

UNIVERSITY OF
BIRMINGHAM

IMSR 

INSTITUTE OF METABOLISM
AND SYSTEMS RESEARCH

*Incidental endocrine lesions –
something or nothing?*

Thyroid nodules

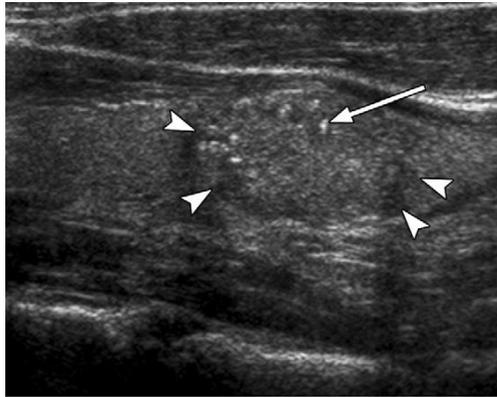
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Thyroid nodules: epidemiology

- **Definition:** *“Discrete lesions within the thyroid gland, radiologically distinct from surrounding parenchyma”*
- May be discovered on **palpation, imaging, incidentally**
- Most common in **women (4:1)** and in **older** populations
- Increased in areas of **low iodine** intake



Thyroid nodules: epidemiology



Roughly in what percentage of the adult population do thyroid nodules occur?

A: 10%

B: 25%

C: 35%

D: 50%

E: 60%



Thyroid nodules: epidemiology

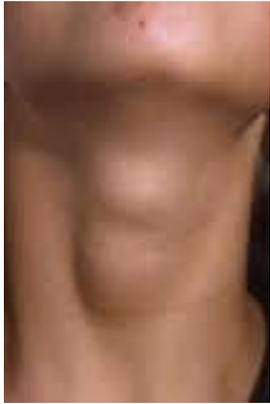


Roughly in what percentage of the adult population do thyroid nodules occur?

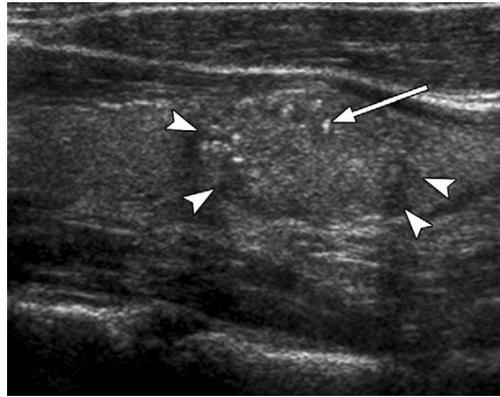
D: 50%



Thyroid nodules: epidemiology



4-7%



20-67%



2-16%

Incidentaloma: **unsuspected**, focal thyroid lesion discovered by **imaging** modality or non-thyroid neck **surgery** in a patient **without history of thyroid disease**

- 16% of cross-sectional neck scans (CT, MRI)
- 9.4% of carotid duplex scans
- 2% to 3% of PET scans



Significance of thyroid nodules

- May cause **thyroid dysfunction**
- May cause **compression**
- **Need to exclude thyroid cancer**

- Prevalence of **malignancy is 4 – 6.5%**
- Independent of nodule **size**
- Malignancy risk in **incidentalomas** remains **controversial**
- Risk of **PET-positive** thyroid nodule: **27%**

