Nuclear medicine I.

KRNM FN BRNO

Nuclear medicine – uses radiopharmaceuticals for:

Diagnostics

Scintigraphy

- **Gama emiters**
  - **^{99m}Tc,** ^{123}I, ^{81m}Kr, ^{111}In
  - Detects **1 photon**
  - **Planar** scintigraphy (sumation) or **SPECT** (tomographic)
  - Static x dynamic
  - Possible hybrid imaging SPECT/CT

PET

- **Beta+ emiters**
  - **^{18}F,** ^{68}Ga, ^{11}C
  - Detects **2 photons**
  - Tomographic method
  - Always hybrid imaging PET/CT or PET/MRI

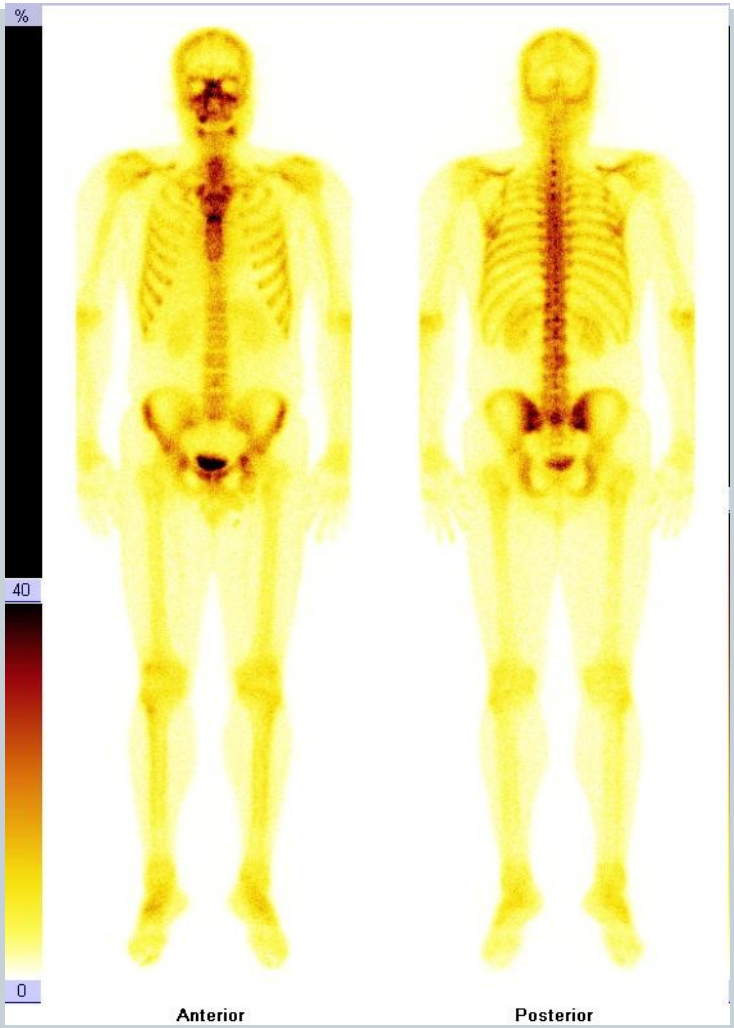
Therapy

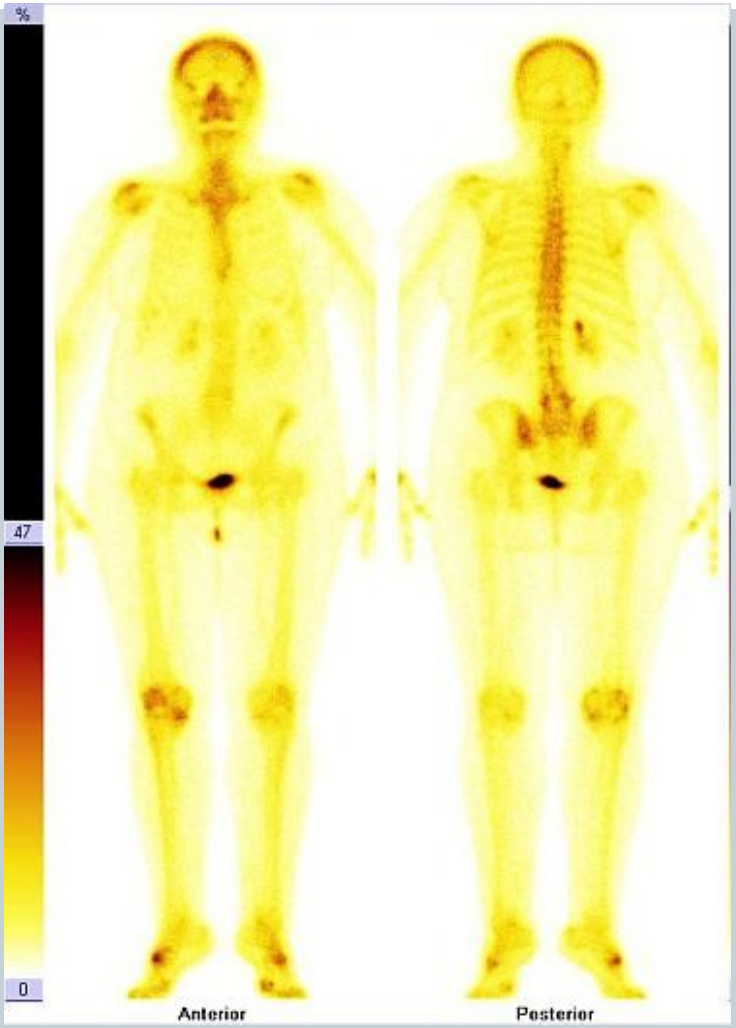
- **Beta- and alfa emiters**
  - **^{131}I** – thyroid carcinoma, hyperthyreosis
  - ^{177}Lu – metastatic prostate cancer, NETs
  - ^{90}Y – synovectomy
  - ^{223}Ra (alfa) – prostate cancer bone mts

Bone scintigraphy

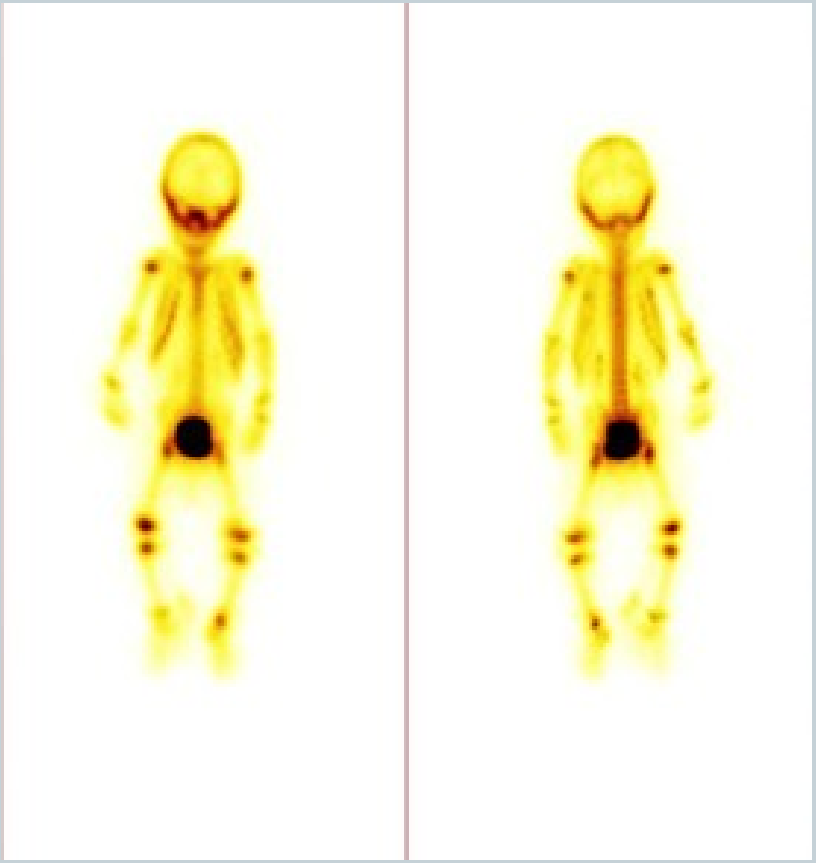
- One of the most commonly used method
- **Principle**: When tracer is injected intravenously, is taken up by adsorbtion onto the surface of bone, distribution in the skeleton is based on differencies in regional perfusion (vascularity) and **bone turnover** as well as other factors – non specific!!!
- High sensitivity, small specifity (clinical context, patient´s history, SPECT, SPECT/CT)
- **RP**: technetium-labeled bisphosphonates (^{99m}Tc-MDP), analogs of some components of the mineral portion of bone
  - (alternatively - 18F-NaF for PET imaging)
- **Imaging technique**: wholebody planar image in anterior and posterior view 2-4h after RP administration, SPECT or SPECT/CT , 3-phase protocol

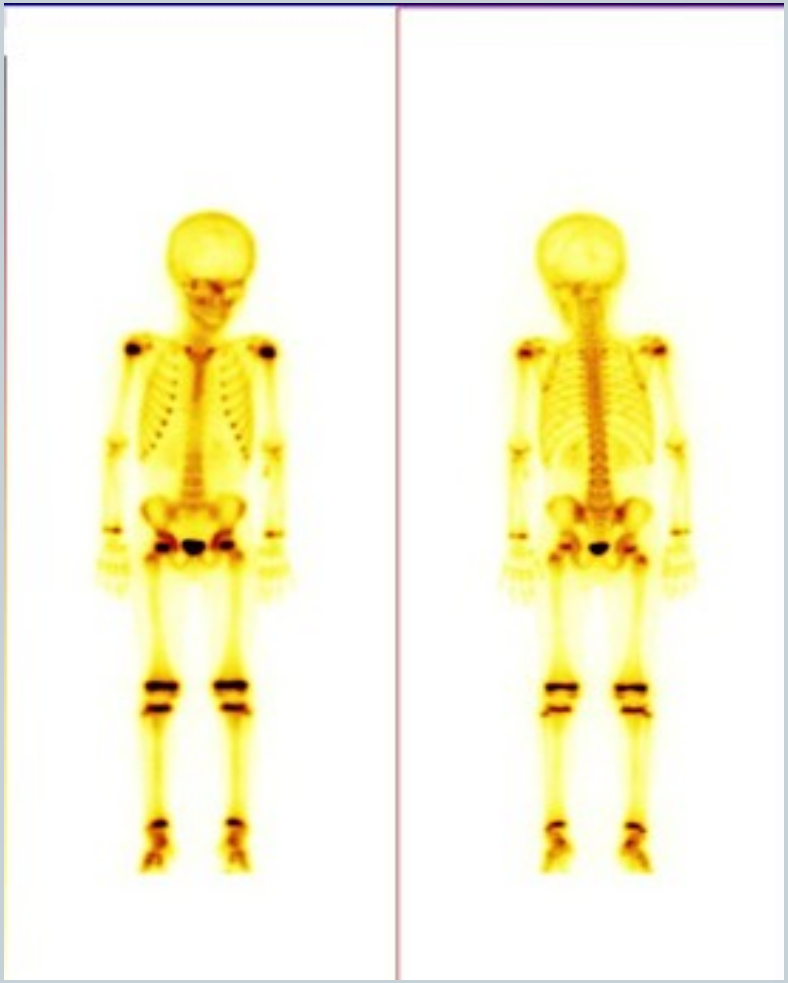
Bone scan





Bone scan





Bone scintigraphy

- **Indications**:

- **Metastatic** bone disease, primary bone tumors
- Osteomyelitis (mostly periferal bones)
- Evaluation of prosthetic joints for loosening and infection

- Skeletal trauma, stress fructures
- Metabolic bone disease : Morbus Paget, hyperparathyroidism
- Evaluation of bone pain in patients with normal radiographs, evaluation of the significance of an incidental bone finding on radiographs, determination of biopsy site

Bone scintigraphy

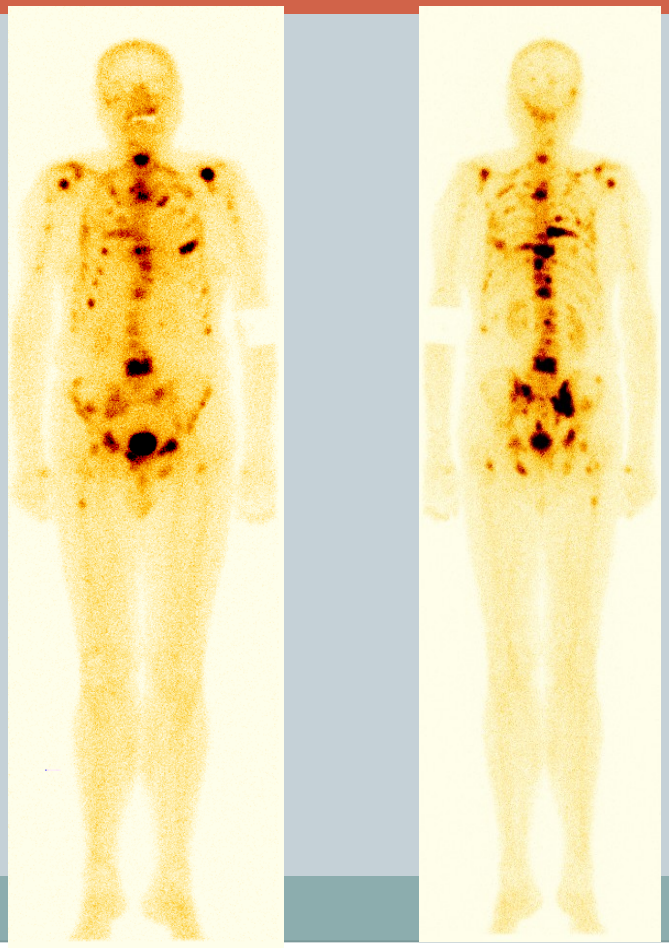
- High sensitivity - predominantly **osteoblastic** sites show **increased activity** (hot spots), whereas mainly osteoclastic or lytic lesions can be difficult to detect (cold lesions) – **tumors that are predominantly lytic have lower sensitivity**

- Highest sensitivity for **prostate cancer**, high sensitivity for **breast** and **lung cancer**, low sensitivity for multiple myeloma, thyroid cancer, renal carcinoma.....

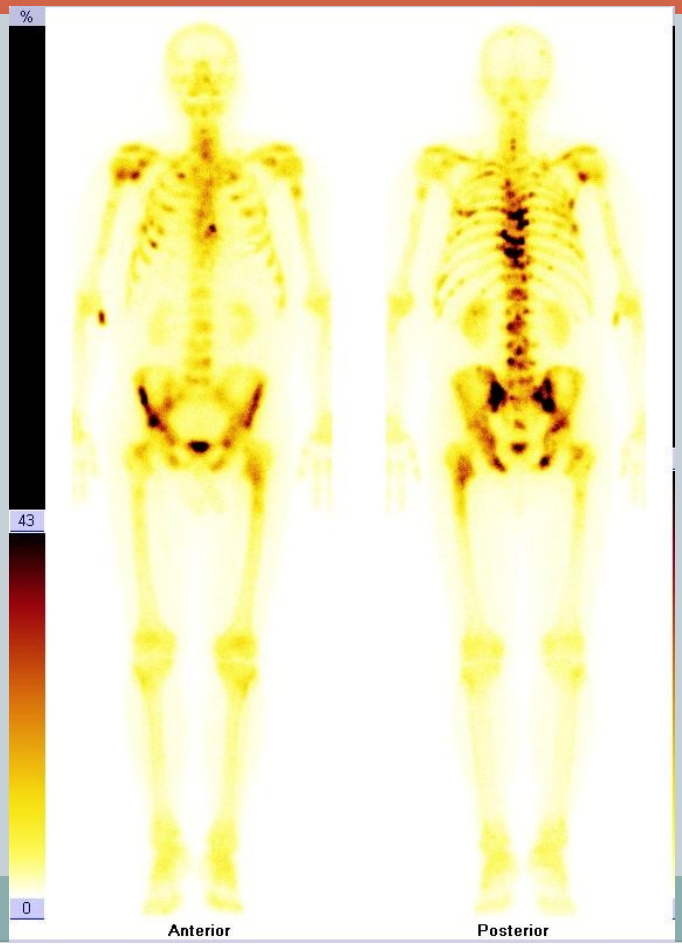
- Bone scan vs FDG PET
  - Higher sensitivity of scintigraphy in osteoplatic metastases
  - Higher sensitivity of PET in osteolytic lesions

