COMO EU CONDUZO A AVALIAÇÃO DE NÓDULOS DE TIREOIDE

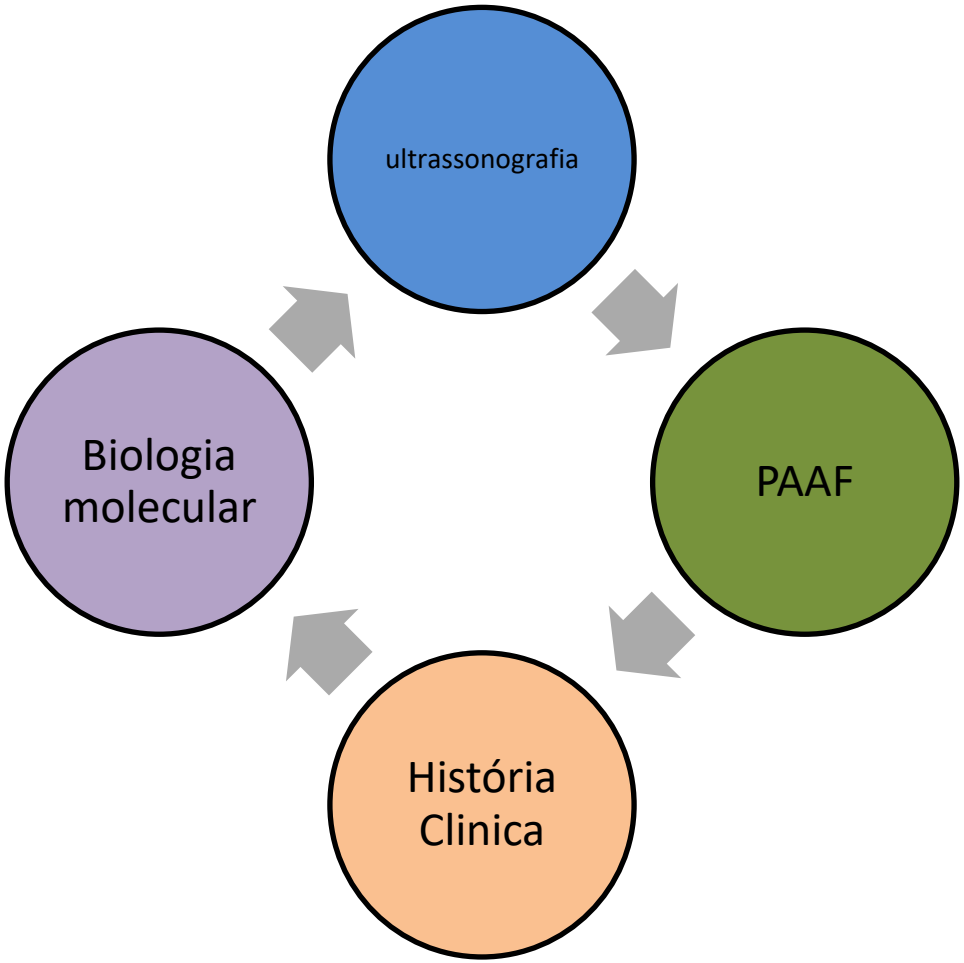
MARIO VAISMAN

UFRJ

Declaração de conflito de interesses

Não tenho conflitos de interesses relacionados a essa apresentação

Ferramentas envolvidas na avaliação de nódulos



PERGUNTAS:

- Quando pedir e quando não pedir US de tireoide?
- Quais os primeiros exames p/ a investigação de um nódulo tireoidiano?
- Quando pedir PAAF?
- Como interpretar a PAAF?
  - Bethesda I
  - Bethesda II
  - Bethesda III e IV (citologias indeterminadas)
  - Bethesda V
  - Bethesda VI

- Quando indicar cirurgia?
- O que pedir antes da cirurgia?

Em que consiste um programa de rastreio universal?

- Aplicar um teste em larga escala, mesmo em assintomáticos, que seja capaz de diagnosticar ou excluir uma doença (alta sensibilidade) em pessoas aparentemente saudáveis

- Desde que…

- A detecção precoce e seu tratamento se associem com benefícios comprovados ao indivíduo e à comunidade

Andermann et al, Bulletin of the World Health Organization. 2008

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Thyroid Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

Conclusions: Although ultrasound of the neck using high-risk sonographic characteristics plus followup cytology from fine-needle aspiration can reasonably identify thyroid cancer, it is unclear if population-based or targeted screening can decrease mortality or improve important patient health outcomes. More importantly, screening results in the identification indolent thyroid cancer, and treatment of these cases of overdiagnosed cancer can pose real patient harms.

2017

Clinical Review & Education

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Thyroid Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

- **Nenhuma sociedade** profissional recomenda *screening* populacional.
- Evidências insuficientes para screening em populaçãp com > risco
  - Concordando com ATA/2015 que tb reporta que não há evidências que suportem *screening* em quem tem história familiar
  - Porém faltam estudo para ver benefícios de estrategia de busca nessas populações de maior risco!
-

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Thyroid Cancer

US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

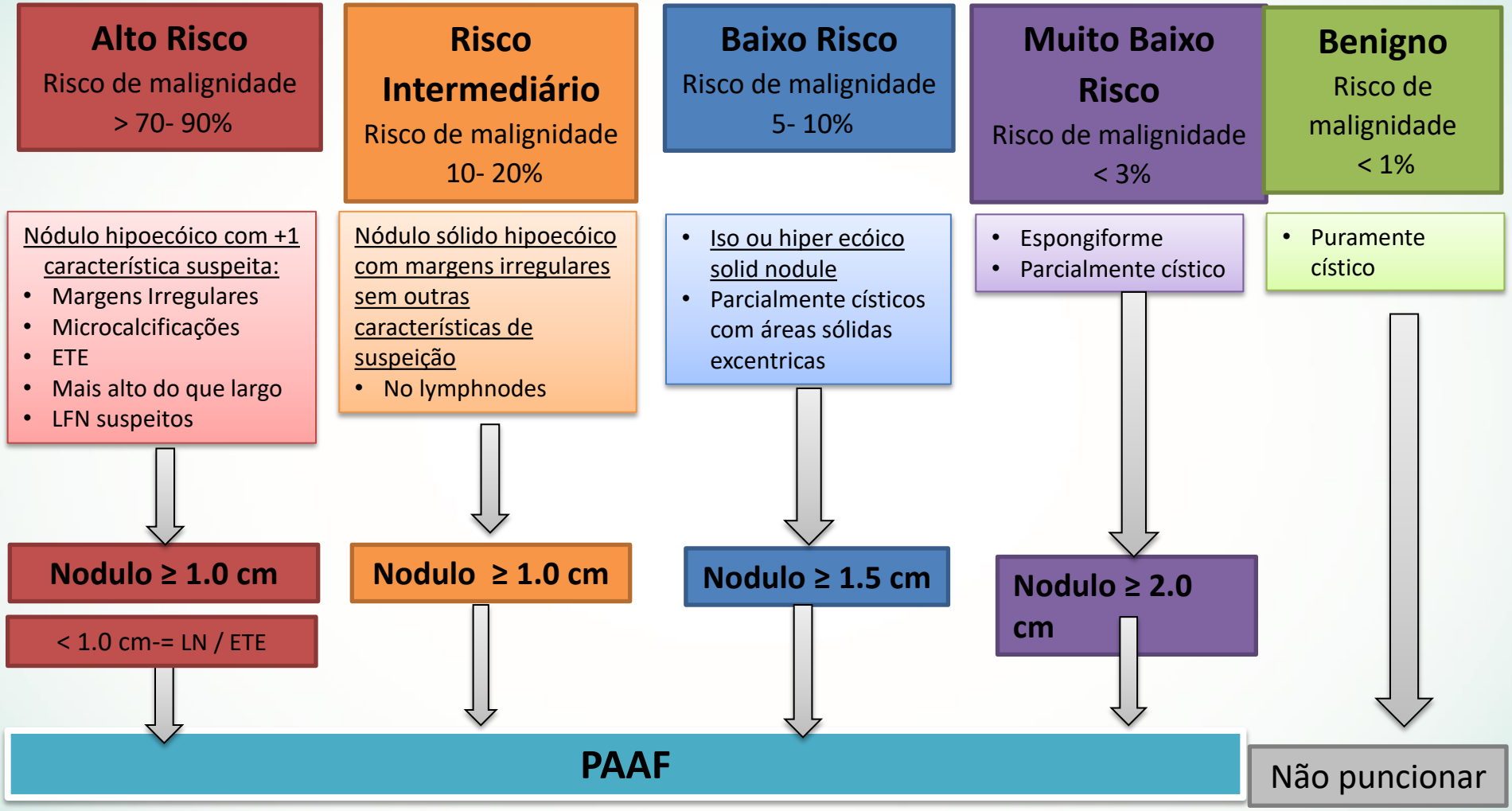
Screening Tests

Although screening for thyroid cancer using neck palpation and ultrasound of the thyroid has been studied, the USPSTF recommends against screening in the general asymptomatic adult population.

