

Thyroid Cancer and Thyroid Nodules

Much ado about nothing?

The untold mystery?

(The bane of my/our existence? !!!)

Premise

- Thyroid Nodules and Thyroid Cancer continue to be a source of confusion and misunderstanding amongst Radiologists and Clinicians, alike.

August 2008

115
Pages!



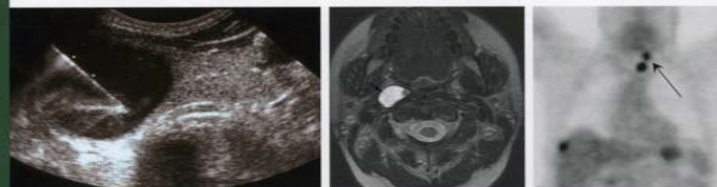
**Thyroid and Parathyroid
Glands: Imaging,
Treatment, and Beyond**

GUEST EDITOR: **Laurie A. Loevner, MD**

**NEUROIMAGING
CLINICS**

OF NORTH AMERICA

Suresh K. Mukherji, MD
CONSULTING EDITOR



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theclinics.com

Objectives

- 1. **Thyroid Cancer** is not a complex disease.
- 2. The management of **Thyroid Nodules** is fairly straightforward.

Robert J. Graziano, M.D.



- How many of you have a Thyroid Nodule?

Nodule Prevalence

- At **autopsy**, **50%–60%** have a thyroid nodule.
- On **US**, up to **67%** will have an incidental thyroid nodule.

Nodule Prevalence

- 90% of women over the age of 60 years.
- 90% of all of us by the age of 80.

Nodules Everywhere!

- That is the very reason I will refuse to do an Ultrasound of my thyroid, although it is obviously readily available to me.
- I don't want to know.

Thyroid Cancer Retrosternal Extension



The Good News

- 1 in 20 nodules will be malignant.
- 80-85% of these cancers will be Papillary Cancer

Papillary Carcinoma

- The 20 year survival is 99% after surgery.
- The 30 year survival is approximately 95%.

Thyroid Cancer

- The **lifetime risk** in the U.S. is **.73%**.

Thyroid Cancer

- Accounts for less **than 1%** of all malignancies.
- Accounts for only **.5%** of all cancer deaths.

Thyroid Cancer

- At **Autopsy**, up to **30%** of adults have incidental cancers smaller than 1 cm.
- **Analogous to Prostate Cancer?**

Roger Ebert

Diagnosed with Papillary Ca 2002



National Cancer Institute Website

- <http://seer.cancer.gov/> 2008

Thyroid Cancer:

- Incidence rate 9.1 per 100,000
- Death rate 0.5 per 100,000

Let's put this further in perspective:

2007 Cancers

	<u>Cases</u>	<u>Deaths</u>
■ Thyroid	33,550	1,530
■ All Cancers	1,437,180	565,650

Thyroid vs Breast

2008 Cancers

	<u>Cases</u>	<u>Deaths</u>
■ Thyroid	37,340	1,590
■ Breast	182,460	40,480

Thyroid vs Lung

2008 Cancers

	<u>Cases</u>	<u>Deaths</u>
■ Thyroid	37,340	1,590
■ Lung	215,020	161,840

Cancer Deaths 2008

Thyroid - 1,590

Bone and Joint - 1,470

- Thyroid cancer deaths are **very uncommon!**
- Average age diagnosis **47 y.o;** death **74 y.o.**
- Should we really worry?

Joe Piscopo - Comedian

Diagnosed with
Medullary Ca
1981



Nodules: Too many to count!

- Population Clocks

- **U.S. 305,164,552**
(Sep 16, 2008)

- **67%** have a Thyroid nodule on imaging.

- **204,460,250** Patients with nodules!

At what cost?

- 200,000,000 Nodules
x 5% malignant
10,000,000 Patients with Thyroid Cancer.

- x \$ 20,000 / Pt Cost Bx and Surgery/Pt
\$ 20,000,000,000

- **\$20,300,000,000 = GNP Iceland 2007**

Postgrad Med J. **1972** February;
48(556): 80–82.

Thyroid nodules in Iraq

H. M. Al-Hashimi

Abstract

Two groups of patients with solitary thyroid nodules have been analysed. One hundred patients of the first group under 20 years of age were managed conservatively with supplementary doses of thyroxin. Three hundred and thirty patients of the second group over the age of 20 were treated surgically.

Seventeen percent of the first group had complete resolution of the thyroid nodule. The majority (eighty-three patients) needed exploration for a residual lesion.

In the two groups, adenomatous goitre constituted the most frequent pathological finding.

True adenoma was the next in frequency.

Malignant nodules were found in ten cases (3.0%) of the second group; none was found in the first group. The overall incidence of carcinoma in solitary thyroid nodules in this study was 2.3%.

Catherine Bell - Actress

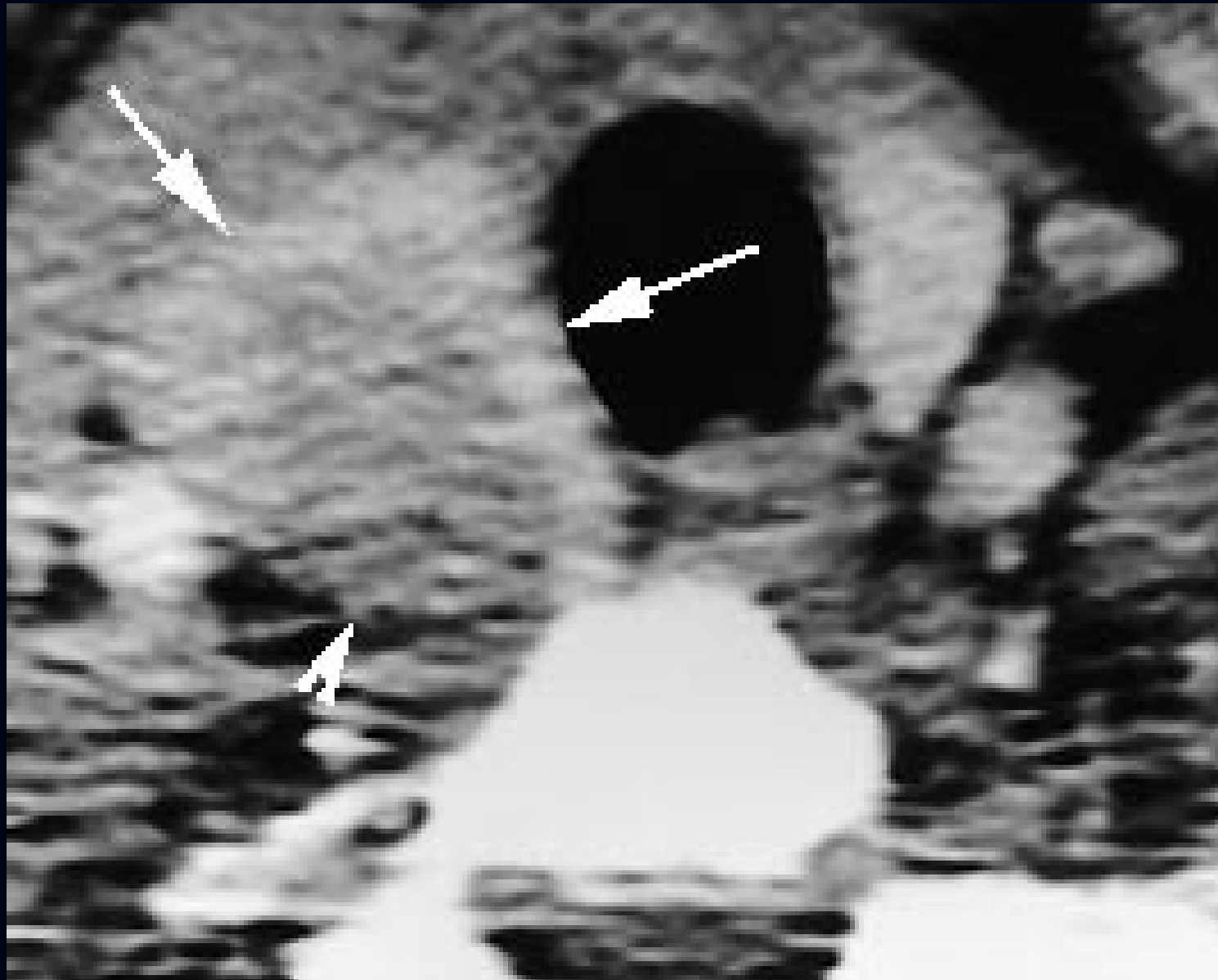
Diagnosed with
Papillary Cancer
1989



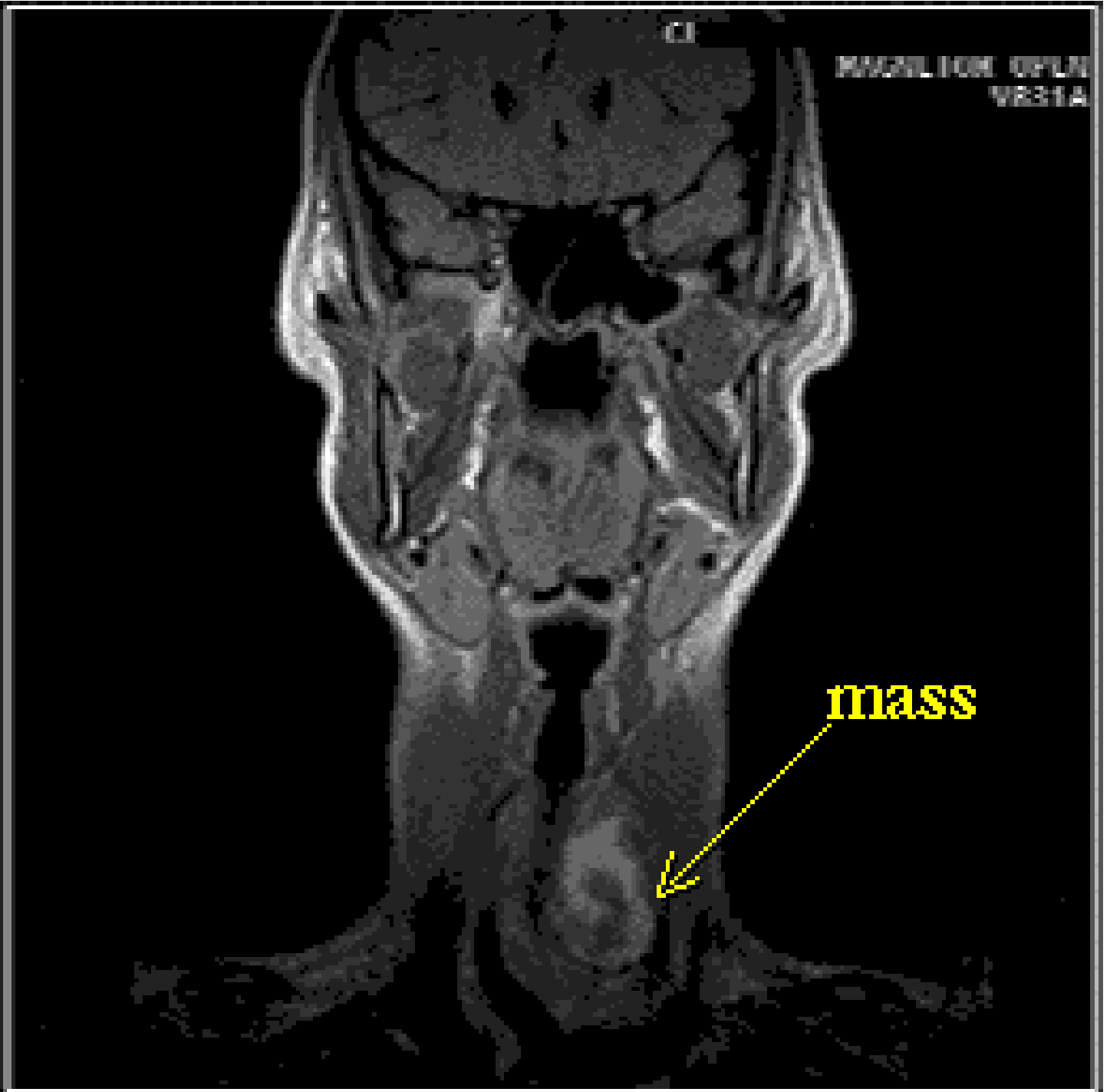
So what do we do??????