Bone scan

Metastatic breast cancer

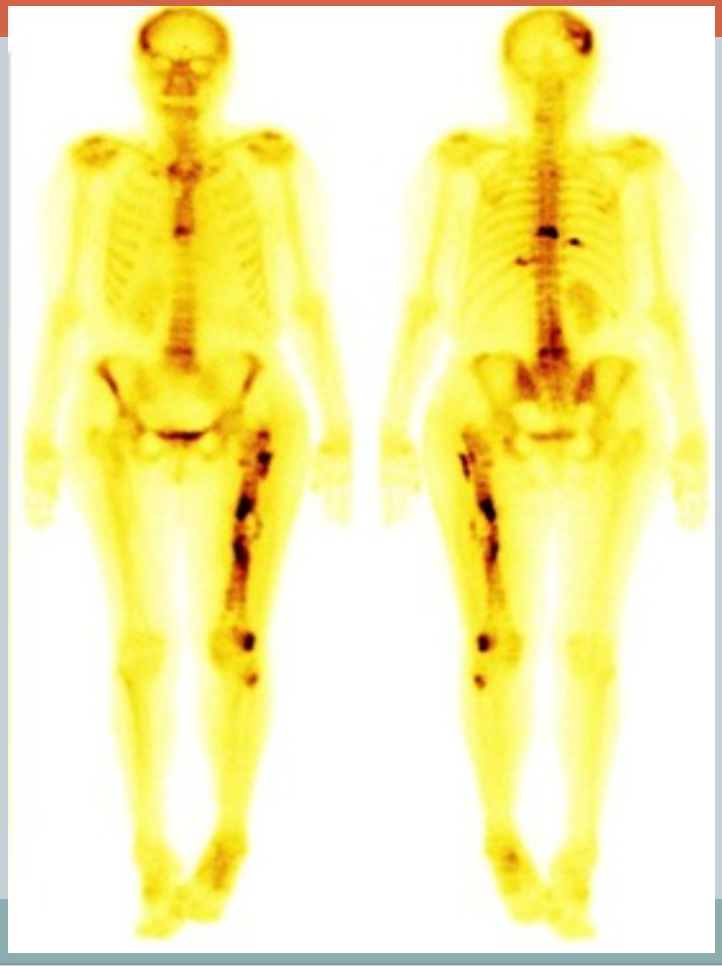


Metastatic prostate cancer

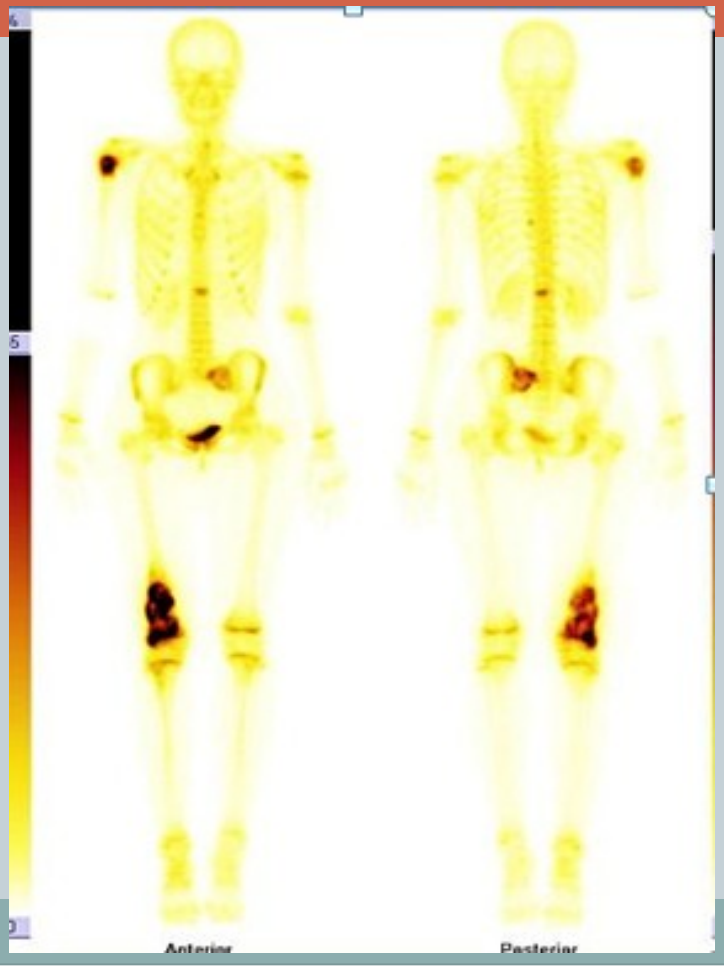


Bone scan

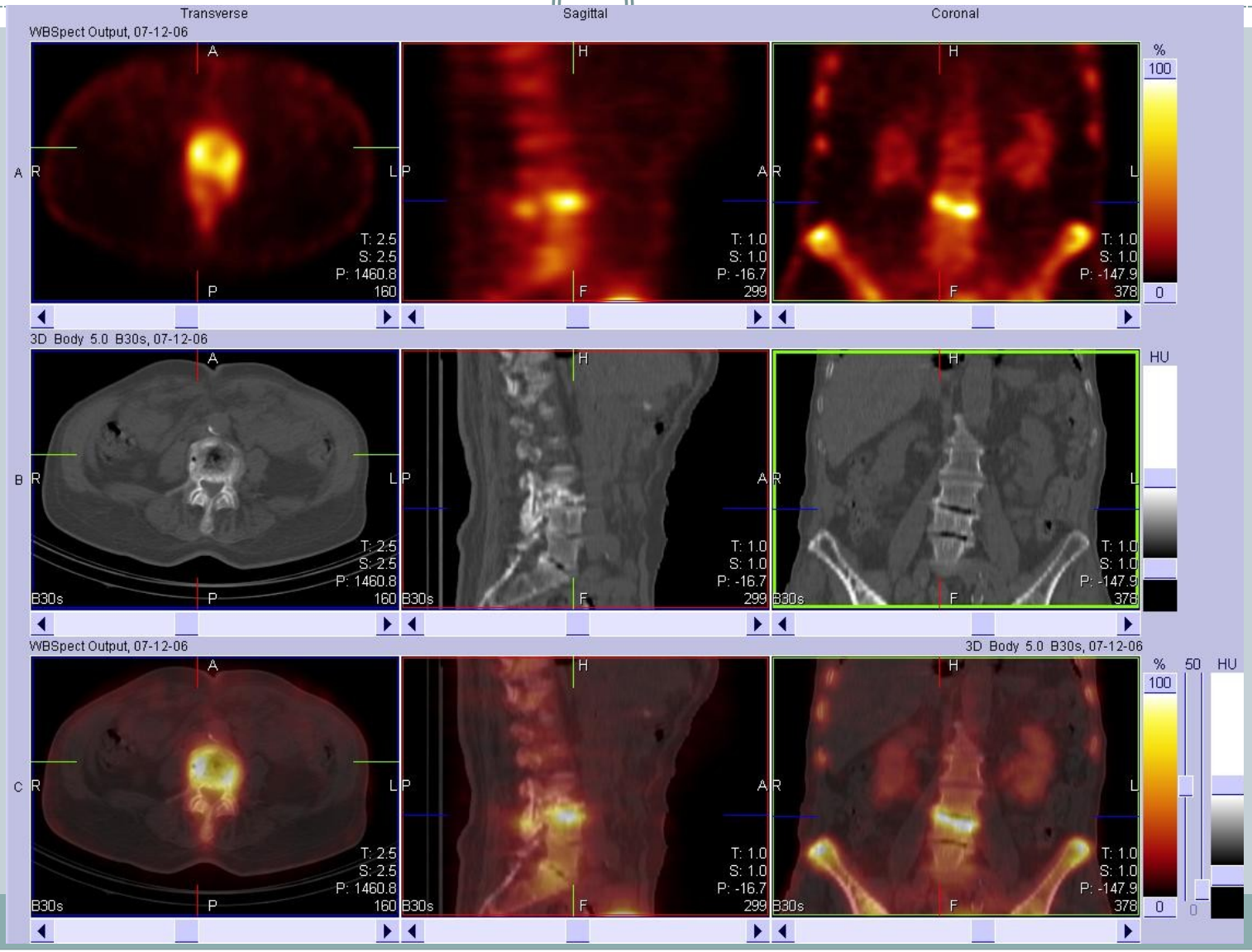
RCC



Osteosarcoma

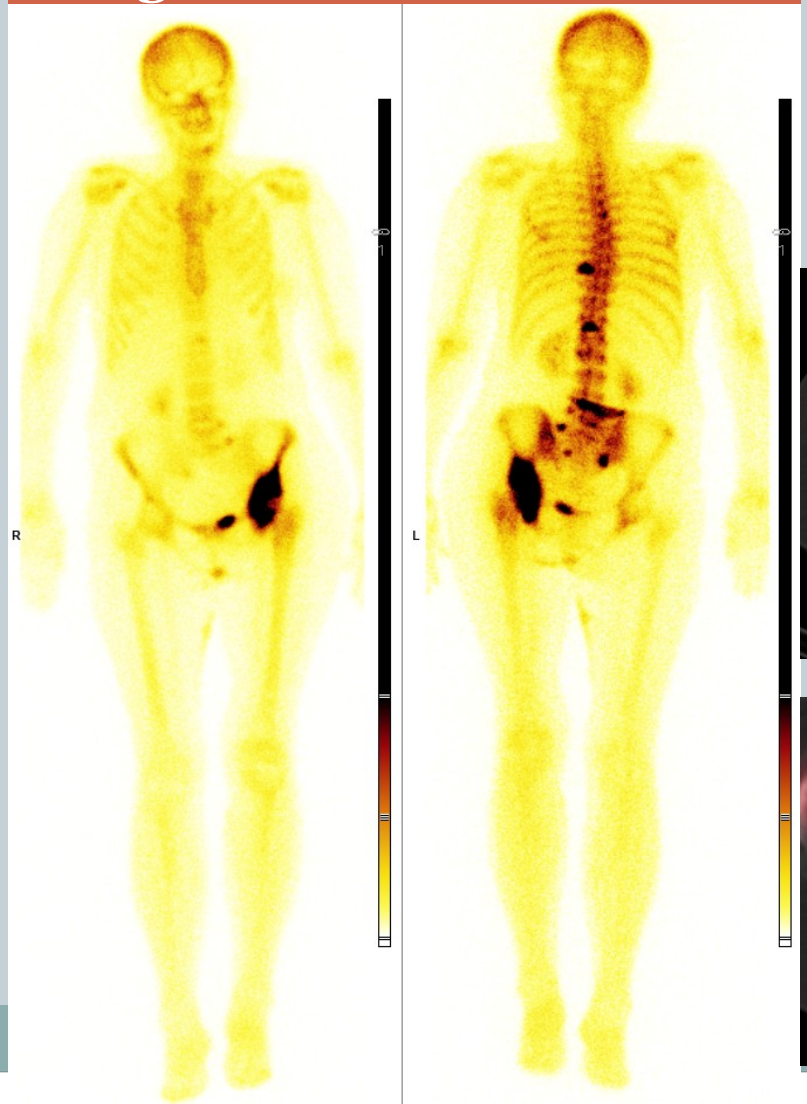


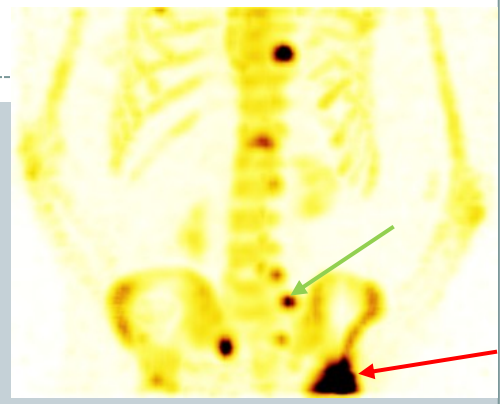
Bone scan – SPECT/CT

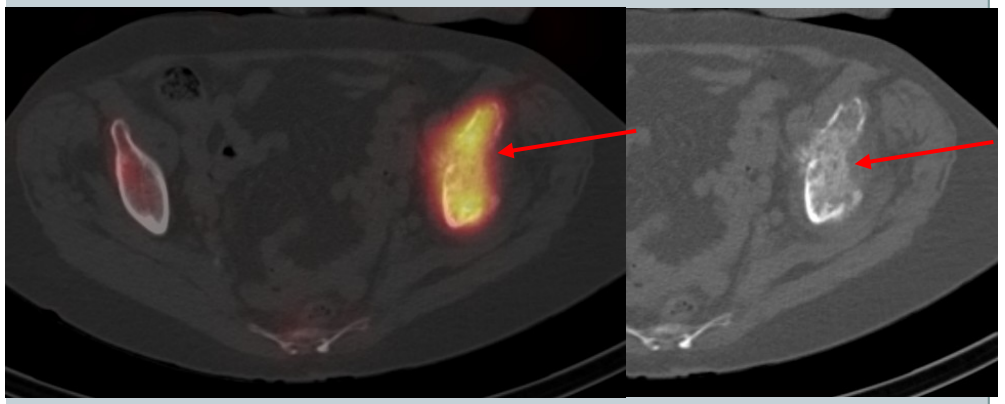


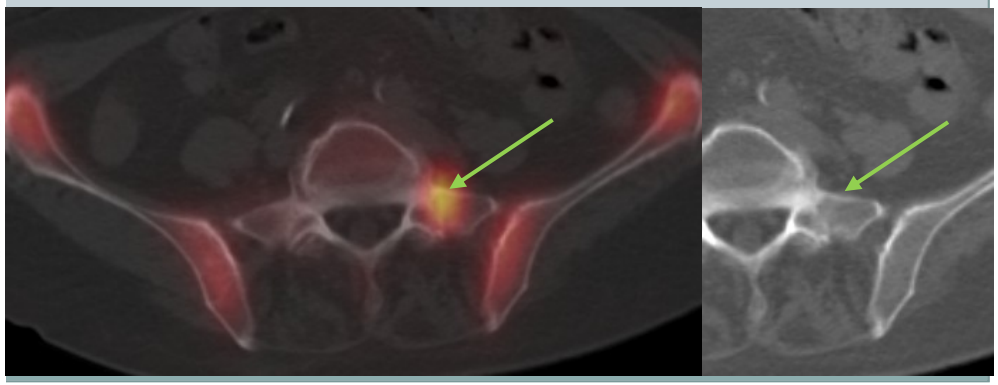
Bone scan– SPECT/CT

Lung cancer

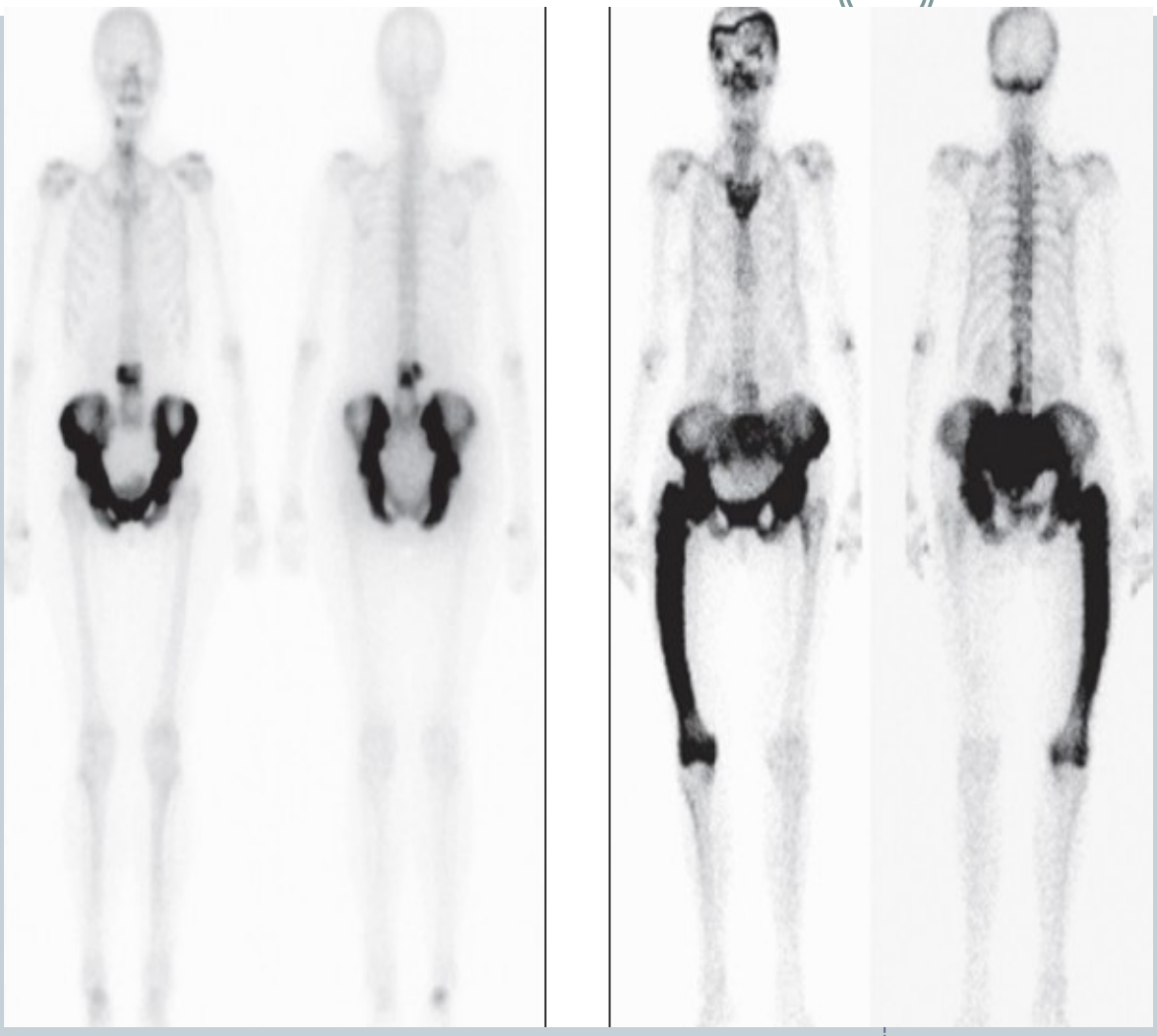








Paget disease



- The pelvis is the most commonly involved site, followed by the spine, skull, femur…

Infection imaging methods

- 3-phase bone scintigraphy – bones only!

- Radiolabeled leukocytes
- Radiolabeled antigranulocyte monoclonal antibodies

- 18F-FDG PET

- Galium imaging (67 galium citrate) – has very limited role today

3-phase bone scintigraphy

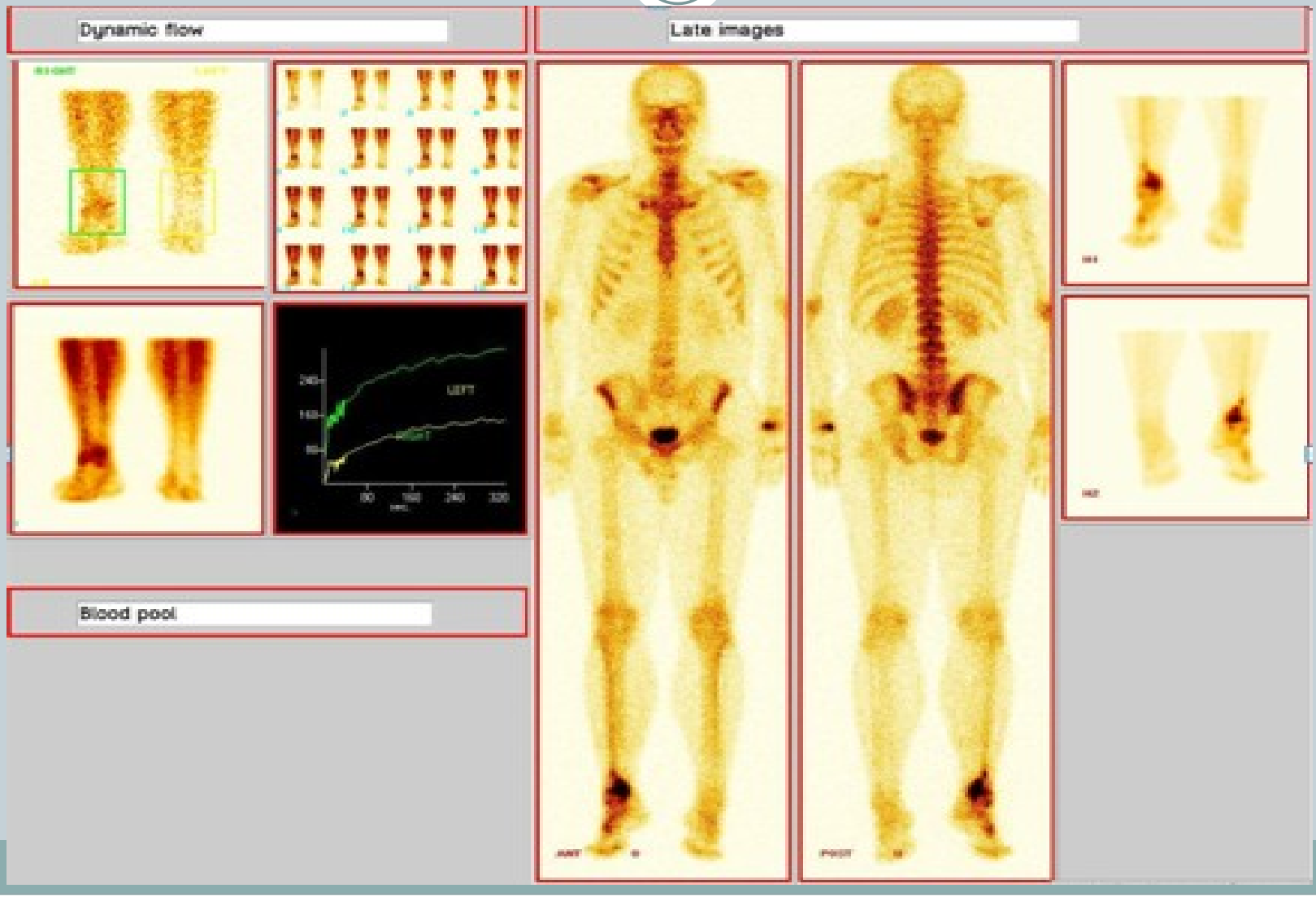
Indication: differentiation between eosteomyelitis and cellulitis (especially in periferal skeleton), evaluation of joint replacement complications (aseptic loosening or infection)

Imaging protocol:

