Clinical PET/CT with other tracers than FDG

JN Talbot

Hôpital Tenon et Université Pierre et Marie Curie, Paris, France

- The **radioactive glucose analogue FDG** is currently the **reference radiopharmaceutical for PET/CT imaging** in **oncology.**
- Overall, FDG has a good diagnostic performance. However, it has some limitations of sensitivity, even in its “well documented” indications.

- The only other radiopharmaceuticals for PET that have been granted a marketing authorisation in the EU, with more restricted indications, are FDOPA (18F) since 2006, sodium fluoride (18F) since 2008, fluorocholine (18F) since 2010 and fluorotyrosine (18F) since 2015. They can be delivered to PET centres by industry.

- Some centres can prepare other radiopharmaceuticals either thanks to an on-site cyclotron, in particular choline (11C), acetate (11C) or methionine (11C), or to a generator 68Ge/68Ga; one has recently been registered in EU.

ONCOLOGY

- A limitation of sensitivity independent of the primary cancer is the small size of neoplastic lesions.
- In contrast with “anatomical” imaging modalities, the size of the lesion on PET is a not considered to be a criterion for malignancy, but there is an interaction between the metabolic activity and the size of a lesion to result in its detection on PET.
- Subcentimeter lesions can be detected and characterised as suspicious on PET, if they are clearly hypermetabolic.

Therefore, even in the primary cancers with a “well documented” utility of FDG, some settings result in a limited sensitivity, in particular:

- Detection of invaded lymph nodes of a normal size at primary staging (e.g. head & neck, breast, oesophagus, colorectal)
- Detection of pleural or peritoneal invasion, when all lesions are of subcentimetre size (e.g. lung, colorectal, ovary).
- However, even in those settings FDG PET has a good PPV and its diagnostic performance is usually better than that of CT or MRI.

In this lecture, we will not further address the limitation of sensitivity due to the size of the lesions but we will focus on its limitation due to metabolic causes.

We will focus on

- particular histologic forms of cancers with "documented FDG utility" that have little or no increase in glucose uptake and metabolism
- cancers with a low FDG PET sensitivity
- or cancers of organs with a high uptake or accumulation of FDG in the non-pathologic tissue.

And discuss alternative PET tracers

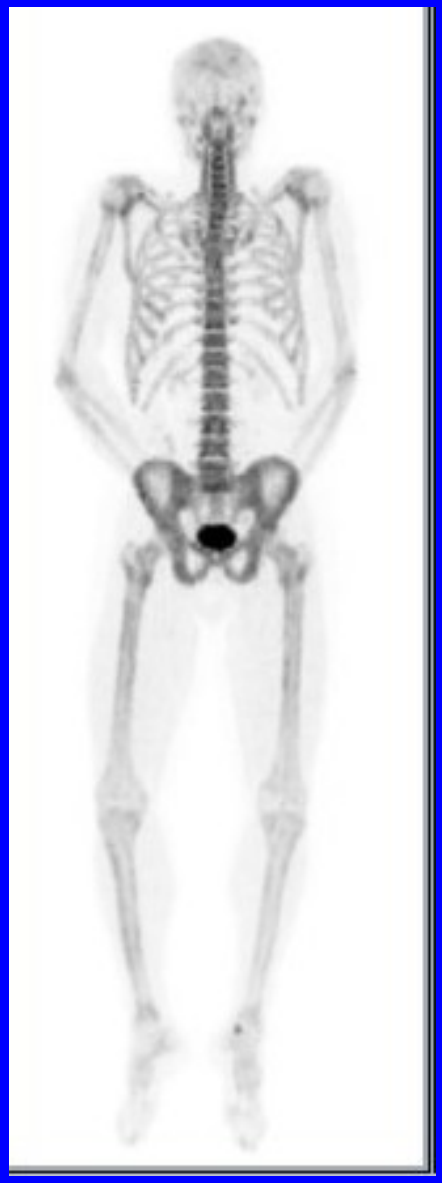
Alternative PET tracers for imaging in oncology which have been granted a marketing authorisation or which routine use has been reported in Europe

Even though it can detect bone metastases, in particular in bone marrow, FDG frequently misses osteoblastic metastases in the cortical bone (most frequent in prostate or breast cancer).

Sodium fluoride (18F) or F Na

tracer of the mineralisation of cortical bone, is currently registered for the detection of bone metastases in adults.

