THYROID NODULE ULTRASOUND
Evidence Base & BTA Guidelines

Dr Steve Colley
Queen Elizabeth Hospital Birmingham

May 2014

AIMS

- Thyroid cancer incidence
- Thyroid nodule appearances
- Scoring systems & Guidelines
- New BTA Guidelines
- Common misunderstandings
- Thyroid US standards

The JAMA Network

All Thyroid Cancer

Incidence Rate per 100 000

9
8
7
6
5
4
3
2
1
0

All
Papillary
Follicular
Poorly Differentiated

1973 1976 1979 1982 1985 1988 1991 1994 1997 2000

Year

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The JAMA Network

Papillary Thyroid Cancer

Incidence Rate per 100 000

4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0

0-1.0 cm
1.1-2.0 cm
2.1-5.0 cm
>5.0 cm

1988 1990 1992 1994 1996 1998 2000 2002

Year

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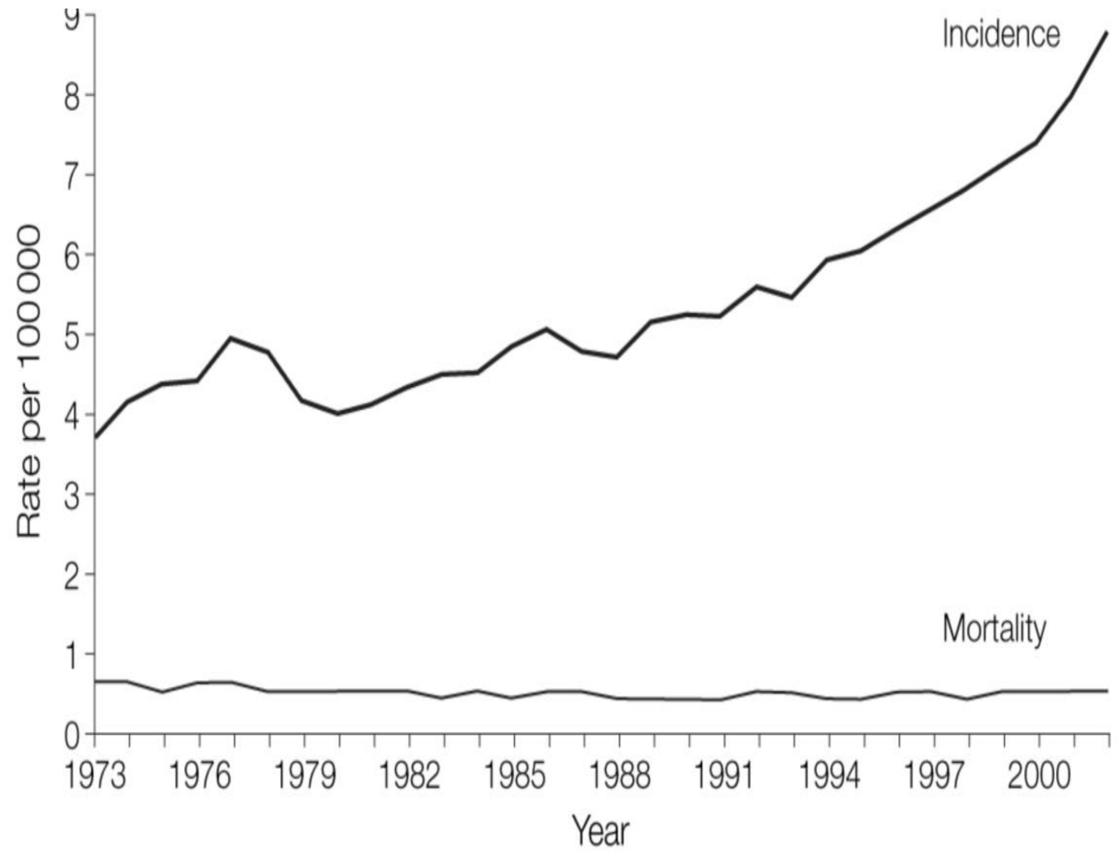

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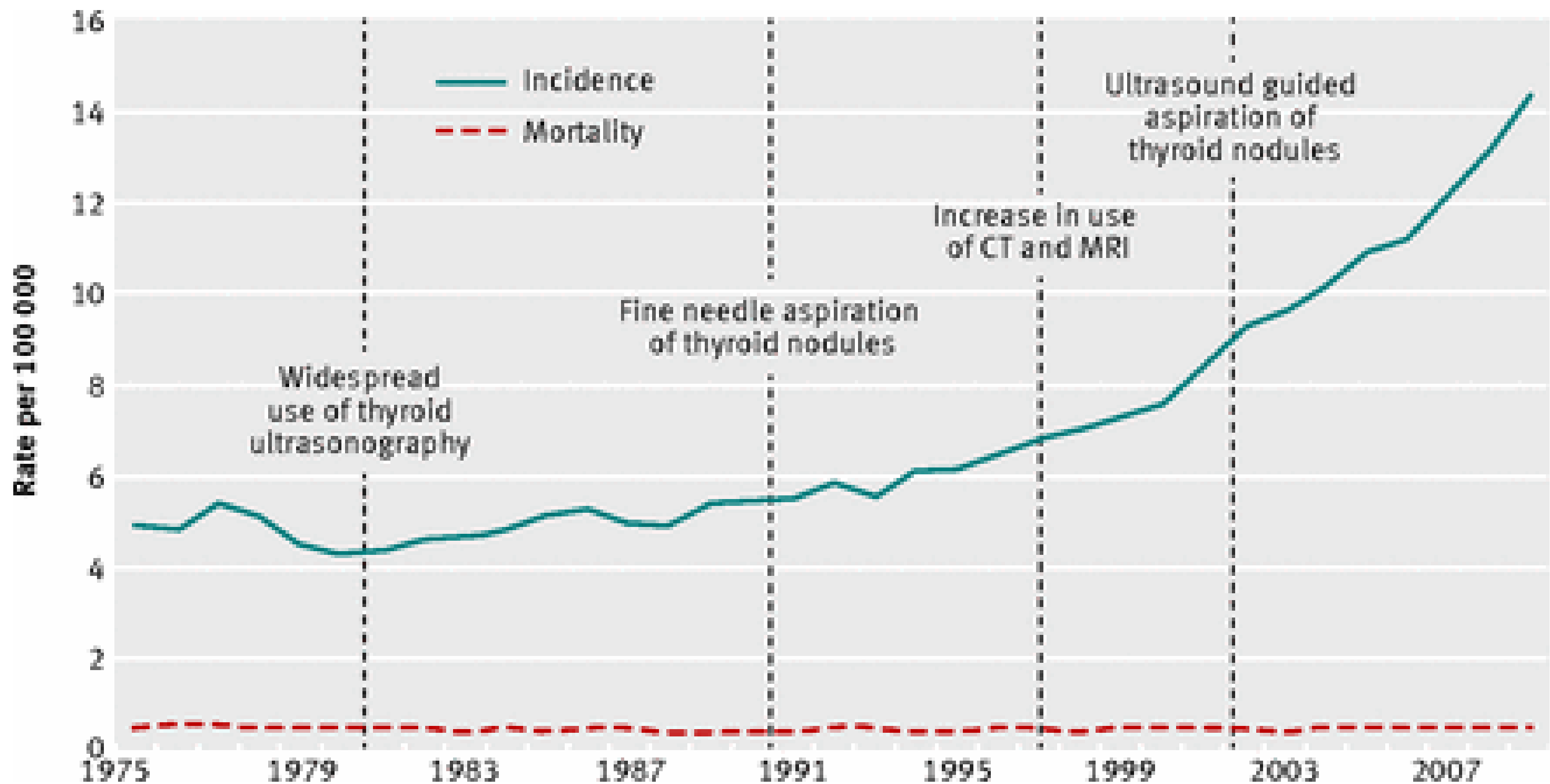
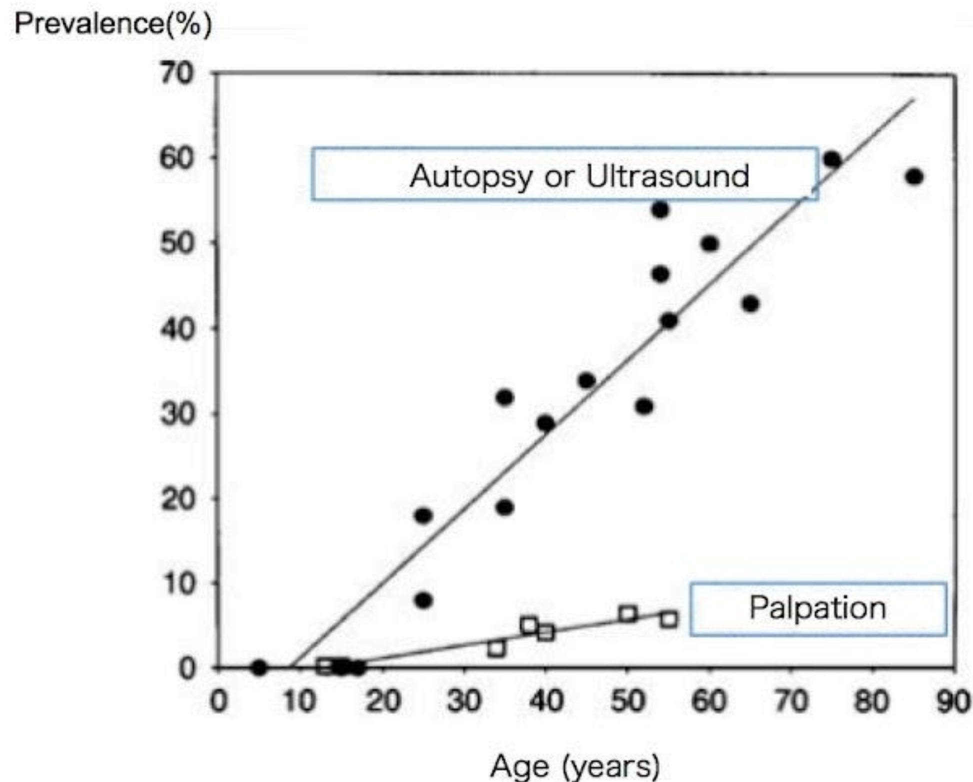
The Role of Imaging…



Thyroid cancer: zealous imaging has increased detection and treatment of low risk tumours. Brito et al. BMJ 2013; 347: 18 – 21.

The Thyroid Nodule Problem



Inappropriate use and reporting of imaging will result in an epidemic of thyroid nodules, the majority of which will be benign.

US Appearances of Nodules

Benign and Malignant Thyroid Nodules: US Differentiation—Multicenter Retrospective Study[1]

Radiology

Radiology 2008; 247:762–770

US Features of Thyroid Malignancy: Pearls and Pitfalls[1]

RadioGraphics 2007; 27:847–865

Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and Color-Doppler Features

Papini *et al.* • Management of Nonpalpable Thyroid Nodules

J Clin Endocrinol Metab, May 2002, 87(5):1941–1946 **1943**

Management of Thyroid Nodules Detected at US: Society of Radiologists in Ultrasound Consensus Conference Statement[1]

Radiology 2005; 237:794–800

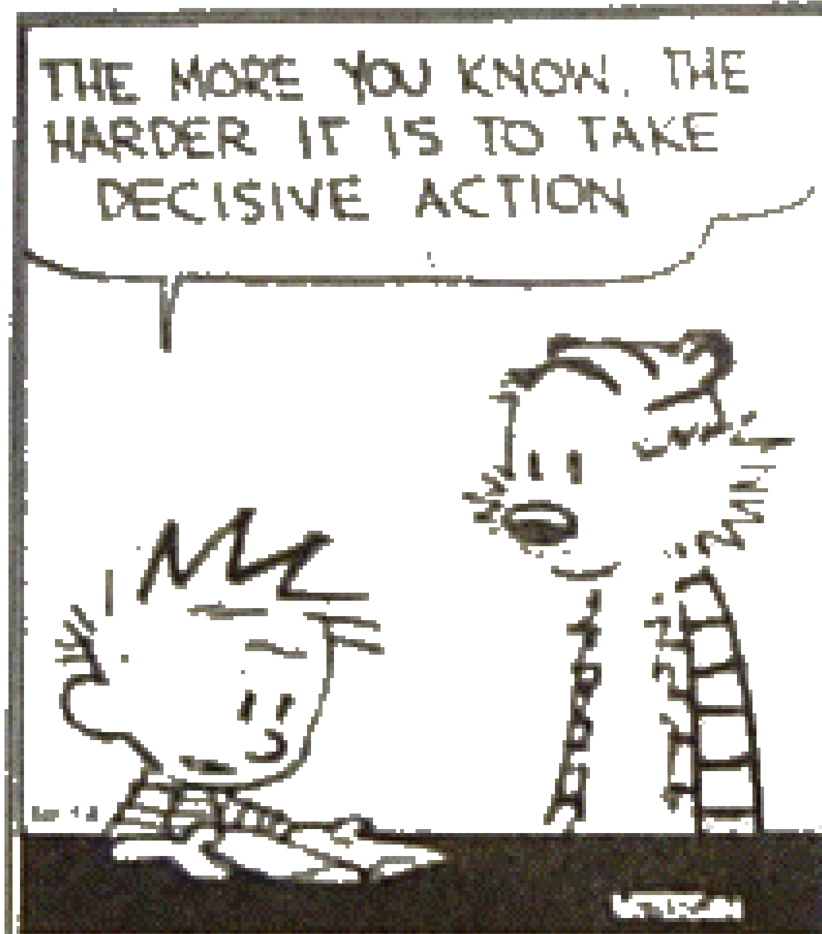
Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

THYROID
Volume 19, Number 11, 2009

Read the Articles…

CALVIN AND HOBBES



US Signs Predictive of Cancer

	Sensitivity	Specificity
Micro-calcifications	40%	90%
Absence of halo	66%	46%
Irregular margins	64%	84%
Hypo-echoic	83%	49%
Intra-nodular flow	70%	65%
MicroCa. & irreg m.	30%	95%
MicroCa. & hypoechoic	28%	95%
Solid & hypoechoic	73%	69%

RSNA 2005

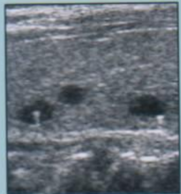
Ultrasound Scoring System

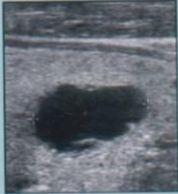
- Mayo Clinic Thyroid US Chart
- TIRADS Scoring System
- U1 – U5 Classification

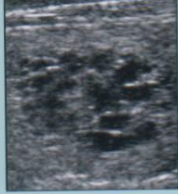
Mayo Clinic Thyroid US Chart

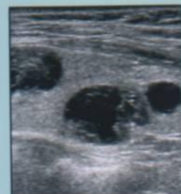
Almost Certainly Benign

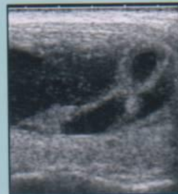
No FNA

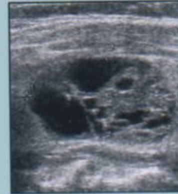

Cysts with bright echo

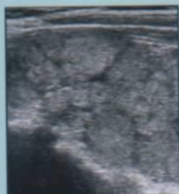
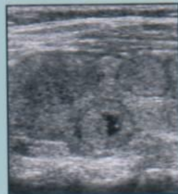

