

VII  
CORSO  
NAZIONALE AME  
DI ENDOCRINOLOGIA  
CLINICA



17/19 MARZO 2016

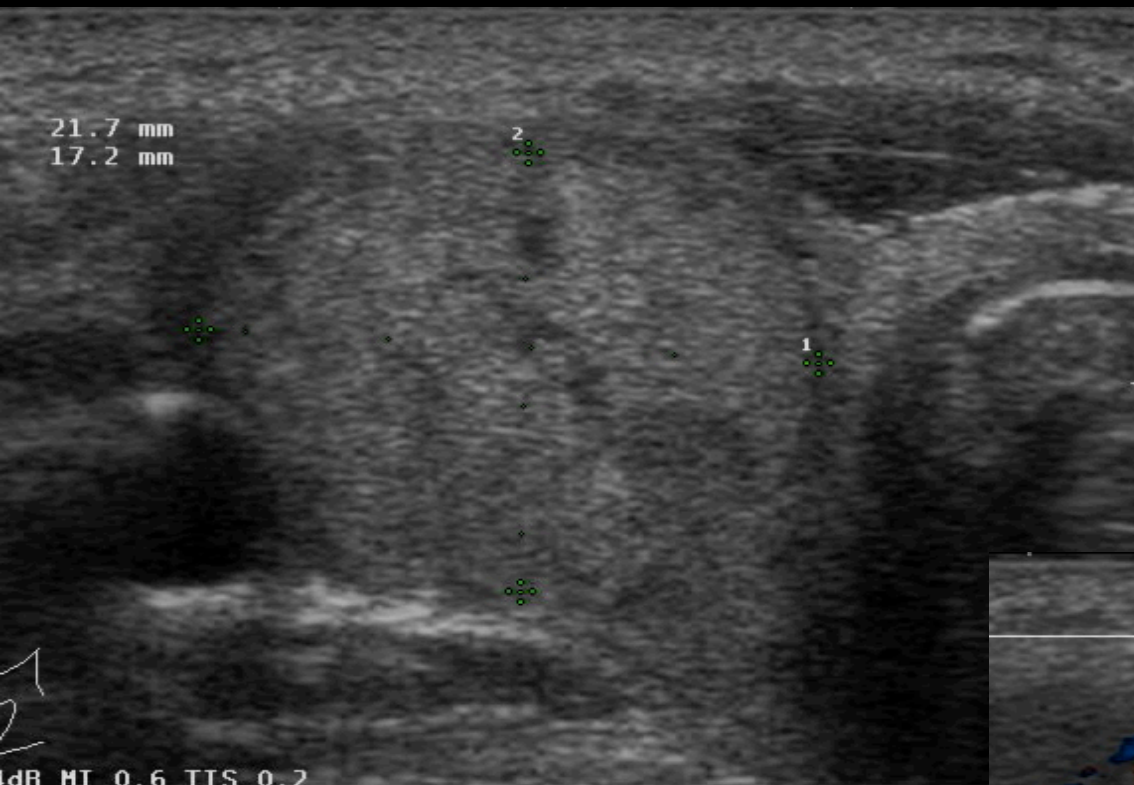
Bari, Hotel Majesty

Ecografia tiroidea e  
classificazione del  
rischio di malignità:  
è possibile? È utile?  
È pericoloso?

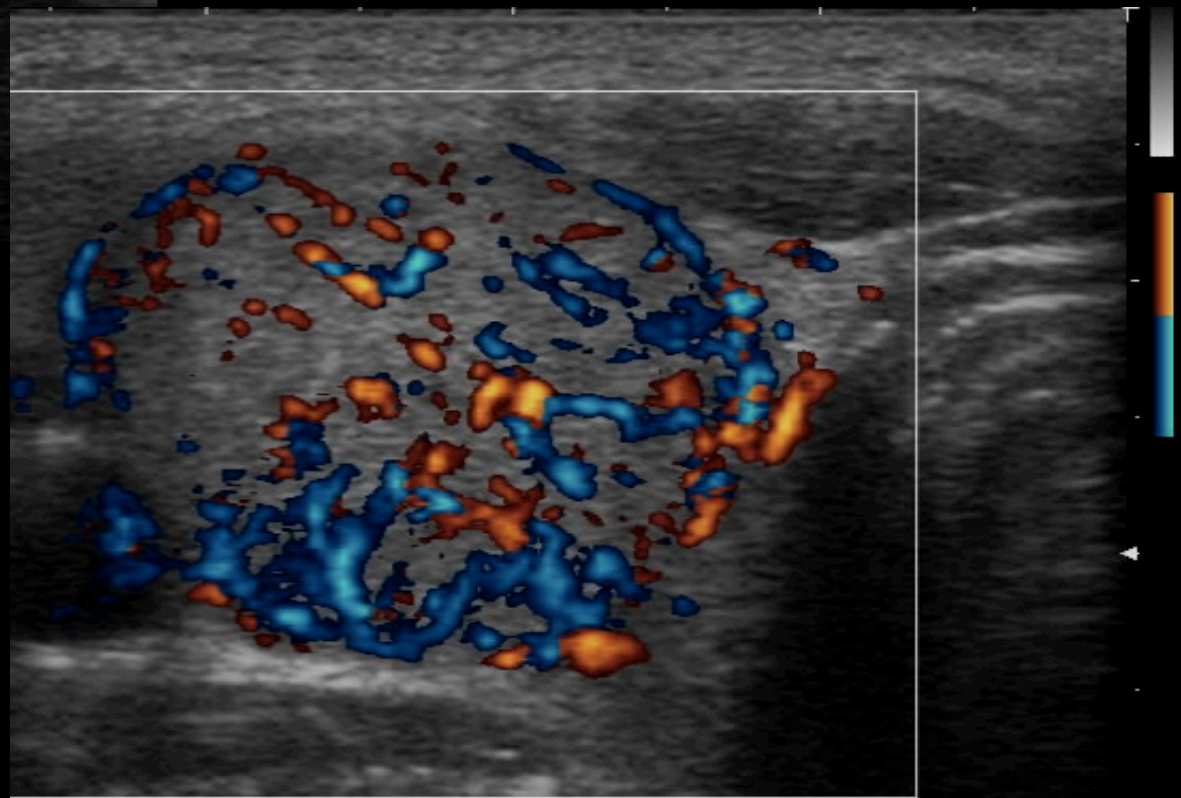
Andrea Frasoldati  
Endocrinologia  
Arcispedale S. Maria  
Nuova IRCCS

# Caso clinico #1

- Paola, aa 35.
- Insegnante. Fuma 1-2 sigarette al dì
- Anamnesi clinica sostanzialmente muta
- Due figli di 3 e 6 anni
- Nel corso di una visita ginecologica, viene sottoposta ad ecografia tiroidea senza un motivo specifico, per “controllo”.



1  
2  
dR MT 0.6 TTS 0.2



1.2 TTS 1.9

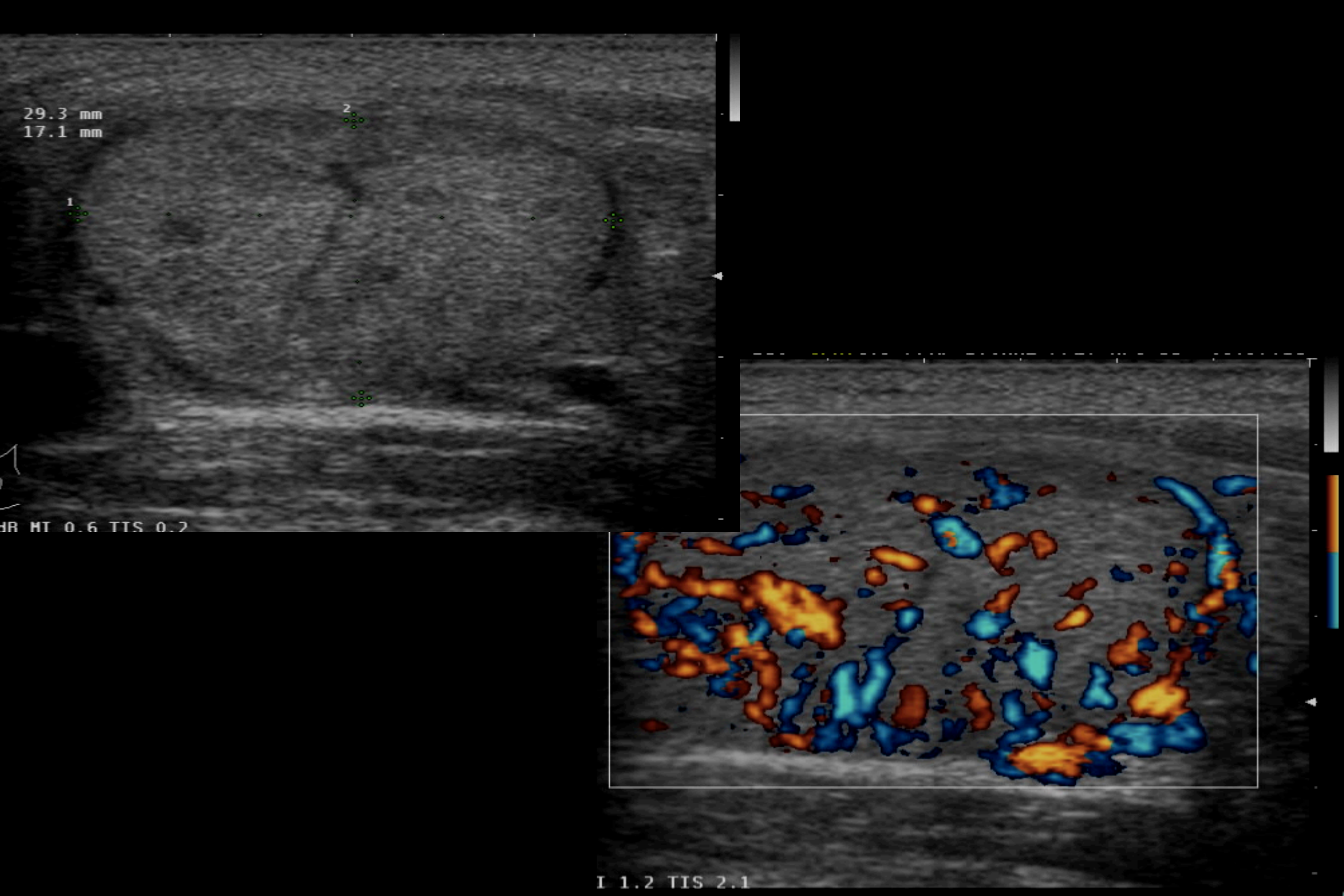
29.3 mm  
17.1 mm

1

2

HR MT 0.6 TTS 0.2

I 1.2 TTS 2.1



# Referto ecografico

- *Tiroide di dimensioni nella norma*
- *Lobo destro: nodulo solido 29 x 21.5 x 17 mm Ø , ad ecostruttura discretamente omogenea, prevalentemente isoecogena, margini netti e regolari, dotato di vascolarizzazione peri- e intranodulare. Non calcificazioni.*
- *Lobo sinistro: non noduli. Ecotessitura di fondo omogenea.*
- *Non evidenza di linfonodi patologici in sede cervicale*

# Dati clinici e laboratoristici

- *Il nodulo è palpabile*
- *Anamnesi familiare negativa per patologia tiroidea di rilievo. Nessuna notizia di interventi sulla tiroide tra i parenti di 1° e 2° grado.*
- *TSH 1.8  $\mu$ U/ml*



# Il referto ecografico è completo?



# Regole per un referto ecografico **ACCURATO** (e soprattutto **UTILE**)

Sintesi  $\longrightarrow$  Chiarezza  $\longrightarrow$  Orientamento clinico

Informazioni generali sulla ghiandola: dimensioni, ecostruttura, asimmetrie maggiori, aspetti flogistici

