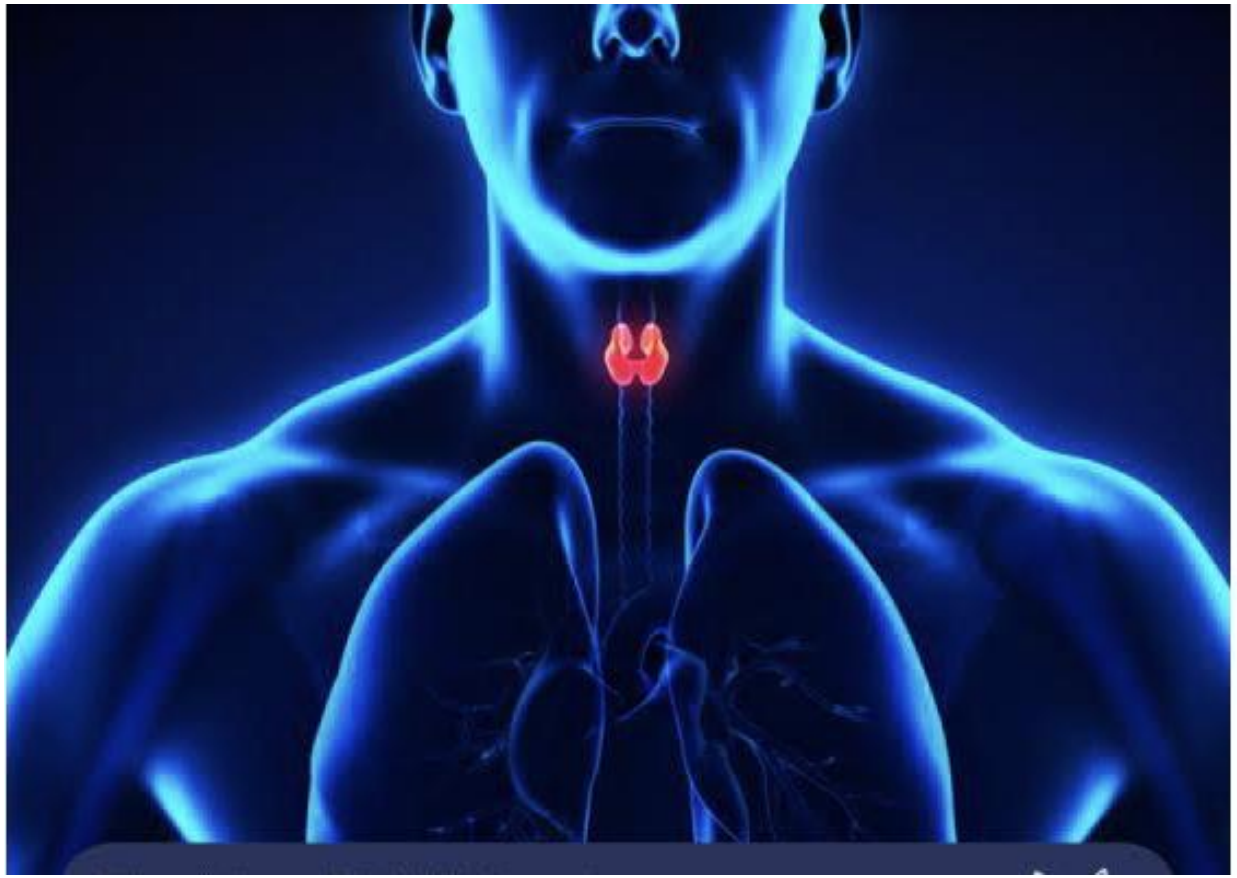
Terapia com Iodo Radioativo. Principios e Racionalidade



Dr. Fábio F. Ribeiro
Médico Nuclear
Bionuclear
ICSC

- O seu uso pode ter objetivos distintos:
  - Ablação
  - Adjuvância
  - Tratamento

Thyroid ©2015 American Thyroid Association DOI: 10.1089/thy.2015.0020

2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

Física das Radiações:

Conceitos de Dosimetria

Dose

É a quantidade de energia (qualquer tipo!) depositada em um certo volume de massa **m.**

$$D = dE/dm \; [\, J \,.\, kg\text{-}1 \,] \,,$$

A unidade antiga de dose absorvida, é o **rad** (radiation absorved dose), que em relação à unidade atual, o **gray** (Gy) no SI, vale:

1 Gy = 100 rad

Física das Radiações: Conceitos

Atividade é diferente de Dose. Pode-se fazer uma analogia com "quantidade" de radiação!

Atividade

A atividade de uma amostra radioativa é o número de desintegrações nucleares de seus átomos por unidade de tempo, denominada becquerel (Bq), no Sistema Internacional (SI).

1 Bq = 1 transformação por segundo.

A unidade antiga de atividade, ainda muito utilizada, é o curie (*Ci*).

1 Ci = $3{,}7.10^{10}$ Bq = $3{,}7.10^{10}$ (transformações por segundo)

Ex.: 1 micro-curie = 1 μCi = 10^{-6}Ci
1 mili-curie = 1 mCi = 10^{-3}Ci

Conceitos de Dosimetria

Dose Equivalente (H)

O Equivalente de Dose, é obtido multiplicando-se a dose absorvida D pelo Fator de qualidade Q da radiação, ou seja,

$$H = D.Q \text{ [Sv] (Sievert)}$$

Dose equivalente no órgão ou tecido (H_T)

O Equivalente de Dose no órgão ou tecido, é o equivalente de dose média em um tecido específico T, expresso por:

$$H_T = D_T\, Q_T \text{ [Gy] (Gray)},$$

onde Q_T é o fator de qualidade médio no órgão ou tecido T e D_T a dose absorvida.

Dose equivalente efetiva (H_E)

A Dose Equivalente Efetiva HE, também denominada de Equivalente de Dose de Corpo Inteiro HWB, (Whole Body) é obtido pela relação,

$$H_E = \sum T.\, W_T\, .H_T \text{ [Sv] (Sievert)}$$

Activity selection strategies

Empirically (based on physician experience)

OR

Quantitative dosimetry to estimate the activity needed to deliver an effective radiation dose of at least 300 Gy (thyroid remnant) or 100 Gy (metastases) (ALARA)

OR

Dosimetry to keep bone marrow exposure $\leq$ 2 Gy (AHASA)

Sherman, Lancet 2003; Benua&Leeper; Lassmann et al., 2008

The New England
Journal of Medicine

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Volume 309 OCTOBER 20, 1983 Number 16

RELATION BETWEEN EFFECTIVE RADIATION DOSE AND OUTCOME OF RADIOIODINE THERAPY FOR THYROID CANCER

- Remanescente
  - 300 Gray (30.000 rad)
- Metastase
  - 80 Gray (8000 rad)

Why Dosimetry?