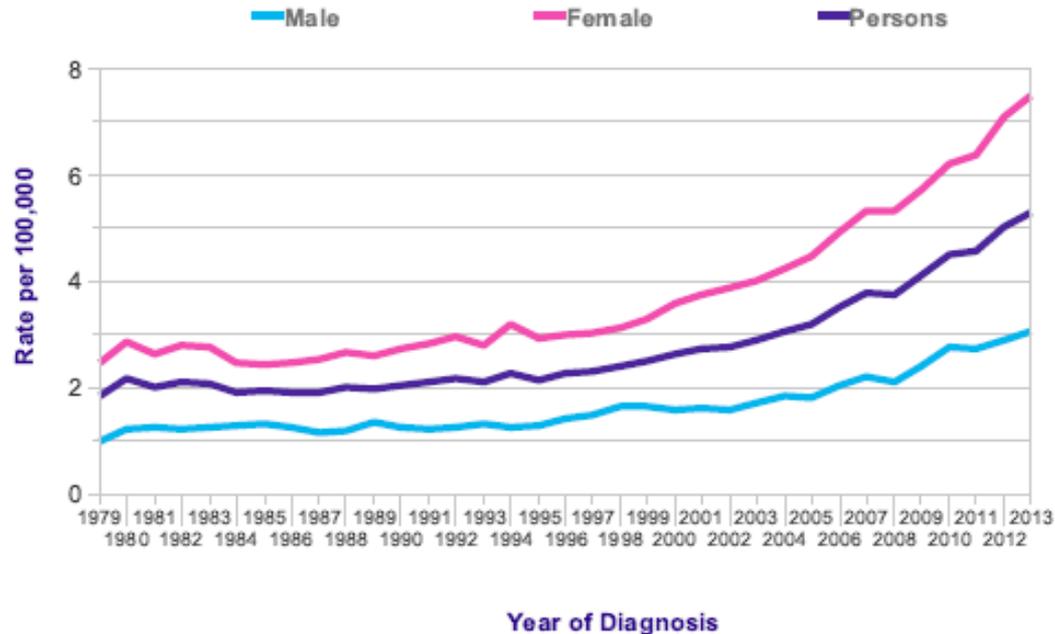


Features suggestive of malignancy

History	Examination	Imaging
Family Hx of MEN, MTC, PTC	Firm nodule	Suspicious US features
History of head and neck irradiation	Nodule fixed to adjacent structures	Lymphadenopathy
History of Hodgkin and non-Hodgkin lymphoma	Growth of nodules, especially during therapy to suppress TSH	
Age < 20	Abnormal cervical lymph nodes	
Age > 70	Vocal cord paralysis	
Male gender		
Symptoms of compression : hoarseness, dysphagia, dyspnoea, cough, dysphonia		



UK Thyroid Cancer Incidence



- **< 1%** of all cancers
- **Incidence** in UK = 3.2 per 100,000
- **Male:female** = 1:3 (1:13 in Japan)
- **2013: 3,241 new cases – 373 deaths**

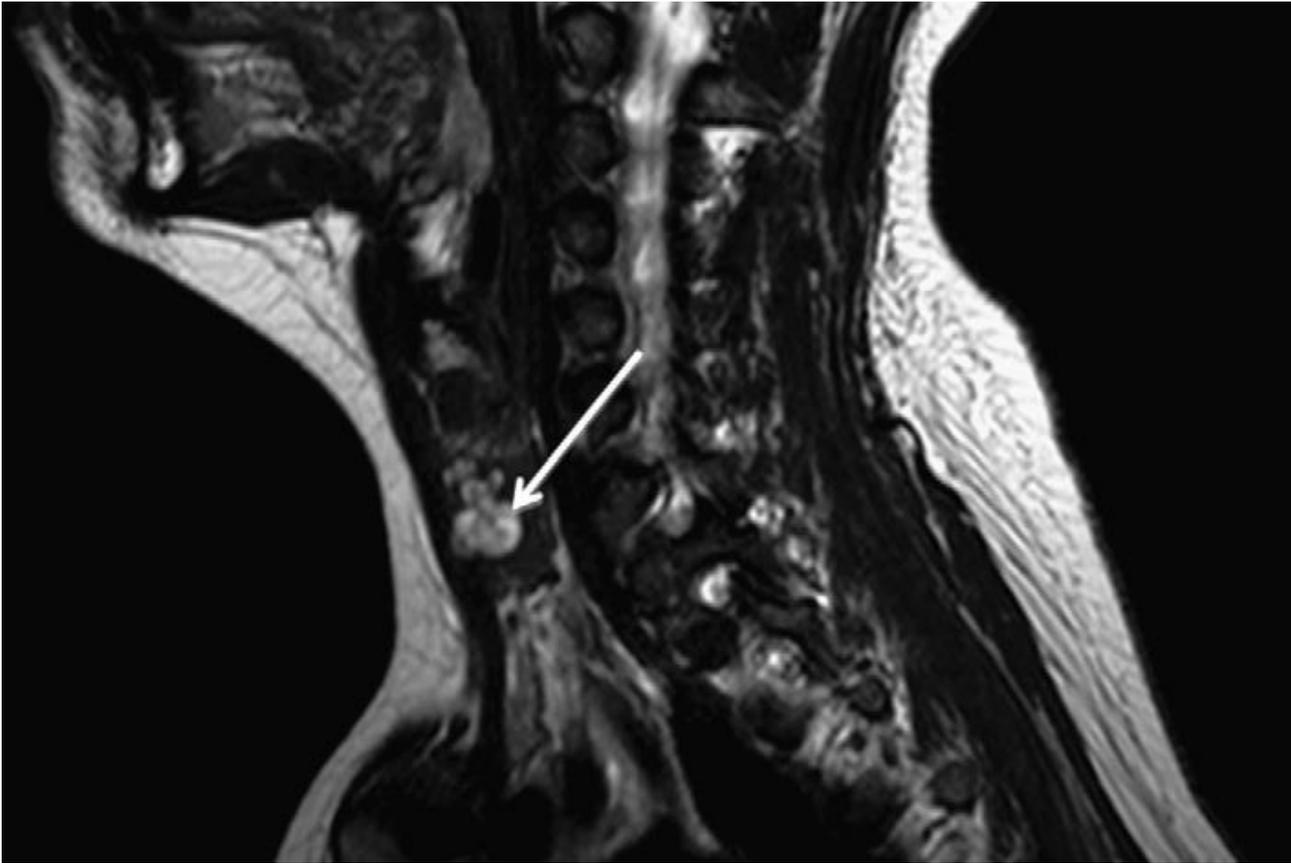


Case report 1

- **52 y old male patient**
- Hx of increasing **lower back and neck pain**
- **PMH:** Hypertension
- **FHx:** Mother: hypothyroidism
Sister: ca colon aged 58 y
- **Rx:** Bendroflumethazide
- **O/E:** P 72/' BP 132/68
 - Normal systems examination
 - Reduced neck movement due to pain
- **MRI neck**



Neck MRI



- **Neck examination:** palpable 1 x 1.5 cm R sided thyroid nodule, thyroid gland not enlarged, no abnormal neck nodes
- **TSH:** 4.2 mU/l





What would you do next?