Se noduli presenti:

a) numero e sede

**b) descrizione dei caratteri ecografici del/dei  
nodulo/i principale/i**



# PPV of different US signs

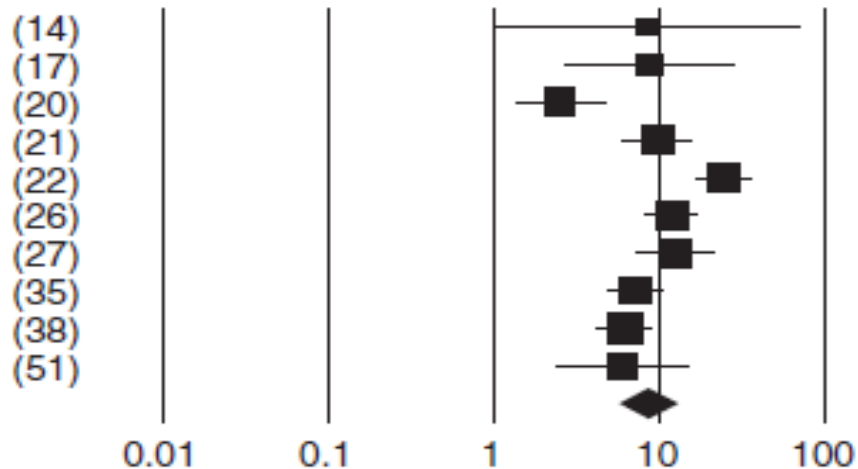
	PPV (%)	
	Kim et al.	Papini et al.
Calcifications	70.7	33.0
Irregular margins	60.0	24.0
Hypoechogenicity	68.4	11.4
“More tall than wide”	66.7	na
Intranodular vascularization	na	24.0
> 10 mm diameter	na	7.0
Solitary nodule	na	66.7

# Flow-chart nella valutazione ecografica dei noduli tiroidei

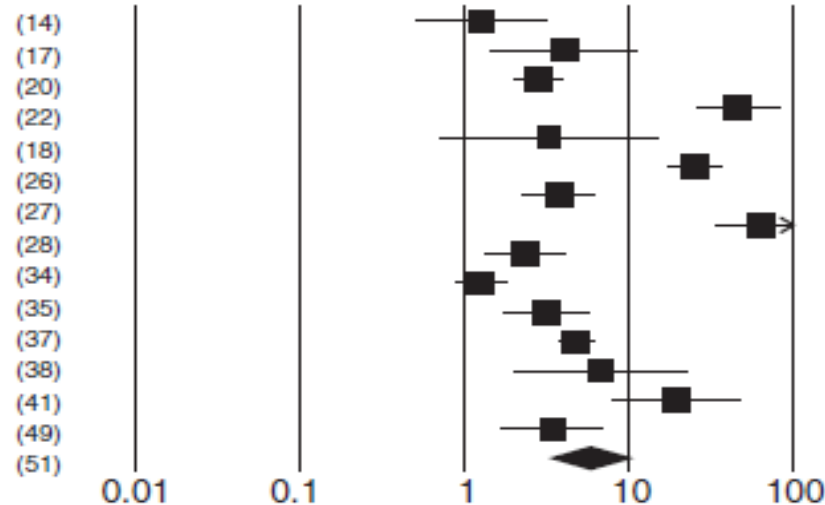
PARAMETRO	Benigno	↔	Sospetto
Struttura	Omogenea	Disomogenea	
	Cistico	Misto	Solido
Ecogenicità	Iperecogena	Isoecogena	Ipoecogena
Margini	Netti	Sfumati	
	Regolari	Irregolari	
Profilo	Ovalare	More tall than wide	
Calcificazioni	A guscio	Grossolane	Puntate
Vascularizzazione	Scarsa/assente	Periferica	Periferica e centrale
Elastografia	ES 0-1 (iper-isoelastico)	ES2 (ipoelastico)	ES 3 (nodulo duro)

# MARGINI E PROFILO

*Sensibilità 70-75% Specificità 65-80%*



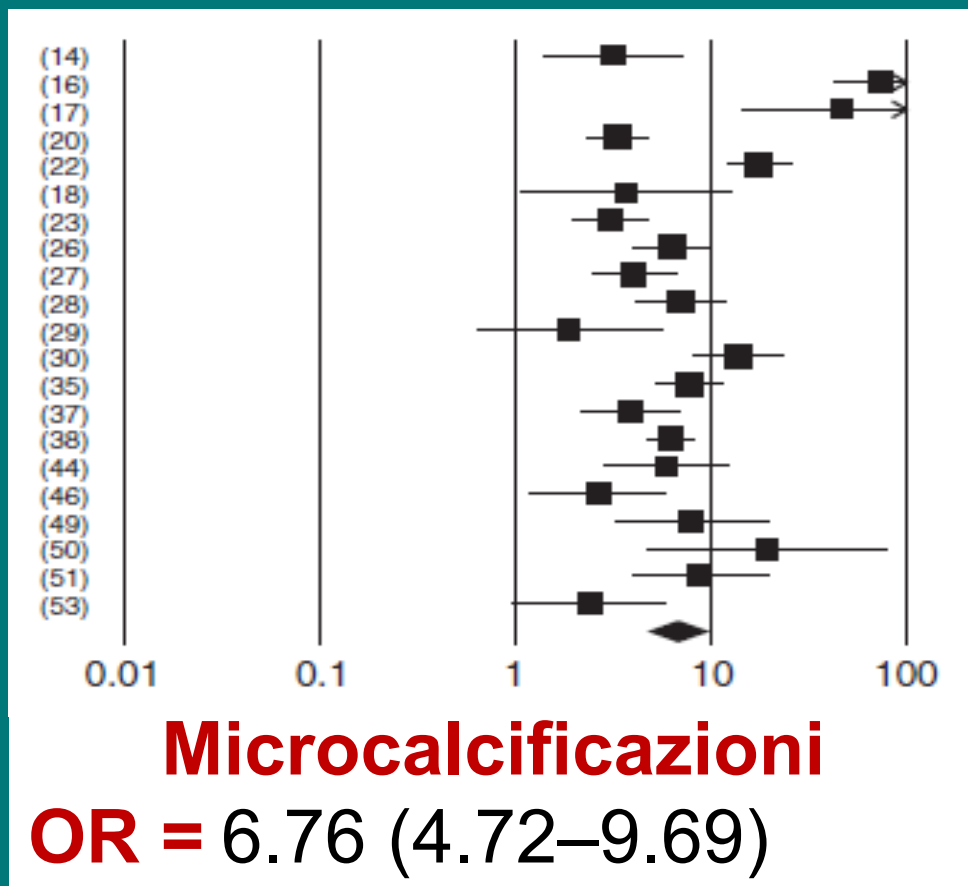
**More tall than wide**  
**OR = 10.15 (6.7–15.3)**



