

# Thyroid Cancer: Resection, Dissection, Surveillance and Recurrence

---

Cord Sturgeon, MD

Associate Professor of Surgery  
Northwestern University Feinberg School of Medicine  
Director of Endocrine Surgery  
Chicago, Illinois

Surgical Oncology Network Fall Update  
Saturday November 2, 2013. Vancouver, BC.

# Disclosures

---

- No financial interests to declare



# Global treatment strategy

---

**Papillary thyroid cancer**

**Follicular thyroid cancer**

**Hürthle cell cancer**

1. Total thyroidectomy with appropriate lymph node clearance
2. Radioiodine ablation (in selected patients)
3. TSH suppression (giving slightly more thyroid hormone than is necessary)
4. Surveillance



# Global treatment strategy

---

## Medullary thyroid cancer

1. Total thyroidectomy with appropriate lymph node clearance
2. Thyroid hormone replacement
3. Surveillance



# Definition of Cure\*

---

- 1) No clinical evidence of tumor
- 2) No imaging evidence of tumor (no uptake outside the thyroid bed on the initial posttreatment WBS, or, if uptake outside the thyroid bed had been present, no imaging evidence of tumor on a recent diagnostic scan and neck US)
- 3) Undetectable serum Tg levels during TSH suppression and stimulation in the absence of interfering antibodies.

\* 2009 ATA



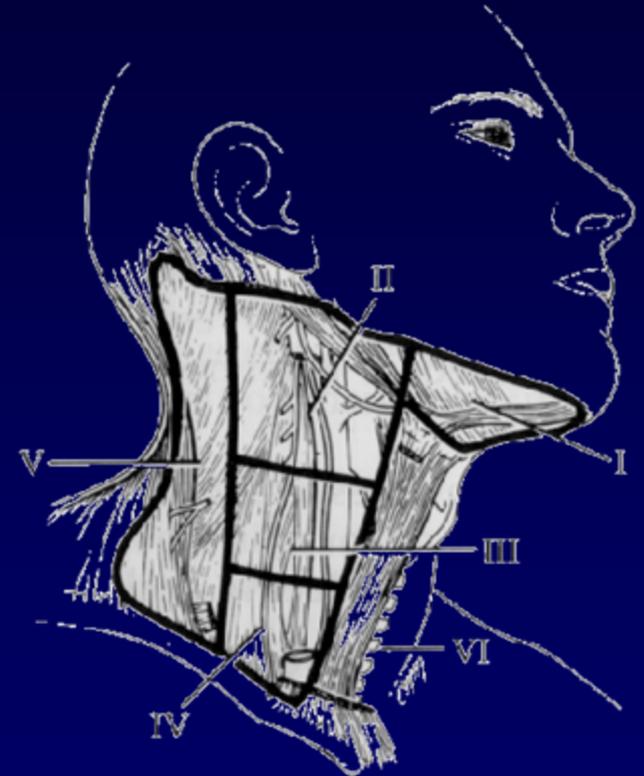
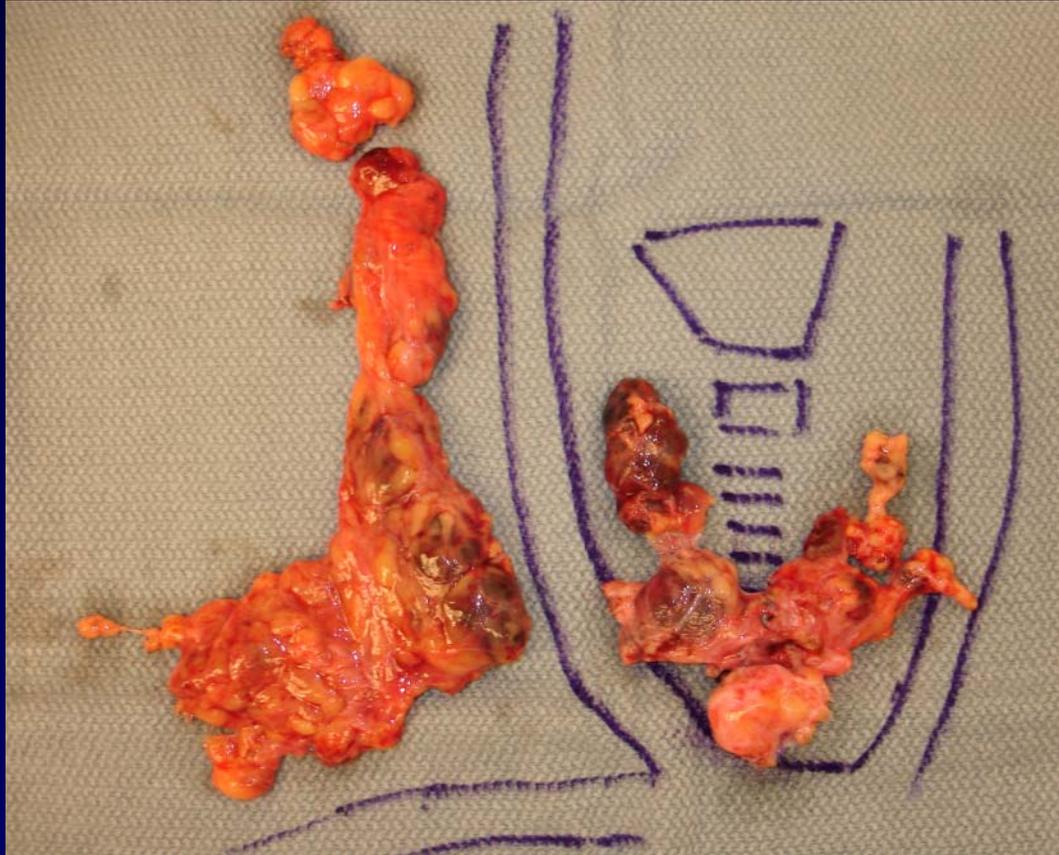
# What Are the Goals of Initial Surgery For Thyroid Cancer?

- Removal of the primary tumor and any extrathyroidal disease
- Minimize disease recurrence and metastatic spread
- Minimize treatment and disease related morbidity
- Permit accurate staging and long-term surveillance
- Facilitate postoperative treatment (e.g. with radioiodine for PTC, FTC, HCC)

# How do you manage lymph nodes in papillary thyroid cancer?

- The preoperative confirmation of metastatic disease in a lymph node basin should lead to a planned formal compartmental lymphadenectomy (usually modified radical neck dissection and/or central neck dissection).
- The intraoperative detection of metastatic disease in a lymph node basin triggers formal compartmental clearance of that basin.
- No cherry picking!

# Formal nodal dissection



# How do you manage lymph nodes in medullary thyroid cancer?

- Lymph node metastases from MTC are common in adults and are a poor prognostic factor.
- In adult MTC, nodal metastases are present in more than 75% of cases and in 30% of tumors smaller than 1 cm.
- Central neck dissection almost always performed.
- Modified radical neck dissection for clinically positive
- No cherry picking!



# Recurrent thyroid cancer

---

How can the cancer come back?

- Probably represents persistence
- A small amount of cells escaped the other treatment(s).

Three types of recurrence

- **Local** (remaining thyroid or nearby structures)
- **Regional** (lymph nodes)
- **Distant** (outside of the neck)

# Survival from thyroid cancer

---

What is the mortality rate of thyroid cancer?

- Papillary <2% at 5 years. <2% at 10 years\*
- Follicular 10% at 5 years. 15% at 10 years\*\*
- Medullary 20% at 5 years. 25% at 10 years\*\*

\*Bilimoria et al. *Ann Surg* 2007;246: 375–384

\*\*Hundahl et al. *Cancer* 1998;83:2638–48

# Recurrent thyroid cancer

---

## How often does thyroid cancer come back?

- **Papillary** 5% at 5 years<sup>1</sup> 10% at 10 years<sup>1</sup> 15% at 25 years<sup>2</sup>
- **Follicular** 18% at 10 years<sup>3</sup> 21% at 20 years<sup>3</sup>
- **Medullary** >50% at 10 years<sup>4</sup>