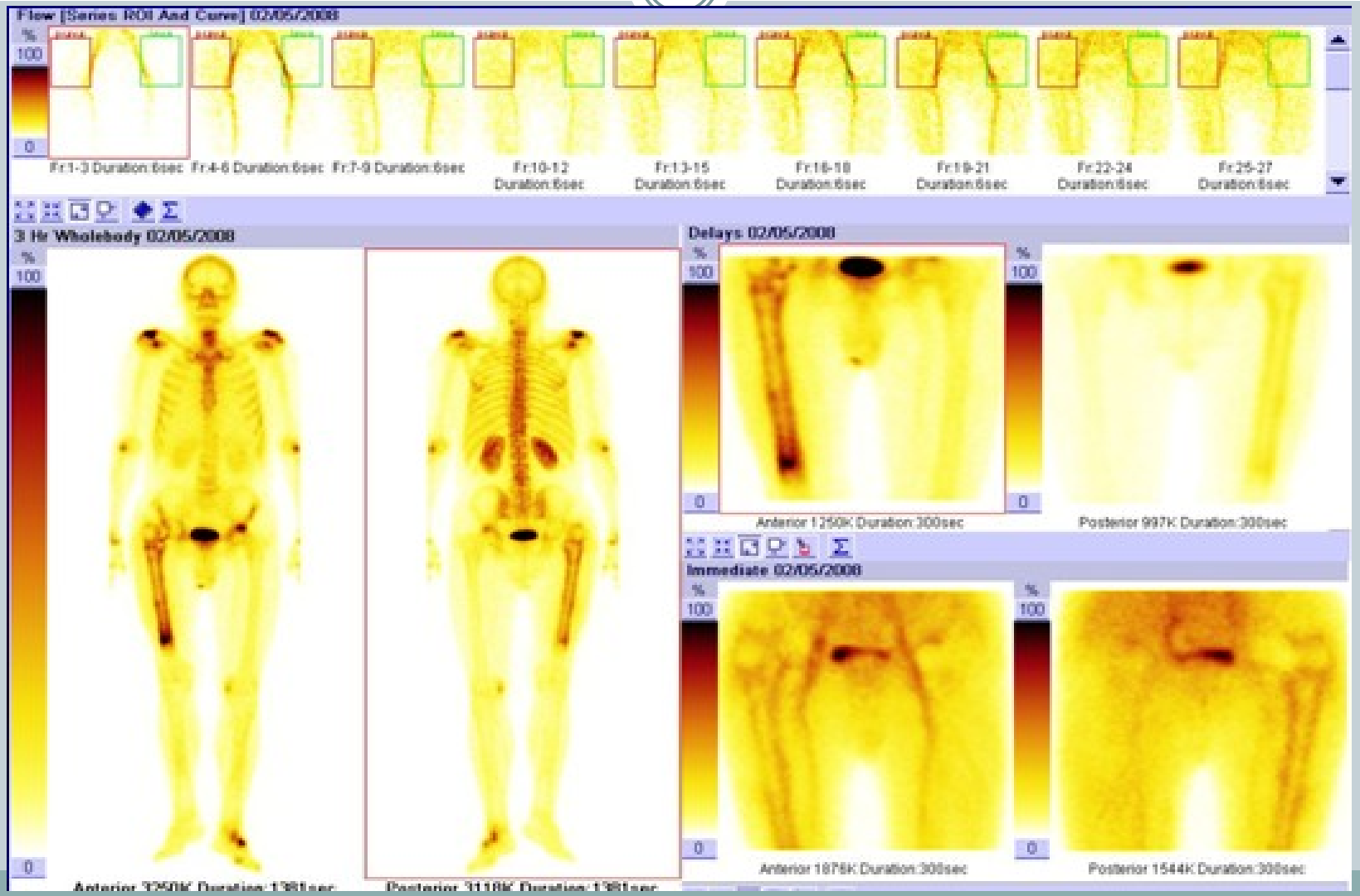
- I. Flow phase: dynamic 2- to 5-second images of the area of interest for 60 seconds after bolus injection
- II. Blood pool and soft tissue phase = immediate static images for time (usually 5 minutes), followed dynamic phase
- III. Skeletal phase : Delayed images at 2-4 hours after injection
- SPECT/CT increasis specifity

- Withouth underlying bone pathology negative study result exludes osteomyelitis with high degree of certainty
- With underlying bone pathology (recent trauma, tumor..) is still sensitivity very high, but specificity only 30-50%

3-phase bone scintigraphy



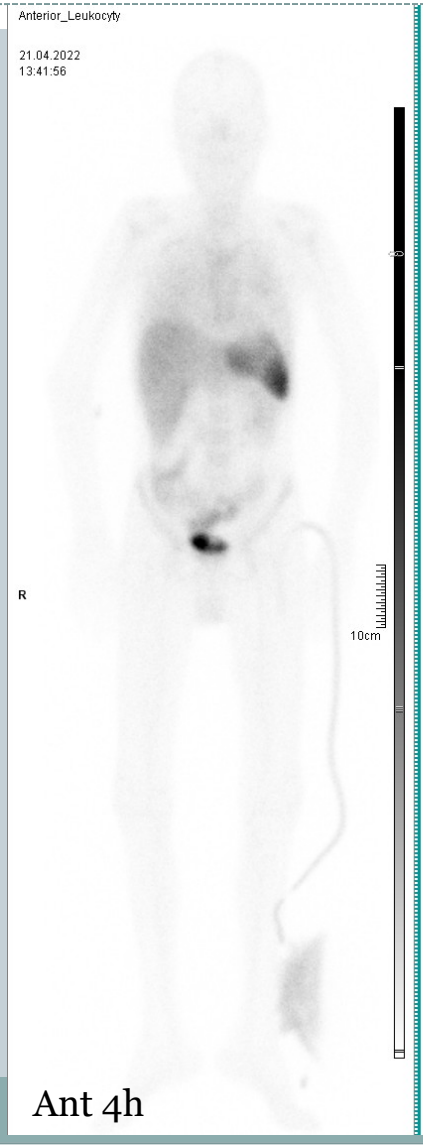
3-phase bone scintigraphy



Radiolabeled leukocytes

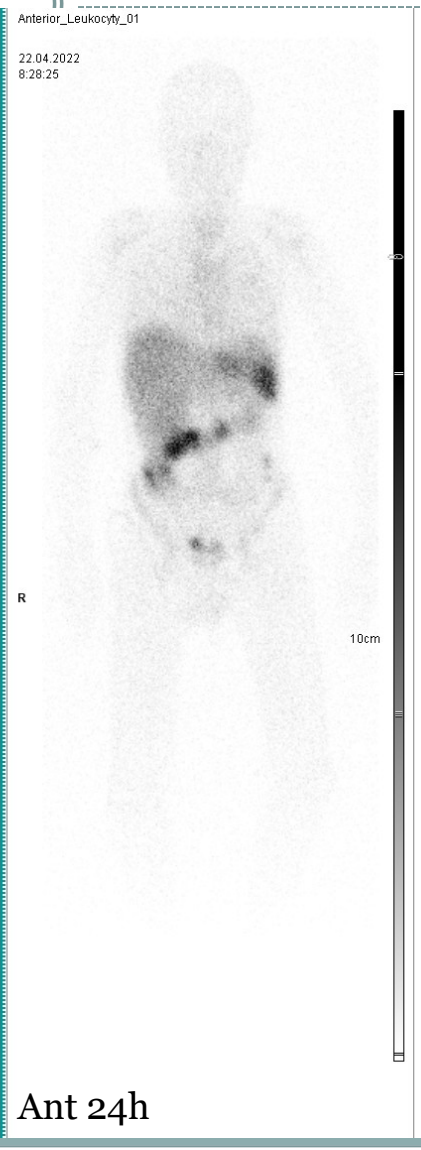
- Leukocyte imaging using in vitro labeling with 111Indium or 99mTc is the nuclear medicine gold standard for diagnosing most infection
- **Principle:** leukocytes are attracted to the site of inflammation – acitive migration, uptake is not specific for infection, may occur in any inflammatory process that incites the leukocytes response
- Leukocytes are isolated from about 60ml anticoagulated blood, labelled in vitro, effectiveness depends on viability, thus is essential to avoid damage to the cells
- (If not possible to label enough leukocytes, examination with radiolabeled antigranulocyte monoclonal antibodies is possible, needs HAMA test, imaging protocol is same)
- **Imaging protocol**: wholebody image in anterior and posterior view at 4 and 24 hours after injection + SPECT/CT , early imaging of the abdomen at 1- 2 hours after injection is obtain in case of inflammatory bowel disease
- **Indication**: acute pyogenic infection, fever of the unknown origo, osteomyelitis, prosthetic joint infection, vascular grafts infection...
- ! MR is the method of the choice once there is a suspicion for spine osteomyelitis and no other underlying bone patology

Radiolabeled leukocytes

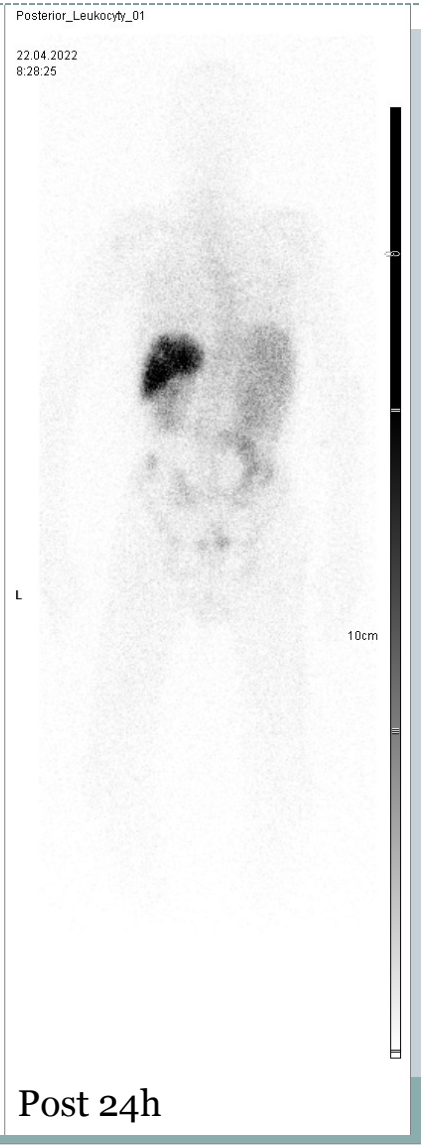


Ant 4h

Post 4h

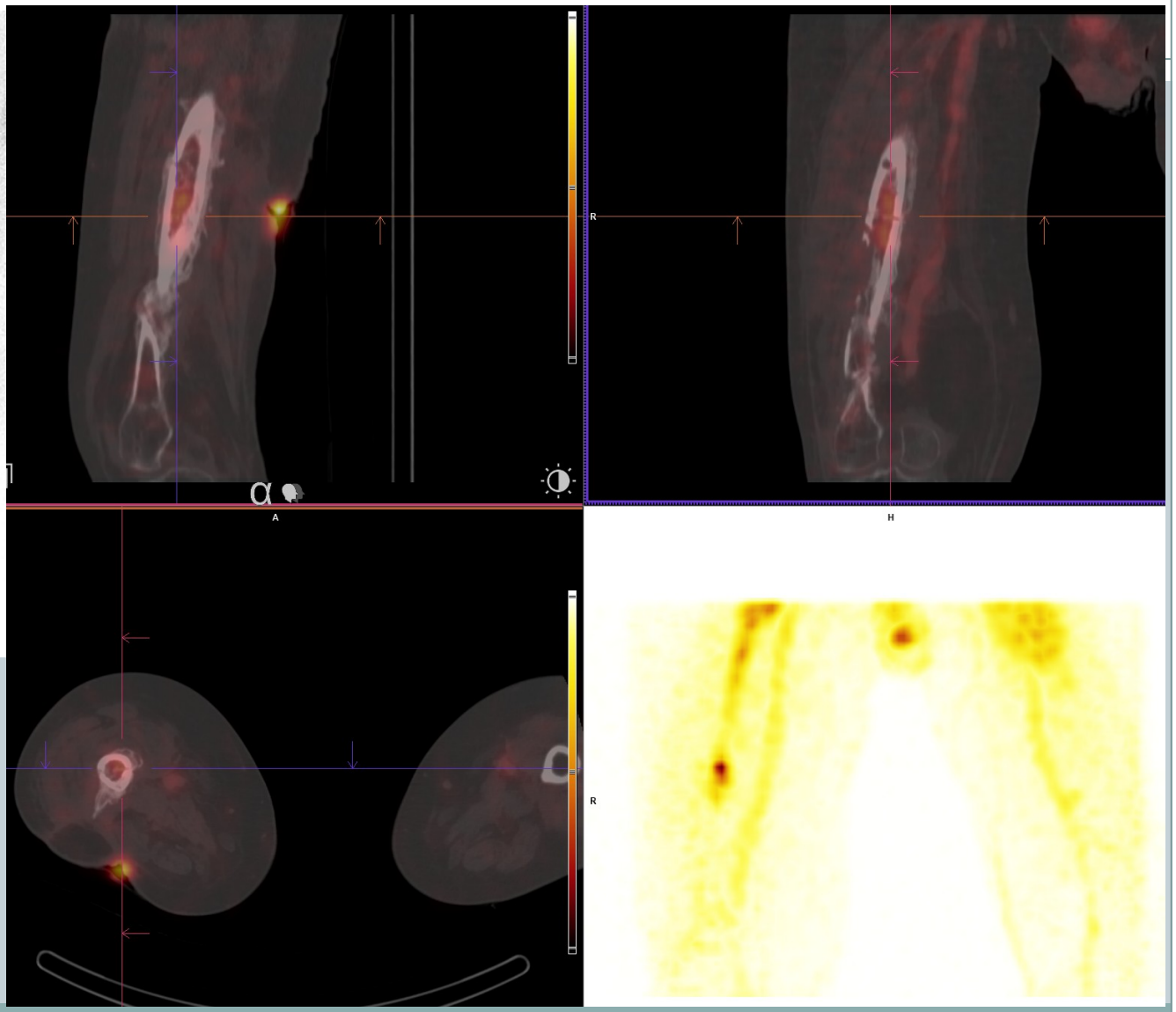


Ant 24h



Post 24h

Radiolabeled leukocytes



Post removal of OS, infection in soft tissues without osteomyelitis

Respiratory system – nuclear imaging methods

- **Perfusion study** : 99mTc-MAA macroaggregated albumin- displays regional lung perfusion

- **Ventilation study**: radiolabeled aerosols (^{99m}Tc-DTPA), radioactive gases (^{81m}Krypton) - display regional lung ventilation

- **18F-FDG PET/CT, PET/MR :** lung carcinoma, infection

Perfusion a ventilation scintigraphy

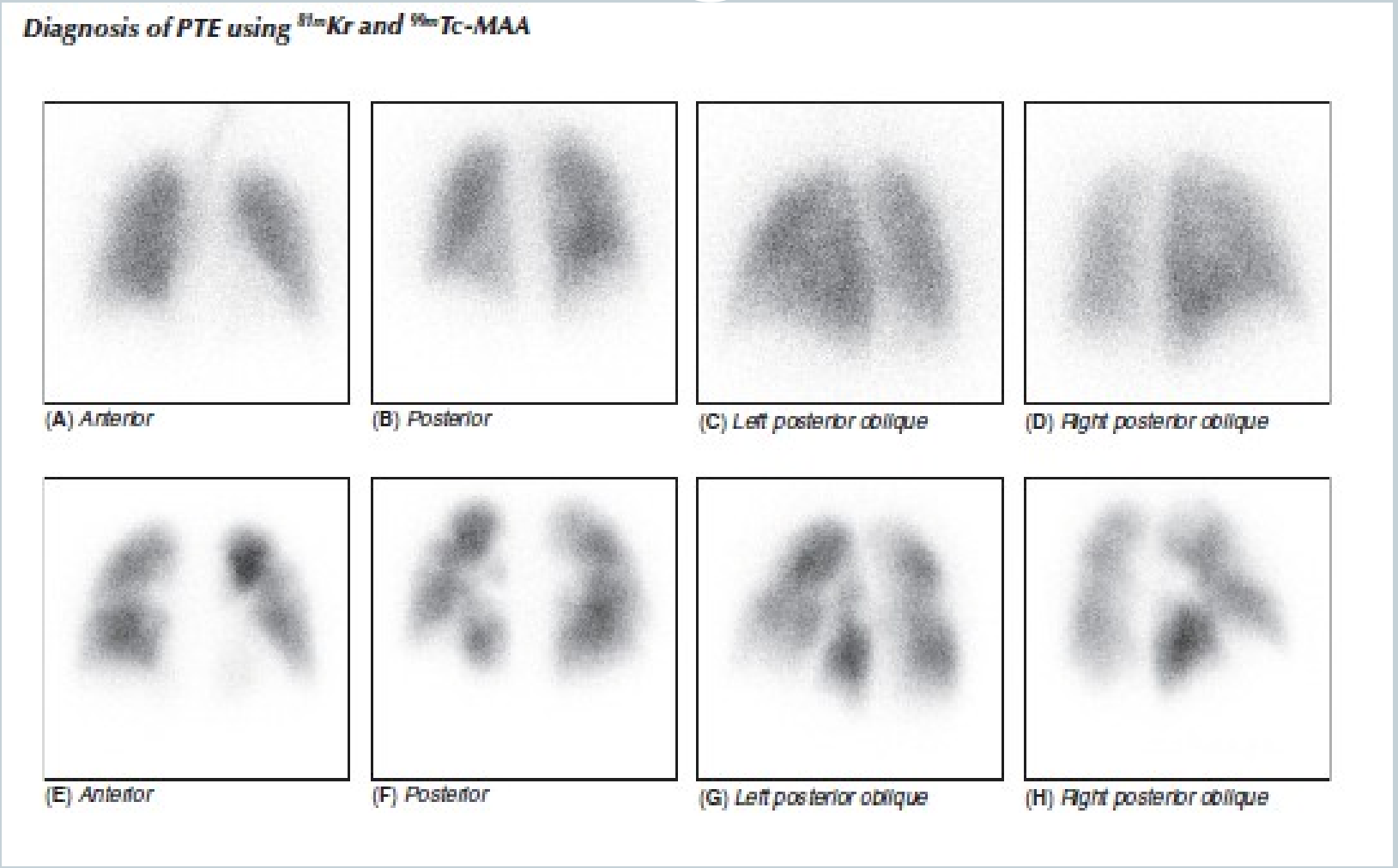
- **Indication**: assess the **probability of pulmonary embolism**, assess regional lung perfusion before lung surgery (semiquantitative evaluation)

- **Imaging:** traditionally perfusion+ventilation (V/Q scan) - V/Q Mismatch
- **SPECT/low-doseCT** perfusion only
  - Ventilation in uclear cases only