História Clinica

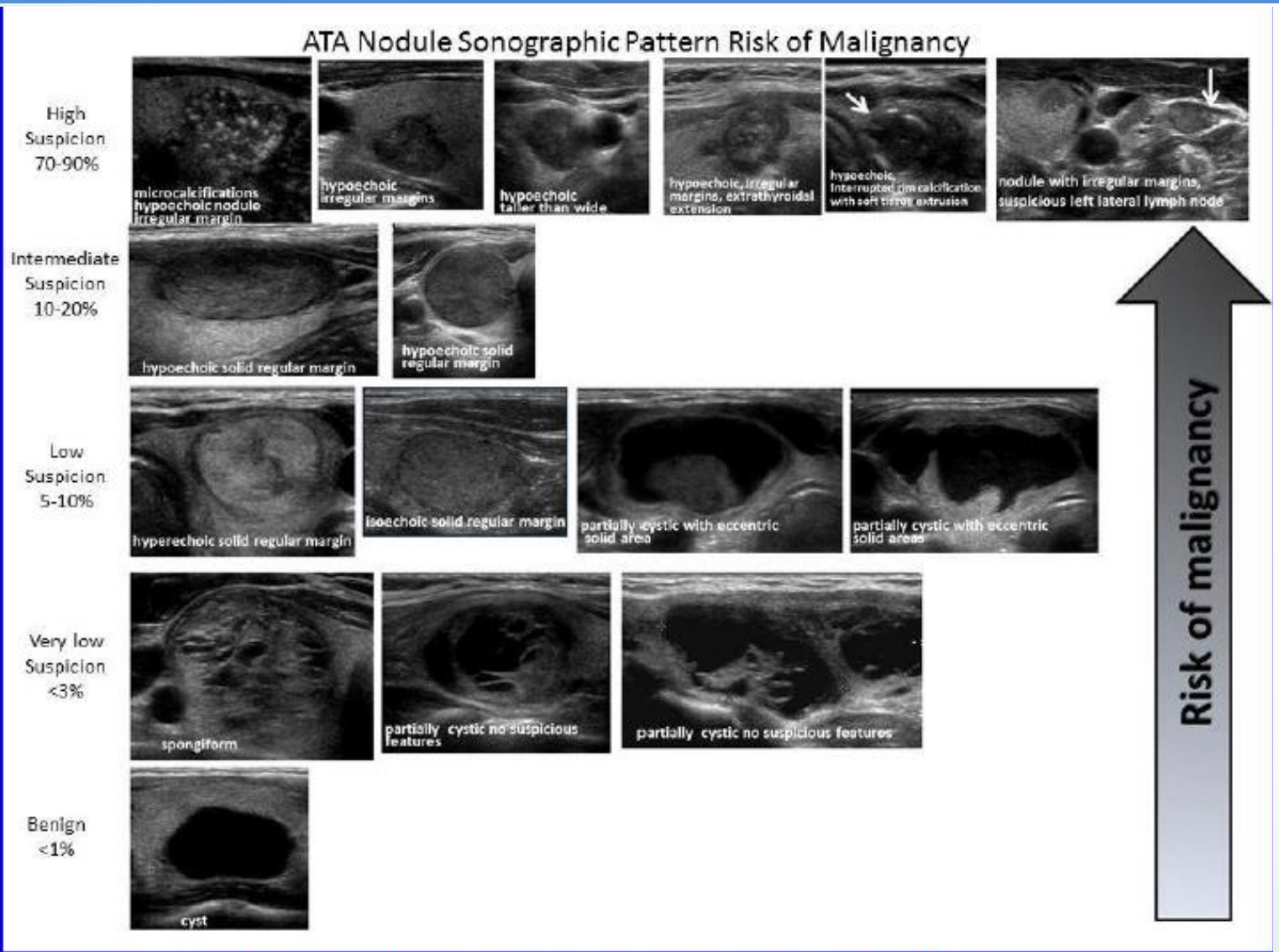
- Nódulo palpável vs nódulo descoberto acidentalmente no US
- Tempo de acompanhamento do nódulo
- História Familiar
- História de Radiação na Infância

ATA SONOGRAPHIC PATTERNS AND ESTIMATED RISK OF MALIGNANCY FOR THYROID NODULES



2017 Guidelines of the American Thyroid association for the Diagnosis and Management of Thyroid Disease During Pregnancy and the Postpartum. Thyroid 2017.

Ultrassonografia



Haugen et al 2015

ACR TI-RADS

COMPOSITION (Choose 1)	
Cystic or almost completely cystic	0 points
Spongiform	0 points
Mixed cystic and solid	1 point
Solid or almost completely solid	2 points

ECHOGENICITY (Choose 1)	
Anechoic	0 points
Hyperechoic or isoechoic	1 point
Hypoechoic	2 points
Very hypoechoic	3 points

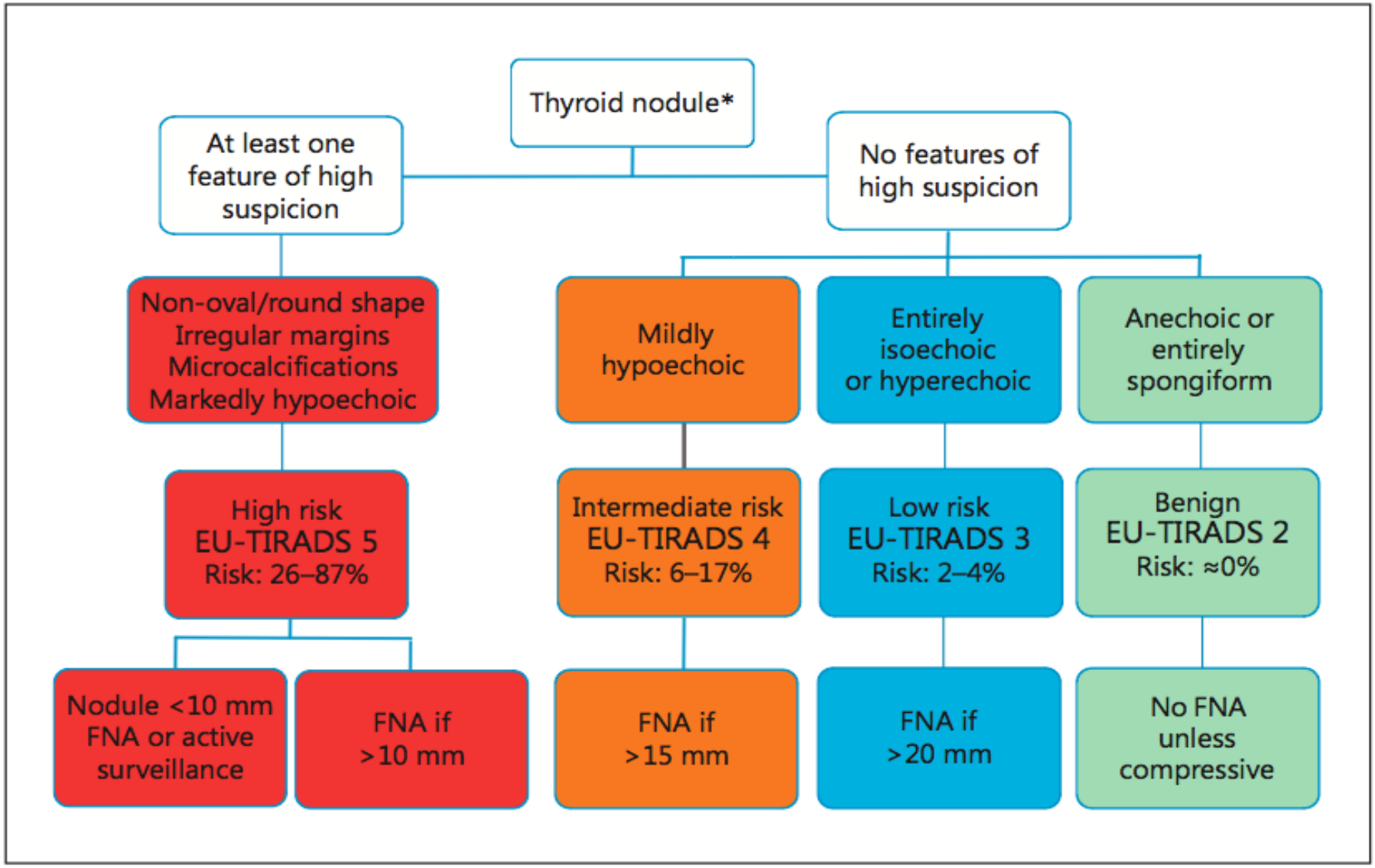
SHAPE (Choose 1)	
Wider-than-tall	0 points
Taller-than-wide	3 points