- 1. **Palpable Thyroid Nodule** detected on physical examination.
(1cm or > nodules occur in 4-7% Adults)
- 2. **Incidental Thyroid Nodule seen on imaging exams** such as Carotid Ultrasound or CT/MRI of the C-spine, Neck, and Chest.
(1-3 mm nodules may be evident on US)

CT Scan



M R I



Rod Stewart - Singer

Diagnosed with
Thyroid Ca
2000



Types of Nodules

- Benign

- Malignant

Benign Nodules

- Colloid (hyperplastic, adenoma) nodules- 80%
- Hashimoto (chronic lymphocytic) thyroiditis
- Cysts: colloid, simple, or hemorrhagic
- Follicular adenomas
- Hürthle-cell (oxyphil-cell) adenomas (variant of follicular adenoma)

Malignant Nodules

- **Papillary carcinoma 80-85%**
- Follicular carcinoma
- Medullary carcinoma
- Anaplastic carcinoma

- Primary thyroid lymphoma
- Metastatic carcinoma (breast, renal cell, others)



CARCINOMA
Papillary 75%
Follicular 10%
Medullary 5%
Anaplastic <5%

Hoang, J. K. et al. Radiography 2007;27:847-860

Lymphoma <5%

Metastases

lung, breast, renal

Sarcoma
rare

Daniel Snyder-
Owner, Washington Redskins

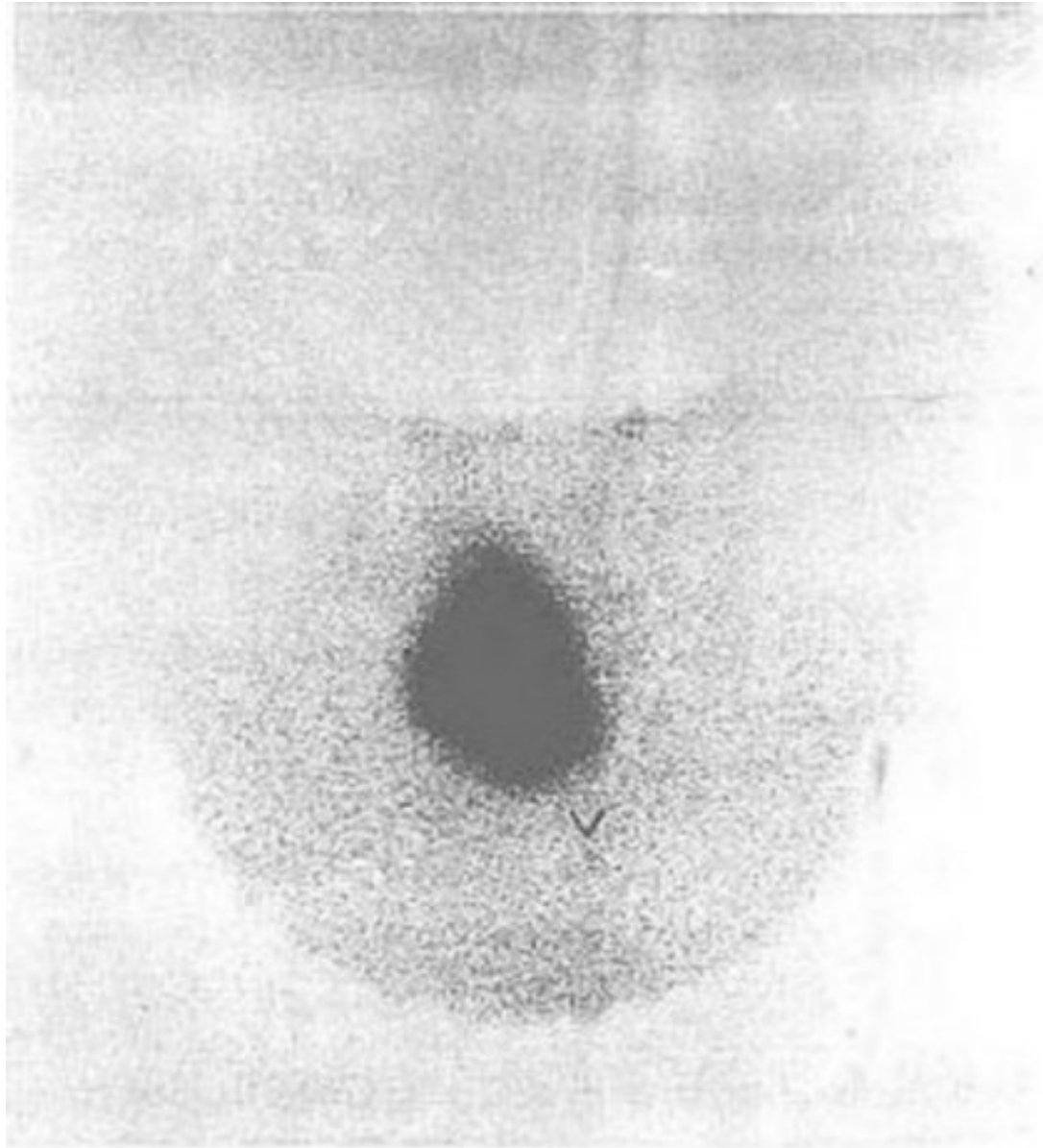
Diagnosed with
Papillary Cancer
2001



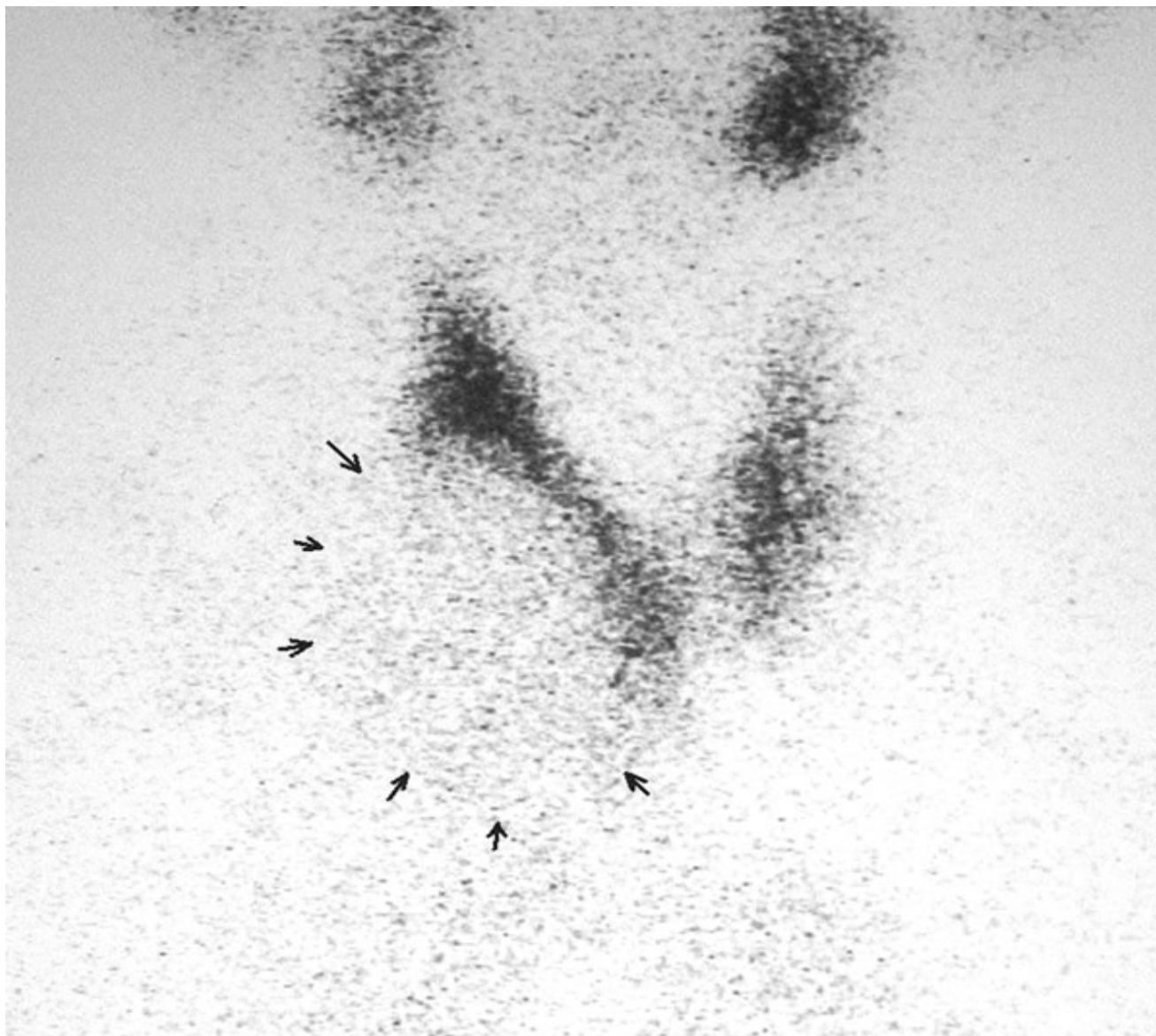
Nuclear Medicine Scan

- For decades, I123- and Tc99m-labeled pertechnetate scans were the initial imaging modalities of choice for the evaluation of a thyroid nodule.
- Less than **1%** of “**Hot Nodules**” are **malignant**.
- **8% to 25%** of “**Cold Nodules**” are **malignant**.

Hot Nodule



Cold Nodule

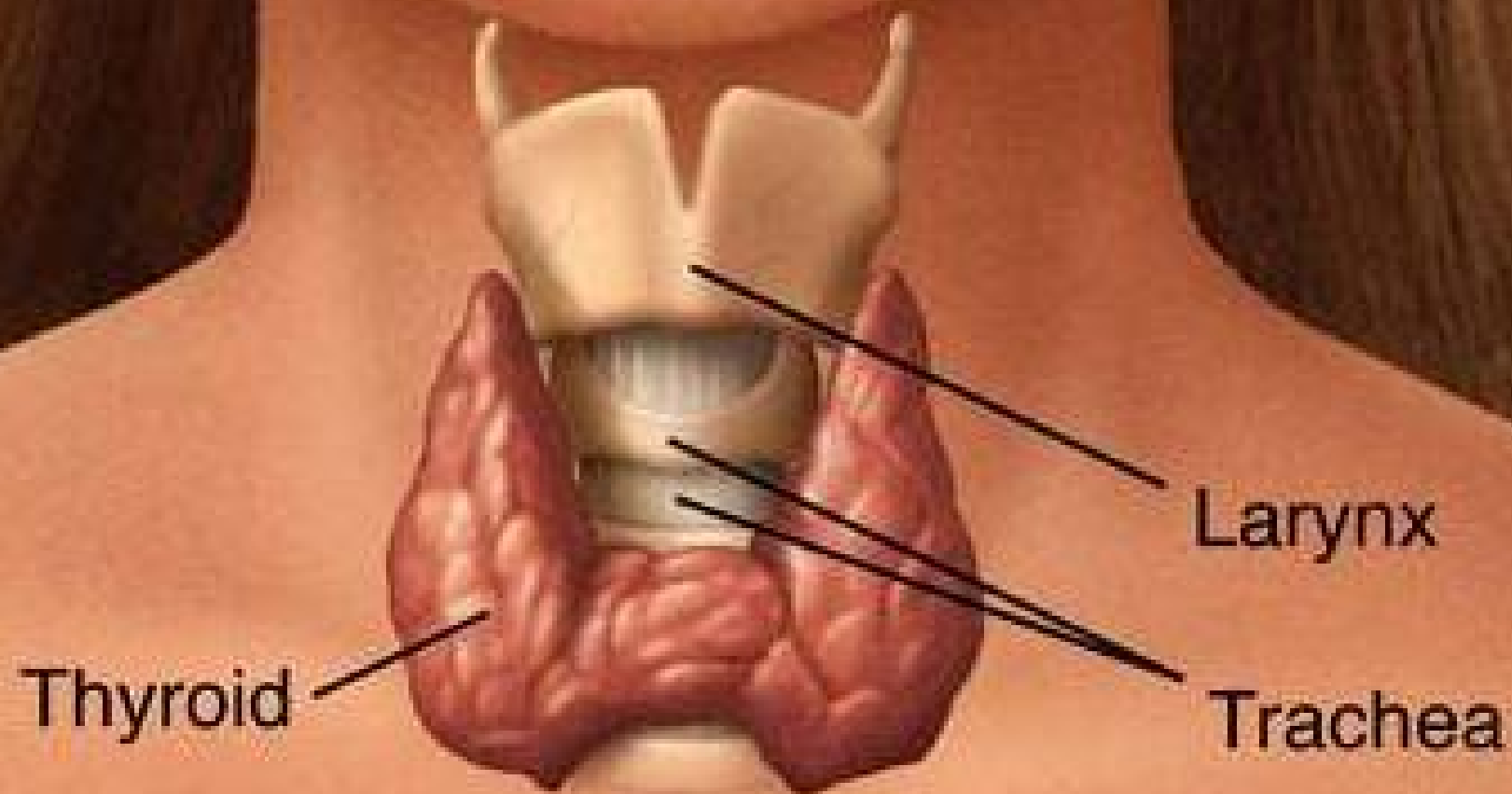


Nuclear Medicine Scan

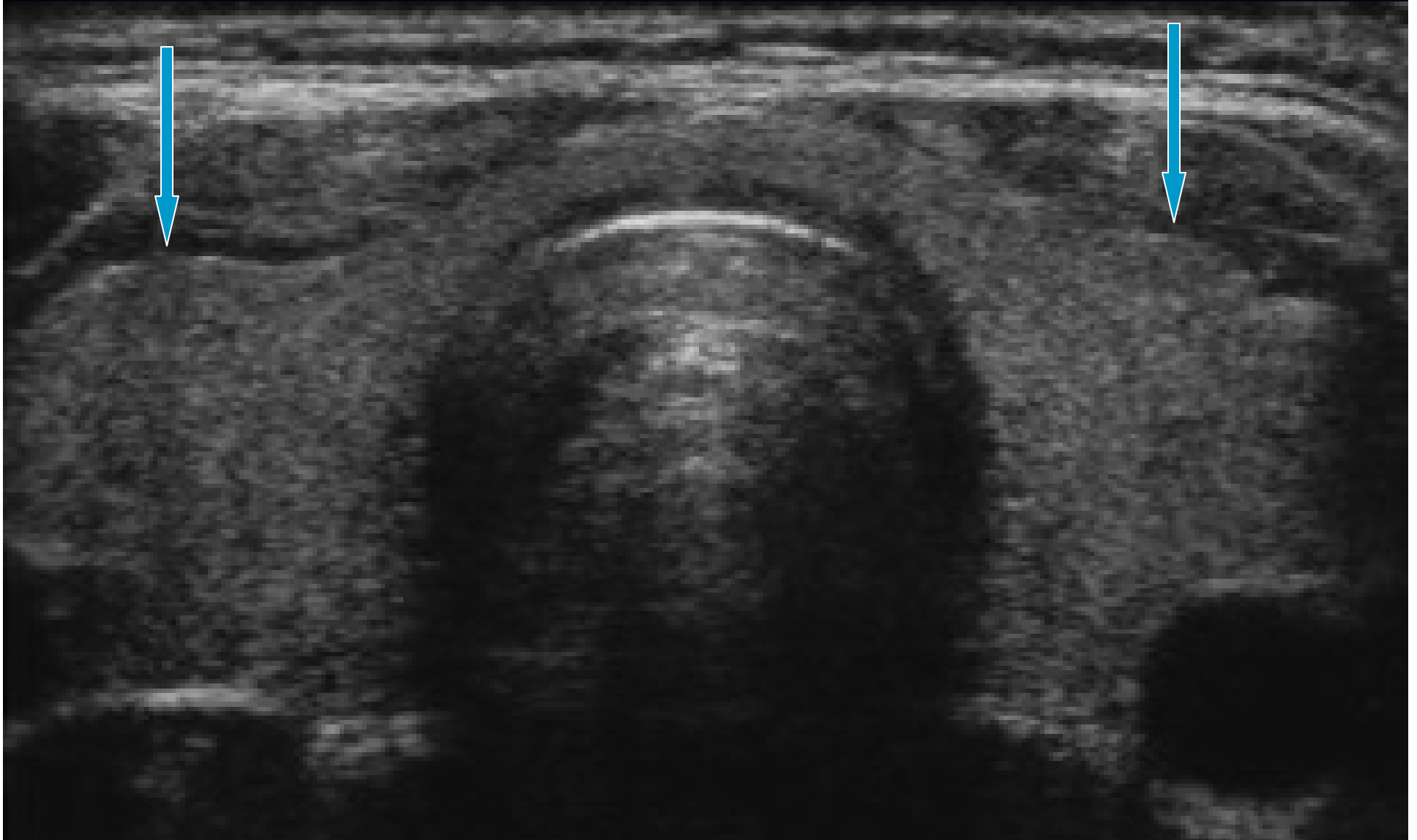
- However, 95% of all thyroid nodules are Cold and therefore nuclear medicine adds little value.
- In addition, in a review of **5000** patients undergoing thyroidectomy regardless of radioimaging findings, Ashcraft and Van Herle (1981) found that 4% of hot nodules harbored malignancy.