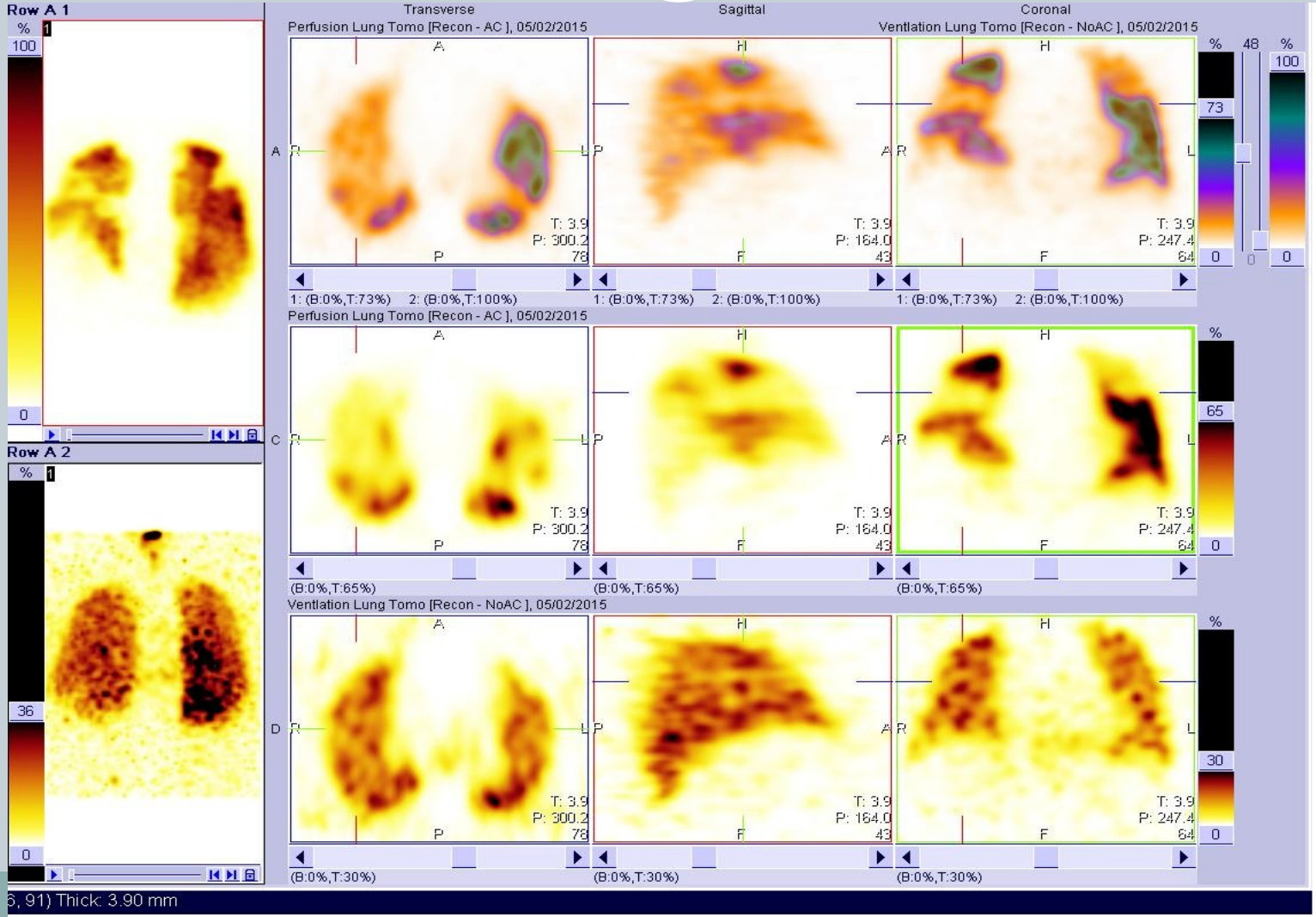
- Many centers performed both the perfusion and ventilation studies, clinical experience show that perfusion study by performing SPECT/CT is fully sufficient (depends on clinical context, technical equipment…)

- R-L shunt may be demostrated at images (activity is seen in the brain, kidneys)

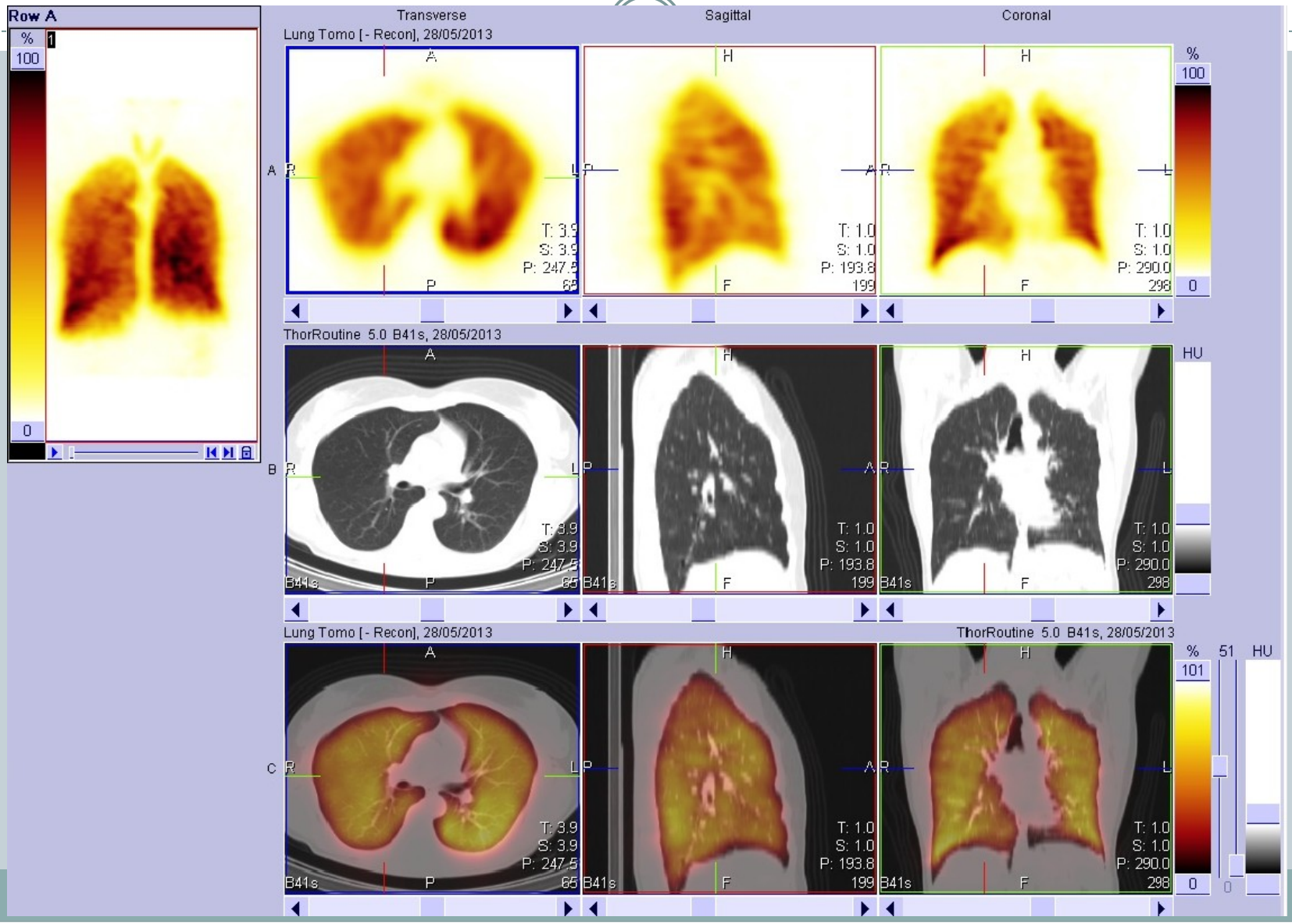
Perfusion ventilation study



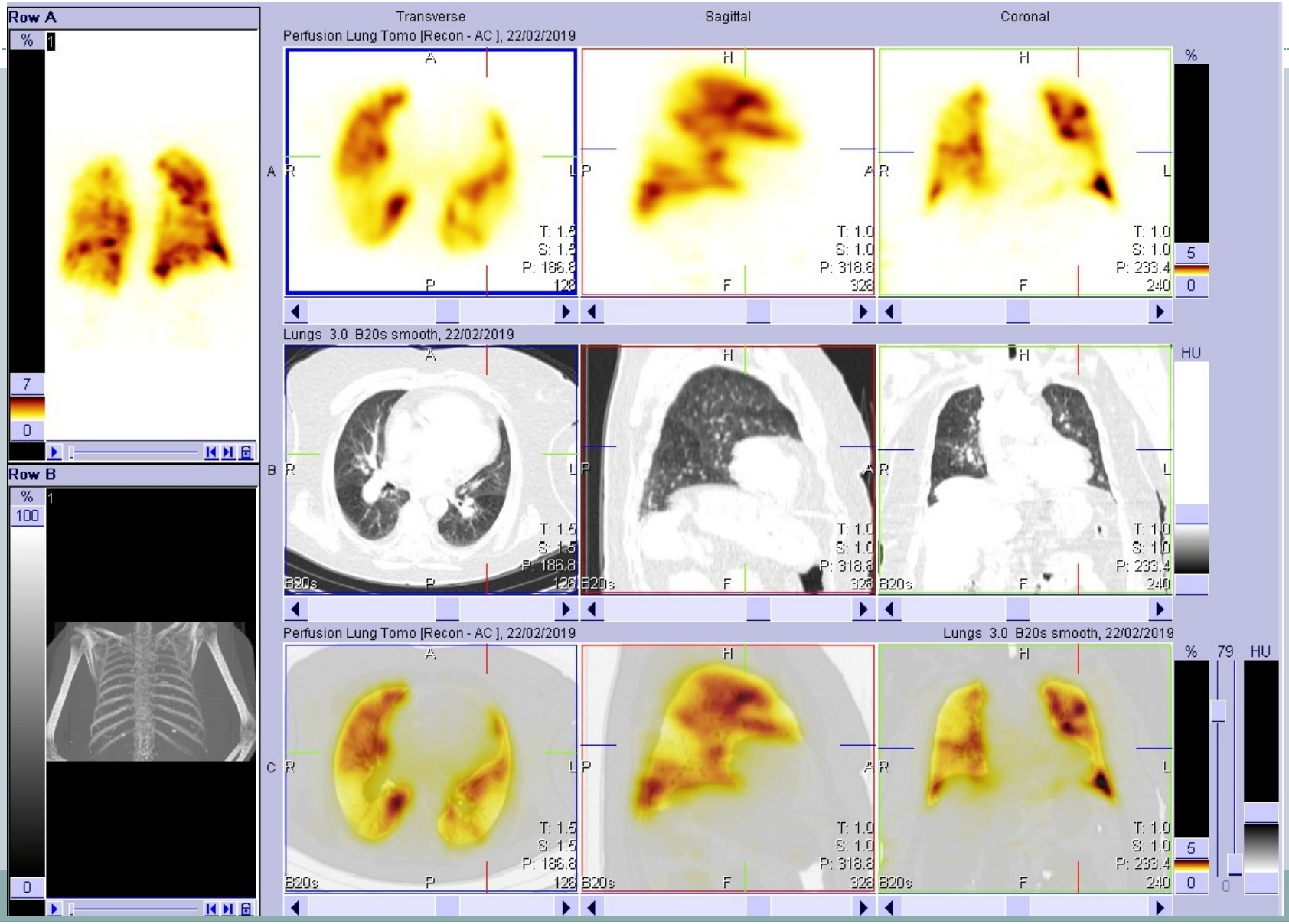
Perfusion ventilation study SPECT



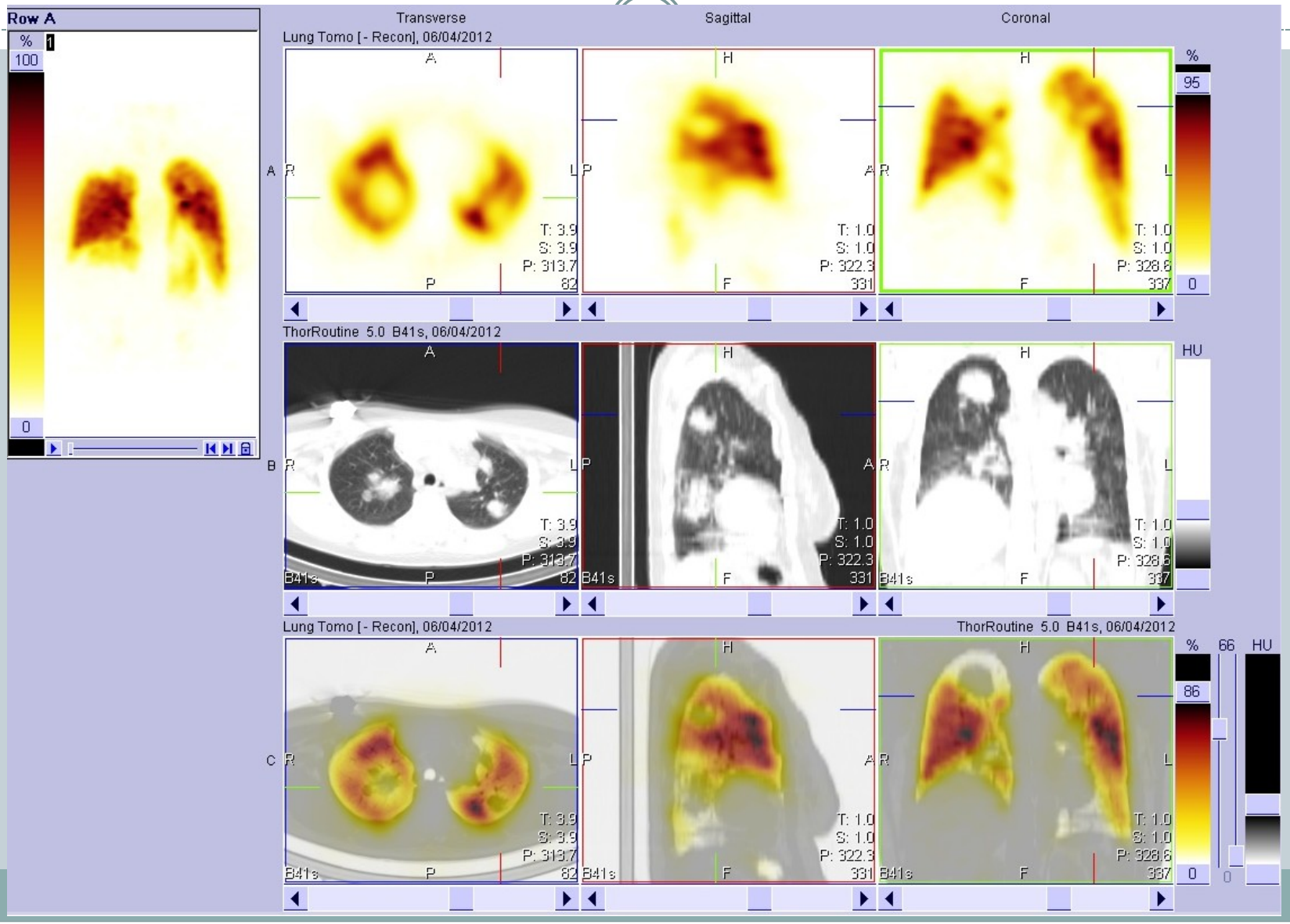
Lung perfusion study, SPECT/CT



Lung perfusion study, SPECT/CT



Lung perfusion study, SPECT/CT



Thyroid imaging

- RP: $^{99m}TcO_4$ (technetium pertechnetate), ^{123}I, ^{131}I
- Planar images, SPECT, SPECT/CT

Thyroid scintigraphy - indication

- **Hyperthyroidism** : autonomous/toxic adenoma, Graves disease, subacute thyreoiditis, compensatory low level TSH due to another disease
- **Thyroid nodules** : to determine their functional status
- **Detection of the ectopic thyroid tissue, evaluation of the retrosternal tissue mass** (**retrosternal goiter**, lingual thyroid, struma ovarii)
- **Thyroid cancer (^{123}I, ^{131}I) staging**

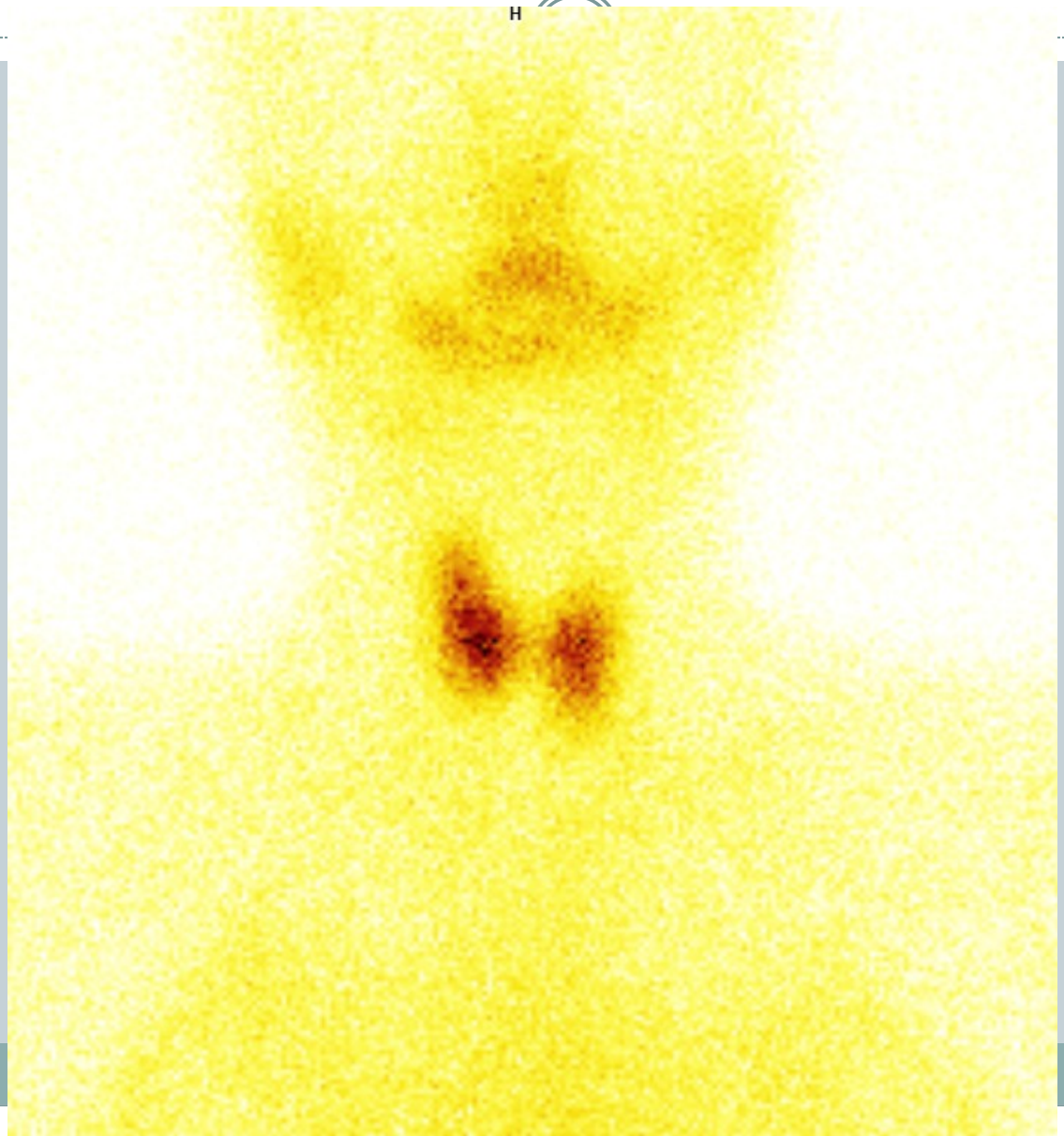
Therapy I 131

- Hospitalization required

- **Malignant -** patients with **differentiated thyroid cancer:**
- Elimination of residues and micrometastases after TTE
- Therapy of metastases found on follow up dg. scan with I131

