Corso EPEC

ITALIAN CHAPTER

Thyroid Nodules US Classification & Indication to FNA

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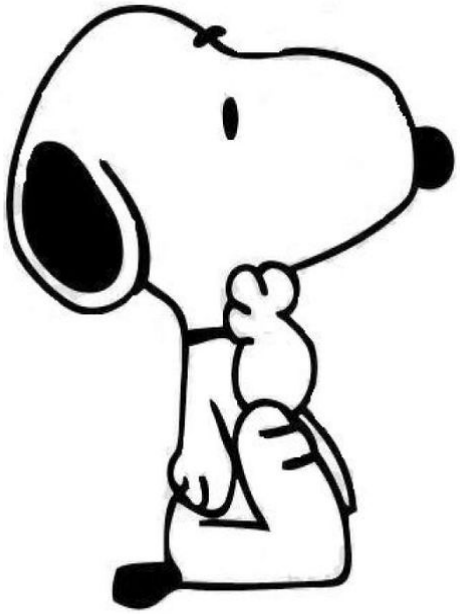
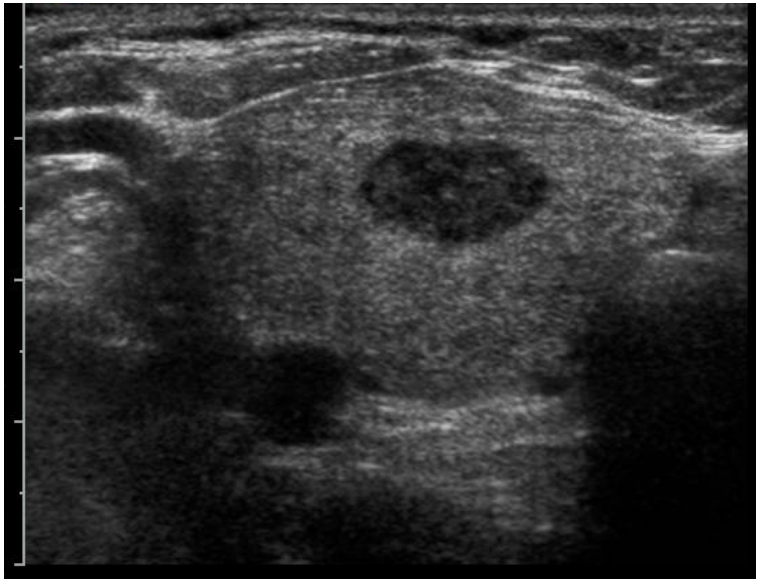
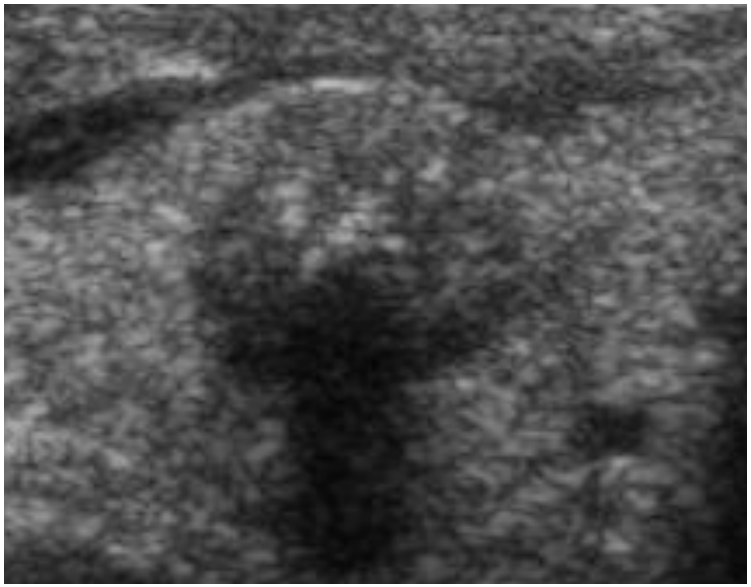
FNA is the best triage system for malignancy but we cannot perform FNA on all detected nodules



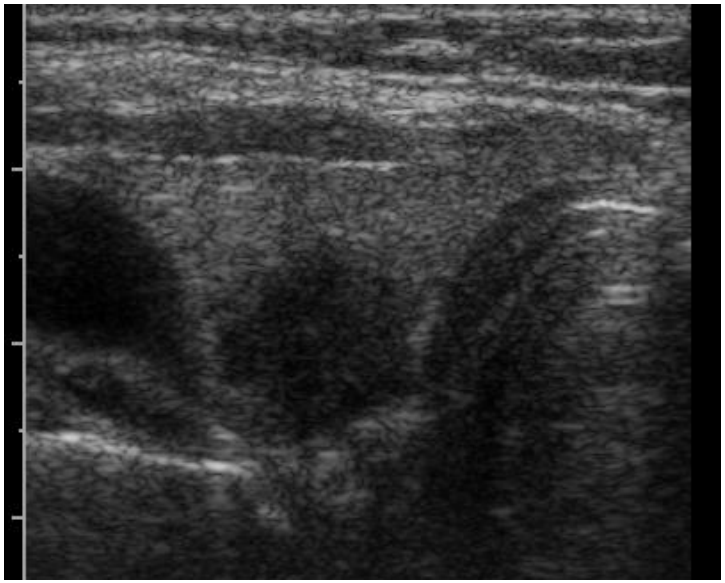
So, we are looking for a few established US findings that are predictive of malignancy

1. Marked Hypoechoic Appearance





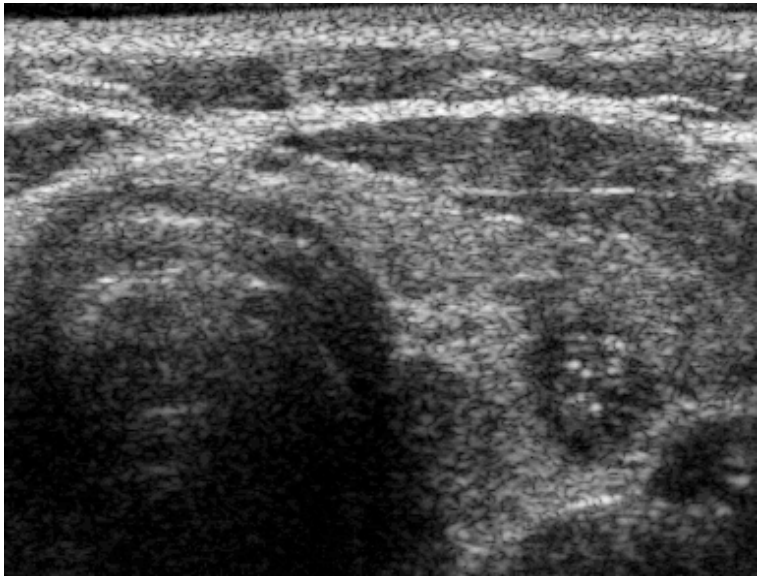
2. Irregular Margins



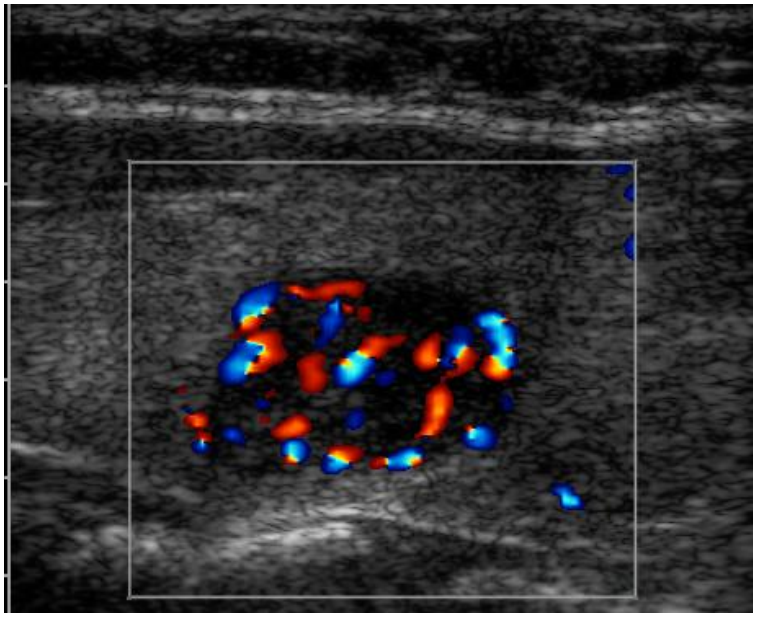
3. Microcalcifications

Papini E et al. JCE&M 2002
Kim et al. Radiology 2002

4.“More Tall than Wide Shape”



Kim et al. 2002



Intranodular Vascular Signals (?)