Fixed activity: Every patient is given the same activity, regardless of biological variation

Old lady

155 cm

49 kg

3,5 l Bloodvolume

T_{eff} in Blood: 36 h

Young man

210 cm

200 kg

8 l Blood volume

T_{eff} in blood: 8 h

Post-surgical ablation

- **Definition:**
  - destruction of remnant thyroid tissue post thyroidectomy

- **Potential Benefits**
  - Decrease recurrence rate
  - Reduce cause-specific mortalities
  - Permit serum Tg measurement as follow up
  - Facilitate I-131 scans to detect recurrence
  - ? Avoid de-differentiation
  - Achieve greater certainty and peace of mind

Uso seletivo- Individualizado

- Decisão deve se basear portanto no risco de cada paciente!

Thyroid ©2015 American Thyroid Association DOI: 10.1089/thy.2015.0020

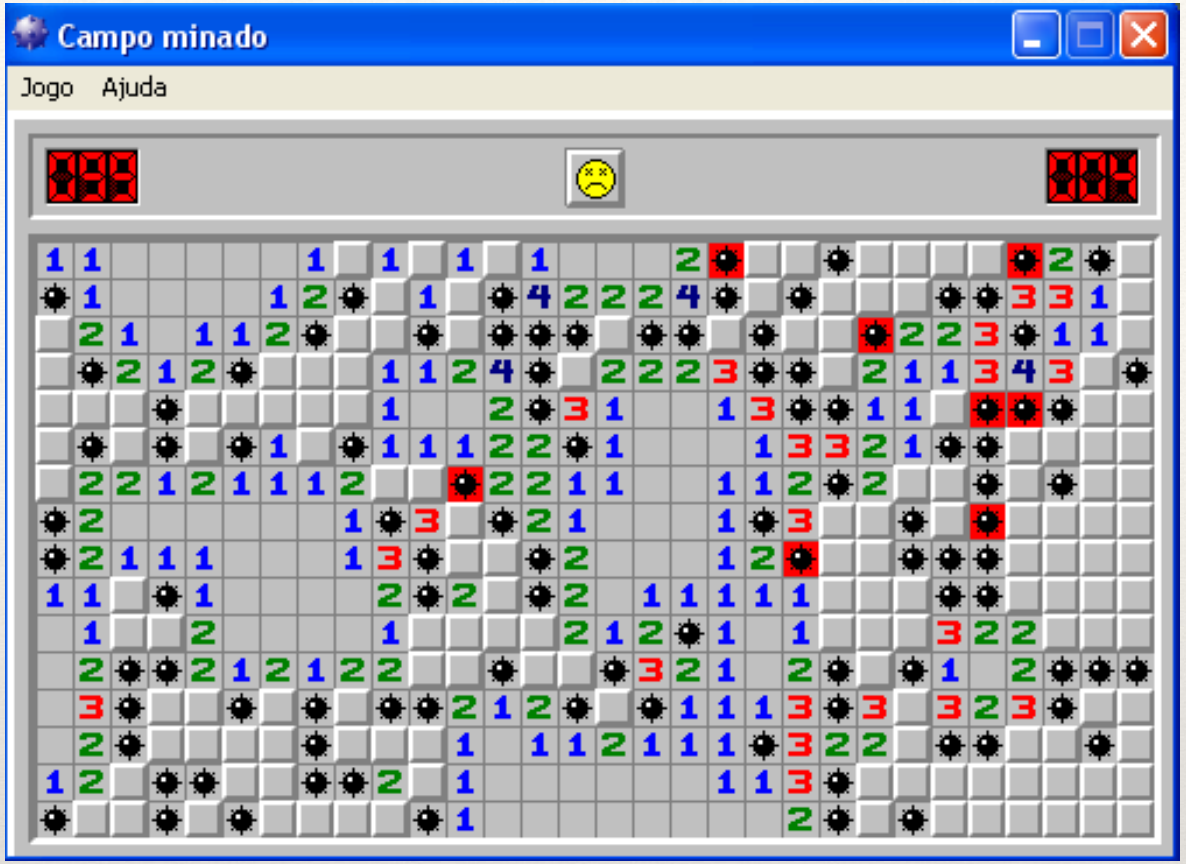
Riscos de um Câncer de Tireoide

- Recorrência
- Morte
- Perda de qualidade/ Não resposta a tratamento convencional

COMO MAPEAR/ DEFINIR ESSES RISCOS?

SE O PACIENTE FOR CANDIDATO A IODO, O RISCO INDUZ A DOSE A SER APLICADA?

E FAZER IODO REDUZ ESSES RISCOS?