Cystic nodule


Sponge-like nodule


Cystic with debris

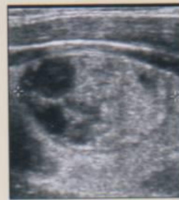
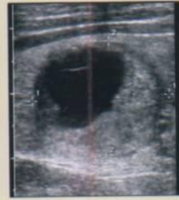

Large cystic nodule with septations

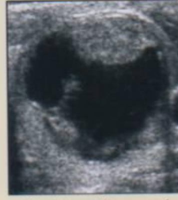

Cystic nodule with debris

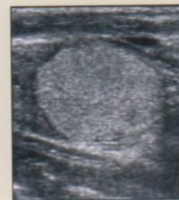
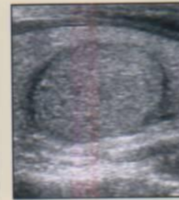


Multiple isoechoic similar nodules (multinodular goiter)

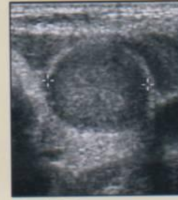
Multiple discrete solid hypoechoic nodules with coarse parenchymal septations (Hashimoto's Thyroiditis)

Indeterminate



Solid with cystic component


Cystic with mural nodule



Solid, homogenous with thin halo


Solid, homogenous

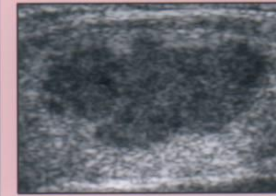
Most are benign, uncommonly follicular or papillary carcinoma

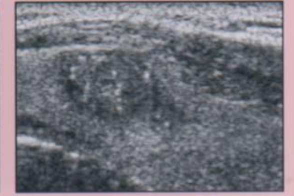
For Indeterminate Nodules Additional Relevant Factors That Would Encourage FNA

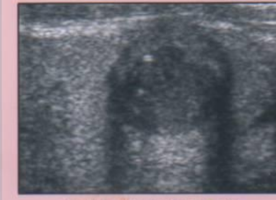
- Family history of thyroid CA
- Previous radiation exposure
- Younger age
- Larger size of nodule

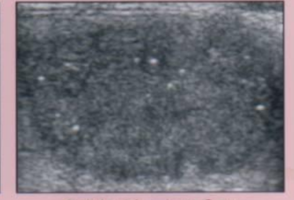
Worrisome for Malignant

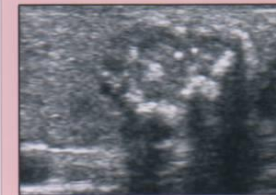
FNA

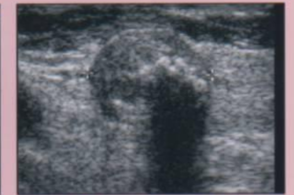

Solid with irregular margins

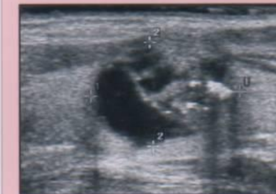

Solid with micro Ca^{++}

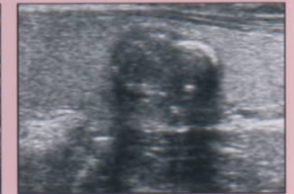

Solid with micro Ca^{++}


Solid with micro Ca^{++}


Fine and coarse Ca^{++}


Solid with Coarse Ca^{++}


Cystic with solid elements and Ca^{++}


Solid with micro and peripheral Ca^{++}

Mayo Clinic Thyroid US Chart

- *"This approach has been effective for the majority of patients with thyroid nodules in our practice. Colour doppler may be of use in selected cases."*

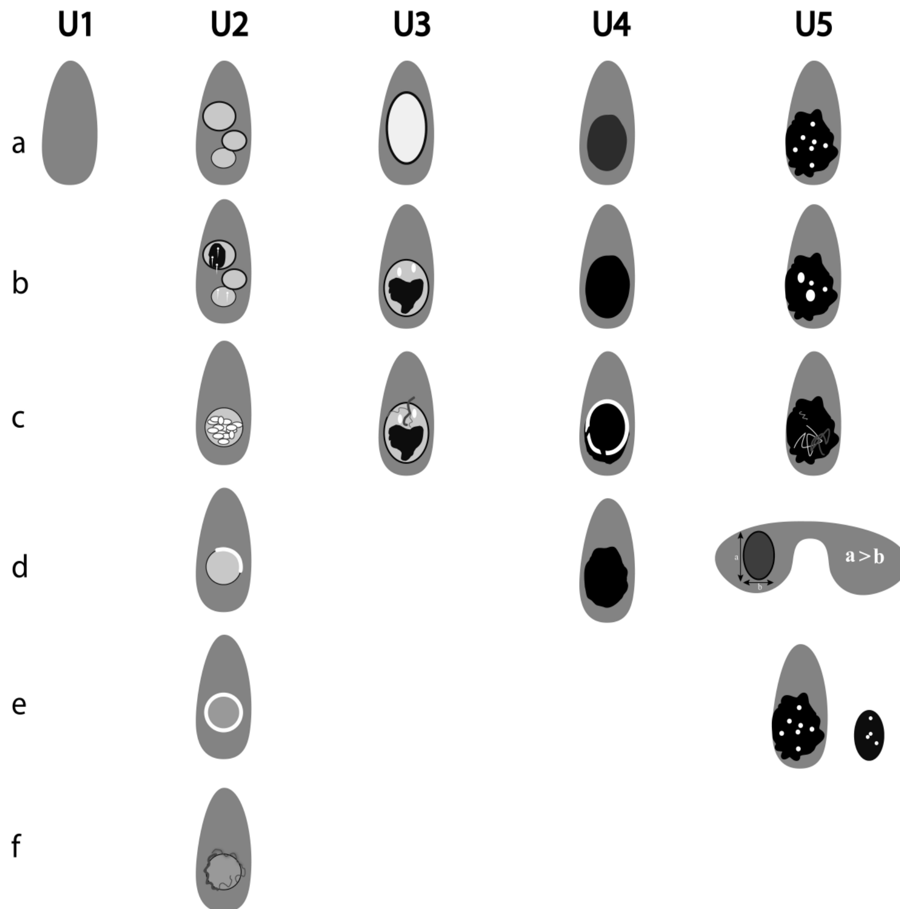
2007 Mayo Clinic Foundation for Medical Education and Research

BTA Guidelines (2007)

- *Ultrasound is rarely of use in assessment of thyroid nodules. It may help guide FNA.*

BTA Guidelines (2014)

- Separate chapter on thyroid nodule US
- Rationalise thyroid US / FNA
  - Suggested standards for reports
  - Indications for FNA
  - Based upon US scoring system
  - U1 – U5
  - Follow up based upon US appearances



U1. Normal.

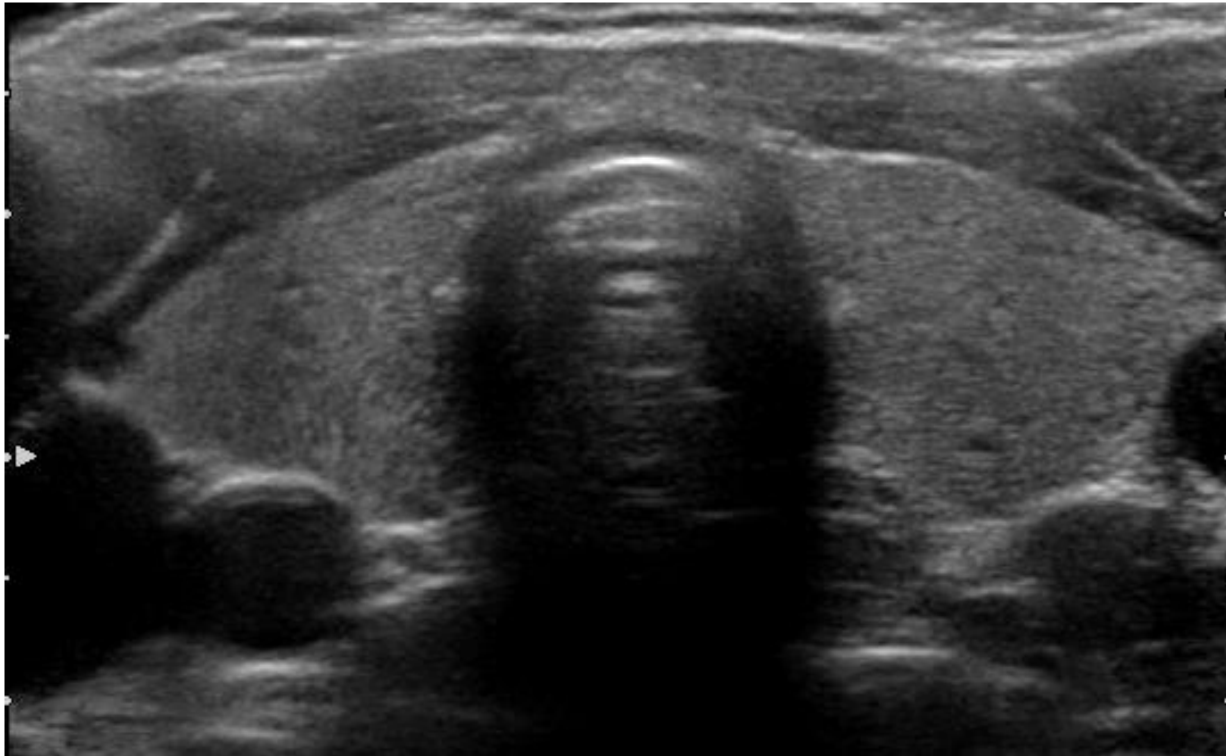
U2. Benign:
(a) halo, hyper- / iso-echoic
(b) cystic change +/- ring down sign (colloid)
(c) micro- cystic / spongiform
(d & e) peripheral egg shell calcification
(f) peripheral vascularity.

U3. Indeterminate/Equivocal:
(a) homogenous, hyper - echoic (markedly), solid, halo (follicular lesion).
(b) ? hypo-echoic, equivocal echogenic foci, cystic change
(c) mixed/central vascularity.

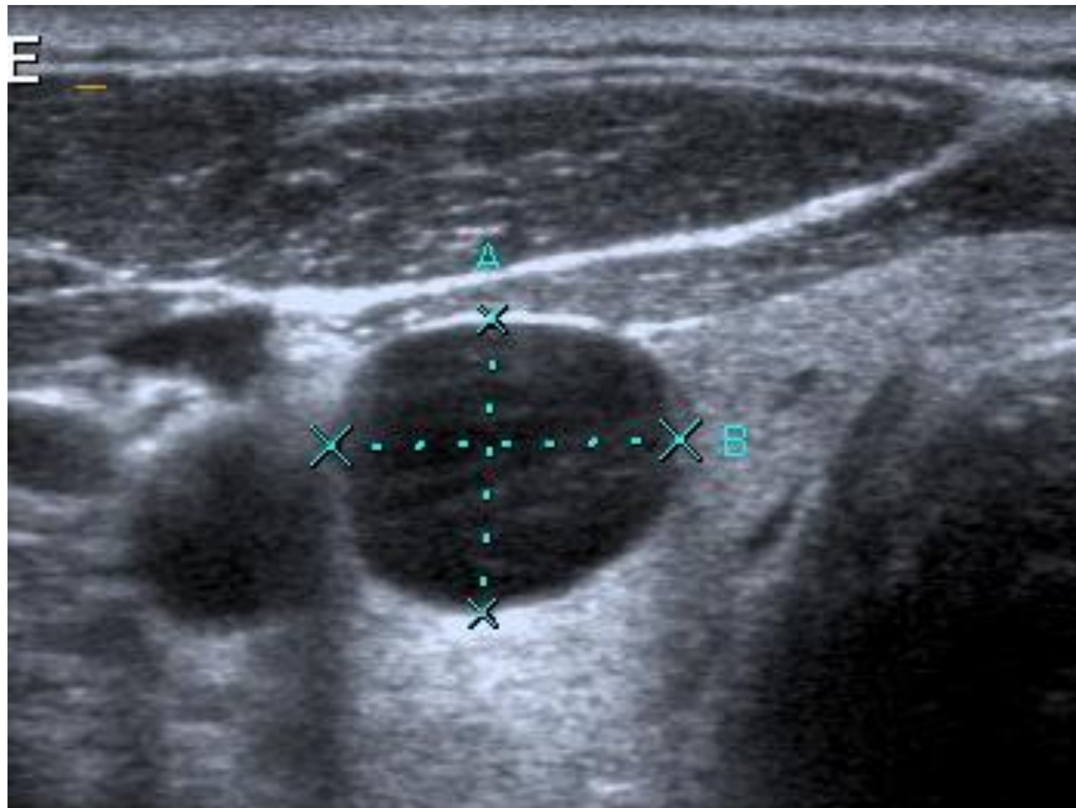
U4. Suspicious:
(a) solid, hypo-echoic (cf thyroid)
(b) solid, very hypo-echoic (cf strap muscle)
(c) disrupted peripheral calcification, hypo-echoic
(d) lobulated outline

U5. Malignant
(a) solid, hypo-echoic, lobulated / irregular outline, micro-calcification. (? Papillary carcinoma)
(b) solid, hypo-echoic, lobulated/irregular outline, globular calcification (? Medullary carcinoma)
(c) intra-nodular vascularity
(d) shape (taller >wide)
(e) characteristic associated lymphadenopathy

