Nuclear medicine in oncology

1. Diagnosis
2. Therapy

Diagnosis

- Conventional methods

- Nonspecific radiopharmaceuticals cumulating in tumours

- Specific radiopharmaceuticals, receptor- and immunoscintigraphy

Hormone synthesis

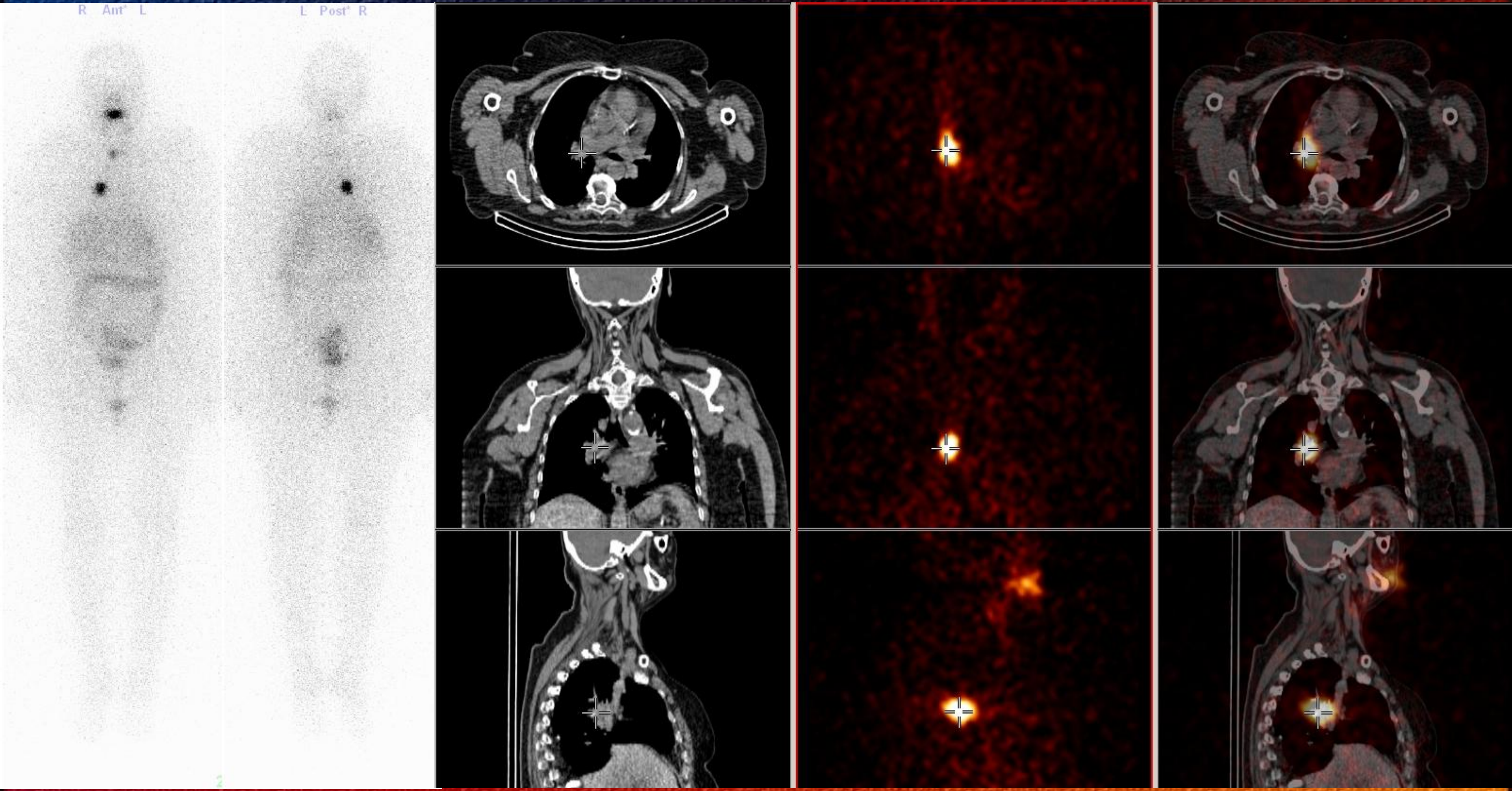
- 123- and 131-I

(in differentiated thyroid cancer: papillary and follicular cc.)

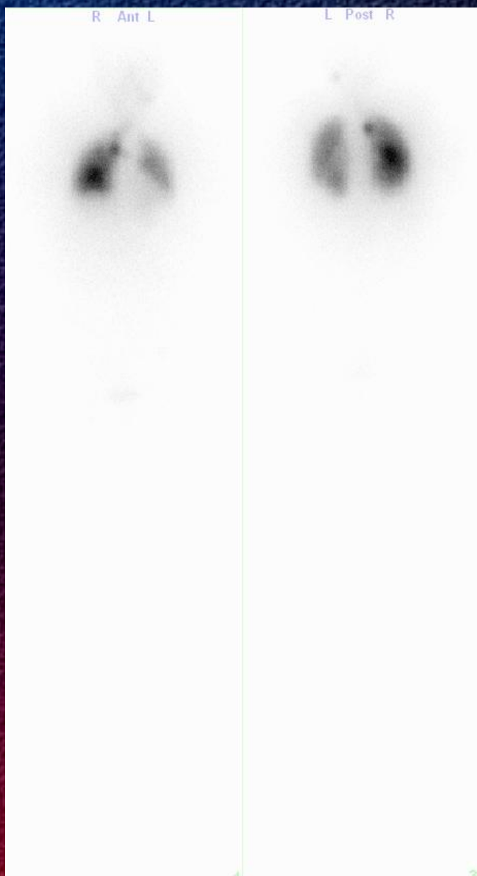
- 131-I-metil-norchoresterol

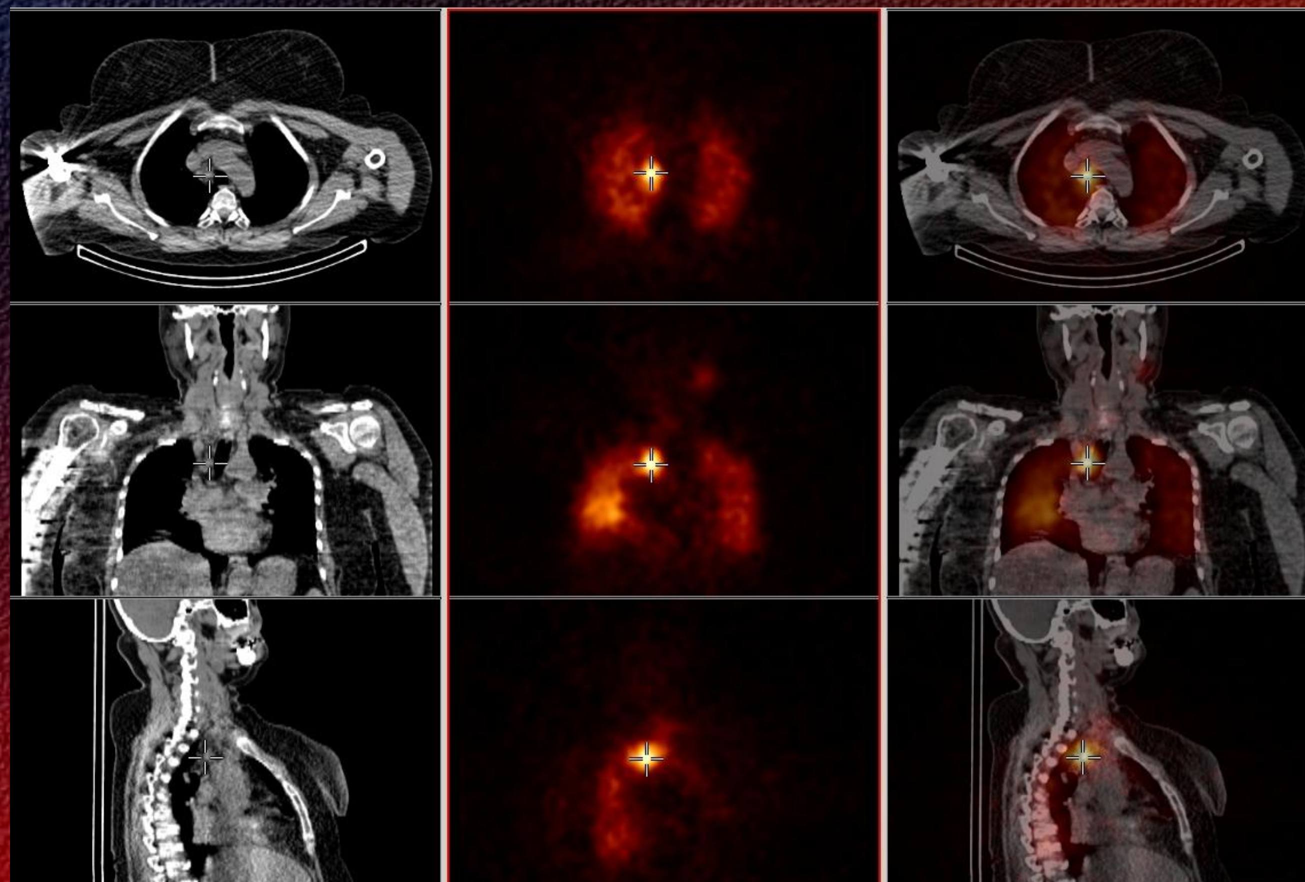
(in differential diagnostic of adrenocortical tumour)

Follicular thyroid cc. – lymph node metastases 131-I

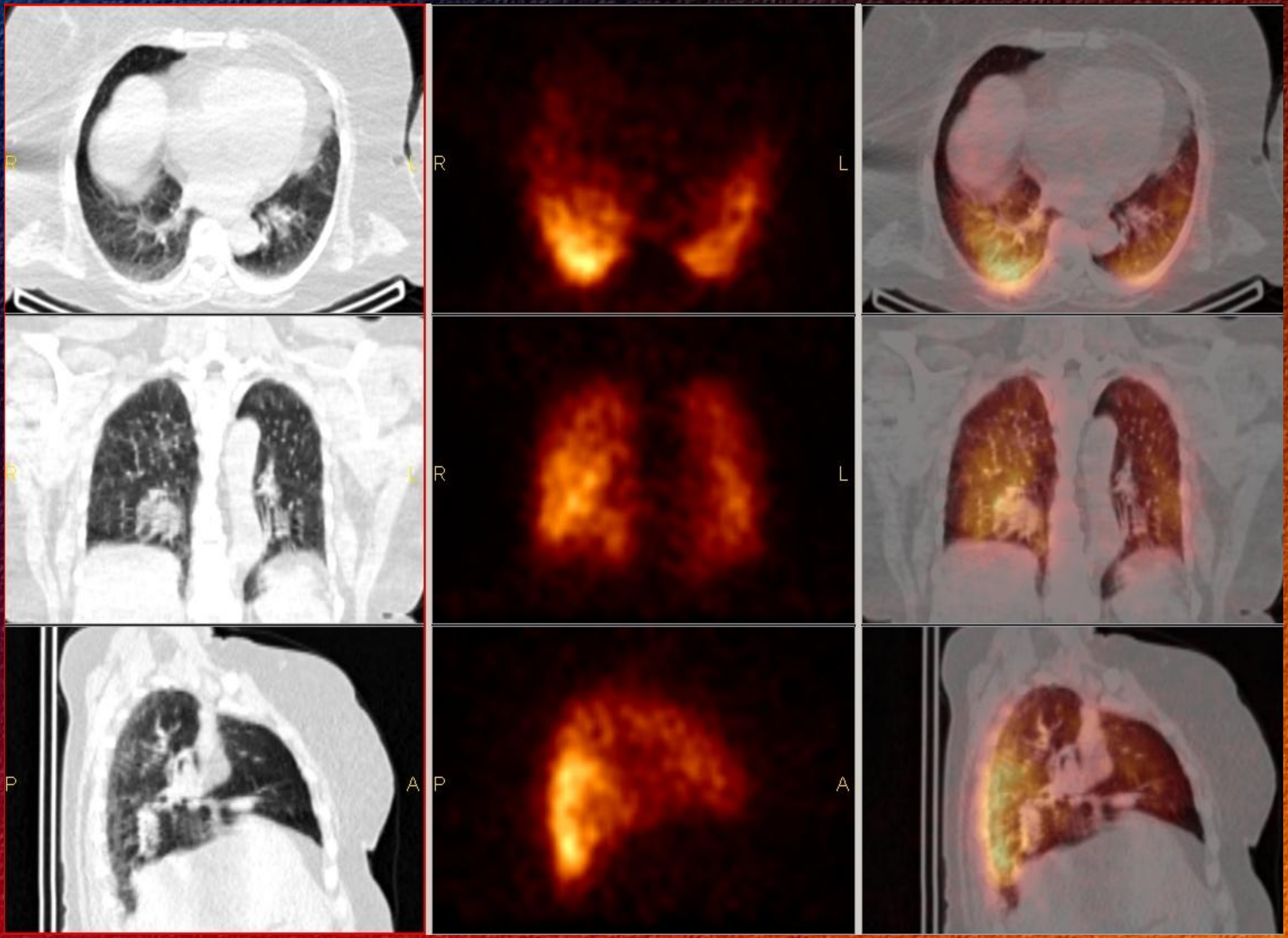


Papillary thyroid cc – mediastinal lymph node metast. and pulmonary micrometast.
131-I

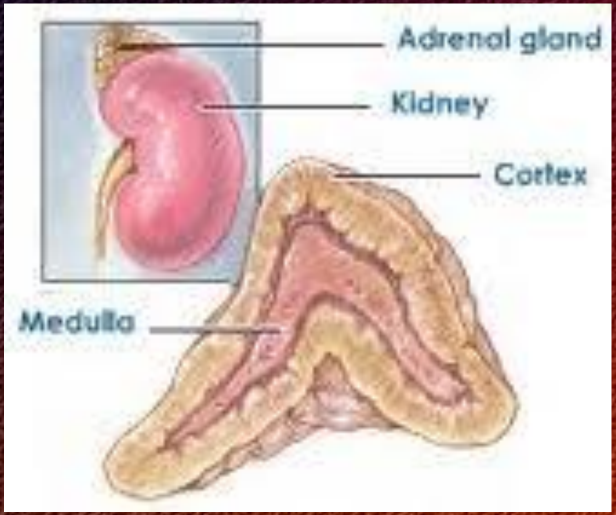




Papillary thyroid cc – mediastinal lymph node metast. and pulmonary micrometast.



Adrenocortical scintigraphy



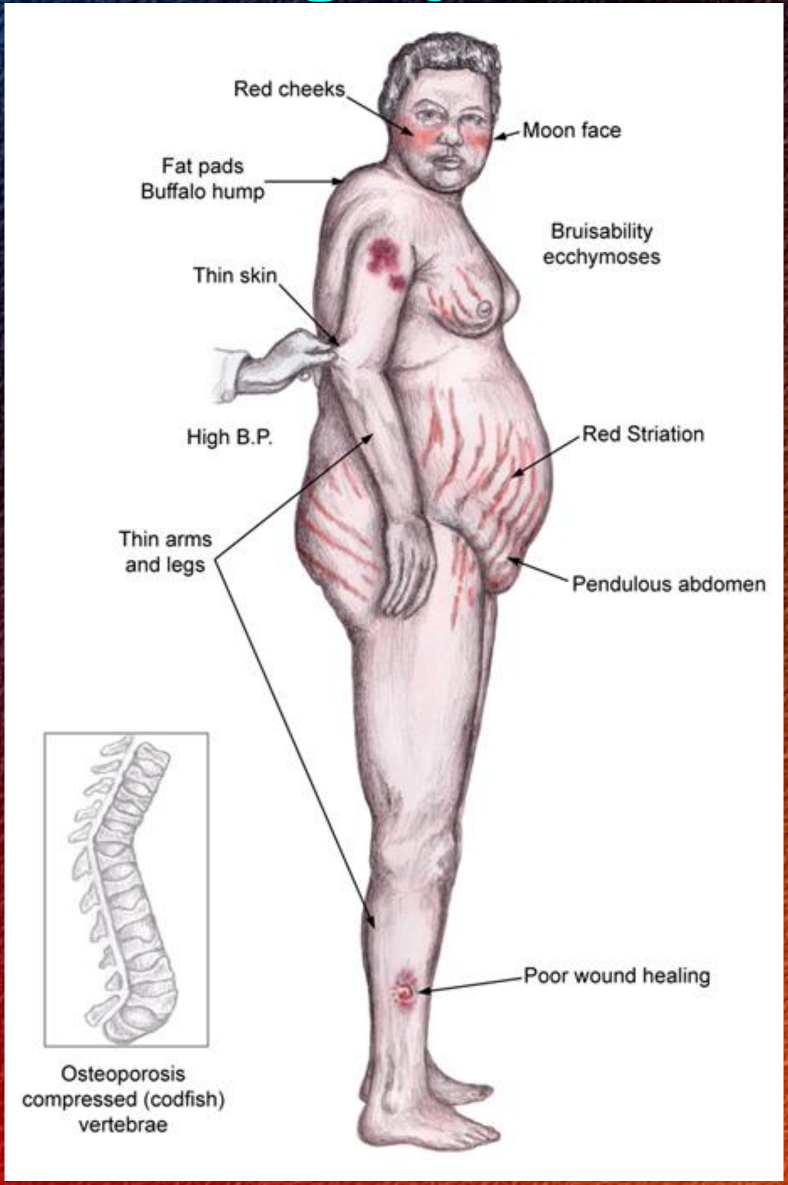
Radiopharmaceutical: **131-I-methyl-norcholesterol (substrate for adrenal hormon synthesis)**

Imaging: **48 hours and 7 days after i.v. administration**

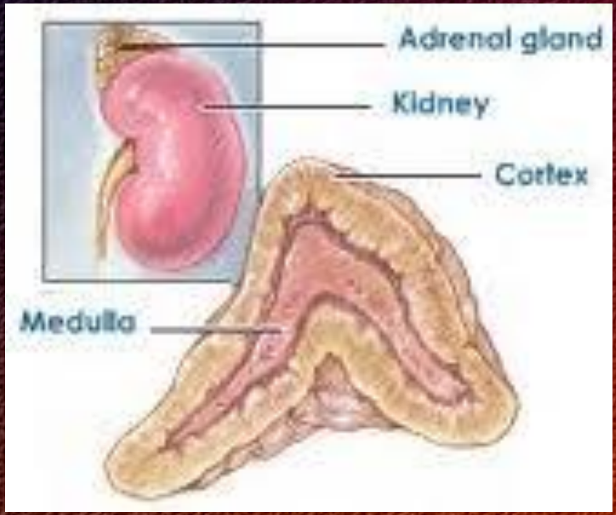
Indications: **- hypersecretory syndromes of adrenal cortex (Cushing syndr., hyperaldosteronism, hyperandrogenism)**

- differential diagnosis of hyperplasia and adenoma, ectopic ACTH syndroma and incidentalomas (incidentally discovered adrenal masses)

Cushing-syndrome



Adrenocortical scintigraphy



Radiopharmaceutical: 131-I-methyl-norcholesterol (substrate for adrenal hormon synthesis)

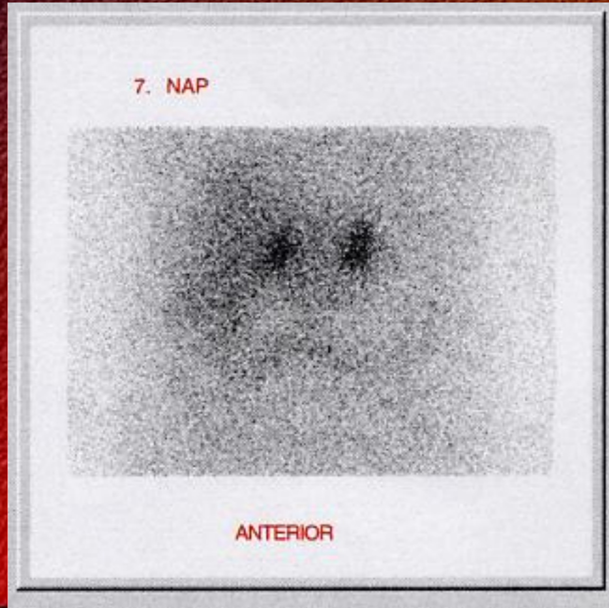
Imaging: 48 hours and 7 days after i.v. administration

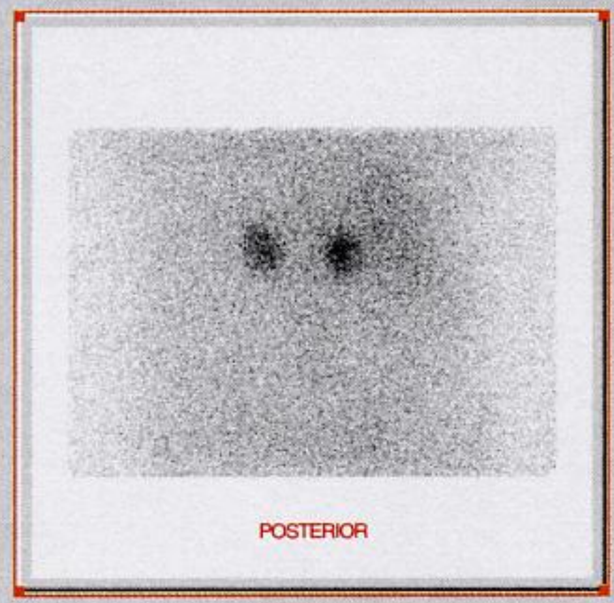
Indications: - hypersecretory syndromes of adrenal cortex (Cushing syndr., hyperaldosteronism, hyperandrogenism)

- differential diagnosis of hyperplasia and adenoma, ectopic ACTH syndroma and incidentalomas (incidentally discovered adrenal masses)

Bilteral adrenal hyperplasia

Planar scans





Bilteral adrenal hyperplasia

48 h.

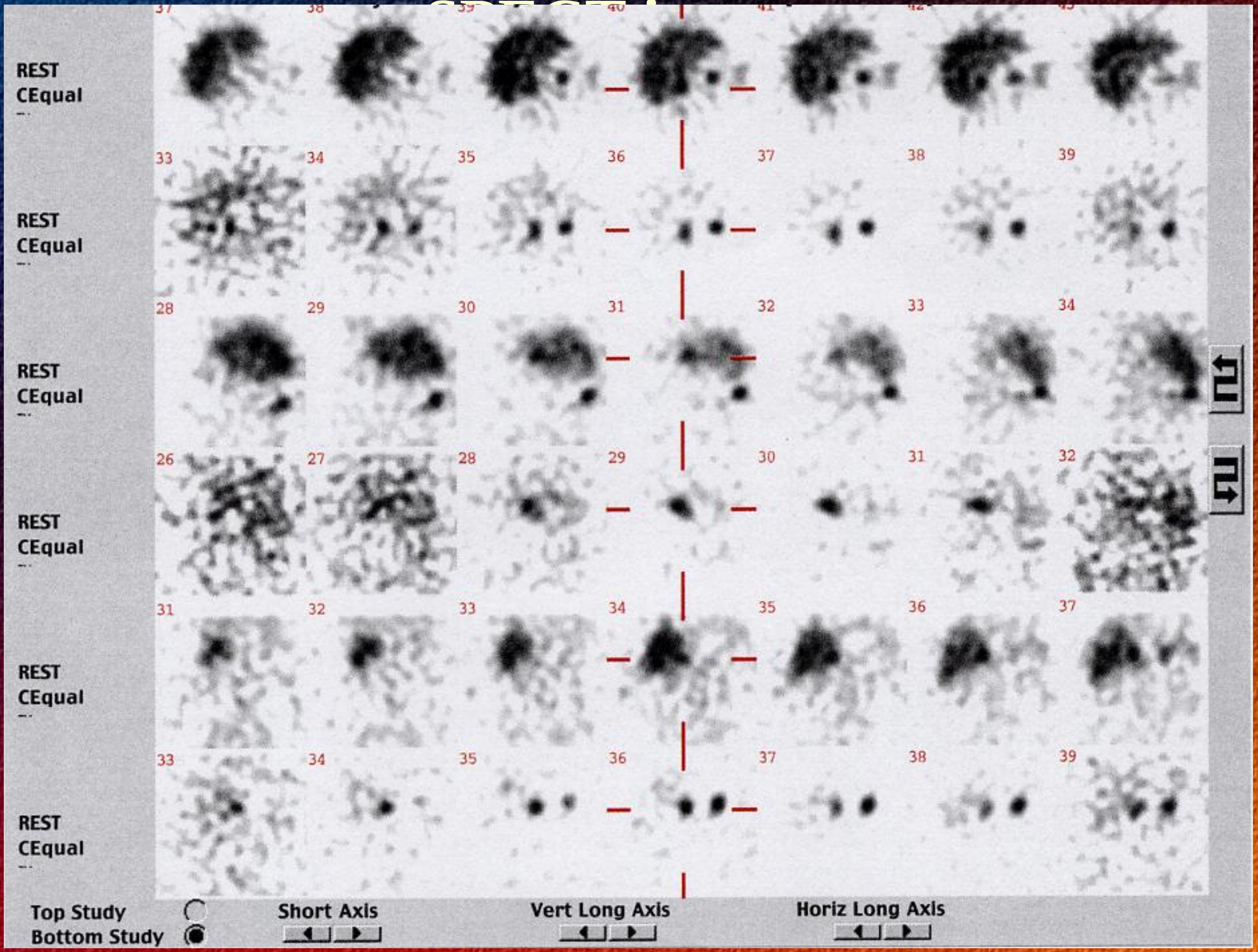
7. day

48 h.