Ultrasound

- Ultrasound is now the study of choice for evaluation of thyroid nodules.
- Has the **highest resolution.**
- **No radiation.**
- **Cost effective.**
- Readily available



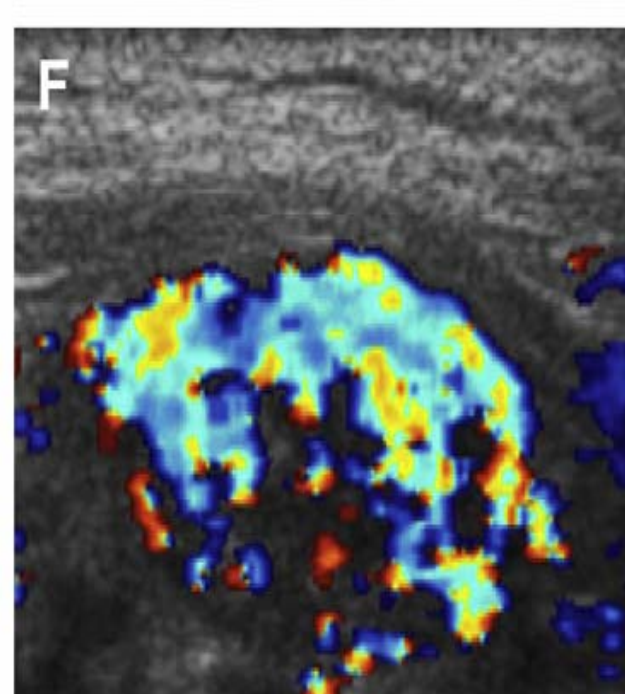
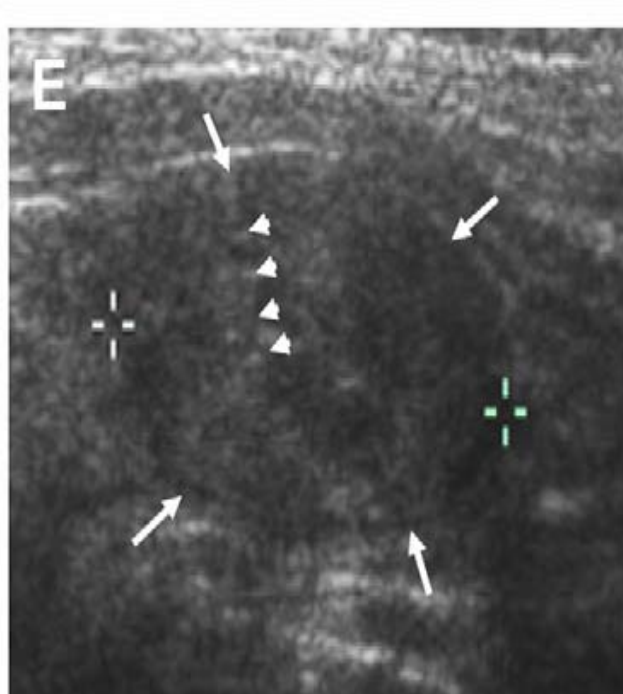
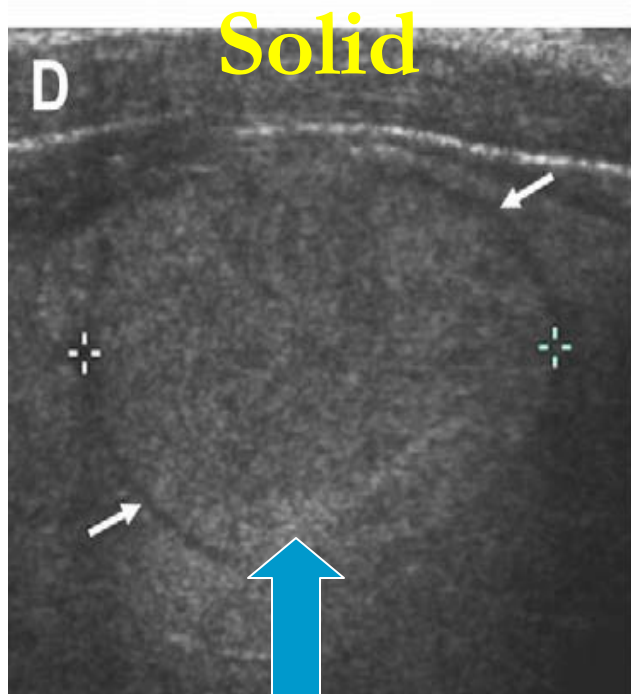
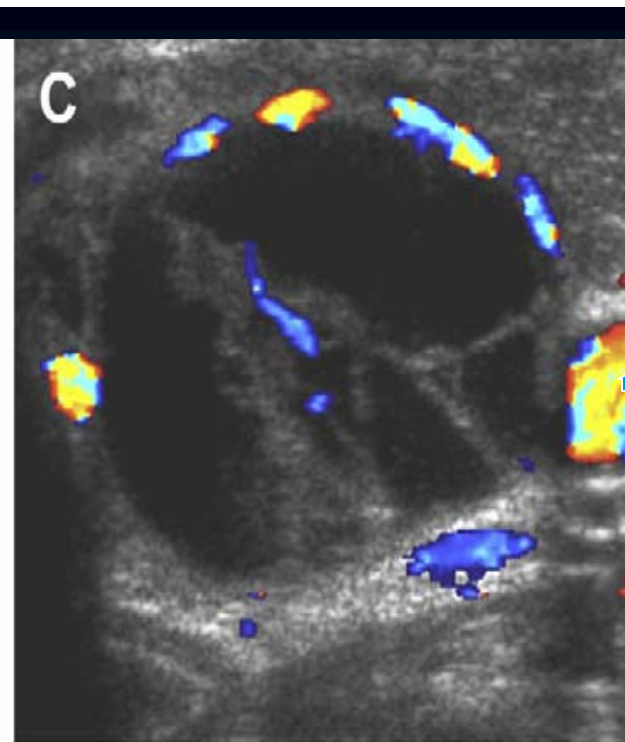
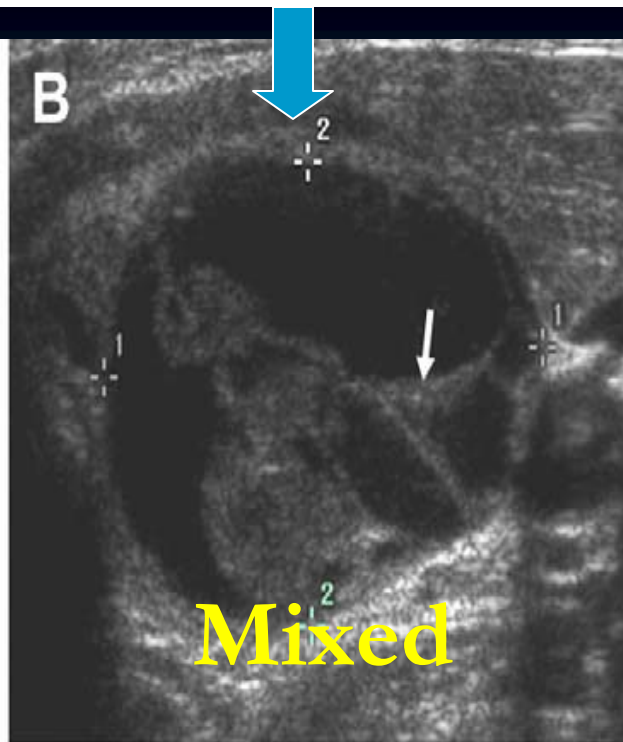
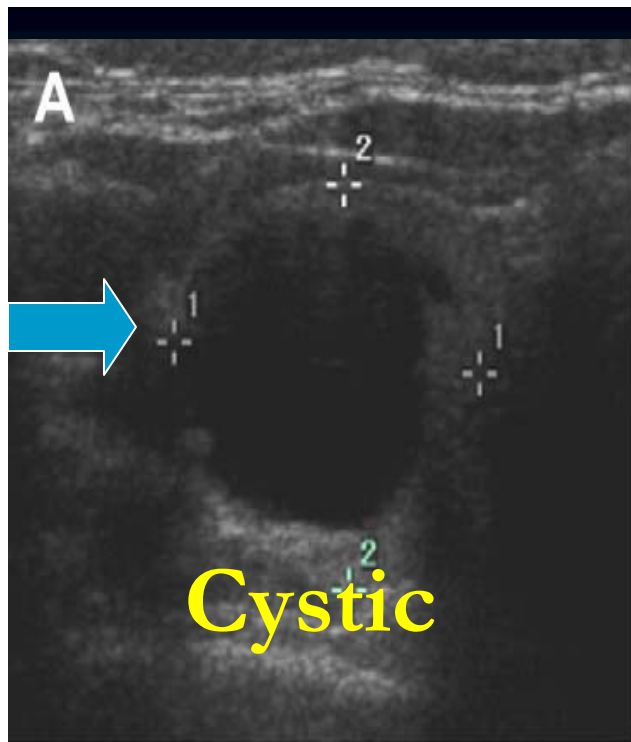
Normal Thyroid US



Ultrasound

■ Nodules may be:

1. **Solid**
2. **Cystic**
3. **Mixed**



Ultrasound of Nodule

■ Characteristics:

1. Shape
2. Margins
3. Echogenicity
4. Calcifications
5. Cystic Change
6. Halo
7. Vascularity
8. Size
9. Multiplicity

Benign Adenoma

- Approximately 80% of nodules .
- Variable appearance.
- Usually well circumscribed.
- Most isoechoic.
- Larger masses more typically echogenic.
- Sometimes coarse internal calcification or peripheral egg-shell calcification.
- Can have cystic degeneration.

Adenoma

A



Papillary Cancer

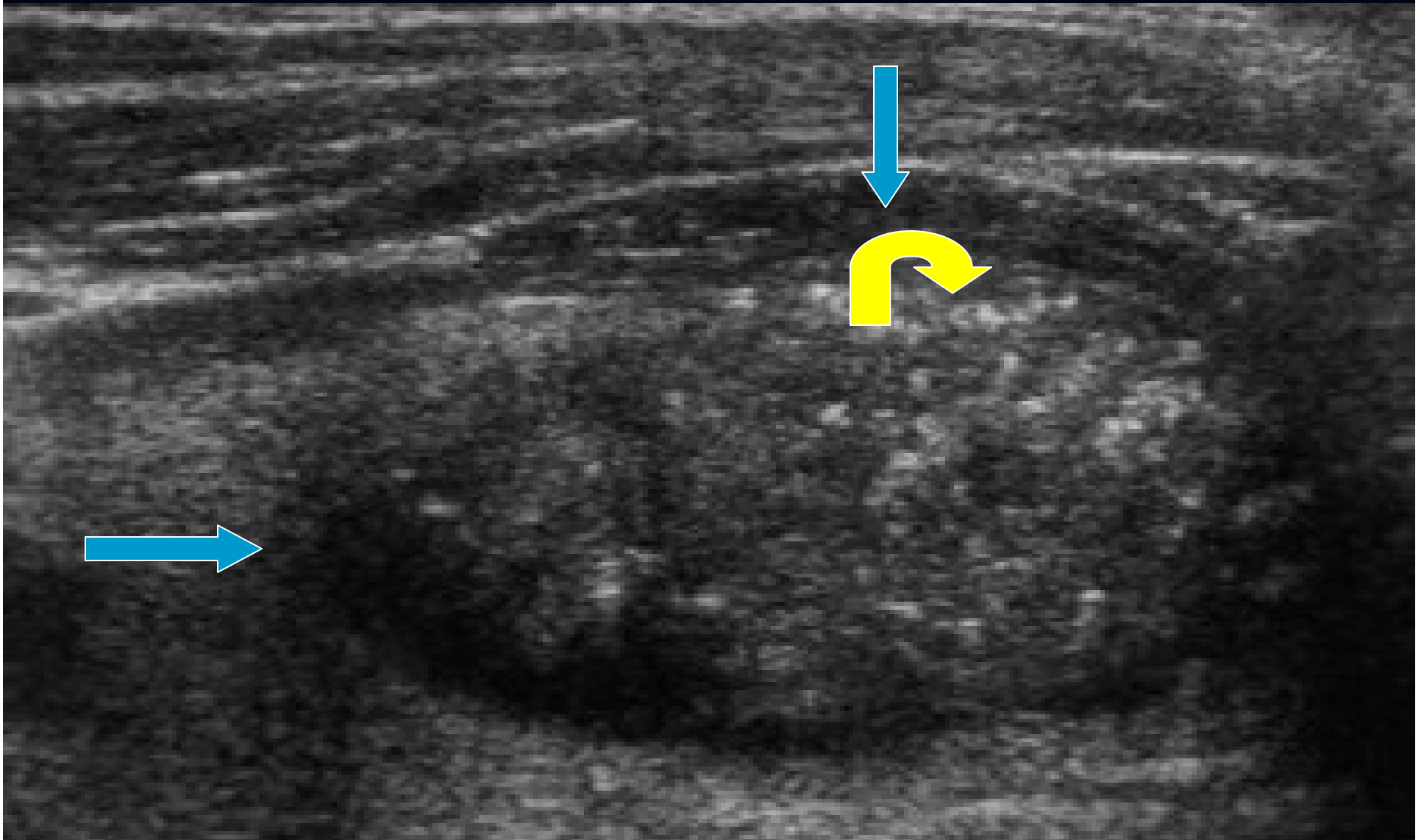
- **Microcalcifications:** most specific finding.

