

Trattamenti percutanei nella patologia tiroidea : stato dell'arte e prospettive future

Milano, 2 Febbraio 2018

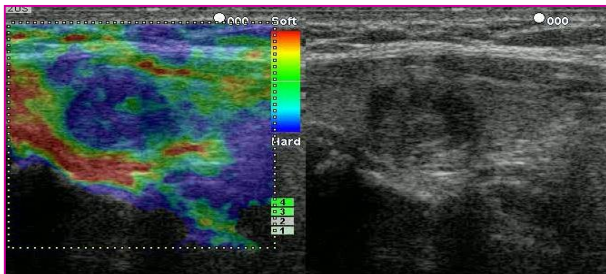


“La diagnostica ecografica nei noduli tiroidei: i criteri TIRADS ”

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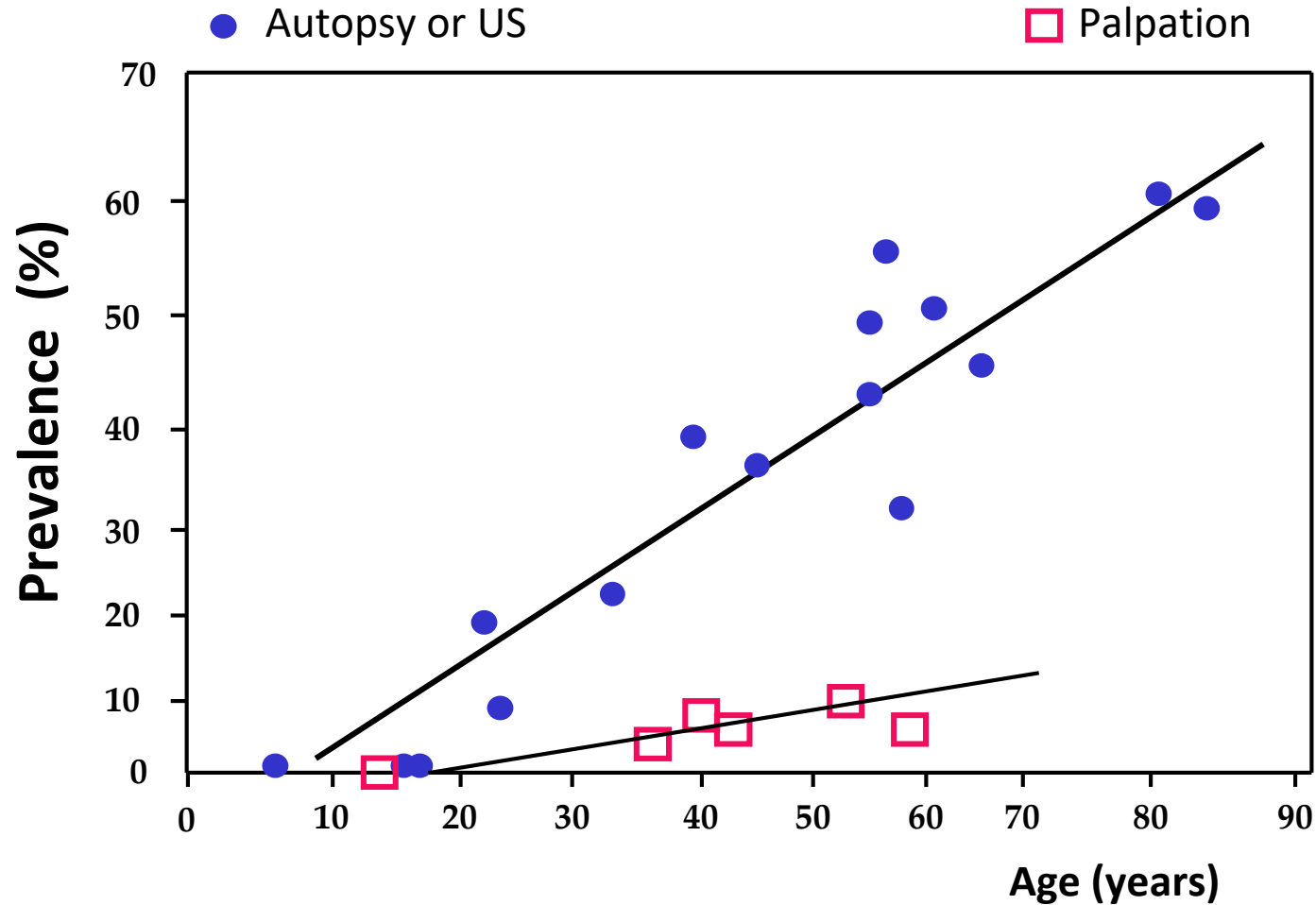
AGENDA



US features

TIRADS systems

Prevalence of thyroid nodules

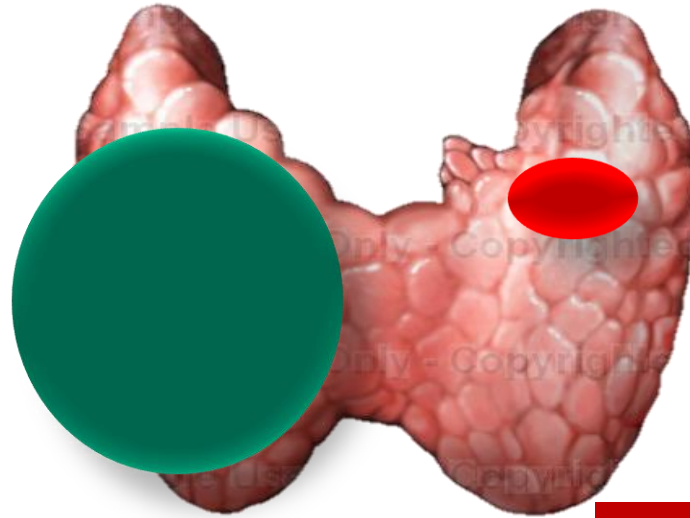


Thyroid Nodule



Large nodules

Pressure symptoms
Hyperthyroidism
Suspicion of cancer



Small nodules

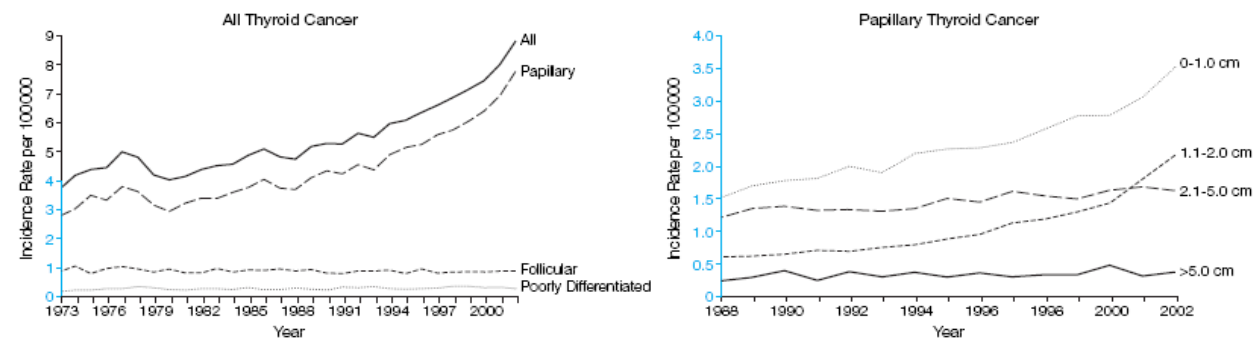
Suspicion of cancer

Thyroid cancer: annual incidence 1988-2002



INCREASING INCIDENCE OF THYROID CANCER IN THE UNITED STATES, 1973-2002

Figure 1. Trends in Incidence of Thyroid Cancer (1973-2002) and Papillary Tumors by Size (1988-2002) in the United States



Poorly differentiated indicates anaplastic and medullary cancers.