MARGIN (Choose 1)	
Smooth	0 points
Ill-defined	0 points
Lobulated or irregular	2 points
Extra-thyroidal extension	3 points

ECHOGENIC FOCI (Choose All That Apply)	
None or large comet-tail artifacts	0 points
Macrocalcifications	1 point
Peripheral (rim) calcifications	2 points
Punctate echogenic foci	3 points

COMPOSITION	ECHOGENICITY	SHAPE	MARGIN	ECHOGENIC FOCI
Spongiform: Composed predominantly (> 50%) of small cystic spaces. Do not add further points for other categories. *Mixed cystic and solid:* Assign points for predominant solid component. Assign 2 points if composition cannot be determined because of calcification.	*Anechoic:* Applies to cystic or almost completely cystic nodules. *Hyperechoic/isoechoic/hypoechoic:* Compared to adjacent parenchyma. *Very hypoechoic:* More hypoechoic than strap muscles. Assign 1 point if echogenicity cannot be determined.	*Taller-than-wide:* Should be assessed on a transverse image with measurements parallel to sound beam for height and perpendicular to sound beam for width. This can usually be assessed by visual inspection.	*Lobulated:* Protrusions into adjacent tissue. *Irregular:* Jagged, spiculated, or sharp angles. *Extrathyroidal extension:* Obvious invasion = malignancy. Assign 0 points if margin cannot be determined.	*Large comet-tail artifacts:* V-shaped, >1 mm, in cystic components. *Macrocalcifications:* Cause acoustic shadowing. *Peripheral:* Complete or incomplete along margin. *Punctate echogenic foci:* May have small comet-tail artifacts.

EU-TIRADS


Thyroid nodule*
At least one feature of high suspicion
No features of high suspicion
Non-oval/round shape
Irregular margins
Microcalcifications
Markedly hypoechoic
Mildly hypoechoic
Entirely isoechoic or hyperechoic
Anechoic or entirely spongiform
High risk
EU-TIRADS 5
Risk: 26–87%
Intermediate risk
EU-TIRADS 4
Risk: 6–17%
Low risk
EU-TIRADS 3
Risk: 2–4%
Benign
EU-TIRADS 2
Risk: ≈0%
Nodule <10 mm
FNA or active surveillance
FNA if >10 mm
FNA if >15 mm
FNA if >20 mm
No FNA unless compressive

Likelihood of malignancy in thyroid nodules according to a proposed Thyroid Imaging Reporting and Data System (TI-RADS) classification merging suspicious and benign ultrasound features

Ricardo Luiz Costantin Delfim[1], Leticia Carrrasco Garcez da Veiga[2], Ana Paula Aguiar Vidal[2], Flávia Paiva Proença Lobo Lopes[3], Mário Vaisman[2], Patrícia de Fatima dos Santos Teixeira[2]

1413 nódulos

TIRADS-Delfim

Ultrasound features	Score
Marked hypoechogenicity	+5
Moderate hypoechogenicity	+4
Microcalcification	+3
Irregular/microlobu lated margin	+3
Mild hypoechogenicity	+2
Solid appearance	+2
Undefined hyperechoic spot	+2
Predominantly central flow	+2
Non-ovoid shape	+1
Macrocalcification	+1
Absence of a halo	+1
Irregular/thick halo	+1
Regular thin halo	-1
Crystal colloid	-1
Hyperechogenicity	-1
Spongiform appearance	-1
Blurred margin	-2

Table 4. Propose TI-RADS categories

TI-RADS 1: Negative
TI-RADS 2: Benign*
TI-RADS 3 (final score ≤ 2): Probably benign
TI-RADS 4a (final score 3–5): Low suspicion for malignancy
TI-RADS 4b (final score 6–9): Moderate suspicion for malignancy
TI-RADS 5 (final scores ≥ 10): Highly suggestive of malignancy

Conclusion: Both TIRADS and the ATA guidelines provide effective malignancy risk stratification for thyroid nodules. Nodules that

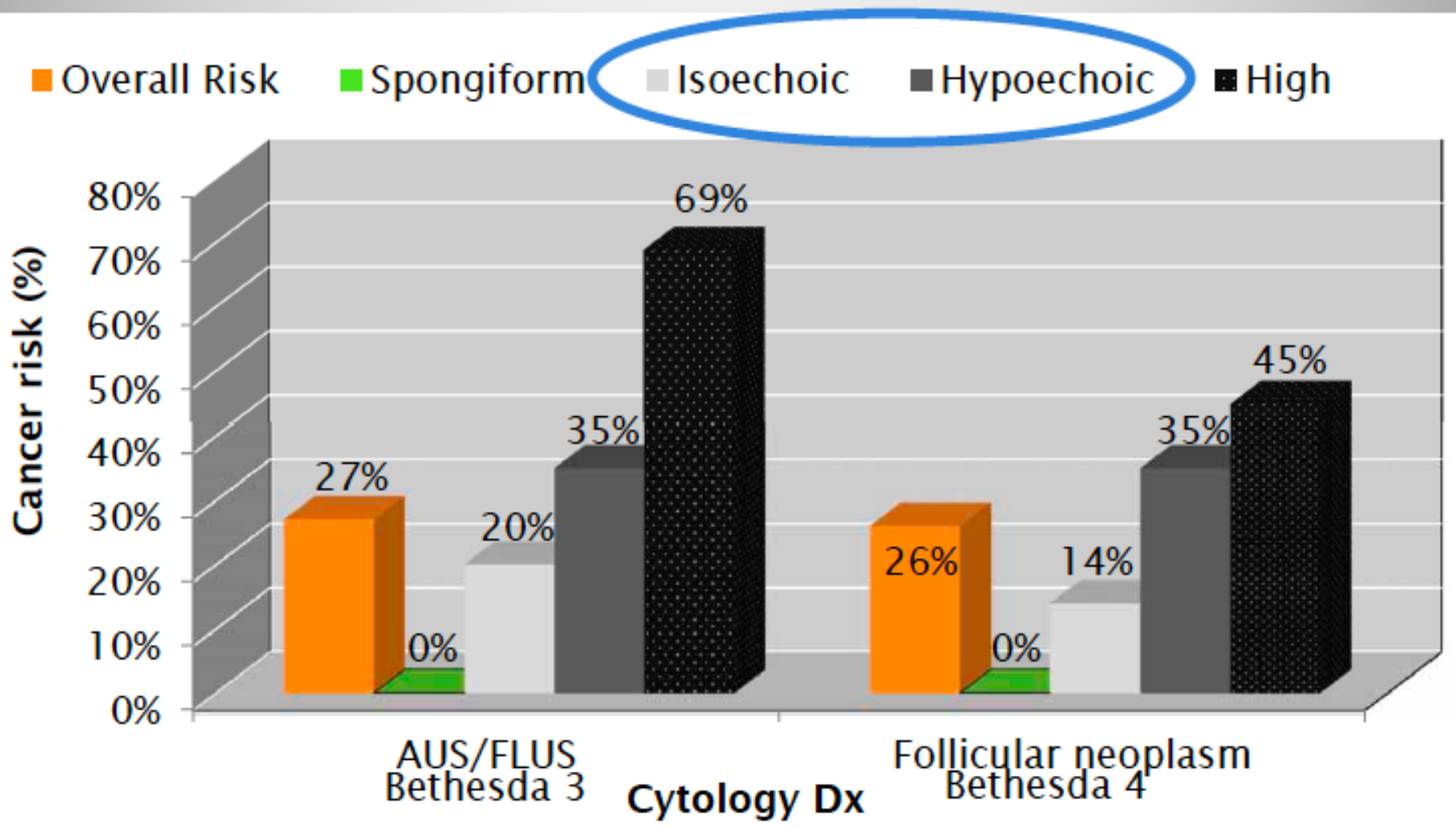
Conclusions: Classification systems had elevated predictive value of malignancy in high-risk classes. ATA and AACE/ACE/AME systems were effective for ruling out indication to FNA in low-US-risk nodules. A similar diagnostic accuracy and a substantial interobserver agreement was provided by the three- and the five-category classifications. ***(J Clin Endocrinol Metab* 103: 1359–1368, 2018)**