85-95% Specific

25-59% Sensitive

- Usually hypoechoic
- **Ill defined more worrisome;** can be well defined.

Papillary Cancer



Diagnostic Ultrasound-

Rumack 1998

- The Incidentally Detected Nodule.

1. **Biopsy Criteria:**

- A. **Malignant features-**

Microcalcifications, irregular margin, thick halo, and internal flow pattern.

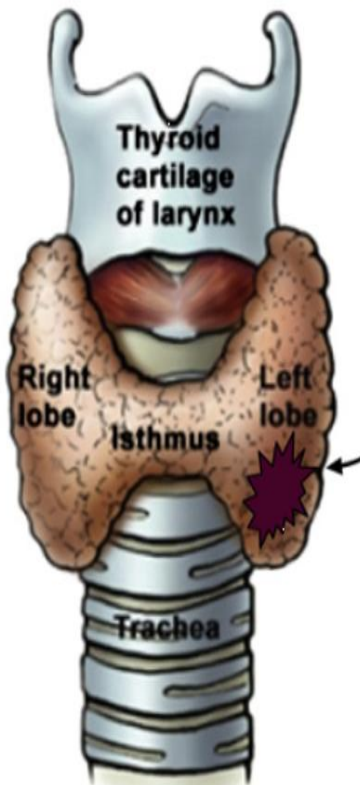
- B. **Size > 1.5 c.m.**

Biopsy

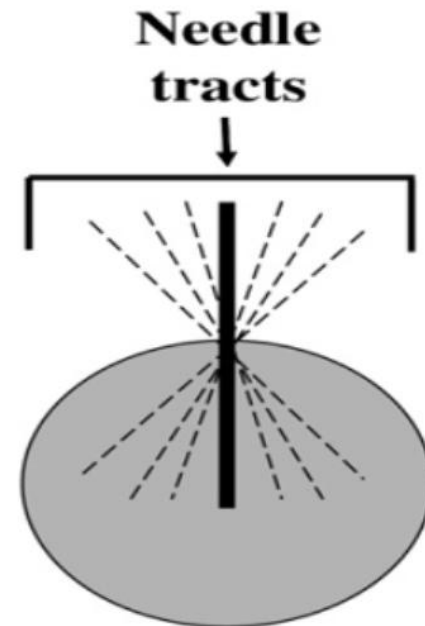
- Some even recommended Bx of any Nodule
for **Size > 1.0 c.m**

1. **Thyroid Nodule Clinic, MGH – Harvard**
2. **Delaware Valley Ultrasound Society**
Lecture 1998, Jill Langer **U of Penn**

BIOPSY

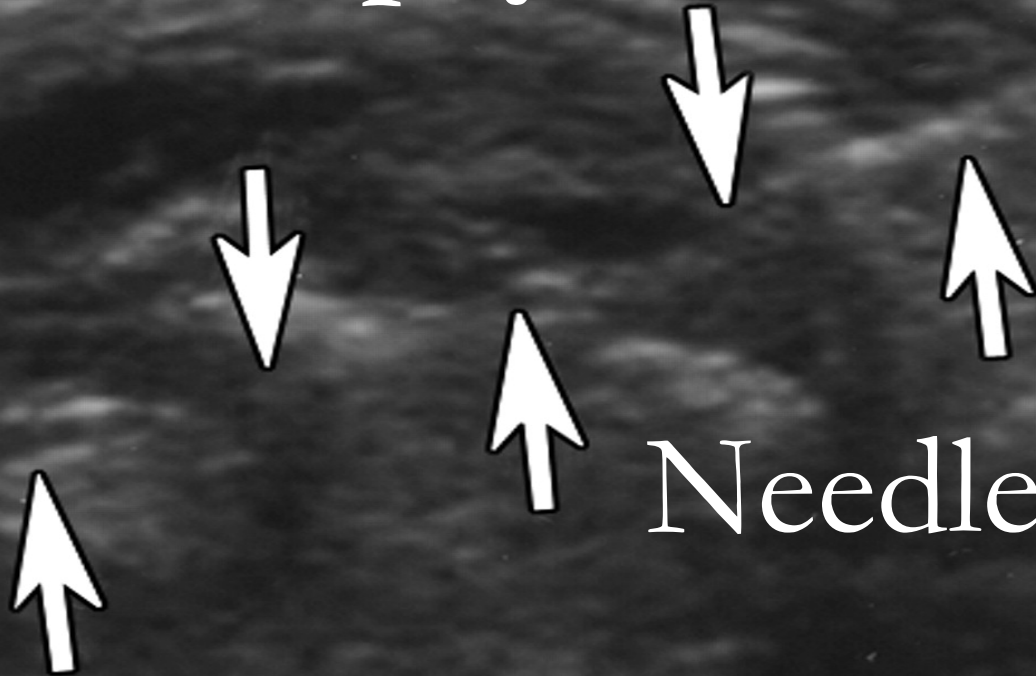


Fine-needle Aspiration



Biopsy

Needle tract



FNA

Adequate Sample

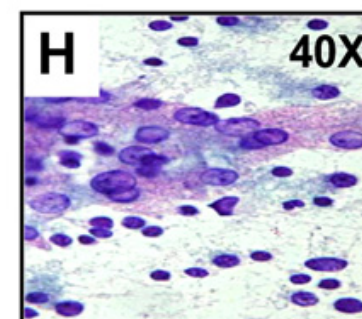
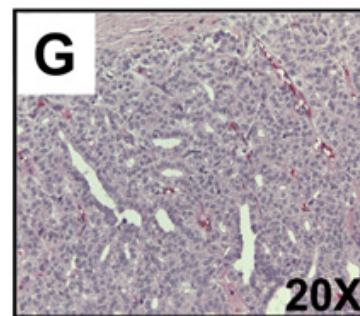
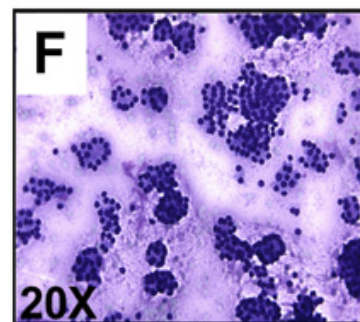
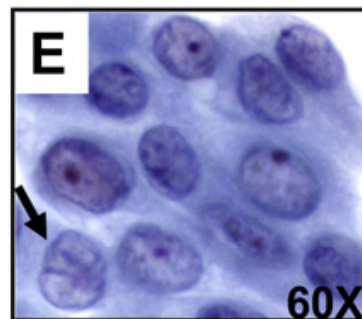
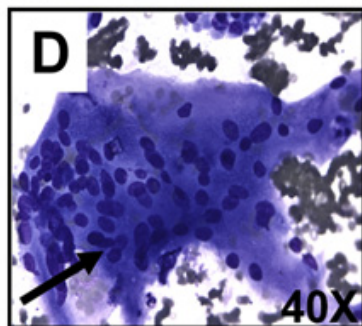
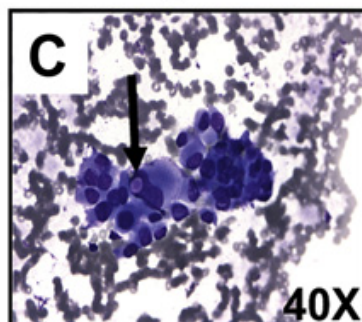
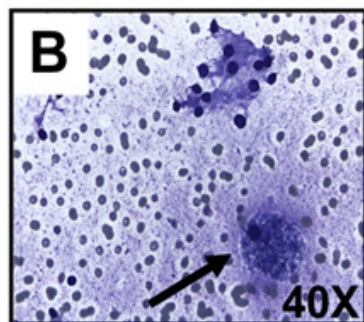
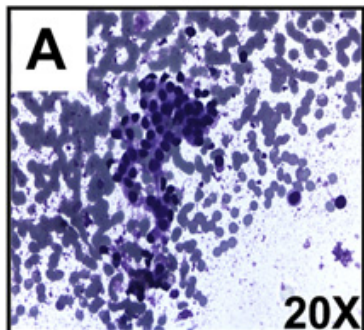
Benign

Suspicious

Malignant
(usually papillary)

Follicular
Neoplasm

Indeterminate



Biopsy

- Gold Standard
- However 5–20% will be insufficient or nondiagnostic.

Sofia Vergara – Model/Actress

Diagnosed with
Thyroid Ca
2001



Newer Exceptions

- Unfortunately recent Studies have shown exceptions:
- *** In one study of papillary carcinomas, more than **HALF** had at least one feature not commonly associated with malignancy. ***
- *** In another study of benign nodules, **69%** of them had at least one finding usually associated with malignancy. ***

Echogenicity

- Previously increased echogenicity was typically associated with a benign nodule, yet now has been seen in **follicular neoplasms** and **papillary cancer**.

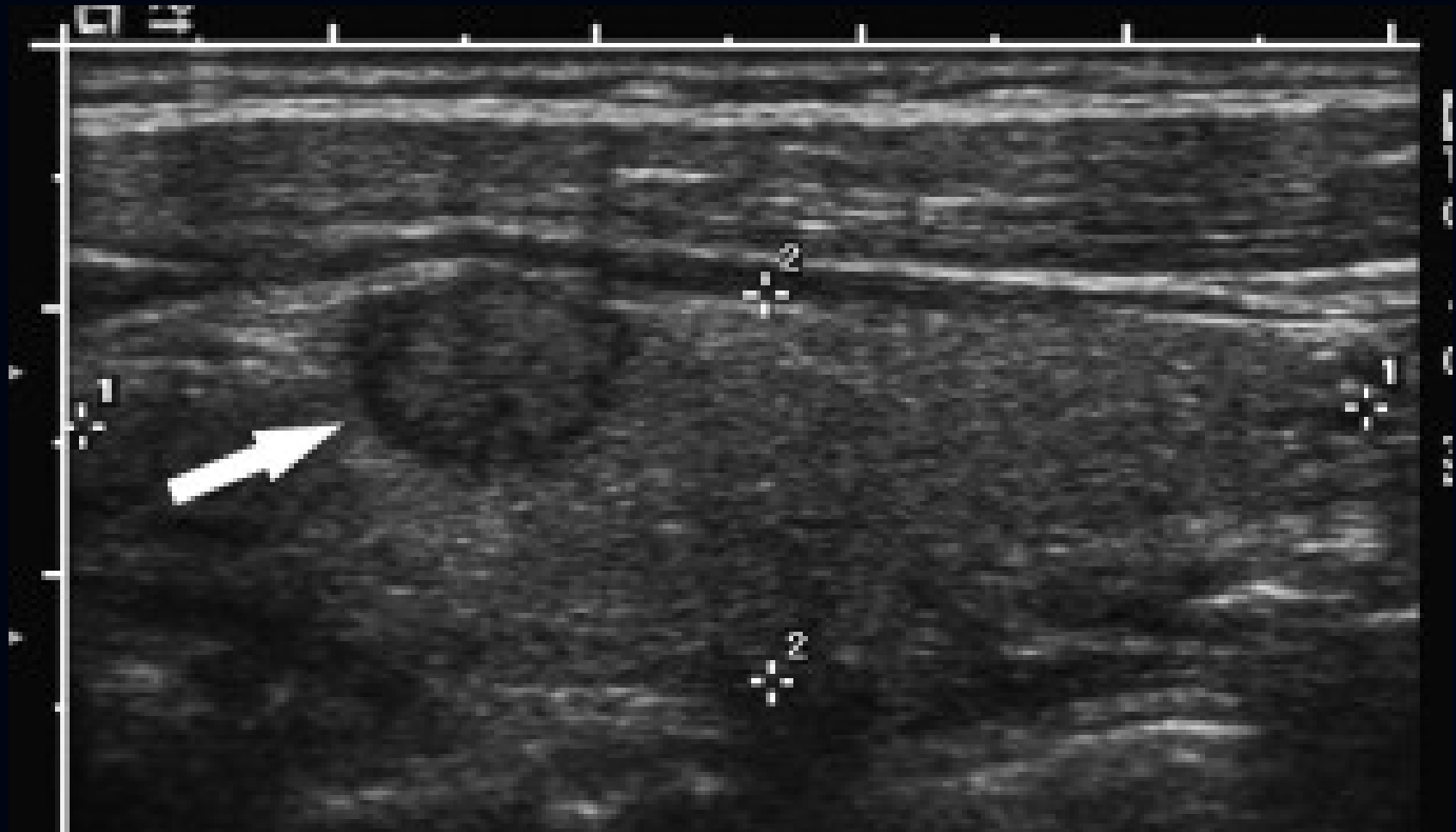
Follicular Neoplasm



Sonolucent Halo

- Previously a sonolucent halo was thought to be representative of a benign nodule, yet now has been seen in **10% to 24%** of **papillary cancers**.

Halo in Papillary Cancer



Calcifications

- Even **eggshell calcifications** which are usually considered a benign finding, have been reported in **thyroid cancers** .

Eggshell Calcifications Papillary Cancer



Margins

- Furthermore, an **irregular margin**, which is typically the most worrisome feature, has the **highest interobserver variability**.
- In addition, small benign nodules $< 1\text{cm}$ can show a spiculated margin therefore mimicking cancer.

Size

- **Size is not a good predictor of malignancy.**
- (Trend toward higher rate of malignancy in nodules larger than 3-4 cm.)

Now what?!!!



204,460,250 Patients with nodules!

