



**19. Endokrinológiai  
Továbbképző Tanfolyam**

Radisson Blu Béke | 2023. november 23-25.

Semmelweis Egyetem  
Belgyógyászati és  
Onkológiai Klinika  
Magyar Endokrinológiai és  
Anyagcsere Társaság  
közös rendezvénye

**Budapest, Hungary, 25 Nov. 2023**

**European Thyroid Association Clinical Practice Guideline  
for Thyroid Nodule Management**

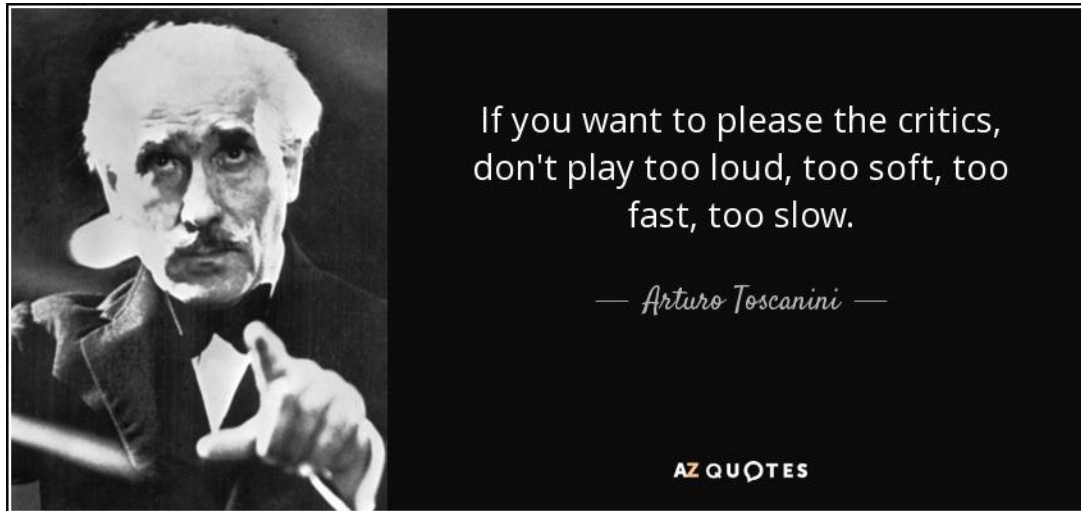
**Laszlo Hegedüs**



# Current Disclosures

- Receive fees and/or grant support from: Novo Nordisk, IBSA, Lundbeck, Merck, Berlin-Chemie, Horizon, Bracco
- None of the above perceived as influencing the present talk
- Did not use ChatGPT (AI)
- Be aware that I understand Hungarian!

# Paraphrasing a master



If you want to please a scientific audience  
Don't underestimate, or overestimate it  
Don't speak too loud or too soft  
Don't speak too fast or too slow  
Curb your humor but do not bore

Arturo Toscanini  
Parma, Italy, 1867 – New York, USA; 1957

# Who did the work?

## 2023 European Thyroid Association Clinical Practice Guidelines for Thyroid Nodule Management

Cosimo Durante,<sup>1, §</sup> Laszlo Hegedüs,<sup>2, §</sup> Agnieszka Czarniecka,<sup>3</sup> Ralf Paschke,<sup>4</sup> Gilles Russ,<sup>5</sup> Fernando Schmitt,<sup>6</sup> Paula Soares,<sup>7</sup> Tamas Solymosi,<sup>8</sup> and Enrico Papini<sup>9</sup>

<sup>§</sup> C.D. and L.H co-chaired and provided equal first-author-level contribution to this work.



CS

LH

AC

RP

GR

FS

PS

**TS**

EP

# On behalf of the 2023 ETA "Guideliners"\*



\*The anatomical division of the work

On behalf of the 2023 ETA "Guideliners"\*

European Thyroid  
JOURNAL

C Durante, L Hegedüs *et al.*

12:5

e230067

GUIDELINES

# 2023 European Thyroid Association Clinical Practice Guidelines for thyroid nodule management

Cosimo Durante<sup>ID1,\*</sup>, Laszlo Hegedüs<sup>ID2,\*</sup>, Agnieszka Czarniecka<sup>3</sup>, Ralf Paschke<sup>ID4</sup>, Gilles Russ<sup>ID5</sup>,  
Fernando Schmitt<sup>ID6</sup>, Paula Soares<sup>ID7</sup>, Tamas Solymosi<sup>8</sup> and Enrico Papini<sup>9</sup>



\*The anatomical division of the work

# Can this theme be covered in one single guideline? Max 5000 words and ca. 100 references



European  
Thyroid Journal

Eur Thyroid J 2013;2:147–159  
DOI: 10.1159/000354537

Received: April 11, 2013  
Accepted after revision: July 18, 2013  
Published online: September 5, 2013

## 2013 European Thyroid Association Guidelines for the Management of Thyroid Cancer

L. Leenhardt<sup>a</sup> M.F. Erdogan  
T. Rago<sup>f</sup> G. Russ<sup>a</sup>

<sup>a</sup>Department of Nuclear Medicine, Pitié S  
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Odense, Denmark; <sup>d</sup>Division of Endocrin  
of Pennsylvania, Philadelphia, Pa., USA; <sup>e</sup>I  
<sup>f</sup>Endocrine Unit 1, Department of Interna

European  
Thyroid Journal

## European Thyroid Association Guidelines for the Management of Thyroid Cancer

Ralf Paschke<sup>a</sup> Silvia Ca  
Thomas J. Musholt<sup>e</sup> M.

<sup>a</sup>Division of Endocrinology and Me  
Charbonneau Cancer Institute, Cal  
Endocrinology Section, University  
Rome, Italy; <sup>d</sup>Department of Nucl  
Center and Institute of Oncology,  
General, Visceral, and Transplant  
Mainz, Germany; <sup>f</sup>Institute of Mole

European  
Thyroid Journal

## European Thyroid Association Guidelines for the Management of Thyroid Cancer

Gilles Russ<sup>a</sup> Stee  
Rose Ngu<sup>e</sup> Laur

<sup>a</sup>Thyroid and Endocrine  
University, Paris, France; <sup>c</sup>Department of Endocrir  
Ankara, Turkey; <sup>d</sup>Depar  
Italy; <sup>e</sup>Head Neck and Th  
Trust, London, UK

Eur Thyroid J 2017;6:225–237  
DOI: 10.1159/000478927

Received: May 4, 2017  
Accepted: June 17, 2017

European  
Thyroid Journal

European  
Thyroid Journal

## 2020 European Thyroid Association Guidelines for the Management of Thyroid Cancer

Enrico Papini<sup>a</sup> Hervé Monpeys:

<sup>a</sup>Department of Endocrinology and Metabolis  
Hospital, Paris, France; <sup>c</sup>Department of Endocr  
Reggio Emilia, Italy; <sup>d</sup>Department of Endocrin

Guidelines

Eur Thyroid J 2021;10:185–197  
DOI: 10.1159/000516469

Received: 03/23/2021  
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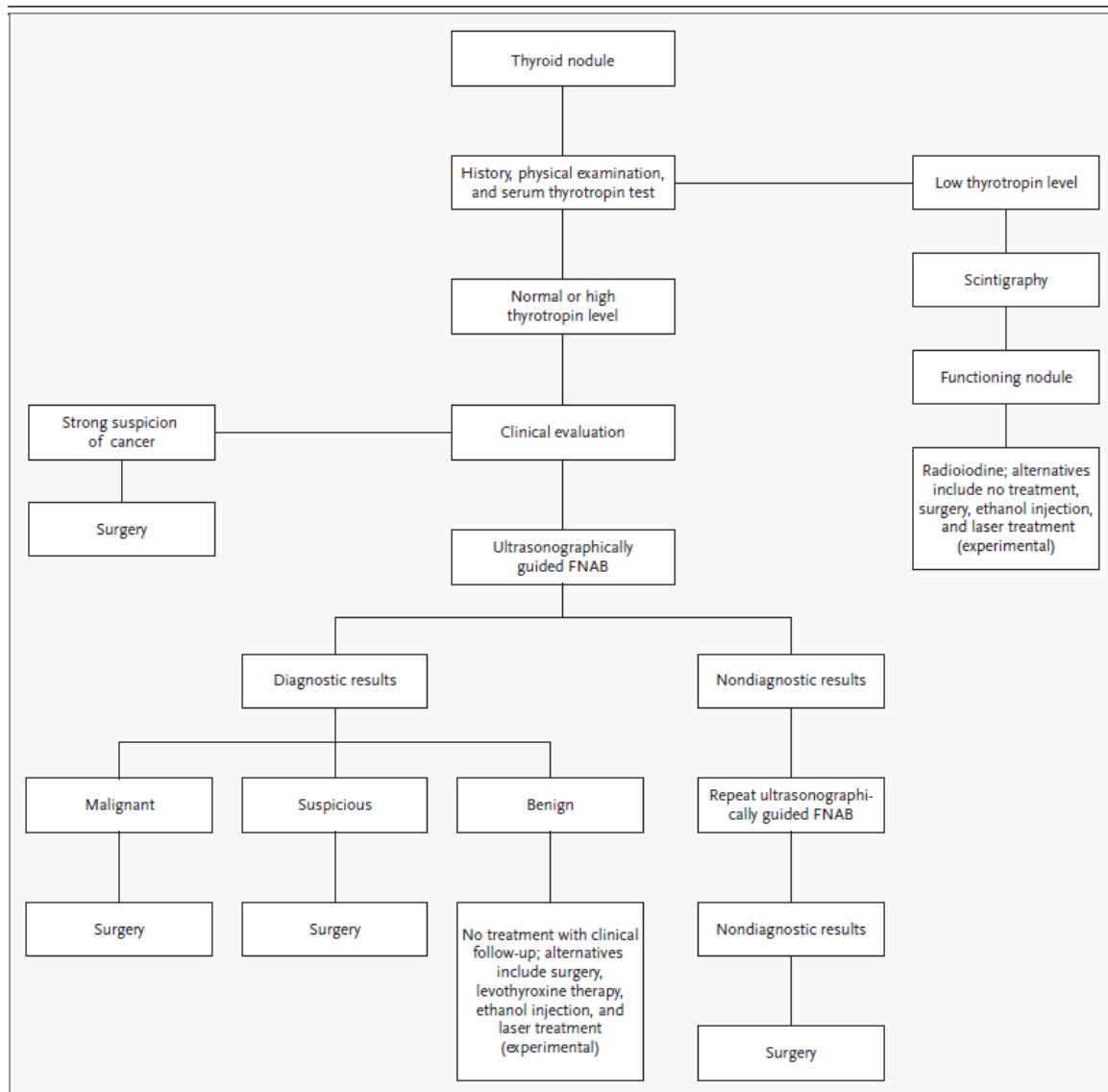
## European Thyroid Association and Cardiovascular and Interventional Radiological Society of Europe 2021 Clinical Practice Guideline for the Use of Minimally Invasive Treatments in Malignant Thyroid Lesions