Conclusions: ETA and ATA US risk stratification systems provide effective malignancy risk stratification for thyroid nodules. In clinical practice, using this approach, we should be able to reduce the number of unnecessary FNAC without losing clinically relevant thyroid cancer. ***(J Clin Endocrinol Metab* 103: 2362–2368, 2018)**

Effective malignancy risk stratification
Effective for ruling out FNA

Yoon Radiology 2016;278:917; Persichetti J Clin Endocrinol Metab 2018;103:1359; Maino J Clin Endocrinolo Metab 2018; 2362

ULTRASOUND modifies cytology associated cancer risk for Bethesda 3 and 4 nodules

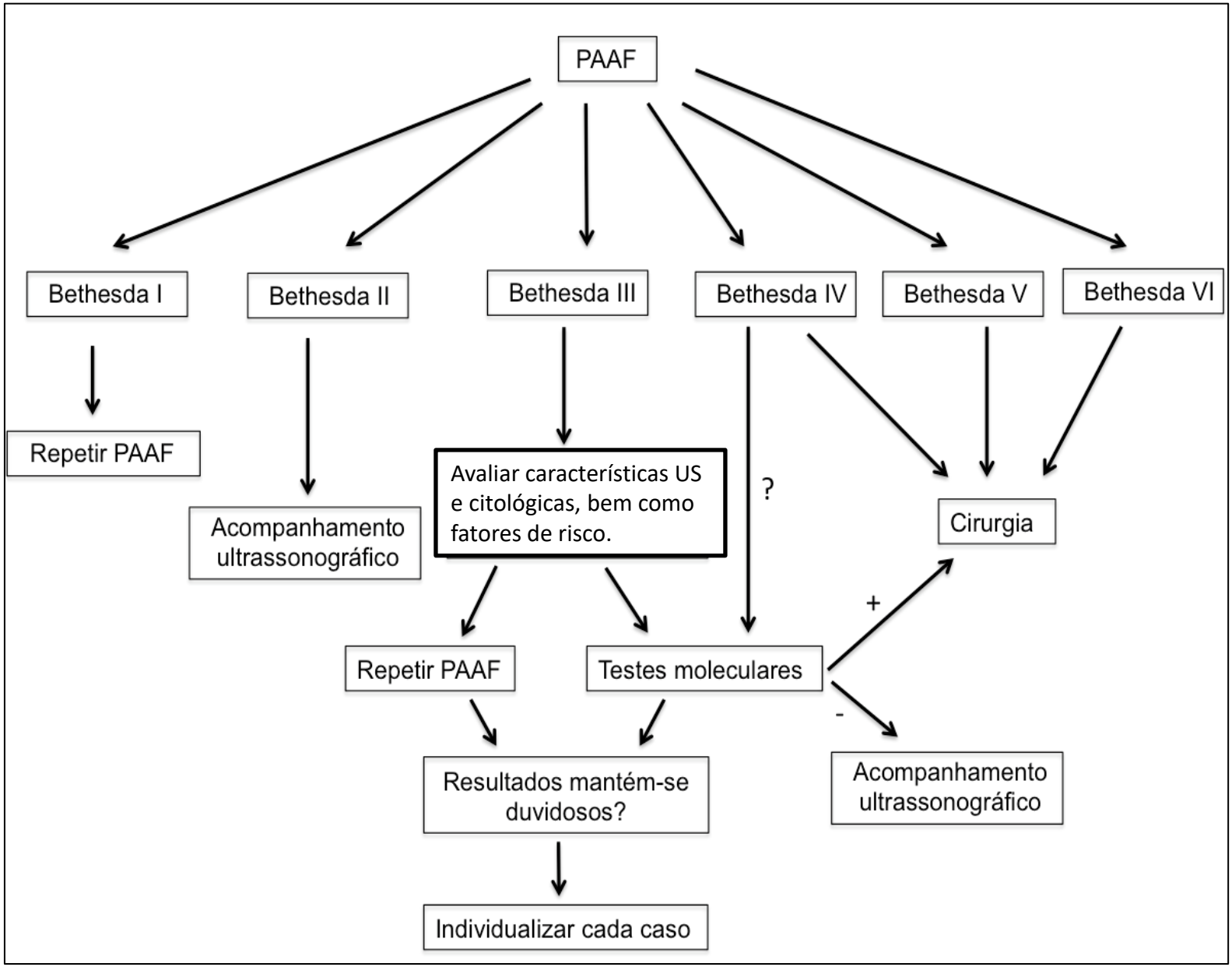


Hong Thyroid 2017;27:953; Valderrabano Thyroid epub May 2019

Generally speaking, you don't operate and diagnose thyroid cancer unless you FNA . . .

- From 2006 to 2011 in USA
  - doubling of the number of thyroid FNAs/year
  - 31% increase in number of thyroid surgeries 99K →131K
- 92% of FNAs are US guided, c/w only 8% performed with palpation
- ~ 600,000 thyroid nodule FNAs done in USA in 2015

Sosa Surgery 2013;154:1420
http://www.thyroidmanager.org/chapter/fine-needle-aspiration-biopsy-of-the-thyroid-gland


PAAF
Bethesda I
Bethesda II
Bethesda III
Bethesda IV
Bethesda V
Bethesda VI
Repetir PAAF
Acompanhamento ultrassonográfico
Avaliar características US e citológicas, bem como fatores de risco.
?
Cirurgia
+
Repetir PAAF
Testes moleculares
-
Resultados mantém-se duvidosos?
Acompanhamento ultrassonográfico
Individualizar cada caso

Citologia Nódulo Tireoide

TABLE 8. THE BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY: DIAGNOSTIC CATEGORIES AND RISK OF MALIGNANCY[a]

Diagnostic category	*Estimated/predicted risk of malignancy by the Bethesda system, %*[a]	*Actual risk of malignancy in nodules surgically excised, % median (range)*[b]
Nondiagnostic or unsatisfactory	1–4	20 (9–32)
Benign	0–3	2.5 (1–10)
Atypia of undetermined significance or follicular lesion of undetermined significance	5–15	14 (6–48)
Follicular neoplasm or suspicious for a follicular neoplasm	15–30	25 (14–34)
Suspicious for malignancy	60–75	70 (53–97)
Malignant	97–99	99 (94–100)

[a]As reported in The Bethesda System by Cibas and Ali (1076).
[b]Based on the meta-analysis of eight studies reported by Bongiovanni *et al.* (103). The risk was calculated based on the portion of nodules in each diagnostic category that underwent surgical excision and likely is not representative of the entire population, particularly of nondiagnostic and benign diagnostic categories.

Haugen BR. Thyroid 2016.

JAMA Oncology

Original Investigation | April 14, 2016

Nomenclature Revision for Encapsulated Follicular Variant of Papillary Thyroid Carcinoma

A Paradigm Shift to Reduce Overtreatment of Indolent Tumors

OPEN ACCESS ONLINE FIRST

Yuri E. Nikiforov, MD, PhD[1]; Raja R. Seethala, MD[1]; Giovanni Tallini, MD[2]; Zubair W. Baloch, MD, PhD[3]; Fulvio Basolo, MD[4]; Lester D. R. Thompson, MD[5]; Justine A. Barletta, MD[6]; Bruce M. Wenig, MD[7]; Abir Al Ghuzlan, MD[8]; Kennichi Kakudo, MD, PhD[9]; Thomas J. Giordano, MD, PhD[10]; Venancio A. Alves, MD, PhD[12,13]; Elham Khanafshar, MD, MS[14]; Sylvia L. Asa, MD, PhD[15]; Adel K. El-Naggar, MD[16]; William E. Gooding, MS[17]; Steven P. Hodak, MD[18]; Ricardo V. Lloyd, MD, PhD[19]; Guy Maytal, MD[20]; Ozgur Mete, MD[15]; Marina N. Nikiforova, MD[1]; Vania Nosé, MD, PhD[21,22]; Mauro Papotti, MD[23]; David N. Poller, MB, ChB, MD, FRCPath[24]; Peter M. Sadow, MD, PhD[21,22]; Arthur S. Tischler, MD[25]; R. Michael Tuttle, MD[26]; Kathryn B. Wall[27]; Virginia A. LiVolsi, MD[3]; Gregory W. Randolph, MD[28]; Ronald A. Ghossein, MD[29]

[+] Author Affiliations

JAMA Oncol. Published online April 14, 2016. doi:10.1001/jamaoncol.2016.0386

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

- Uma nova denominação para o “antigo” Carcinoma papilífero variante folicular encapsulado não invasivo (EFVPTC)”

Padrão	Atipias nucleares típicas de CPT	Oncogene importante			
Papilífero	SIM	BRAF	Micro CPT	➔➔➔	Clássico CPT
Folicular	SIM	RAS	NIFTP	➔➔➔	EFVPTC invasivo
Folicular	NÃO	RAS	Adenoma Folicular	➔➔➔	Ca folicular

Adaptado de Nikiforov et al, 2016

Bethesda e risco de malignidade

TABLE 2. THE 2017 BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY: IMPLIED RISK OF MALIGNANCY AND RECOMMENDED CLINICAL MANAGEMENT

Diagnostic category	*Risk of malignancy if NIFTP ≠ CA (%)*	*Risk of malignancy if NIFTP = CA (%)*	*Usual management*[a]
Nondiagnostic or unsatisfactory	5–10	5–10	Repeat FNA with ultrasound guidance
Benign	0–3	0–3	Clinical and sonographic follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	6–18	~10–30	Repeat FNA, molecular testing, or lobectomy
Follicular neoplasm or suspicious for a follicular neoplasm	10–40	25–40	Molecular testing, lobectomy
Suspicious for malignancy	45–60	50–75	Near-total thyroidectomy or lobectomy[b,c]
Malignant	94–96	97–99	Near-total thyroidectomy or lobectomy[c]

Adapted with permision from Ali and Cibas (7).