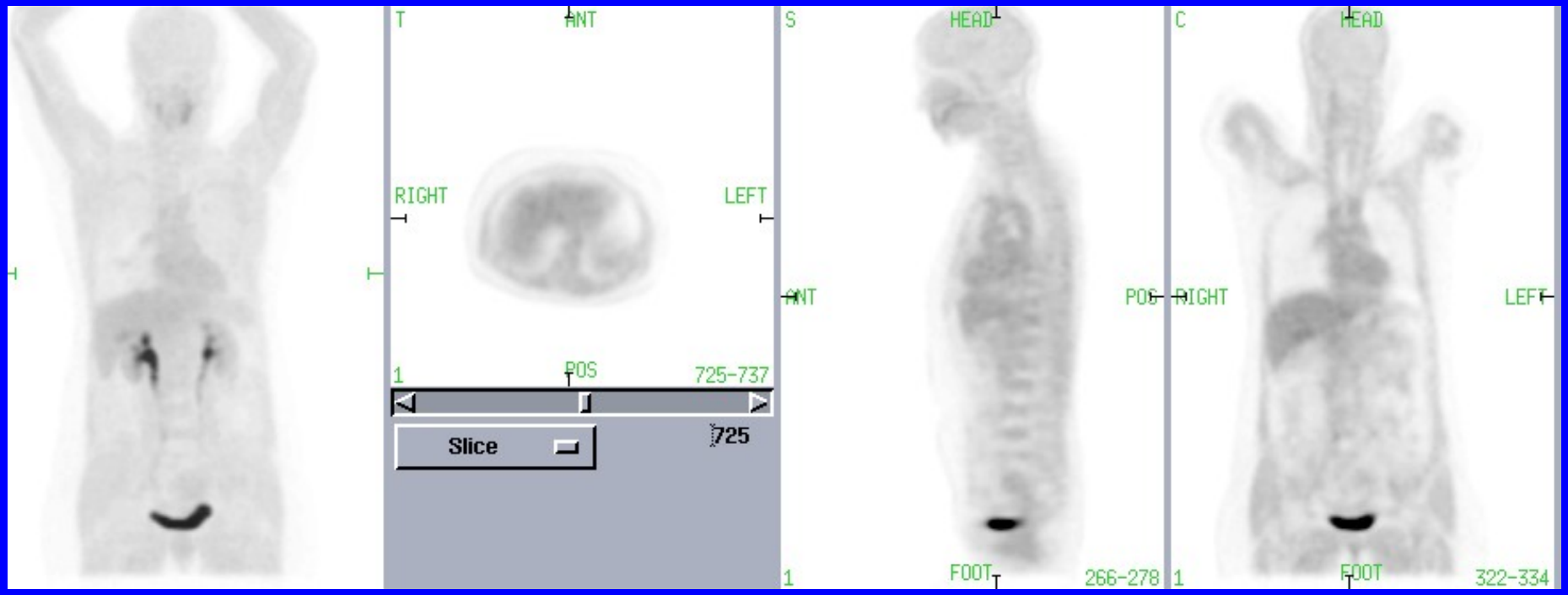
(Almost) normal F Na biodistribution



Aminoacids

- Aminoacids or aminoacid analogues have little background activity in the brain and are less taken-up by inflammatory lesions.
- The most frequently reported for routine use are:
  - Methionine (11C), with the logistic problems of 11C
  - Fluorethyl thyrosine (18F) or FET
  - Fluorodihydroxyphenylalanin (18F) or FDOPA

Normal biodistribution of FET

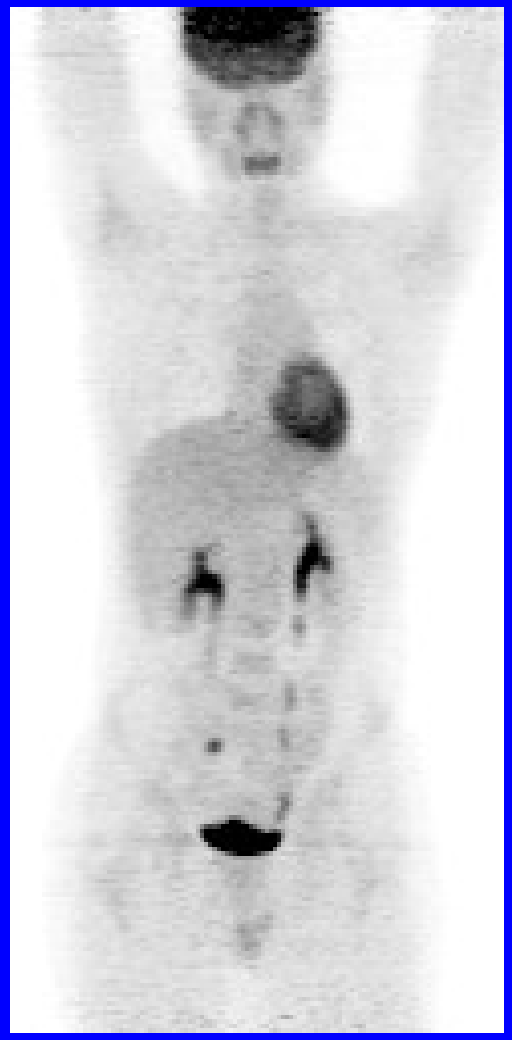


FluoroDOPA (18F)