Radiology

May 2008

Editorials

**Thyroid Nodules: Is It Time to
Turn Off the US Machines?**

John J. Cronan, MD

Brown University

Washington, DC, October 26–27, 2004

- A **Conference** was convened to determine which thyroid nodules should undergo US-guided fine-needle aspiration (FNA) and which need not undergo FNA.
- **19 Panelists:**
 - ✓ **Radiology**
 - ✓ **Endocrinology**
 - ✓ **Pathology**
 - ✓ **Surgery**

Washington, DC, October 26–27, 2004

- Depts of Radiology, Pathology, Endocrinology, Medicine at Brigham and Women's Hosp, **Harvard Medical School**.
- Depts of Radiology, Pathology, and Endocrinology (I.D.H.), **Mayo Clinic**, Rochester, Minn.
- Dept of Surgery, **UCSF**

Washington, DC, October 26–27, 2004

- Dept of Radiology, Endocrinology, Hosp of the **Univ of Pennsylvania.**
- Dept of Radiology, **Brown** Univ
- Depts of Surgery and Endocrine, Univ of Texas **M.D. Anderson**
- Dept of Radiology, **Duke** Univ Medical School, Cancer Ctr, Medical School

Washington, DC, October 26–27, 2004

- Dept of Radiology, Thomas **Jefferson** Univ
- Dept of Radiology, **Stanford** Univ
- Dept of Radiology, Mallinckrodt Inst,
Washington Univ School of
- Dept of Radiology, **Univ of Alabama**

Radiology

December 2005

Consensus Statement

Management of Thyroid Nodules Detected at US

US Feature	Recommendation
Solitary nodule	
Microcalcifications	Strongly consider US-guided FNA if ≥ 1 cm
Solid (or almost entirely solid) or coarse calcifications	Strongly consider US-guided FNA if ≥ 1.5 cm
Mixed solid and cystic or almost entirely cystic with solid mural component	Consider US-guided FNA if ≥ 2 cm
None of the above but substantial growth since prior US examination	Consider US-guided FNA
Almost entirely cystic and none of the above and no substantial growth (or no prior US)	US-guided FNA probably unnecessary
Multiple nodules	Consider US-guided FNA of one or more nodules, with selection prioritized on basis of criteria (in order listed) for solitary nodule*

5 Features

- Microcalcifications
- Coarse Calcifications and/or Solid
- Predominantly Cystic
- Almost entirely Cystic
- Size

Calcifications

- **Microcalcifications** -
High specificity for Papillary Cancer.
85-95%
- **Coarse calcifications** - Are a common feature of **Medullary carcinoma** (.4% Nodules)
But also seen in **Hyperplastic Nodules**.

Cystic versus Solid

- **Thyroid cancer is not common in predominantly cystic nodules.**
- **Nodules that are nearly completely cystic are virtually never cancers** in the absence of other concerning features.

Microcalcifications

■ Biopsy ≥ 1 cm

Coarse Calcifications or Solid Nodule without calcifications

■ Biopsy ≥ 1.5 cm

Mixed Solid and Cystic

■ Biopsy ≥ 2 cm

Almost Entirely Cystic

- Biopsy Unnecessary

What about size?

Size

- Size is a good predictor of **PROGNOSIS !**

- Size is not a good predictor of **malignancy**

(except there is a trend to higher rate of malignancy in nodules greater than 3 – 4 cm).

Size

- Some studies have shown that Papillary Microcarcinomas (<10mm) demonstrate no difference in mortality between patients who underwent surgical resection versus observation alone.
- Autopsy series have shown that up to 30% of adults have incidental occult cancers smaller than 1 cm at time of death.

Size

- Well differentiated thyroid neoplasms are typically slow growing tumors with an excellent prognosis.

Is it really “Prostate Cancer” in disguise?

- Some refer back to the early days of prostate ultrasound, which led to an increase in biopsies, more cancer diagnoses, and many prostatectomies, but had little impact on the mortality rate.

The agreement then was to observe longer.

Size

- However tumor size > 1.0 cm is associated with:

1. Multifocal or bilateral thyroid tumor
2. Extrathyroidal invasion
3. Local lymph node metastases

- * All can affect prognosis

Or is it closer to Breast Cancer?

Breast Imaging: Kopans 2007

1. Size does not predict malignancy
2. However size is the most important prognostic feature.
3. Worsening of prognosis when cancers are $> 1\text{cm}$.

* However, unlike Thyroid Cancers, there is a proven great benefit to diagnosing small tumors.

Consensus Panel Summary

■ Compromise -

“The size limitations for each category are based on consideration of the excessive number of biopsies of small nodules, and the likelihood that treatment of **microcarcinomas** (< 1 cm) does not improve life expectancy.”

Microcalcifications

■ Biopsy ≥ 1 cm

Coarse Calcifications or Solid Nodule without calcifications

■ Biopsy ≥ 1.5 cm

Mixed Solid and Cystic

■ Biopsy ≥ 2 cm

Almost Entirely Cystic

- Biopsy Unnecessary

What about Multiple Nodules?

Multiple Breast Nodules

Breast Imaging: Kopans 2007

“Multiple rounded densities with sharp margins almost invariably represent a benign process.”

“Sickles has coined the rule of multiplicity. Three or more of the same lesion are almost always benign (with the exception of spiculated or irregularly shaped masses) and do not require further investigation.”

Multiple Thyroid Nodules

- However with multiple thyroid nodules, while the cancer rate per nodule decreases, the decrease is approximately proportional to the number of nodules, so that the overall rate of cancer is the same as that in patients with a solitary nodule.

Multiple Nodules

- Therefore it is recommend to biopsy 1 or more suspicious nodules, prioritizing the selection based on criteria described for a solitary nodule.

Multiple Thyroid Nodules

- Biopsy of only the dominant nodule will result in detection only of approximately two-thirds of thyroid cancers.

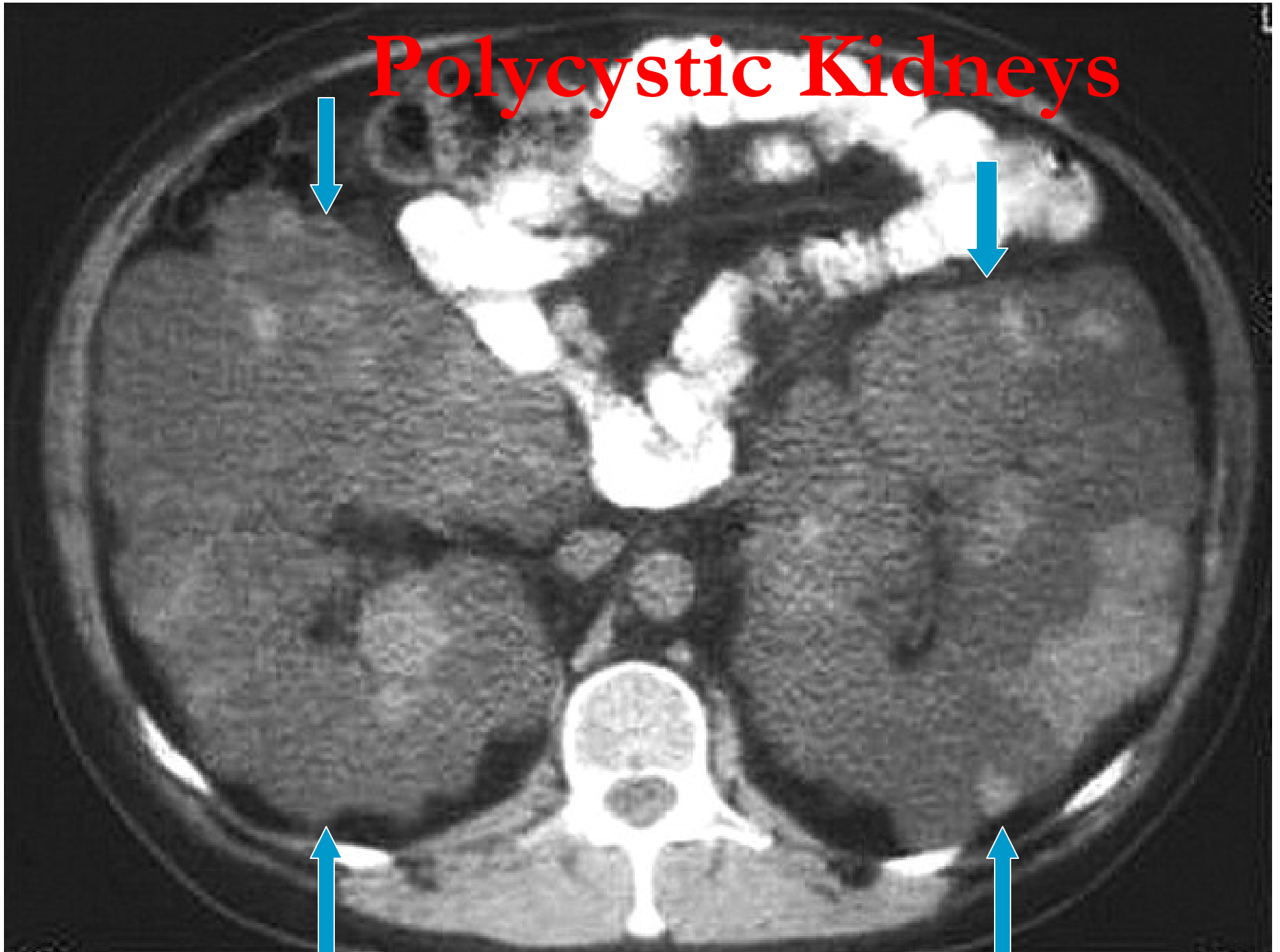
Multiple Thyroid Nodules

- A Thyroid Gland with Multiple Nodules is **NOT** a Multinodular Goiter.

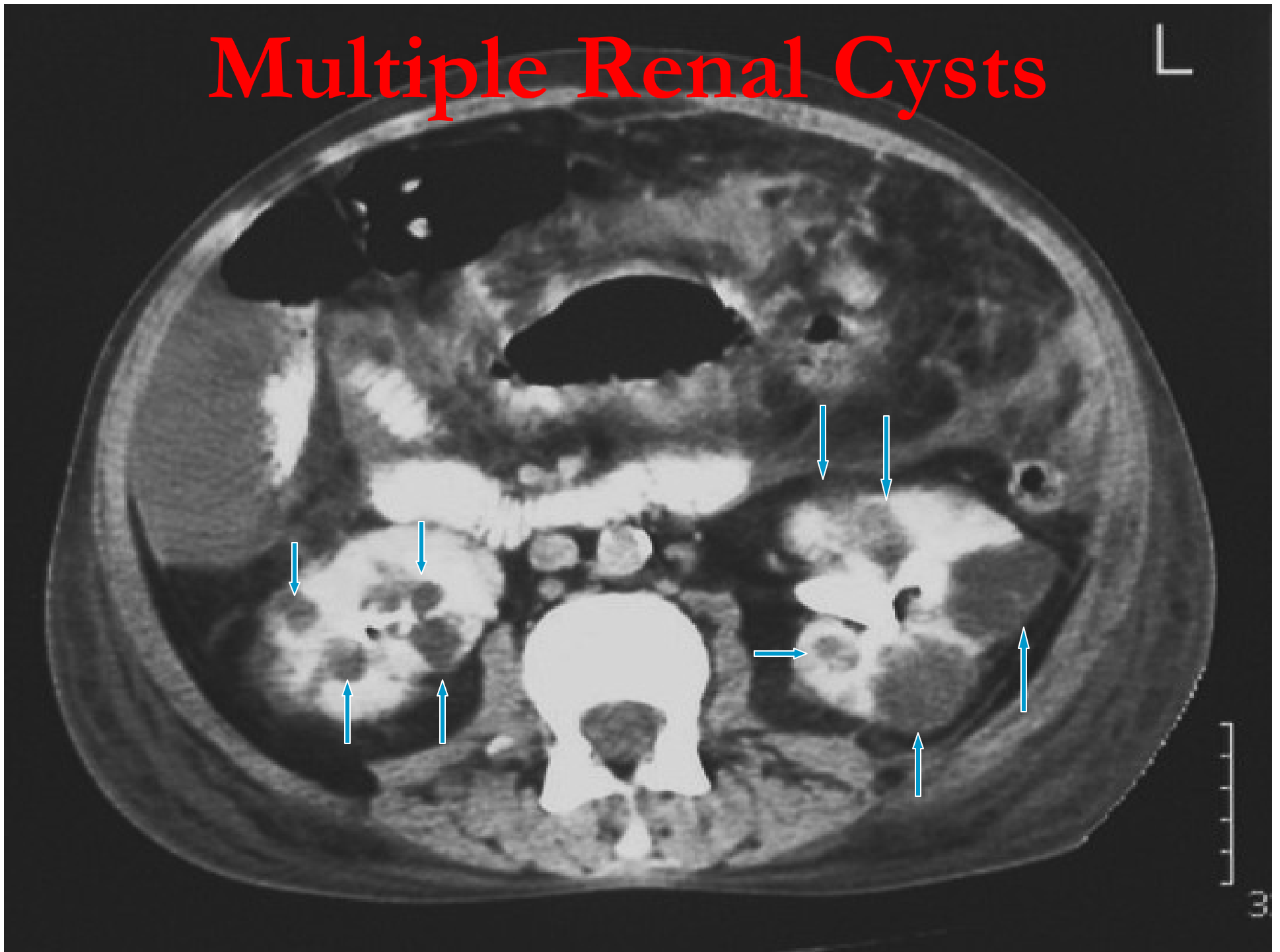
Multiple Thyroid Nodules

- Similarly Polycystic Kidneys are different than Multiple Renal Cysts.

