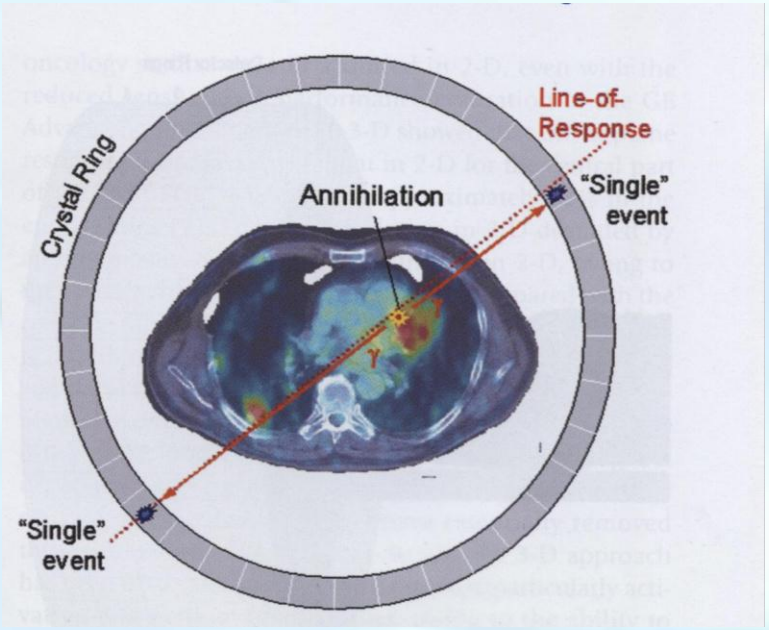
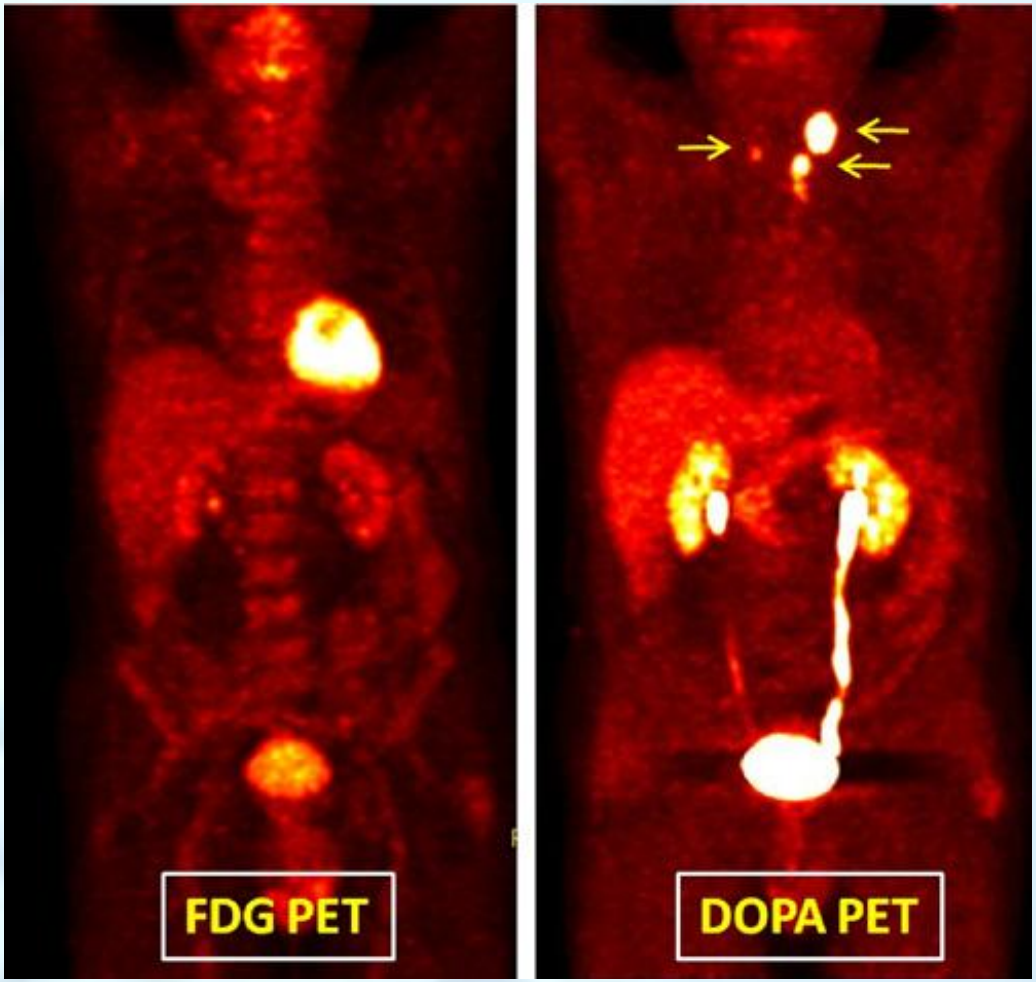
PET and PET-CT





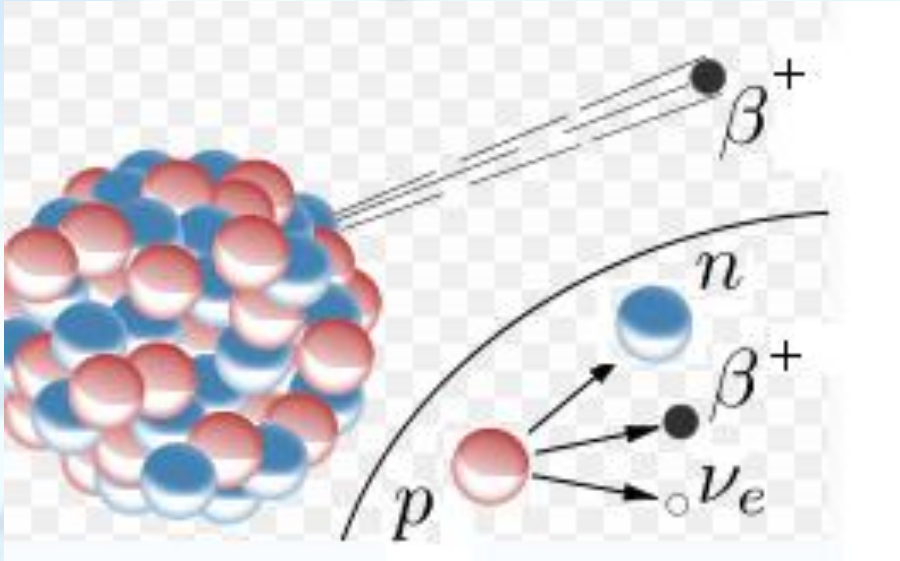
Assoc. prof. Vinko Marković, MD, PhD
Assoc. prof. Ante Punda, MD, PhD
A. Barić, MD, nucl. med. spec.

Beta plus decay- positron decay

A nucleus that has a lack of neutrons converts one proton into a neutron while releasing a positron and one neutrino

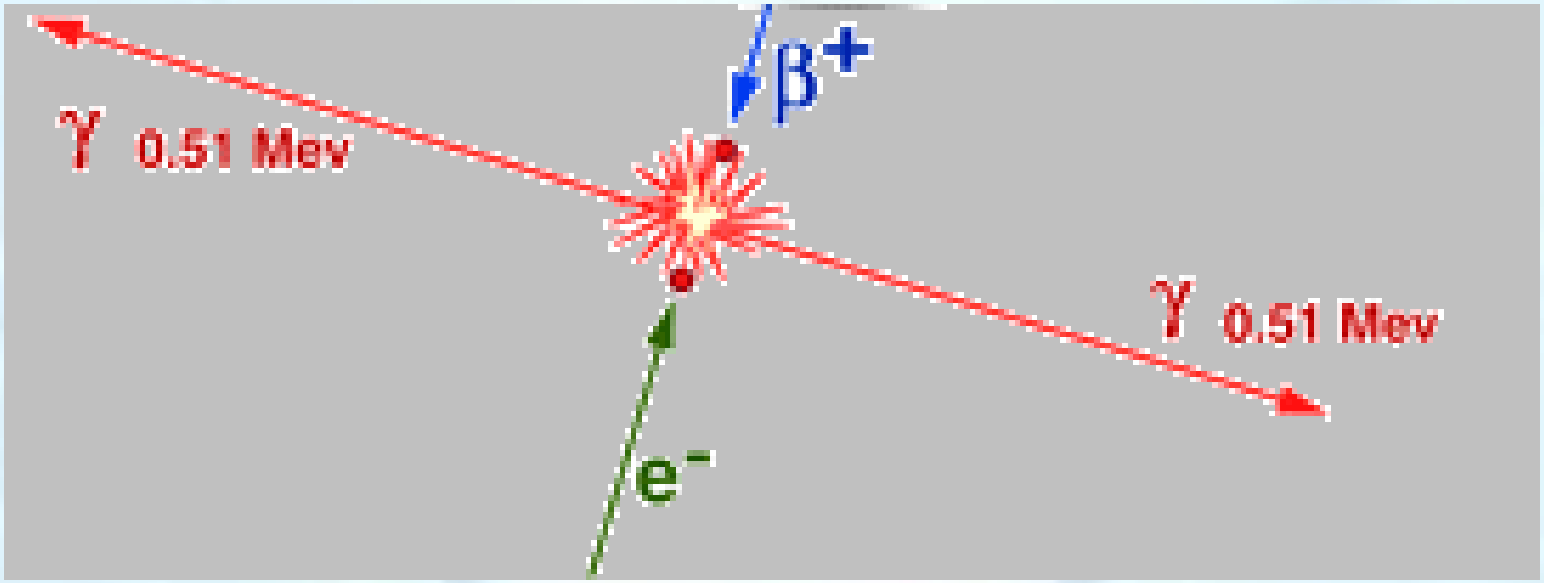
Atomic number is reduced by one, and a new element has been created.

During positron decay- one particle disappear while the other is created



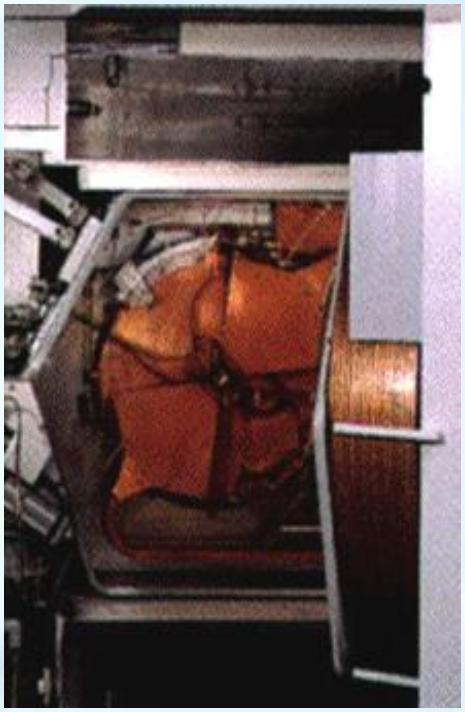
- Positron is emitted (β^+) with energy of: 0-E_{max} and neutrino.
- ie. ^{18}F, E_{max} = 0.633 MeV.

Positron decay- Annihilation radiation



β^+ decay is followed by **annihilation radiation**.
Passing through the tissue positron slows down and meets its antiparticle (free electron) wich leads to **annihilation (disappearance)** of both particles, with emission of two photons of 511 keV (energy equivalents of their mass at rest) in opposite direction.

Nuclear reactions for positron emitter production in cyclotron



Target Material	Nuclear Reaction[a]	Radionuclide
^{18}O water	$^{18}O(p,n)\ ^{18}F$	^{18}F
^{20}Ne gas	$^{20}Ne(d,\alpha)\ ^{18}F$	^{18}F
$^{14}N_2$ gas	$^{14}N\ (p,\alpha)\ ^{11}C$	^{11}C
^{16}O water	$^{16}O\ (p,\alpha)\ ^{13}N$	^{13}N
Enriched $^{15}N_2$ gas	$^{15}N\ (p,n)\ ^{15}O$	^{15}O

Positron emitters

PET imaging			
^{11}C	20 min	Beta-plus	511 (200%)
^{13}N	10 min	Beta-plus	511 (200%)
^{15}O	2 min	Beta-plus	511 (200%)
^{18}F	110 min	Beta-plus	511 (193%)
^{82}Rb	1.3 min	Beta-plus	511 (191%)
^{62}Cu	9.7 min	Beta-plus	511 (196%)
^{68}Ga	1.1 h	Beta-plus	511 (178%)
^{124}I	4.18 d	Beta-plus	511 (47%)

Characteristics of some of positron emitters

Nuclide	Half-life (min)	SA (Ci/μmol)	Decay % β^+	β^+ Energy (MeV)		Range in Water (mm)	
				Max.	Mean	Max.	Mean
^{11}C	20.4	9220	99.77	0.9601	0.3856	4.1	1.1
^{68}Ga	68.3	2766	87.7	1.8991	0.836	8.2	2.9
^{18}F	110	1710	96.7	0.6335	0.2498	2.4	0.6
^{64}Cu	768	245	17.87	0.6529	0.2781	2.9	0.64
^{86}Y	884	213	12.4	1.2535	0.55	5.2	1.8
			5.6	1.578	0.696	6.5	2.9
^{124}I	6048	31	11.0	1.5323	0.6859	6.3	2.3
			12.0	2.1350	0.9736	8.7	3.5

Why is the F-18 the most ideal positron emitter?

1. It has the lowest positron energy (640 keV), and therefore a short range in tissue (max. 2,4 mm, average 0,6 mm), what provides scintigrams with highest resolution (location of positron emission and annihilation detection are different, the difference is lower as the positron range is shorter- greater precision of positron emission detection)

2. It can be produced with a high specific activity

3. High activity can be produced (10 Ci)

4. It has a relatively large percentage of labeled PET tracer (20-40%)

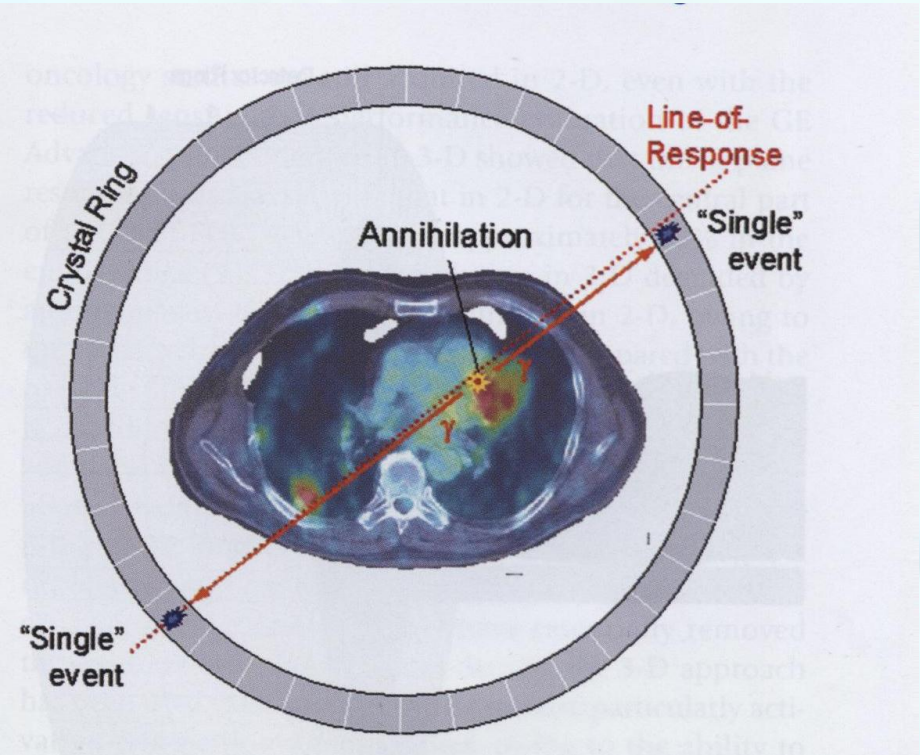
5. Acceptable radiation dose for patients

6. Half-life of 110 minutes- long enough to enable transportation from the place of production to the point of use

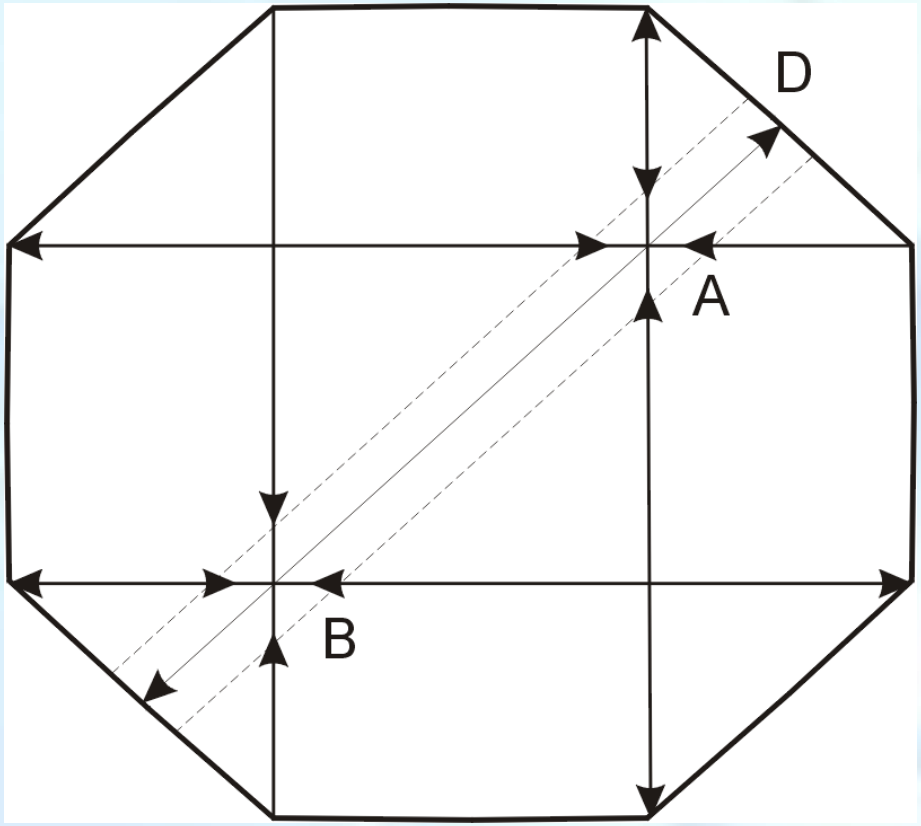
Scintilation detectors in PET

- BGO: bismuth-germanate-oxide
- LSO: lutetium oxy-ortho-silicate
- GSO: gadolinium oxy-ortho-silicate