**Margini irregolari**  
**OR = 6.12 (3.1–12.0)**

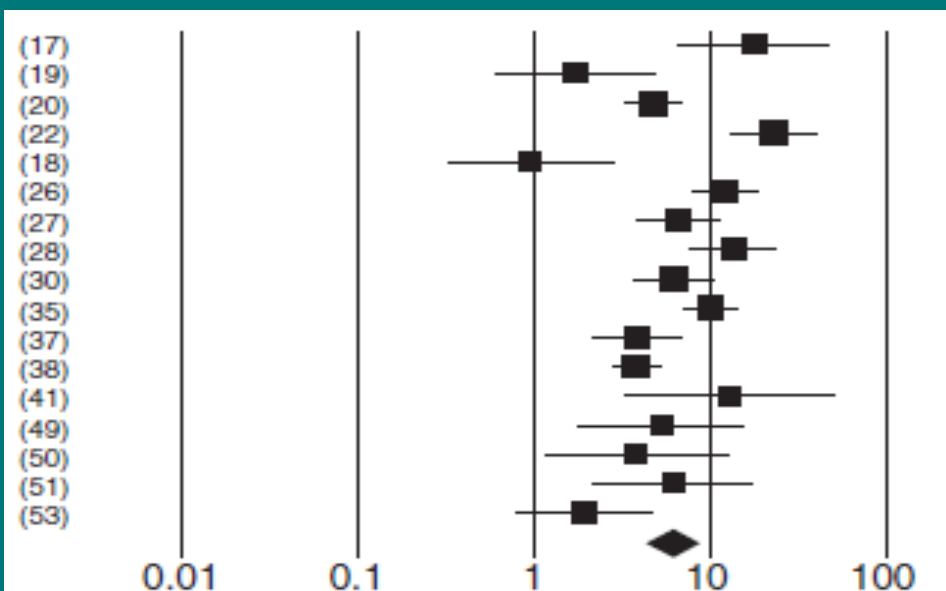
# CALCIFICAZIONI

*Sensibilità 20-35% Specificità 80-95%*



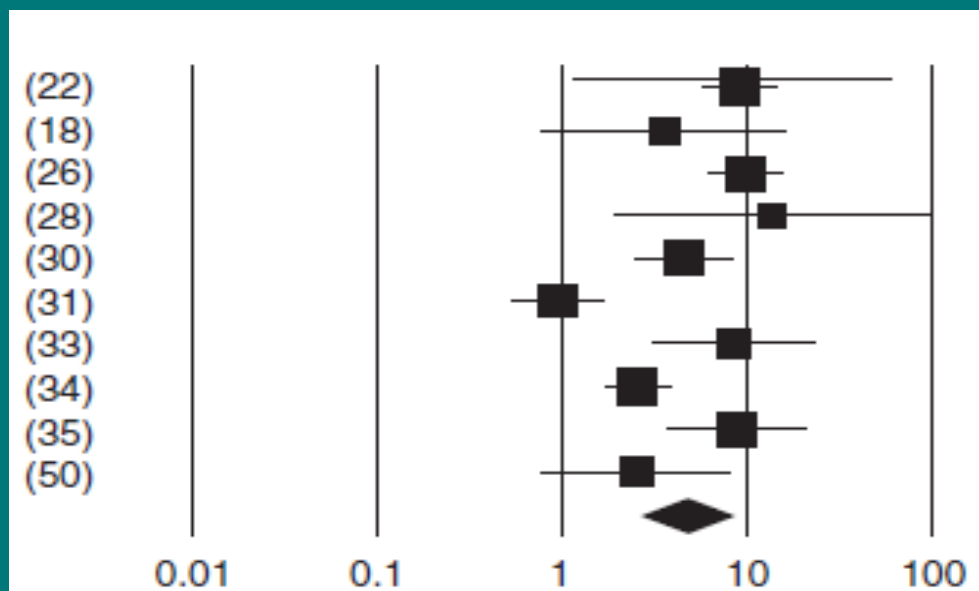
# ECOGENICITA' ED ECOSTRUTTURA

*Sensibilità 80-85% Specificità 45-50%*



**Ipoecogenicità**

**OR = 5.07 (3.47–7.43)**

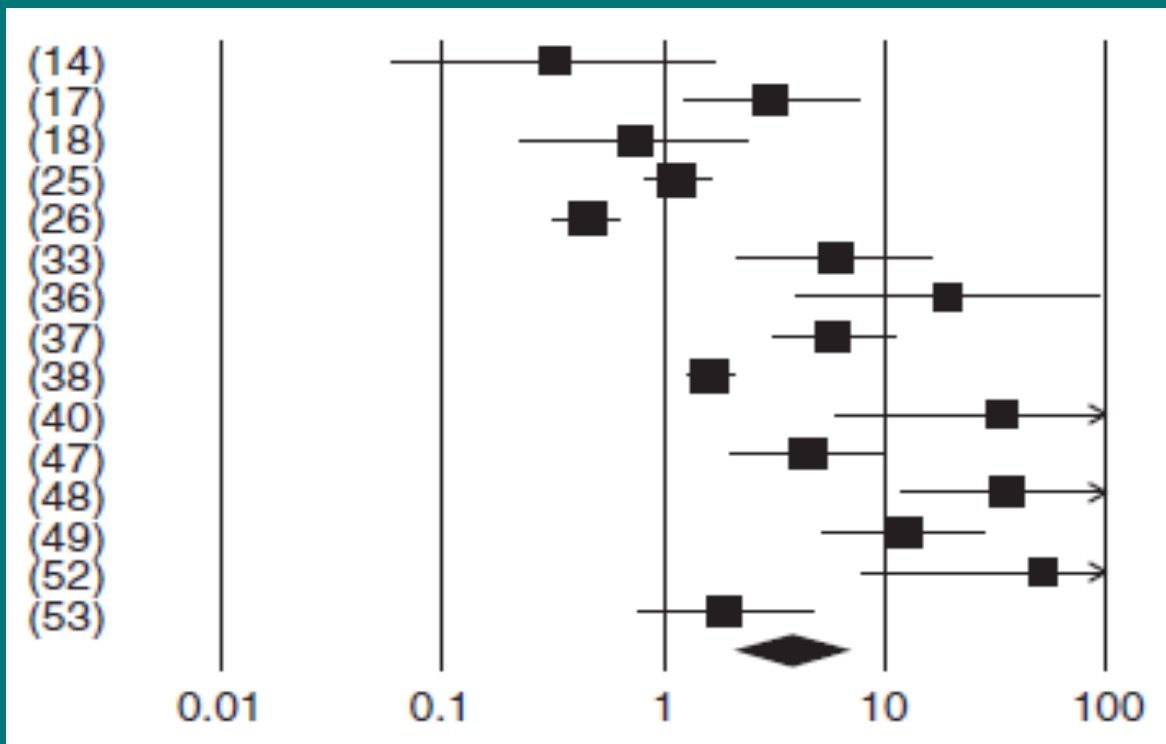


**Struttura solida**

**OR = 4.69 (2.63–8.36)**

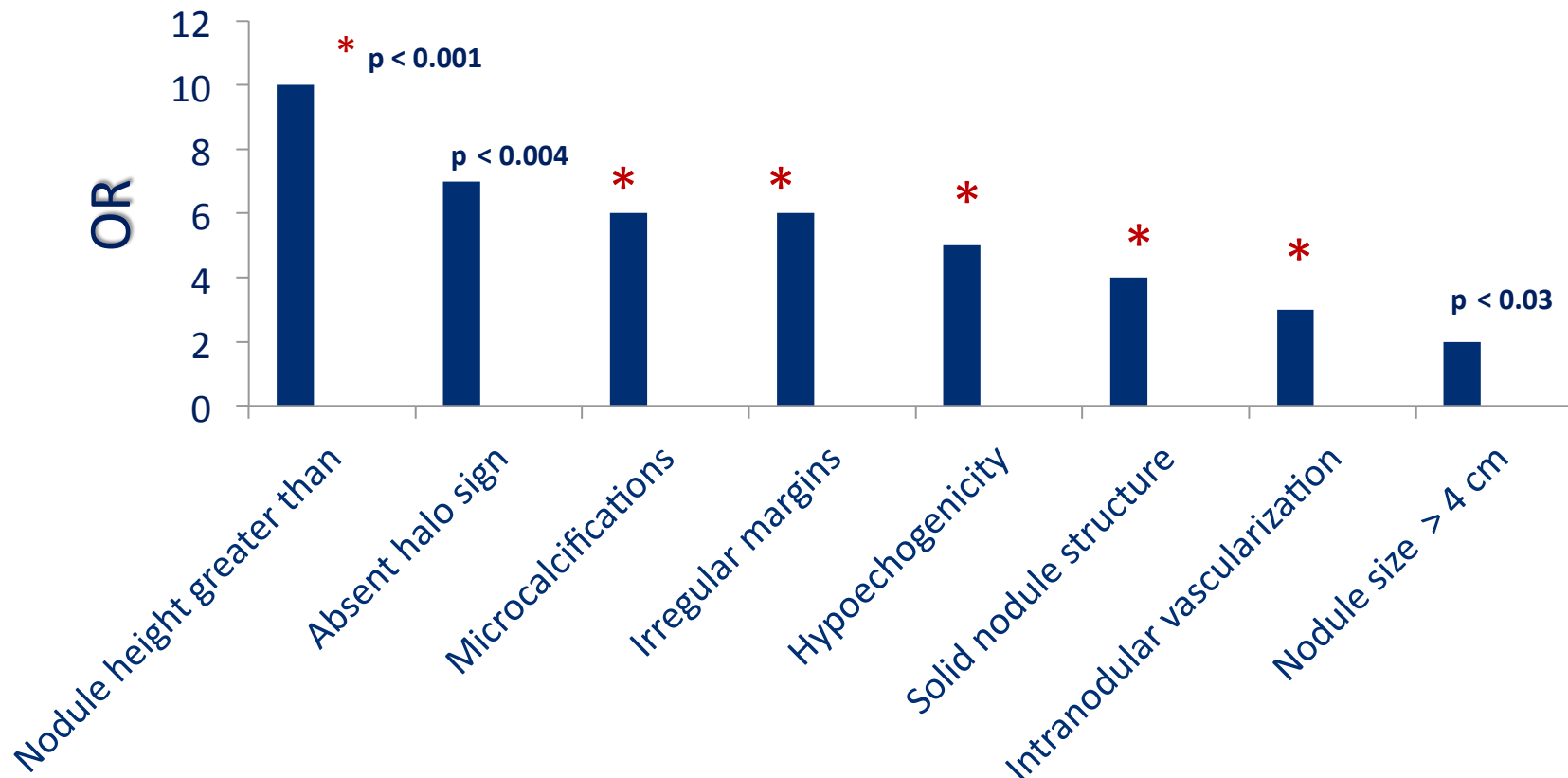
# VASCOLARIZZAZIONE

*Sensibilità 60-75% Specificità 70-80%*



**Vascularizzazione intranodulare**  
**OR = 3.76 (2.04–6.95)**

## Results of the meta-analysis of TN clinical and US features associated with an increased risk of thyroid cancer



# Caratteristiche US di malignità



1. Marcata ipoecogenicità (i.e. ecogenicità  $\leq$  muscoli pre-tiroidei)
2. Irregolarità dei margini (indentature, aspetto lobulato, infiltrazione e/o superamento capsula tiroidea)
3. Microcalcificazioni spot iperecogeni puntati ( $< 1$  mm diametro) in assenza di artefatti tipo comet-tail
4. Profilo *more tall than-wide* (i.e diametro anteroposteriore  $>$  diametro trasverso)
5. Associata linfadenopatia con caratteri sospetti





## Identikit US del nodulo benigno

1. Profilo ovalare o appiattito
2. Isoecogenicità
3. Margini regolari
4. Vascolarizzazione periferica

## Identikit del nodulo borderline

1. Ipoecogenicità rispetto al tessuto circostante
2. Prevalente vascolarizzazione intranodulare
3. Macrocalcificazioni (a guscio o intranodulari)

# REGOLE PER UN REFERTO ACCURATO (E SOPRATTUTTO UTILE)

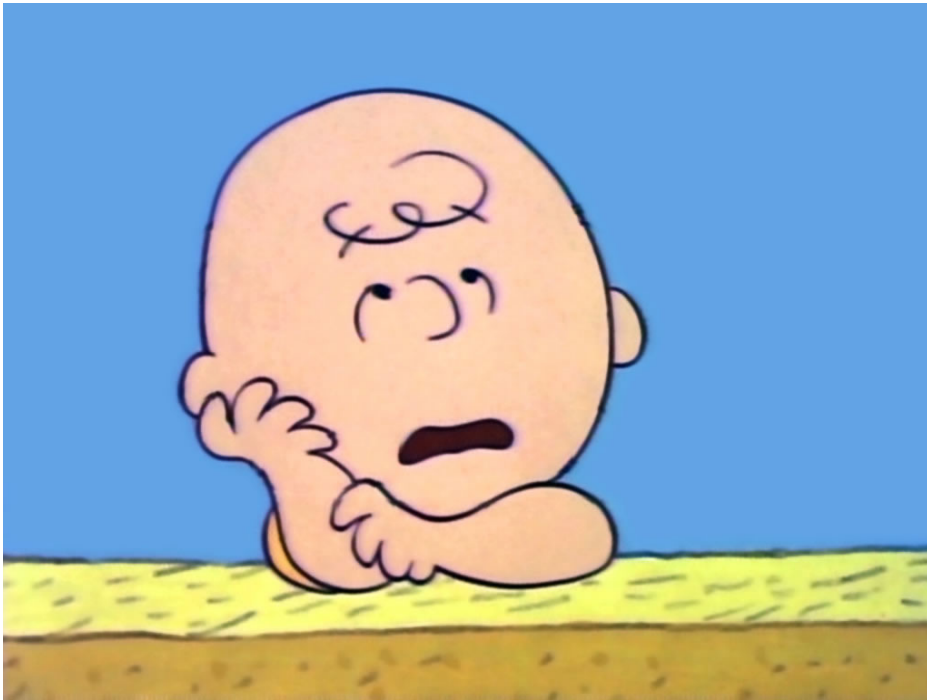
Sintesi – Chiarezza – Orientamento clinico

Informazioni generali sulla ghiandola: dimensioni, ecostruttura, asimmetrie.

Se noduli presenti:

- a) numero e sede
- b) Descrizione dei caratteri ecografici del/dei nodulo/i lesioni principale/i
- c) Stratificazione del rischio di malignità del nodulo:  
benigno/indeterminato/maligno U2/U3/U4**

# Classificazione ecografica del rischio di malignità



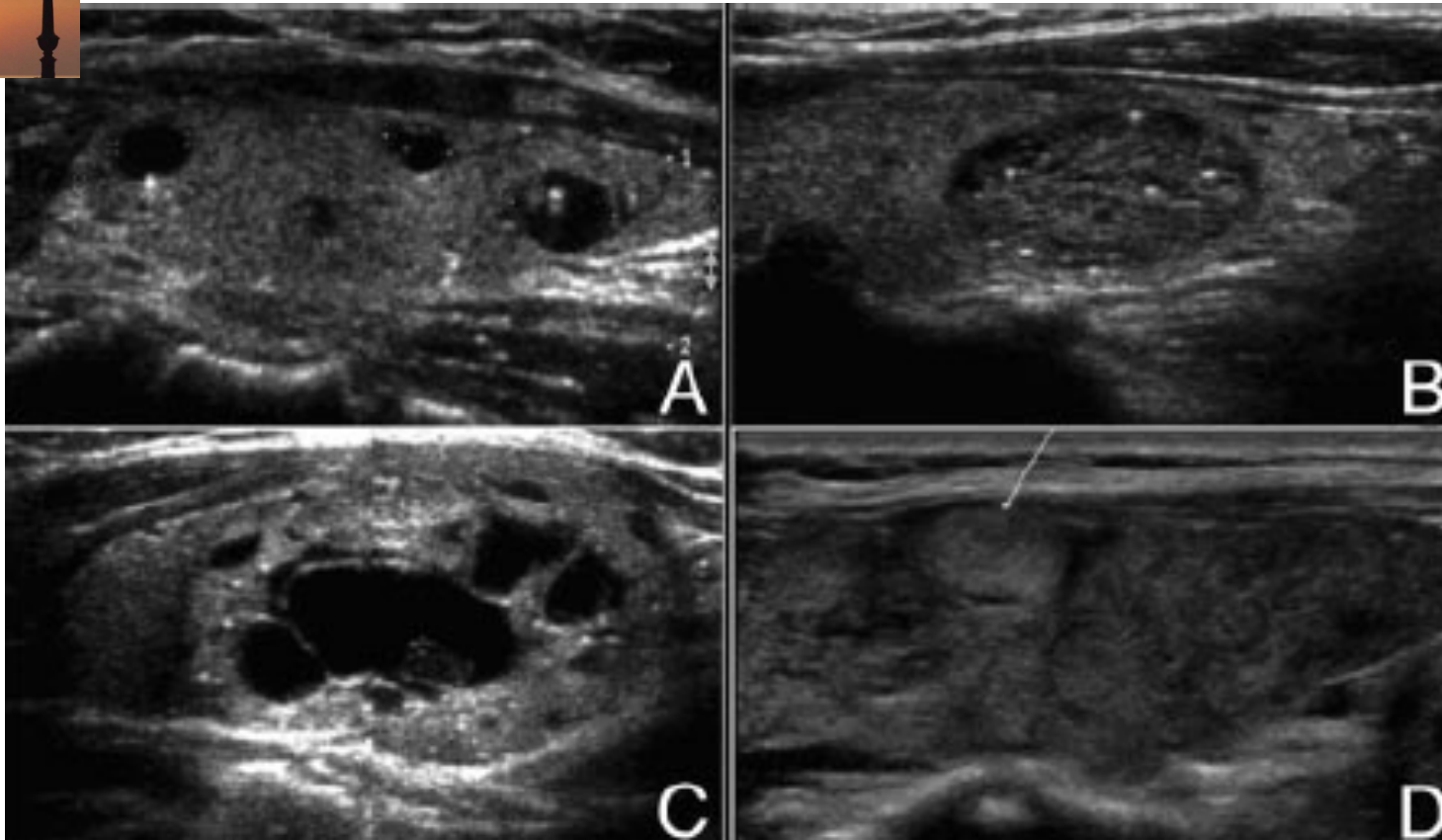
- **È possibile?**

# An US Reporting System for Thyroid Nodules Stratifying Cancer Risk for Clinical Management

- 1959 lesions biopsied under US guidance and studied histologically during an 8-yr period.
- 10 US patterns defined and 4 TIRADS groups defined.
- **TIRADS classification evaluated in 1097 nodules** (benign: 703; follicular lesions: 238; carcinoma: 156).
- Sens 88%, Spec 49%, PPV 49%, NPV 88% ; accuracy 94%