1. Bilimoria *et al.* *Ann Surg* 2007; 246: 375–384 – 10 year survival >98%

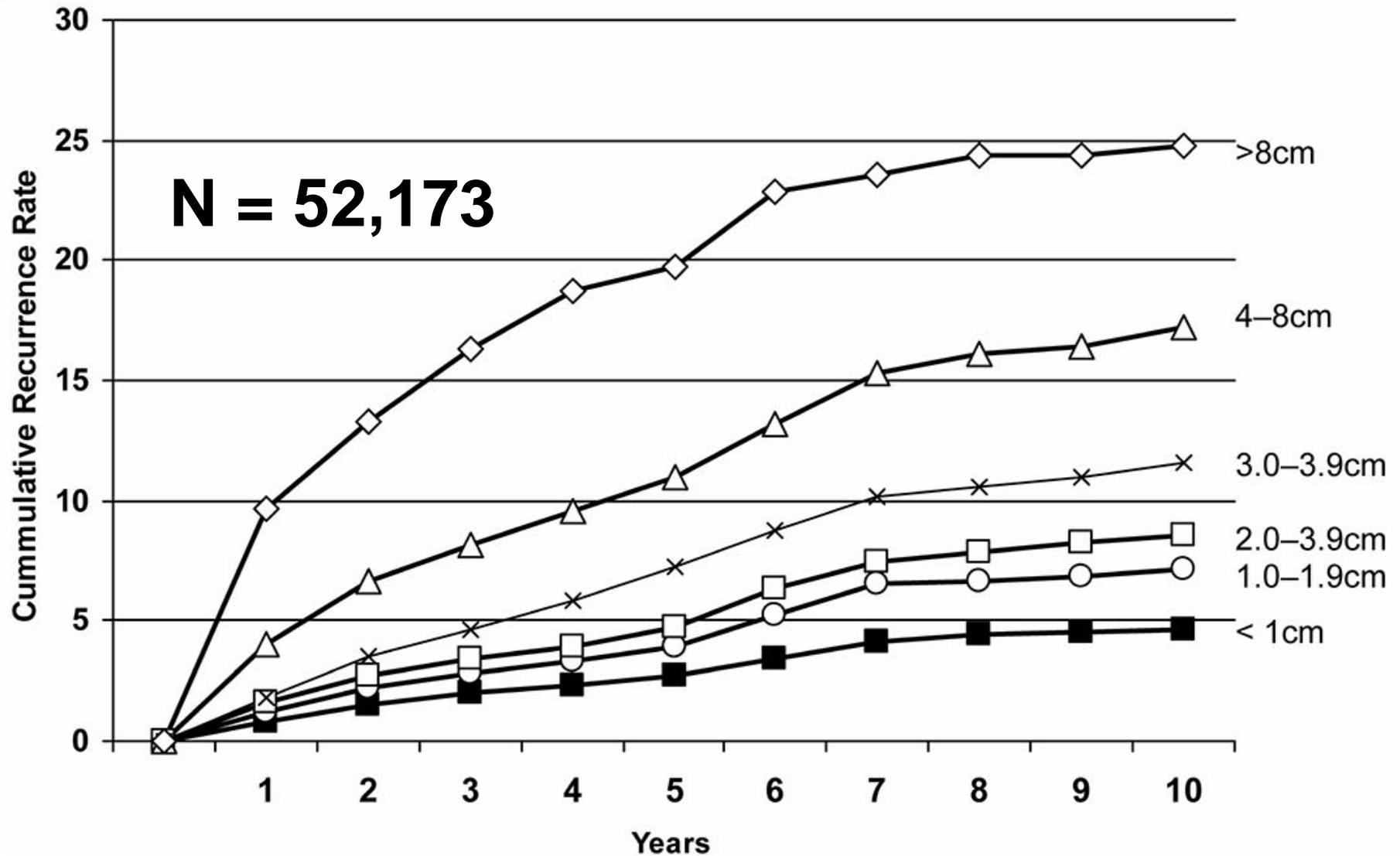
2. Hay *et al.* *World J. Surg.* 2002; 26, 879–885,– 25 year survival 95%

3. Mazzaferri and Jhiang. *Am. J. Med.* 1994; 97, 418-428

4. Dottorini *et al.* *Cancer* 1996; 77:1556-65.

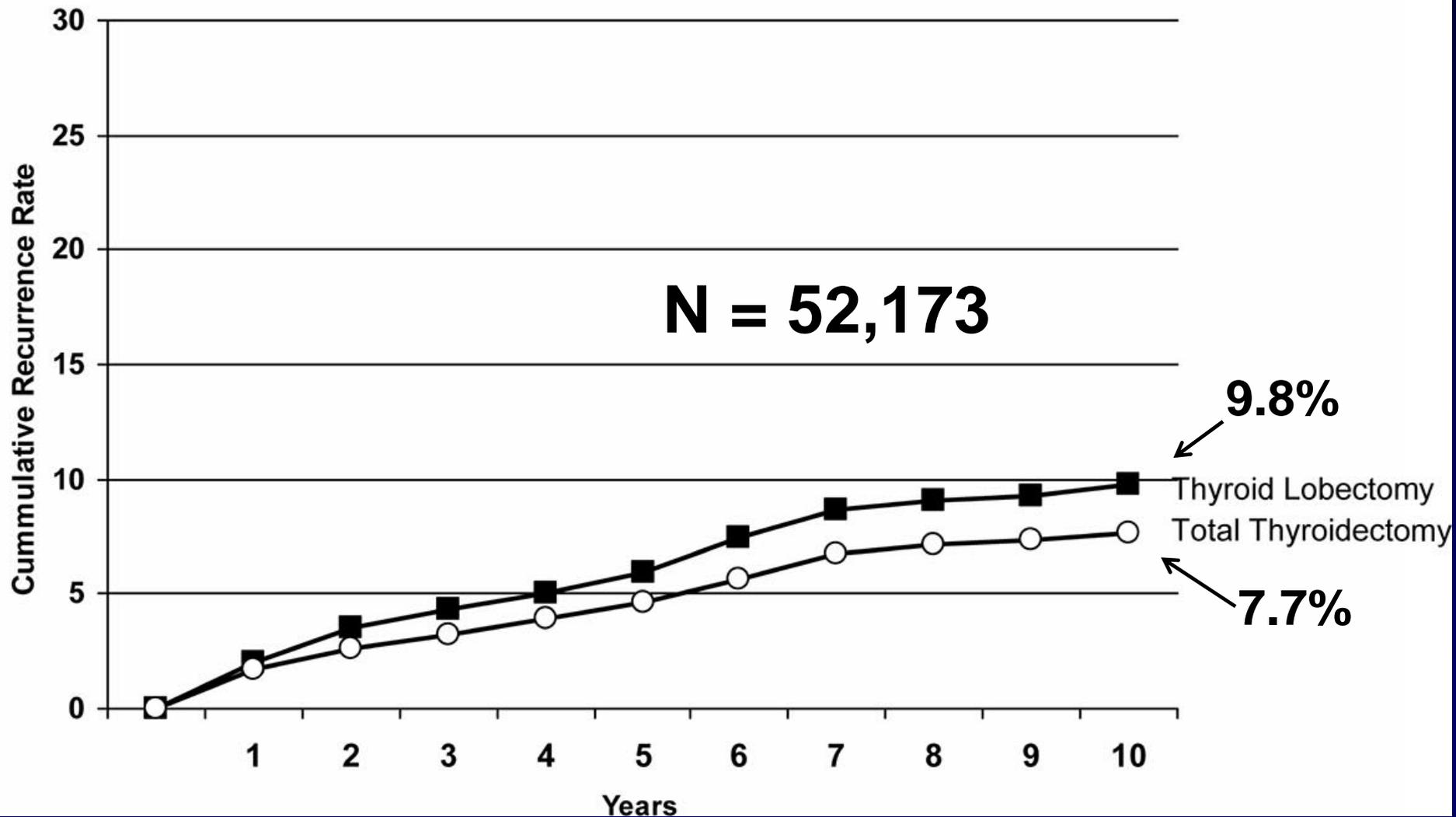
# Recurrence of PTC based on tumor size

A.