Unfortunately, none of these signs is both sensitive and specific

Grouping together different data could be more predictive than searching for a single feature

US Classification systems may be used to communicate risk of malignancy and indication to FNA

Tuscany landscape

An Ultrasonogram Reporting System for Thyroid Nodules Stratifying Cancer Risk for Clinical Management

- TIRADS 1: normal thyroid gland.
- TIRADS 2: benign conditions (0% malignancy).
- TIRADS 3: probably benign nodules (5% malignancy).
- TIRADS 4: suspicious nodules (5–80% malignancy rate).
  - 4a (malignancy between 5 and 10%)
  - 4b (malignancy between 10 and 80%).
- TIRADS 5: probably malignant nodules (malignancy 80%).
- TIRADS 6: category included biopsy proven malignant nodules.

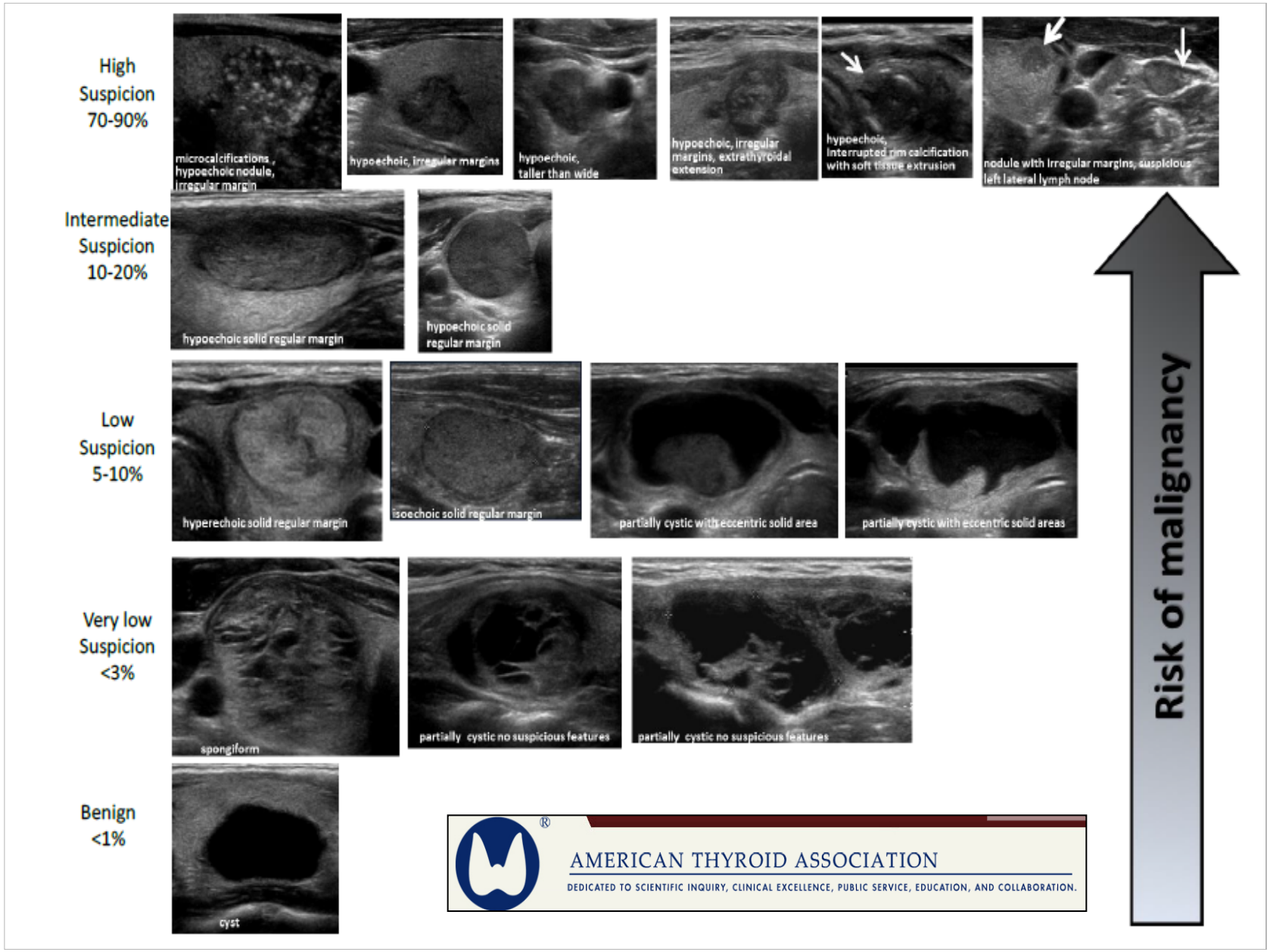
Horvath E et al. J Clin Endocrinol Metab, May 2009, 90(5):1748–1751

The practitioner should be competent in identifying the signs that allow a differentiation of thyroid nodules:

- **benign (U2)**
- **equivocal/indeterminate (U3)**
- **suspicious (U4)**
- **malignant (U5)**

In multinodular thyroids, the score for the most suspicious nodule should be recorded.

