

# Die ATA-Leitlinien aus europäischer/österreichischer Sicht

Martha Hoffmann

JAMA | Original Investigation



# Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013

Hyeyeun Lim, PhD; Susan S. Devesa, PhD; Julie A. Sosa, MD; David Check, BS; Cari M. Kitahara, PhD, MHS

77 276 TC patients diagnosed during 1974-2013

2371 TC related deaths during 1994-2013

3,6% annual increase in incidence

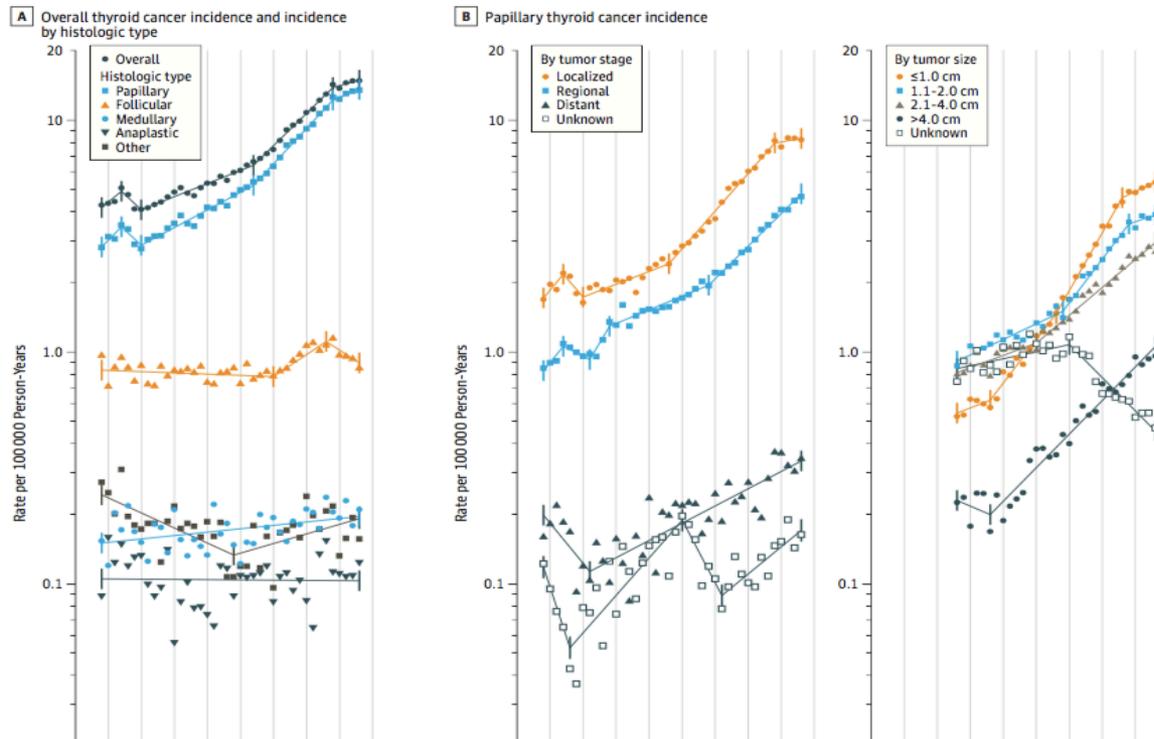
1,1% annual increase in mortality

RC

JAMA 2017;317(13):1338-1348

# 3,6% annual increase in incidence

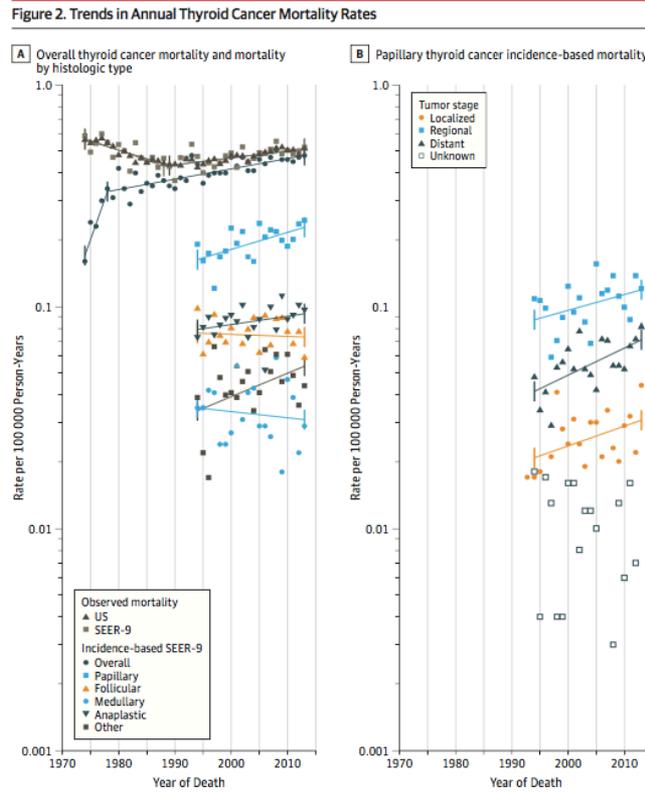
Figure 1. Trends in Annual Thyroid Cancer Incidence Rates



2,4% for advanced PTC

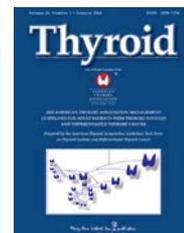
JAMA 2017;317(13):1338-1348

# 1,1% annual increase in mortality



2,9% for patients diagnosed with advanced PTC

JAMA 2017;317(13):1338-1348



2016 Jan;26(1):1-133

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

The American Thyroid Association Guidelines Task Force  
on Thyroid Nodules and Differentiated Thyroid Cancer

Bryan R. Haugen,<sup>1,\*</sup> Erik K. Alexander,<sup>2</sup> Keith C. Bible,<sup>3</sup> Gerard M. Doherty,<sup>4</sup> Susan J. Mandel,<sup>5</sup>  