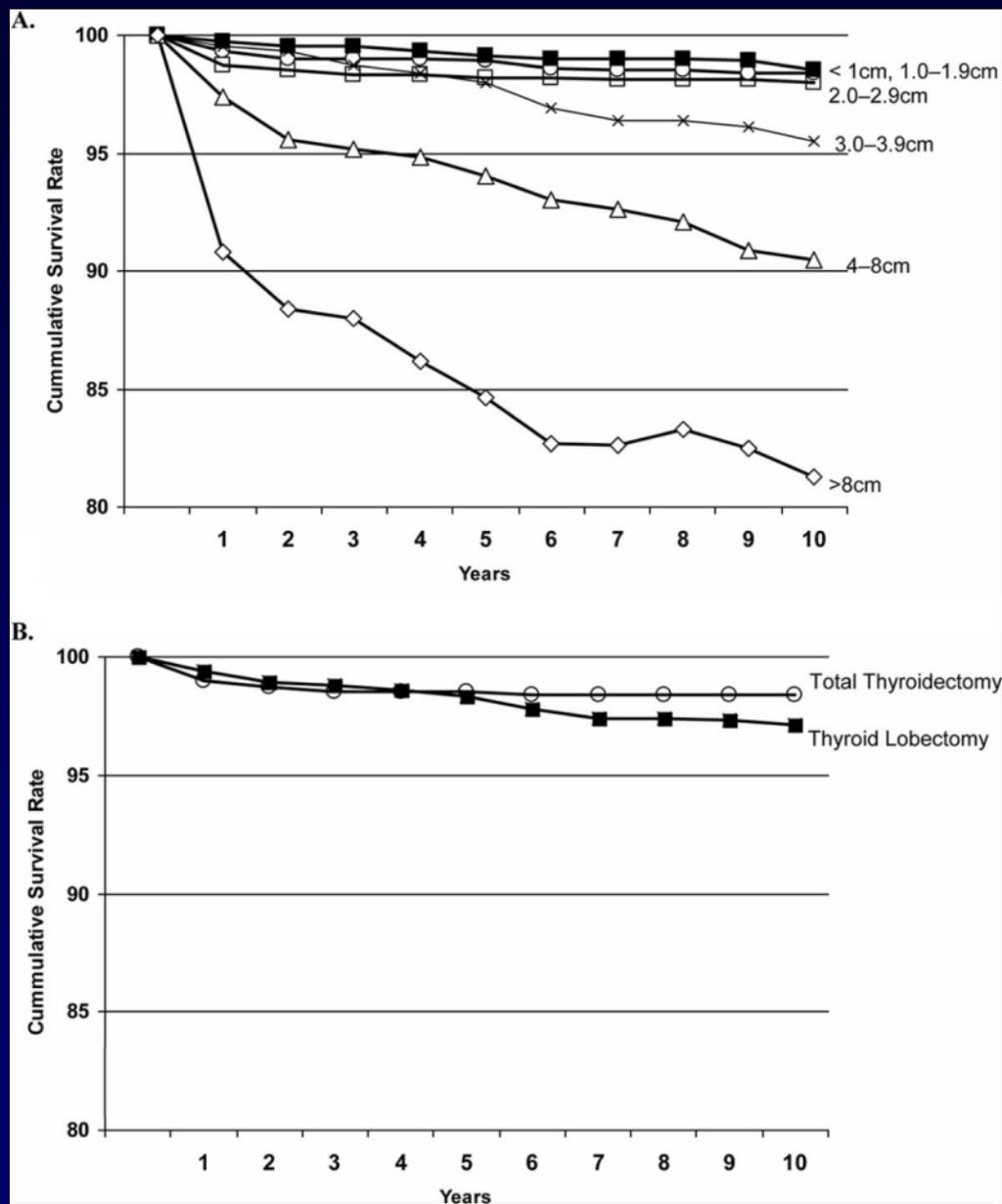


# Recurrence of PTC based on surgery

B.



# Survival from PTC based on tumor size and surgery



# Recurrent thyroid cancer

---

Why is the recurrence rate so much higher than the mortality rate?

- Metastases discovered during follow-up are probably actually persistent disease that survived the initial treatment.
- Because of detection and treatment.

Early detection and treatment of recurrence *probably* improves survival.

# Recurrent thyroid cancer

---

## What are the risk factors for PTC recurrence?

- Tumor size (larger size)
- Local tumor invasion
- Tumor subtype (tall cell, columnar, diffuse sclerosing)
- Extent of initial surgery (less-extensive)\*<sup>1</sup>
- TSH (non-suppressed)<sup>1,2</sup>
- Radioactive iodine ablation (none)\*<sup>1</sup>
- Clinically positive nodal metastases (esp lateral neck)<sup>3</sup>

\*Probably does not apply to small, low risk cancers.

<sup>1</sup>Jonklaas et al. 2006. Thyroid 16:1229–1242.

<sup>2</sup>Pujol et al. 1996. J Clin Endocrinol Metab 81:4318–4323.

<sup>3</sup>Randolph et al. 2012. Thyroid. Aug 10.

# Metastatic thyroid cancer

---

- Lymph nodes (PTC, FTC, HCC, MTC)
- Local tissues (all)
- Lung (PTC, FTC, HCC)
- Bone (PTC, FTC, HCC)
- Brain (PTC, FTC, HCC)
- Liver (MTC)

# Lymph nodes in PTC

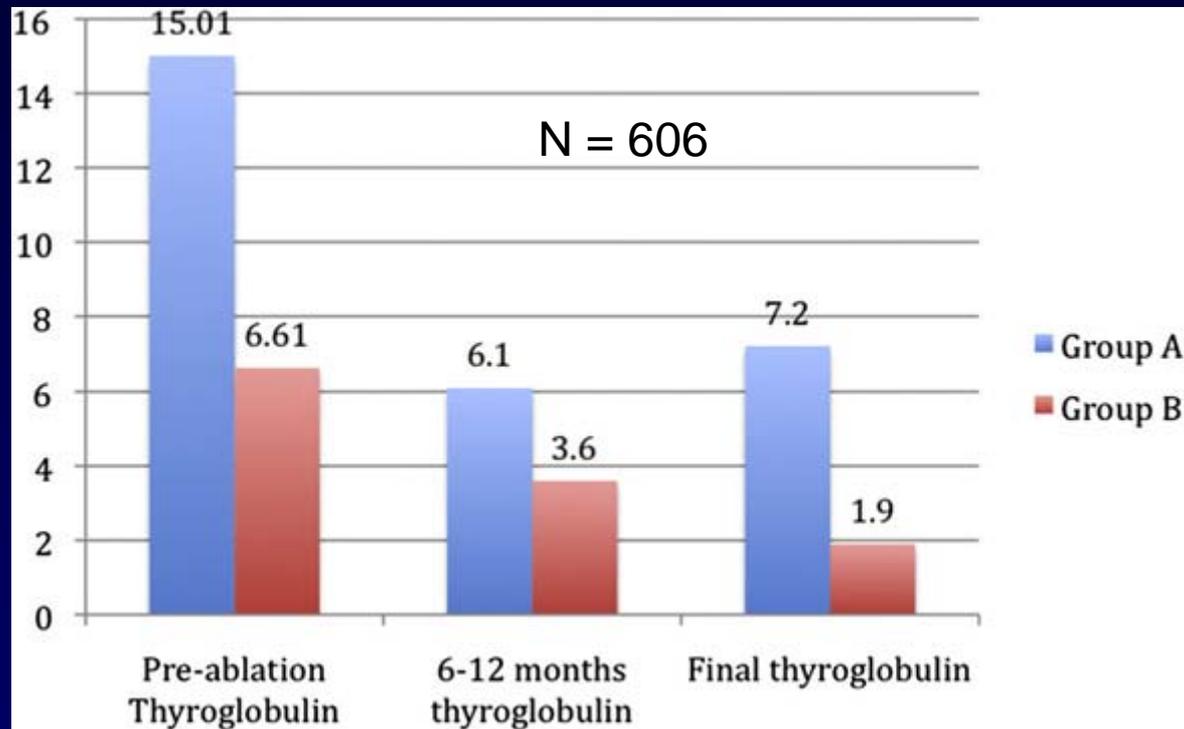
---

- Cervical lymph node metastases are found in approximately two-thirds (up to 80%) of PTC patients if they undergo central neck dissection at the time of their diagnosis.
- Metastatic lymph nodes identified by prophylactic neck dissection are usually quite small (3-5mm) and are few in number (3-5 positive of 10-15 nodes).
- When using the size of the largest metastatic lymph node, a spectrum of recurrence risk is seen ranging from approximately 4% in patients with microscopic nodal disease to 34% in patients with large bulky nodes
- Large nodal metastases, a large number of positive nodes, and the presence of extranodal extension are risk factors for recurrence.**