Clin Endocrinol 2014

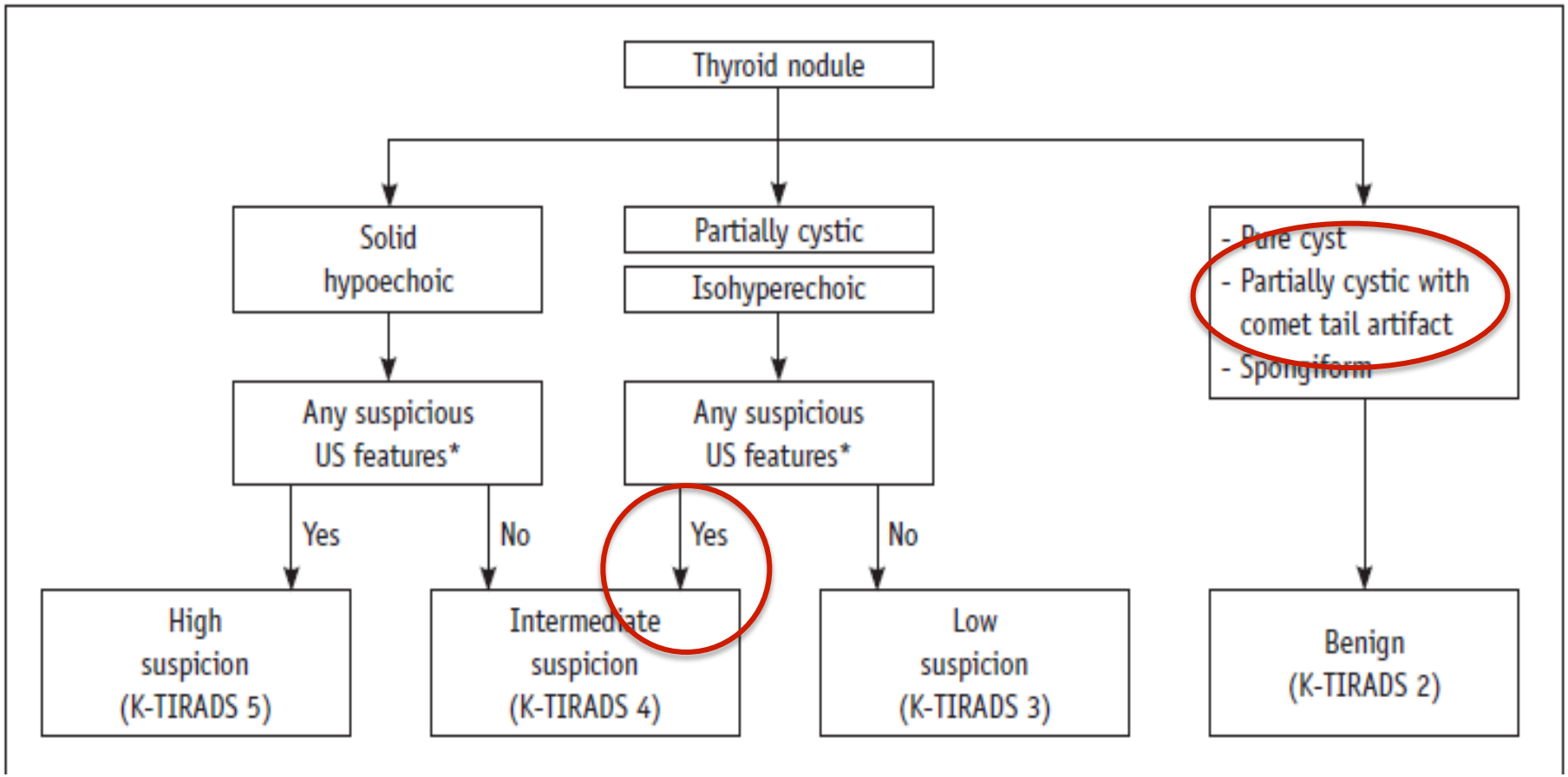


Thyroid, 2015

Review Article | Thyroid
http://dx.doi.org/10.3348/kjr.2016.17.3.370
pISSN 1229-6929 · eISSN 2005-8330
Korean J Radiol 2016;17(3):370-395

Korean Journal of Radiology
KJR

Ultrasonography Diagnosis and Imaging-Based Management of Thyroid Nodules: Revised Korean Society of Thyroid Radiology Consensus Statement and Recommendations



European Thyroid Association Guidelines for Ultrasound Malignancy Risk Stratification of Thyroid Nodules in Adults: The EU-TIRADS

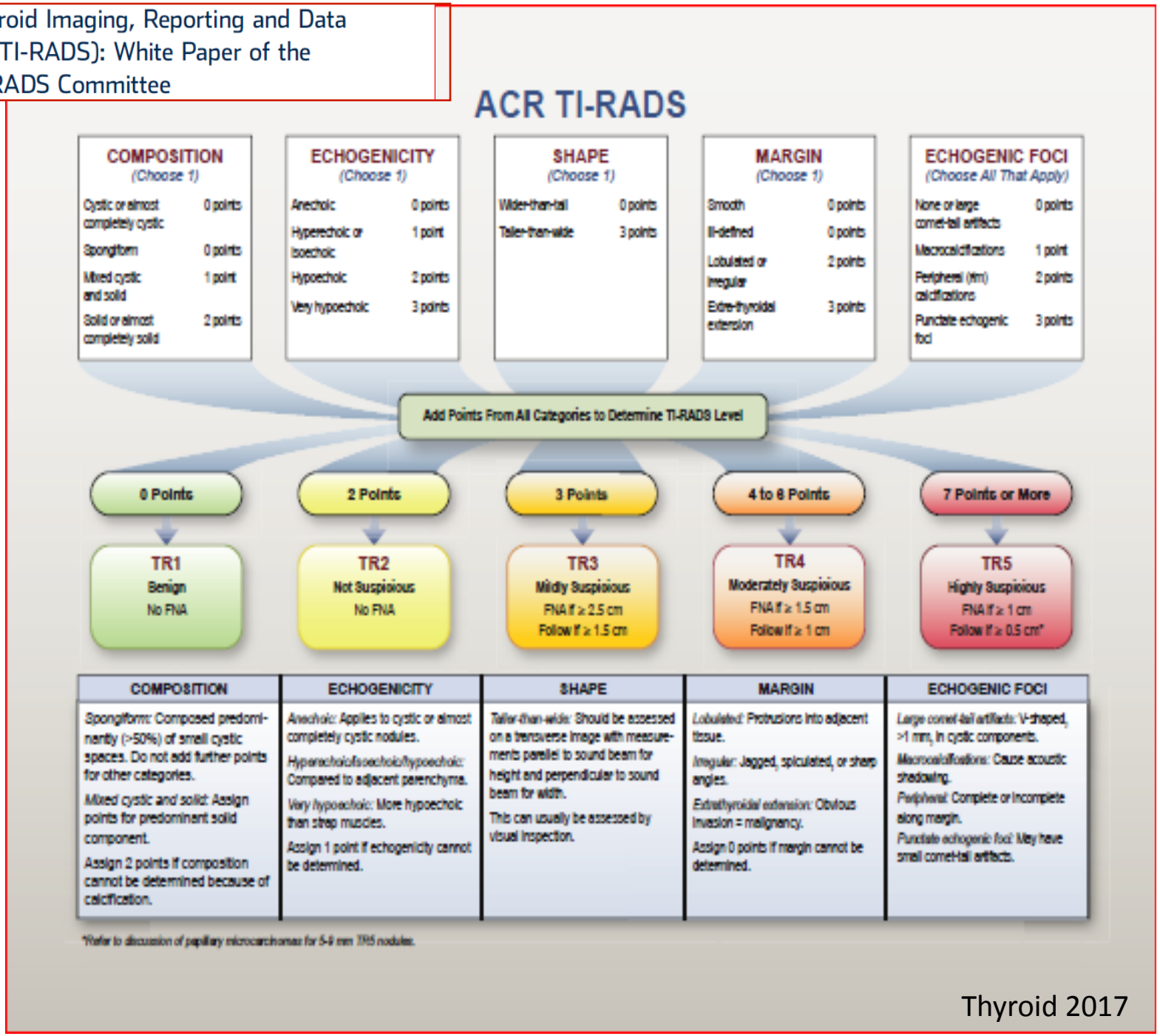
Gilles Russ[a] Steen J. Bonnema[b] Murat Faik Erdogan[c] Cosimo Durante[d] Rose Ngu[e] Laurence Leenhardt[a]

Category	US features	Malignancy risk, %
EU-TIRADS 1: normal	No nodules	None
EU-TIRADS 2: benign	Pure cyst Entirely spongiform	≅0
EU-TIRADS 3: low risk	Ovoid, smooth isoechoic/hyperechoic No features of high suspicion	2–4
EU-TIRADS 4: intermediate risk	Ovoid, smooth, mildly hypoechoic No features of high suspicion	6–17
EU-TIRADS 5: high risk	At least 1 of the following features of high suspicion: – Irregular shape – Irregular margins – Microcalcifications – Marked hypoechogenicity (and solid)	26–87

EU-TIRADS, European Thyroid Imaging Reporting and Data System; US, ultrasound.