# An US Reporting System for Thyroid Nodules Stratifying Cancer Risk for Clinical Management

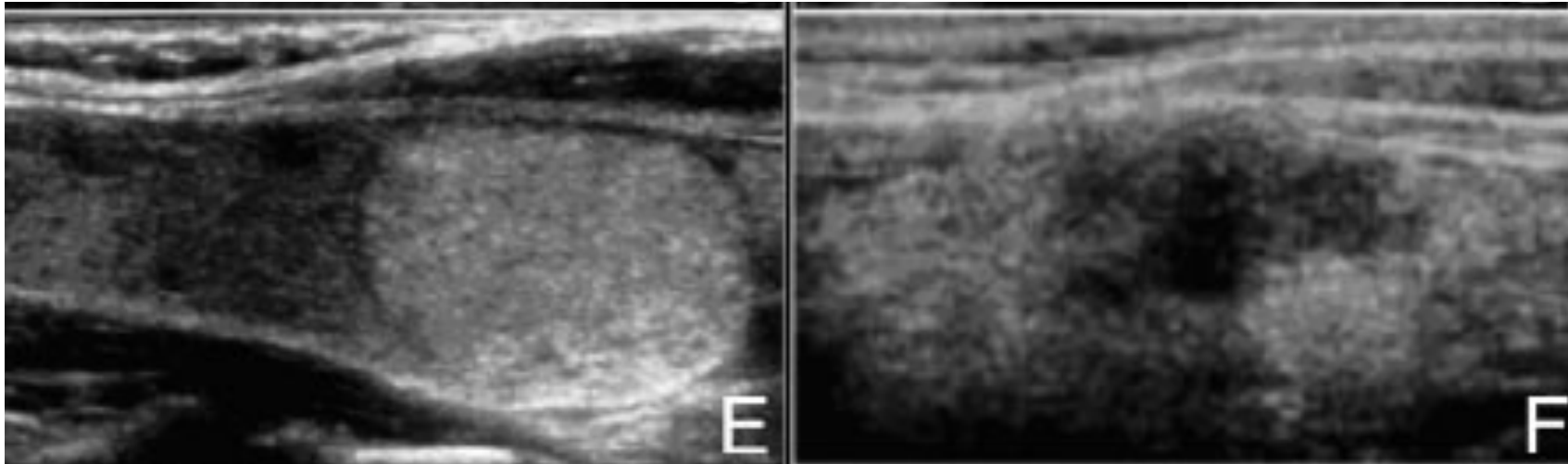
- TIRADS 1: normal thyroid gland.
- TIRADS 2: benign conditions (0% malignancy).
- TIRADS 3: probably benign nodules (5% malignancy).
- TIRADS 4: suspicious nodules (5–80% malignancy rate).
  - 4a (malignancy between 5 and 10%)
  - 4b (malignancy between 10 and 80%).
- TIRADS 5: probably malignant nodules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



- A Type 1 colloid pattern.
- B Type 2 colloid nodule:
- C Type 3 pattern:
- D hyperechoic pseudo-nodule

**TIRADS 2**

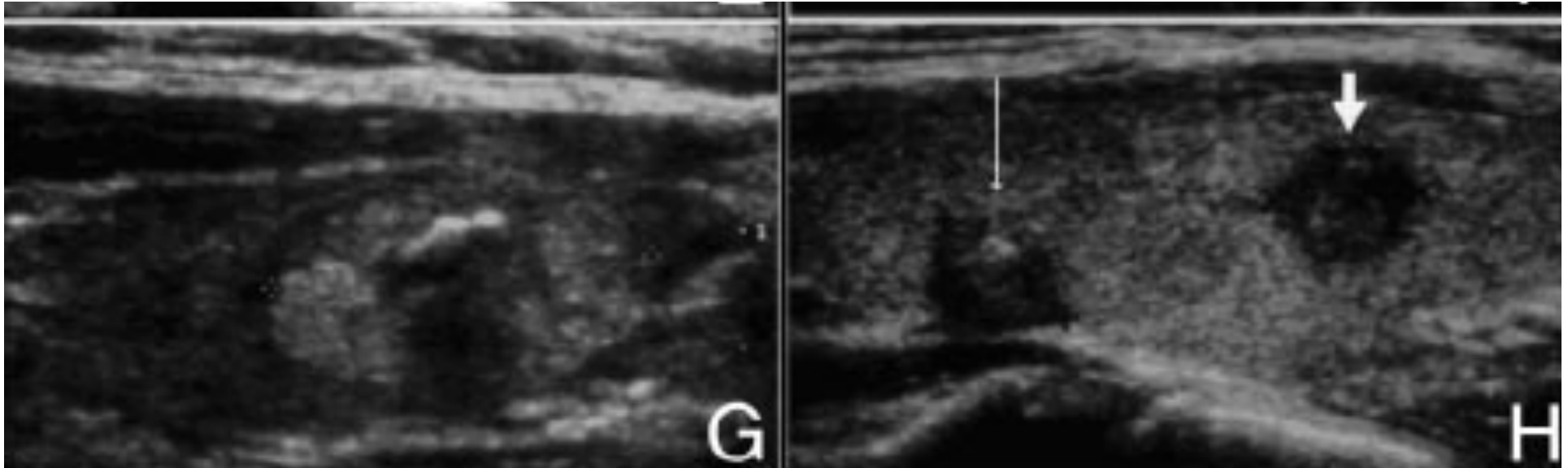
**TIRADS 3**



E : a solid hyperechoic nodule without calcifications, surrounded by a thin capsule.

F: a hypoechoic area with ill-defined borders, without calcifications. This pattern may be found in both subacute thyroiditis and carcinomas.

## **TIRADS 4A**

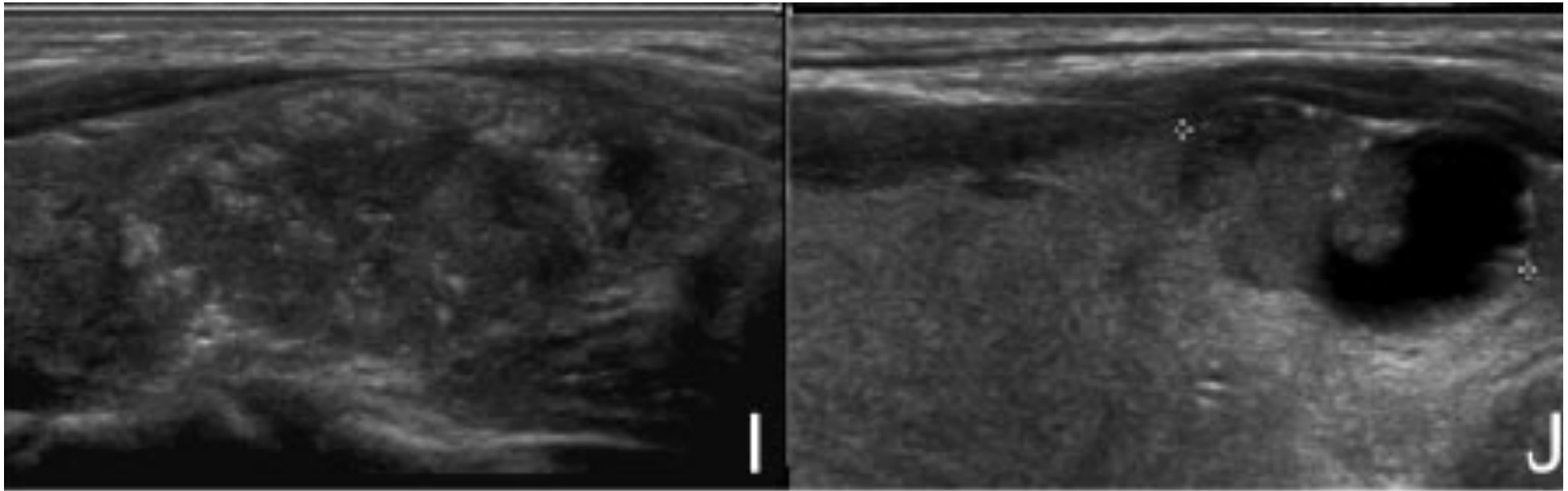


**G:** encapsulated heterogeneous nodule with coarse calcifications, surrounded by a thick capsule.

**H:** malignant pattern A: solid hypoechoic, irregular nodules with ill-defined margins, calcifications

**TIRADS 4B**





**I:** malignant pattern B : solid, nonencapsulated, isoechoic, ill-defined nodule with a “salt and pepper” aspect, due to peripheral microcalcifications.

**J:** malignant pattern C: a mixed, isoechoic, vascularized, nonencapsulated nodule with calcifications and no hyperechoic spots. **T IRADS 5**

### HIGH SUSPICIOUS ASPECTS

- Taller-than-wide shape
- Irregular or microlobulated margins
- Microcalcifications
- Marked hypoechogenicity

≥ 3 signs and/or  
adenopathy  
**TIRADS 5**

1 or 2 signs and  
no adenopathy  
**TIRADS 4B**

### LOW SUSPICIOUS ASPECT

- None of the high suspicious aspect
- Moderately hypoechogenic

**TIRADS 4A**

### PROBABLY BENIGN ASPECTS

- None of the high suspicious aspect
- Isoechogenic
- Hyperechogenic

**TIRADS 3**

### BENIGN ASPECTS

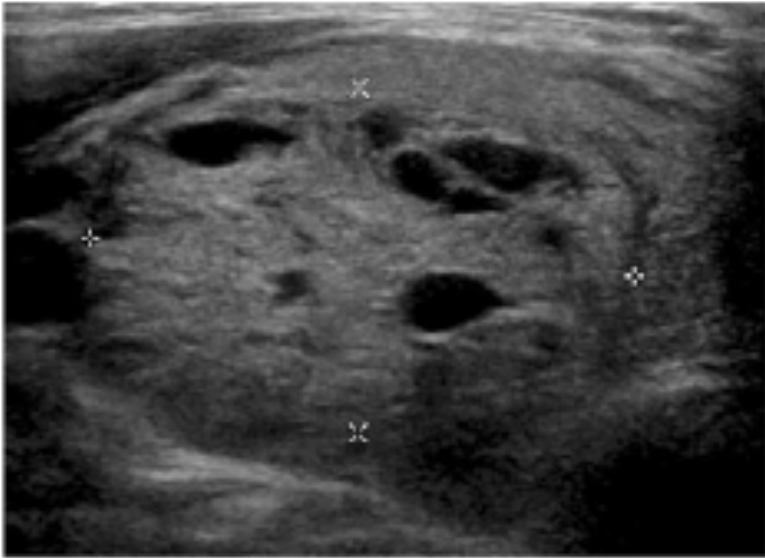
- Simple cyst
- Spongiform nodule
- 'White knight' aspect
- Isolated macrocalcification
- Typical subacute thyroiditis