Giovanni Mauri<sup>a,b</sup> Laszlo Hegedüs<sup>c</sup> Steven Bandula<sup>d</sup> Roberto Luigi Cazzato<sup>e</sup>  
Agnieszka Czarniecka<sup>f</sup> Oliver Dudeck<sup>g</sup> Laura Fugazzola<sup>h,i</sup>  
Romana Netea-Maier<sup>j</sup> Gilles Russ<sup>k</sup> Göran Wallin<sup>l</sup> Enrico Papini<sup>m</sup>

<sup>a</sup>Department of Oncology and Hemato-Oncology, University of Milan, Milan, Italy; <sup>b</sup>Division of Interventional Radiology, European Institute of Oncology, IRCCS, Milan, Italy; <sup>c</sup>Department of Endocrinology, Odense University Hospital, University of Southern Denmark, Odense, Denmark; <sup>d</sup>Interventional Oncology Service, University College Hospital, London, United Kingdom; <sup>e</sup>Department of Interventional Radiology, University Hospital of Strasbourg, Strasbourg, France; <sup>f</sup>The Oncologic and Reconstructive Surgery Clinic, Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland; <sup>g</sup>Center for Microtherapy, Klinik Hirslanden, Zurich, Switzerland; <sup>h</sup>Department of Endocrinology and Metabolic Diseases, IRCCS Istituto Auxologico Italiano, Milan, Italy; <sup>i</sup>Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; <sup>j</sup>Division of Endocrinology, Department of Internal Medicine, Radboud University Medical Center, Nijmegen, The Netherlands; <sup>k</sup>Thyroid and Endocrine Tumors Unit, La Pitié-Salpêtrière Hospital, Sorbonne University, Paris, France; <sup>l</sup>Department of Surgery, Faculty of Medicine and Health, Örebro University, Örebro, Sweden; <sup>m</sup>Department of Endocrinology & Metabolism, Ospedale Regina Apostolorum, Albano, Italy

5 guidelines at the price of one?





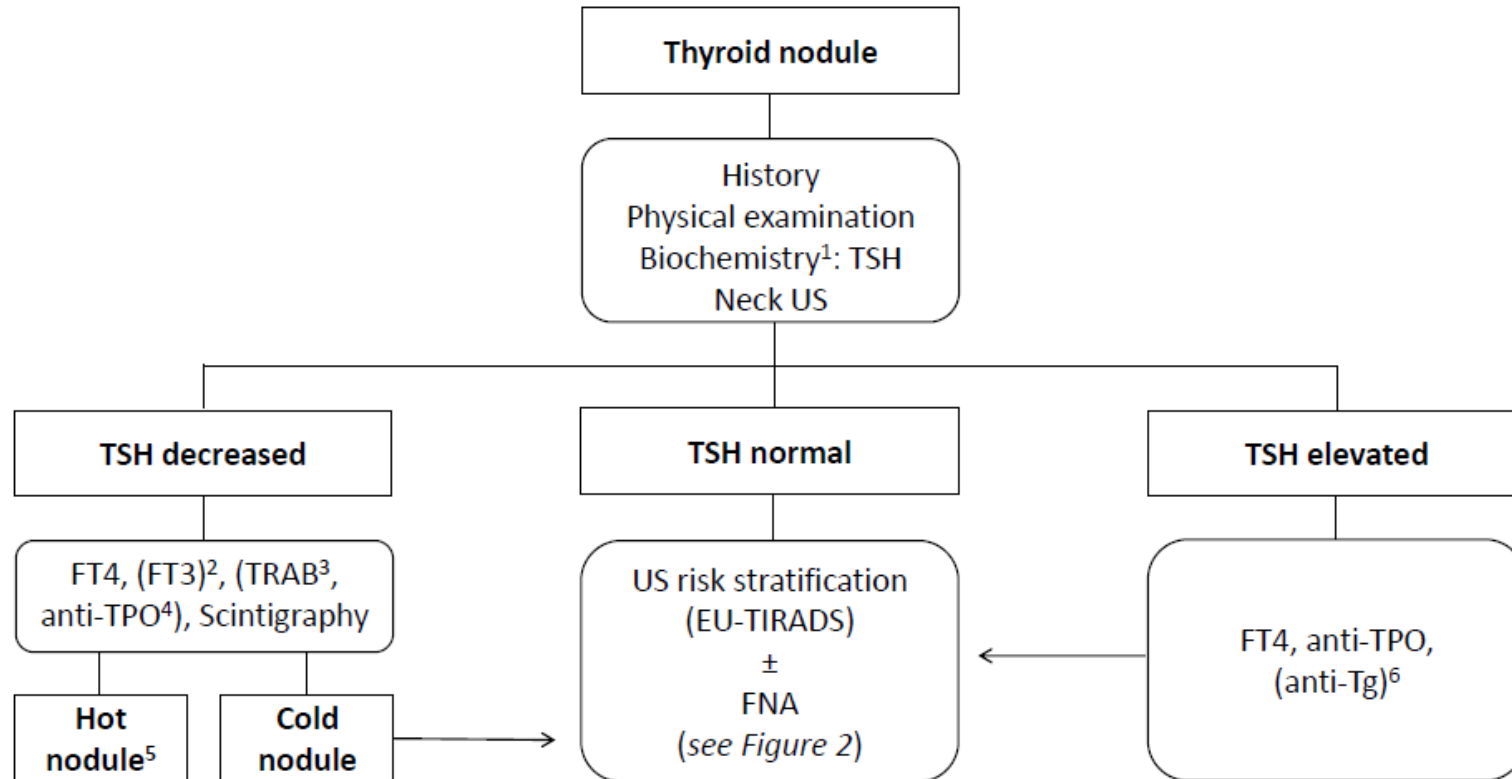
**Figure 1. Algorithm for the Cost-Effective Evaluation and Treatment of a Clinically Detectable Solitary Thyroid Nodule.**

In the case of a strong clinical suspicion of cancer, surgery is recommended, regardless of the results of fine-needle aspiration biopsy (FNAB). In the case of a suppressed level of serum thyrotropin, thyroid scintigraphy should be performed, since a functioning nodule almost invariably rules out cancer. In the case of a nondiagnostic FNAB, a repeated biopsy yields a satisfactory aspirate in 50 percent of cases. If ultrasonography reveals additional nodules that are more than 10 mm in diameter, FNAB could be performed on one other nodule, in addition to the one that is clinically detectable. The therapeutic options shown cover both solid and cystic nodules. In the case of a recurrent cyst, the possibilities of treatment are repeated FNAB, surgery, and ethanol injection. I do not recommend levothyroxine therapy for the thyroid nodule.

- An algorithm for the management of thyroid lesions from 2004\*
- How much has changed?



# The 2023 ETA guideline on thyroid nodule management



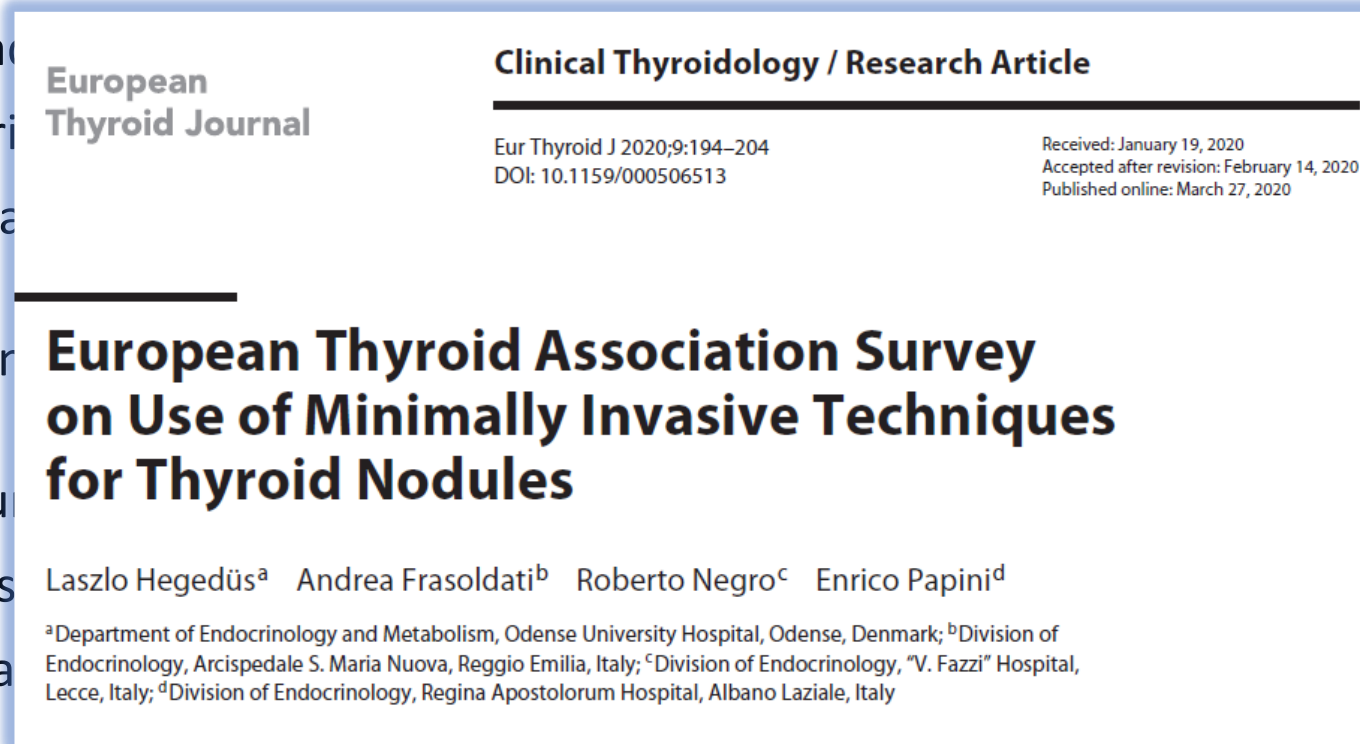
- A simplification, certainly
- But, you cannot see the treatment part
- Neither all our footnotes

## Important background information, often forgotten....

- Up to **60% of adults** harbor thyroid nodules
- In **most** countries 90-95% are **benign**
- Vast **majority asymptomatic** in no need of treatment
- Many small cancers **can be managed conservatively**
- **Superfluous surgery** an issue
- Unfavorable risk and cost-benefit ratio
- Active surveillance and **MIT underutilized**
- Huge geographic **variation in access** to management options
- **Lack of considering patient's voice**

# Important background information, often forgotten....

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**Lack of availability!** Hegedüs L et al. Eur. Thyroid J. 2020

## Important background information, often forgotten....

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- Lack of considering patient's voice
- Provide a clinical practice guideline for initial workup and subsequent management
- **Does not cover** management of thyroid **malignancy**
- Recommendations should **take into consideration** e.g. clinical setting, expertise, available technology, legislation, **pat. preference**
- Should be based on evidence
- Is a guideline **NOT A LEGAL DOCUMENT**

## Important background information, often forgotten....

- Up to 60% of adults harbor thyroid nodules
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- Provide a clinical practice guideline for initial workup and subsequent management
- Do not cover management of thyroid malignancy
- Recommendations should take into consideration e.g. clinical setting, expertise, available technology, legislation, pat. preference
- Should be based on evidence
- Is a guideline **NOT A LEGAL DOCUMENT**
- **We think that any country can translate it into their own language, copy  $\geq 95\%$ , and amend with necessary footnotes as a local National Guideline**