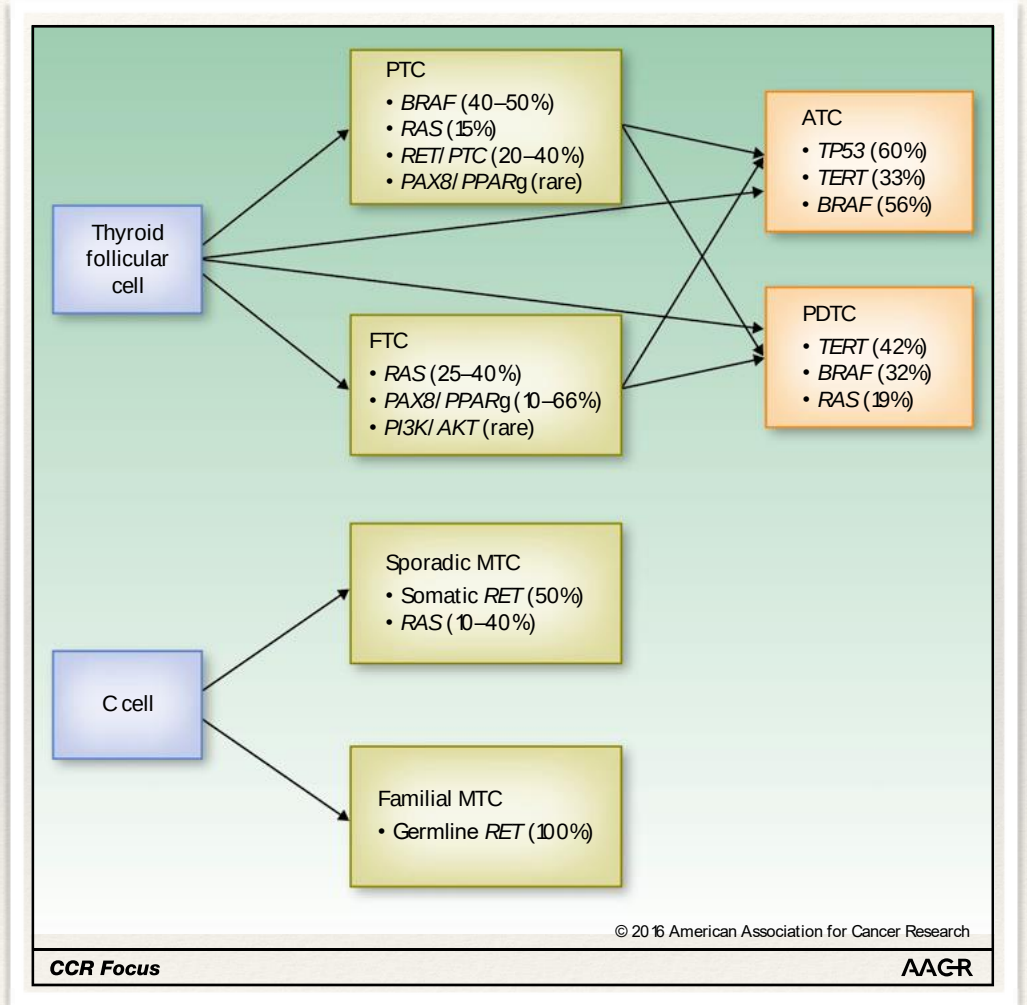


MAPEANDO OS RISCOS...

Análise de Risco

- Idade e gênero
- Tamanho do tumor
- Histologia
- Invasividade
- Doença multifocal (+ 3 focos)
- Presença de metástases locoregionais
- Presença de metástases à distância
- **Nível da reoglobulina sérica**

Avaliação Molecular



Clin Cancer Res; 22(20) October 15, 2016

RACIONALIDADE

Consenso Brasileiro - 2013

ATA 2009

Consenso Europeu - 2012

ATA 2015

Classificações de Risco do Memorial Sloan Kettering

Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

F. Pacini[1], M. G. Castagna[1], L. Brilli[1] & G. Pentheroudakis[2], on behalf of the ESM Working Group*

[1]Department of Internal Medicine, Endocrinology and Metabolism and Biochemistry, Section of Endocrinology and Metabolism, University o
[2]Department of Medical Oncology, Medical School, University of Ioannina, Ioannina, Greece

ETA risk stratification		
Very low risk	Low risk	High risk
Complete surgery Patients with unifocal microcarcinoma (<1 cm) with no extension beyond the thyroid capsule and without lymph node metastases	No local or distant metastases No tumor invasion of locoregional tissues or structures No aggressive histology or vascular invasion	Less than total thyroidectomy Tumor invasion of locoregional tissues or structures Cervical lymph node metastases Distant metastases Aggressive histology or vascular invasion

RAI is recommended	RAI is not recommended
All patients with	
Known distant metastases	Patients with unifocal cancer <1 cm without other higher risk features[a]
Documented lymph node metastases	Patients with multifocal cancer when all foci are <1 cm in the absence of other higher risk features[a]
Gross extrathyroidal extension of the tumor regardless of tumor size	
Primary tumor size >2 cm even in the absence of other higher risk features[a]	

[a]Higher risk features: histological subtypes (tall cell, columnar, insular and solid variant as well as poorly DTC and follicular and Hurthle cell cancer), intrathyroidal vascular invasion, gross or microscopic multifocal disease.

Annals of Oncology 23 (Supplement 7): vii110–vii119, 2012
doi:10.1093/annonc/mds230

Nódulo tireoidiano e câncer diferenciado de tireoide: atualização do consenso brasileiro

Thyroid nodule and differentiated thyroid cancer: update on the Brazilian consensus

Pedro Weslley Rosário[1], Laura S. Ward[2], Gisah A. Carvalho[3], Hans Graf[3], Rui M. B. Maciel[4], Léa Maria Z. Maciel[5], Ana Luiza Maia[6], Mário Vaisman[7]

Baixo (todos achados)	≤ 4 cm sem invasão extratireoidiana	cN0[c]	M0[a]	Clássica, sem invasão vascular	Completa	Leito tireoidiano[d]
	≤ 2 cm sem invasão extratireoidiana (pT1)	1-3 LN sem EEC				
	≤ 2 cm com invasão extratireoidiana mínima (pT3)	cN0[c]				
Muito baixo (todos achados)	≤ 1 cm sem invasão extratireoidiana (pT1a)	cN0[c]	M0[a]	Clássica, sem invasão vascular	Completa	
	1-2 cm sem invasão extratireoidiana (pT1b), único					

Risco	Tamanho do tumor e invasão extratireoidiana	Metástases linfonodais	Metástases distantes	Histologia	Ressecção tumoral[b]	Captação na PCI
Alto (qualquer um dos achados)	Invasão extratireoidiana extensa (pT4)	> 10 LN acometidos ou > 3 LN com EEC ou algum LN metastático > 3 cm	M1[a]		Incompleta	A distância (M1)
Intermediário (qualquer um dos achados)	> 4 cm	4-10 LN acometidos ou 1-3 LN com EEC		Subtipo agressivo ou invasão vascular		Cervical ectópica (LN)
Intermediário (ambos achados)	≤ 4 cm com invasão extratireoidiana mínima (pT3)	1-3 LN sem EEC				
	2-4 cm sem invasão extratireoidiana (pT2)	1-3 LN sem EEC				
	2-4 cm com invasão extratireoidiana mínima (pT3)	cN0[c]				

Arq Bras Endocrinol Metab. 2013;57/4

Quando indicar a ablação/terapia com ^{131}I após a tireoidectomia total?

Nos pacientes com ressecção tumoral incompleta ou metástases aparentes após a tireoidectomia e que não são candidatos à reintervenção cirúrgica, o tratamento com ^{131}I está indicado. Também em pacientes com ressecção tumoral aparentemente completa, mas classificados como de risco alto ou intermediário para doença persistente (87,91), a terapia adjuvante com ^{131}I tem impacto no prognóstico (92), sendo assim recomendada.

Opostamente, nos indivíduos considerados de muito baixo risco, a ablação com ^{131}I não é indicada (67,72,73,75,93-95).

Nos demais pacientes, de baixo risco para doença persistente/ recorrente, a ablação é controversa (67,96).

todos os direitos reservados.