Annihilation radiation detection

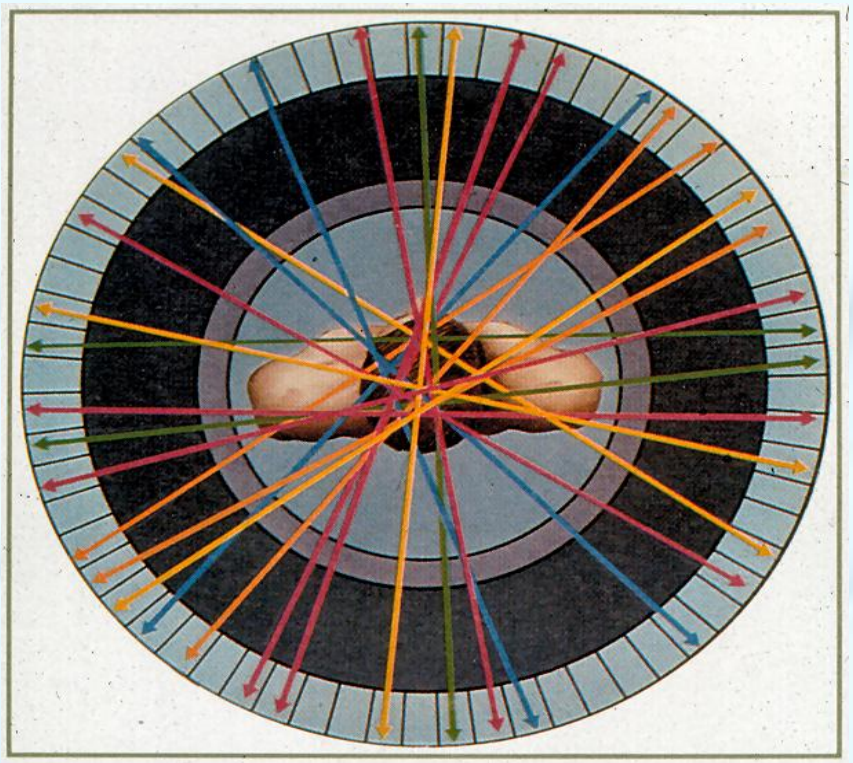


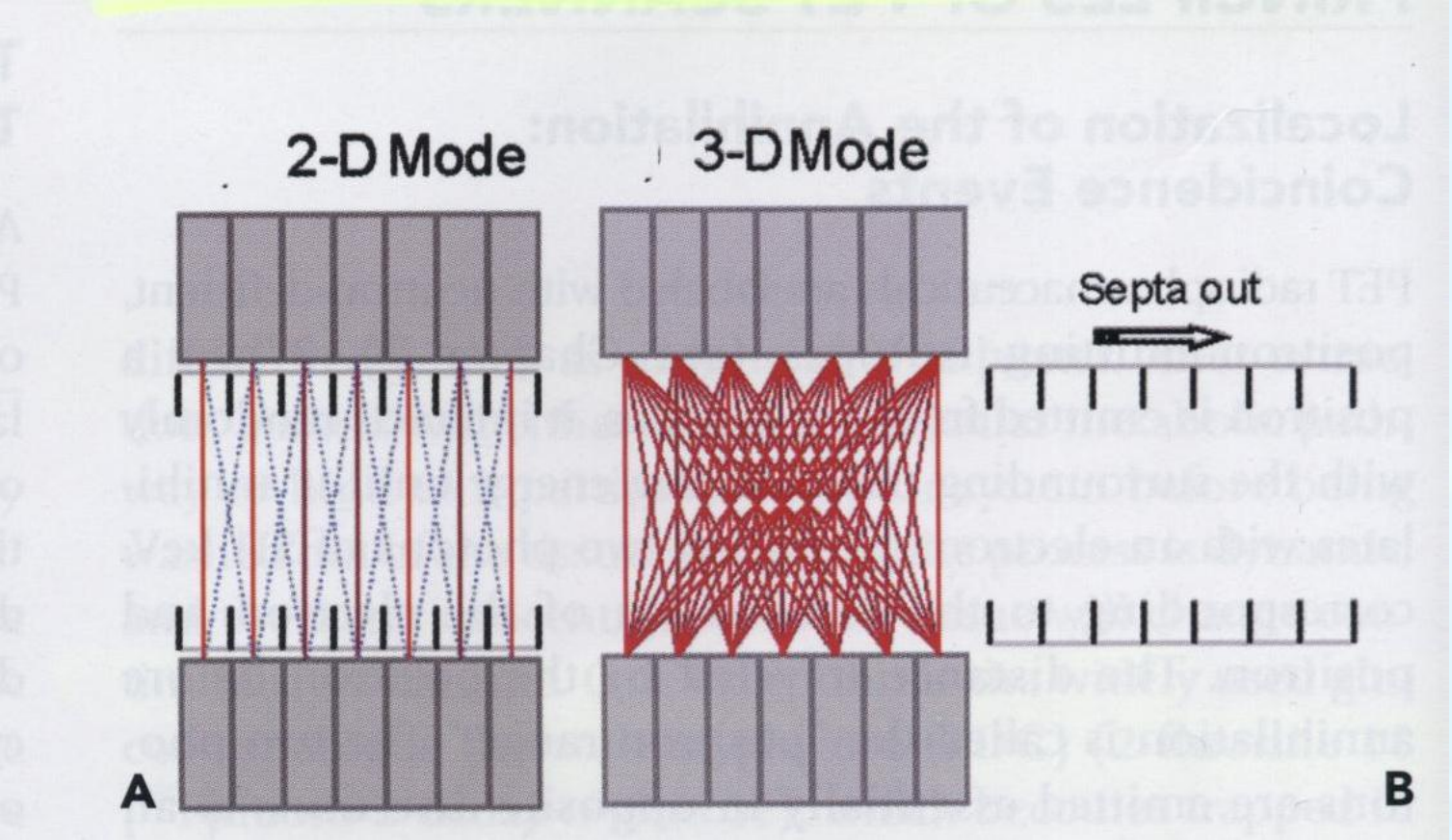
PET image formation



The location of positron sources (A, B) are the intersections of routes that pass through the detector pairs

Annihilation radiation detection

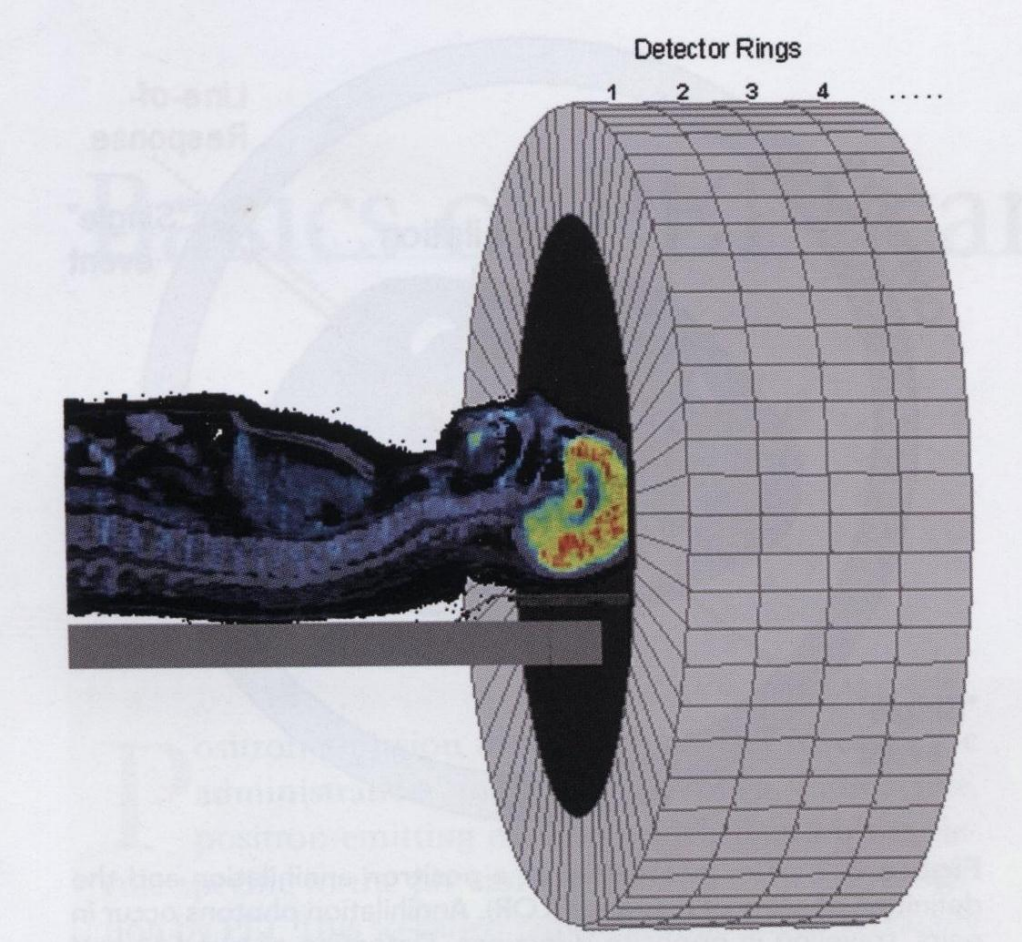




2D mode: collimator's septa blocks annihilation radiation coming from an oblique angle; allow only opposite and adjacent detectors to register annihilation radiation

3D mode: without collimator's septa, annihilation radiation is detected from all directions. Sensitivity is increased for 5 times, but reconstruction is more complicated.
3D aquisition mode is used for CNS because the brain has less of surrounding structures (wich are also sources of annihilation), comapared with other organs.

Detector design



The detectors are arranged in several loops to form a cylinder, in which patient is pulled in.
The length of the cylinder is 15-25 cm.
Smaller organs (brain and heart) can be scanned without longitudinal movement of the detector.

PET camera

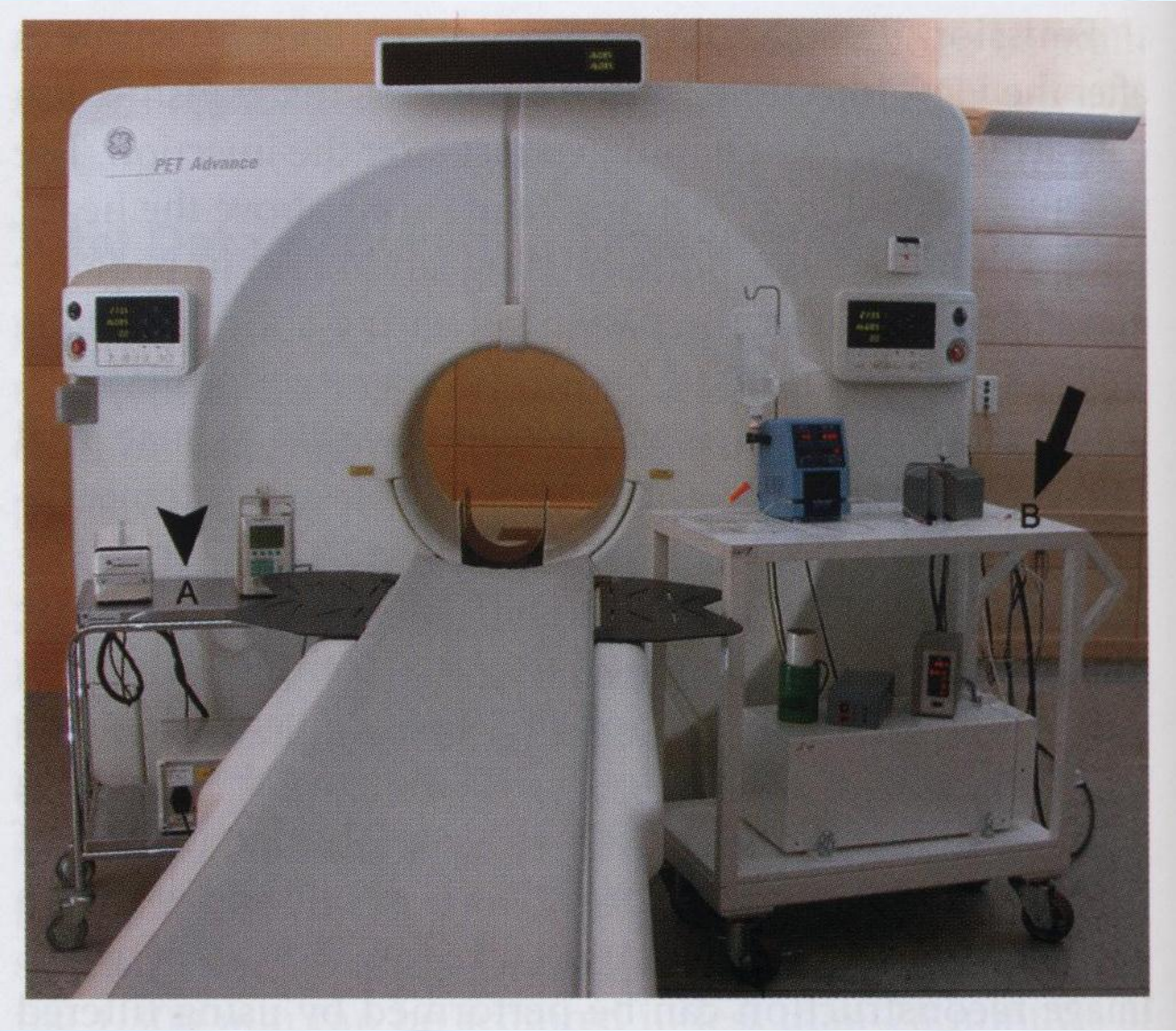
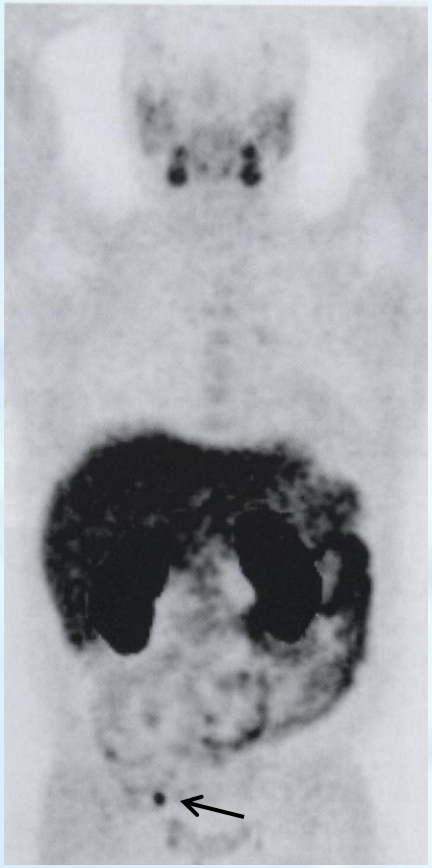
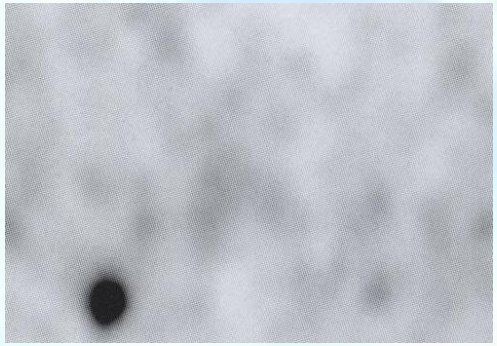


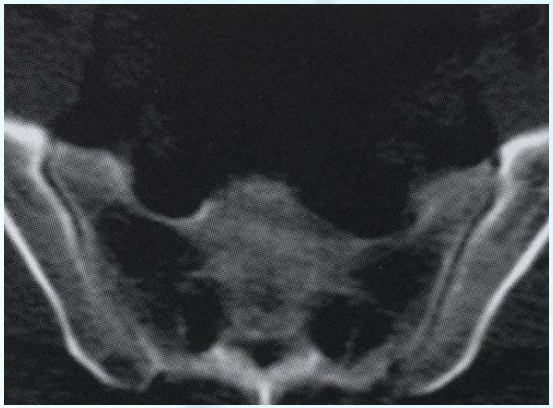
Image fusion

Fusion of functional and morphological images

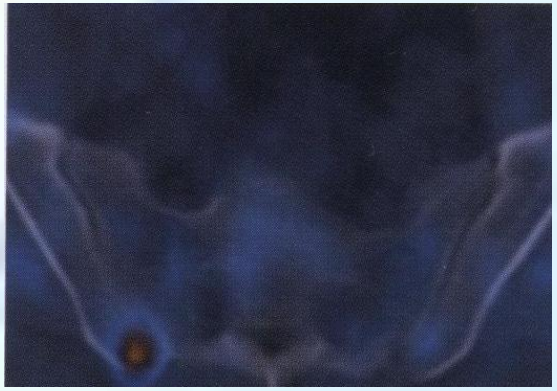




F-choline PET



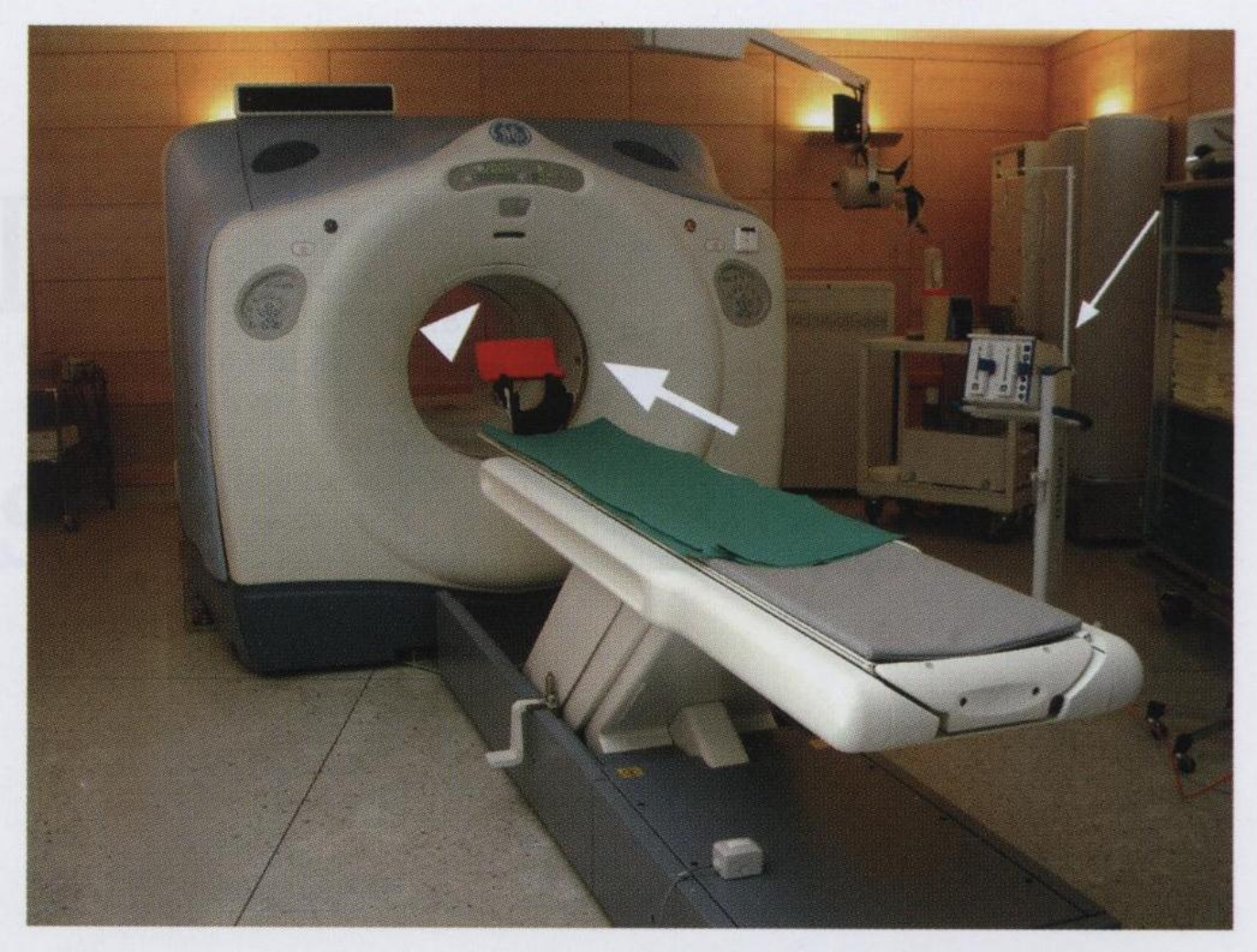
CT



PET-CT

Prostatic cancer, 6 yr after prostatectomy, increase in PSA
Metastasis in the pelvic bone on the right side