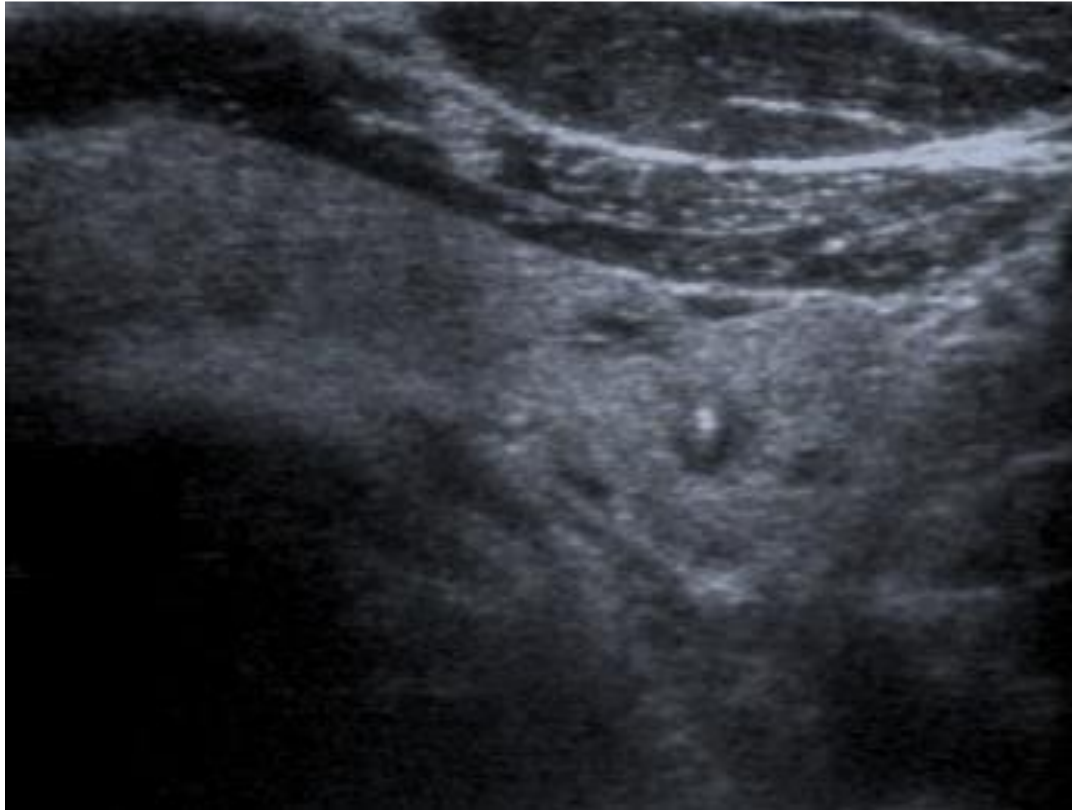
U1 - Normal



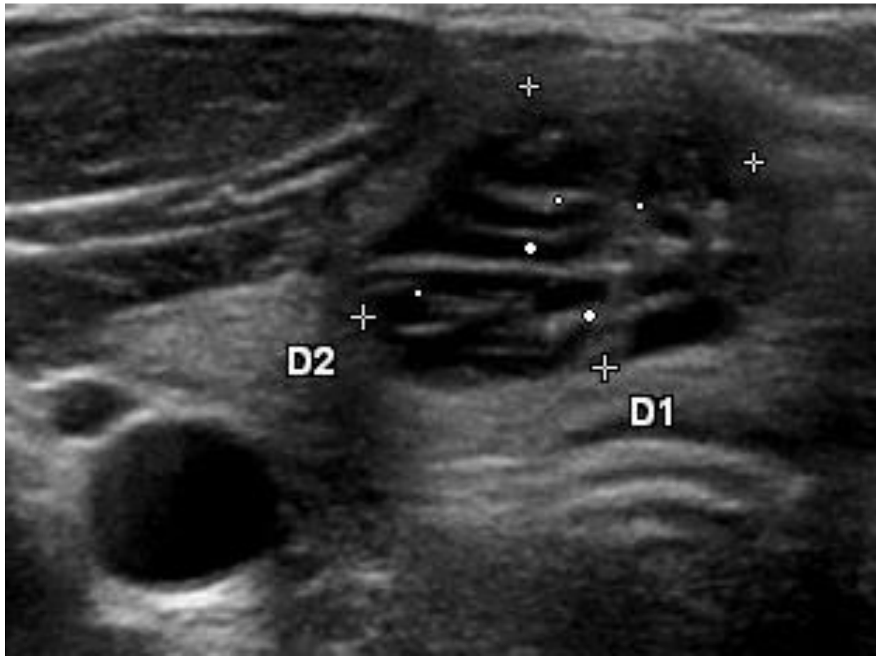
U2 – Benign (cyst)

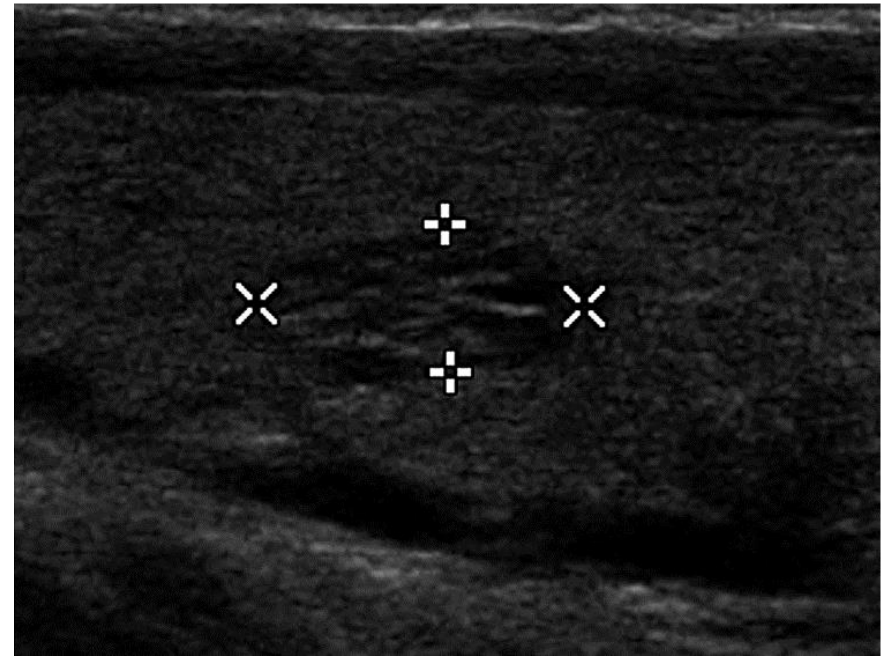


U2 – Benign (cyst with colloid)



U2 – Benign (spongiform nodule)

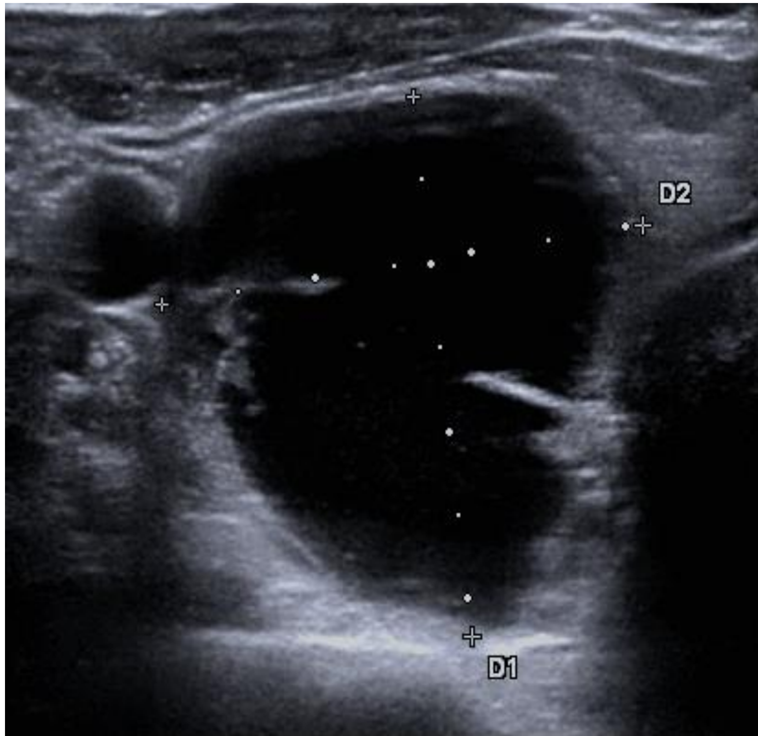


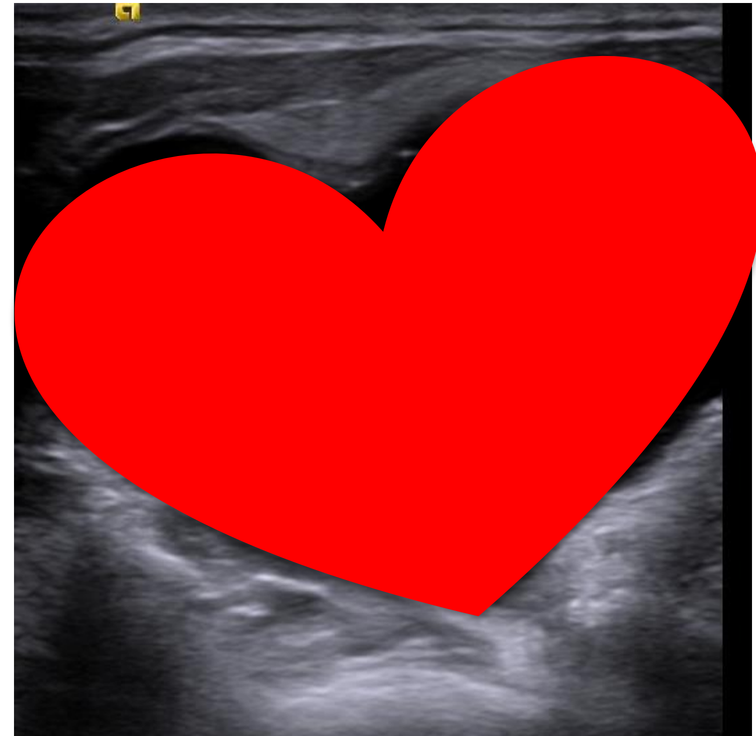


Aggregation of micro-cystic spaces comprising >50% of a nodule
99.7% specificity, 100% if isoechoic nodule

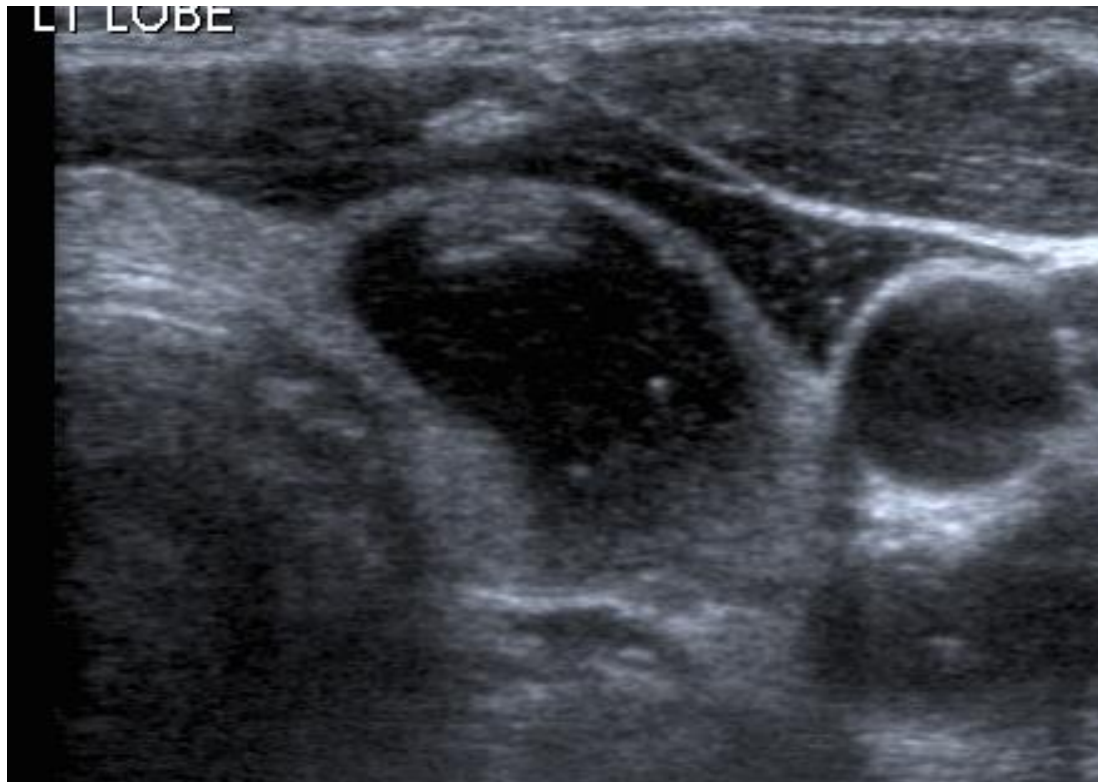
Moon W-J et al. Benign and Malignant Thyroid Nodules: US Differentiation, a multi-center retrospective study. *Radiology* 2008; 247(3): 762 – 770.

U2 – Benign
(large cyst with septations)

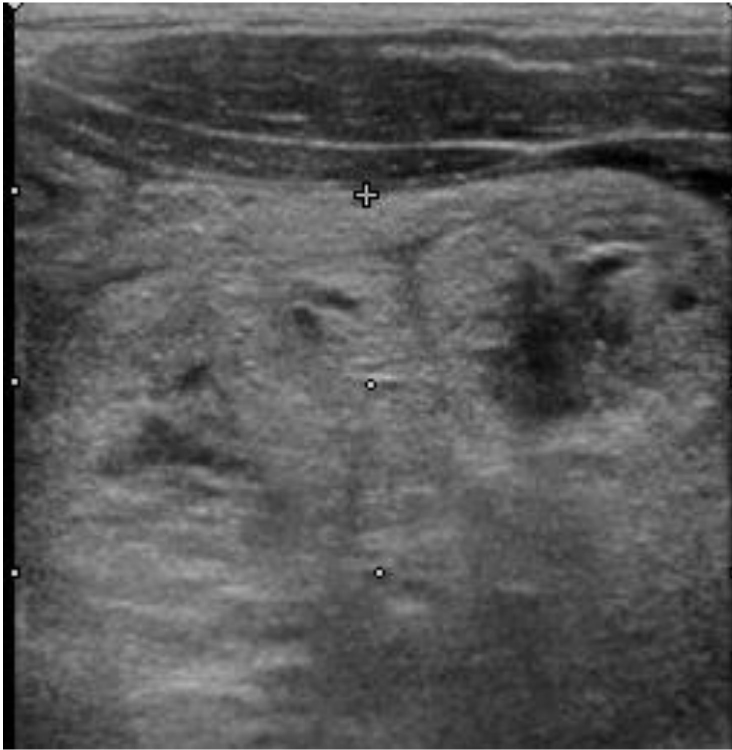


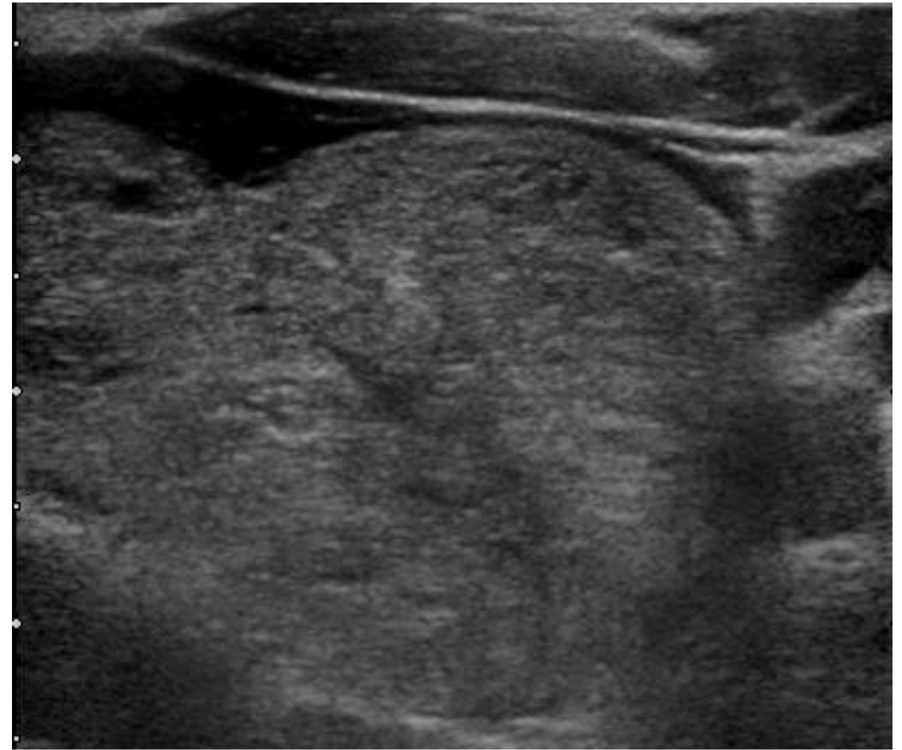


U2 – Benign (cyst with debris)