**TIRADS 2**

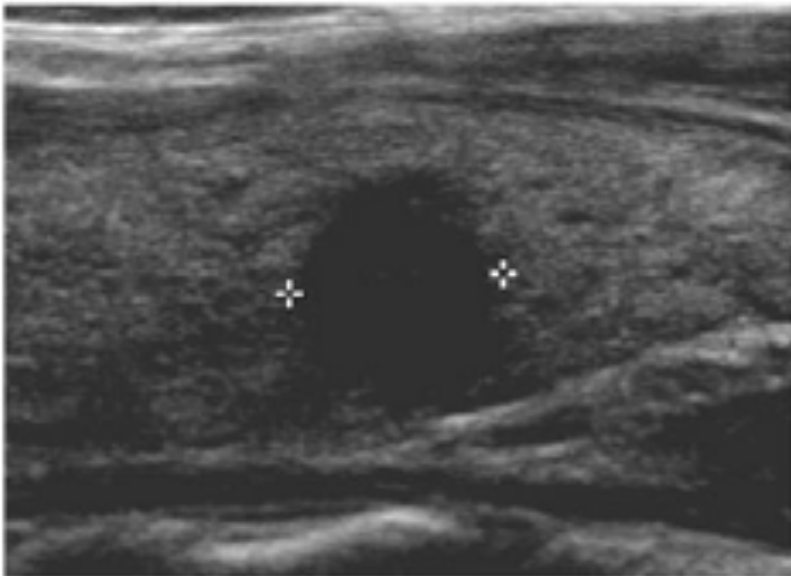
**Normal thyroid US**

**TIRADS 1**

# TIRADS classification algorithm



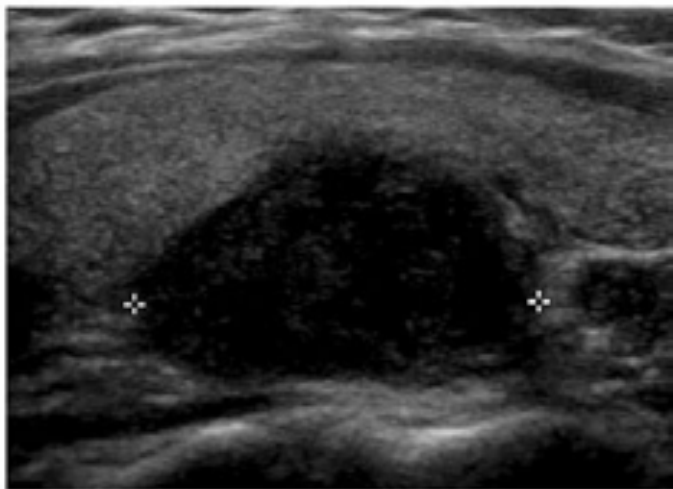
**TIR2**



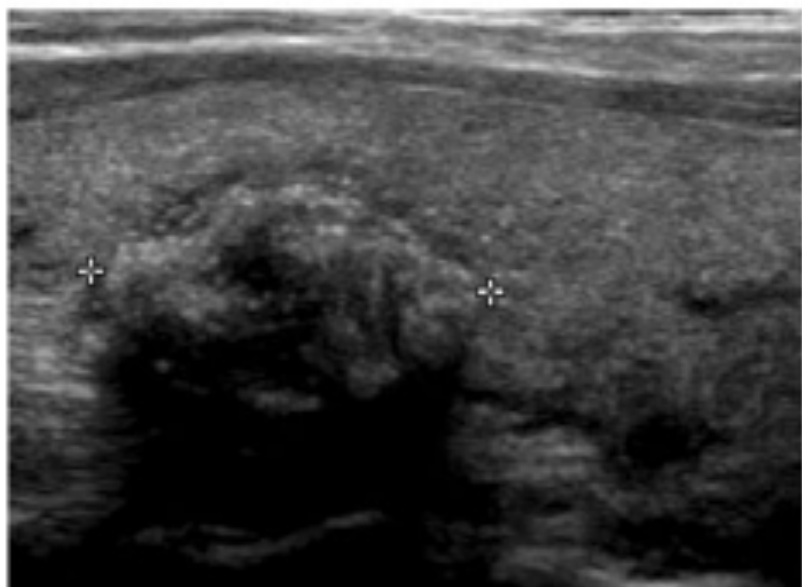
**TIR4b**



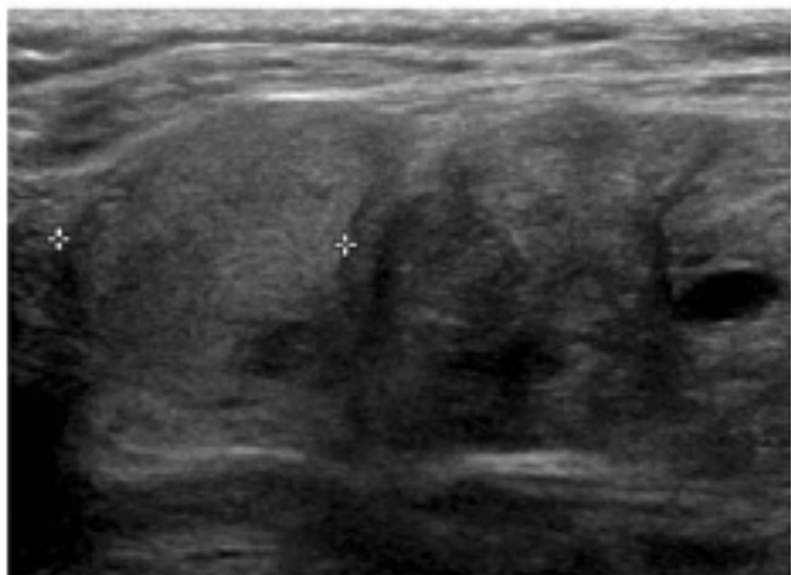
TIR4a



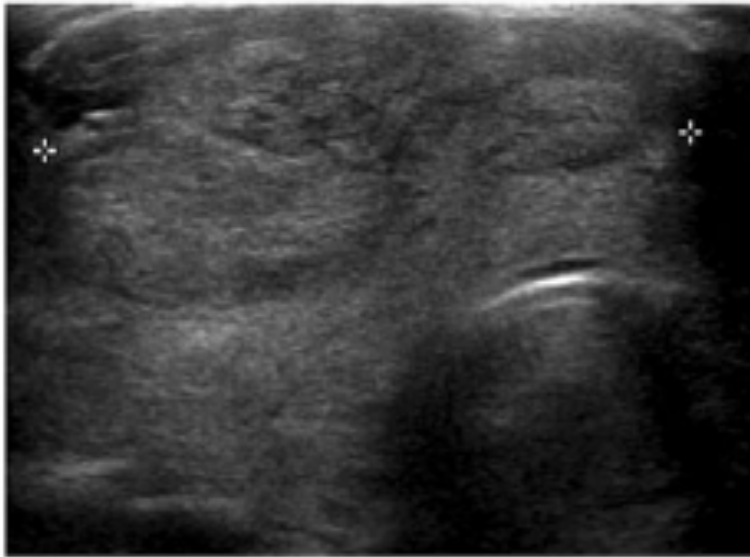
TIR4b



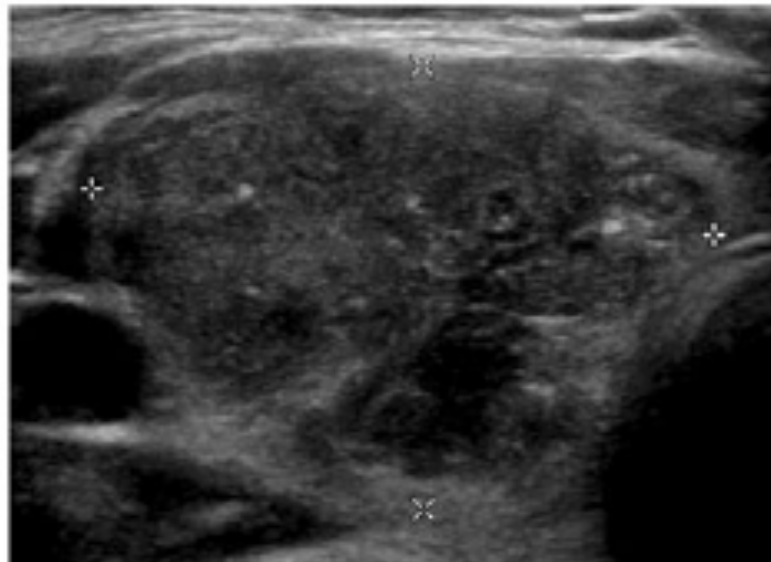
**TIR5**



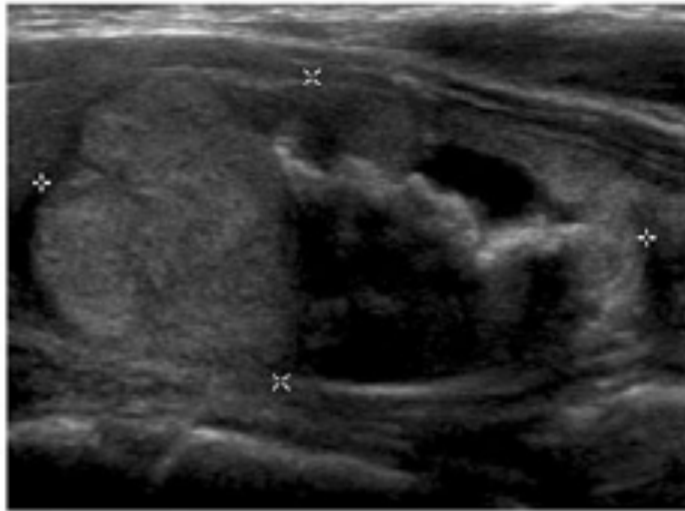
**TIR3**



**TIR3**



**TIR5**

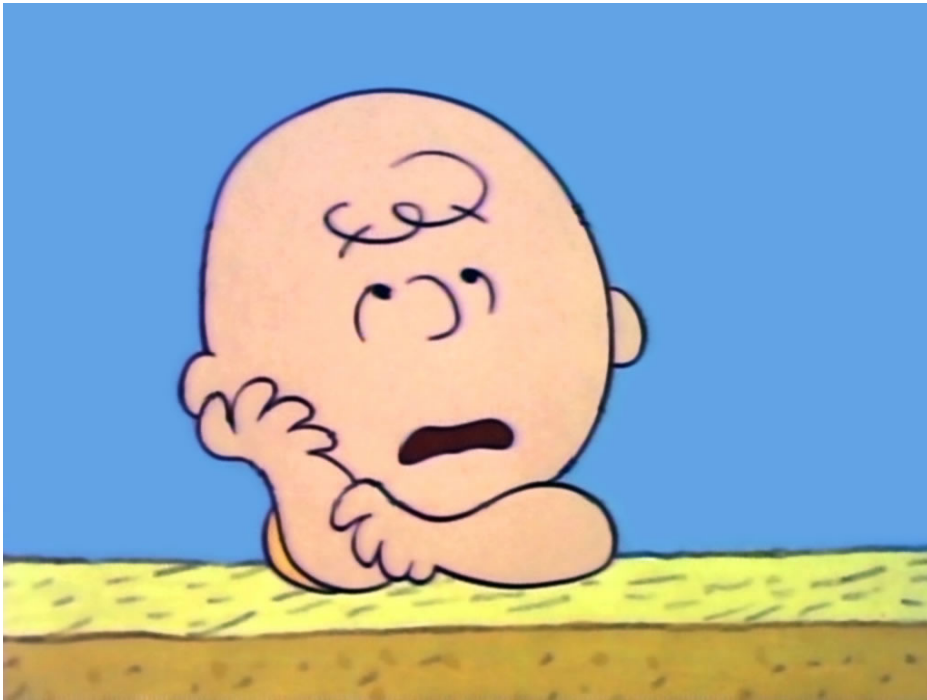


TIR4a



TIR2

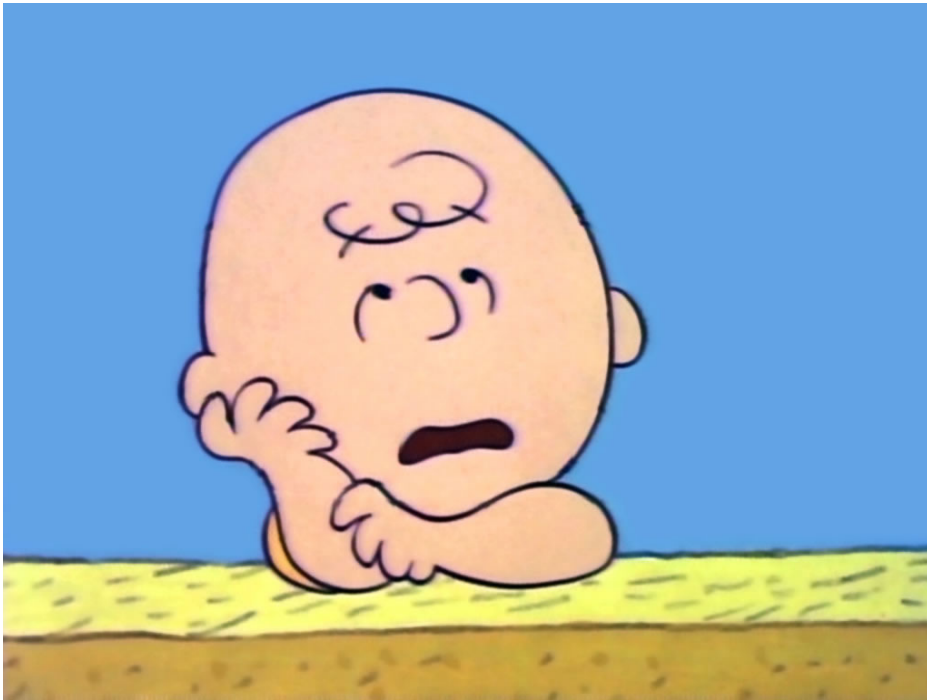
# Classificazione ecografica del rischio di malignità



- **È possibile?**
- **SI'!**



# Classificazione ecografica del rischio di malignità



- È utile?