# Methodology and grading of evidence

- Available evidence, knowledge and experience
- Panellists ETA members
- Literature search via MEDLINE through PubMed
- **European literature prioritized**
- **GRADE** (Grading of Recommendations, Assessment, Development, and Evaluation) used to grade quality of evidence and making recommendations
- **Quality of evidence** rated: high (∅∅∅∅), moderate (∅∅∅0), low (∅∅00), or very low (∅000)
- **Strength of recommendation**: strong (1) or weak (2).
- On occasion we used "ungraded good practice statement"
- **Consent** (e.g. agreement 8/9; 88.9%) demanded ≥80% (that is a minimum of 8/9 panellists) and at which out of a max of 2 voting rounds this was achieved

# Contents

Initial evaluation

Thyroid ultrasound

Thyroid biopsy

Pathology

Molecular diagnostics

Non ultrasound imaging modalities

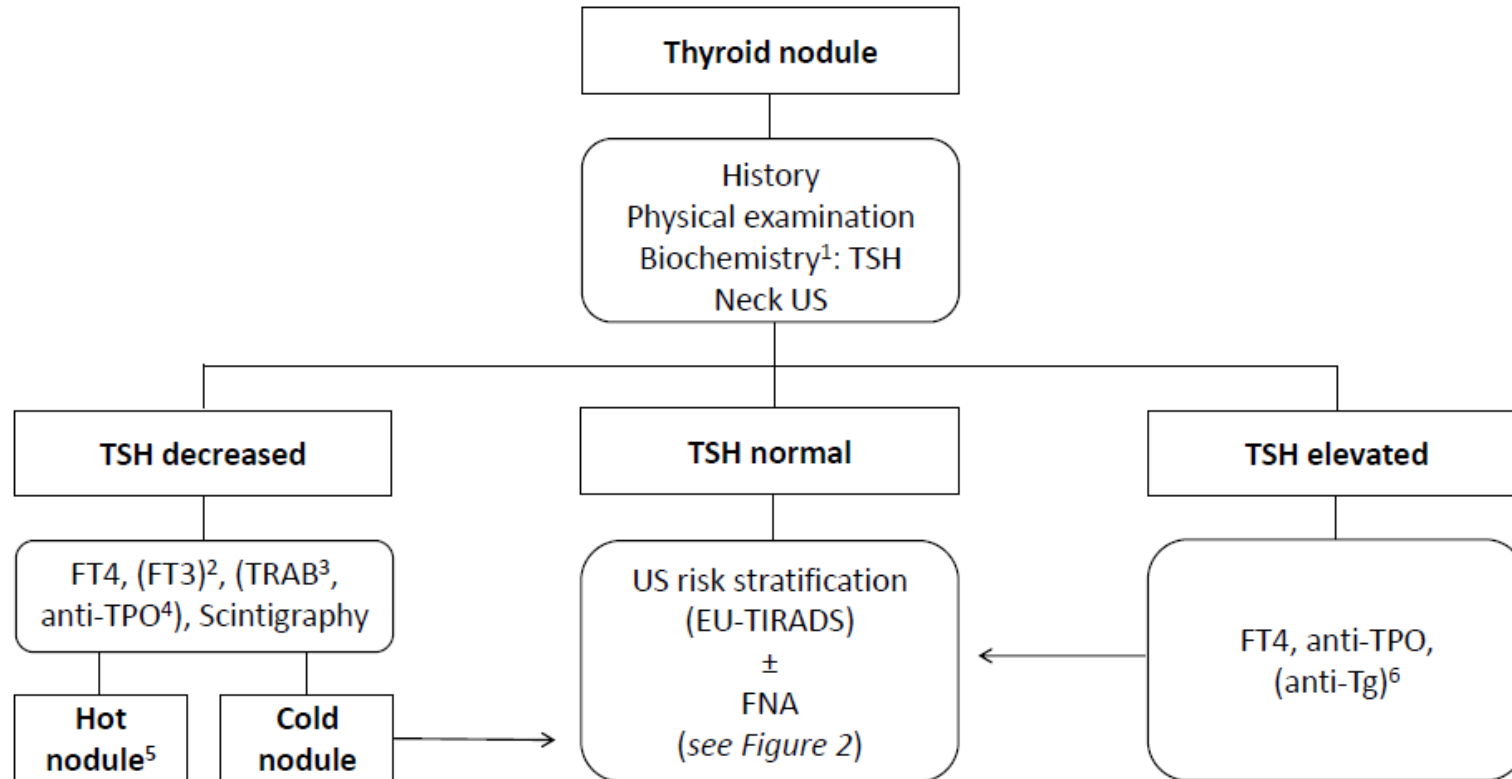
Therapeutic options: non-surgical approaches

Therapeutic options: surgical approach

**35**  
**recommendations**

# The 2023 ETA guideline on thyroid nodule management

## Initial evaluation

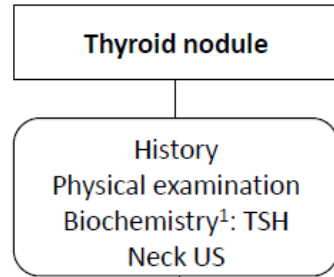


- Should include personal and family history, physical evaluation, thyroid function testing (a min of TSH), and neck US (1; ØØØØ; 9/9; round 1). Calcitonin? 🙅 🙆



# The 2023 ETA guideline on thyroid nodule management

## Initial evaluation



ORIGINAL ARTICLE

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Endocrine Care

### The Thyroid-Related Quality of Life Measure ThyPRO Has Good Responsiveness and Ability to Detect Relevant Treatment Effects

Torquil Watt, Per Cramon, Laszlo Hegedüs, Jakob Bue Bjorner, Steen Joop Bonnema, Åse Krogh Rasmussen, Ulla Feldt-Rasmussen, and Mogens Groenvold

Department of Endocrinology (T.W., P.C., Å.K.R., U.F.-R.), Copenhagen University Hospital Rigshospitalet, DK-2100 Copenhagen, Denmark; Department of Endocrinology and Metabolism (L.H., S.J.B.), Odense University Hospital, DK-5000 Odense, Denmark; QualityMetric (J.B.B.), Lincoln, Rhode Island 02865; Department of Public Health (M.G., J.B.B.), University of Copenhagen, DK-1353 Copenhagen, Denmark; National Research Institute for the Working Environment (J.B.B.), DK-2200 Copenhagen, Denmark; and Department of Palliative Medicine (M.G.), Bispebjerg Hospital, DK-2400 Copenhagen, Denmark

- Should include personal and family history, physical evaluation, thyroid function testing (a min of TSH), and neck US (1; 9/9; ØØØØ, round 1). Calcitonin?
- Consider the use of a PRO (patient related outcome measure) for evaluation of symptomatology (1; 8/9; ØØØØ; round 1)

## Factors other than size and US-risk level, which strengthen or weaken the indication for FNA

### Strengthens FNA

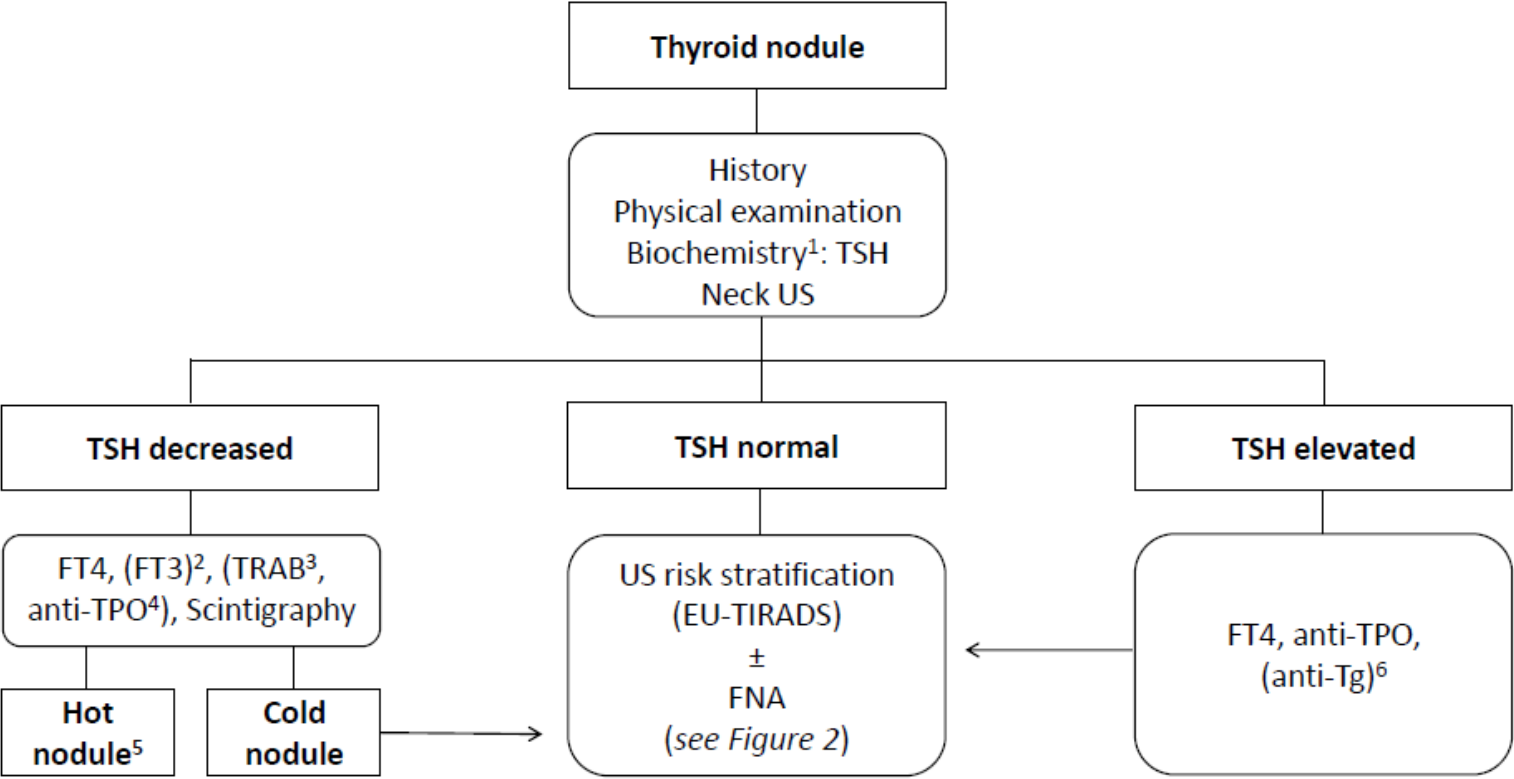
- Male sex
- Young age
- Solitary nodule
- Compressive symptoms
- Family history of MTC or MEN-2
- Head and neck radiation
- Planned thyr. or parathyr. surgery
- **Patient preference**
- Monogenic syndromic thyroid suscep.
- History of thyroid cancer
- Elevated s-calcitonin
- 18-FDG or MIBI uptake

### Weakens FNA

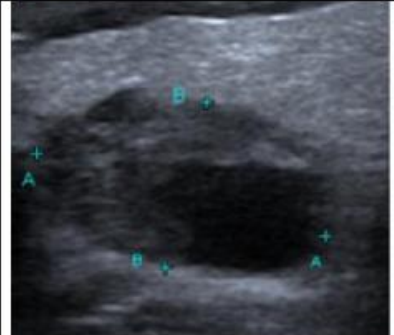
- Long history of stable or slowly growing MNG
- Limited life expectancy
- Significant comorbidity
- Family history of benign nodular thyroid disease
- Subnormal TSH
- Autonomous nodule on isotope scan
- **Patient preference**

# The 2023 ETA guideline on thyroid nodule management

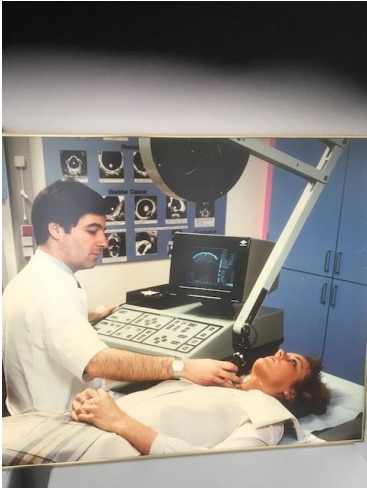
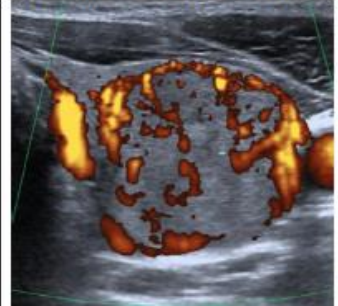
## Thyroid ultrasound



a. A markedly hyper-echogenic nodule is considered indeterminate regarding its malignant risk.



