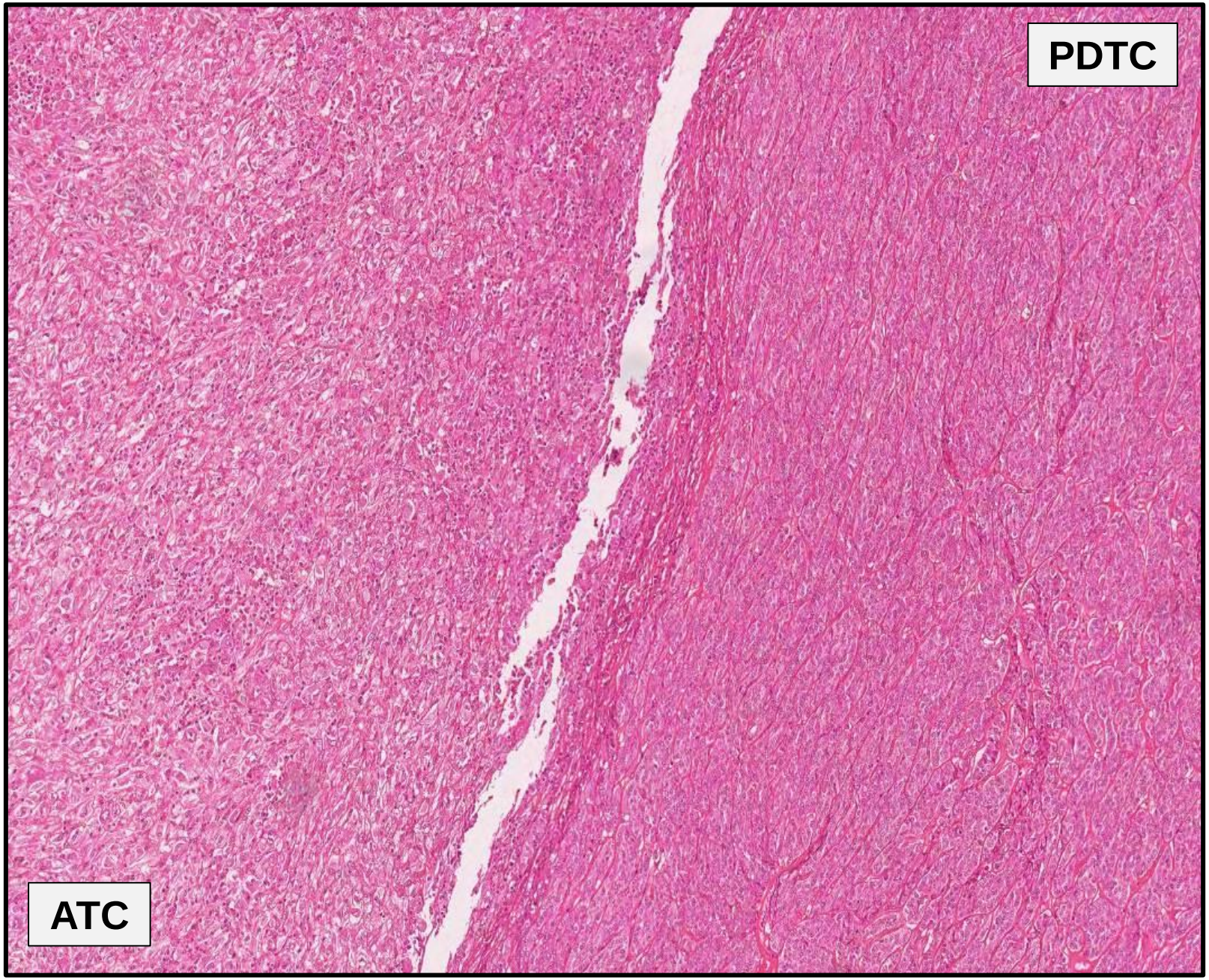

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