Eur Thyroid J 2017

ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee



Thyroid 2017

2016 AACE/ACE/AME Thyroid US Classification

- Class 1. Low-risk US lesion (1%)*
- Class 2. Intermediate-risk US lesion (5 - 15%)
- Class 3. High-risk US lesion (50-90%)

*estimated risk of malignancy

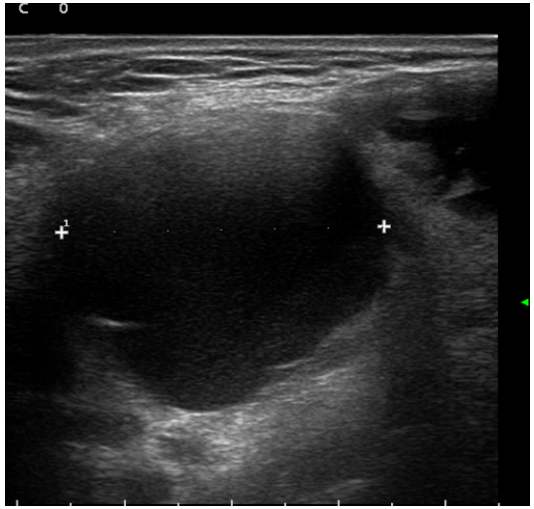
Gharib et al. Endocrine Practice, 2016

AACE Class 1. Low risk lesion
EU-TIRADS Class 1 and 2

- Pure cyst
- Mostly cystic nodule (fluid >80%) with reverberating artifacts, not associated with suspicious US signs
- Spongiform nodules.

Class 1. Ultrasound Low-Risk Thyroid Nodules

A



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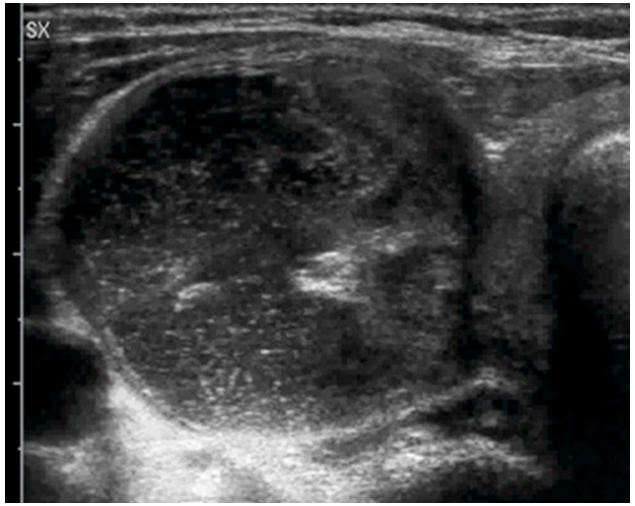

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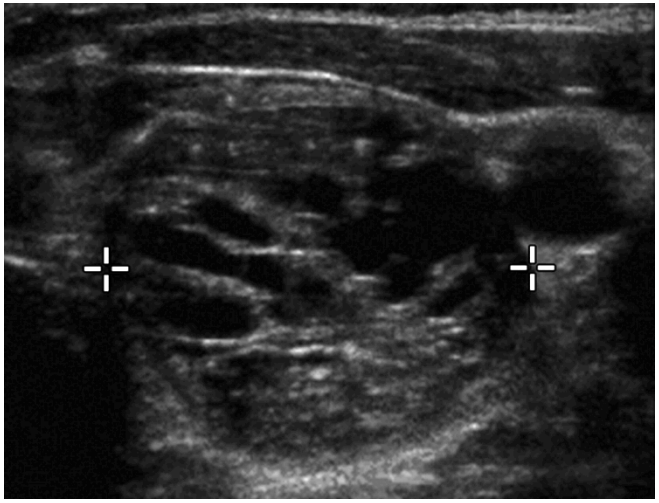


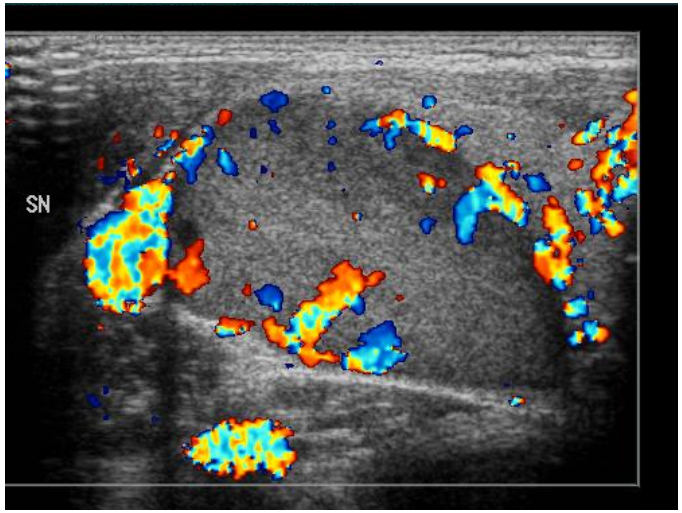
- A. Thyroid cyst
- B. Mostly cystic nodule with reverberating artifacts, not associated with suspicious signs
- C. Spongiform nodule

AACE Class 2. Intermediate risk lesion
EU TIRADS Class 3 and 4

- Slightly hypo- (vs thyroid tissue) or iso-echoic nodules with ovoid-to-round shape, not associated with suspicious findings
- May be present and increase risk:
  - intranodular vascularization
  - elevated stiffness
  - macro- or incomplete-rim calcifications
  - “indeterminate” hyperechoic spots.

Class 2. US Intermediate-Risk Thyroid Nodules

A



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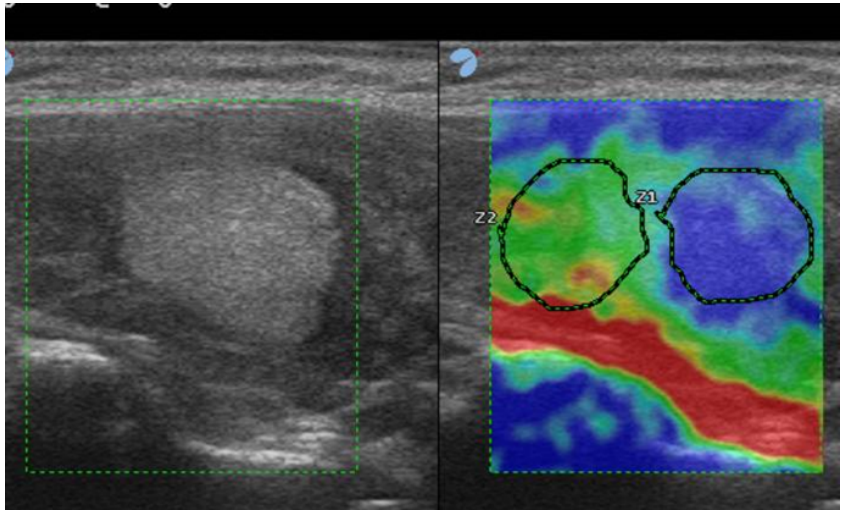