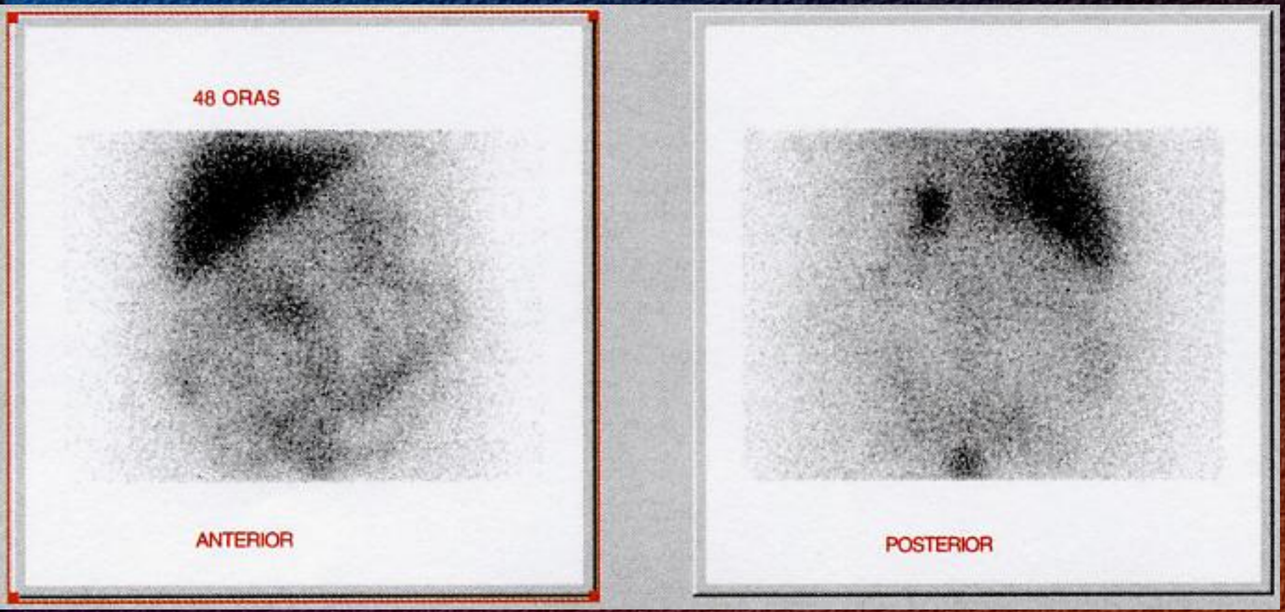
7. day

48 h.

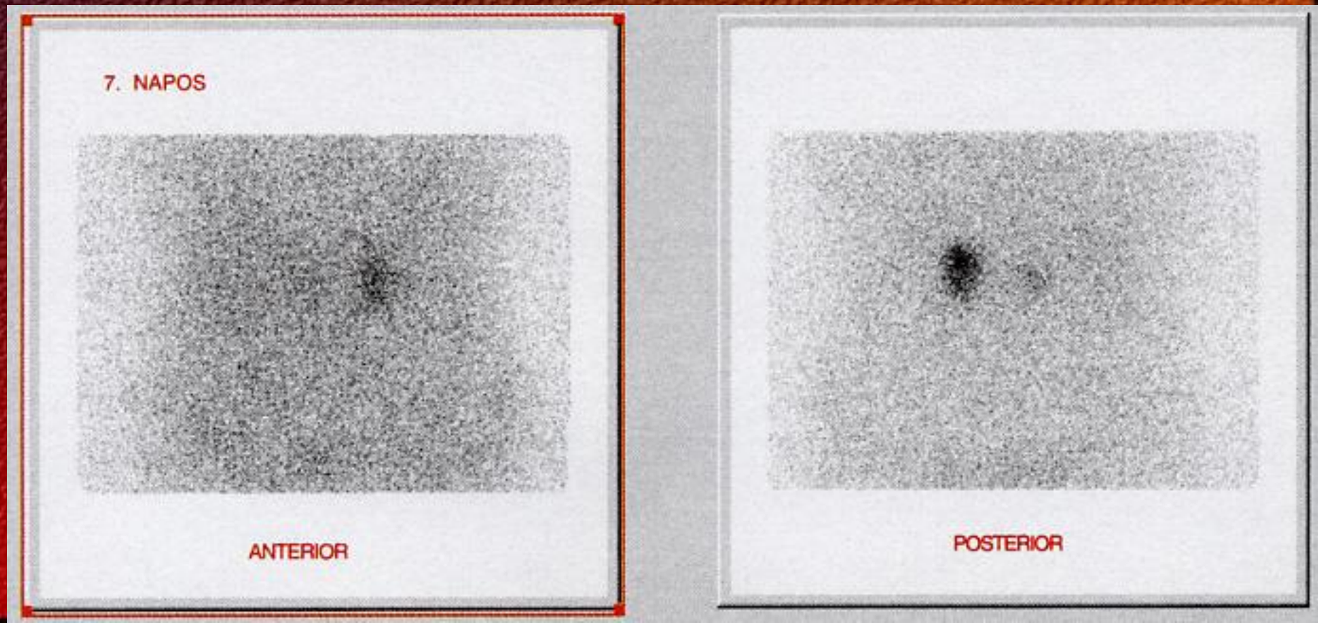
7. day



Unilateral abnormal increased uptake - adenoma



Static scans



Unilateral abnormal increased uptake - adenoma

SPECT image

48 h.

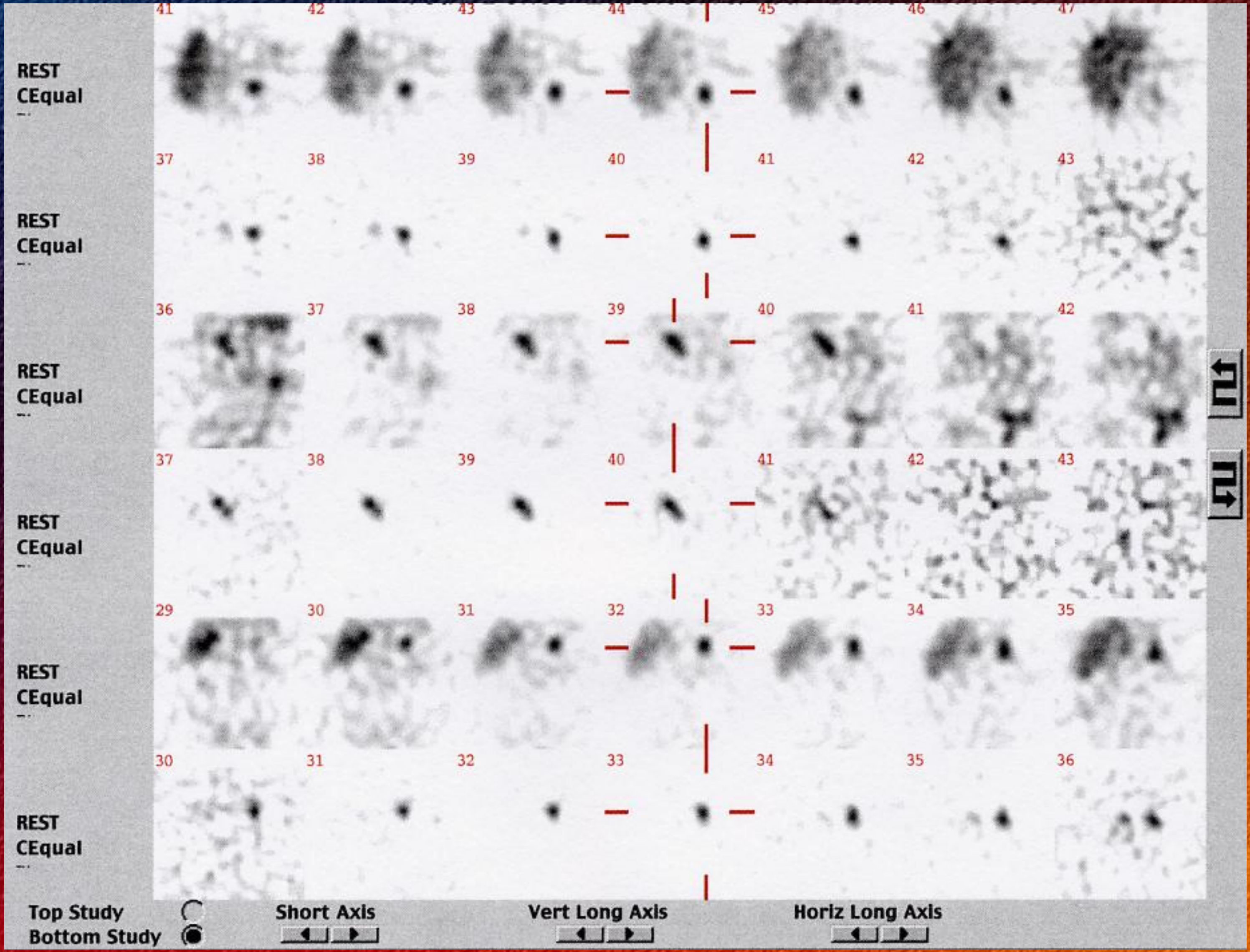
7. day

48 h.

7. day

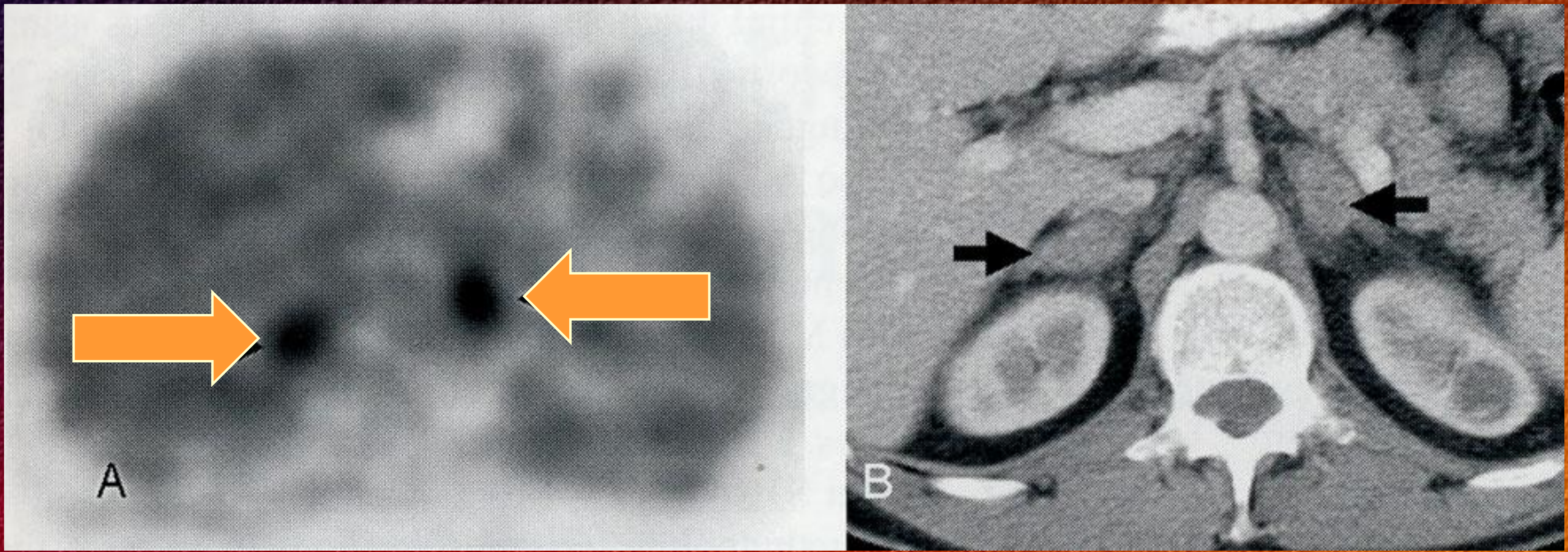
48 h.

7. day



Bilateral adrenocortical metastasis(!) in SCLC

18F-FDG PET **CT**



Receptorscintigraphy

- Adrenerg receptor scintigraphy:

- noradrenaline analogous:

I-123- or I-131-MIBG (meta-iodobenzil-guanidin)

(taken up actively by cell membranes and then stored by neurosecretory cytoplasmic granules in neuroendocrine tumors, pheochromocytoma, neuroblastoma, medullary thyroid cc.)

- Somatostatin receptor scintigraphy:

- somatostatin analogous peptides

In-111- Octreoscan (pentetreotide)

99mTc-Neospect (depreotide)

(somatostatin analogues bind to somatostatin cell surface receptors; GEP tumours, carcinoid, brain and lung tumours, medullary thyroid cc.)

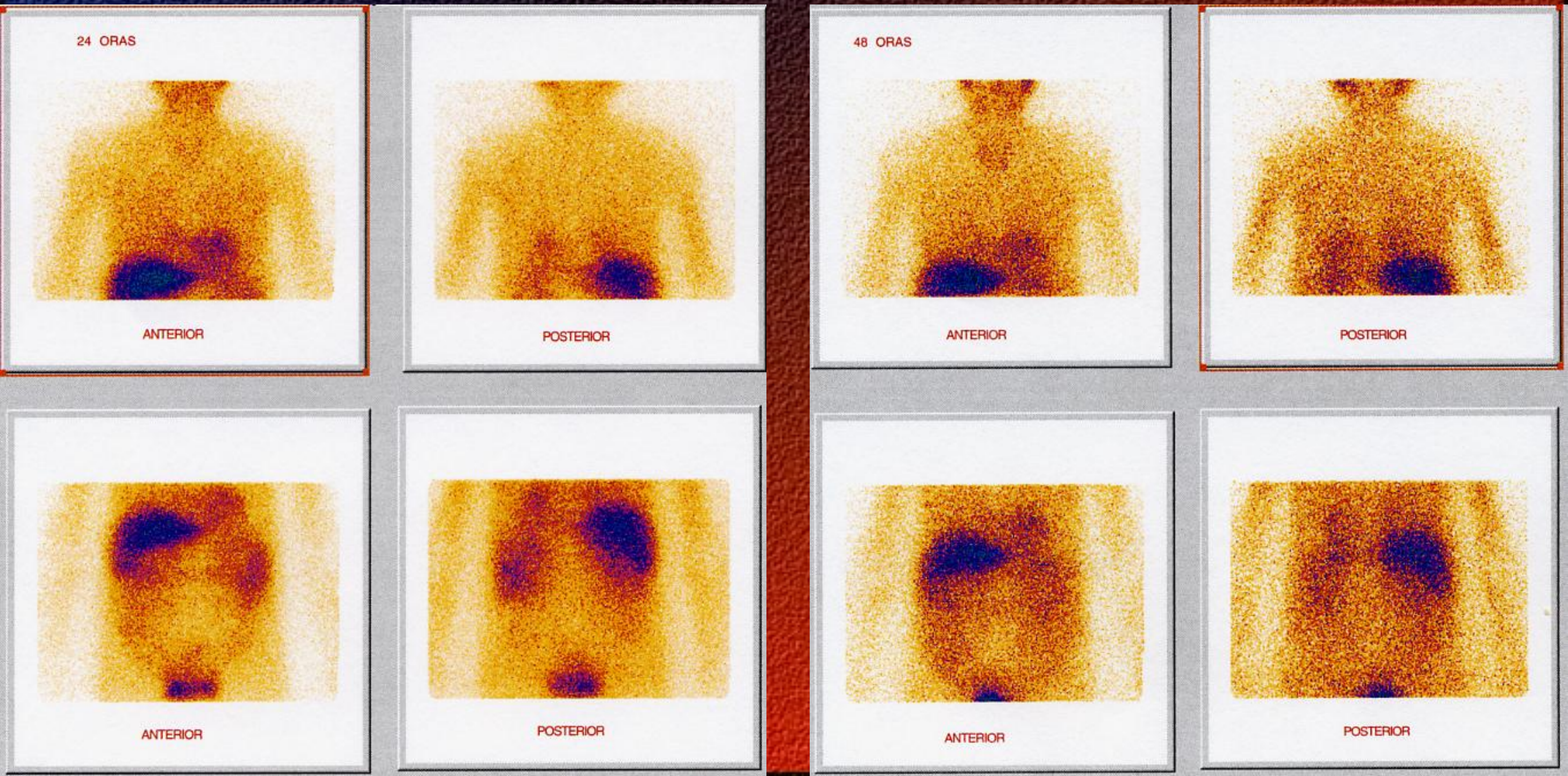
- **Neuroblastoma is the most common extracranial solid cancer in childhood and the most common cancer in infancy. It is a neuroendocrine tumor, arising from any neural crest element of the sympathetic nervous system.**

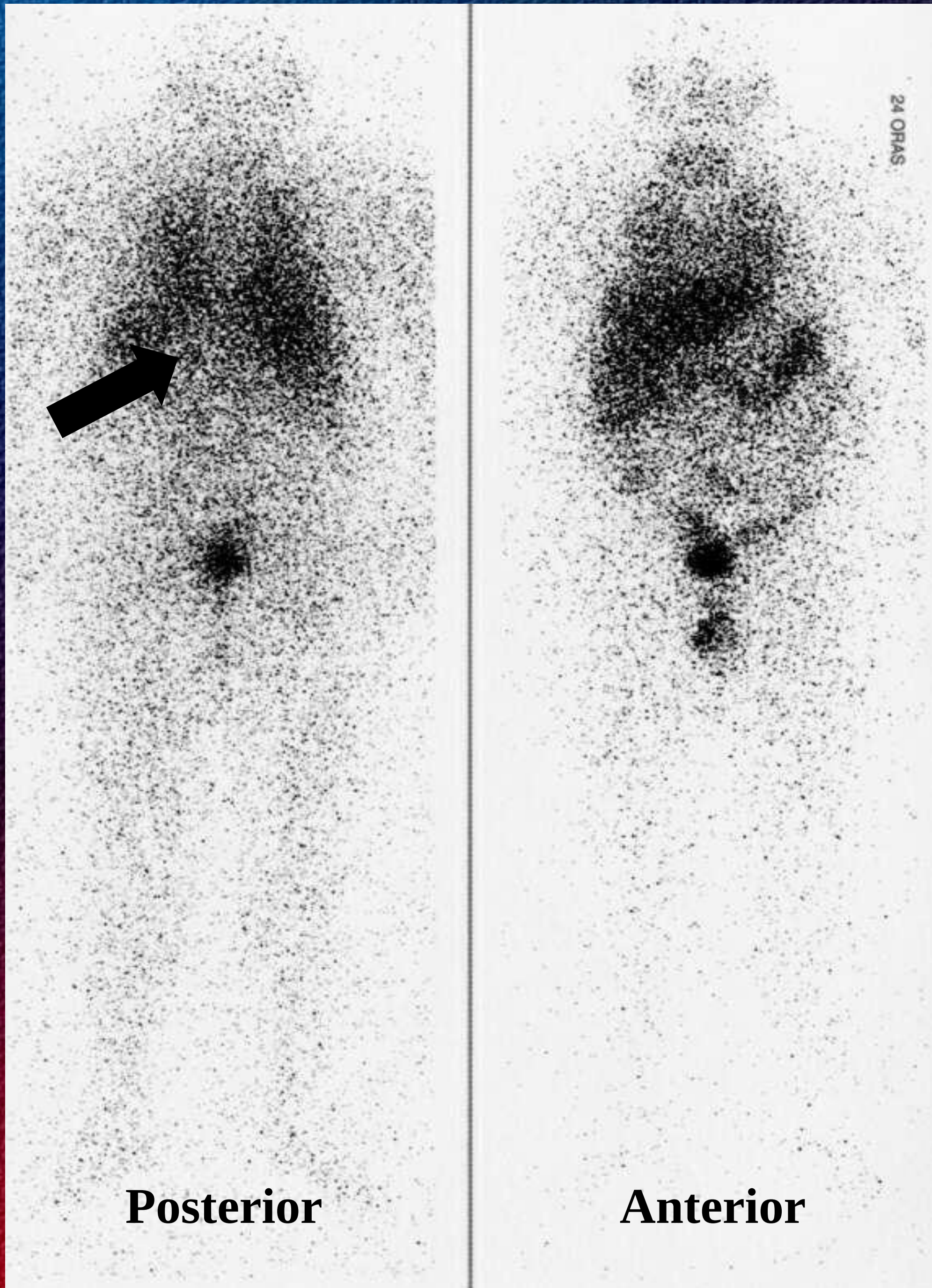
- **Pheochromocytoma is a neuroendocrine tumor of the medulla of the adrenal glands (originating in the chromaffin cells), and secretes excessive amounts of catecholamines, usually noradrenaline (norepinephrine), and adrenaline (epinephrine) to a lesser extent.**

- **Medullary thyroid cancer (MTC) is a form of thyroid carcinoma which originates from the parafollicular cells (C cells), which produce the hormone calcitonin.**

- **Carcinoid is a slow-growing type of neuroendocrine tumor, originating in the cells of the neuroendocrine system. Carcinoid metastasis can lead to carcinoid syndrome. This is due to the over-production of many substances, including serotonin, which is released into the systemic circulation, and which can lead to symptoms of cutaneous flushing, diarrhea, bronchoconstriction**