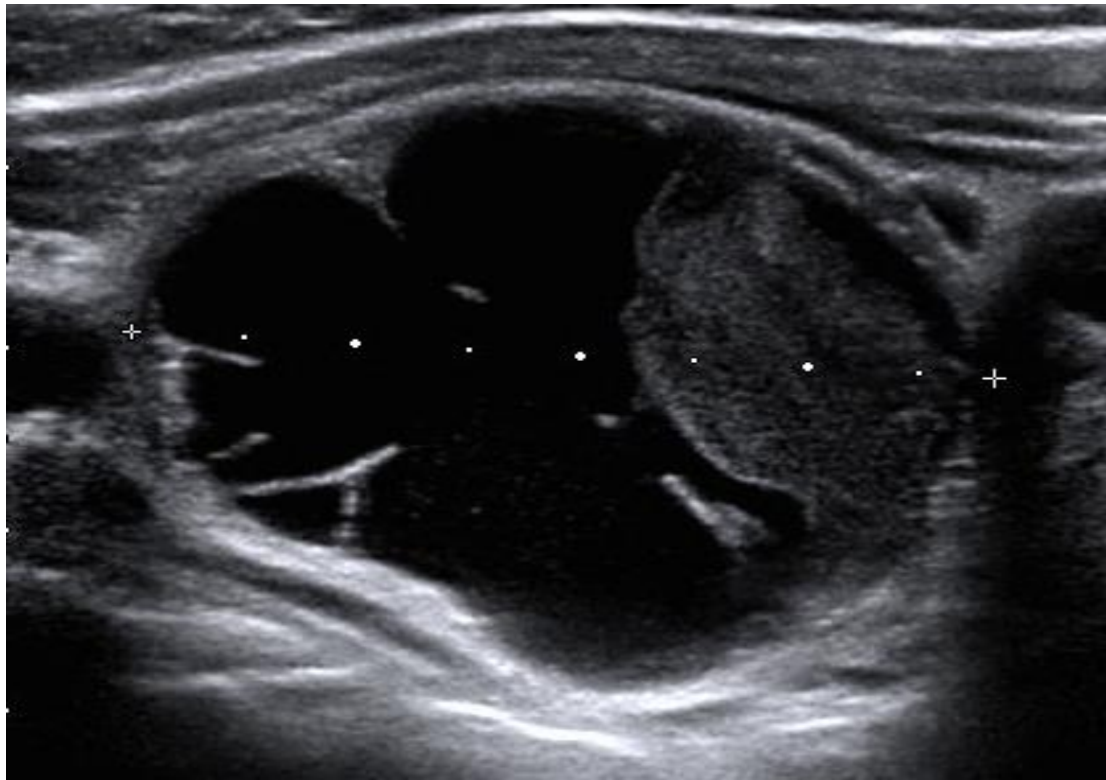


U2 – Benign (multiple isoechoic nodules)

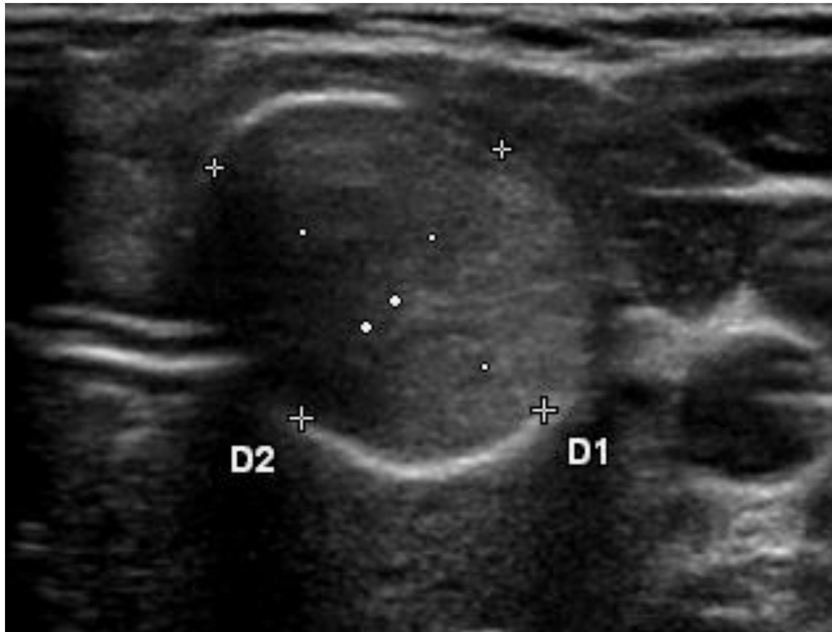


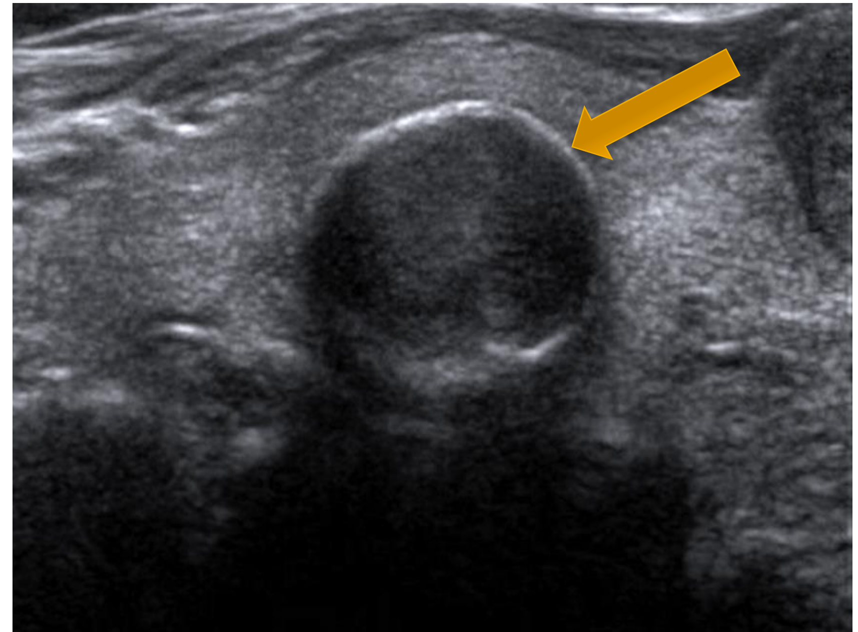


U2 – Benign
(cyst with retracting clot)

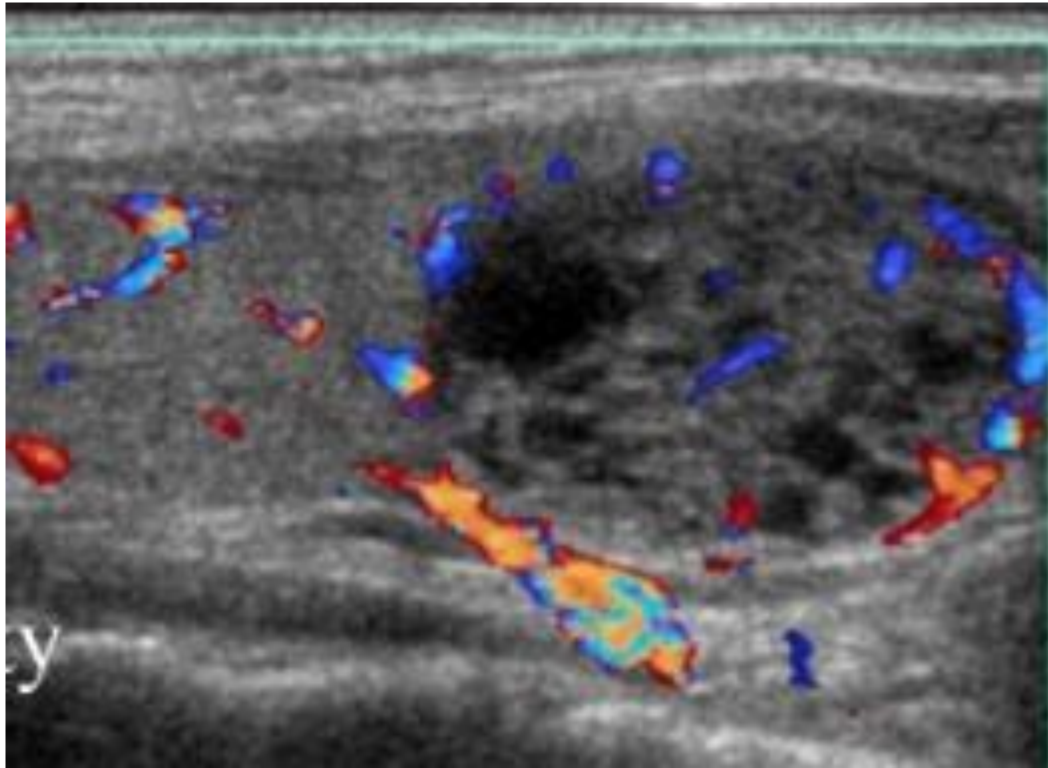


U2 – Benign (peripheral egg shell calcification)

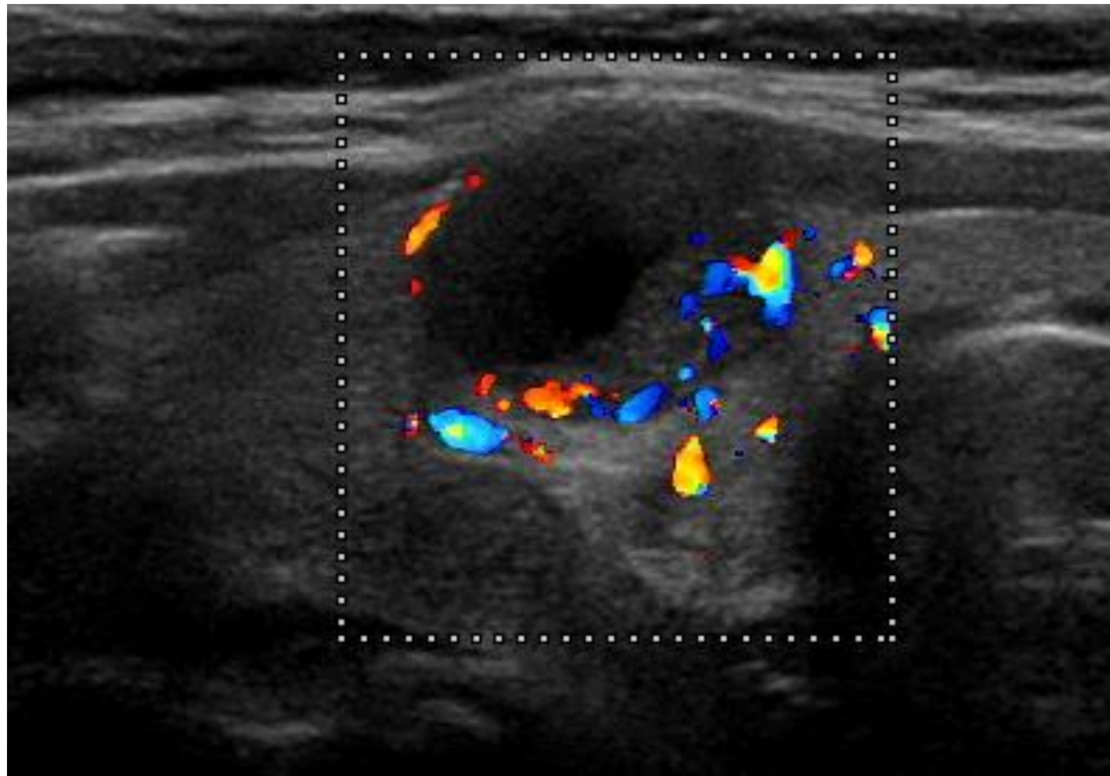




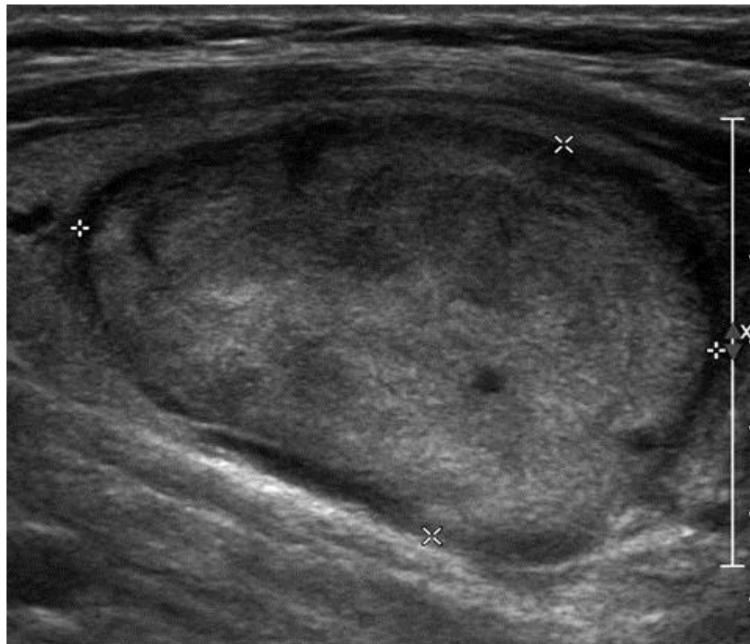
U2 – Benign (peripheral blood flow)