PET-CT camera



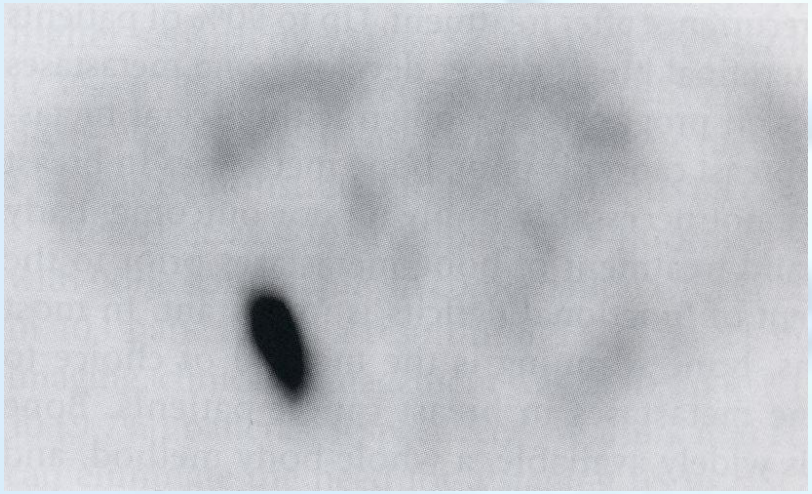
PET/CT

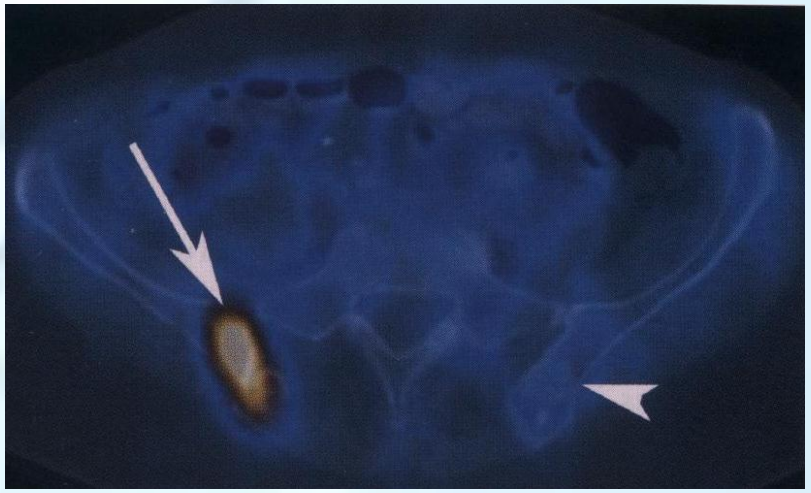
PET/CT

Combination of PET and CT allows:

1. Attenuation correction (transmission maps) for PET, completed in a few seconds. Attenuation correction is used to correct attenuation effects of radiation in the body

2. Morphological presentation provides precise anatomical location of radiotracer accumulation





Compared to the findings of the PET and CT,

PET/CT fusion provides:

1. Better detection of lesions
2. Better differentiation of physiological from pathological accumulation
3. Precise localization of malignant focus at connections of certain tissues, ie. bone/soft tissue, liver/bowel or adjacent lymph nodes.

PET radiotracers: indicators of various metabolic processes

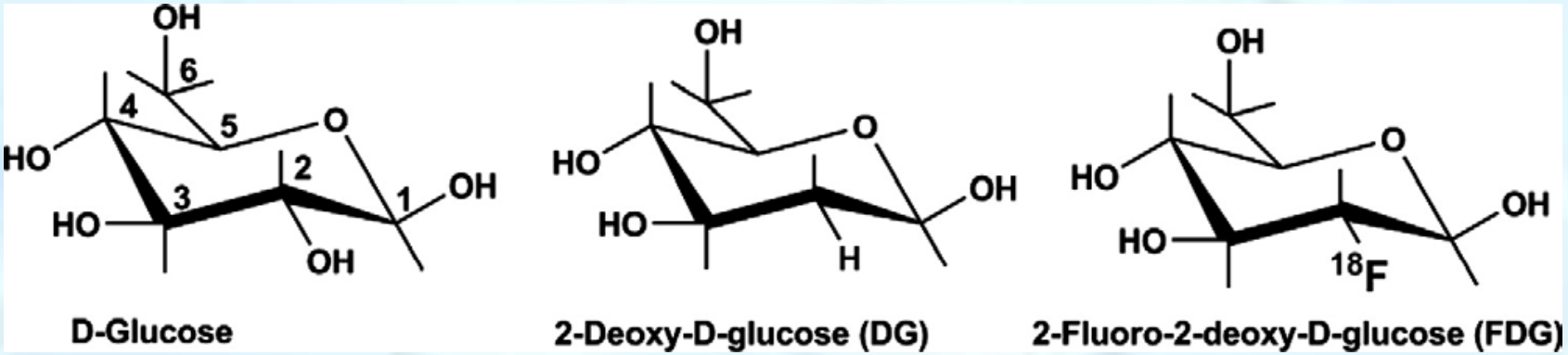
- glucose metabolism: **FDG**
- bones: **Fluoride**
- DNA synthesis: **FLT** (Fluorthymidine)
- synthesis of membrane lipids:

  FCH (Florcholine), **C-11-choline, Flor-acetate, C-11-acetate**
- protein and amino acid transporters synthesis :

  FET (fluoro-ethyl-tyrosine), **C-11-thyrosine, C11- methionine, FDOPA**

  (presinaptic dopaminergic receptors), **Ga-68-DOTA-TOC** (somatostatin receptors analogue, neuroendocrine tumors)
- cellular hypoxia: **FMISO** (fluoro-miso-nidazole)
- estrogene receptors: **FES** (fluor-estradiol)

FDG

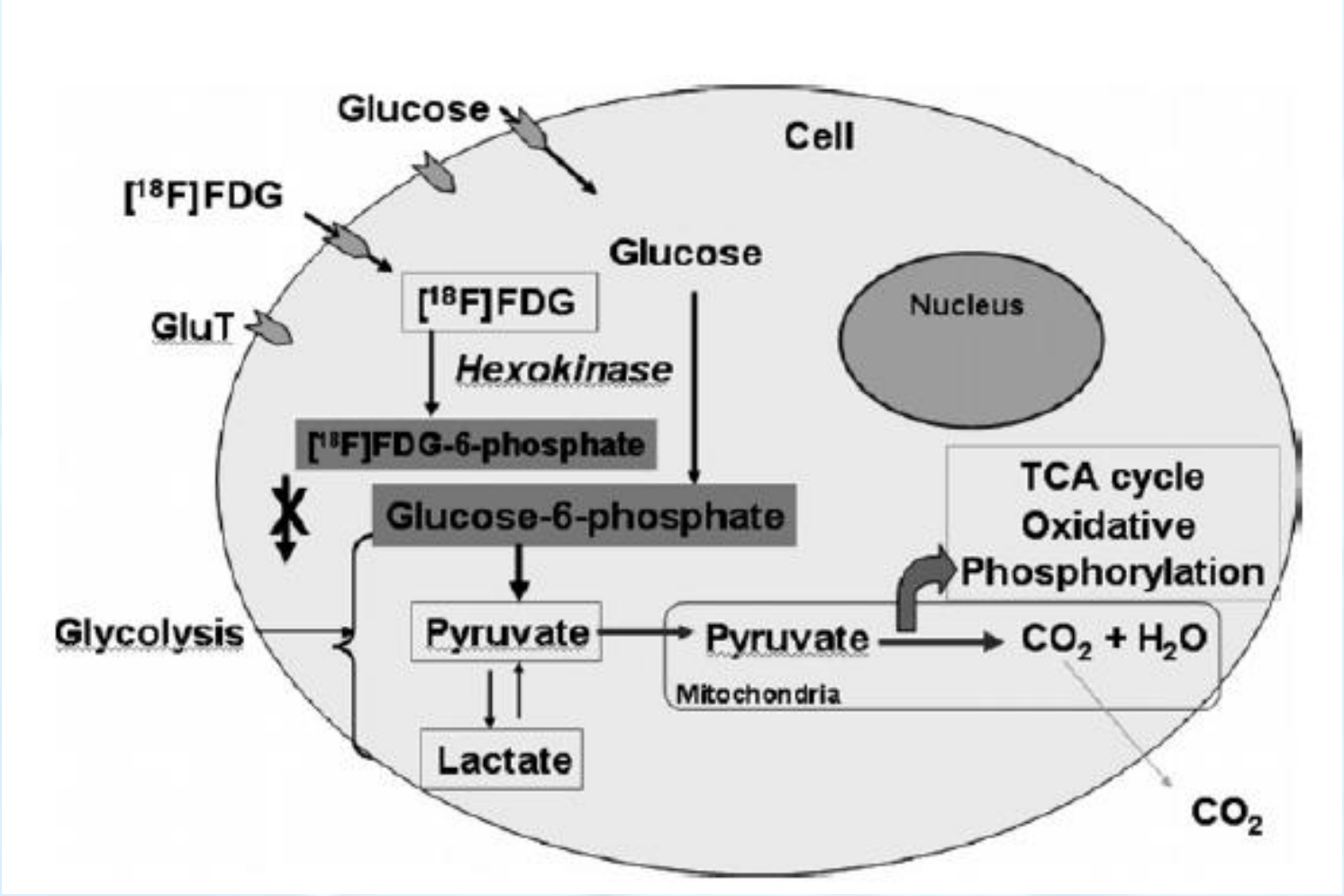


Glucose and its analogues, 2-deoxyglucose (DG) and fluorodeoxyglucose (FDG).

FDG

- FDG has broad application: oncology, inflammation, neurology and cardiology.
- FDG in cells undergoes 6-phosphorilation (hexokinase), but is not further metabolised –difference from glucose! – **FDG is trapped in the tumor cells**
- Accumulation on PET/CT presents only FDG-6P activity
- Tumor cells have increased level of phosphorilation, incresed glucose consumption, and Glut 1, 3 expression

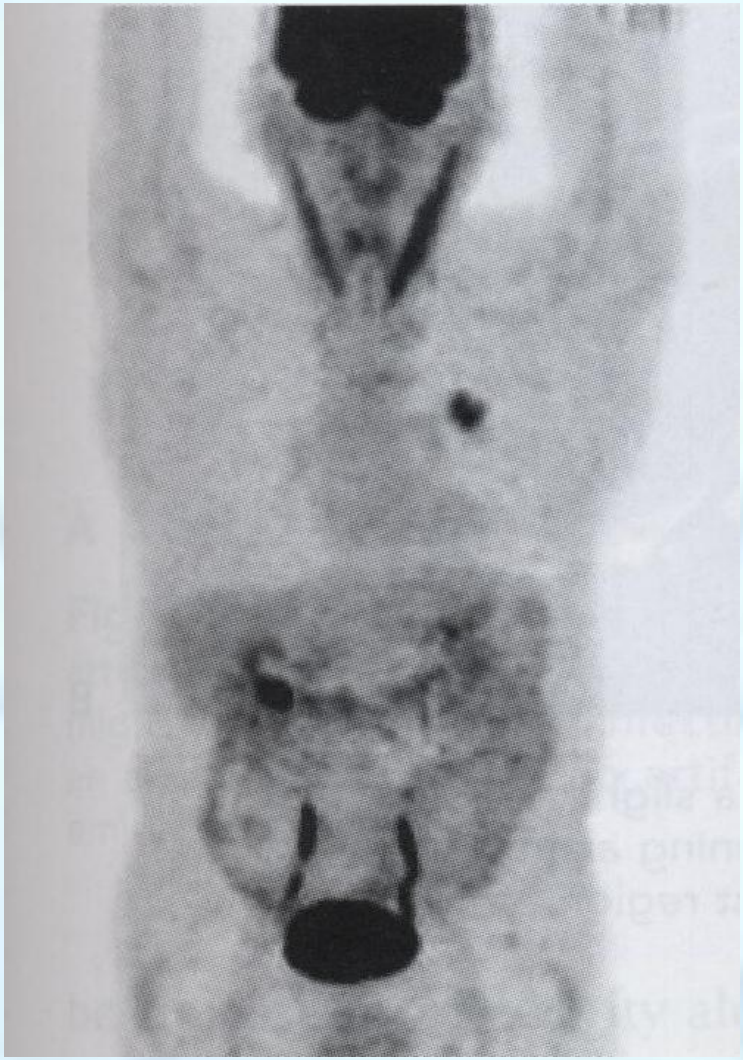
The cellular mechanism of D-glucose and (^{18}F) FDG



FDG

- It is used in 90% of PET imaging
- Patient needs to fast for at least **4 hours** before time of injection
- No need to interrupt medications (with some exceptions)
- Patients on intravenus therapy should not be given glucose!
- Previously check level of glucose in the blood (<10 mmol/l), body weight
- Dose: **10 mCi,** scaning after 45-60 min p.i. (WBS 10-15 min)
- After iv application, patient needs to lay still, in a quiet ambient, eyes closed, no speaking (to prevent FDG accumulation in the visual cortex or oropharingeal muscles)
- Empty bladder before scanning

FDG biodistribution



Assessment of uptake intensity in PET

Qualitatively

- **Gr.IV**: intensive uptake, comparable with the intensity of the brain uptake where the brain is dark, almost black (SUV mostly greater than 4)
- **Gr.III**: uptake intensity between brain and liver
- **Gr. II**: moderately increased, uptake as in liver, SUV arround 1,5
- **Gr.I**: weak uptake, similar to the rest of the body

SUV (Standardized uptake values)

$$SUV_{ibw}[g/ml] = 1000\frac{A}{D}\Big(45.5 + 0.91\,(height[cm] - 152)\Big) \qquad \textit{ideal body weight}$$

$$SUV_{lbm}[g/ml] = 1000\frac{A}{D}\left(1.07\,weight[kg] - 148\left(\frac{weight[kg]}{height[cm]}\right)^2\right) \qquad \textit{lean body mass (female)}$$

$$SUV_{lbm}[g/ml] = 1000\frac{A}{D}\left(1.1\,weight[kg] - 128\left(\frac{weight[kg]}{height[cm]}\right)^2\right) \qquad \textit{lean body mass (male)} \qquad (2)$$

$$SUV_{bsa}[m^2/ml] = \frac{A}{D}\,(weight[kg])^{0.425} \times (height[cm])^{0.725}\,0.007184 \qquad \textit{body surface area}$$

Activity in certain lesion: activity in voxel (volumetric pixel)- kBq/cm^3, divided with injected activity, normalised on the gram of body weight (kBq/cm$^{3)}$

Indication

Oncology

FGD- PET/CT can not be used for primary diagnosis of tumor

It is used for evaluation :

1. staging
2. therapy effectivness: surgical, radiotherapy, chemotherapy or concomitant chemoradiotherapy
3. detection of local recurrence and distant metastases
4. localization of the primary tumor (in patients with established metastases from unknown primary location)
5. in patients with dubious CT/MRI- for the detection of recurrence, especially if this finding will change the further course of treatment

Oncology

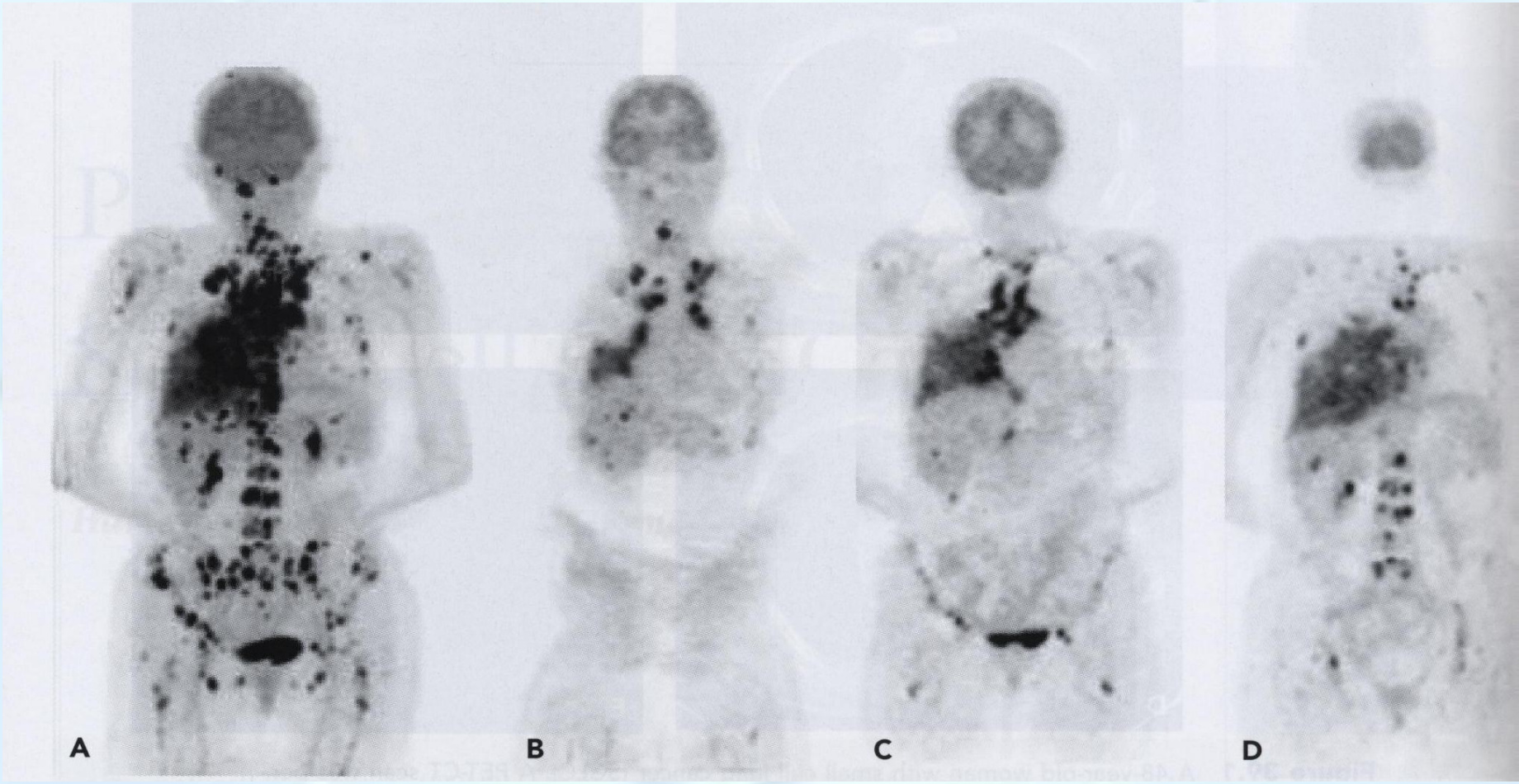
6. during chemotherapy, reduction of SUV over **50 %** indicates positive therapeutic effect.