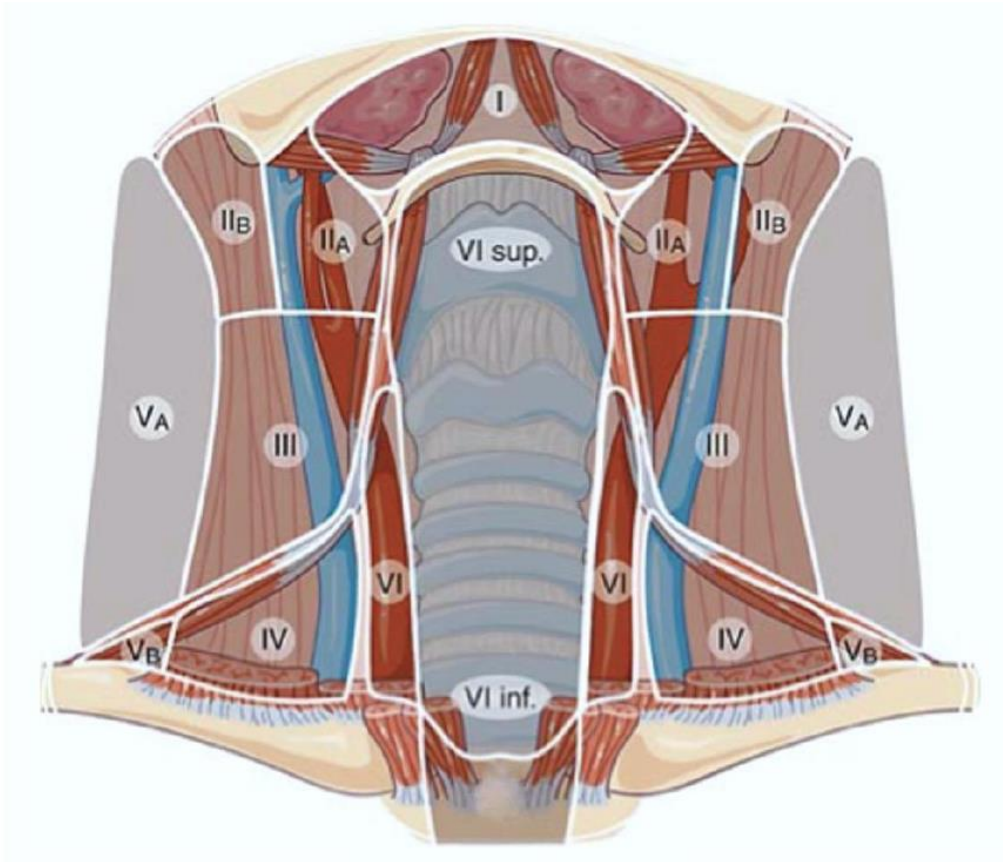
b. A nodule containing an echogenic focus that appears to be cystic is indeterminate.



Unidentified individuals early 1980s

# The 2023 ETA guideline on thyroid nodule management

## Thyroid ultrasound

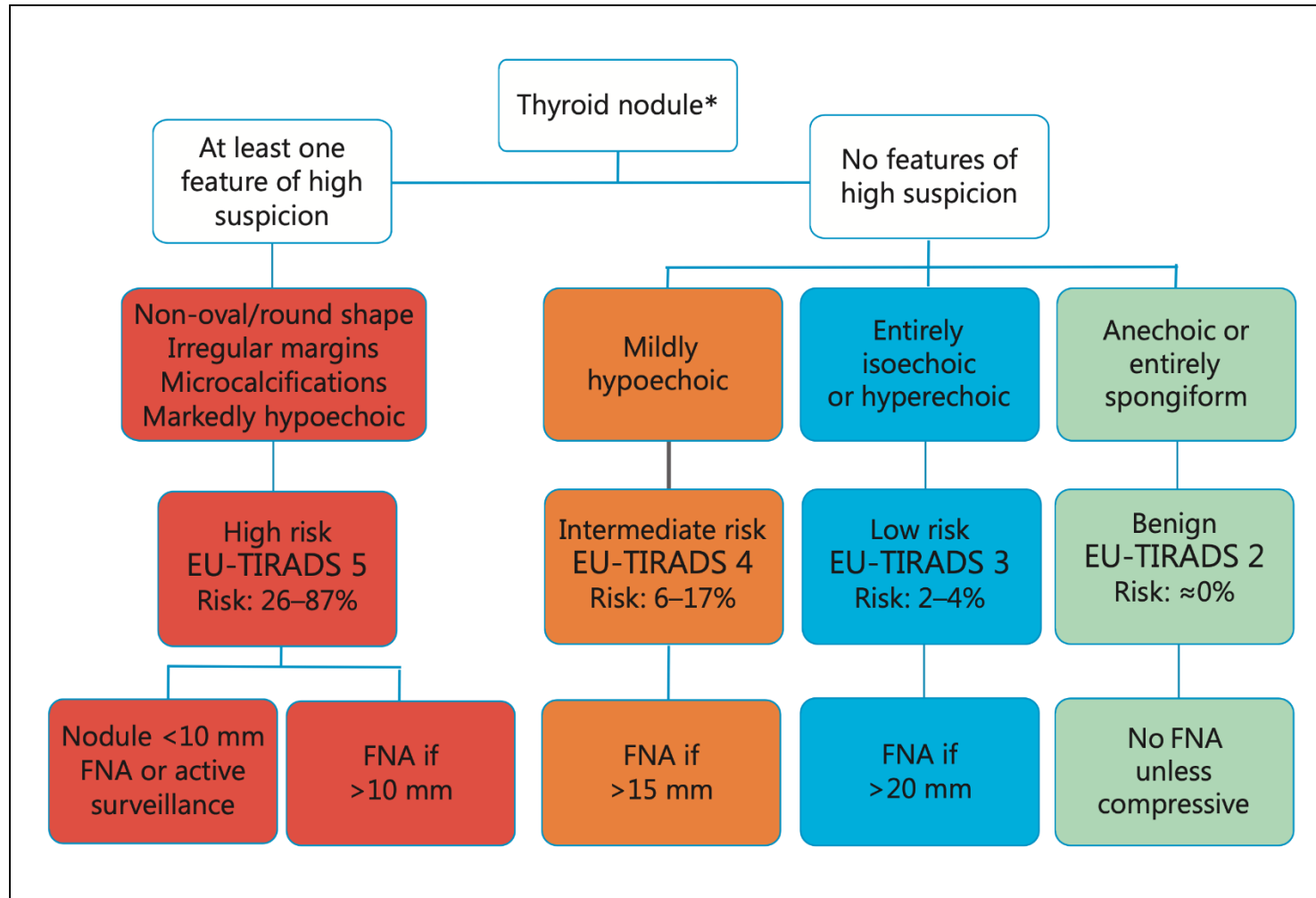


- Neck US (thyroid and the central and lateral cervical compartm. In all suspected of nodular thyroid disease (1; ØØ00; 9/9; round 1)
- Use **EU-TIRADS\*** for nodule description (risk of cancer) (1; ØØ00; 9/9; round 1)
- If multinodular, describe all with susp. Features
- Doppler imaging, elasto-sonography and contrast enhanced US (CEUS) considered ancillary techniques (2; Ø000; 9/9; round 1)

\*ETA Thyroid Imaging Reporting and Data Systems

# The 2023 ETA guideline on thyroid nodule management

## Thyroid ultrasound and use of EU-TIRADS\*



\*ETA Thyroid Imaging Reporting and Data Systems

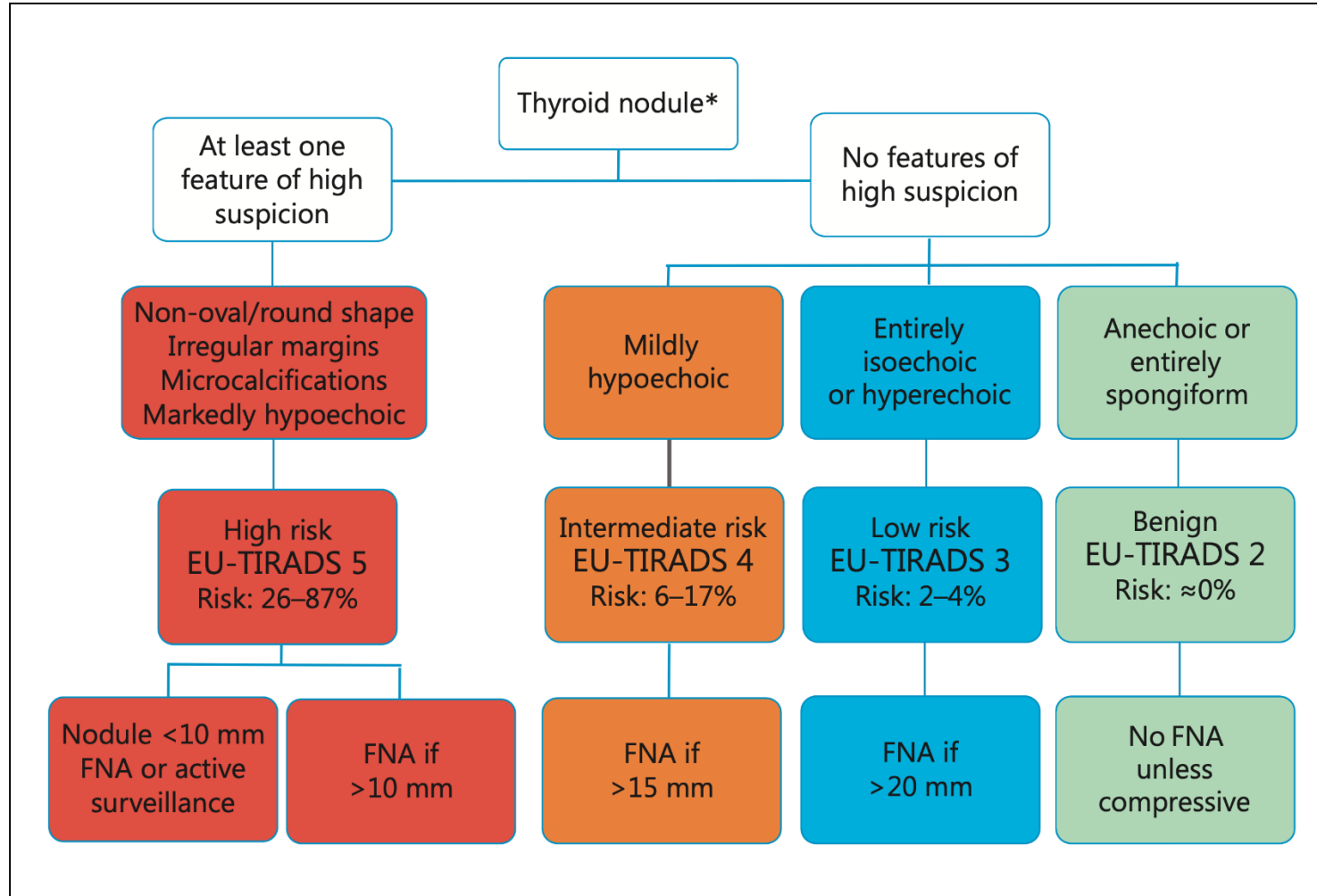
\*Russ G et al. Eur. Thyroid J. 2017;6:225-37.

