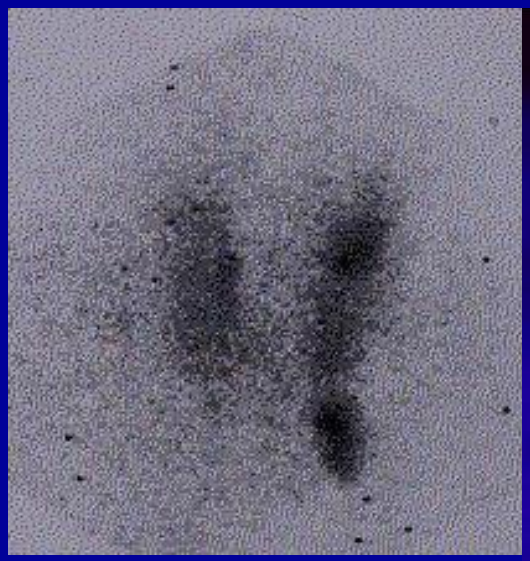
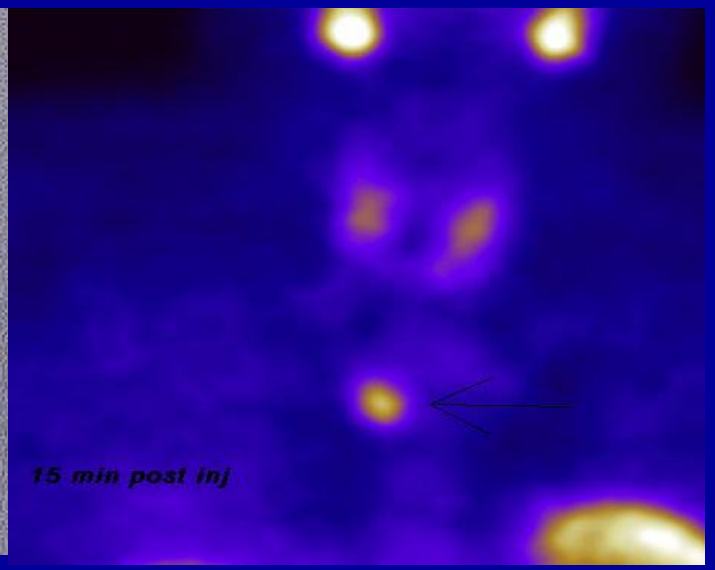
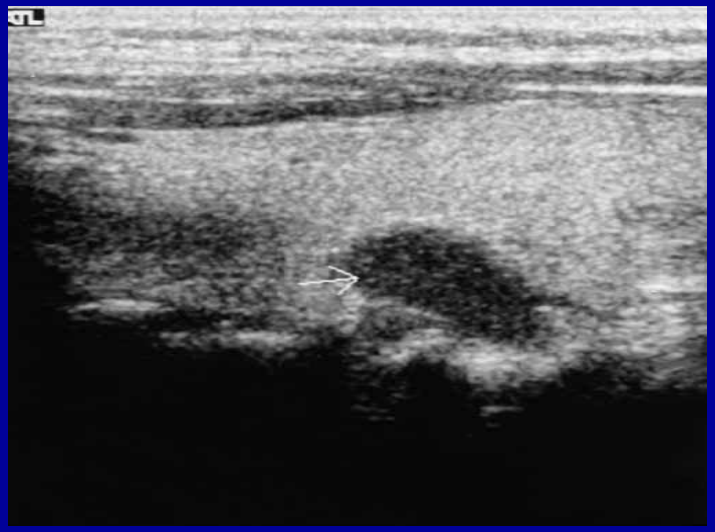
Parathyroid and adrenal glands







Assoc. prof. V. Marković, MD, PhD

Assoc. prof. A. Punda, MD, PhD

D. Brdar, MD, nucl. med. spec.

Hyperparathyroidism (HPT)

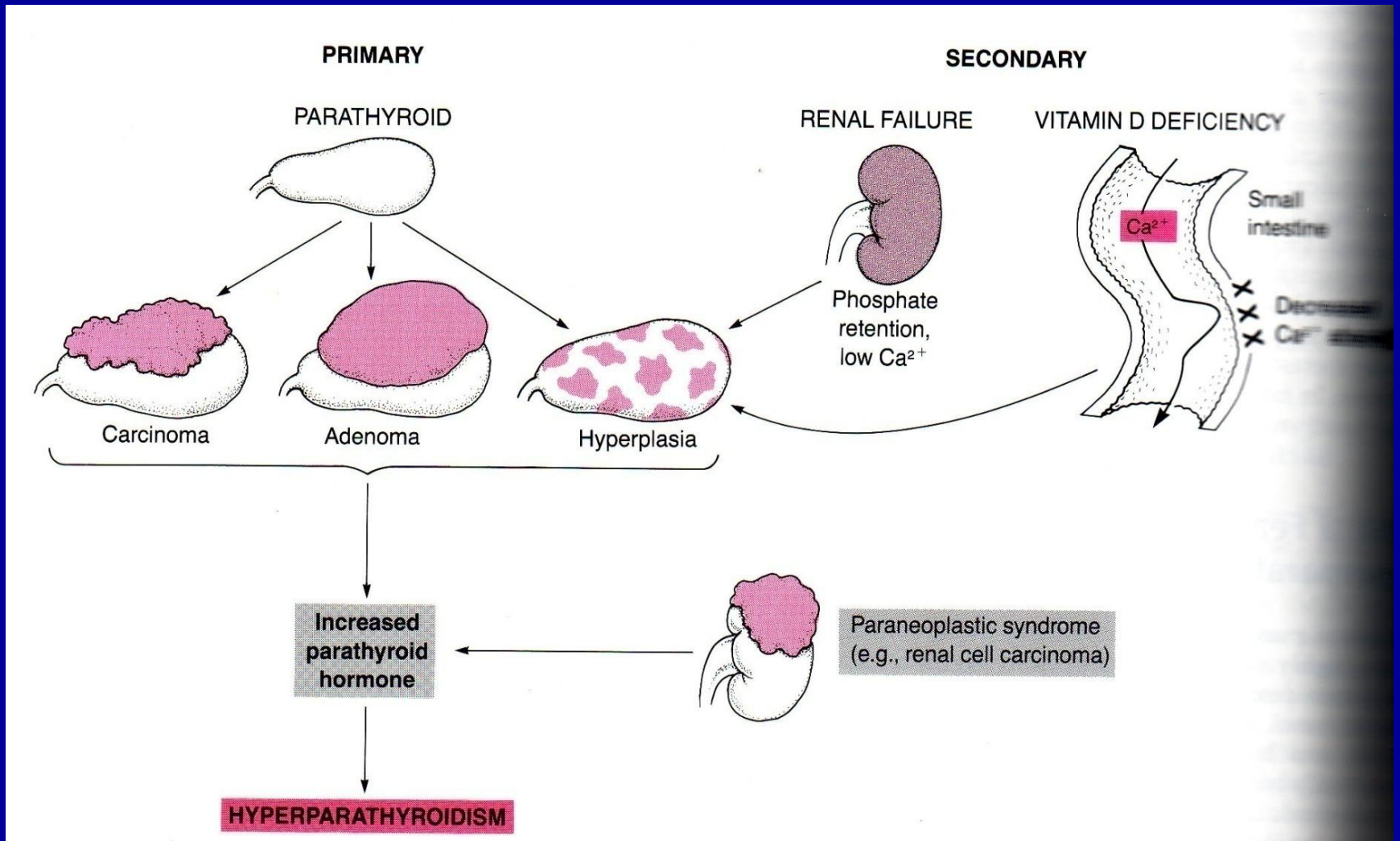


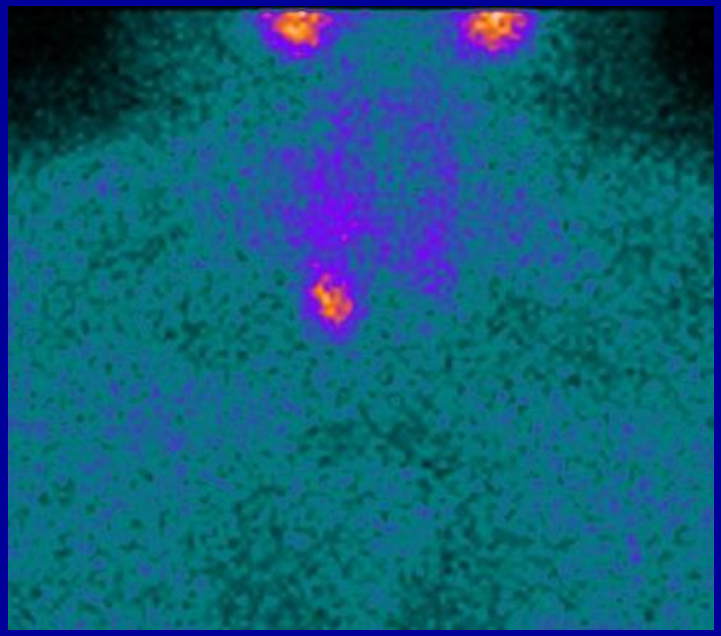
FIGURE *21-30*
Major pathogenetic pathways leading to clinical primary and secondary hyperparathyroidism.

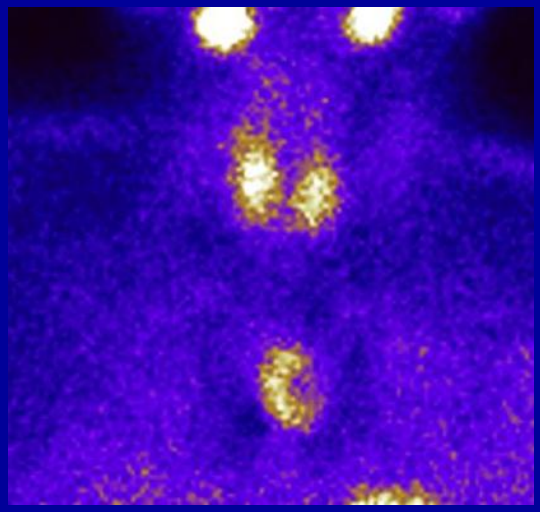
Primary hyperparathyroidism

- The autonomous, spontaneous, excessive production of PTH
- Hypercalcemia and hypophosphatemia

Adenoma - 80-90 %

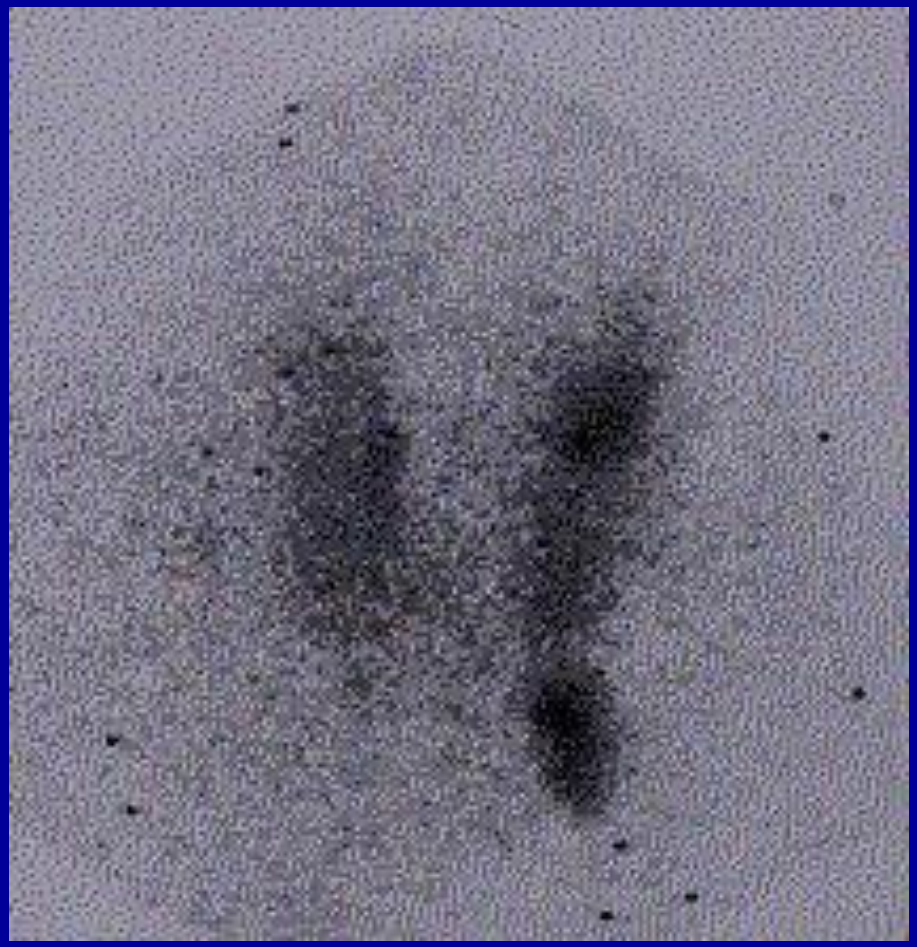
- Sharply restricted, soft capsule, up to 5 g
- Edge squeezed the rest of parathyroid





Ectopic parathyroid adenoma

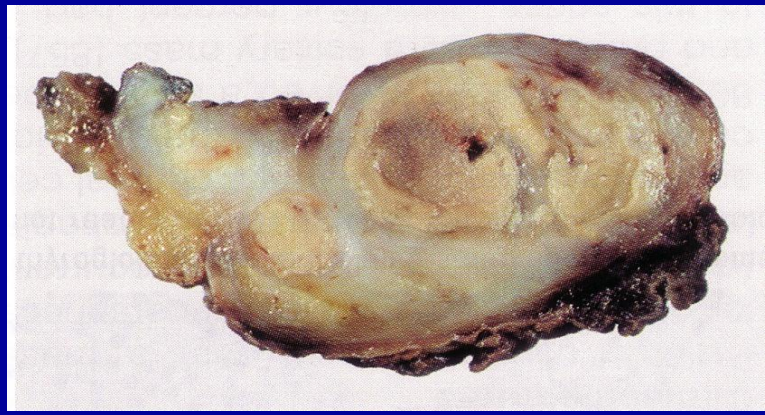
Multiple adenomas 2-4%



Hyperplasia 15%

- Sporadically or as part of MEN type 1 or type 2

Carcinoma < 0,5%



- solid
- Bigger than adenomas
- One gland
- Polymorphism and mitosis
- Necrosis and hemorrhage

- Metastases and infiltration

What can we find?

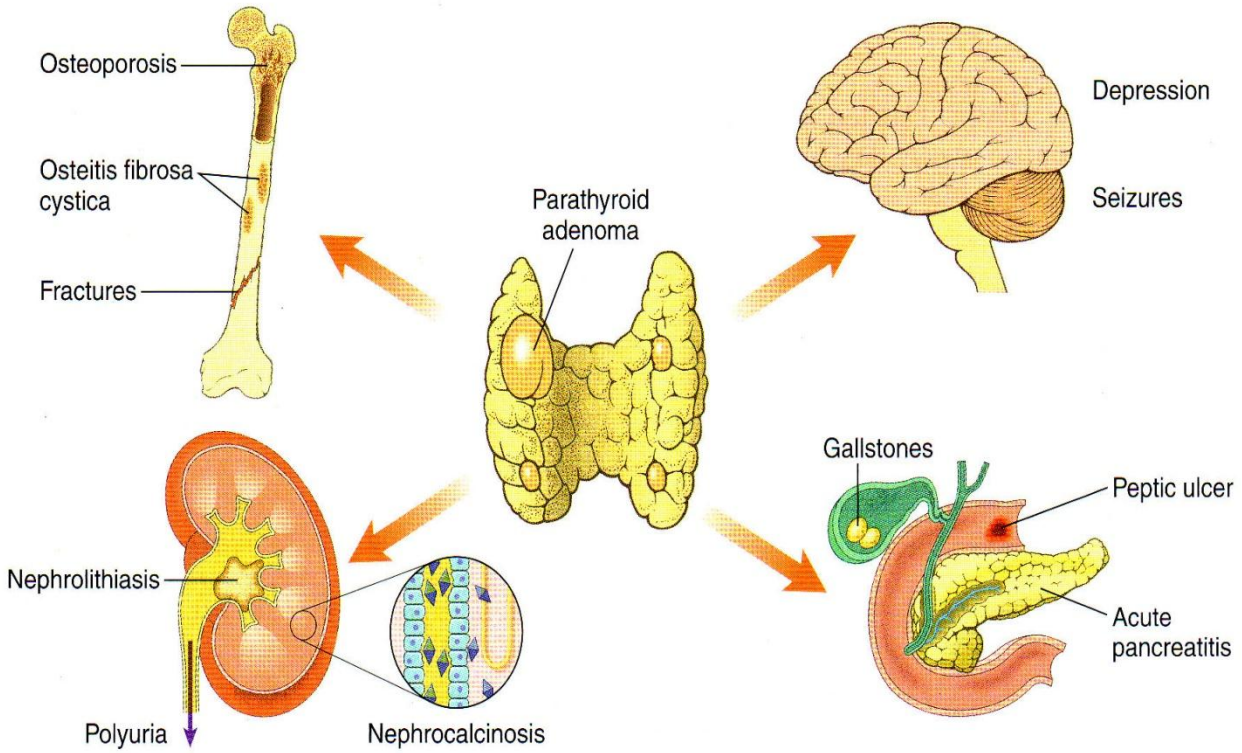


Figure 20-19

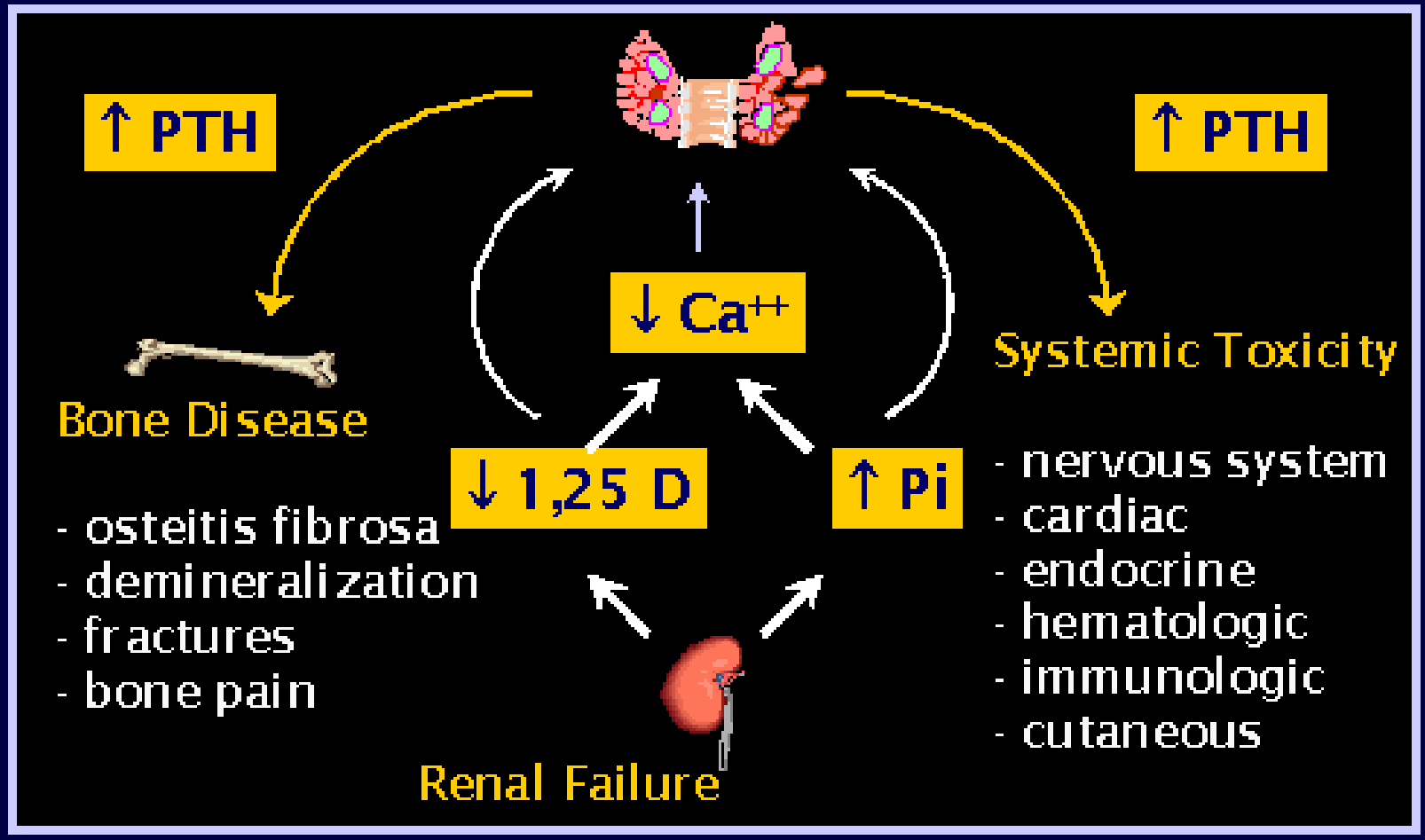
Cardinal features of hyperparathyroidism. With routine evaluation of calcium levels in most patients, primary hyperparathyroidism is often detected at a clinically silent stage. Hypercalcemia from any other cause can also give rise to the same symptoms.