131-I-MIBG - physiological distribution

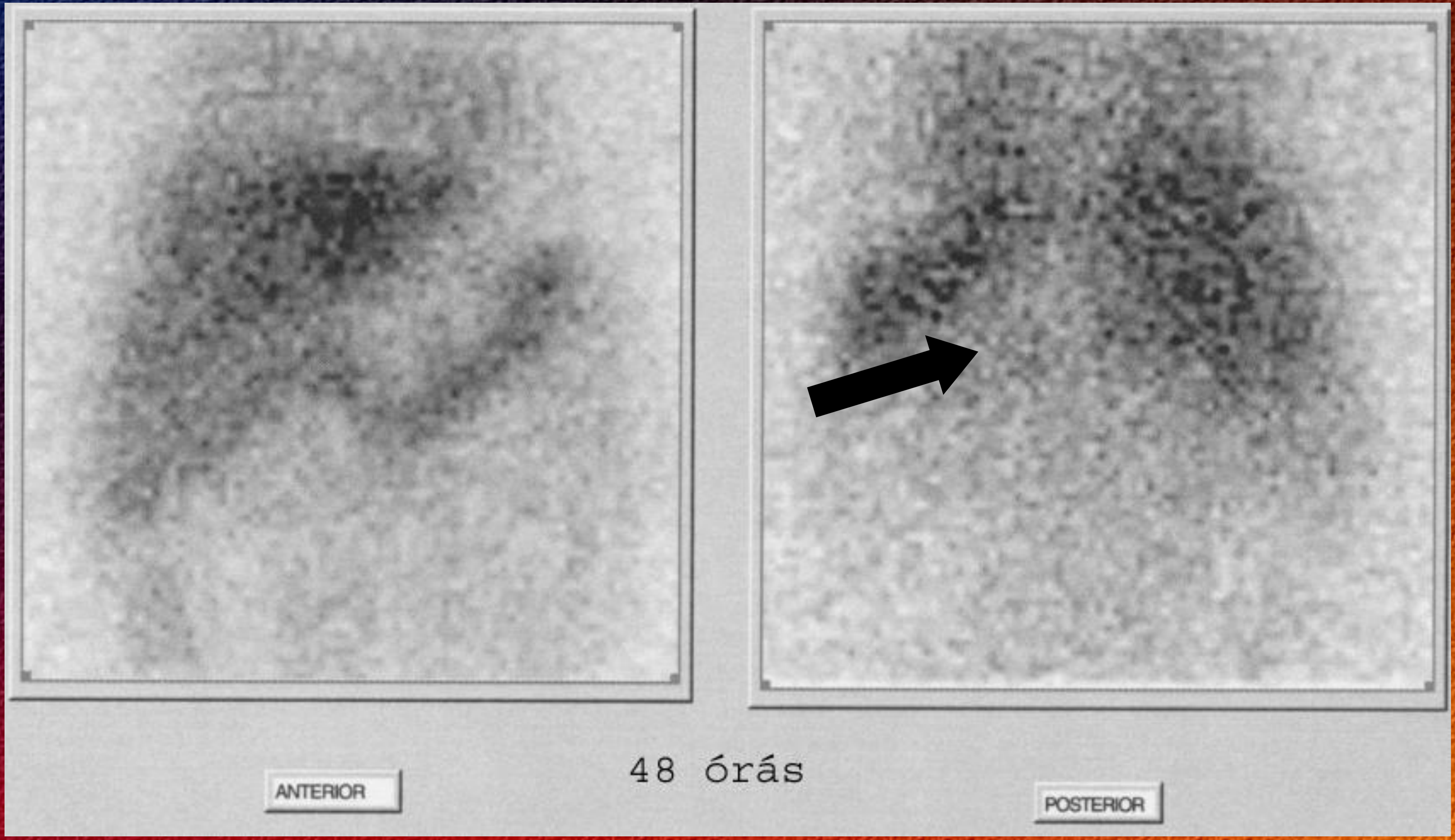


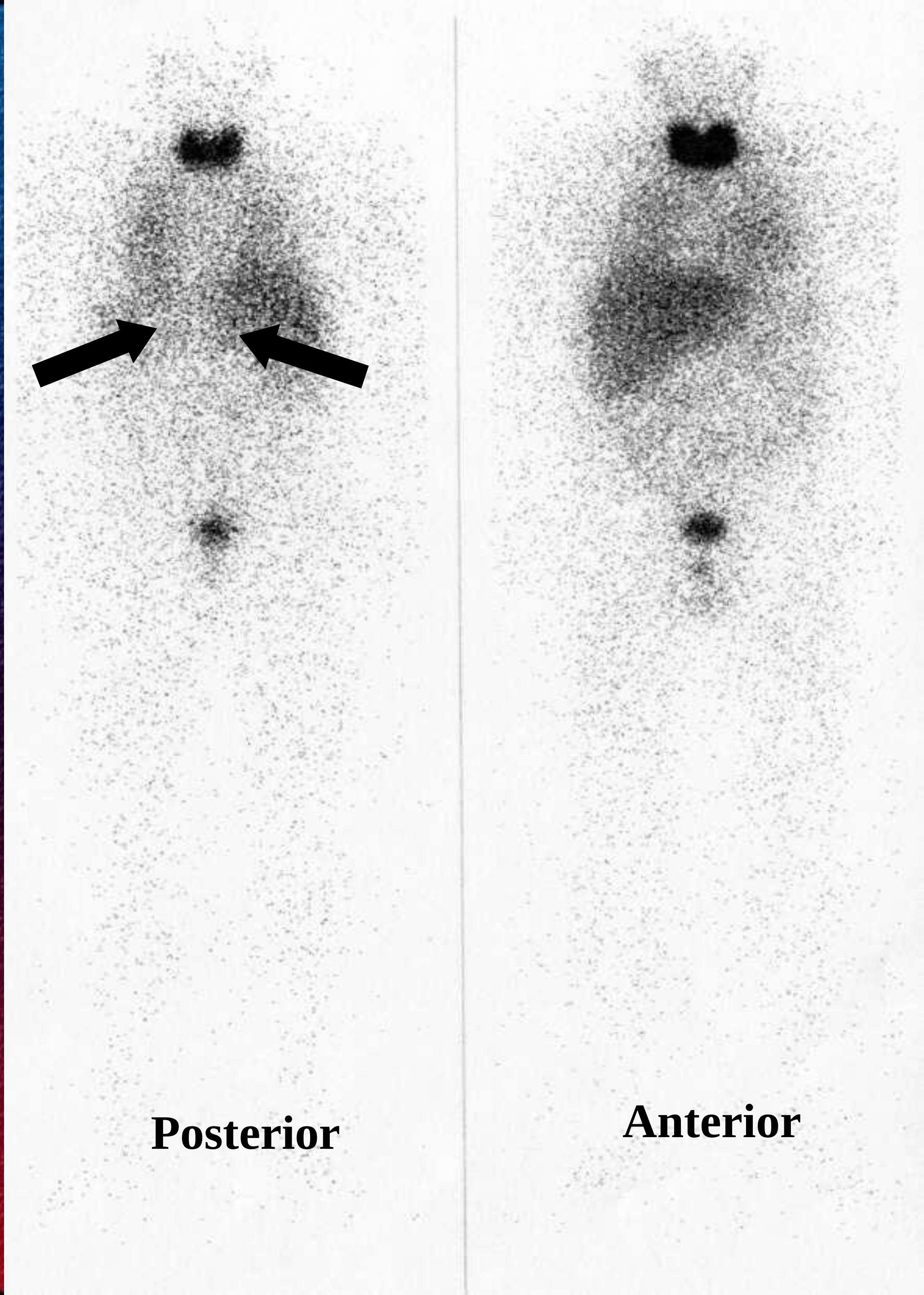


Pheochromocytoma
on the left side
131-I-MIBG
whole body scan

Pheochromocytoma on the left side -131-I-MIBG

48 hours after i.v. injection, static images

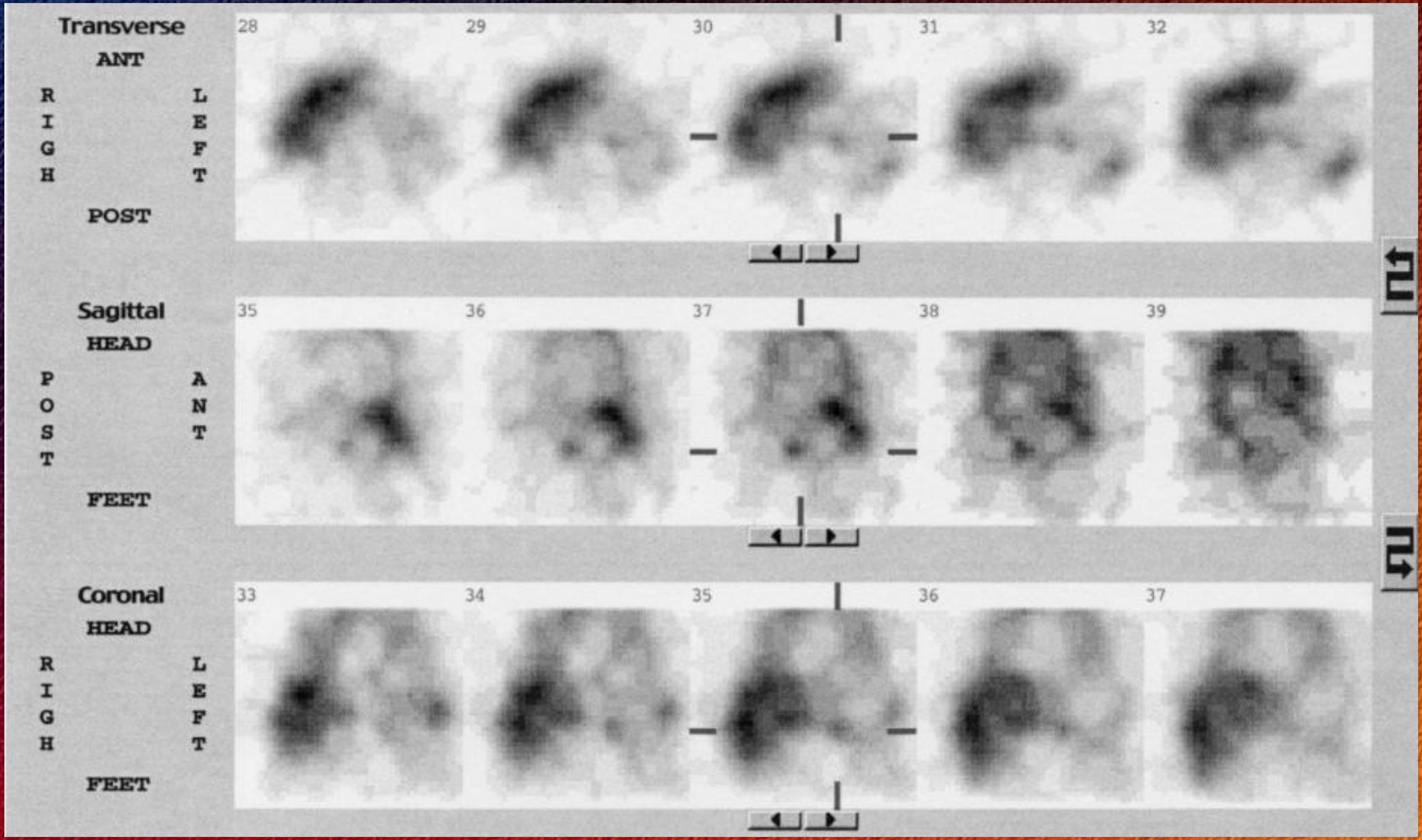




Bilateral pheochromocytoma
131-I-MIBG
whole body scan

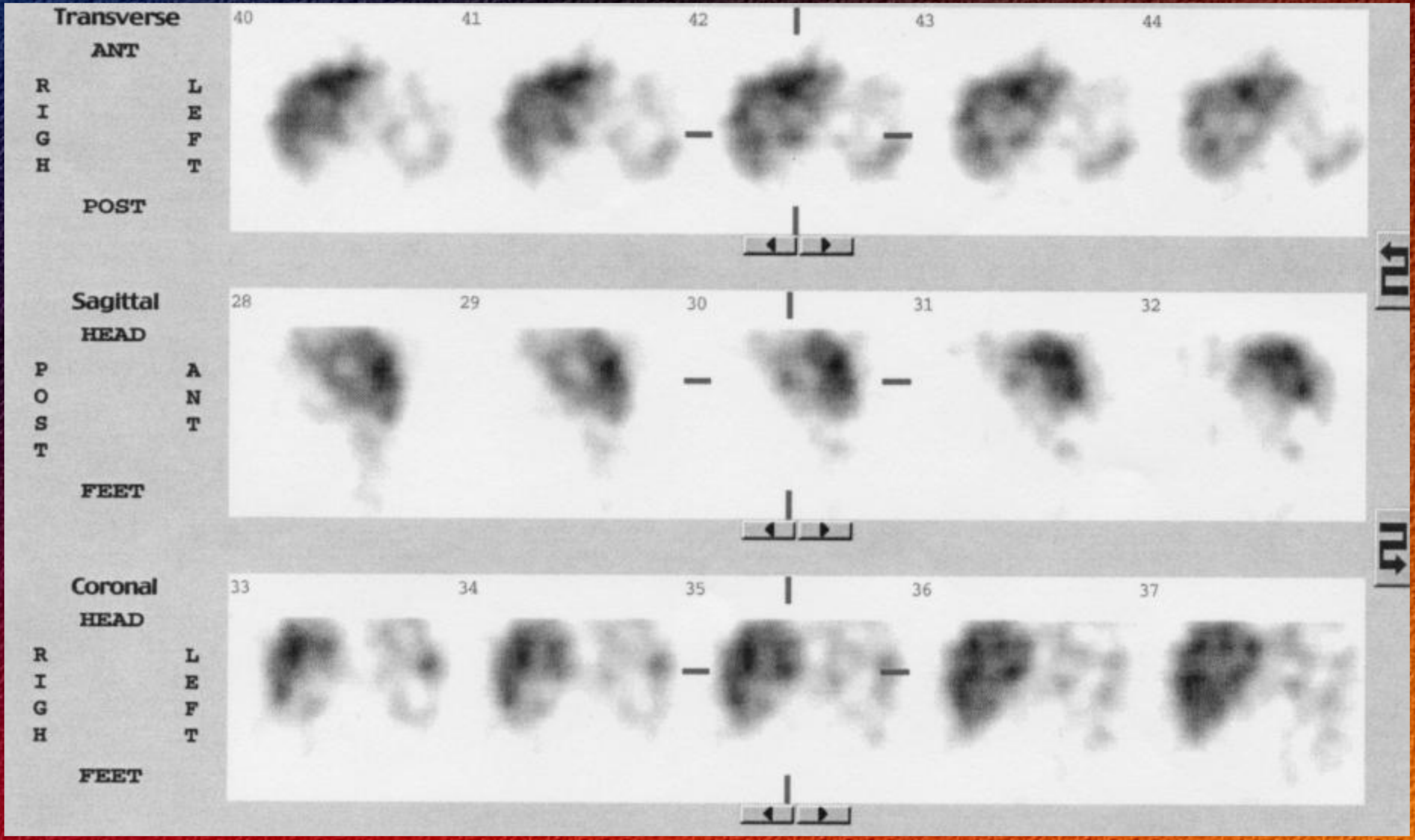
Bilateral pheochromocytoma - 131-I-MIBG

SPECT – image (left side)

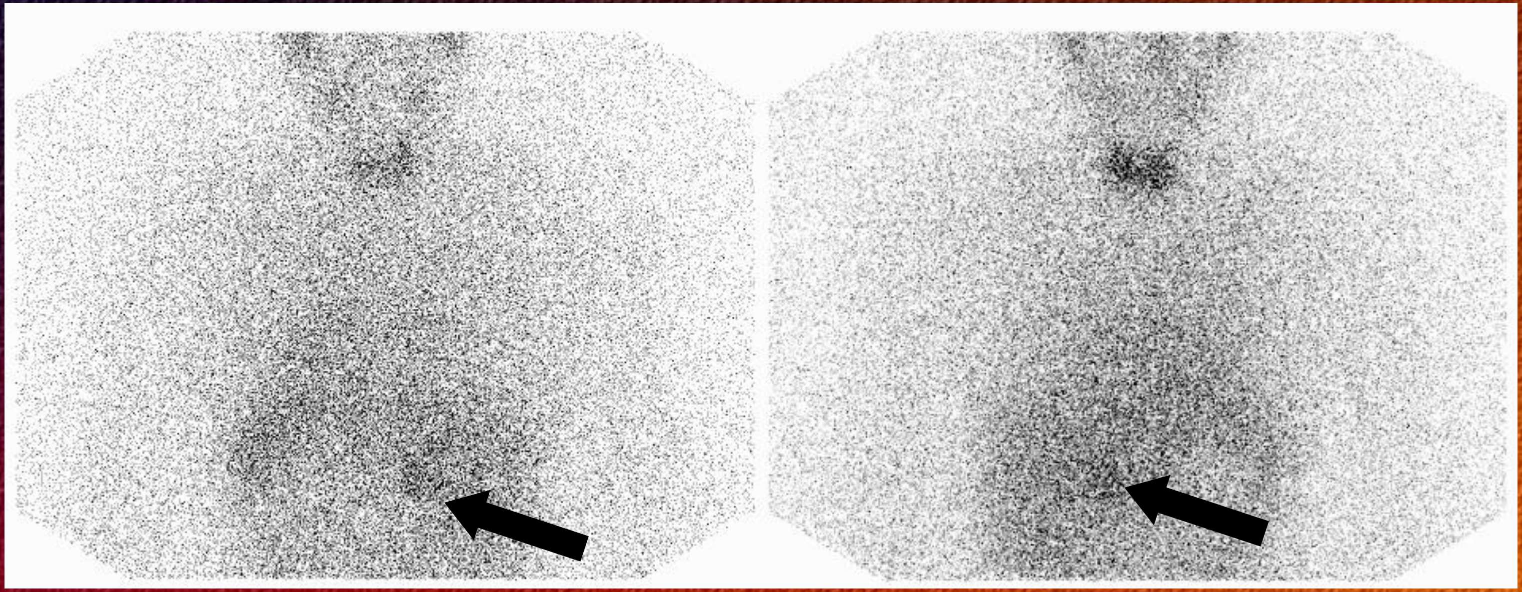


Bilateral pheochromocytoma - 131-I-MIBG

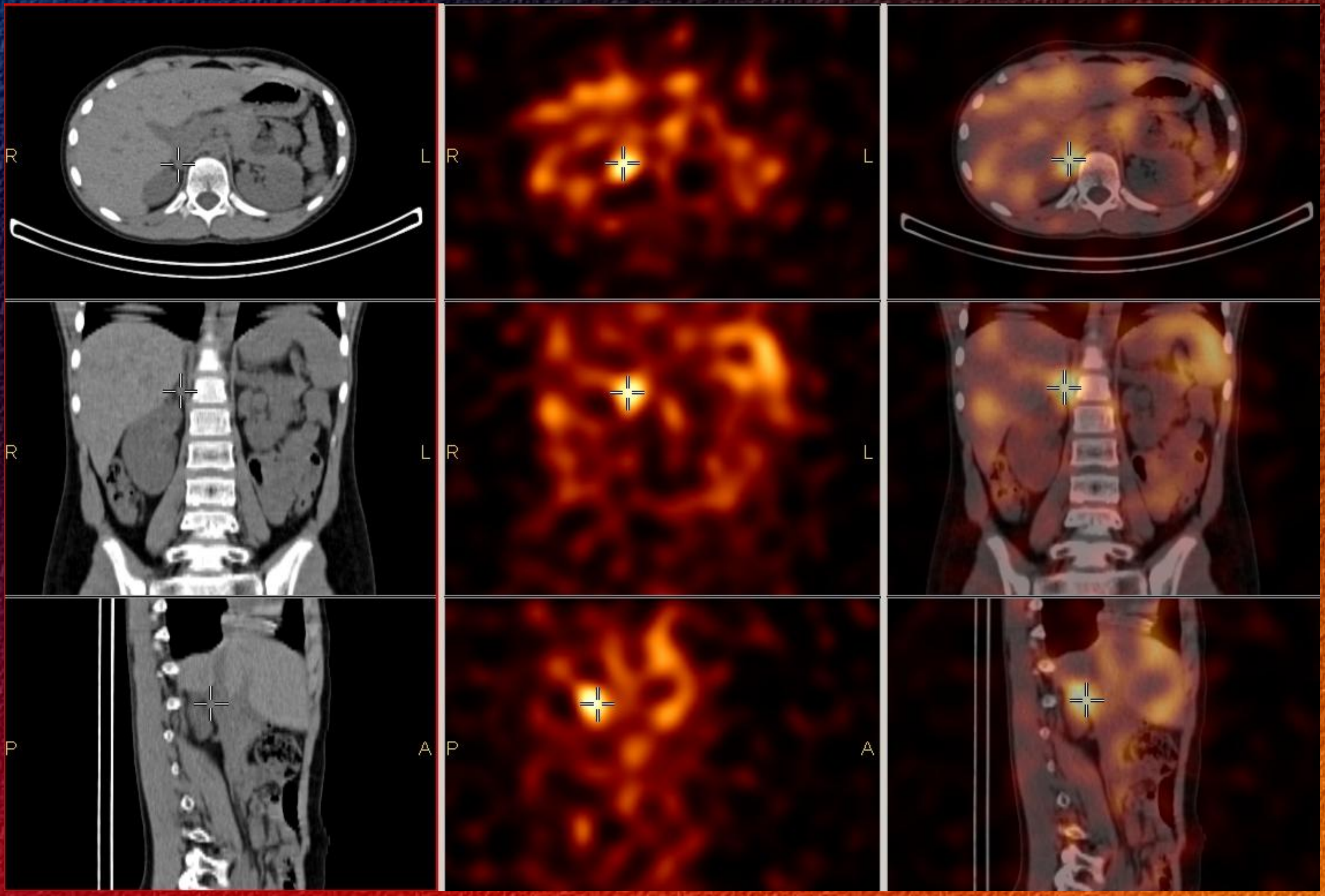
SPECT – image (right side)



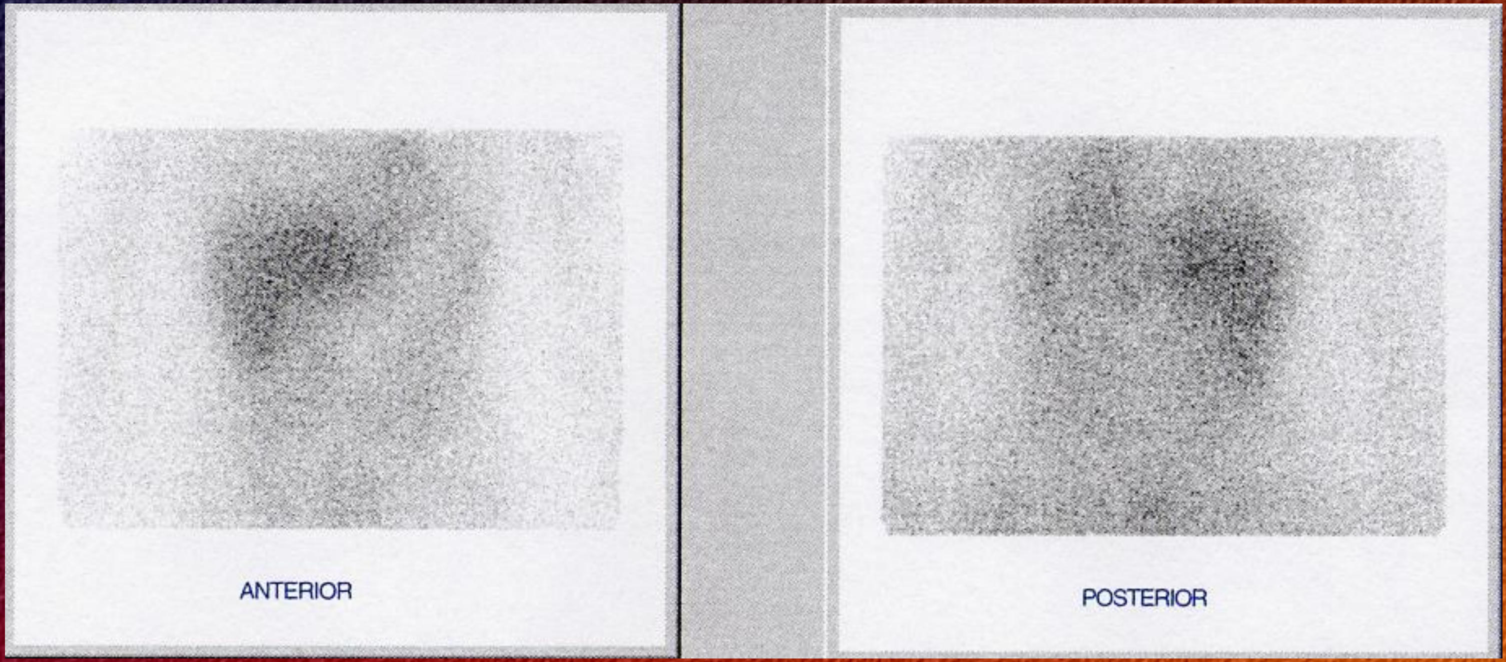
Pheochromocytoma on the right side, 131-I-MIBG 48 hours after i.v. injection, planar images



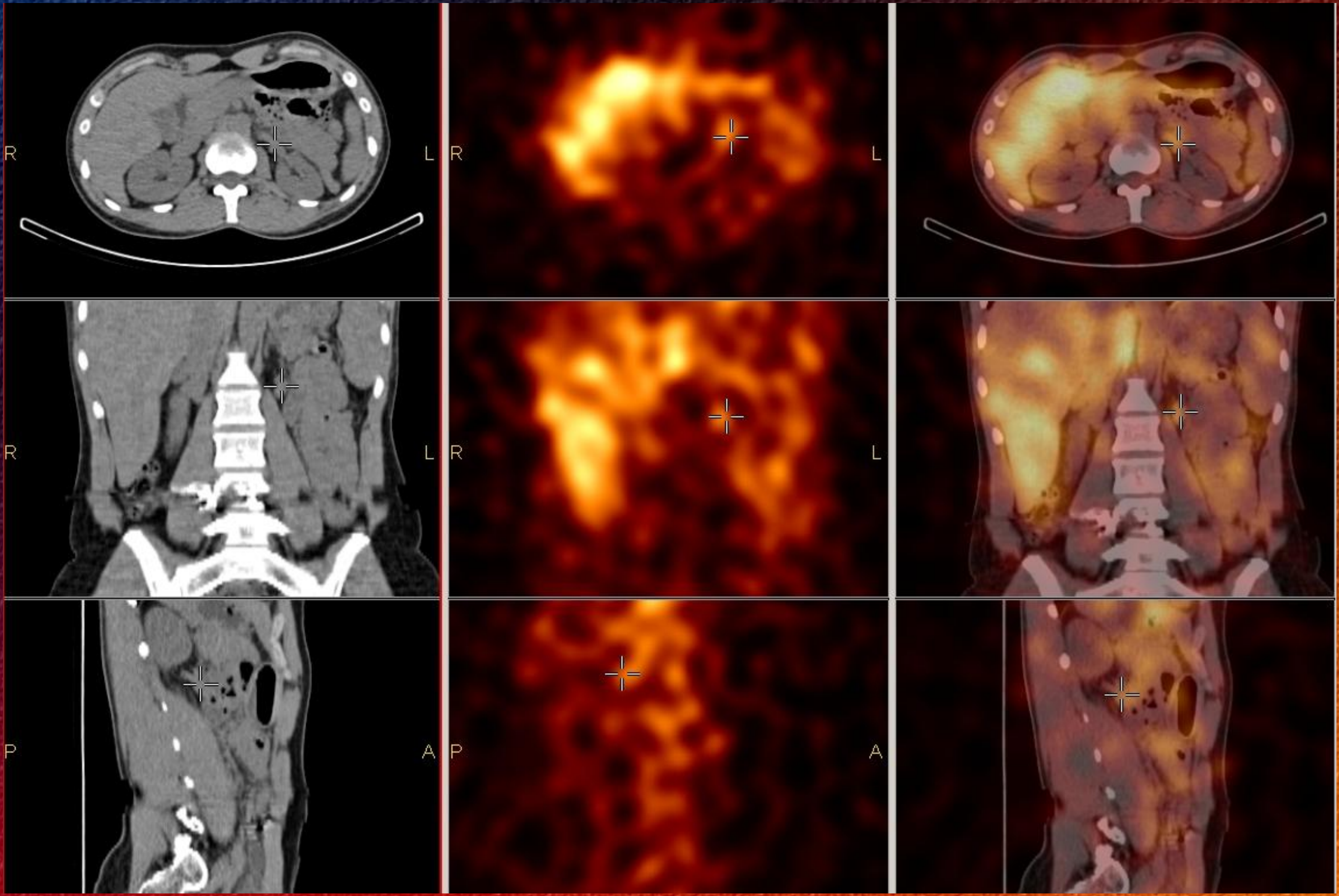
Pheochromocytoma on the right side, 131-I-MIBG 48 hours after i.v. injection, SPECT – CT images



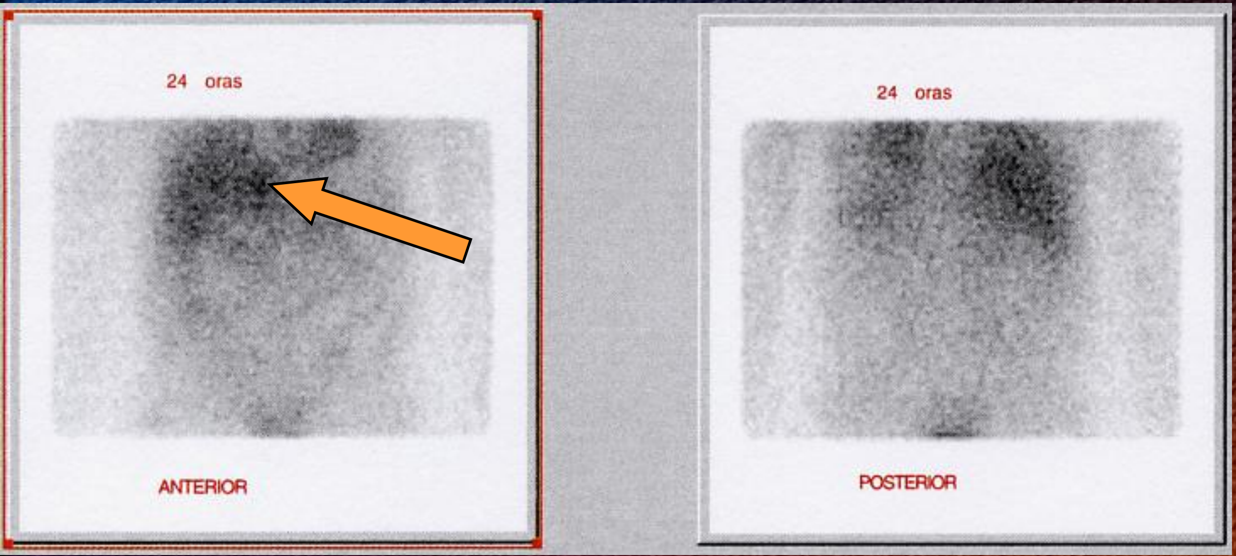
Ectopic pheochromocytoma on the left side, 131-I-MIBG
48 hours after i.v. injection,
planar images