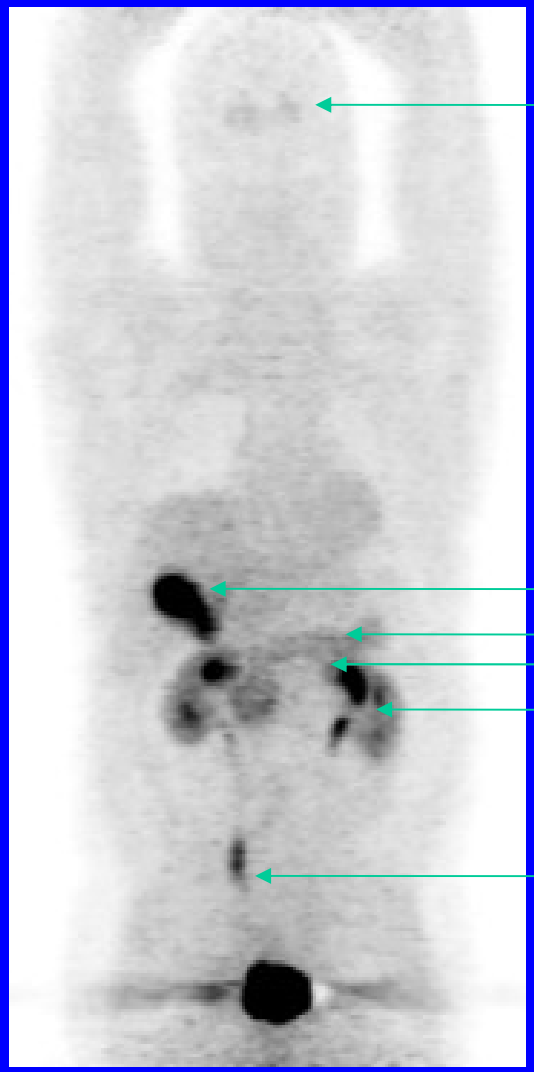
Analogue of DOPA, the aminoacid precursor of the bioamines in the endocrine cells and of the dopaminergic mediators.

It was initially used to quantify the loss of dopaminergic neurons in Parkinson's disease. It has also been shown to be clinically useful in the evaluation of glioma and above all of endocrine tumours

Normal biodistribution FDOPA



FDG



Basal ganglia

Gallbladder

Pancreas

Adrenals, faint and variable

Kidneys

Urinary tract and bladder

FDOPA

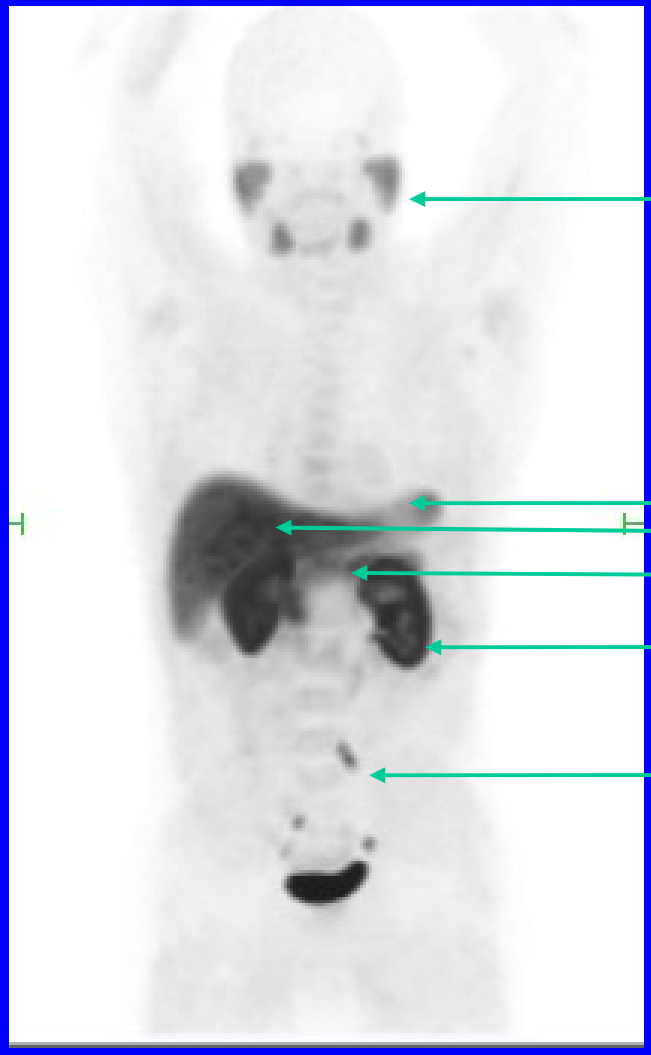
Tracers of the lipid metabolism

- Tracers of the lipid metabolism have been proposed in indications where the renal excretion of the tracer is a drawback : renal cancer and prostate cancer. The rational for tumour detection is the enhanced uptake for membrane accretion in the cancer cell.
- Several PET tracers have been proposed, the best documented are:
  - Acetate (11C)
  - Choline (11C)
  - Fluorocholine (18F) or FCH and fluoroethylcholine (18F)

Fluorocholine (18F) or FCH

FCH is behaving as choline (11C), except for urinary excretion which is almost absent for choline (11C).

