EUROPEAN SOCIETY OF RADIOLOGY

eBook for Undergraduate Education in Radiology

CHAPTER: Endocrine System

Preface

Undergraduate teaching of radiology in Europe is provided according to national schemes and may vary considerably from one academic institution to another. Sometimes, the field of radiology is considered as a "cross-cutting discipline" or taught within the context of other clinical disciplines, e.g., internal medicine or surgery.

This e-book has been created in order to serve medical students and academic teachers throughout Europe to understand and teach radiology as a whole coherent discipline, respectively. Its contents are based on the *Undergraduate Level of the ESR European Training Curriculum for Radiology* and summarize the so-called ***core elements*** that may be considered as the basics that every medical student should be familiar with. Although specific radiologic diagnostic skills for image interpretation cannot be acquired by all students and rather belong to the learning objectives of the *Postgraduate Levels of the ESR Training Curricula*, the present eBook also contains some ***further insights*** related to modern imaging in the form of examples of key pathologies, as seen by the different imaging modalities. These are intended to give the interested undergraduate student an understanding of modern radiology, reflecting its multidisciplinary character as an organ-based specialty.

We would like to extend our special thanks to the authors and members of the ESR Education Committee who have contributed to this eBook, to Carlo Catalano, Andrea Laghi and Andras Palko, who initiated this project, and to the ESR Office, in particular Bettina Leimberger and Danijel Lepir, for all their support in realising this project.

We hope that this eBook may fulfil its purpose as a useful tool for undergraduate academic radiology teaching.

Minerva Becker   Vicky Goh

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Based on the ESR Curriculum for Undergraduate Radiological Education

Chapter: Endocrine System

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Pancreas, ovaries and testes are not included in this chapter. They are dealt with in separate eBook chapters.

Anatomy & Function: Thyroid and Parathyroids

The **thyroid gland** is located in the anterior lower visceral space of the neck. The gland has two lobes, connected by a thin midline portion called isthmus (Fig. 1). It produces hormones that regulate metabolism, growth, and development, including thyroxine (T4), triiodothyronine (T3) and calcitonin.

The parathyroids are small paired endocrine glands, typically located on the posterior surface of thyroid lobes (Fig. 1). Most individuals have four parathyroid glands, i.e., two superior and two inferior glands; however, about 15% of individuals have supernumerary parathyroids. Ectopy of the parathyroids is common. Typical ectopic locations include the superior mediastinum, the submental space and the retro-oesophageal area (most common). The parathyroid glands produce the parathyroid hormone (PTH), which regulates the calcium level in the blood.

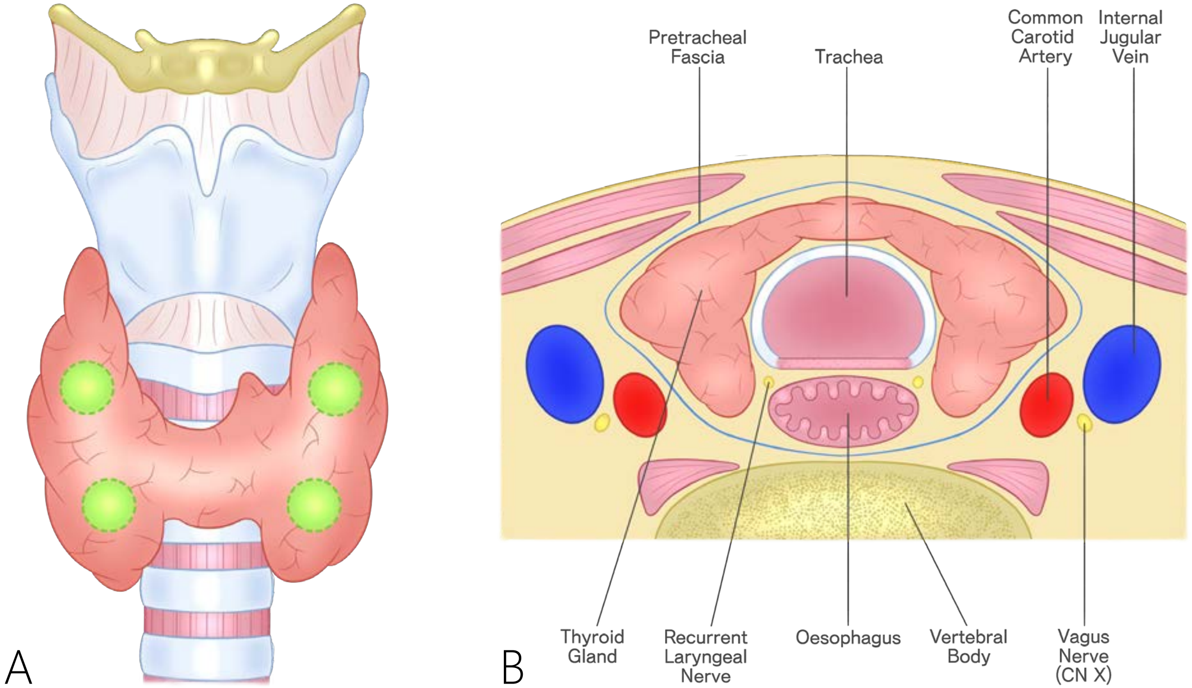

Fig. 1. Schematic diagram of the thyroid and parathyroid glands (green dots) and their relationship to important anatomical landmarks. A. Frontal view. B. Axial cross-section.

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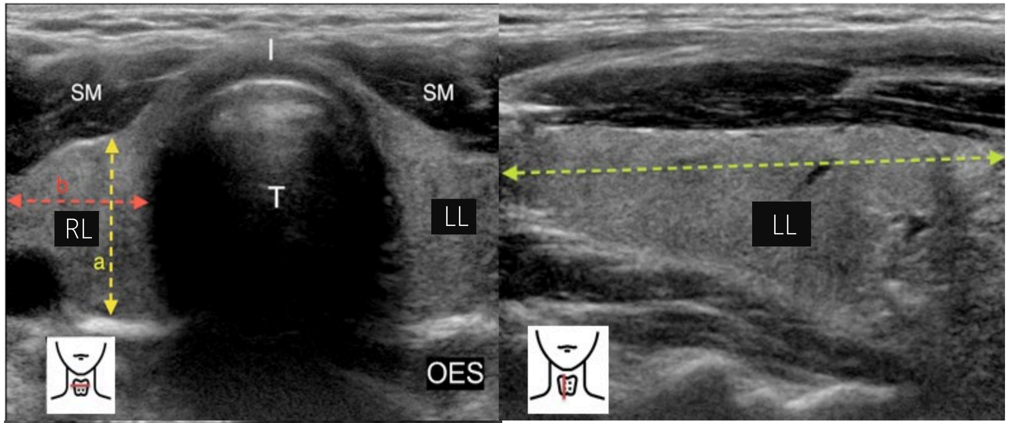
Anatomy & Function: Thyroid and Parathyroids

Due to its superficial position, ultrasonography (US) is the imaging modality of choice to explore the thyroid gland (Fig. 2). On US, the gland appears hyperechogenic compared to muscles and weakly vascularised. The volume (which depends on gender) is measured to diagnose gland atrophy versus enlargement (goitre).

CT or MRI (Fig. 3) are useful to evaluate gland extension into the mediastinum, tracheal compression or deep extension of a thyroid mass. The normal parathyroids are not visible on CT and MRI, however their position can be estimated based on the location of the inferior thyroid artery.



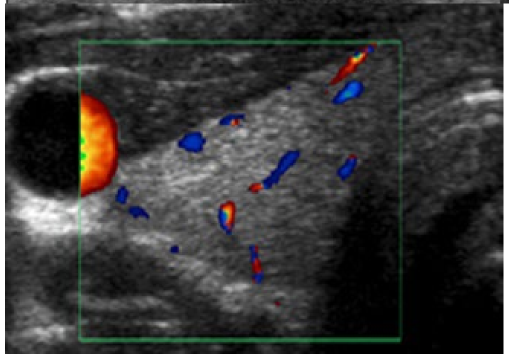


Fig. 2. Axial (A) and sagittal (B) US image illustrating the normal anatomy of thyroid gland with normal vascularisation seen at Doppler US (C). RL = right lobe; LL = left lobe; I= isthmus; SM = strap muscles; T = trachea; a = antero-posterior diameter; b = left right diameter; c = cranio-caudal diameter.

Normal weight = 25 - 30 g
Normal volume = 5 cm^3 - 18 cm^3 ♀ / 20 cm^3 ♂

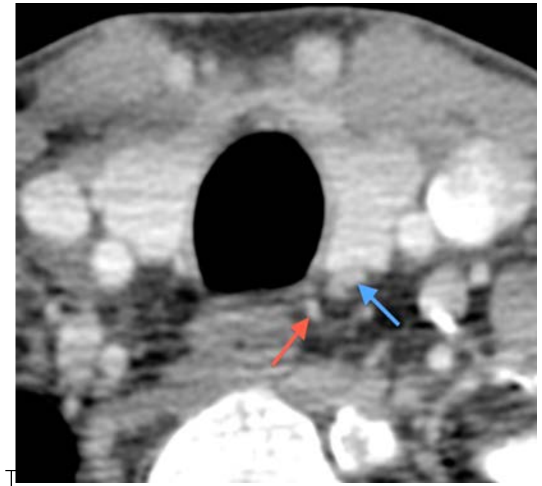


Fig 3. Normal thyroid gland on an axial contrast-enhanced CT image at the level of the cervical trachea. Red arrow (inferior thyroid artery) and blue arrow (inferior thyroid vein).

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Anatomy & Function: Pituitary Gland

The **pituitary gland** is a small endocrine gland located at the base of the brain, in a saddle-shaped depression of the sphenoid bone called the sella turcica (Fig. 4). The gland is divided into two parts, the anterior pituitary (ante-hypophysis or adenohypophysis) and the posterior pituitary (post-hypophysis). The pituitary stalk (also called infundibulum) connects the pituitary gland (especially the post-hypophysis) to the hypothalamus. The pituitary gland and stalk are located outside the blood-brain barrier. The cavernous sinuses are dural venous sinuses, which are located on both sides of the sphenoid bone and pituitary gland (Fig. 5).

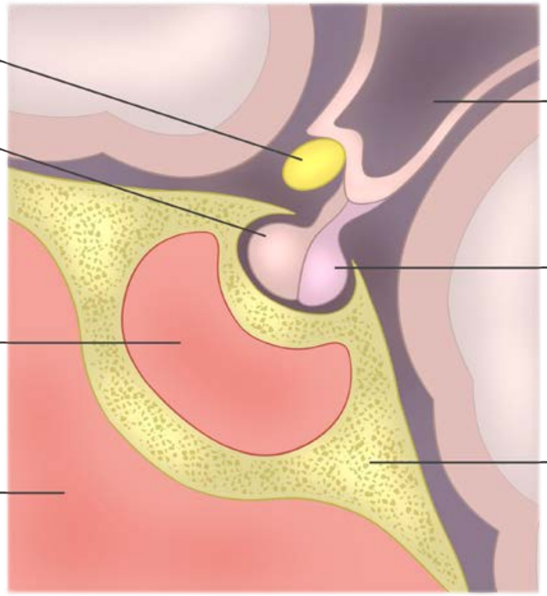

Fig. 4 . Schematic diagram of the sella turcica (sagittal view) with the anterior and posterior parts of the pituitary gland (adenohypophysis and post-hypophysis).

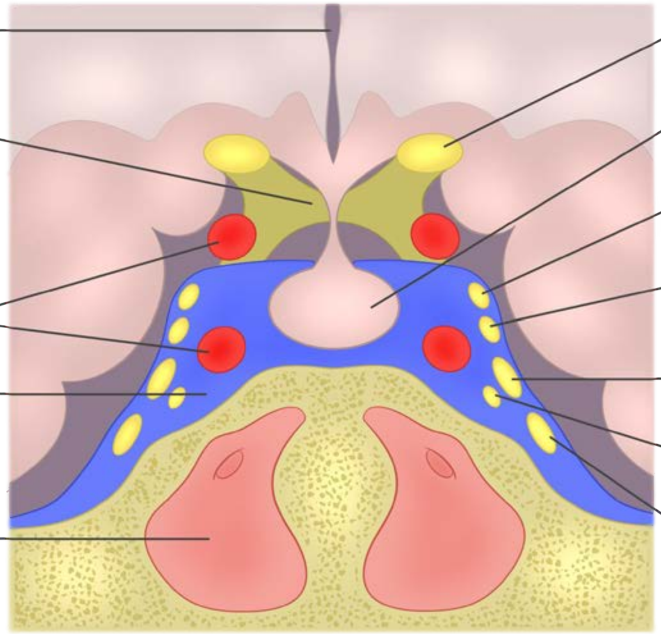

Fig 5. Schematic diagram of the sella turcica with the pituitary gland (coronal view). The cavernous sinuses are rendered in blue. The internal carotid artery and cranial nerves III, IV, V1, V2 and VI traverse the cavernous sinuses. Superiorly the main suprasellar structure located in proximity is the optic chiasm.

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Anatomy & Function: Pituitary Gland

The volume of the pituitary gland changes depending on hormonal status and age. In adults > 50 years, the gland gradually decreases in size.

MRI is the imaging modality of choice to evaluate the pituitary gland (Fig. 6).

On MRI, the posterior pituitary gland has a high signal on T1-weighted (T1W) images because of the storage of vasopressin (see next page).

Because the pituitary gland and the stalk are located outside the brain blood barrier, they both show enhancement after intravenous administration of contrast material on CT and MRI.

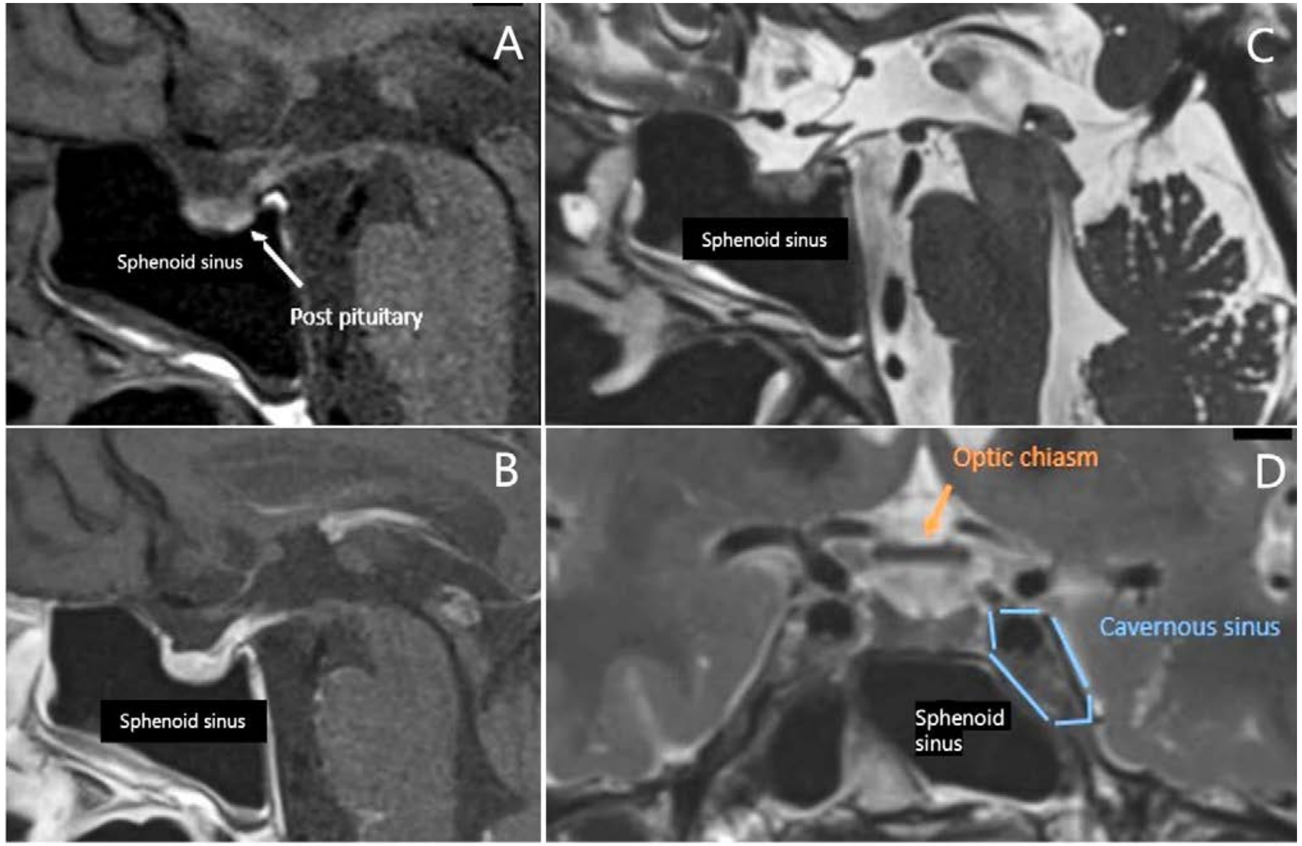

Fig. 6. Sagittal T1W MR image (A) shows normal high signal of the post-hypophysis. Corresponding contrast-enhanced T1W (B) image demonstrates normal homogenous enhancement of the gland and pituitary stalk. Sagittal (C) and coronal (D) T2W images show the anatomical position of pituitary fossa just above the sphenoid sinus, in between the paired cavernous sinuses and below the optic chiasm.

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Anatomy & Function: Pituitary Gland

The pituitary gland plays an important role in controlling the hormonal secretion of most other endocrine glands (Fig. 7). Its activity is mainly controlled by the hypothalamus. The hormones produced by the pituitary gland are released in bursts of a few hours, following a circadian rhythm or depending on other factors (e.g., menstrual cycle).

The adenohypophysis produces five hormones :
- Growth hormone (GH) or somatotropin
- Prolactin (PRL)
- Adrenocorticotropic hormone (ACTH)
- Thyroid stimulating hormone (TSH)
- Follicle stimulating hormone (FSH) and
- Luteinizing hormone (LH)

The post-hypophysis stores and releases two hormones produced by the hypothalamus :
- Antidiuretic hormone (ADH), also known as vasopressin, which regulates water balance.
- Oxytocin, which stimulates uterine contractions during childbirth and promotes milk ejection during breastfeeding.

Hormonal testing is crucial in the context of adrenal pathologies. However hormonal assessment may be challenging due to circardian rhythm , sex /age, drug interactions, etc.
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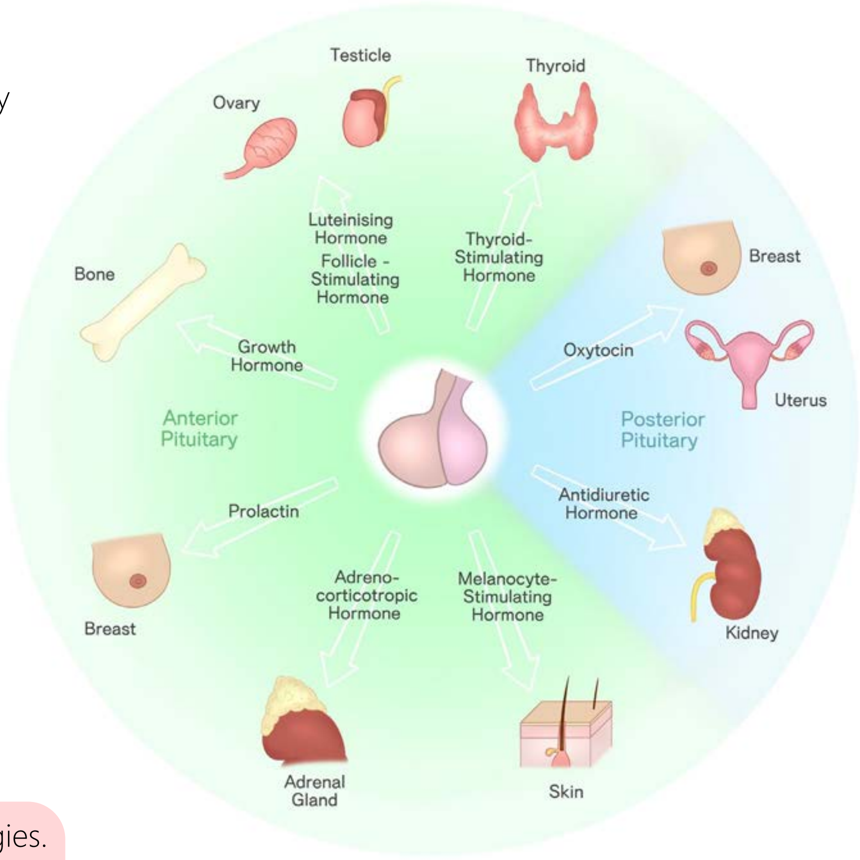

Fig. 7. Schematic diagram of pituitary hormal secretions and their different functions on the target organs

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Anatomy & Function: Adrenal Glands

The **adrenal glands** (**Figs. 8 and 9**) are a pair of small, triangular-shaped glands located on top of each kidney. Each gland is formed by an outer cortex and an inner medulla. The adrenal cortex is divided into three zones. The **zona glomerulosa** produces mineralocorticoids, e.g., aldosterone, which regulates the balance of electrolytes and blood pressure. The **zona fasciculata** produces glucocorticoids (cortisol and cortisone), which regulate metabolism, immune system and stress response. The **zona reticularis** produces androgens.

The adrenal medulla releases two hormones, i.e., epinephrine (adrenaline) and norepinephrine (noradrenaline). These hormones are involved in the "fight or flight" rapid body response to stress.

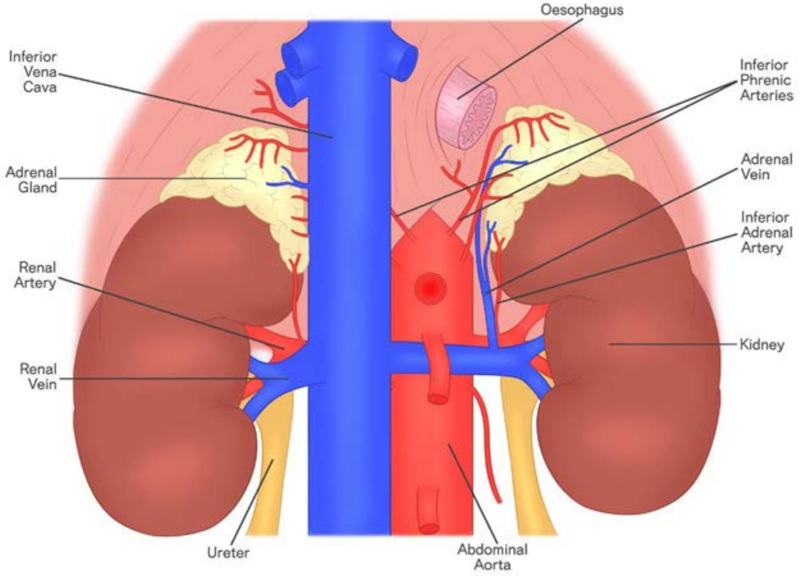

Fig. 8. Schematic illustration of the adrenal glands and surrounding anatomic structures (coronal view).