Ectopic pheochromocytoma on the left side, 131-I-MIBG 48 hours after i.v. injection, SPECT – CT images



Liver metastasis in the left liver lobe
131-I- MIBG accumulation

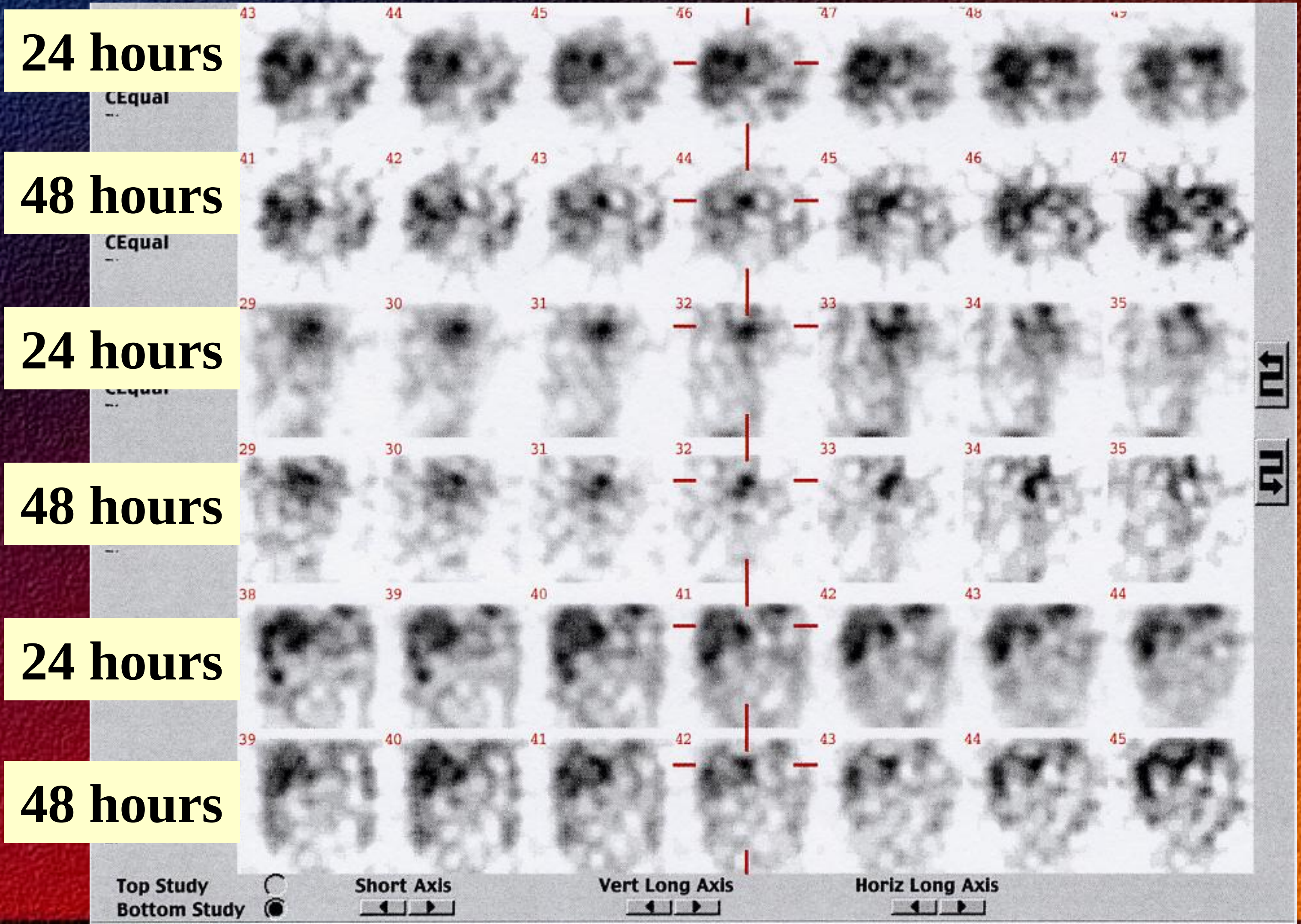


Planar images

[redacted]

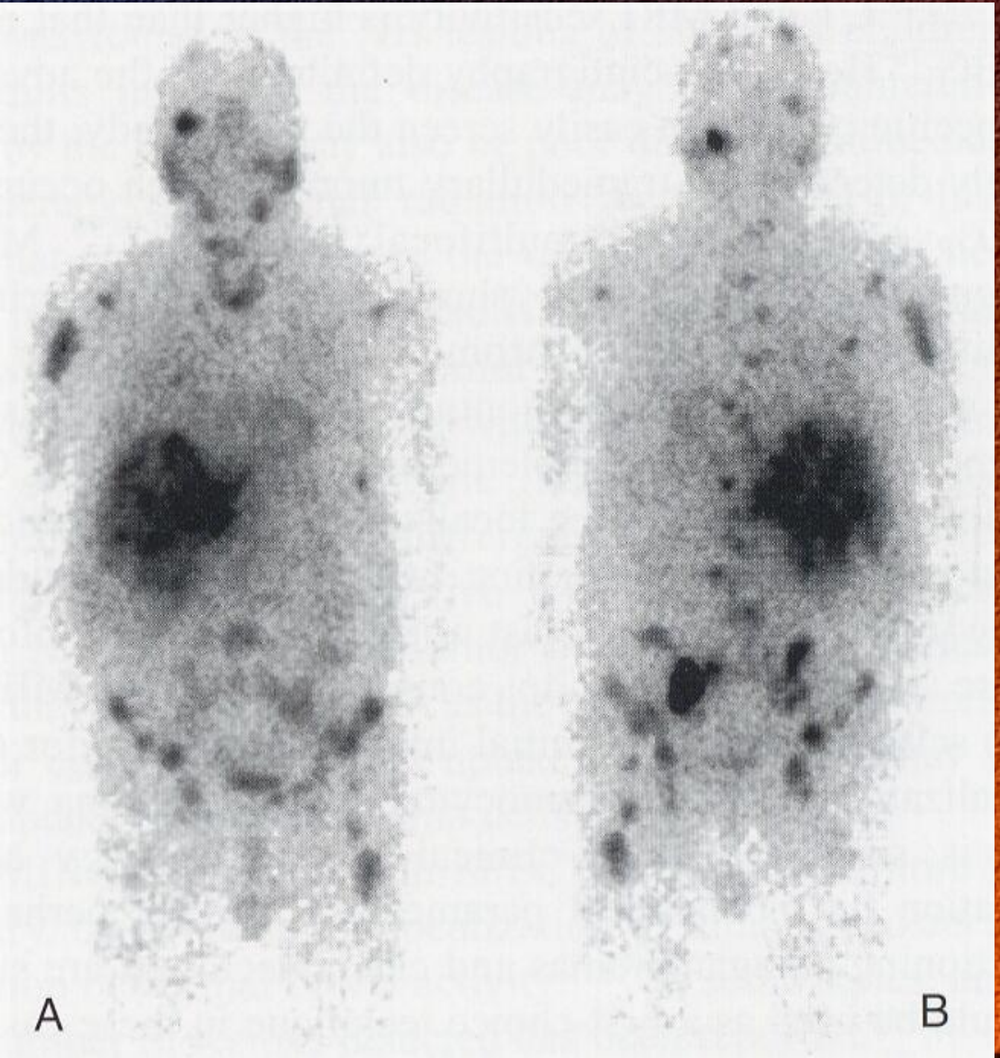
Liver metastasis in the left liver lobe
131-I- MIBG accumulation

SPECT image



123-I-MIBG accumolation in malignant pheochromocytoma

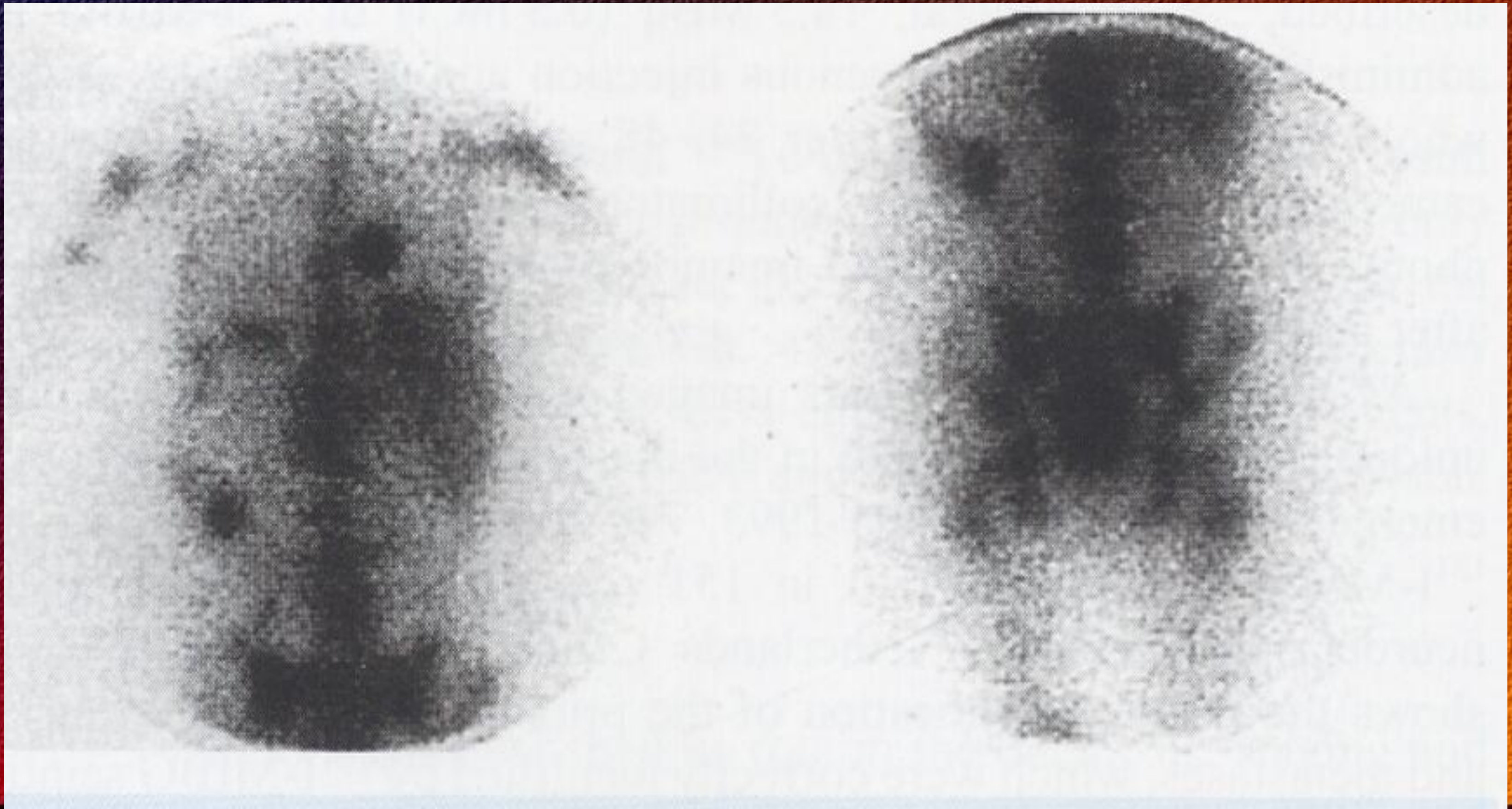
ANTERIOR



POSTERIOR

131-I-MIBG accumulation in neuroblastoma

ANTERIOR POSTERIOR

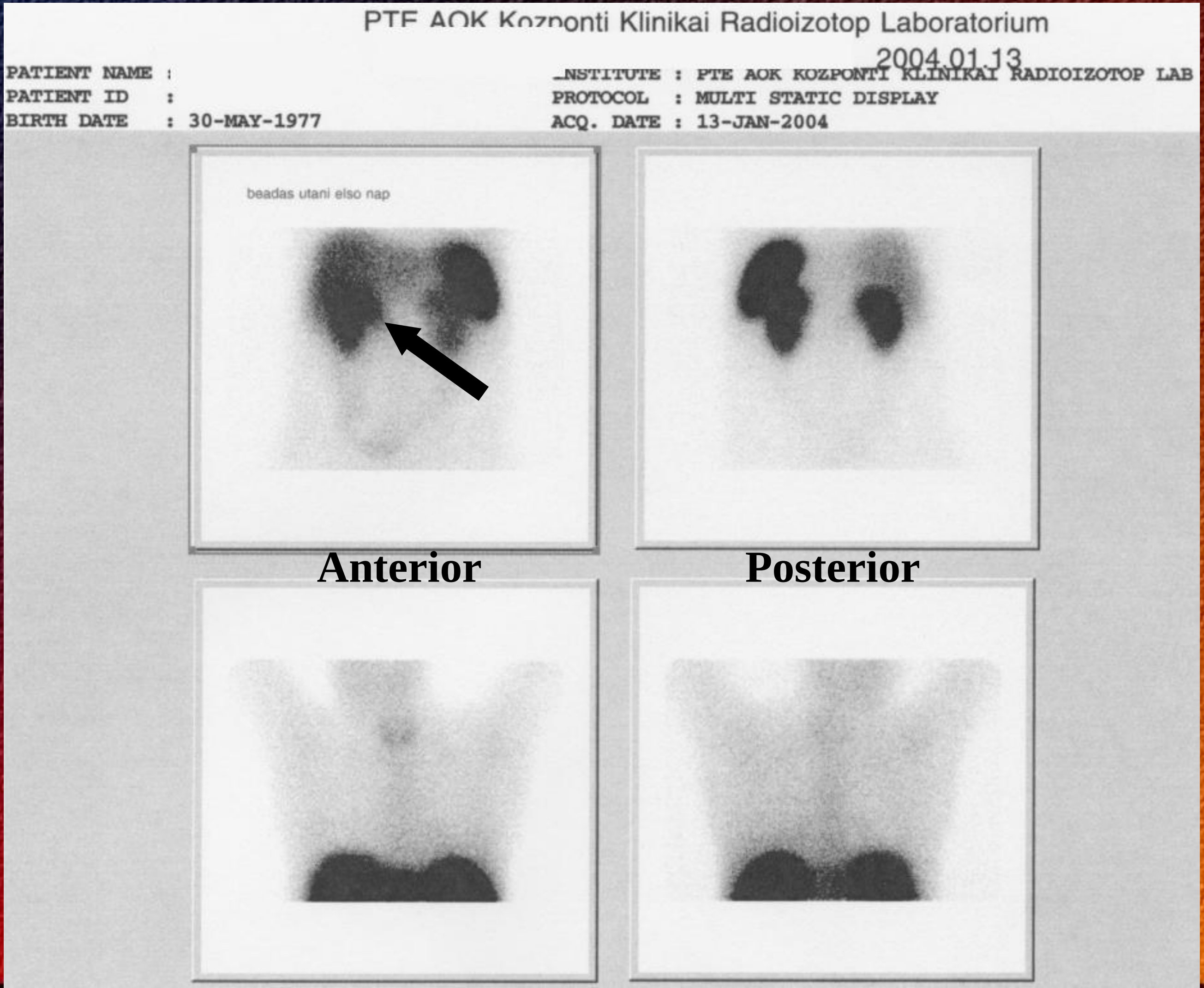


Carcinoid tumour of the pancreatic head - 111-In - Octreoscan

planar images

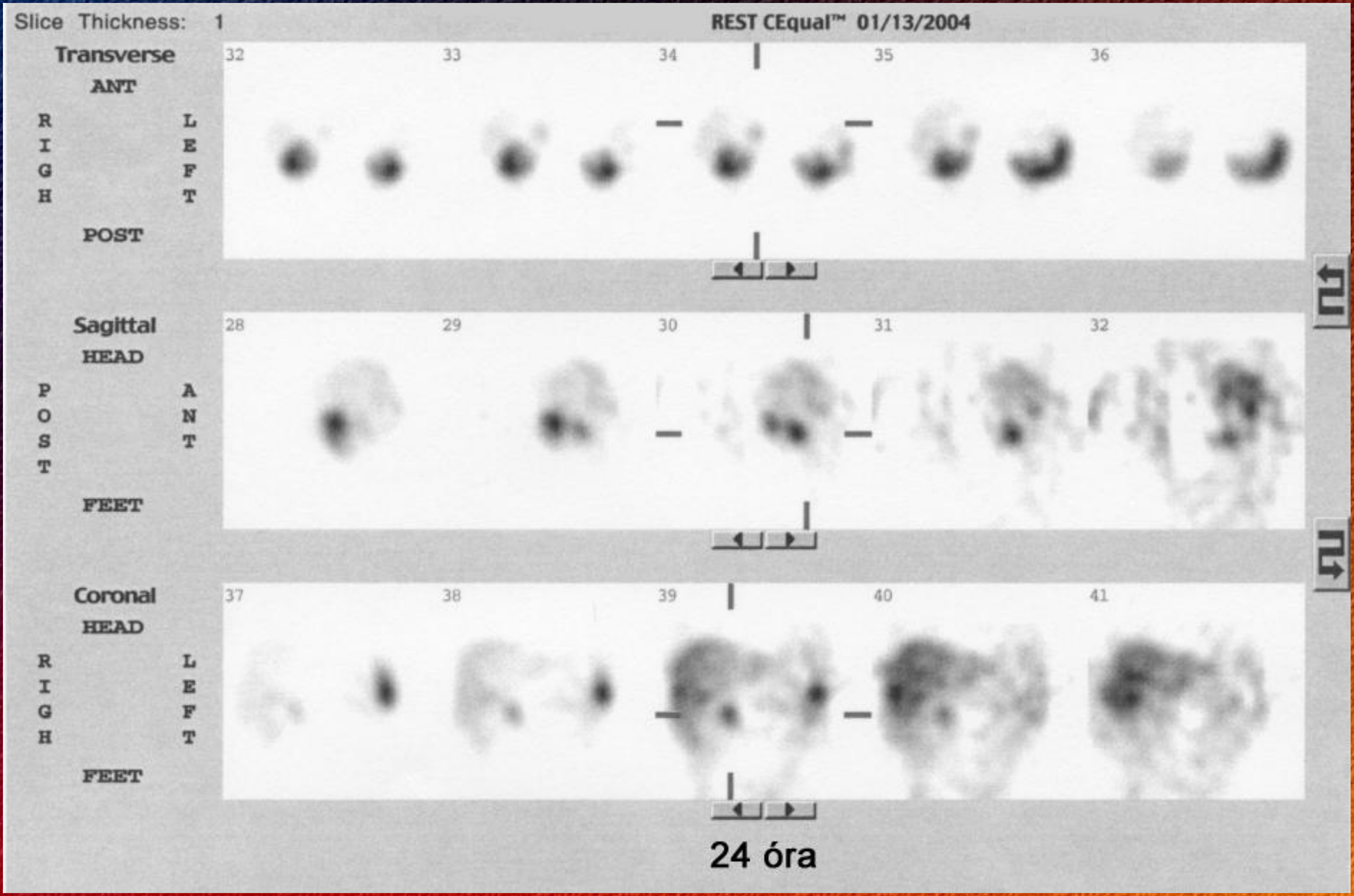
Abdomen

Chest

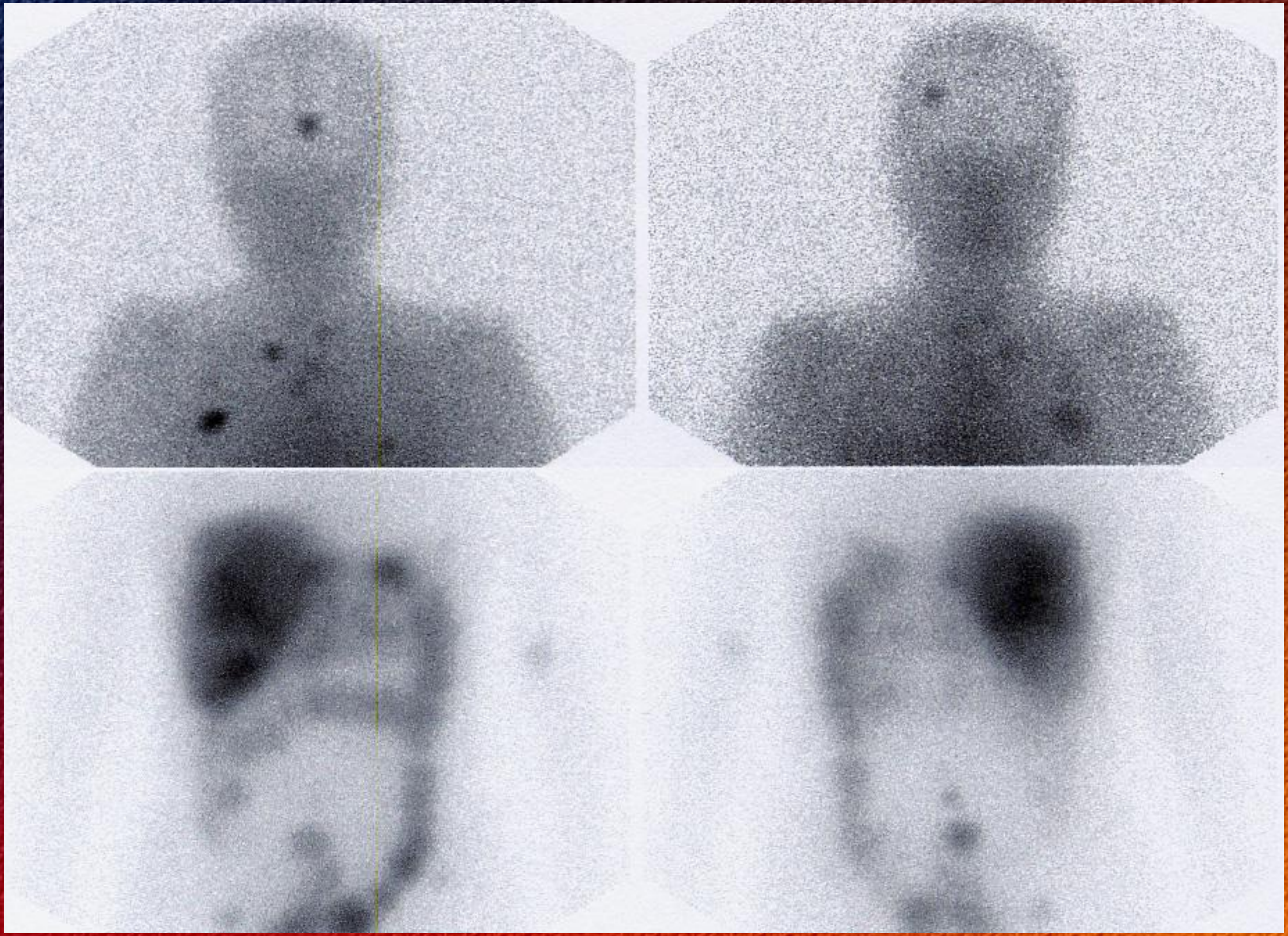


Carcinoid tumour of the pancreatic head - 111-In - Octreoscan

SPECT image



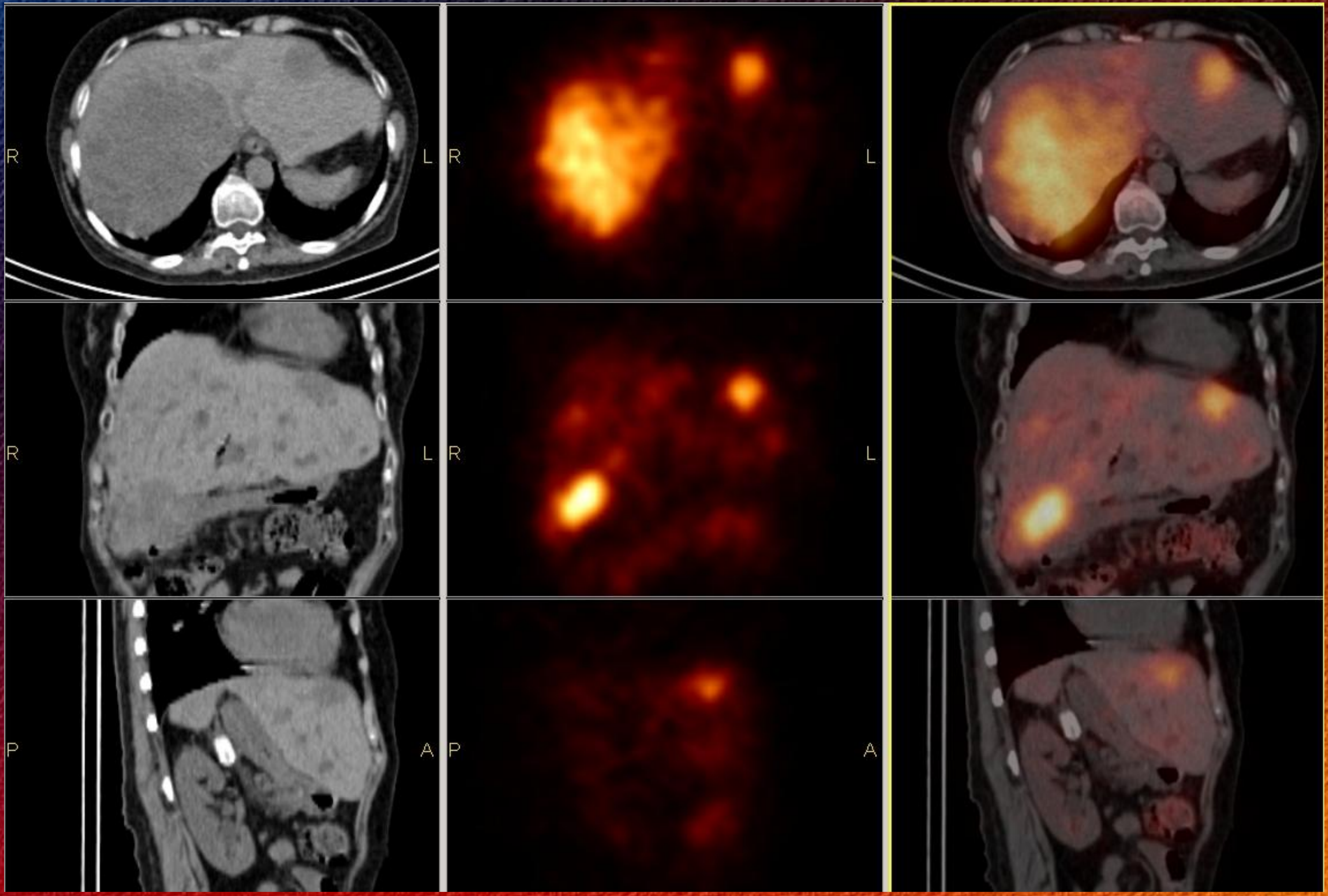
Carcinoid tumour of the pancreatic head – multiplex metastases
111-In - Octreoscan
Static images