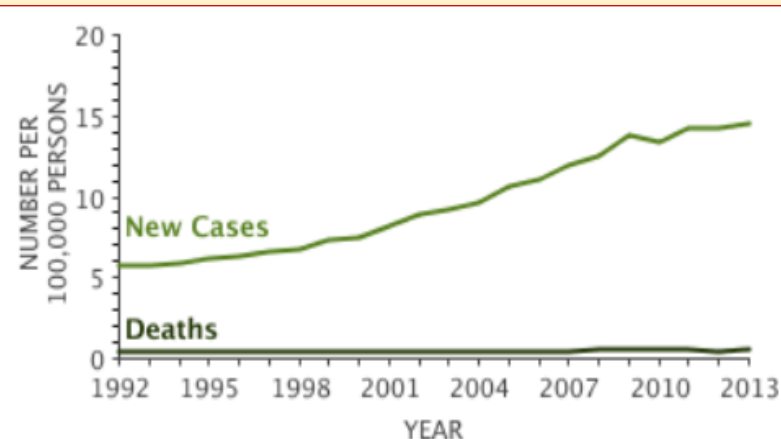
Davies et al, Jama 2006



NATIONAL CANCER INSTITUTE

Surveillance, Epidemiology, and End Results Program

Estimated New Cases in 2016	64,300
% of All New Cancer Cases	3.8%
Estimated Deaths in 2016	1,980
% of All Cancer Deaths	0.3%



Percent Surviving
5 Years

98.1%

2006-2012

Thyroid Nodules



AACE/AME/ETA Guidelines

American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association
Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules

© 2016 AACE.

These guidelines are based on *Endocr Pract.* 2016

Thyroid Ultrasound

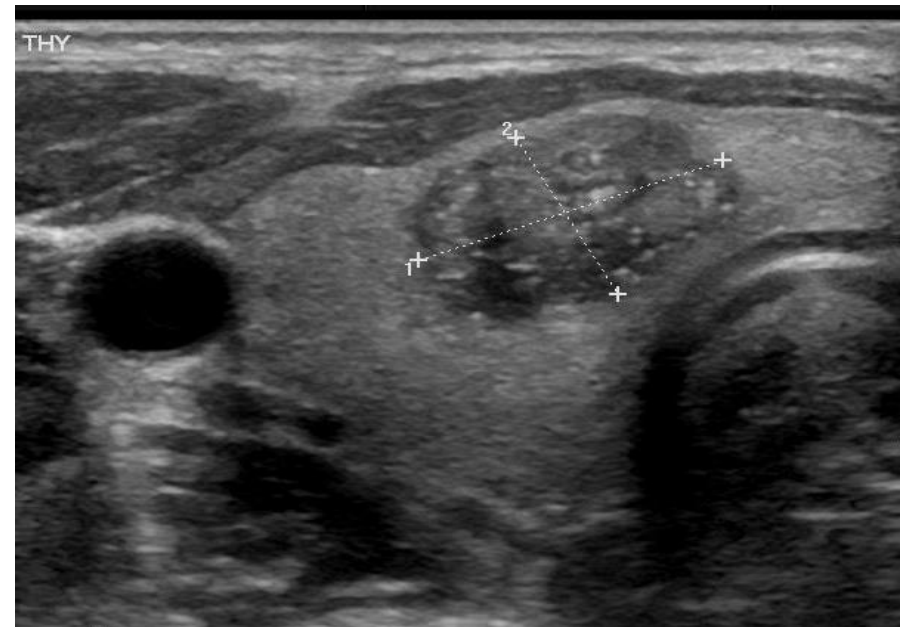
.....is the most valuable technique for evaluating thyroid nodule...

....is considered the gold standard for detecting nodular thyroid disease.....

DIAGNOSTIC IMPORTANCE



- ✓ Nodule size and position
- ✓ Suspicious US features
- ✓ Presence of other nodules/lymph-nodes
- ✓ Increases FNAC accuracy

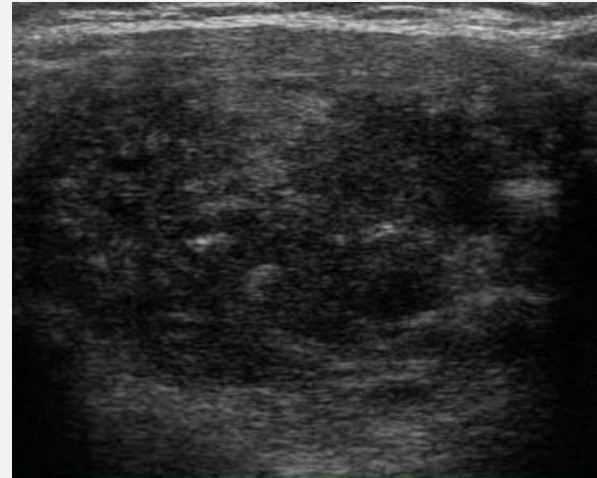


BENIGN



- Anechogenic / hyperechogenic
- Thin Halo
- Regular margins
- Egg shell calcifications

MALIGNANT



- Hypoechogenic
- Absent halo
- Irregular margins
- Microcalcifications
- Taller than wide

US Features



US features	CA (n=30)	BN (n=74)	P	Spe %	Sen %
Halo -	20	17	<0.001	77.0	66.6
Microcalcification	13	18	<0.05	75.6	54
Hypoechoic	20	38	<0.15	48.6	66.6

US features	CA (n=30)	BN (n=74)	P	Spe %	Sen %
Halo -/Microcalcification/Type III	5	2	<0.01	97.2	16.6
Halo -/Hypoech/ Type III	13	6	<0.001	91.8	43.3
Hypoech/Microcalcification/Type III	6	8	<0.20	89.1	20

Thyroid Nodule US: Considerations



1. Specificity of US increases at expense of sensitivity

Role of conventional ultrasonography and color flow Doppler in predicting malignancy in “cold” thyroid nodules.

Rago et al. Eur. J. Endocrinol, 1998

2. Echographic pattern useful to select nodules to submit to FNA

Risk of malignancy in nonpalpable thyroid nodules: predictive value of ultrasound and color Doppler features.