Secondary hyperparathyroidism

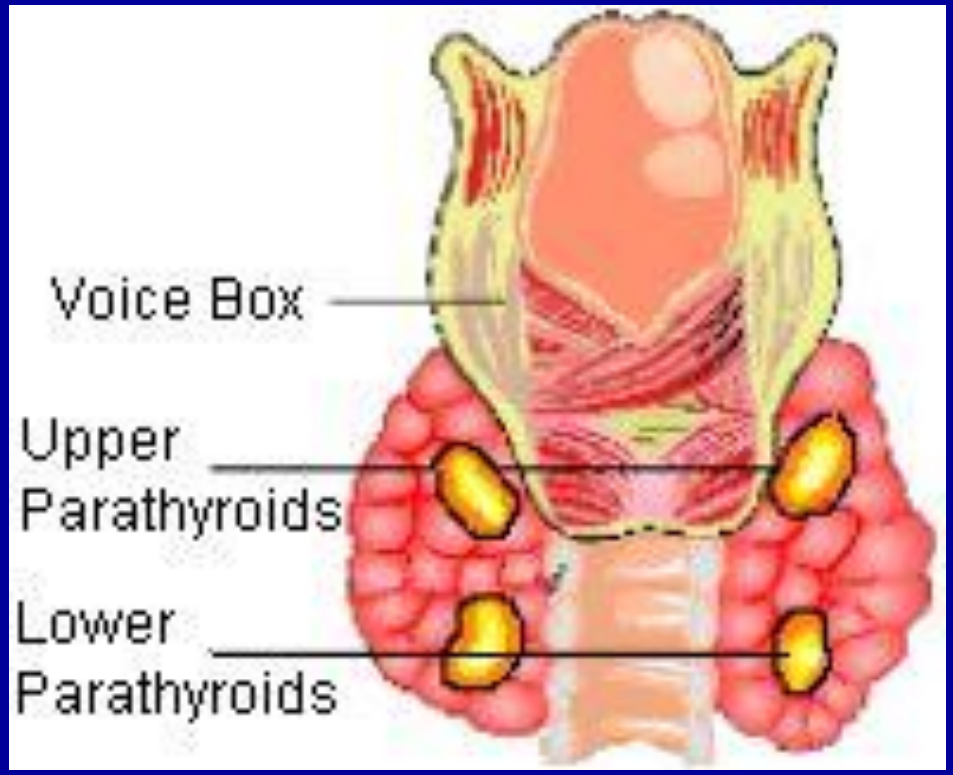
Diseases caused by adequate secretion of PTH

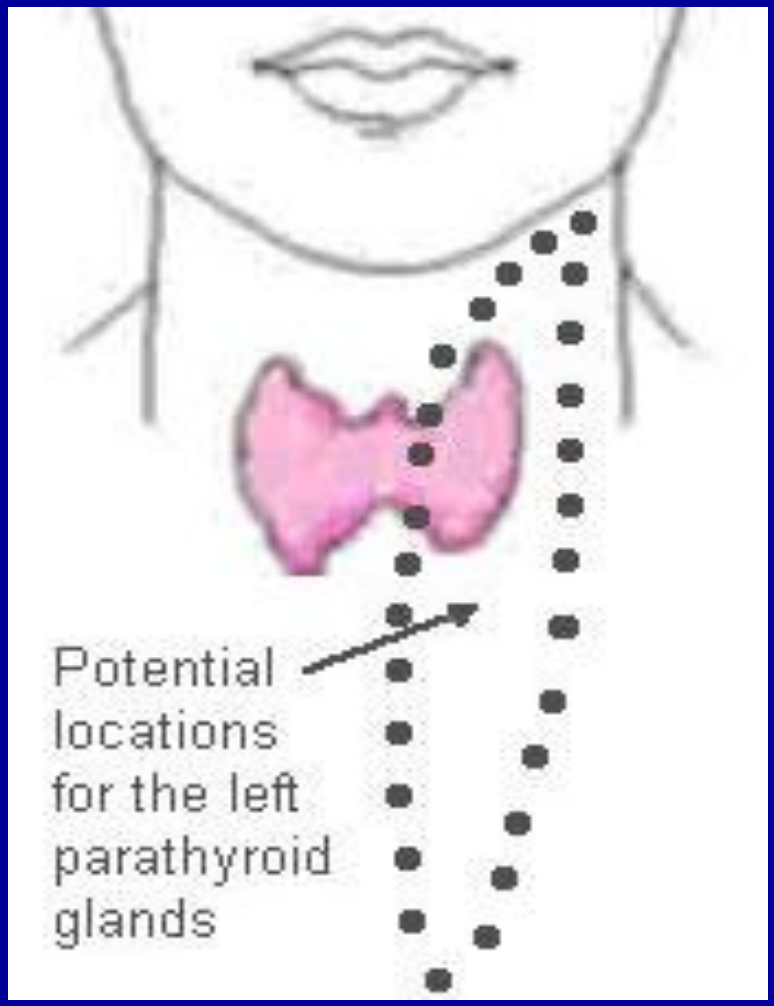
- Every state of hypocalcemia causes compensatory secretion of PTH: rachitis, osteomalacia, intestinal malabsorption, disorders of the pancreas, obstructive disease of the bile ducts, after gastrectomy, gluten sensitive enteropathy, renal osteodystrophy, renal tubular acidosis, Fanconi syndrome, rachitis resistant to vitamin. D, hypofosfatasis.

Secondary Hyperparathyroidism



Normal and ectopic positions of parathyroid glands





Radiopharmaceuticals

- Se -75 - methionine
- Tl-201
- Tc-99m - MIBI
- Tc-99m - MIBI

Methods

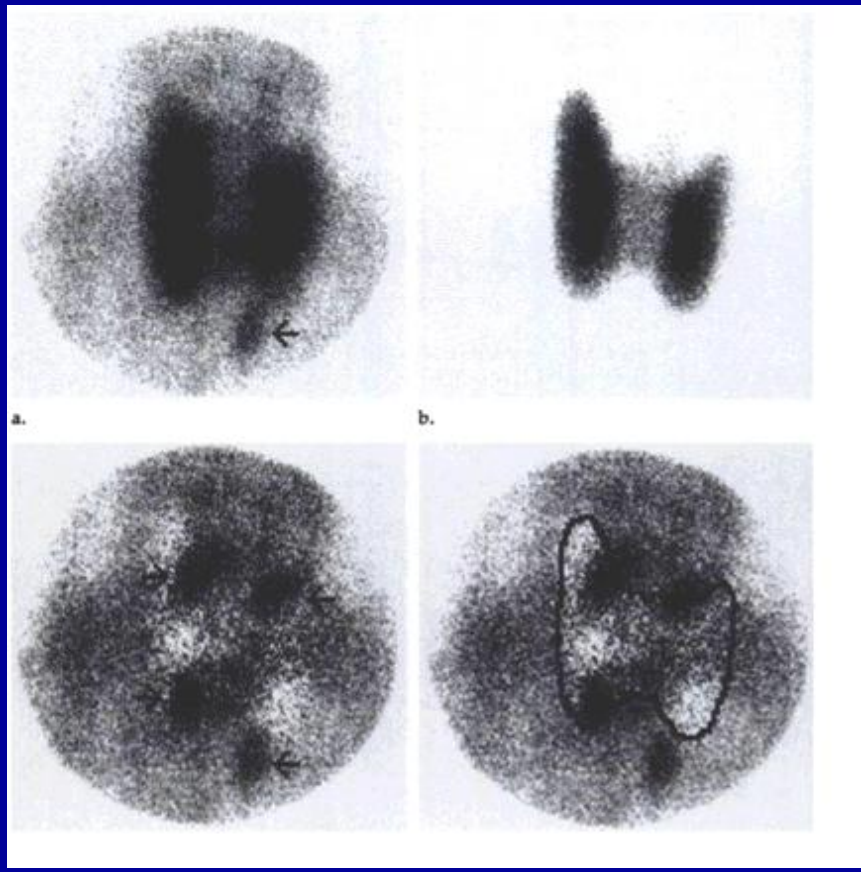
- Subtraction scintigraphy:
  - Tl201 - Tc99m
  - Tc99m MIBI – Tc 99m O4
  - Tc99m MIBI – I 123
- Dual phase: Tc-99m-MIBI

Mechanism of accumulation

- MIBI - lipophilic substance that accumulates in cells with increased metabolic activity, active transport and passive diffusion within the mitochondria

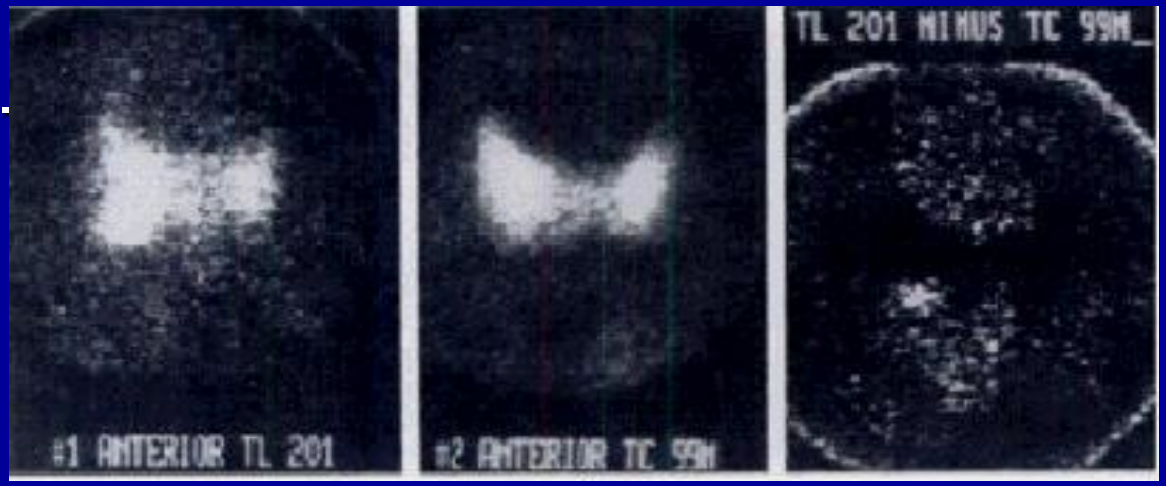
Subtraction scintigraphy

- Radiopharmaceuticals: Tl 201 (accumulates in the thyroid and parathyroid glands); Tc 99m O4 (accumulates only in the thyroid gland)
- Scintigrams of the neck and chest
- Technetium scintigrams of the neck ″subtracted″ from thalium scintigrams



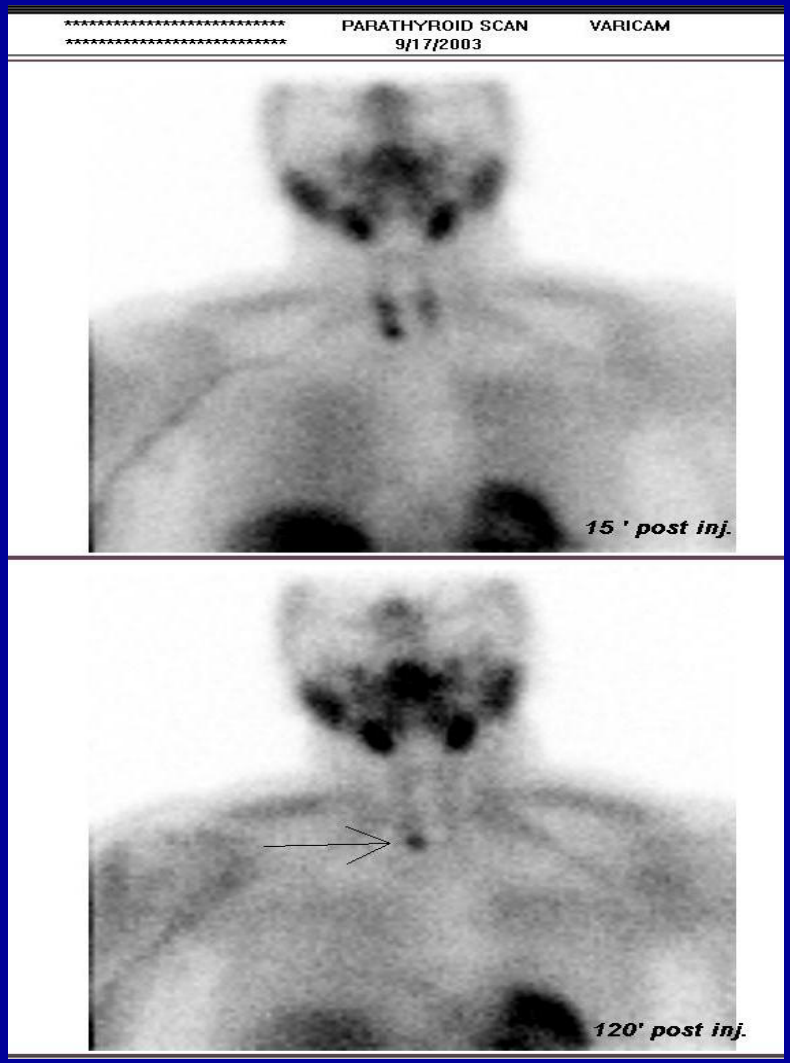
Subtraction scintigraphy

- Disadvantages:
  -The existence of artifacts due to patient movement
  - A relatively small dose of thallium (technically poor images)
  - Thallium is expensive and not always available



Dual phase scintigraphy

- Radiopharmaceutical:Tc 99m MIBI or Tc 99m tetrofosmin
- Dual phases: 15 and 120 min after injection
- Region: neck and chest
- The use of oblique and lateral projections, tomography (SPECT) and pin hole collimator



Preoperative application

For

- Ectopic glands
- Multiple adenomas
- Supernumerary glands
- Minimally invasive surgery

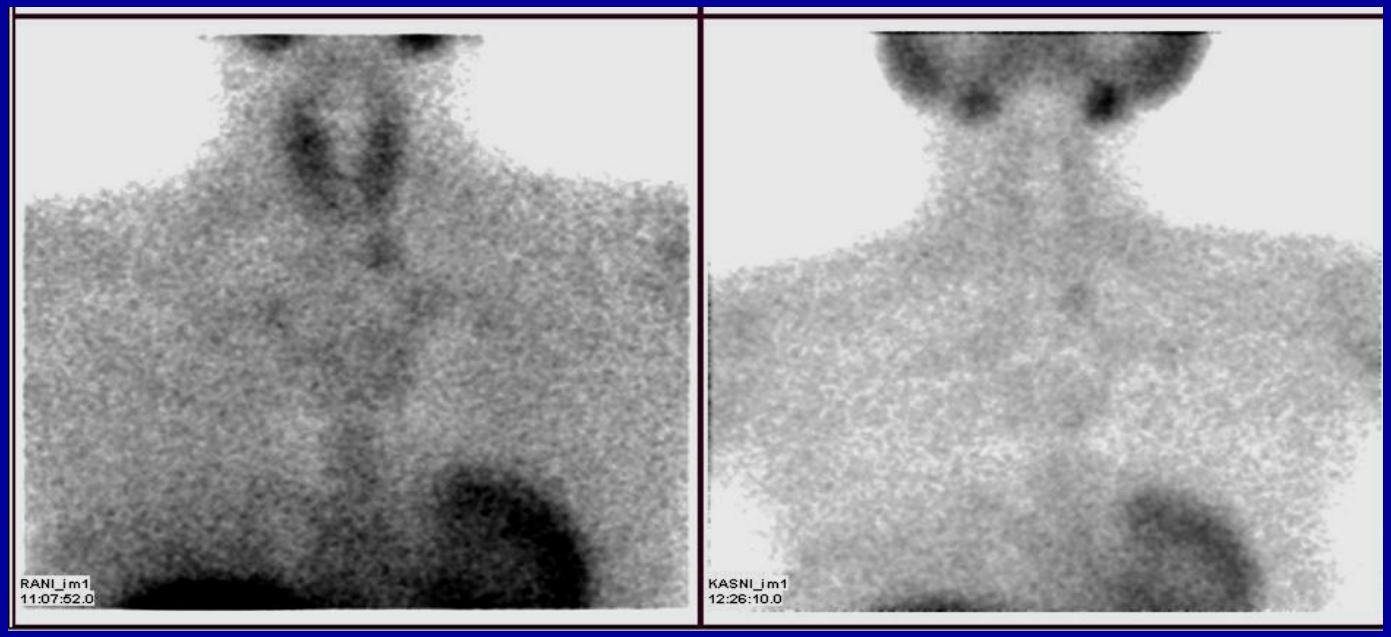
against

- Insufficiently sensitive for ″experienced operators″
- Price
- Complexity of the method

Primary HPT

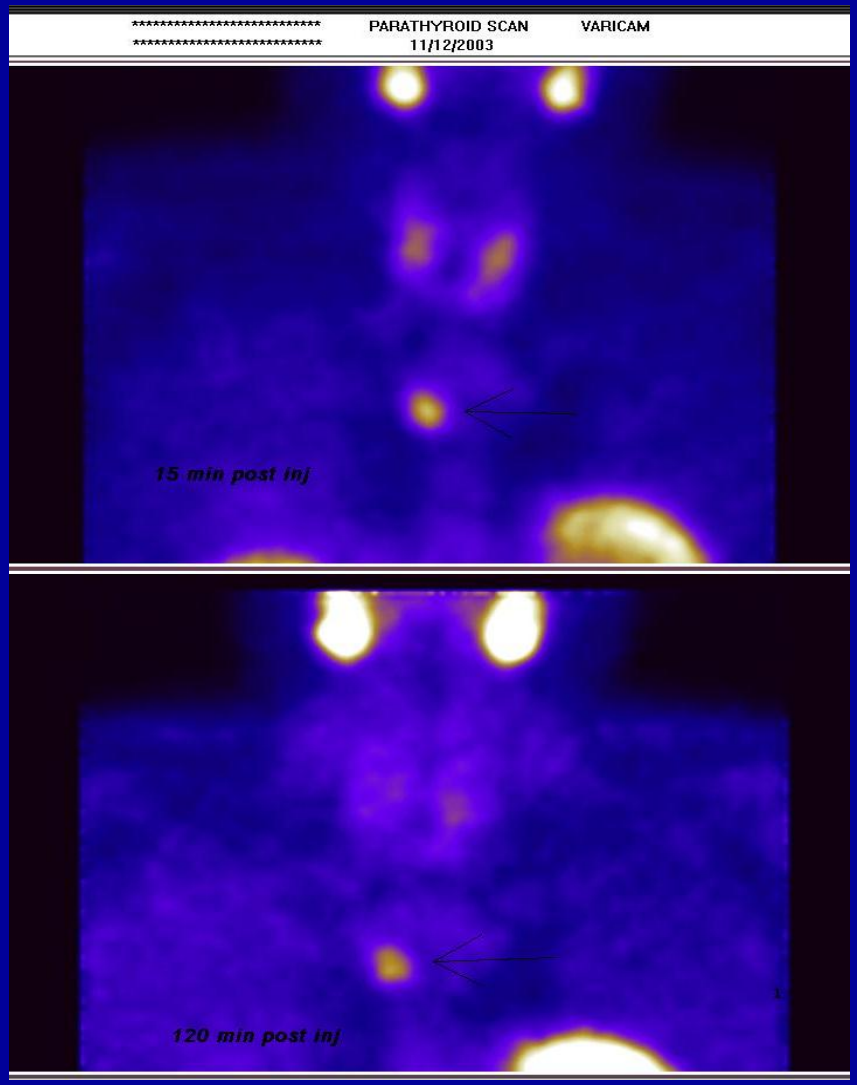
- High sensitivity (> 95%) and specificity (98%)
- Appearance of the ectopic (10-15%) and supernumerary (5%) glands
- A positive result even at slightly elevated PTH serum