# Elements of thyroid ultrasound reporting

Thyroid lobes	Echogenicity Size (three diameters and volume) Presence of substernal extension or compression of cervical structures
Nodule	Size (three diameters and volume) Location (according to the three axes) Echogenicity Composition Suspicious and non-suspicious signs if present <sup>a</sup> Possible extrathyroidal extension
Which discrete lesions should be described?	Nodules larger than 10 mm. Nodules between 5 and 10 mm with suspicious signs
How many nodules should be described in detail?	The largest one and those with suspicious signs if the number of nodules is >3 in a lobe <sup>b</sup>
Pathological <sup>c</sup> lymph nodes if present	Location, three diameters, features

# The 2023 ETA guideline on thyroid nodule management

## Thyroid ultrasound and use of EU-TIRADS\*

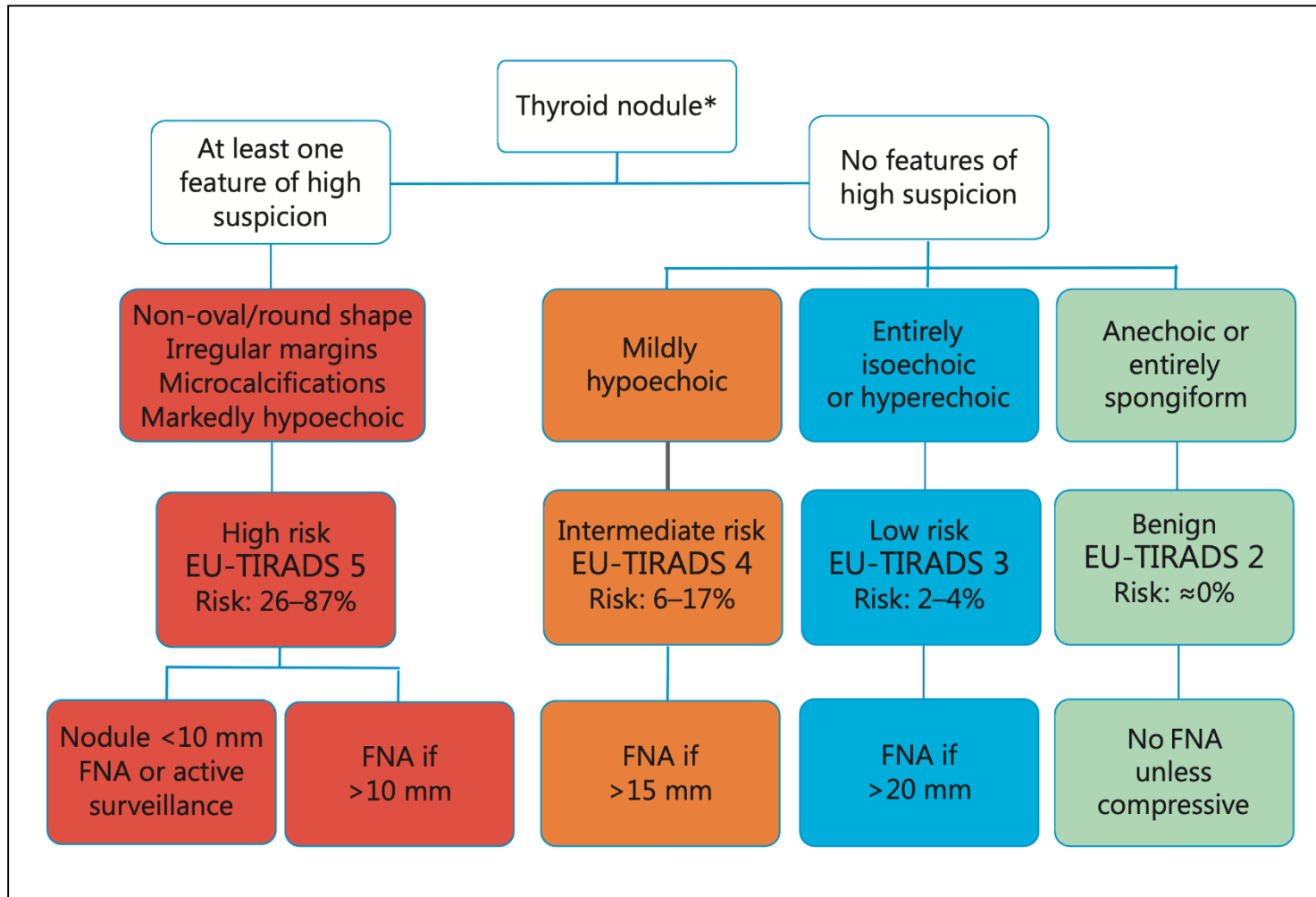


How well-described are these descriptors?  
E.g. hypoechoic?

\*Russ G et al. Eur. Thyroid J. 2017;6:225-37.

# The 2023 ETA guideline on thyroid nodule management

## Thyroid ultrasound and use of EU-TIRADS for FNA indication



- Combine all evaluations, in shared decision with pat. when deciding on FNA
- Use US-guidance; capillary action or suction\*
- FNA indication as in the Fig.
- Repeat FNA (non-diagnostic; Bethesda class III; discrepancy between US and FNA; signif. nodule growth)
- FNA of suspicious lymph nodes
- Core-needle biopsy; second line
- \*Todsén T et al. Head Neck 2021



# The 2023 ETA guideline on thyroid nodule management

## Thyroid ultrasound and use of EU-TIRADS for FNA indication

- Combine all evaluations, in shared decision with pat. when deciding on FNA

Thyroid nodule\*

Received: 14 August 2020 | Revised: 8 December 2020 | Accepted: 17 December 2020  
DOI: 10.1002/hed.26598

**OPERATIVE TECHNIQUES**

This article supplements the Operative Techniques video presentation, which can be viewed online on Head & Neck's home page at [http://onlinelibrary.wiley.com/journal/10.1002/\(ISSN\)1097-0347](http://onlinelibrary.wiley.com/journal/10.1002/(ISSN)1097-0347)

**WILEY**

### Ultrasound-guided fine-needle aspiration biopsy of thyroid nodules

Tobias Todsén MD, PhD<sup>1,2</sup> | Finn Noe Bennedbæk MD, PhD<sup>3</sup> | Katalin Kiss MD<sup>4</sup> | Laszlo Hegedüs MD, DMSc<sup>5</sup>

Nodule <10 mm FNA or active surveillance	FNA if >10 mm	FNA if >15 mm	FNA if >20 mm	No FNA unless compressive
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guidance; capillary action or

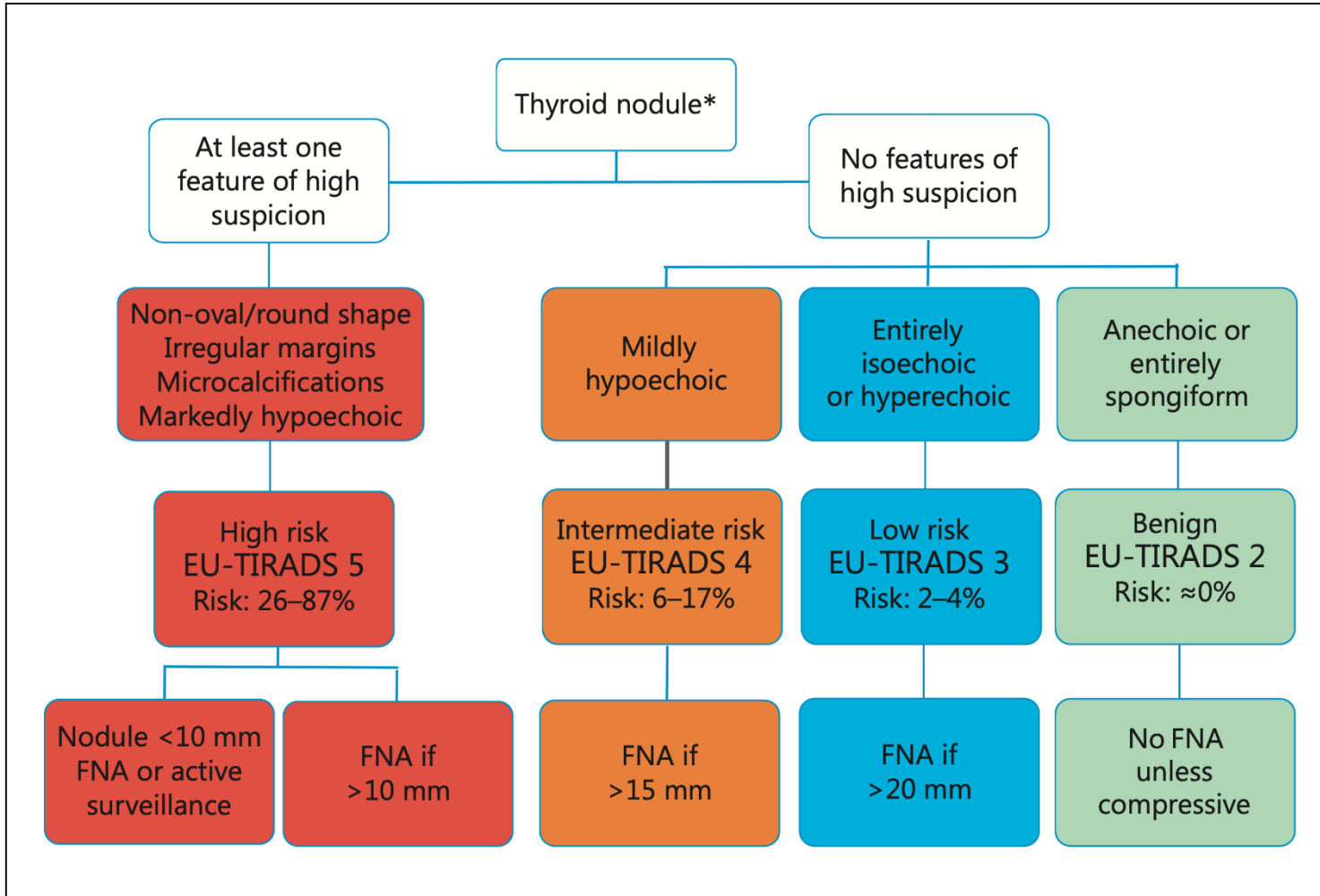
ication as in the fig.