Yuri E. Nikiforov,<sup>6</sup> Furio Pacini,<sup>7</sup> Gregory W. Randolph,<sup>8</sup> Anna M. Sawka,<sup>9</sup> Martin Schlumberger,<sup>10</sup>  
Kathryn G. Schuff,<sup>11</sup> Steven I. Sherman,<sup>12</sup> Julie Ann Sosa,<sup>13</sup> David L. Steward,<sup>14</sup>  
R. Michael Tuttle,<sup>15</sup> and Leonard Wartofsky<sup>16</sup>

# European perspective on the 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer. Proceedings of an interactive international symposium.



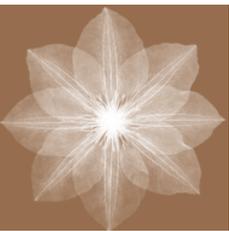
Eur J Nucl Med Mol Imaging (2016) 43:1001–1005  
DOI 10.1007/s00259-016-3327-3



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**

Frederik A. Verburg<sup>1</sup> · Cumali Aktolun<sup>2</sup> · Arturo Chiti<sup>3,4</sup> · Savvas Frangos<sup>5</sup> · Luca Giovannella<sup>6</sup> · Martha Hoffmann<sup>7</sup> · Ioannis Iakovou<sup>8</sup> · Jasna Mihailovic<sup>9</sup> · Bernd J. Krause<sup>10</sup> · Werner Langsteiger<sup>11</sup> · Markus Luster<sup>12</sup> · on behalf of the EANM and the EANM Thyroid Committee



# Thyroid nodules

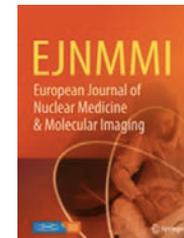
## ■ RECOMMENDATION 2

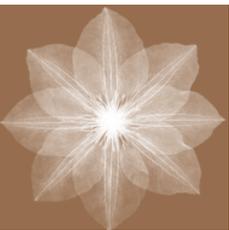
(B) If the serum TSH is subnormal, a radionuclide (preferably  $^{123}\text{I}$ ) thyroid scan should be performed.