Primary HPT - ectopia

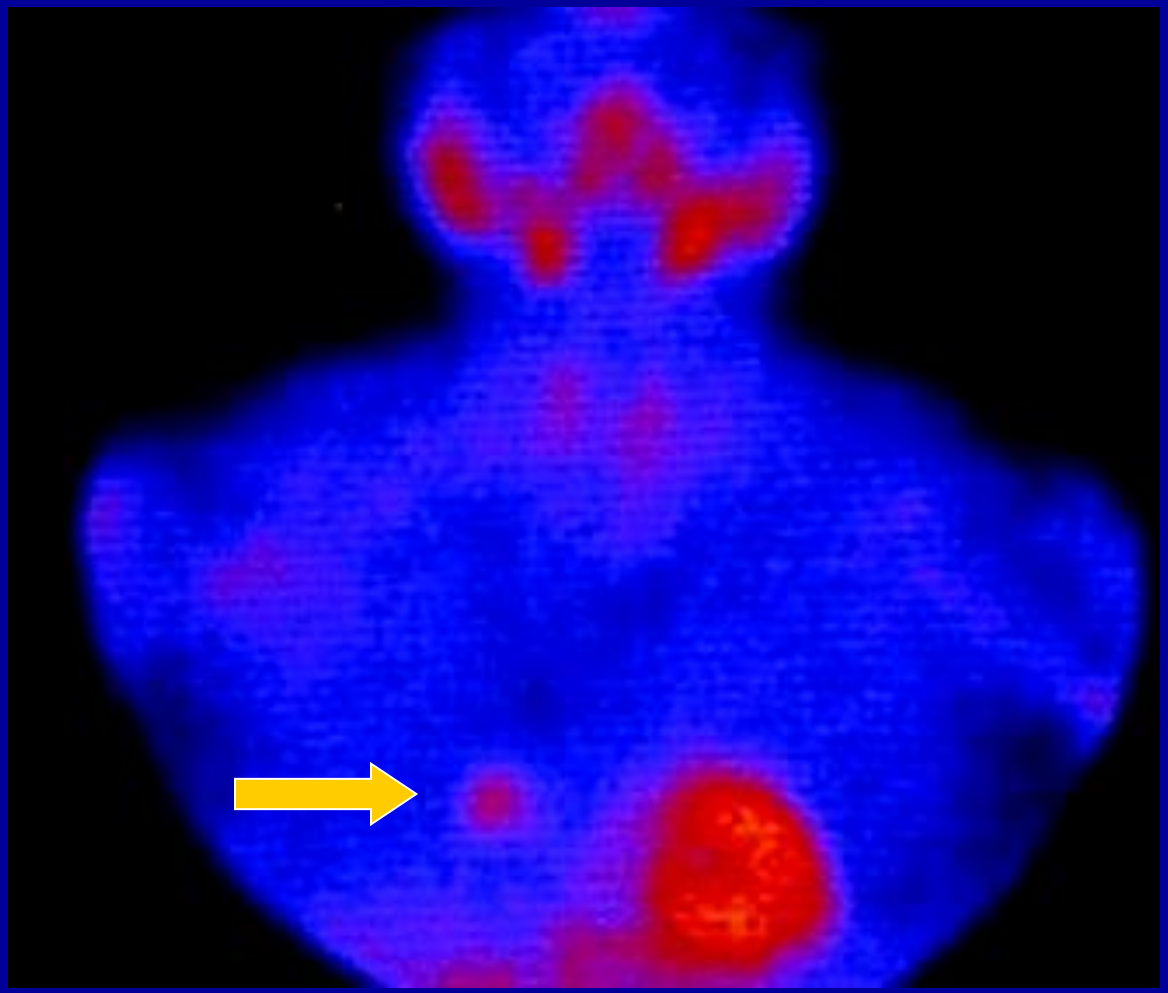


- Ectopia = distance from thyroid greater than 1cm
- in 10-15% (20%)

Primary HPT - ectopia

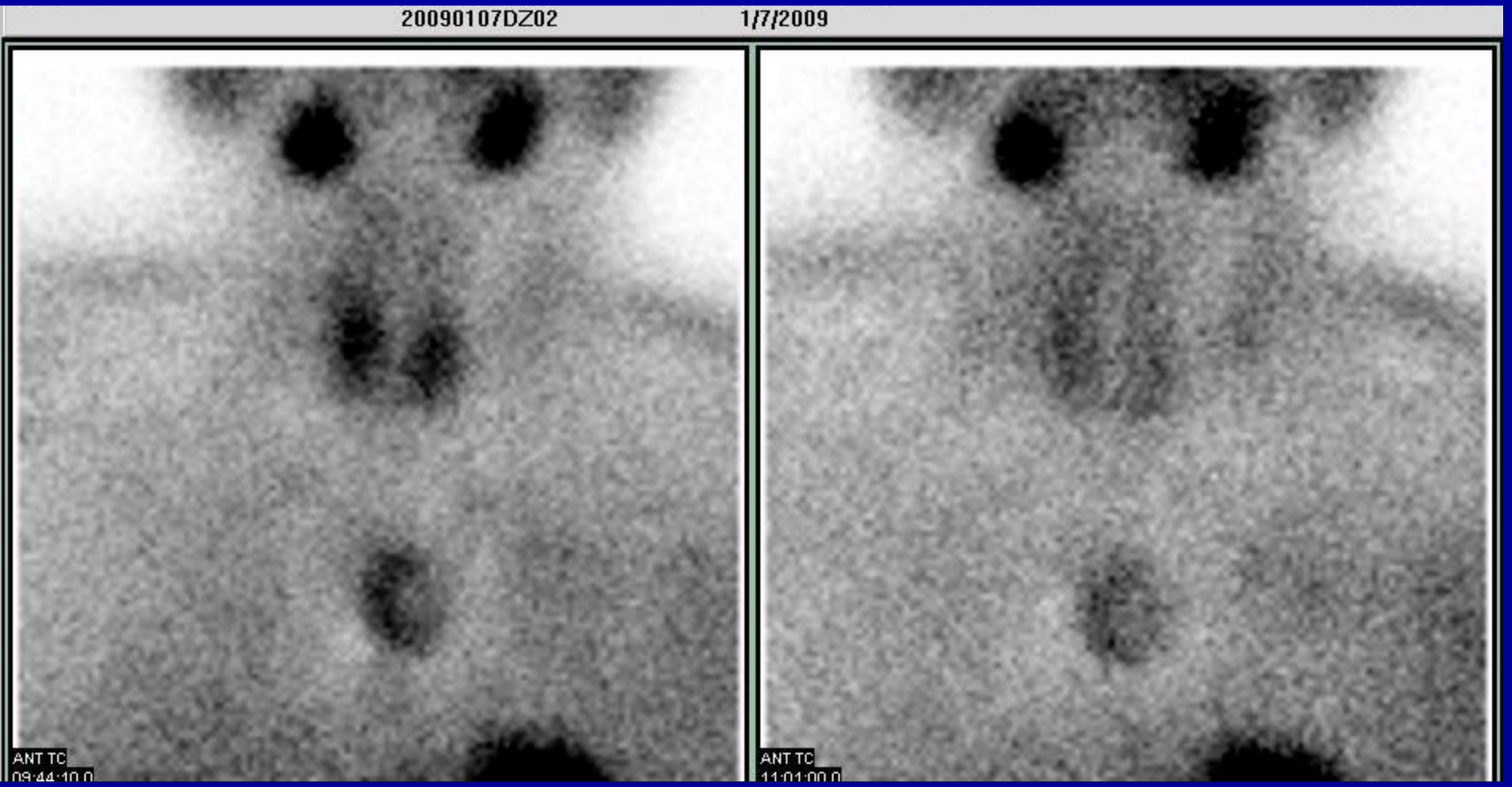


Primary HPT - ectopia

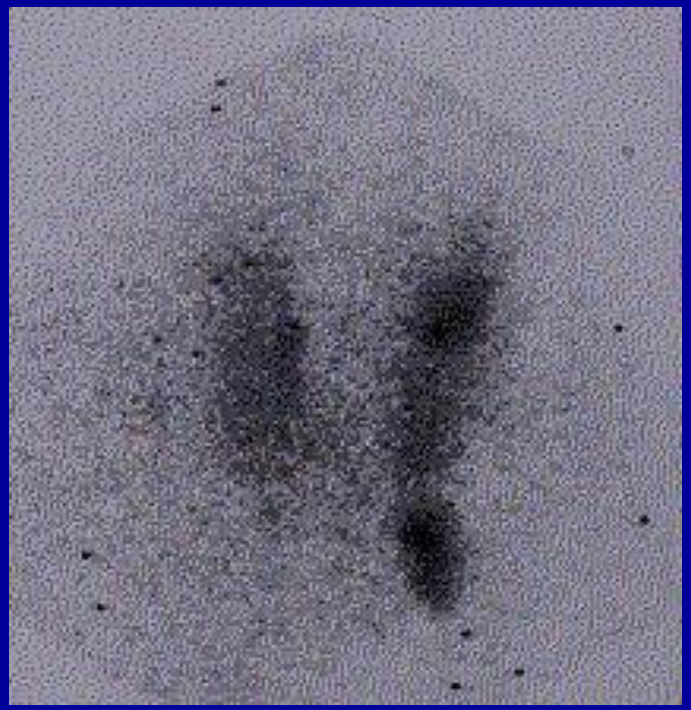


Tc99m MIBI, 120 min p.i., pHPT

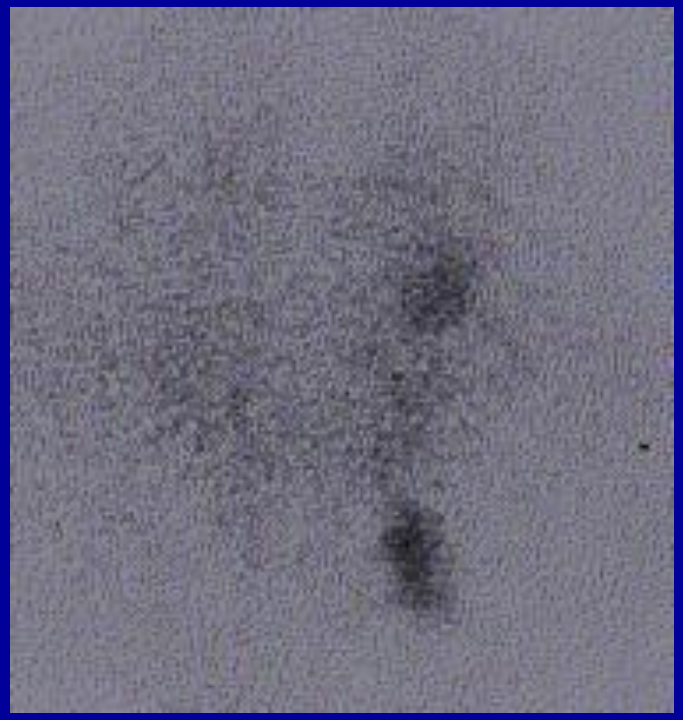
Primary HPT - ectopia



Primary HPT– multiple adenomas



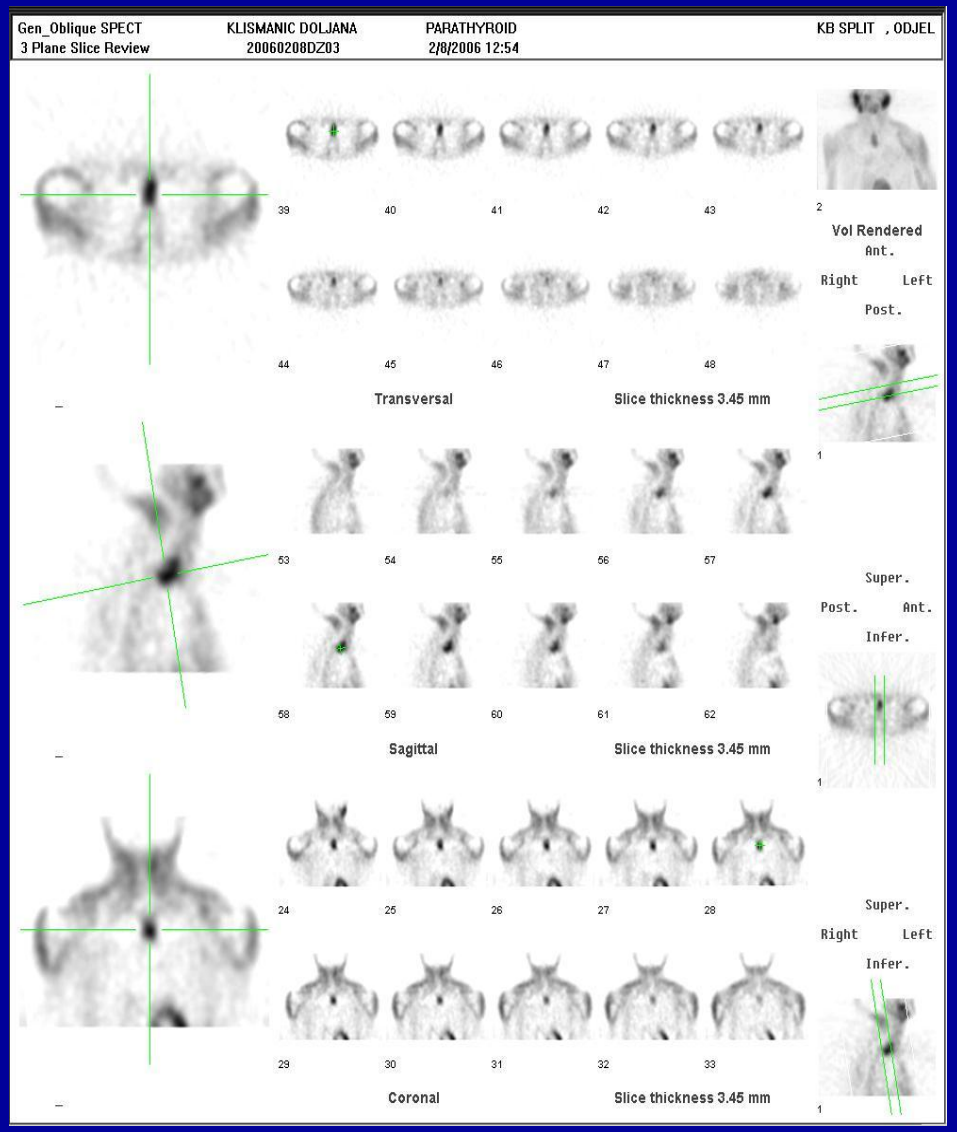
15 min p.i.



120 min p.i.

Primary HPT - SPECT

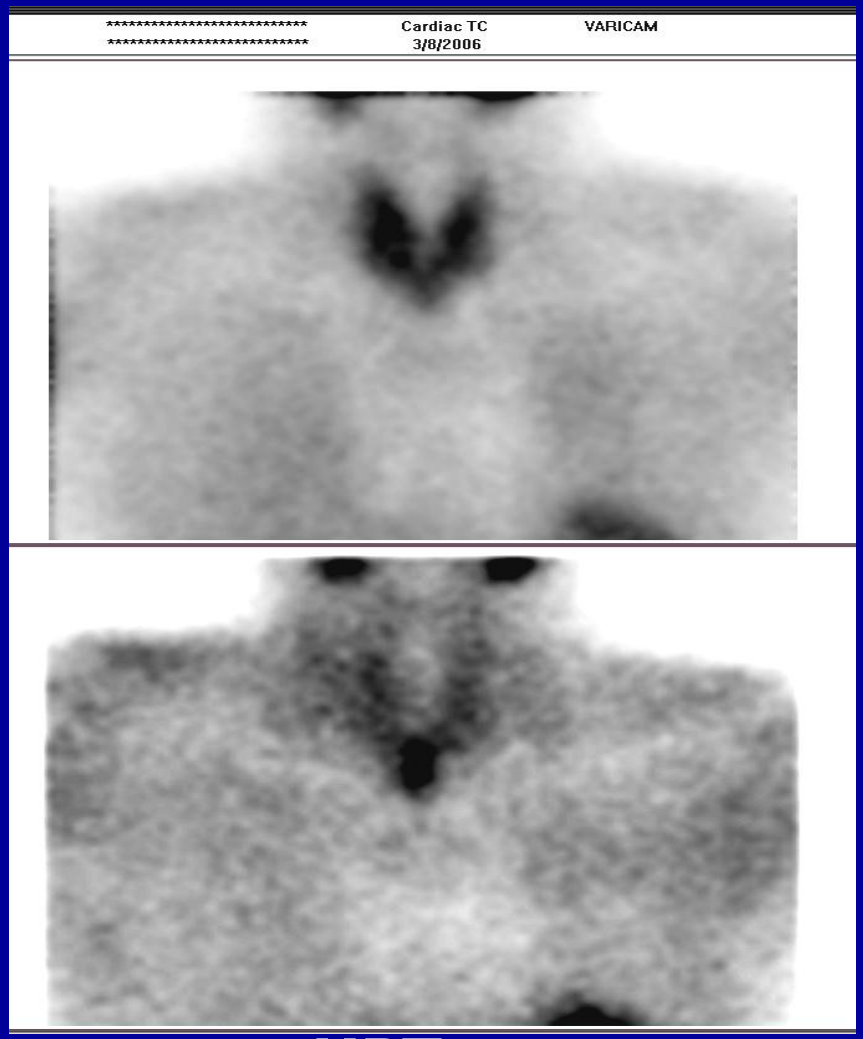
- Useful for better localization, especially in ectopic glands, nodular goiter
- Requires more time than planar scintigraphy



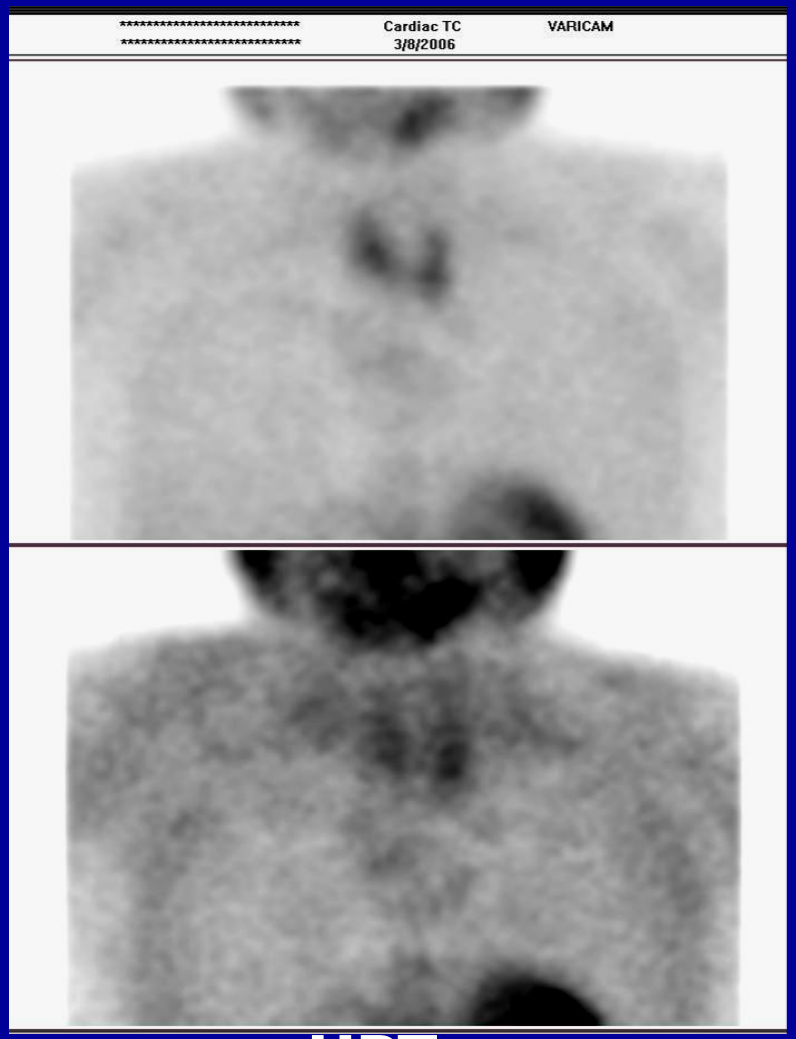
Secondary HPT

- Often enlarged more (all) glands
- Scintigraphic appearance weaker than primary
- The coexistence of MIBI positive and MIBI negative gland
- The role of scintigraphy: to differentiate diffuse and nodular hyperplasia - valuable for therapy selection