Papini et al. JCEM, 2002



New Sonographic Criteria for Recommending Fine-Needle Aspiration Biopsy of Nonpalpable Solid Nodules of the Thyroid

OBJECTIVE. The purpose of our study was to provide new sonographic criteria for fine-needle aspiration biopsy of nonpalpable solid thyroid nodules.

MATERIALS AND METHODS. Sonographic scans of 155 nonpalpable thyroid nodules in 132 patients were prospectively classified as having positive or negative findings. Sonographic findings that suggested malignancy included microcalcifications, an irregular or microlobulated margin, marked hypoechogenicity, and a shape that was more tall than it was wide. If even one of these sonographic features was present, the nodule was classified as positive (malignant). If a nodule had none of the features described, it was classified as negative (benign). The final diagnosis of a lesion as benign ($n = 106$) or malignant ($n = 49$) was confirmed by fine-needle aspiration biopsy and follow-up (>6 months) in 83 benign nodules, by fine-needle aspiration biopsy and surgery in 44 malignant and 15 benign lesions, and by surgery alone in five malignant and eight benign lesions. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated on the basis of our proposed classification method.

RESULTS. Of 82 lesions classified as positive, 46 were malignant. Of 73 lesions classified as negative, three were malignant. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy based on our sonographic classification method were 93.8%, 66%, 56.1%, 95.9%, and 74.8%, respectively.

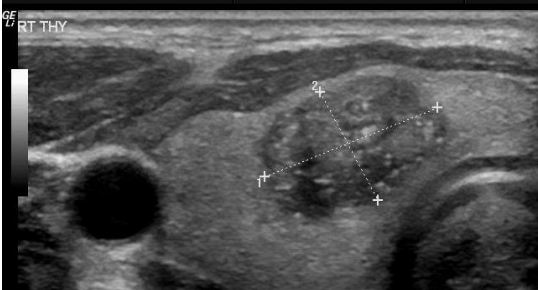
CONCLUSION. Considering the high level of sensitivity of our proposed sonographic classification, fine-needle aspiration biopsy should be performed on thyroid nodules classified as positive, regardless of palpability.

Suspicious US features



Society of Radiologists in Ultrasound Consensus Statement

Frates et al. Radiology 2005



US characteristics (references)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
Microcalcifications (1-5)	26-59	86-95	24-71	42-94
Hypoechoogenicity (2-5)	27-87	43-94	11-68	74-94
Irregular margins or no halo (2-5)	17-78	39-85	9-60	39-98
Solid (4-6)	69-75	53-56	16-27	88-92

1. Khoo et al. Head Neck 2002
2. Kim et al. Am J Roentgenol 2002
3. Papini et al. J Clin Endocrinol Metab

4. Rago et al. EJE 1998
5. Frates et al. Radiological Society of Noth America 2004
6. Frates et al. J Ultrasound Med 2003



Can vascularity at power Doppler US help predict thyroid malignancy?

1024 patients : 1083 thyroid nodules
Benign: 814, Malignant 269

Intranodular vascularity was frequently seen in benign nodules and no vascularity was more frequent in malignant nodules ($p < 0.0001$)

Conclusion: Vascularity was not useful for predicting thyroid malignancy.

Benign and malignant thyroid nodules: US differentiation--multicenter retrospective study.



PURPOSE:

To retrospectively evaluate the diagnostic accuracy of ultrasonographic (US) criteria for the depiction of benign and malignant thyroid nodules by using tissue diagnosis as the reference standard.

MATERIALS AND METHODS:

This study had institutional review board approval, and informed consent was waived. From January 2003 through June 2003, 8024 consecutive patients had undergone thyroid US at nine affiliated hospitals. A total of 831 patients (716 women, 115 men; mean age, 49.5 years +/- 13.8 [standard deviation]) with 849 nodules (360 malignant, 489 benign) that were diagnosed at surgery or biopsy were included in this study. Three radiologists retrospectively evaluated the following characteristics on US images: nodule size, presence of spongiform appearance, shape, margin, echotexture, echogenicity, and presence of microcalcification, macrocalcification, or rim calcification. A chi(2) test and multiple regression analysis were performed. Sensitivity, specificity, and positive and negative predictive values were obtained.

RESULTS:

Statistically significant ($P < .05$) findings of malignancy were a taller-than-wide shape (sensitivity, 40.0%; specificity, 91.4%), a spiculated margin (sensitivity, 48.3%; specificity, 91.8%), marked hypoechogenicity (sensitivity, 41.4%; specificity, 92.2%), microcalcification (sensitivity, 44.2%; specificity, 90.8%), and macrocalcification (sensitivity, 9.7%; specificity, 96.1%). The US findings for benign nodules were isoechogenicity (sensitivity, 56.6%; specificity, 88.1%; $P < .001$) and a spongiform appearance (sensitivity, 10.4%; specificity, 99.7%; $P < .001$). The presence of at least one malignant US finding had a sensitivity of 83.3%, a specificity of 74.0%, and a diagnostic accuracy of 78.0%. For thyroid nodules with a diameter of 1 cm or less, the sensitivity of microcalcifications was lower than that in larger nodules (36.6% vs 51.4%, $P < .05$).

CONCLUSION:

Shape, margin, echogenicity, and presence of calcification are helpful criteria for the discrimination of malignant from benign nodules; the diagnostic accuracy of US criteria is dependent on tumor size.



TIRADS Systems

TIRADS: thyroid imaging reporting and data system

10 US patterns with their malignancy risk and thyroid imaging reporting and data system (TIRADS) category

Description of US pattern	US patterns	Malignancy	TIRADS
Anechoic with hyperechoic spots, nonvascularized lesion.	Colloid type 1		
Nonencapsulated, mixed, nonexpansile, with hyperechoic spots, vascularized lesion, "grid" aspect (spongiform nodule).	Colloid type 2	0%	TIRADS 2: benign findings
Nonencapsulated, mixed with solid portion, isoechogenic, expansile, vascularized nodule with hyperechoic spots.	Colloid type 3		
Hyper, iso, or hypoechoic, partially encapsulated nodule with peripheral vascularization, in Hashimoto's thyroiditis.	Hashimoto pseudo-nodule	<5%	TIRADS 3: probably benign
Solid or mixed hyper, iso, or hypoechoic nodule, with a thin capsule.	Simple neoplastic pattern	5–10%	TIRADS 4A: undetermined
Hypoechoic lesion with ill-defined borders, without calcifications.	de Quervain pattern		
Hyper, iso, or hypoechoic, hypervascularized, encapsulated nodule with a thick capsule, containing calcifications (coarse or microcalcifications).	Suspicious neoplastic pattern		
Hypoechoic, nonencapsulated nodule, with irregular shape and margins, penetrating vessels, with or without calcifications	Malignant pattern A	10–80%	TIRADS 4B: suspicious
Iso or hypoechoic, nonencapsulated nodule with multiple peripheral microcalcifications and hypervascularization.	Malignant pattern B	>80%	TIRADS 5: consistent with malignancy
Nonencapsulated, isoechoic mixed hypervascularized nodule with or without calcifications, without hyperechoic spots.	Malignant pattern C Cancer, confirmed by previous biopsy	100%	TIRADS 6: malignant



TIRADS Systems

10 US patterns with their malignancy risk and thyroid imaging reporting and data system (TIRADS) category

FNAB	TIRADS 2	TIRADS 3	TIRADS 4	TIRADS 5
Benign	100 %	85,9 %	55 %	10,4 %
Cancer	0 %	3,4 %	14 %	86,5 %

Thyroid imaging reporting and data system for US features of nodules: a step in establishing better stratification of cancer risk.