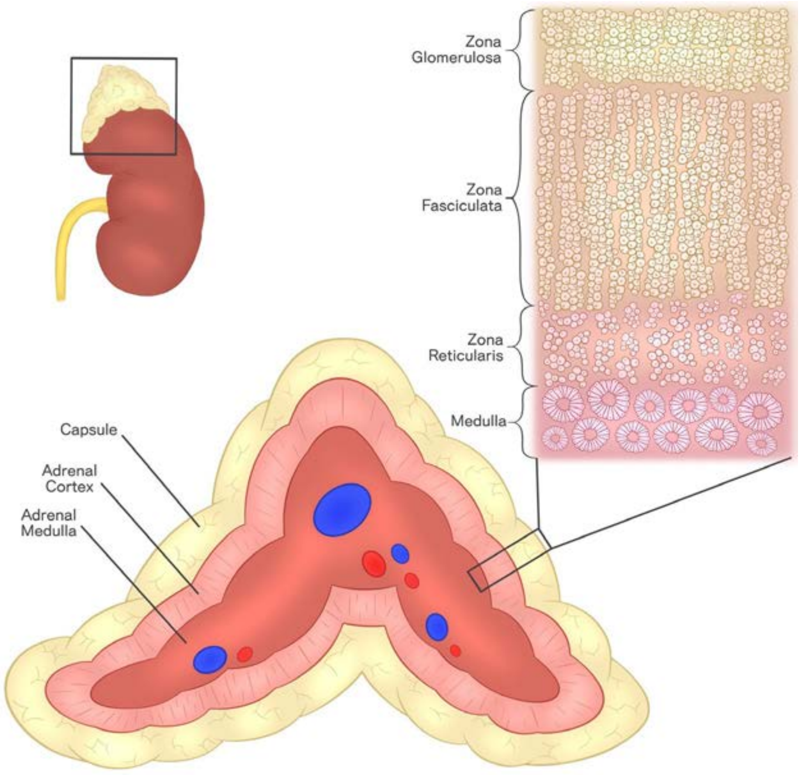

Fig. 9. Schematic drawing of an adrenal gland and its different components.

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Anatomy & Function: Adrenal Glands

The right adrenal gland has a maximum width of 6 mm and the left adrenal gland has a maximum width of 8 mm. Proportionally, the size of the adrenal glands is larger in new-borns and infants, being almost a third of the size of the kidneys. In young children, the adrenal glands are easily seen on abdominal US (Fig. 10). However, in adolescents and adults, the normal adrenal glands are less well visible on US (Fig. 11), especially in large or obese patients unless they are enlarged. In general, the left adrenal gland is more difficult to visualise than the right.

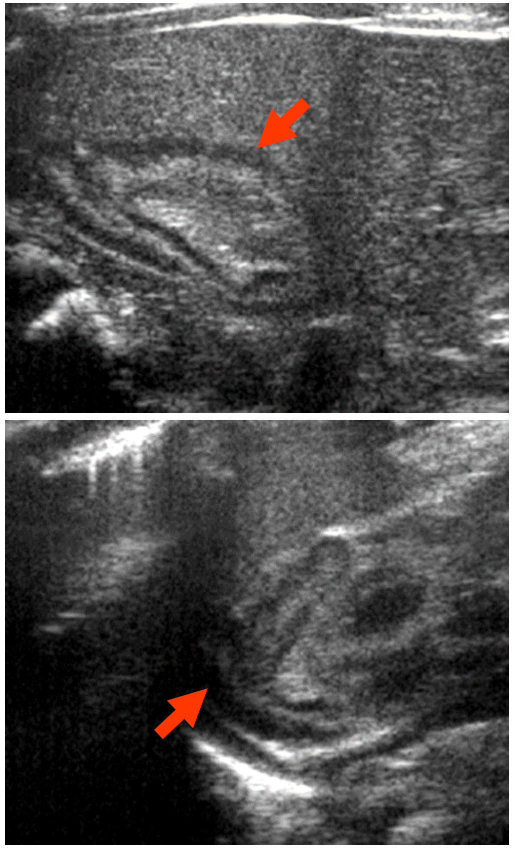

Fig. 10. Newborn abdominal ultrasound showing normal adrenal glands. The glands appear as an Y shaped structure surrounded by a hypoechogenic rim (arrows).

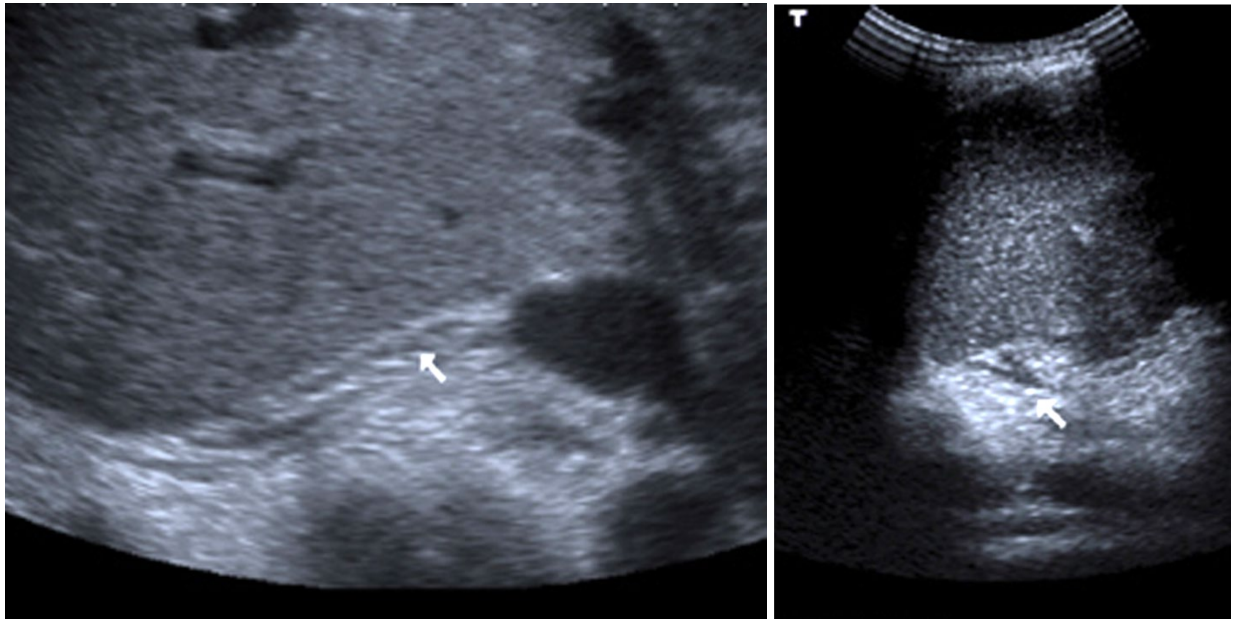

Fig. 11. Adult abdominal ultrasound. White arrows showing two small adrenal glands. As mentioned above, it's not uncommon not to see them on US. In adults, CT or MRI are better suited for adrenal gland imaging.

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Anatomy & Function: Adrenal Glands

In general, the right adrenal gland is slightly smaller than the left adrenal gland and it has a triangular shape on axial images (Fig. 12).

In contrast, the left adrenal gland can either appear as crescent shaped or as triangular on axial images (Fig. 12).

The right adrenal gland is posterior to the inferior vena cava and adjacent to the right liver.

The left adrenal gland is located medially to the spleen with the splenic pedicle running along its lateral limb.

The adrenal glands typically show enhancement after intravenous contrast administration.

On coronal images , both adrenal glands have a triangular shape (Fig. 12).

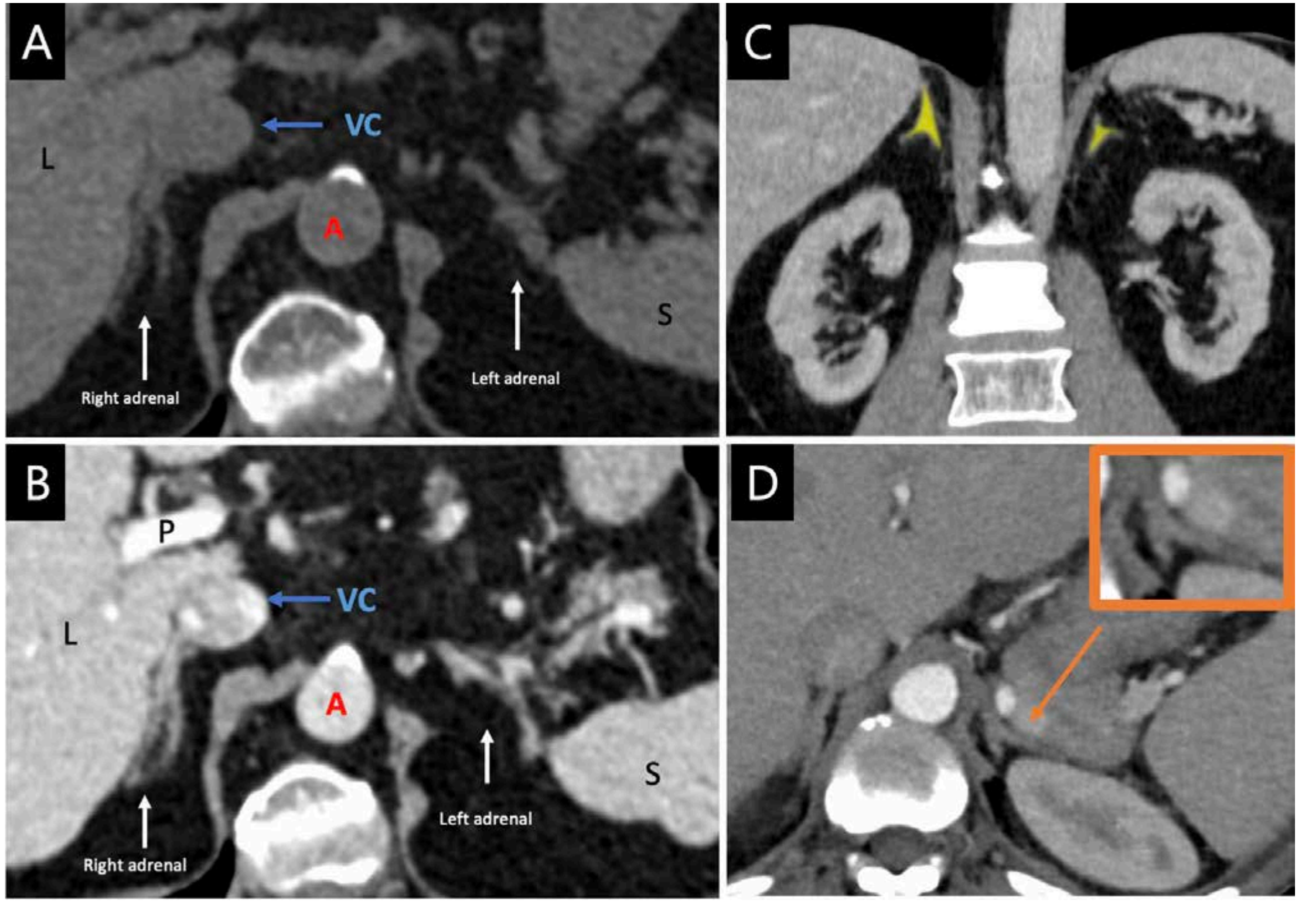

Fig. 12. Axial (A and B) CT images obtained in the same patient without (A) and with contrast administration (B). Liver (L), spleen (S), aorta (A). Coronal (C) and axial (D) images in a different patient. On the coronal image, the adrenal glands are rendered in yellow.

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Anatomy & Function: Paraganglia

Paraganglia are neuroendocrine cell clusters associated with the autonomic nervous system.

Depending on their location, they can be classified as sympathetic (made of chromaffin cells) or parasympathetic (made of nonchromaffin glomus cells).

Sympathetic paraganglia have an endocrine function, whereas parasympathetic paraganglia have primary chemoreceptor function. Paraganglia with chemoreceptor function detect changes in blood pH, O_2 and $C0_2$ levels and thus regulate circulation and respiration.

Sympathetic paraganglia can be found in the adrenal medulla or in extra-adrenal locations along the sympathetic nervous system, including the organ of Zuckerkandl.

Parasympathetic paraganglia are found the carotid and aortic bodies, along the vagus (X) and glosso-pharyngeal (IX) nerves and their branches.

Tumours arising in paraganglia are called paragangliomas.
Chromaffin paragangliomas are called pheochromocytomas.

=> See pages 47-49 in this chapter.

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Choice of Imaging Techniques:
Ultrasonography for the Thyroid Gland

INDICATIONS
- Characterisation and classification of thyroid lesions.
- US has a high sensitivity for identifying malignant lesions based on certain sonographic criteria such as: hypoechogenic, ill-defined margins, microcalcifications, shape (taller-than-wide), high vascularity (Fig. 13).
- US is used to distinguish benign from malignant lymph nodes based on their shape, size and pattern of vascularity (Fig. 14).

Advantages:
- Quick and cheap
- Non-invasive
- No ionising radiation
- Aids in guiding fine needle aspiration (FNA) or biopsy in suspected thyroid gland lesions or lymph node metastases.
- Excellent spatial resolution (the ability to distinguish small structures or features).

Disadvantages:
- Operator dependent
- No standardised, reproducible imaging documentation
- Unable to assess retrosternal lesions.
- Cannot reliably distinguish benign from malignant follicular lesions (see below)

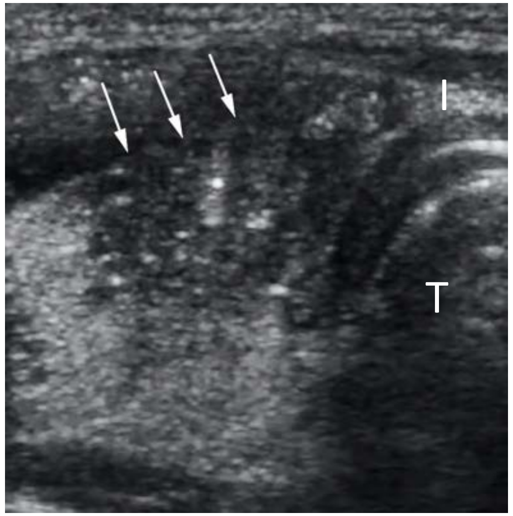

Fig. 13. Transverse US shows a strongly hypoechogenic lesion with irregular margins, containing microcalcifications (small hyperechoic areas) in the right thyroid lobe. This was a histologically proven papillary carcinoma. T = trachea; I = isthmus

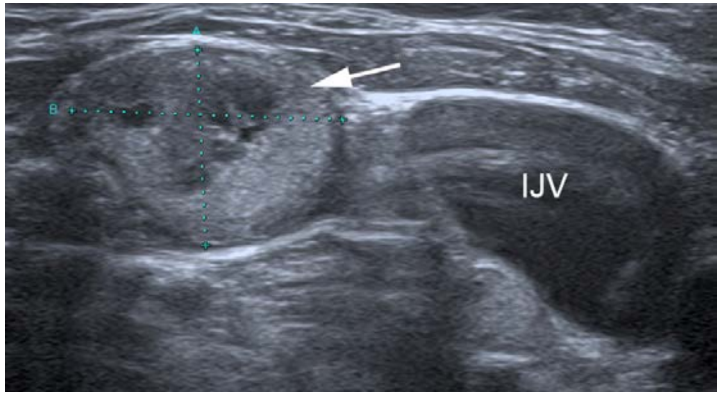

Fig. 14 US shows a pathological lymph node (white arrow) lying lateral to the internal jugular vein (IJV), with no fatty hilum, internal cystic changes and internal echogenic foci, consistent with microcalcifications.

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Choice of Imaging Techniques:
Ultrasonography Guided Fine Needle Aspiration (FNA)

INDICATIONS
- Characterising thyroid nodules or lymph nodes

Advantages:
- No ionising radiation
- Aids in guiding the exact site of fine needle aspiration (FNA) or biopsy in suspected thyroid gland lesions (Figs. 15 & 16) or lymph node metastases.

Disadvantages:
- Operator dependent
- If lymphoma is suspected, a biopsy is necessary

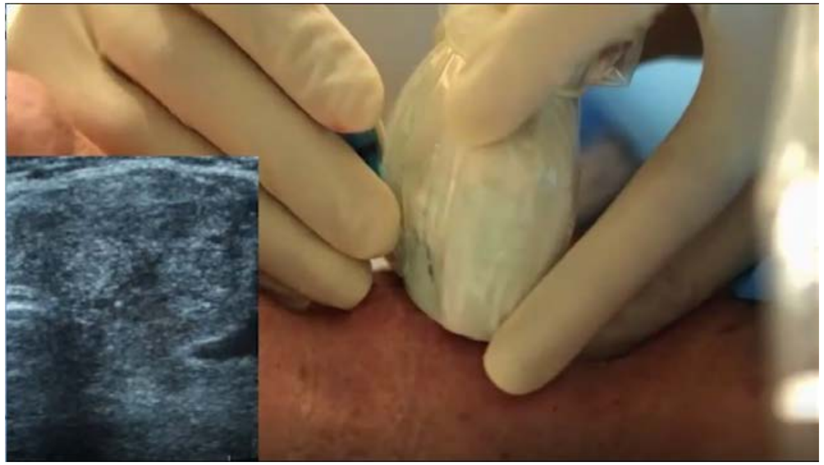

Fig 15. Photograph of an FNA being performed with the corresponding US image.

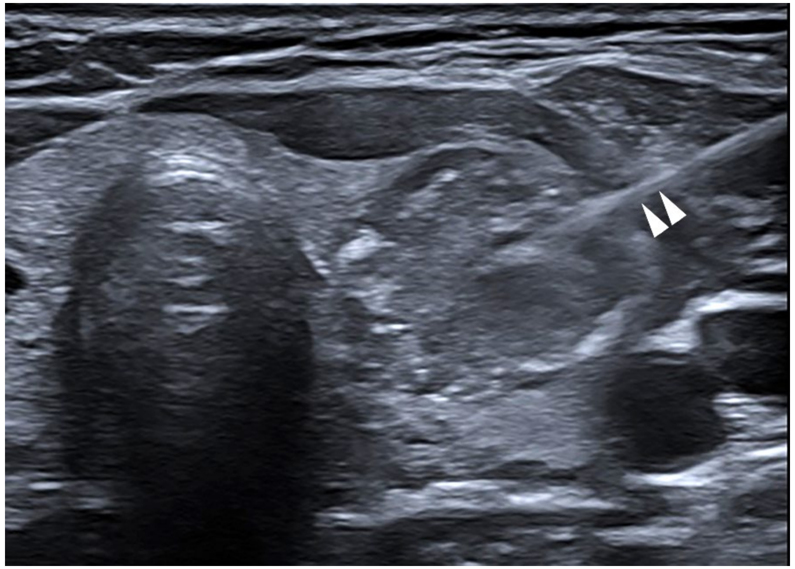

Fig 16. US image demonstrates the needle (double arrowheads) within a nodule in the left thyroid lobe.

In cases where lymphoma is suspected, whether in the thyroid gland or in pathological lymph nodes, US guided biopsy is preferred to FNA as it aids in reaching a more conclusive and precise diagnosis in certain lymphoma types.

Bernadette Koch, Bronwyn E. Hamilton, Patricia Hudgins, H. Ric Harnsberger (2017). Diagnostic Imaging: Head and Neck, 3rd edn. Elsevier, Philadelphia.

https://www.sciencedirect.com/science/article/pii/S1879729616301399

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Choice of Imaging Techniques:
Computed Tomography (CT) for the Thyroid Gland

INDICATIONS

Reserved for locally advanced cases where there is a strong suspicion of deep invasion and/or metastatic disease and for surgical planning

Advantages:

- Can allow evaluation of retrosternal extent in large lesions to guide surgical management
- Helps characterise large lesions and clearly demonstrates necrosis and extracapsular extension (Fig. 17)
- Able to identify deep seated metastatic lymph nodes lying behind the manubrium or behind the clavicle
- High resolution CT can be used to detect very small lung metastases
- MRI is superior to CT for assessing invasion of trachea/oesophagus (less suited for the lungs)

Disadvantages:

- Iodine based contrast agents are contraindicated in differentiated thyroid malignancies because they delay radioiodine therapy by 6 months
- Radiation penalty
- Unable to characterise smaller thyroid nodules due to its limited spatial resolution compared to US

https://radiopaedia.org/articles/thyroid-malignancies

Fig. 17. CT scan of the neck after contrast administration demonstrates a thyroid mass with necrotic centre (asterisk) and ill-defined margins, causing severe contralateral tracheal shift, and associated with intraluminal invasion of the trachea (arrow). This was a biopsy proven poorly differentiated thyroid carcinoma.

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Choice of Imaging Techniques:
Magnetic Resonance Imaging (MRI) for the Thyroid Gland

INDICATIONS
- Not the first imaging modality
- Can help identify retropharyngeal lymph node metastases (rare)

Advantages:
- Non-invasive
- No ionising radiation
- Useful in the context of locally advanced thyroid cancer to determine extrathyroidal extension and invasion of regional structures
- Staging of lymph node metastases
- Can determine the degree of retrosternal extension in large thyroid goitre and the degree of locoregional spread including the degree of vessel encasement (Fig. 18)
- Can be used in the follow-up of goitres in patients who are not ideal candidates for surgery avoiding repeated ionising radiation exposure

Disadvantages:
- Limited spatial resolution in comparison to US
- Patient claustrophobia may preclude its use.
- Motion and swallowing artifacts in lesions with tracheal compression/invasion degrade image quality.