Weaker scintigraphic appearance at sHPT compared to pHPT

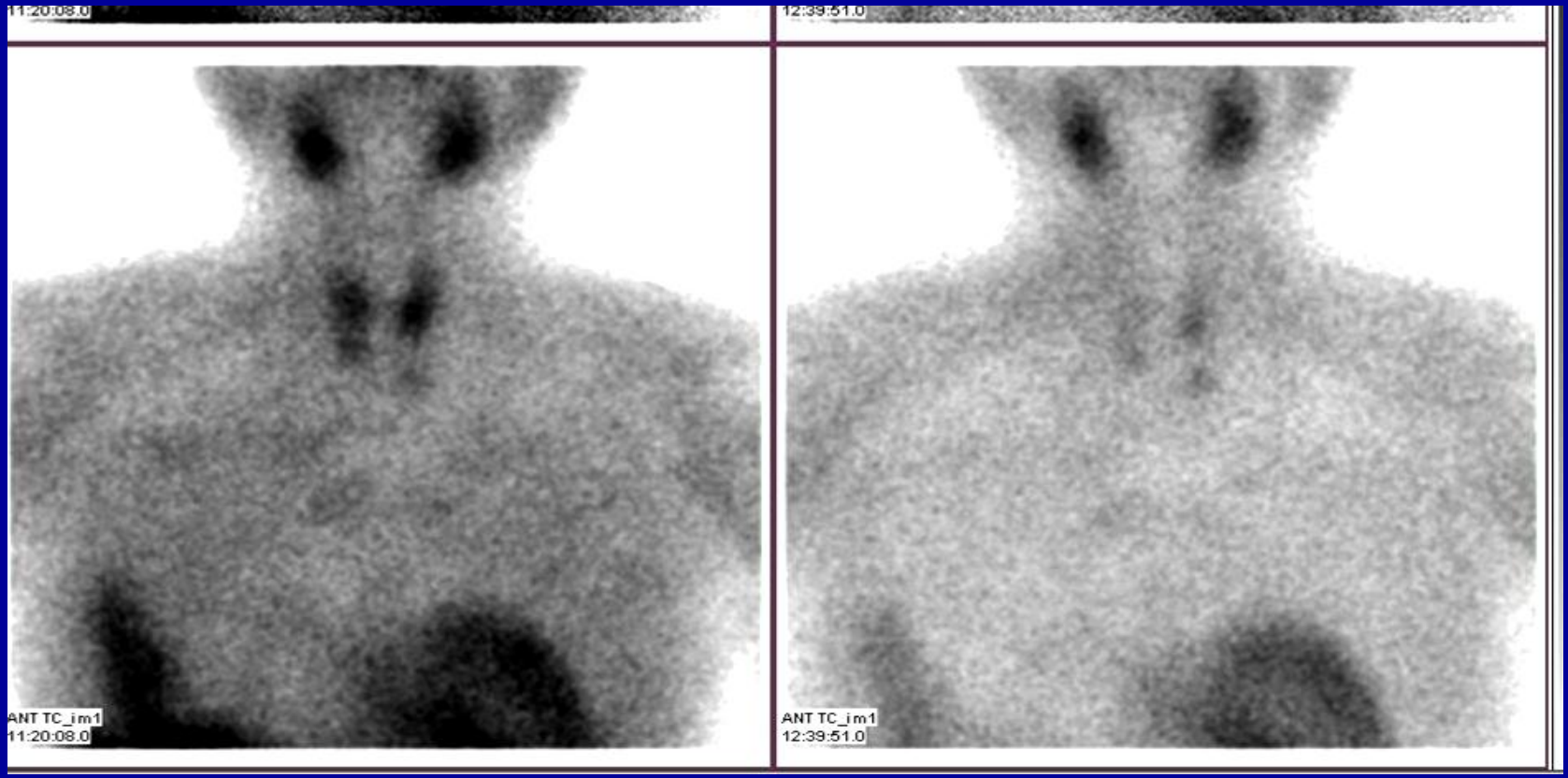


p HPT

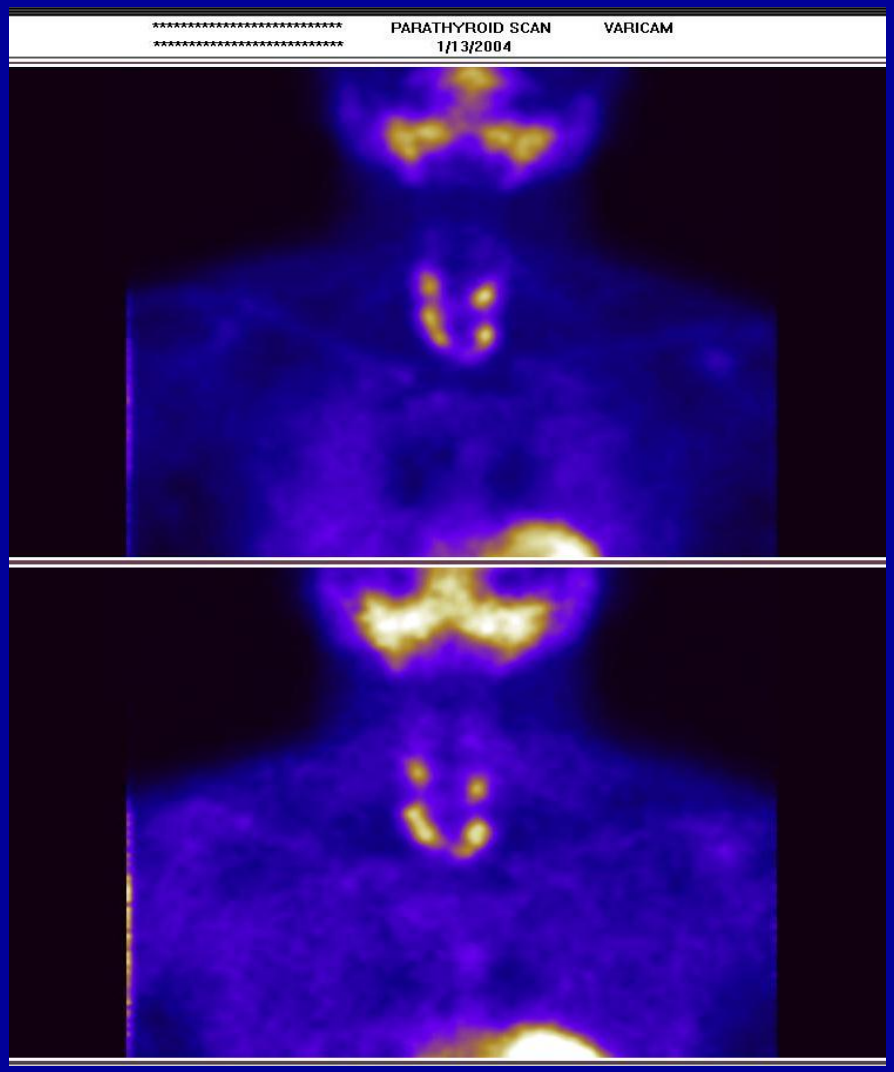


s HPT

Often enlarged more or all four glands

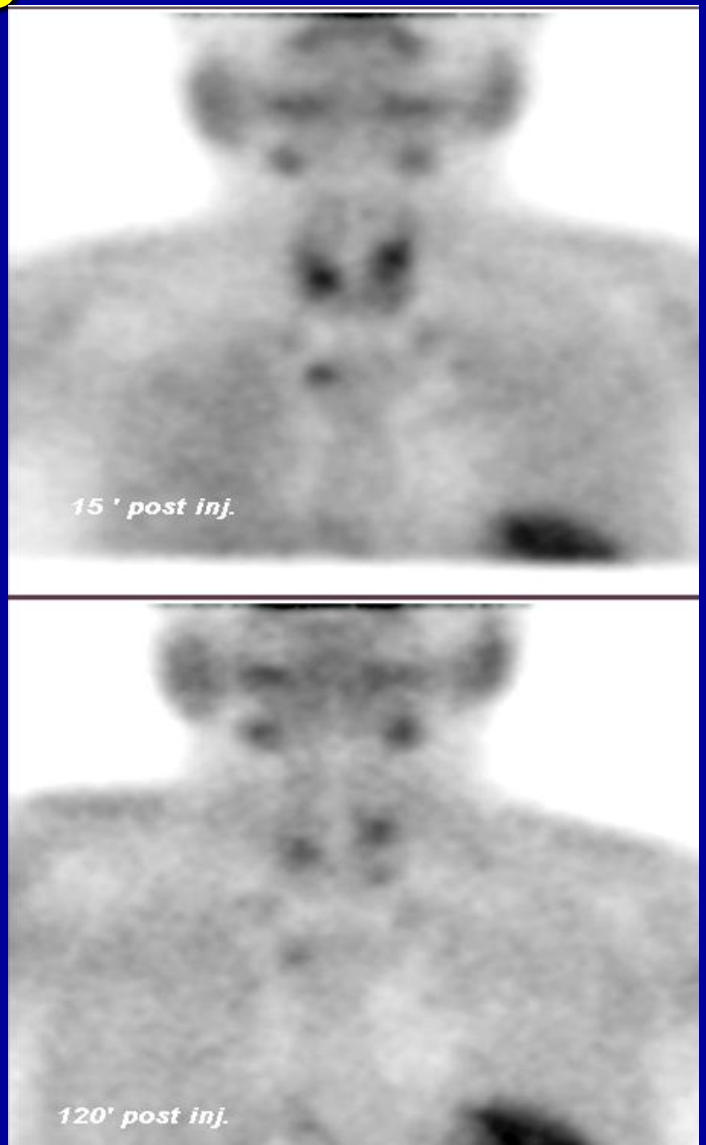


Supernumerary glands



The coexistence of MIBI positive and MIBI negative glands

- MIBI positive glands often with nodular hyperplasia
- Nodular hyperplasia often resistant to conservative therapy
- Planning surgical therapy?



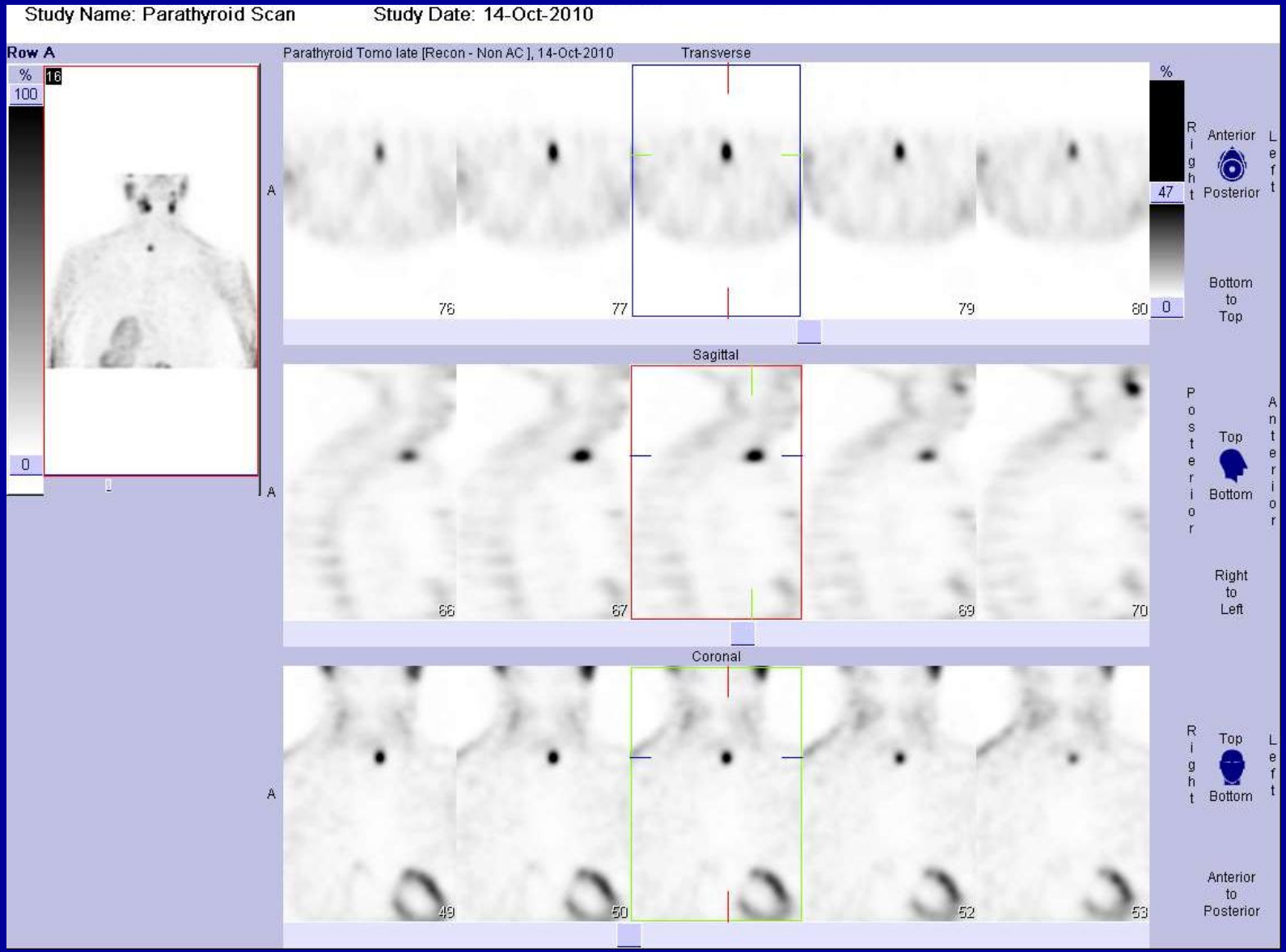
SPECT / CT

It can't be seen on ultrasound

And there is no thyroid to bother you!

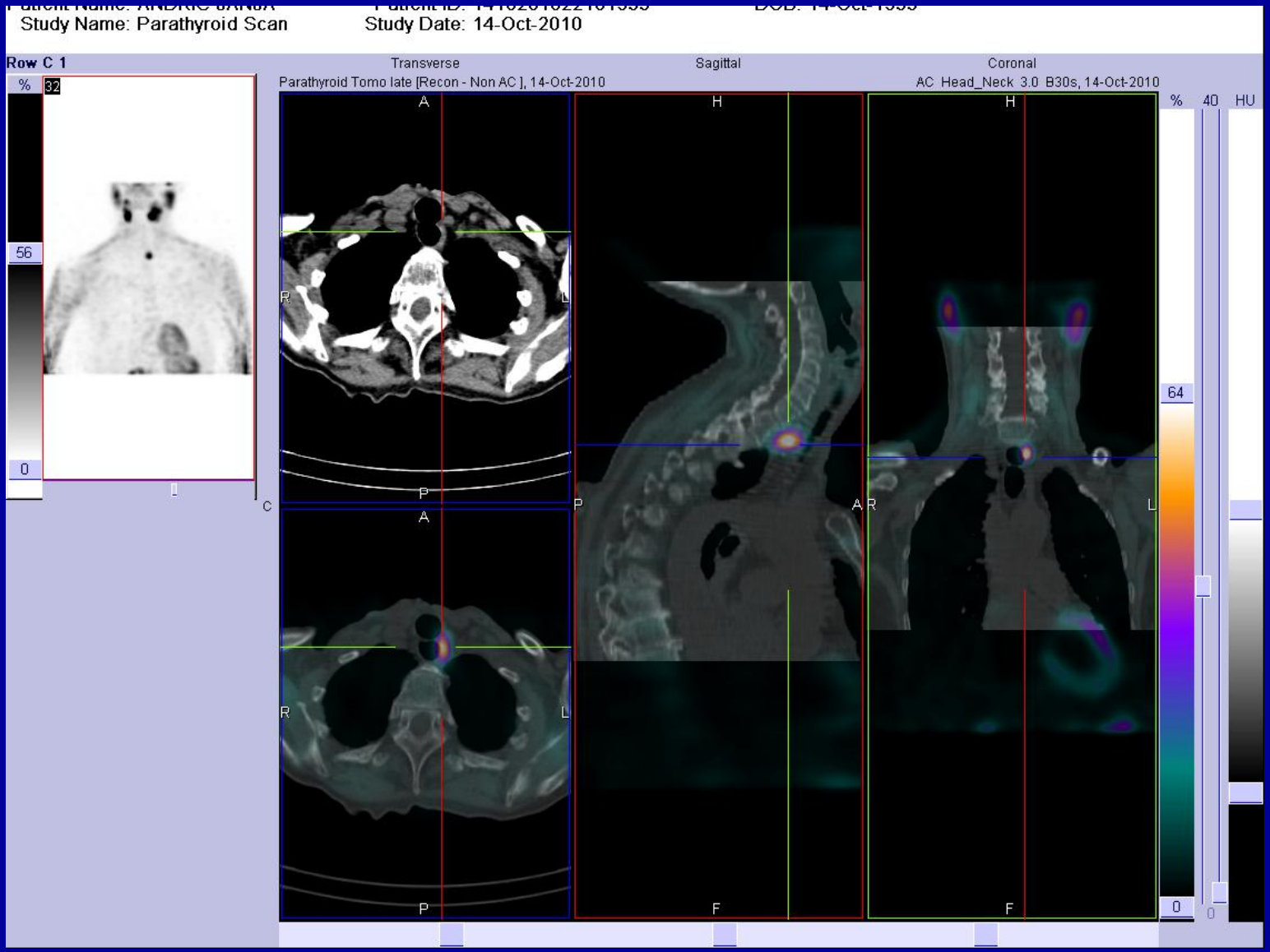
And where is it?

SPECT


Study Name: Parathyroid Scan
Study Date: 14-Oct-2010
Row A
%
100
16
0
A
A
Parathyroid Tomo late [Recon - Non AC], 14-Oct-2010
Transverse
76
77
79
80
%
47
0
Right
Anterior
Posterior
Left
Bottom
to
Top
Sagittal
66
67
69
70
Posterior
Top
Bottom
Anterior
Right
to
Left
Coronal
A
49
50
52
53
Right
Top
Bottom
Left
Anterior
to
Posterior

SPECT/CT

And there you are. Behind the trachea, along esophagus!



CONCLUSIONS

- Scintigraphy is the most sensitive localization method in preoperative preparation of patients with HPT
- In patients with primary HPT significantly shortens the time of the operation, enabling the application of minimally invasive surgery
- In patients with secondary HPT has a lower sensitivity, but is useful in preoperative preparation for possible ectopic and supernumerary glands
- The combination with ultrasound increases the sensitivity and specificity of the method.

Ultrasonography of the parathyroid glands

Normal parathyroid gland

Ultrasound cannot differentiate normal PG (up to 25 mg) from the thyroid because of the narrow contact with it, similar echographic appearance and small size

Thus, ultrasound can not show normal, healthy PG (as it is not possible using other diagnostic methods)

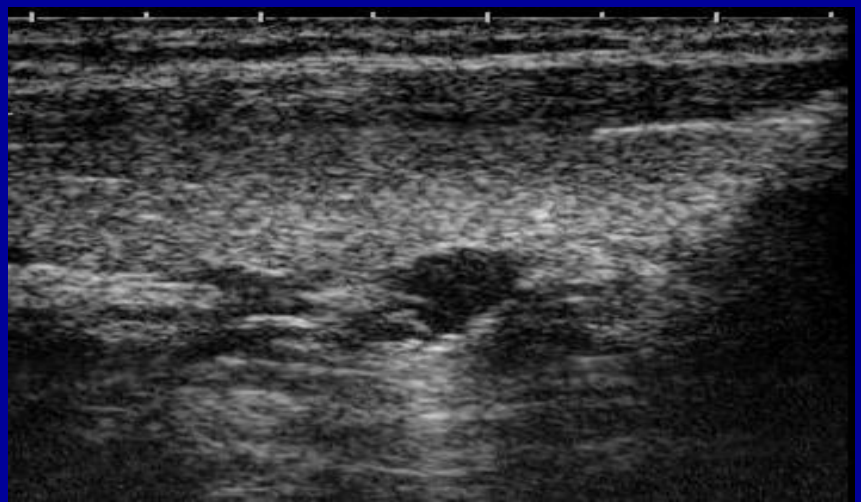
Hypoparathyroidism

In hypoparathyroidism parathyroids are atrophic, aplastic or surgically removed so they can not be detected by echography

Hypoparathyroidism is not an indication of echographic examination of the parathyroid glands

Enlarged parathyroid glands

Because of pathological changes in the HPT, parathyroid glands **become enlarged, but also change echostructure**- and are presented as more or less hypoechoic, well-defined formation behind the lobes of the thyroid.
Because of hypoechoic appearance glands can be seen with minimum enlargment and can not be detected by other methods



During the US examination of the parathyroid glands the number of found PG, their size is described in all three dimensions, their shape and localization, echostructure and blood flow by Doppler is analyzed

The most common diseases that are diagnosed by US (ultrasonography) are adenomas and hyperplasia, while carcinoma and cysts are rarely diagnosed.