## Risk of recurrence based on characteristics of cervical lymph node metastases

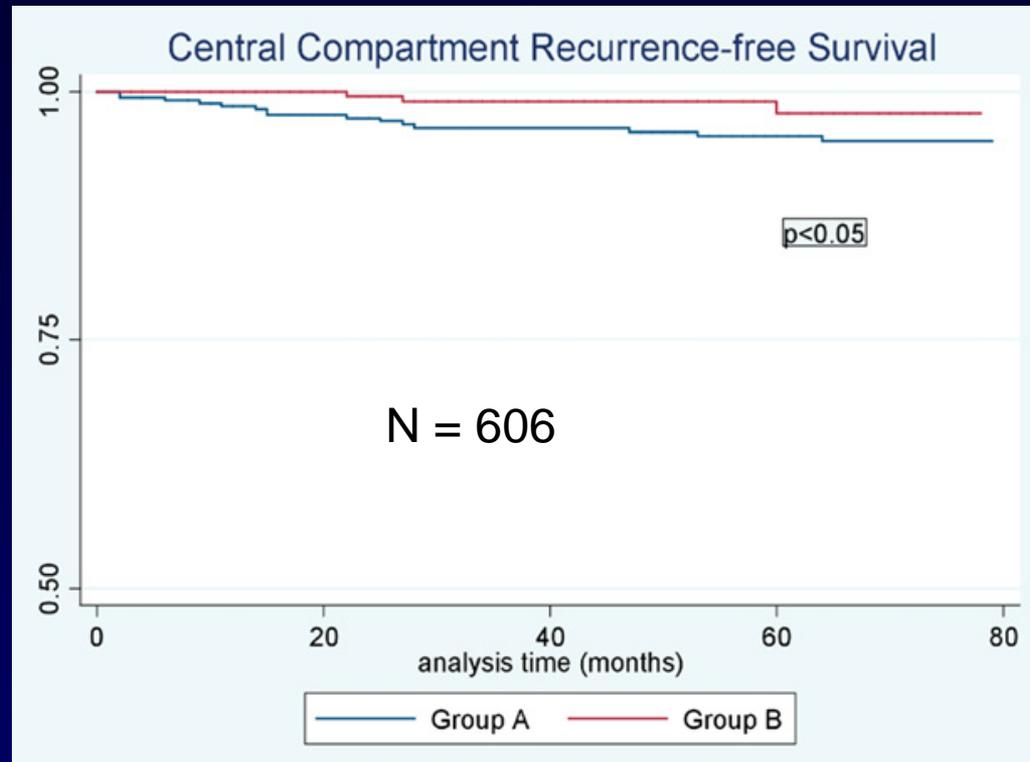
Pathology	Specific Characteristic	Median	Range	Source
<b>Pathological N1</b>	<b>Clinical N0</b>	2%	0-9%	Wada 2008, Bardet 2008, Yamashita 2009, Cranshaw 2008
	<b>&lt; 5 metastatic nodes</b>	4%	3-8%	Leboulleux 2005, Bardet 2008, Sugitani 2004
	<b>&gt; 5 metastatic nodes</b>	19%	7-21%	Leboulleux 2005, Sugitani 2004
	<b>Clinical N1</b>	22%	10-42%	Ito 2004, Cranshaw 2008, Ito 2009, Wada 2003, Bardet 2008, Ito 2006, Ito 2005, Wada 2008, Moreno 2011, Wada 2008
	<b>Clinical N1 with extranodal extension</b>	24%	15-32%	Leboulleux 2005, Yamashita 2009

# Prophylactic CND in PTC



Popadich A, Levin O, Lee JC, Smooke-Praw S, Ro K, Fazel M, Arora A, Tolley NS, Palazzo F, Learoyd DL, et al. A multicenter cohort study of total thyroidectomy and routine central lymph node dissection for cN0 papillary thyroid cancer. *Surgery* 2011;150:1048-57.

The rate of central neck reoperation in the group A patients compared with group B patients was 6.1% vs 1.5%;  $P = .004$ . The number of procedures required to prevent one reoperation was 20.



Popadich A, Levin O, Lee JC, Smooke-Praw S, Ro K, Fazel M, Arora A, Tolley NS, Palazzo F, Learoyd DL, et al. A multicenter cohort study of total thyroidectomy and routine central lymph node dissection for cN0 papillary thyroid cancer. *Surgery* 2011;150:1048-57.

# Risks of CND

Group A = No CND. Group B = Unilateral CND. Group C = Bilateral CND

**Table 1.** Incidence of Transient and Permanent RLNP and Transient and Permanent Hypoparathyroidism (%).

Group	A	B	C	P Value*
Transient RLNP	3.6	3.9	5.5	0.40 (NS)
Permanent RLNP	1.0	0.5	2.3	0.10 (NS)
Transient hypoparathyroidism	28	36	52	See below
Permanent hypoparathyroidism	6	7	16	See below

\* NS denotes not significant.

Giordano D, Valcavi R, Thompson GB, Pedroni C, Renna L, Gradoni P, Barbieri V. Complications of central neck dissection in patients with papillary thyroid carcinoma: results of a study on 1087 patients and review of the literature. *Thyroid* 2012;22:911-7.

# Recurrent thyroid cancer

---

## How can you screen for thyroid cancer recurrence?

- Physical exam
- Neck ultrasound and other imaging (CT, MRI)
- Blood tests (TSH, TG, anti-TG\*, calcitonin, CEA)
- Radioiodine scans
- PET scans?

\*10% of the population and 25% of differentiated thyroid cancer patients have anti-TG antibodies

## SURVEILLANCE AND MAINTENANCE

- Physical examination, TSH and Tg measurement  
+ antithyroglobulin antibodies at 6 and 12 mo, then annually if disease-free
- Periodic neck ultrasound<sup>n</sup>
- Consider TSH stimulated Tg measurement in patients previously treated with RAI and with negative TSH-suppressed Tg and anti-thyroglobulin antibodies<sup>o</sup>
- Consider TSH-stimulated radioiodine imaging in high-risk patients, patients with previous RAI avid metastases, or patients with abnormal Tg levels (either TSH-suppressed or TSH-stimulated), stable or rising antithyroglobulin antibodies, or abnormal ultrasound during surveillance
- In iodine responsive tumors, if detectable Tg or distant metastases or soft tissue invasion on initial staging, radioiodine imaging every 12-24 mo until no clinically significant response is seen to RAI treatment (either withdrawal of thyroid hormone or rhTSH)<sup>p</sup>
- If <sup>131</sup>I imaging negative and stimulated Tg > 2-5 ng/mL, consider additional nonradioiodine imaging (eg, central and lateral neck compartments ultrasound, neck CT, chest CT, FDG-PET/CT)
- Patients treated with <sup>131</sup>I ablation, with a negative ultrasound, stimulated Tg < 2ng/mL (with negative Tg antibodies), and negative RAI imaging (if performed) may be followed by unstimulated thyroglobulin annually and by periodic neck ultrasound. TSH-stimulated testing, or other imaging as clinically appropriate, may be considered if clinical suggestion of recurrent disease.

<sup>9</sup>See Principles of TSH Suppression (THYR-A).

<sup>1</sup>The administered activity of RAI therapy should be adjusted for pediatric patients.

<sup>n</sup>A subgroup of low risk patients may only require an ultrasound if there is a reasonable suspicion for recurrence.

<sup>o</sup>In selected patients who may be at higher risk for residual/recurrent disease (eg, N1 patients), obtain a stimulated Tg and consider concomitant diagnostic RAI imaging. With a positive stimulated Tg, concomitant RAI imaging may help determine whether treatment with RAI is indicated (ie, RAI is often beneficial in iodine-avid disease but not in non-iodine avid disease).

## RECURRENT DISEASE

- Stimulated Tg 1-10 ng/mL
- Non-resectable tumors
- Non-radioiodine responsive

→ Suppress TSH with levothyroxine<sup>9</sup>

Locoregional recurrence →

Surgery (preferred) if resectable<sup>9</sup> and/or Radioiodine treatment,<sup>1</sup> if radioiodine imaging positive and/or EBRT, if radioiodine imaging negative

- Stimulated Tg > 10 ng/mL and rising
- Scans (including PET) negative

→ Consider radioiodine therapy with 100-150 mCi<sup>1</sup> and post-treatment <sup>131</sup>I imaging (category 3); additional RAI treatments should be limited to patients who responded to previous RAI therapy

Metastatic disease →

→ [See Treatment of Metastases \(PAP-7\)](#)

<sup>o</sup>In selected patients who may be at higher risk for residual/recurrent disease (eg, N1 patients), obtain a stimulated Tg and consider concomitant diagnostic RAI imaging. With a positive stimulated Tg, concomitant RAI imaging may help determine whether treatment with RAI is indicated (ie, RAI is often beneficial in iodine-avid disease but not in non-iodine avid disease).

<sup>p</sup>If there is a high likelihood of therapy, thyroid hormone withdrawal suggested; if not, suggest using rhTSH.

<sup>9</sup>Preoperative vocal cord assessment, if central neck recurrence.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

# Screening for recurrent thyroid cancer

---

- Physical exam – 6 mos, 12 mos, annually
- Neck ultrasound – “periodic”
- Tumor markers – 6 mos, 12 mos, annually
- Radioiodine scans: TSH stimulated scan every 1-2 years for high risk patients with radioiodine avid cancers, or sooner for rising TG/Anti-TG, or abnormal imaging.
- CT / PET. For radioiodine negative, US negative patients with stimulated Tg >2-5
- Patients treated with <sup>131</sup>I ablation may be followed with unstimulated Tg annually with periodic neck ultrasound if they have negative ultrasounds, stimulated Tg less than 2 ng/ml, negative anti-Tg and negative RAI imaging.