FNA (non-diagnostic; a class III; discrepancy in US and FNA; signif. Nodule

- FNA of suspicious lymph nodes
- Core-needle biopsy; second line

\*Todsén T et al. Head Neck 2021;43:1009-13

The 2023 ETA guideline on thyroid nodule management  
 Thyroid ultrasound and use of EU-TIRADS\*, **when asymptomatic and no FNA performed**



- EU-TIRADS 2 and 3. 5-10 mm no further evaluation. If 10-20 mm. Repeat US in 3-5 yr.
- EU-TIRADS 4  $\leq$  15 mm, re-evaluate in 12 months. EU-TIRADS 5  $\leq$  10 mm. Re-evaluate every 6-12 months.

TABLE 3. OPINIONS ON VALUE AND STRUCTURE OF THYROID ULTRASOUND RISK STRATIFICATION SYSTEMS

<i>Question and answers</i>	<i>Responses, n (%)</i>
Total respondents	724
Aware of RSS	
Yes	560 (77.3)
Somewhat	125 (17.3)
No	39 (5.4)
See value in RSS	
Strongly agree	330 (45.6)
Agree	329 (45.4)
Neutral	51 (7.0)
Disagree	13 (1.8)
Strongly disagree	1 (0.1)
How should an RSS be structured?	
Points-based	285 (39.4)
Patterns	206 (28.5)
Presence of 1 or more suspicious features	161 (22.2)
No preference	66 (9.1)
Other	6 (0.83)
How many risk categories should an RSS have?	
No more than 3	125 (17.3)
No more than 4	244 (33.7)
No more than 5	320 (44.2)
More than 5	21 (2.9)
Other	14 (1.9)

There are many US risk stratification systems

94%, aware of...

95% agree or strongly agree..

More than 30% used more than one risk stratification system

*Hoang et al. An International Survey on Utilization of Five Thyroid Nodule Risk Stratification Systems: A Needs Assessment with Future Implications. Thyroid 2022;32:675-81.*

# Use of Risk Stratification Systems amongst specialists

- >30% of respondents used more than 1 Risk Stratification System

TABLE 4. USE OF SINGLE VERSUS MULTIPLE THYROID ULTRASOUND RISK STRATIFICATION SYSTEMS IN RESPONDENT'S PRACTICE

	n	%
Use 1 or more RSSs in practice	692	
4 RSSs		
AACE, ACR TI-RADS, ATA, EU-TIRADS	1	0.1
3 RSSs		
AACE, ATA, EU-TIRADS		
AACE, ACR TI-RADS		
ACR TI-RADS, ATA		
ACR TI-RADS, ATA, AACE, ACR TI-RADS		
AACE, EU-TIRADS		
ACR TI-RADS, EU-TIRADS		
ACR TI-RADS, EU-TIRADS, ATA		
2 RSSs		
ACR TI-RADS, ATA		
ATA, EU-TIRADS		
AACE, ATA		
AACE, EU-TIRADS		
ATA, K-TIRADS		
ACR TI-RADS, EU-TIRADS		
AACE, ACR TI-RADS		
ACR TI-RADS, other		
ACR TI-RADS, K-TIRADS		
EU-TIRADS, other		
1 RSS		
EU-TIRADS		
ACR TI-RADS		
K-TIRADS		
AACE		
ATA		
Other		

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THYROID RADIOLOGY AND NUCLEAR MEDICINE

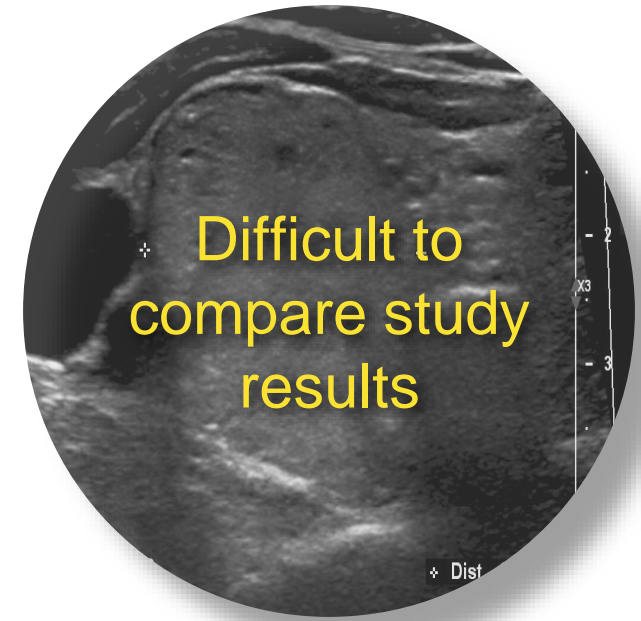
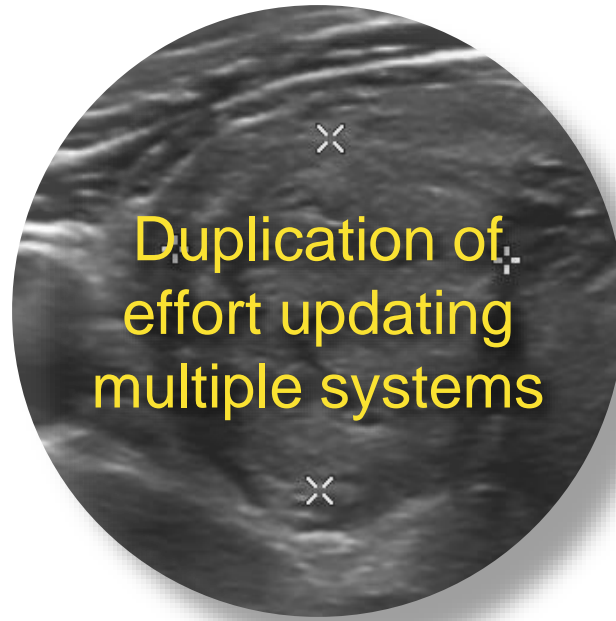
Open camera or QR reader and scan code to access this article and other resources online.



## An International Survey on Utilization of Five Thyroid Nodule Risk Stratification Systems: A Needs Assessment with Future Implications

Jenny K. Hoang,<sup>1</sup> Shadi Asadollahi,<sup>1</sup> Cosimo Durante,<sup>2</sup> Laszlo Hegedüs,<sup>3</sup> Enrico Papini,<sup>4</sup> and Franklin N. Tessler<sup>5</sup>

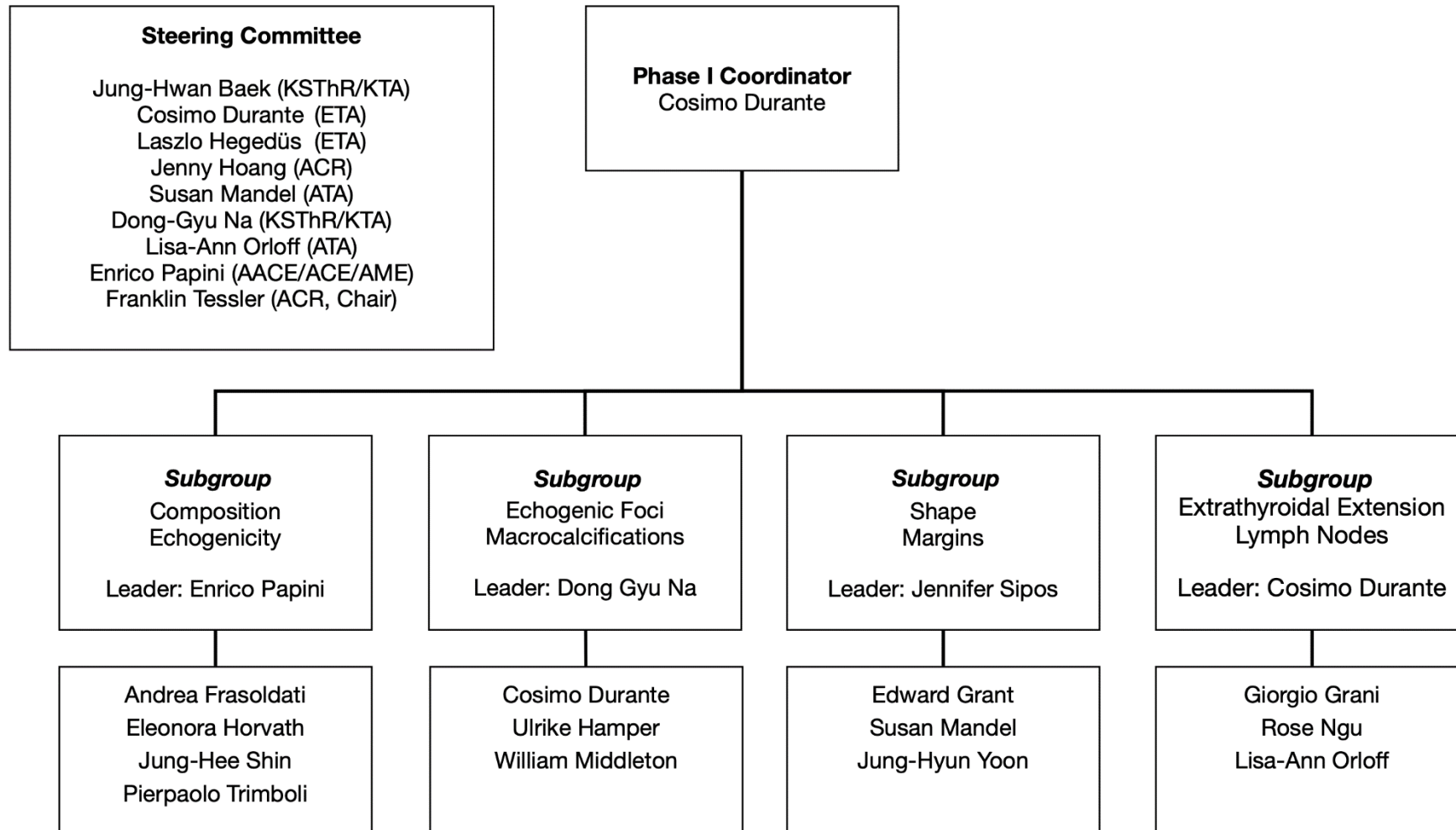
# Why is it problematic with several TIRADS?