US characteristics of adenomas

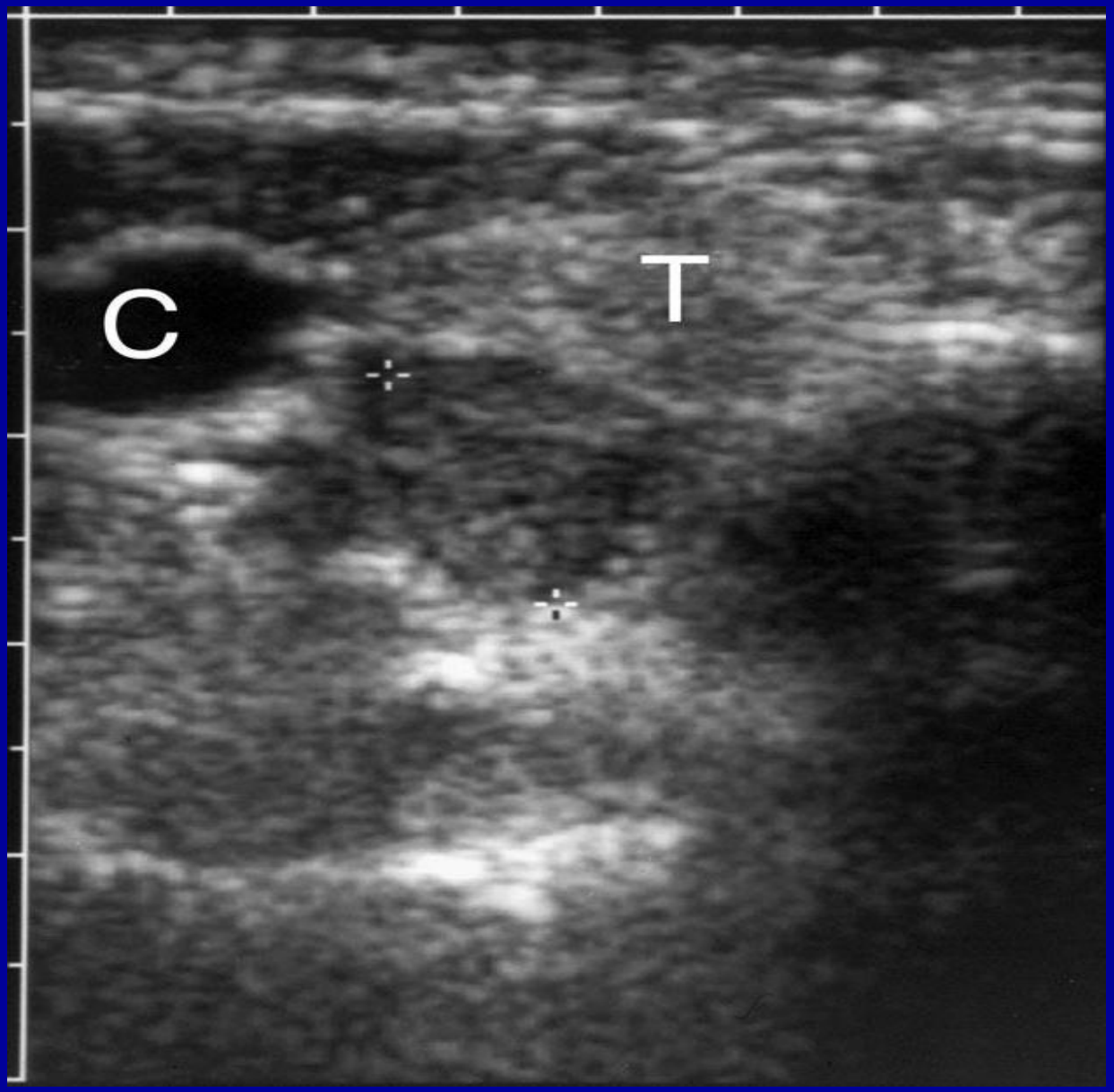
Usually solitary, sometimes there are two or more.

More common in the lower glands

Echographically appear as rounded or oblong, more or less hypoechoic formations behind the lobes of the thyroid gland, often surrounded by hyperechogenic rim

Smaller adenomas are homogenous appearance, while the larger can be found degenerative changes-cystic, fibrotic, calcified

Sizes are beetwen 0.5-5 cm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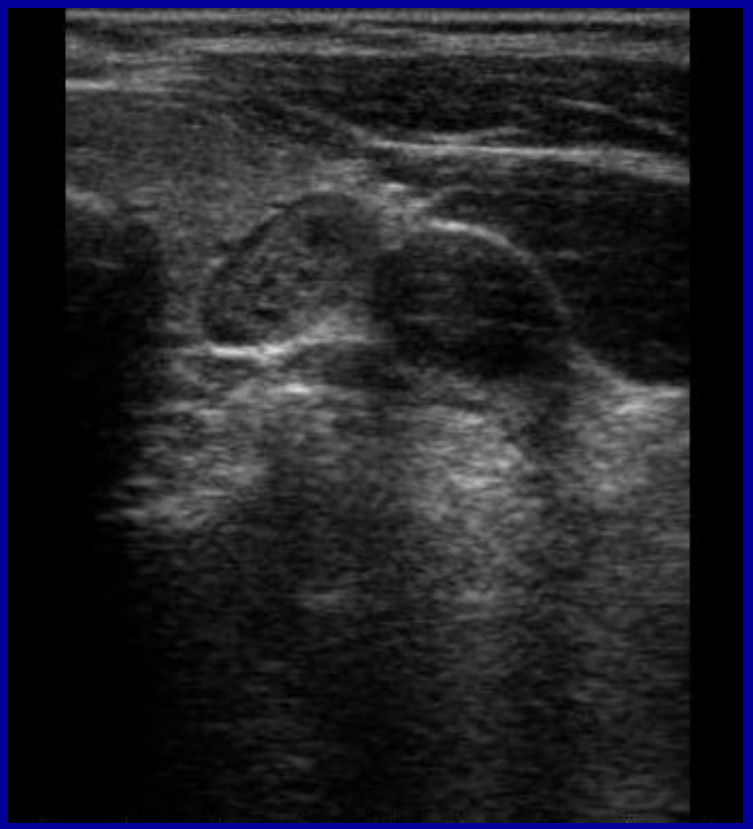
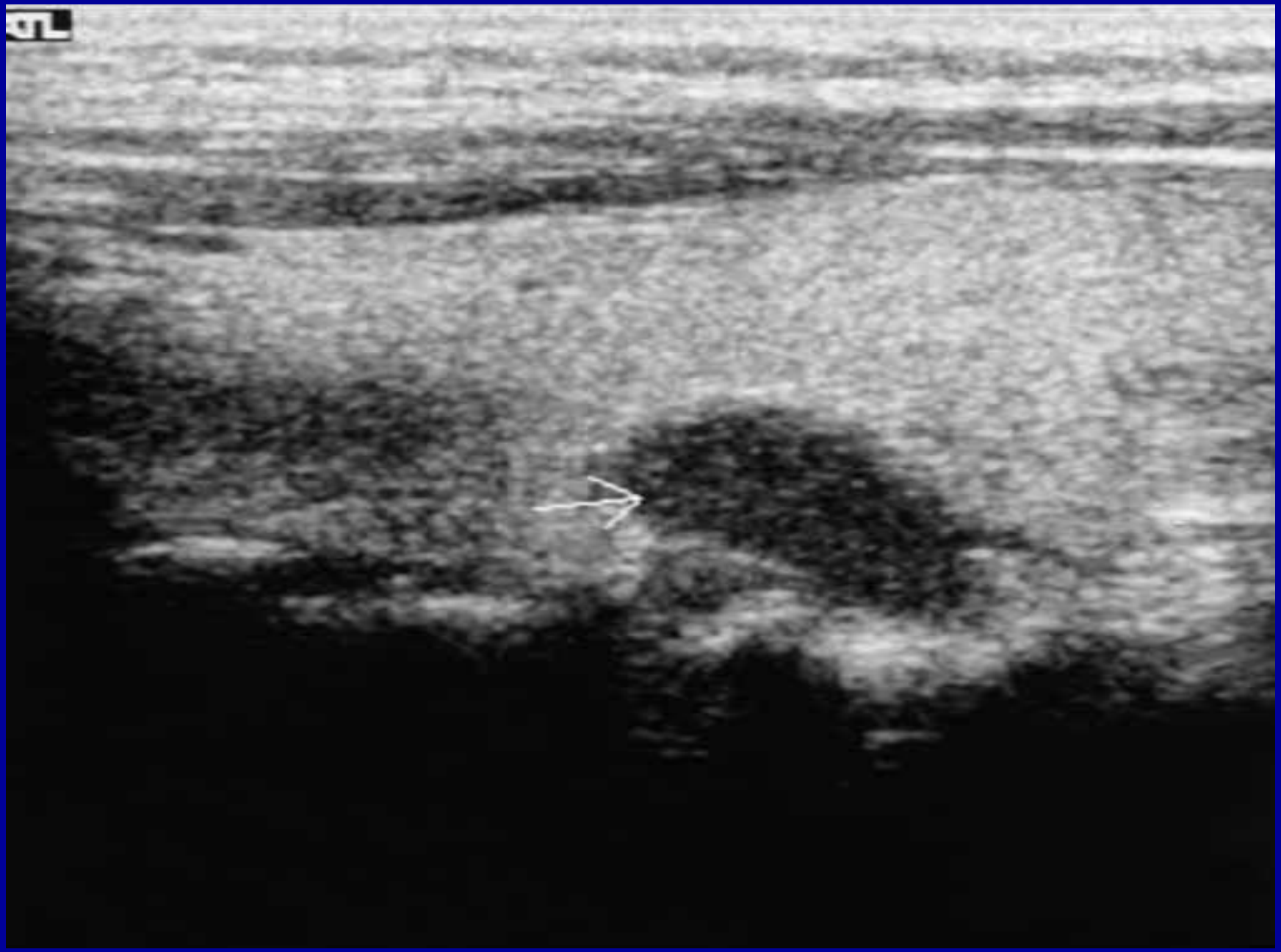
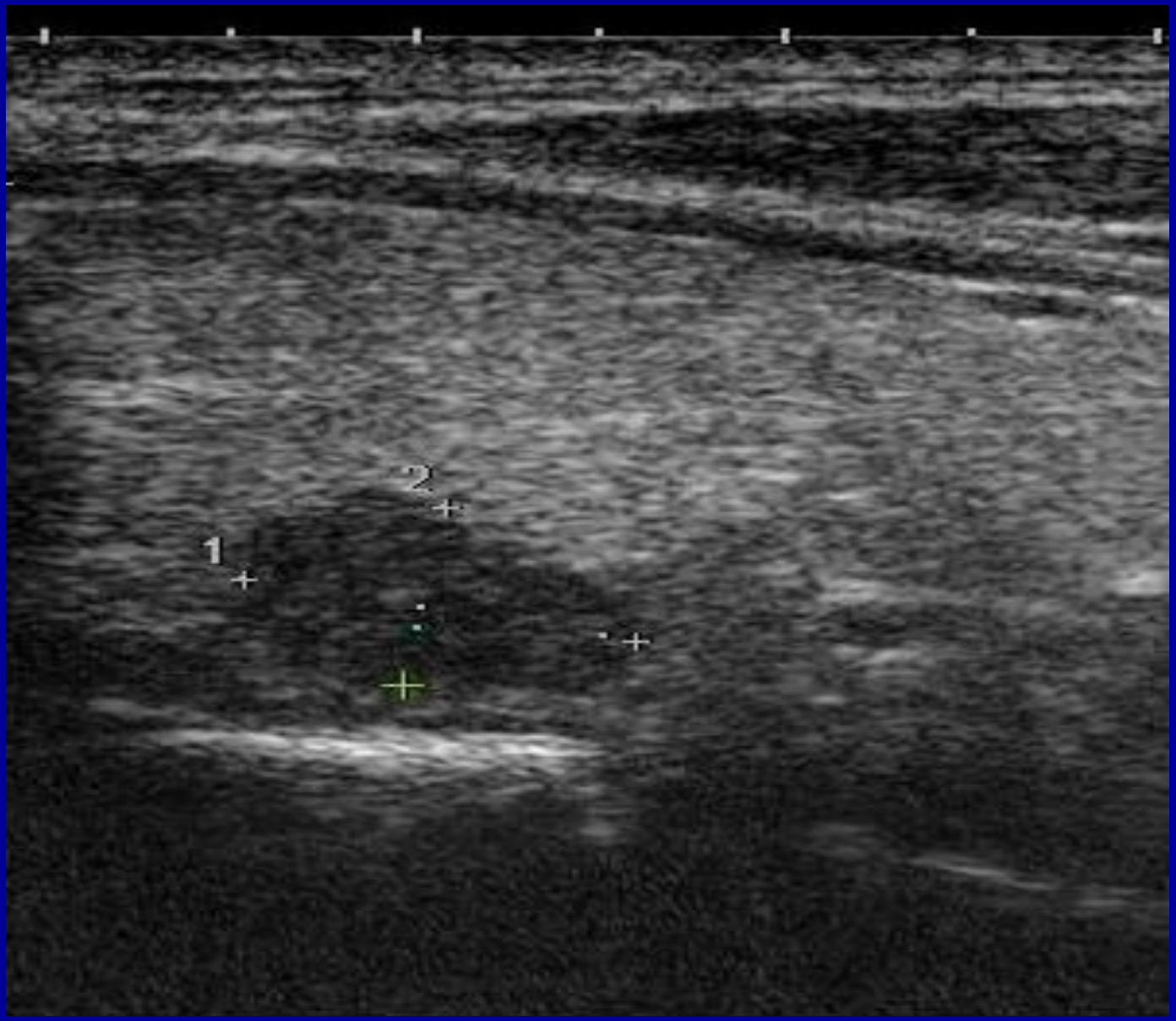
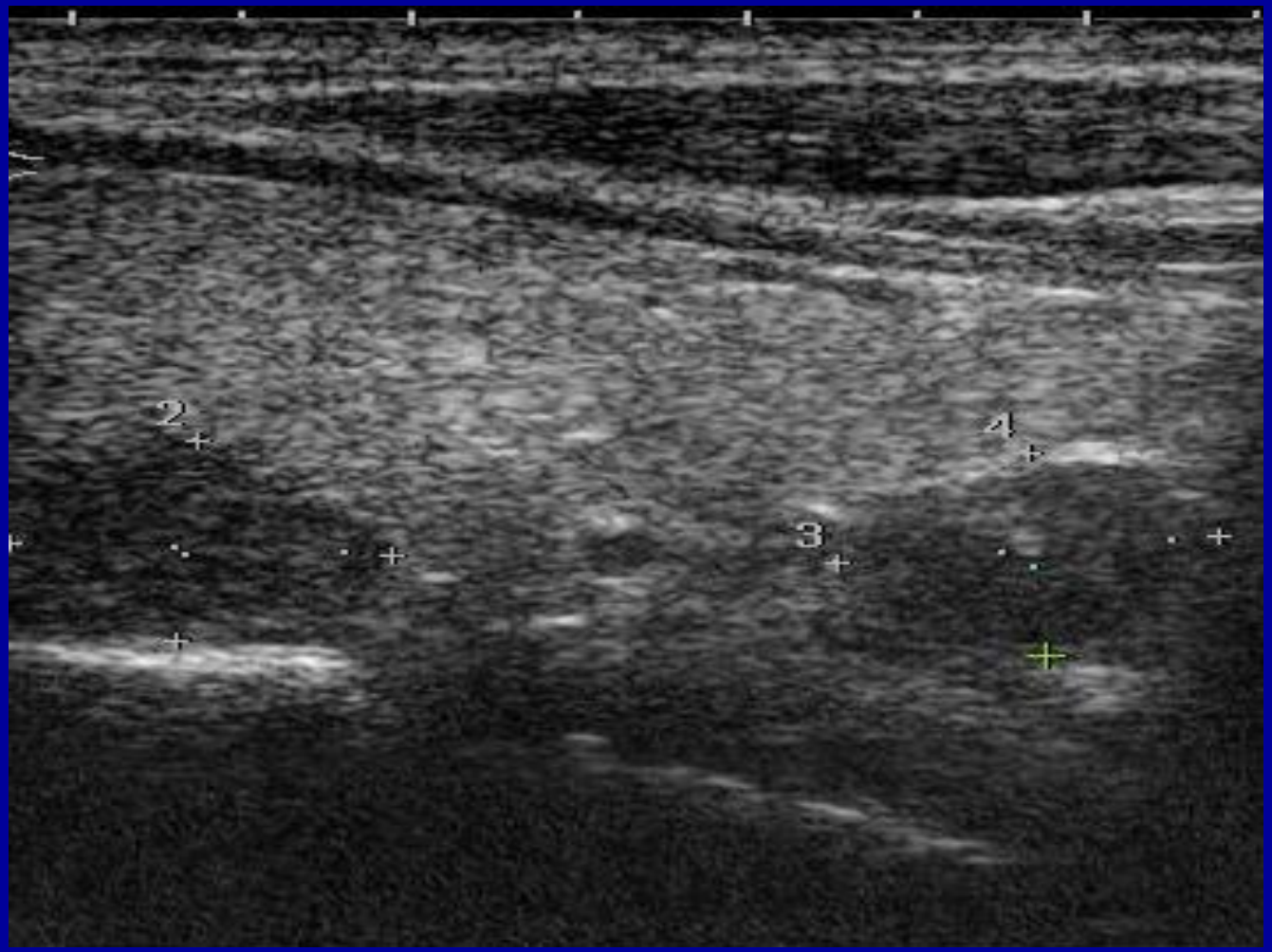