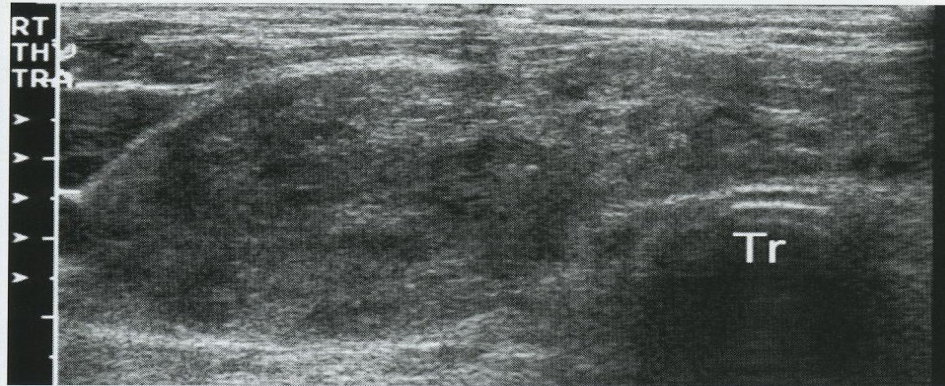
Polycystic Kidneys



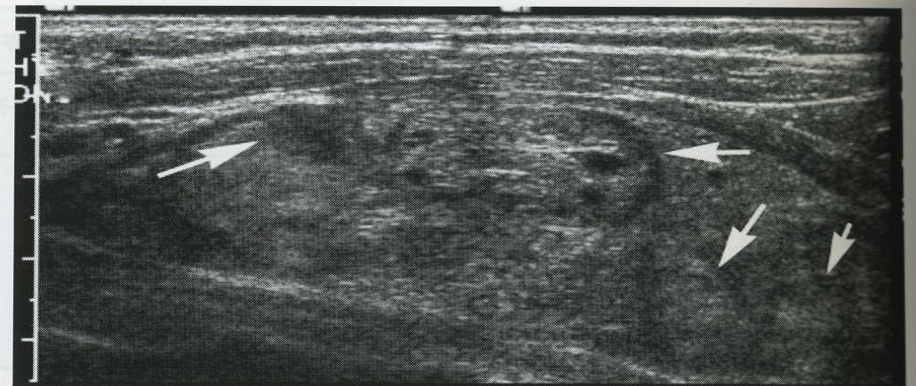
Multiple Renal Cysts



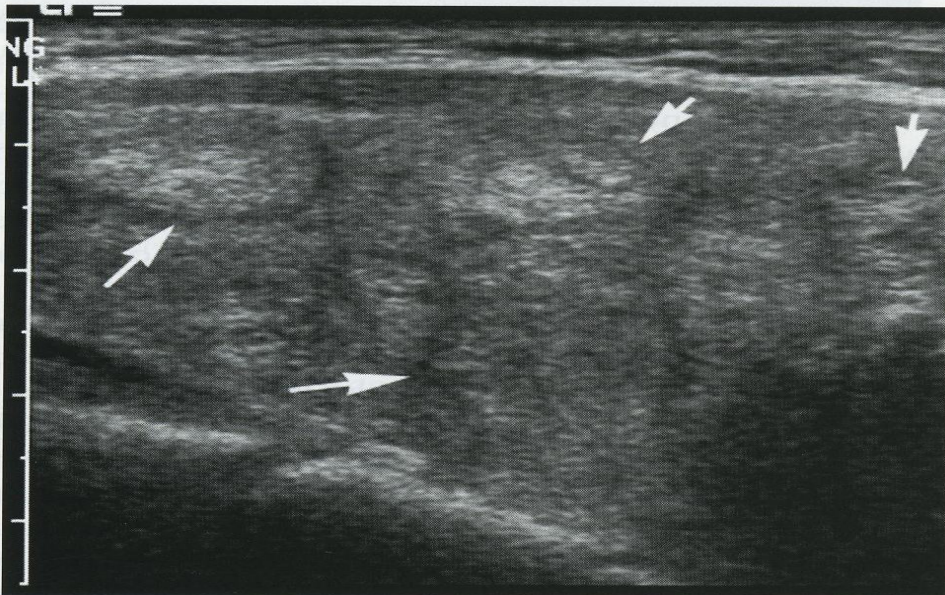
Multinodular Goiter



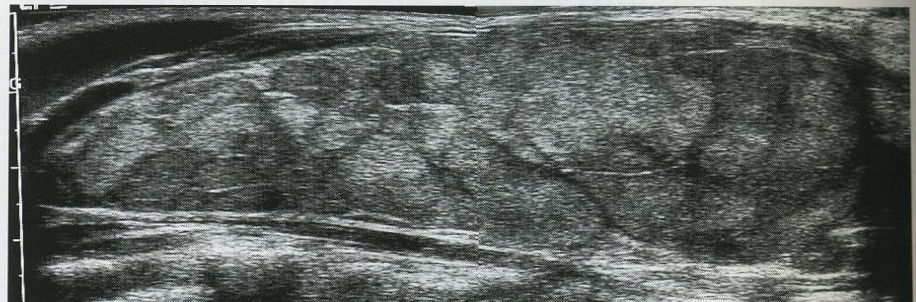
A



B

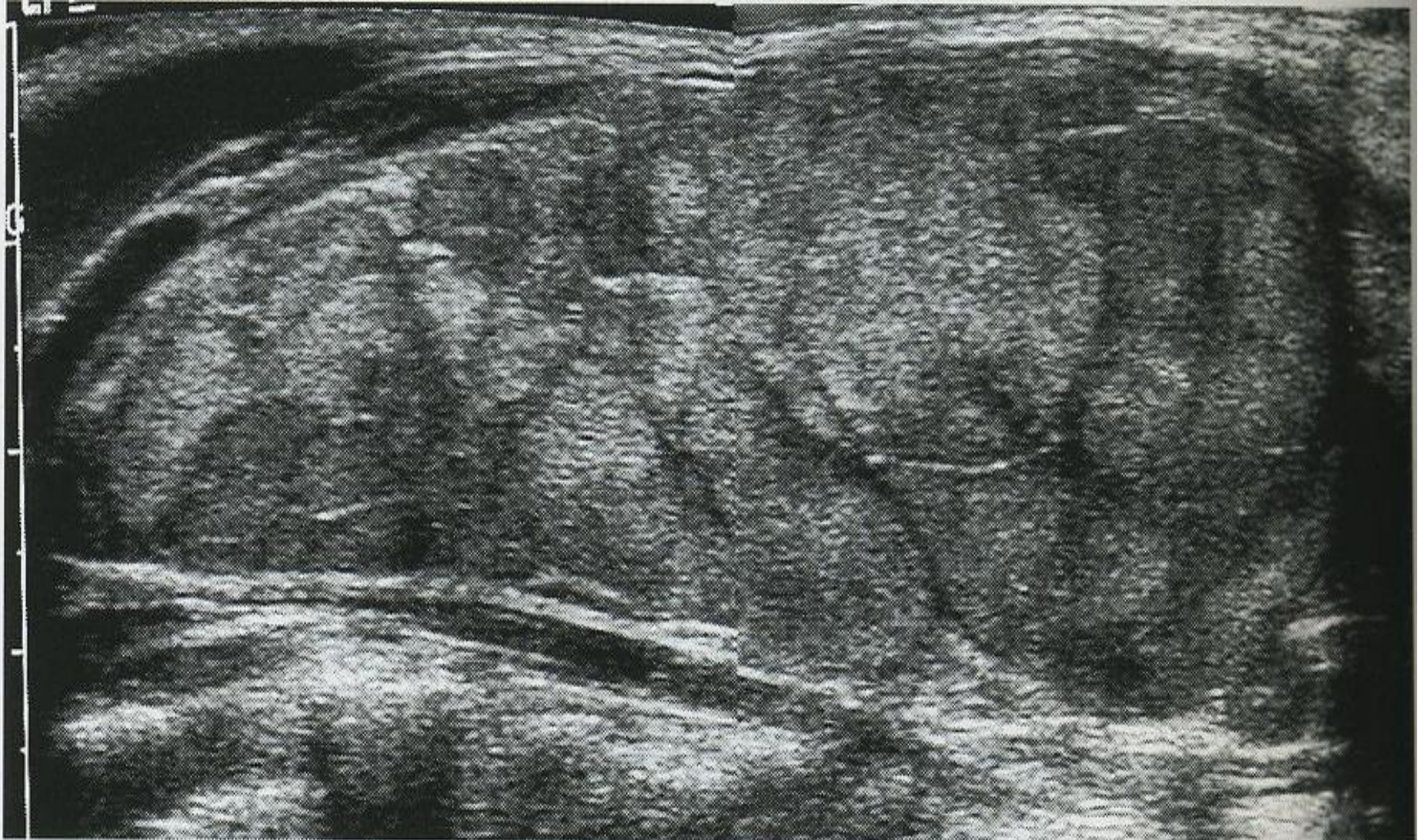


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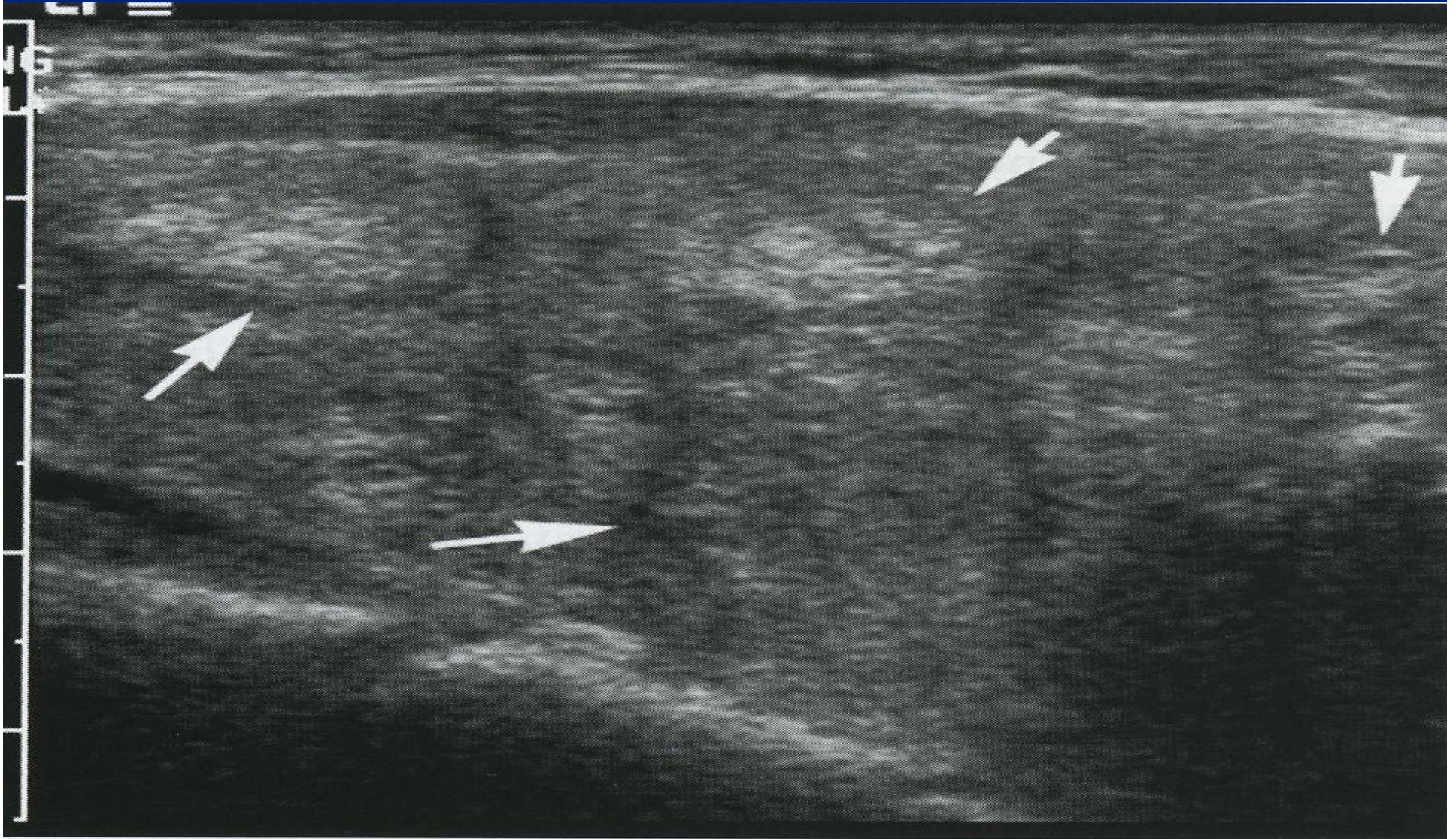