# Ultrasound Recommendations\*

---

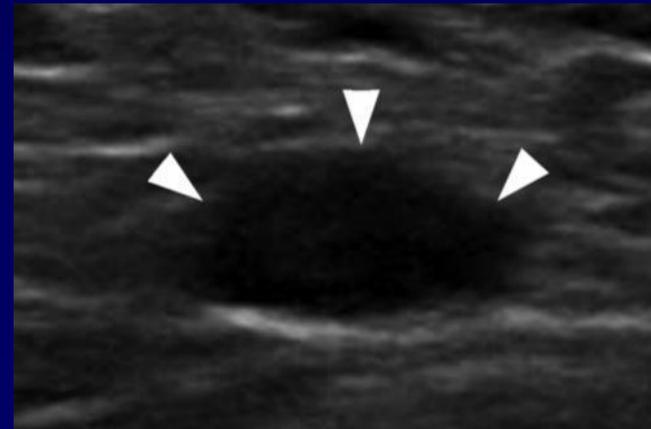
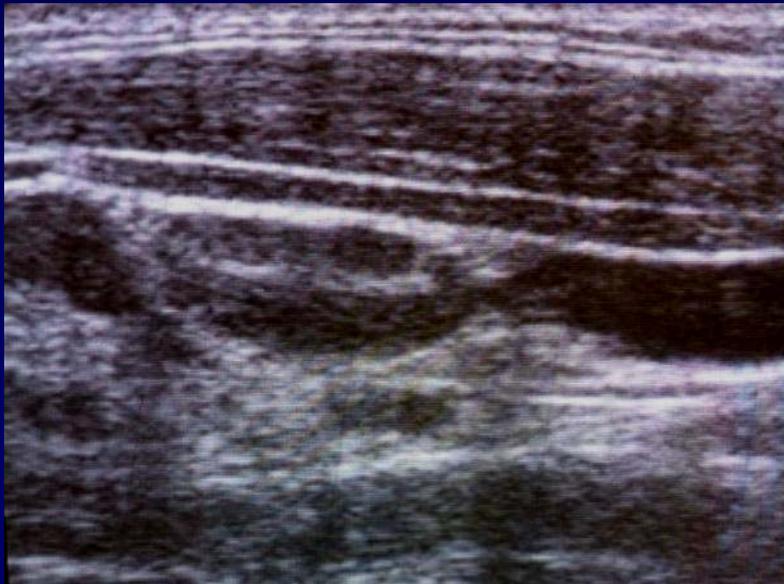
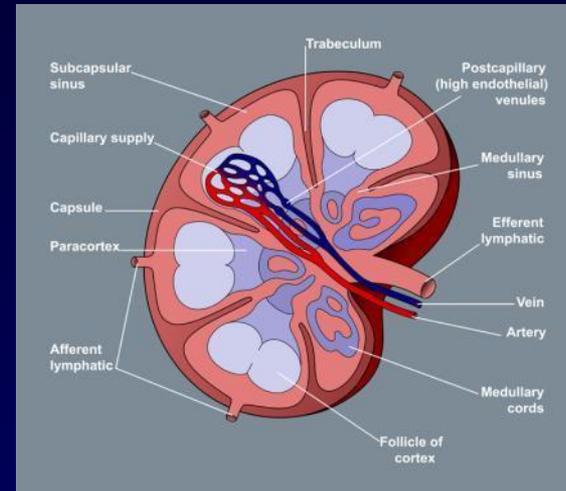
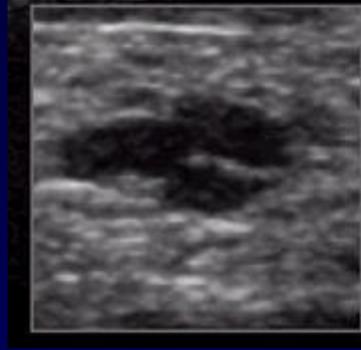
(a) Following surgery, cervical US to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6–12 months and then periodically, depending on the patient's risk for recurrent disease and Tg status

(b) If a positive result would change management, ultrasonographically suspicious lymph nodes greater than 5–8mm in the smallest diameter should be biopsied for cytology with Tg measurement in the needle washout fluid

(c) Suspicious lymph nodes less than 5–8mm in largest diameter may be followed without biopsy with consideration for intervention if there is growth or if the node threatens vital structures

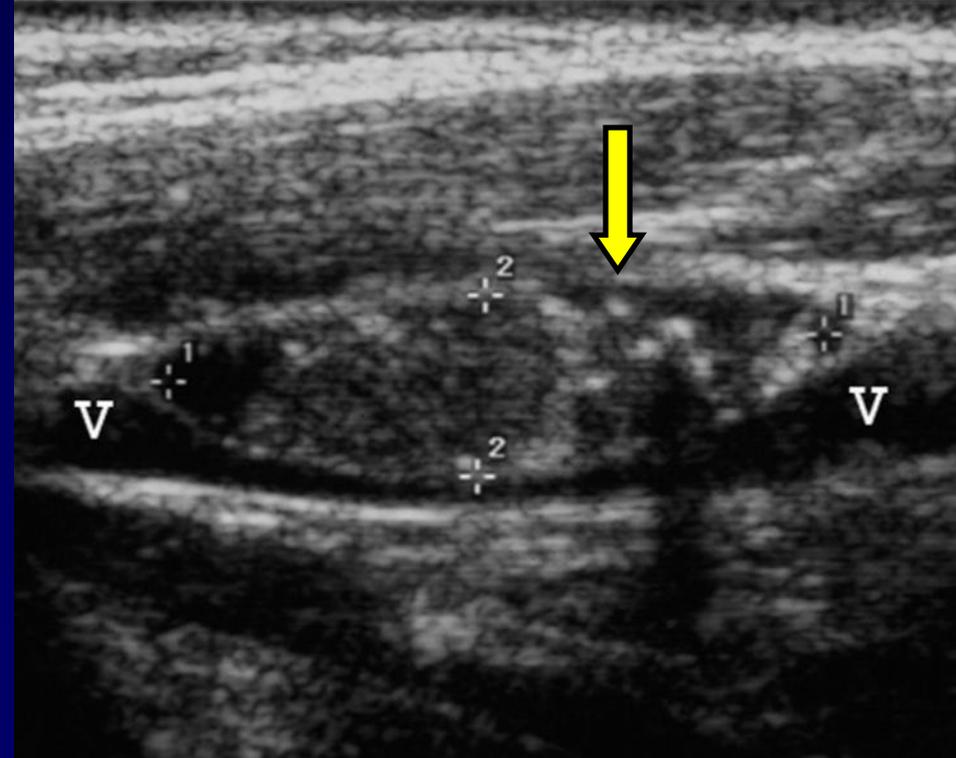
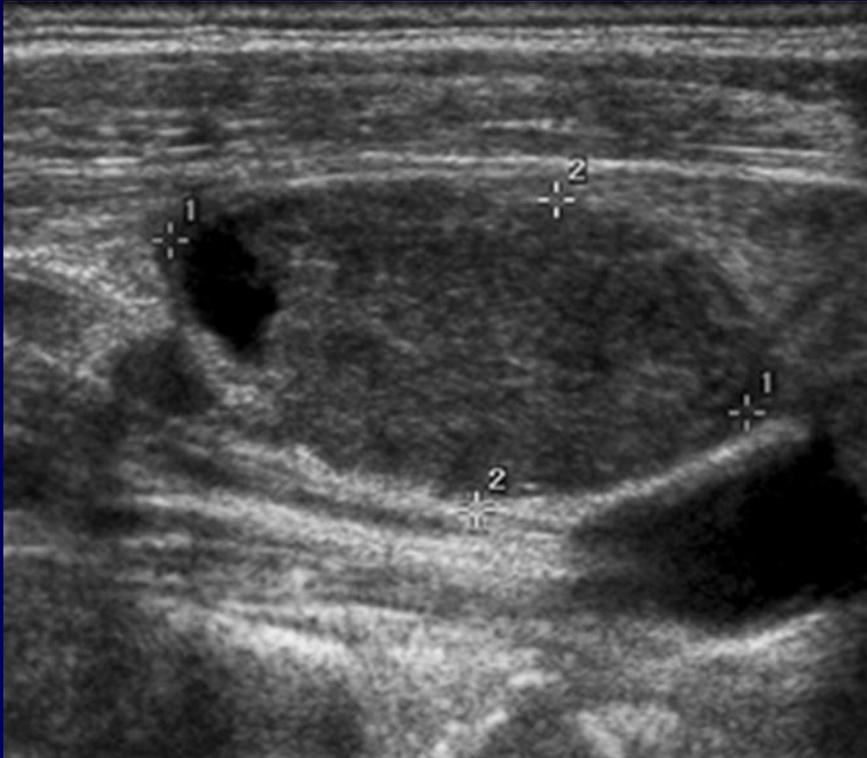
# Sonographically Suspicious Nodes