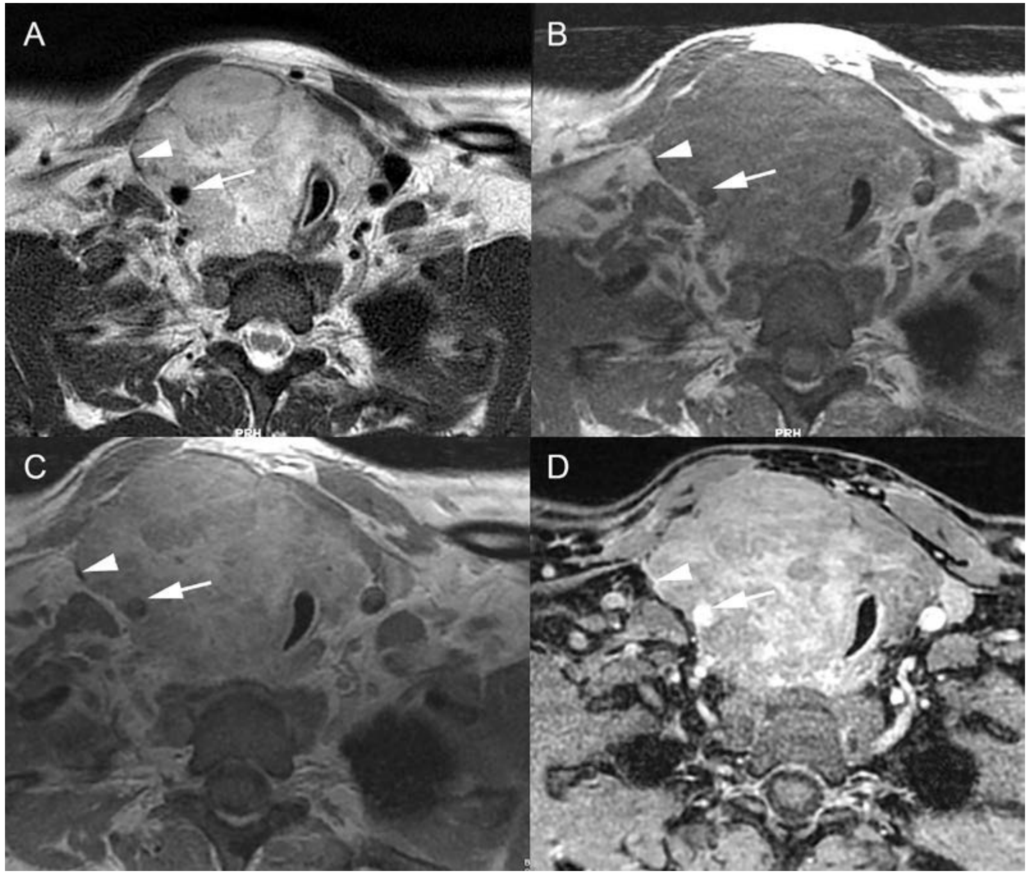

Fig. 18. A. T2 weighted sequence at the level of the thyroid gland shows complete infiltration of the thyroid gland, particularly on the right, by a hyperintense mass, encasing the right common carotid artery (arrow) and effacing the internal jugular vein (arrowhead). The mass has a low signal onT1 (B) and enhances in a heterogeneous fashion after contrast on T1 sequences before and after fat suppression (C and D).

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Choice of Imaging Techniques:
Nuclear Medicine Studies for the Thyroid Gland

INDICATIONS

- Iodine-123 and Iodine-131 in cases of differentiated thyroid cancer for the detection of nodal and distant metastases (staging) and also in the diagnosis of Graves disease
- Iodine-131 is useful as ablation therapy in post-thyroidectomy patients, detection of nodal recurrence and ablative therapy in patients with Graves disease
- Indium-111 labelled octreotide and PET / CT with 68Ga-DOTA-TATE are used for medullary thyroid cancer
- FDG PET-CT is useful in staging medullary thyroid cancer and in poorly differentiated thyroid cancers that are non-iodine avid (Fig. 19).
- Technetium-99m pertechnetate used in the diagnosis of Graves disease
- SPECT/CT improves the diagnostic accuracy of the 131I scan in the context of differentiated thyroid cancer

Advantages:

- Can sometimes differentiate benign from malignant nodules based on their uptake, with "hot" nodules conventionally suggestive a benign aetiology. Conversely "cold" nodules raise the suspicion of malignancy
- Can distinguish between Graves disease and other thyroid disorders
- Iodine-123 produces the best whole body image quality in follow-up studies and is most sensitive in differentiated thyroid cancer metastases (*Sarkar et al. 2002*)
- SPECT/CT helps to better distinguish cervical lymph node metastases from residual thyroid tissue, lung from mediastinal metastases and bone from soft tissue metastases

Disadvantages:

- Radiation exposure
- Contraindicated in pregnancy and lactation within past two months
- Iodine-131 is contraindicated in severe uncontrolled thyrotoxicosis, while its effect on thyroid orbitopathy is somewhat controversial
- With respect to cancer imaging sensitivity :
    - depends on tumour volume and histology
    - is reduced by increased total body iodine from diet, intravenous iodinated contrast material, amiodarone and carbimazole.

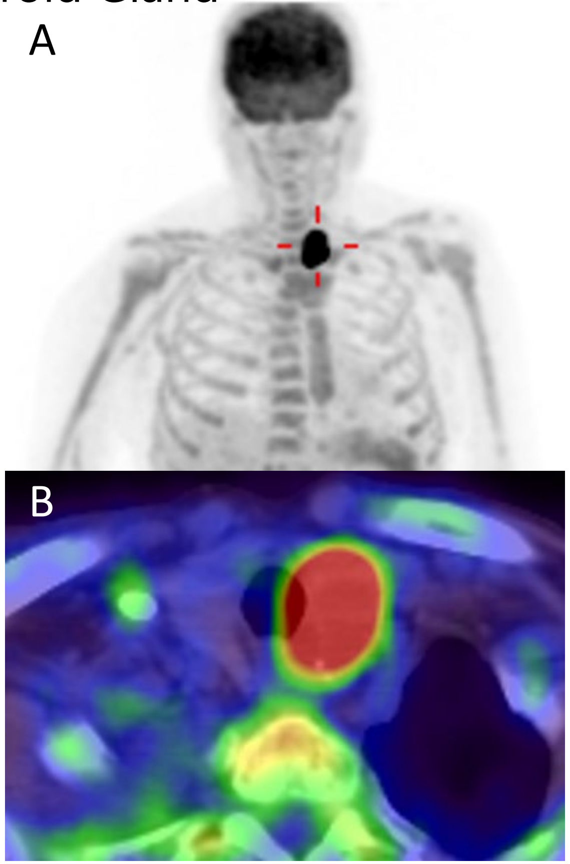

Fig. 19. A. MIP and B. fused axial 18F-FDG PET/CT scan demonstrating avid uptake of FDG in the left thyroid bed. This was histologically proven medullary thyroid carcinoma detected incidentally on a staging PET performed for multiple myeloma

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Choice of Imaging Techniques:
Ultrasonography for the Parathyroid Glands

INDICATIONS
- Excellent at identifying parathyroid lesions adjacent to the thyroid gland (Fig. 20).
- Pivotal role in diagnosing parathyroid lesions in patients with clinically confirmed hyperparathyroidism but a negative 99mTc-Sestamibi SPECT study.
- Complimentary to nuclear medicine studies.

Advantages:
- Quick and cheap
- Non-invasive
- No ionising radiation
- Excellent spatial resolution and morphological evaluation
- Allows concurrent US guided aspiration for PTH levels in case of intrathyroidal lesions.

Disadvantages:
- Operator dependent
- Relies only on the structural characteristics of the lesion
- Limited to superficial evaluation
- May be more difficult to detect in patients with short necks or patients with large thyroid goitres
- No standardised, reproducible imaging documentation
- Unable to assess ectopic parathyroid lesions
- It can be difficult to distinguish between the following:
  - ✓ Parathyroid lesions within the thyroid gland
  - ✓ Small solitary parathyroid nodules and paratracheal lymph nodes
  - ✓ Cystic parathyroid lesions (Fig. 21) and cystic metastases from thyroid papillary or squamous cell carcinoma

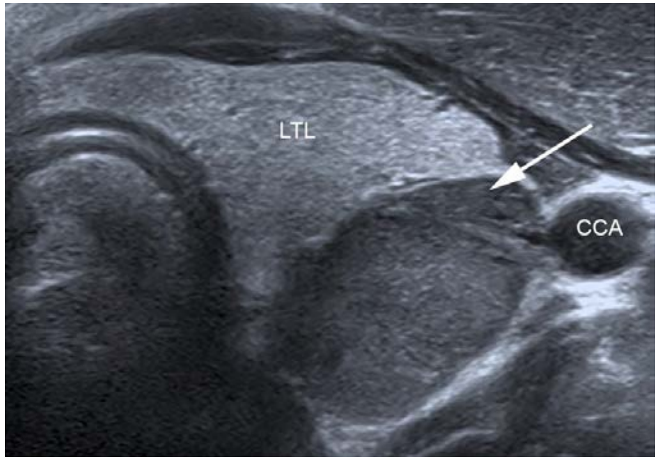

Fig. 20. US image shows a sizeable, sharply circumscribed, hypoechoic, solid nodule (white arrow), lying inferior to the left thyroid lobe (LTL) and medial to the common carotid artery (CCA). This was a histologically proven parathyroid adenoma.

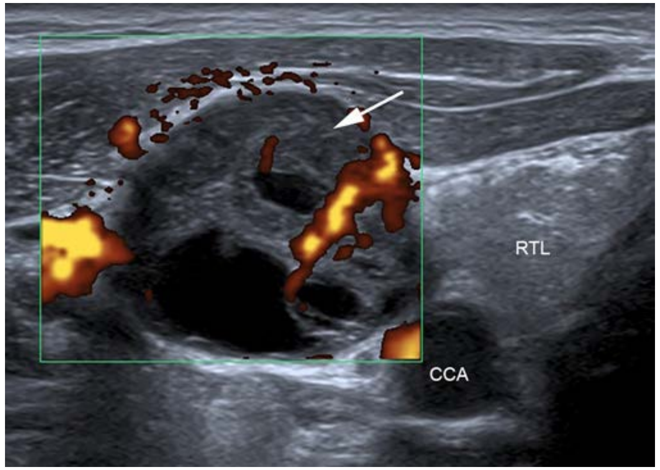

Fig. 21. US image shows a hypoechoic nodule (arrow) of mixed cystic and solid composition lying lateral to the right thyroid lobe (RTL) and common carotid artery (CCA). It exhibits modest vascularity at Doppler interrogation. This was a histologically confirmed parathyroid adenoma with cystic degeneration.

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Choice of Imaging Techniques:
Computed Tomography (CT) for the Parathyroid Glands

INDICATIONS

- Sometimes referred to as 4D CT, CT is the imaging modality of choice in patients with primary hyperparathyroidism who are being worked-up for surgery

Advantages:

- Allows accurate preoperative imaging localisation of a single adenoma thereby allowing minimally invasive parathyroidectomy (Fig. 22)
- Provides anatomic localisation of ectopic PTA discovered with radionuclide exam
- Useful when there are discordant findings between US and scintigraphy studies
- Provides clarification in the context of multinodular goitre which may obscure findings on both US and Technetium scans
- Provides critical information about number, size and specific location of the parathyroid lesion with respect to important anatomical landmarks
- Can identify important vascular anomalies associated with a nonrecurrent laryngeal nerve.
- Used in the postoperative neck (recurrent/persistent hyperparathyroidism, failed surgery) in combination with scintigraphy

Disadvantages:

- Ionising radiation particularly given that it is a multiphase study
- Uses iodinated contrast agents, which are contraindicated in patients with severe renal failure (see chapter on contrast media)
- Cannot reliably distinguish an intrathyroidal parathyroid adenoma from a thyroid nodule.

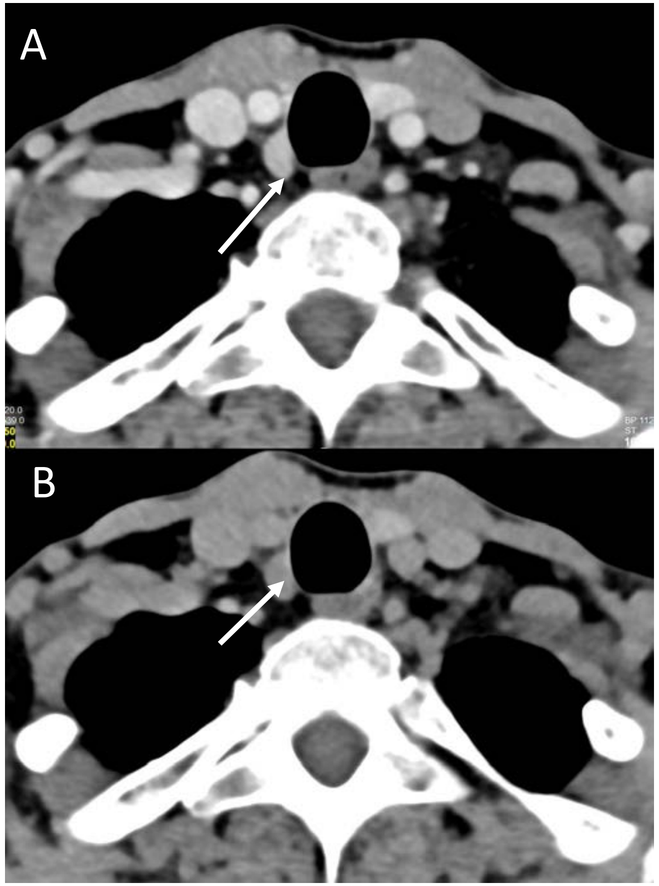

Fig. 22. Images from a 4DCT in the arterial and venous phases (A and B) demonstrate a small parathyroid adenoma below and separate from the right thyroid lobe.

Images courtesy of Dr Reuben Grech MD FRCR ESHNRD ESNRD PhD (Mater Dei Hospital Malta)

Bunch PM, Randolph GW, Brooks JA, George V, Cannon J, Kelly HR. Parathyroid 4D CT: What the Surgeon Wants to Know. Radiographics. 2020 Sep-Oct;40(5):1383-1394. doi: 10.1148/rg.2020190190.

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Choice of Imaging Techniques:
Magnetic Resonance Imaging (MRI) for the Parathyroid Glands

INDICATIONS
- Complimentary to nuclear medicine studies.

Advantages:
- No ionising radiation
- High spatial and temporal resolution
- Can allow identification of ectopic parathyroid tissue
- In a small proportion of patients with atypical parathyroid lesion characteristics, contrast enhanced MRI can increase sensitivity
- In addition to providing information on structural features, it also provides information on enhancement characteristics which can better help distinguish parathyroid from adjacent structures

Disadvantages:
- Long scanning times
- It can be difficult to distinguish between the following:
    - ✓ Parathyroid lesions within the thyroid gland
    - ✓ Small solitary parathyroid nodules and paratracheal lymph nodes
    - ✓ Cystic parathyroid lesions and cystic metastases from thyroid papillary or squamous cell carcinoma

Lopez Hänninen E, et al. Preoperative contrast-enhanced MRI of the parathyroid glands in hyperparathyroidism. Invest Radiol. 2000 Jul;35(7):426-30.

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Choice of Imaging Techniques:
Nuclear Medicine Studies for the Parathyroid Glands

INDICATIONS

Tc-99m MIBI (methoxyisobutylisonitrile) scan

- Often used as a first line imaging tool in primary hyperparathyroidism
- Similar sensitivity and specificity to US in experienced hands
- Works on the principle that MIBI washes out more rapidly from the thyroid than from abnormal parathyroid tissue (Fig. 23)

Advantages:

- Single radiotracer, dual-phase acquisition
- Can be combined with SPECT with/without CT for accurate localisation.

SUBTRACTION TECHNIQUE:

- Dual radiotracer, dual-phase acquisition
- The radioisotopes Tc-99m pertechnetate and I-123 (radioiodine) are only taken up by the thyroid gland
- Conversely, the radioisotope Tc-99m MIBI is taken up by thyroid and parathyroid glands
- Subtraction studies remove the thyroid uptake, leaving only parathyroid uptake.

Advantages:

- Can be used when multinodular goitre or thyroid masses risk obscuring parathyroid uptake.

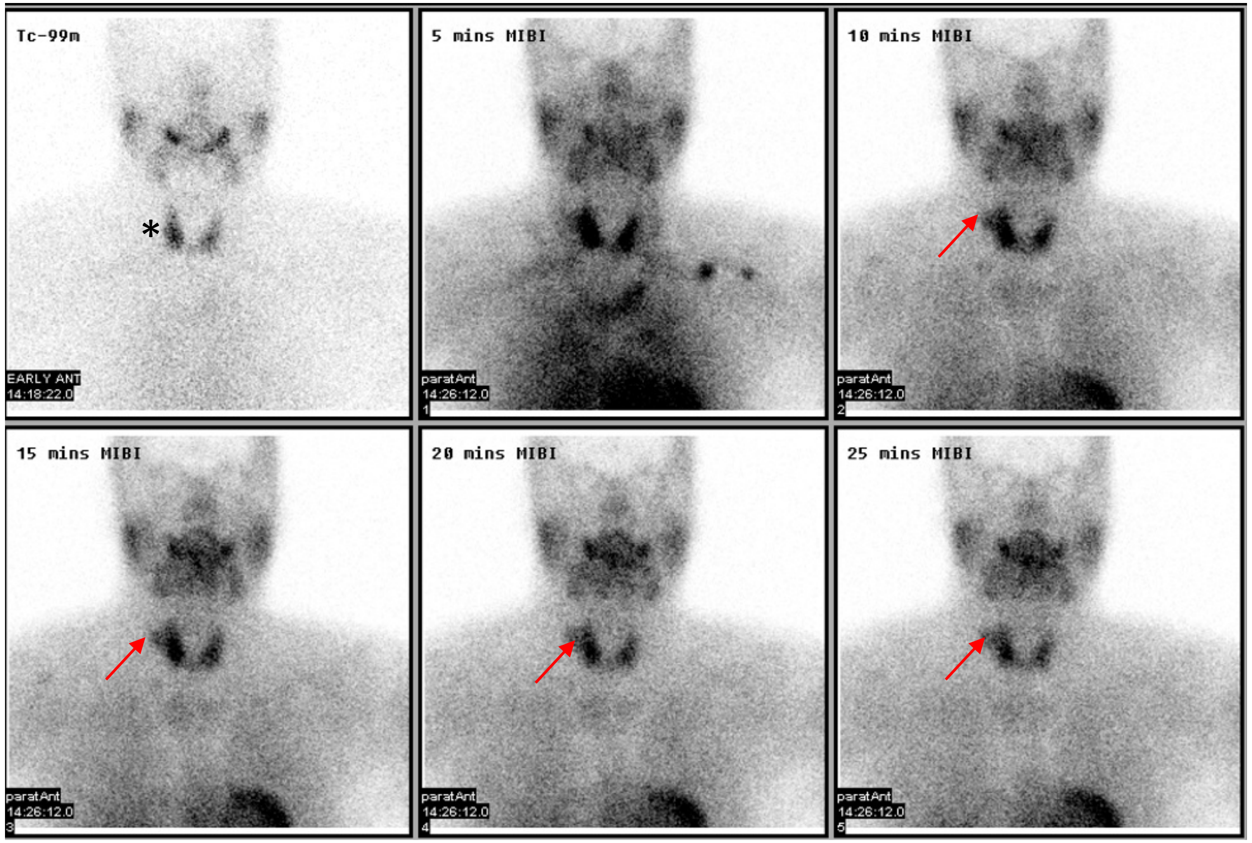

Fig. 23. Thyroid and parathyroid scintigraphy performed following IV administration of Tc 99m and Tc 99m MIBI respectively show a focus of increased tracer uptake lateral to the upper pole of the right thyroid lobe on the Tc 99m MIBI images (red arrows) that is not evident on technetium thyroid map (asterisk).

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Both Tc-99m MIBI scan and subtraction techniques:
✓ Have a crucial role in diagnosing ectopic and intrathyroidal parathyroid lesions in the context of hyperparathyroidism.

Disadvantages:
- low spatial resolution in localising parathyroid lesions
- Sometimes difficult to differentiate thyroid nodules from parathyroid lesions (*Spanu A, et al. SPECT/CT in hyperparathyroidism. Clin Transl Imag. 2014*)
- May give false negatives in cases of cystic parathyroid lesions, small size
- False positive may occur in the presence of a solid thyroid nodule, thyroid carcinoma, lymphoma and lymphadenopathy
- Less sensitive for detecting hyperplastic parathyroid glands
- Less sensitive for detecting multi-gland disease than solitary gland disease.

SPECT-CT offers a number of advantages over 131-Iodine scan including:
- better attenuation correction
- increased specificity
- accurate depiction of the localisation of disease and of possible involvement of adjacent tissue

Christopher J. Palestro, Maria B. Tomas, Gene G. Tronco, Radionuclide Imaging of the Parathyroid Glands, Seminars in Nuclear Medicine, Volume 35, Issue 4, 2005, Pages 266-276, ISSN 0001-2998

Ishii, S. et al. Causes of false negatives in technetium-99 m methoxyisobutylisonitrile scintigraphy for hyperparathyroidism: influence of size and cysts in parathyroid lesions. Ann Nucl Med 34, 892–898 (2020).

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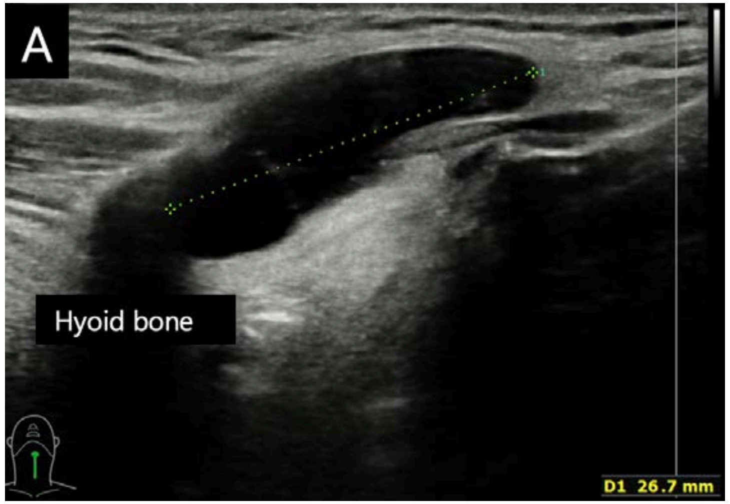
Congenital Malformations: Thyroglossal Duct Cyst

- During embryologic development, the thyroid gland originates as a small outpouching of endodermal tissue in the base of the tongue. This tissue migrates downwards along the neck midline guided by the thyroglossal duct (TGD), to reach its final position in the lower neck. As the thyroid gland descends, the TGD normally disappears, leaving behind a solid thyroid gland.
- However, in some cases, the TGD fails to disappear completely, leaving behind a cystic structure that can become infected or inflamed, causing pain and swelling in the neck.