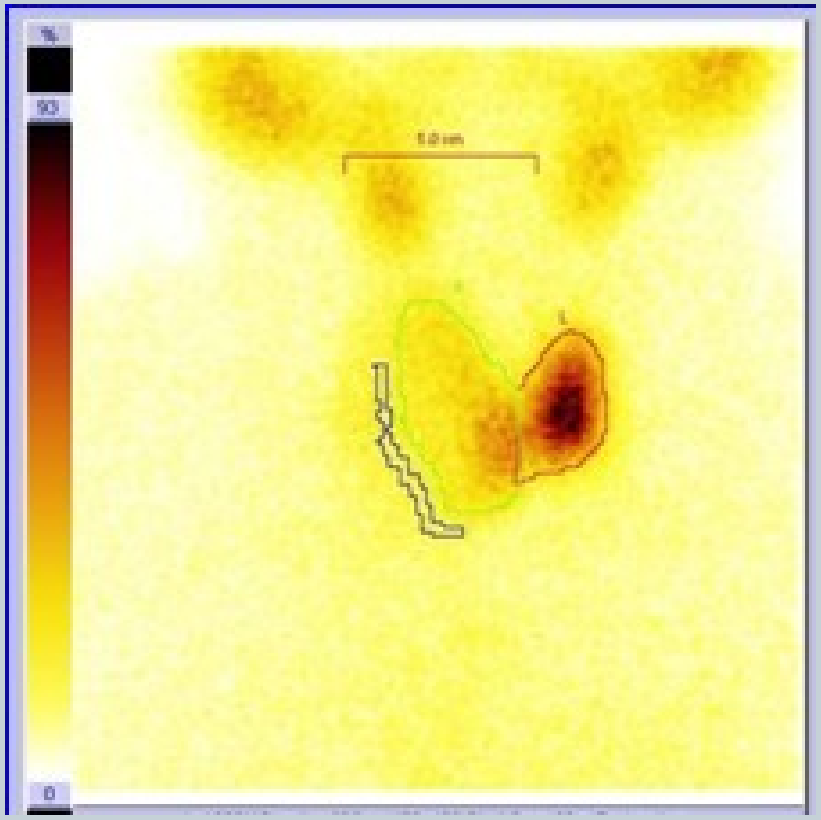
- **Benign:**
- Autonomous adenoma
- Relapse of autoimmune hyperthyroidism (Graves-Basedow) without endocrine orbitopathy

Thyroid scintigraphy – normal finding

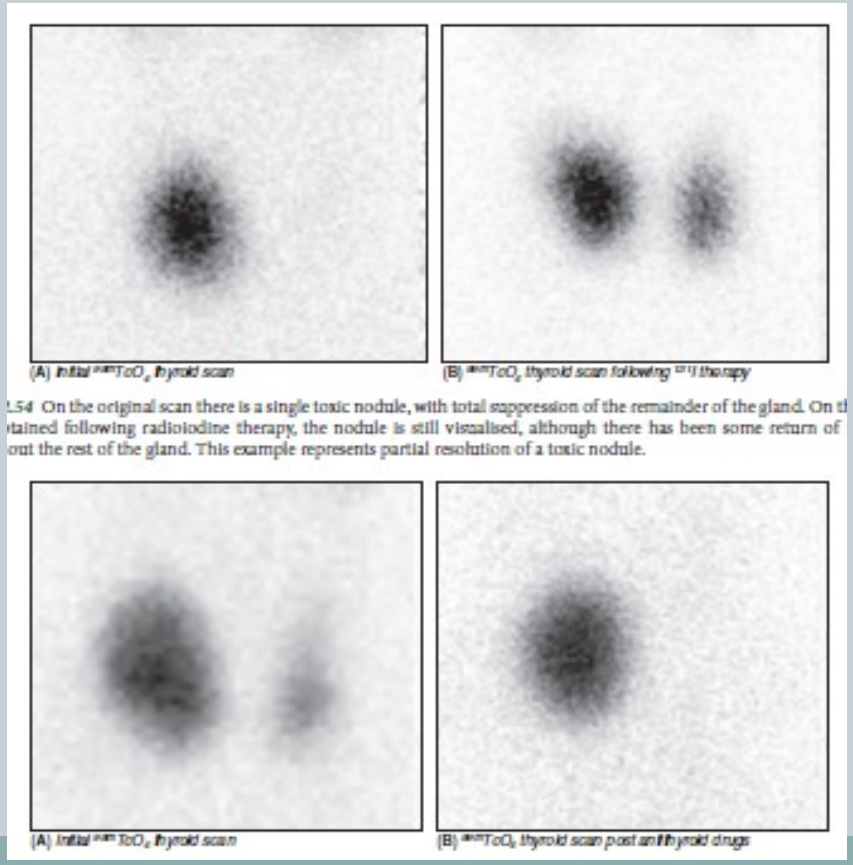


Thyroid study

Cold nodule

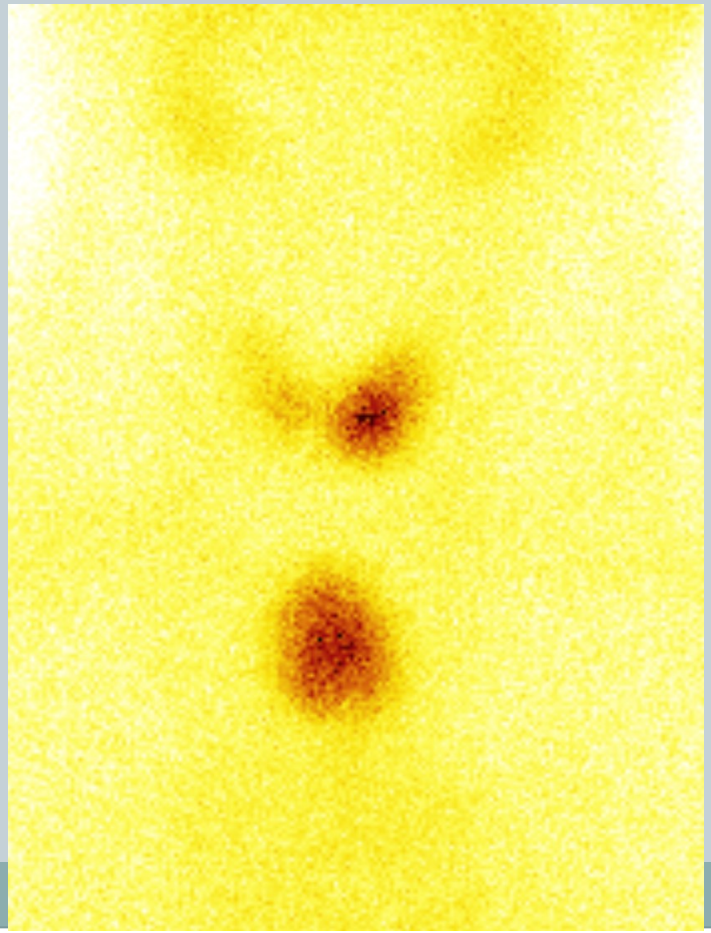


Toxic adenoma

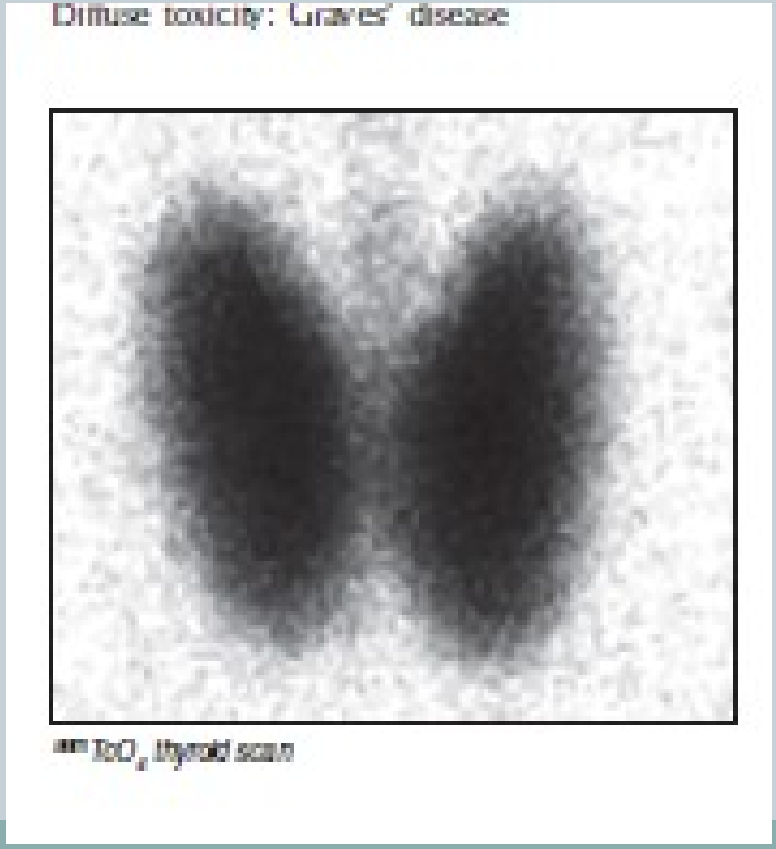


Thyroid scintigraphy

Ectopic thyroid - substernal



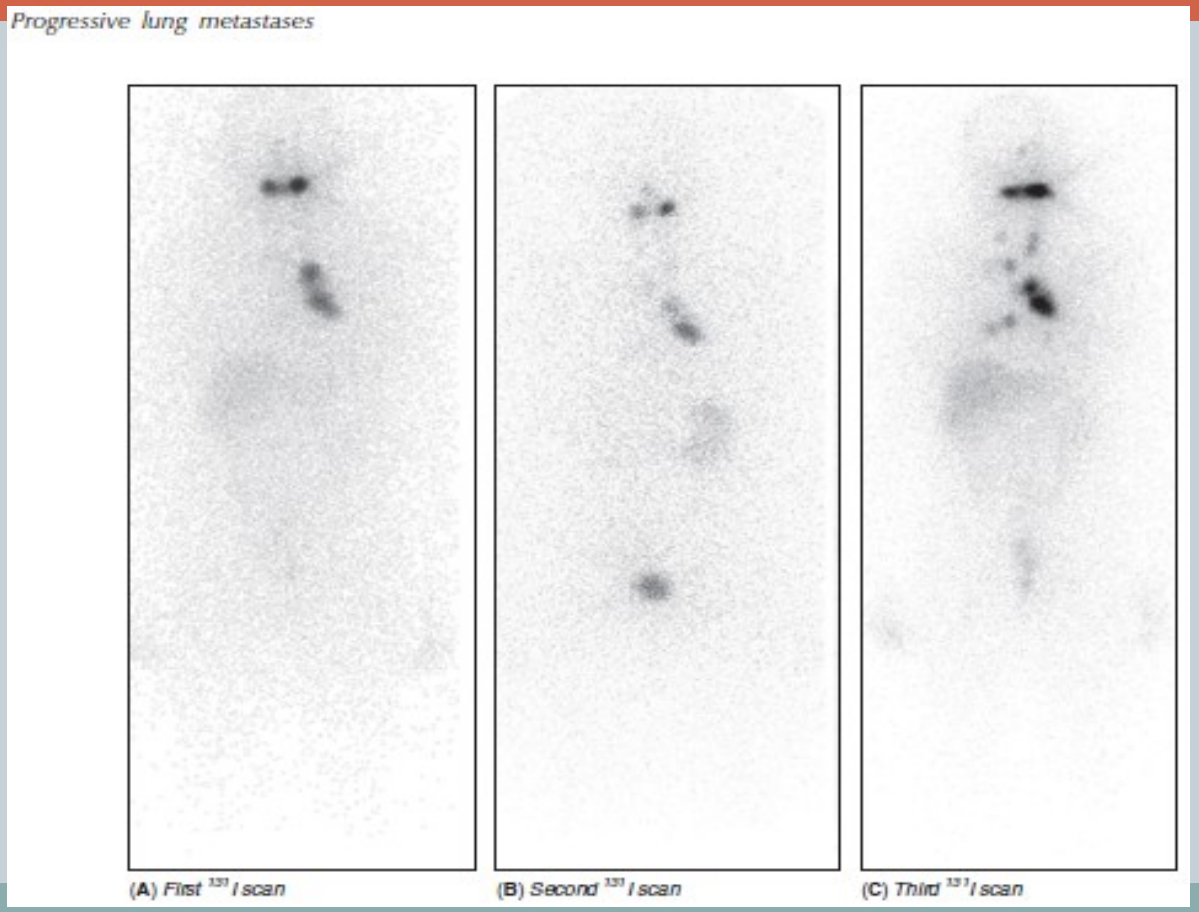
Graves-Basedow disease



Iodine 131

131I –normal finding

131I-dissemination



Parathyroid scintigraphy

- **Indication**: preoperative localization of hyperfunctioning parathyroid glands making possible minimally invasive surgery
- **RP:** ^{99m}Tc-MIBI – unspecific uptake in paratahyroid and thyroid gland

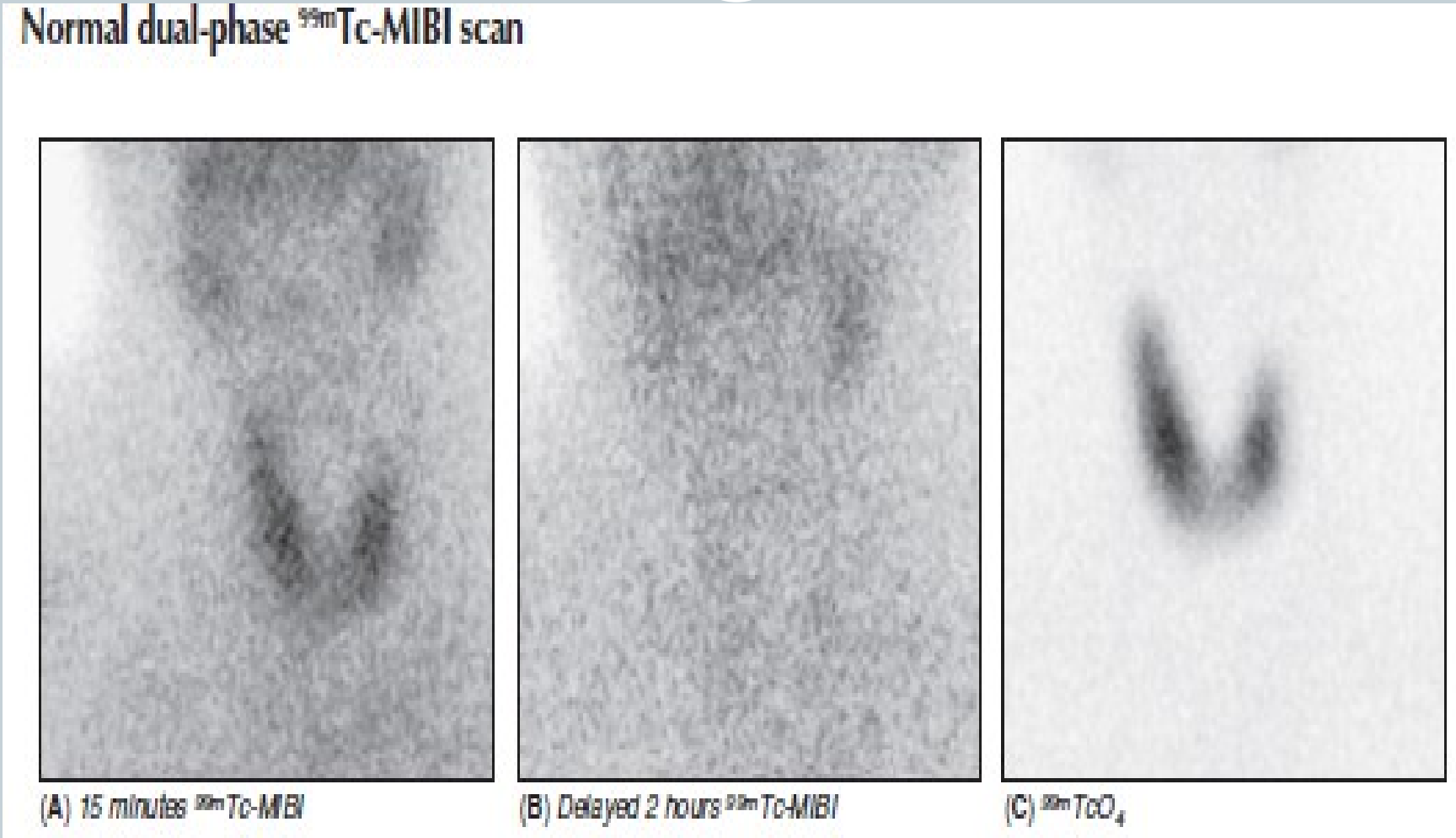
- **Protocol**:

- Two-phase scan (^{99m}Tc-MIBI), initial images 10 min after injection, second set of images at 2 hours, there is more rapid washout fromt the thyroid, so delayed images show hyperfunctioning parathyroid gland)

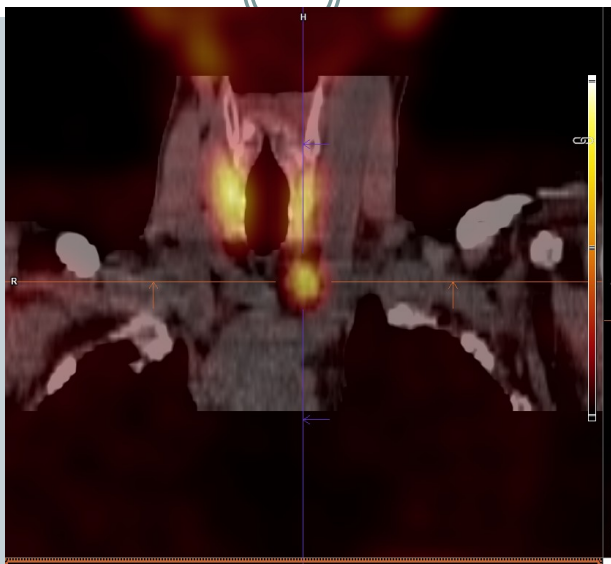
- Subtraction methodology (compares ^{99m}Tc-pertechnate study and ^{99m}Tc-MIBI study by digital subtraction)

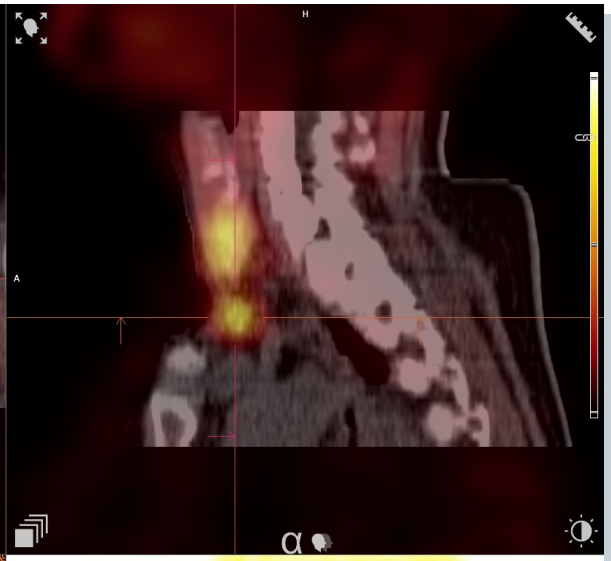
- Planar images, but SPECT, SPECT/CT with better accuracy, localization of the parathyroid gland
- If unclear/negative result – posibility of ^{18}F-choline PET