Arq Bras Endocrinol Metab. 2013;57/ 4

2015 American Thyroid Association Management Guidelines for Adult Patient with Thyroid Nodules and Differentiated Thyroid Cancer

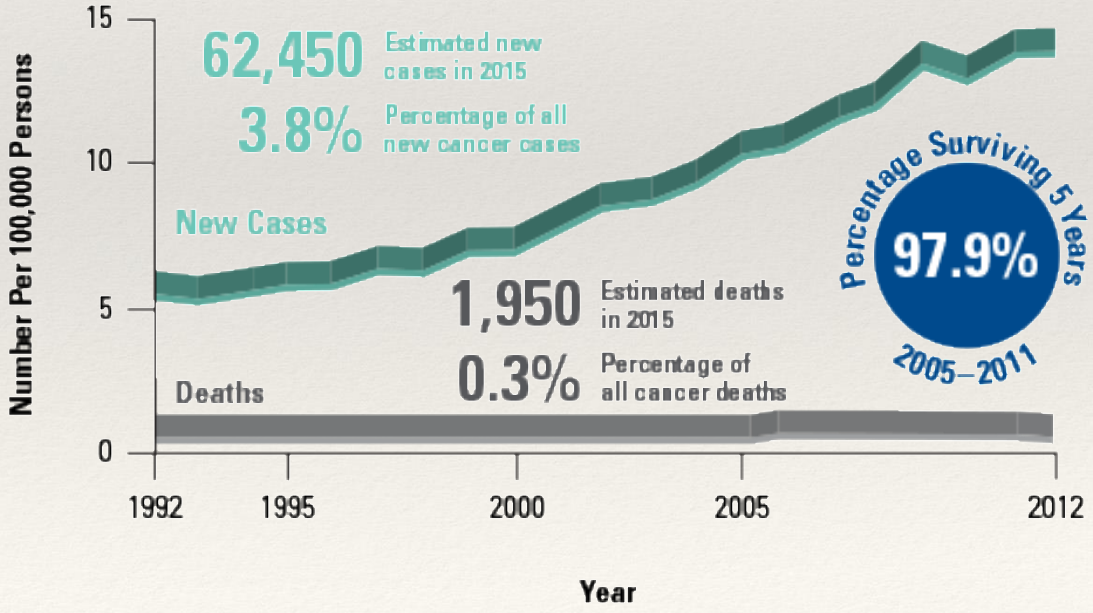
The American Thyroid Association (ATA) Guidelines Taskforce
on Thyroid Nodules and Differentiated Thyroid CancerBryan R. Haugen, M.D.[1] (Chair)*,
Erik K. Alexander, M.D.[2], Keith C. Bible, M.D., Ph.D.[3], Gerard M. Doherty, M.D.[4], Susan J. Mandel,
M.D., M.P.H.[5], Yuri E. Nikiforov, M.D., Ph.D.[6],
Furio Pacini, M.D.[7], Gregory W. Randolph, M.D.[8], Anna M. Sawka, M.D., Ph.D.[9],
Martin Schlumberger, M.D.[10], Kathryn Schuff, M.D.[11], Steven I. Sherman, M.D.[12],
Julie Ann Sosa, M.D.[13], David L. Steward, M.D.[14], R. Michael Tuttle, M.D.[15],
and Leonard Wartofsky, M.D.[16]

ATA - A “Evolução" ou “Involução” com o passar dos Tempos.....

ATA 1996 - 7 paginas

ATA 2009 - 47 páginas

ATA 2015 - 133 páginas



Updated risk stratification criteria.

Risk Category	2009 ATA Guidelines	2015 ATA Guidelines additions	2015 RAI recommendation	% NED after TT/RAI
Low risk	• No local or distant metastasis • No macroscopic tumor remaining • No ETE • No vascular invasion • Nonaggressive histology • If RAI given, no RAI-avid metastatic foci outside the thyroid bed on the post-treatment whole body RAI scan	• Clinical N0 • $\leq$5 pathologic N1 micrometastases (< 2 mm in size) • Intrathyroidal encapsulated follicular variant of PTC • Intrathyroidal FTC with capsular invasion and minimal vascular invasion (< 4 foci) • Intrathyroidal papillary microcarcinoma, unifocal or multifocal, including BRAF mutation	Not routinely recommended	78e 86%
Intermediate risk	• Minimal ETE • RAI-avid metastatic foci in neck on first post-treatment whole body RAI scan • Aggressive histology (tall cell, columnar) • PTC with vascular invasion	• Clinical N1 • > 5 pathologic N1 (all involved LN < 3 cm in size) • Multifocal papillary microcarcinoma with ETE and BRAF mutation	Can be considered	52e 63%
High risk	• Gross ETE • Incomplete tumor resection • Distant metastases • Postoperative TG suggesting distant metastases	• Pathologic N1 with LN $\geq$3 cm in size • FTC with extensive vascular invasion (> 4 foci)	Routinely recommended	14e 31%

ATA, American Thyroid Association; ETE, extrathyroidal extension; TT, total thyroidectomy; RAI, radioactive iodine; NED, no evidence of disease; PTC, papillary thyroid carcinoma; FTC, follicular thyroid carcinoma.

Goals of I-131 initial treatment

A. Remnant ablation → „usual activity 30 mCi (1110 MBq)"
   Reduction/destruction of a sufficient part of the„healthy" thyroid remnant tissue to allow sensitive Tg based follow-up

B. Adjuvant therapy → „Activities of up to 150 mCi can be given"
   Treatment of unknown (micro)metastases
   Prevention of local recurrence through therapy (unknown) remaining DTC foci

C. Therapy → No activity mentioned (≤150 mCi if age ≥70)
   Treatment of known micro- or macroscopic local DTC remnants / metastases

ATA guidelines 2016

THYROID CANCER
131-I Ablation & Adjunctive Therapy

- ATA Cancer Guidelines
  - Who to Ablate? Who not to ablate?
  - 30 mCi or 100 mCi ?
- rhTSH for Ablation
  - Efficacy
  - Safety
  - Cost effectiveness

EDITORIAL

Why the European Association of Nuclear Medicine has declined to endorse the 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer

Eur J Nucl Med Mol Imaging. 2016 Jun;43(6):1001-5. doi: 10.1007/s00259-016-3327-3. Epub 2016 Feb 17.

Why the European Association of Nuclear Medicine has declined to endorse the 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer.

Verburg FA[1], Aktolun C[2], Chiti A[3,4], Frangos S[5], Giovanella L[6], Hoffmann M[7], Iakovou I[8], Mihailovic J[9], Krause BJ[10], Langsteger W[11], Luster M[12]; EANM and the EANM Thyroid Committee.

For future editions of the ATA management guidelines for adult patients with thyroid nodules and DTC, we sincerely offer our support in order to include more experts in nuclear thyroidology and thus create a more balanced set of recommendations which do justice to the role of nuclear medicine in the care of patients with nodular thyroid disease and DTC. Guidelines created in such a manner would indeed gladly be endorsed by the EANM.

Posicionamento da SBMN em relação às atuais diretrizes da Associação Americana de Tireóide para Manejo de Pacientes Adultos com Nódulos Tireoidianos e Câncer Diferenciado da Tireoide (ATA 2015)

corroborando com o posicionamento da Sociedade Europeia de Medicina Nuclear e Imagem Molecular (EANMMI) -,

A entidade expressa reconhecer o valor e o empenho da Associação Americana de Tireoide na elaboração de diretrizes que objetivam oferecer a melhor prática médica baseada em evidências para os pacientes. Entretanto a SBMN não pode recomendar ao momento a adoção plena desta diretriz visto que ainda existem importantes pontos controversos e não abordados, principalmente nos cenários de populações que possam diferir das populações mais comumente estudadas em literatura científica internacional, e recomenda aos profissionais que optarem por seu uso, que o mesmo seja feito com a cautela e particularização desejável para que não haja prejuízo ao paciente.