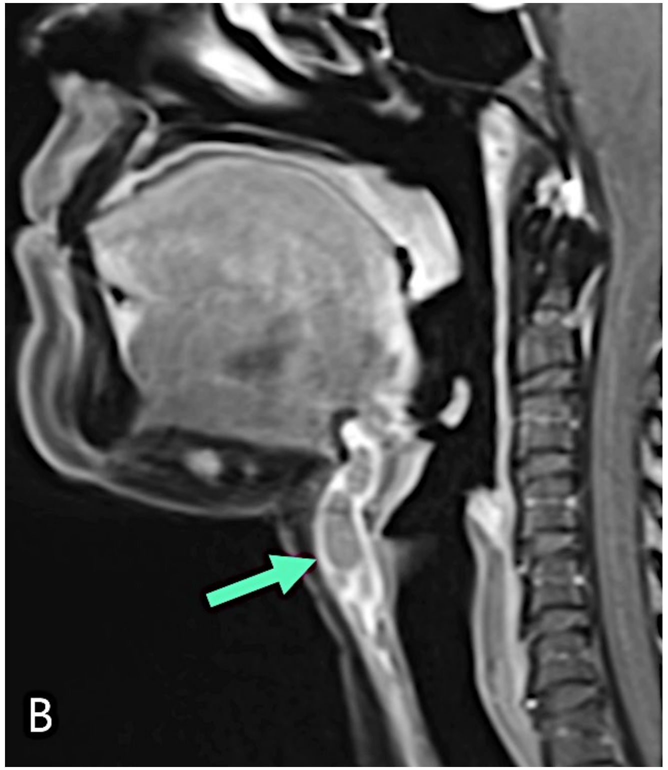


Fig. 24. Sagittal US (A) and sagittal T1W post-gadolinium with fat saturation (B) showing a homogenous hypoechoic and non-enhancing cystic formation in the midline right below the hyoid bone, typical of a TGD cyst. As shown in B, the wall of the cyst is thin and frequently shows enhancement (green arrow). In case of infection, the wall becomes thicker.

The cyst can be located anywhere along the path of the TGD, but it is most commonly found in the midline of the neck, just below the hyoid bone (Fig. 24).

Less frequently, migration arrest can lead to persistent thyroid tissue in the base of the tongue, called «lingual thyroid».

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Congenital Malformations: Ectopic Parathyroid

- The parathyroid glands descend embryologically from the third and fourth pharyngeal pouches (Fig. 25).
- Ectopic parathyroid glands are the result of aberrant migration during early development.
- If missed during initial patient work-up these can result in failed surgery and persistent hyperparathyroidism. Prevalence is about 2–43% in anatomical series and up to 16% and 14% in patients with primary and secondary hyperparathyroidism, respectively.
- The most common location for ectopic inferior parathyroid glands is the anterior mediastinum, adjacent to the thymus or thyroid gland. Conversely, ectopic superior parathyroids are usually located in the tracheo-oesophageal groove and retro-oesophageal region. Ectopic parathyroid glands can also be found in the carotid sheath and in the thyroid gland itself. To complicate matters, supernumerary gland are not uncommon accounting for about 13% of cases.
- In general, US has a low sensitivity for detecting ectopic parathyroid glands. This can however, be improved when combined with 99mTc MIBI scans and with the addition of SPECT or SPECT/CT.

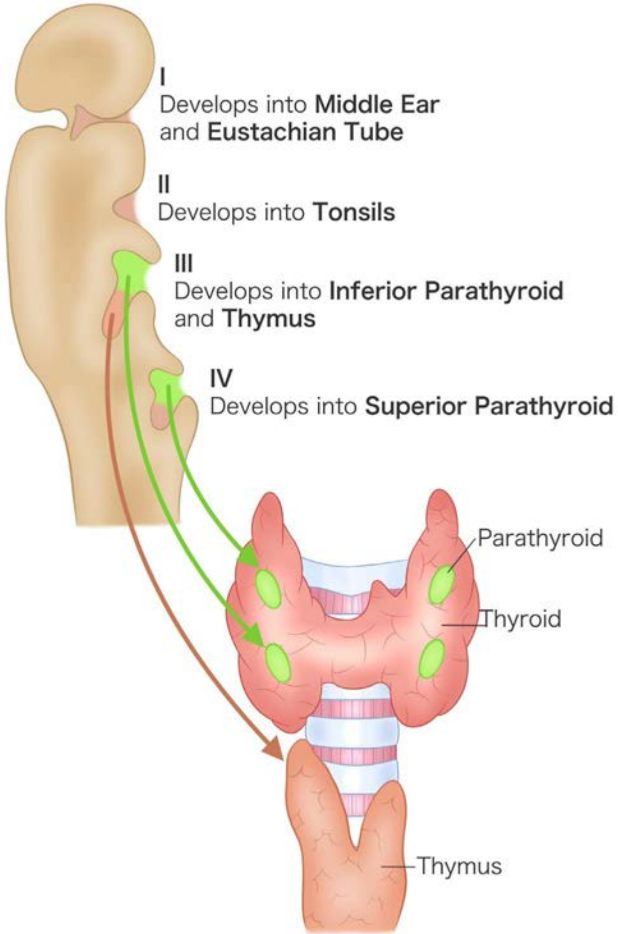

Fig. 25. Schematic drawing depicting the embryology of the parathyroid glands.

Farah Karipineni, Zeyad Sahli, Helina Somervell, Aarti Mathur, Jason D. Prescott, Ralph P. Tufano, Martha A. Zeiger, Are preoperative sestamibi scans useful for identifying ectopic parathyroid glands in patients with expected multigland parathyroid disease?, Surgery, Volume 163, Issue 1, 2018, Pages 35-41, ISSN 0039-6060

Experimental and Clinical Endocrinology & Diabetes 2012; 120(10): 604 – 610

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Dysthyroidism: Graves' Disease (Basedow Disease)

Graves' disease or Basedow disease is an autoimmune disease. It is the most common cause of hyperthyroidism. In Graves' disease, the body produces antibodies called TRAK (Thyrotropin Receptor Antibodies) that bind to the TSH receptor resulting in increased T3 and T4 production and release. Symptoms include: tremor, heat sensitivity, goitre, anxiety and weight loss.

On US, Graves' disease causes diffuse enlargement of the thyroid gland («diffuse toxic goitre»). Typically, the gland appears homogeneously enlarged with a lobular surface contour. (Fig. 26) Thyroid parenchyma is diffusely hypoechogenic and vascularity is increased. This pattern at Doppler US is called "thyroid inferno" or "thyroid storm". Doppler US can be useful to detect increased velocity in the thyroid arteries (mean systolic velocity >100 cm/sec in most patients at initial evaluation). Diastolic velocity can also be increased due to vascular shunts.

On iodine-123 and Tc-99m pertechnetate scans, there is a homogenously increased activity of the enlarged gland.

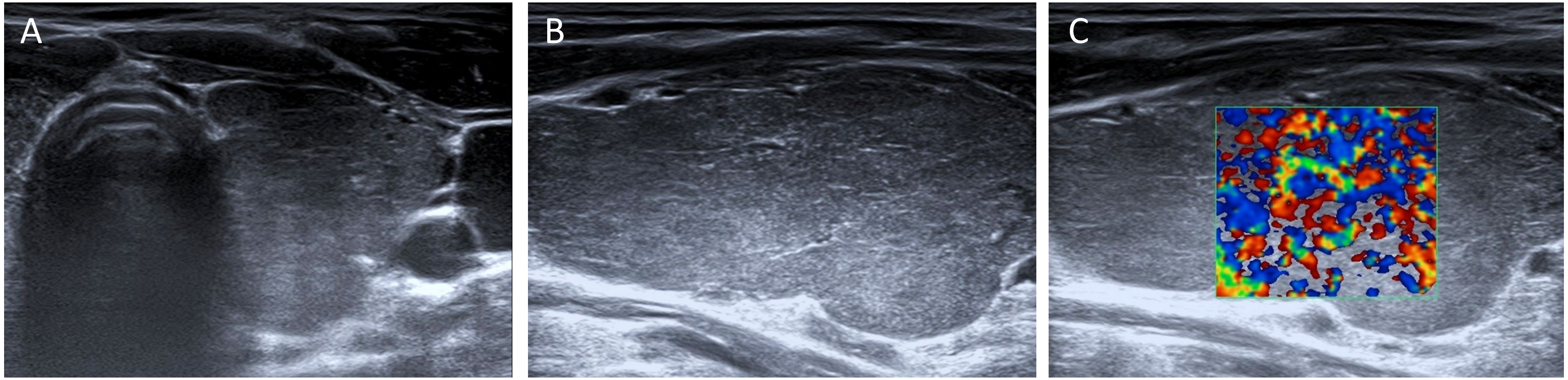

Fig. 26. Axial (A) and longitudinal (B) US views showing a lobulated, enlarged left thyroid lobe and diffuse hypoechogenicity with fine reticulations. C. Power Doppler US demonstrating the typical aspect of a « thyroid inferno » due to diffusely increased parenchymal vascularity.

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Dysthyroidism: Thyroid-Associated Orbitopathy (TAO)

In Graves' disease, the autoimmune response can cause inflammation and swelling of the tissues surrounding the eyes. Up to 50% of individuals with Graves' disease develop thyroid-associated orbitopathy (TAO) clinically presenting with proptosis and lid retraction.

On orbital MRI (Fig. 27), the changes due TAO include thickening and enhancement of extra-ocular muscles, lacrimal gland enlargement, and accumulation of fat in the orbit. In long-standing cases; chronic inflammation and collagen deposition leads to fibrosis.

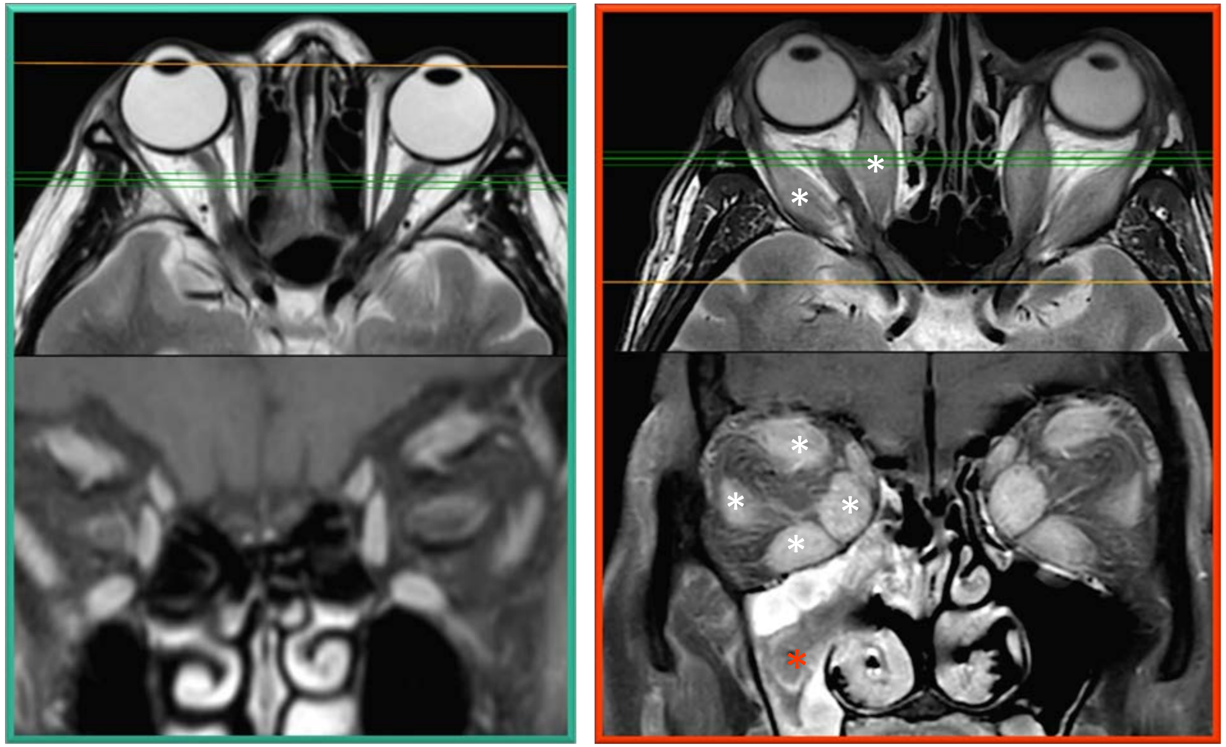
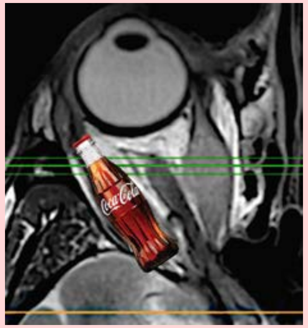


Fig. 27. Axial T2W and coronal post-gadolinium fat saturated T1W MRI in two different patients. Normal MRI (images on the left, contoured in green). MRI findings in TAO (images on the right, contoured in red). Note exophthalmos and bilateral extra-ocular muscle enlargement (white asterisks show enlarged muscles in the right orbit). Red asterisk shows sinusitis of the right maxillary sinus.

In TAO, muscle enlargement typically spares the anterior tendon. This appearance is described as the «Coca-Cola bottle» sign.



Muscle enlargement most often affects (in decreasing order) the inferior rectus, medial rectus, superior rectus and lateral rectus muscles.

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Dysthyroidism: Hashimoto Thyroiditis

Hashimoto thyroiditis, also known as **chronic lymphocytic thyroiditis** is an autoimmune disorder leading to hypothyroidism.

In Hashimoto thyroiditis, the thyroid gland may appear enlarged, normal, or reduced in size on an US scan, depending on the stage and severity of the disease. Initially, the gland may appear enlarged due to inflammation, which can cause transitory elevation of thyroid hormones («hashitoxicosis»), but over time, it may become scarred and atrophied, resulting in a smaller-than-normal gland and hypothyroidism.

US can show an heterogeneous aspect, with areas of increased and decreased echogenicity also known as the pseudo-nodular appearance or «**giraffe pattern**» (**Fig. 28**).

Hashimoto thyroiditis patients have an increased risk of developing papillary thyroid cancer and lymphoma compared to the general population :

- ✓ The risk is estimated to be up to 3-4 times higher in individuals with Hashimoto thyroiditis than those without.
- ✓ > 85% of patients with primary thyroid lymphoma have coexistent Hashimoto thyroiditis

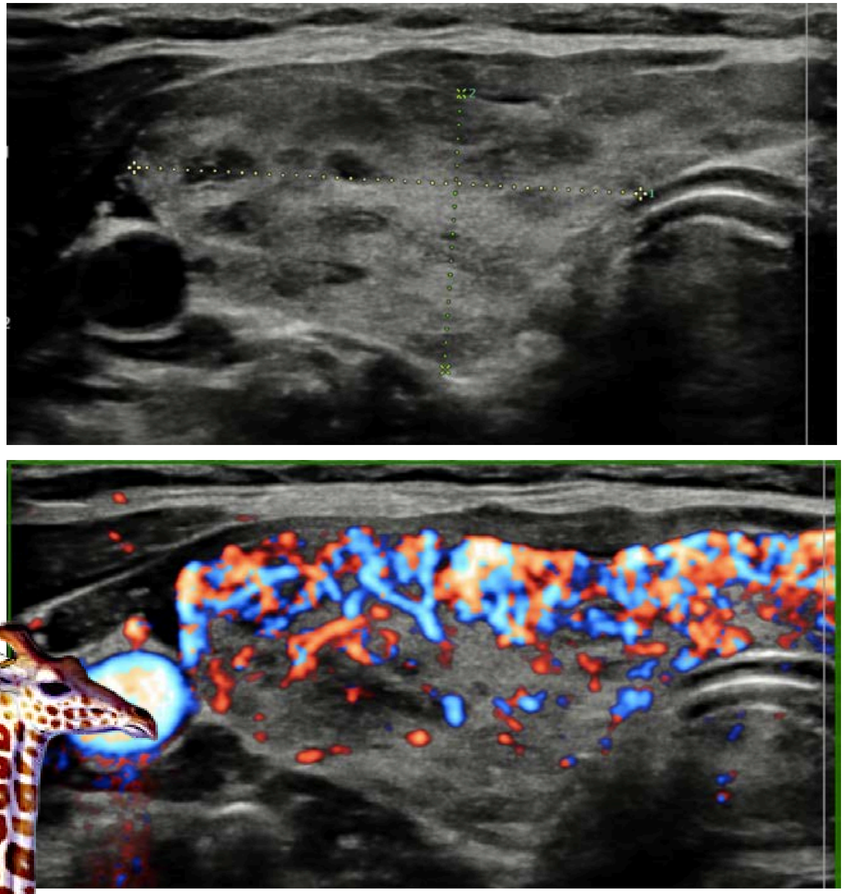

Fig. 28. Transverse US and corresponding Doppler US image of the right thyroid lobe in a patient with an initial stage Hashimoto thyroiditis presenting with a characteristic «giraffe pattern»

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Thyroid Nodules: Toxic Nodule

In some cases, hyperthyroidism may be due to the presence of a «toxic nodule ». The exact cause of toxic nodules is not fully understood, but it is believed to be related to TSH receptor mutations in the gland cells leading to autonomous production of excess thyroid hormone.
Toxic nodules can mimic malignancy and present as solid nodules with irregular borders and increased vascularity at US (Fig. 29).

If a toxic nodule is suspected, scintigraphy can help in combination with FNA. Scintigraphy will help identify areas of overactivity, such as a "hot" nodule (Fig. 29), and it can also help to differentiate benign from malignant nodules based on the pattern of iodine uptake.

=> Hot nodules are rarely malignant. Cold nodules carry an estimated 10% - 20% risk of malignancy (Fig. 30).

Treatment options include medication to control the symptoms of hyperthyroidism, radioactive iodine therapy to destroy the abnormal thyroid tissue, or surgery to remove the nodule. Treatment choice will depend on factors such as the size and location of the nodule.

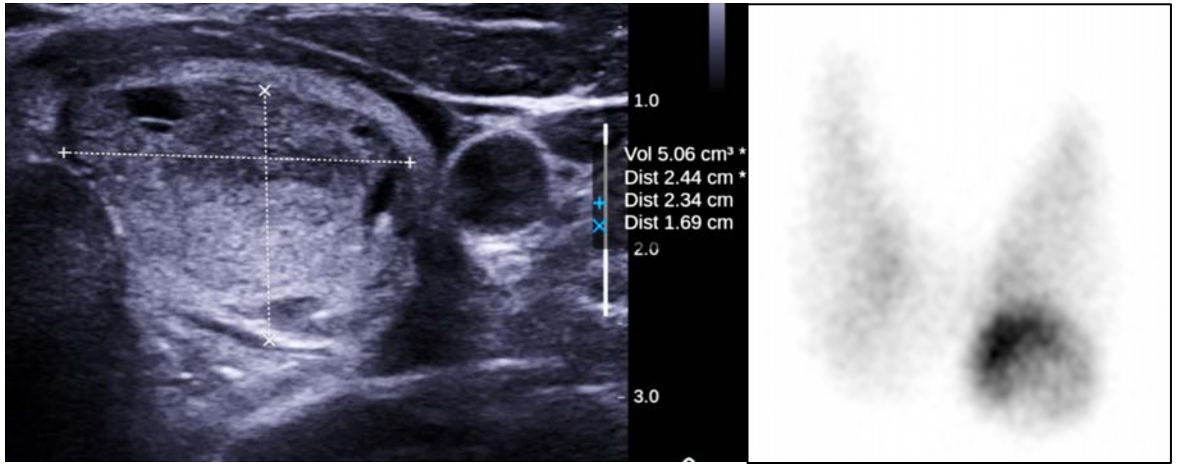

Fig. 29. Axial US showing a solid nodule of the left thyroid lobe. Scintigraphy showing an increased focal uptake of Iodine-123 in the left thyroid lobe corresponding to a « hot » nodule.

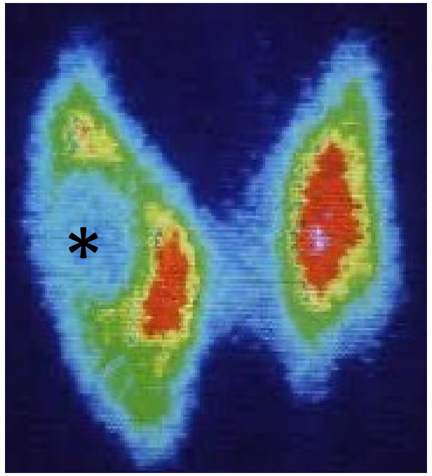

Fig. 30. Scintigraphy showing focal absence of fixation (asterisk), due to a « cold » nodule in the right thyroid lobe.

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Thyroid Nodules: Multinodular Goitre (MNG)

Multinodular goitre (MNG) is defined as an enlarged thyroid gland with multiple nodules. It develops following repeated episodes of stimulation and involution. MNG occurs in females in the 4th – 6th decades. Most goitres have euthyroid nodules. However, hyper- or hypofunctioning nodules can lead to systemic symptoms. A MNG with hyperthyroidism is called «toxic MNG».

- US is the imaging modality of choice allowing to screen for suspicious malignant nodules (see ACR-TIRADS criteria) and to perform FNA, whenever indicated. Benign nodules in MNG are typically iso- or hyperechoic and usually have a hypoechoic halo (Fig. 31).
- On nuclear medicine studies, MNG is seen as an enlarged gland with heterogeneous Tc-99m pertechnetate or radioiodine uptake.
- Although CT is not the primary imaging modality for MNG, it is used to plan surgery in patients with airway compression and to assess the retrosternal extent.
- On frontal chest radiography, a MNG extending into the anterior mediastinum manifests with a positive cervico-thoracic sign (CTS) and it can also deviate the trachea (Fig. 31). A positive CTS is caused by anterior mediastinal masses as the anterior mediastinum ends at the level of the clavicles. Posterior mediastinal masses have a negative CTS (see e book chapter on chest imaging)

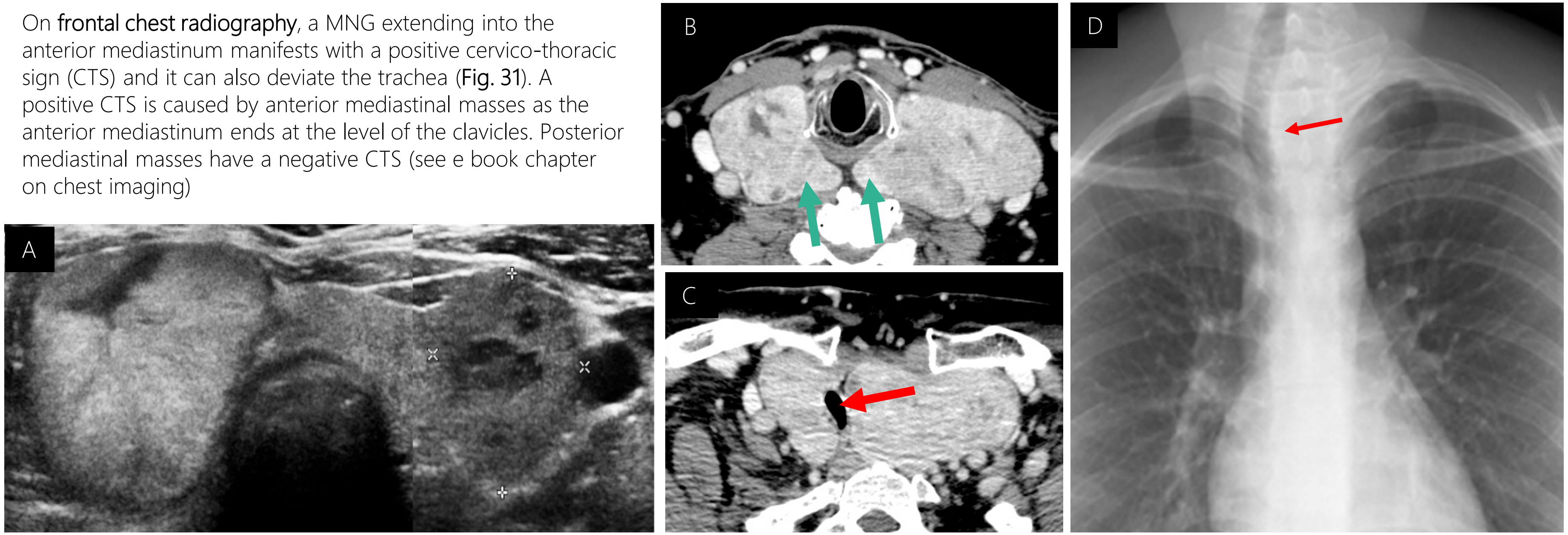

Fig. 31. Different patients with MNG. A. Transverse US image showing an enlarged thyroid gland with bilateral nodules. B and C. Contrast-enhanced CT showing a MNG with retropharyngeal spread (green arrows) and massive tracheal compression (red arrow). D. Deviation of the trachea (arrow) and positive cervico-thoracic sign, i.e., indistinct borders above the clavicles in a patient with MNG.