D

Multinodular Goiter



Multinodular Goiter



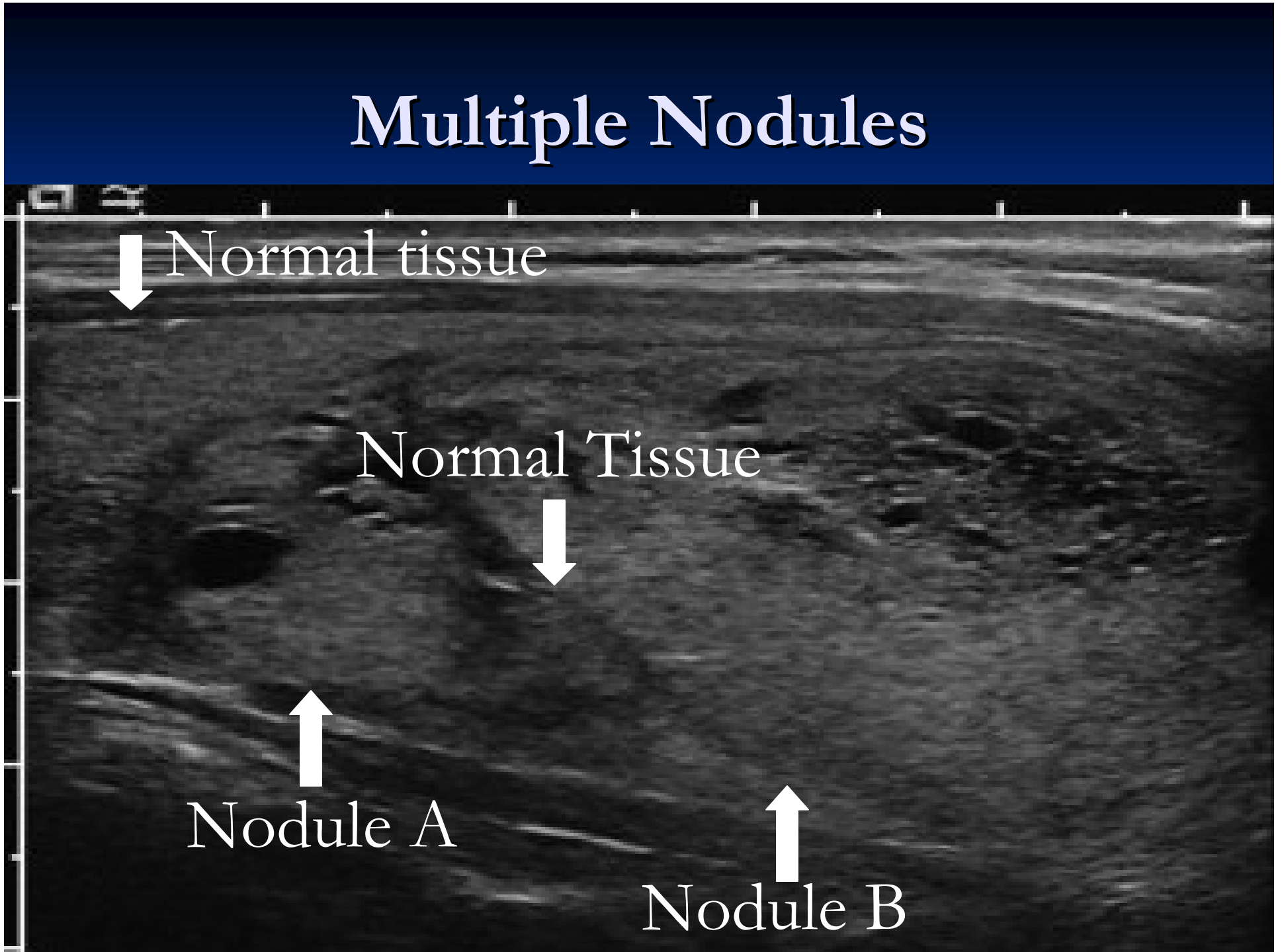
Multiple Nodules

↓ Normal tissue

Normal Tissue
↓

↑
Nodule A

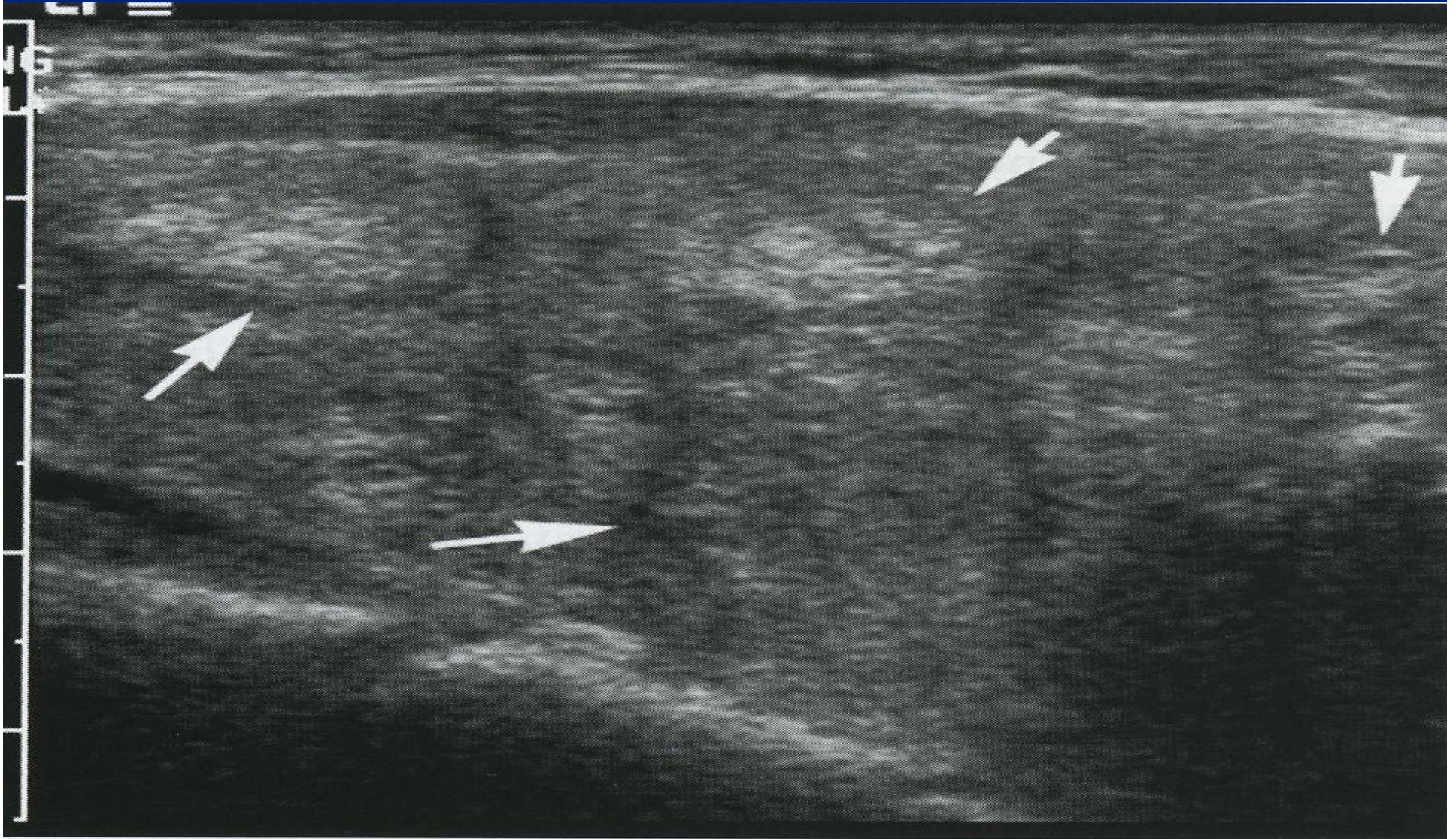
↑
Nodule B



Multiple Thyroid Nodules

- *“FNA is likely unnecessary in diffusely enlarged glands with multiple nodules of similar US appearance **without intervening normal parenchyma.**”*
- (Biopsy is however recommended if there is a dominant nodule.)

Multinodular Goiter



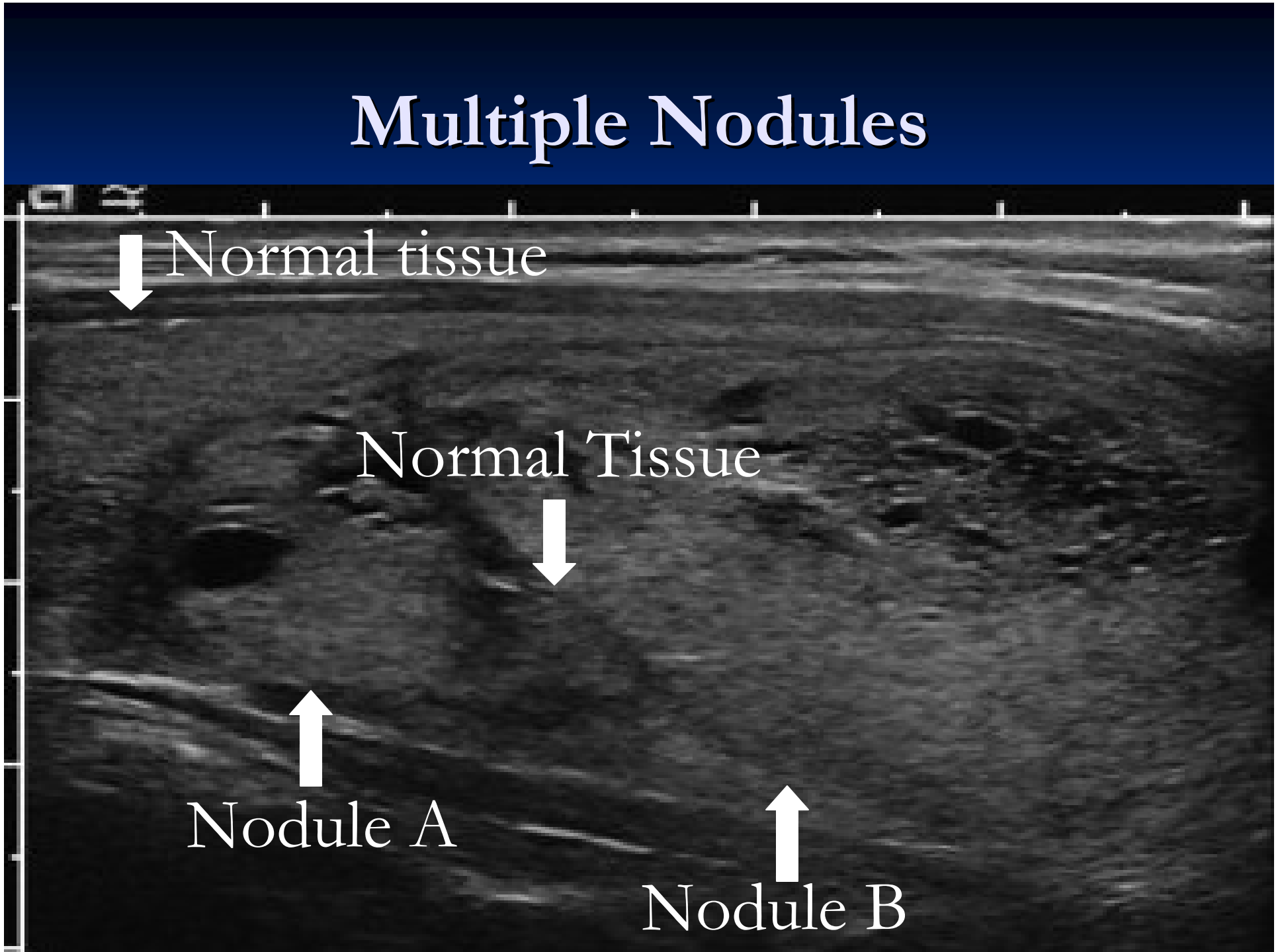
Multiple Nodules

↓ Normal tissue

Normal Tissue
↓

↑
Nodule A

↑
Nodule B



Unanswered Questions

- How often should we monitor growth.
- What constitutes significant growth?

Follow-up Interval

- Many use 6-12 months, with several using 9-12 months (Thyroid Nodule Clinic MGH).
- I use 9-12 months generally for most nodules.
- However if I have any concerns I will use 6-9 months on occasion.

Significant Growth ?

- A. Maximal diameter increase $>$ than 50%.
- B. Maximal diameter increase of 3 mm or more.
- C. Calculated volume increase of 15% or more .

Volume of Nodule

- Rotational Ellipsoid.

- $L \times W \times D \times \pi / 6 = \text{Volume}$

Recommendations-Not Absolute!

- The recommendations may not apply to all patients, including those who have historical, physical, or any other features suggesting they are at increased risk for cancer or who have a history of thyroid cancer.

High Risk

- History of head and neck or total body radiation
- Family history
- Rapid growth
- Hard, fixed nodule
- Regional, cervical lymphadenopathy.

Moderate Risk

- Male gender
- Age younger than 30 or older than 60 years
- Persistent local symptoms (hoarseness, dysphagia, dysphonia, dyspnea)