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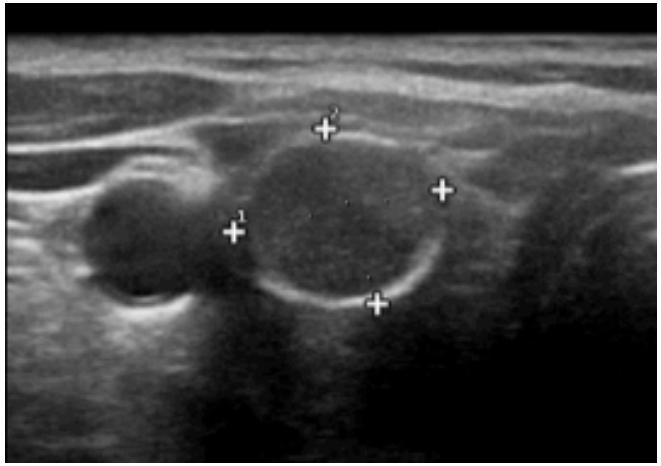

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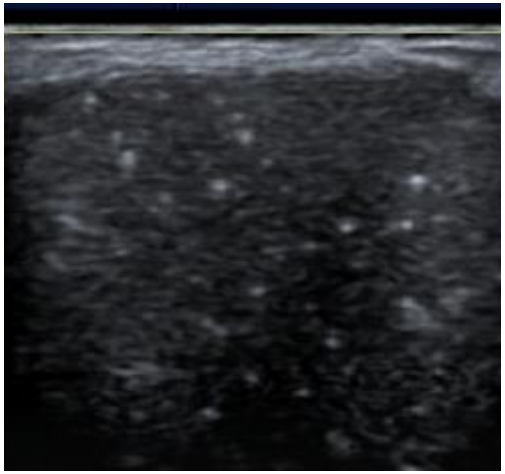


Slightly hypo- or iso-echoic nodules with no suspicious findings. May be present and increase risk: A. intranodular vascularization; B. elevated stiffness at elastography; C. incomplete rim calcification; D. indeterminate hyperechoic spots.

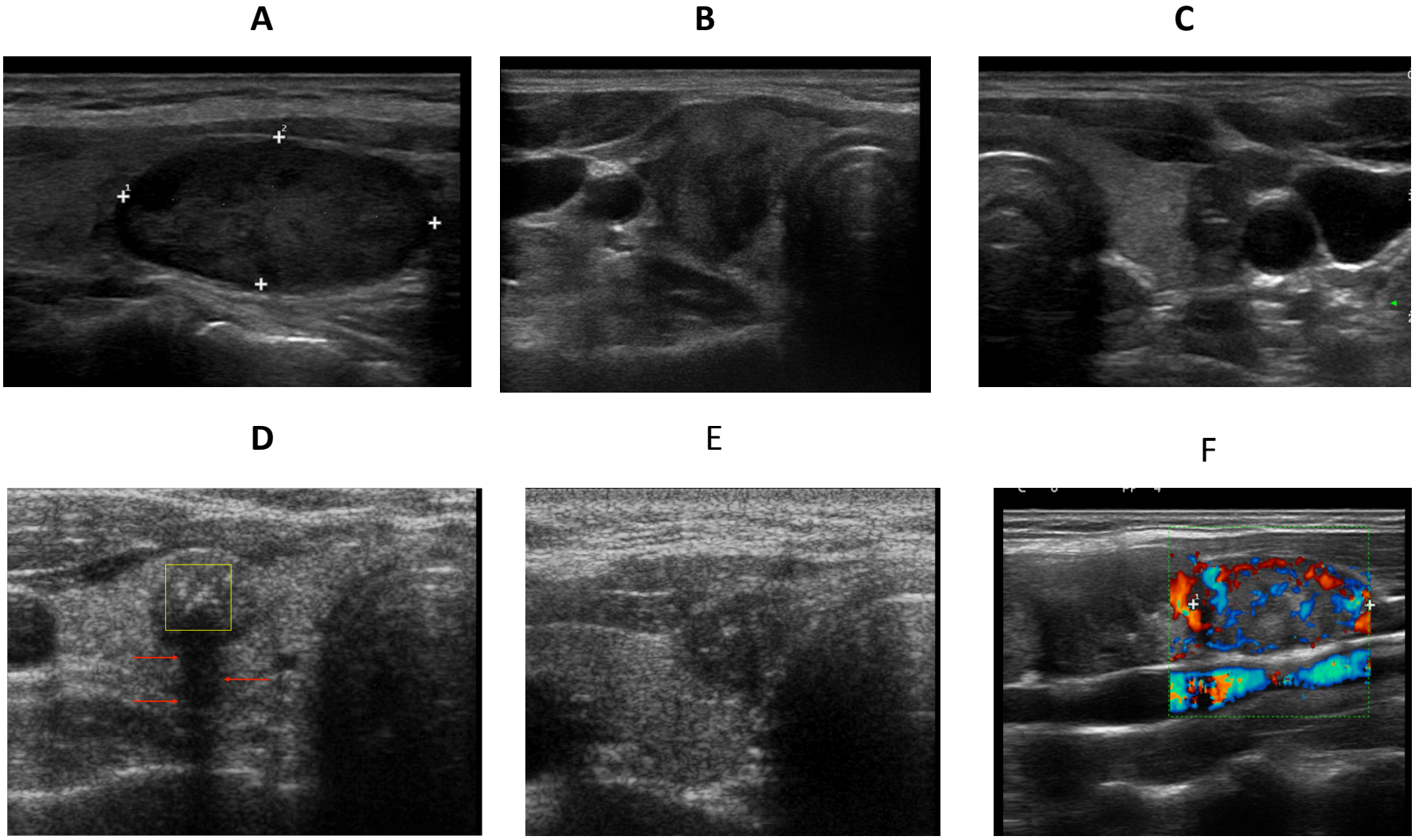
AACE Class 3. High risk lesion
EU-TIRADS Class 5

Nodules with one of the following:

- Marked hypoechogenicity (vs muscles)
- Spiculated or lobulated margins
- Microcalcifications
- Taller-than-wide shape
- Extra-thyroid growth or pathologic adenopathy

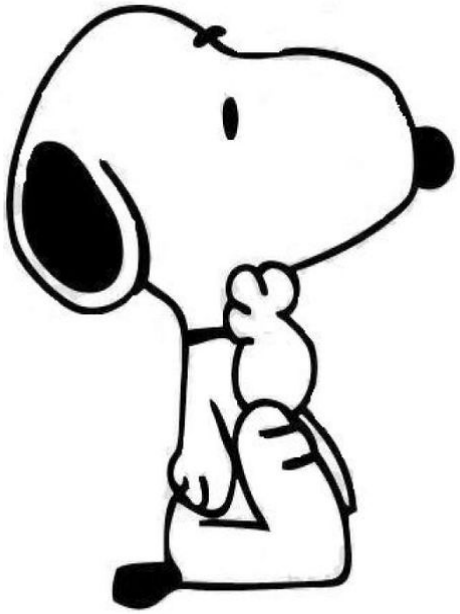
The expected risk of malignancy increases with the increase of the number of suspicious findings or with extra-thyroid spread.

Class 3. US High-Risk Thyroid Nodules



A. Marked hypoechogenicity; B. Spiculated or lobulated margins; C. More tall than wide shape; D. Microcalcifications; E. Extracapsular growth; F. Pathologic adenopathy.

Question # 1



Is the actual prevalence of malignancy similar to the expected rate in the different US classes?