Niente di meglio che le linee guida per conciliare il sonno!

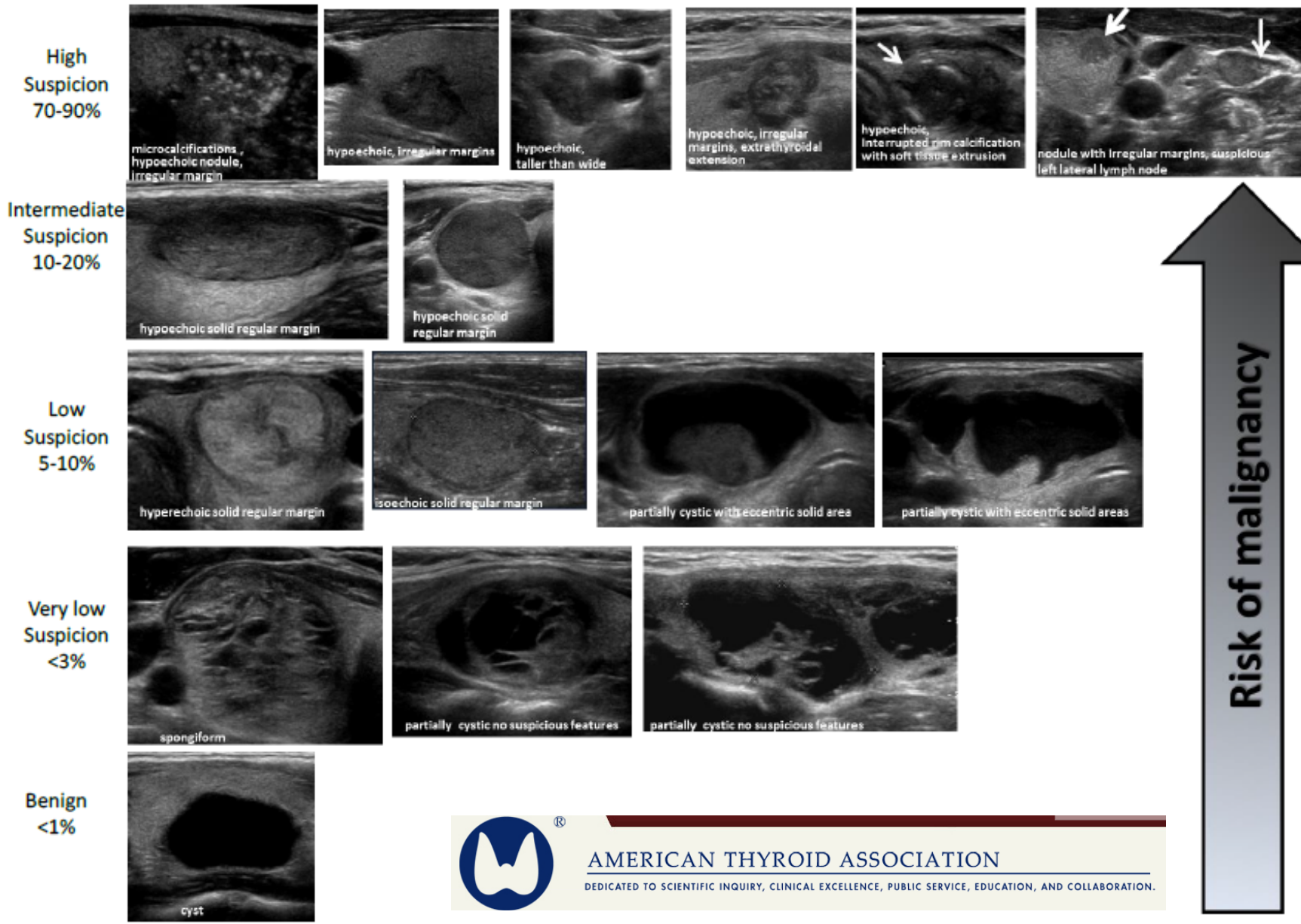


# *Thyroid sonography*

- The ultrasound report should convey nodule size (in 3 dimensions) and location (e.g. right upper lobe) and a description of the nodule's sonographic features including: composition (solid, cystic proportion, or spongiform), echogenicity, margins, presence and type of calcifications, and shape if taller than wide, and vascularity.
- **The pattern of sonographic features associated with a nodule confers a risk of malignancy, and combined with nodule size, guides FNA decision making**

Sonographic Pattern	US features	Estimated risk of malignancy
High suspicion	Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule <b>with</b> one or more 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	>70-90%*
Intermediate suspicion	Hypoechoic solid nodule with smooth margins <b>without</b> microcalcifications, extrathyroidal extension, or taller than wide shape	10-20%
Low suspicion	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid areas, <b>without</b> microcalcification, irregular margin or extrathyroidal extension, or taller than wide shape.	5-10%
Very low suspicion	Spongiform or partially cystic nodules <b>without</b> any of the sonographic features described in low, intermediate or high suspicion patterns	< 3%
Benign	Purely cystic nodules (no solid component)	< 1%





AMERICAN THYROID ASSOCIATION

DEDICATED TO SCIENTIFIC INQUIRY, CLINICAL EXCELLENCE, PUBLIC SERVICE, EDUCATION, AND COLLABORATION.



# US Thyroid report

- If a nodule is being assessed by US, the practitioner (be they a sonographer, surgeon, endocrinologist or radiologist) should be competent in identifying the characteristic signs that can allow a differentiation of thyroid nodules (i.e. either benign (U2), equivocal/indeterminate (U3), suspicious (U4) or malignant (U5) as outlined in the U classification
- A report should identify the various characteristics and give appropriate measurements of significant thyroid nodules/masses and the U score. In multinodular thyroids, the score for the most suspicious nodule should be recorded.



U2. Benign:

- (a) halo, iso-echoic / mildly hyper-echoic
- (b) cystic change +/- ring down sign (colloid)
- (c) micro- cystic / spongiform
- (d & e) peripheral egg shell calcification
- (f) peripheral vascularity.

U3. Indeterminate/Equivocal:

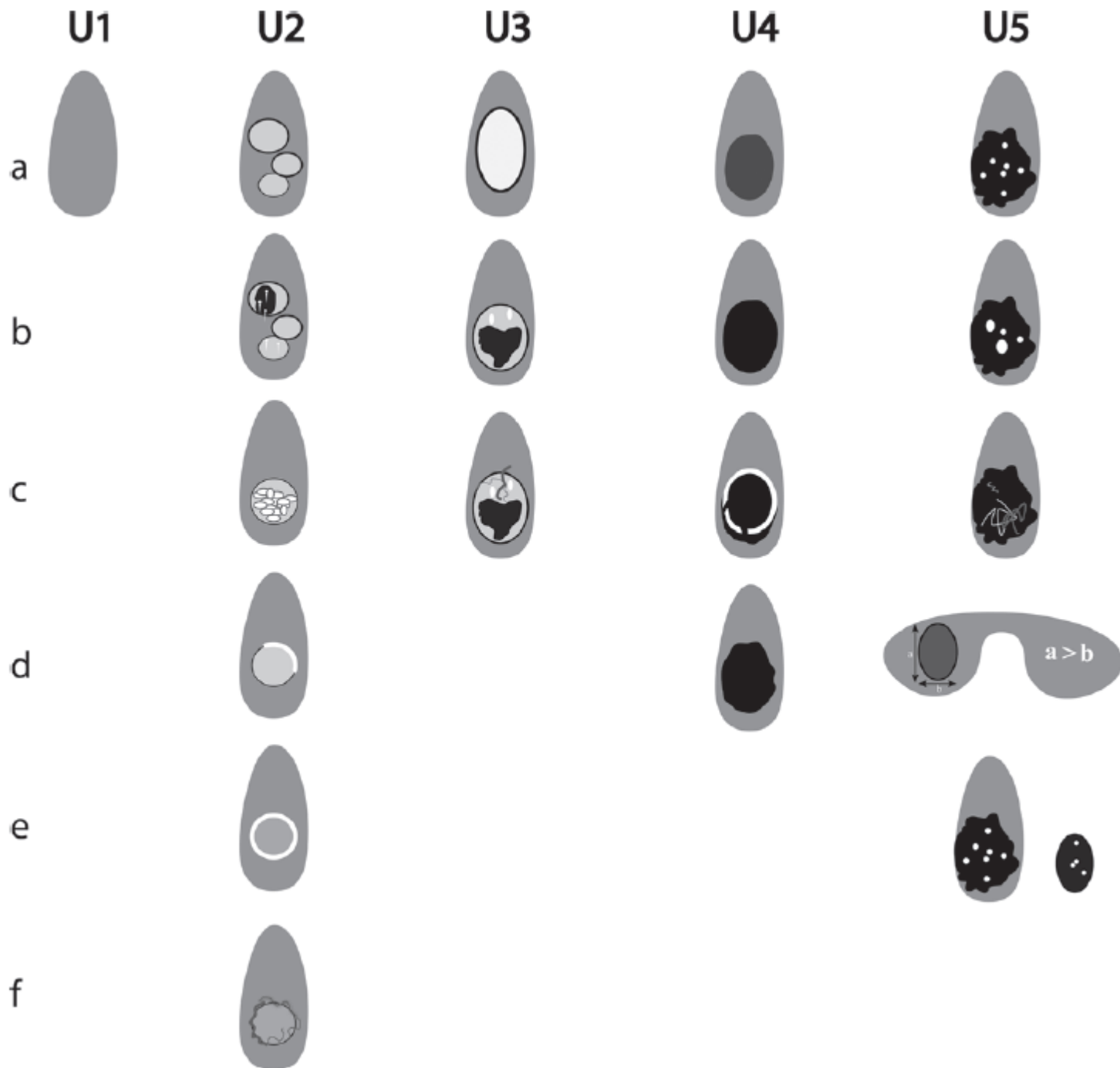
- (a) homogenous, hyper-echoic (markedly), solid, halo (follicular lesion).
- (b) ? hypo-echoic, equivocal echogenic foci, cystic change
- (c) mixed/central vascularity.

U4. Suspicious:

- (a) solid, hypo-echoic (cf thyroid)
- (b) solid, very hypo-echoic (cf strap muscle)
- (c) disrupted peripheral calcification, hypo-echoic
- (d) lobulated outline

U5. Malignant

- (a) solid, hypo-echoic, lobulated / irregular outline, micro-calcification. (? Papillary carcinoma)
- (b) solid, hypo-echoic, lobulated/irregular outline, globular calcification (? Medullary carcinoma)
- (c) intra-nodular vascularity
- (d) shape (taller >wide) (AP>TR)
- (e) characteristic associated lymphadenopathy







# Selection of nodules for FNAC: Key Recommendation

- US appearances that are indicative of a benign nodule (U1–U2) should be regarded as reassuring not requiring fine needle aspiration cytology (FNAC), unless a statistically high risk of malignancy.
- If the US appearances are equivocal, indeterminate or suspicious of malignancy (U3–U5), an US guided FNAC should follow.