Left upper parathyroid gland




2
1

Multiple adenomas



US characteristics of hyperplastic gland

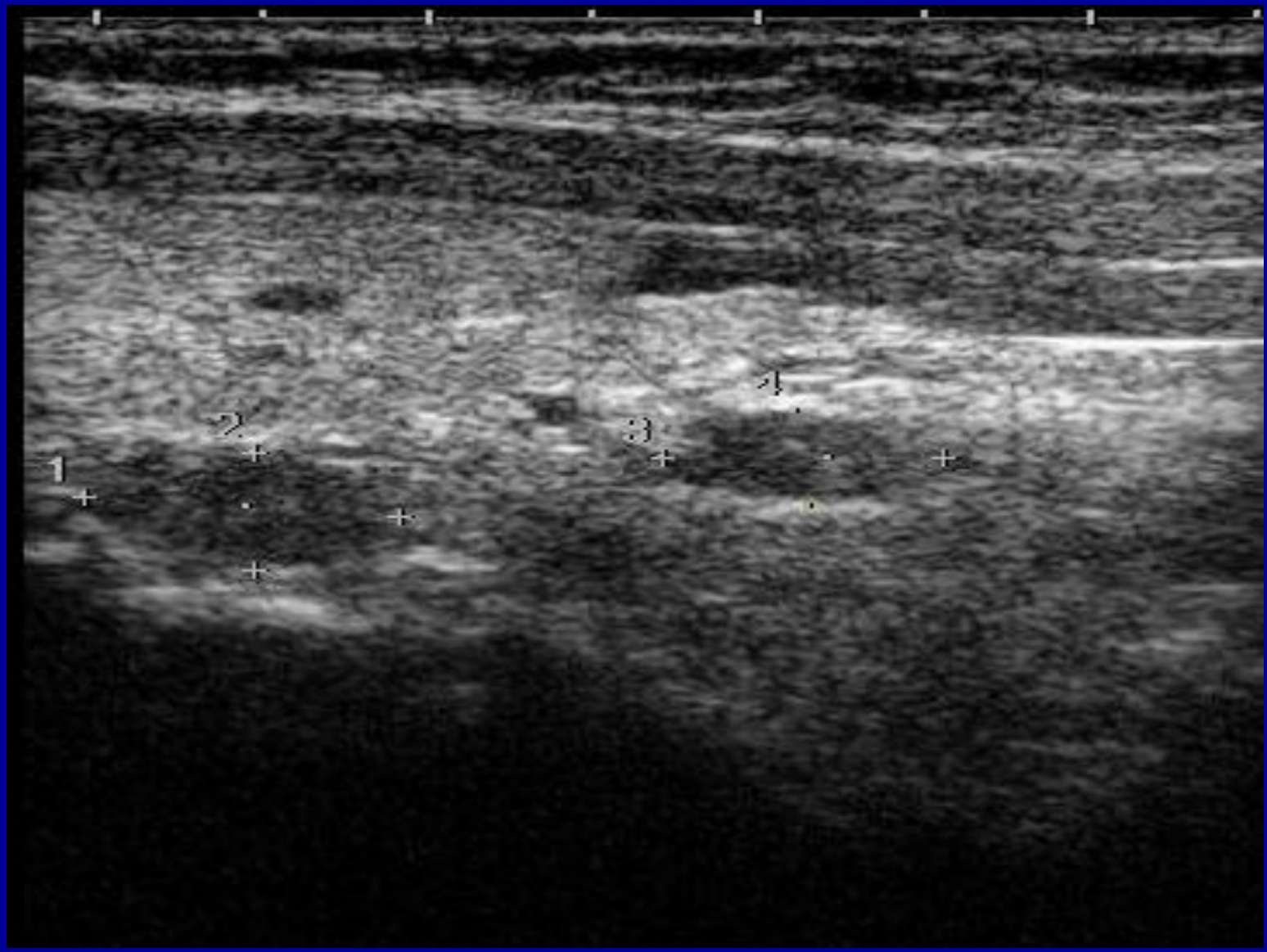
Mostly at Secondary HPT
There are more different sized glands

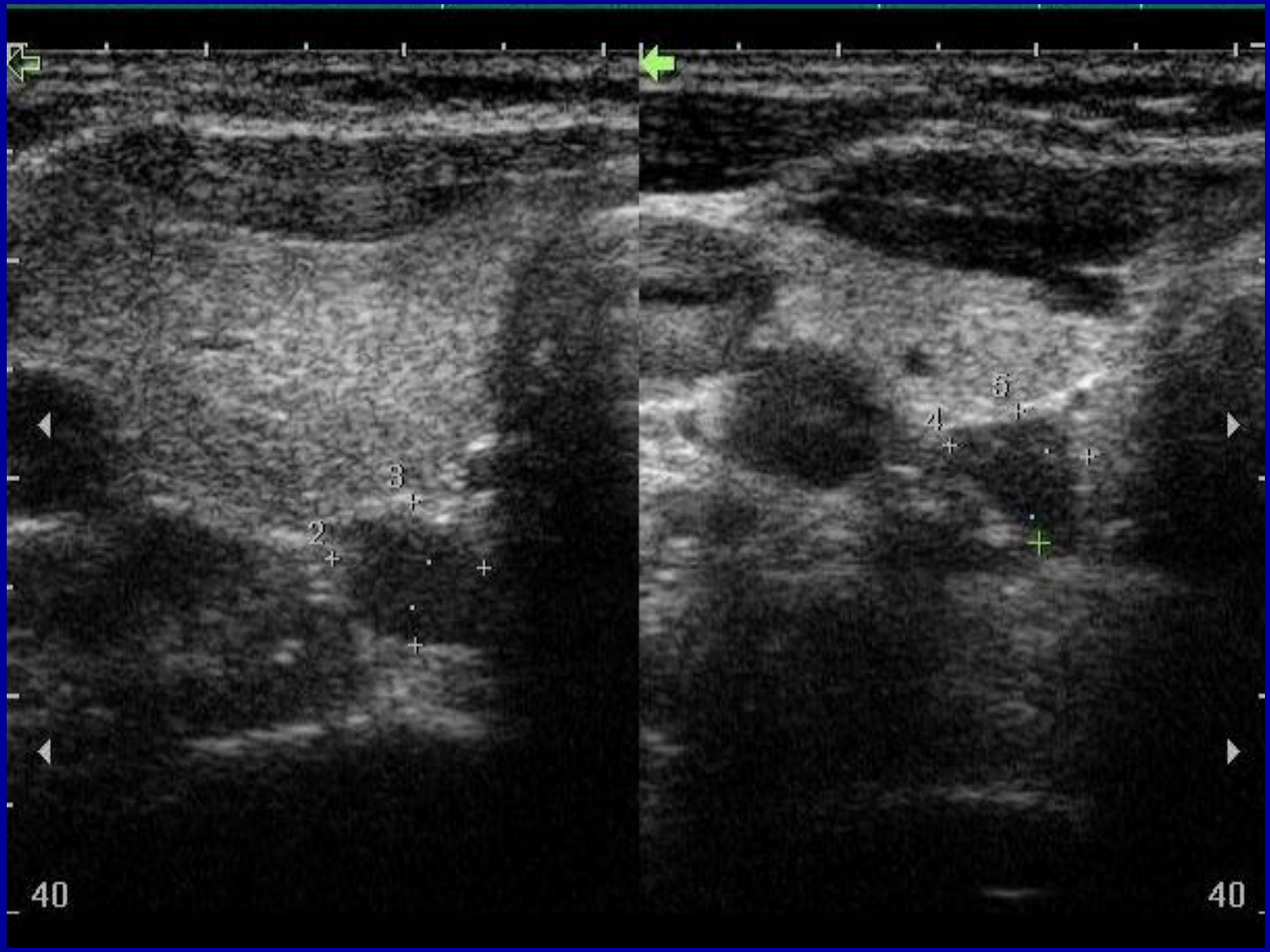
Depending on the duration of the disease can be slightly enlarged (usually oblong and homogeneous appearance) to markedly enlarged (when they are irregular in shape, often with marked degenerative changes)

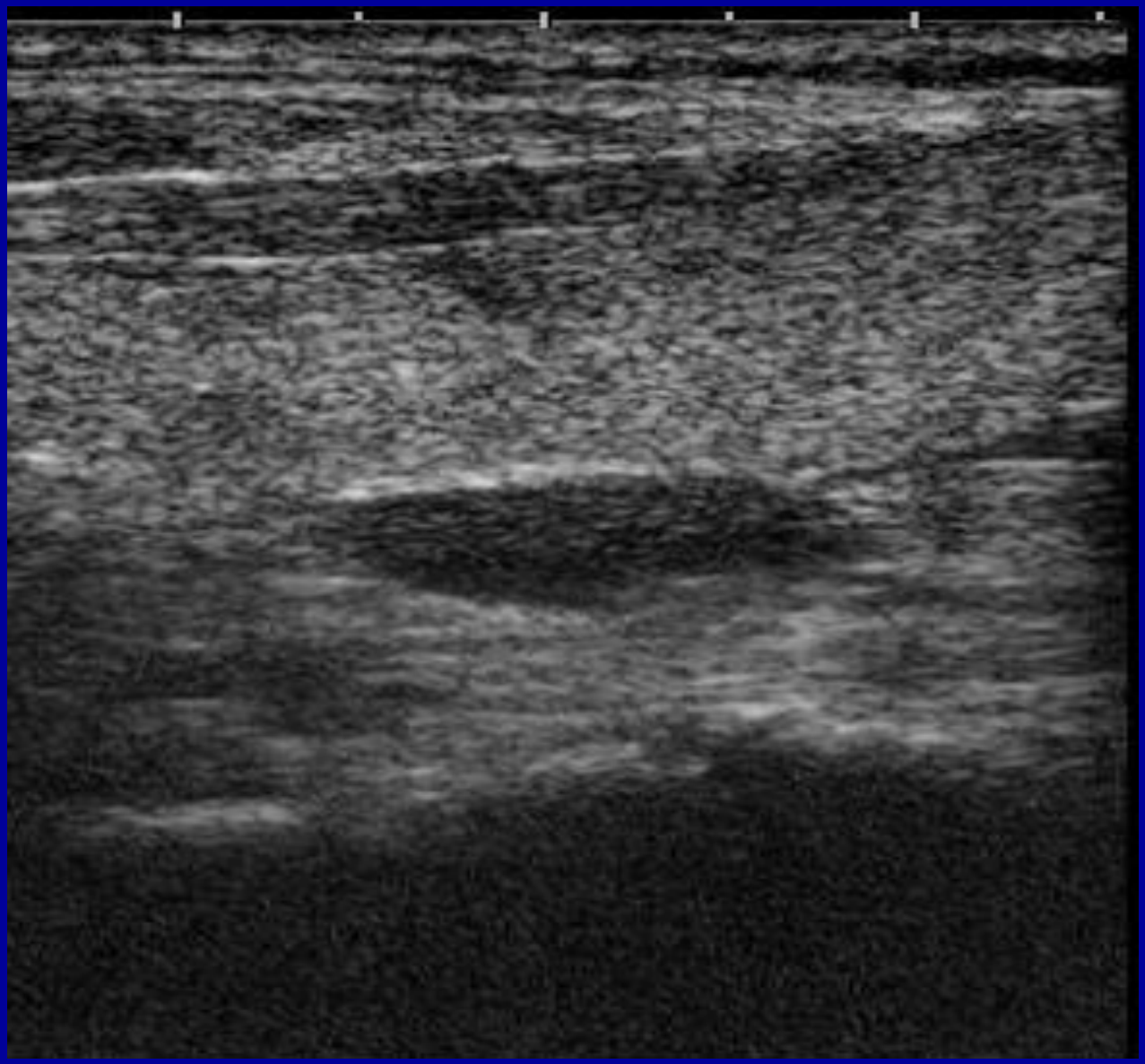
In hyperplastic glands isoechogenic nodes can be seen in hipoechogenic gland, which correspond to nodular hyperplasia

In Tertiary HPT usually there can be found one or more of enlarged PG

Hyperplastic PG




2
3
4
5
40
40

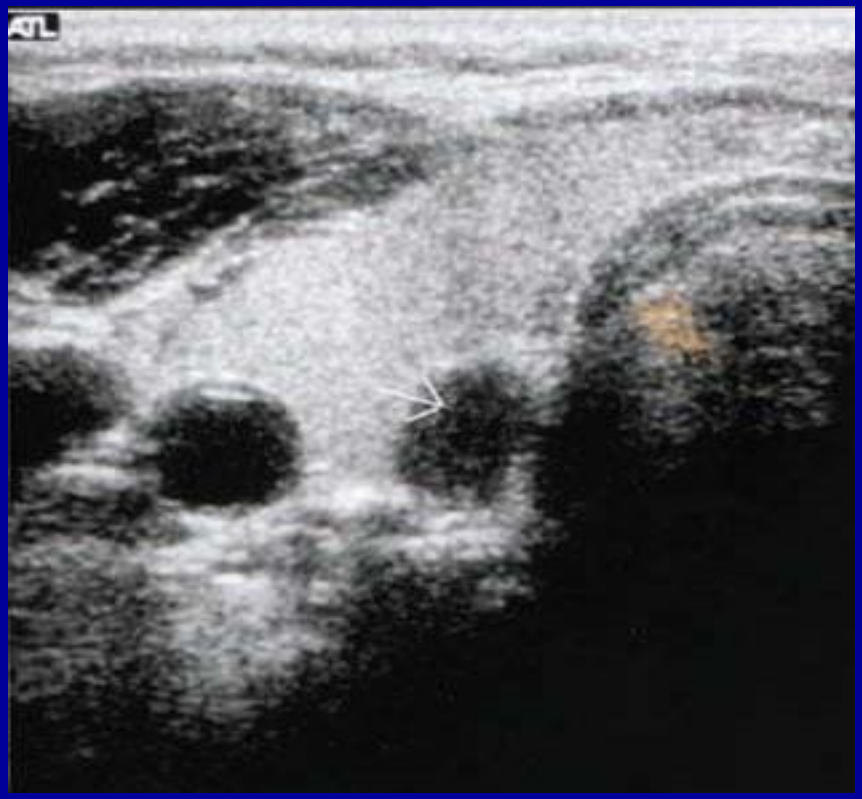


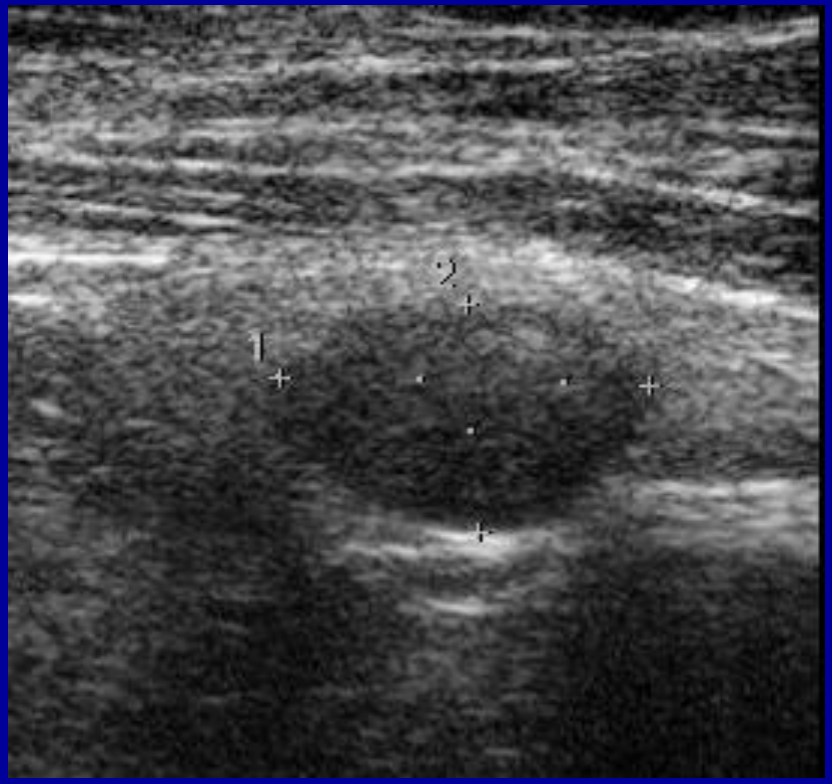
Advantages of US in the diagnosis of hyperparathyroidism

- simplicity
- noninvasive
- does not require any preparation
- the possibility of repeating examination without any restrictions
- no harmful effects
- price
- the ability to perform, under US control, the fine needle aspiration citology and to determine parathormon in aspirate
- this is the only preoperative evidence that suspected formation is PG

Difficulties in ultrasound examinations of the PG

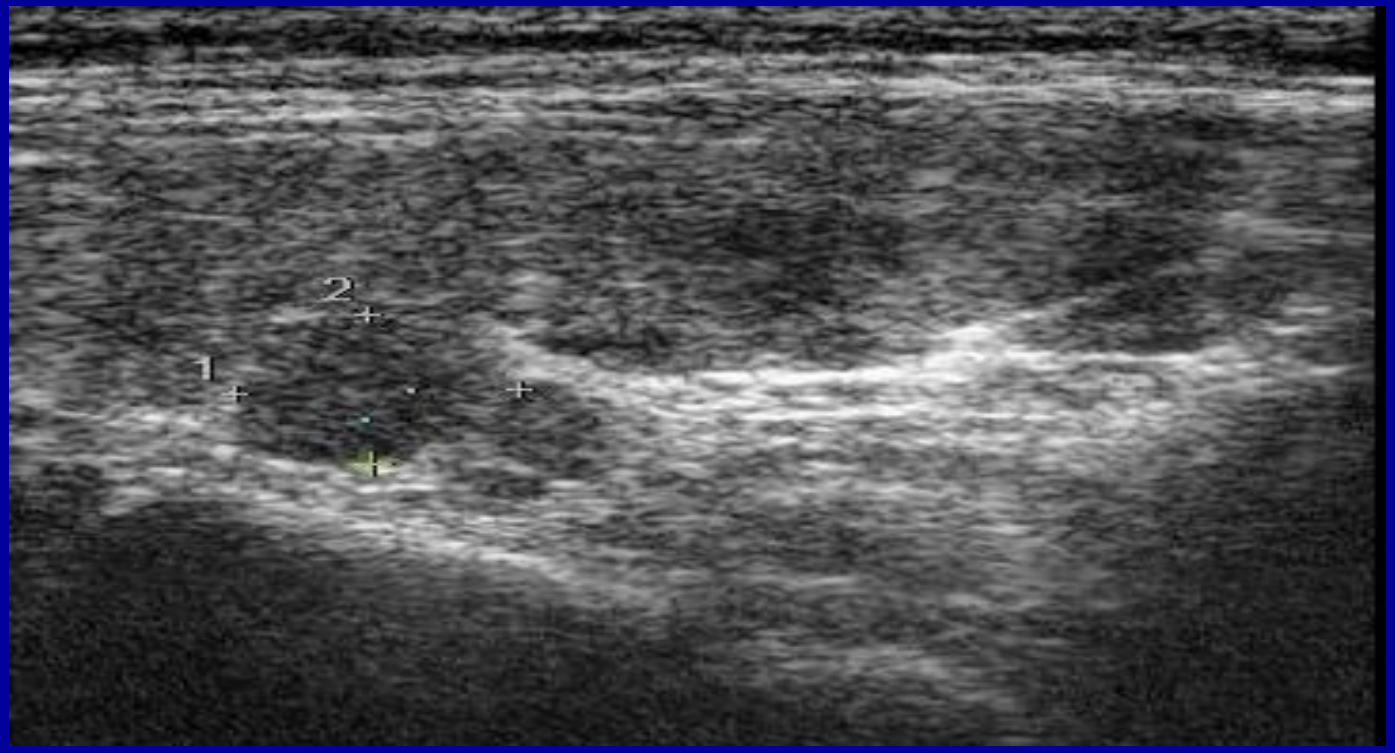
Thyroid nodules located in the posterior parts of the lobes or intrathyroid placed PG or multinodular goiter that suppresses PG deep in the neck





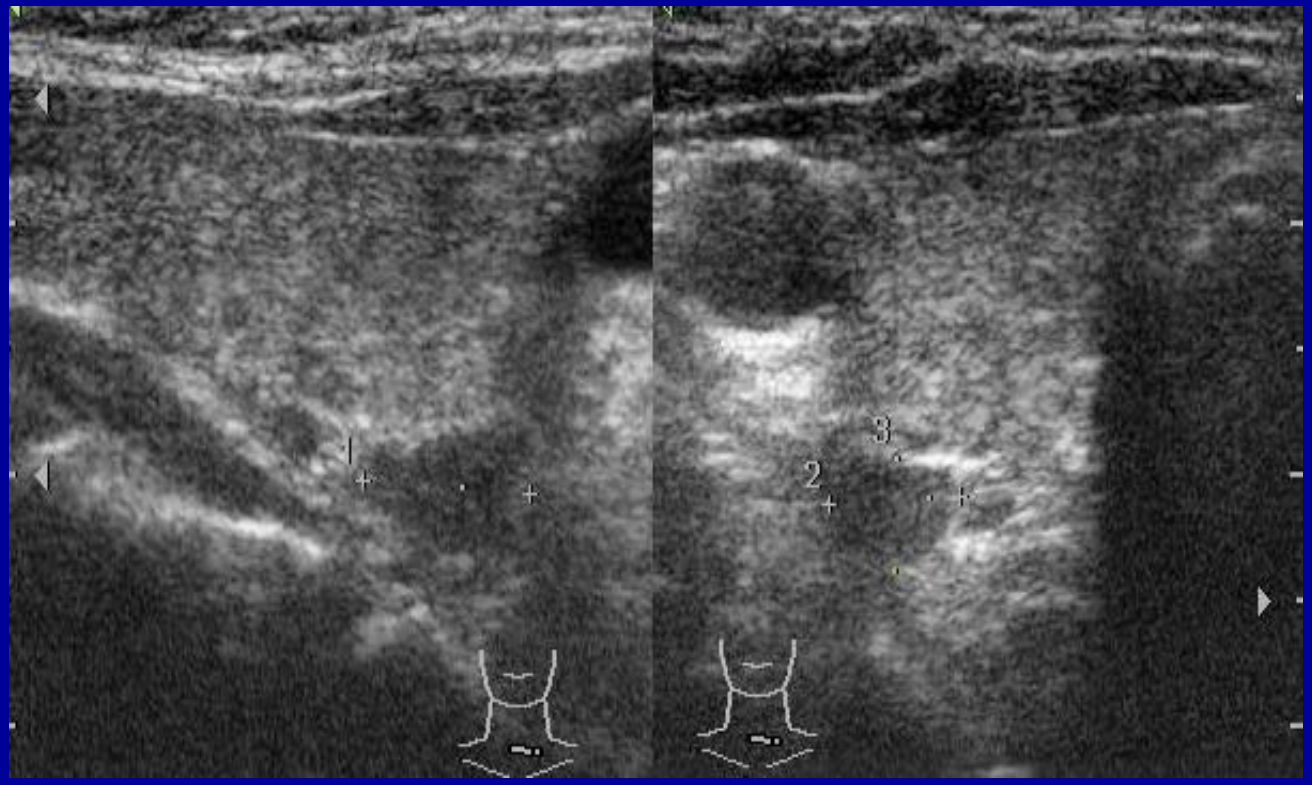
Difficulties in ultrasound examinations of the PG