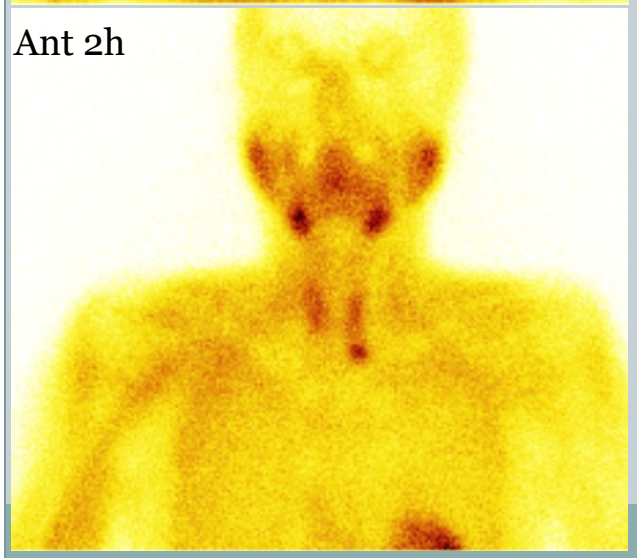
MIBI normal finding

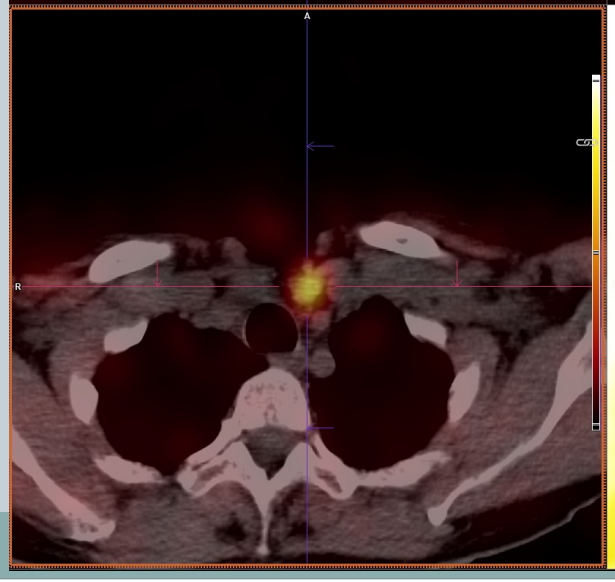


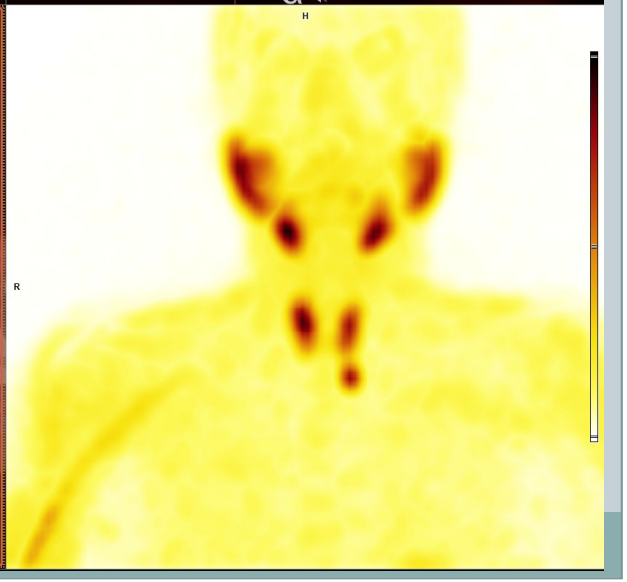
MIBI adenoma



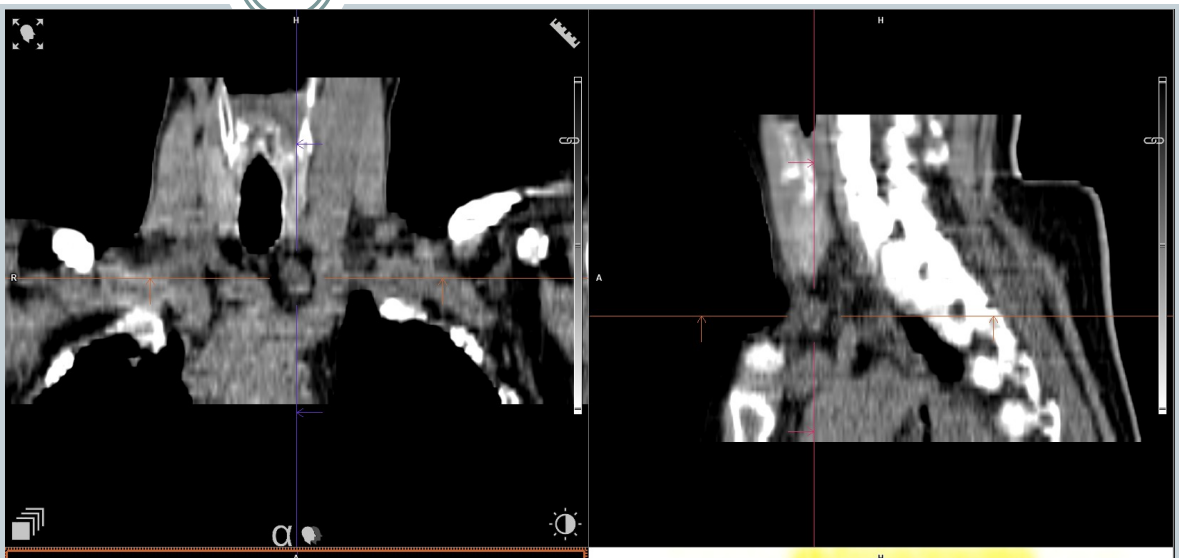


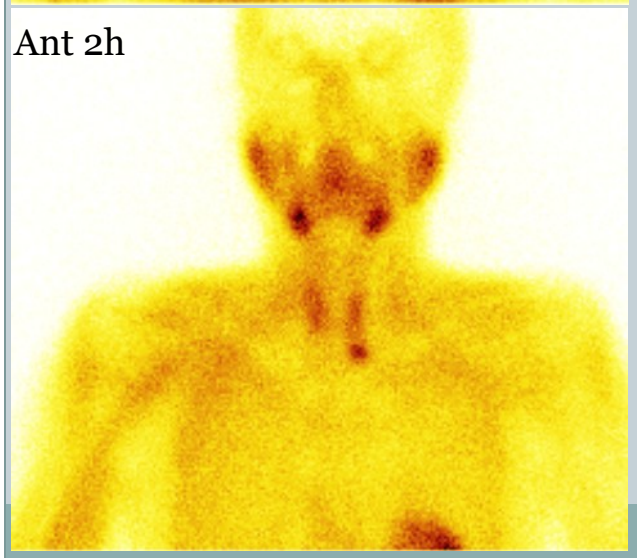


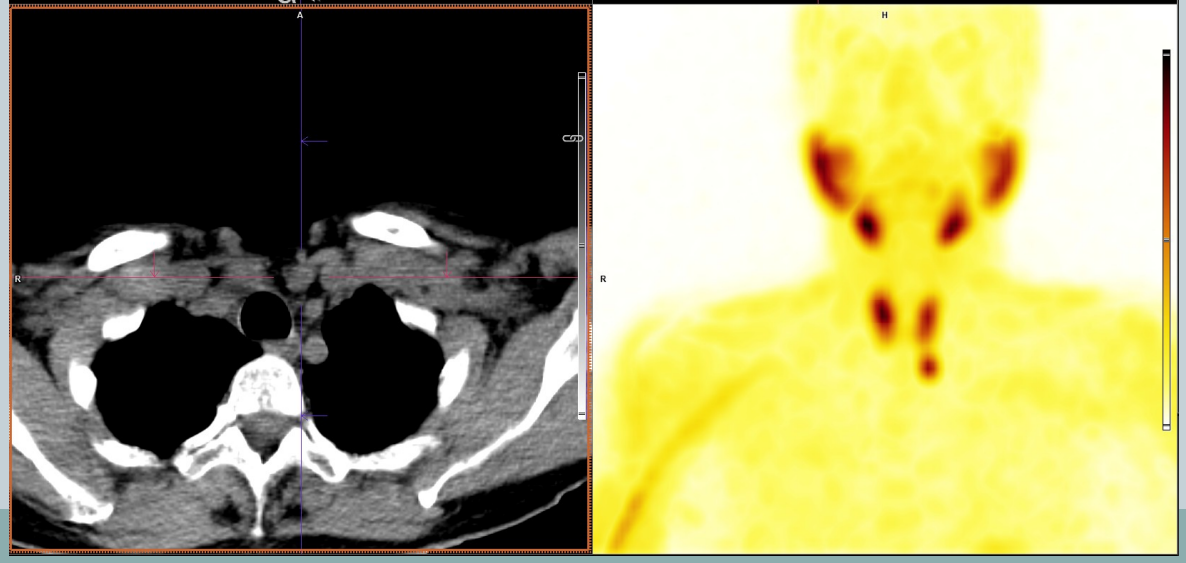




MIBI adenoma







Central nervous system

- **Brain perfusion imaging**
- Epileptogenous focus, Brain death, evaluation of cerebrovascular reserve,, dementia (AD, vascular,…)

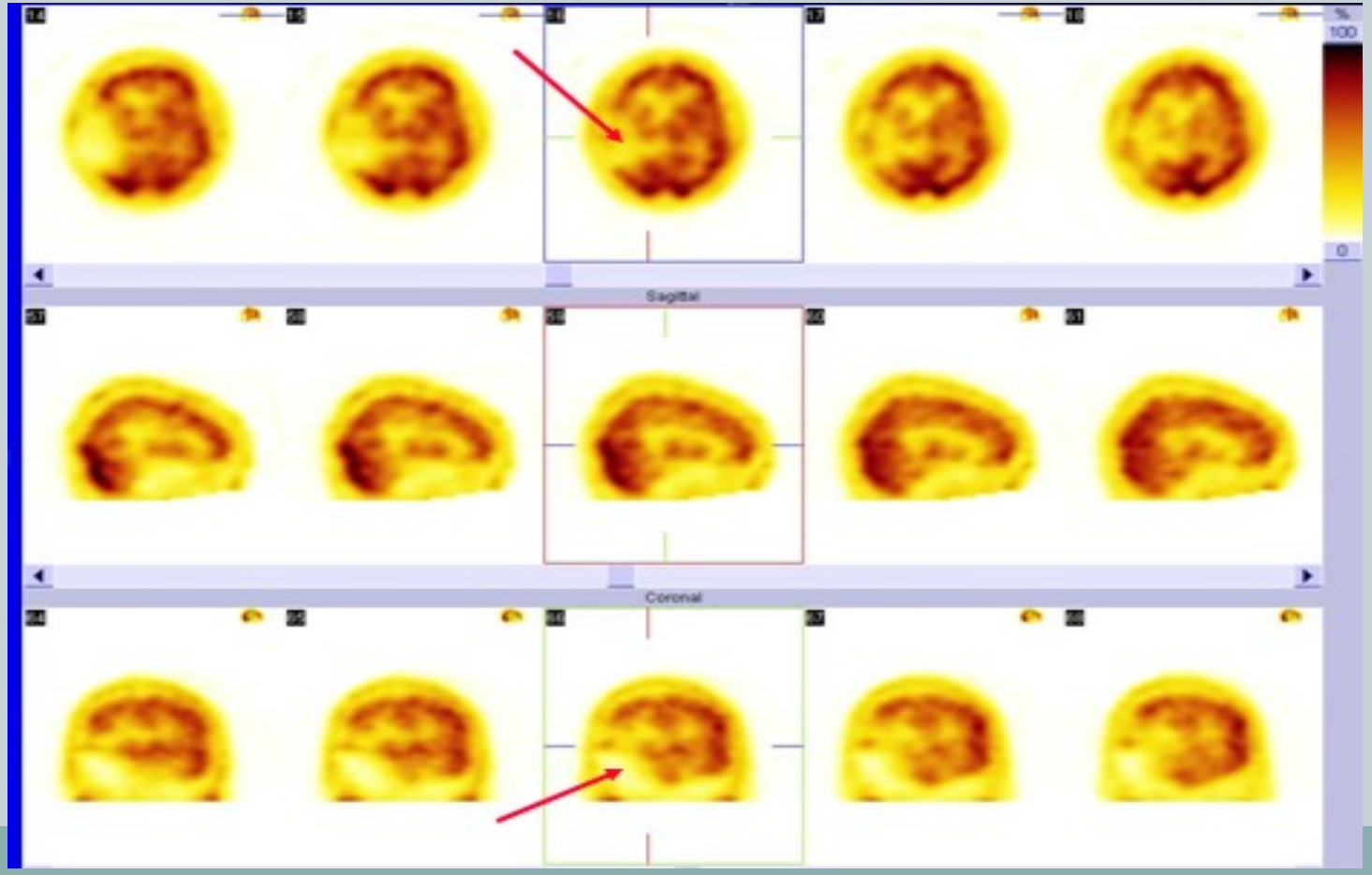
- **Neuroreceptor imaging - DaTscan**
- Parkinson disease and syndromes, essential tremor, Dementia with Lewy Bodies

- **(Cerebrospinal fluid imaging)**
- Evaluation of suspected CSF leaks, investigation of suspected communicating hydrocephalus (normal-pressure hydrocephalus), verification of CSF shunt patency

- **PET : Amyloid imaging, 18F- FDG, 18-F-FLT….**

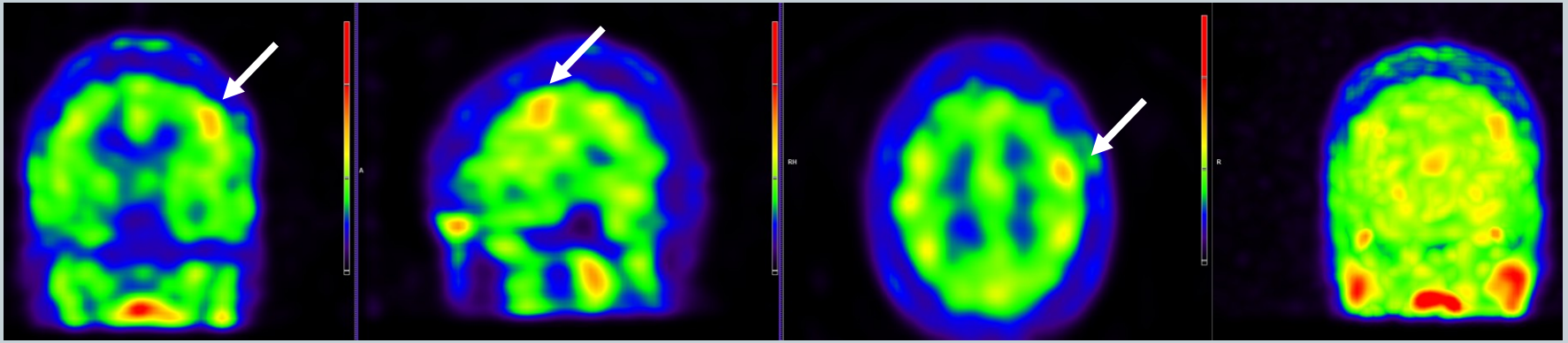
Brain perfusion

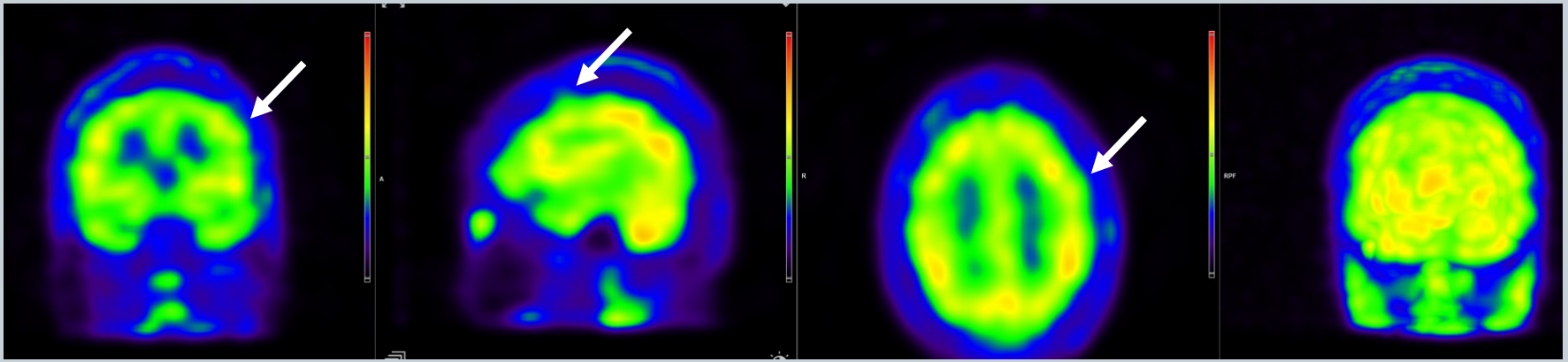
RP: ^{99m}Tc-HMPAO – lipophilic, crosses blood–brain barrier, enter neurons, becomes hydrophilic and is trapped



Brain perfusion – epilepsy

Ictal





Interictal

Brain death

- Imaging methods for diagnosing brain death: Brain perfusion study, angiography, CT angiography, transcranial Doppler ultrasound

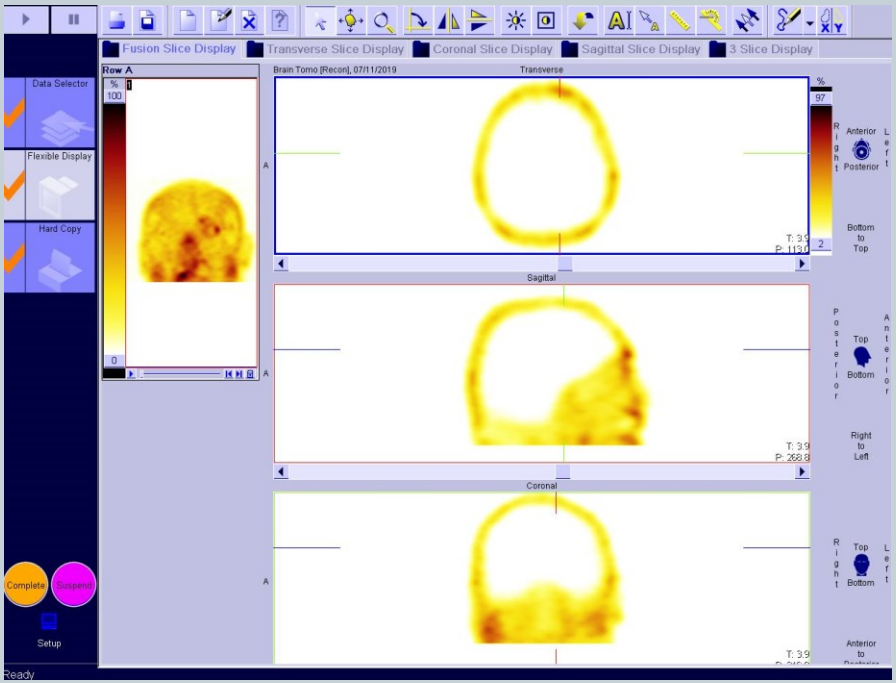
- **Criteria for brain death (brain perfusion study)**: No intracerebral arterial, capillary or venous blood flow/tracer activity on the dynamic study, no visualisation of the sagittal sinus on immediate post-injected images (99mTc-HMPAO, 99mTc-ECD)

- **Protocol**: dynamic study, immediate post-injected images better in multiple projections, SPECT

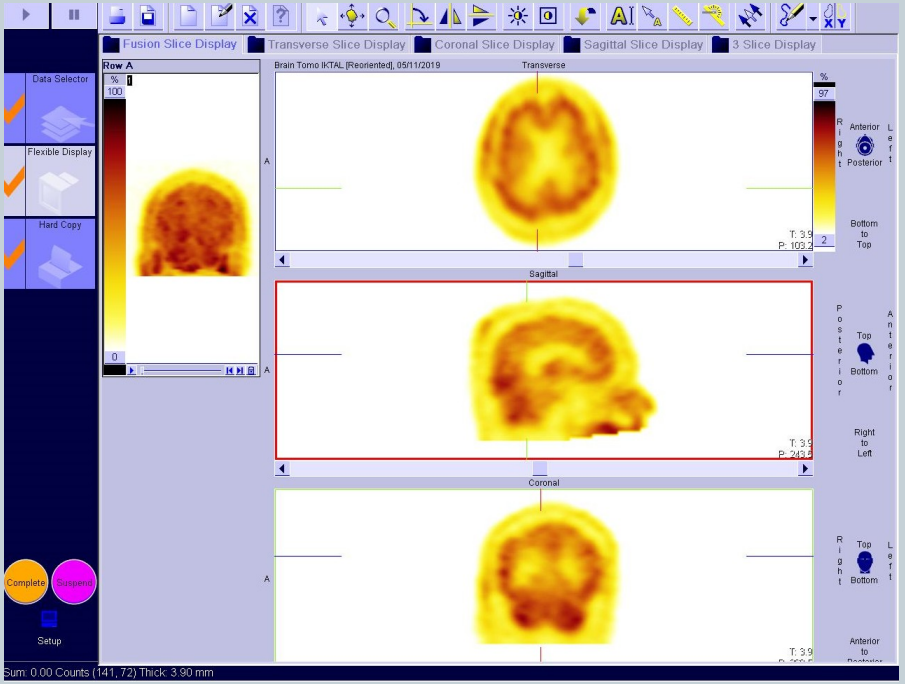
- Advantages: No iodine contrast (possible nephrotoxic effect), simple intravenous injection, preferable in patients with lossy head injury or craniectomy (arteriography can be falsely negative)