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Thyroid Nodules: Epidemiology and Risk Factors

- Thyroid nodules are relatively common, with a prevalence of approximately 49% in the general population. Many studies suggest a prevalence of 2-6% at palpation, up to 35% at US, and 65% in autopsy data.
- Thyroid nodules are often benign.
- Their incidence increases with age, in people with iodine deficiency, and after radiation exposure. They are also more common in women.

Papillary and follicular thyroid carcinomas are the two most common types of thyroid cancer, accounting for approximately 80-90% of all thyroid cancer cases (Fig. 32).

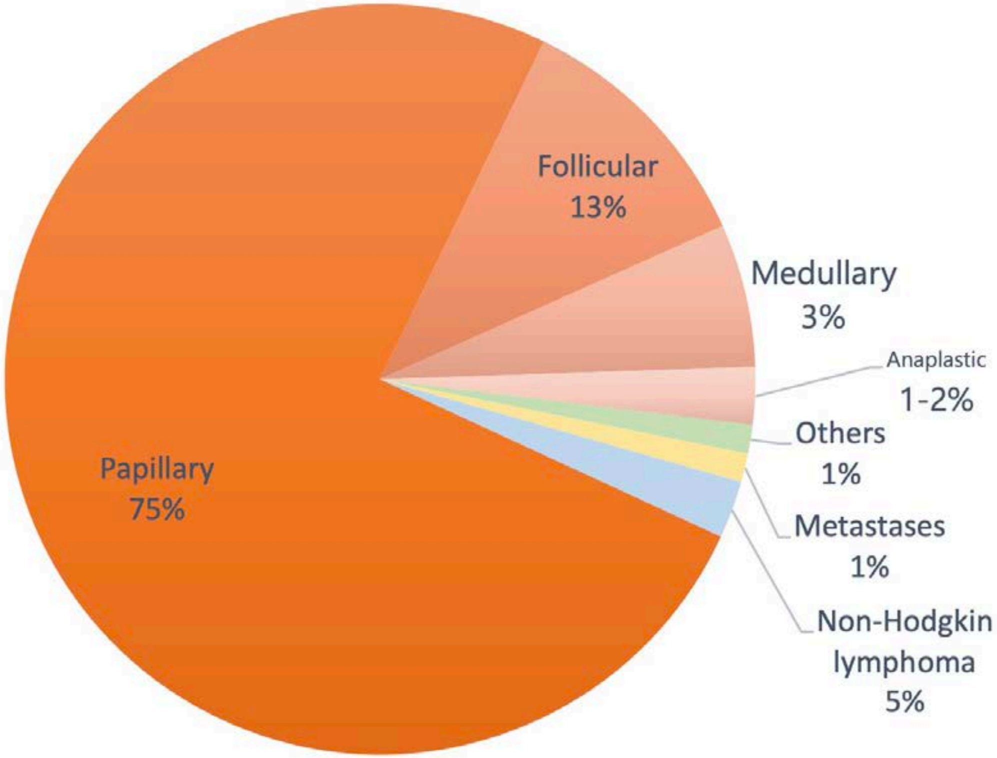

Fig. 32. Diagram showing the distribution of the main histological types of thyroid neoplasms.

Jiang H, et al. The Prevalence of Thyroid Nodules and an Analysis of Related Lifestyle Factors in Beijing Communities. Int J Environ Res Public Health. 2016

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Thyroid Cancer: Aetiology, Genetics & Epidemiology

Thyroid cancer is the most common endocrine malignancy and accounts for 1.8% of all cancers with an increasing incidence during the past decades. Women account for 76% of new cases.

Genetics:

- ✓ 5-10% of patients have a positive family history for papillary thyroid cancer
- ✓ More frequent in women than men (F:M = 3:1)
- ✓ Risk increases with age; peaks earlier for women (40s or 50s) than for men (60s or 70s)
- ✓ Majority are sporadic

Risk factors:

- ✓ Prior radiation to the head and neck increases risk by 30%
- ✓ Iodine deficiency; possibly alcohol excess, Hashimoto's thyroiditis
- ✓ Age:
  - *Papillary*: 30-40 years
  - *Follicular*: 40-70 years
- Follicular and anaplastic carcinoma predominate in areas with iodine-deficient diets
- Papillary carcinoma is more common in areas with iodine-rich diets

Associations:

- ✓ Gardner syndrome: Thyroid cancer has a prevalence of around 0.6% in patients with Gardner's syndrome >= 150-fold risk compared to the general population (Harned RK, et al Extracolonic manifestation of familial adenomatous polyposis syndromes. Am J Radiol. 1991).
- ✓ *Cowden syndrome:* risk of follicular cancer
- ✓ *Hashimoto thyroiditis:* thyroid lymphoma & papillary thyroid carcinoma
- ✓ *Multiple endocrine neoplasia (MEN) 2* : medullary carcinoma

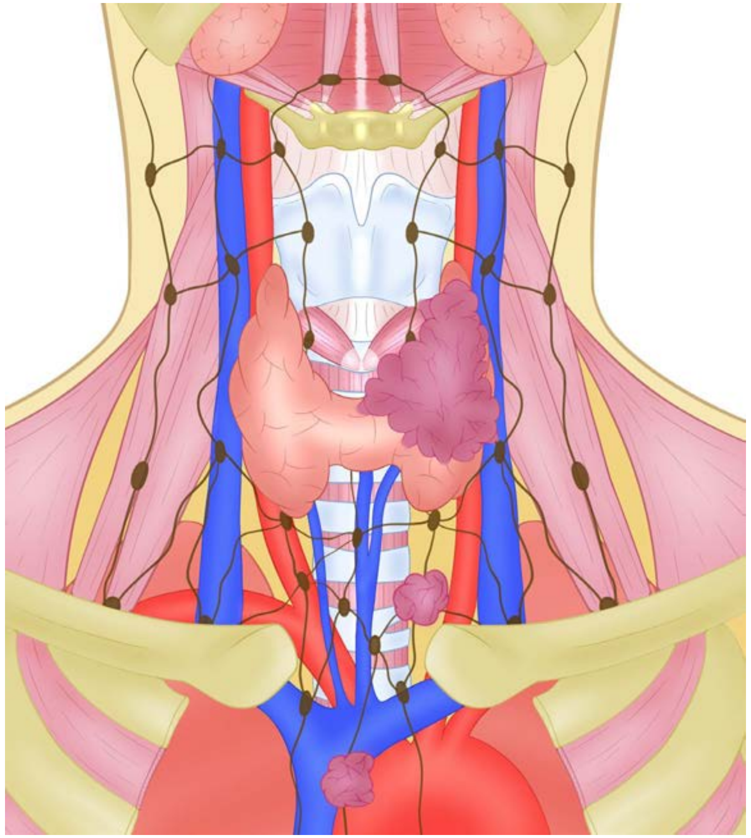

Fig. 33. Schematic diagram depicting malignancy of the thyroid gland with metastatic lymph nodes in the central neck compartment.

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Thyroid Cancer: Classification

According to the 8th edition of the AJCC and TNM staging system for all thyroid cancers, the same T, N and M criteria apply:

- T classification => influenced by tumour size and extent, e.g., invasion of strap muscles, larynx, trachea, …
- N classification => influenced by the presence or absence of nodal metastases in the central compartment (Fig. 33), other neck levels or retropharyngeal nodes
- M classification => influenced by the presence/absence of spread to distant organs

However, the tumour stage (I, II, III, IVA and IVB) depends on

- Tumour type => differentiated thyroid carcinoma (papillary and follicular carcinomas) is staged differently from medullary and anaplastic carcinoma
- Age at diagnosis ≥ 55 years => influences the staging of papillary and follicular carcinoma (as younger individuals have a better prognosis, patients <55 years can have only stage I or II disease, whereas patients ≥ 55 years can have stage I – IVC disease depending on T, N and M category

Prognosis in differentiated thyroid cancer (DTC) is influenced by:

- T, N and M category, post-treatment thyroglobulin levels
- BRAF and V600E mutations and molecular profile
- Age and gender
- Post-treatment residual disease
- Endemic goitre

Prognosis in medullary carcinoma is influenced by:

- Pre- and post-treatment calcitonin level
- MEN
- Age
- Molecular profile

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Papillary Thyroid Carcinoma (PTC)

Papillary thyroid carcinoma (PTC) accounts for 85% of all thyroid cancers (Sipos and Mazzaferri 2010) and for 1% of all malignant tumours.

PTC is usually sporadic, but it can also be associated with increased radiation exposure. It occurs 3 x more frequently in females.

PTC takes up iodine and produces thyroglobulin in response to TSH stimulation. Thyroglobulin levels can be used in the surveillance of patients who have been treated with surgery and radioiodine therapy.

The 10-year survival rate is 96%. Only a minority of PTCs are aggressive.

Lymph node spread is common and distant metastatic spread is seen in 5-10% of cases. About 10-20% of PTCs are multifocal and 70% are solid..

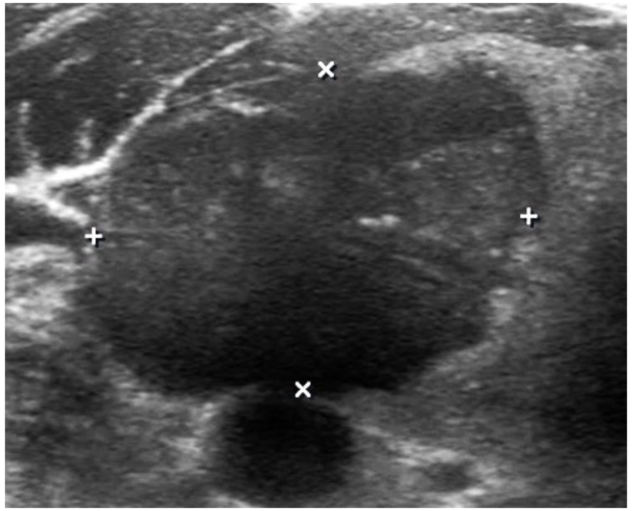

Fig. 34. Profoundly hypoechoic mass in the right thyroid lobe with micro-calcifications confirmed to be papillary carcinoma at histology.

Imaging:

US: Is the imaging modality of choice showing typical features → hypoechoic, irregular margins, internal microcalcifications +/- metastatic lymph nodes with typical microcalcifications and partly cystic components (Fig. 34).

CT/MRI: in locally advanced disease for staging and to exclude distant metastases (Fig. 35).

PETCT: not routinely recommended for the initial staging of DTC. Its role is primarily limited to postoperative follow-up in selected cases and in suspected dedifferentiation.

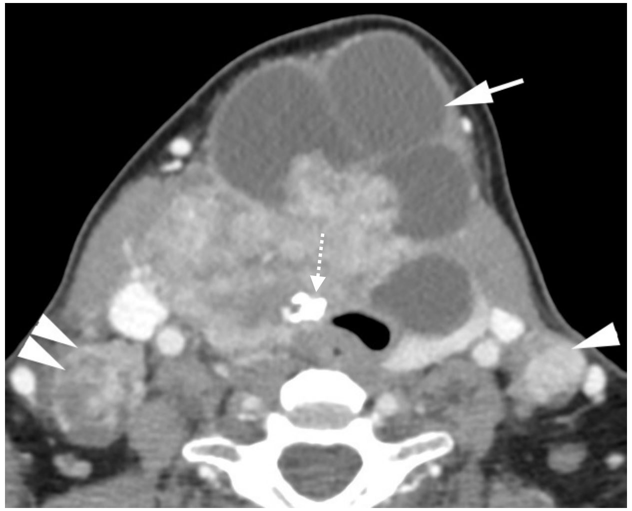

Fig. 35. Massive goitre (arrow) with extensive cystic changes, coarse calcifications (dashed arrow) and severe tracheal compression, accompanied by bilateral metastatic cervical lymph nodes (single and double arrowheads). This was a histologically proven papillary thyroid cancer.

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Follicular Carcinoma

Follicular carcinoma (FC) accounts for 1 in 10 thyroid malignancies. It is a differentiated thyroid cancer with an overall 20-year survival rate of 81% (Shaha et al. 1995). It has a predilection for haematogenous spread to the lungs, bones and central nervous system. It takes up iodine and produces thyroglobulin in response to TSH stimulation.

On US, it usually has characteristic malignant features (Figs. 36-37). It is distinguished from benign follicular adenoma by microscopic vascular invasion and full thickness capsular invasion into adjacent thyroid tissue.

Oncocytic carcinoma (formerly called Hürtle cell carcinoma) is a more aggressive cancer with an intermediate prognosis and a 65% 20-year survival (Shaha et al. 1995).

Minimally invasive follicular cancer may mimic a benign nodule on US! Its appearance can also be that of a heterogenous and locally invasive mass. US is the examination of choice for lesion characterization and to guide FNA.

The role of CT is limited for advanced stage cancers and for surveillance. This should be performed without IV contrast as the latter delays Iodine-131 therapy by up to 6 months.

Surveillance imaging should include:

- ✓ I-131 scan ± US
- ✓ PET/CT if increased serum thyroglobulin levels but negative I-131 scan.

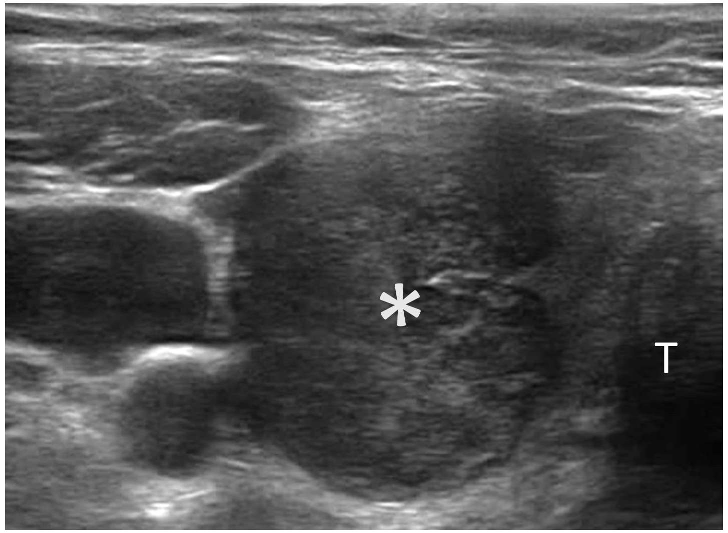

Fig. 36. Profoundly hypoechoic mass in the right thyroid lobe (asterisk), taller than wide confirmed to be follicular carcinoma on histology. T = trachea.

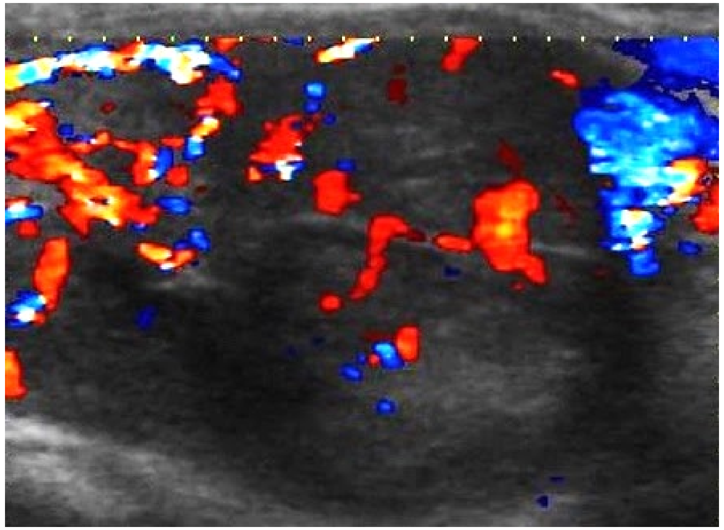

Fig. 37. Same lesion exhibits disorganized, predominantly central Doppler flow.

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Medullary Thyroid Carcinoma

Medullary thyroid cancer (MTC) Is a rare neuroendocrine malignancy. It arises from the calcitonin producing parafollicular C cells. Most cases are sporadic, however, 15-25% are inherited and occur in the context of **multiple endocrine neoplasia (MEN) syndromes** due to a mutation in the RET (Retinoblastoma) protooncogene. These syndromes include MEN 2a (MTC, phaeochromocytoma, parathyroid hyperplasia), MEN 2b (MTC, phaeochromocytoma, multiple mucosal neurinomas), familial medullary thyroid cancer. MTC accounts for10% of paediatric thyroid malignancies
The 20-year survival following adequate treatment of MTC is about 65% (Moley 1995).

MTC has a predilection both lymphatic and haematogenous spread.

Patients require pre-operative biochemical screening for parathyroid and adrenal tumours with phaeochromocytomas needing to be removed prior to thyroidectomy. Genetic screening is offered to family members in the inherited form.

Intravenous iodine-based contrast agents are not contraindicated.

Imaging:

US => first choice modality. The lesion is typically hypoechoic with ill-defined margins and calcifications (Fig. 38).

CT => to assess the degree of local invasion and metastases (Fig. 39).

Ga-68 DOTATATE PET => for metastatic disease

I-131 MIBG or octreotide scintigraphy => for metastases

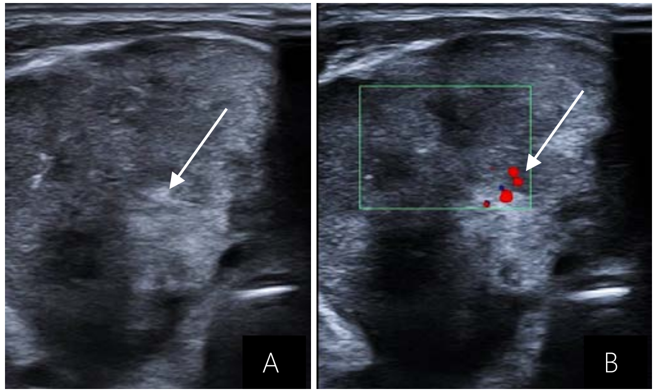

Fig. 38. US shows a strongly hypoechoic mass with irregular margins , internal calcifications (arrow in A) and sparse vascularity (arrow in B), histologically proven medullary carcinoma.

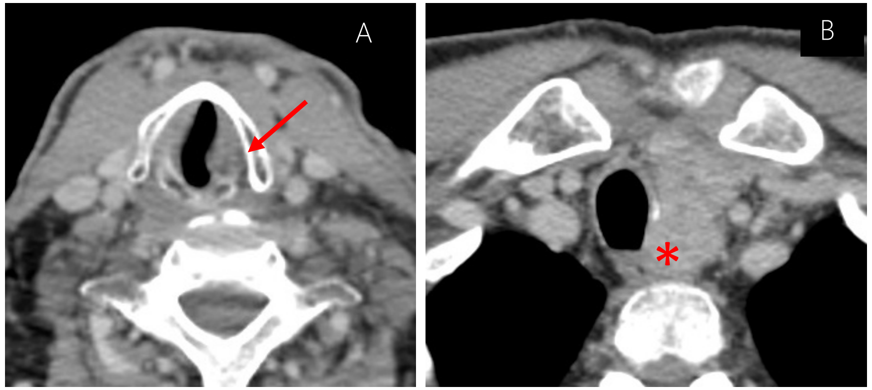

Fig. 39. Contrast enhanced CT in a patient presenting with hoarseness shows a fixed and adducted left vocal (red arrow) due to an infiltrative mass extending into the left tracheo-oesophageal groove (asterix), confirmed medullary thyroid carcinoma.

Kim SH, Kim BS, Jung SL, Lee JW, Yang PS, Kang BJ, Lim HW, Kim JY, Whang IY, Kwon HS, Jung CK. Ultrasonographic findings of medullary thyroid carcinoma: a comparison with papillary thyroid carcinoma. Korean J Radiol. 2009 Mar-Apr;10(2):101-5.

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Anaplastic Thyroid Carcinoma (ATC)

Anaplastic thyroid carcinoma (ATC) is a rare and very aggressive form of thyroid neoplasms, accounting for 1-2% of thyroid cancers & 39% of thyroid deaths.
In most cases, it presents in patients >60 years as a rapidly growing, large, painful neck mass, partially necrotic (75%) and calcified (60%).

Patients tend to have advanced disease at initial presentation, often with extra-thyroid extension, nodal and distant metastases (Fig. 40).

ATC often arises in elderly patients with multinodular goitre and is thought to develop from pre-existing differentiated thyroid cancer (papillary/follicular carcinoma).

The lack of response to radioactive iodine therapy is associated with rapid progression and poor prognosis (average survival : 6 months).

The diagnosis should ideally be made with core biopsy rather than FNA.