PURPOSE:

To develop a practical thyroid imaging reporting and data system (TIRADS) with which to categorize thyroid nodules and stratify their malignant risk.

MATERIALS AND METHODS:

The institutional review board approved this retrospective study, and the requirement to obtain informed consent for the review of images and records was waived. From May to December 2008, ultrasonographically (US)-guided fine-needle aspiration biopsy (FNAB) was performed in 3674 focal thyroid nodules in 3414 consecutive patients. The study included the 1658 thyroid nodules (≥ 1 cm in maximum diameter at US) in 1638 patients (1373 women, 265 men) for which pathologic diagnosis or follow-up findings were available. Univariate and multivariate analyses with generalized estimating equations were performed to investigate the relationship between suspicious US features and thyroid cancer. A score for each significant factor was assigned and multiplied by the β coefficient obtained for each significant factor from multivariate logistic regression analysis. Scores for each significant factor were then added, resulting in an equation that fitted the probability of malignancy in thyroid nodules. The authors evaluated the fitted probability by using a regression equation; the risk of malignancy was determined according to the number of suspicious US features.

RESULTS:

The following US features showed a significant association with malignancy: solid component, hypoechogenicity, marked hypoechogenicity, microlobulated or irregular margins, microcalcifications, and taller-than-wide shape. As the number of suspicious US features increased, the fitted probability and risk of malignancy also increased. Positive predictive values according to the number of suspicious US features were significantly different ($P < .001$).

CONCLUSION:

Risk stratification of thyroid malignancy by using the number of suspicious US features allows for a practical and convenient TIRADS.

Risk stratification of thyroid nodules on ultrasonography with the French TI-RADS

Table 2. Summary of the French TI-RADS categorization system

TI-RADS classification	Meaning	Main features	Risk of malignancy (%)
1	Normal thyroid gland	Absence of nodule	
2	Effectively certainly benign	Simple cyst	≈ 0
		Septated cyst	
		Isolated macrocalcification	
3	Very probably benign	Isoechoic spongiform nodule	0.25
		Oval-shaped	
		Regular borders	
4A	Suspicious nodules; low risk of malignancy	Isoechoic or hyperechoic	6
		Oval-shaped	
		Regular borders	
4B	Suspicious nodules; high risk of malignancy	Mildly hypoechoic	69
		One or two features of high suspicion	
		Taller-than-wide/taller-than-long	
		Spiculated or lobulated borders	
		Marked hypoechogenicity	
		Microcalcifications	≈ 100
5	Effectively certainly malignant nodules	High stiffness on elastography	
		Three to five features of high suspicion and/or presence of a lymph node suspected to contain metastasis of thyroid origin	

Risk of malignancy corresponds to the positive predictive value of each category.

TI-RADS, thyroid imaging reporting and database system.



TIRADS Systems and Risk of malignancy

AACE/ACE-AME	ATA	BTA
1 Low-risk lesion - Cysts (fluid component >80%) - Mostly cystic nodules with reverberating artifacts and not associated with suspicious US signs - Isoechoic spongiform nodules, either confluent or with regular halo	Benign Purely cystic nodules (no solid component) Very low suspicion Spongiform or partially cystic nodules without any of the US features described in low-, intermediate- or high-suspicion patterns Low suspicion Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid area <u>without</u> : - Microcalcifications - Irregular margin - Extrathyroidal extension - Taller than wide shape	U1 Normal U2 Benign A. Halo, isoechoic, mildly hyperechoic B. Cystic change ± ring-down sign (colloid) C. Microcystic/spongiform - D-E. Peripheral eggshell calcification F. Peripheral vascularity
2 Intermediate-risk thyroid lesion Slightly hypoechoic (vs. thyroid tissue) or isoechoic nodules, with ovoid-to-round shape, smooth or ill-defined margins May be present: - Intranodular vascularization - Elevated stiffness at elastography, - Macro or continuous rim calcifications - Indeterminate hyperechoic spots	Intermediate suspicion Hypoechoic solid nodule with smooth margins <u>without</u> : - Microcalcifications - Extrathyroidal extension - Or taller than wide shape	U3 Indeterminate/equivocal A. Homogeneous, markedly hyperechoic, solid, halo (follicular lesion) B. Hypoechoic (?), equivocal echogenic foci, cystic change (irregular) C. Mixed/central vascularity
3 High-risk thyroid lesion (50-90%) Nodules <u>with at least 1</u> of the following features: - Marked hypoechogenicity (vs. prethyroid muscles) - Spiculated or lobulated margins - Microcalcifications - Taller-than-wide shape (AP>TR) - Extrathyroidal growth - Pathologic adenopathy Expected risk of malignancy in accordance with the presence of 1 or more suspicious findings.	High suspicion Solid hypoechoic nodule or solid hypoechoic component of partially cystic nodule <u>with 1 or more</u> of the following features: - Irregular margins (infiltrative, microlobulated) - Microcalcifications - Taller than wide shape - Rim calcifications with small extrusive soft tissue component - Evidence of extrathyroidal extension	U4 suspicious A. Solid, hypoechoic (cf. thyroid) B. Solid, very hypoechoic (cf. strap muscle) C. Disrupted peripheral calcification, hypoechoic D. Lobulated outline U5 Malignant A. Solid, hypoechoic, lobulated/irregular outline, microcalcification (papillary carcinoma?) B. Solid, hypoechoic, lobulated/irregular outline, globular calcification (medullary carcinoma?) C. Intranodular vascularity D. Shape tall>wide (AP>TR) E. Characteristic associated lymphadenopathy

	Category	US feature	Malignancy risk, %
5	High suspicion	Solid hypoechoic nodule with any of 3 suspicious US features ^b	>60
4	Intermediate suspicion	Solid hypoechoic nodule without any of 3 suspicious US features ^b or Partially cystic or isohyperechoic nodule with any of 3 suspicious US features ^b	15–50
3	Low suspicion	Partially cystic or isohyperechoic nodule without any of 3 suspicious US features ^b	3–15
2	Benign ^d	Spongiform Partially cystic nodule with comet tail artifact Pure cyst	<3 <1
1	No nodule	-	-

Ka Hee Yi Endocrinol Metab. 2016

TIRADS Systems: similarity



US features in favor

- very low risk: Cystic, spongiform, isoechoic appearance
- Low risk: Isoechogenicity, hyperechogenicity with no feature of high suspicion OR partially cystic
- Intermediate risk: Solid and hypoechoic and no feature of high suspicion
- High risk: Solid and hypoechoic and any of 3 features of high suspicion



- Controversial value in the literature
- Not Retained in ATA and Korean systems
- Feeble added value to B mode
- BUT, in isoechoic solid nodules > 20mm:
 - Central vascularity increases a little the risk of carcinoma
 - Peripheral vascularity lowers the risk of follicular carcinoma



2016 ATA Guidelines: consideration

Marked hypoechogenicity

hypoechogenicity have been excluded.