Even after 1 or 2 cycles of chemotherapy, therapy response can be estimated, if there is suspicion of disease progression or the side effects

7. re-staging, when other diagnostic prcedures reveal suspicious metastaic disease

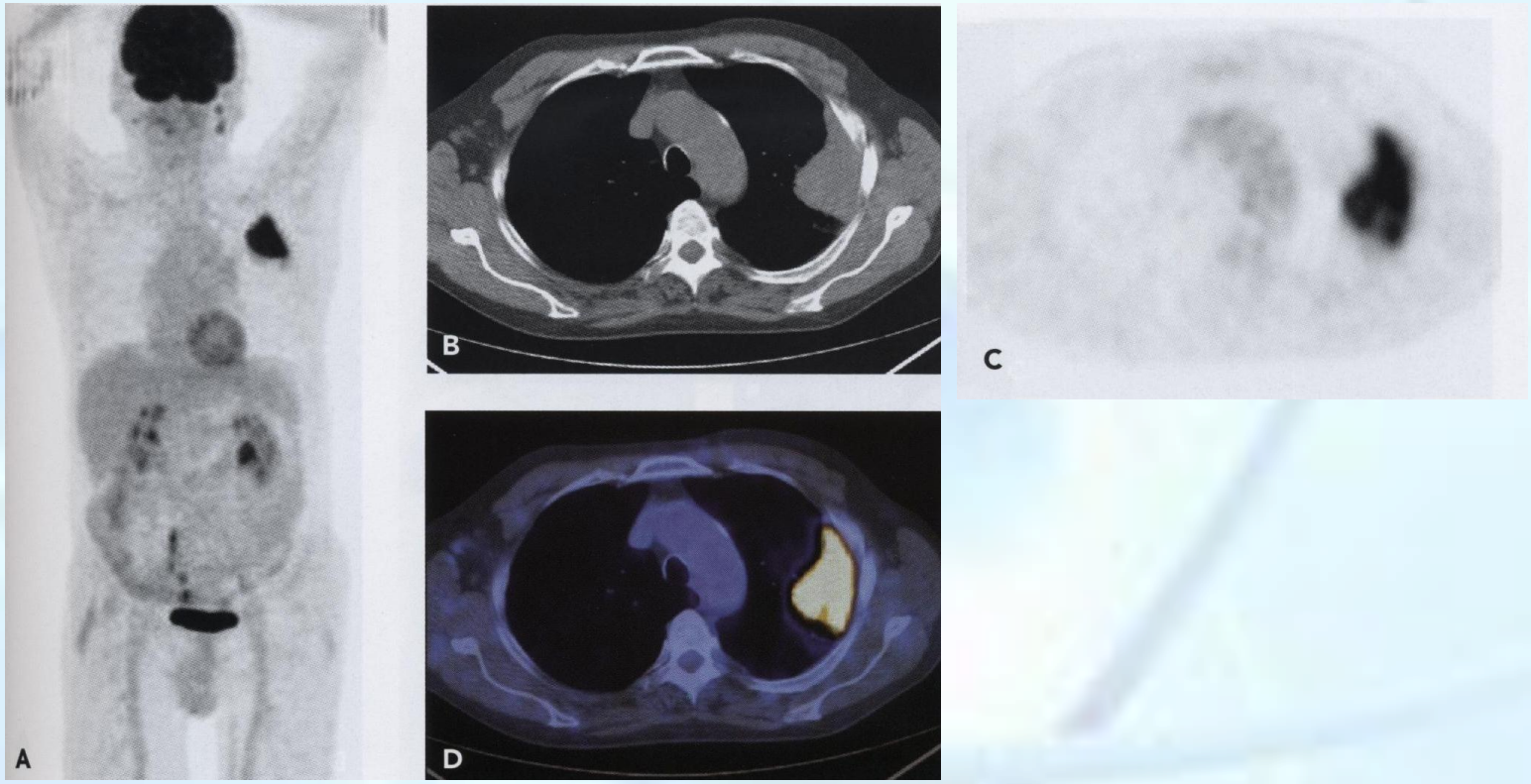
8. precise planning of radiation therapy field

Lung cancer staging: FDG PET



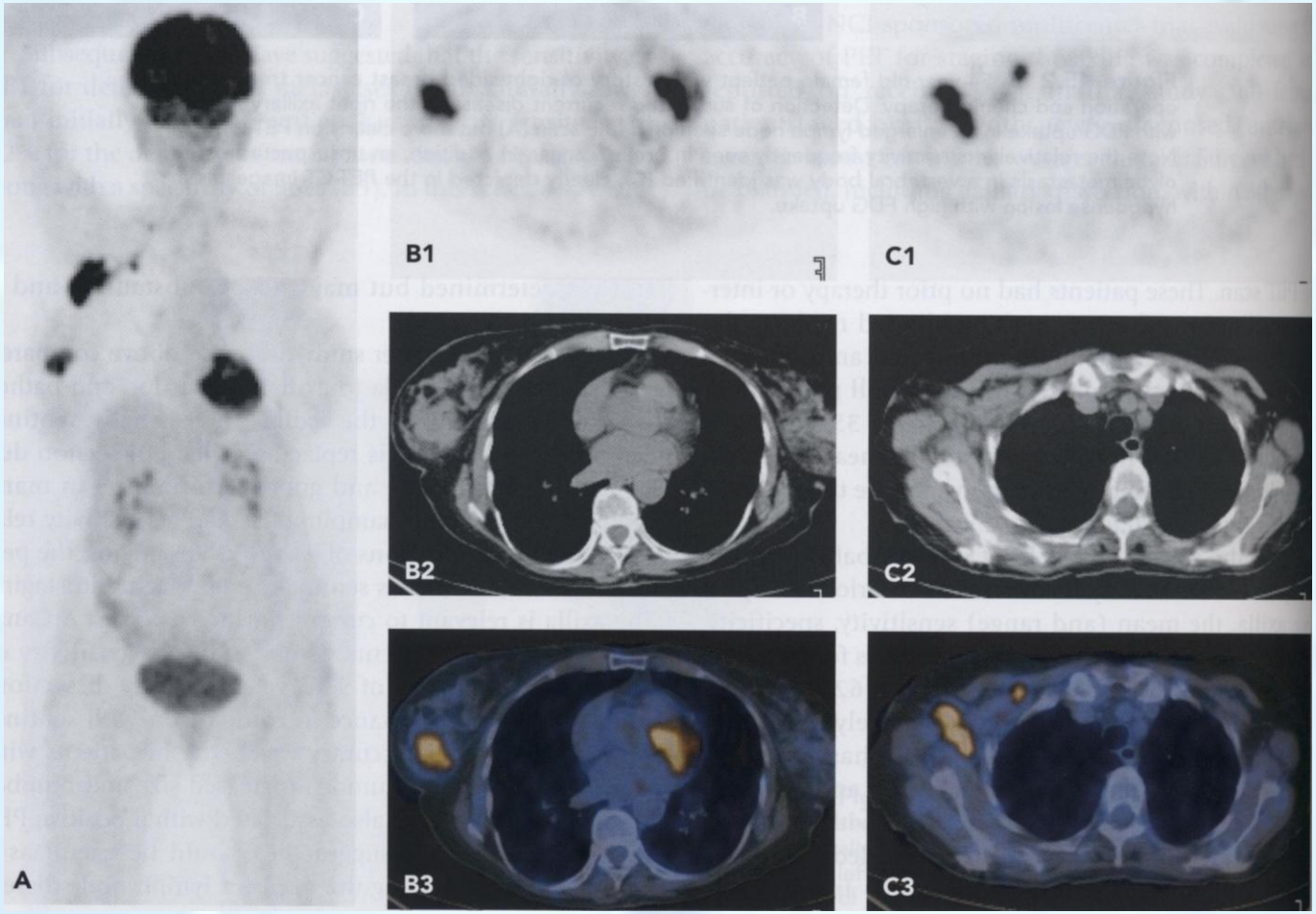
Multiple metastases; palliative treatment

FDG-PET/CT staging



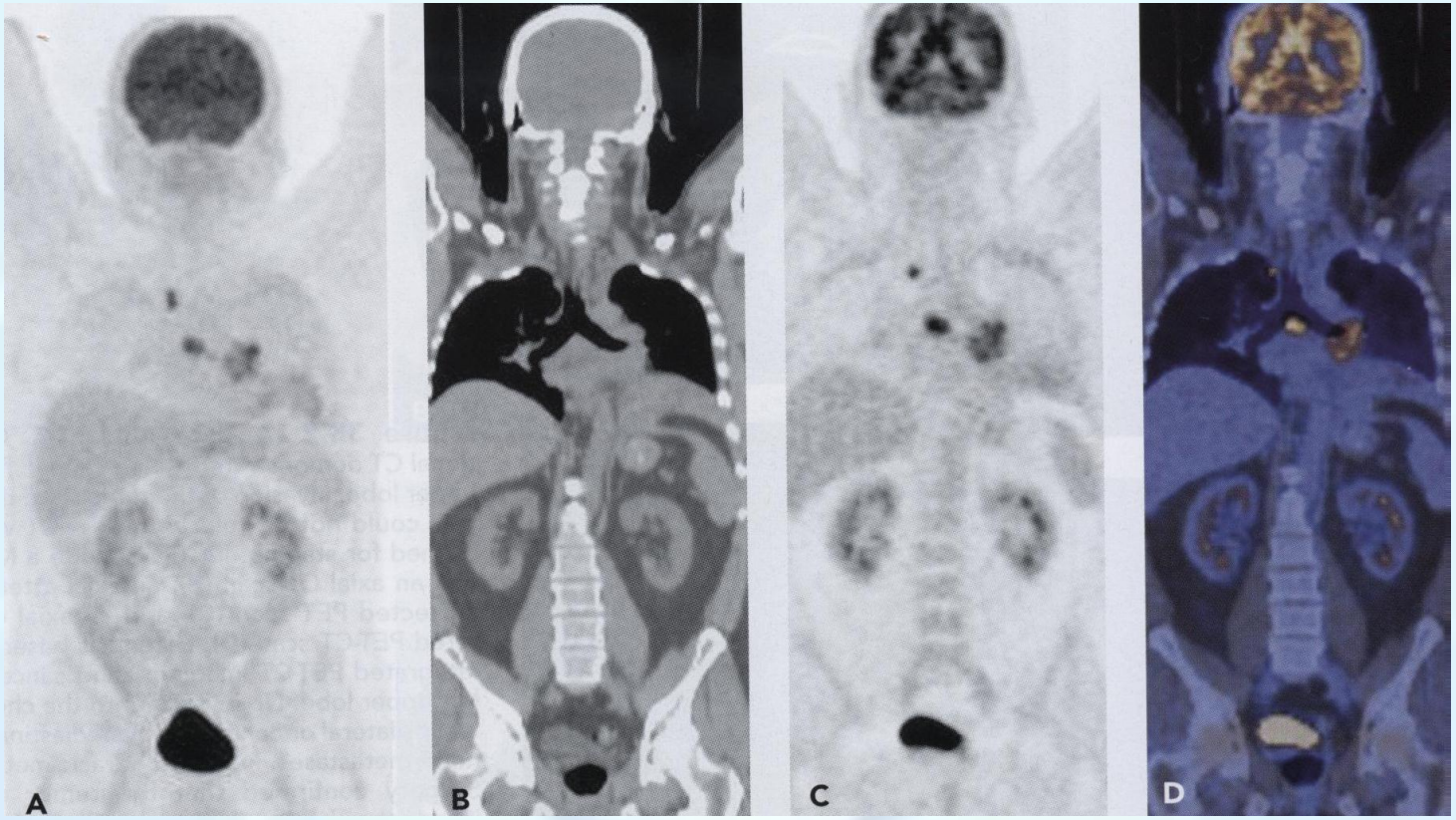
CT: cancer in the upper lobe of the left lung, infiltration of the chest wall
FDG-PET/CT: chest wall is not infiltrated, there is no extrathoracic disemmiantion
Patient was operated.

Right breast cancer staging



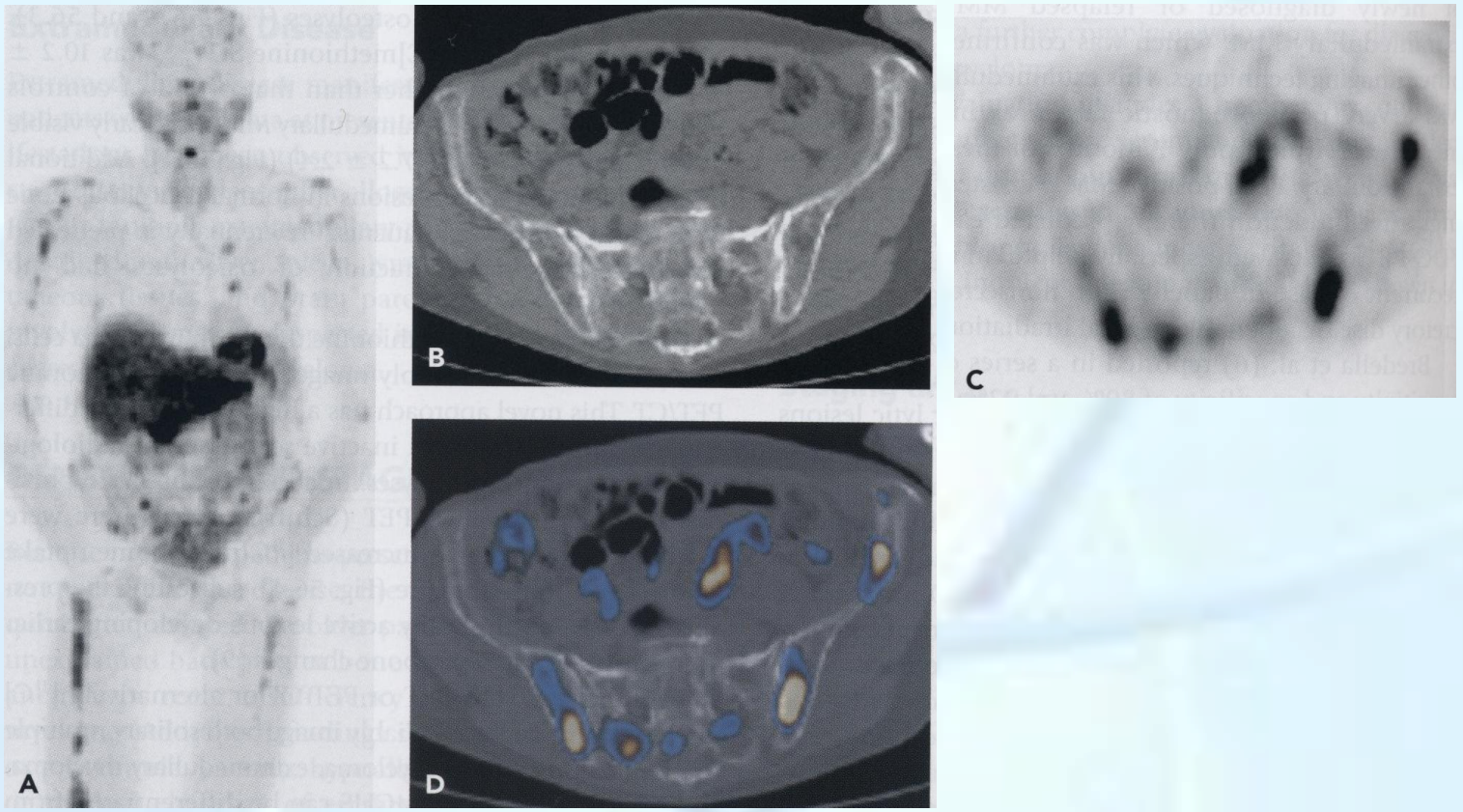
Metastases in the right axillary lymph nodes; no distant metastases

FDG PET/CT staging



Cancer in the lower lobe of the left lung- bronchoscopy and biopsy.
FDG PET-CT: beside the cancer, there are metastases in the subcarinal and contralateral hilar lymph node; without extrathoracic dissemination