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

(C) If the serum TSH is normal or elevated, a radionuclide scan should not be performed as the initial imaging evaluation.

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



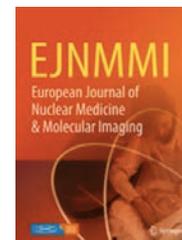


# Sonography

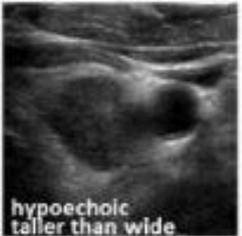
## ■ RECOMMENDATION 6

Thyroid sonography **with survey of the cervical lymph nodes** should be performed in all patients with known or suspected thyroid nodules.

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



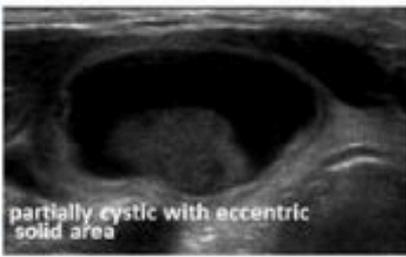
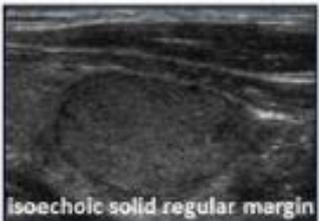
High  
Suspicion  
70-90%



Intermediate  
Suspicion  
10-20%



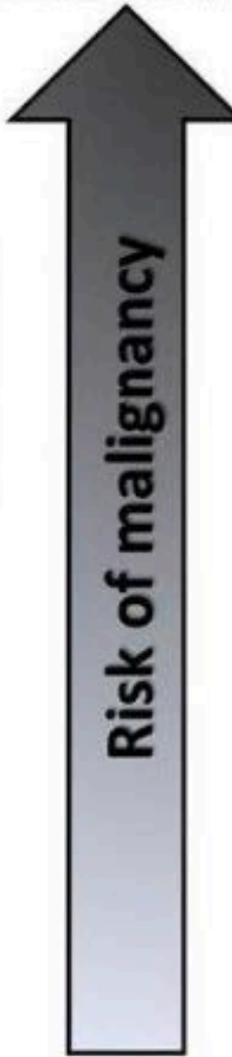
Low  
Suspicion  
5-10%

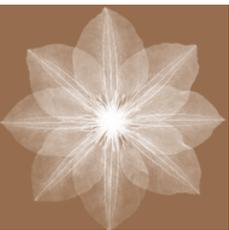


Very low  
Suspicion  
<3%



Benign  
<1%





**FNA**

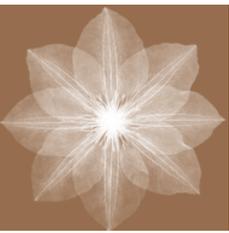


■ **RECOMMENDATION 8**

<b>Sonographic Pattern</b>	<b>Estimated malignancy risk</b>	<b>Biopsy suggested</b>
<b>High suspicion</b>	<b>&gt;70-90%</b>	<b><math>\geq 1</math> cm</b>
<b>Intermediate suspicion</b>	<b>10-20%</b>	<b><math>\geq 1</math> cm</b>
<b>Low suspicion</b>	<b>5-10%</b>	<b><math>\geq 1.5</math> cm</b>
<b>Very low suspicion</b>	<b>&lt; 3%</b>	<b><math>\geq 2</math> cm*</b>
<b>Benign</b>	<b>&lt; 1%</b>	<b>No biopsy</b>

**\*Biopsy considered, surveillance as reasonable alternative**

**FNA is not recommended for nodules that do not meet the above criteria, including **all nodules < 1 cm****



# Cytology



## ■ RECOMMENDATION 9

Thyroid nodule FNA cytology should be reported using diagnostic groups outlined in the **Bethesda System** for Reporting Thyroid Cytopathology.