More than half of benign nodules are hypoechoic in US especially when their size is small which makes nodule hypoechogenicity less specific

Vascularization

Increased nodular vascularity did not show significant association with malignancy.

The increased vascularity can be related to the cellular proliferation in a neoplastic condition.

Intranodular vascularity is useful for differentiating benign and malignant thyroid nodules.

Benign nodules with hyperplastic follicular proliferation can also show increased vascularity.

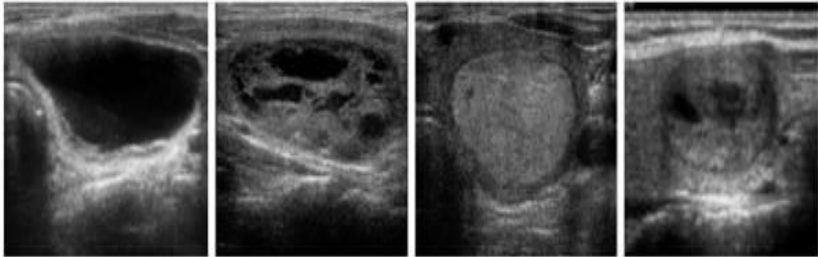
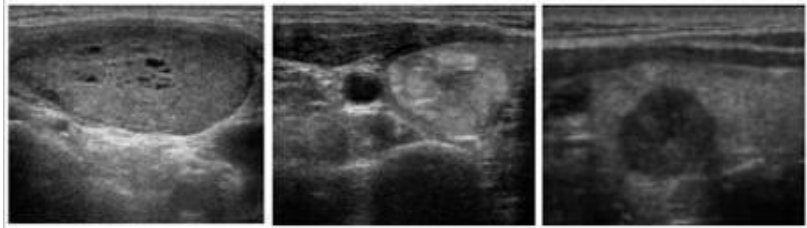
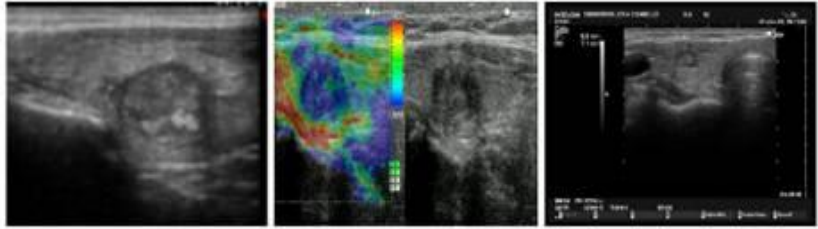
Therefore, removing increased vascularity from the suspicious features by the ATA guidelines

Elastonography

Elastosonography have been excluded

Echographic Classification Of thyroid Nodules According to the Risk of Malignancy (ECON-ARM)

Teresa Rago, Maria Scutari, Francesco Latrofa, Ivo Marchetti, Rossana Romani, Agnese Proietti, Fulvio Basolo, Paolo Vitti

ECON-ARM	US Features	Example	Risk Of Malignancy
0-1	Cystic, spongiform, iso-hyperechoic, complete halo sign, macrocalcifications, perinodular vascularization		Low
2-3	iso-hypoechoic with one of US pattern suggestive of malignancy,		Intermediate
4-5	hypoechoic, with 3 or more US pattern suggestive of malignancy, extrathyroid extension, presence of lymph nodes		High

Echographic Classification Of thyroid Nodules According to the Risk of Malignancy (ECON-ARM)

Teresa Rago, Maria Scutari, Francesco Latrofa, Ivo Marchetti, Rossana Romani, Agnese Proietti, Fulvio Basolo, Paolo Vitti

		TIR-1		TIR-2	TIR-3		TIR-4	TIR-5
		1	1C		A	B		
ECON-ARM	n° %							
0-1	493 66.5	36	27	374	45	11	0	0
2-3	208 28.0	16	1	127	42	13	5	4
4-5	40 5.4	1	/	3	2	4	9	22
Total	741	81		503	89	28	14	26

Cat 0-1: none had TIR 4-5 cytology.

Cat 2-3: 4.3% had TIR 4-5 cytology.

Cat 4-5: 77.5% had TIR 4-5 cytology

		TIR-4	TIR-5
ECON-ARM	n°		
0-1	493	0	0
2-3	208	5	4
4-5	40	9	22
Total	741	16	26

Echographic Classification Of thyroid Nodules According to the Risk of Malignancy (ECON-ARM)

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Histology of 126 nodules according to FNA cytology

Cytology	Tx n.	Ca n.	BN n.
Thy 1 (n=53)	1	/	1
Thy 2 (n=503)	32	7 (21%)	25
Thy 3A (n=89)	37	16 (42,8%)	21
Thy B (n=28)	21	6 (28,5)	15
Thy 4 (n=14)	13	12 (92,3%)	1°
Thy 5 (n=26)	22	22 (100%)	0

° Adenoma with foci of PTC

Conclusions: this new US classification of the risk of malignancy in the thyroid nodule allows to establish the strength of the indication to perform FNA in each thyroid nodule