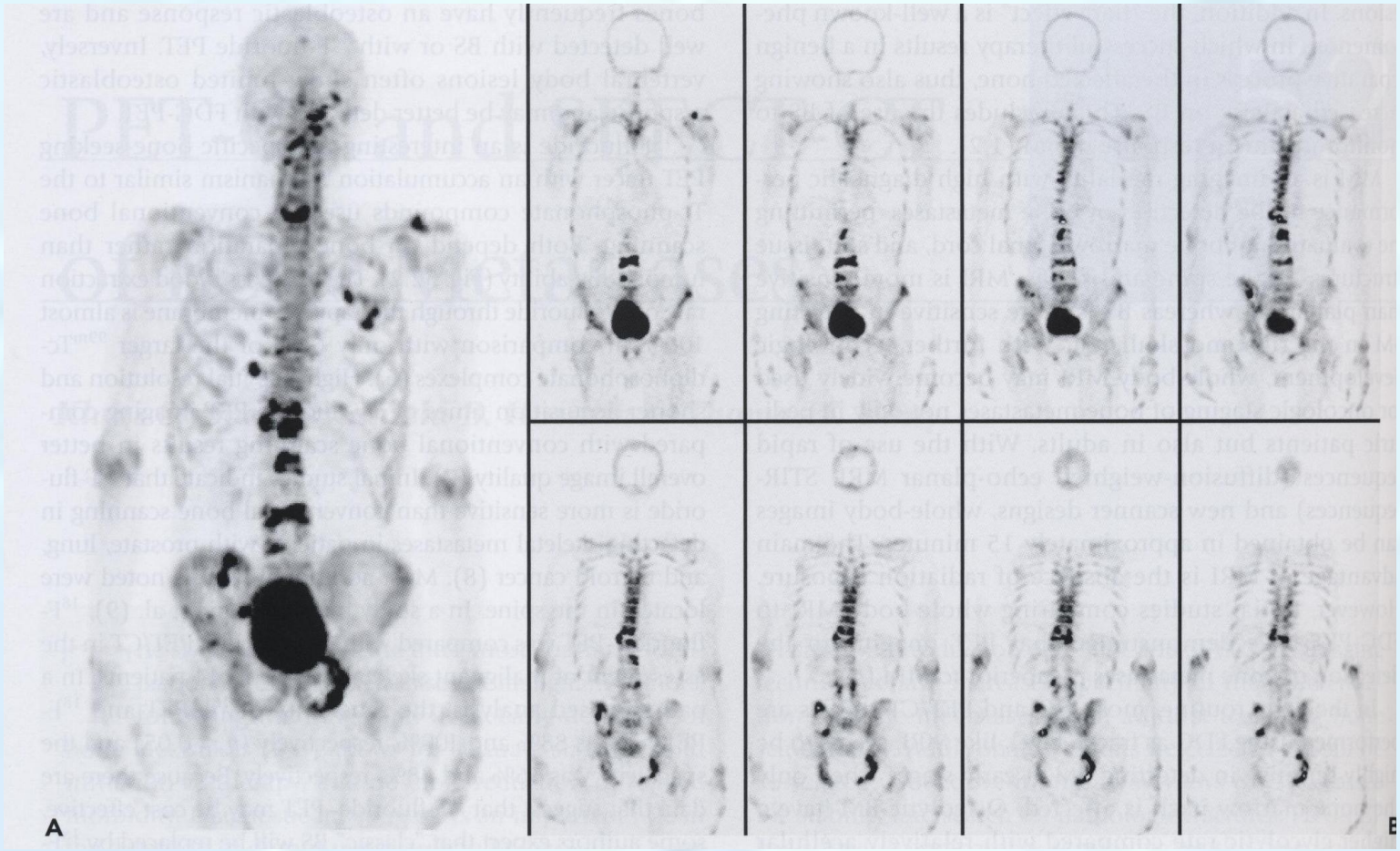
C-11- methionine: multiple myeloma staging



dissemination

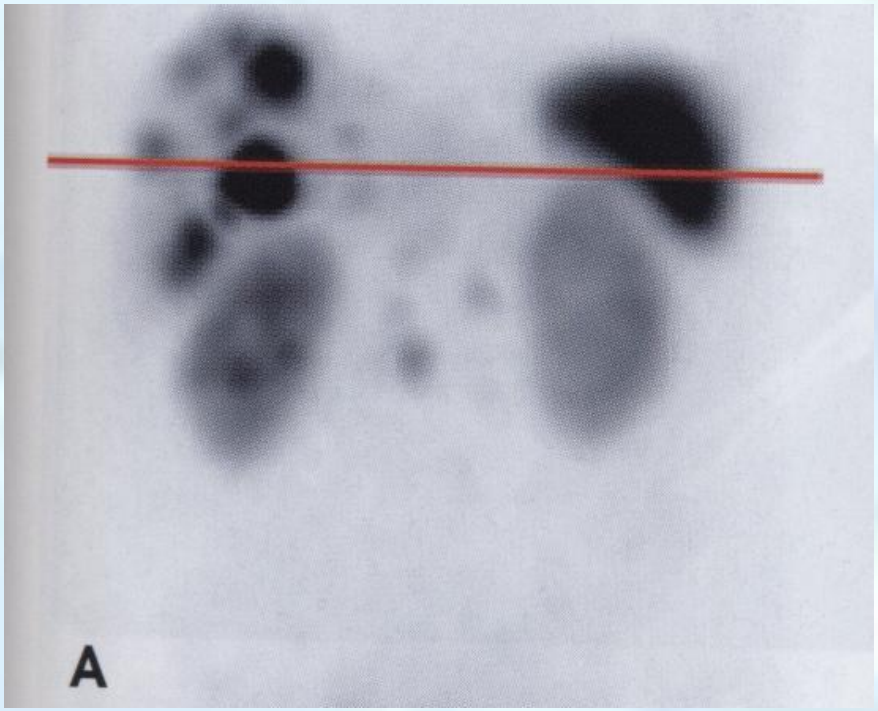
Initial staging

F-18-fluoride-PET: bone metabolism

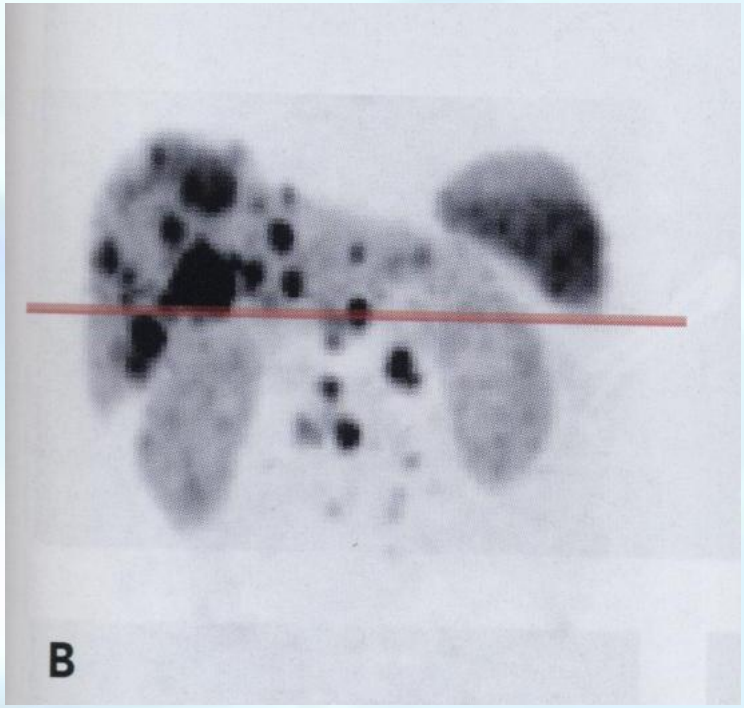


Renal cancer with multiple bone metastasis

Evaluation of the disease stage in pancreatic NETs Ga-68-DOTA-TOC



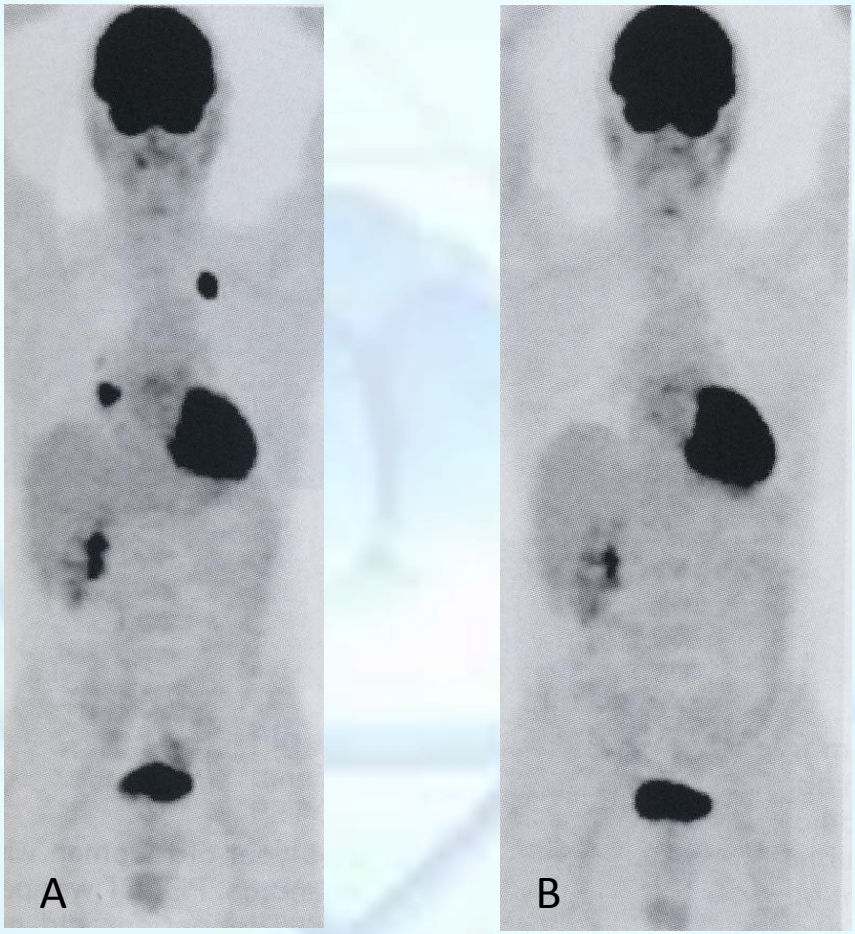
SPECT In-111Octreotid
(DTPA- Octreotid)



PET Ga-68- DOTA-TOC (DOCA-octreotid)

Patient with pancreatic NET, after palliative surgical treatment.
Ga-68-DOTA-TOC PET revealed even more metastases in liver and abdomen

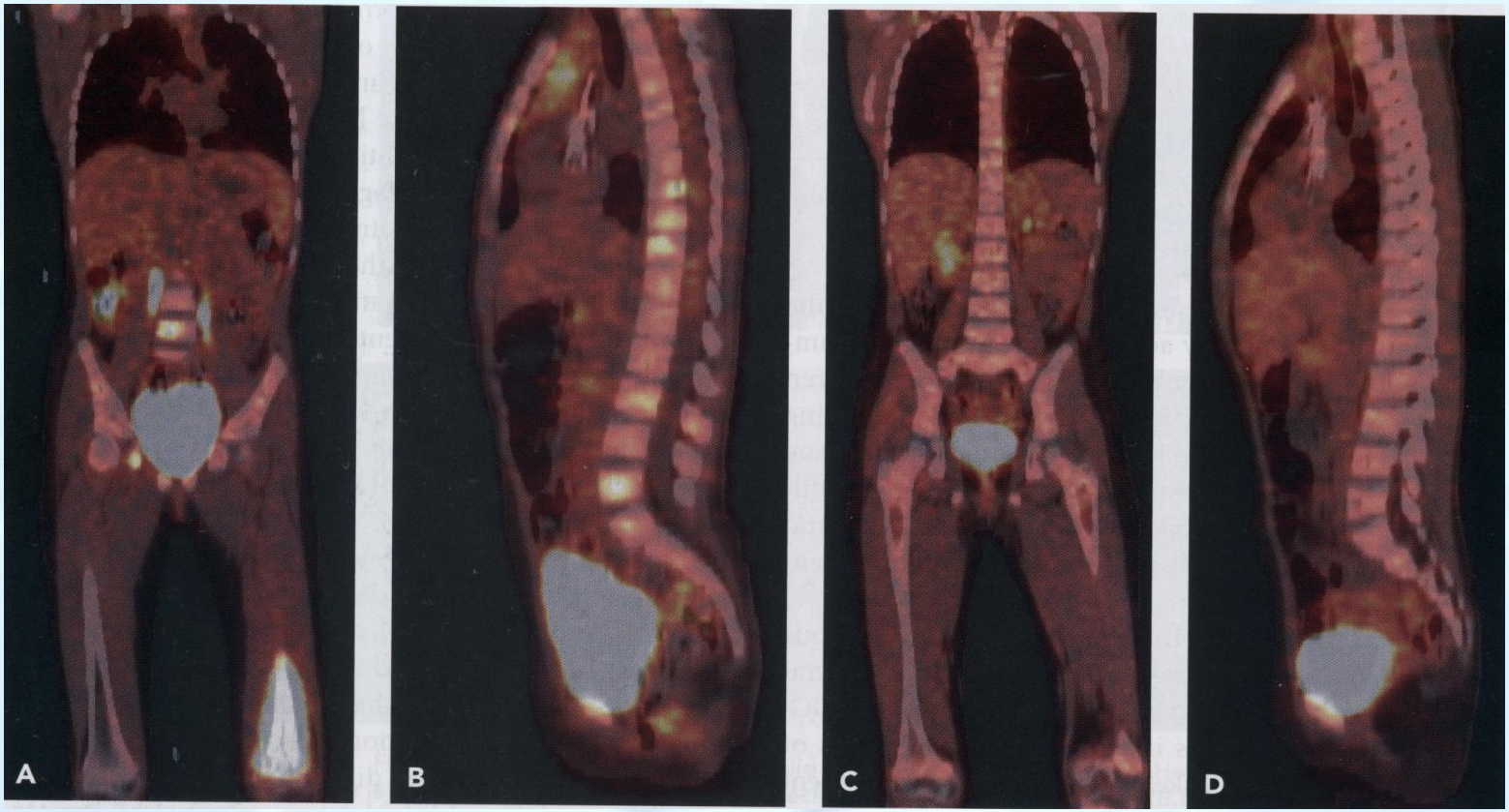
Initial staging after excision of the melanoma in the nasal region, post-chemotherapy re-staging



FDG PET

Initial staging: lung metastases (A).
Re-staging after chemotherapy: complete regression (B).

1. i 2. Osteosarcoma: staging before therapy and evaluation of therapeutic response

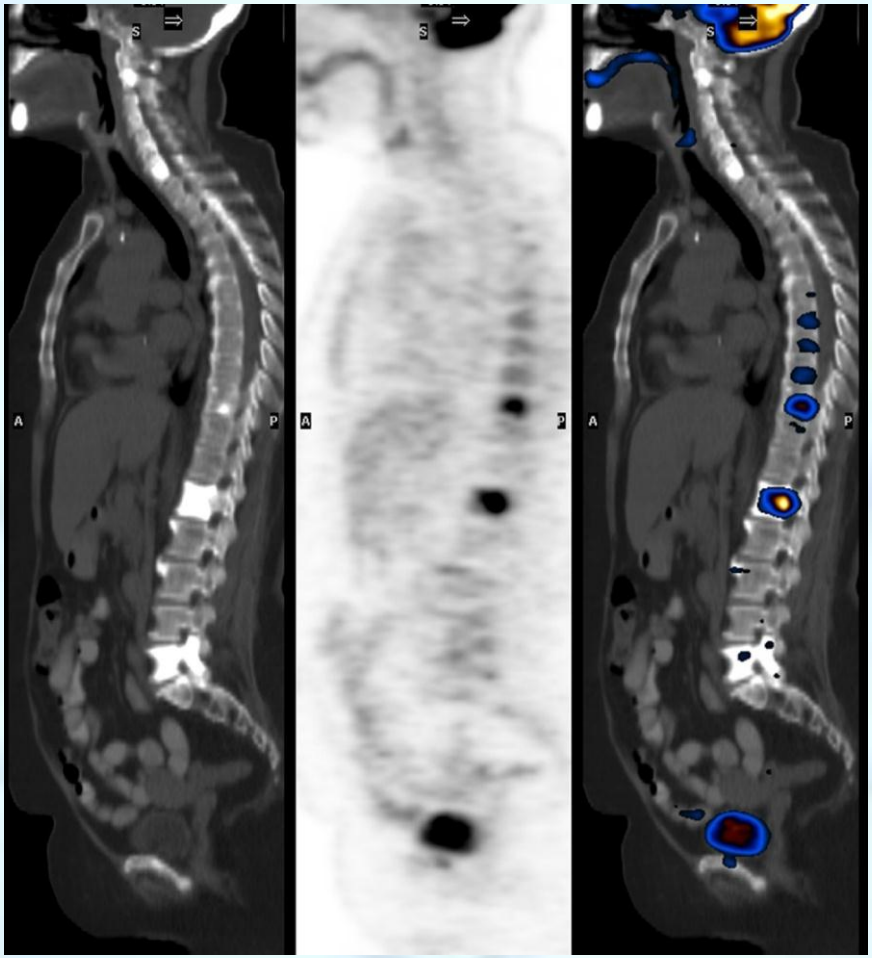


FDG PET/CT

6-yr old boy, osteosarcoma on the distal part of the left femour, multiple vertebral metastases

2 months after therapy- minimal metabolic activity in the primary tumor, while metastases are cured

2. Monitoring of therapy response

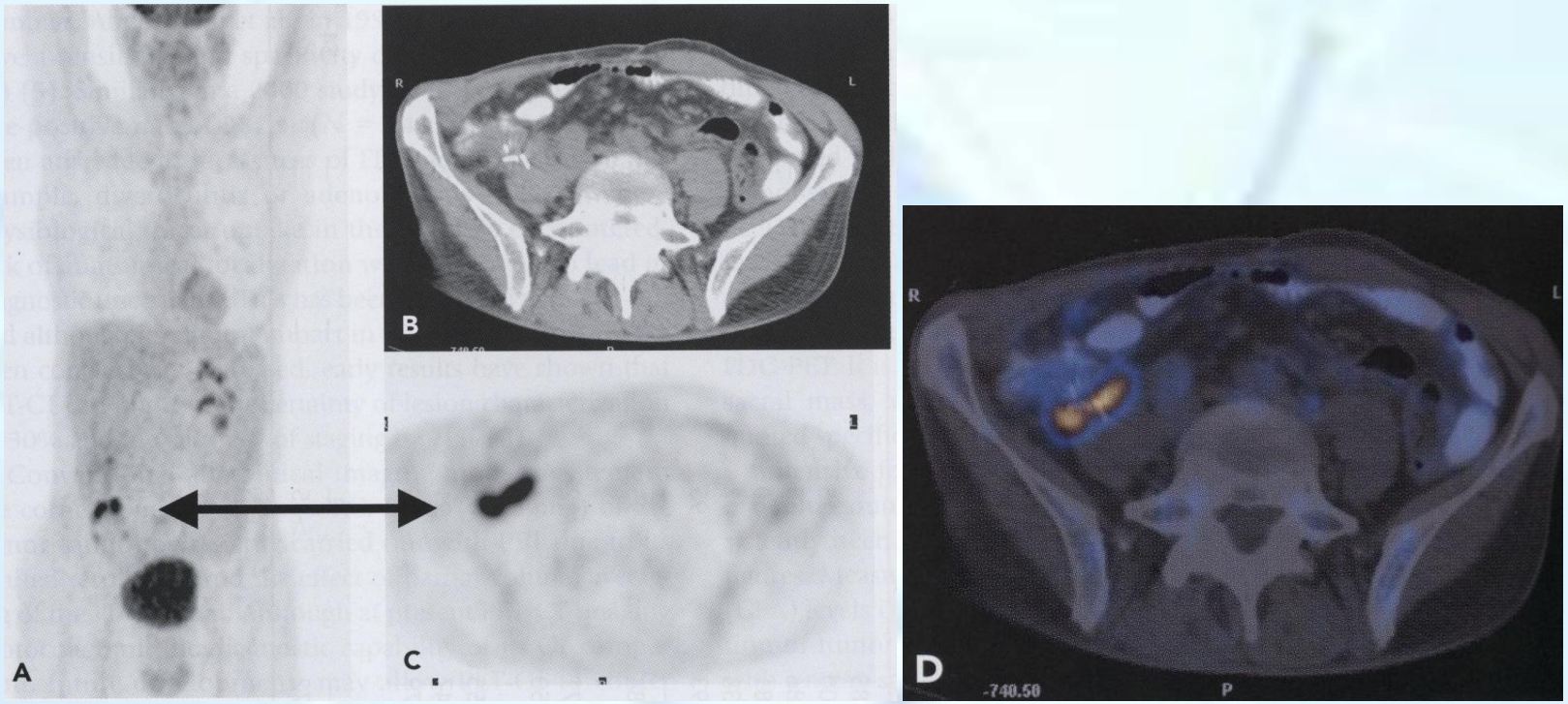


Patent with breast cancer and bone metastases, after therapy.