Normal biodistribution of fluorocholine (18F) or FCH



Salivary glands

Stomach

Liver

Pancreas

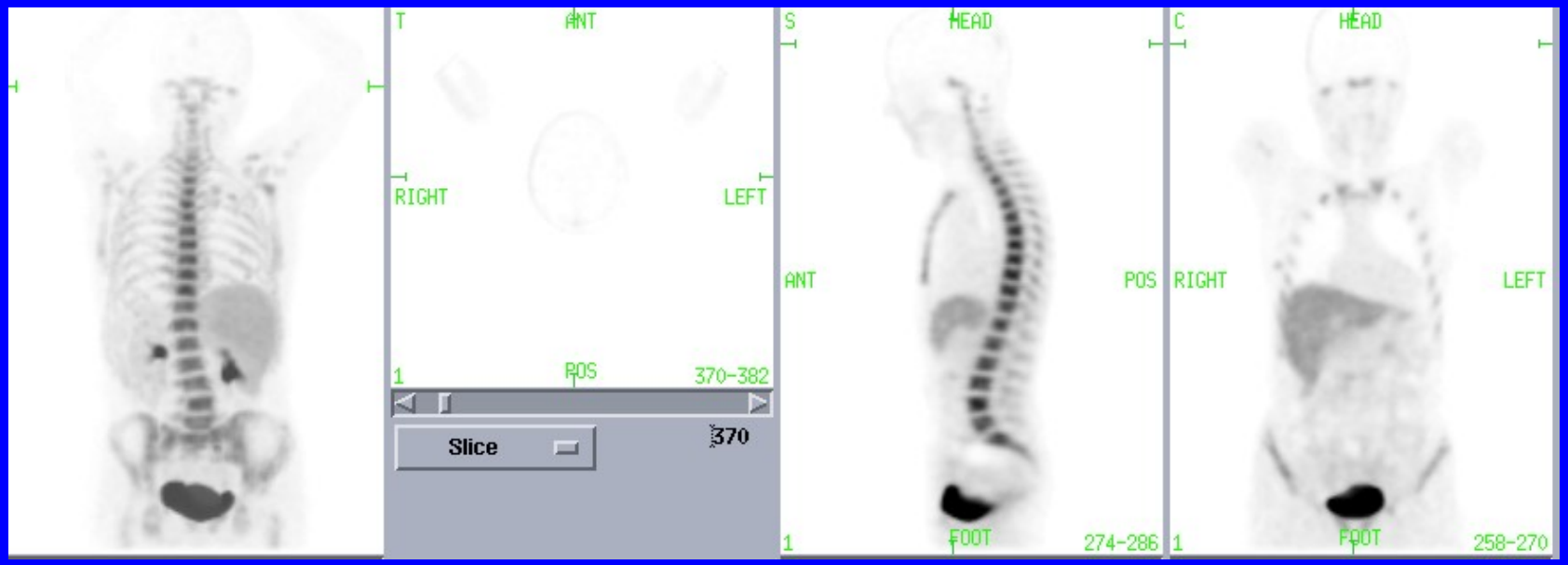
Renal cortex

Urinary tract and bladder

Fluoro-L-thymidine (18F) or FLT

tracer of phosphorylation of thymine, a DNA base, is expected to reflect earlier than FDG the response to therapy

Normal biodistribution of FLT



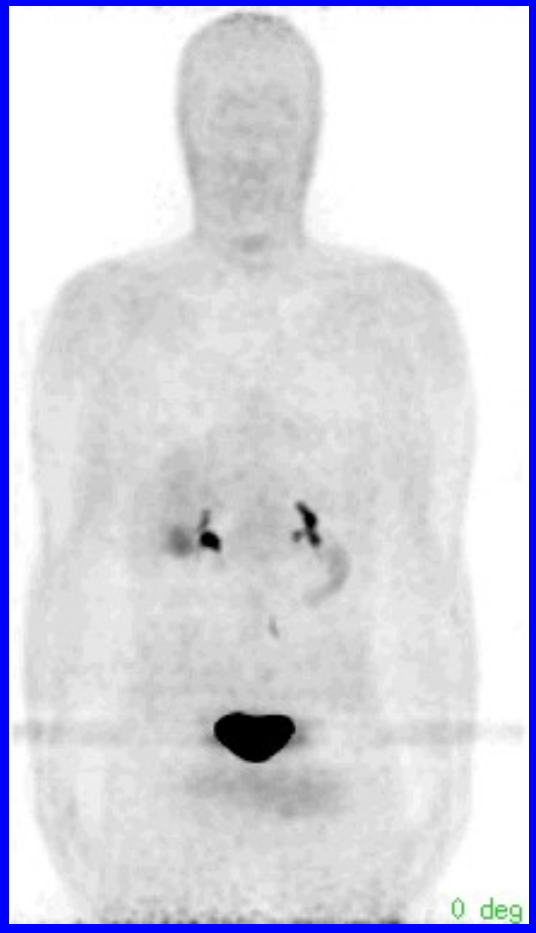
FLT is non cancer-specific and may accumulate in non malignant lesions such as sarcoidosis or inflammatory adenopathies, possibly less than FDG

Evaluation of hypoxia

- Hypoxic tissue may take-up FDG without difference with non-hypoxic tissue
- It is important to delineate hypoxic tissue since it can resist to radiotherapy
- The consequences of treatment with the new antiangiogenic anticancer agents on hypoxia are important to explore
- Several PET tracers which give a positive signal in case of hypoxia have been proposed. The most studied among the imidazole family is FMISO (18F)

Normal biodistribution of FMISO (18F)

3h after injection (slow clearance); ca 4h waiting time is recommended by some authors *(Abolmaali N Nuklearmedizin 2011: 22)*



In relation with the slow clearance, PET tracers labeled with 64Cu have been proposed, ATSM in particular.