Pseudolobulation of the thyroid lobes in lymphomatous goiter



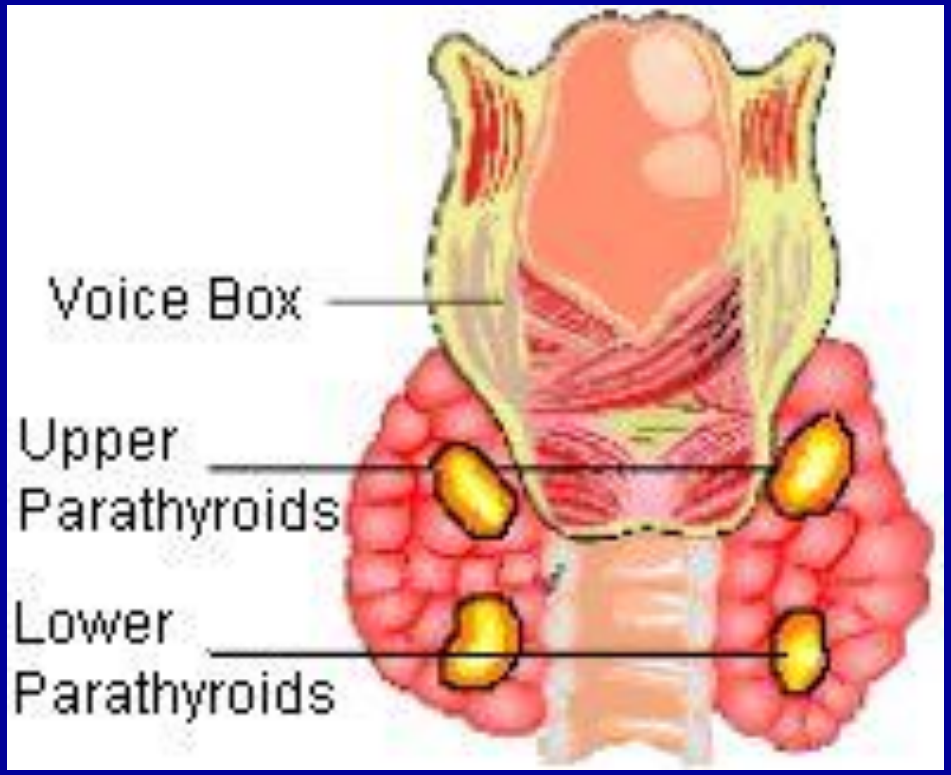
Difficulties in ultrasound examinations of the PG

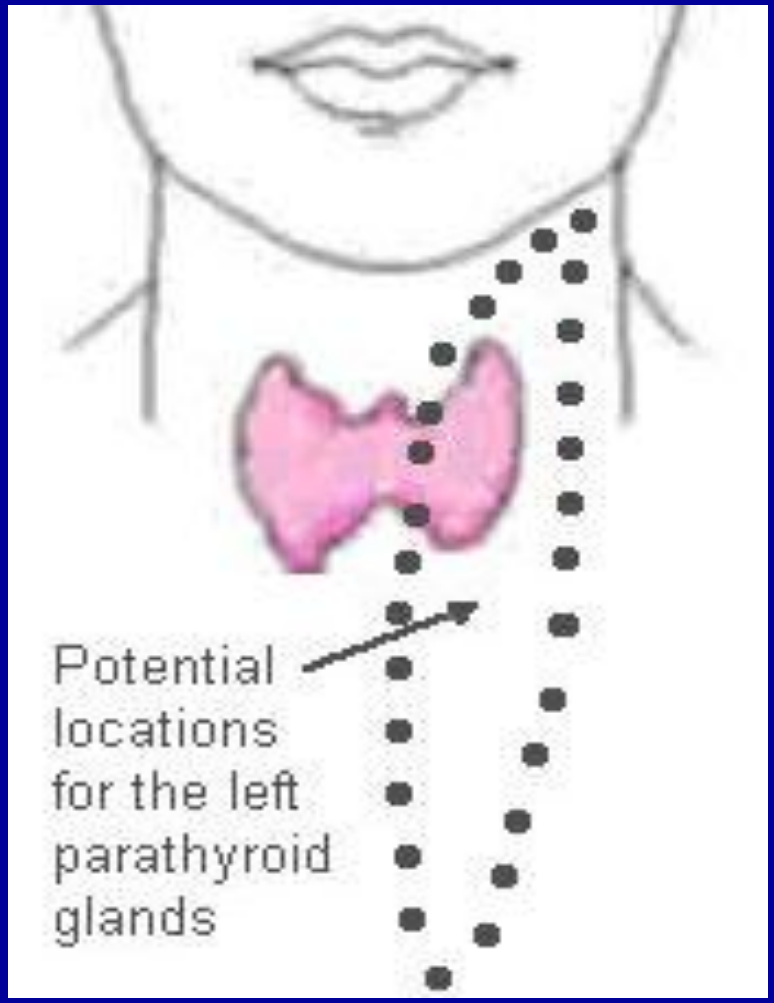
Lymph nodes or tm. on the neck located behind the thyroid lobes



Difficulties in ultrasound examinations of the PG

PG that are not available to the US detection- placed retrotracheally, retropharyngeally, retroesophageally, retrosternal or mediastinal





US in PHPT

Aim: To locate the gland responsible for PHPT and to enable application of minimally invasive parathyroidectomy (MIP)

It has to be confirmed by determination of PTH in aspirate, or (and) FNAC (fine needle aspiration cytology) under US control

Scintigraphy with Tc-99m-MIBI?

Scintigraphy with Tc-99m-MIBI to exclude possible ectopia or possible second adenoma, which in addition is not detected by ultrasound?

P350

Patient with parathyroid adenoma, thyroid toxic adenoma and metastatic papillary thyroid carcinoma

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Introduction

The occurrence of primary hyperparathyroidism, toxic adenoma of the thyroid and metastatic papillary thyroid carcinoma simultaneously in the same patient is extremely rare and diagnostically challenging. Only a few cases are reported in the literature.

Case Report

A 75-year-old woman with hypercalcemia was referred to our Outpatient Clinic for ultrasound examination of the neck.

Sonography revealed large hypoechogenic nodule in the right thyroid lobe that measured 42x32x25 mm (Fig. 1.a and b). In the upper third of the left lobe there was hypoechogenic nodule with microcalcifications that measured 15x10x11 mm (Fig. 1.c).

Figure 1.

Behind the midle third of the left thyroid lobe we found hypoechogenic nodule that measured 16x12x5 mm (Fig. 2.a and b). In the upper third of the left side of the neck there were two small lymph nodes with microcalcifications, larger one measured 16x9x6 mm (Fig. 2.c).

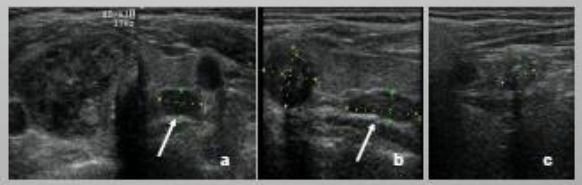

Figure 2.

Accidental concomitant finding of the toxic adenoma of the thyroid, metastatic thyroid carcinoma and parathyroid adenoma was suspected. Laboratory findings showed T3 thyrotoxicosis and increased serum PTH level. Tc-99m-scintigraphy showed hot nodule in the right thyroid lobe.

Parathyroid adenoma was indiscernible on Tc-99m-MIBI scintigraphy because a huge activity was accumulated in the toxic thyroid adenoma (Fig. 3.), but PTH in the aspirate of the hypoechogenic nodule behind left thyroid lobe was high (> 2 096 pg) and thus confirmed parathyroid adenoma.

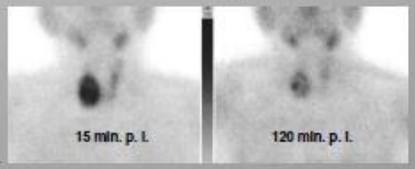

Figure 3.

FNA cytology of the hypoechogenic nodule in the upper third of the left thyroid lobe and the lymph node on the left side of the neck revealed metastatic papillary carcinoma. After short course of thyrostatic preparation, total thyroidectomy, parathyroid adenomectomy and functional dissection of the left side of the neck was performed

Results

Pathohistology confirmed papillary thyroid carcinoma of the left thyroid lobe with metastases in cervical lymph nodes, follicular adenoma of the right thyroid lobe and left-upper parathyroid adenoma (Fig. 4.). Patient received ablative-therapeutic dose of 3,98 GBq of I-131 and is now disease-free, 3 years after the operation and radioiodine treatment. PTH and calcium levels remained normal during follow-up.

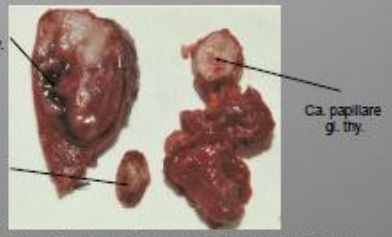

Figure 4.

Conclusion

This case illustrates the need for clinical awareness of possibility of concomitant multiple thyroid and parathyroid diseases and emphasizes high diagnostic utility of ultrasound. It also points out the necessity for PTH determination in aspirate of suspected lesion in patient with concomitant toxic adenoma of the thyroid because scintigraphic visualization of hyperfunctioning parathyroid adenoma is difficult in that case.

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US in SHPT

Aim:

Detection of enlarged PG within preoperative examination

Sensitivity of parathyroid ultrasonography in patients with secondary hyperparathyroidism

Reference	Year	No. of pts.	No. of gl.	TP	Sens. (%)
Jeanguillaume et al.	1998.	14	50	27	54
Nishida H. et al.	2004	14	49	34	71
Perie et al.	2005.	20	79	59	75
Fuster D. et al.	2006	48	192	109	55

US in SHPT

Aim?

Detection of enlarged PG within preoperative examination ??

No! Insufficient sensitivity

Surgery in SHPT: bilateral neck exploration with the success of surgery of 95% in the hands of an experienced surgeon

US in SHPT

Aim?

Detection of enlarged PH within preoperative examination? - No. Do only scintigraphy with Tc-99m-MIBI-em for possible ectopia

The aim of ultrasound examinations?

Assessment of disease severity based on the number and size enlarged PG

Assessment type hyperplasia (and thus the type of th.): Diffuse or nodular

Follow-up the effect of conservative therapy-regression or progression

Sclerotherapy

PG sclerotherapy

The method of percutaneous injection of 95% alcohol in PG, US controlled, in order to cause necrosis, fibrosis, or reduction in gland sizes and normalizing of their functions

The method is simple, performed on an outpatient, without special preparation of the patient

The amount of injected alcohol is half the volume of the gland, usually 0.5-1.5 ml of alcohol

During the injection the patient feels short sharp pain

Complications are rare: mostly transient hoarseness, a rare bleeding

This is the method of choice in patients with persistent or recurrent HPT after op., especially with SHPT

The process should be repeated until you achieve the target values of PTH and gland significantly reduces and gets fibrosed

The method is considered a way of conservative treatment and assistance to medical therapy and not an alternative to surgical treatment

It is recommended in SHPT and THPT, in patients with PHPT gives weaker results

With method there is no complete healing, but the satisfactory state can be maintained for longer time and the development of severe forms of renal osteodystrophy can be prevented

This is the method of choice in patients with persistent or recurrent HPT after op., especially with SHPT

Minimally invasive surgery

- Use of gamma probe that facilitates location of glands
- The combination of scintigraphic appearance (one dose of radiopharmaceuticals) or separately (two doses)

Scintigraphy of the adrenal glands

Scintigraphy of the adrenal cortex

- The functional assesment of adrenal cortex morphological changes
  -The base of detection is (hyper)functionality, not the size or type of structural disorder

Radiopharmaceuticals

I-131-6β-19-iodinemetilnorcholesterol and selenium 75 -6β-19-selenomethylnorcholesterol analogs are cholesterol

Bind to circulating low density lipoproteins (LDL) which are accumulated via LDL receptor in cells of the adrenal cortex

0.07% -0.03% is accumulated in each adrenal gland

Excreted in the liver and kidneys

Activities

- i.v. application of 10 MBq (0.27 mCi) norcholesterol marked with selenium-75; Scintigraphy 7^{th} - 14^{th} day after application of Se-75 norcholesterol

- Norcholesterol marked with I-131; 37-74 MBq (1-2 mCi). Scinitgraphy 3^{rd} - 7^{th} day after application of I-131 norcholesterol

Scintigrams

- Posterior lumbar scintigram

- If necessary, the anterior and lateral scintigrams

- Dexamethasone suppression of ACTH

Indications

- **Cushing's syndrome**

- adrenal adenoma: increased uptake in adenoma and nonvisualization of the contralateral normal gland due to the suppression of ACTH

- Bilateral cortical nodular hyperplasia: increased accumulation bilaterally, often asymmetrically

- Carcinoma of the adrenal gland: no appearance of the adrenal gland. Increased secretion of cortisol suppresses contralateral normal gland, but carcinomas are not accumulating radiopharmaceutical sufficiently to be visualized by scintigraphy

Primary aldosteronism

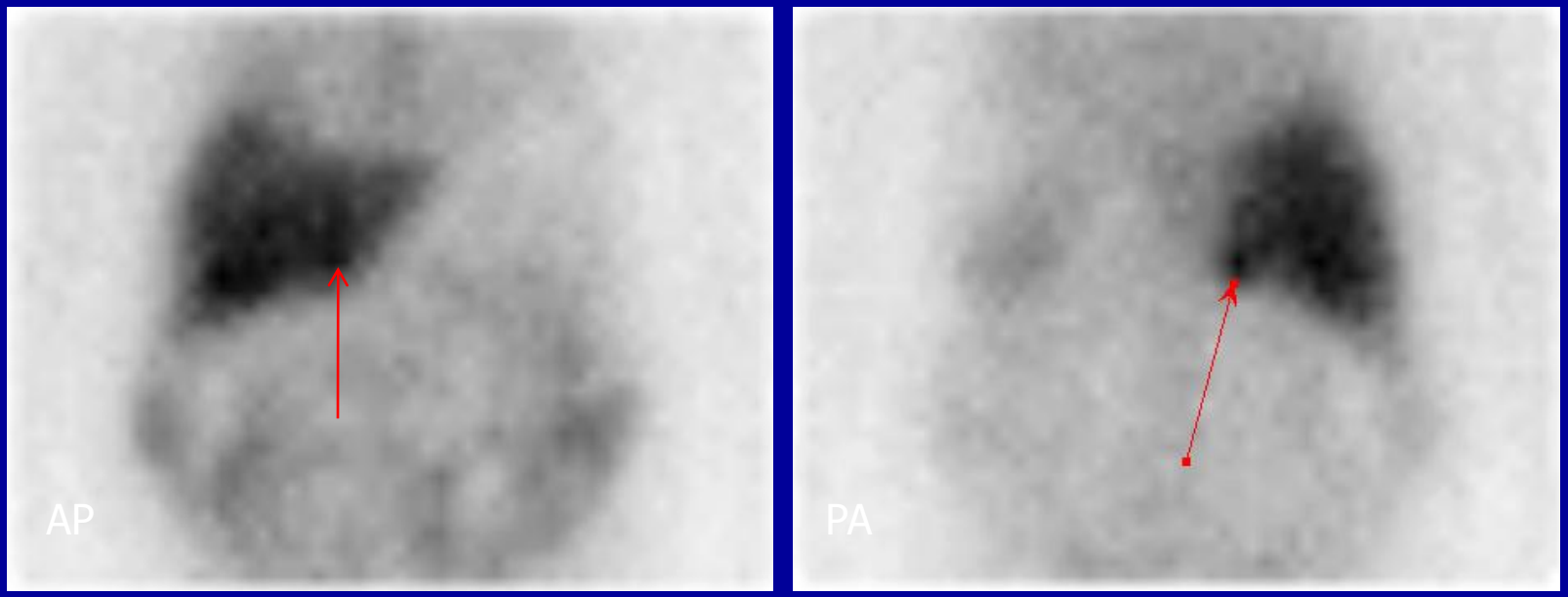
- Differentiating between aldosteronoma and other unilateral disorder from the bilateral hyperplasia

- Always apply dexamethasone suppression

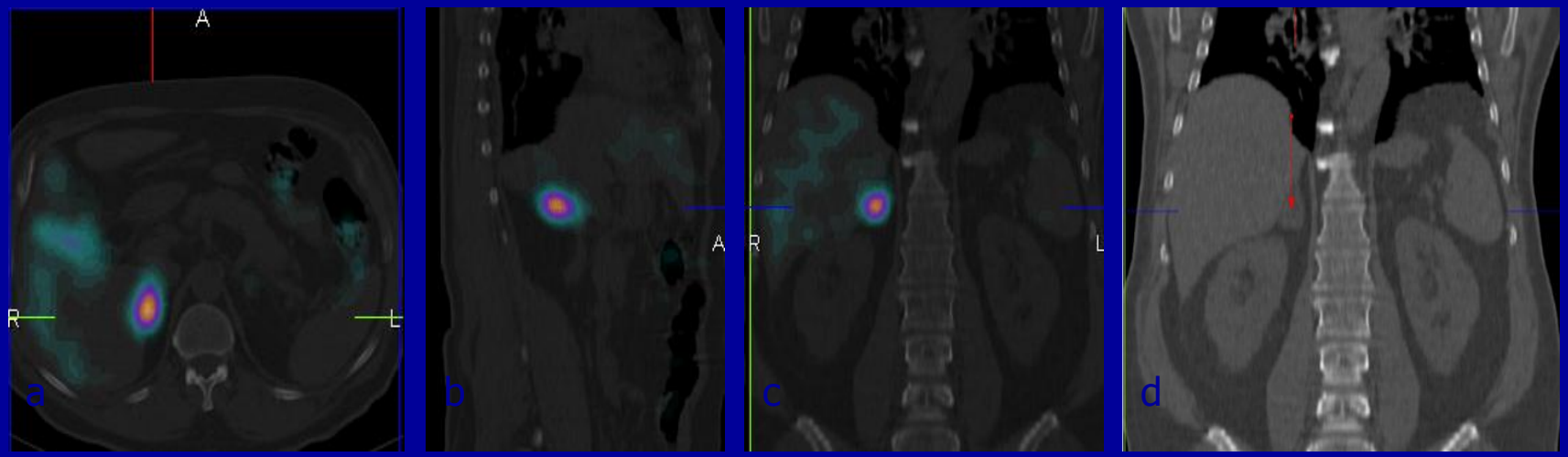
Primary aldosteronism

Primary aldosteronism may be caused by bilateral idiopatic adrenal hyperplasia or adrenal cortical adenoma. It is important to distinguish theese two conditions because they require different treatment. Adrenal venous sampling is the gold standard in determining the source of aldosterone excess in patients with primary aldosteronism, but it is invasive and technically demanding with possible severe complications and doubtful success. I-131-6β-iodomethyl-19-norcholesterol (NP-59) scintigraphy is simple, nonivasive, without any complications and may be used as a supplementary diagnostic tool.