Diagnostic Category	Risk of Malignancy (%)
Non-diagnostic or Unsatisfactory	
Benign	0-3%
<u>Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance (AUS/FLUS)</u>	<u>~ 5-15%</u>
<u>Follicular Neoplasm or Suspicious for a Follicular Neoplasm (Specify if Hurthle type or Oncocytic)</u>	<u>15-30%</u>
Suspicious for Malignancy	60-75%
Malignant	97-99%

**Strong recommendation, Moderate-quality evidence**



## Surgery for malignancy

### ■ RECOMMENDATION 35

(A) Near-total or **total thyroidectomy** for patients with **thyroid cancer >4 cm**, or with gross extrathyroidal extension (**clinical T4**), or clinically apparent metastatic disease to nodes (**clinical N1**) or distant sites (**clinical M1**),

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

(B) ...Thyroid **lobectomy** alone **may** be sufficient initial treatment for **low-risk carcinomas (>1 cm and <4 cm** without extrathyroidal extension, and without clinical evidence of any lymph node metastases (**cN0**)) ; however, the treatment team may choose total thyroidectomy to enable RAI therapy or to enhance follow-up based upon disease features and/or patient preferences.

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



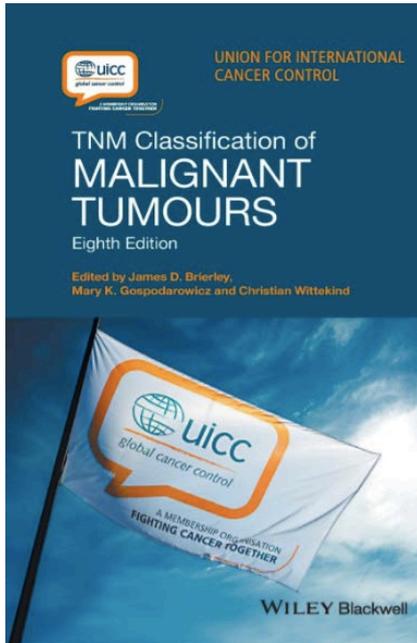
(C) Thyroid **lobectomy** alone **is** sufficient treatment **for small, unifocal**, intrathyroidal carcinomas in the absence of prior head and neck

# Radioiodine

## ■ RECOMMENDATION 51

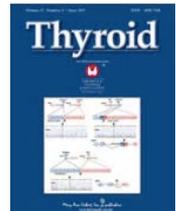
ATA recurrence risk Staging	Description	Grade of Recommendation	Quality of Evidence	RAI indicated?
<b>microPTC</b>	Tumor size ≤1cm (unifocal)	<b>Strong</b>	<b>Moderate</b>	No
	(multifocal)	<b>Weak</b>	<b>Low</b>	
<b>low risk</b>	Tumor size > 1 - < 4 cm	<b>Weak</b>	<b>Low</b>	Not routine
<b>high risk</b>	gross extrathy. extension, large Lnn , R1	<b>Strong</b>	<b>Moderate</b>	Routinely recommended
<b>intermediate risk</b>	Microscopic extra thy. extension, aggressive histology	<b>Weak</b>	<b>Low</b>	Should be considered





## The Updated AJCC/TNM Staging System for Differentiated and Anaplastic Thyroid Cancer (8<sup>th</sup> edition): What changed and why?

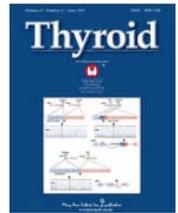
R Michael Tuttle<sup>1</sup>, Bryan Haugen<sup>2</sup>, and Nancy D. Perrier<sup>3</sup>



Thyroid. 2017 Jun;27(6):751-756.