Quando o Bethesda I é diagnóstico...

- Colóide abundante
- Hipocelular sem atipias
- Nódulos mistos de baixa suspeição

Quando repetir a PAAF?

BETHESDA I não diagnóstica

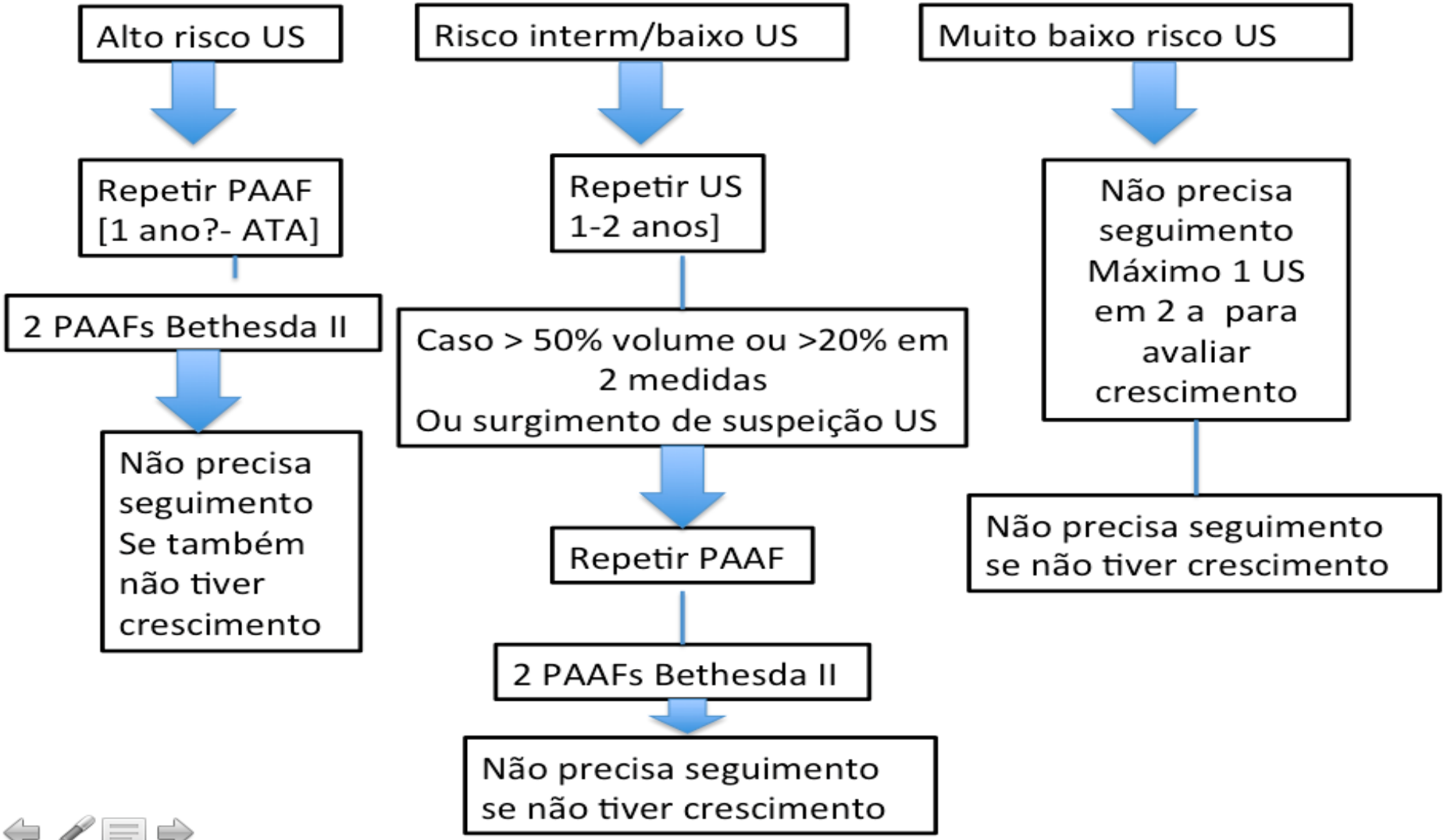
Quando repetir a PAAF?

- Idealmente imediatamente ou após 3 meses (desde que não seja muito suspeito)
  - 2 estudos sugerem que não precisa esperar 3 meses
  - Falso positivo por danos reparativos/ reativos?

Bethesda I

- Caso segunda PAAF BETHESDA I novamente:
  - Hipocelular sem atipias + nódulos mistos = benigno
  - Sem suspeição à US =observação com US ou cirurgia (preferência do paciente)
  - Suspeito à US=cirurgia
  - Crescimento no seguimento=cirurgia
  - Fatores de risco clínicos=cirurgia

Bethesda II


Alto risco US
Repetir PAAF
[1 ano?- ATA]
2 PAAFs Bethesda II
Não precisa seguimento
Se também não tiver crescimento
Risco interm/baixo US
Repetir US
1-2 anos]
Caso > 50% volume ou >20% em 2 medidas
Ou surgimento de suspeição US
Repetir PAAF
2 PAAFs Bethesda II
Não precisa seguimento
se não tiver crescimento
Muito baixo risco US
Não precisa seguimento
Máximo 1 US em 2 a para avaliar crescimento
Não precisa seguimento
se não tiver crescimento

Conduta nos nódulos benignos

- Terapia supressiva= não recomendada
- Coorte recente = LT4 não supressiva previne crescimento
- >4 cm= operar se crescimento c/ sintomas compressivos.
- Cistos que refazem = cirurgia ou injeção percutânea de etanol

Bethesda III

- REPETIR PAAF (10-30% mantém BIII/IV)
- Considerar características clínicas de risco e US
  - Repetir PAAF ou não
- Considerar testes moleculares
  - Afirma ®– alto VPN
  - Thyroseck ® - alta especificidade/ baixa sensibilidade

AUS/FLUS

Atipias

- Citologia com atipias não bem definidas
- > risco de malignidade se confirmada
- Comumente na repunção= PODE evidenciar benigna, insuficiente ou suspeita

Desarranjos

- Arranjo arquitetural atípico
- Menor risco
- Porém menor chance de mudar na 2ª PAAF

Bethesda IV

- Pode ser por predomínio de céls de Hurtle
- Arranjo arquitetural alterado
  - Sobreposição marcada
  - Microfolicular

Bethesda IV

(B) If molecular testing is either not performed or inconclusive, surgical excision may be considered for removal and definitive diagnosis of an FN/SFN thyroid nodule.

(Strong recommendation, Low-quality evidence)

Bethesda V (comparável ao VI ou III/IV?)

- Cirurgia=maioria
- Pode acompanhar:
  - MicroPTC sem Ln etc..
  - idoso sem citologia de risco
  - Alto risco cirúrgico
  - Sobrevida curta
  - Outras urgências médicas…
  - Longe da traqueia/ cápsula
  - Estável no *follow-up*

■ **RECOMMENDATION 17**

(A) If the cytology is reported as suspicious for papillary carcinoma (SUSP), surgical management should be similar to that of malignant cytology, depending on clinical risk factors, sonographic features, patient preference, and possibly results of mutational testing (if performed).