- Loss of the hilar line



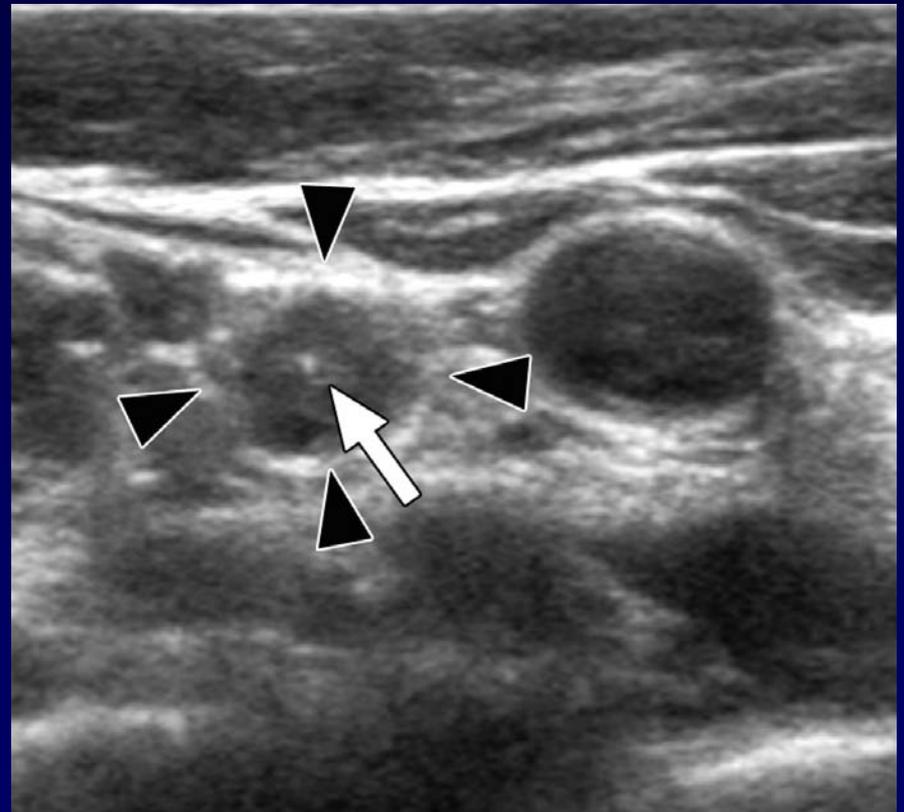
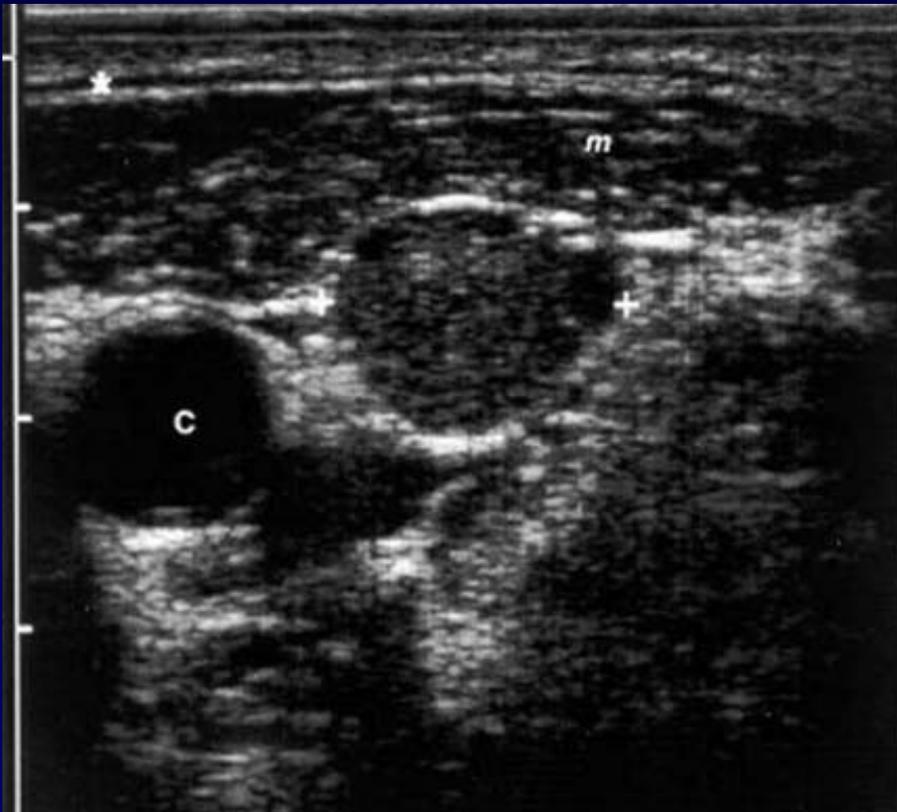
# Sonographically Suspicious Nodes