Role of 131-I-6β-iodomethyl-19-norcholesterol scintigraphy with SPECT/CT in patient with primary aldosteronism caused by aldosteron secreting cortical adenoma



Planar scintigrams with I-131-6β-iodomethyl-19-norcholesterol (NP-59) showed intensive focal radiotracer accumulation in the right hemiabdomen, under the lower edge of the liver.



SPECT/CT confirmed accumulation of with I-131-6β-iodomethyl-19-norcholesterol in the right adrenal mass.

Role of 131-I-6β-iodomethyl-19-norcholesterol scintigraphy with SPECT/CT in patient with primary aldosteronism caused by aldosteron secreting cortical adenoma

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Introduction

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Case Report

58-year-old man has arterial hypertension during last 10 years and has been unsuccesfully treated with various combination of antihipertensive drugs. He had one cerebrovascular insult with no consequences. Because only aldosterone antagonist spironolactone had effects the aldosteronism was suspected. He had no hypokalemia. Aldosterone-to-renin ratio indicate primary aldosteronism. MSCT of adrenal glands revealed expansive right adrenal mass, 25 mm in diameter. During preparation for NP-59 scintigraphy spironolactone and ACEI were excluded during 6 weeks before applying NP-59, and replaced with monoxydine, amlodipine and doxazosin.

Methods

Dexamethason suppression has been applyed to decrease ACTH- dependant accumulation of norcholesterol in the zona fasciculata. Patient received 4 mg/day of dexamethasone per os, during seven days before applying radiotracer and throughout the imaging period. NP-59 was intravenously applyed in dose of 37 MBq (1 mCi). Thyroid blocade with Na-perchlorate had been started 30 min before injection of NP-59 and continued during next 10 days.

Results

On the third and the fourth day NP-59 planar scintigram (Figure 1.) showed intensive focal radiotracer accumulation in the right hemiabdomen, under the lower edge of the liver, and abscent accumulation on the left side of lumbar region. Physiological accumulation has been seen in the liver, gallbladder and colon. SPECT/CT (Figure 2., a-transverse, b-sagital, c-coronal section) confirmed accumulation of NP-59 in the right adrenal mass (Figure 2d-low-dose CT). Laparoscopic partial right adrenalectomy was done and pathohistology confirmed aldosteronom.

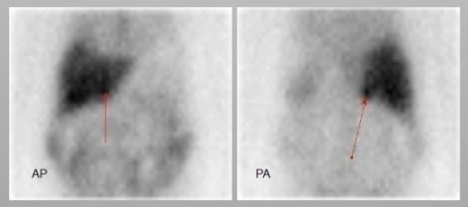

Figure 1. Planar scintigrams with I-131-6β-iodomethyl-19-norcholesterol (NP-59) showed intensive focal radiotracer accumulation in the right hemiabdomen, under the lower edge of the liver.

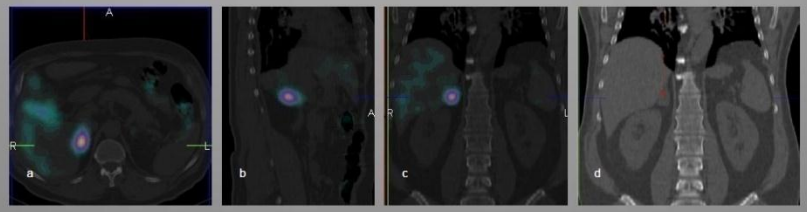

Figure 2. SPECT/CT confirmed accumulation of with I-131-6β-iodomethyl-19-norcholesterol in the right adrenal mass.

Conclusion

Considering invasiveness, possible severe complications and doubtful success of adrenal venous sampling, we suggest simple and noninvasive 131-I-6β-iodomethyl-19-norcholesterol scintigraphy using SPECT/ CT as the first lateralization modality for patients with a clinically confirmed primary aldosteronism.

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- Normal adrenal glands are shown by scintigraphy only five days after the administration of radiopharmaceuticals

Unilateral or bilateral changes 3-4 days after application

Ultrasound- for change bigger than 2 cm

CT – differentiating adenoma from hyperplasia

Nonfunctional tumors of the adrenal glands

Revealed by the CT

Increased radiopharmaceutical uptake with a high probability confirms malignancy

Non-accumulation with a high probability excludes malignancy

Scintigraphy of the adrenal medulla

- Scintigraphy of the adrenal medulla is possible with the I-131- methyl-iodinebenzylguanadine (MIBG)

  Due to the similarity with norepinephrine, MIBG accumulates in the adrenal medulla, but also in pheochromocytoma, neuroblastoma and other APUD-tumors (amine precursor uptake deamination)

Radiopharmaceuticals

- I-131 – MIBG
- i.v. 18,5-37 MBq (0,5-1 mCi)
- Protection of the thyroid gland from free iodine day before MIBG injection with KI or with Na-perchlorate on the day of MIBG injection
- Scintigrams 24, 48 and 72 hours

Scintigrams

- Physiological accumulation of MIBG:

  - salivary glands
  - liver
  - spleen
  - urinary bladder
  - heart
  - lung
  - colon

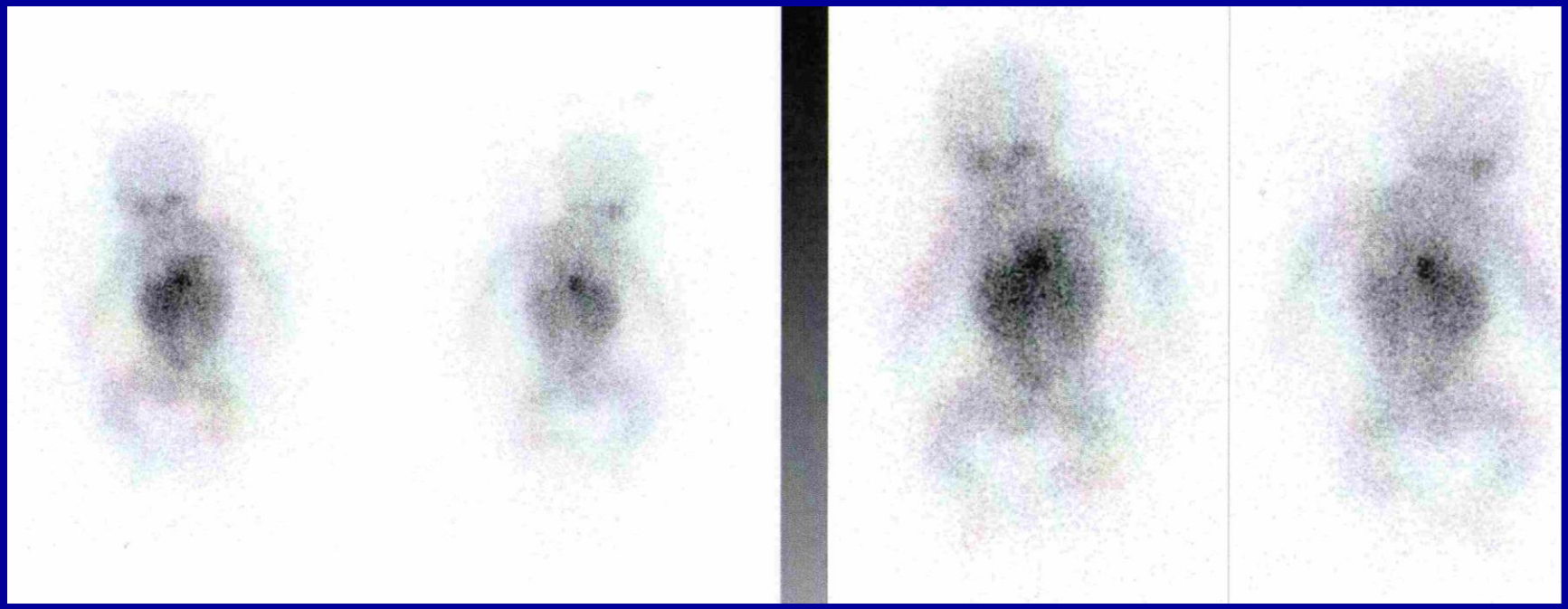
- Adrenal gland can be seen in 1/5 of the healthy subjects on scintigram 48 hours after application

- Indications:

- pheochromocytoma
- paraganglioma
- hyperplasia of the adrenal glands as part of the MEN syndrome
- Neuroblastoma
- medullary thyroid cancer
- APUD-tumors

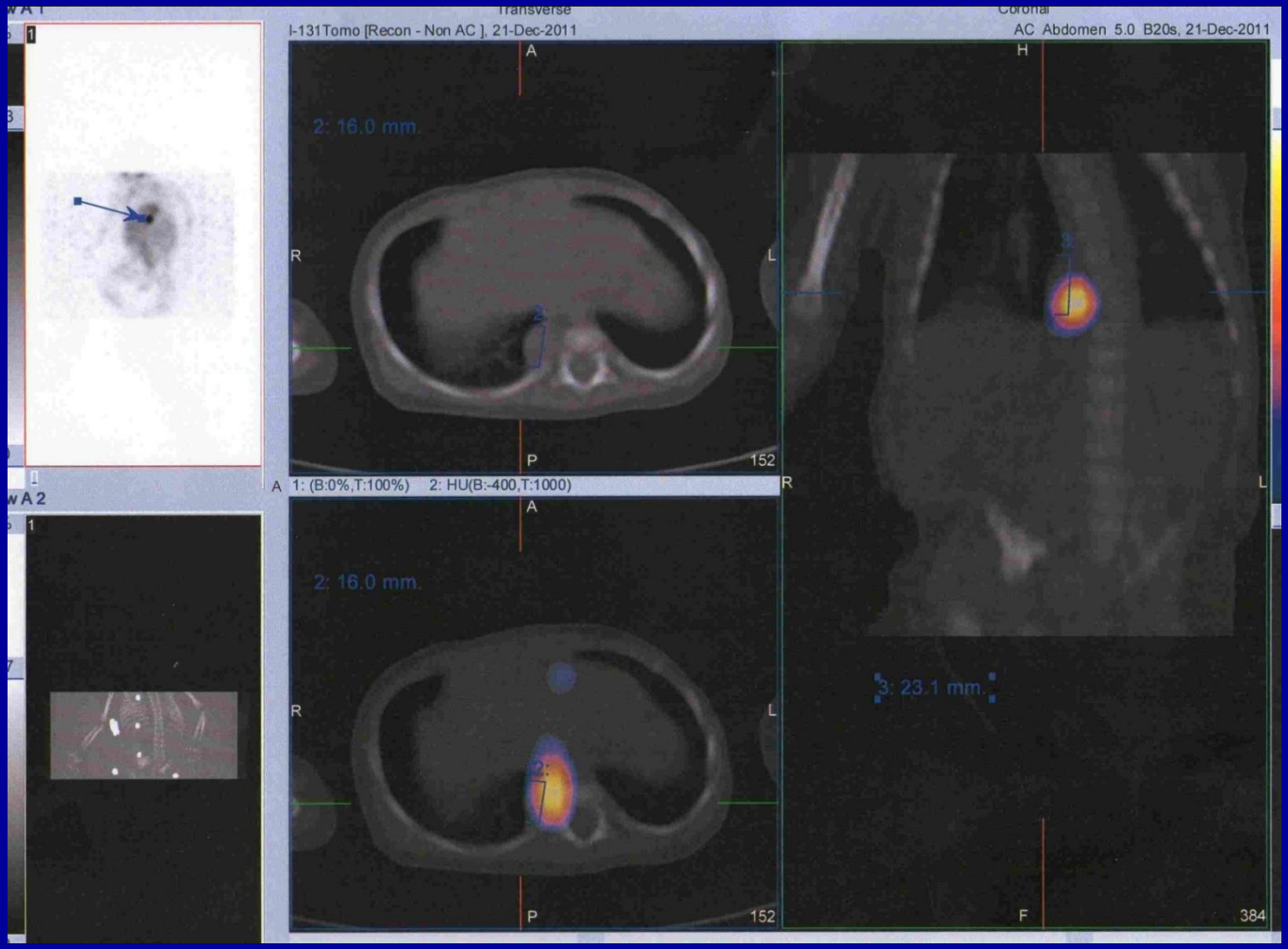
Picture 2-12. Patological accumulation I-131-MIBG in pheochromocytoma of the left adrenal gland. There is excreted activity in bladder with slightly activity in the liver. The contours of kidneys are marked.

I-131- MIBG



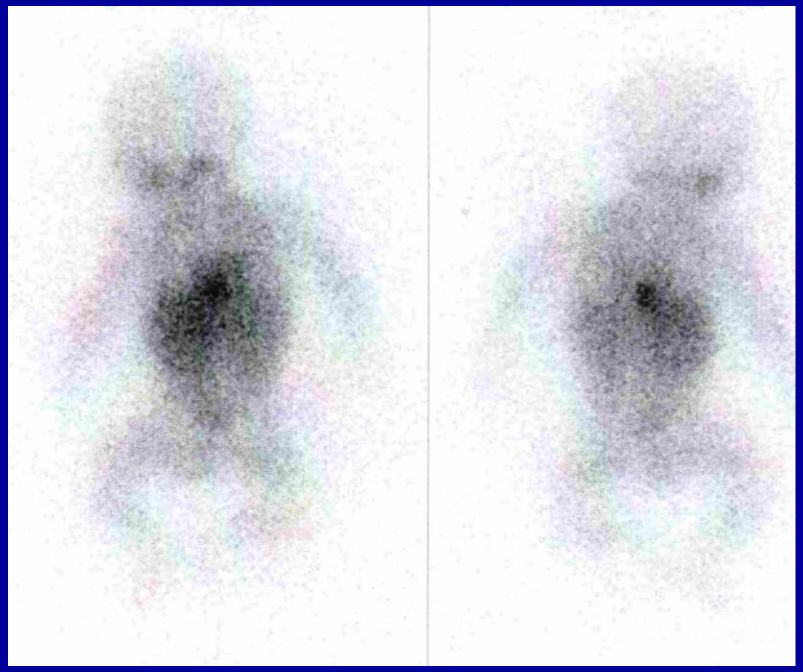
Neuroblastoma in the paravertebral area

I-131- MIBG; SPECT/CT

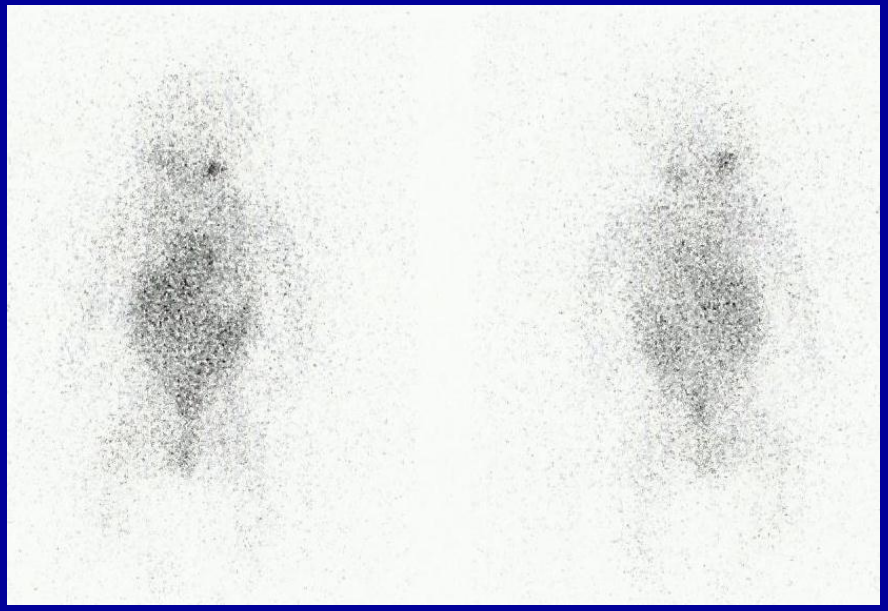


Neuroblastoma: paravertebral localization

I-131- MIBG

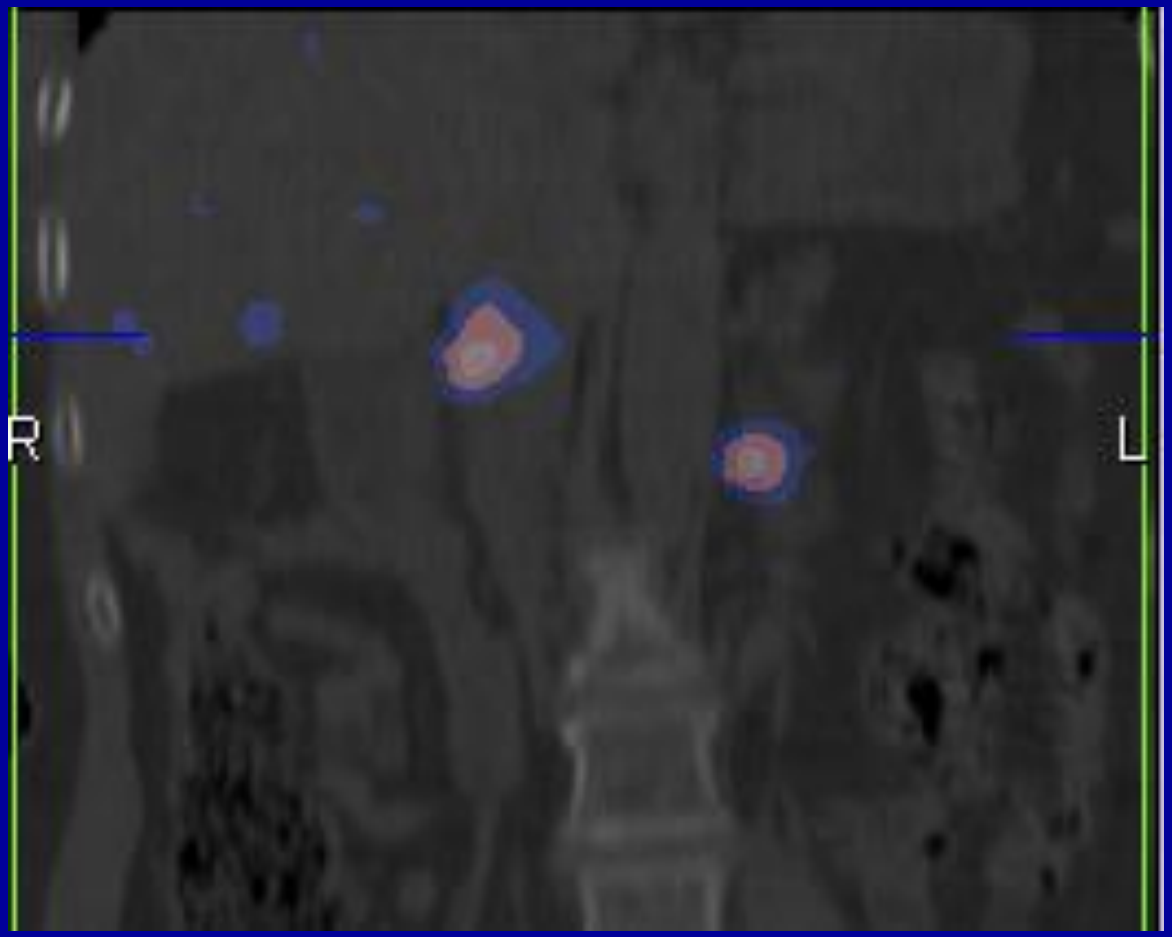


Before surgery



After surgery

J-131- MIBG; SPECT/CT



Bilateral pheochromocytoma

Indications for I-131 MIBG

- In the diagnosis of pheochromocytoma in patients with adrenal tumors, which was detected with other diagnostic methods

- For detection and localization of pheochromocytoma or paraganglioma in hypertensive patients with clinical and laboratory signs of disease
- For detecting hyperplasia of the adrenal medulla and pheochromocytoma in MEN syndromes
- In the diagnosis of tumors suspected of neuroblastoma
- For detecting recurrence of neuroblastoma

- The planning and evaluation of the success of the radionuclide therapy of malignant pheochromocytoma and neuroblastoma with I-131-MIBG

- The detection of recurrence

- Sensitivity and specificity of MIBG scintigraphy = 90% for pheochromocytoma and neuroblastoma

  For medullary carcinoma and carcinoid 50% and less

  The advantage over CT and MRI in paraganglioma detection.

The end!