A: Reassure patient

B: Check serum thyroglobulin

C: Request thyroid ultrasound and FNAB

D: Request thyroid isotope scan

E: Check serum calcitonin



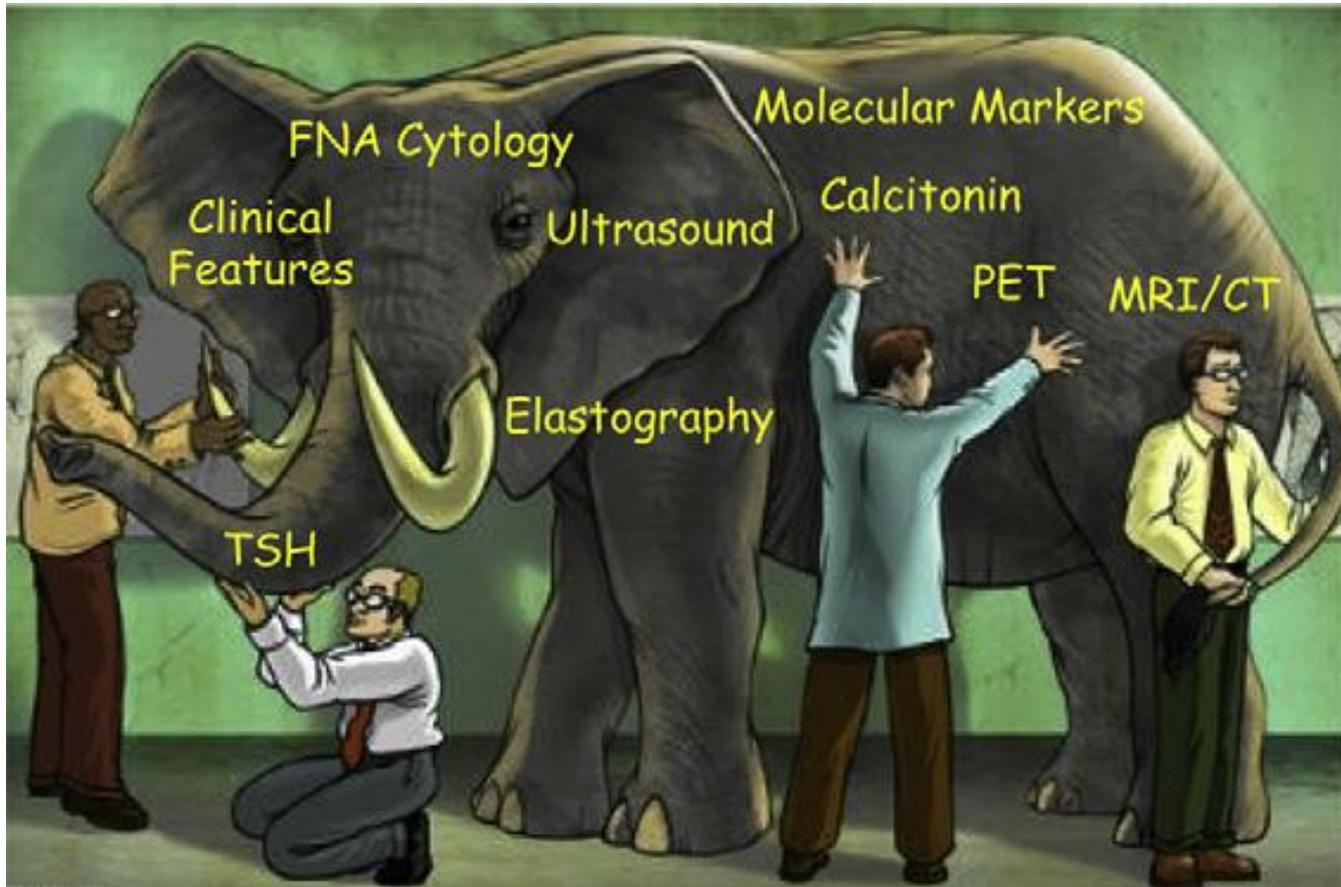


What would you do next?

C: Request thyroid ultrasound and FNAB



Diagnostic evaluation of thyroid nodules



Serum markers and thyroid nodules

- **Serum TSH** guides further management
- **Serum calcitonin:**
 - Sensitive marker of C-cell hyperplasia/MTC
 - Screening not recommended in UK and US but routinely done in Europe
 - Useful in FU of MTC
- **Serum thyroglobulin:**
 - Not sensitive / specific for diagnosis of thyroid malignancy
 - Useful in FU of differentiated thyroid cancer