Brain death

Positive



Negative

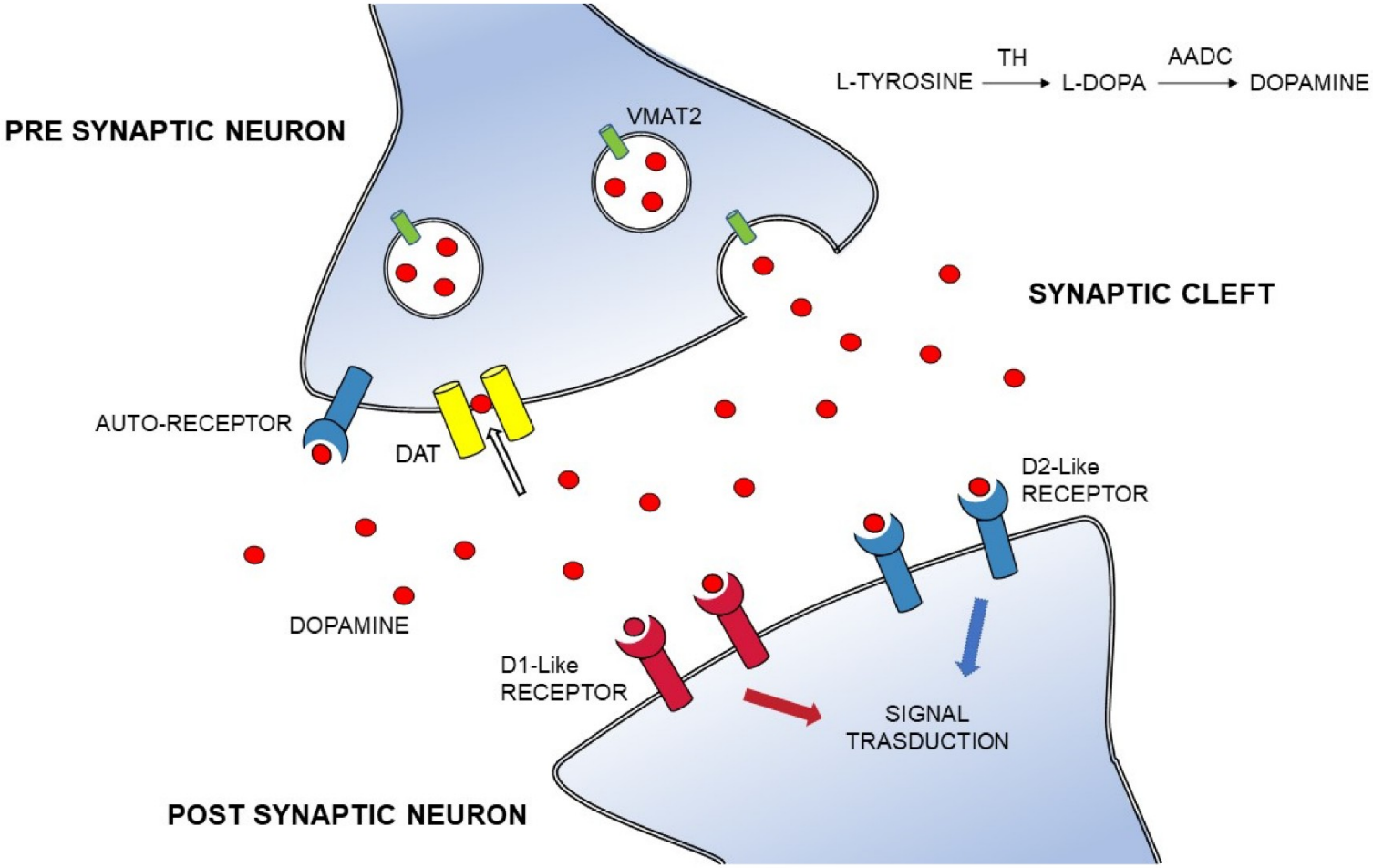


Datscan – 123Ioflupan

- Idiopatic Parkinson disease – degeneration of nigrostriatal pathways, impairment of afferent pathway from substantia nigra to BG = presynaptic impairment
- Parkinson's disease plus diseases (MSA, PSP…) - directly affected striatum, affected pre- and postsynaptically
- Essential tremor, parkinsonism secondary to medication = no dopamine synapse disorder

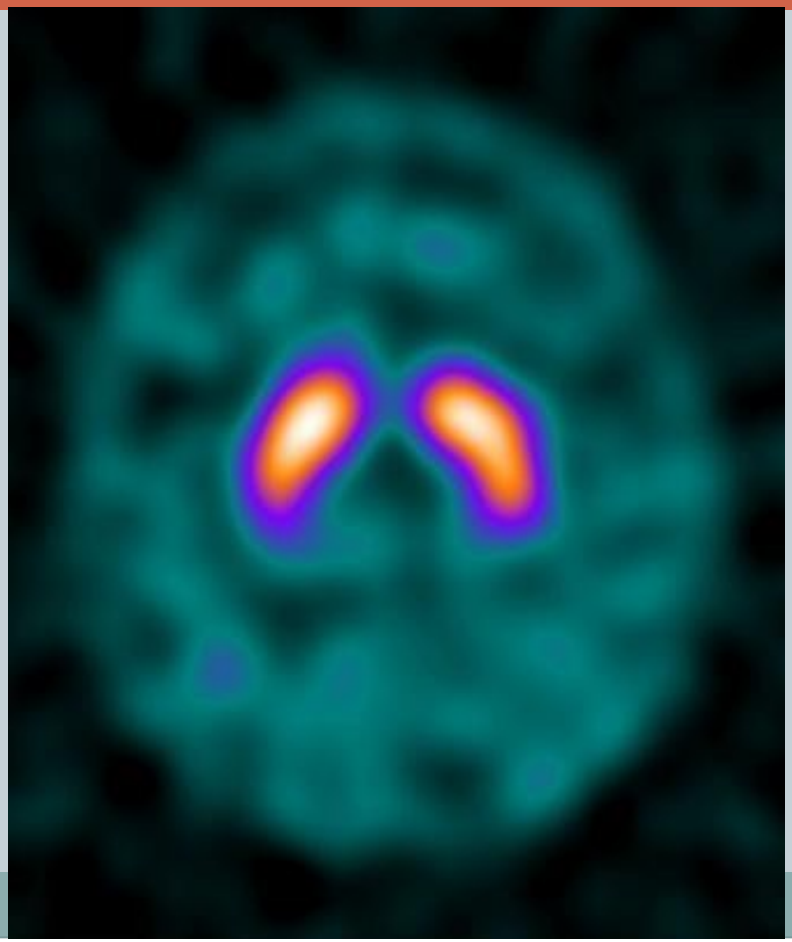
- **^{123}I-Ioflupan** : distribution of **presynaptic dopamine transporters**, cocaine analogue, thyroid blockade preparation

- **Indications**: differentiation of Parkinson's disease and Parkinson plus diseases from essential tremor, dg. dementia with Lewy bodies

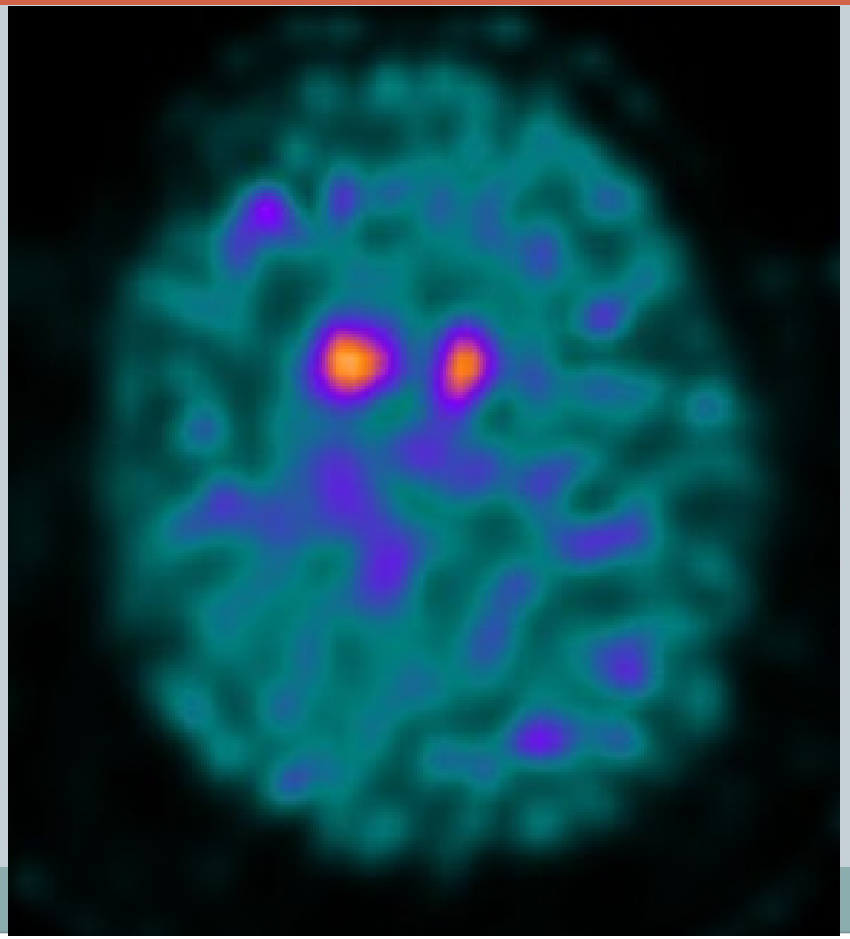

L-TYROSINE
TH
L-DOPA
AADC
DOPAMINE
PRE SYNAPTIC NEURON
VMAT2
SYNAPTIC CLEFT
AUTO-RECEPTOR
DAT
D2-Like
RECEPTOR
DOPAMINE
D1-Like
RECEPTOR
SIGNAL
TRASDUCTION
POST SYNAPTIC NEURON

Datscan

Normal



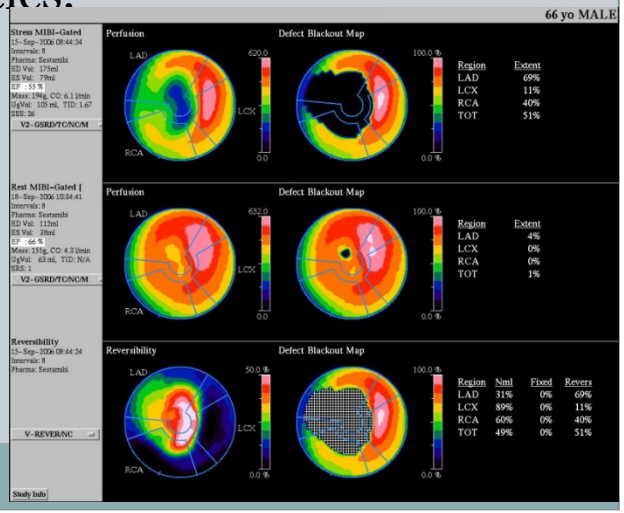
Positive – Parkinson disease



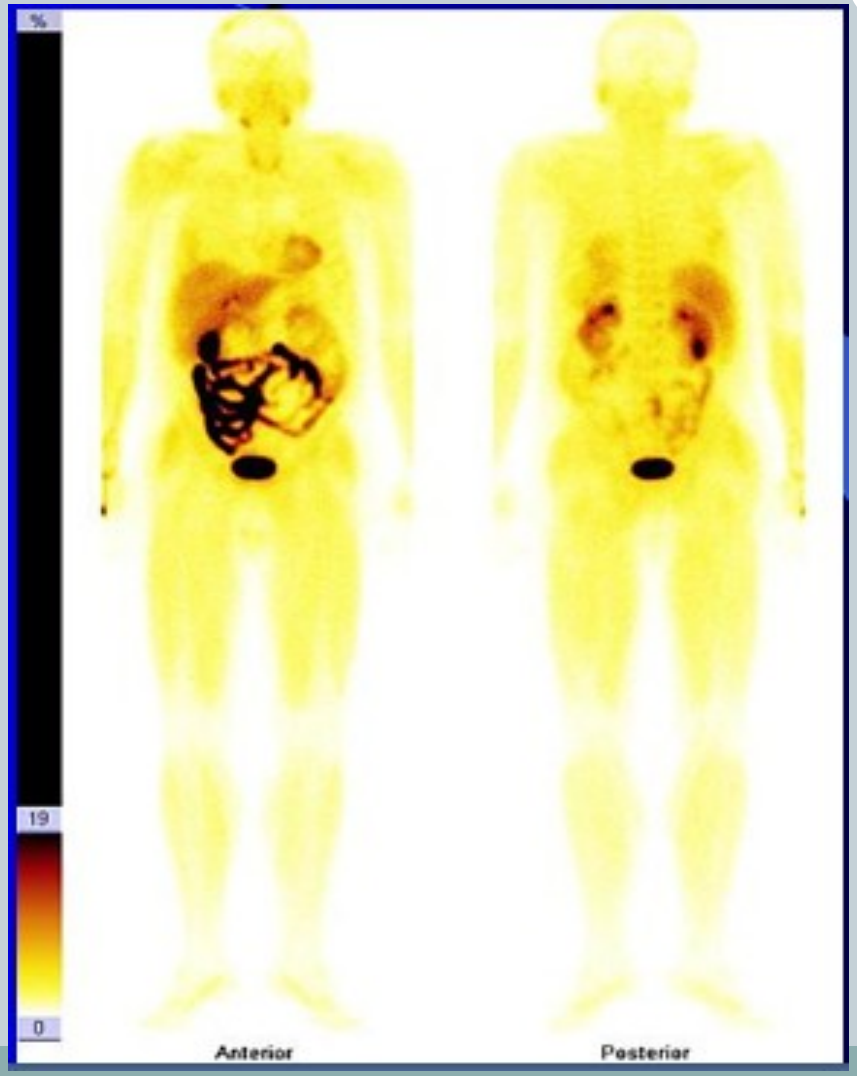
99mTc-MIBI (sestamibi)

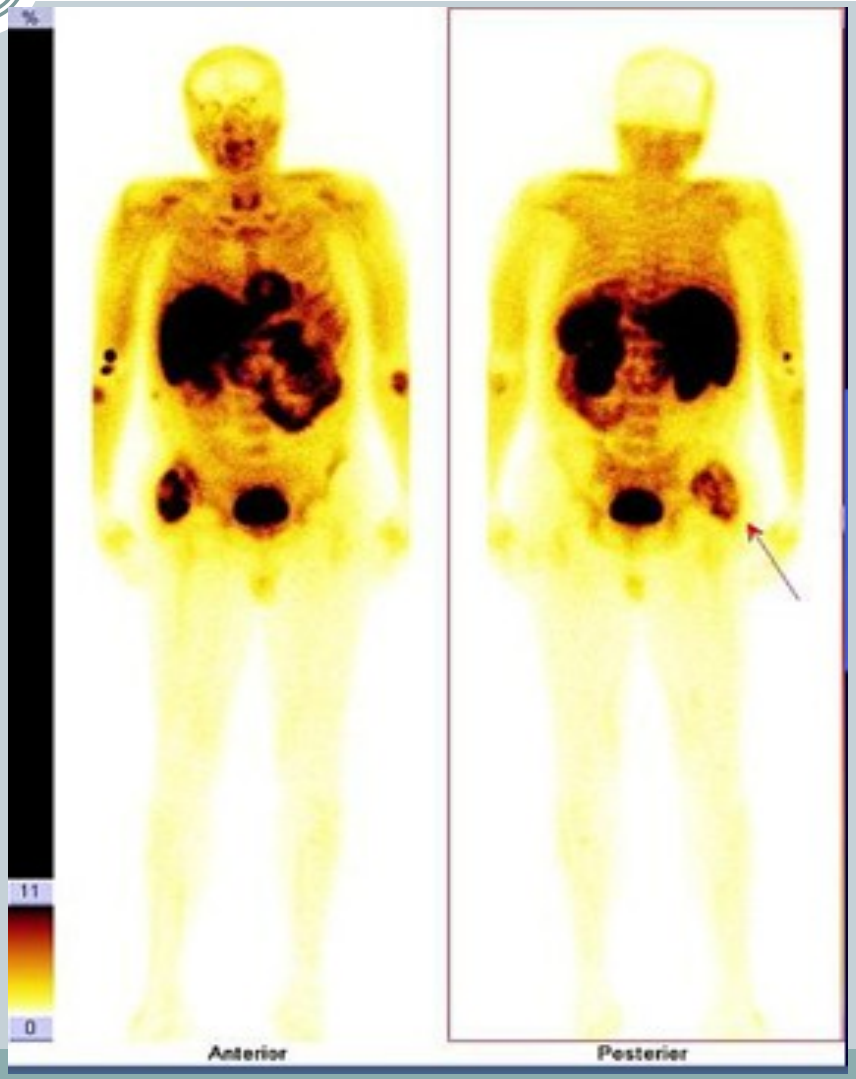
- Nonspecific tumor binding agent, it is concentrated in mitochodria of the viable cells as a result of the passive difusion
- **Use**:
- **cardiology** (cardiac perfusion studies – dg. ICD)
- **endocrinology** (localisation of hyperparathyroid gland)
- oncology – follow up of patients with differentiated thyroid cancer as an alternative to ^{131}I

  - earlier in pts. with multiple myeloma, breast ca, soft tissue sarcomas
  - accumulation also in other types of malignancies.