# *Recommendations for diagnostic FNA based on sonographic features*

Thyroid nodule diagnostic FNA is recommended for :

- A) Nodules > 1cm with high suspicion sonographic pattern (**Strong recommendation, Moderate-quality evidence**)
- B) Nodules > 1 cm with intermediate suspicion sonographic (**Strong recommendation, Low-quality evidence**)
- C) Nodules > 1.5cm with low suspicion sonographic pattern (**Weak recommendation, Low-quality evidence**)
- D) Nodules > 2cm with very low suspicion sonographic pattern (e.g. - spongiform) (**Weak recommendation, Moderate-quality evidence**)

# *Recommendations for diagnostic FNA based on sonographic features*

Thyroid nodule diagnostic FNA is not required for:

E) Nodules that do not meet the above criteria.

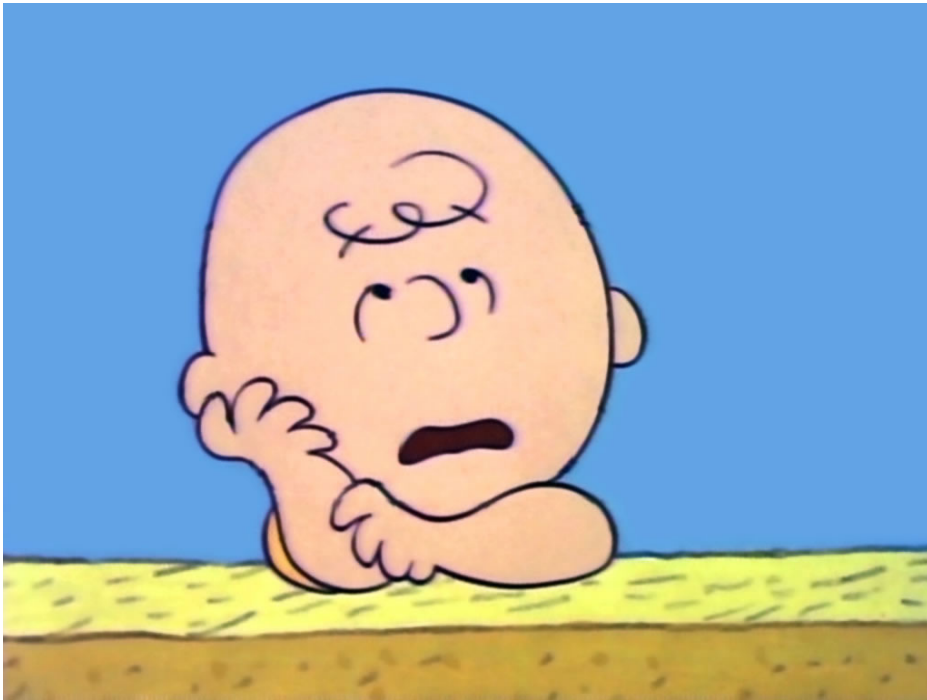
**(Strong recommendation, Moderate-quality evidence)**

F) Nodules that are purely cystic (**Strong**

**recommendation, Moderate-quality evidence)**



# Classificazione ecografica del rischio di malignità



- È utile?
- SI'

# FNA is recommended for:

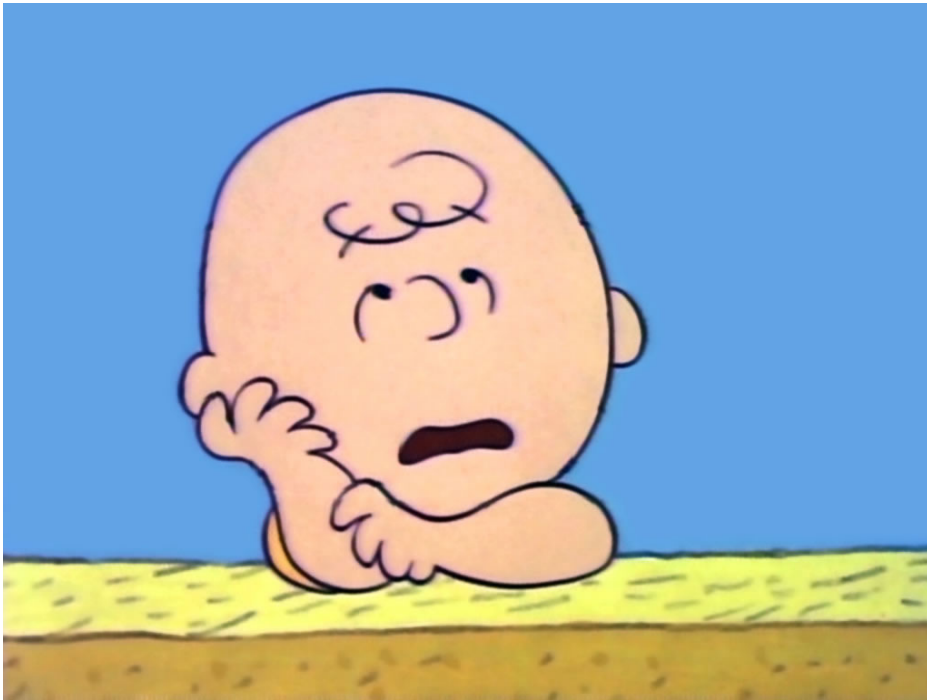


- High-US-risk thyroid lesions  $\geq 10$  mm
- Intermediate-US-risk thyroid lesions  $> 20$  mm
- Low-US-risk thyroid lesions only when  $> 20$  mm and increasing in size or associated with a risk history and before thyroid surgery or minimally invasive ablation therapy

# Utilità della classificazione ecografica

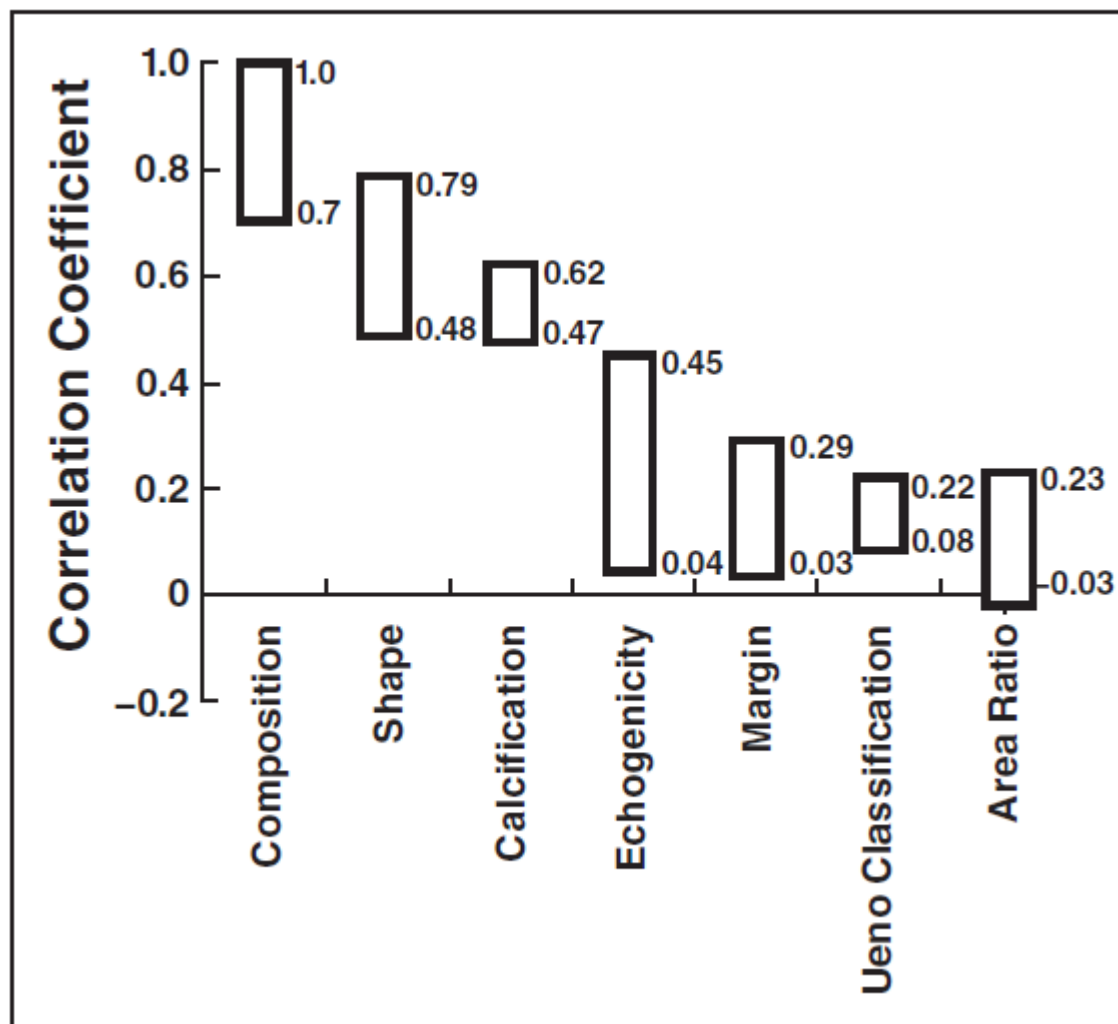
- Rendere omogenea e sistematica la valutazione dell'operatore
- Standardizzare le indicazioni all'agoaspirato
- Fornire una sintesi del dato ecografico utile a “pesare” il referto citologico

# Classificazione ecografica del rischio di malignità



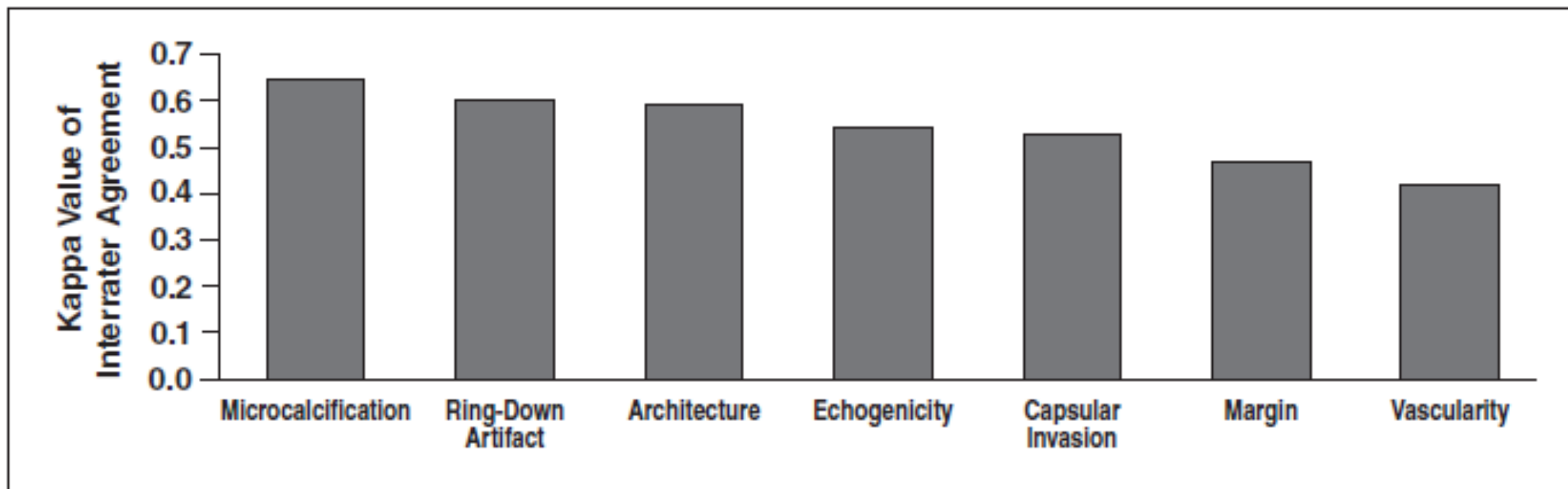
- **È pericoloso?**

# Interobserver Agreement in Assessing the US Features of Thyroid Nodules





# Agreement between two radiologists for each sonographic feature



# Interobserver Agreement of Thyroid Imaging Reporting and Data System (TIRADS)

- The IA between the 3 observers was only fair for TIRADS categories 2–5 (Cohens kappa = 0.27,  $p = 0.000001$ ) and TIRADS categories 2/3 versus 4/5 ( $ck = 0.25, p = 0.0020$ ).
- 92–100% of patients with TIRADS-2 had benign lesions, while 28–42% with TIRADS-5 had malignant cytology/histology.
- The negative-predictive-value (NPV) was 92–100% for TIRADS using TIRADS-categories 4&5 for the diagnosis of malignancy,
- This demonstrates the difficulties of categorizing according to TIRADS.