Posicionamento da SBMN em relação ATA 2015

- A falta de ensaios clínicos prospectivos aleatorizados e preferencialmente duplo-cegos
- particularizar nossas observações dentro da realidade brasileira
- essencial a maior efetividade e resolutividade no primeiro tratamento.
- recomendação 35B da ATA 2015: lobectomia para os ca > 1 cm < 4 cm, sem extensão extra-tireoidiana e sem metástases LNs.
- Mazzaferi et al.3: enorme redução de mortalidade e recorrência nos pctes com TT e RIT.
- Bilimoria et al.4 TT X lobectomia, 52.173 pacientes =Lobectomia tu > 1 cm ➔maior recorrência mortalidade.
- Detectação novos focos de tumor
- seguimento TG prejudicados com a lobectomia.
- SUS

Preocupação: Ablação com Baixas doses de RIT tragam pior prognóticos aos pacientes.

- cuidado em alterar uma prática de longo tempo e que tem tido sucesso, antes que haja evidência suficiente em literatura médica indicando se é seguro omitir a RIT de ablação ou adjuvância em pacientes com TU > que os microcarcinomas.
- microcarcinoma papilífero = bom prognóstico mas.. a sua evolução depende de alguns fatores como a presença de metástase linfonodal ao diagnóstico > recorrência
- experiência do cirurgião, médico que irá acompanhar

Surgical Treatment

American Thyroid Association Guidelines 2016

20:42

CANCER DO ESTADO DE SÃO PAULO

- Tumor >4 cm
- Gross extrathyroidal extension Clinically apparent LN mets (N1)
- Distant Mets (M1)

→ Total Thyroidectomy +/- LN dissection

Tumor >1 cm and <4 cm
No extrathyroidal extension, and without clinical evidence of LN mets (cN0)

→ Lobectomy or Total Thyroidectomy

<1 cm without extrathyroidal extension and cN0

→ Lobectomy
*unless there are clear indications to remove the contralateral lobe

(Strong recommendation, Moderate-quality evidence)

** pre-operative US: extremely important

Haugen BR et al. THYROID Volume 26, Number 1, 2016

AJCC

Thyroid
The Updated AJCC/TNM Staging System for Differentiated and Anaplastic Thyroid Cancer (8th edition): What changed and why? (DOI: 10.1089/thy.2017.0102)
This paper has been peer-reviewed and accepted for publication, but has yet to undergo copyediting and proof correction. The final published version may differ from this proof.

Table 2: Comparison of the AJCC 7th and 8th edition staging system.

	Stage	7th Edition Description	7th Edition 10 yr DSS	8th Edition Description	8th Edition Expected 10 yr DSS
Younger patients	I	< 45 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	97-100%	< 55 years old All patients without distant metastases regardless of tumor size, lymph node status or extrathyroidal extension	98-100%
	II	< 45 years old Distant metastases	95-99%	< 55 years old Distant metastases	85-95%
Older patients	I	45 years old 2 cm tumor Confined to the thyroid	97-100%	55 years old 4 cm tumor Confined to the thyroid	98-100%
	II	45 years old 2-4 cm tumor Confined to the thyroid	97-100%	55 years old Tumors > 4cm, Or tumors of any size with central or lateral neck lymph nodes, Or gross extrathyroidal extension into strap muscles	85-95%
	III	45 years old >4 cm tumor, Or minimal extrathyroidal extension, Or central neck lymph node metastasis	88-95%	55 years old Tumors of any size with gross extrathyroidal extension into subcutaneous tissue, larynx, trachea, esophagus, recurrent laryngeal nerve	60-70%
	IV	45 years old Gross extrathyroidal extension, Or lateral neck lymph node metastasis, Or distant metastasis	50-75%	55 years old Tumors of any size or lymph node status with gross extrathyroidal extension into prevertebral fascia, encasing major vessels Or distant metastasis	< 50%

Table 3: A clinically based approach to staging in differentiated thyroid cancer using the 8th edition AJCC/TNM update.

	Distant Metastasis	Gross ETE present?	Structures involved with gross ETE	T category	N Category	Stage
< 55 yrs	No	Yes or No	Any or None	Any	Any	I
	Yes	Yes or No	Any or None	Any	Any	II
≥ 55 yrs	No	No	None	≤4 cm (T1-2)	N0/Nx N1a/N1b	I II
				> 4 cm (T3a)	N0/Nx/N1a/N1b	II
		Yes	Only strap muscle (T3b)	Any	Any	II
			Subcutaneous, larynx, trachea, esophagus, recurrent laryngeal nerve (T4a)	Any	Any	III
			Prevertebral fascia, encasing major vessels (T4b)	Any	Any	IVA
	Yes	Yes or No	Any or None	Any	Any	IVB

Summary of Changes

Change	Details of Change	Level of Evidence
Prognostic Factors Required for Stage Grouping	The age at diagnosis cutoff used for staging was increased from 45 years to 55 years.	I
Definition of Primary Tumor (T)	Minor extrathyroidal extension was removed from the definition of T3 disease. As a result, minor extrathyroidal extension does not affect either T category or overall stage.	I
Definition of Primary Tumor (T)	T3a is a new category and refers to a tumor >4 cm in greatest dimension limited to the thyroid gland.	I
Definition of Primary Tumor (T)	T3b is a new category and is defined as a tumor of any size with gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles).	I
Definition of Regional Lymph Node (N)	The definition of central neck (N1a) was expanded to include both level VI and level VII (upper mediastinal) lymph node compartments. Previously, level VII lymph nodes were classified as lateral neck lymph nodes (N1b).	II
Definition of Regional Lymph Node (N)	The pN0 designation is clarified as one or more cytologically or histologically confirmed benign lymph node(s).	II

Change	Details of Changes	Level of Evidence
AJCC Prognostic Stage Groups	The definition of Stages I, II, III, IV was changed for patients older than 55 years at diagnosis.	I
AJCC Prognostic Stage Groups	Stage I now includes T1 and T2 tumors if N0/NX and M0 in patients older than 55 years at diagnosis.	I
AJCC Prognostic Stage Groups	Stage II now includes T1 and T2 tumors if N1 and T3a/T3b tumors with any N if M0 in patients older than 55 years at diagnosis.	I
AJCC Prognostic Stage Groups	Stage III now includes only T4a with any N, if M0 in patients older than 55 years at diagnosis.	I
AJCC Prognostic Stage Groups	Stage IV now includes T4b with any N, any M and M1 with any T or N in patients older than 55 years at diagnosis.	I
Definition of Primary Tumor (T)	Unlike previous editions where all anaplastic tumors were classified as having T4 disease, the T category for anaplastic thyroid cancers will now use the same definitions used for differentiated thyroid cancers.	II
AJCC Prognostic Stage Groups	With anaplastic carcinoma, intrathyroidal disease is stage IVA, gross extrathyroidal extension or cervical node metastases is stage IVB, and distant metastases is stage IVC	II
Histologic Grade (G)	GX–G4 grading system was removed.	II