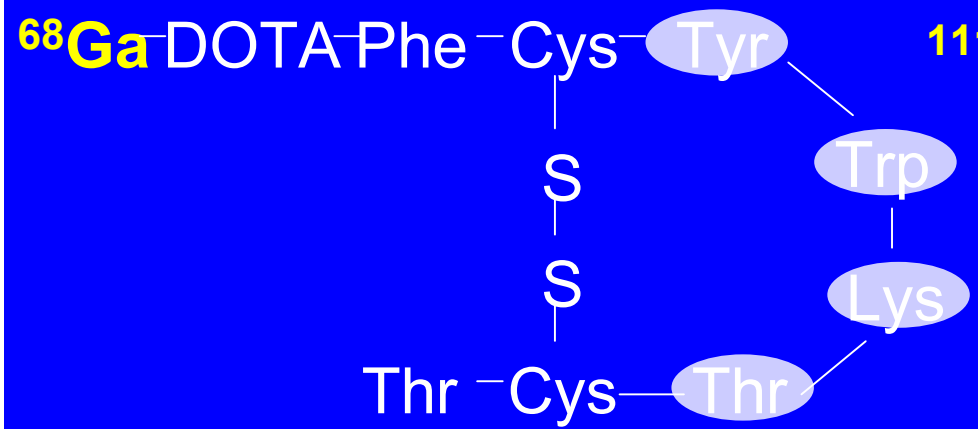
124 I

Has been proposed to search for iodine-avid lesions in thyroid cancer after initial initial treatment. The dosimetry is less unfavourable than that of a « diagnostic » activity of 131I, without risking stunning effect.