## The Updated AJCC/TNM Staging System for Differentiated and Anaplastic Thyroid Cancer

(8<sup>th</sup> edition): What changed and why?



- Minor extrathyroidal extension detected only on histological examination was removed from the definition of T3 disease and therefore has no impact on either T category or overall stage.
- T3a is a new category for tumors > 4 cm confined to the thyroid gland
- T3b is a new category for tumors of any size demonstrating gross extrathyroidal extension into strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) (AJCC Cancer Staging Manual, 8th ed. (2017):751-756.



## RAI activity

### ■ RECOMMENDATION 55 **Ablation**

A low administered activity of approximately **30 mCi (1,1 GBq)** is generally favored over higher administered activities.

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

Higher administered activities may need to be considered for patients receiving less than a total or near-total thyroidectomy in which a larger remnant is suspected or in which adjuvant therapy is intended.

**(Weak recommendation, Low-quality evidence)**

### ■ RECOMMENDATION 56 **Adjuvant therapy**

Administered activities above those used for remnant ablation **up to 150 mCi (5,5 GBq)** are generally recommended (in absence of known distant metastases).

**(Weak recommendation, Low-quality evidence)**



# rhTSH

## ■ RECOMMENDATION 54

(A) In patients with ATA low-risk and ATA intermediate-risk DTC **without extensive lymph node involvement** rhTSH stimulation is an **acceptable alternative**, based on evidence of superior short-term quality of life, noninferiority of remnant ablation efficacy, and multiple consistent observations suggesting no significant difference in long-term outcomes.

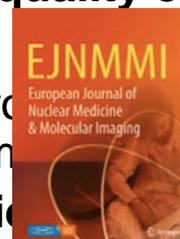
**(Strong recommendation, Moderate-quality evidence)**

(B) In patients with ATA intermediate-risk DTC who have **extensive lymph node disease** (multiple clinically involved LN) in the absence of distant metastases, preparation with rhTSH stimulation **may be considered as an alternative** prior to adjuvant RAI treatment.

**(Weak recommendation, Low-quality evidence)**

(C) In patients with ATA **high-risk** DTC more controlled data from randomized controlled studies are needed before rhTSH preparation can be recommended.

**(No recommendation, Insufficient evidence)**



(D) In patients with DTC of any risk level with significant **comorbidity** that may preclude thyroid hormone withdrawal prior to iodine RAI administration, rhTSH preparation should be considered.

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



# ATA Dynamic Risk Stratification

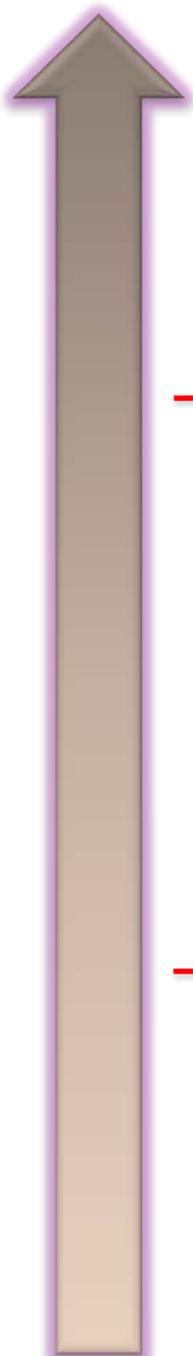
= Reclassification according to response to therapy

THYROID  
Volume 20, Number 12, 2010  
© Mary Ann Liebert, Inc.  
DOI: 10.1089/thy.2010.0178

THYROID CANCER AND NODULES

Estimating Risk of Recurrence in Differentiated  
Thyroid Cancer After Total Thyroidectomy and Radioactive  
Iodine Remnant Ablation: Using Response to Therapy  
Variables to Modify the Initial Risk Estimates Predicted  
by the New American Thyroid Association Staging System