1. Risk Stratification of Thyroid Nodules on Ultrasonography: Current Status and Perspectives.

Ha EJ et al. Thyroid 2017

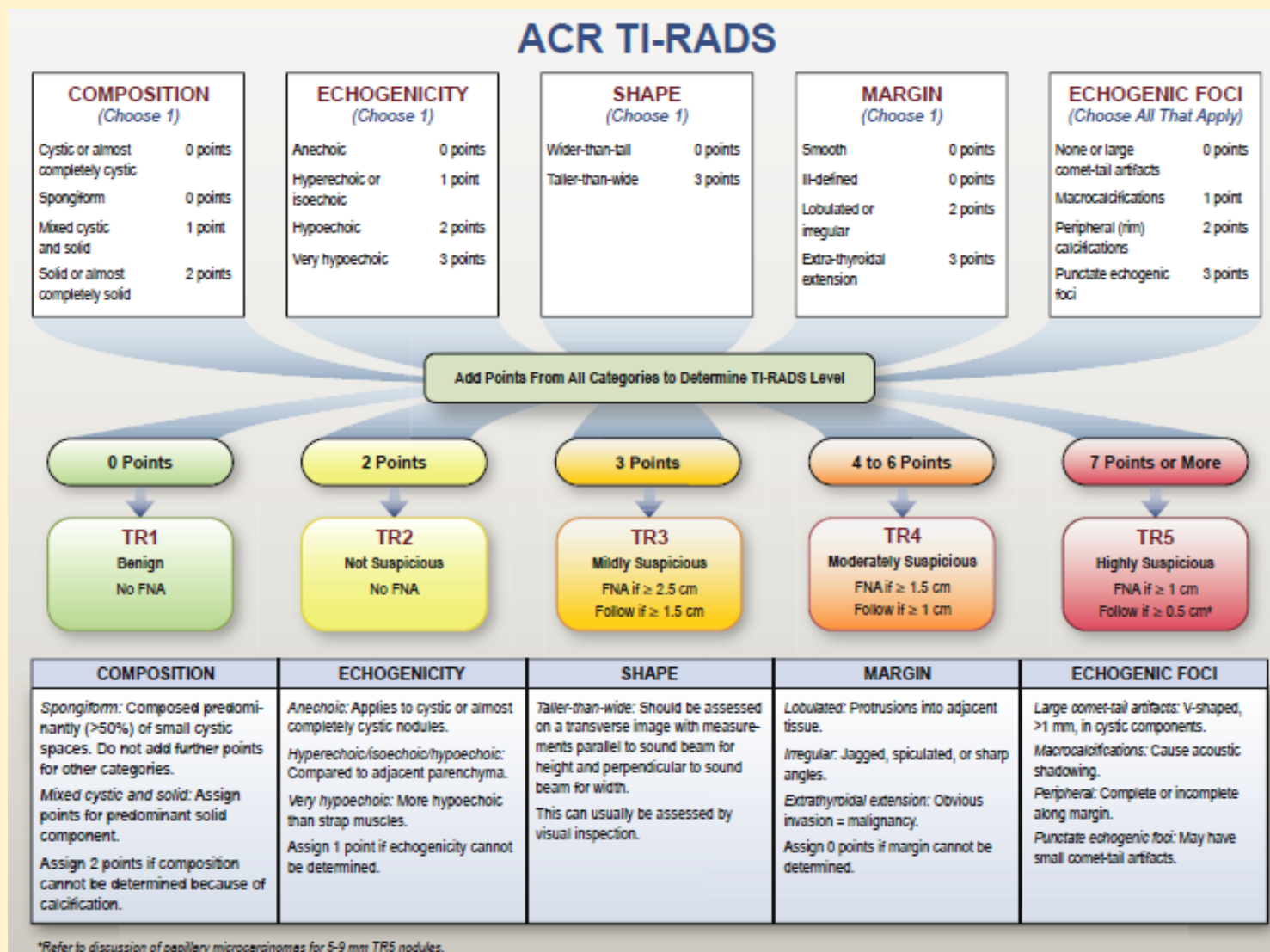
2. Validation of Three Scoring Risk-Stratification Models for Thyroid Nodules.

Ha SM et al. Thyroid 2017

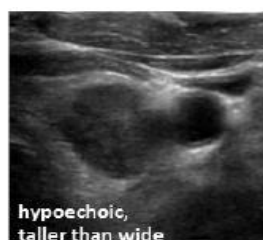
3. Striving toward standardization of reporting of ultrasound features of thyroid nodules and lymph nodes: a multidisciplinary consensus statement.

Su HK EJ et al. Thyroid 2017

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



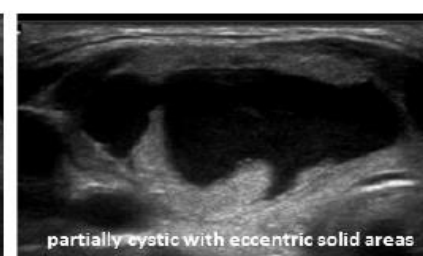
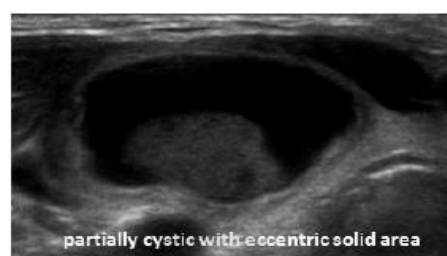
High
Suspicion
70-90%



Intermediate
Suspicion
10-20%



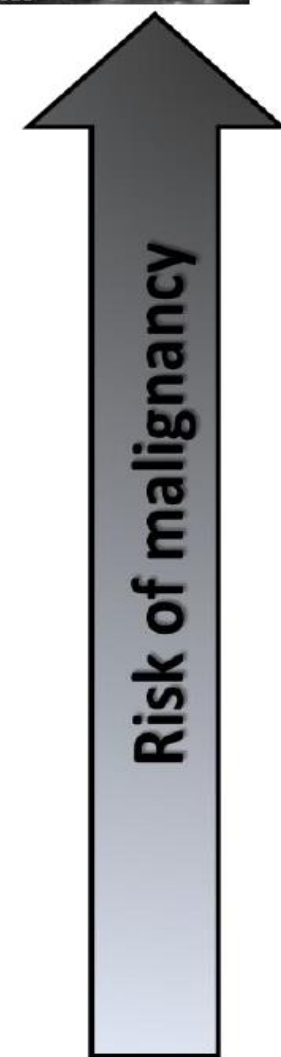
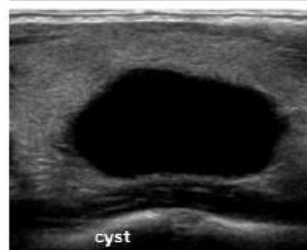
Low
Suspicion
5-10%