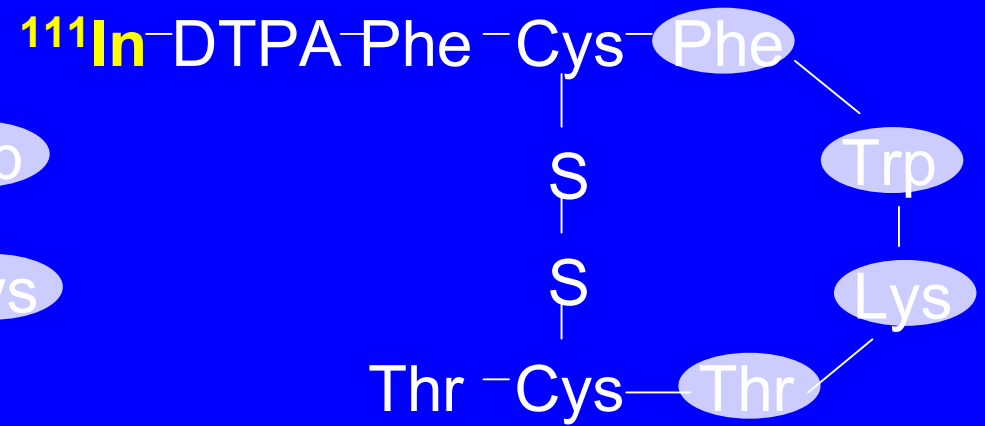
Normal biodistribution 124I

Gallium-68 labelled tracers for PET imaging

Somatostatine receceptor ligands for nuclear imaging

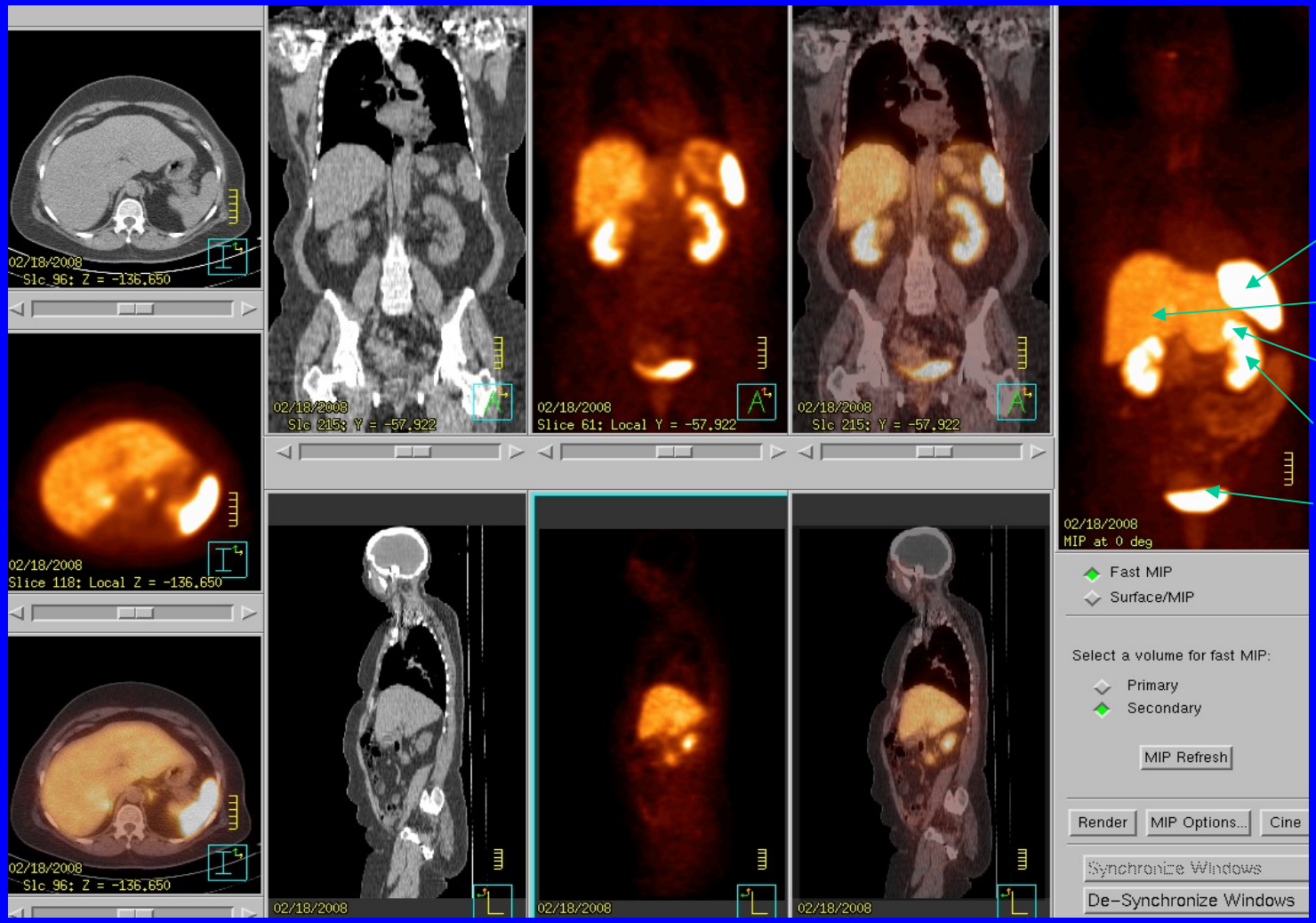


DOTATOC-(Ga-68)
Receptor subtypes :
2, (5)



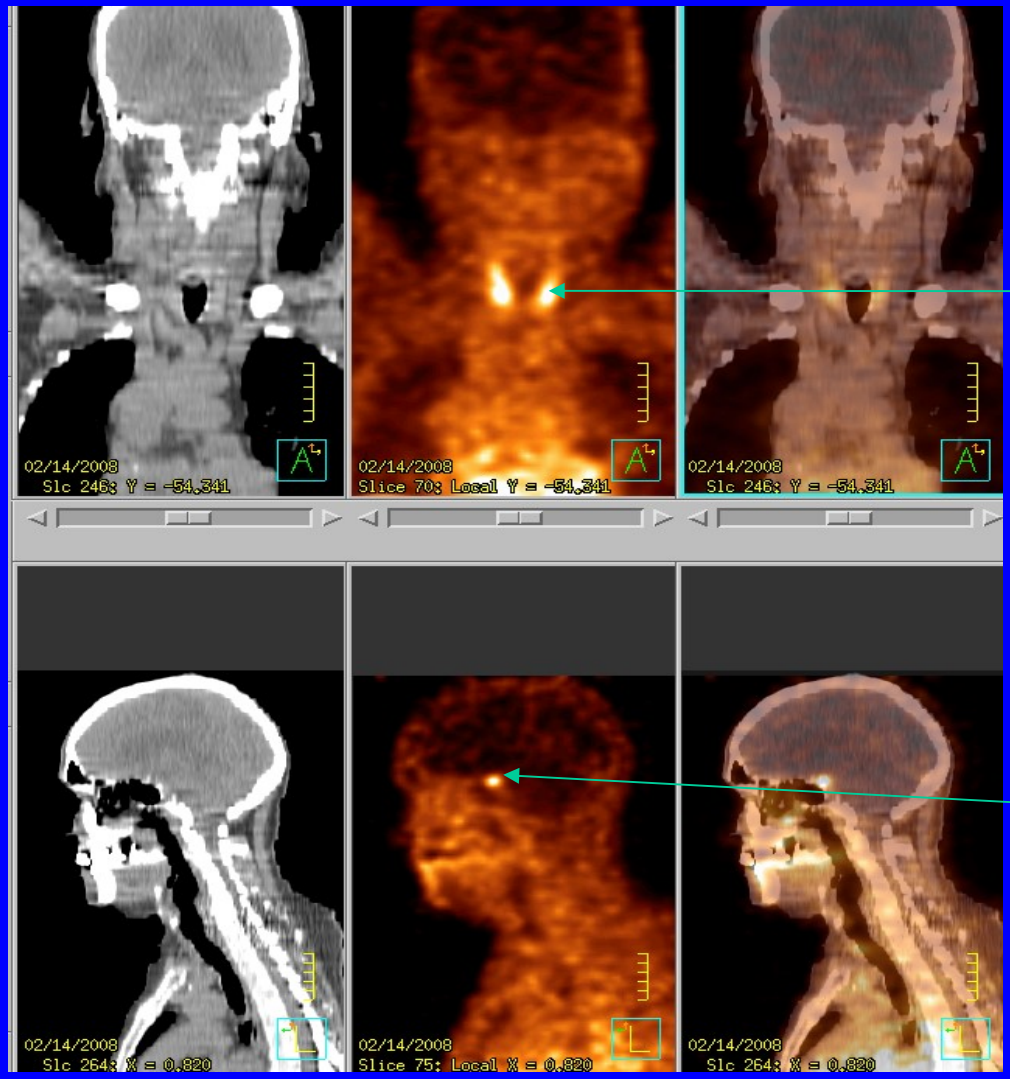
Pentetreotide-(In-111)
Receptor subtypes : 2,
5, (3)