- Jugular deviation or compression
- Microcalcifications



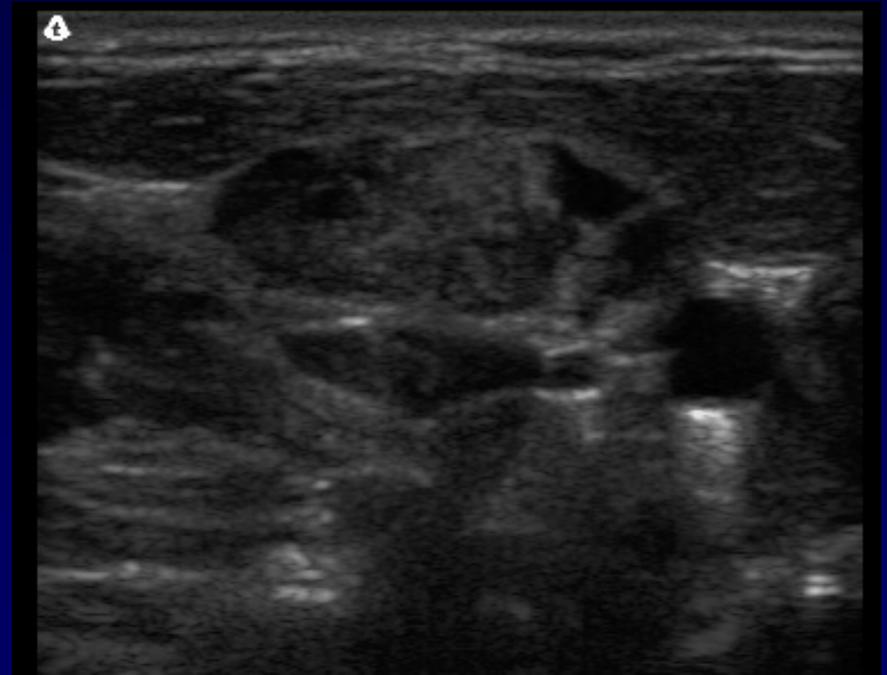
# Sonographically Suspicious Nodes

- Rounded shape



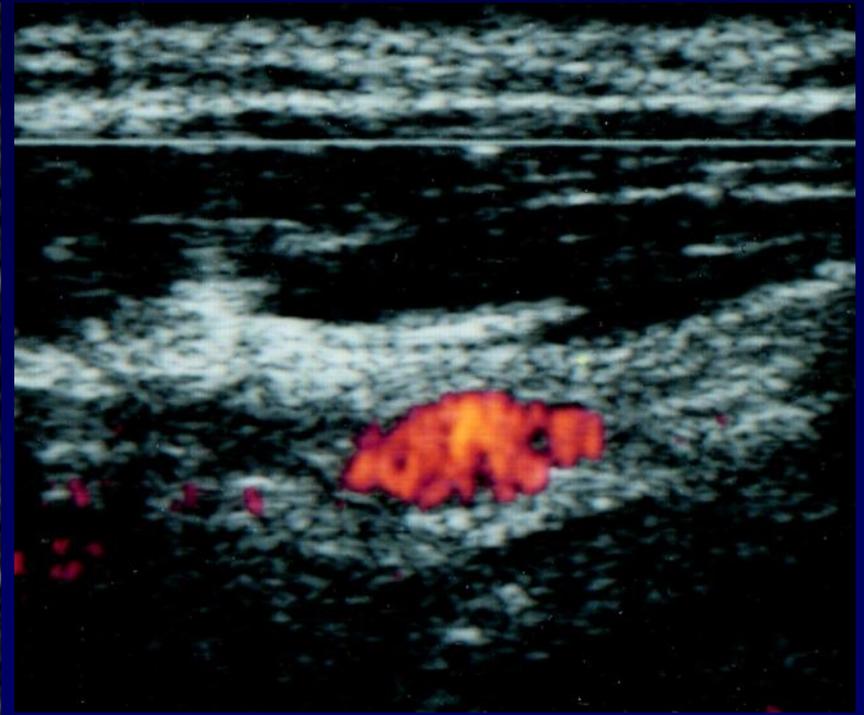
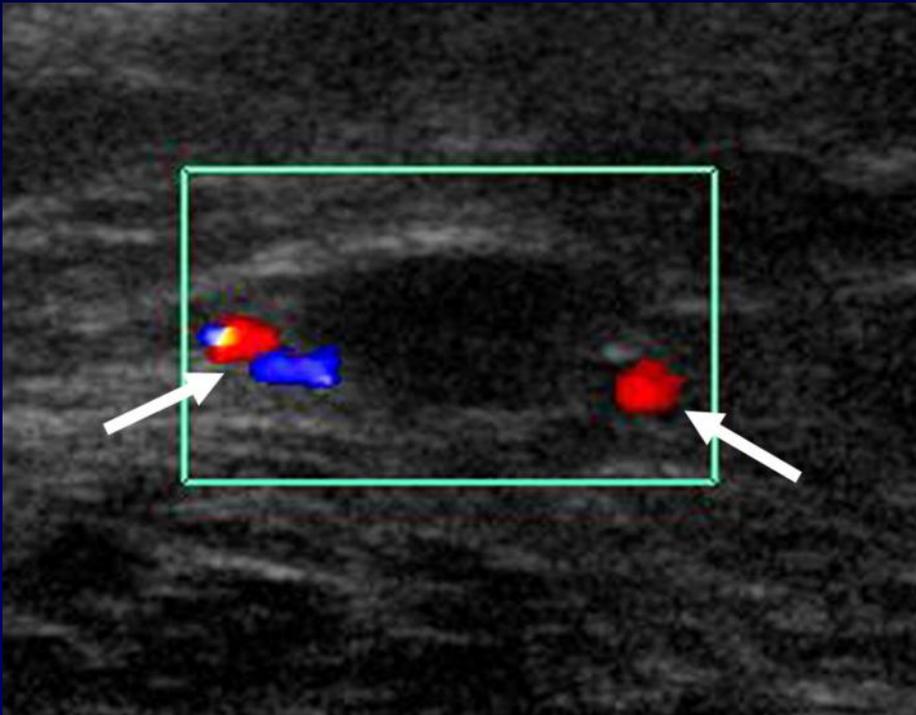
# Sonographically Suspicious Nodes

- Cystification



# Sonographically Suspicious Nodes

- Chaotic or peripheral vascularity



# Recurrent thyroid cancer

---

## How can you treat thyroid cancer recurrence?

Depends on:

- What kind of cancer?
- Where it is
- What you've done in the past
- How well it worked
- How much cancer is left (tumor burden)



# Recurrent thyroid cancer

---

How can you treat thyroid cancer recurrence?

**The preferred treatment for recurrent thyroid cancer is surgery if it can be localized and is resectable<sup>1,2</sup>**

<sup>1</sup>NCCN 2013

<sup>2</sup>ATA 2009



# Recurrent PTC, FTC, HTC

---

## Local recurrence

Cancer in residual thyroid tissue or nearby tissues.

- FNA biopsy to confirm diagnosis
  - Surgery
  - Radioiodine ablation
  - Watchful waiting
  - *Consider* external beam radiation
  - *Consider* kinase inhibitors or experimental trials
- 

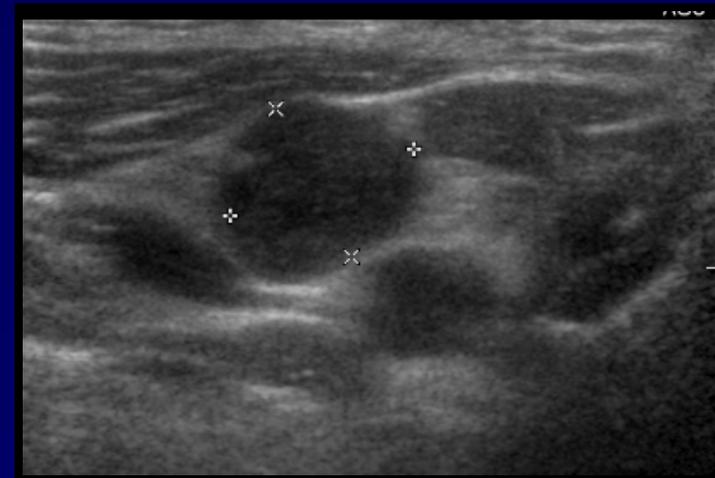
# Recurrent PTC, FTC, HTC

---

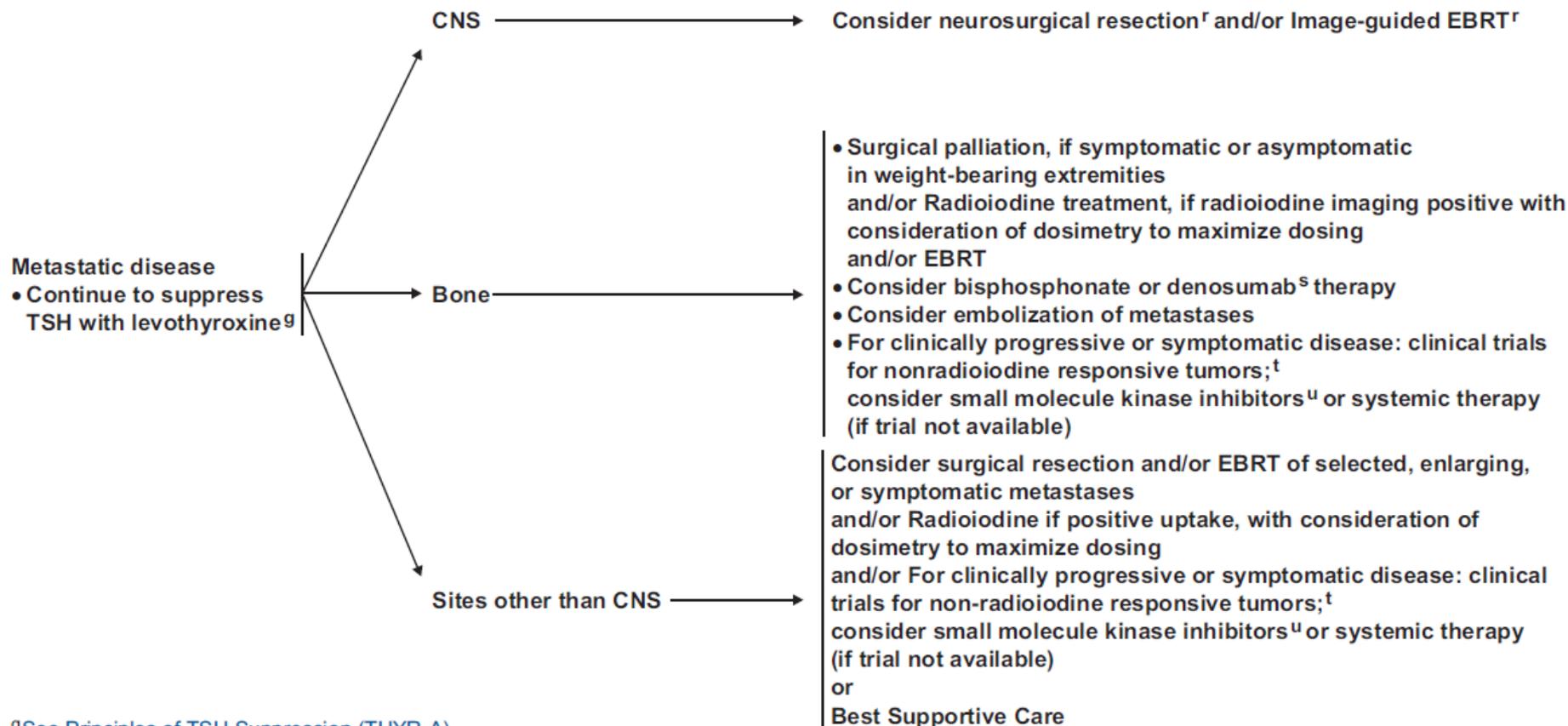
## Regional recurrence

Cancer spread to lymph nodes in the neck

- FNA biopsy (cytology and tumor marker)
- Surgery (formal compartmental clearance)
- Radioiodine ablation
- External beam radiation (rare)
- Watchful waiting



## TREATMENT OF METASTASES



<sup>9</sup>See [Principles of TSH Suppression \(THYR-A\)](#).