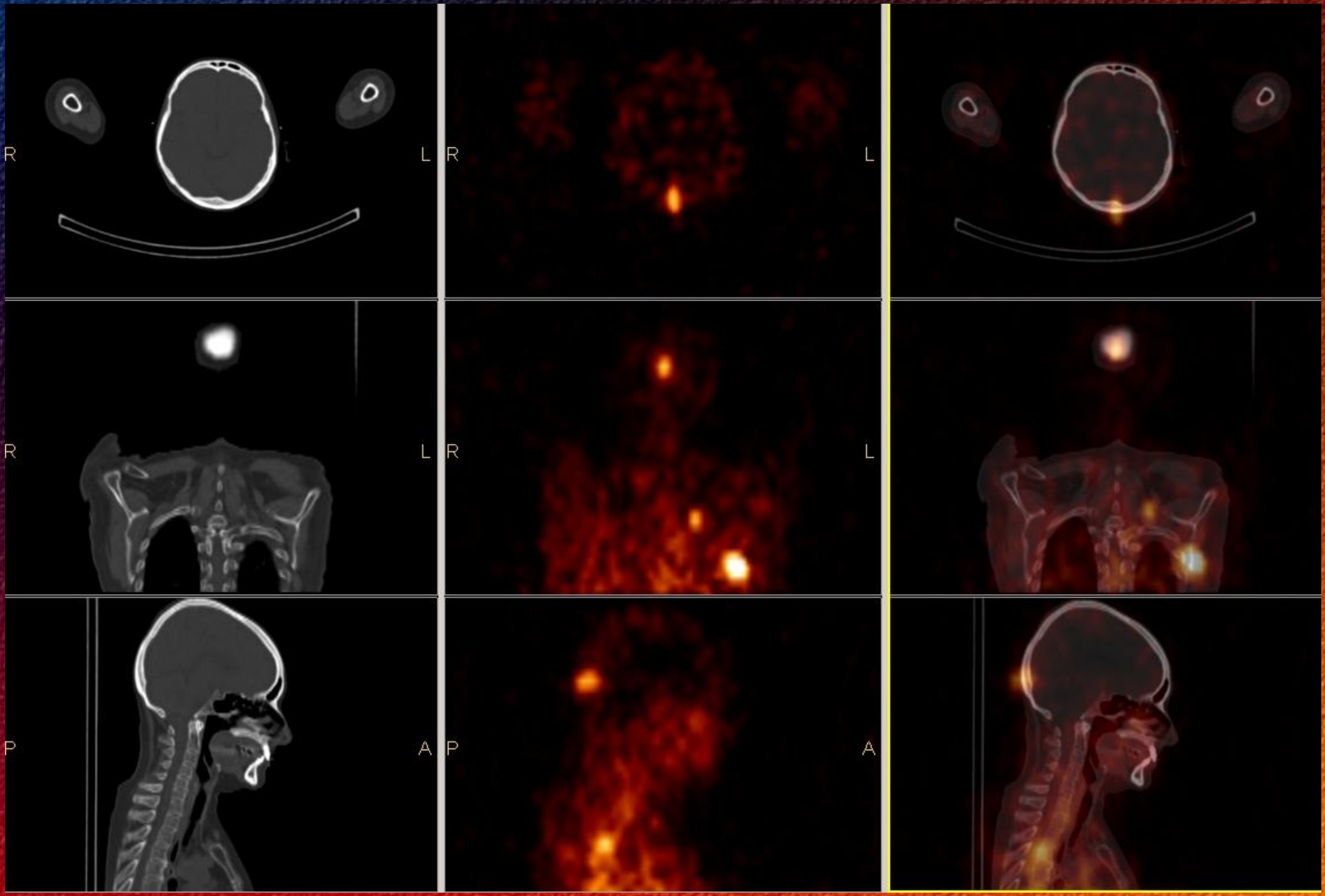
Carcinoid tumour of the pancreatic head – multiplex liver metastases

111-In - Octreoscan

SPECT -CT images



Carcinoid tumour of the pancreatic head – multiplex bone metastases
111-In - Octreoscan
SPECT -CT images

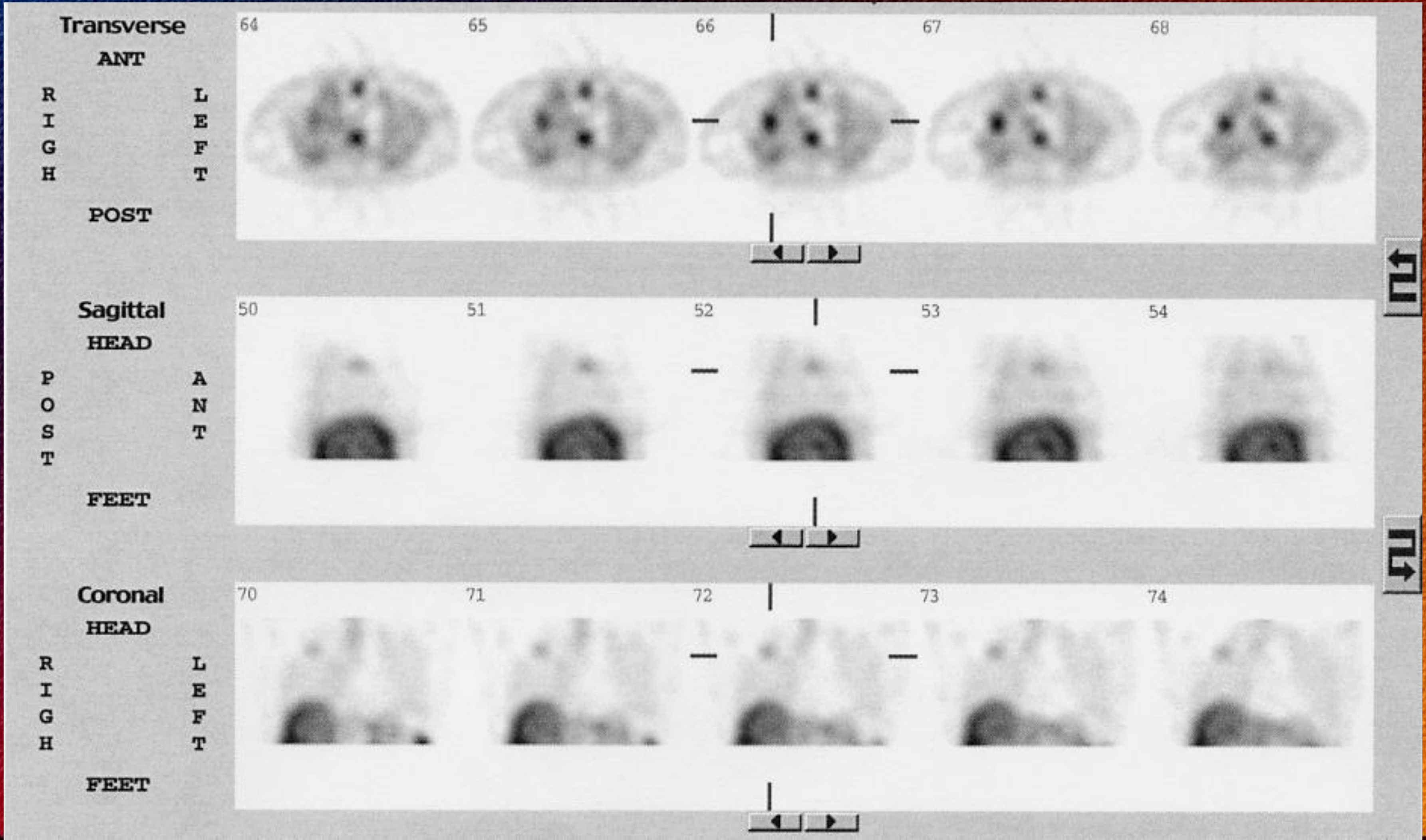


Small cell carcinoma in the right lung

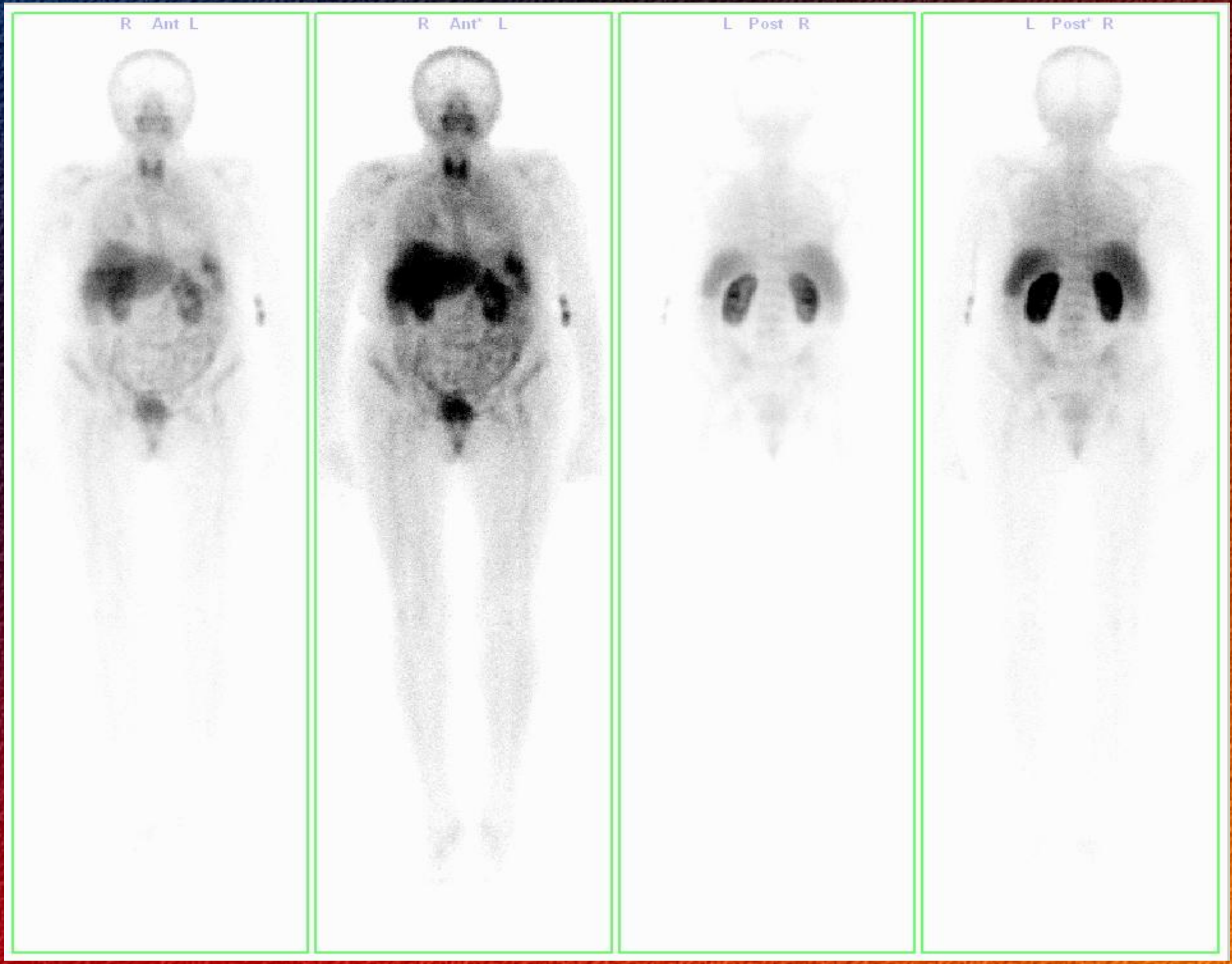
99mTc-Neospect

Whole body scan

Small cell carcinoma in the right lung
99mTc-Neospect
SPECT study

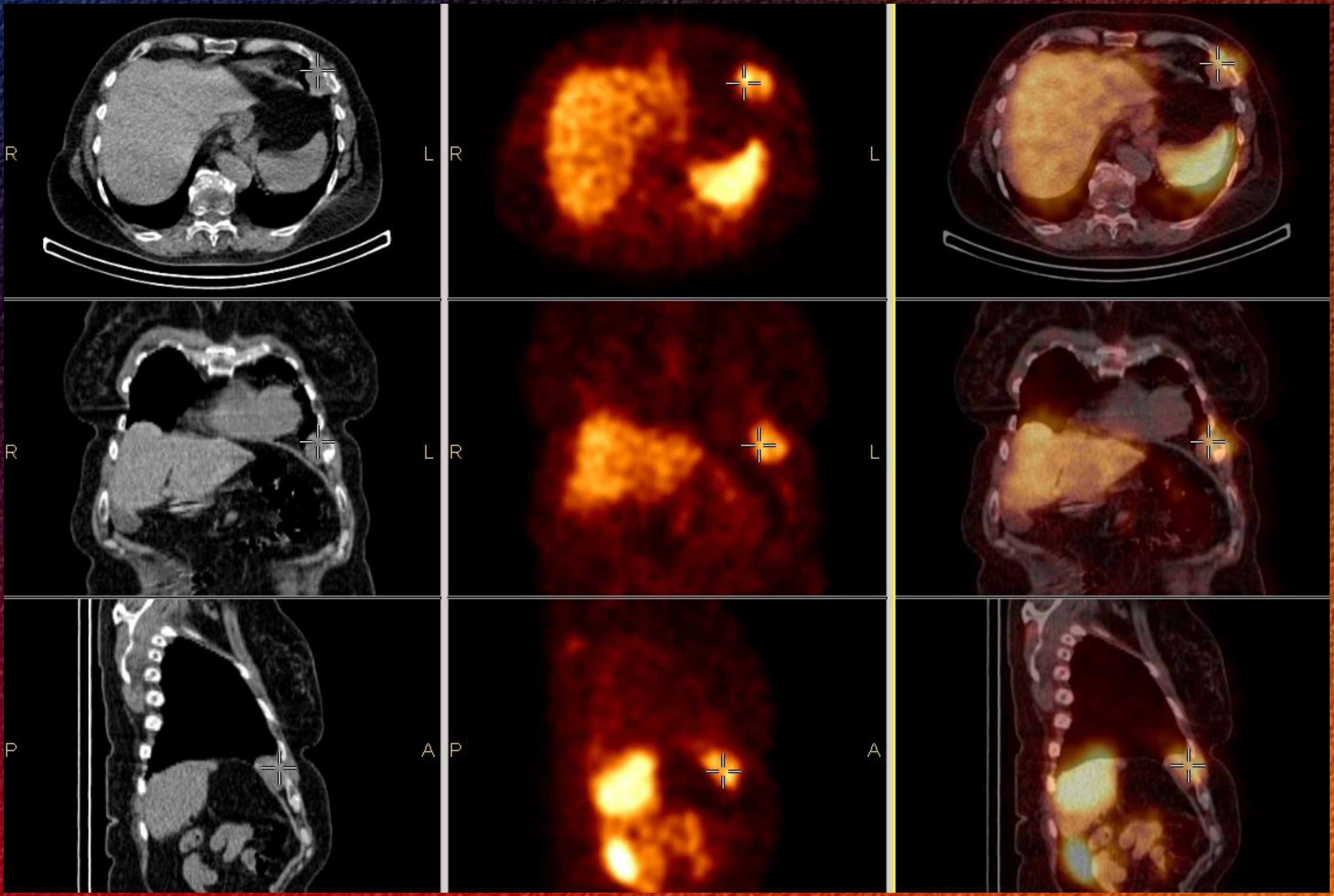


Carcinoid metastasis in chest
99mTc-Neospect
Whole body scan



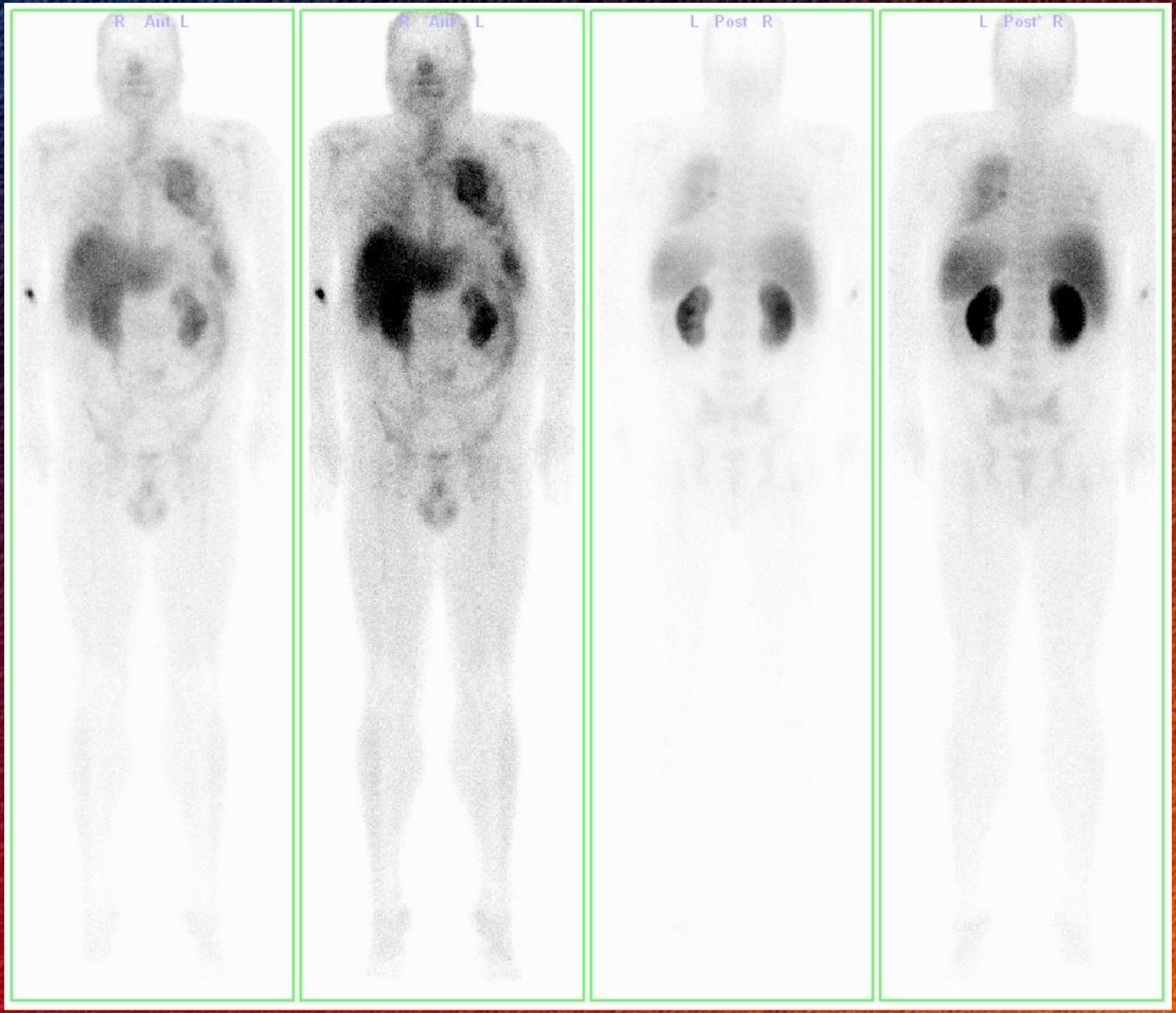
Carcinoid metastasis in chest 99mTc-Neospect