Predictive Value of Malignancy of Thyroid Nodule Ultrasound Classification Systems: A Prospective Study

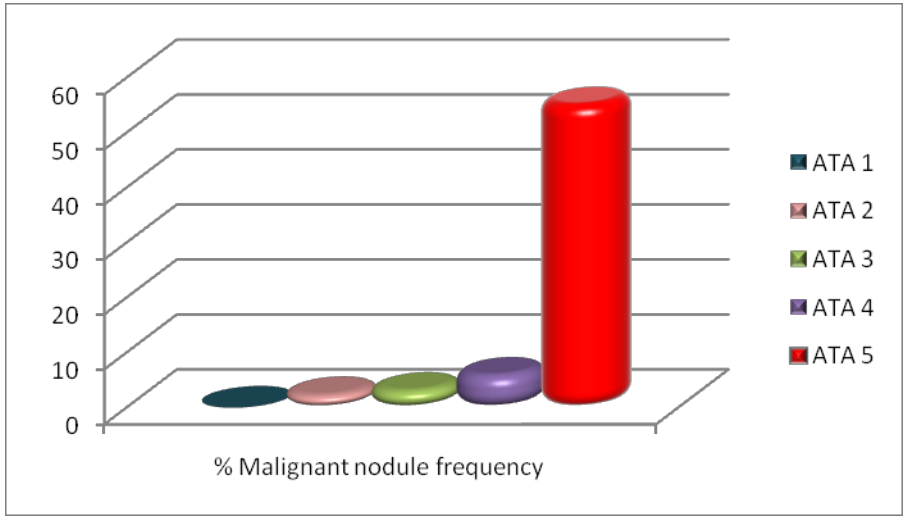
Agnese Persichetti,[1,2] Enrico Di Stasio,[3] Rinaldo Guglielmi,[1] Giancarlo Bizzarri,[4] Silvia Taccogna,[5] Irene Misischi,[1] Filomena Graziano,[1] Lucilla Petrucci,[1] Antonio Bianchini,[4] and Enrico Papini[1]

J Clin Endocrinol Metab, April 2018, 103(4):1359–1368

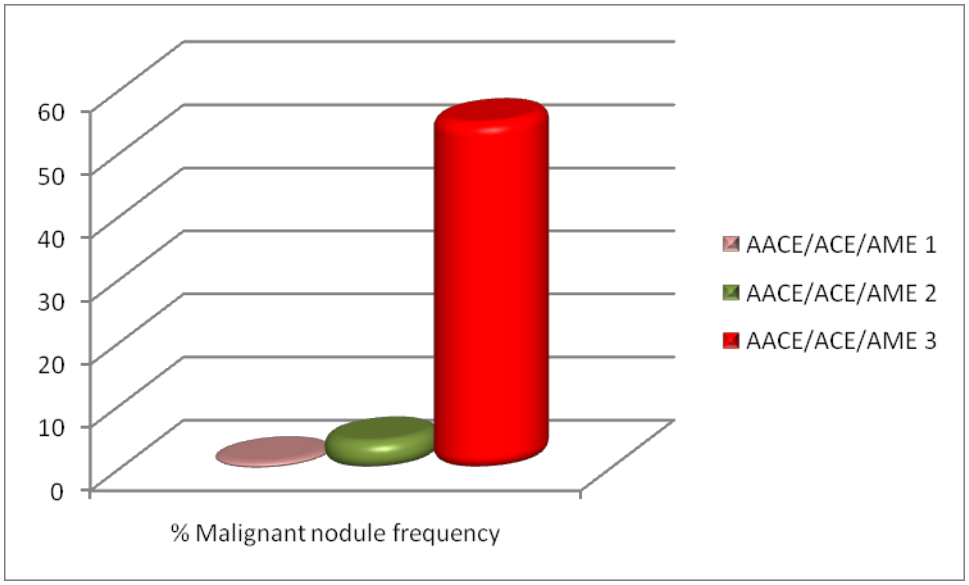
- prospective study
- 1100 thyroid nodules consecutively referred for FNA
- 987 nodules controlled with surgery (Bethesda IV-V-VI) or a repeat FNA after 12 months (Bethesda II and III)
- blinded real time scoring of three US classification systems by sonographers with specific experience
- independent statistical analysis.

Malignancy rate in the different classes of ATA & AACE/ACE/ AME US classification systems

ATA US classification



AACE/ACE/AME US classification



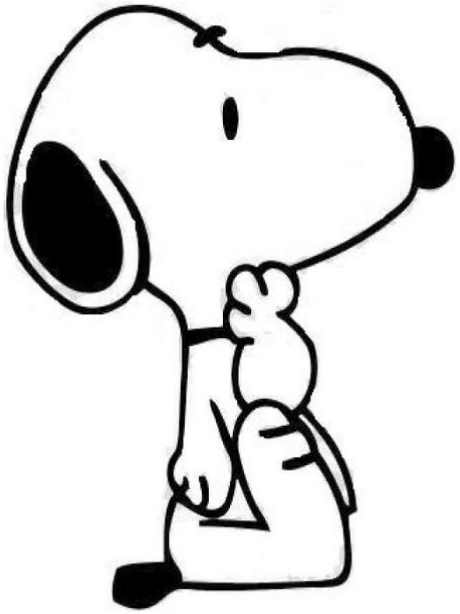
Persichetti et al., JCE&M 2018

Malignancy rate in the US Classes

BTA		ATA		AACE/ACE/AME	
Benign	2.8%	Benign	0.0%	Low-risk	1.1%
		Very low suspicion	2.2%		
		Low-suspicion	3.3%		
Indeterminate	10%	Indeterminate	5.8%	Intermediate risk	4.4%
Suspicious	58.3%	High suspicion	55.0%	High-risk	54.9%
Malignant	80.9%				

Persichetti et al., J Clin Endocrinol Metab. 2018

Question # 2



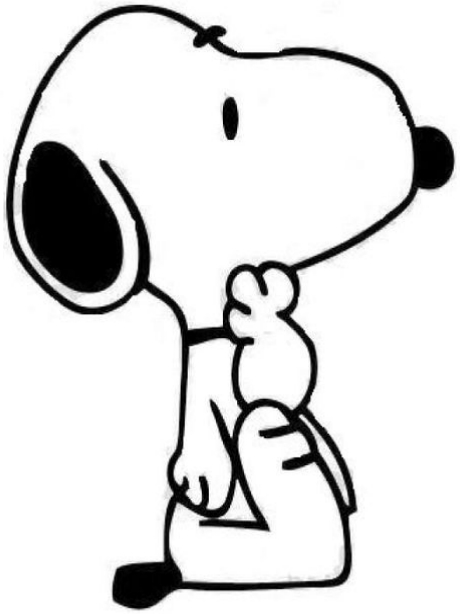
What is the diagnostic accuracy and the predictive value for malignancy of the higher risk classes?

US Stratification of the Risk of malignancy

	BTA	ATA	AACE/ACE/AME
Sensitivity	0.74	0.81	0.82
Specificity	0.92	0.87	0.87
Accuracy	0.89	0.86	0.86

Persichetti et al., J Clin Endocrinol Metab. 2018

Question # 3



How many FNA can we spare with the combined use of US classes and size cut-offs (and at what risk of missing malignancies)?