Isotope scanning and thyroid nodules



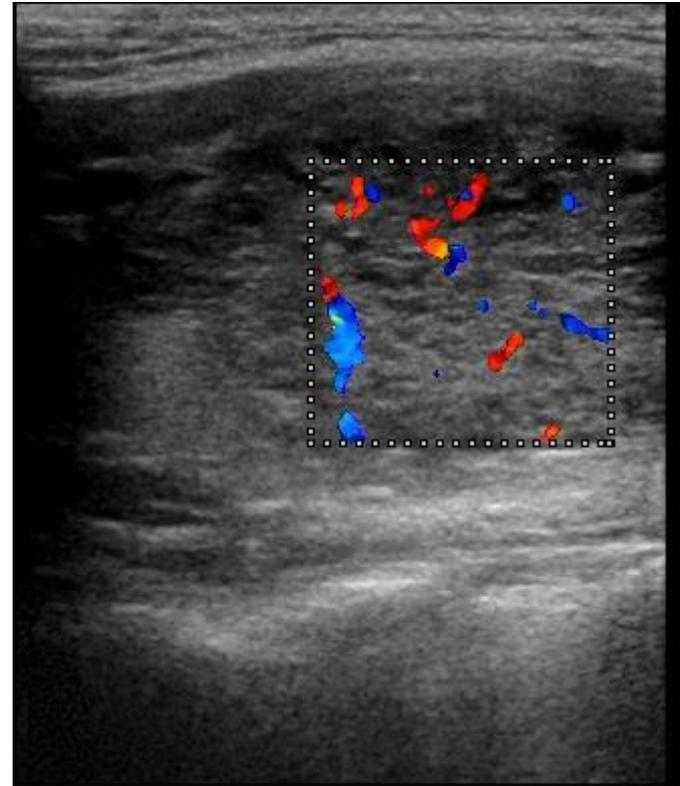
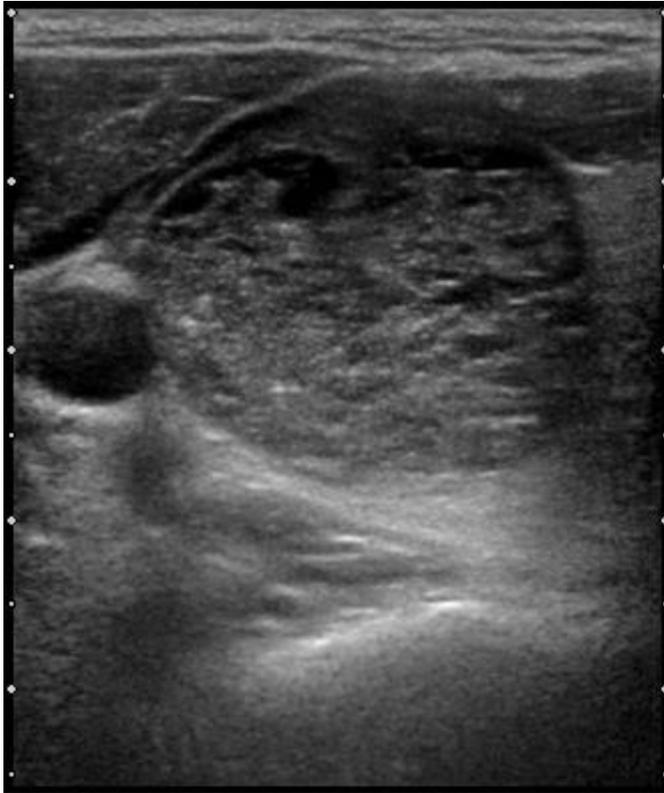
Hot nodule – likely benign



Cold nodule – possibly malignant



Case report 1



- **Neck examination:** palpable 1 x 1.5 cm R sided thyroid nodule, thyroid gland not enlarged
- **TSH:** 4.2 mIU/l





Which is the most appropriate next step?

A: Reassure and discharge patient

B: Perform fine needle aspiration biopsy

C: Repeat US after 6-12 months

D: Surgical excision of nodule





**Which is the most appropriate
next step?**

B: Perform fine needle aspiration biopsy



Thyroid ultrasonography

- Extremely **sensitive** for diagnosis of thyroid nodules
- **Specific** for thyroid ca diagnosis (papillary)
- Aids decision making to **select** nodules for **FNA**
- Increases **yield** of diagnostic **FNA**
- Patients with possible thyroid cancer should undergo ultrasonographic evaluation of neck by **experienced** operator