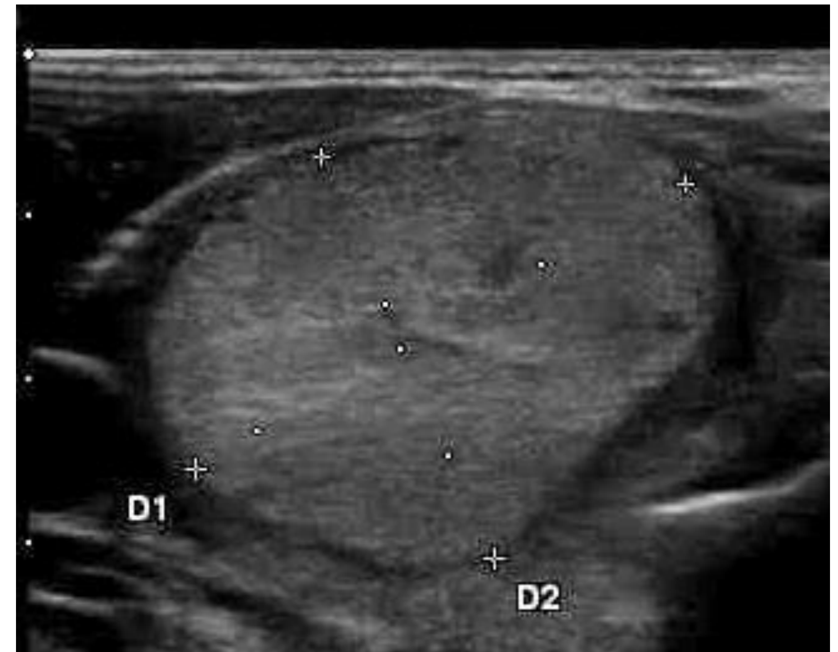


U_3 – Indeterminate (cystic / solid nodule + doppler flow)

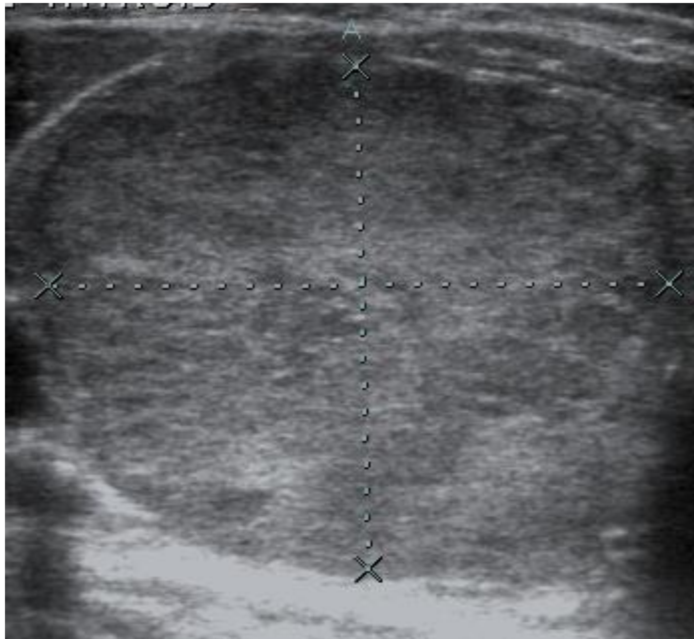


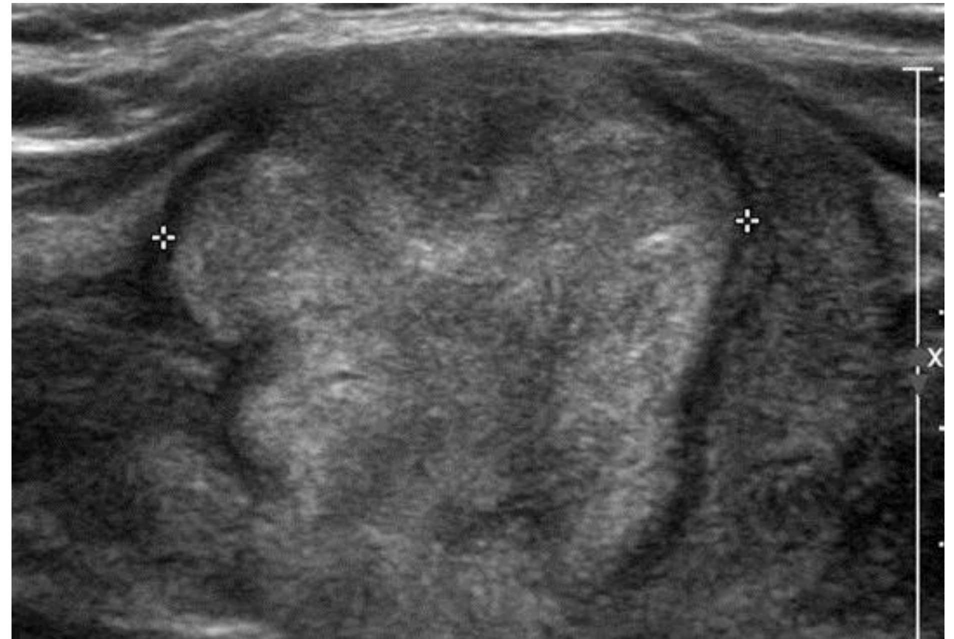
U3 – Indeterminate (follicular lesions)



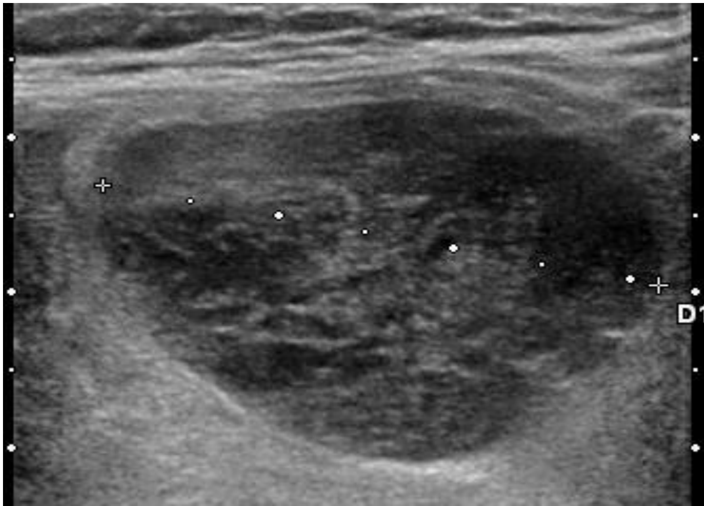


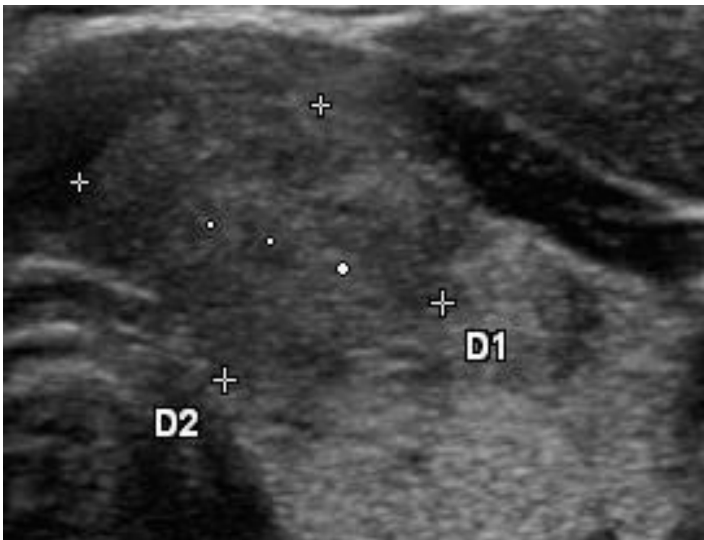
U3 – Indeterminate (follicular lesions)

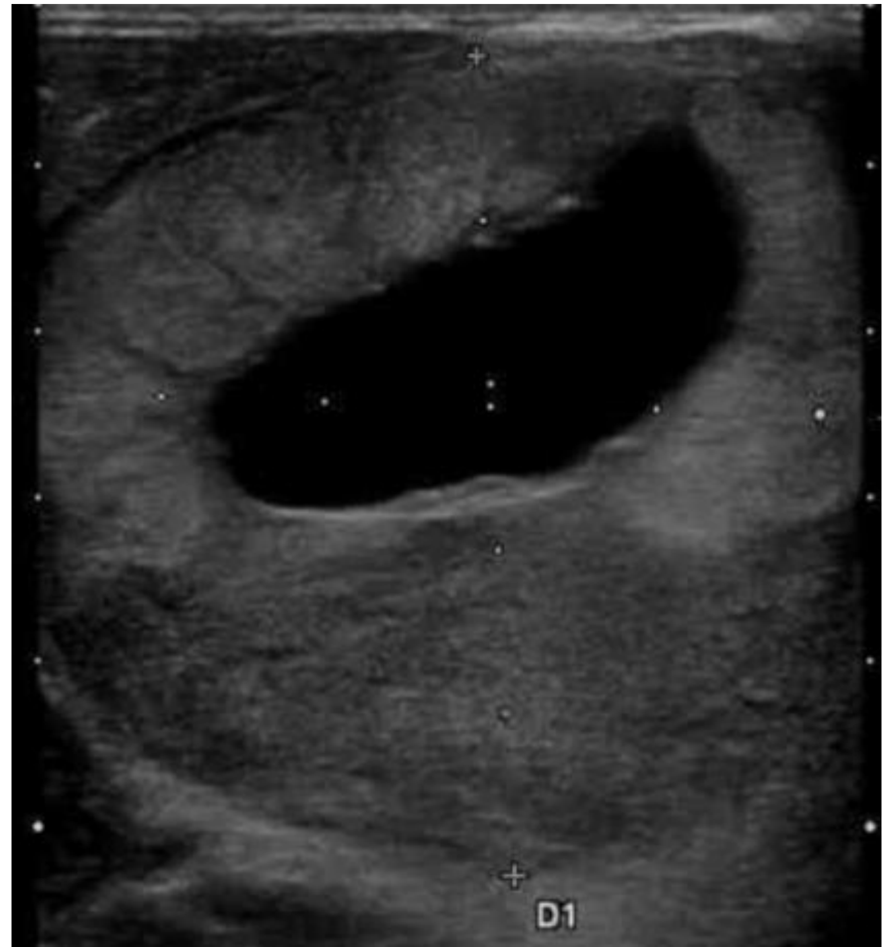




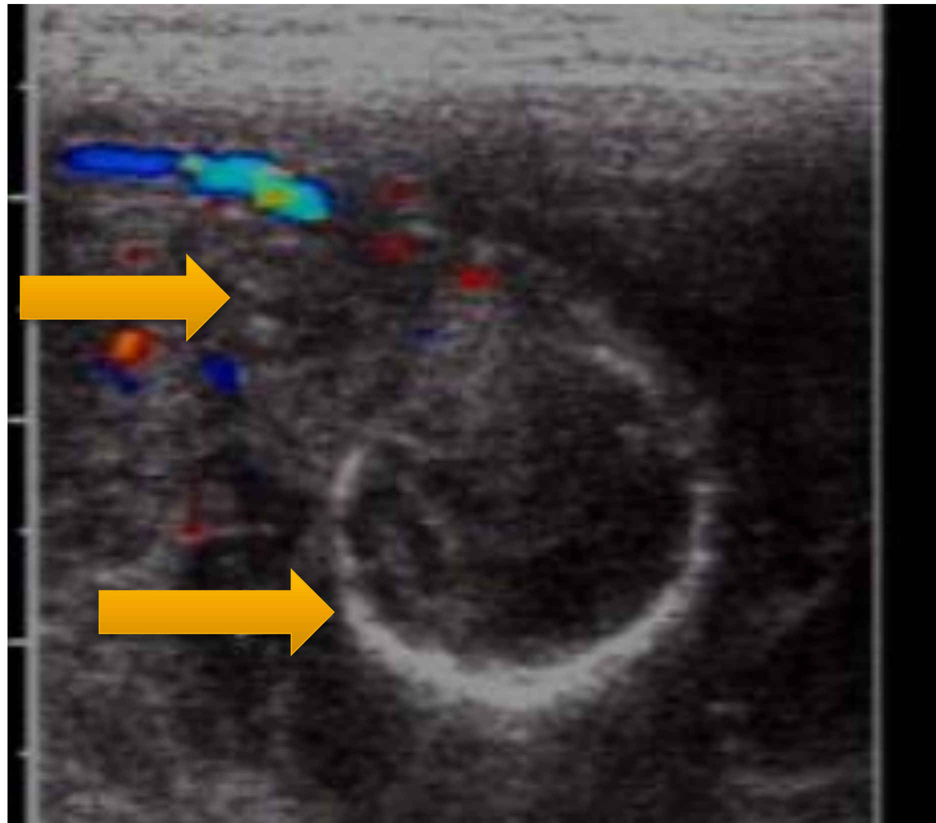
U4 – Suspicious
(slightly hypoechoic, heterogenous nodules)