CT: multiple osteoblastic lesions in vertebrae

FDG PET/CT: only active metastases are presented

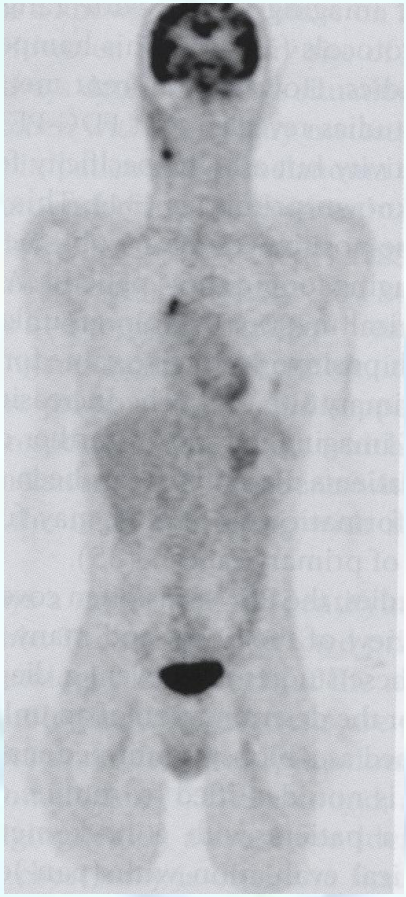
Detection of local recurence



FDG PET-CT

Carcinoma of the cecum- local recurrence in the anastomosis.

Detection and localisation of the primary tumor in patients with disseminated disease from unknown primary

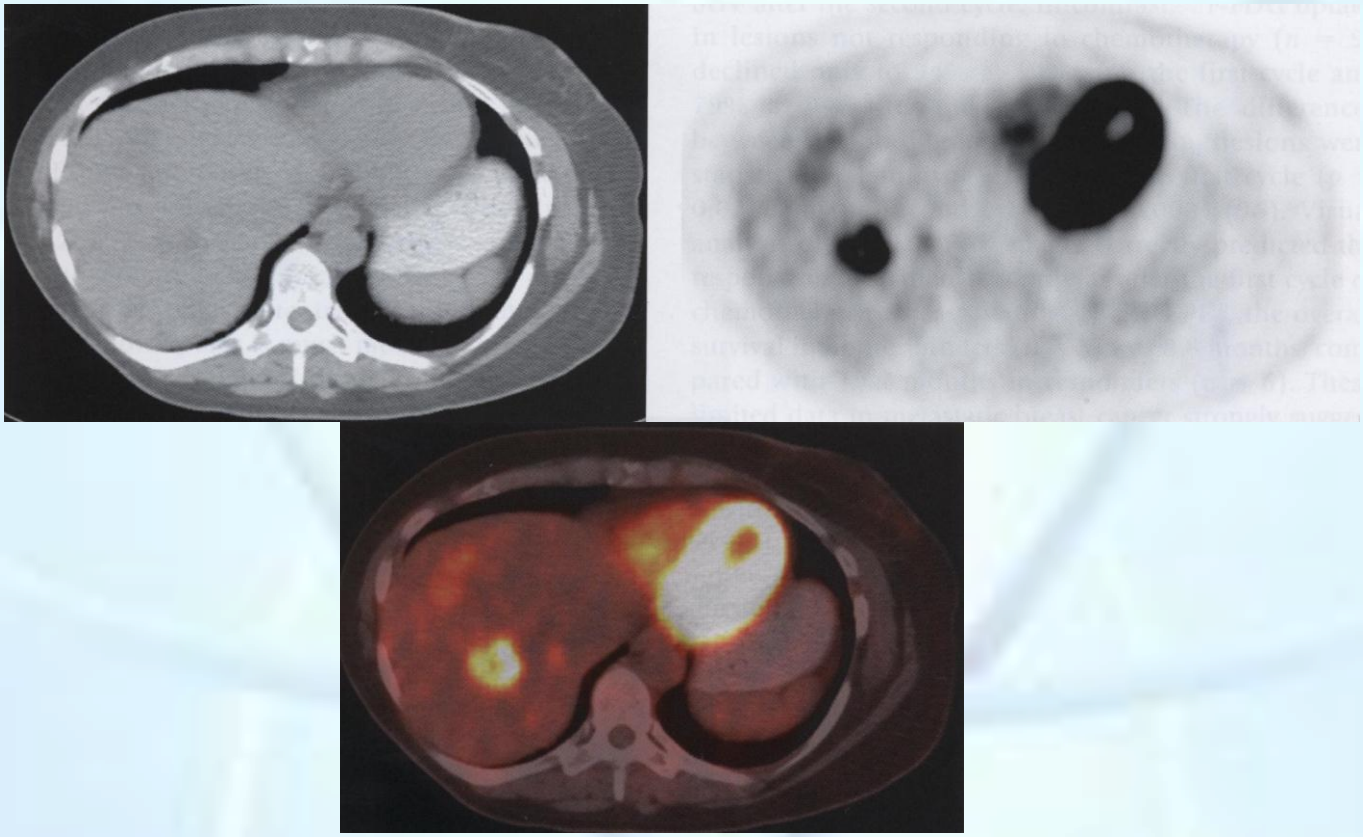


Metastasis on the right side of the neck- unknown primary location.
Chest X-ray negative

FDG PET: beside neck metastases, FDG PET reveals peribroncheal lesion on the right side. Further diagnostic procedure confirmed bronchial carcinoma

In patients with doubtful, CT/MR findings, to reveal recurrence

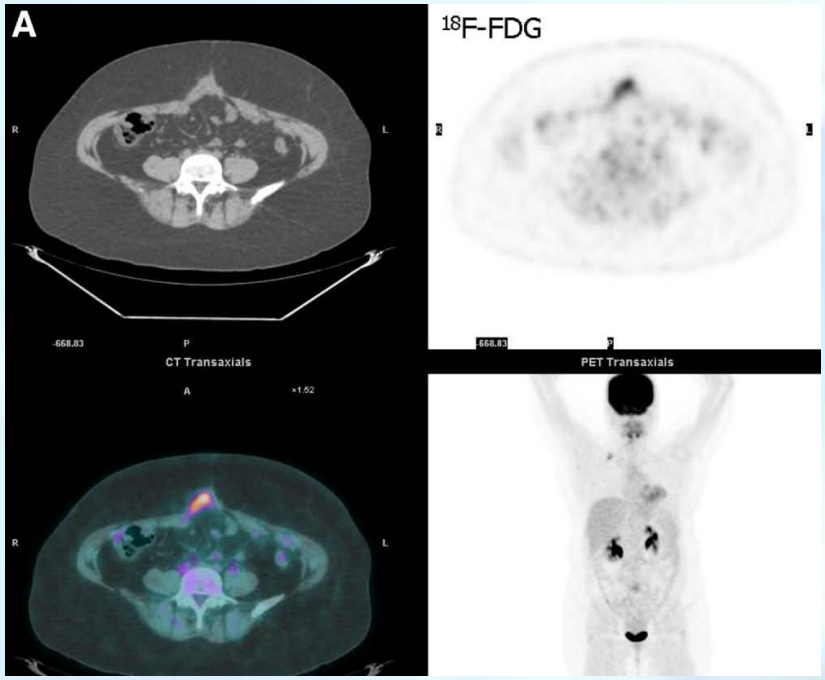
Breast cancer metastasis

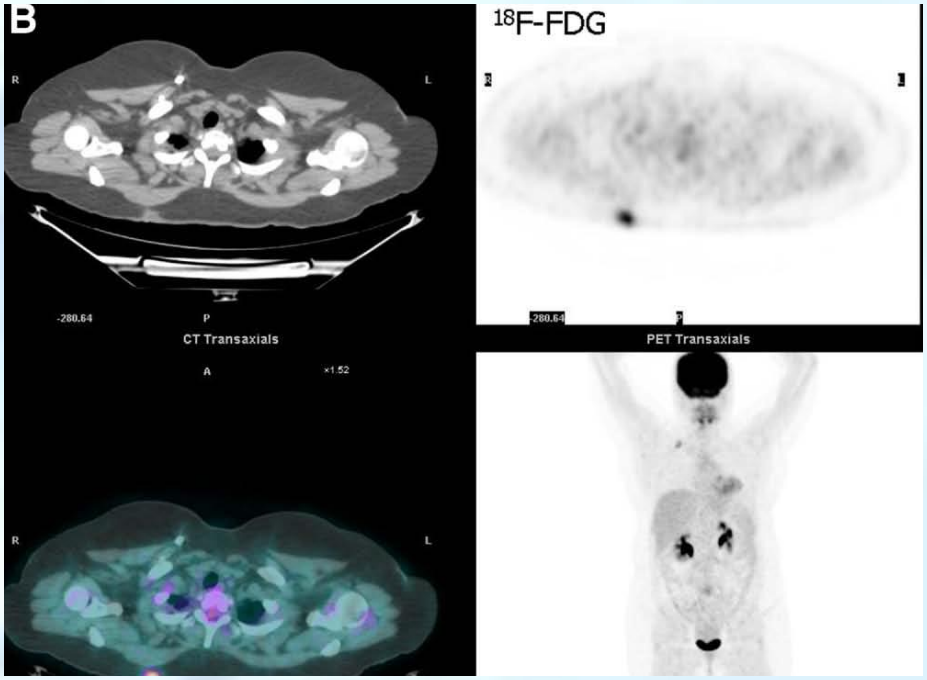


Doubtful liver CT scan
FDG PET/CT: liver metastasis

Restaging- if other diagnostic procedures reveals disemination

Restaging- ovarian cancer





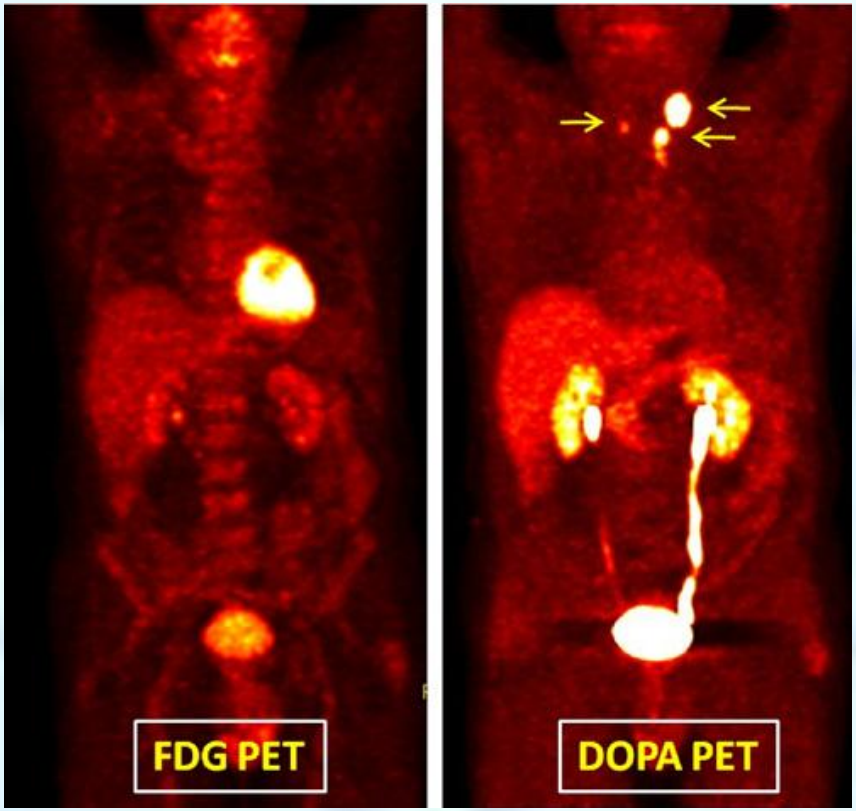
Ovarihysterectomy and chemotherapy were provided 2 yr before. Restaging was indicated because of **Ca-125 elevation**

FDG-PET/CT: metastasis in the scar

Other focus, in the skin on the shoulder: inflamed atheroma

Restaging- if other diagnostic procedures reveals disemination

FDOPA-PET: multiple metastases of the medullary thyroid cancer



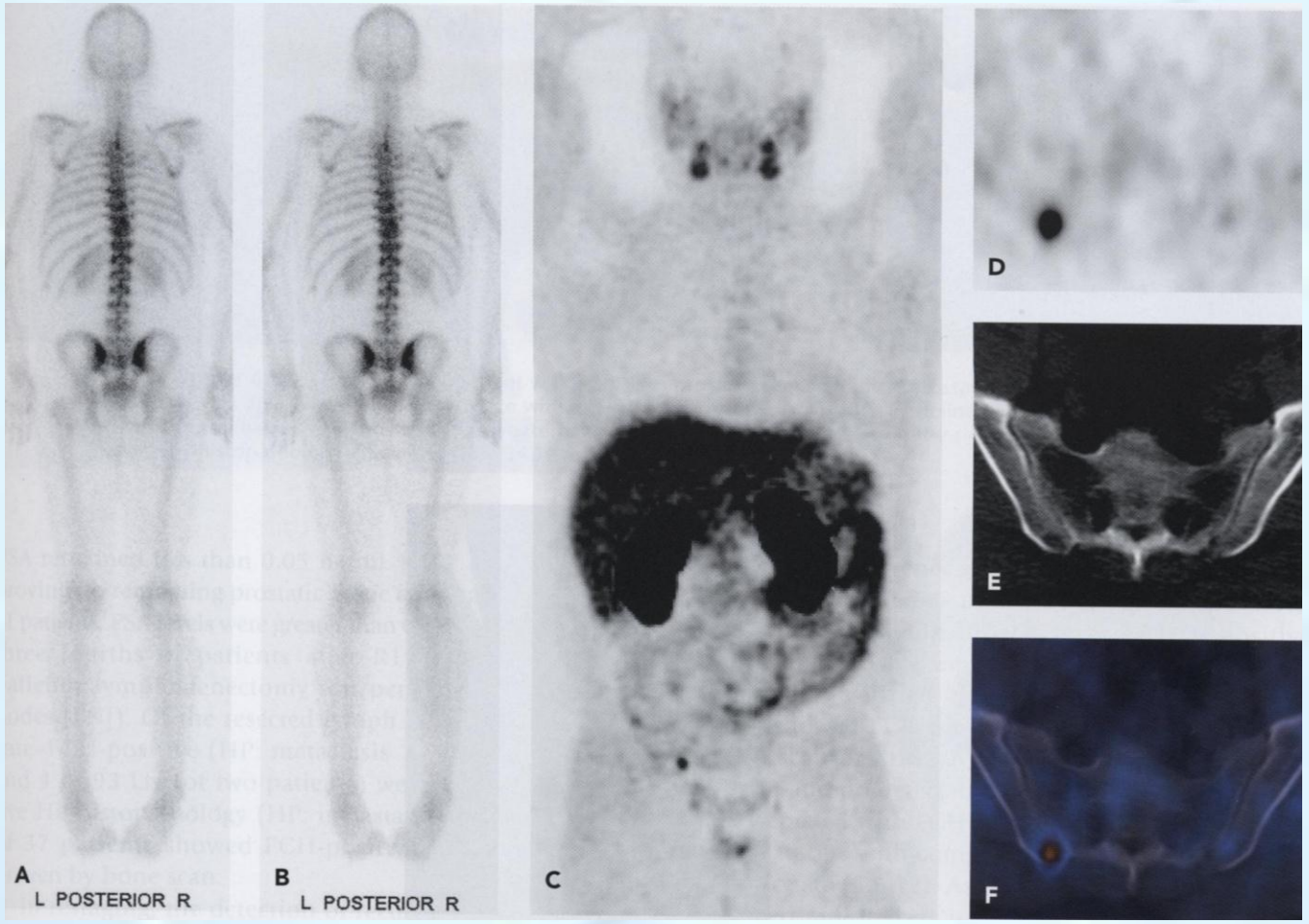
Total thyroidectomy was performed in patient with medullary thyroid cancer, **Calcitonin=597** pg/ml

FDG-PET negative.