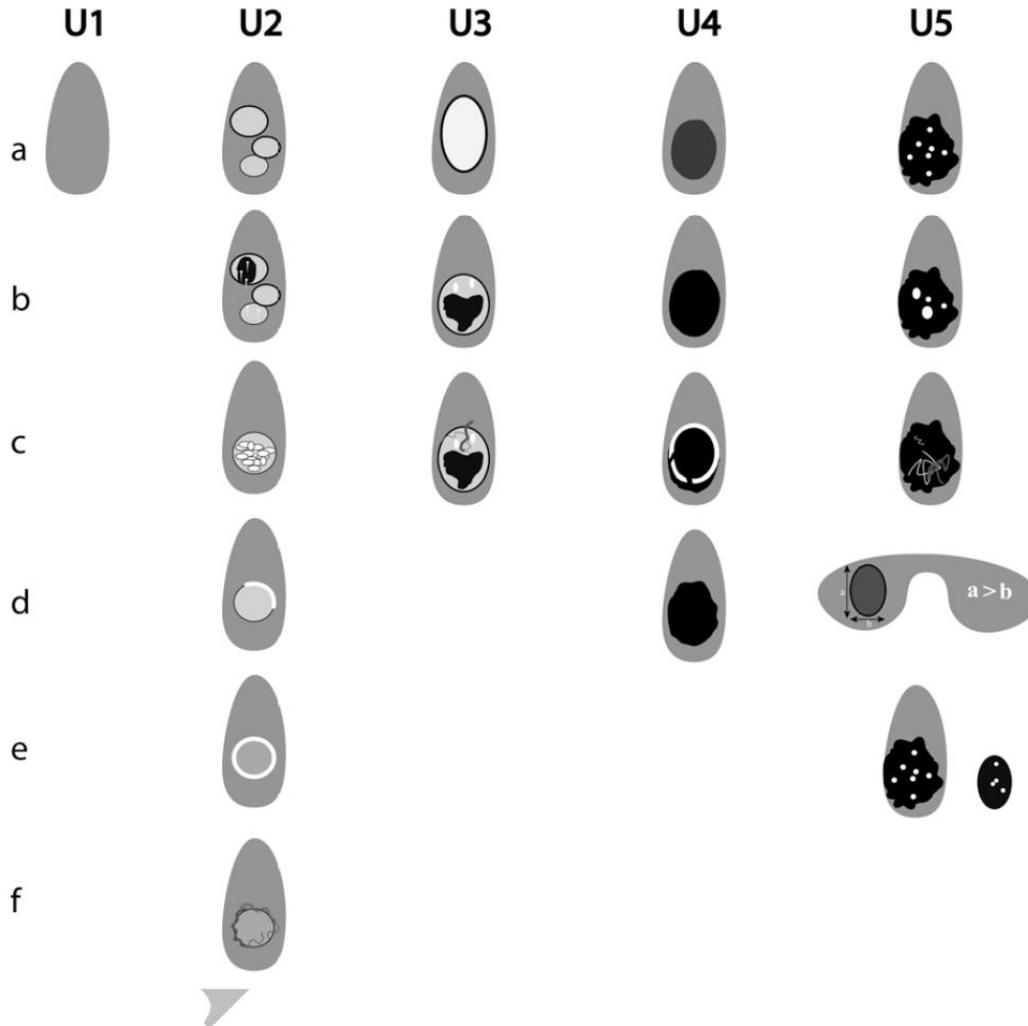
Ultrasound features

Benign nodule	Malignant nodule: Papillary/medullary	Follicular lesion
Spongiform/honeycomb	Solid and hypoechoic	Hyperechoic / homogeneous/halo benign
Purely cystic	Irregular margin	Hypoechoic ity/loss of halo suspicious
Egg shell calcification	Intranodular vascularity	
Iso/hyper echoic (hypoechoic halo)	Absence of halo	
Peripheral vascularity	Taller than wide	
	Microcalcifications	



Scoring system:U1-U5

Thyroid nodules – Ultrasound(U) classification



U1: Normal

U2: Benign

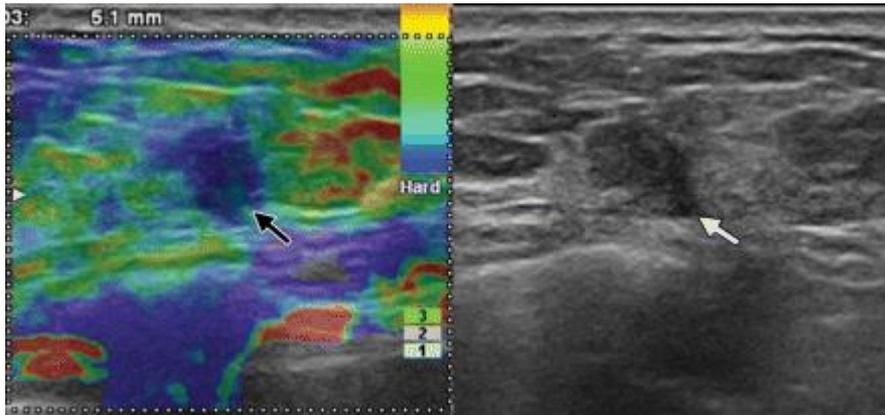
U3: Indeterminate

U4: Suspicious

U5: Malignant

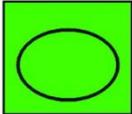
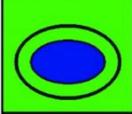
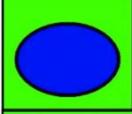
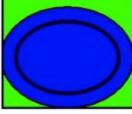


Elastography



**Measurement of tissue stiffness:
distortion on application of
external force**

Tsukuba Scores

Score	Diagram	Description
1		Entire lesion evenly shaded in green - Even strain for the entire hypoechoic lesion
2		Mosaic pattern of green and blue (no strain) - Strain (green) in most of the hypoechoic lesion
3		Peripheral area of lesion is green; central area is blue - Strain is in the peripheral area of lesion
4		Entire lesion is blue - No strain within entire hypoechoic lesion
5		Entire lesion AND surrounding area are blue - No strain within entire hypoechoic lesion and and surrounding area

ELATION-trial: HTA-funded multi-centre trial



Which Thyroid nodules require FNAB?