Doug Davis - Professional Baseball Player

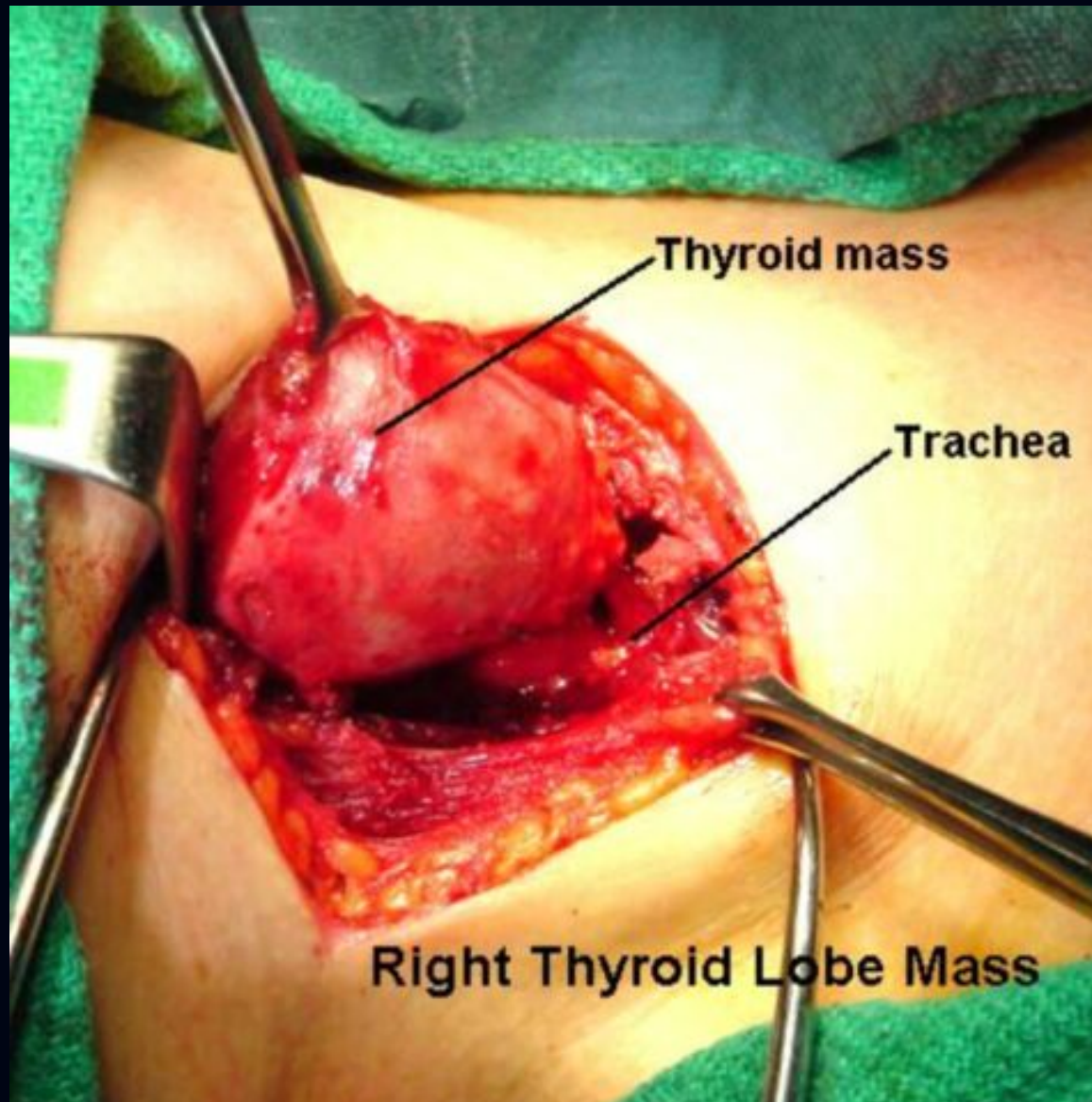
Diagnosed
Thyroid Ca
Mar 2008

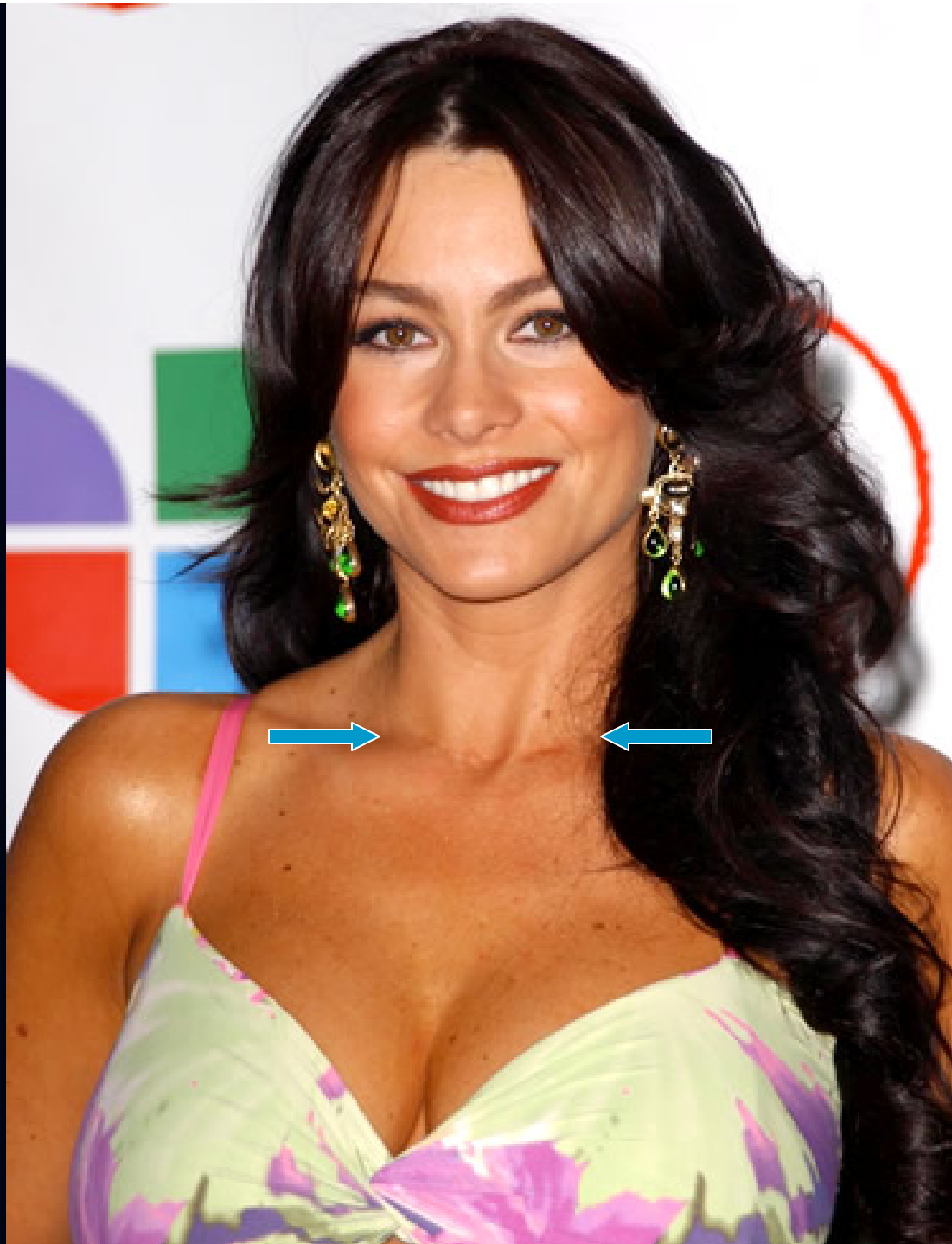


Treatment

- **Papillary cancer is commonly multifocal;** histologically as high as 80%.
- **Therefore many prefer total thyroidectomy.**
- Younger age is associated with an improved prognosis.

Thyroidectomy







Treatment

- Nodal involvement has little impact on prognosis, yet does affect likelihood of recurrence.
- May be evaluated surgically.
- Nodes affected are treated with iodine radioablation following thyroidectomy

CT and MRI

- Lymph node metastases are noted in up to 60-80% of patients.
- However up to 65% of cancerous nodes are normal in size so CT/MRI adds little value.
- (Benign hyperplastic nodes may be large.)

CT and MRI

- Rarely used except:

1. For symptoms such as hoarseness, airway compromise, dysphagia, or a rapidly enlarging neck mass, all of which suggest extension beyond the thyroid gland.
2. Palpable cervical nodal disease for surgical planning.

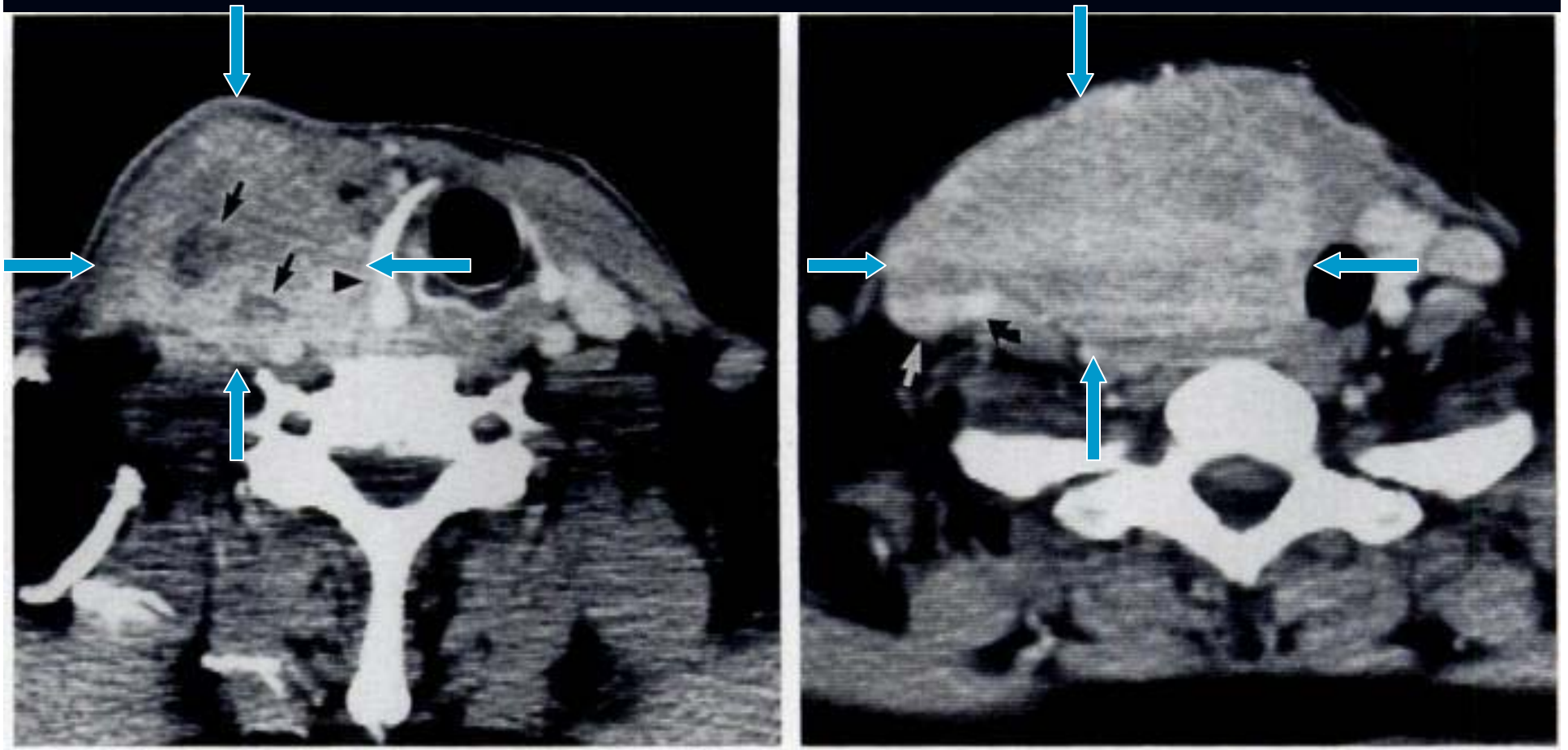
Anaplastic carcinoma

- Rare
- Usually in older patients and is highly aggressive and rapidly fatal.
- Generally large, at least 5 to 10 cm
- Life expectancy is measured in months.

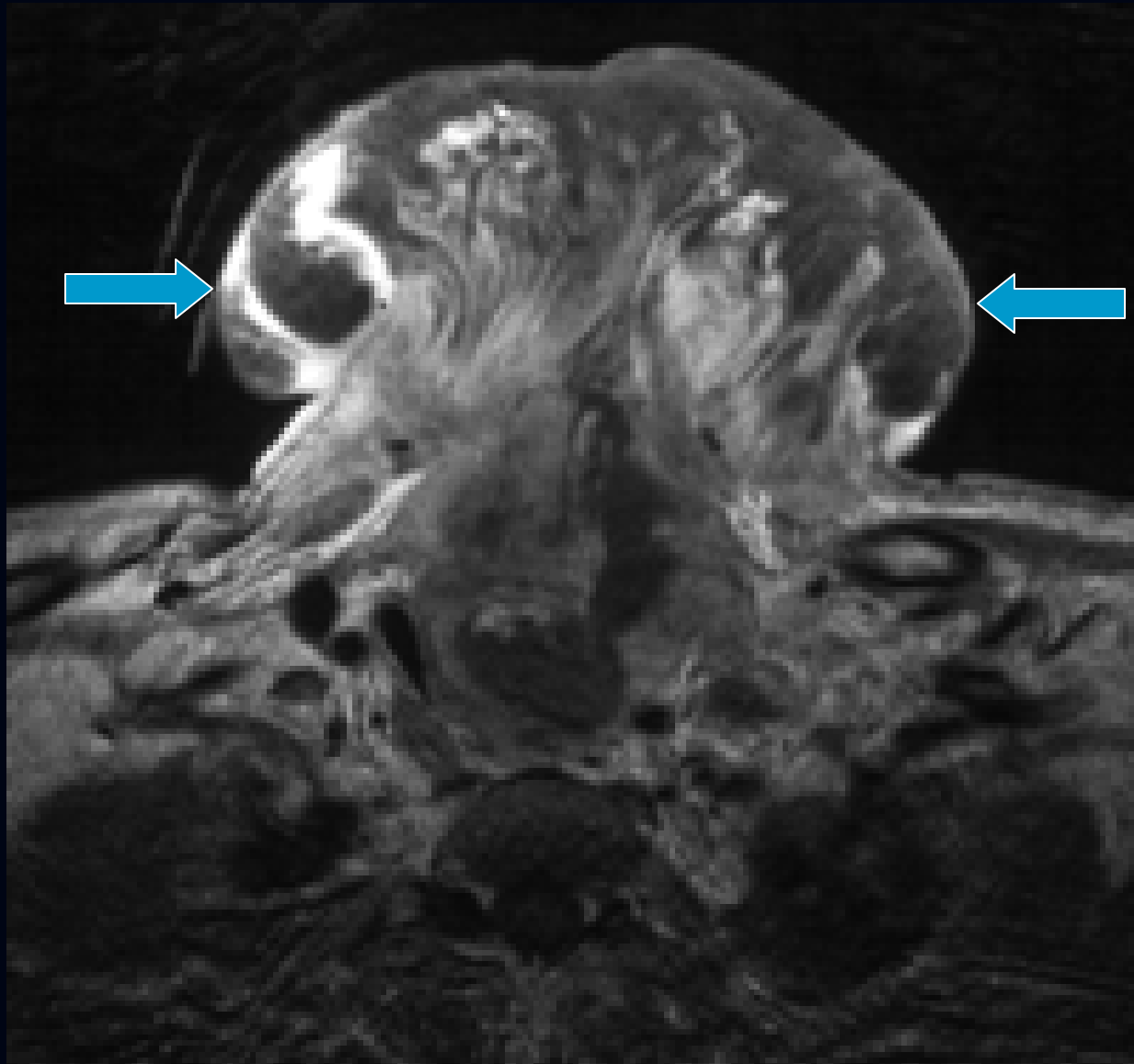
Anaplastic Thyroid Cancer



Anaplastic Thyroid Cancer



Anaplastic Thyroid Cancer



Occupational Exposure

- There is a case where a **speech pathologist** successfully won a lawsuit claiming their thyroid cancer was related to radiation exposure during modified barium swallow examinations.

Occupational Exposure

- *THYROID DOSE MEASUREMENTS FOR STAFF INVOLVED IN MODIFIED BARIUM SWALLOW EXAMS.*

Paper

- Health Physics. 90(1):38-41, **January 2006.**

**There is a linear dose–response
relationship between 100 and 2000
rads and Thyroid Cancer**



In Summary

- Thyroid nodules continue to be a diagnostic dilemma radiologist encounter far too frequently.
- However, now with the aid of the Consensus Panel Recommendations, we can now make more educated decisions and improve patient care.
- One must also use common sense, or at the very least suggest an Endocrinology consult !

Table 2**Management recommendations for thyroid nodules 1 cm or larger in maximal diameter¹**

Sonographic Feature	Recommendation
Solitary nodule	
Microcalcifications	Strongly consider US-guided FNA if ≥ 1 cm
Solid or coarse calcification	Strongly consider US-guided FNA if ≥ 1.5 cm
Mixed cystic and solid or almost entirely cystic with solid mural component	Consider US-guided FNA if ≥ 2 cm
None of the above but substantial growth since prior US	Consider US-guided FNA
Almost completely cystic and without significant growth or features above	US-guided FNA probably not necessary
Multiple nodules	Consider US-guided FNA of one or more nodules, prioritizing selection based on criteria for solid nodules in order listed above

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Thyroid Nodule



Questions?