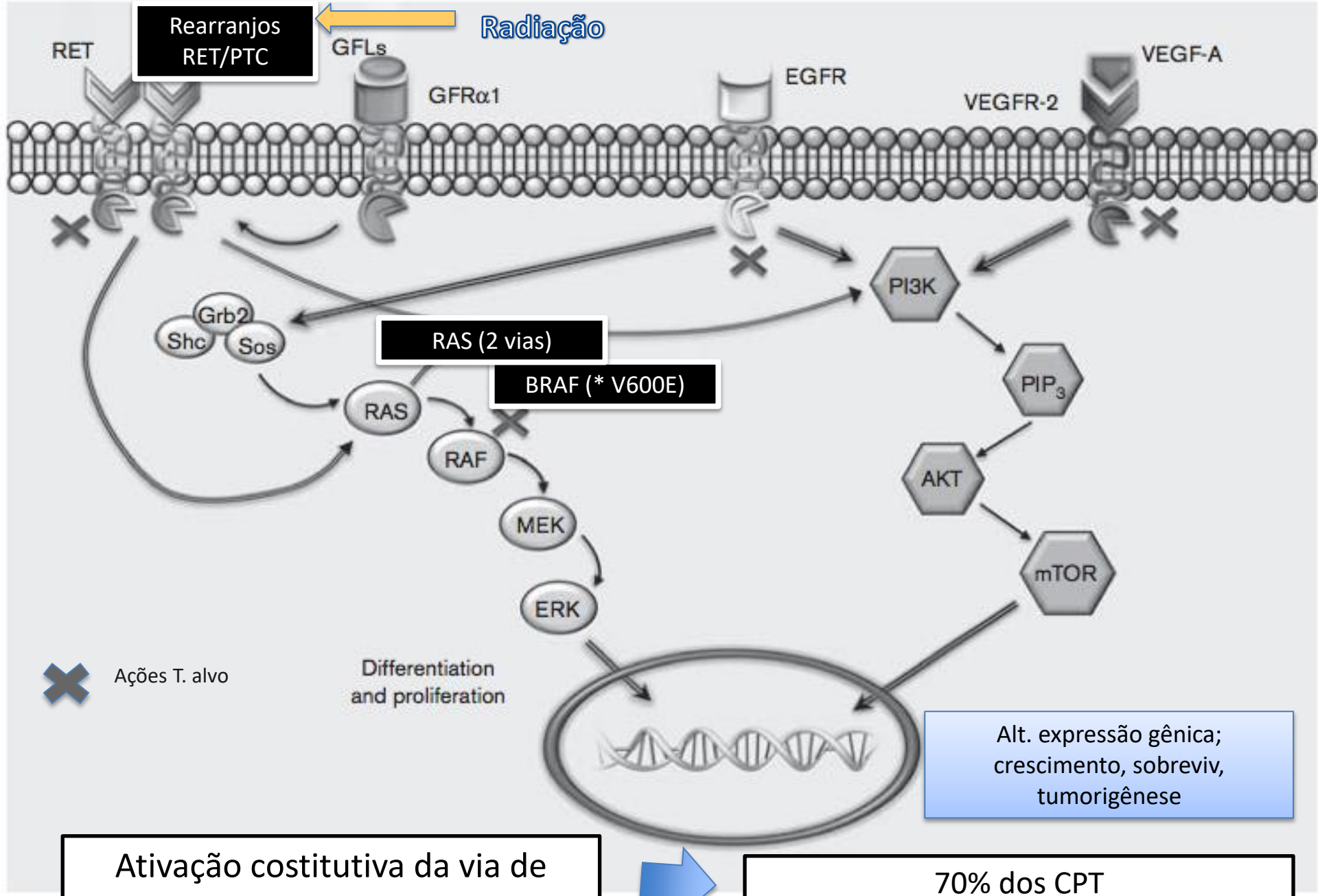
(Strong recommendation, Low-quality evidence)

Bethesda V

- Molecular testing using the 167 GEC has a PPV that is similar to cytology alone (76%) and a NPV of 85%, and it is therefore not indicated in patients with this cytologic diagnosis.

Citologias indeterminadas

TESTES MOLECULARES



Ativação costitutiva da via de sinalizacão MAPK

70% dos CPT

Fonte Wang et al, 2015 Anti Cancer Drugs

PREVALÊNCIA DE CÂNCER (% AMOSTRAS MALIGNAS)

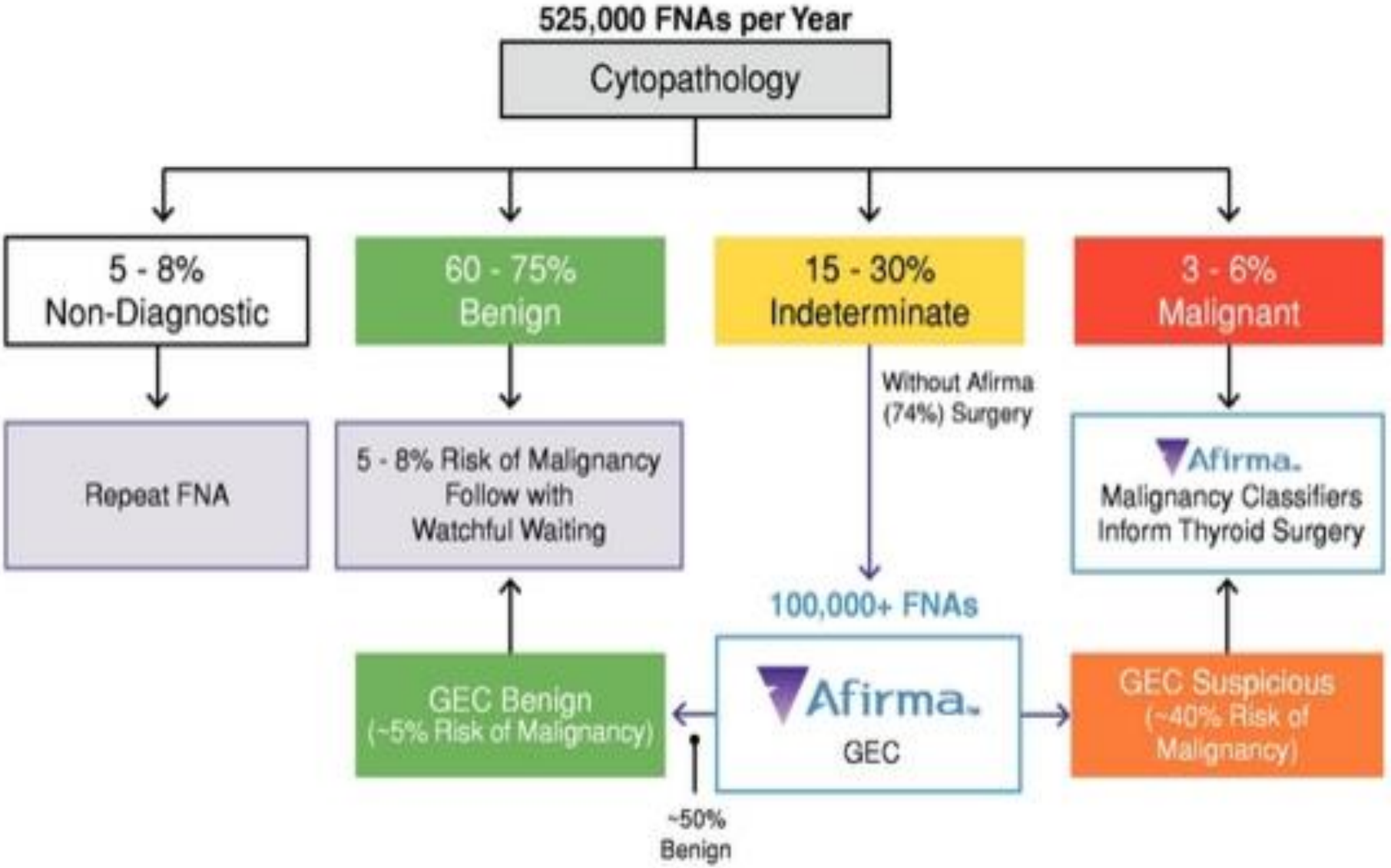
Positive and Negative Predictive Value

Need to know Institutional Prevalence of CA for Indeterminate FNAC!

- PPV= (Sensitivity)(Prevalence) / (Sens)(Prev)+(1-Prev)(1-Spec)
- PPV: will decrease if prevalence decreases.
- NPV= (Specificity)(1-Prevalence) / Spec(1-Prev)+Prev(1-Sens)
- NPV: will decrease if the prevalence increases.

Figure 1. Positive predictive value (PPV) and negative predictive value (NPV) are impacted by the prevalence (Prev) of cancer. Sens indicates sensitivity; Spec, specificity.