- **U1-2:** FNA not required unless high risk
- **U3-5:** US guided FNA
- **FNA** of abnormal lymph nodes (diagnosis/staging)
- **Incidental** nodules on CT: clinical evaluation and further Ix (US) in high risk groups
- **PET-CT positive nodules:** US and FNA – higher risk of malignancy (35%)



THY classification

Classification	Cytology	Action
Thy 1	Non-diagnostic	US +/- repeat FNA
Thy 2	Non-neoplastic	Correlate with clinical and US findings
Thy 3a	Neoplasm possible (atypical features)	Further US +/- FNA MDT discussion if Thy3a on repeat sample
Thy 3f	Follicular neoplasm	Diagnostic hemi-thyroidectomy
Thy 4	Suspicious of malignancy	Diagnostic hemi-thyroidectomy
Thy 5	Diagnostic of malignancy	Therapy appropriate to tumour type: usually surgery

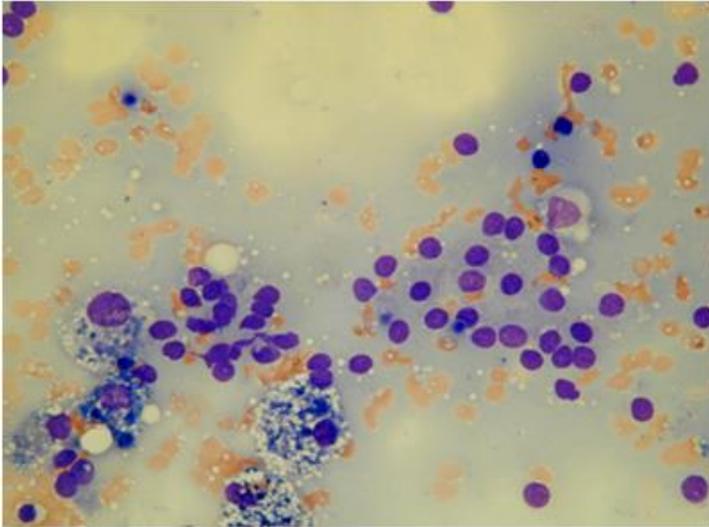


THY Classification

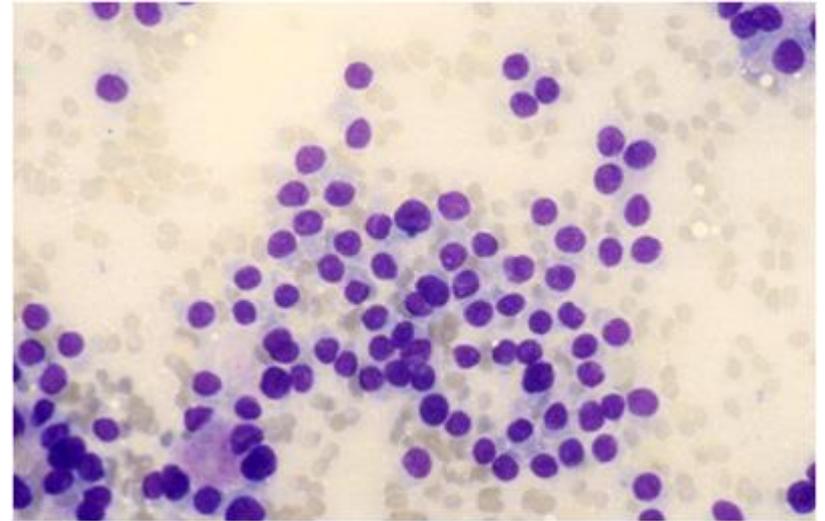
Classification	Frequency	Risk of malignancy
Thy 1	1-11% (mean 6%)	4.5-8%
Thy 2	62-85% (mean 72%)	<3%
Thy 3a	10-26% (mean 17%)	9.5-43%
Thy 3f		
Thy 4		
Thy 5	1-8% (mean 5%)	68-70%
		98-99%

➤ Median **34%** (14-48%) of patients with **indeterminate** cytology have malignancy