R. Michael Tuttle,<sup>1</sup> Hernan Tala,<sup>1</sup> Jatin Shah,<sup>2</sup> Rebecca Leboeuf,<sup>1</sup> Ronald Ghossein,<sup>3</sup>  
Mithat Gonen,<sup>4</sup> Matvey Brokhin,<sup>1</sup> Gal Omry,<sup>1</sup> James A. Fagin,<sup>1</sup> and Ashok Shaha<sup>2</sup>



### High risk

*Gross extrathyroidal extension,  
incomplete tumor resection  
or lymph node >3 cm*

### Intermediate risk

*Agressive histology, minor extrathyroidal  
extension, vascular invasion  
or >5 involved lymph nodes (0.2-3 cm)*

### Low risk

*Intrathyroidal DTC,  
≤5 LN micrometastases (<0.2 cm)*

FTC, extensive vascular invasion (~30-55%)

pT4a gross ETE (~30-40%)

>30%

pN1 with extranodal extension, >3LN involved (~40%)

PTC, >1cm, TERT mutated ± BRAF mutated\* (>40%)

pN1, any LN >3cm (~30%)

PTC, extrathyroidal, BRAF mutated\* (~10-40%)

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PTC, vascular invasion (~15-30%)

Clinical N1 (~20%)

5%-30%

pN1, >5 LN involved (~20%)

Intrathyroidal PTC, <4cm, BRAF mutated\* (~10%)

pT3 minor ETE (~3-8%)

pN1, all LN <0.2 cm (~5%)

pN1, ≤5 LN involved (~5%)

Intrathyroidal PTC, 2-4cm (~5%)

Multifocal PMC (~4-6%)

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pN1 without extranodal extension, ≤3LN involved (~2%)

Minimally invasive FTC (~2-3%)

<5%

Intrathyroidal, BRAF wild type\* (~1-2%)

Intrathyroidal, unifocal PMC, BRAF mutated\* (~1-2%)

Intrathyroidal, encapsulated, FV-PTC (~1-2%)

Unifocal PMC (~1-2%)



# ATA Dynamic Risk Stratification

## **Excellent response =**

no clinical, biochemical, or structural evidence of disease

## **Biochemical incomplete response =**

abnormal Tg or rising anti-Tg antibody levels in the absence of localizable disease.

## **Structural incomplete response =**

persistent or newly identified loco-regional disease or distant metastases

## **Indeterminate response =**

nonspecific biochemical or structural findings that cannot be confidently classified as either benign or malignant. This includes patients with stable or declining anti-Tg antibody levels without definitive structural evidence of disease.



# TSH - Suppression

Increasing risk of TSH suppression	Excellent	Indeterminate	Biochemical Incomplete**	Structural incomplete
No known risk	No Suppression. TSH target 0.5*-2.0 mU/L	Mild Suppression.	Moderate or Complete Suppression. TSH target <0.1 mU/L	
Menopause				
Tachycardia				
Osteopenia		TSH target 0.1-0.5*mU/L		
Age > 60				
Osteoporosis				
Atrial fibrillation				

\* - 0.5 mU/L represents the lower limit of the reference range for the TSH assay which can be 0.3-0.5 mU/L depending on the specific assay

\*\* - TSH target for patients with a biochemical incomplete response can be quite different based on original ATA risk, Tg level, Tg trend over time and risk of TSH suppression



No suppression. TSH target 0.5\*-2.0 mU/L



Mild suppression. TSH target 0.1-0.5\* mU/L



Moderate or Complete suppression. TSH target <0.1 mU/L



# Follow Up (Stimulation Test)



## ■ RECOMMENDATION 63

(A) In ATA low-risk and intermediate-risk patients who have had remnant ablation or adjuvant therapy and negative cervical US, serum Tg should be measured at 6–18 months on thyroxine therapy with a sensitive Tg assay ( $<0.2$  ng/mL) or after TSH stimulation.

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

(B) Repeat TSH-stimulated Tg testing is not recommended for low- and intermediate-risk patients with an excellent response to therapy.