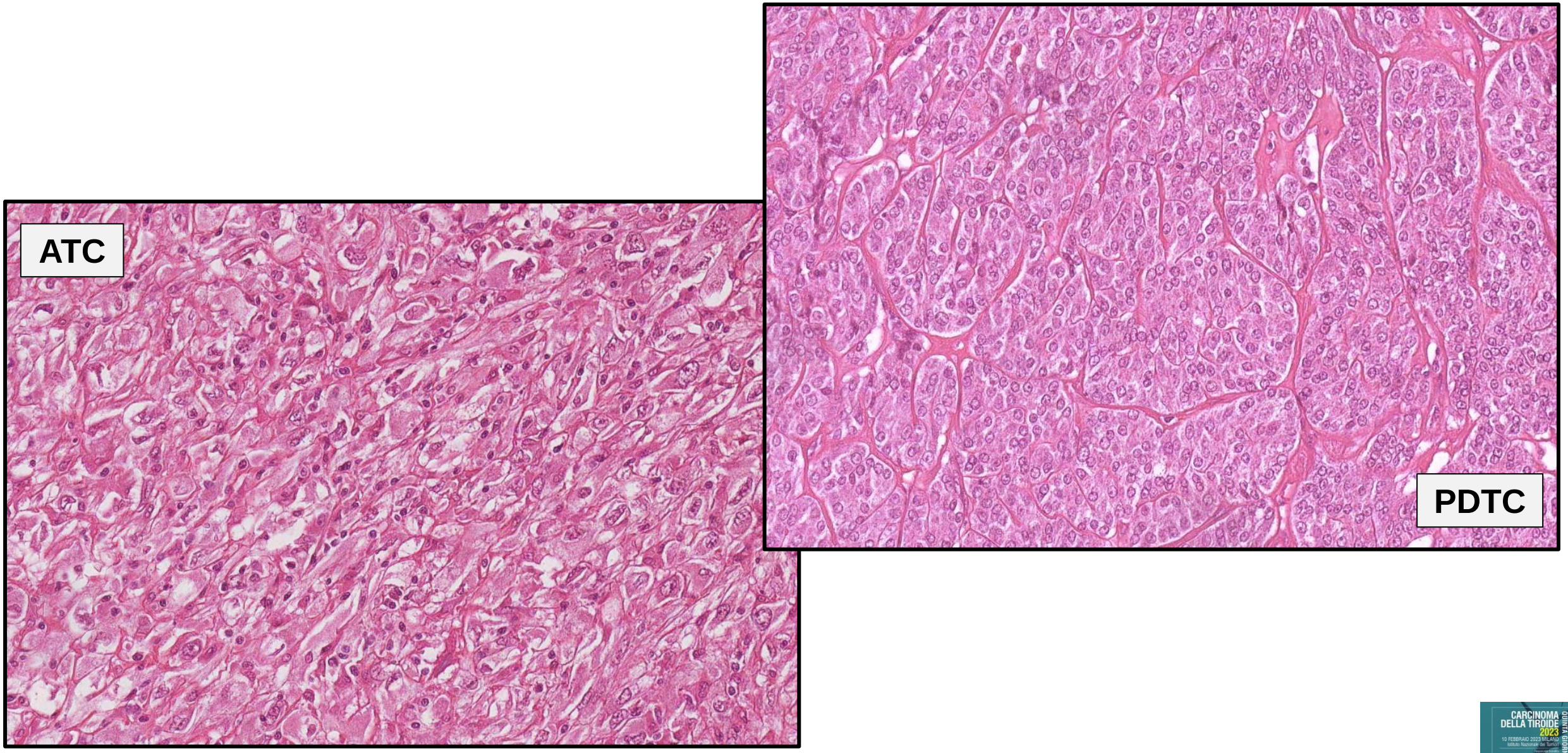


What's New in the Understanding of ATC?