Várias publicações apontam controvérsias

0 1:02

- Nabhan F end Ringelm 2017 Endocrine Related Cancer

- Verburg F et al EJMMI 2016; 43:1001-1005

-Força tarefa 13/14 janeiro 2018

  - European Association Nuclear Med
  - Society Nuclear Medicine Molecular Imaging
  - American Thyroid Association
  - European Thyroid Association

-Princípios de "Martinique Principles"

Câncer de Tireóide – Dose terapêutica

- Resíduos: 30 a 100 mCi
- Linfonodos cervicais ou mediastinais: 150 a 200 mCi
- Metástase à distância: ≥ 200 mCi

- < 80 mCi se risco de pneumonite
- < 120 mCi se risco de mielossupressao

High X Low Iodine Activity

- Comparisons:
  - THW vs rhTSH
  - 30 vs 100 mCi

- No significant differences between groups

N Engl J Med 2012;366:1674-85.

N Engl J Med 2012;366:1663-73.

Conclusão

- **SBMN** – reconhece importância do consenso ATA 15

- **SBMN** – não recomenda a adoção plena
  – pontos controversos – dose fixa
  – diferentes populações

USO DE CONSENSO COM BOMSENSO

- Conduta individualizada

RADIOLOGISTA

ENDOCRINOLOGISTA

CIRURGIÃO

CA TIREOIDE

BIOL MOLECULAR
GENETICA

MEDICINA NUCLEAR

PATOLOGISTA

"Join those who seek the truth;
doubt those who think
they know the truth"

- Vamos pela escada que se atribui ao progresso, à civilização e à cultura. Mas aonde se vai? Realmente, não sei.

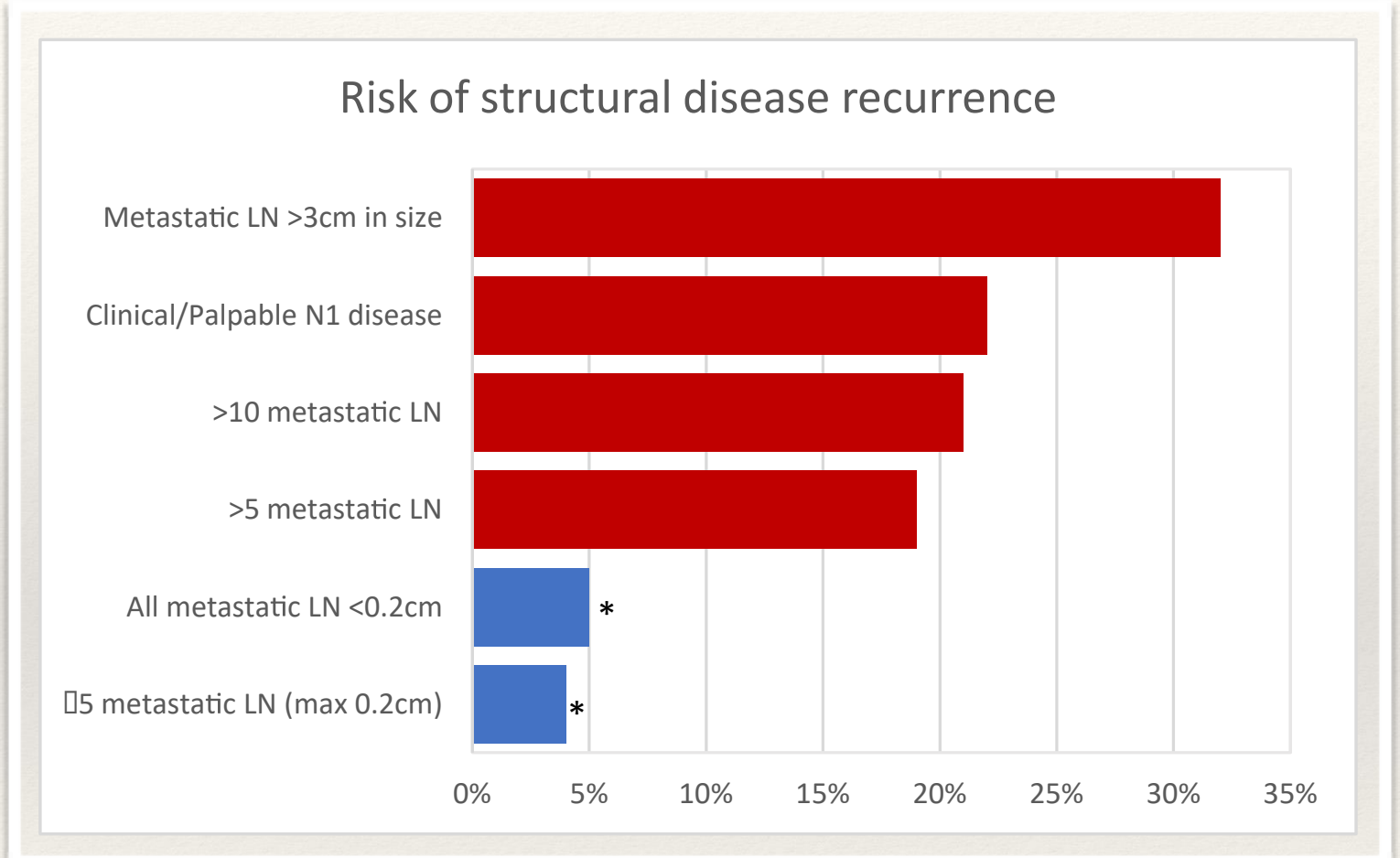
Anton Tchekhov

OBRIGADO

ATA Low Risk	Papillary Thyroid Cancer (with all of the following) • No local or distant metastases; • All macroscopic tumor has been resected • No tumor invasion of loco-regional tissues or structures • The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) • If ^{131}I is given, there are no RAI avid metastatic foci outside the thyroid bed on the first post-treatment whole-body RAI scan • ***No vascular invasion*** • ***Clinical N0 or ≤ 5 pathologic N1 micrometastases (<0.2 cm in largest dimension)**** ***Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer**** ***Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci) vascular invasion**** ***Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including V600E BRAF mutated (if known)****

ATA Intermediate Risk	Microscopic invasion of tumor into the perithyroidal soft tissues
	RAI avid metastatic foci in the neck on the first post-treatment whole-body RAI scan
	Aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma)
	Papillary thyroid cancer with vascular invasion
	Clinical N1 or >5 pathologic N1 with all involved lymph nodes < 3 cm in largest dimension*
	Intrathyroid, papillary thyroid cancer, primary tumor 1-4 cm, V600E BRAF mutated (if known)*
	Multifocal papillary microcarcinoma with extrathyroidal extension and V600E BRAF mutated (if known)*