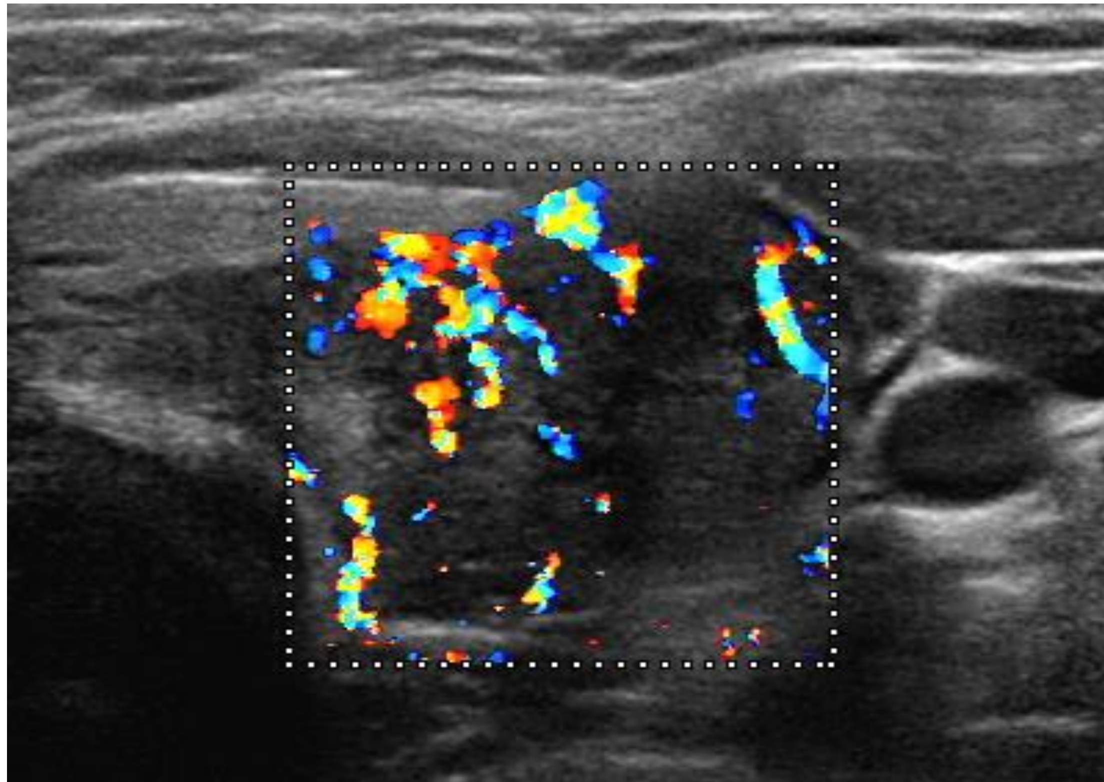




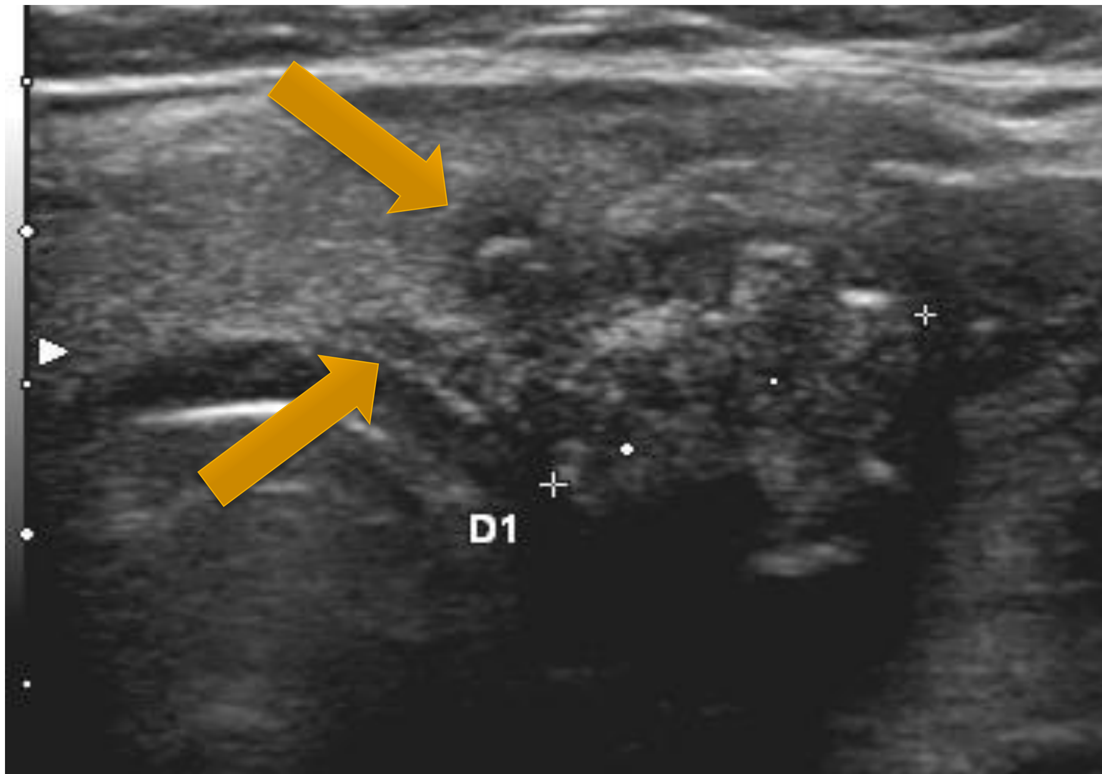
U4 – Suspicious (extension beyond eggshell rim)



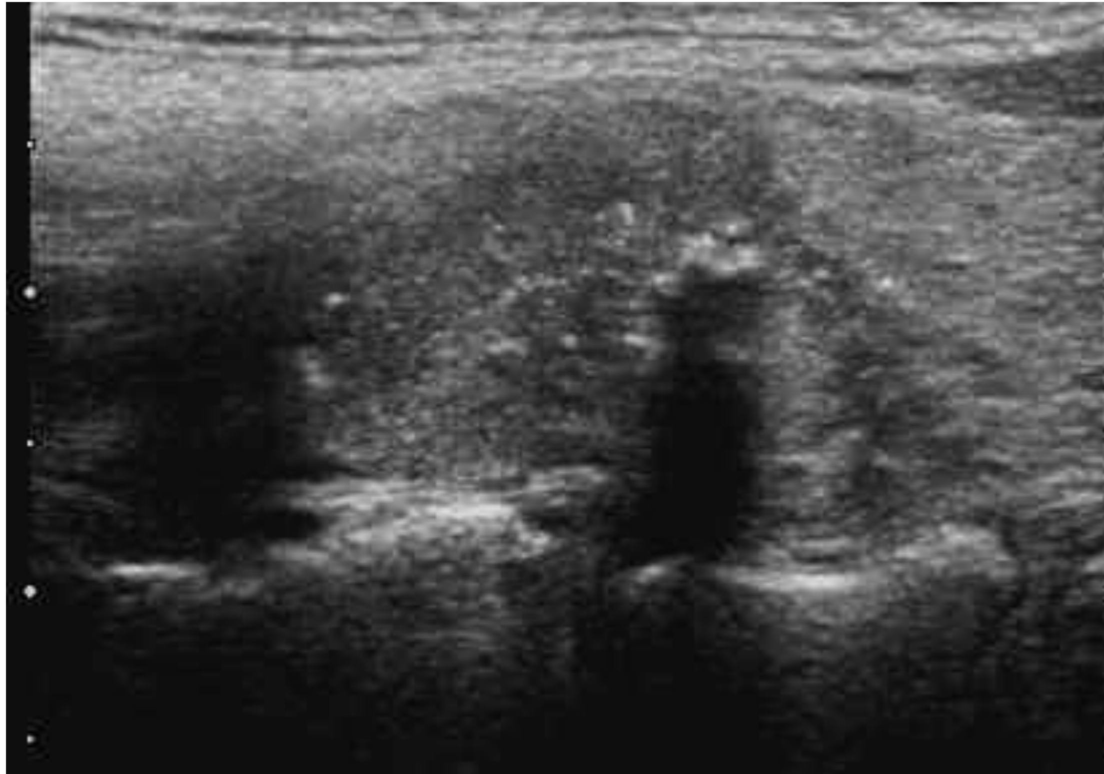
U5 – Malignant (markedly hypoechoic)



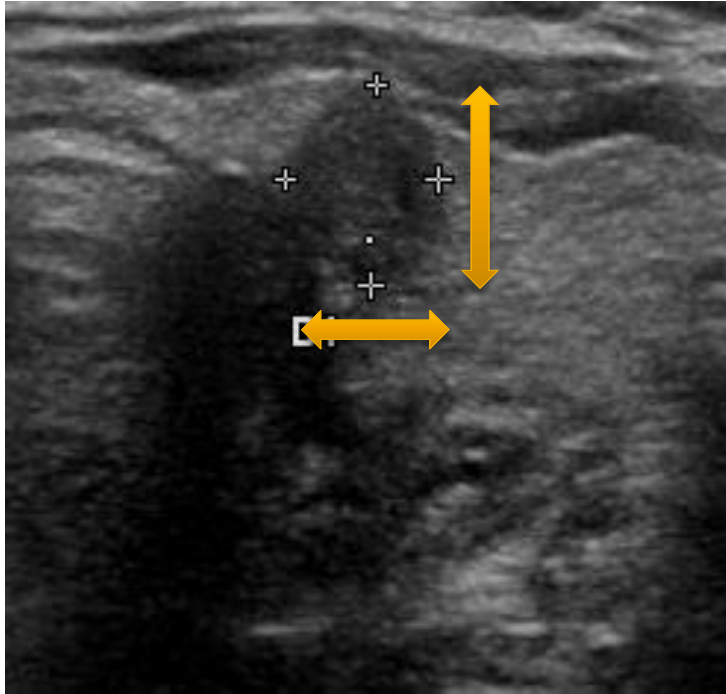
U5 – Malignant (ill defined margins)

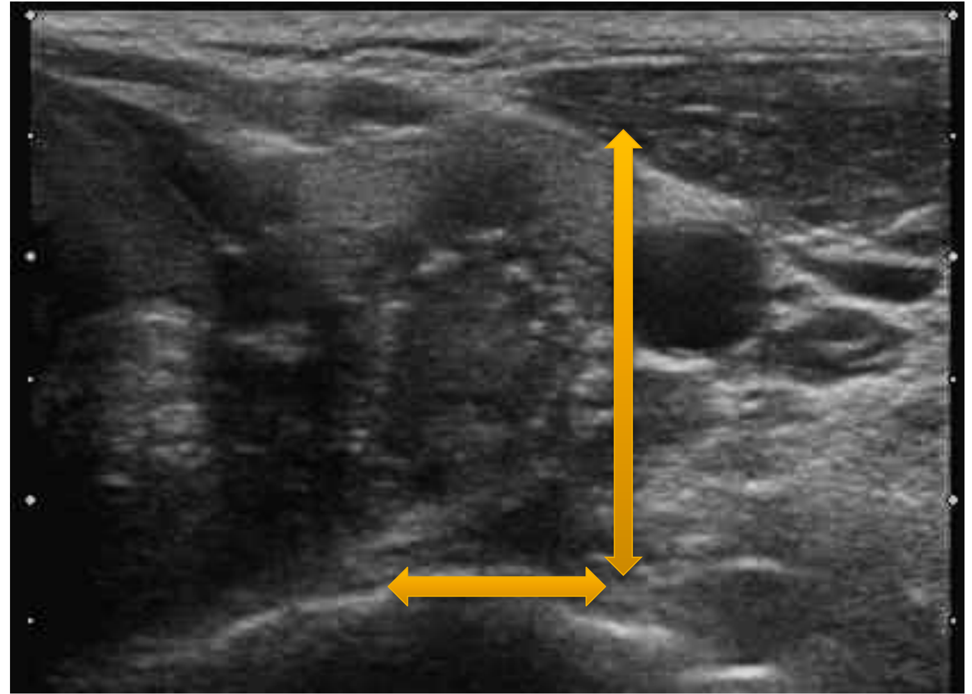


U5 – Malignant (micro-calcification)



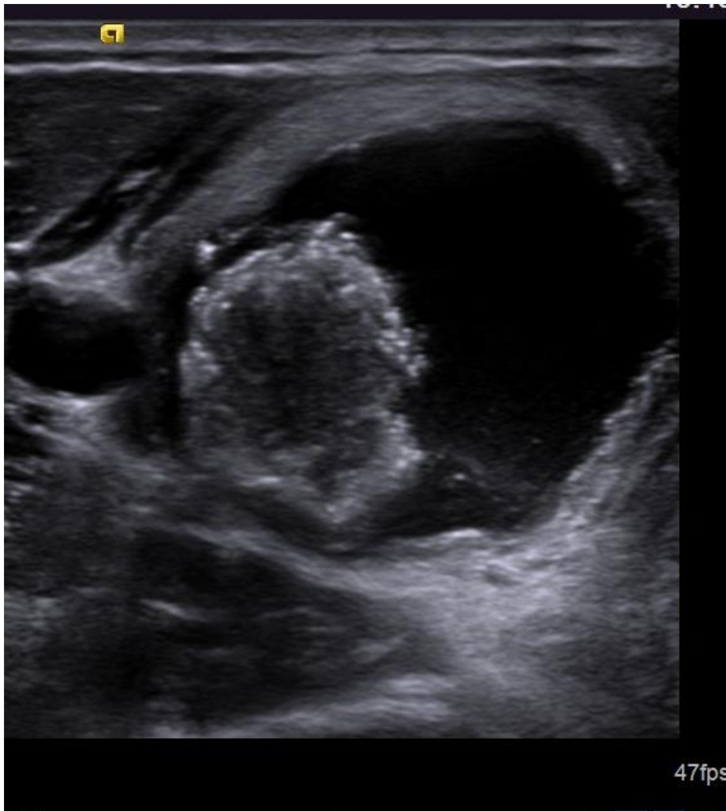
U5 – Malignant (taller than wide)

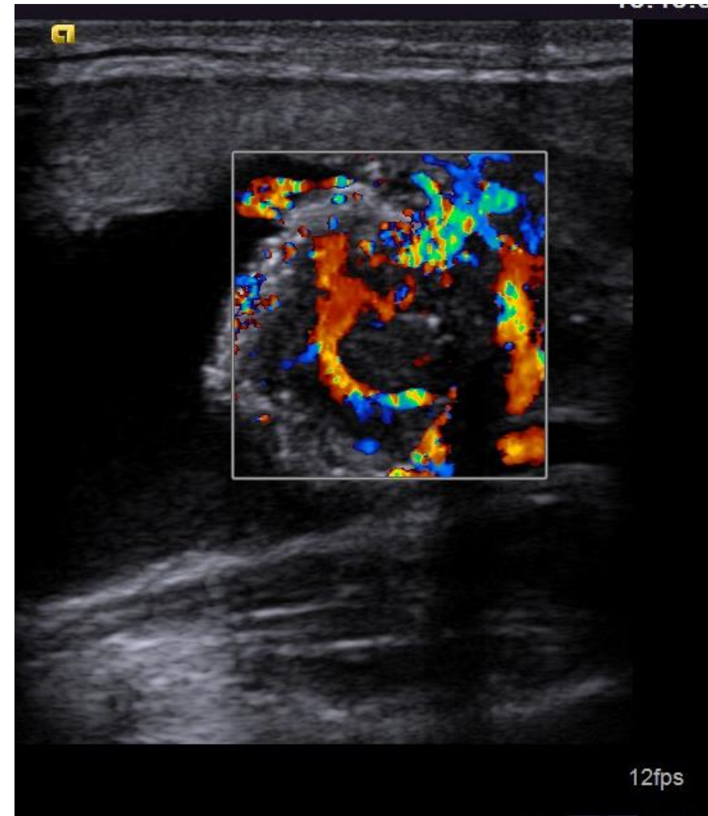




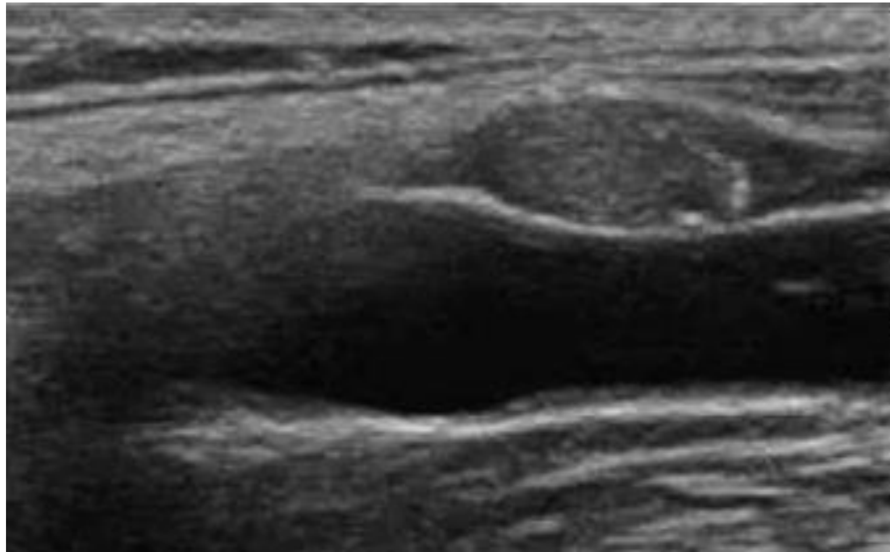
AP > TR in the transverse plane

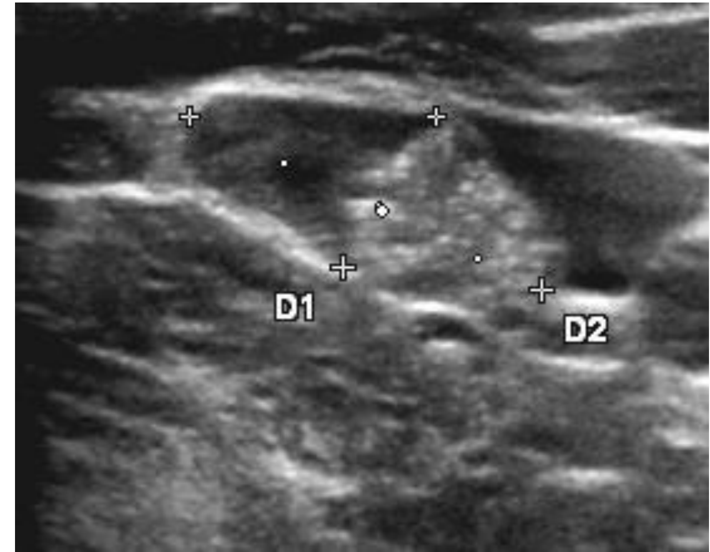
U5 – Malignant (cystic papillary cancer)