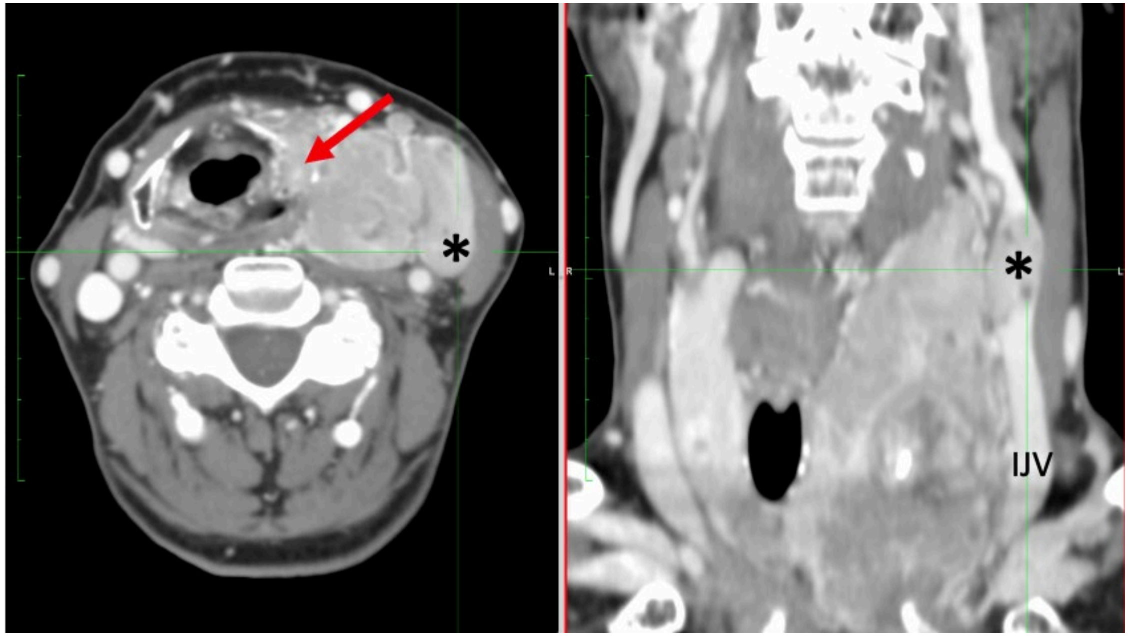

Fig. 40. Contrast-enhanced CT scan showing an invasive cervical mass developped from left thyroid lobe. The lesion invades thyroid cartilage (arrow) and left larynx and extends into the ipsilateral jugular vein. Intravenous tumour thronbus (asterisks). IJV = internal jugular vein.

Imaging:

US => mostly used to guide core biopsy

CT/MRI => for staging, to delineate the extent of trans-spatial invasion; PETCT => tumours are highly FDG avid

Iodine scintigraphy is not used in the evaluation or treatment of anaplastic carcinoma

IV iodine contrast agents can be used.

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ACR-TIRADS

The ACR Thyroid Imaging Reporting System (TIRADS) provides a structured approach to assess the risk of malignancy of a thyroid nodule based on the size of the nodule and on the following US features:

- Composition
- Echogenicity
- Shape
- Margin
- Echogenic foci

This classification uses a standardised scoring system and the sum of the different scores determines the TIRADS level or grade (range 1 – 5)

It also provides guidelines indicating which nodules warrant FNA cytology, e.g., TIRADS 1 corresponds to a benign lesion & no cytology is required, whereas TIRADS 5 is a highly suspicious lesion requiring cytology if nodule size ≥ 1cm.

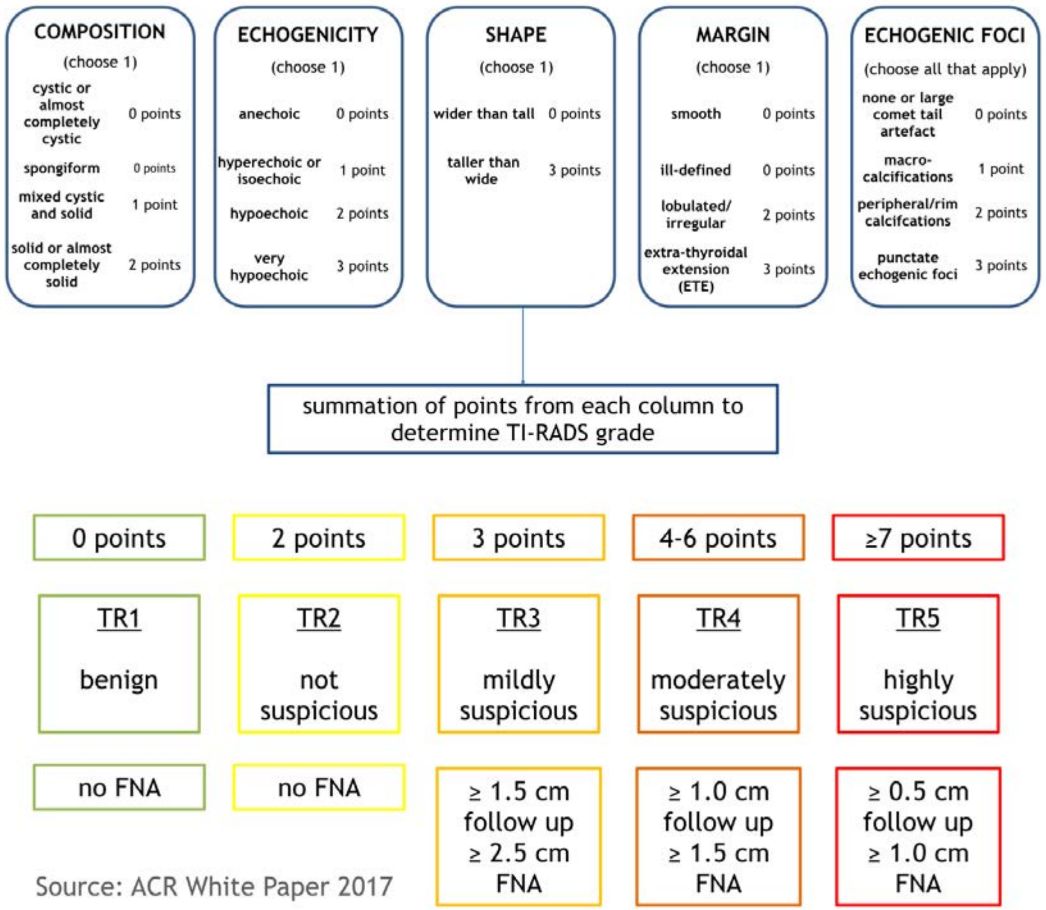

Diagram: Courtesy of Derek Smith, Radiopaedia.org, rID: 52373

https://doi.org/10.1016/j.jacr.2017.01.046

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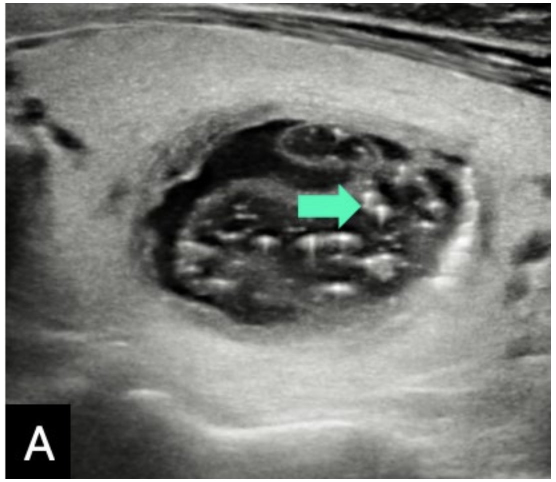
ACR-TIRADS 1 and 2

These two categories are used to describe benign nodules (Fig. 41):

- TIRADS 1 => corresponds to a homogenous thyroid gland / absence of nodule.
- TIRADS 2 => includes pure anechoic cysts, «colloid cysts» and «spongiform nodules», which are composed of tiny cystic spaces involving the entire nodule, separated by isoechoic linear septa.



FNA cytology is not indicated unless for comfort treatment such as emptying a cyst in case of compression symptoms.

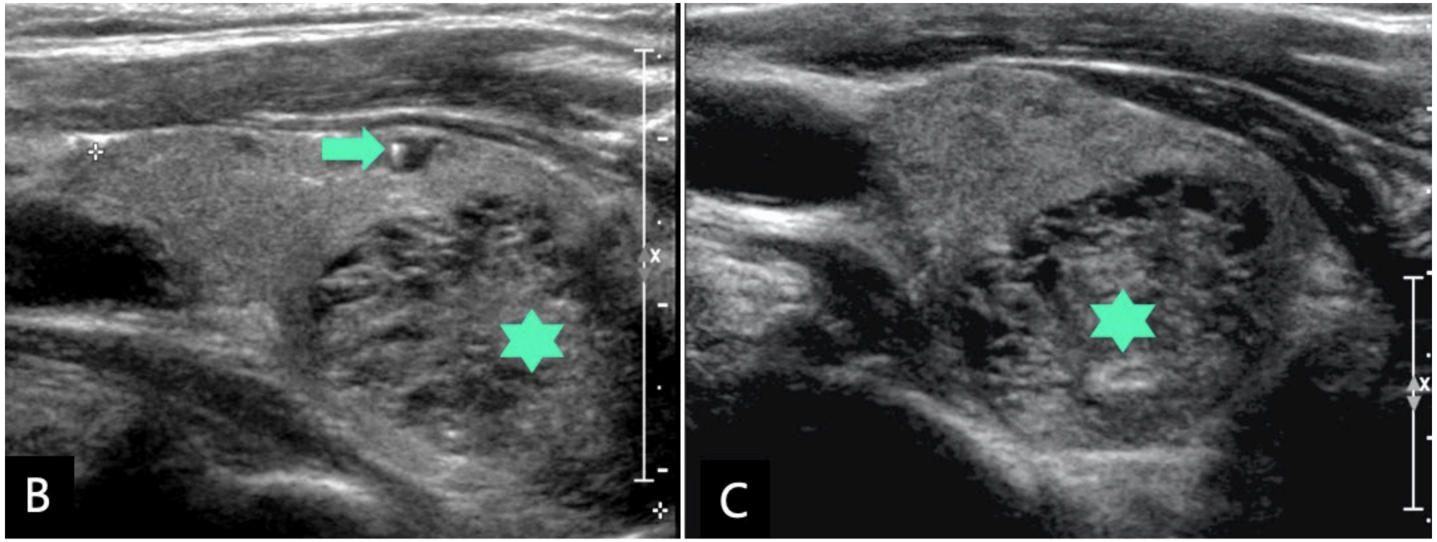


Fig. 41. US of different thyroid glands with nodules classified as TIRADS 2. On images A and B colloid cysts are shown with arrows pointing at the typical « comet tail artifact ». On images B and C, stars indicate large spongiform nodules.

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ACR-TIRADS 3 and 4

TIRADS 3 and 4 correspond to low and intermediate-risk categories (Fig. 42).

They are used to describe nodules with oval shape and smooth margins and without any feature of high risk.

The main difference between these 2 categories is the relative echogenicity of the nodule compared to the adjacent gland parenchyma.

- Iso or hyperechogenic => TIRADS 3 (risk of malignancy < 5%)
- Mildly hypoechogenic => TIRADS 4 (risk of malignancy: 6-17%)

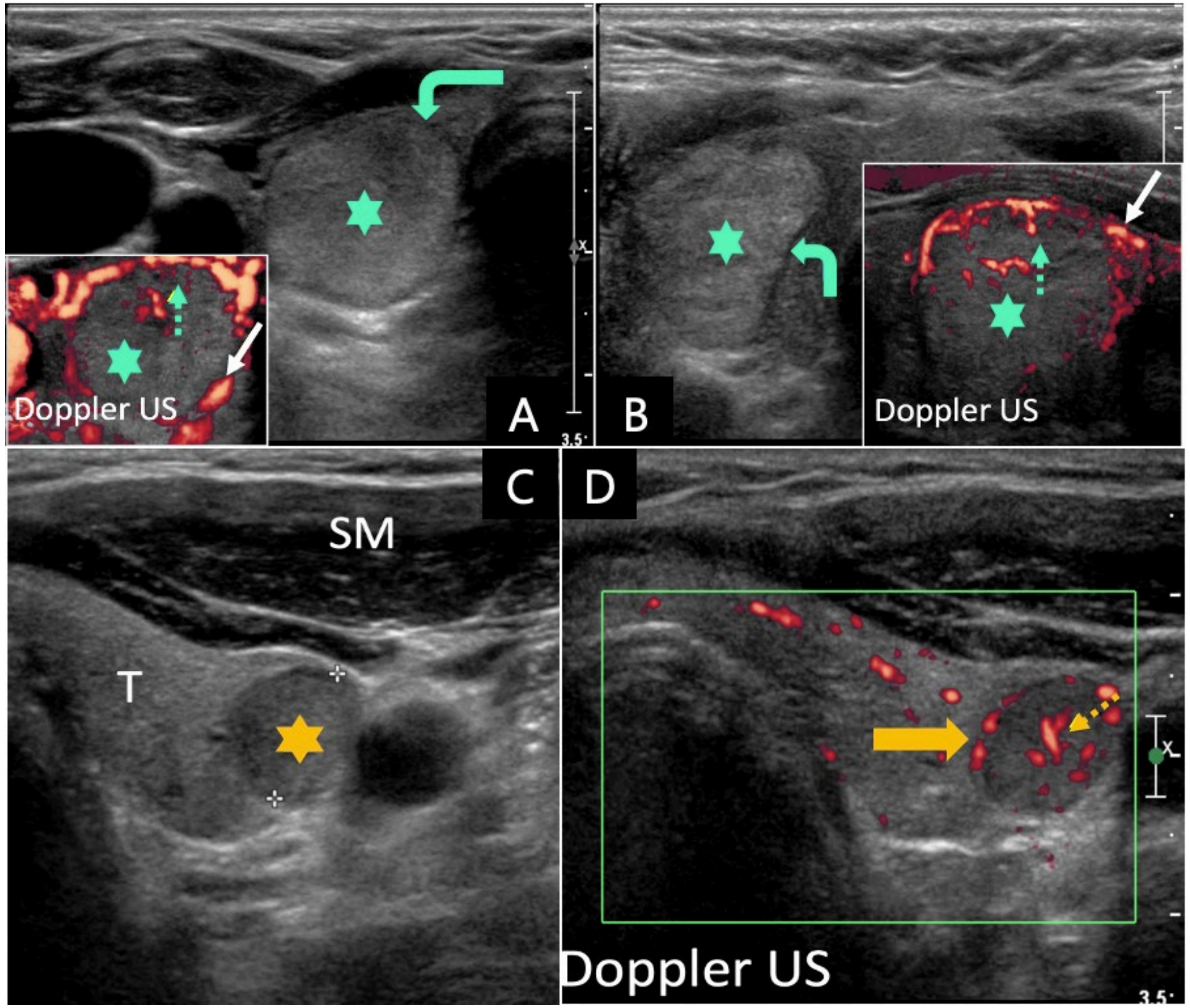

Fig. 42. Images A and B show a homogenous isoechoic nodule (TIRADS 3) with a typical vascular ring (white arrows). The nodule (star) has an oval shape and well-defined margins (green arrows) Images C and D show a slightly hypoechoic nodule (TIRADS 4, star) with peripheral (arrow) and central (dashed arrow) vascularisation.

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ACR-TIRADS 5

TIRADS-5 correspond to the high-risk category with a risk of malignancy estimated between 26 % and 87% (Fig. 43).

High-risk features include:
- ✓ Taller than wide
- ✓ Irregular margins
- ✓ Microcalcifications
- ✓ Marked hypoechogenicity

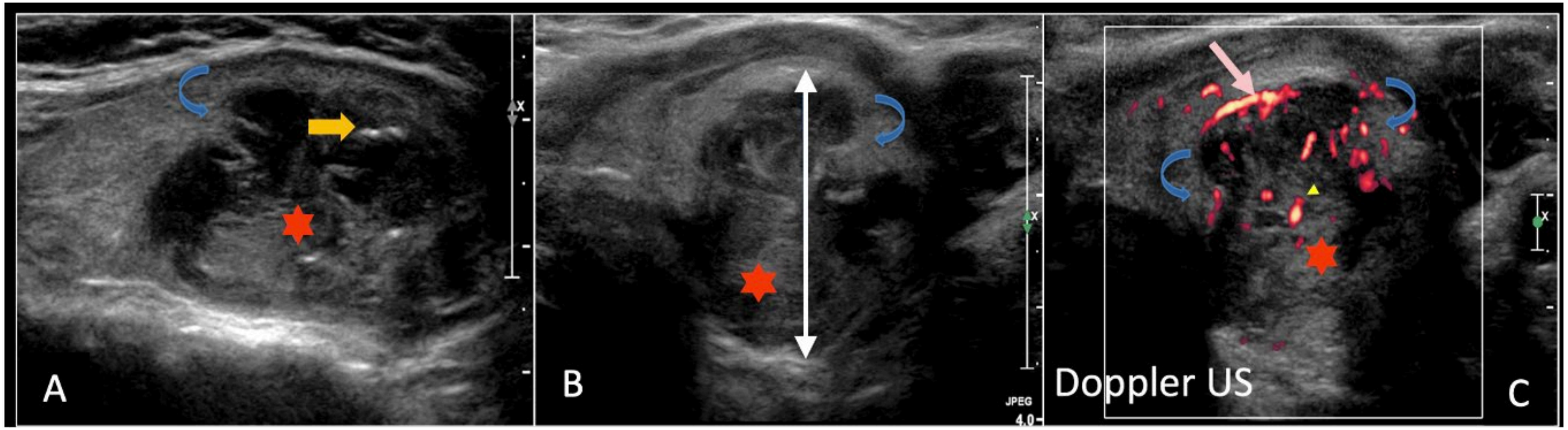

Fig. 43. US showing a TIRDAS 5 strongly hypoechogenic nodule with microcalcifications (yellow arrow in A), a taller than wide shape on the transverse image (B). Doppler US demonstrates an anarchic vascularisation with peripheral (large pink arrow) and central (small yellow arrow) vessels. Note poorly defined margins (curved blue arrows on all images).

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Hyperparathyroidism: Definition and Epidemiology

- Hyperparathyroidism is a pathological condition in which one or multiple parathyroid glands produce an excess amount of parathyroid hormone (PTH), leading to hypercalcemia and reduced bone density.
- There are three types of hyperparathyroidism: primary, secondary and tertiary.
  - Primary hyperparathyroidism is the most common type and is usually caused by a single hyperfunctioning adenoma.
  - Secondary hyperparathyroidism is caused by chronic kidney disease or vitamin D deficiency.
  - Tertiary hyperparathyroidism occurs after longstanding secondary hyperparathyroidism in which hypercalcaemia has resulted
- Symptoms of hyperparathyroidism can include fatigue, weakness, bone fragility, kidney stones, and gastrointestinal symptoms. However, many patients are asymptomatic and the condition is discovered incidentally during routine blood tests.
- Severe osteoporosis is the most feared complication of hyperparathyroidism. Acute hypercalcemia can lead to cardiac complications, however it is rarely observed in hyperparathyroidism.
- Surgical resection is the only curative treatment. Minimally invasive parathyroidectomy is the technique of choice, which requires precise preoperative imaging studies to locate the hyper-functional glands.

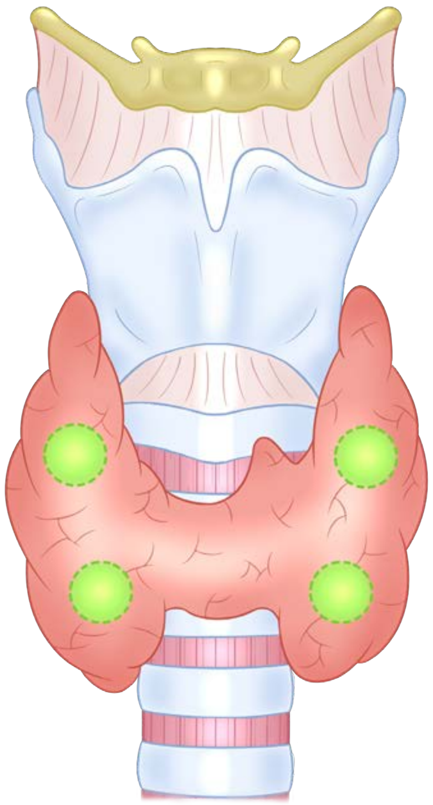

Fig. 44. Schematic drawing of the thyroid and parathyroid glands (green dots). However, many parathyroid glands have an ectopic location in the neck and in the thoracic cavity.

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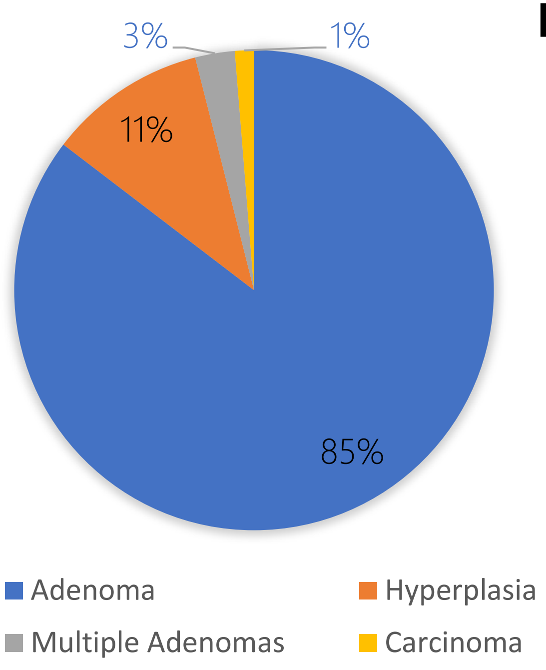

Fig. 45. Main aetiologies in primary hyperparathyroidism.

Primary Hyperparathyroidism: Adenoma

As shown in the chart on the left (Fig. 45), adenomas and diffuse parathyroid hyperplasia represent the main aetiologies of primary hyperparathyroidism.

Radiological exploration plays an important role to determine the number and size of pathological glands. Facilitated by a precise imaging localisation (Fig. 46) surgeons can operate using microincision, thus avoiding bilateral neck exploration and limiting the risk of recurrent laryngeal nerve damage.