ATA High Risk	Macroscopic invasion of tumor into the perithyroidal soft tissues (gross extrathyroidal extension),
	Incomplete tumor resection
	Distant metastases
	Post-operative serum thyroglobulin suggestive of distant metastases
	Pathologic N1 with any metastatic lymph node ≥ 3 in largest dimension*
	Follicular thyroid cancer with extensive vascular invasion (> 4 foci of vascular invasion)*



Please cite this article in press as: Marti JL, et al., Selective use of radioactive iodine (RAI) in thyroid cancer: No longer "one size fits all", Eur J Surg Oncol (2017), http://dx.doi.org/10.1016/j.ejso.2017.04.002

Análise de Risco - MSKCC

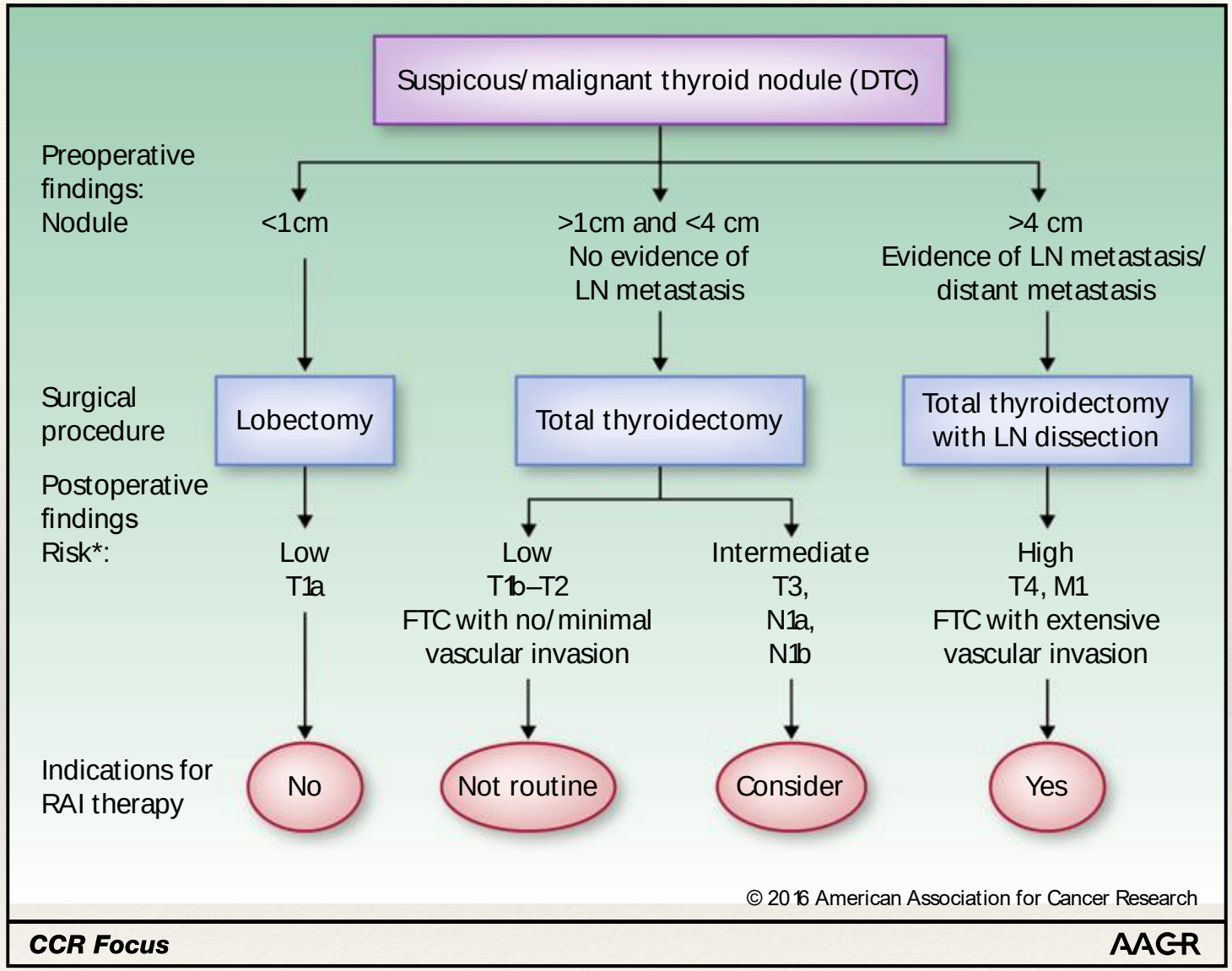
TABLE I. Risk of Death From Thyroid Cancer

	Very low risk	Low risk	Intermediate risk	High risk
Age at diagnosis	< 45 years	< 45 years	Young patients (< 45 years) Classic PTC > 4 cm Or vascular invasion Or extrathyroidal extension Or worrisome histology of any size[c]	> 45 years
Primary tumor size	< 1 cm	1–4 cm	Older patients (> 45 years) Classic PTC < 4 cm Or extrathyroidal extension Or worrisome histology < 1–2 cm confined to the thyroid[c]	> 4 cm classic PTC
Histology	Classic PTC, confined to the thyroid gland[a]	Classic PTC, confined to the thyroid gland[a]	Histology in conjunction with age as above	Worrisome histology > 1–2 cm[c]
Completeness of resection	Complete resection	Complete resection	Complete resection	Incomplete tumor resection
Lymph node involvement	None apparent	Present or absent[b]	Present or absent[b]	Present or absent[b]
Distant metastasis	None apparent	None apparent	None apparent	Present

Re-análise de Risco MSKCC

TABLE III. Response to Therapy Variables

	Excellent response[a]	Acceptable response	Incomplete response
Suppressed T_g[b]	Undetectable	Detectable but < 1 ng/ml	> 1 ng/ml
Stimulated T_g[b]	Undetectable	< 10 ng/ml	> 10 ng/ml
Trend in suppressed T_g[c]	Remains undetectable	Declining	Stable or rising
Anti-T_g antibodies	Absent	Absent or declining	Persistent or rising
Neck examination	Normal	Normal	Palpable disease
Neck ultrasonography	No evidence of disease	Non-specific changes in thyroid bed	Evidence of structurally significant recurrent/persistent disease in the thyroid bed (> 1 cm)
		Probable inflammatory lymph nodes	Cervical lymph nodes (> 1cm), or distant metastases, particularly if structurally progressive or FDG avid
		Stable millimeter sized cervical LN even if abnormal by US criteria	
Diagnostic RAI WBS[d]	No evidence for RAI avid disease	No evidence for RAI avid disease	Persistent/recurrent RAI avid disease present
		Very faint uptake in thyroid bed only	
Cross-sectional imaging (MRI, CT)[d]	No evidence of disease	Non-specific changes	Structural disease present
FDG PET scanning[d]	No evidence of disease	Non-specific changes consistent with normal variants or inflammatory changes	FDG avid disease present