SPECT – CT images

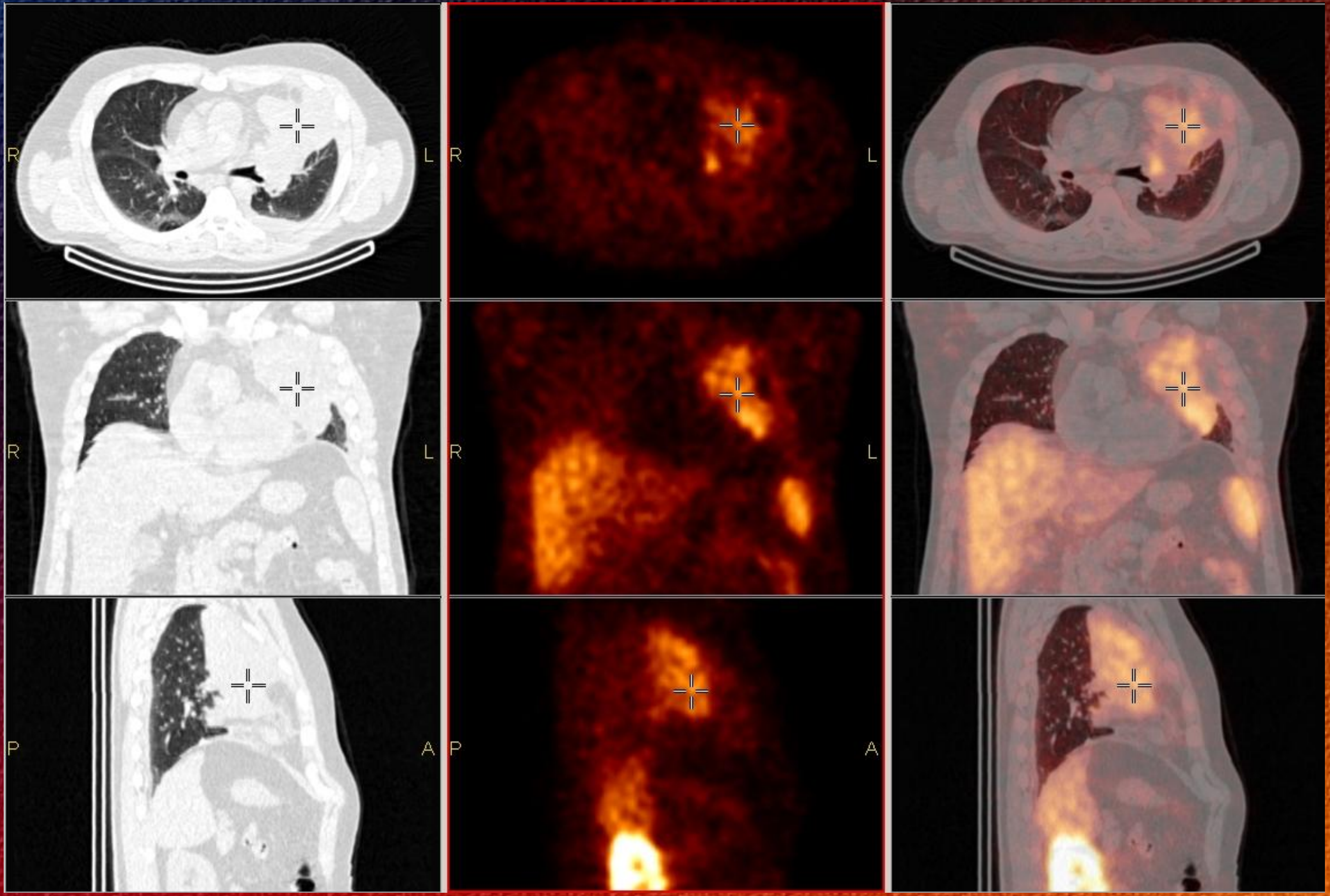


Carcinoid in left lung
99mTc-Neospect

Whole body scan

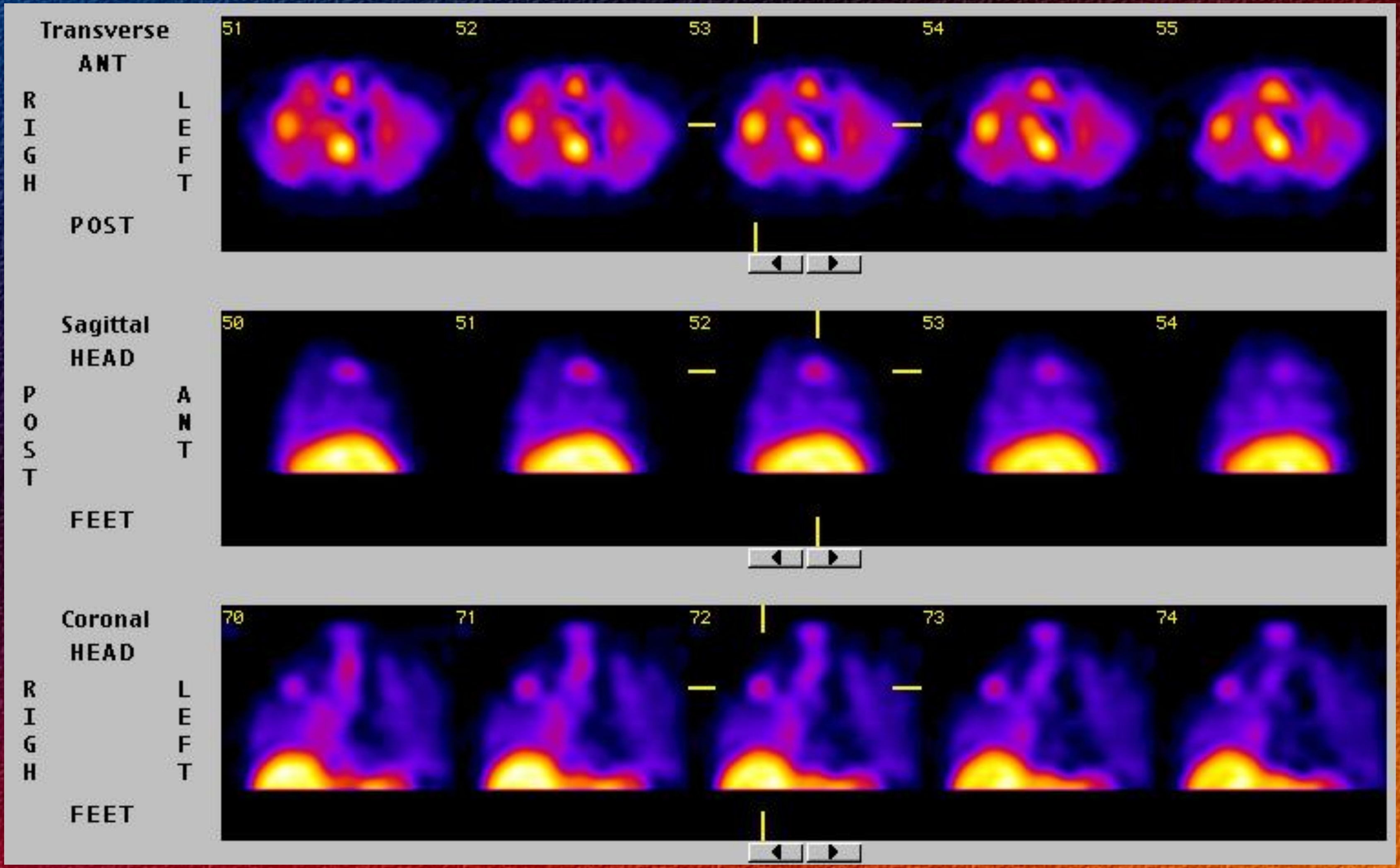


Carcinoid in left lung
99mTc-Neospect
SPECT – CT images



False positive results: sarcoidosis - 99mTc-Neospect

SPECT study



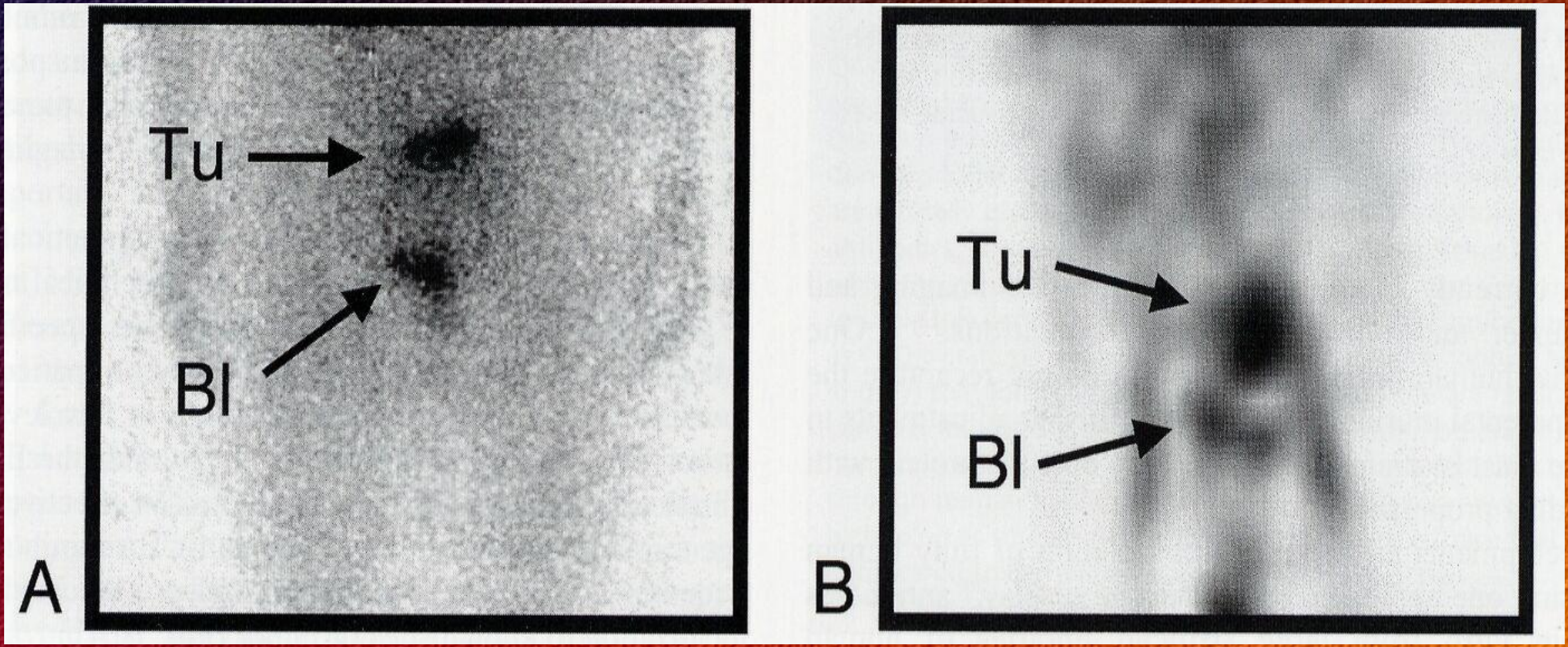
Sarcoidosis: a disease in which abnormal collections of chronic inflammatory cells (granulomas) form as nodules in multiple organs.

Immunoscintigraphy

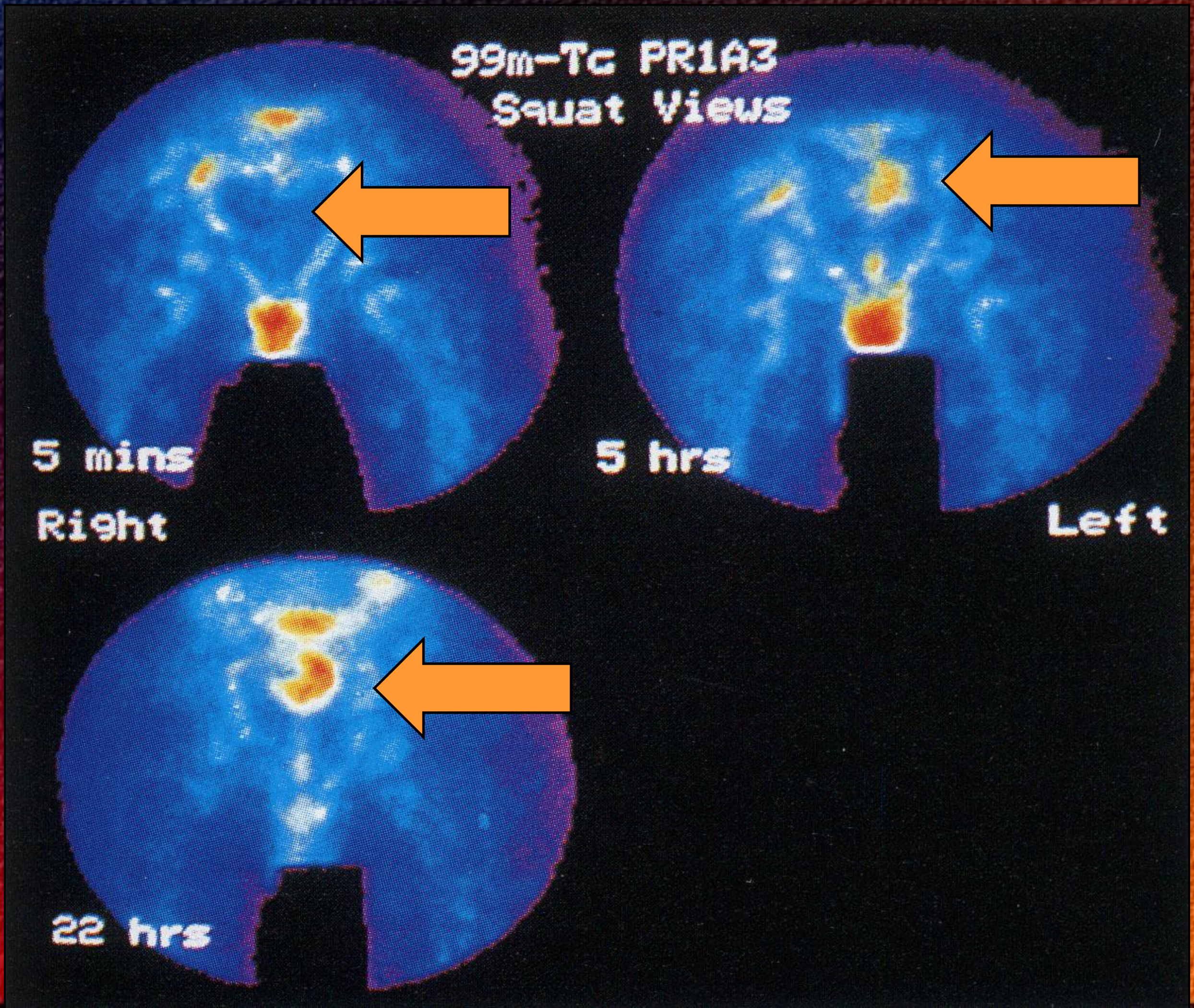
Antigen-antibody reactions (111-In- or 99m-Tc labeled antibodies against tumor specific antigens)

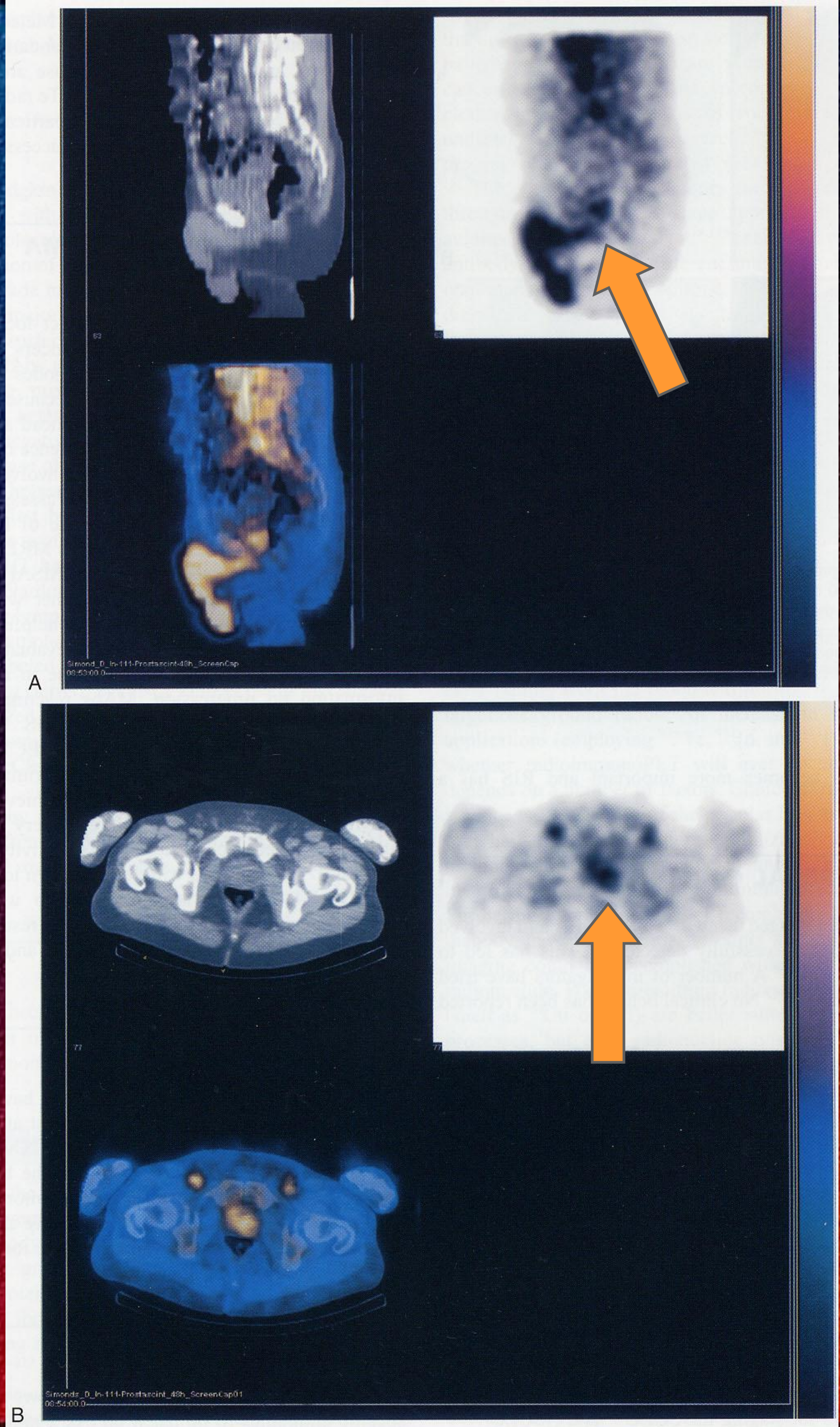
Indications: colorectal-, ovarial-, prostate carcinoma, lung tumours, melanoma malignum, lymphomas, breast cancer

Immunoscintigraphy in colorectal carcinoma
I-123 anti-CEA



Immunoscintigraphy in colorectal carcinoma 99mTc-PR1A3 fragment





Prostate cc.

In-111-Prostascint

SPECT-CT images

Therapy

Principle of radionuclid therapy

- carrying a cytotoxic agent, such as radionuclid, direct to an aberrant cell

- an alternative form of radiation treatment

- the contact between the radioactive conjugate and tumour cell enables the absorbed radiation dose to be concentrated at the site of abnormality with minimal injury to normal tissue

Therapeutical applications

- Systematic therapy:
  - oral or i.v. administration
  - Accumulation
    - intracellularly accumulation
    - cell-surface accumulation
    - extracellular accumulation
- Local therapy: directly at the tumor site
    - Intraarterial
    - Intracavital
    - Intratumoral
    - Intralymphatic

Therapeutical effect

- <u>D</u> – absorbed dose (Gy)
- <u>C</u> – activity per unit mass of tumour (MBq/gramm)
- <u>E</u> – energy emitted by the radionuclide (MeV)
- <u>Teff</u> – effektív half life

$$D \sim C \cdot E \cdot T_{eff}$$

INDIVIDUALIZED DOSE CALCULATION!!!

Radionuclides used for therapy

- β -emitters: 131-I, 89-Sr, 32-P, 186-Re, 188-Re, 90-Y, 153-Sm, 166-Ho, 169-Er, 177-Lu
- α sugárzók: 224-Ra
- Auger electron emitters:123-I, 111-In, 125-I

Special rules of radionuclide therapy

- Official licence
- Special proficiency (physicist, nuclear medicine specialist, oncologist)
- radiohygenic rules and regulations should be kept
- Information
- Isolation, if it is necessary (radiation protection)

Systematic therapy

- Thyroid cancer
- Bone metastases
- Neuroendokrin tumorok
- Non-Hodgkin lymphoma
- Polycythaema vera, essentialis thrombocythaemia

Thyroid cancer (after near total or total thyreoidectomy)

- In differenciated thyroid cancer (papillary and follicular cc.) :

  131-I therapy (oral administration):

  - For ablation 131-I is usually given in a dosage of 1.85-3.7 GBq (50-100 mCi) 4 to 6 weeks after total or near-total thyroidectomy.
  - For treatment of metastases 131I is often administered, following TSH stimulation obtained after thyroid hormone withdrawal, in a dosage of 3,7-7.4 GBq (100-200 mCi)

- Therapy possibilities in 131-I-non-avid thyroid carcinoma

  131-I-MIBG has been used for medullary thyroid cancer

  111-In-DTPAOC in Hürthle cell carcinoma, papillary thyroid carcinoma and medullary thyroid carcinoma (in experimental phase)

Systematic therapy

- Thyroid cancer
- Bone metastases
- Neuroendokrin tumorok
- Non-Hodgkin lymphoma
- Polycythaema vera, essentialis thrombocythaemia

Radionuclide therapy in bone metastases

Indication: in case of painful bone metastases of breast, prostate and small cell lung carcinomas if the combinations of non-narcotic analgesics and anti-tumor drugs are ineffective.

Aim of the radionuclide therapy is the reduction of the pain caused by bone metastases, to improve significantly the patients' quality of life and to restore their ability to move.

Essence of the therapy: Pain relief by systemic and selective ß-radiotherapy. The therapeutic effect is caused by the local energy transfer of the beta particles absorbed in the tissues of the bone metastases and the surrounding bone, hibition of production and release of pain mediators

Radionuclide therapy in bone metastases

Selection of patients

- Patients are selected on the basis of whole-body bone scintigraphy performed at least one week before the therapy.

- The most important patient selection criterion is the presence of proved multiple bone metastases associated with increased osteoblastic activity, established by the evaluation of the bone scintigram.

- A further precondition of the use of radionuclide therapy is that the laboratory test results of the patients conform to the following values:
  - Serum creatinine< 120 µmol/litre
  - Thrombocyte count> 120 × 10^9/litre
  - Leukocyte count> 3 × 10^9/litre

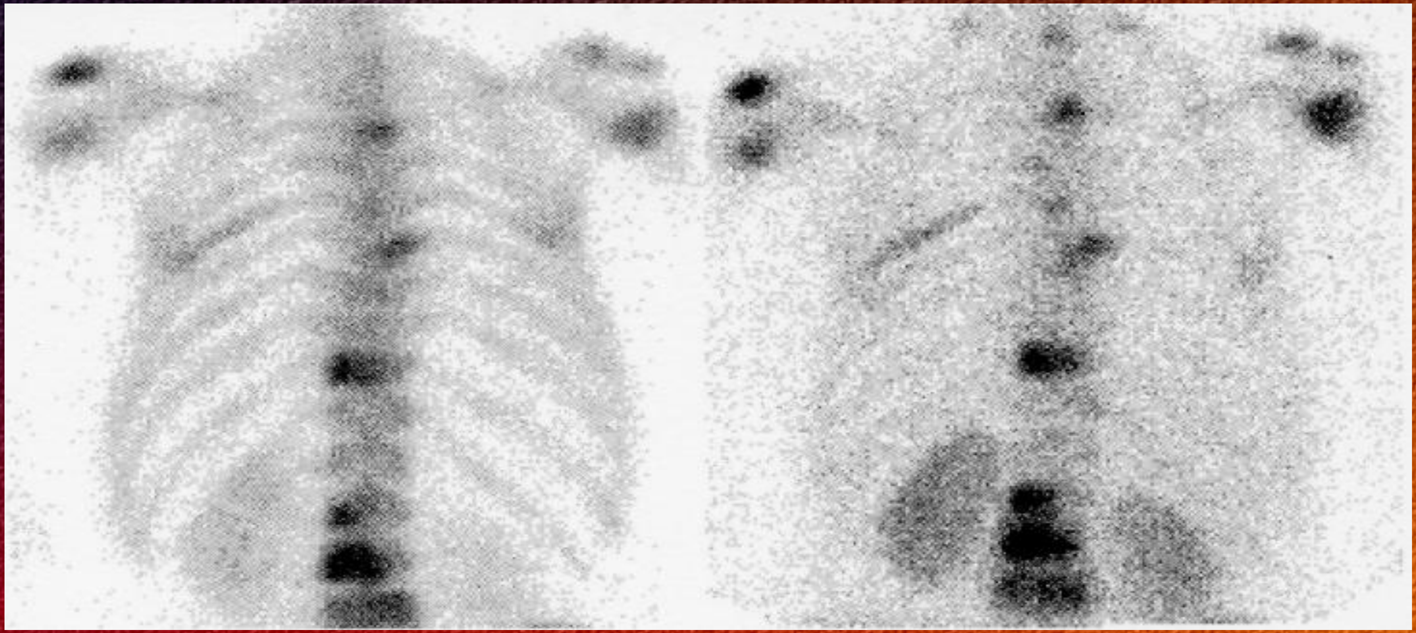
Contraindications

- Treatment is contraindicated on the basis of laboratory parameters
- in case of pregnancy and lactation.

Palliation of bone pain

(the therapautic principle is the same as in the diagnostic)

99mTc-MDP **186-Re-HEDP**



Radionuclide therapy in bone metastases

Selection of patients

- Patients are selected on the basis of whole-body bone scintigraphy performed at least one week before the therapy.

- The most important patient selection criterion is the presence of proved multiple bone metastases associated with increased osteoblastic activity, established by the evaluation of the bone scintigram.

- A further precondition of the use of radionuclide therapy is that the laboratory test results of the patients conform to the following values:
  - Serum creatinine < 120 μmol/litre
  - Thrombocyte count $> 120 \times 10^9$/litre
  - Leukocyte count $> 3 \times 10^9$/litre

Contraindications

- Treatment is contraindicated on the basis of laboratory parameters
- in case of pregnancy and lactation.

Radiopharmaceuticals for palliative bone therapy

Radionuclide	89-Sr	90-Y	186-Re	153-Sm
Half life (days)	50,5	2,675	3,77	1,95
E max (β) (MeV)	1,46	2,25	1,07	0,81
Max. range in tissue (mm)	8	12	5	3
γ-energia (Kev)	-	-	137	103
Pharmaceutical	klorid	EDTMP	HEDP	EDTMP
Product	Metastron	Multibone	Osteopal-R Diphoter-R	Multibone
Administered activity (MBq)	150	400	1300-2600	1300
Therapeutic effect (months)	6-9	3-4	3-4	3-4

Systematic therapy

- Thyroid cancer
- Bone metastases
- Neuroendokrin tumorok
- Non-Hodgkin lymphoma
- Polycythaema vera, essentialis thrombocythaemia

Neuroendokrin tumours I.
131-I-MIBG therapy

The therapautic principle is the same as in the diagnostic:

- noradrenaline analogous

- 131-I-MIBG is taken up actively by cell membranes and then stored by neurosecretory cytoplasmic granules in neuroendocrine tumors, e.g. pheochromocytoma, neuroblastoma.