Outcomes of the combined use of ATA US classes and size cut-offs for thyroid FNA

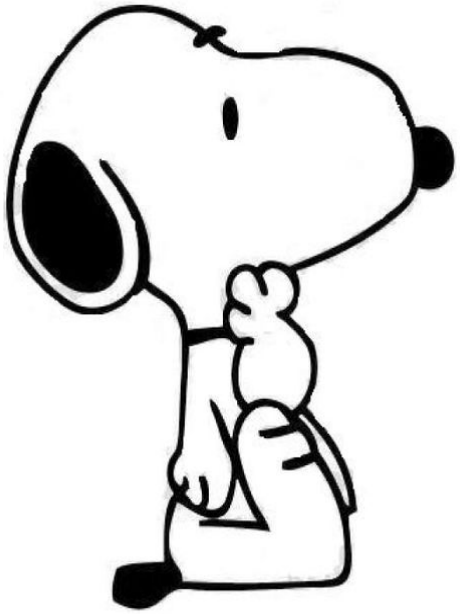
US Class	Size cut-off	Number	Spared FNA	Malignancy rate
Benign	no	43	100.0%	0.0%
Very low	≥ 20 mm	137	48.9%	0.0%
Low	≥ 15 mm	263	28.1%	0.8%
Indeterminate	≥ 10 mm	313	12.7%	0.7%
High risk	≥ 10 mm*	231	18.6%	25.5%

Outcomes of the combined use of AACE US classes and size cut-offs for thyroid FNA

US Class	Size cut-off	Number	Spared FNA	Malignancy rate
Low risk	> 20 mm	180	42.8%	0.0%
Intermediate risk	≥ 20 mm	572	45.3%	2.0%
High risk	≥ 10 mm*	235	18.7%	25.5%

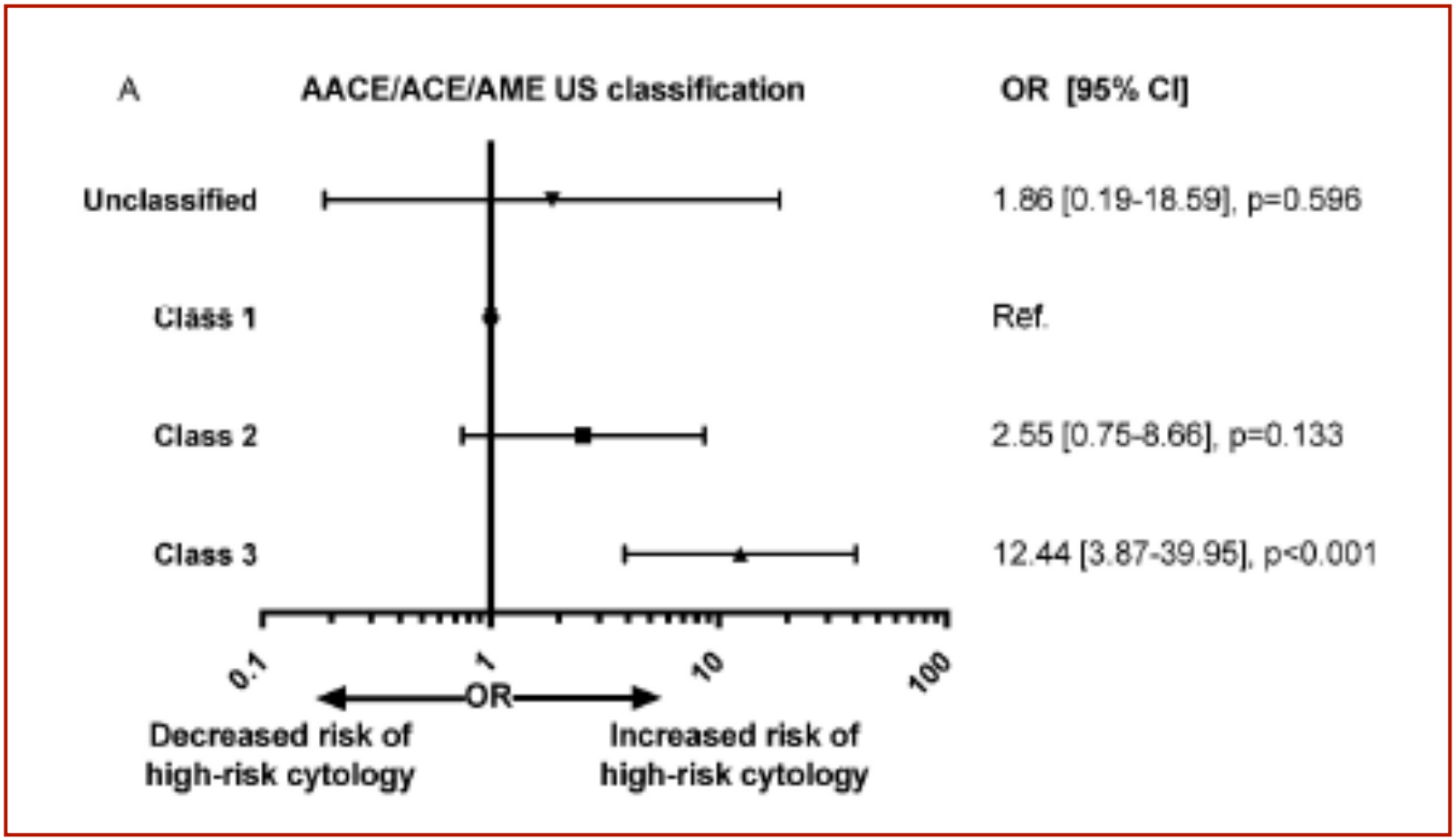
* Virtual data: the actual AACE size cut-off for FNA is 6 mm in the US high-risk class

Question # 4



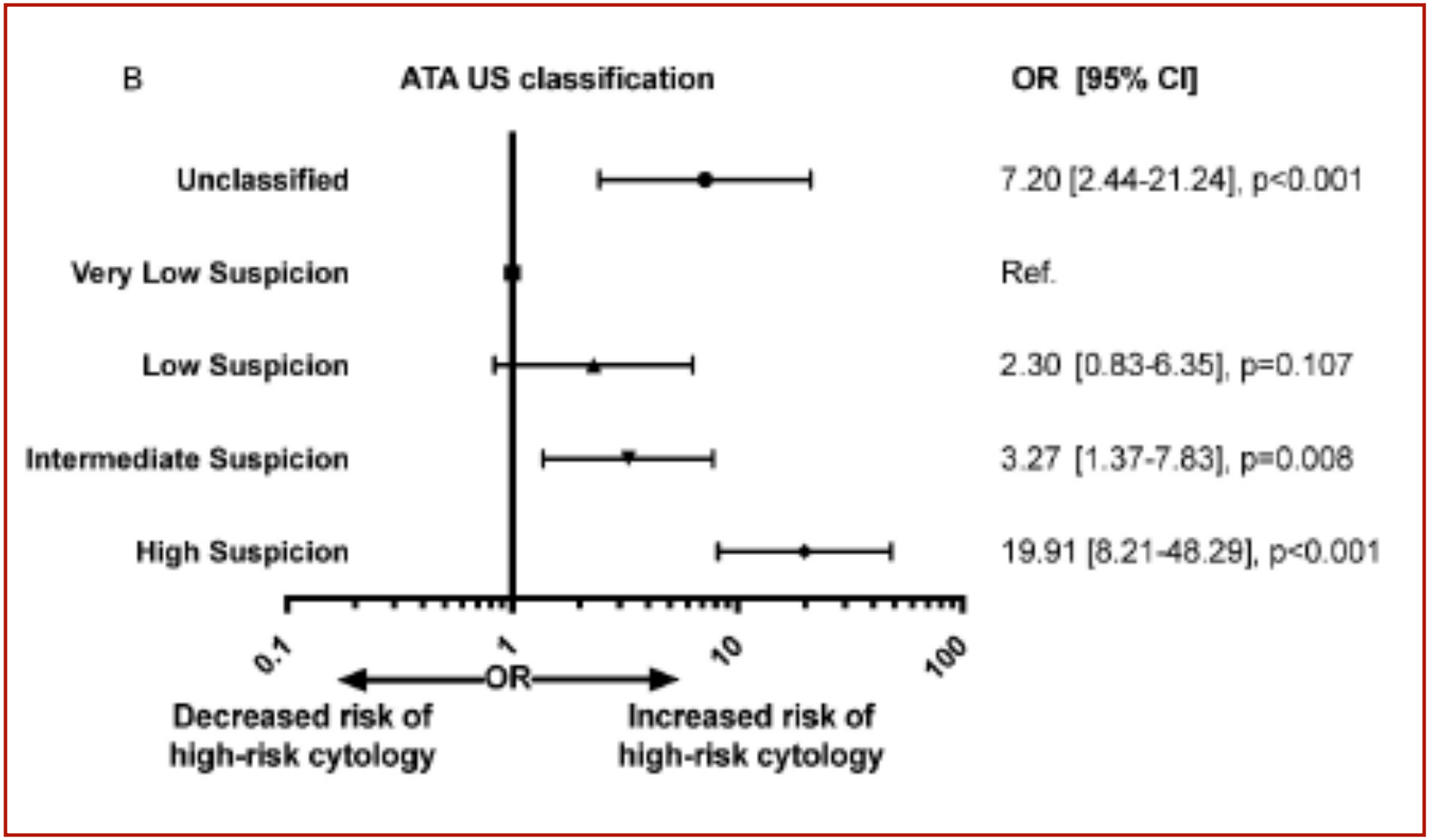
What about the recent white paper on the ACR-TIRADS US Classification System?