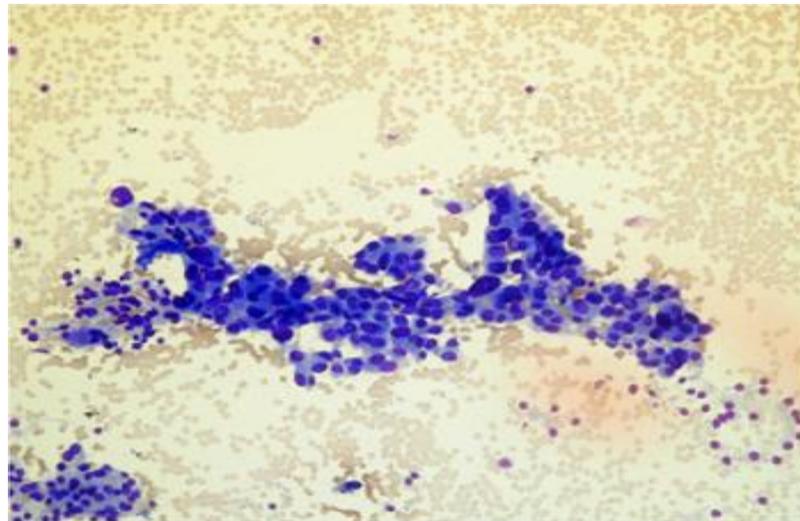
Fine needle aspiration biopsy



Benign: Thy 2



Follicular lesion: Thy 3f



Malignant: Thy 5



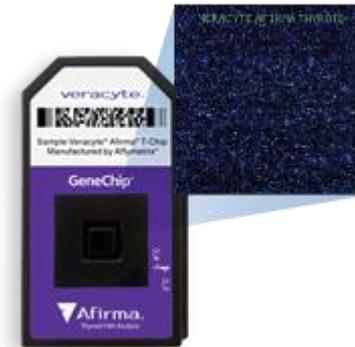
Case report 1

- **Neck examination:** palpable 1 x 1.5 cm R sided thyroid nodule, thyroid gland not enlarged
- **TSH:** 4.2 mIU/l
- **Thyroid US:** no neck node involvement
- **Fine needle aspiration biopsy (US-guided)**
- **Thy 3f lesion**
- **Recommendation:** hemi-thyroidectomy



Molecular markers to refine diagnosis

- BRAF^{V600E}, RAS, RET/PTC, PAX-PPARY, galectin 3 may be considered if **indeterminate cytology**
- May be combined with **US** criteria to improve specificity and PPV.
- Gene expression **classifiers/gene chips** to refine diagnosis of indeterminate lesions: expensive – validity to be proven
- **Avoid** diagnostic hemi-thyroidectomy?



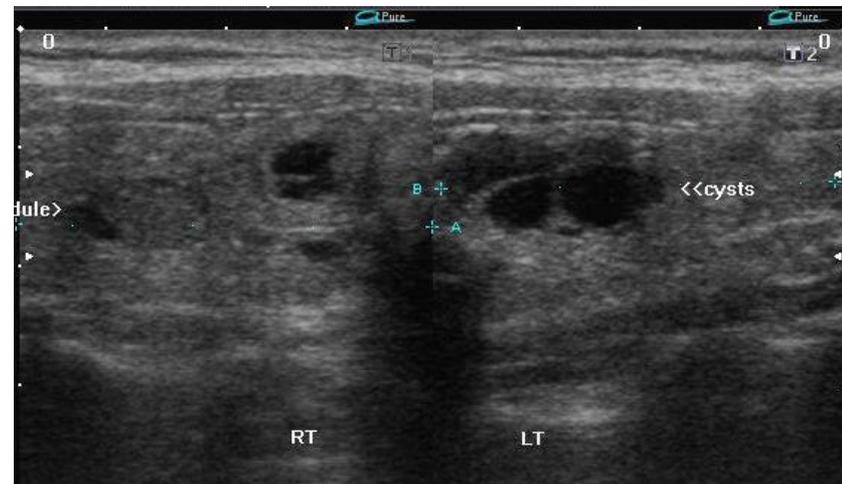
Alexander EK et al 2012 NEJM 376: 705-715

Xing et al. Lancet (2013) 381, 1058



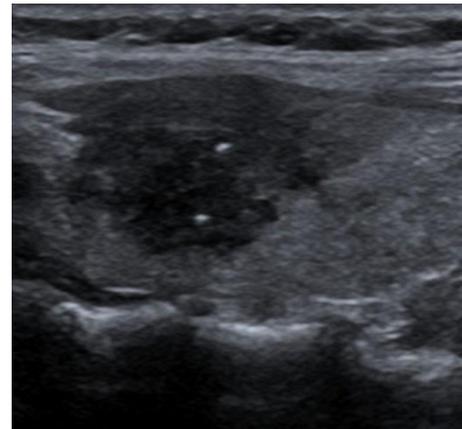
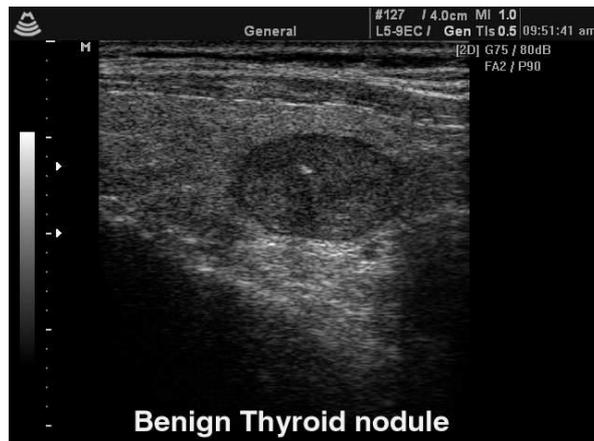
Multi-nodular thyroids

- **Same risk** of malignancy as in patient with **single nodule**
- **US** will provide information about **appearance** and **size** of thyroid and **number of nodules**
- **Palpable nodule** is not necessarily the **suspicious/ malignant** one
- Aspirate those with **suspicious US features**
- If none suspicious – **risk is low**
- **Suppressive levothyroxine** treatment not recommended