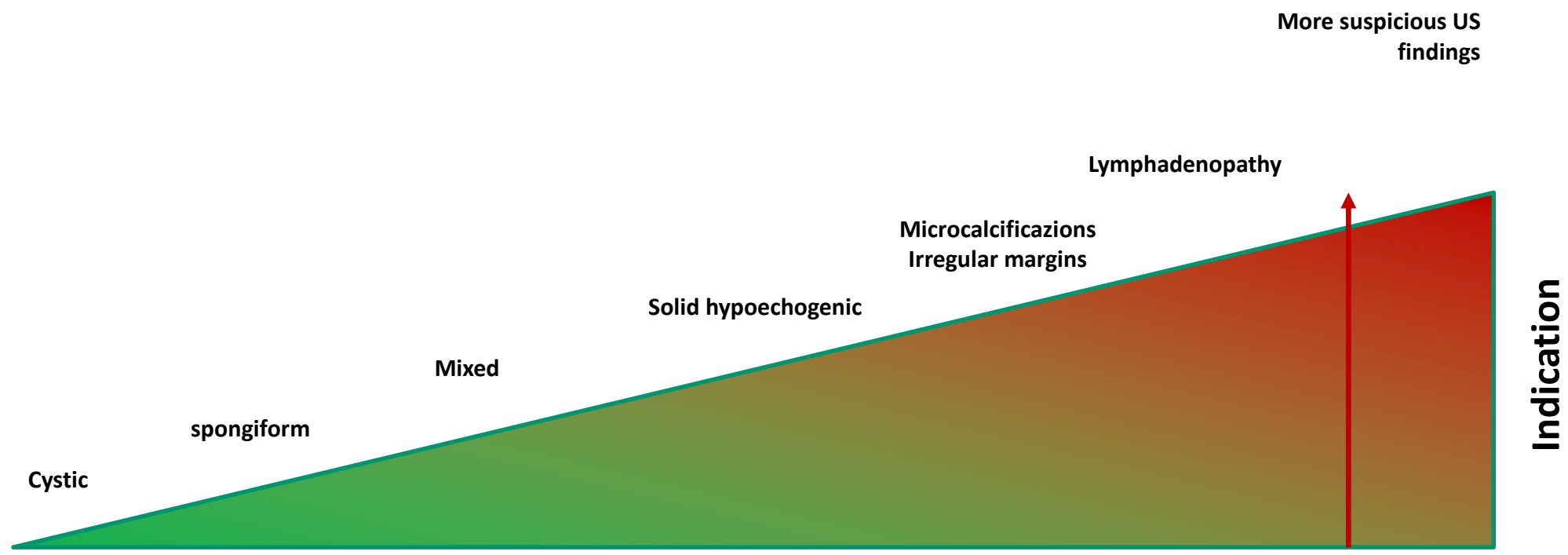
Very low
Suspicion
<3%



Benign
<1%



Strength of indication for FNA depending on US features



Strength of indication for fine-needle aspiration (FNA) biopsy of thyroid nodules on the basis of ultrasonography (US) findings.



US findings and FNA indications

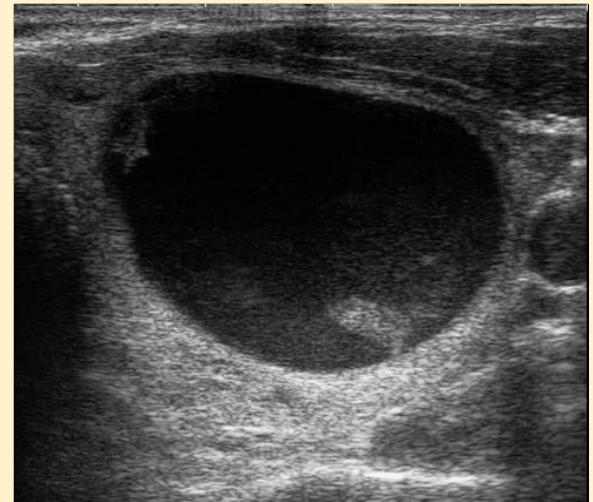
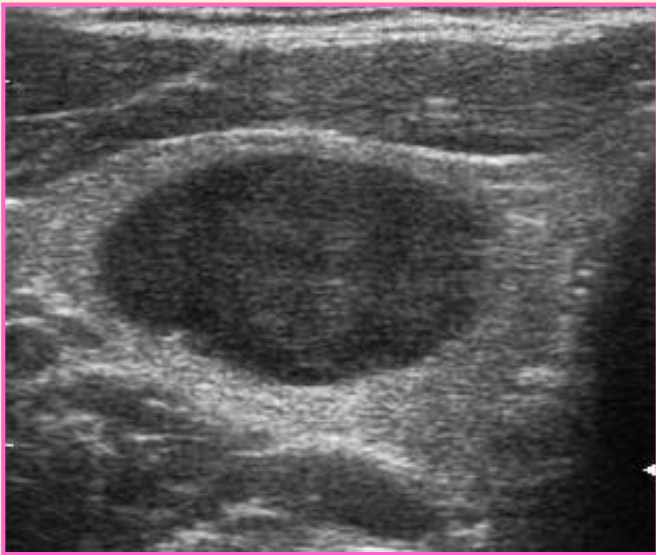
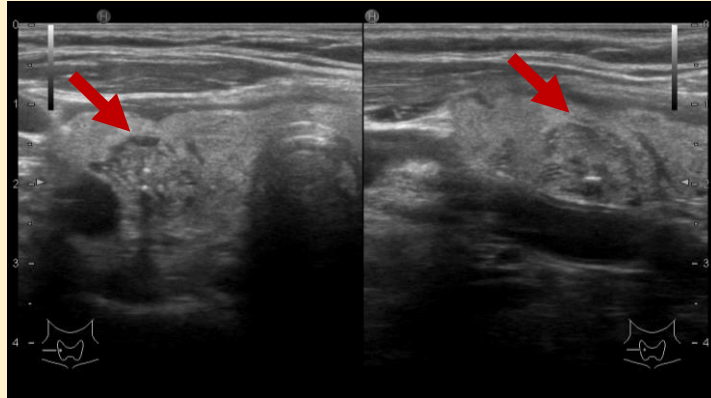
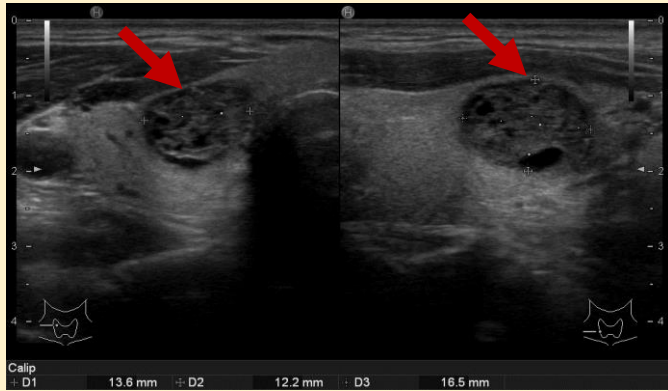
Sonographic pattern Suspicion	FNA size
High	<u>Recommend</u> > 1 cm
Intermediate	Recommend ≥ 1 cm
Low	Recommend ≥ 1.5 cm
Very low	consider ≥ 2 cm Observation without FNA is also a reasonable option
Benign	No biopsy

Sonographic pattern Suspicion	FNA size
High	≥ 1 cm
Intermediate	> 2 cm
Low	≥ 2 cm