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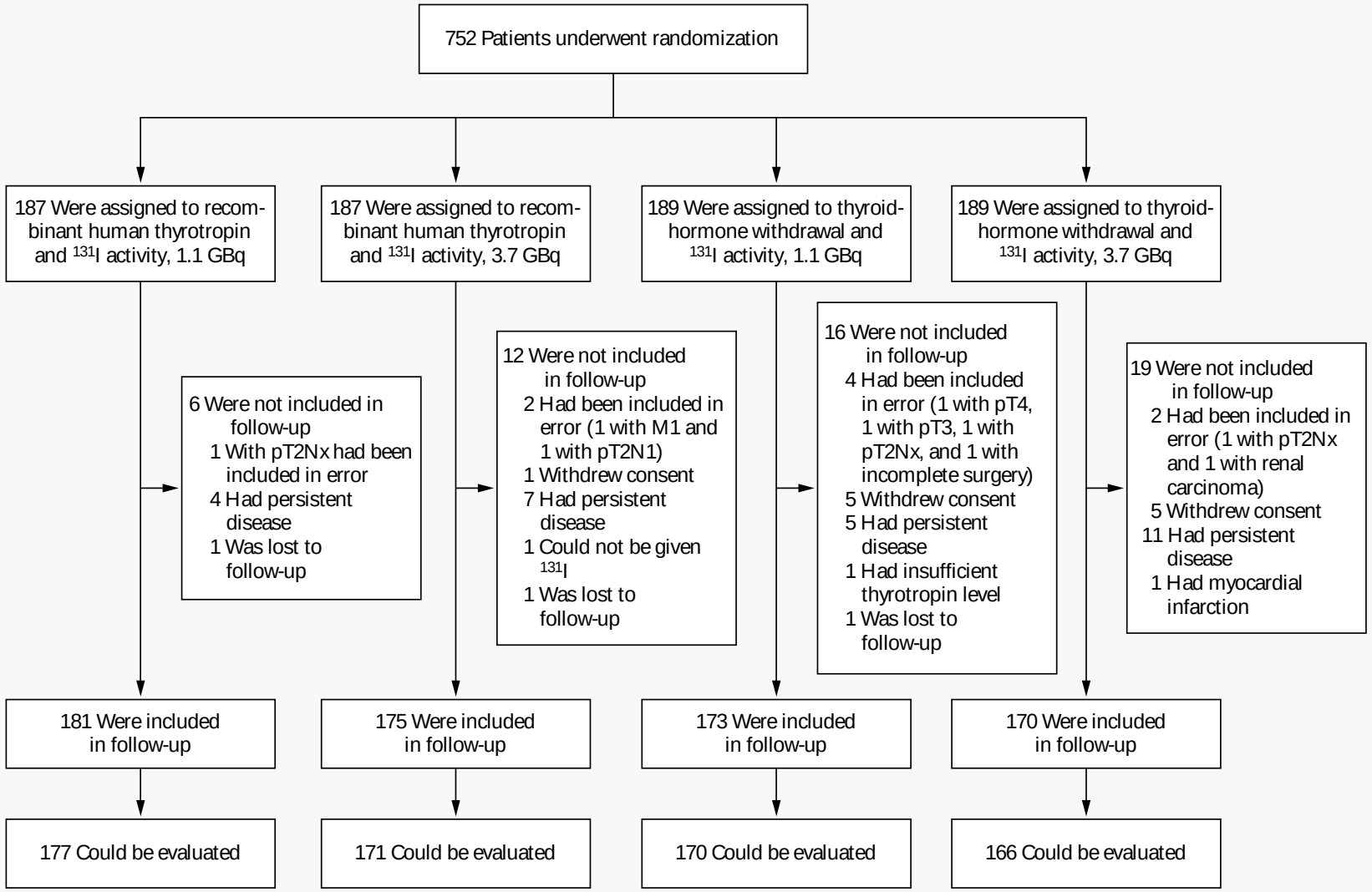

Figure 1. Randomization and Follow-up of the Study Patients.

The tumor–node–metastasis (TNM) stage noted was ascertained on pathological examination of a surgical specimen of the tumor (pT) and lymph node (N). Stage Nx indicates that the lymph nodes could not be evaluated; stage N0, that tumor cells were absent from regional lymph nodes; and stage N1, that tumor cells were present in regional lymph nodes. Fifteen patients could not be evaluated because not all diagnostic tests were performed.

Table 3. Follow-up Testing of Thyroid Ablation 6–10 Months after ^{131}I Administration in the 684 Patients Who Could Be Evaluated, According to Thyrotropin-Stimulation Method and ^{131}I Dose.

Characteristic	Recombinant Human Thyrotropin		Thyroid Hormone Withdrawal	
	1.1 GBq (N=177)	3.7 GBq (N=171)	1.1 GBq (N=170)	3.7 GBq (N=166)
Neck ultrasonography — no. (%)				
Normal	171 (97)	161 (94)	163 (96)	157 (95)
Suspicious	6 (3)	10 (6)	7 (4)	9 (5)
Cytologic test normal	1 (<1)	3 (2)	1 (<1)	3 (2)
Cytologic test abnormal	0	1 (<1)	0	2 (1)
Cytologic test not performed	5 (3)	6 (4)	6 (4)	4 (2)
Presence of antithyroglobulin antibody — no. (%)	10 (6)	4 (2)	10 (6)	8 (5)
Total-body scan normal	6 (3)	3 (2)	7 (4)	7 (4)
Total-body scan abnormal	0	0	1 (<1)	0
Total-body scan not performed*	4 (2)	1 (<1)	2 (1)	1 (<1)
Absence of antithyroglobulin antibody				
Local determination				
Thyroglobulin ≤1 ng/ml — no./total no. (%)	157/167 (94)	160/167 (96)	152/160 (95)	152/158 (96)
Central determination				
Thyroglobulin ≤1 ng/ml — no./total no. (%)	148/158 (94)	155/160 (97)	146/152 (96)	142/148 (96)
Thyroglobulin ≤1.4 ng/ml — no./total no. (%)	150/158 (95)	156/160 (98)	146/152 (96)	143/148 (97)
Missing data — no.	9	7	8	10
Thyroid ablation				
With local thyroglobulin determination — no. (%)				
Complete	160 (90)	159 (93)	156 (92)	156 (94)
Incomplete	17 (10)	12 (7)	14 (8)	10 (6)
With central thyroglobulin determination — no./total no. (%)†				
Complete	151/168 (90)	154/164 (94)	150/162 (93)	145/156 (93)
Incomplete	17/168 (10)	10/164 (6)	12/162 (7)	11/156 (7)