Odds ratio for cytological high risk nodules by AACE/ACE/AME US classification system



Pantano AL et al EJE 2018, in press

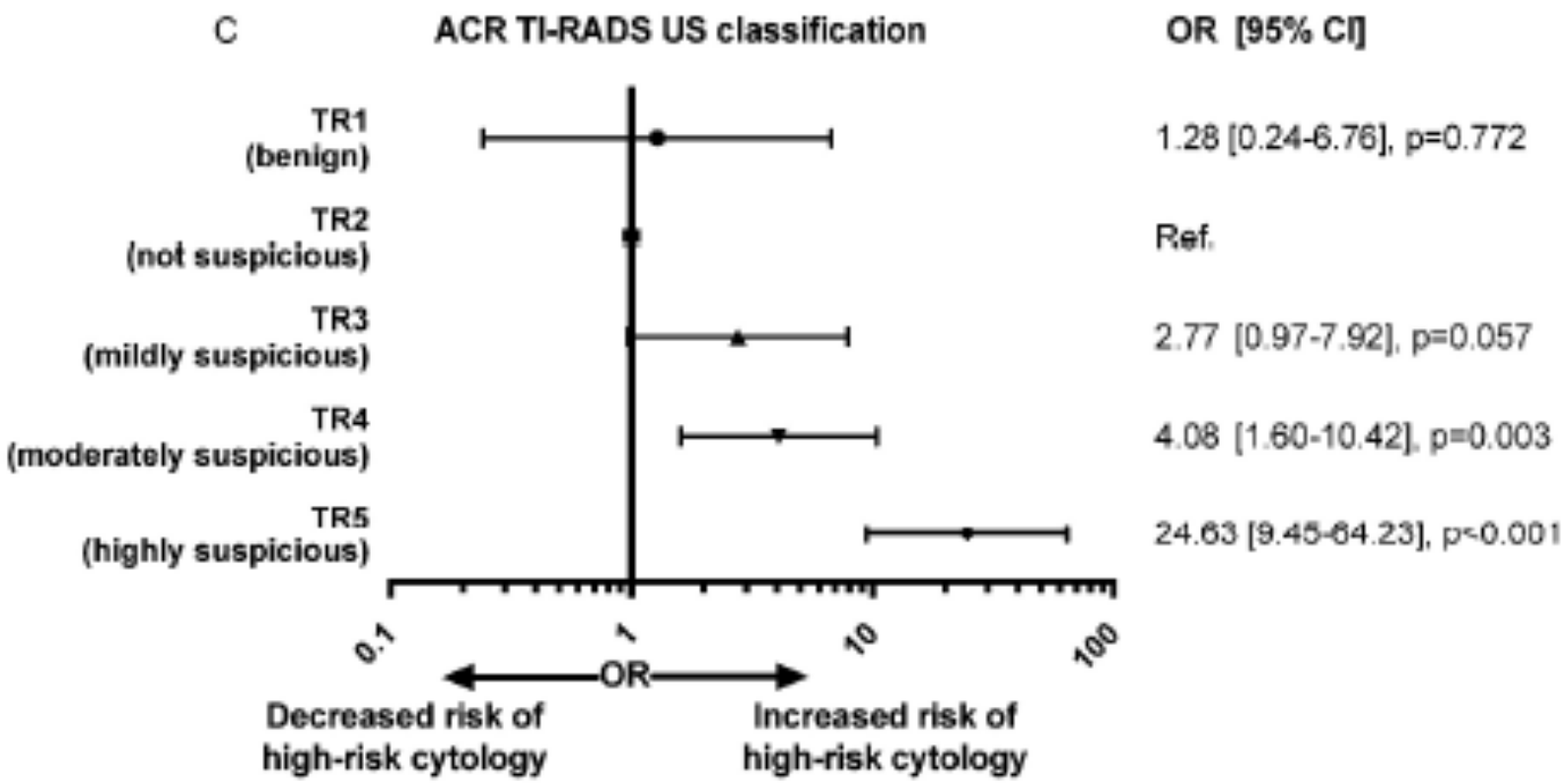
Odds ratio for cytological high risk nodules by ATA US classification system



*Unclassified nodules were 7 times more likely to be cytologically malignant than very low suspicion nodules.

Pantano AL et al EJE 2018, in press

Odds ratio for cytological high risk nodules by ACR TI-RADS US classification systems



Pantano AL et al EJE 2018, in press

Conclusions for clinical practice

NODULE VOCABULARY

Echogenicity	Anechoic Hyperechoic Isoechoic Hypoechoic - mildly - markedly	Shape	Oval Irregular: taller than wide and/or long taller than long
Halo	Present - Thin - Thick Absent	Content	Solid - Homogeneous - Heterogeneous Mixt - Mainly solid - Mainly cystic Cystic - Purely - With sediments Spongiform
Calcifications	Macrocalcifications - Central - Peripheral +/- disrupted Microcalcifications	Margins	Regular Blurred, ill-defined Irregular: - Microlobulated - Spiculated, angular
Capsular contact	Absent Present - <50% - >=50%	Other hyperechoic punctuations	Colloidal granulations Acoustic enhancement in cystic microcavities
		Vascularization	Absent (avascular) Mainly peripheral Mixt Mainly central Diffuse Resistive index

Similarities between the systems

- US features in favor of very low risk:

  Cystic, spongiform appearance

- US features in favor of low risk:

  Iso- or hyper-echoic without high-risk features

- US features in favor of intermediate risk:

  Hypoechoic and no high-risk features

- US features in favor of high risk:

  Solid and hypoechoic with any high-risk feature

Remaining problems

- Is the use of Doppler to be forgotten ?
- Should we use elastography ?
- Should we consider ‘indeterminate spots’?
- Should we remove marked hypoechogenicity ?
- Partially cystic nodules without suspicious features are always benign?
- Should we exclude isoechoic nodules from highly suspicious (follicular carcinoma may be isoechoic)?
- What is the strength of evidence of all this?

Use in Clinical Practice

- AACE-ACE-AME and EU-TIRADS are similar classification systems, easy to be used and with elevated predictivity
- ATA classification may pose some difficulty in every day practice and is missing a few relevant features
- ACR TI-RADS is a promising US classification, based on a numeric score of the main US features, and is well suited for electronic algorithms and a future “global classification”
- Indication to FNA should be always evaluated in the context of clinical setting and patient preferences.

ITNWG

- American College of Radiology
- AACE/ACE/AME
- American Thyroid Association
- Endocrine Society
- European Thyroid Association
- Latin American Society of Endocrinology
- South Korean Society Thyroid Radiologists

Thank You!