•

Neuroendokrin tumours I.
131-I-MIBG therapy

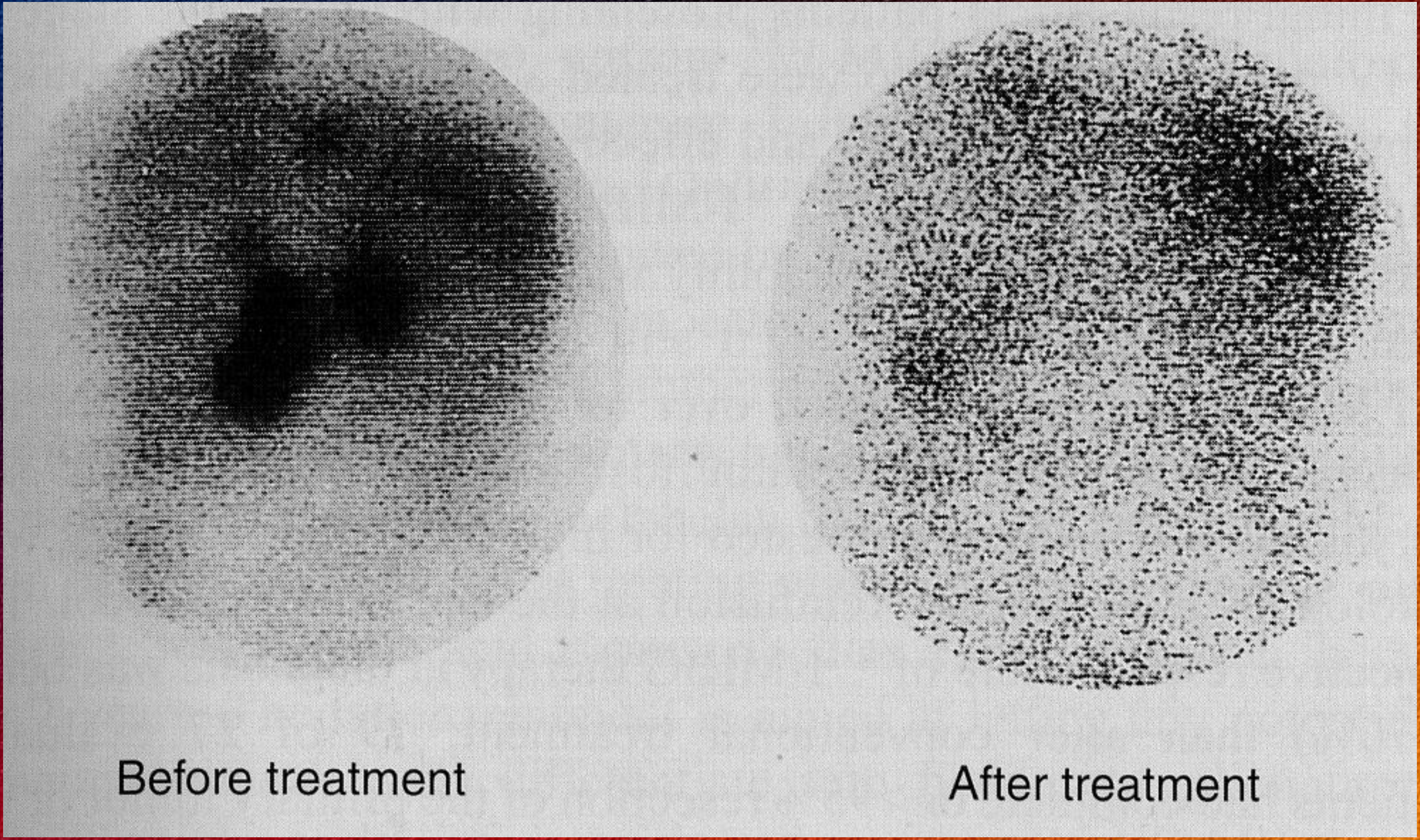
- **Indications:** **late-stage, therapy resistant tumours**
  - **Malignant pheochromocytoma (inoperable, multiplex metastases)**
  - **Neuroblastoma III.-VI. stage**
  - **Malignant paraganglioma**
  - **Medullary thyroid cancer**
  - **Metastatic carcinoid tumours**

- **Kontraindications:**
  - **severe myelosuppression**
  - **impairment of renal function**
  - **pregnancy**
  - **Breast-feeding**

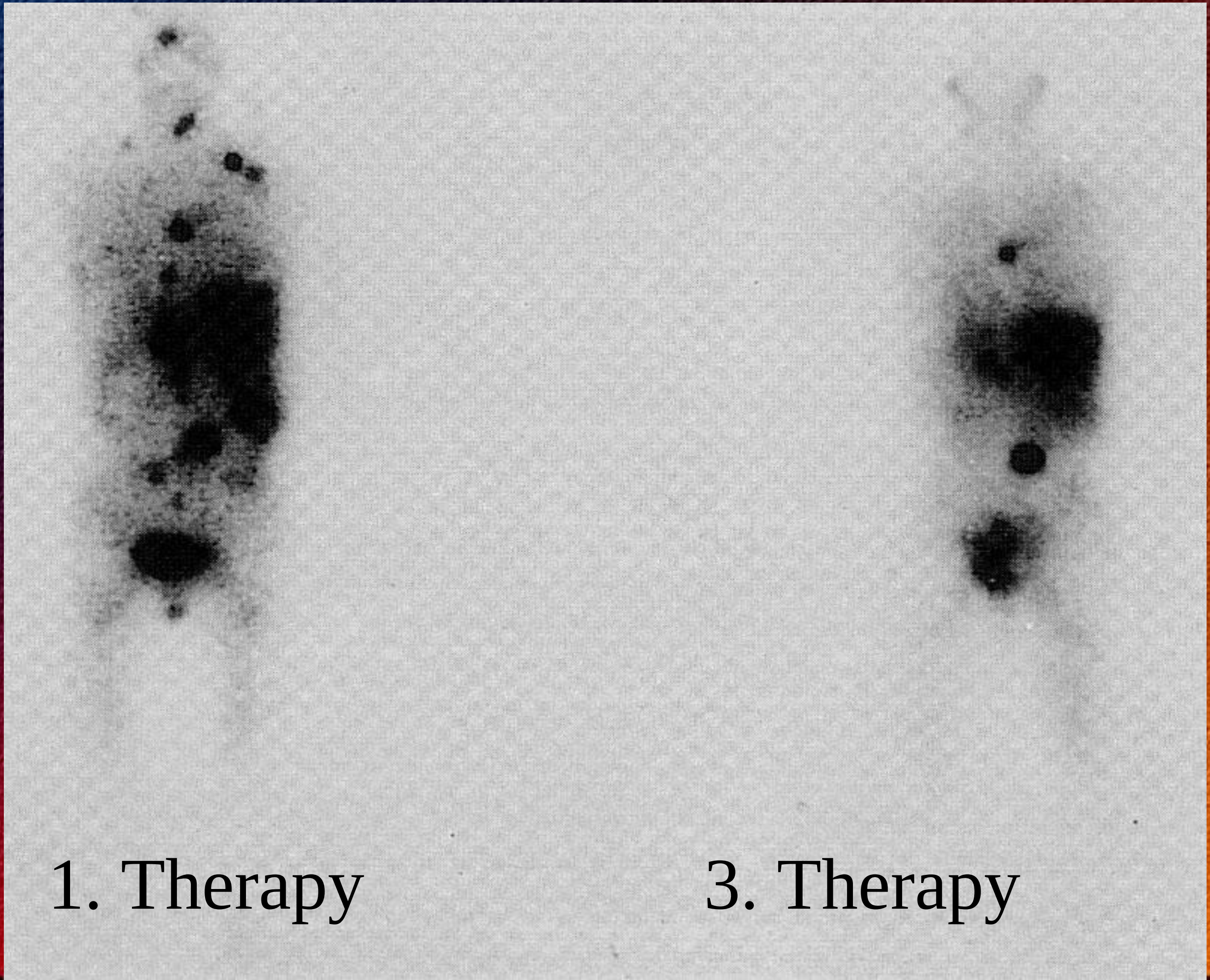
Neuroendokrin tumours I.
131-I-MIBG therapy

- **Implementation of therapy**
  - **Preparation of the patient:**
    - **Before therapy diagnostic image**
    - **leaving drug therapy, which block the MIBG uptake 2 weeks before the planned therapy (α-blockers, Ca-antagonists, tricikl. antidepr., sympathomimetics)**
    - **Blockade of thyroid (Lugol's and perchlorate)**
  - **Administration of the radiopharmaceutical:**
    - **Dose: 3,7-11,1 GBq 131-I-MIBG**
    - **Slow infusion (4 hours) – hazard of hypertensive crisis!**
    - **Isolation for a few days**
    - **Possibility of repetition after 4 weeks**

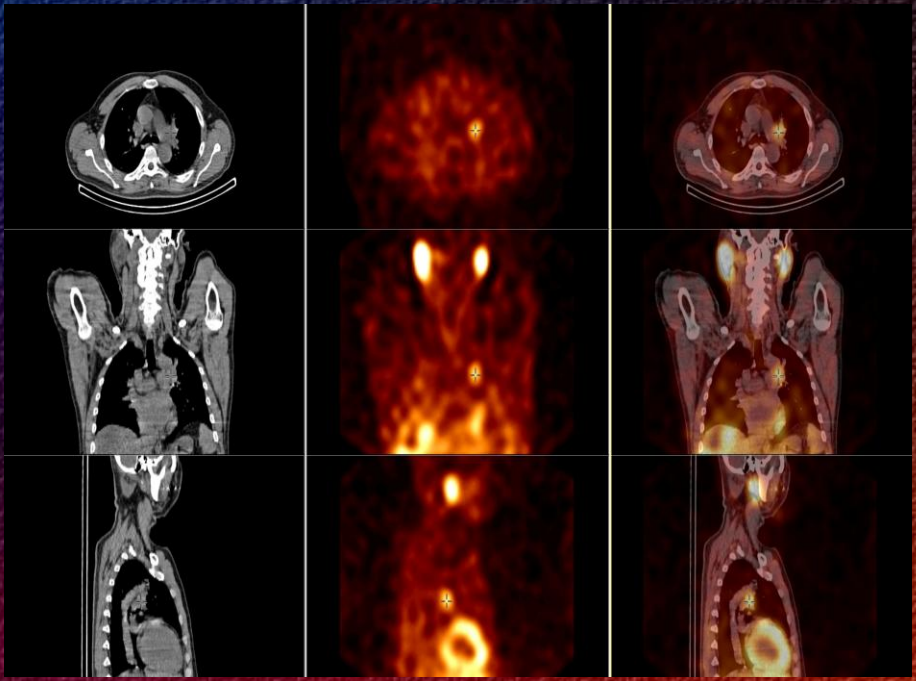
Regression of neuroblastoma after 131-I-MIBG therapy

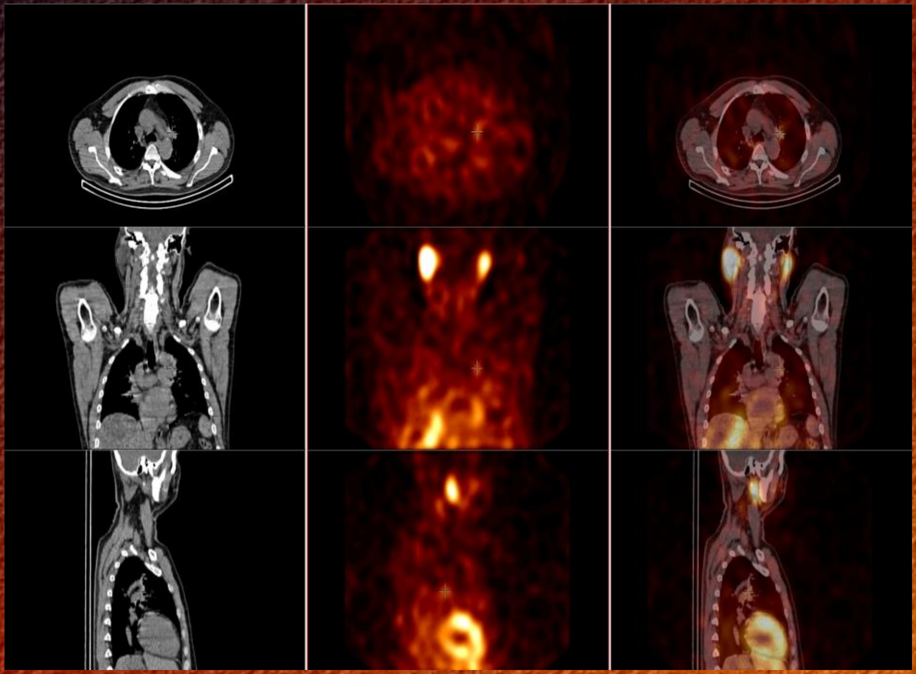


Partial regression of malignant paraganglioma after 131-I-MIBG therapy



Partial regression of metastatatic carcinoid after 131-I-MIBG therapy

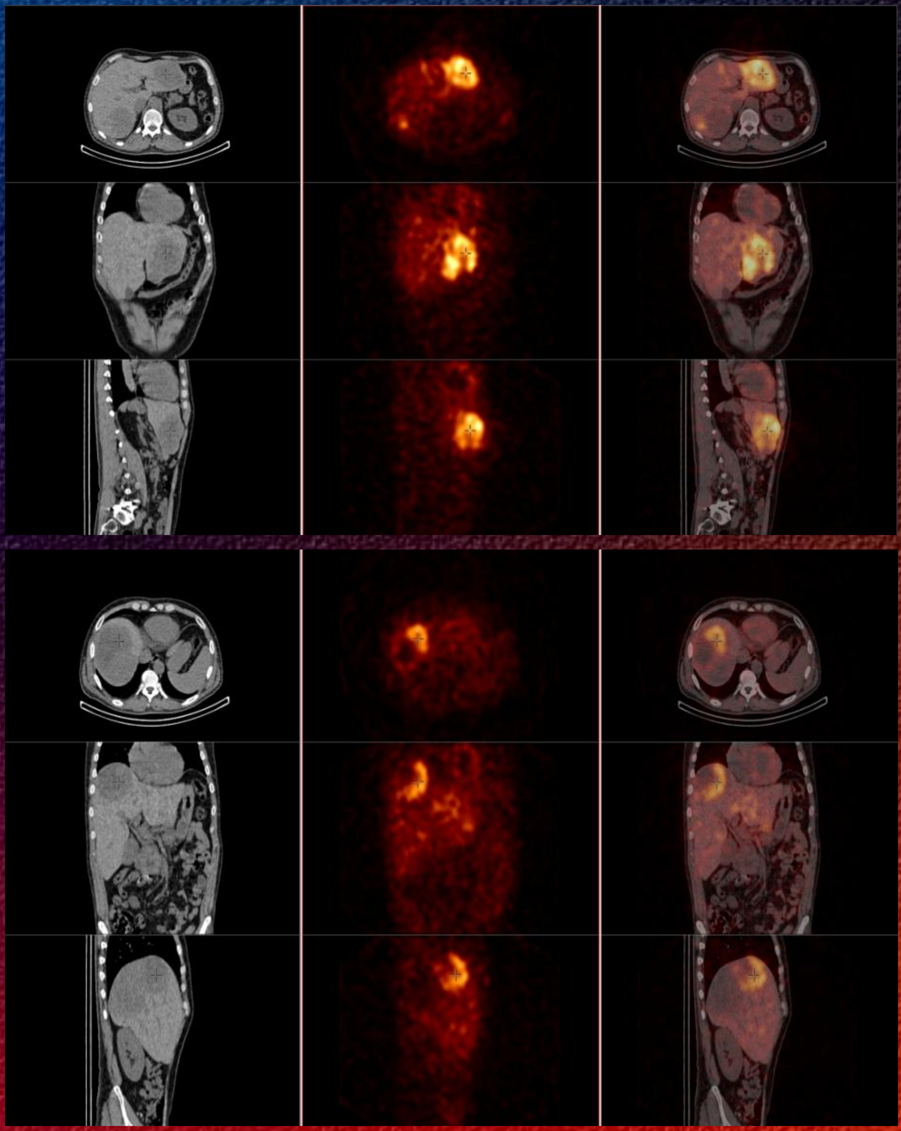




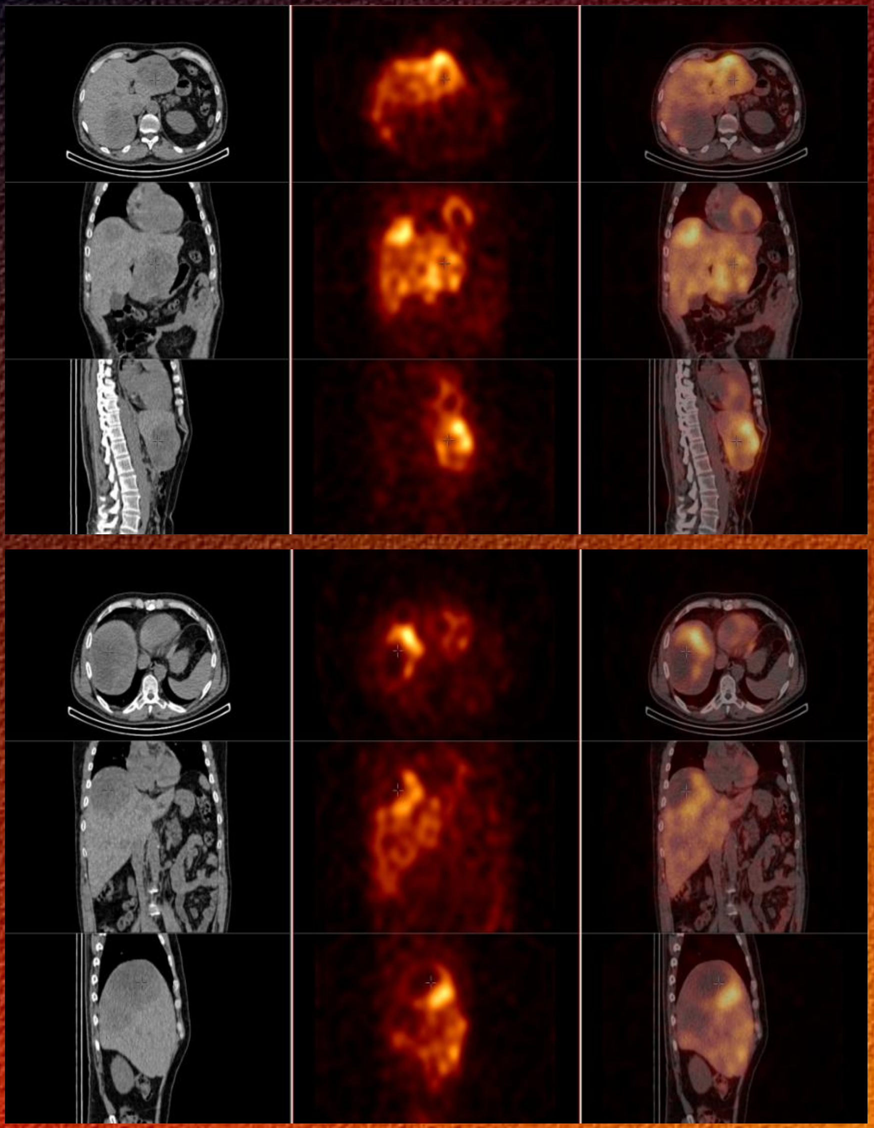
Before therapy

After therapy

Partial regression of metastatatic carcinoid after 131-I-MIBG therapy



Before therapy



After therapy

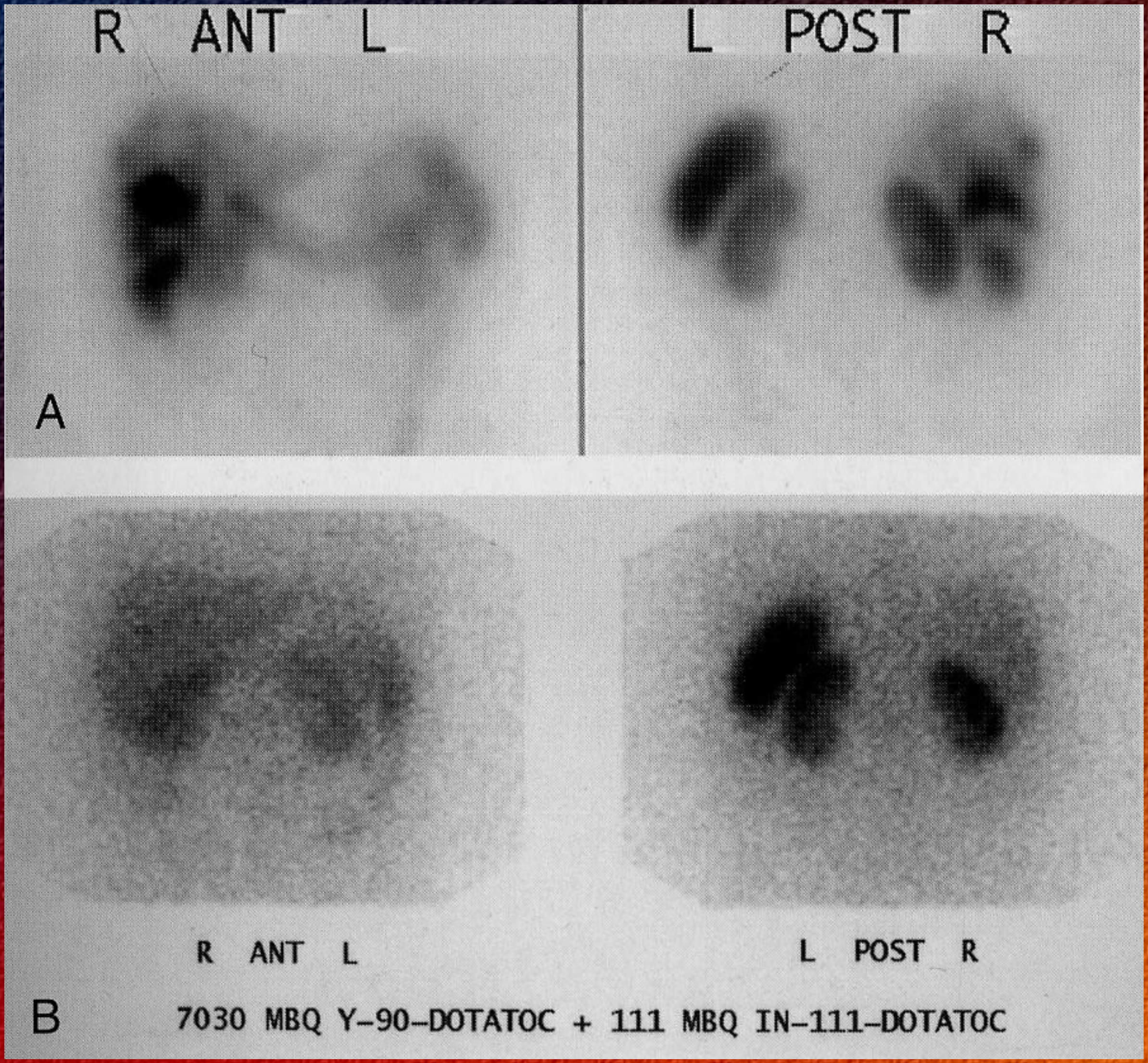
Neuroendokrine tumours II.
somatostatin analogous peptides
(111-In-DTPA-Octreotid, 90-Y-DOTATOC, 90-Y-lanreotid, 177-Lu-DOTA Tyr3-Octreotid)

- The therapautic principle is the same as in the diagnostic: somatostatin analogues bind to somatostatin cell surface receptors;

- Indications: neuroendokrine tumours (malignant carcinoid, pheochromocytoma, paraganglioma)

- Side effects: nephrotoxicity, myelosuppression, emesis

Regression of neuroendocrine tumour after 90-Y-DOTADOC therapy



Systematic therapy

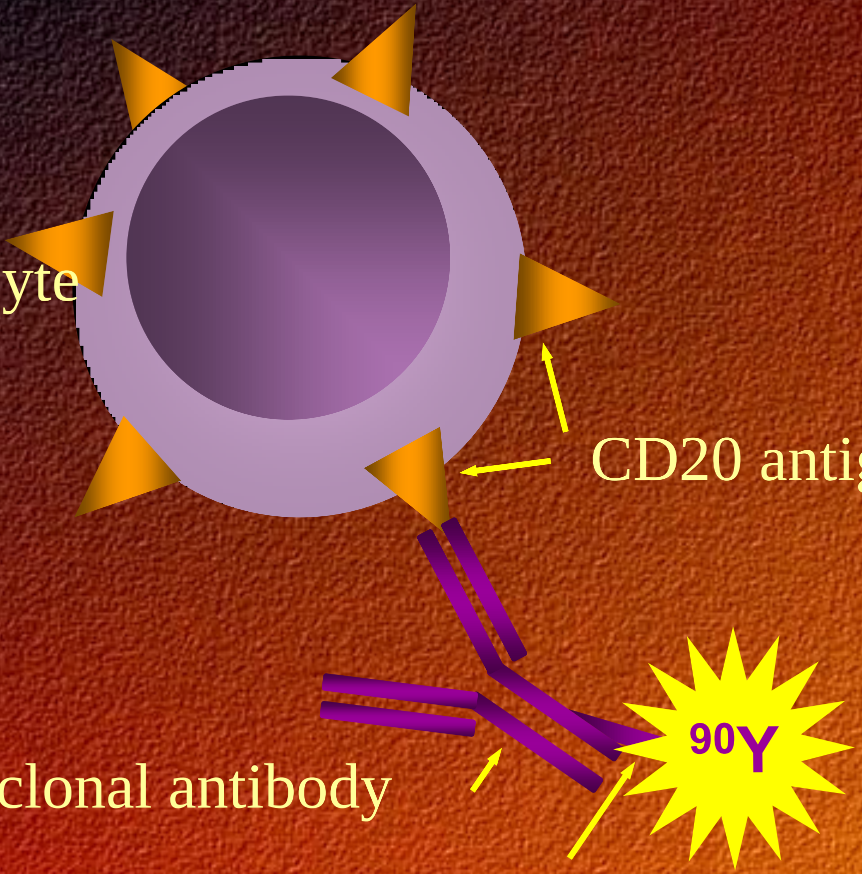
- Thyroid cancer
- Bone metastases
- Neuroendokrin tumorok
- Non-Hodgkin lymphoma
- Polycythaema vera, essentialis thrombocythaemia

Non-Hodgkin lymphoma

- **Radiopharmaceuticals:**
  - **90-Y-antiCD20 monoclonal antibody (Zevalin)**
  - **131-J-antiCD20 monoclonal antibody (Bexxar)**

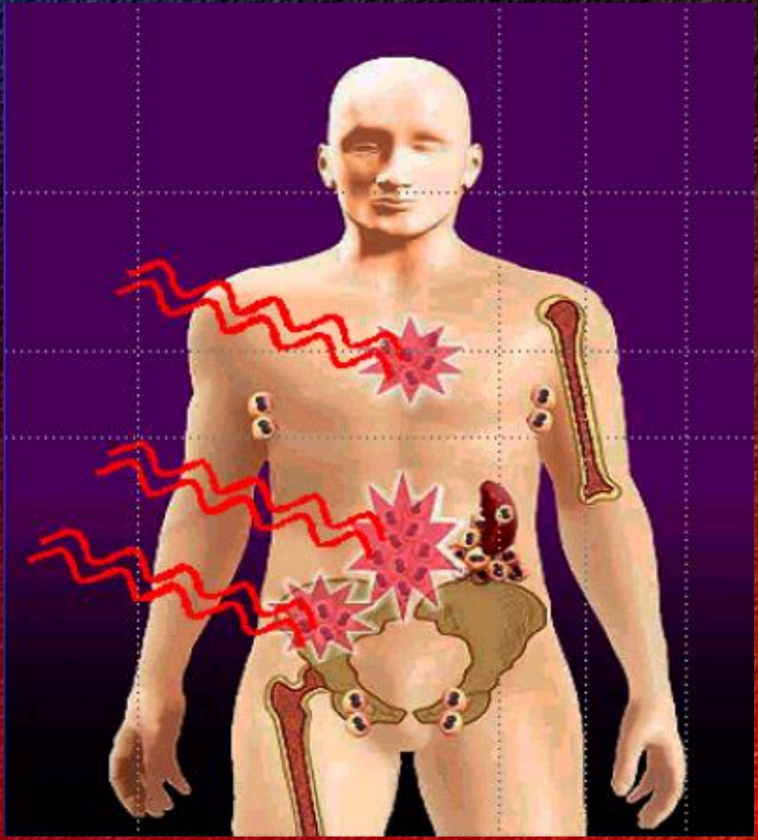
- **The therapautic principle: immunotherapy, antigen-antibody reaction**

Immunotherapy - mechanism of action

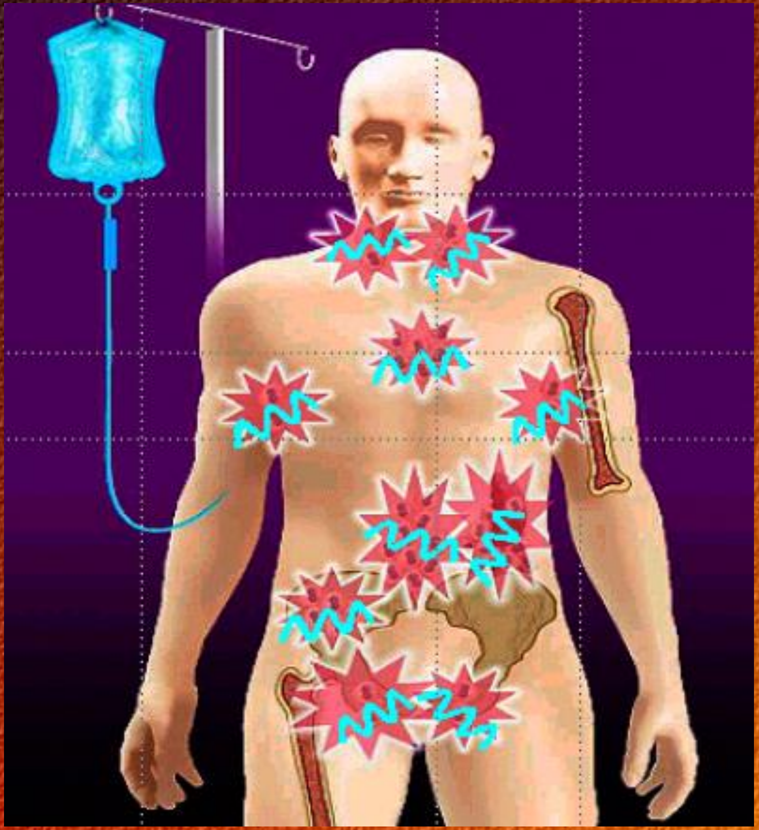


Immunotherapy - mechanism of action

Irradiation



Immunotherapy



Non-Hodgkin lymphoma

- **Indication:**

  The [90Y]-radiolabelled Zevalin is indicated for the treatment of adult patients with rituximab relapsed or refractory CD20+ follicular B-cell non-Hodgkin's lymphoma (NHL).