**(Weak recommendation, Low-quality evidence)**

(C) Subsequent TSH-stimulated Tg testing may be considered in patients with an indeterminate, biochemical incomplete, or structural incomplete response following either additional therapies or a spontaneous decline in Tg values on thyroid hormone therapy over time.

**(Weak recommendation, Low-quality evidence)**



## Follow Up (WBS )

### ■ RECOMMENDATION 66

After the first posttreatment WBS following RAI remnant ablation or adjuvant therapy, **low-risk and intermediate-risk patients** with an undetectable Tg on thyroid hormone with negative anti-Tg antibodies and a negative US **do not require routine diagnostic WBS** during follow-up.

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

### ■ RECOMMENDATION 67

(A) Diagnostic WBS, either following thyroid hormone withdrawal or rhTSH, 6–12 months after adjuvant RAI therapy **can be useful** in the follow-up of patients with **high or intermediate risk** of persistence and should be done with  $^{123}\text{I}$  or low activity  $^{131}\text{I}$ .

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

(B) **SPECT/CT** imaging is preferred over planar imaging in patients with uptake on WBS to better anatomically localize the RAI uptake.

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

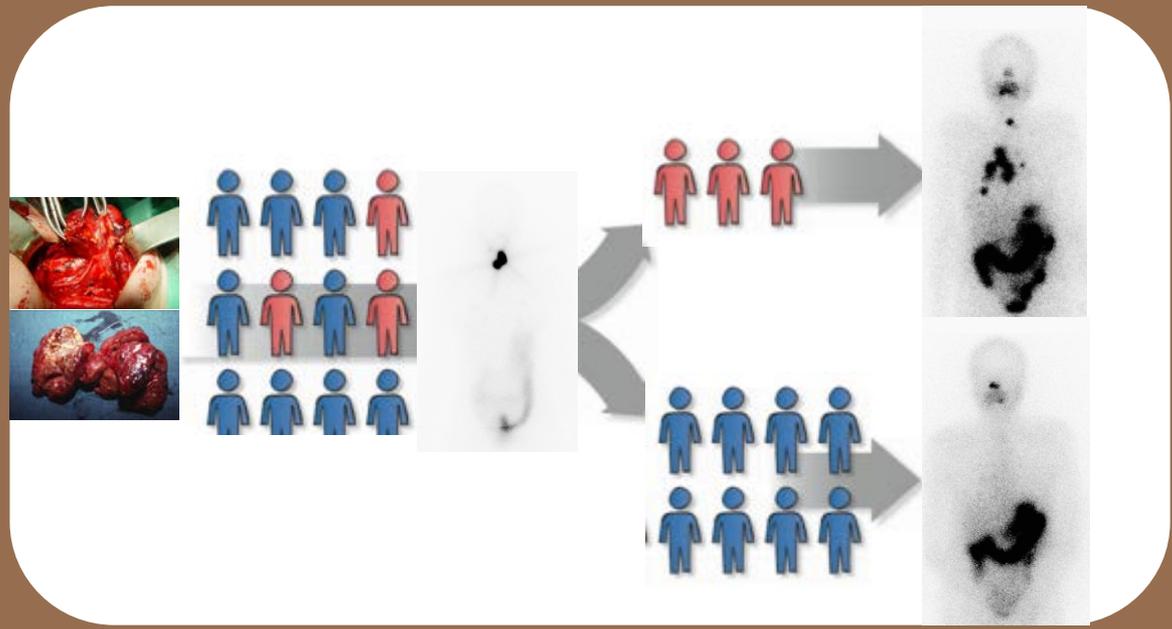
## 48jährige Patientin.

Struma uninodosa. 26mm Knoten im rechten SD-Lappen  
echoarm, hypervaskularisiert, ...

Zytologie Bethesda IV foll. Neopl.

OP: pap. SDCa pT2 (2017)





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Vielen Dank für Ihre Aufmerksamkeit

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