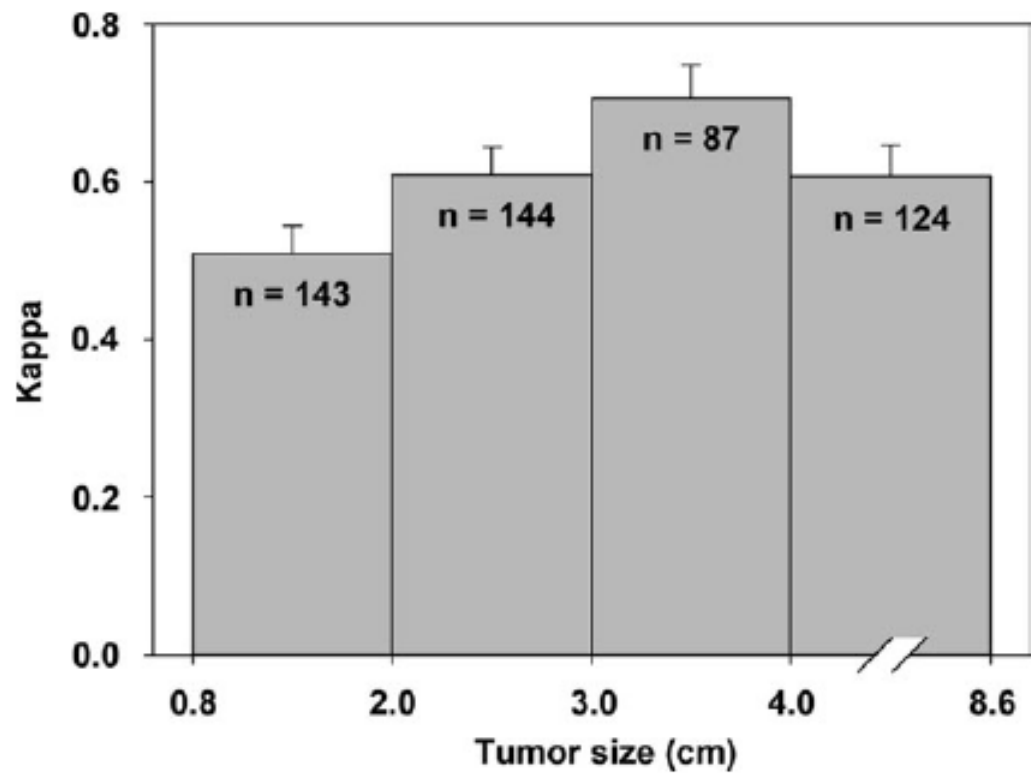
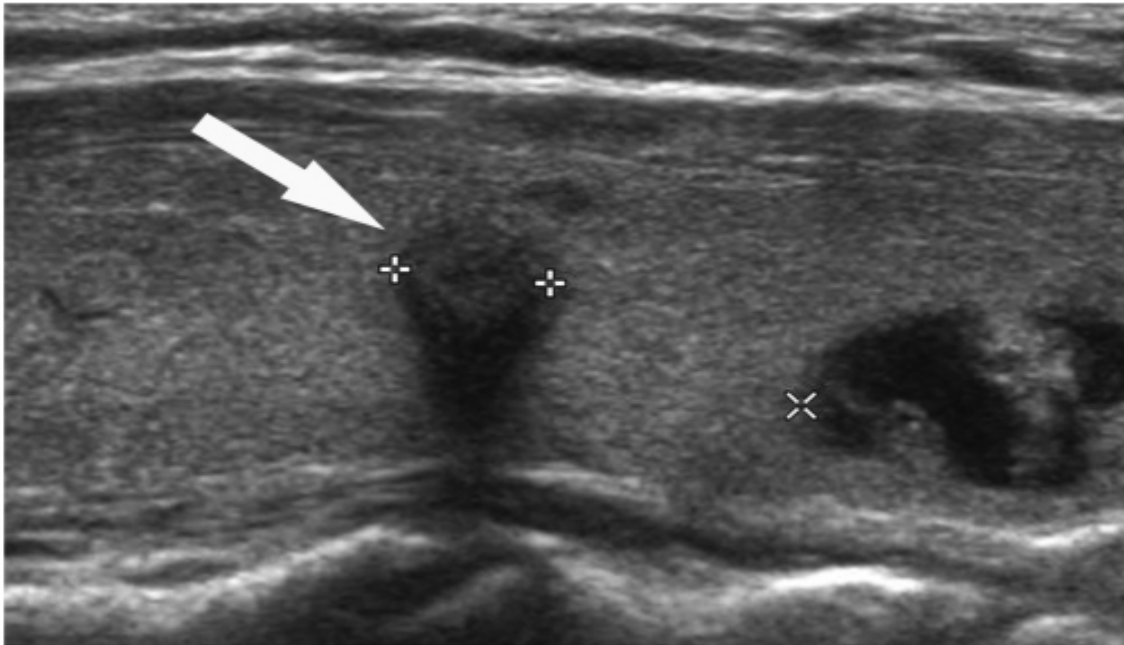
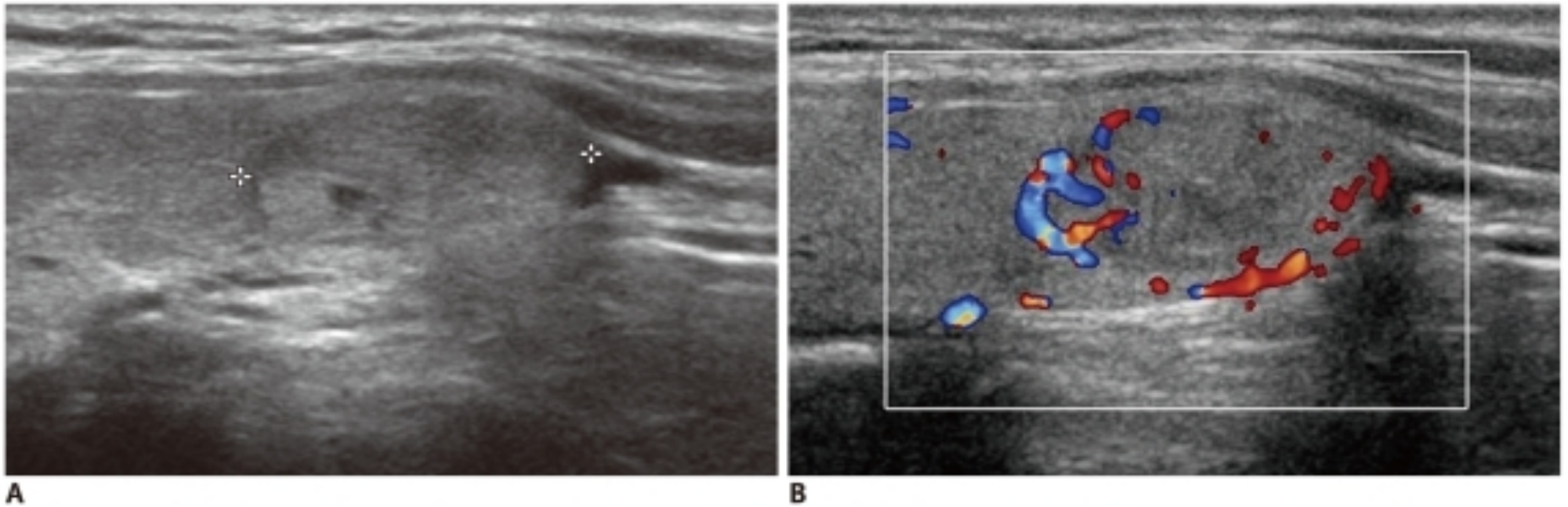


FIGURE 2. Interobserver agreement for the Thyroid Imaging Reporting and Data System (TI-RADS) classification of thyroid nodules stratified for tumor size. The filled shapes indicate the kappa value; the bars indicate the SEs of the means.



[Fig. 5](#)

Benign nodule designated as suspicious for malignancy as result of thyroid US in 52-year-old woman (false positive).

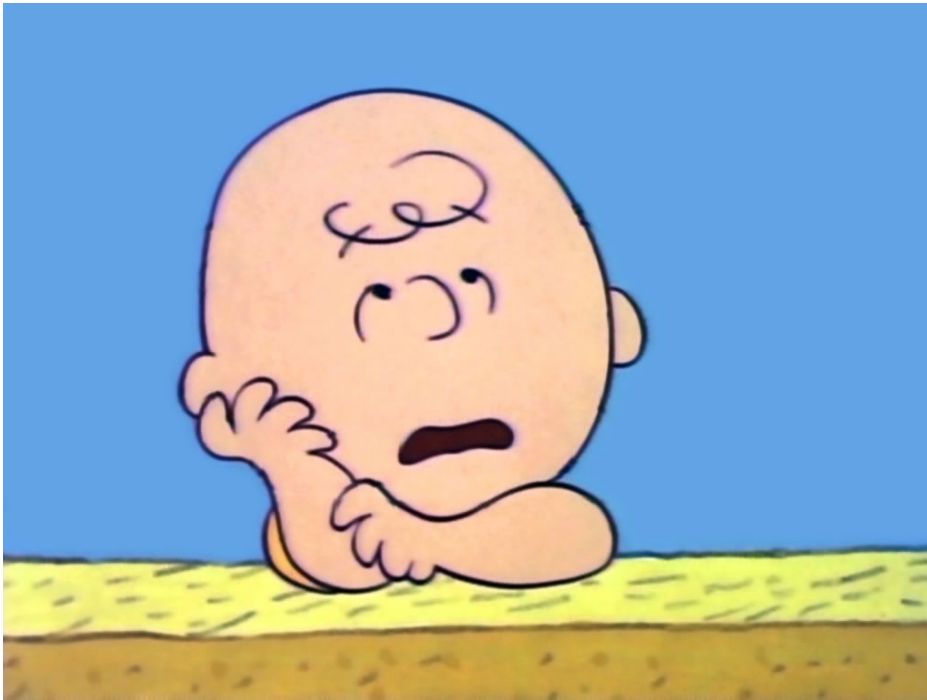


Papillary thyroid carcinoma designated as benign from thyroid US in 18-year-old woman (false negative).

Longitudinal US image of right thyroid nodule shows ovoid shape, isoechogenicity, smooth margin, and peripheral vascularity (**A, B**).

Korean J Radiol. 2011 Sep-Oct; 12(5): 559–567

# Classificazione ecografica del rischio di malignità



- **È pericoloso?**
- **NO, ma il sistema non è infallibile...**

# AAACE AME thyroid nodule guidelines

- **Class 1. Low-risk thyroid lesion –**
  - Mostly cystic nodules with reverberating artifacts that are not associated with suspicious US signs
  - Isoechoic spongiform nodules confluent or with regular halo
- **Class 2. Intermediate-risk thyroid lesion.**
  - Slightly hypoechoic nodules and isoechoic nodules with ovoid-to-round shape and smooth or ill-defined margins. Intranodular vascularization, elevated stiffness at elastography and macro- or continuous rim calcifications may be present
- **Class 3. High-risk thyroid lesion:** at least one of the following suspicious features:
  - marked hypoechogenicity (ch pre-thyroid muscles)
  - spiculated or microlobulated margins
  - microcalcifications
  - taller-than-wide shape
  - evidence of extrathyroidal growth or pathologic adenopathy

- **Possibile** se vogliamo veramente metterci la mano sulla coscienza
- **Utile** Se vogliamo frenare su OVERDIAGNOSIS/ OVERTREATMENT di noduli tiroidei e ridurre ansie ingiustificate per i pazienti
- **Pericoloso** Per chi sarà costretto a cambiare mestiere per paura di sbagliare



dott. VINCENZO GIAMMARCO



**Grazie per l'attenzione!**