FDOPA-PET – reveals multiple metastases on the neck and upper mediastinum

Restaging- if other diagnostic procedures reveal disemination

^{18}F-choline

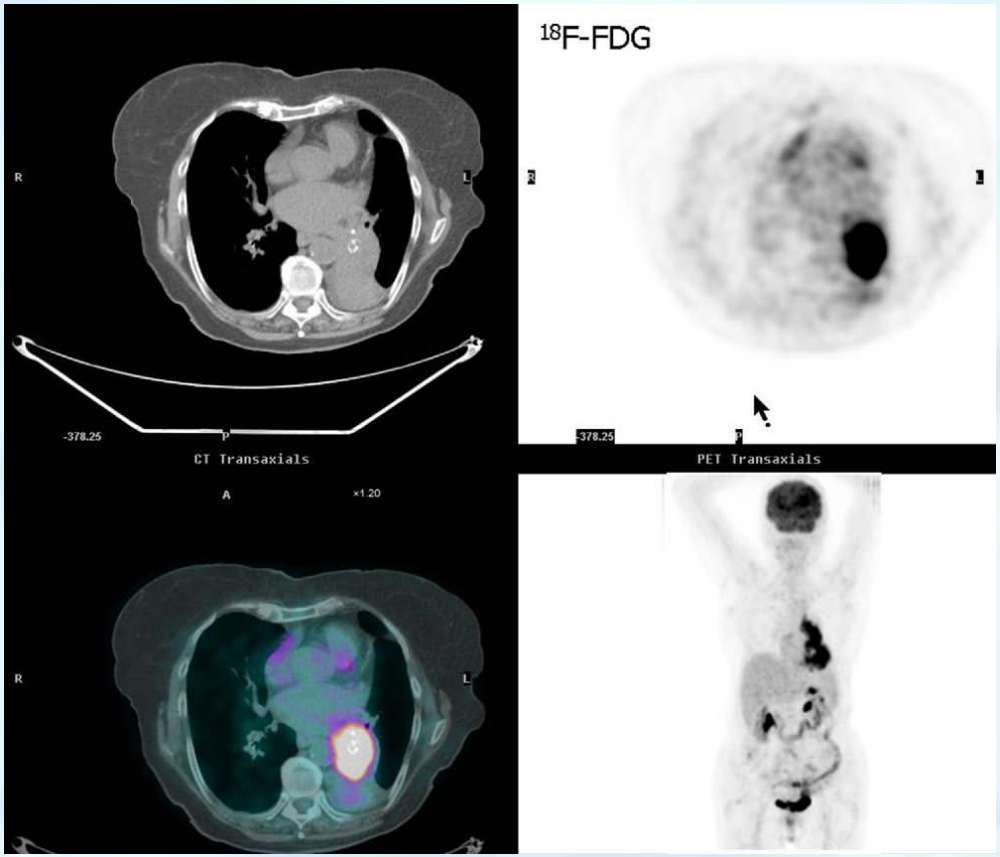


Prostatic cancer, 6 yr after prostatectomy, elevated PSA

Bone scan (Tc-99m MDP) negative.

^{18}F-choline PET-CT: metastasis in the right illiac bone

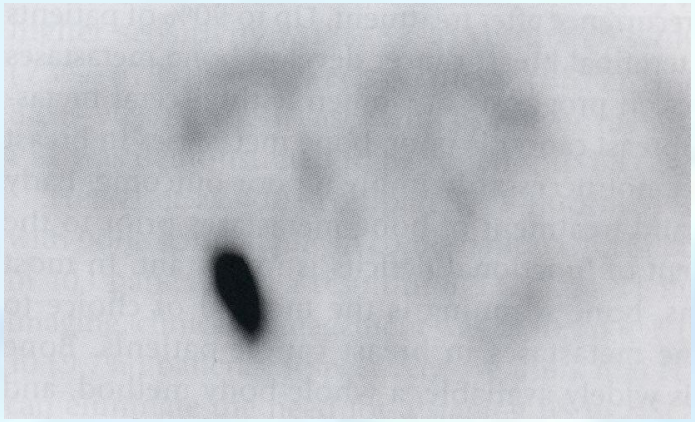
Planning of radiation therapy field

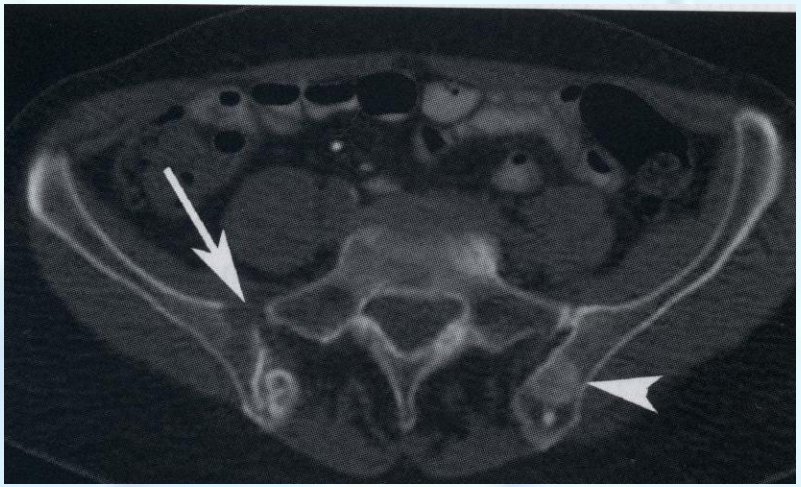


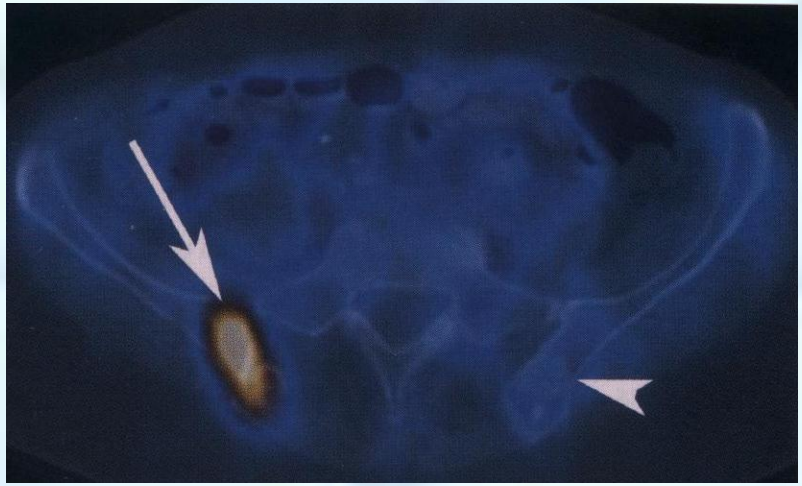
Lung carcinoma

CT: extensive consolidation in the lower lobe of the left lung, hilar metastases
FDG-PET/CT: tumor size is lower than on CT- bacause of surrounding atelectasis
Irradiation filed will be more precisely directed on the tumor

FDG PET: Osteolytic and osteoblastic lesions







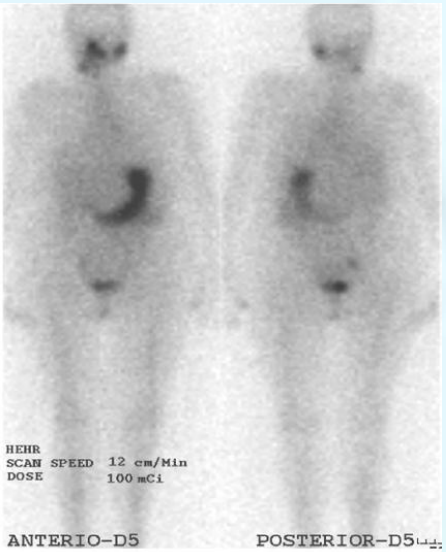
Breast cancer metastasis in the pelvis

PET: higher sensitivity for the osteolytic, lower for osteoblastic lesions

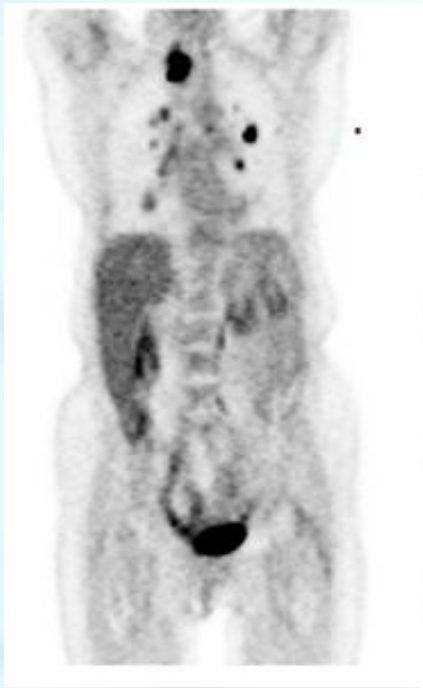
Thyroid carcinoma

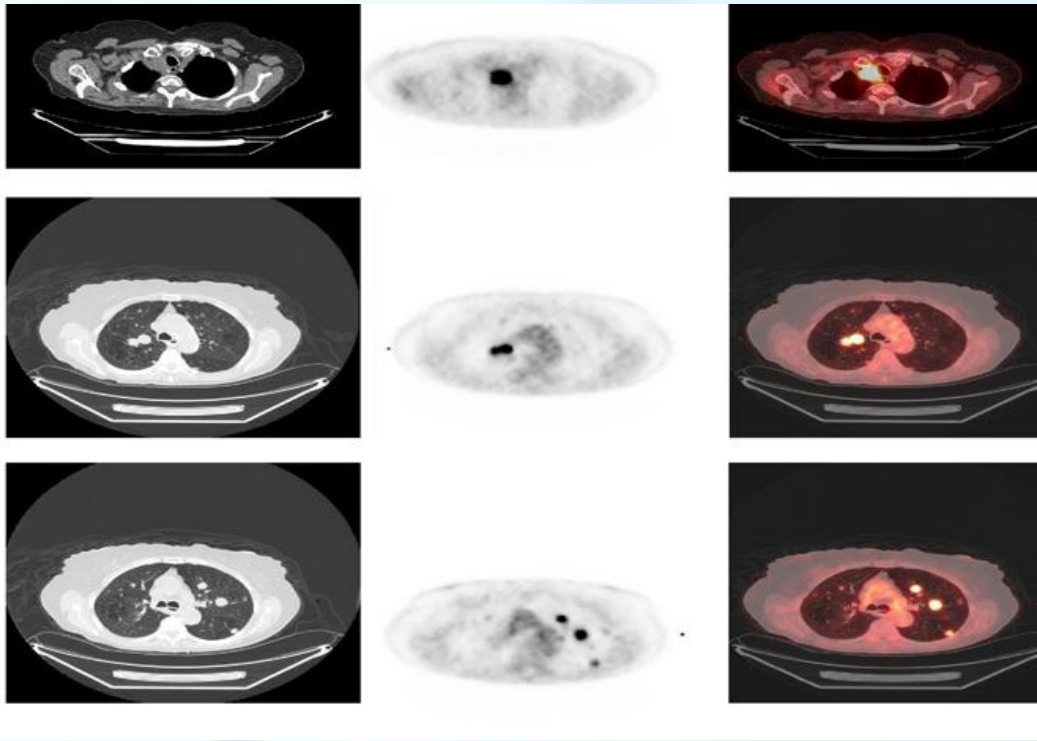
1. Increased Tg (or Tg>10), negative I-131 scintigram
2. Disseminated disease with suspicious iodine-negative metastasis
3. In evaluation of the surgical therapy sucess/ recurrece/ evaluation of chemotherapy in iodine-negative metastases, surically non-resectable
4. Agressive variant (tall cell, Hurthle cancer), poorly differentiated (insular, solide, trabecular), anaplastic thyroid cancer
5. Increasing calcitonin and CEA in patients with MTC

Iodine-negative metastases of the PTC



Post-therapy

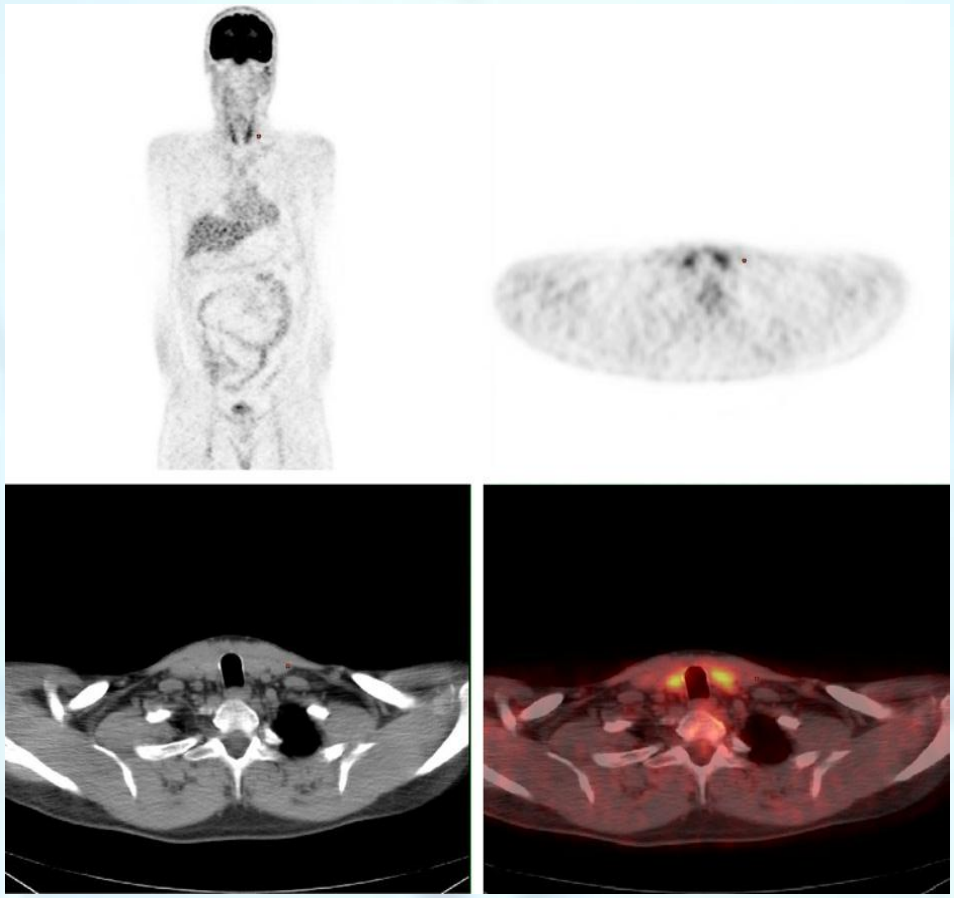




PTC, increased Tg and I-131 negative mts.

FDG PET/CT reveals paratracheal reccurence and multiple lung metastses

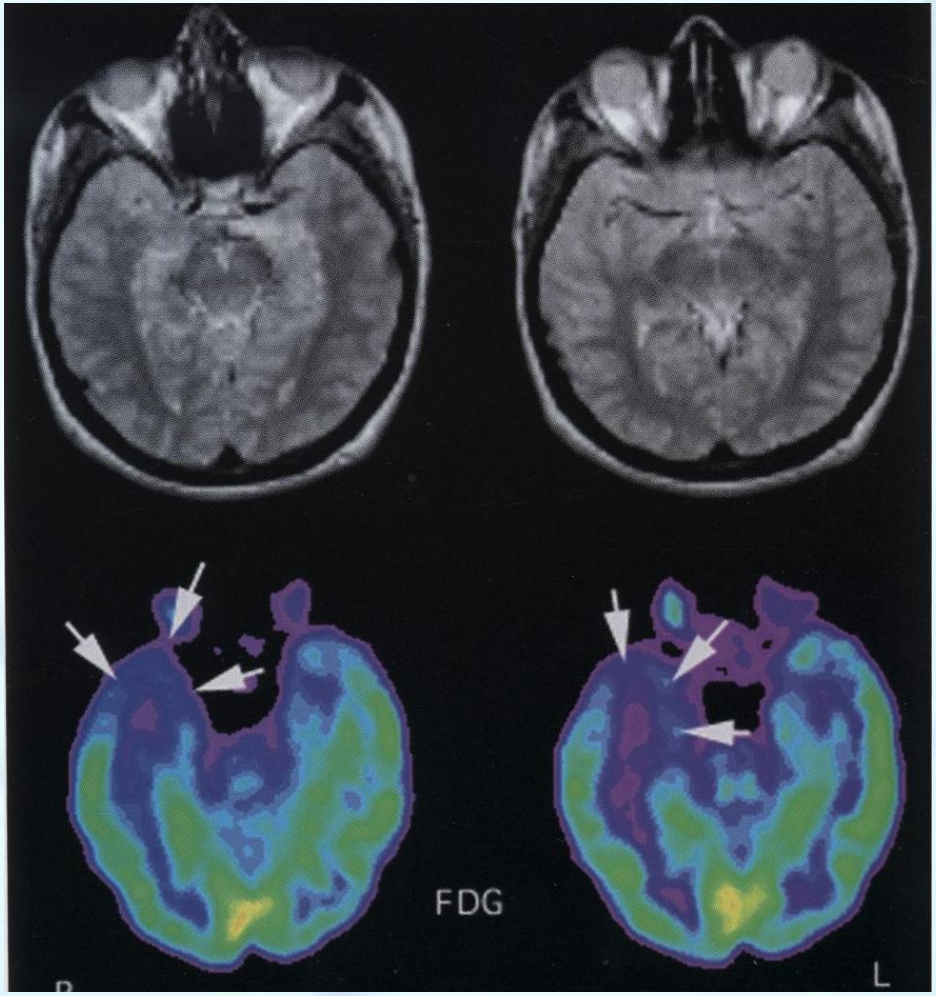
Chronic thyroiditis and diffuse toxic goiter