- **Potency:** **75% of patients**

Non-Hodgkin lymphoma – regression after Zevalin therapy

FDG-PET

Before therapy

After therapy

Systematic therapy

- Thyroid cancer
- Bone metastases
- Neuroendokrin tumorok
- Non-Hodgkin lymphoma
- Polycythaema vera, essentialis thrombocythaemia

Polycythaema vera, essential thrombocythaemia

- **Radiopharmaceutical:** 32-P (β-emitter, Emax 1,71 MeV, T1/2 14,3 days)
- **The therapautic principle:** After intravenous administration of a 120- to 185-MBq dose, 32P sodium phosphate concentrates in blood cell precursors and destroys or damages cell production functions.
- **Indications:** myeloproliferative diseases, polycythaemia vera, essential thrombocythaemia
- **Side effect:** myelosuppression,

Local therapy

- **Intraarterial**
- **Intracavital**
- **Intratumoral**
- **Intralymphatic**

Local therapy

- **Intraarterial administration: e.g. hepatocellular carcinoma (Inoperable tumour, liver transplantation contraindicated)**
- **Radiopharmaceutical:**
  - **131-I-lipiodol**
  - **90-Y-microsphaera**
  - **166-Ho-microsphaera**
- **Advantages:**
  - **Available in multifocal tumours**
  - **good tumor. regression**

Local therapy

- Intraarterial
- Intracavital
- Intratumoral
- Intralymphatic

Local therapy

- **Intracavital administration**
  - **intraperitoneal**
  - **intrapleural**
- **Radiopharmaceuticals:**
  - **90-Y-colloid,**
  - **32-P**
  - **labelled monoclonal antibodies**
- **Indications:**
  - **carcinosis peritonei**
  - **carcinosis pleurae ,**

Local therapy

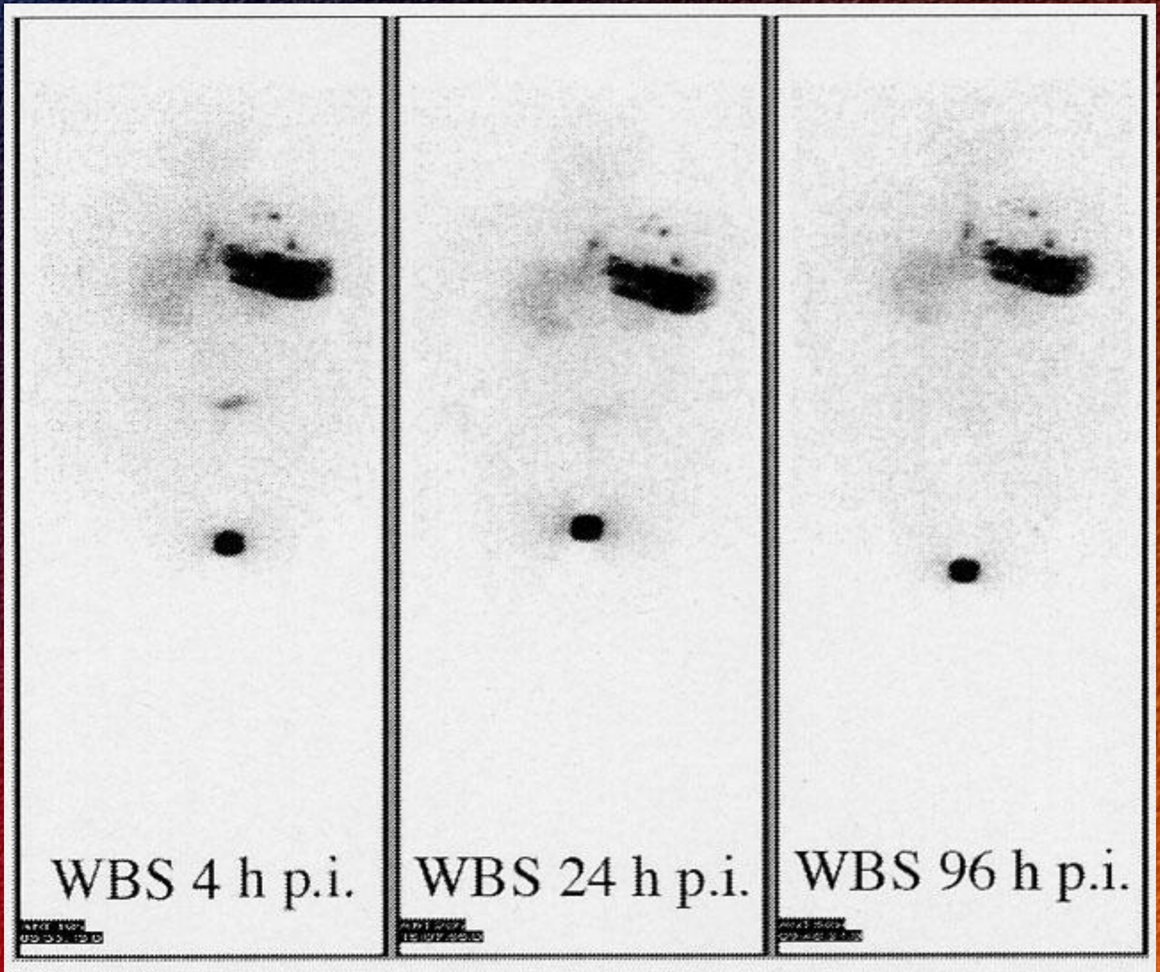
- **Intraarterial**
- **Intracavital**
- **Intratumoral**
- **Intralymphatic**

Local therapy

- Intratumoral administration:
  E.g. brain tumours (astrocytoma, craniopharingeoma)
  - Administration : using stereotaxis
  - Radiopharmaceutical: 90-Y-kolloid,

  E.g. in postoperative therapy of breast tumours:
  - local injected avidin,
  - later i.v. injected labelled biotin (90-Y, 177-Lu)

Intraoperative radionuclide therapy of breast tumour



Local therapy

- Intraarterial
- Intracavital
- Intratumoral
- Intralymphatic

Local therapy

- **Intralymphatic administration: together with rtg lymphography, (32-P-Tri-n-octyl- phosphat) the radiopharmaceutical accumulates in the lymph nodes, effects local radiation**
- **Indications: e.g. melanoma malignum of the limbs with lymph node metastases**

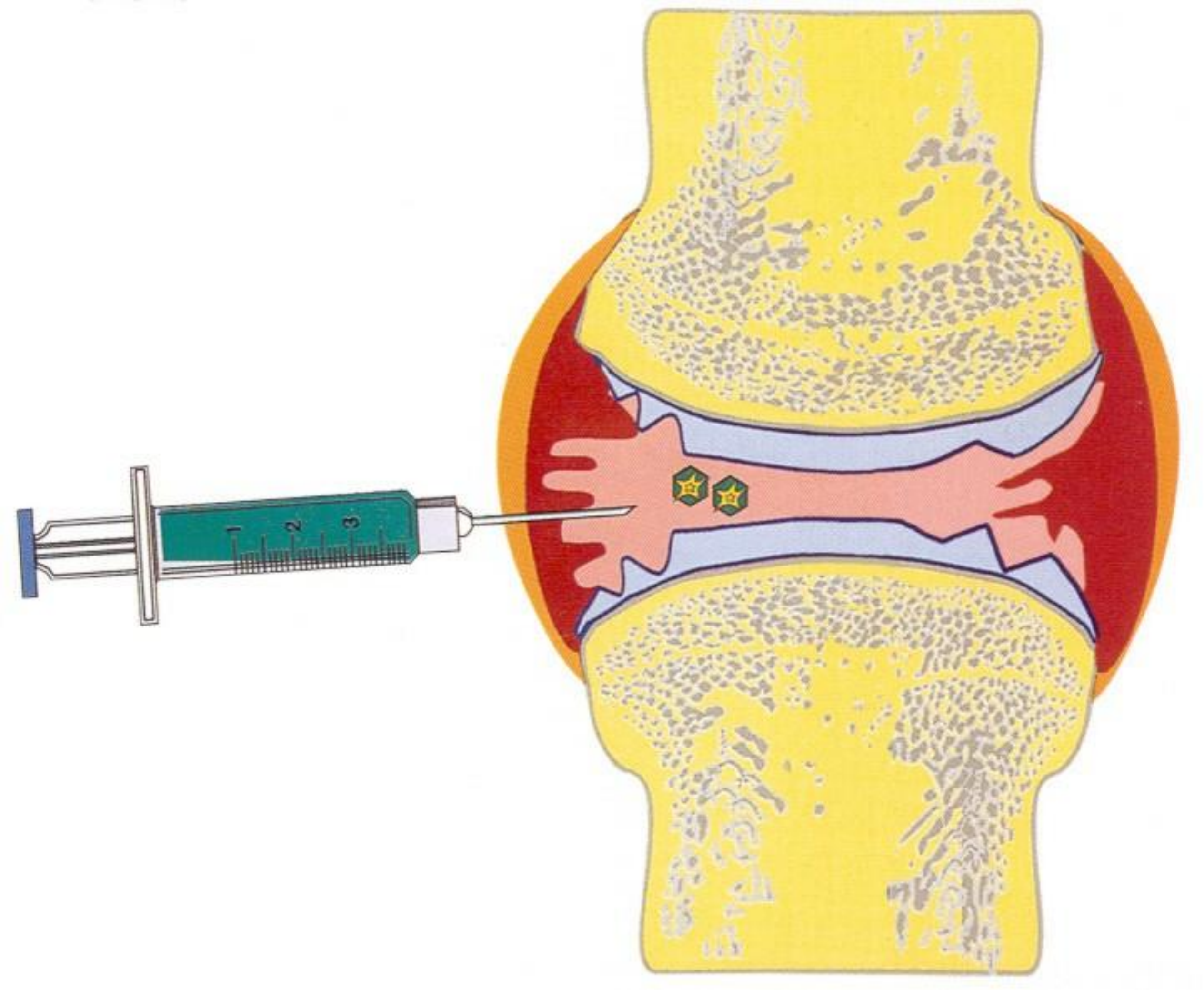
Therapy of the joints (radio-synovectomy) I.

- Local therapy: directly in the joints
- Stops inflammation and pain
- Prevents the deformation of the joints
- Effective combined with long- term systemic therapy

Therapy of the joints (radio-synovectomy) II.

- Indication: arthritis
- Radiopharmaceuticals: β-emitter isotopes
- Important:
  - the accurate injection (x-ray-control!)
  - homogeneous distribution in the synovial liquid
- The synovial cells fagocytate the radioaktiv colloid
- Immobilisation for 72 hours (!)

Method of radio-synovectomy



Therapy of the joints (radio-synovectomy) II.

- Indication: arthritis
- Radiopharmaceuticals: β-emitter isotopes
- Important:
  - the accurate injection (x-ray-control!)
  - homogeneous distribution in the synovial liquid (immobilisation for 72 hours !)

- The synovial cells fagocytate the radioaktiv colloid

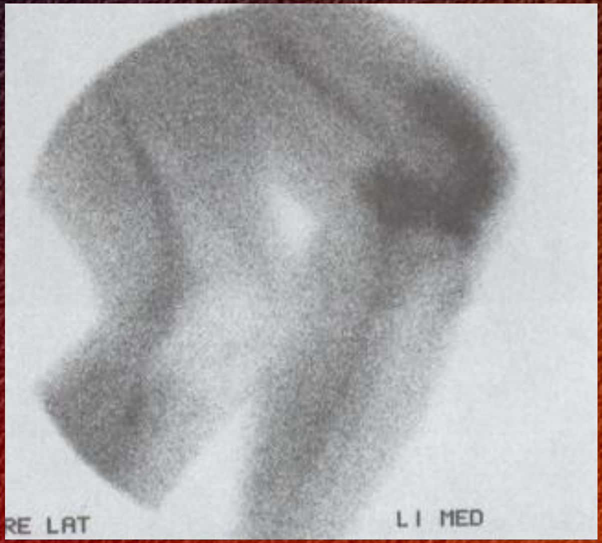
Radiopharmaceuticals used for radio-synovectomy

	Yttrium-90	Rhenium-186	Erbium-169
T ½:	2.7 nap	3.7 nap	9.5 nap
Radiation:	β	β +y	β
Beta energy	2.26 MeV	0.98 MeV	0.34 MeV
Max. range in tissue	11.0 mm	3.7 mm	1.0 mm
Treated joint:	knee	shoulder, elbow, wrist, hip, ankle	small joints of hands and feet

Synovitis and arthrosis in the left knee

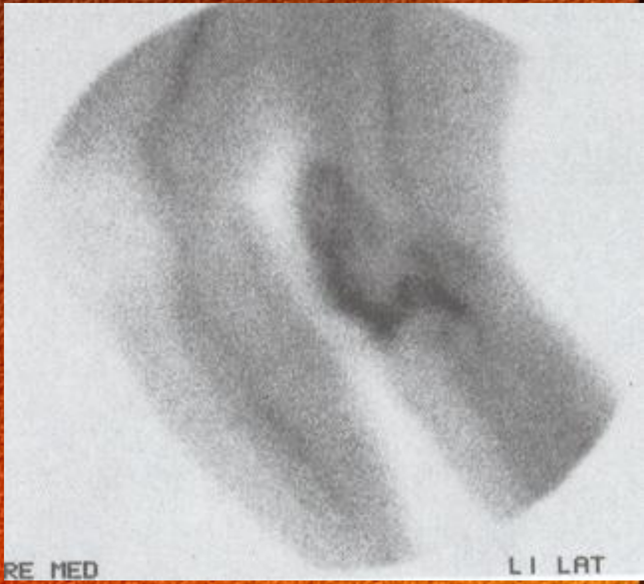
blood-pool scans

Anterior



right lateral

left lateral



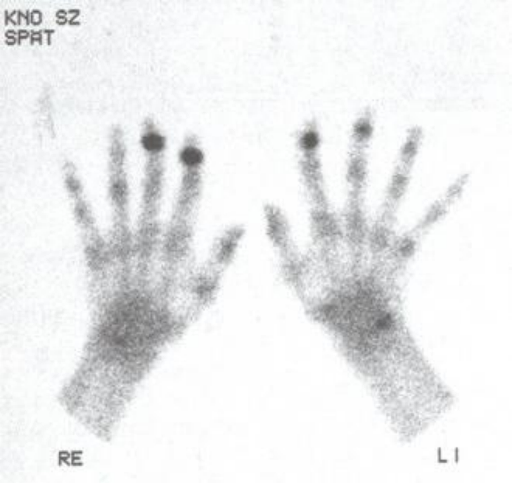
Polyarthrosis in the small joints of both hands

blood-pool scan

Ventral projection

Dorsal projection

Bone scan

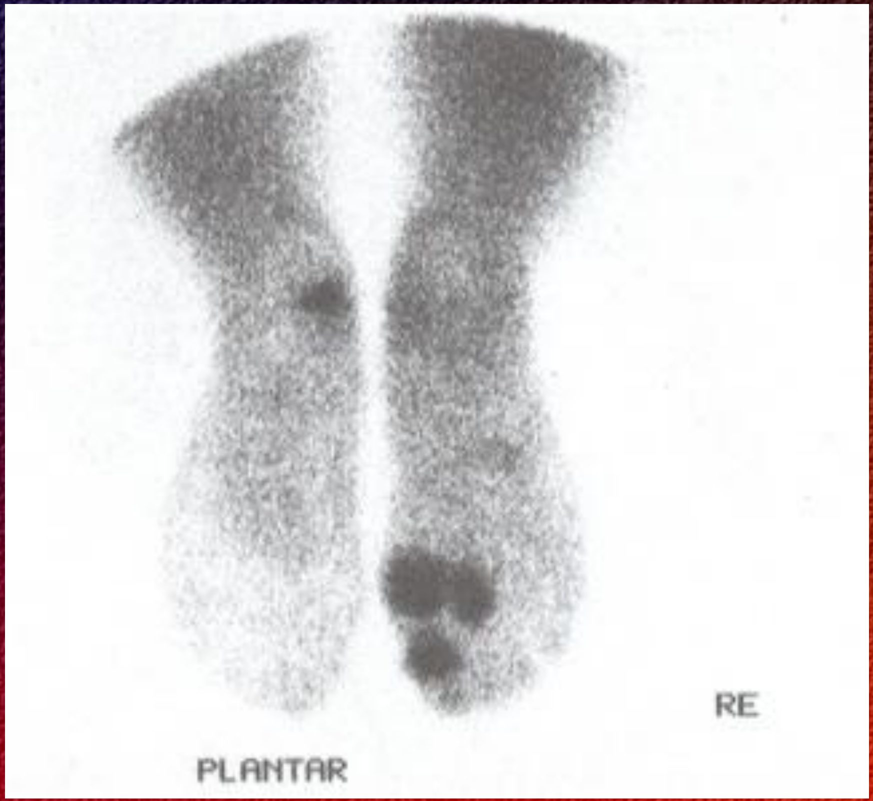


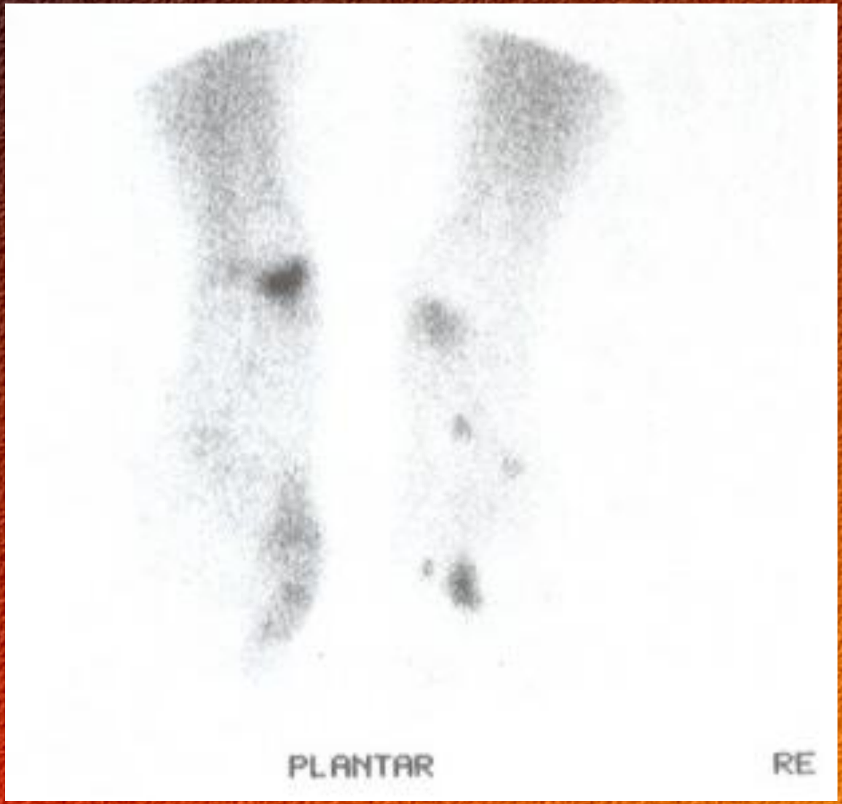
Rheumatoid arthritis in the small joints of feet

blood-pool scan

Before therapy

after therapy, 4 month later



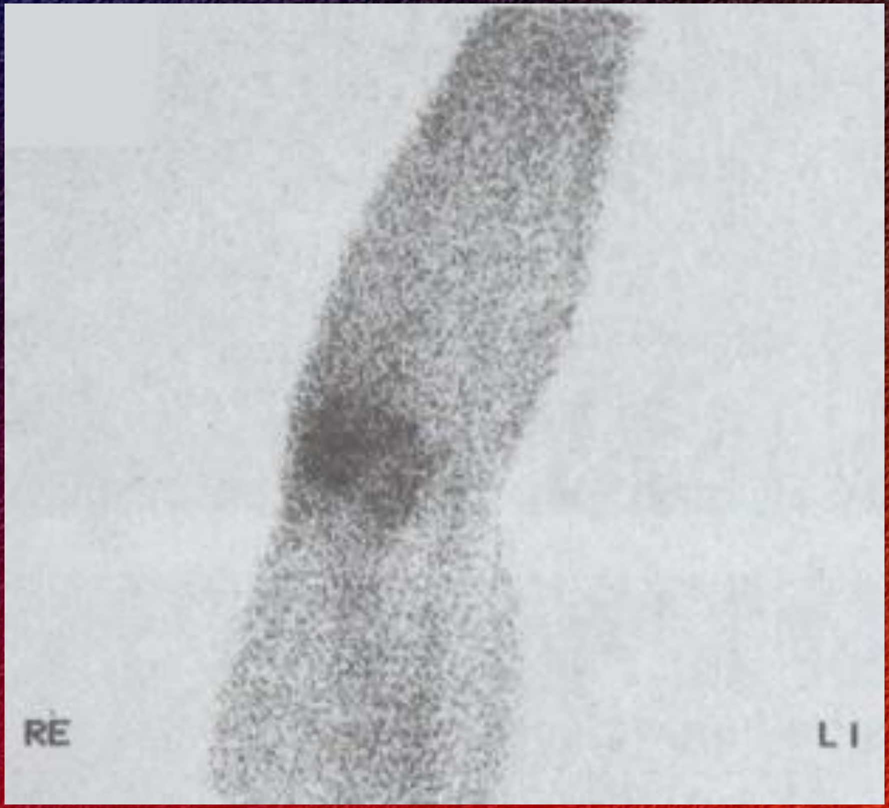


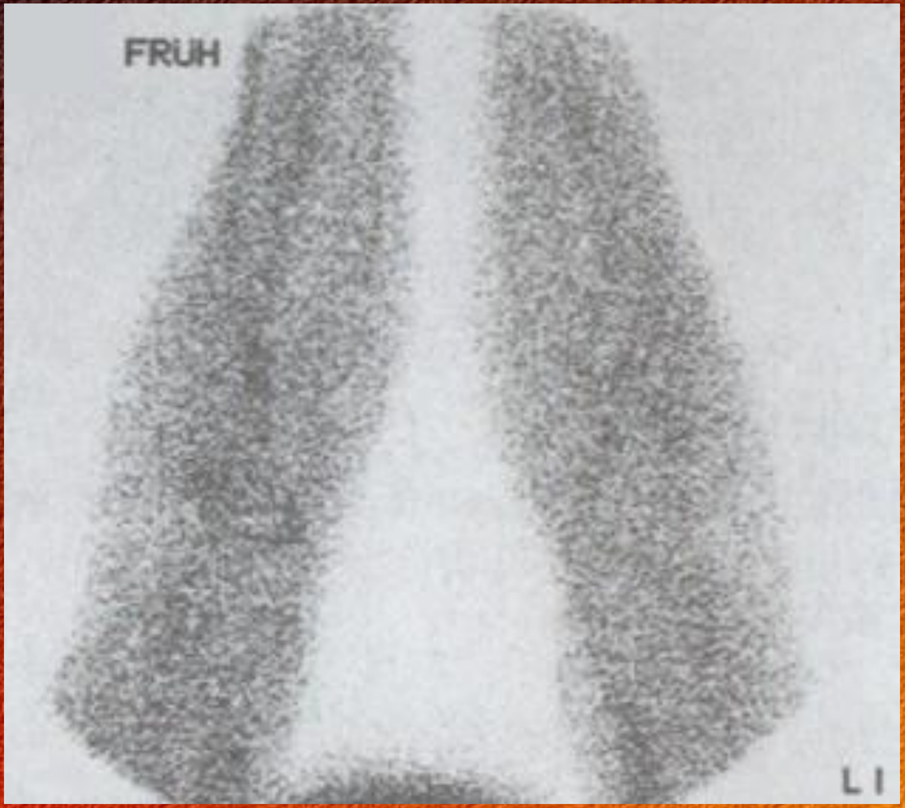
Synovitis in the right elbow

Blood-pool scan

before therapy

after therapy, 7 month later





Therapy of the joints (radio-synovectomy) II.

- **Contraindications:**
  - absolute: pregnancy, breast feeding
  - relative:

    children and adolescent
    unstable joint
    periarticular sepsis


Thanks for your attention!