SCC of the thyroid was considered a separate entity from ATC

-Pure SCC with or without a WDTC component

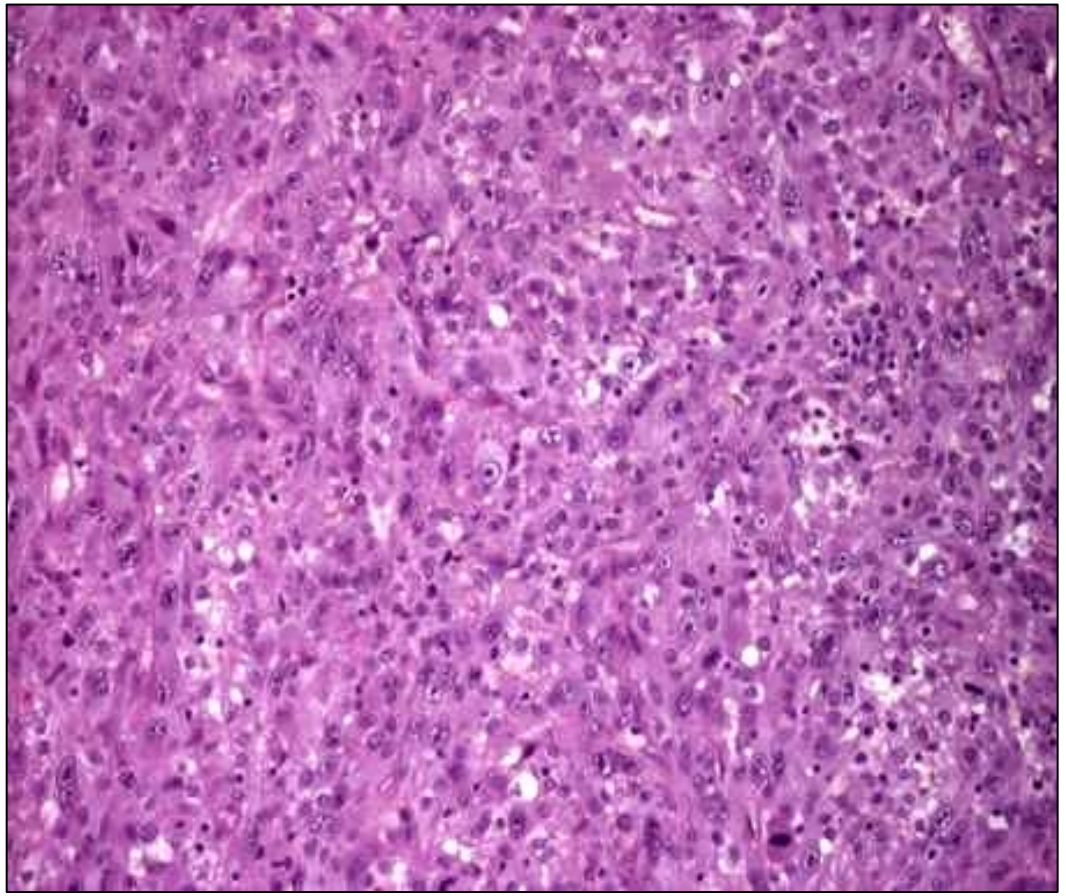
-*BRAF*V600E mutation 60% to 87% of cases

-PAX8 and TTF1 in 91% and 38% of cases

-Confirming their follicular cell origin

-Outcome similar to ATC

-Morphologic pattern of ATC



What's New in the Understanding of ATC?