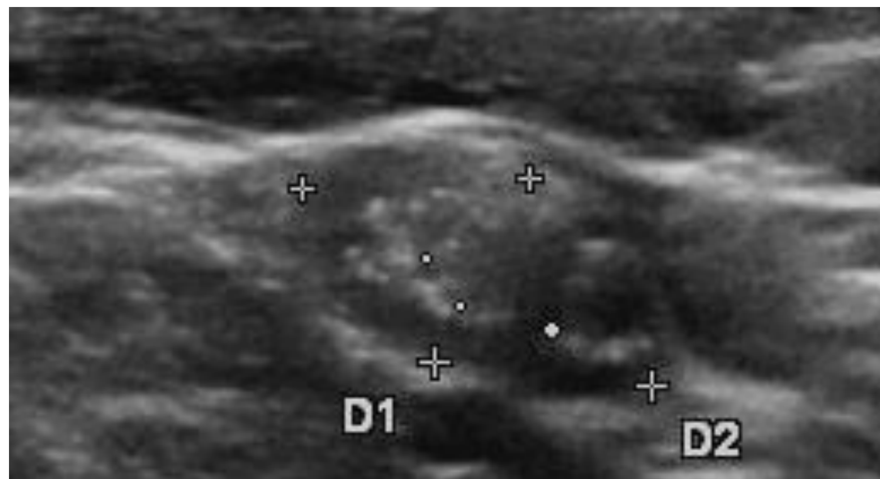




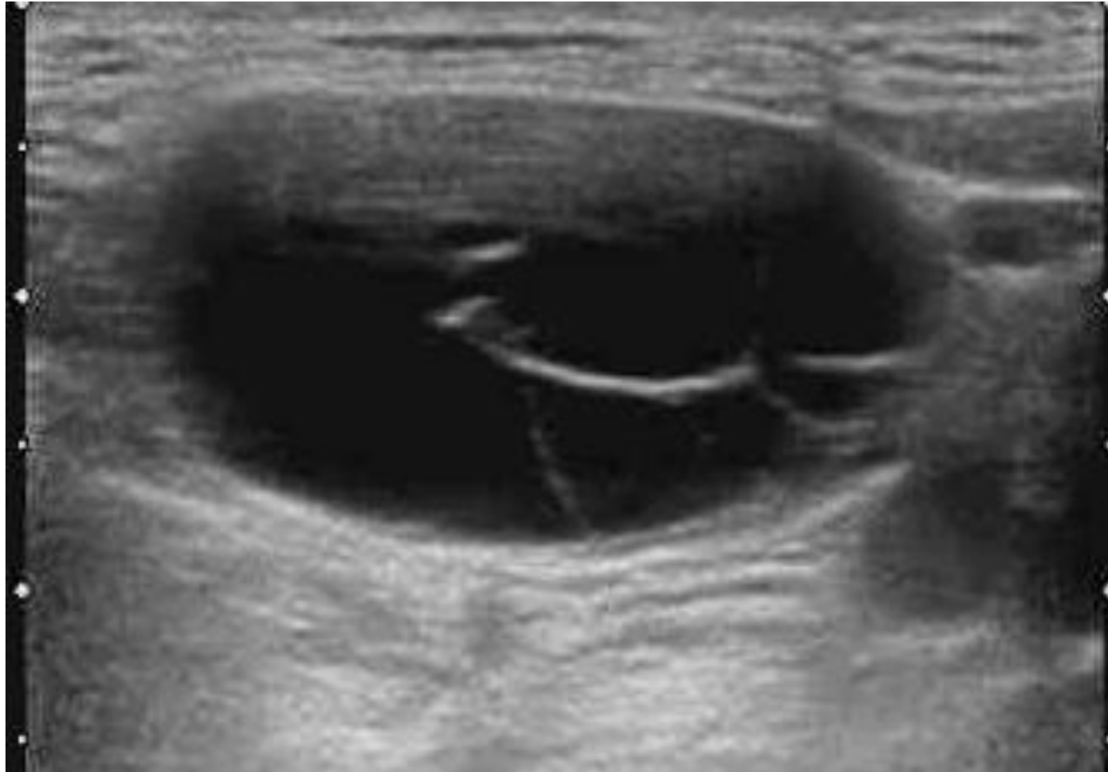
U5 – Malignant (nodes with micro-calcification)







U5 – Malignant (cystic nodes)

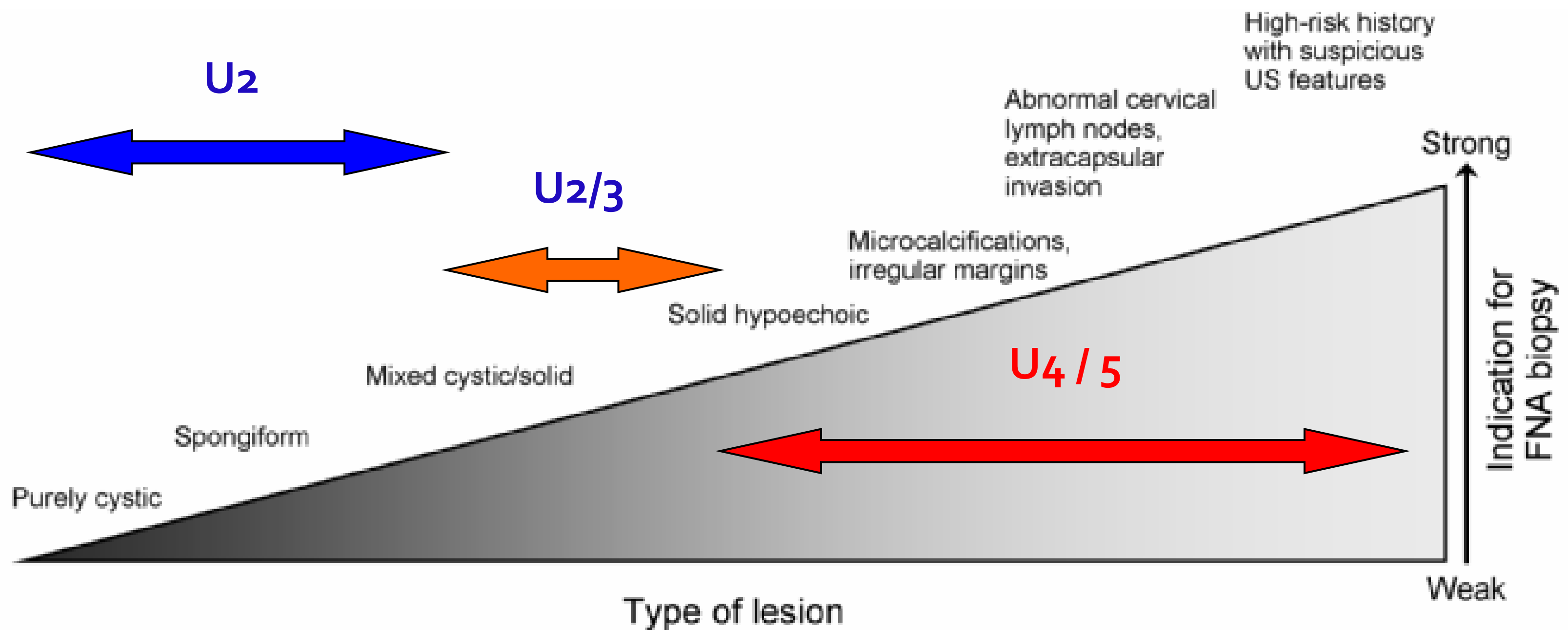


Ultrasound Rating (U1 – U5)

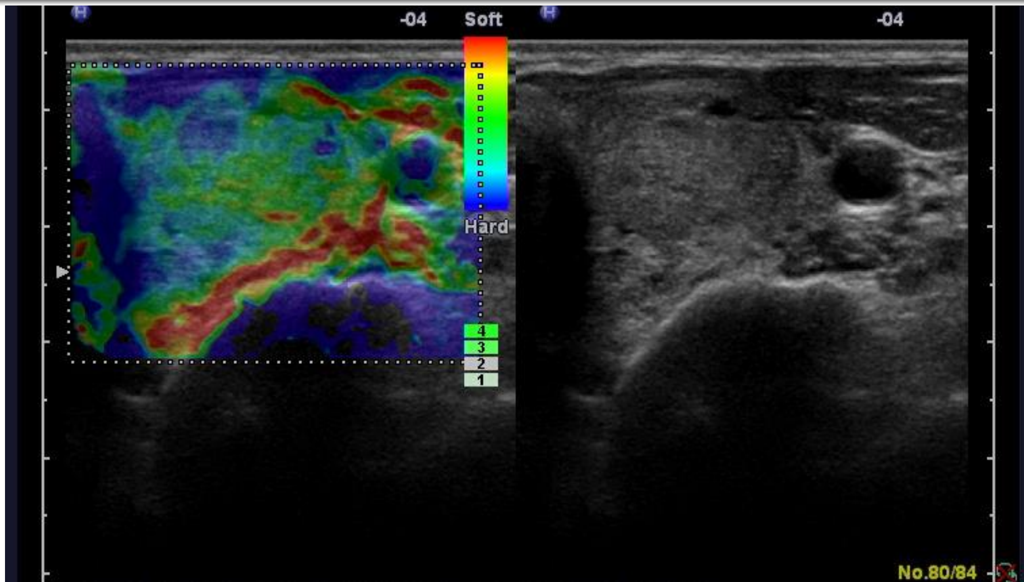
- FNA any indeterminate or suspicious / malignant nodules
- FNA of U3 – U5
- U3 – most will be benign, but follicular lesions are included, and the occasional cancer may be present

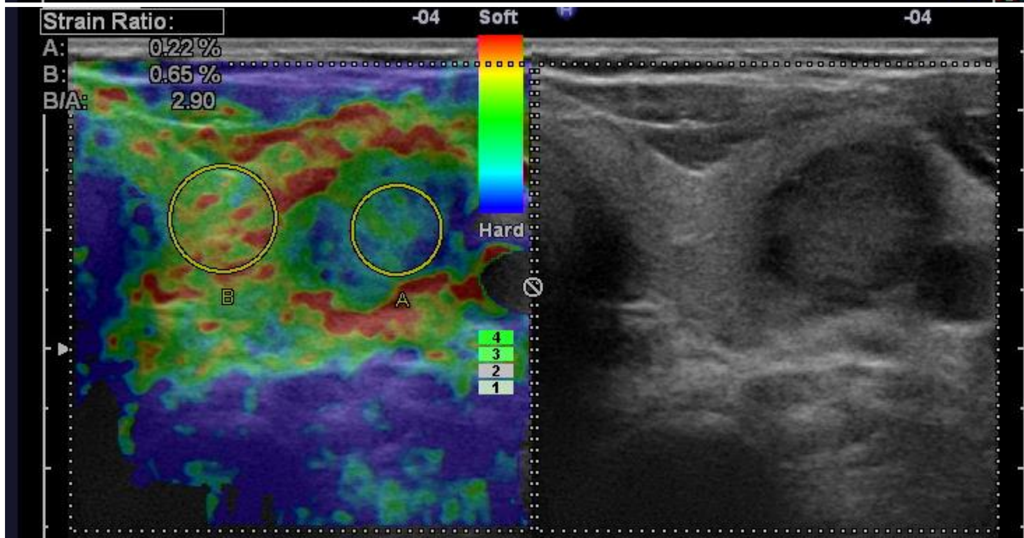
Ultrasound Rating (U1 – U5)

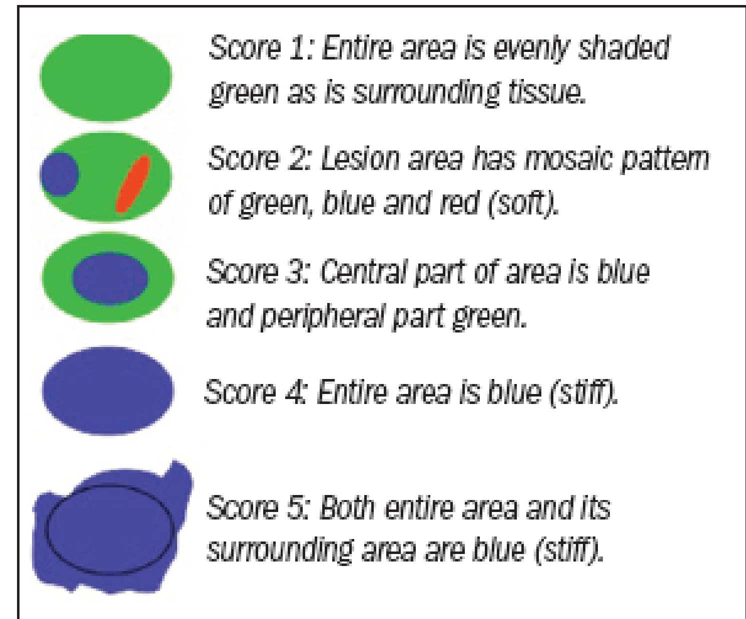
- FNA of U3 – U5



Ultrasound Rating – additions…







Score 1: Entire area is evenly shaded green as is surrounding tissue.

Score 2: Lesion area has mosaic pattern of green, blue and red (soft).

Score 3: Central part of area is blue and peripheral part green.

Score 4: Entire area is blue (stiff).

Score 5: Both entire area and its surrounding area are blue (stiff).

FIGURE 3. Ueno classification (Hitachi software).