Normal biodistribution (torso) of the most studied somatostatin analogue for PET imaging: DOTATOC (68 Ga)



- spleen
- liver
- adrenals
- kidneys
- urinary tract and bladder

Normal biodistribution (head & neck) DOTATOC (68 Ga)



- thyroid
- pituitary

Prostate Specific Membrane Antigen (PSMA)

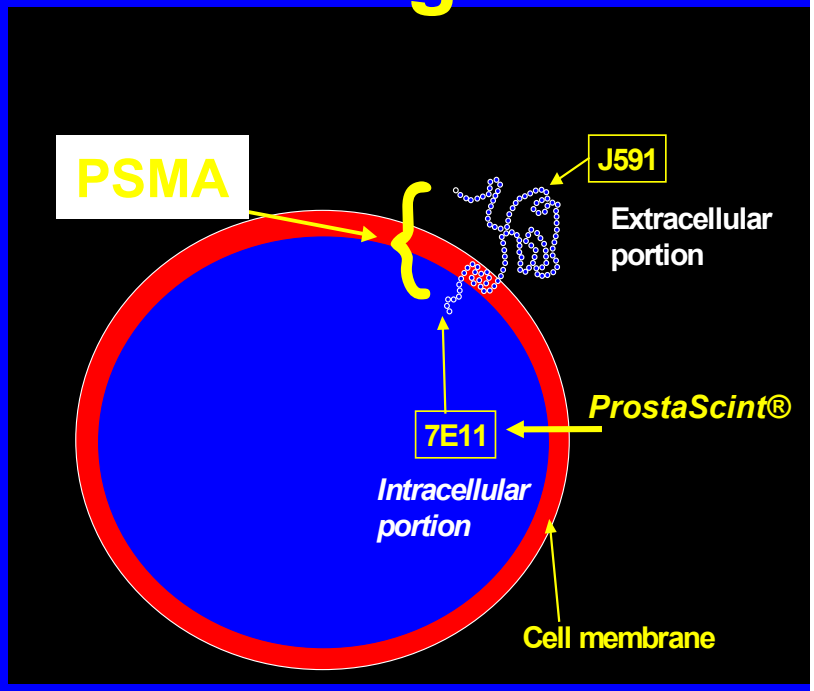
PSMA is a surface antigen expressed on virtually all prostate cancer cells

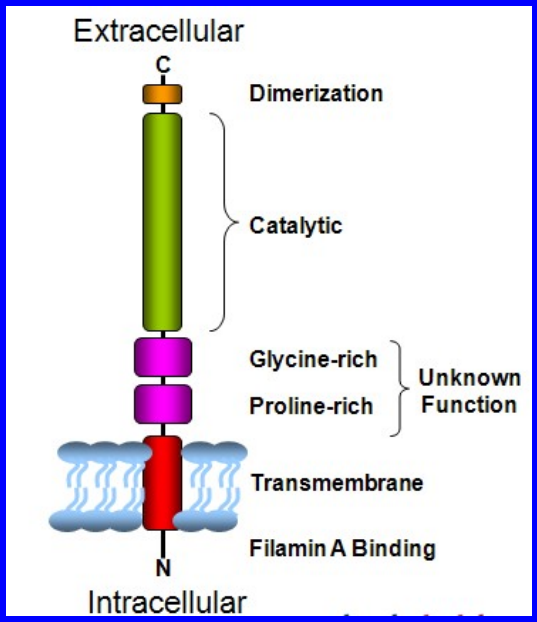
PSMA expression increases progressively in:

- Higher grade tumors
- Metastastic disease
- Castration resitsant stage

PSMA has an enzymatic function as a *glutamate carboxypeptidase*

- Several PSMA ligands have been proposed for PET imaging.
- Currently 68Ga labeled ligands are the most effective





Particular histologic forms of cancers with “documented FDG utility” that have little or no increase in glucose uptake and metabolism

Non-Hodgkin lymphoma

- It has been recognised for more than a decade that some types NHL are variably FDG avid
- These include aggressive NHL subtypes other than DLBCL, such as T-cell lymphomas,
  and all subtypes of indolent NHL other than follicular lymphoma, such as extranodal marginal zone lymphoma of mucosa associated lymphoid tissue and small lymphocytic lymphoma.

- Choline (11C) or FCH could be more sensitive in those NHL

- In contrast, FLT, which has been proposed for treatment monitoring of aggressive lymphomas, is of no help in indolent lymphoma *(Buchmann I, Cancer Biother Radiopharm. 2004: 436).*

Bronchoalveolar carcinoma (BAC)