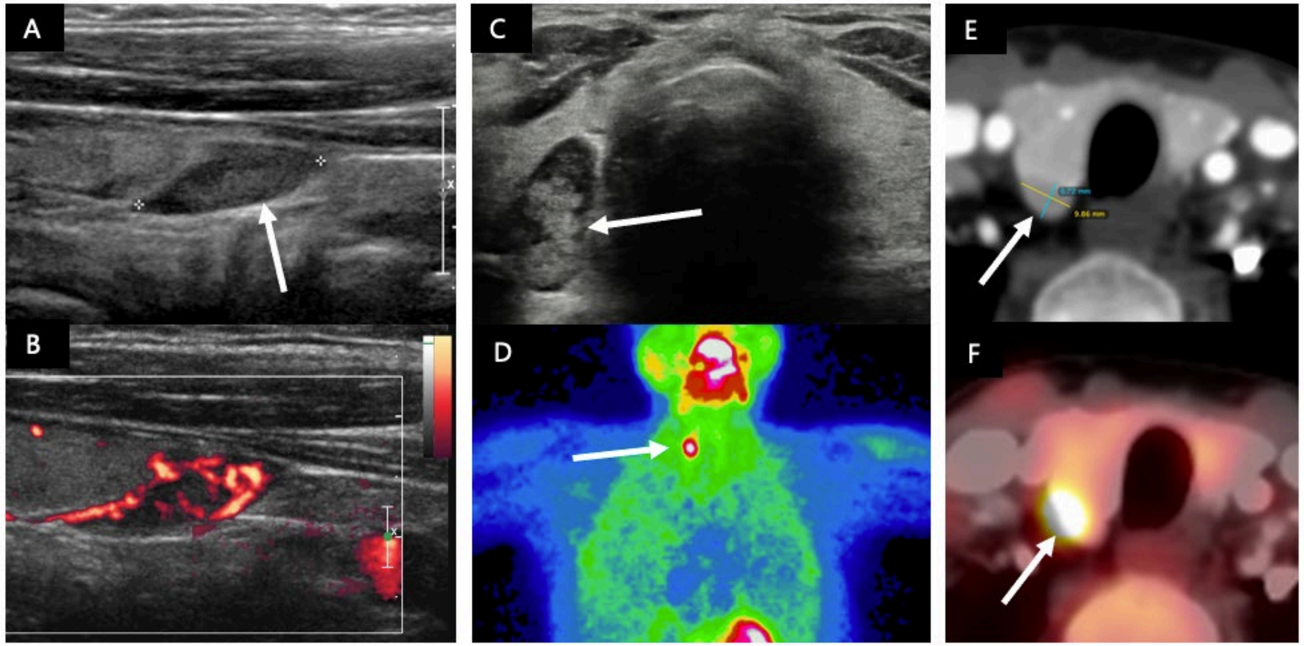

Fig. 46. Three different patients with surgically proven parathyroid adenomas. Patient 1: Longitudinal US image (A) shows a hypoechoic nodule (arrow) below the right thyroid lobe with increased vascularisation on the power Doppler image (B). Patient 2: large parathyroid adenoma on US (C) and corresponding MIBIscintigraphy (D). Patient 3: 18F choline PET CT (E and F) shows focal uptake of an enlarged parathyroid gland (arrows) corresponding to an adenoma.

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Hyperparathyroidism: Renal and Skeletal Involvement

To regulate calcium blood levels, parathormone influences bone and kidney homeostasis.

Regarding the kidneys, it increases tubular reabsorption of calcium, it inhibits tubular reabsorption of phosphate and stimulates calcitriol (active form of vitamin D) synthesis.

Chronic hypercalciuria predisposes to stone formation, renal colic being one of the more frequent symptoms associated with hyperparathyroidism.

Primary hyperparathyroidism induces both bone resorption and formation. Consequently, it causes excessive and constant bone remodelling, which affects bone mineralisation.

As illustrated in Fig. 47, different types of skeletal lesions can be observed on conventional X-ray images including osteopenia (Fig. 27A), brown tumours (Fig. 27B) and acro-osteolysis (Fig. 27C).

For skeletal manifestations of hyperparathyroidism, see also the e book chapter on musculoskeletal radiology!

Fig. 47. Lateral X-Ray (A) showing multiple vertebral compression fractures due to severe osteoporosis. Tibial radiograph (B) showing well-defined lytic lesions, corresponding to brown tumours (white arrows), which manifest as expansive lesions causing cortical thinning. Image C showing subperiosteal resorption of the middle phalange of the second finger (arrowheads) and terminal tuft resorption acro-osteolysis (curved arrows).

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Paraganglioma (PGL): Epidemiology and Risk Factors

Paragangliomas (PGL) are rare tumours arising from the paraganglia cells of neural crest origin.

These tumours can develop in various parts of the body along the parasympathetic chain of the head and neck (Fig. 48) and along the sympathetic chain in the chest and abdomen (Fig. 49).

Above the aortic arch, the carotid bifurcation is the most common location of PGL, followed by the jugular fossa, tympanic cavity and along the vagus nerve. In the abdomen, the main sites are the adrenal glands and the retroperitoneal « organ of Zuckerkandl ».

Adrenal paragangliomas are usually called « pheochromocytomas ».

Hereditary cases represent 33% - 50% of all PGL and -as specific genetic alterations increase the malignancy risk- genotyping is always recommended.

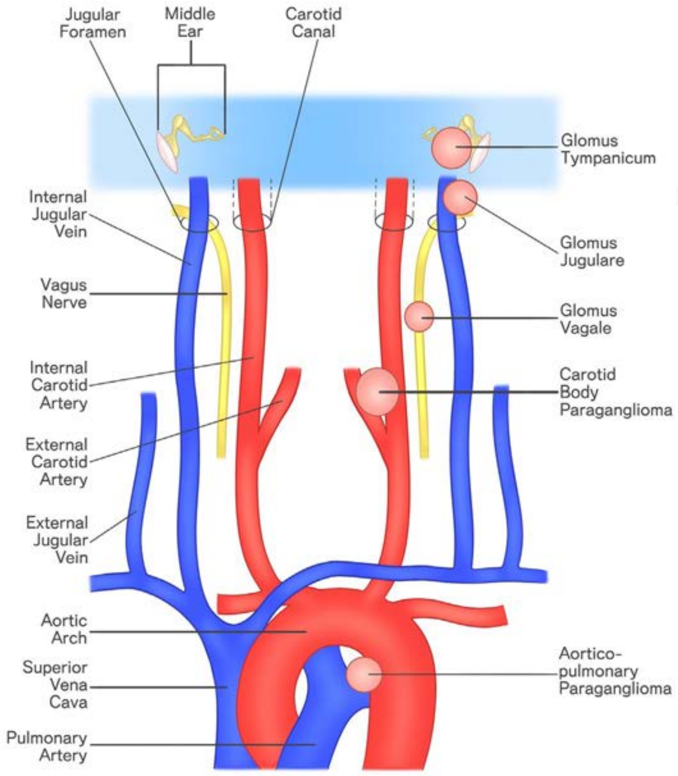

Fig. 48. Diagram representing the main PGL locations in the head and neck along the parasympathetic chain.

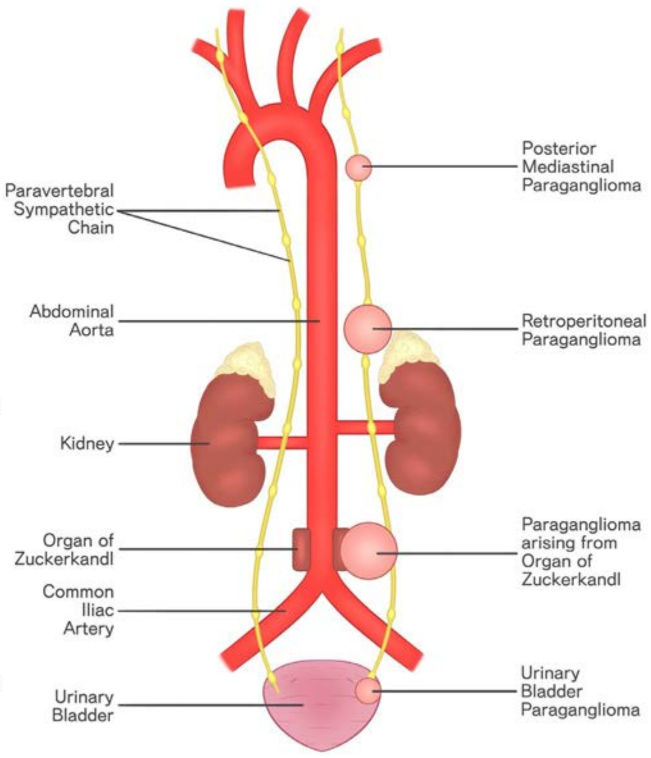

Fig. 49. Schematic diagram of the sympathetic chain from the aortic arch to the bladder.

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Carotid Body Paraganglioma

Paragangliomas (PGL) located in the carotid bifurcation are commonly called « carotid body PGL ». They are slow-growing tumours and rarely functional. Symptoms are generally due to mass effect. Alternatively, they can present as pulsatile cervical masses, causing submucosal oropharyngeal swelling or they represent an incidental imaging finding. PGL can be familial and multicentric (bilateral in 5 to 10 % of cases).

Imaging features on contrast-enhanced CT/MRI (Figs. 50 and 51) include:
- Well-defined mass with a heterogenous central portion in larger lesions.
- Typical splaying of the internal and external carotid arteries (« lyre sign »).
- Rapid enhancement due to increased vascularisation.
- « Salt and pepper » appearance on MRI due to flow voids and/or haemorrhage.

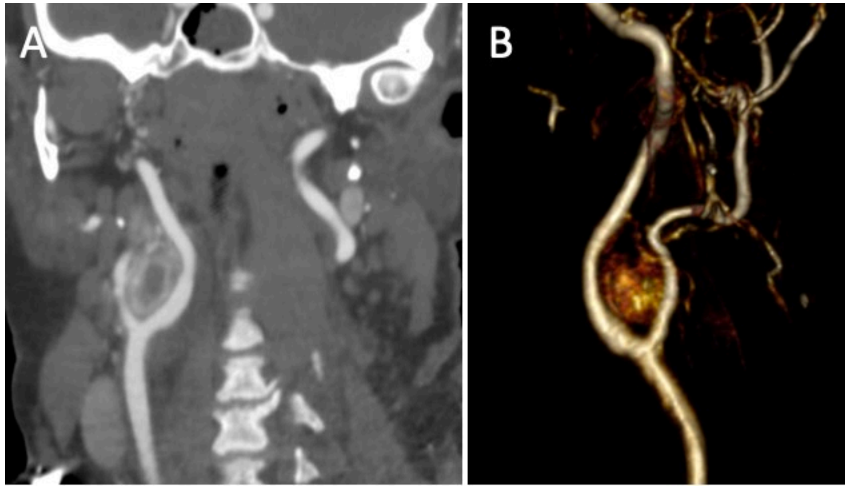
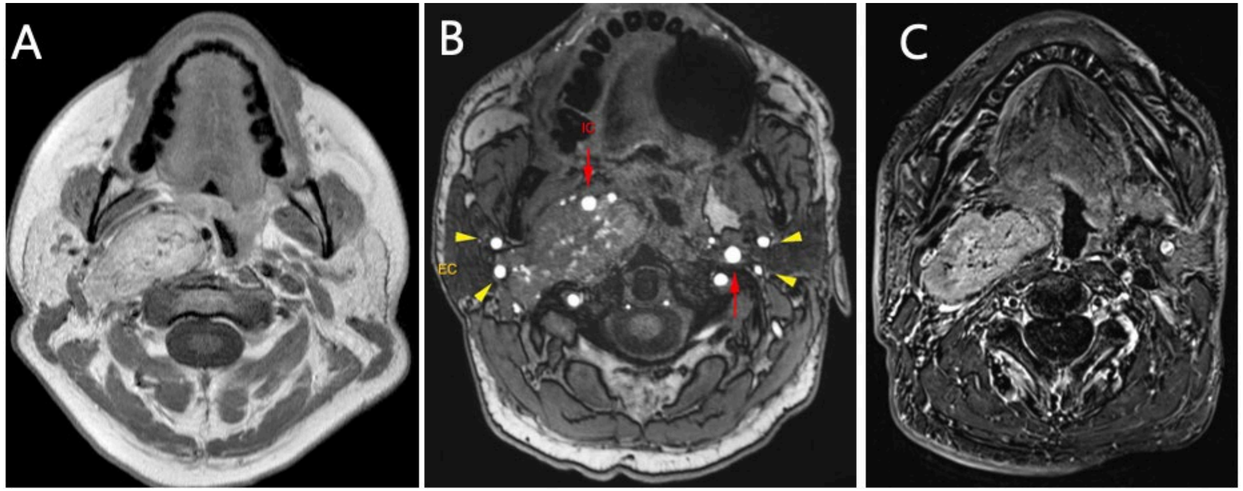


Fig. 50. A. Coronal reconstruction of an arterial phase CT showing a carotid body tumour on the right. B. 3D Volume rendering reconstruction of the same tumour.



See also e book chapter on head and neck imaging!

Fig. 51. Axial MRI demonstrates a right cervical lesion with mass effect on the oropharynx. On the contrast-enhanced T1W image (A), the lesion appears hyperintense with « flow voids » corresponding to a « salt and pepper aspect ». The contrast-free angiography (Time-of-flight, B) image demonstrates increased distance between the internal (IC) and external (EC) carotid arteries compared to the contralateral side. Numerous arterial vessels in the tumour. Marked and global enhancement after gadolinium is visible on the subtraction T1W image (C).

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Jugulo-Tympanic Paraganglioma

Paraganglia of the temporal bone are located along Arnold's and Jacobson's nerve.

Jacobson's nerve is a branch of the glossopharyngeal nerve, passing in the tympanic cavity along the cochlear promontory where tympanic paragangliomas are most frequently found. In this location, patients present with a retrotympanic mass which can cause pulsatile tinnitus (Figs. 52 and 53).

Arnold's nerve is an auricular branch of the vagus nerve which runs posteriorly in the jugular foramen. An expanding paraganglioma may progressively compress surrounding nerves (IX, X and XI) causing symptoms.

In large tumours involving both the cochlear promontory and the jugular fossa, lesion origin cannot always be established. These tumours are called « jugulo-tympanic ».

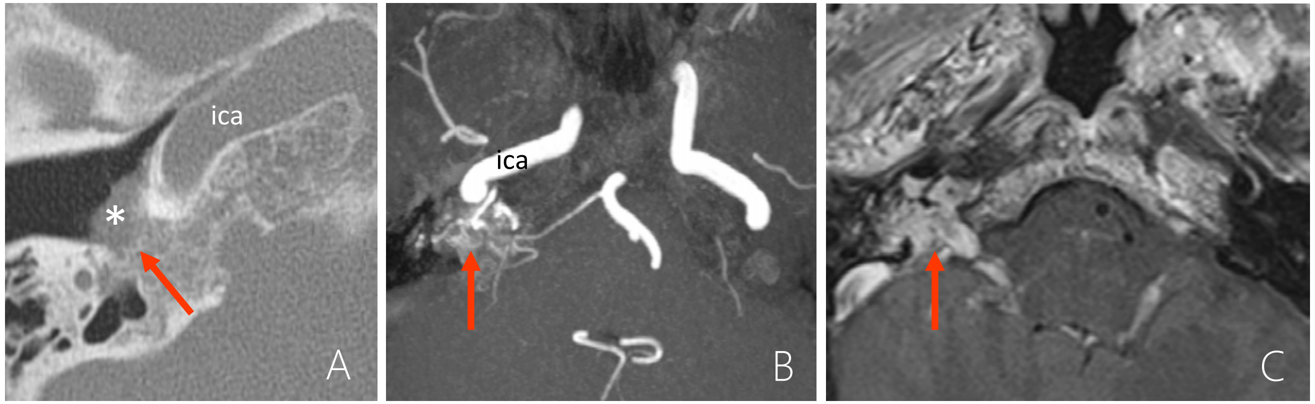

Fig. 53. Axial CBCT image shows a hypotympanic lesion (asterisk) along the promontory associated with petrous bone erosion (arrow). Axial MR angiography sequence (TOF, B) and T1W contrast-enhanced image (C) show a strongly enhancing mass with important neovascularization (arrows) partly arising from the internal carotid artery (ica).

Fig. 52. Otoscopic view showing a red retrotympanic mass (asterisk).

Case courtesy: Pascal Senn, University Hospitals Geneva.

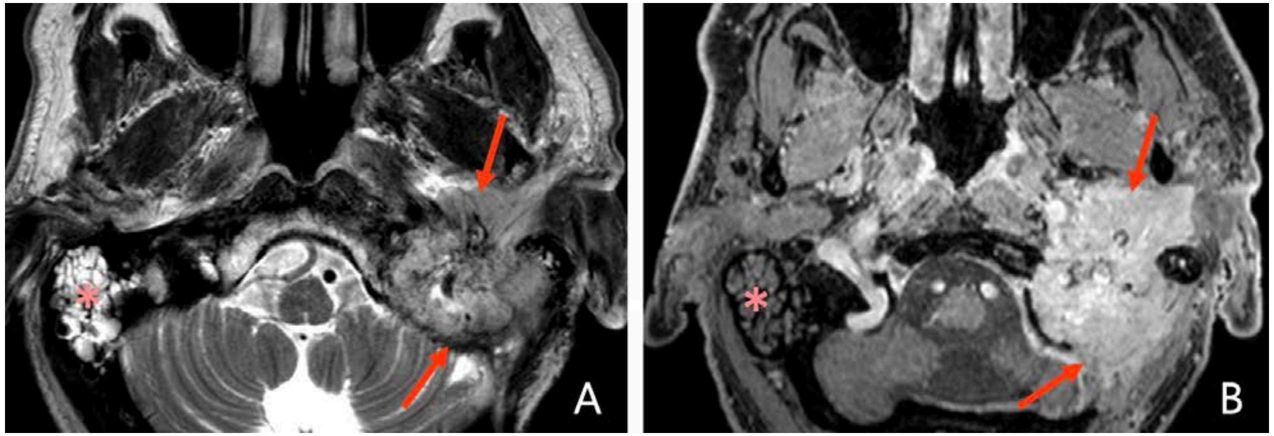

Fig. 54. Axial T2W image (A) shows a heterogenous mass (arrows) arising from the left jugular foramen with strong enhancement on the axial T1W image post gadolinium (B). The mass invades the left skull base, the left parotid gland and extends intracranially into the posterior fossa. Fluid in the right mastoid cells (asterisk)

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Pituitary Gland Adenoma

- Adenomas are the most common tumors of the sella turcica in the adult population. They are benign lesions arising from the adenohypophysis. Due to the increased amount of brain imaging, completely asymptomatic adenomas are commonly diagnosed.
- Parallel to these "incidentalomas", two main types of symptomatic adenomas can be distinguished:
  - ✓ secreting microadenomas (Fig. 55. A and B) with endocrine dysfunction allowing early diagnosis, and
  - ✓ non-secreting macroadenomas causing compression of adjacent neural structures (Fig. 55. C and D).
- Typically, a macroadenoma will induce hypopituitarism due to compression of the stalk or of the pituitary gland, superior extension will cause hemianopia due to optic chiasm compression, while lateral extension to cavernous sinus is rarely symptomatic but can compromise surgical resection if surrounding the internal carotid artery.

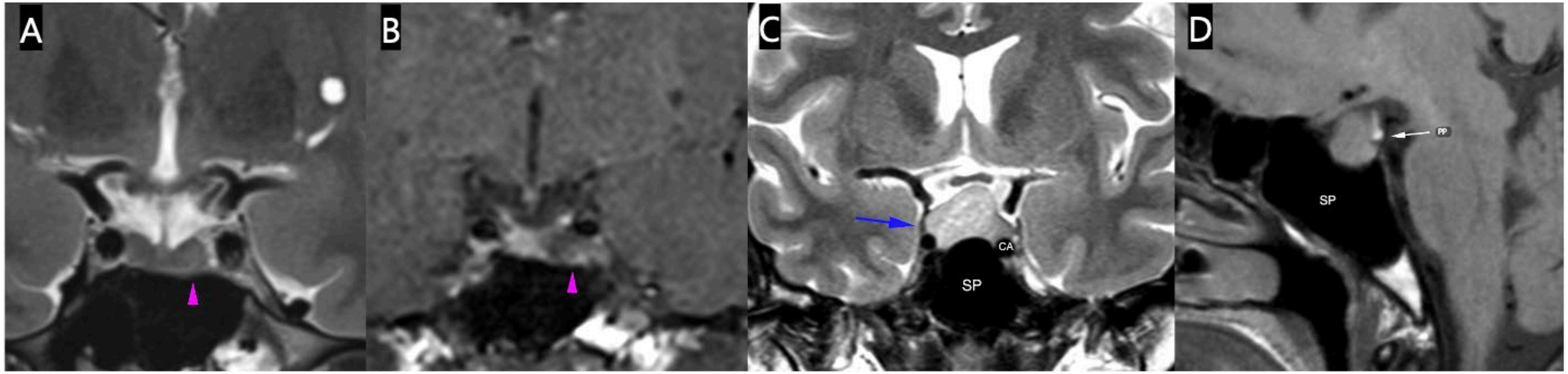

Fig. 55. Coronal and sagittal MR images of two different patients. Images A and B show a pituitary micro-adenoma (purple arrowheads) seen as a slightly hyperintense image on the T2W sequence (A) and as a focal hypo-enhancing region on the fat suppressed T1W image (B). Macro-adenoma appearing as a hyperintense mass on the coronal T2W (C) with extension to the right cavernous sinus (blue arrow) and surrounding the internal carotid artery. The lesion is isointense on the sagittal T1W image (D). On D, the tumor has a mass effect on the neurohypophysis that appears as a bright spot on the non-contrast T1W image (white arrow). SP = sphenoid sinus. CA = Internal carotid artery.

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Craniopharyngioma

Craniopharyngioma is a benign epithelial tumour derived from Rathke's pouch epithelium. Frequent in the paediatric population, it represents >50 % of all paediatric sellar tumours. The lesions tend to be partially cystic and to grow intracranially along the pituitary stalk. Large tumours may reach the hypothalamus and are associated with a high risk of injury in case of surgical resection.

There are two histologic subtypes, namely adamantinomatous and papillary craniopharyngioma. They can be differentiated based on molecular testing, age of predilection and imaging/histologic findings. In the paediatric population, adamantinomatous craniopharyngioma is the most common subtype (Fig. 56).

Rathke's cleft cyst shares a common origin with craniopharyngioma, and it can occasionally be difficult to differentiate one from the other.

Calcifications and thick parietal enhancement favour the diagnosis of craniopharyngioma.

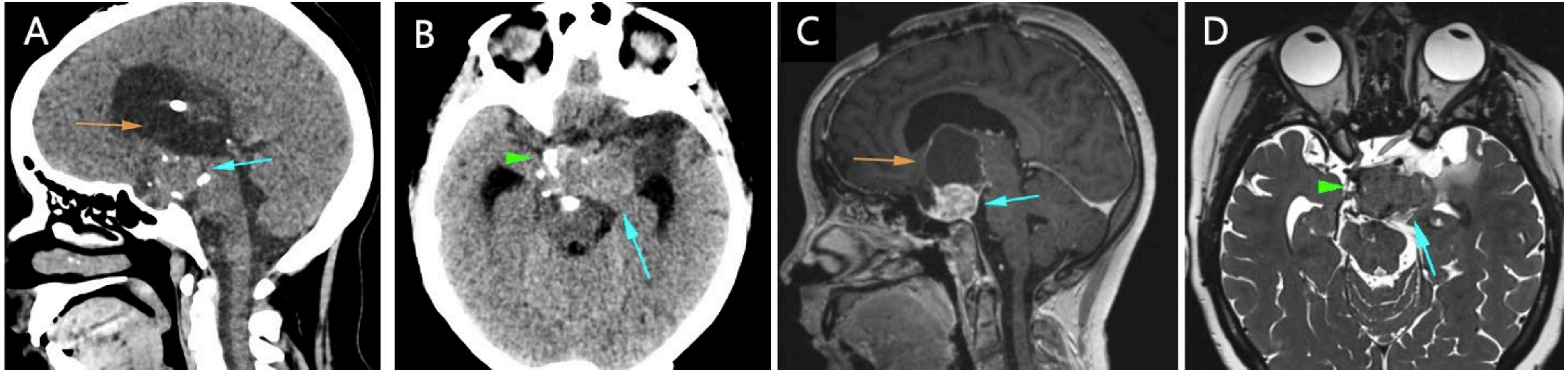

Fig. 56. Adamantinomatous craniopharyngioma in a 9-year-old girl with headache and vision loss. Sagittal and axial CT images (A and B) show a heterogenous partially solid mass (blue arrows) with calcifications (green arrowhead) and cystic parts (brown arrow). Corresponding MR images show mixed solid and cystic components. The solid parts display heterogenous enhancement (blue arrow) on the contrast-enhanced T1W image (C) and isointensity to brain parenchyma on the T2W sequence (D). The pituitary stalk is inside the mass and cannot be identified. Brown arrow in C points at the cystic component.