Courtesy of Dr Andrew McQueen

Ultrasound Scoring Systems

Niamh M. Hambly[1,2]
Mithat Gonen[3]
Scott R. Gerst[1]
Duan Li[1]
Xiaoyu Jia[3]
Svetlana Mironov[1]
Debra Sarasohn[1]
Stephen E. Fleming[1]
Lucy E. Hann[1]

Implementation of Evidence-Based Guidelines for Thyroid Nodule Biopsy: A Model for Establishment of Practice Standards

AJR 2011;196: 655 - 660

- Use of scoring systems is robust
  - Training possible
  - Good inter observer variability
  - Allows effective audit / follow

Ultrasound Scoring Systems

- *Ultrasound based reporting system for thyroid nodules improves patient management and cost-effectiveness by reducing unnecessary FNA*

Horvath E et al. An ultrasonogram reporting system for thyroid nodules stratifying cancer risk for clinical management. *J Clin Endocrinol Metab* 2009; 94: 1748 - 1751

Guidelines

- American Thyroid Association (ATA)
- American Association of Clinical Endocrinologists (AACE)
- Kim / Korean Society of Radiologists
- Society of Radiologists in US (SRUS)
- *British Thyroid Association (BTA)*
- *Mayo Clinic Thyroid US Chart*

- *Guidelines represent expert opinion based upon a selection of retrospective studies*

- *There is a lack of prospective randomised control trials assessing effectiveness of Guidelines in detecting thyroid cancer*

- The majority of guidelines currently available still recommend biopsy for the majority of thyroid nodules
- This leads to a massive cost implication, with resultant surgery for often benign disease, and all to exclude a cancer with excellent long term survival rates

GUIDELINES FOR FNA

Neuroradiology/Head and Neck Imaging • Origina

Biopsy of Thyroid Nodules: Comparison of Three Sets of Guidelines

Sung Soo Ahn[1]
Eun-Kyung Kim[1]
Dae Ryong Kang[2]
Sung-Kil Lim[3]
Jin Young Kwak[1]
Min Jung Kim[1]

AJR 2010; 194:31–37

Kim

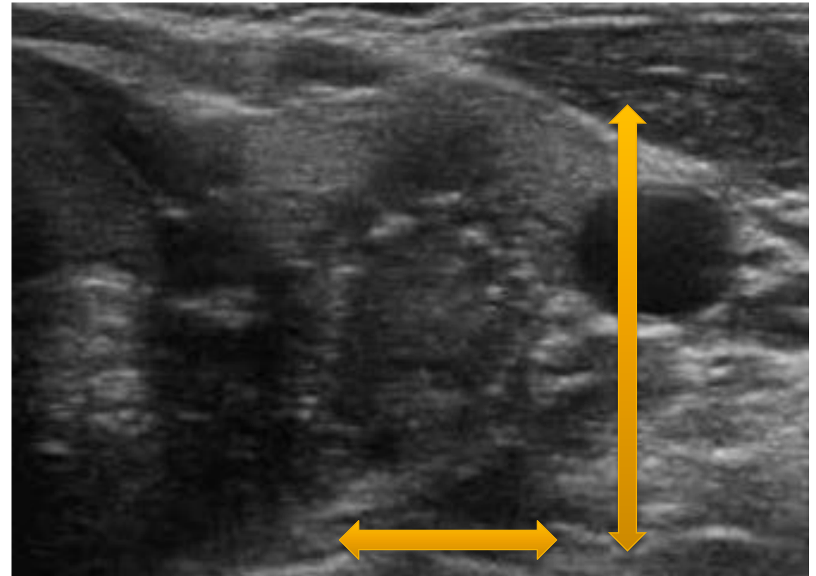
AACE

SRUS

1398 nodules

Kim Criteria

- FNA of any nodule with <u>one</u> of:
  - Markedly hypo-echoic
  - Micro-calcification
  - Irregular margins
  - Taller-than –wide shape



Kim EK, Park CS, Chung WY et al. New sonographic criteria for recommending fine needle aspiration biopsy of nonpalpable solid nodules of the thyroid. *AJR* 2002; 178: 687 – 691.

AACE Criteria

- FNA of any nodule with:
  - Marked hypo-echogenicity + one other:

  - Micro-calcification
  - Irregular margins
  - Taller-than-wide shape

Gharib H, Papini E, Valcavi R et al. American Association of Clinical Endocrinologists and Associazone Medici Endocrinologi medical guidelines for the diagnosis and management of thryoid nodules. *Enodcr Pract* 2006; 12: 63 – 102.

Society of Radiologists in US

- FNA any nodule with:
  - > 10mm with micro-calcification
  - >15mm if solid
  - >15mm if coarse calcification
  - >20mm if solid and cystic

Frates MC, Benson CB, Charboneau JW et al. Management of thyroid nodules detected at US: Society of Radiologists in Ultrasound consensus conference statement. *Radiology* 2005; 237: 794 – 800.

- Kim Criteria
  - Sensitivity 92.7% Specificity 80.9%
  - NPV 97.3%
- AACE Criteria
  - Sensitivity 74% Specificity 94.4%
  - NPV 95%

- SRUS
  - Uses size criteria

  - Sensitivity 35%
  - Specificity 54%
  - NPV 80%

Common Misunderstandings

- Nodule size
- Dominant Nodule FNA
- Follow up post benign FNA
- Nodule growth

Nodule Size

- Nodules > 4cm have been claimed as having malignancy rates > 20%
- Nodule size > 4cm increases neither the false negative rate of FNA, nor the rate of malignancy

Shrestha M, Crothers BA, Burch HB. The impact of thyroid nodule size on the risk of malignancy and accuracy of fine-needle aspiration: a 10-year study from a single institution. *Thyroid*. 2012;22:1251-6

Nodule Size

- 661 nodules > 3cm diameter
- US and FNA are accurate in nodules > 3cm.
- US features are still predictive even with larger nodule size

Yoon JH, Kwak JY, Moon HJ. The diagnostic accuracy of ultrasound guided fine needle aspiration biopsy and the sonographic differences between benign and malignant thyroid nodules 3cm or larger. *Thyroid* 2011: 21(9): 993 – 1000

Dominant Nodule FNA

- *FNA of a dominant nodule is a common but mistaken practice*
  - Decision to FNA should be based upon US appearances.
  - Selecting nodules purely on size criteria encourages lazy / incomplete assessment

Its all about the apples….

Follow Up Post FNA

Value of US Correlation of a Thyroid Nodule with Initially Benign Cytologic Results[1]

Radiology

Jin Young Kwak, MD
Hyeryoung Koo, MD
Ji Hyun Youk, MD

Purpose: To investigate the value of ultrasonographic (US) features in thyroid nodules with initially benign cytologic results.

Radiology 2010. 254 (1): 292 - 300

1343 nodules with US, FNA, pathological correlation

Total:	Benign 98.1%	Malignant 1.9%
Benign initial US + Thy 2 FNA:	**Benign 99.4%**	**Malignant 0.6%**
Suspicious initial US + Thy 2 FNA:	**Benign 79.6%**	**Malignant 20.4%**

Follow Up Post FNA

- Clinico-radiologic-cytologic correlation
- Benign US and benign FNAC does not need repeating after 6 – 12 months
  - Low cost effectiveness
- Suspicious US and Thy 2 must be repeated as malignancy rates are significant

Follow Up Post FNA

- Long term follow up of benign nodules

  - *Associated with increased US studies*
  - *Associated with increased FNA rates*

  - *No improvement in malignancy detection rates*

Lee S, Skelton TS, Zheng F. Biopsy proven benign thyroid nodule: is long term follow up necessary. *J Am Coll Surg* 2013, 217(1): 81 – 8.

Nodule Growth

- Presence or absence of growth is not an indicator of malignancy or benignity
- Interval growth has low PPV for malignancy

Nodule Growth

- 294 / 330 Thy 2 nodules enlarged
- Average 15% growth
- 74 nodules had significant growth (≈ 69%)
- Re-FNA showed cancer in only 1 / 74.

Alexander EK et al. Natural History of Benign Solid & Cystic Thyroid Nodules. *Ann Int Medicine* 2003; 138: 315 - 318

- *Growth of nodules is an expected finding in benign thyroid disease*

US Standards

Images & Reports

- Radiologist, sonographer, surgeon, endocrinologist
- Formal images, recorded on PACS, with appropriate formal report on RIS system
- Training in accordance with RCR Guidelines / Non–radiologist US Training Document
- Assessment of any indeterminate or suspicious nodules

TABLE 4.4

Suggested features to consider/include in US reporting/assessment of thyroid nodules:

Relevant Nodule Size:	
Nodule Composition:	Solid, cystic, mixed solid /cystic, micro-cystic/spongiform.
Cystic Component:	? Ring down sign - colloid
Echogenicity:	Markedly hypo-echoic, hypo-echoic, iso-echoic, hyper-echoic
Calcifications:	Micro-calcification, macro-calcification, rim / egg shell
Margin:	Well defined, irregular/lobulated, spiculated
Taller than Wide:	AP> TR : Y / N
Halo:	Regular / continuous, interrupted, absent
Colour flow:	Central, peripheral, mixed, none
Extent:	Retrosternal extension / tracheal deviation
Classification:	Benign (U2), equivocal / indeterminate (U3), suspicious (U4), malignant (U5)
Lymphadenopathy:	Suspected malignancy – ? metastases: anatomical location/levels
Biopsy:	FNAC / core biopsy, needle gauge, number of passes. Location of nodule biopsied. Complications : Y/N.

Ultrasound Standards

- Interest / regular practice of thyroid imaging
- Participation at Thyroid MDT
- US images / report stored on PACS system
  - Report attached to images
  - Assess the likelihood of cancer
  - Regular audit of cases / FNA results
- *MINIMUM STANDARD OF PRACTICE*

Incidental Thyroid Nodules

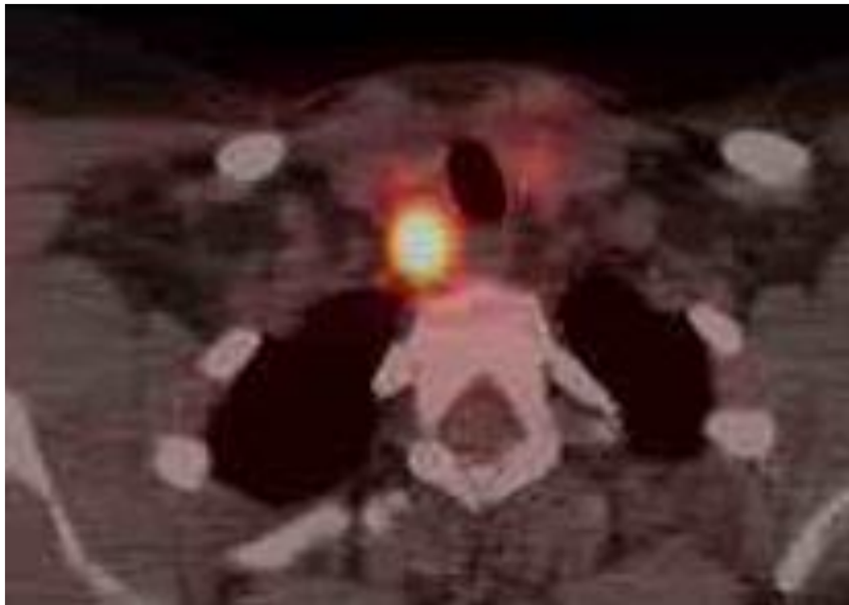
- Massive cost to NHS of follow up / FNA
  - >£5 million per annum for UHB NHSFT for US + FNA
  - Stable mortality rates despite investigation
- No CT feature reliably characterises nodules
- Clinical evaluation (not US / FNA), but consider US / FNA initially if:
  - Risk factors in history
  - Ill defined margins, young age, micro-calcification

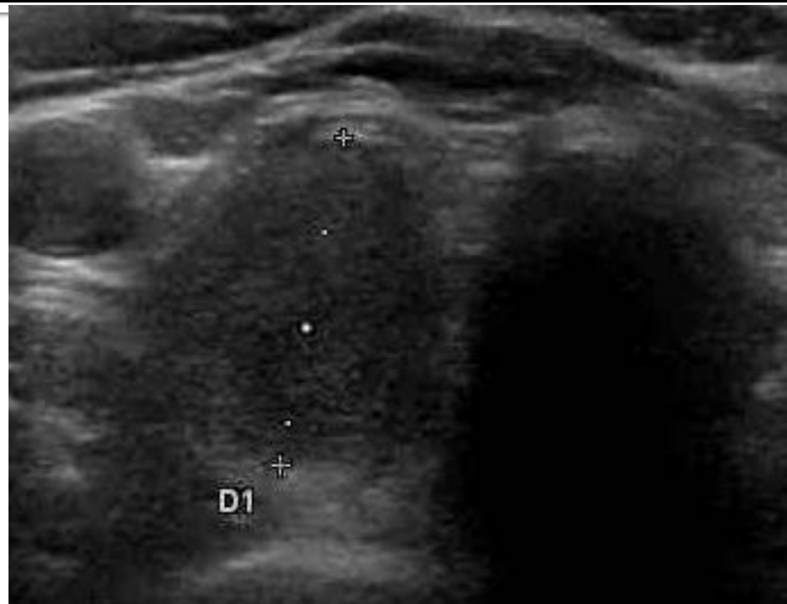
Incidental Nodules on PET CT

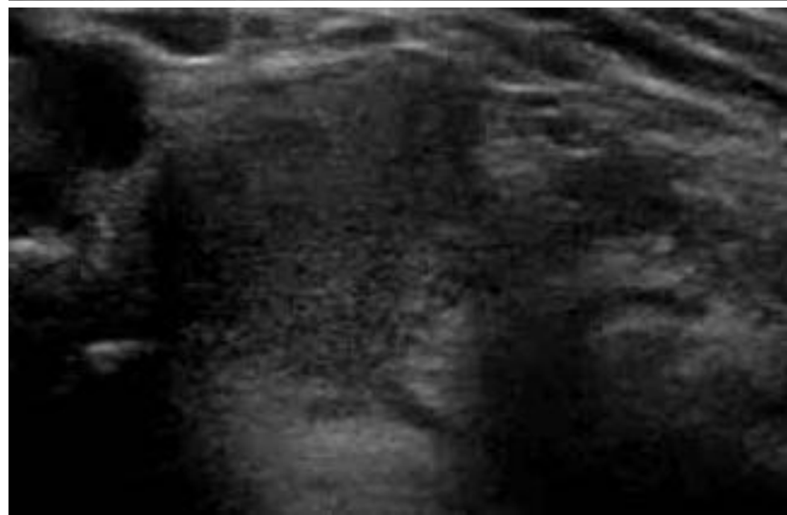
- Focal FDG activity within thyroid
- Meta-analysis shows malignancy ≈ 35%

- US / FNA must be performed for focal uptake

Soelberg KK, Bonnema SJ, Brix TH, Hegedus L.
Risk of malignancy in thyroid incidentalomas detected by 18 FDG PET: a systematic review. *Thyroid* 2012; 22(9): 918 – 925.




D1



Summary (1)

- US images stored on PACS system
  - Formal documented report
  - Report attached to images
  - Regular audit of cases / FNA results
- Interest / regular practice of thyroid imaging
- Participation at Thyroid MDT

Summary (2)

- FNA of a dominant nodule in a MNG is a common but mistaken practice
- Use ultrasound to risk stratify nodules
  - Mayo Clinic
  - BTA U1-U5 scoring system
- FNA indeterminate or suspicious / malignant nodules

Summary (3)

- Follow up post FNA should be based upon nodule appearances on US
- Close liaison with thyroid / endocrine team
  - Clinical history is important
  - Repeat sampling of Thy 2 but suspicious US
- Incidental FDG avid nodules on PET CT need definite follow up with US / FNAC

Any Questions?