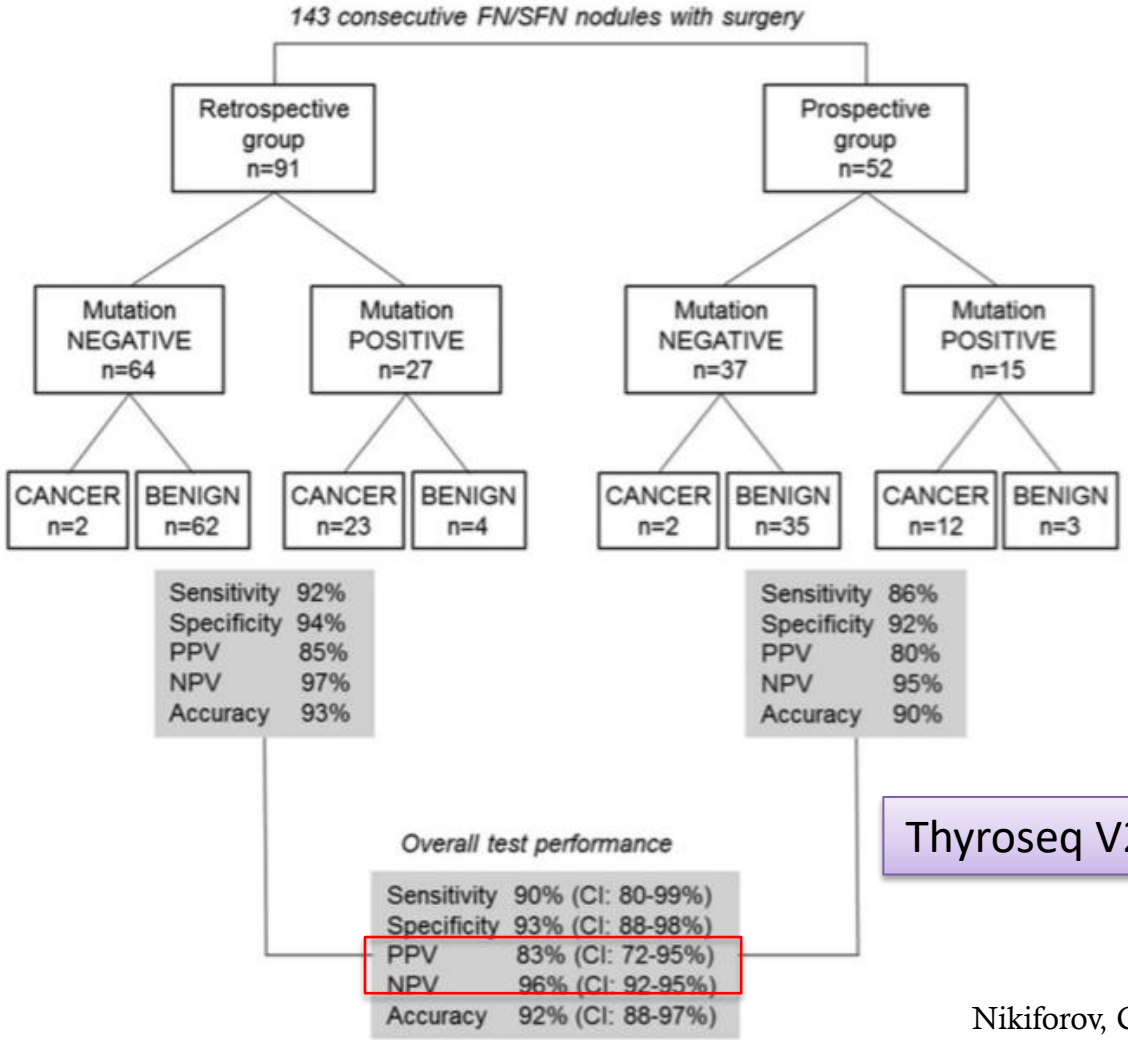
AFIRMA performance



Thyroseq V2- Next generation sequencing panel

MOLECULAR ANALYSIS: 14 gens e 42 fusions

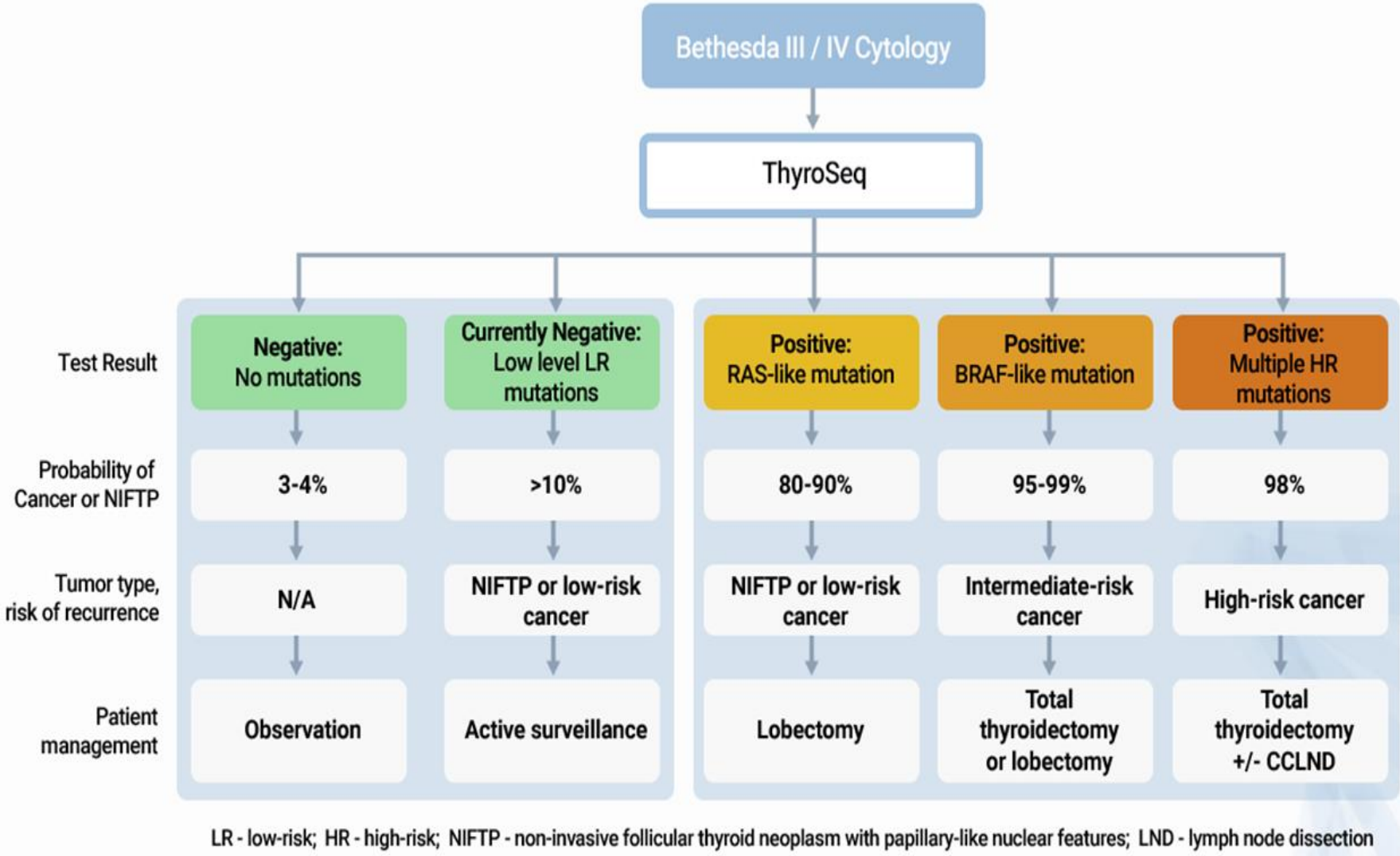
BRAF, NRAS, HRAS, KRAS, RET (RET/PTC, RET/PTC3), PAX8/PPARY, TSHR, PTEN, AKT1, TP53, GNAS, CTNNB1, PIK3CA, TERT



Thyroseq V2- ⇧ VPP ⇧VPN

Nikiforov, Cancer 2014

Thyroseq V3



LR - low-risk; HR - high-risk; NIFTP - non-invasive follicular thyroid neoplasm with papillary-like nuclear features; LND - lymph node dissection

Gene Expression Classifier vs Targeted Next-Generation Sequencing in the Management of Indeterminate Thyroid Nodules

J Clin Endocrinol Metab JUNE 2018

Context: Molecular testing has reduced the need for diagnostic hemithyroidectomy for indeterminate thyroid nodules. No studies have directly compared molecular testing techniques.

Objective: Compare the diagnostic performance of Afirma Gene Expression Classifier (GEC) with that of ThyroSeq v2 next-generation sequencing assay.