<sup>r</sup>For solitary lesions, either neurosurgical resection or stereotactic radiosurgery preferred. (See [NCCN Guidelines for Central Nervous System Cancers](#))

<sup>s</sup>Denosumab and bisphosphonates can be associated with severe hypocalcemia; patients with hypoparathyroidism and vitamin D deficiency are at increased risk.

<sup>t</sup>Cytotoxic chemotherapy has shown to have minimal efficacy. Clinical trials investigating novel targeted therapies are ongoing.

[See Clinical trials available at the NCCN member institutions.](#)

<sup>u</sup>While not FDA approved for treatment of thyroid cancer, commercially available small molecule kinase inhibitors (such as sorafenib, sunitinib, or pazopanib [category 2B for pazopanib]) can be considered if clinical trials are not available or appropriate.

**Note:** All recommendations are category 2A unless otherwise indicated.

**Clinical Trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

# Recurrent PTC, FTC, HTC

---

## Distant metastases - lung

- Usually treated with radioactive iodine  
and/or
- Surgery could be considered for large resectable discrete lesions  
and/or
- Clinical trials  
and/or
- Systemic chemotherapy (kinase inhibitors)

# Recurrent PTC, FTC, HTC

---

## Distant metastases - bone

- Resection  
and/or
- Radioactive iodine  
and/or
- External beam radiation
- *Consider* bisphosphonates or denosumab
- *Consider* embolization
- Clinical trials, kinase inhibitors

# Recurrent PTC, FTC, HTC

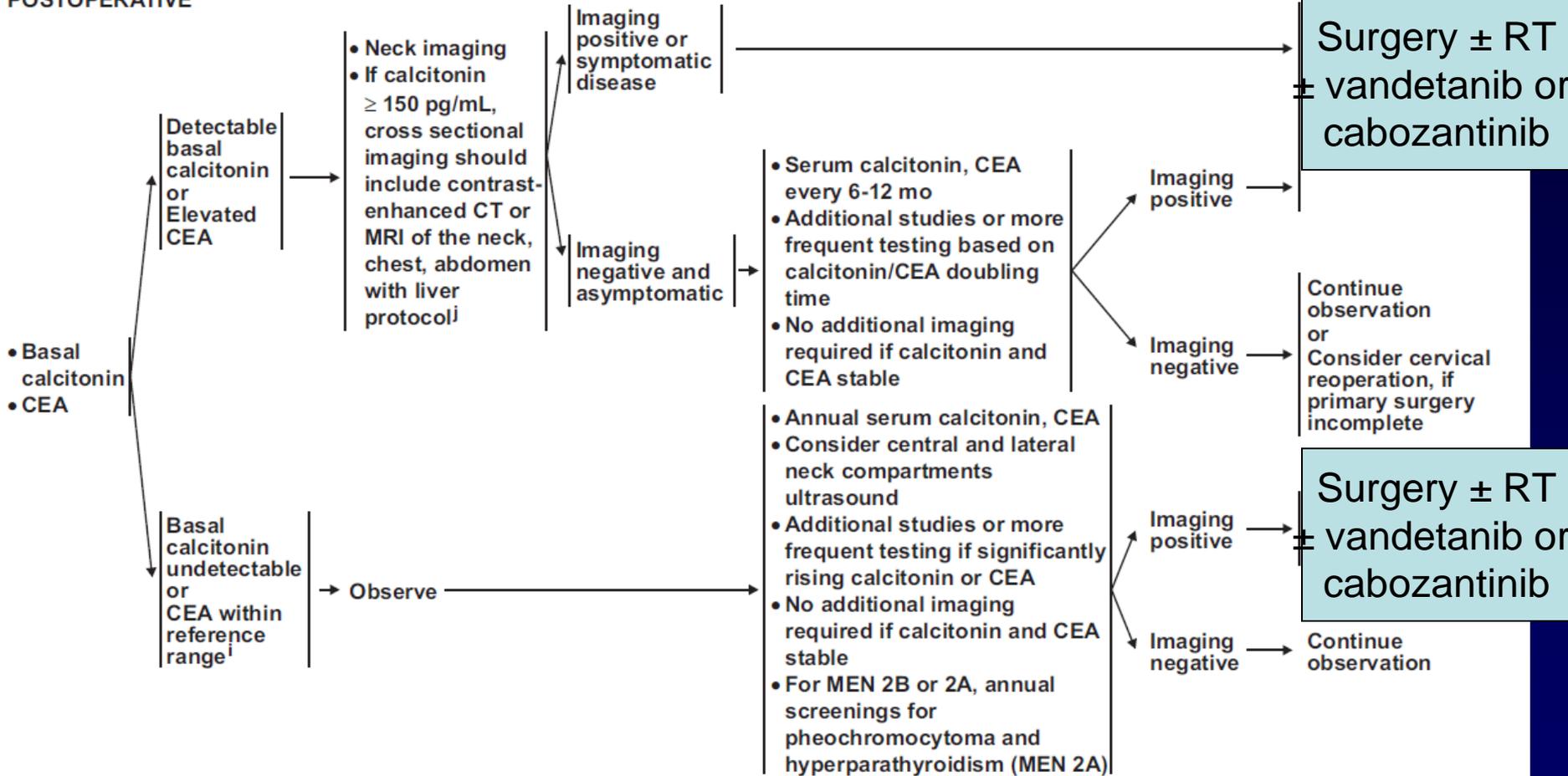
---

## Distant metastases - CNS

- Resection  
and/or
- Gamma knife

MANAGEMENT  
2-3 MONTHS  
POSTOPERATIVE

SURVEILLANCE



<sup>i</sup>The likelihood of significant residual disease with an undetectable basal calcitonin is very low.  
<sup>j</sup>Bone scan and MRI of axial skeleton should be considered in patients with very elevated calcitonin levels.

**Note:** All recommendations are category 2A unless otherwise indicated.  
**Clinical Trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

# Recurrent Medullary Cancer

 **AMERICAN THYROID ASSOCIATION**  
DEDICATED TO SCIENTIFIC INQUIRY, CLINICAL EXCELLENCE, PUBLIC SERVICE, EDUCATION, AND COLLABORATION.

Google™ Custom Search

ABOUT THE ATA    GIVE ONLINE    JOIN THE ATA    FELLOWS' CORNER    MEMBERS ONLY

ATA PUBLICATIONS    PUBLIC & PATIENTS    PHYSICIANS & PROFESSIONALS

### CALCITONIN AND CARCINOEMBRYONIC ANTIGEN (CEA) DOUBLING TIME CALCULATOR

[Print page](#) [Email page](#)

 Please note: Due to HIPAA regulations, the information entered into the calculator is not retained by the ATA system. Once you exit the calculator page, any calculated data and results will no longer be available. However, you may enter a non-HIPAA patient identifier and print the calculator results to maintain for your record-keeping purposes.

The monitoring of calcitonin levels play an important role in the follow-up and management of patients with medullary thyroid cancer. Calcitonin doubling times of > 2 years seem to be associated with a better long term prognosis than those < 6 months. The calculator is intended for use by healthcare providers as appropriate medical training and clinical experience is required for interpretation of the results and application to care of individual patients. Providers are referred to the recently published ATA Guidelines on Medullary Thyroid Cancer.

Based on available data, it is recommended to use a minimum of 4 calcitonin values preferably spread over a 2 year period. For a valid result, it is essential that all the calcitonin results have been obtained from the same laboratory and assay.

(One record per line. The two tables should have equal number of records.)

Patient Reference

Date of Test (mm/dd/yyyy)	Calcitonin (must be number)	CEA (must be number)
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>

Doubling Time:

< 6 months =  
Bad

6-24 months =  
Not as bad

>24 months =  
Good

# Recurrent Medullary Cancer

---

- Locoregional
  - Surgery
  - External beam radiation
  - Vandetanib / cabozantinib
  - Observe
- Distant
  - Resection / embolization
  - Vandetanib / cabozantinib
  - Observe

# Recurrent thyroid cancer

---

What are the problems (limitations) with screening for thyroid cancer recurrence?

- **Physical exam** – not very sensitive
- **Neck ultrasound** – may miss deep nodes, or those behind airway
- **Blood tests** – some patients have interfering antibodies in the blood, or cancers that don't make the tumor markers
- **Radioiodine scans** - some cancers lose their appetite for iodine and don't show up on the scans.
- **PET scans** – OK for poorly differentiated cancers, or radioiodine neg / TG pos. Not very sensitive for others.

# Conclusions

---

## How do you prevent recurrence?

- Early diagnosis and treatment of the primary cancer
- Complete removal of the cancer at the first operation
- Appropriate lymph node clearance during the first operation
- Use of radioiodine in high risk patients (not MTC)
- TSH suppression (not MTC)

**Thank you for your attention**

---

**Cord Sturgeon MD**