Diffusely inceased FDG uptake in the thyoid gland -chronic thyroiditis

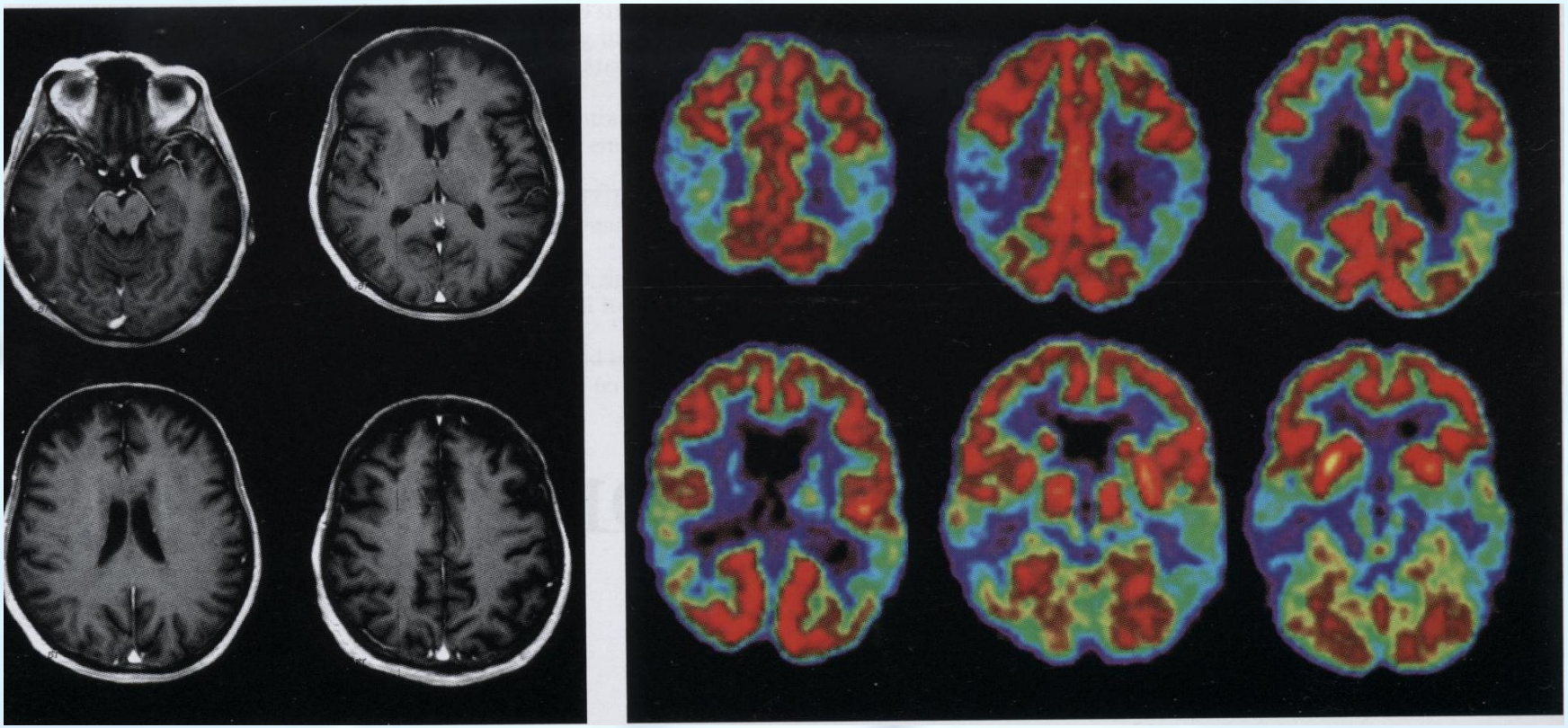
Neurology

Epilepsy



MR normal.
FDG: FDG uptake decreased in the right temporal lobe

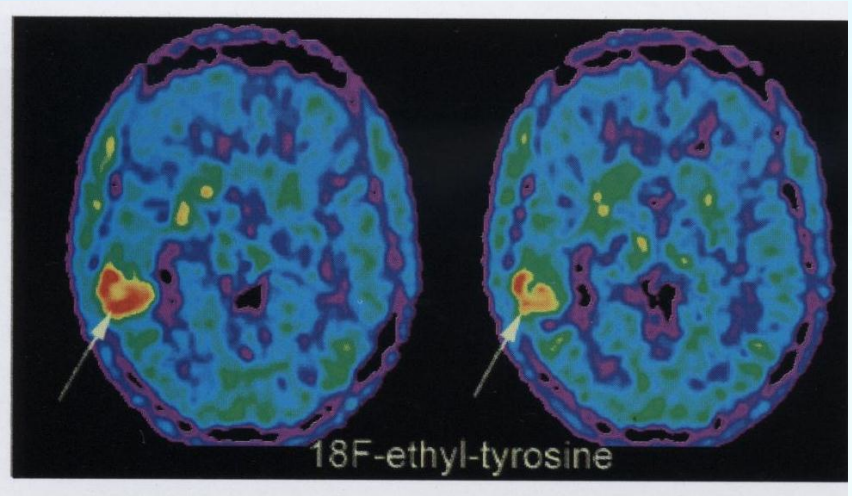
Dementia

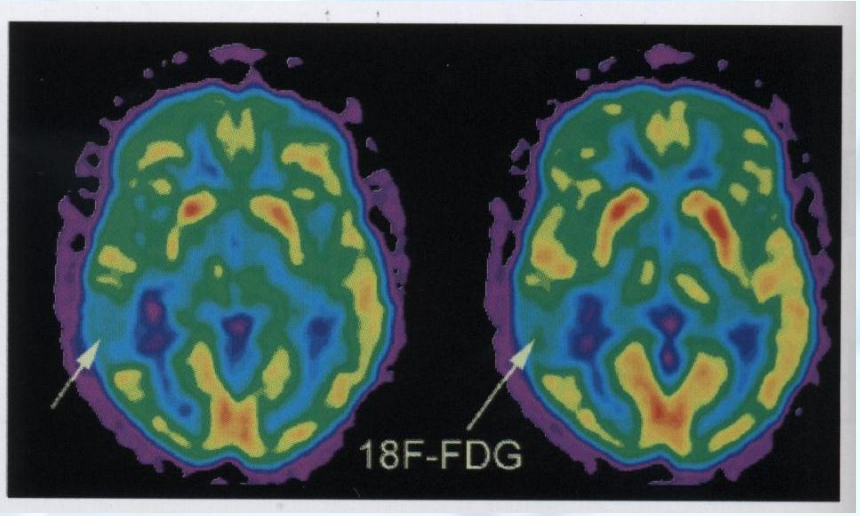


Mb Alzheimer

MR: cortical atrophy
FDG PET: billateral temporoparietal hypometabolism

FET and FDG in brain tumors





FET- selective uptake in brain tumor

Low FDG uptake indicates a low degree of aggressiveness

INFLAMMATION

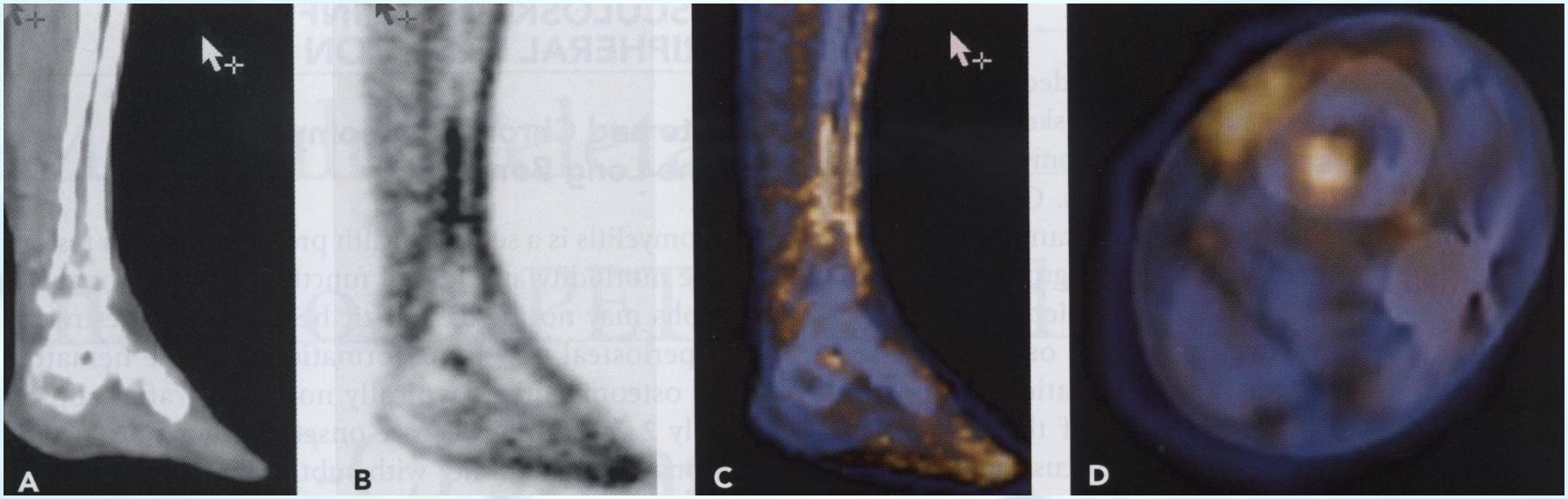
MR- good for acute inflammation (hyperemia and edema).

Less usefull for chronic inflammaton.

- FDG labels only activated granulocytes.
- Stimulated neutrophils, eosinophils and mononuclears take large amounts of glucose and oxygen (up to 50x more than normally).

- FDG uptake is proportional to activity of the infammation

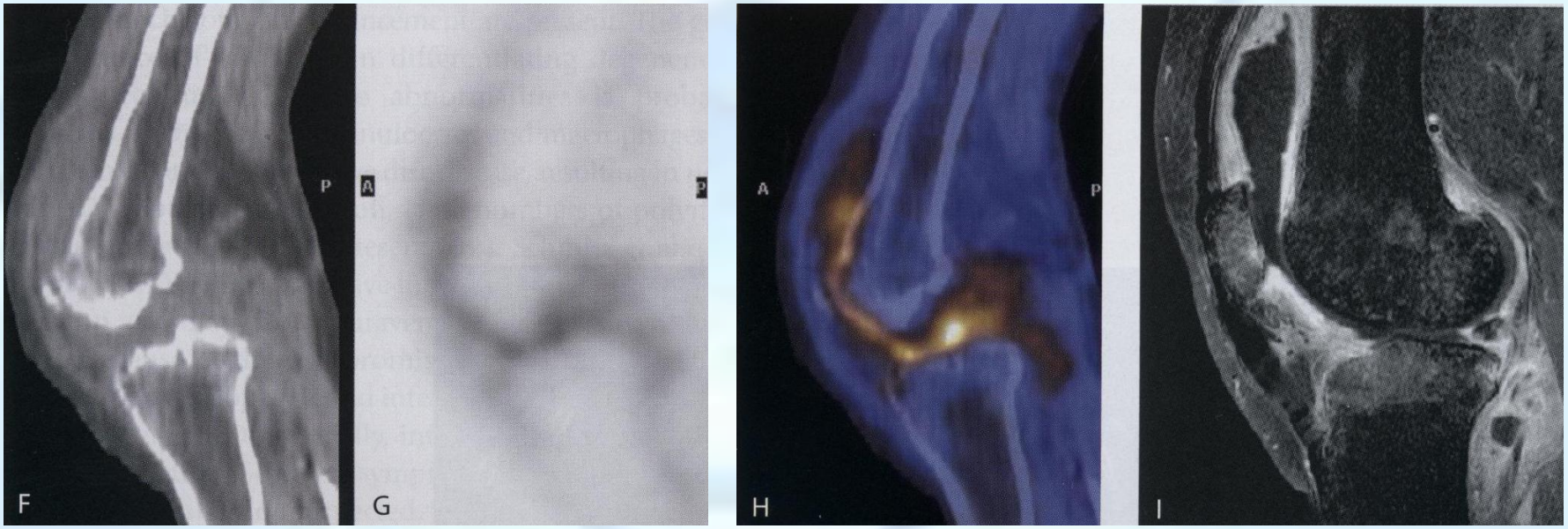
FDG- INFLAMMATION



Patiend had a car accidence, few years ago. Now presented with swelling and pain in the left lower leg.

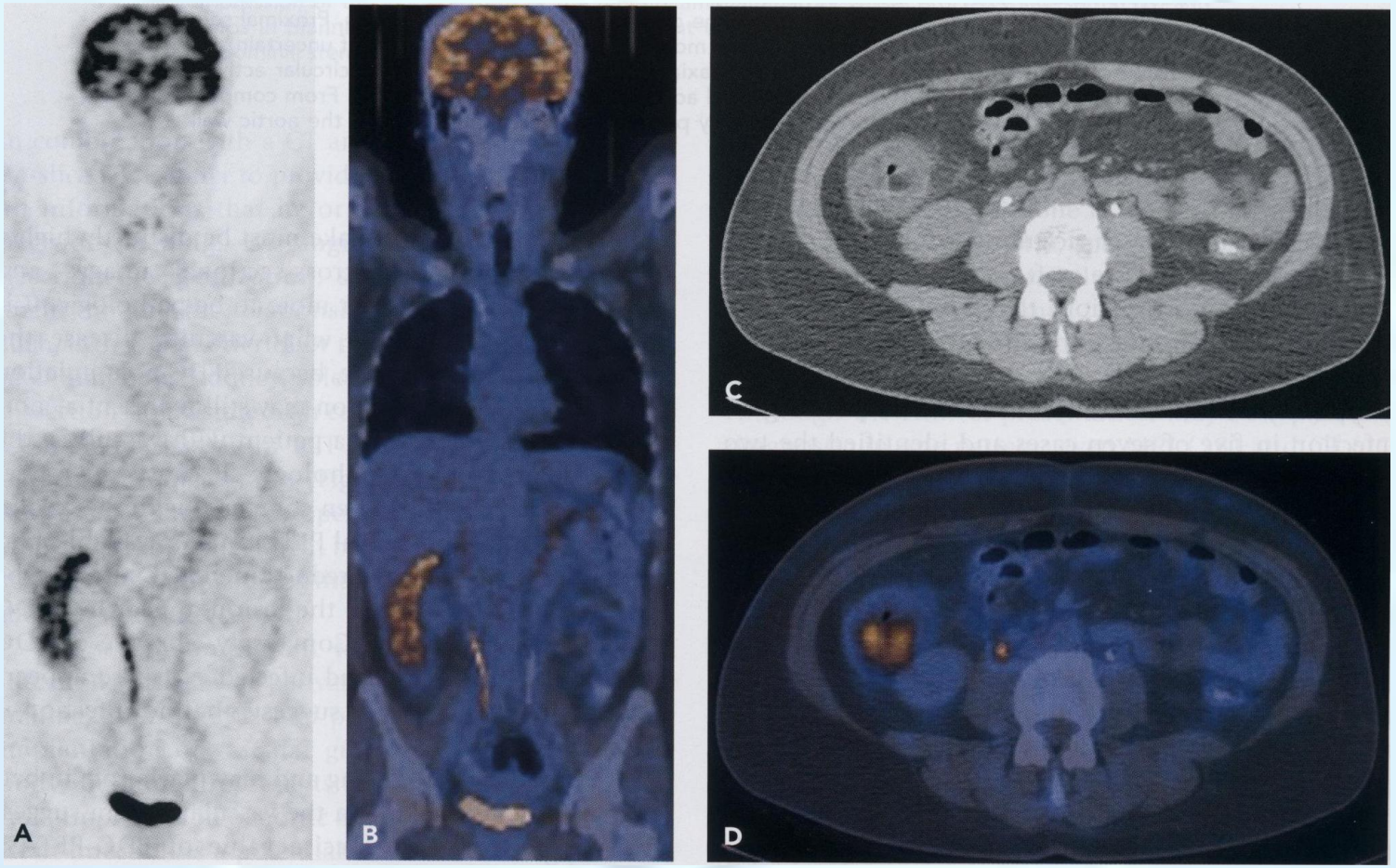
FDG PET-CT: increased uptake in the left fibula and soft tissues- osteomyelitis.

FDG- INFLAMMATION



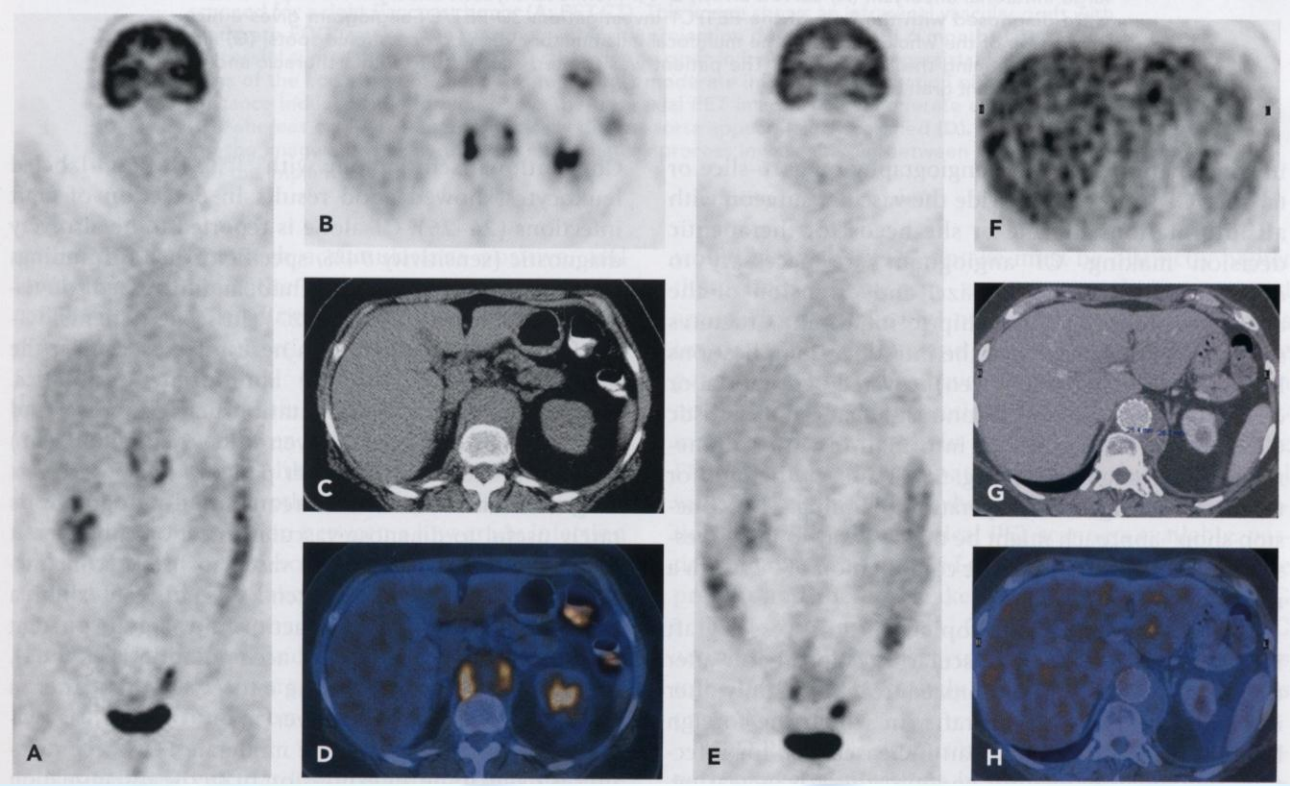
Septic gonarthritis

FDG- INFLAMMATION



Colitis of the ascending colon

FUO (**f**ever of **u**known **o**rigin)



The patient with fever, back pain and elevated inflammatory blood parameters, pneumococcus has been isolated from blood culture.

PET-CT: increased FDG accumulation around aortic aneurysm.

PET/CT one month after antibiotic treatment and implantation of the aortic stent – normal findings.

Patient has no symptoms, normal laboratory findings.

THE END