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Pituitary Gland: Other Pathologies

Besides tumors, the pituitary gland can be the target of congenital or inflammatory disorders, as well as cystic lesions and infectious diseases.

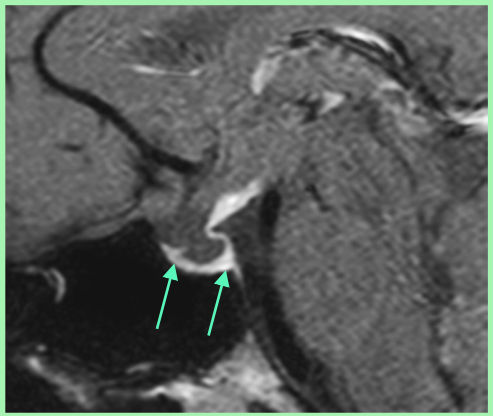
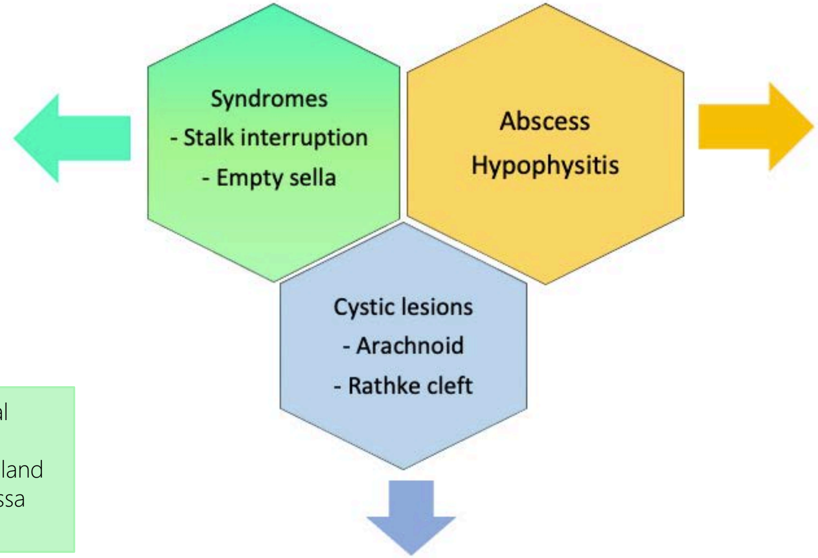


Fig. 57. Asymptomatic 38-year old woman, sagittal post-contrast T1W image shows a partially empty sella, filled with cerebrospinal fluid. The pituitary gland is small and located in the floor of the pituitary fossa (arrows).



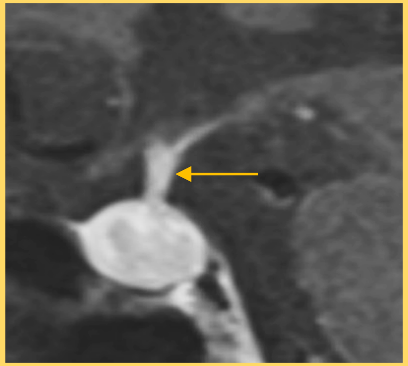


Fig. 58. Sagittal T1W post contrast shows an enlarged pituitary gland and stalk (arrow) with homogenous contrast enhancement due to hypophysitis.

Fig. 58. Rathke cleft cyst (orange arrows) seen as midline strongly hyperintense on T2W (A) and isointense on sagittal T1W image (B), with mass effect on the neurohypophysis and in contact with the optic chiasm (yellow star). Some cysts may appear as hyperintense on T1W and low on T2W images, due to proteinaceous or haemorragic content. The location between anterior and posterior pituitary is typical.

DOI 10.1016/j.eprac.2022.10.004

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Adrenal Incidentaloma, Epidemiology and Diagnostic Algorithm

Adrenal incidentalomas are frequently encountered following the use of high resolution cross sectional imaging.

The majority of these lesions are benign and do not require further investigation or follow-up.

The role of the radiologist is to primarily identify signs of potential malignancy and recognize which patients would benefit from further investigation.

For the purpose of standardised practice the following algorithm (Fig. 59) is used.

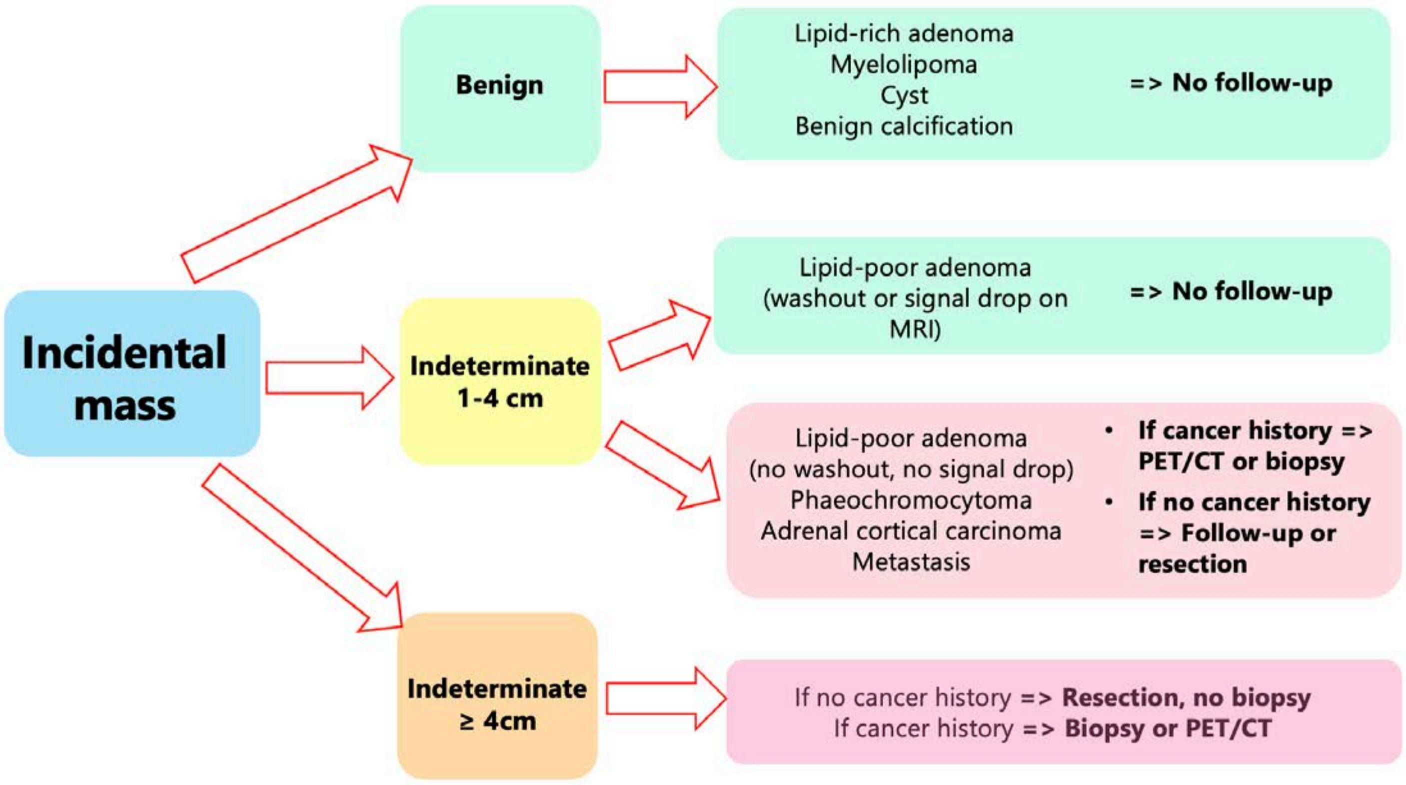

Fig. 59. Schematic algorithm for adrenal incidentaloma characterisation and management.

Doi: 10.1530/EJE-16-0467

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Adrenal Gland Pathology: Adenoma

Depending on hormonal secretion, there are two types of adenomas:

- « functional adenomas », which produce either cortico-steroids causing Cushing syndrome or aldosterone (discovered because of uncontrollable hypertension)
- « non-functional adenomas », which are more frequent and most of the time incidentally discovered.

The majority of non secreting tumours are lipid rich adenomas which display typical features at imaging: small (<4cm), round or oval shaped, well delineated, homogenous lesions with attenuation values <10 Hounsfield Units (HU) at CT (Fig. 60).

However, in 30% of adenomas with lower lipid content, the attenuation value is above 10 HU. In this situation, an additional delayed contrast-enhanced CT or MRI should be performed. The CT protocol includes delayed phase acquisitions obtained 15 min after contrast injection to calculate the absolute washout that should be ⩾ 60%. MRI can also be used as an alternative to CT and shows ⩾ 20% drop in signal on opposed- phase MRI (Fig. 61).

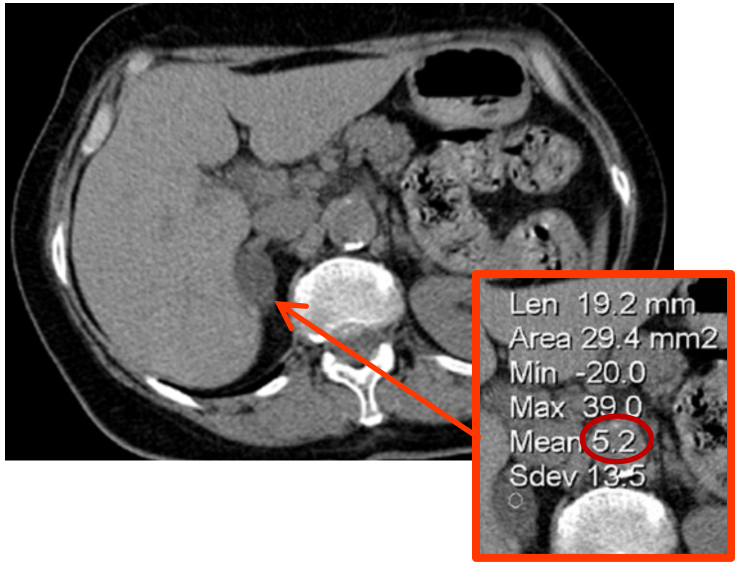

Fig. 60. Unenhanced CT with right adrenal incidentaloma, mean attenuation = 5.2 HU, in keeping with a lipid-rich adenoma

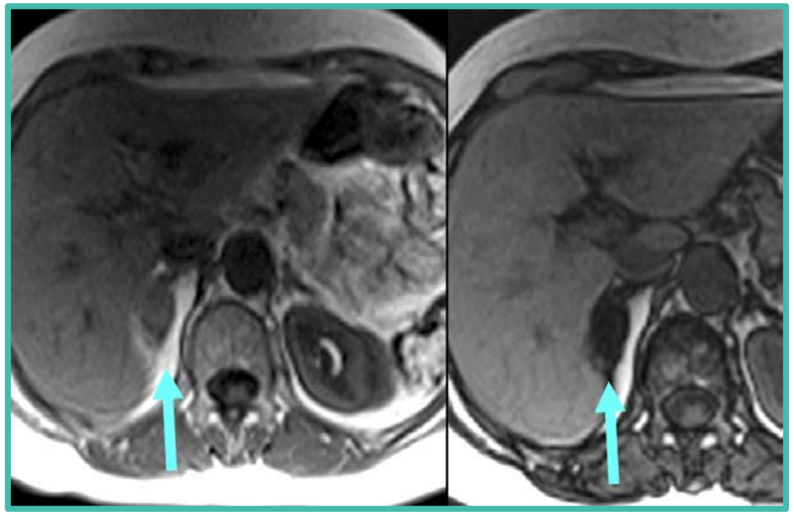

Fig 61. MRI chemical-shift sequence demonstrating homogenous signal drop in the right adrenal lesion on the opposed-phase compared to the in-phase (blue arrows)

Doi: 10.21037/gs-20-559

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Adrenal Gland Pathology: Pheochromocytoma

<u>The 10% rule:</u>
- ✓ 10% bilateral
- ✓ 10% non-secreting
- ✓ 10% malignant
- ✓ 10% genetic (NEM, von Hippel Lindau, ...)

Pheochromocytoma is a rare neuroendocrine tumour that originates in the adrenal medulla. The tumour is usually benign and can secrete adrenaline and noradrenaline. When the tumour is secreting, high blood pressure, rapid heartbeat, sweating, headaches, anxiety, and weight loss are the result. Non-secreting tumours are usually asymptomatic and detected later. These are often larger in size at the time of diagnosis.

Several genes have been identified that are associated with the development of pheochromocytoma, including the RET, VHL, NF1, SDHA, SDHB, SDHC, and SDHD genes.

Metaiodobenzylguanidine (MIBG) is a radioactive substance taken up by the adrenal glands. MIBG scintigraphy is commonly used to diagnose pheochromocytoma or to determine tumour extent.

PETCT can also be used (Fig. 62. A-B) but has a low specificy. PET/CT is useful in the context of a known cancer to look for metastatic disease.

Dynamic contrast enhanced MRI can also help to better characterise these lesions (Fig. 62.C-D).

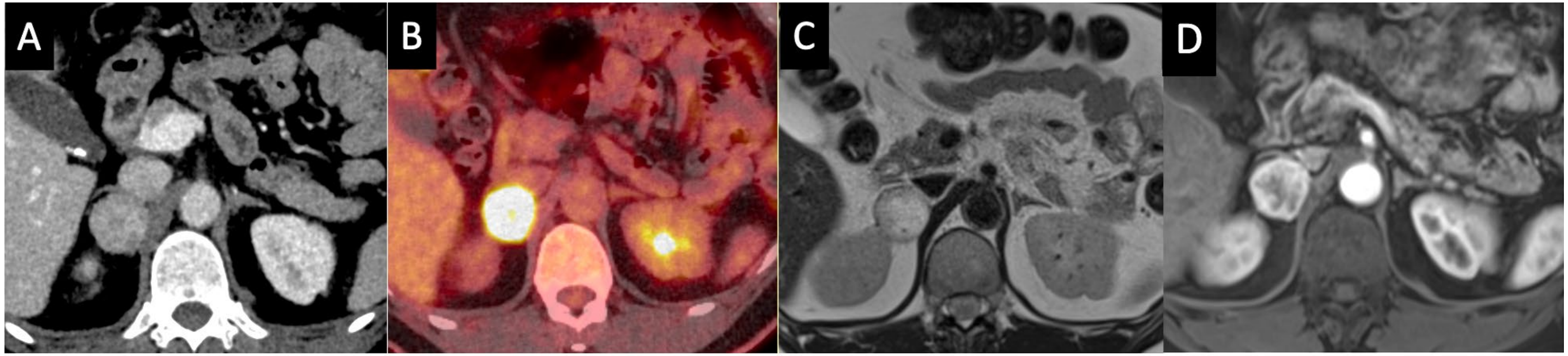

Fig. 62. Contrast-enhanced CT (A) and PET 18FDG fusion demonstrating intense tracer uptake in the heterogenous right adrenal mass. On MRI, the lesion has a high signal on T2W (C) and cystic unenhanced portions on T1W post Gadolinium (D) sequences.

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Adrenal Gland Pathology: Other lesions

While adenomas are the most frequent adrenal tumours, other adrenal lesions can also occur including cysts, haematomas, myelolipomas or metastases.

Benign

Myelolipoma present as solid tumours with macroscopic fat representing > 50% of the tumour volume (Fig. 63).

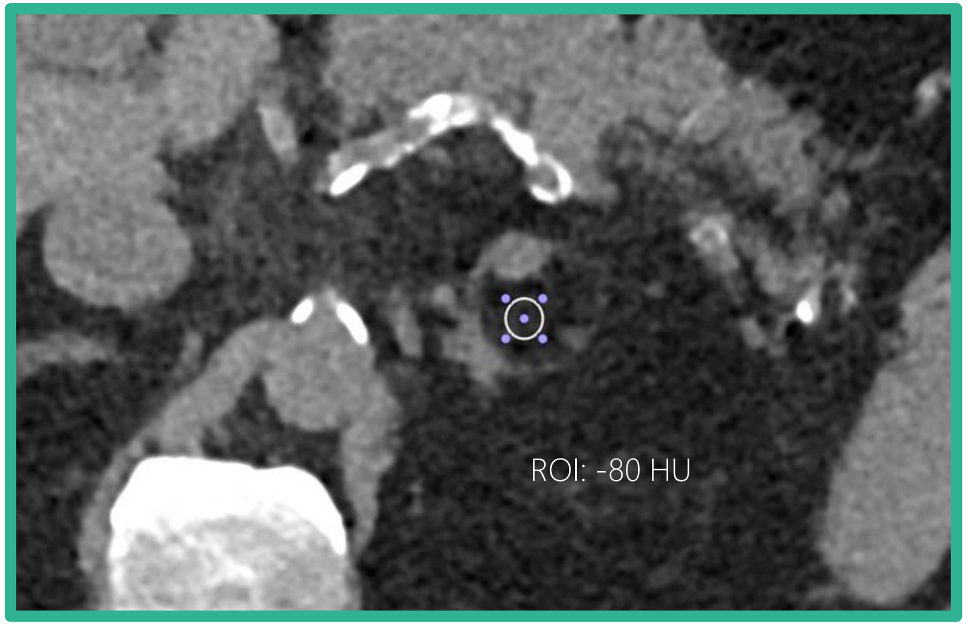

Fig. 63. Axial abdominal unenhanced CT showing a tumour with macroscopic fat (Region of Interest attenuation measurement = -80 HU) suggesting a myelolipoma.

Malignant

Some criteria, e.g., actual or previous cancer history, large size (> 4cm) or heterogenous mass are red flags for malignancy (Fig. 64).

Fig 64. Axial contrast-enhanced CT showing a large and heterogenous mass of the left adrenal gland (red arrow), in a patient treated for lung cancer

https://doi.org/10.7861/clinmed.2023-0042.

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- The endocrine system is a complex network of glands with intricate hormonal interactions responsible for almost every organ and function in the body. It is because of its complexity that a thorough knowledge of the radiological anatomy is crucial to understand underlying pathology and corresponding symptoms.
- The choice of the most appropriate imaging technique depends on the involved organ and on patient symptoms. Knowledge and familiarity with all imaging modalities and their respective roles depending on the clinical situation are, therefore, crucial.
- Both radiological and biological tests must be correctly utilised and closely integrated with each other, thereby allowing accurate clinical interpretation.
- The radiologist plays an important role in identifying signs of potential malignancy and in recommending which patients would benefit from further investigations.
- To improve practices for lesion characterisation, standardised radiological algorithms and classifications have been developed and are routinely used in every-day practice.

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1 – Which of the following statements is correct?

- The thyroid gland is located in the carotid space
- Ultrasonography is the imaging modality of choice for assessing thyroid pathology
- The thyroid gland often has an ectopic location
- ACR-TIRADS grades are used to classify thyroid cancer grades

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2 – On US, the thyroid gland has the following appearance:

- Isoechogenic to the overlying strap muscles
- Hyperechogenic compared to the overlying strap muscles
- Isoechogenic to the subcutaneous tissues
- Hypervascularised at Doppler studies

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3 – Regarding the parathyroid glands, which of the following statements is correct ?

- Ectopic parathyroid glands are rare
- They are usually located on the anterior surface of the thyroid gland
- A typical ectopic location is in the retro-oesophageal region
- Are commonly located within the thyroid gland

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4 – Regarding the adrenal glands, which statement is correct?

- In adults US is better suited for assessing the adrenal glands
- The adrenal glands do not enhance after contrast administration on CT
- In children, adrenal glands are readily visible on ultrasound
- Phaeochromoctyomas are indistinguishable from adrenal adenomas on imaging

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5. Regarding imaging of the thyroid gland, which statement is correct?

- Iodine based contrast agents are not contraindicated in the work-up of thyroid cancer
- MRI has a superior spatial resolution compared to US
- PET CT is routinely used as part of the preoperative management of thyroid cancer
- One of the disadvantages of nuclear medicine studies is lower spatial resolution

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6. Regarding imaging of the parathyroid glands, which statement is correct ?

- US always requires correlation with 4DCT in the standard work-up of patients with hyperparathyroidism
- Parathyroid lesions can be of mixed cystic and solid composition and very large
- Parathyroid lesions ectopically located within the thyroid gland are easily distinguished from nodules of thyroid origin
- MRI is recommended to distinguish parathyroid adenomas from lymph nodes

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7. Which of the following statements regarding thyroid cancer is correct ?

- Is the least common endocrine malignancy
- Medullary carcinoma occurs more frequently than follicular carcinoma
- Hashimoto's thyroiditis has an increased risk for thyroid malignancy
- Papillary carcinoma is a type of dedifferentiated thyroid cancer

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8. Which of the following statements regarding paragangliomas is correct ?

- They occasionally occur along the sympathetic chain of the head and neck
- They rarely occur in the context of hereditary disorders
- The jugular fossa is the most common location above the aortic arch
- They are rare neuroendocrine tumours

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9. Regarding imaging in paragangliomas, which statement is correct ?

- Tympanic paraganglioma is often found along the cochlear promontory
- Jacobson's nerve is an auricular branch from the vagus nerve
- Carotid body tumours have a characteristic salt and pepper appearance on contrast enhanced CT
- In jugular paraganglioma, splaying of the internal and external carotid arteries is common

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10. Regarding pituitary lesions, which of the following statements is correct ?

- Adenomas are the commonest tumours of the sella turcica in the paediatric population
- They most often arise from the neurohypophysis
- They are often asymptomatic and rarely cause mass effect on the adjacent structures
- Craniopharyngiomas frequently occur in the paediatric population

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10. Regarding pituitary lesions, which of the following statements is correct ?

- Adenomas are the commonest tumours of the sella turcica in the paediatric population
- They most often arise from the neurohypophysis
- They are often asymptomatic and rarely cause mass effect on the adjacent structures
- ✓ Craniopharyngiomas frequently occur in the paediatric population

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