MIBI scan





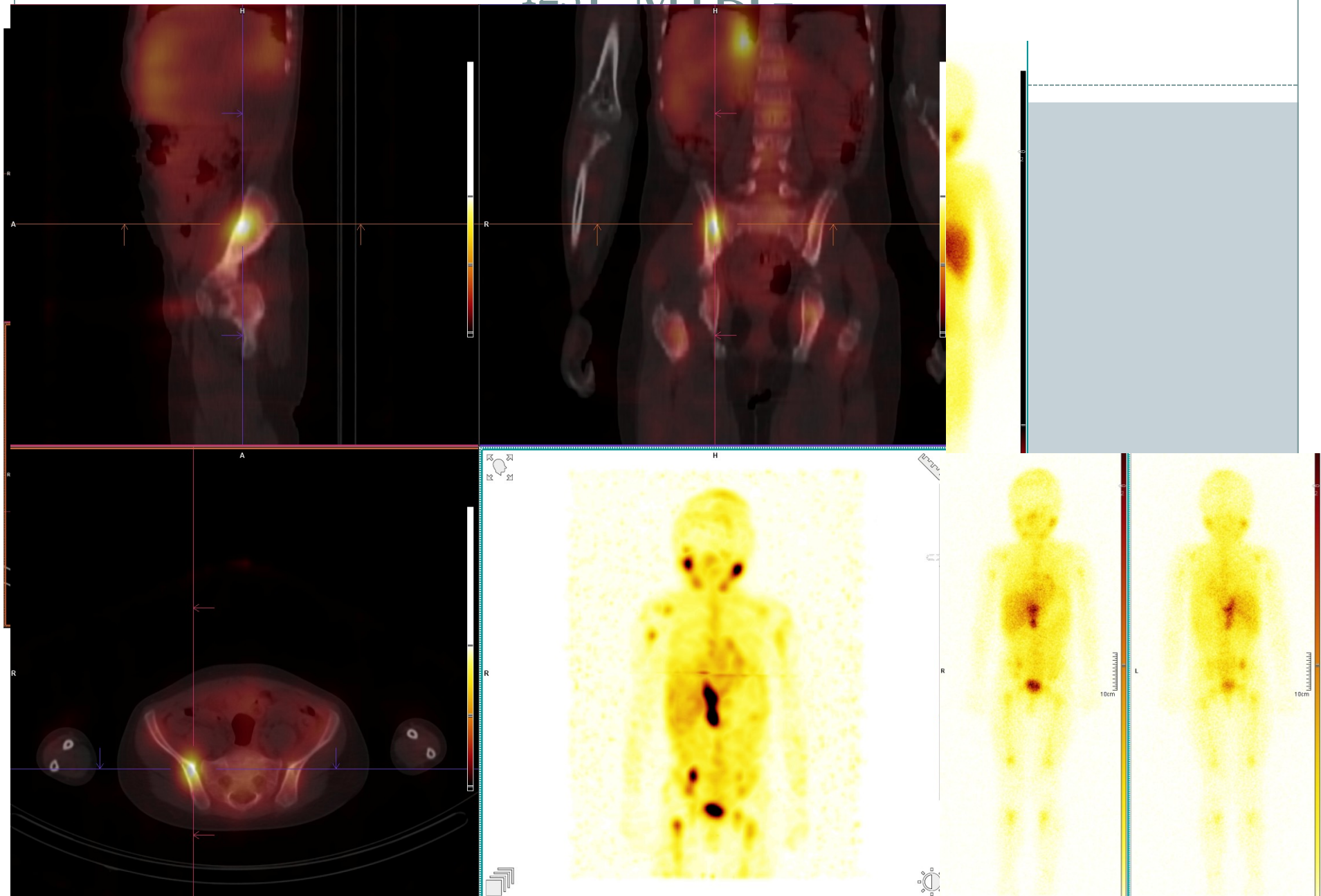
123I-MIBG – adrenal medullary scintigraphy

- Metajodobenzylguanidin = guanethidin analogue (similar to norepinephrin) that accumulates in adrenergic and neuroblastic tumors
- Protocol: Wholebody planar scan + SPECT/CT at 4 and 24 hours after injection, patient preparation before study! (thyroid blockade)

- **Indication** : diagnosis, staging, management of adrenergic neuroectodermal tumors (pheochromocytomas, extraadrenal paragangliomas, neuroblastomas), before planned 131I-MIBG therapy of medullary thyroid cancer

- **Pheochromocytoma/paraganglioma** – catecholamine-secreting tumors (hypertension, arrytmias), 10%bilateral pheochr., 10% extraadrenal paragangliomas, 10% malignant, found from the bladder up to the base of the skull
- **Neuroblastoma** – embryonal malignancy of the sympathetic nervous system, typically in children younger than 4years of age, 70% originate in retroperitoneal area, 131I-MIBG for therapy after the failure of previous conventional therapies

123I-MIBG



Imaging of somatostatin receptors

- Imaging of the distribution of somatostatin receptors, which are highly expressed in neuroendocrine tumors (especially pulmonary and gastro-enteropancreatic NETs)

- **^{111}In-Pentetreotid** (Octreoscan) - synthetic somatostatin analogue with high affinity to SSTR2, SSTR5

  Protocol : wholebody scan + SPECT/CT at 4h, 24h (sometimes 48h) after injection

Newer alternative:

- **Tektrotyd** = ^{99m}Tc-EDDA/HYNIC-TOC – at 1h and 4h

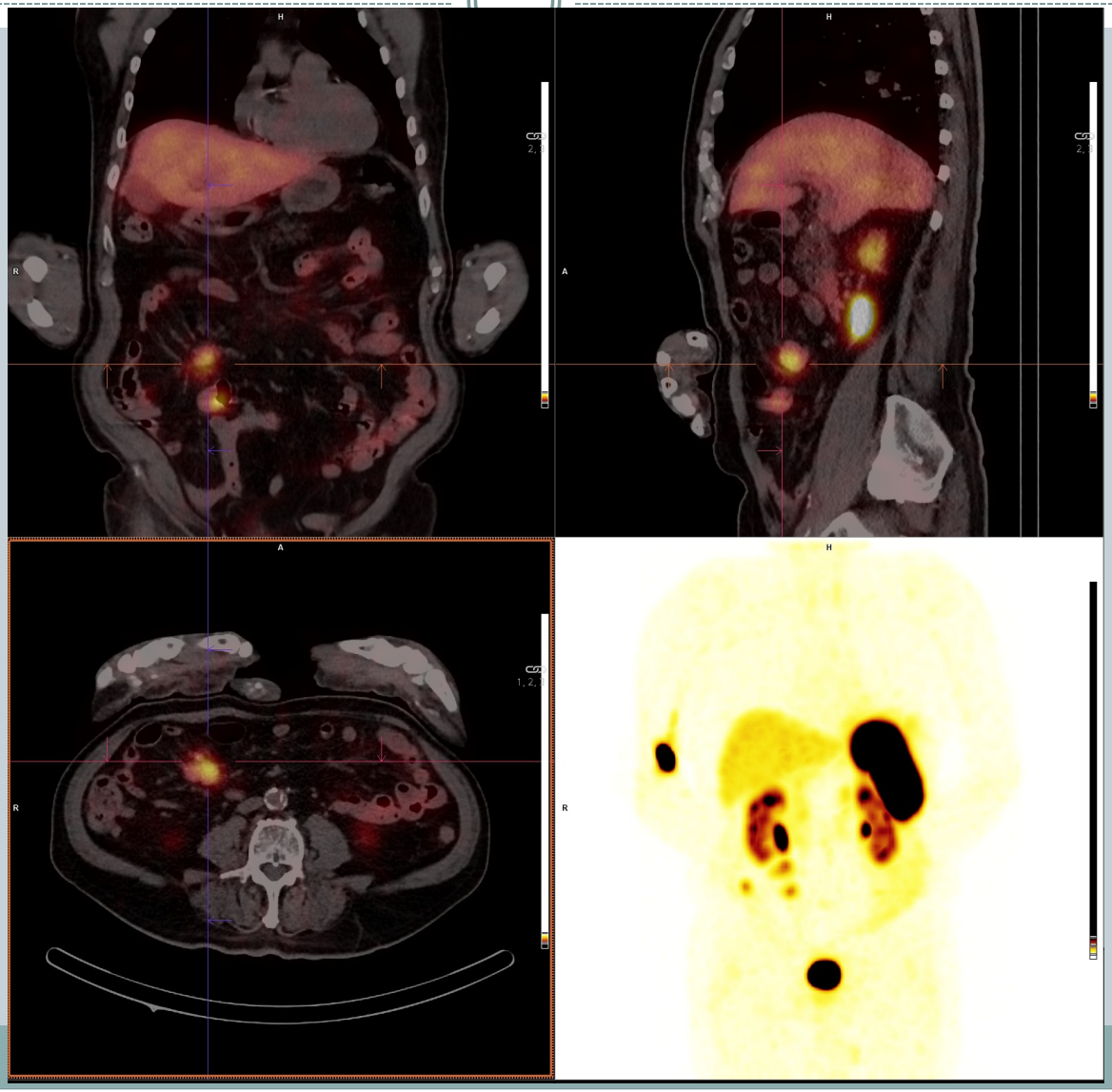
  - better image quality than Octreoscan (energy of ^{99m}Tc), 1-day exam, lower radiaton dose, lower price

- **Indication**: evaluating neuroendocrine tumors, especially carcinoid , gastroenteropanctreatic tumors, small cell lung cancer, meningioma, variable affinity for medullary thyroid cancer, insulinoma
- **Limitation** : false positive uptake in bening inflammmatory granulomatous disease (sarcoidosis, TBC, IBD...), in tumors expressing lack of appropriate receptor subtype

- PET alternatives:
- **68Ga-DOTA-TOC** - best sensitivity and image quality, lower availability (^{68}Ga), higher price
- 18F-FDG PET useful in poorly differentiated neuroendocrine tumors

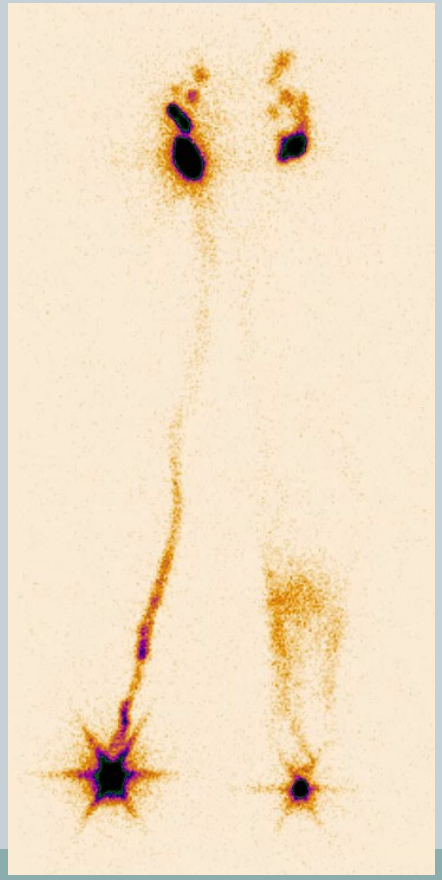
- **Therapy**: **^{177}Lu-**DOTA-TATE – beta- radiation therapy in patients with progressing GEP NETs

Tektrotyde – NET in ileum + lymph nodes



Lymfoscintigraphy of limbs

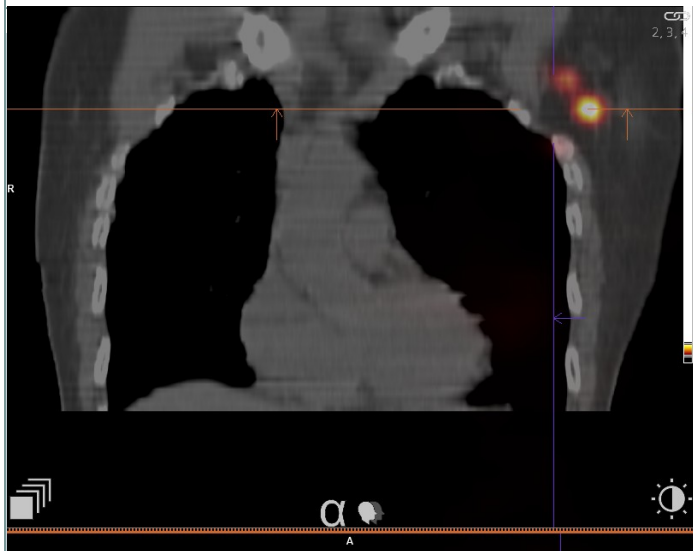
- RF: **^{99m}Tc-nanocoloid**, subcutaneus
- **Indication**: lymphedema

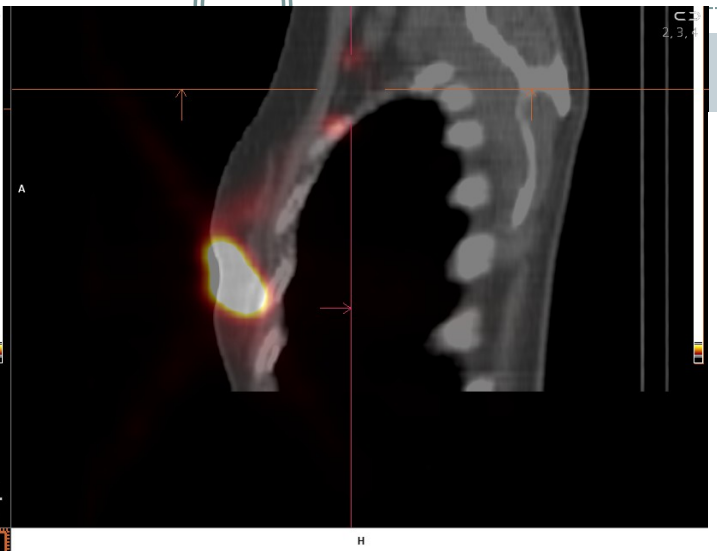


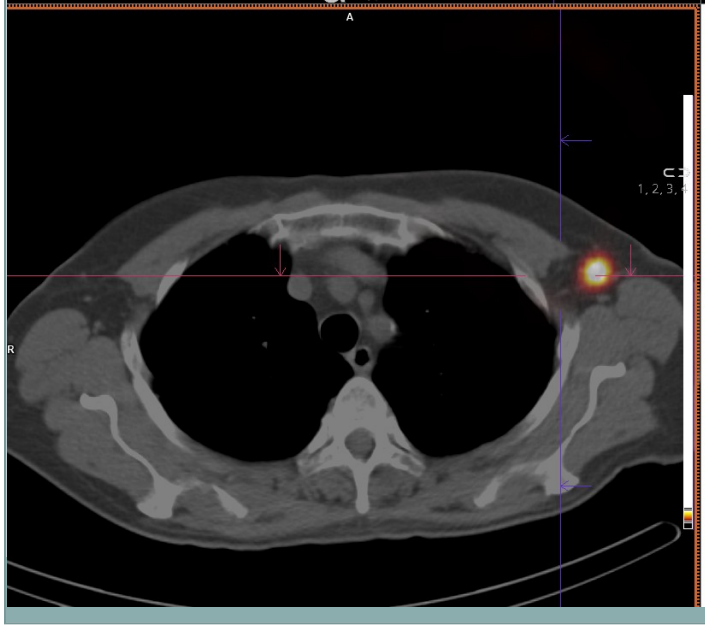
Lymphoscintigraphy – SLN detection

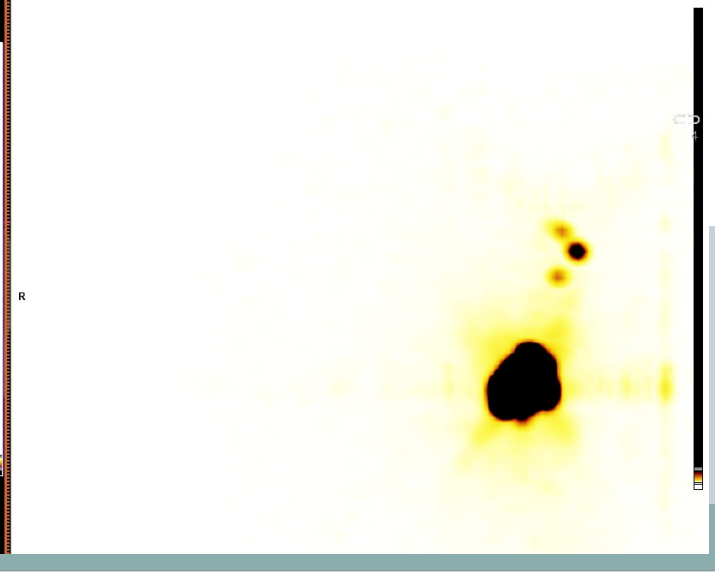
- **Small amount of radioactive active colloidal tracer is injected into the skin in proximity to tumor leasion to determine the SLU receiveing drainage and thus possibly metastasizing tumor cells**
- **SLN** (sentinel lymph node) = the first lymph node (nodes) which is first on a direct lymphatic drainage pathway from a primary tumor site, and as such is the most likely the location of metastasis
- Identification and histopathological examination of the SLU (after surgical removal) allow us to predict a regional metastatic potential of that given tumor and thus to choose optimal therapy
- **99mTc-nannocolloid**
- **Indication** : malignant melanoma, breast cancer, cancer of the tonque, neck, head, vulva
- **Contraindication**: already known metastatic disease indicated fo systemic therapy, suspected altered lymphatic drainage due to the previous surgery procedure

Breast cancer – detection of SLN

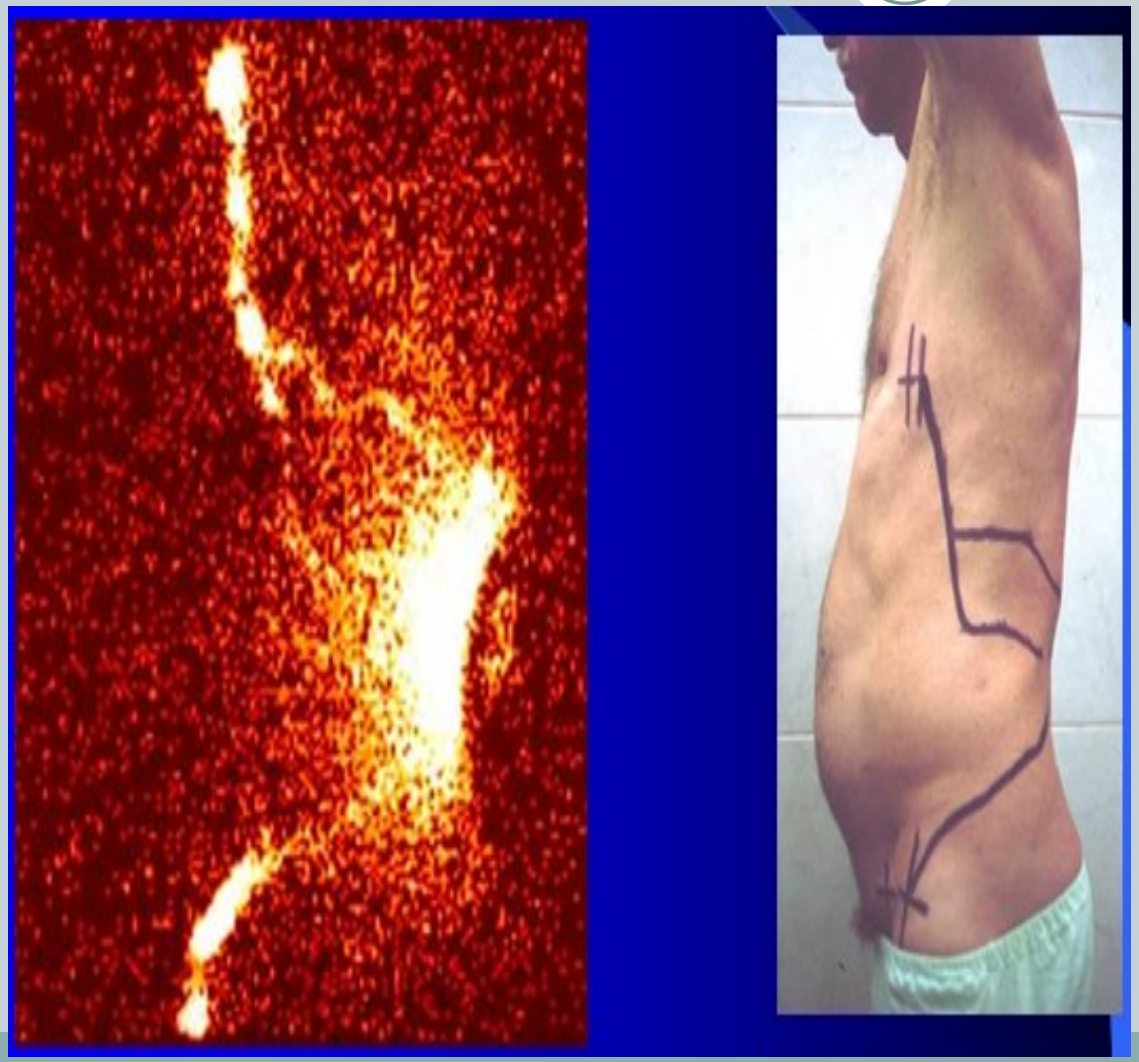








SLU imaging – patient with melanoma



- Tracer was injected around the leasion on the lower back and drained to 2 lymph nodes. They were marked superficially over the skin