# International Thyroid Nodule Ultrasound Working Group (ITNUWG)

Name	Institution	Country	Organization Represented (Steering Committee)
Jung-Hwan Baek	Department of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine	South Korea	KSThR/KTA
Cosimo Durante	Dipartimento di Medicina Interna e Specialità Mediche, SAPIENZA Università di Roma	Italy	ETA
Andrea Frasoldati	Sapienza Università di Roma	Italy	N/A
Gioglio Grani	Sapienza Università di Roma	Italy	N/A
Edward Grant	Department of Radiology, Keck School of Medicine, University of Southern California	USA	N/A
Laszlo Hegedüs	Department of Endocrinology and Metabolism, Odense University Hospital	Denmark	ETA
Jenny Hoang	Department of Radiology, Duke University School of Medicine	USA	ACR
Eleonora Horvath	Radiology Department, Clinica Alemana, Facultad de Medicina Clinica Alemana, Universidad del Desarrollo	Chile	N/A
Susan Mandel	Division of Endocrinology, Diabetes, and Metabolism, Perelman School of Medicine, University of Pennsylvania	USA	ATA
William Middleton	Mallinckrodt Institute of Radiology, Washington University	USA	N/A
Dong-Gyu Na	Department of Radiology, GangNeung Asan Hospital, University of Ulsan College of Medicine	South Korea	KSThR/KTA
Rose Ngu	Department of Radiology, Guy's Hospital	UK	N/A
Lisa-Ann Orloff	Stanford University School of Medicine	USA	ATA
Enrico Papini	Ospedale Regina Apostolorum, "La Sapienza" University of Rome	Italy	AACE/ACE/AME
Jung-Hee Shin	Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine	Korea	N/A
Jennifer Sipos	Ohio State University	USA	N/A
Franklin Tessler	Department of Radiology, University of Alabama at Birmingham	USA	ACR
Pierpaolo Trimboli	Department of Nuclear Medicine and Thyroid Centre, Oncology Institute of Southern Switzerland	Switzerland	N/A
Jung-Hyun Yoon	Department of Radiology, Research Institute of Radiological Science, Yonsei University College of Medicine	South Korea	N/A

# Phase I organization (Descriptors nodule characteristics)



# I-TIRADS Lexicon Part I

## Echogenicity

Echogenicity of the non-calcified solid components of a nodule when compared to the reference structures represented either by the normal thyroid parenchyma or the anterior neck muscles

- **Anechoic** No internal echoes
- **Hyperechoic** Increased echogenicity relative to the surrounding normal thyroid parenchyma
- **Isoechoic** Similar echogenicity relative to the surrounding normal parenchyma
- **Mildly hypoechoic** Decreased echogenicity compared to the normal thyroid parenchyma, but still increased echogenicity relative to the anterior neck muscles
- **Markedly hypoech.** Echogenicity less than or equal to the anterior neck muscles

In all, there are 25 descriptors! We voted on all (Delphi process);  $\geq 80\%$  agreed = consent



Echogenicity

Radiology

REVIEWS AND COMMENTARY • STATEMENTS AND GUIDELINES

# International Expert Consensus on US Lexicon for Thyroid Nodules

Radiology 2023; 309(1):e231481 • <https://doi.org/10.1148/radiol.231481>

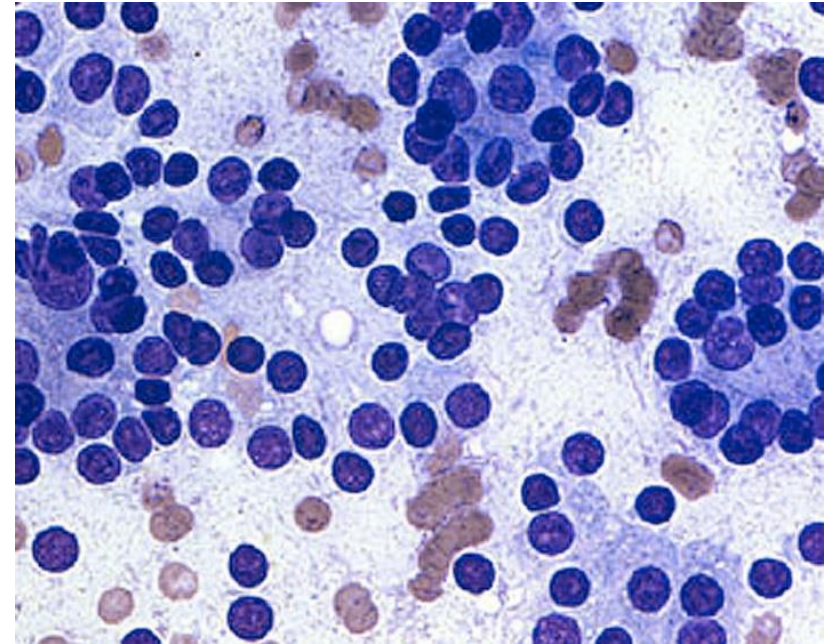
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*Cosimo Durante, MD, PhD • Laszlo Hegedüs, MD • Dong Gyu Na, MD, PhD • Enrico Papini, MD • Jennifer A. Sipos, MD • Jung Hwan Baek, MD, PhD • Andrea Frasoldati, MD • Giorgio Grani, MD • Edward Grant, MD • Eleonora Horvath, MD • Jenny K. Hoang, MBBS • Susan J. Mandel, MD • William D. Middleton, MD • Rose Ngu, BDS, EDS • Lisa Ann Orloff, MD • Jung Hee Shin, MD • Pierpaolo Trimboli, MD • Jung Hyun Yoon, MD, PhD • Franklin N. Tessler, MD, CM*

In all, there are 25 descriptors! We voted on all (Delphi process); ≥ 80% agreed = consent

# Cytology-based management of nodular thyroid disease

- Use an endorsed classification system (e.g. Bethesda)
- Cytology report should *(ideally)* include:
  - Patient id
  - Imaging finding, TIRADS score
  - Sample adequacy
  - Microscopic description of the lesion
  - Ancillary testing, if performed
  - Reporting category and diagnosis
  - **The local Risk Of Malignancy (ROM) of the diagnostic category**



# Cytology-based management of nodular thyroid disease

**2<sup>st</sup> line approach:** perform FNA cytology

BETHESDA I ROM (%): 1-4	BETHESDA II ROM (%): <3	BETHESDA III ROM (%): 5-15	BETHESDA IV ROM (%): 15-30	BETHESDA V ROM (%): 60-75	BETHESDA VI ROM (%): 97-99
<p><b>EU-TIRADS 3 (&gt;20 mm)</b> <b>Repeat FNA.<sup>1</sup></b> <i>If Bethesda class I, consider CNB.</i></p> <p><b>EU-TIRADS 4 (&gt;15 mm) and 5 (&gt;10 mm)</b> <b>Repeat FNA.<sup>1</sup></b> <i>If Bethesda class I, consider CNB or molecular testing (if available and sufficient material).</i></p>	<p><b>EU-TIRADS 3 (&gt;20 mm) and 4 (&gt;15 mm)</b> <b>Repeat US</b> in 3-5 yrs<sup>2</sup> <b>Repeat FNA<sup>1,3</sup></b> if significant growth<sup>4</sup> or new worrisome features</p> <p><b>EU-TIRADS 5 (&gt;10 mm)</b> <b>Repeat FNA<sup>1,5</sup></b> (imaging and pathology not concordant)</p>	<p><b>EU-TIRADS 3 (&gt;10 mm)</b> <b>Repeat FNA.<sup>1</sup></b> <i>If Bethesda class III, repeat US within 1 yr or consider molecular testing (if available) or offer surgery</i></p> <p><b>EU-TIRADS 4 and 5 (&gt;10 mm)</b> <b>Repeat FNA.<sup>1</sup></b> <i>If Bethesda class III, offer surgery, or surveillance, or molecular testing (if available)</i></p>	<p><b>EU-TIRADS 3, 4 and 5 (&gt;10 mm)</b> <i>Offer surgery or molecular testing (if available)<sup>6</sup></i></p>	<p><b>EU-TIRADS 3, 4 and 5 (&gt;10 mm)</b> <i>Recommend:</i></p> <ul style="list-style-type: none"><li>▪ <i>Surgery<sup>7</sup></i></li></ul>	

# The use of molecular testing in nodular thyroid disease

## When to use it

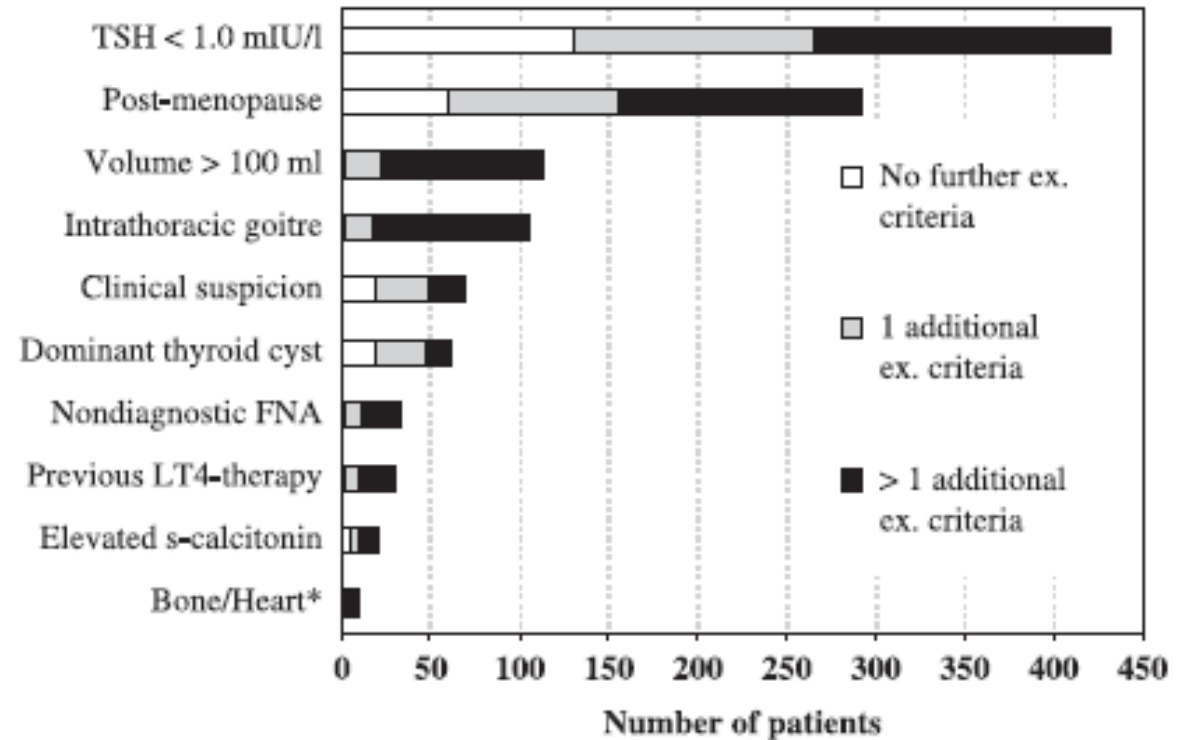
- Consider molecular testing in indeterminate thyroid nodules, if available
- 1; 0000; 9/9, round 1