Follow-up of nodules

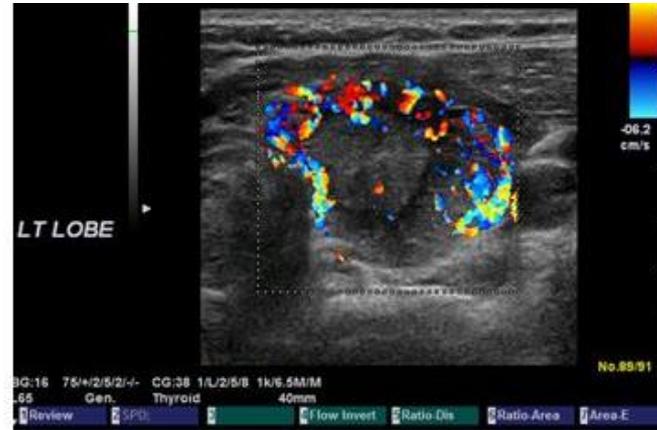
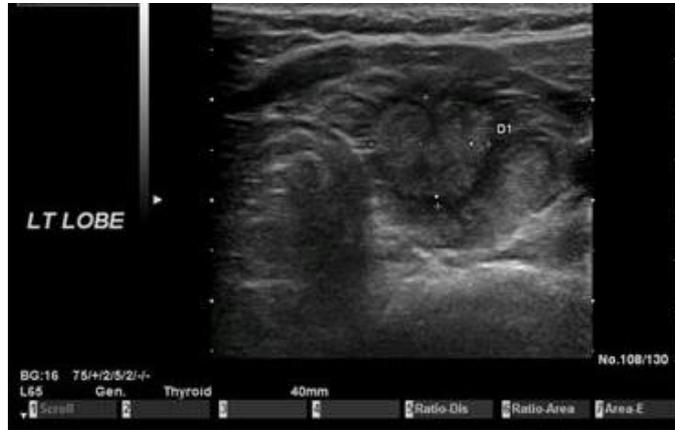
- Asymptomatic and **benign**: discharge
- **Benign** US and **Thy2**: no repeat FNA required
- **Suspicious** US and **Thy1**: repeat FNA
- **Suspicious/indeterminate** US and **Thy2**: repeat FNA
- **MDT** discussion if discordance between clinical suspicion, US, FNA



Case report 2

- **28y old female** patient – 8/40 pregnant
- **G2 P1** – healthy 3 y old boy
- Noticed **lump in neck** 4 weeks ago – slight **increase** in size
- **No** symptoms of **obstruction**
- **FHx:** Father: head and neck cancer
- **O/E:**
 - Thyroid **not enlarged**
 - Palpable L sided **1 cm thyroid nodule**

Case report 2



- **US neck: hypoechoic 12 x 11 x 12-mm nodule with markedly increased adjacent Doppler blood flow and ill-defined, low-echogenicity halo – U4**
- **TSH: 1.5 mU/l**



Which is the most appropriate next step?

- A: Perform fine needle aspiration biopsy now**
- B. Postpone FNAB until postpartum period**
- C: Perform L hemithyroidectomy in 2nd trimester**
- D: Repeat US after 8 weeks**
- E: Start levothyroxine therapy**



**Which is the most appropriate
next step?**

A: Perform fine needle aspiration biopsy now

Pregnancy



Nodules

- **New thyroid nodules** in pregnancy: **TFT, US**
- Investigate in **same way** as outside pregnancy: **FNA no risk to pregnancy**
- Consider **surgery** only for **suspicious nodules that grow rapidly**

New thyroid cancer diagnosis

- **Surgery** if **rapid growth** or development of **LN**
- Sx in **second** trimester
- **Risks** to foetus and mother lowest with **high volume surgeons**
- Avoid **131-I ablation**



Conclusions

- **Thyroid nodules are common clinical entities**
- **Clinical importance relates to malignant potential**
- **The initial evaluation should include history and clinical evaluation**
- **Serum TSH and US are pivotal in the evaluation of malignancy in thyroid nodules**
- **FNAC remains the gold standard for diagnosis of malignancy**
- **The use of molecular markers and ultrasound elastography may provide refinement of the diagnosis of malignancy**





Which of the following statements is TRUE?

- A:** An **incidental** thyroid nodule has a **higher risk of malignancy** than a **clinically** identified thyroid nodule
- B:** A thyroid nodule in a **30 year old female** has a **lower risk** of malignancy than that in a **75 year old male**
- C:** A thyroid nodule found in **pregnancy** carries a **higher risk** of malignancy
- D:** In a patient with a **multinodular** thyroid it is advisable to aspirate the largest **nodule**
- E:** An **hyperechoic** nodule is **more likely malignant** than a **hypo-echoic** nodule



Which of the following statements is TRUE?



B: A thyroid nodule in a 30 year old female has a lower risk of malignancy than that in a 75 year old male





Which of the following statements is TRUE?

- A:** The current **increased incidence** in differentiated thyroid cancer is largely due to increases in **ionising radiation exposure**
- B:** A thyroid FNA which is **suspicious of malignancy (Thy4)** is associated with a **25% risk of malignancy**
- C:** Fine needle aspiration biopsy should be **avoided** in **pregnancy** as it is associated with an increased risk of **miscarriage**
- D:** **Molecular markers** are now **widely used** to refine the diagnosis of malignancy in thyroid nodules
- E:** The presence of **microcalcifications** and increased **intranodular blood flow** on US are associated with **increased risks** of malignancy



Which of the following statements is TRUE?



E: The presence of **microcalcifications** and increased **intranodular blood flow** on US are associated with **increased risks** of malignancy