-Rapid and prompt testing of all ATC for ***BRAF^{V600E}*** mutation

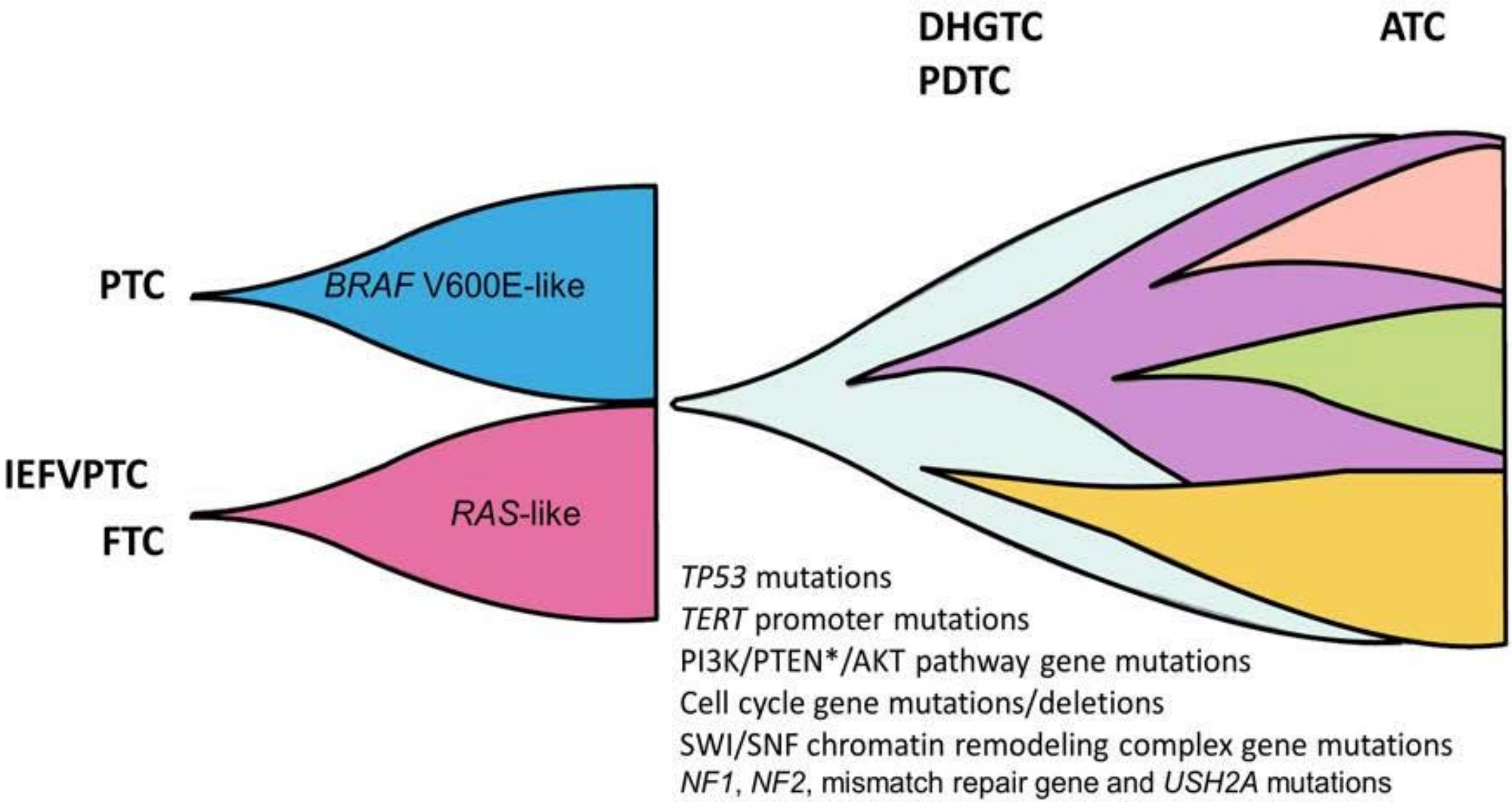
-This testing is mandatory

-BRAF and MEK inhibitors active against ***BRAF^{V600E}*** ATC

-IHC against mutated protein or NGS

-Massive sequencing for serarching targetable mutations

What's New in the Understanding of ATC?



TAKE HOME MESSAGES

WHAT CHANGES?
THE ANSWER TO LIFE, UNIVERSE AND EVERYTHING

-A better mix of old and new

-Application of the new WHO 2022 classification leads to…

-A correct diagnosis (tissue is the issue!)

-A prompt deep molecular analysis

-Future perspective: digital, Deep Learning, A.I. algorithms

TAKE HOME MESSAGES

GIANTS IN THYROID TUMOR PATHOLOGY

Virchows Archiv (2020) 477:471–472
https://doi.org/10.1007/s00428-020-02905-6

OBITUARY

Manuel Sobrinho Simões
Porto, July 17, 2020

Memorial tribute Juan Rosai (1940–2020)

“I don’t really know much about it, but it seems this molecular trend could take over pathology like immunohistochemistry”

Juan Rosai, Yale University (1991), talking about the role of p53

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