Design: Par Afirma GEC or ThyroSeq v2 nts with Bethesda III/IV cytology to

Setting: University of California, Los Angeles

Participants: Thyroid biopsy 4/16 to 6/17

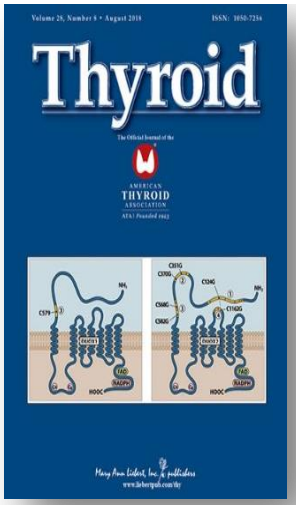
Intervention: Testing with GEC or ThyroSeq v2.

Further studies are required for comparison with other available molecular diagnostics and for newer tests as they are developed

Molecular Classification of Thyroid Nodules with Indeterminate Cytology: Development and Validation of a Highly Sensitive and Specific New miRNA-Based Classifier Test Using Fine-Needle Aspiration Smear Slides

Marcos Tadeu dos Santos,[1,2] Ana Lígia Buzolin,[1] Ricardo Ribeiro Gama,[2,3] Eduardo Caetano Albino da Silva,[4] Rozany Mucha Dufloth,[4] David Livingstone Alves Figueiredo,[5] and André Lopes Carvalho[2,3]

THYROID
Volume 28, Number 12, 2018
Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2018.0254



ONKOS DIAGNÓSTICOS MOLECULARES

HOSPITAL DE CÂNCER DE BARRETOS
Fundação Pio XII
O HOSPITAL DO AMOR

FAPESP

RESULTADOS

"Rule-in" test: Specificity > 80%

"Rule-out" test: Sensitivity>

Performance in the Study FNA Validation Set Cohort	mir-THYpe	ThyroSeq v3[1]	ThyroidPrint	ThyraMIR / ThyGenX	Rosetta GX Reveal[a]	Afirma GSC
"Rule-in" Test?[§]	Yes	Yes	Yes	Yes	No	No
"Rule-out" Test?[§]	Yes	Yes	Yes	No	No	No
Performed from FNA smear slides?	Yes	No	No	Yes	Yes	No
Sensitivity	94·6%	98·0%	95·5%	88·6%	85·2%	91·0%
Specificity	81·0%	81·8%	86·7%	85·1%	71·9%	68·0%
NPV	95·9%	97·4%*	97·5%	94·0%	91·1%	96·0%
PPV	76·1%	85·7%*	77·8%	73·8%	59·1%	47·0%
Cancer Prevalence	38·9%	52·6%	32·8%	32·1%	32·3%	24·0%
Number of Samples in the Study	95	175	67	109	189	191
Out-of-Network Cost[ǂ]	$	$$$	n.a.	$$$**	$$	$$$$

[a] Considering the entire validation set (n=189). [§]According to the thresholds proposed by Vargas-Salas and colleagues in 2018. *Calculated based on Bayes' theorem, using the cancer prevalence, sensitivity, and specificity published. **Aggregated price of ThyraMIR ($$$) + ThyGenX ($). [ǂ] The prices are typically different from payers' reimbursement schedules. Prices ranges in USD: $; 0-1999. $$; 2000-3999; $$$; 4000-5999. $$$$: >6000.

CONCLUSÕES

O mir-THYpe:

- ✓ é o único teste que pode ser considerado tanto "Rule-In" como "Rule-Out" que é feito a partir de lâminas da PAAF;
- ✓ tem um custo significativamente menor;
- ✓ pode ser considerado para uso na prática clínica como uma ferramenta complementar para apoiar a tomada de decisão clínica;
- ✓ Tem grande potencial para contribuir na redução nas taxas de cirurgias desnecessárias e gastos desnecessários com

Resumindo…

- Teste de expressão genética não tem valor:
  - Lesão de células de Hurthle!
  - Bethesda V
  - Nódulos < 1cm
  - Pediatria
  - Nódulos > 4cm
  - Citologias: benigna, maligna ou suspeita
  - Preferência do paciente por cirurgia
  - Sintoma compressivo
  - Alta suspeita clínica ou US

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REVIEWS and SCHOLARLY DIALOG

American Thyroid Association Guidelines on the Management of Thyroid Nodules and Differentiated Thyroid Cancer Task Force Review and Recommendation on the Proposed Renaming of Encapsulated Follicular Variant Papillary Thyroid Carcinoma Without Invasion to Noninvasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features

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NIFTP – guideline ATA 2017

- It is also unclear how these patients should be monitored.

- Based on the low risk for recurrence DTC recommendations in the 2015 ATA guidelines (lobectomy sufficient—Recommendation 38A and 51B; remnant ablation not recommended—Recommendation 38B; thyrotropin target 0.5–2mIU/L—Recommendation 59C and 59E), these general recommendations would not be different for patients with tumors classified as NIFTP.

- Until more long-term follow-up data are available, occasional monitoring with serum thyroglobulin and neck ultrasound can be considered, depending upon patient context, but this is not mandatory.

NIFTP e testes moleculares...

- Since NIFTP, like follicular adenoma, requires surgery for a definitive diagnosis, the changes in PPV and NPV of the molecular tests will not alter the requirement of surgical intervention for these patients.

Bethesda VI - CDT

- Tireoidectomia=maioria
  - Total X parcial

- Considerar acompanhar:
  - Micro PTC sem Ln, longe de cápsula/traquéia, >40 anos (Ito *et al*); estável no *follow-up*
  - idoso sem citologia de risco
  - Alto risco cirúrgico
  - Sobrevida curta
  - Outras urgências médicas…
  - Gestante até o melhor *time* cirúrgico

Estudos seguimento micro PTC s/ operar

Eur J Surg Oncol. 2018 Mar;44(3):307-315. doi: 10.1016/j.ejso.2017.03.004. Epub 2017 Mar 16.

Low-risk papillary microcarcinoma of the thyroid: A review of active surveillance trials.

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Abstract

Papillary microcarcinoma (PMC) of the thyroid is defined as papillary thyroid carcinoma (PTC) measuring ≤1 cm. Many autopsy studies on subjects who died of non-thyroidal diseases reported latent small thyroid carcinoma in up to 5.2% of the subjects. A mass screening study for thyroid cancer in Japanese adult women detected small thyroid cancer in 3.5% of the examinees. This incidence was close to the incidence of latent thyroid cancer and more than 1000 times the prevalence of clinical thyroid cancer in Japanese women reported at that time. The question of whether it was correct to treat such PMCs surgically then arose. In 1993, according to Dr. Miyauchi's proposal, Kuma Hospital initiated an active surveillance trial for low-risk PMC as defined in the text. In 1995, Cancer Institute Hospital in Tokyo, Japan, started a similar observation trial. The accumulated data from the trials at these two institutions strongly suggest that active surveillance (i.e., observation without immediate surgery) can be the first-line management for low-risk PMC. Although our data showed that young age and pregnancy might be risk factors of disease progression, we think that these patients can also be candidates for active surveillance, because all of the patients who showed progression signs were treated successfully with a rescue surgery, and none of them died of PTC. In this review, we summarize the data regarding the active surveillance of low-risk PMC as support for physicians and institutions that are considering adopting this strategy.

Table 2. Results and findings of observation for low-risk PMC at Kuma Hospital and the Cancer Institute Hospital

Kuma Hospital [12–15]	Cancer Institute Hospital [17–19]
1. Of 1235 patients, 8% and 3.8% showed size enlargement and novel node metastasis, respectively, at 10-year observation. 2. The PMC of young patients are likely progress, and those of old patients are most unlikely to grow. Although the number of patients is small, none of the young patients with TSH suppression showed progression. 3. Only 8% of the patients showed PMC progression during pregnancy, and rescue surgery after delivery was successful. 4. In Japan, the medical cost of observation was lower than that of immediate surgery. 5. None of the patients who underwent surgery after the detection of progression signs showed significant recurrence or died of PTC.	1. Of 230 patients (300 lesions), 7% and 1% showed size enlargement and novel node metastasis, respectively, during observation. 2. The TSH value was not linked to the progression of PMC during observation. 3. PMC with rich blood supply or lack of strong calcification on ultrasound were signs of high growth activity. Rich vascularity often decreased over time. 4. None of the patients who underwent surgery after the detection of progression signs showed significant recurrence or died of PTC.

Table 1. Contraindications for the active surveillance of PMC

Type	Contraindications
Clinically high-risk features	1. N1 (may present) or M1 (very rare) 2. Signs or symptoms of invasion to the recurrent laryngeal nerve or trachea 3. High-grade malignancy on cytology (very rare) 4. Cases with size enlargement or novel appearance of lymph node metastasis during observation
A feature unsuitable for observation, although unclear whether it is clinically aggressive	Tumors attaching the trachea or located in the course of the recurrent laryngeal nerve

Obrigado

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