## Considerations

- **Availability poor** in Europe (mainly research setting)
- **Considerable observer-variation** in adenomatous nodules, thyroid adenomas, and minimally invasive FTCs
- **Costly**; lack of reimbursement in Europe
- **Lack of independent validation**
- **Lack of long-term outcome studies**

# Therapeutic options - Non-surgical approaches I


- In case of non-intervention, follow-up per the previous
- **Thyroid hormone treatment is not indicated** in the euthyroid patient (1; ØØØØ; 9/9; round 1)
- **Because of ineligibility and lack of efficacy**



# Therapeutic options - Non-surgical approaches II

- In case of non-intervention, follow-up per the previous
- Thyroid hormone treatment is not indicated in the euthyroid patient (1; 0000; 9/9; round 1)
- Because of ineligibility and lack of efficacy
- **Selenium and iodine supplementation is not indicated, unless deficient in this nutraceutical (1; 0000; 9/9; round 1)**

## Selenium in thyroid disorders — essential knowledge for clinicians

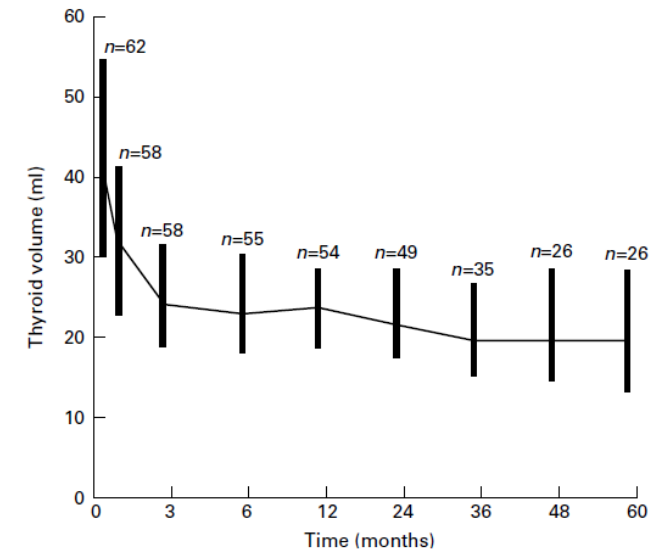
*Kristian Hillert Winther<sup>1</sup>, Margaret Philomena Rayman<sup>1</sup>, Steen Joop Bonnema<sup>1</sup> and Laszlo Hegedüs<sup>1</sup> \**

Nature Reviews Endocrinology 2020;16(3):165-176.

# Therapeutic options - Non-surgical approaches III

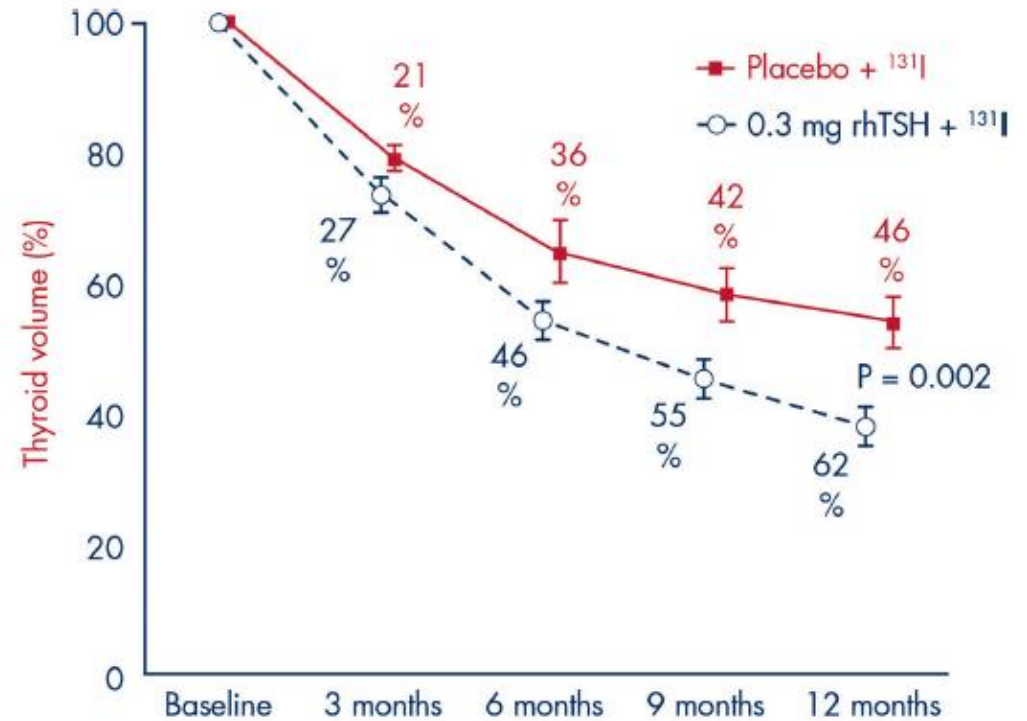
- In case of non-intervention, follow-up per the previous
- Thyroid hormone treatment is not indicated in the euthyroid patient (1; ØØØØ; 9/9; round 1)
- Because of ineligibility and lack of efficacy
- Selenium supplementation is not indicated, unless deficient in this nutraceutic (1; ØØØØ; 9/9, round 1)
- **RAI is recommended as an alternative to surgery and MIT in functioning solitary thyroid nodules (1; ØØØØ; 9/9; round 1)**

## Long-term effect of radioactive iodine on thyroid function and size in patients with solitary autonomously functioning toxic thyroid nodules



# Therapeutic options - Non-surgical approaches IV

- Consider RAI in benign multinodular goiter (2; ØØØØ; 9/9; round 1)





# Therapeutic options - Non-surgical approaches V

- Consider Ethanol Ablation as first line treatment for pure or dominantly recurring cystic thyroid lesions (1; ØØØØ; 9/9; round 1)

## **Treatment of Recurrent Thyroid Cysts with Ethanol: A Randomized Double-Blind Controlled Trial**

FINN NOE BENNEDBÆK AND LASZLO HEGEDÜS

*Department of Endocrinology, Odense University Hospital, DK-5000 Odense C, Denmark*

Remission in 27/33 in the ethanol group and 16/33 in the saline group.

J. Clin. Endocrinol Metab. 2003;88:5773-5777.

# Therapeutic options - Non-surgical approaches VI

- Consider Thyroid Ablation (Thermal ablation) for symptomatic solid benign thyroid nodules or cystic thyroid nodules that recur after ethanol ablation – as an alternative to surgery (1; ØØØØ; 8/9; round 1)

European  
Thyroid Journal

Guidelines

Eur Thyroid J 2020;9:172–185  
DOI: 10.1159/000508484

Received: April 24, 2020  
Accepted: May 7, 2020  
Published online: June 8, 2020

## 2020 European Thyroid Association Clinical Practice Guideline for the Use of Image-Guided Ablation in Benign Thyroid Nodules

Enrico Papini<sup>a</sup> Hervé Monpeyssen<sup>b</sup> Andrea Frasoldati<sup>c</sup> Laszlo Hegedüs<sup>d</sup>

<sup>a</sup>Department of Endocrinology and Metabolism, Regina Apostolorum Hospital, Rome, Italy; <sup>b</sup>Thyroid Unit, American Hospital, Paris, France; <sup>c</sup>Department of Endocrinology and Metabolism, Arcispedale Santa Maria Nuova IRCCS-ASL, Reggio Emilia, Italy; <sup>d</sup>Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark

# Therapeutic options - Non-surgical approaches VI



Charlie Chaplin in "Modern Times"  
Who rules. The technique or we?

THYROID  
Volume 32, Number 8, 2022  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/thy.2021.0665

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scan code to access this article  
and other resources online.



## The Effect of Laser Thermal Ablation on Quality of Life: Improvements in Patients with Solid-Cystic Thyroid Nodules

Jesper Roed Sorensen,<sup>1</sup> Helle Døssing,<sup>1</sup> Torquil Watt,<sup>2</sup> Per Cramon,<sup>2</sup> Laszlo Hegedüs,<sup>3</sup>  
Steen Joop Bonnema,<sup>3</sup> and Lars Folkestad<sup>3</sup>

Using disease-specific QoL-instrument (ThyPRO). 3-6 months post-laser ablation anxiety and goiter symptom scales improved significantly and were indistinguishable from the control population. 79% had large and clinically significant improvement in effect sizes.

# Therapeutic options - Surgery

- Symptomatic nodular disease as **alternative to MIT**
- Benign nodules that become symptomatic over time
- **Indeterminate cytology** (Bethesda class III and IV and unsuitable for active surveillance)
- Nodules with a **Bethesda class V and VI cytology**
- **Patient choice**
- **1; ØØØØ; 8/9; round 1**

European  
Thyroid Journal

Clinical Thyroidology / Original Paper

Eur Thyroid J 2017;6:307-314  
DOI: 10.1159/000480348

Received: June 16, 2017  
Accepted after revision: August 14, 2017  
Published online: September 12, 2017

## Thyroidectomy Improves Tracheal Anatomy and Airflow in Patients with Nodular Goiter: A Prospective Cohort Study

Jesper Roed Sorensen<sup>a, b</sup> Jeppe Faurholdt Lauridsen<sup>c</sup> Helle Døssing<sup>a</sup>  
Nina Nguyen<sup>d</sup> Laszlo Hegedüs<sup>e</sup> Steen Joop Bonnema<sup>e</sup> Christian Godballe<sup>a</sup>

<sup>a</sup>Department of ORL Head and Neck Surgery, Odense University Hospital, Odense, Denmark; <sup>b</sup>OPEN, Odense Patient Data Explorative Network, Odense University Hospital, Odense, Denmark; <sup>c</sup>Department of Nuclear Medicine, Odense University Hospital, Odense, Denmark; <sup>d</sup>Department of Radiology, Odense University Hospital, Odense, Denmark; <sup>e</sup>Department of Endocrinology and Metabolism, Odense University Hospital, Odense, Denmark

The above paralleled significant improvements in health-related quality of life (ThyPRO)

# 2023 ETA Thyroid Nodule Guidelines Conclusions

- The **initial evaluations** based on
  - **symptomatology** (history)
  - classification of **thyroid function** (TSH)
  - **imaging** (primarily US) and using EU-TIRADS
  - **FNA** (Bethesda classification)
- Focused on evaluation of risk of thyroid cancer
- Tries to **limit** need of **follow-up**
- Emphasizes offering **no treatment** and **non-surgical options**
- Emphasizes the **patient perspective** (HRQoL; PRO)
- Could with a minimum of alterations be translated and **implemented in any European national guideline** (?)

# 2023 ETA Thyroid Nodule Guidelines Conclusions

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- Emphasizes the patient perspective (HRQoL; PRO)
- Could with a minimum of alterations be translated and implemented in any European national guideline (?)
- **Over ambitious?** Time for simplification?
- **Obsolete** when published?
- Dependent on who develops it?
- Overzealous in our search for malignancy?
- Too fascinated with technology and offering MIT to the non-needy?
- **None of our undertakings have adequately been proven to prolong life**
- Inadequate focus on thyroid-disease related QoL
- **Lack of adequately sized and long-term follow-up studies comparing the various treatment options (efficacy; side-effects; cost; QoL)**

# On behalf of the 2023 ETA "Guideliners"\*



\*Thank you for your patience