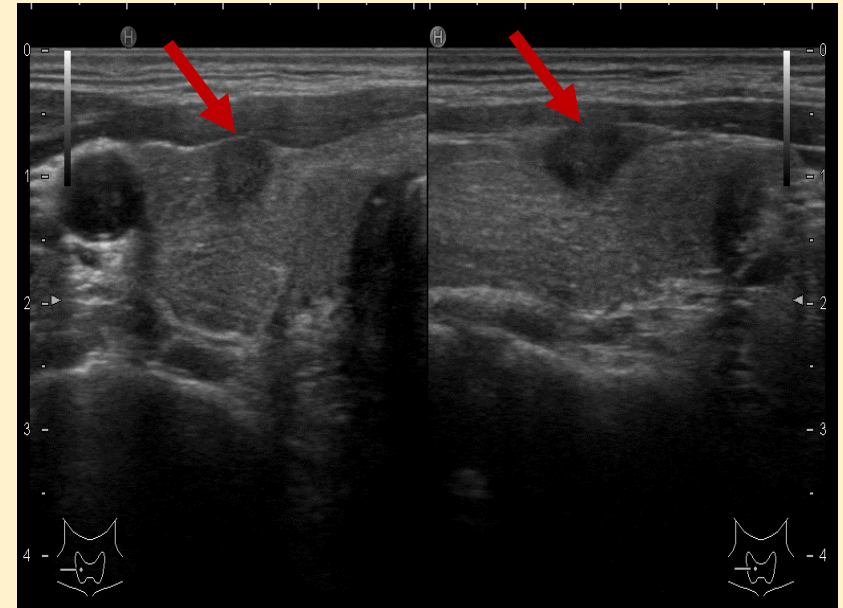
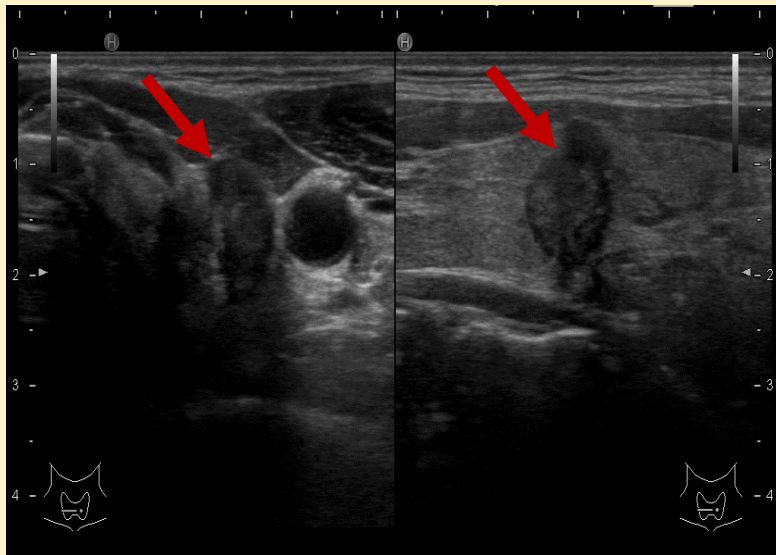
Sonographic pattern Suspicion	FNA size
High	≥ 1 cm (>0.5 cm, selective)
Intermediate	≥ 1 cm
Low	≥ 1.5 cm
Benign	≥ 2 cm NA
No nodule	NA

INDICATIONS FOR FNA FRENCH ENDOCRINE SOCIETY CONSENSUS 2011 (adapted)		
>20mm	>10mm	≤ 10mm if
• Scores TI-RADS 3 to 5 • Simple cyst if compressive symptoms and fluid	• Scores 4A, 4B, 5 (intermediate and high risk nodules)	• Search for the primary cancer of : • a distant metastasis • a suspect cervical lymph node* • Score 4B or 5 (high risk) if: • Increase in size • Juxta-capsular location • Polar superior location • Suspected multifocality • Age < 40 years
Following this algorithm, more than 75% of all nodules do not require FNA and only 2% of nodules <10mm.		
* FNA of suspect lymph node with in-situ Tg assay is mandatory **Such as X-ray cervical therapy during childhood or thyroid carcinoma in a first-degree relative		

Cases



Cases



What is and Why should We use US Risk Stratification ?



- The main aims are to:
 - Help to define the optimal management strategy
 - Reduce the number of unnecessary investigations:
 - Help to select what patients should be operated on
- Secondary goals are to:
 - Facilitate communication between practitioners and with the patient
 - Facilitate cross-talk between clinicians and pathologists
 - Enhance the inter-observer agreement of US reports: decrease the variation seen in reporting of thyroid nodules in current practice.
- No single US feature has enough accuracy to distinguish benign from malignant thyroid lesions, but the combination of multiple features greatly increases sensitivity and specificity.



- US can clearly be used as a risk stratification tool for thyroid nodules
- TIRADS scores and risk stratification systems:

have many US features in common

have high sensitivity (81-98 %) and negative predictive Values (88-99 %) for detection of CA

- Help to select which nodule should undergo FNA in very similar ways
- The next step is to come up with a global system and test in multicenter studies

Patients  **Guidelines**

Grazie

...





2016 ATA Guidelines: consideration

ATA 2009

Biopsy thyroid nodules primarily based on thyroid size: Size 5-10 mm and individual sonographic features

ATA 2016

Recommendation 8: Biopsy thyroid nodules primarily based on sonographic features, followed by size

FNA $\geq$ 10 mm in nodules with high suspicious US features

What is the evidence for changing the size criteria for high suspicion nodules from >0.5 cm in the 2009 ATA guidelines to $\geq$ 1.0 cm in the 2016 ATA guidelines?

1. This is because most subcentimeter nodules show an indolent course, a low malignancy rate, and good prognosis
2. as nodule size decreases there is a higher possibility of an inadequate FNAB results

Mazzaferri et al. were opposed to recommending FNAB for 5mm or smaller nodules

Indication for FNA: US is not alone



AT RISK CONTEXT:

- Age
- History of external X-ray therapy during childhood
- Family history of papillary carcinoma (at the first degree)
- Family history of MTC or MEN2
- Personal or family history of Cowden's disease, Carney's complex, familial polyposis, McCune-Albright
- Elevated serum calcitonin (checked)
- Cervical suspicious lymph node or distant metastasis
- Thyroid auto-immune disease
- AT RISK NODULE:
 - Fast increase of the solid portion
 - Focal uptake using PET-FDG
 - Location: juxta-capsular, isthmus



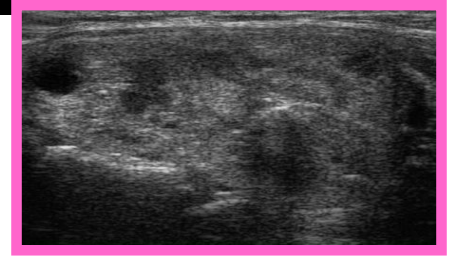
Which nodules?

3.5.1. Indications for UGFNA

High-US-risk thyroid lesions ≥ 10 mm

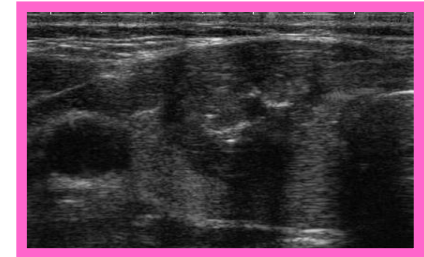
Intermediate-US-risk thyroid lesions > 20 mm

Low-US-risk thyroid lesions only when > 20 mm and increasing in size or associated with a risk history and before thyroid surgery or minimally invasive ablation therapy [BEL 2, GRADE A]



3.5.2. UGFNA of multinodular glands \

We do not recommend the biopsy of more than 2 nodules when they are selected on the basis of previously described criteria [BEL 3, GRADE C]





- The nodule's size is not a predictor of malignancy in 1/3 of the cases of multinodular goiter, the carcinoma is not in the biggest nodule.
- The risk of carcinoma is identical in palpable and in non palpable nodules

Kim EK, AJR 2002
Papini E, JCEM 2002
Kunreuther E, ATA 2004