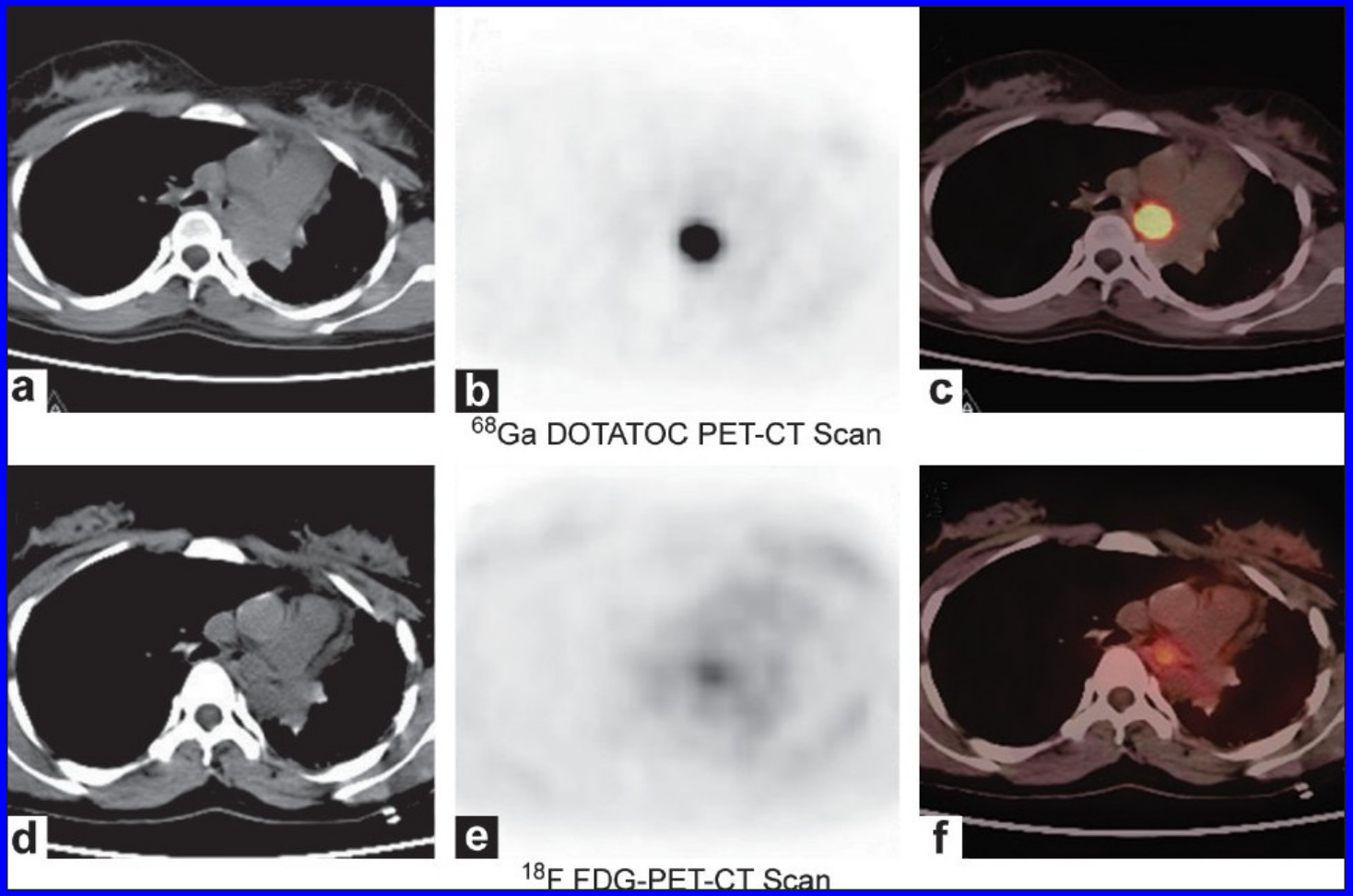
- *Yap C (EJNM 2002: 1166)* in the rare tumours with a pure BAC pattern, FDG PET missed a majority (67%) of lesions.
- We considered FCH to be a potential PET alternative in BAC but did not find a better sensitivity than FDG in our pilot study of 12 BAC lesions (*Balogova S. Nucl Med Commun 2010: 389*)

Bronchial NET (carcinoid)

- FDG sensitivity is limited, in particular in case of typical bronchial NET:
  - 50% in 12 patients imaged with FDG PET/CT (*Krüger S. J Intern Med 2006: 545*),
  - 75% in 16 patients with FDG PET (*Daniels CE. Chest 2007: 255*).

- PET alternative : DOTATOC (68Ga) or another ligand of somatostatin receptors.
- PET/CT provided additional information in 9 of 11 patients leading to the changes in the clinical management of 3 of 9 patients (*Ambrosini Nucl Med Commun 2009: 281*).

FDG and DOTATOC (68Ga) in a case of bronchial carcinoid



Jindal T. J postgrad Med 2009: 272

Breast cancer

- EMA FDG : Staging locally advanced breast cancer
- ESMO : Suspicion of metastatic breast cancer. Clinical suspicion must be confirmed by imaging including functional imaging such as PET-CT or dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI)

Factors influencing FDG uptake by breast cancer

- **Type : ductal > lobular > carcinoma in situ**
- **Tumour size** (without correction of the partial volume effect) :

pT1 Se = **68%**
(pT1a : Se = **25**%, pT1b : Se =**25**%, pT1c : Se = **84**%)

pT2 Se = **92%**

pT3 Se = **100%**

(Avril N. J Clin Oncol 2000: 3495 & J Nucl Med 2001: 9)

Breast cancer : distant metastases

- **<u>Brain mets :</u> low FDG sensitivity due to the physiologic uptake by the brain cortex**

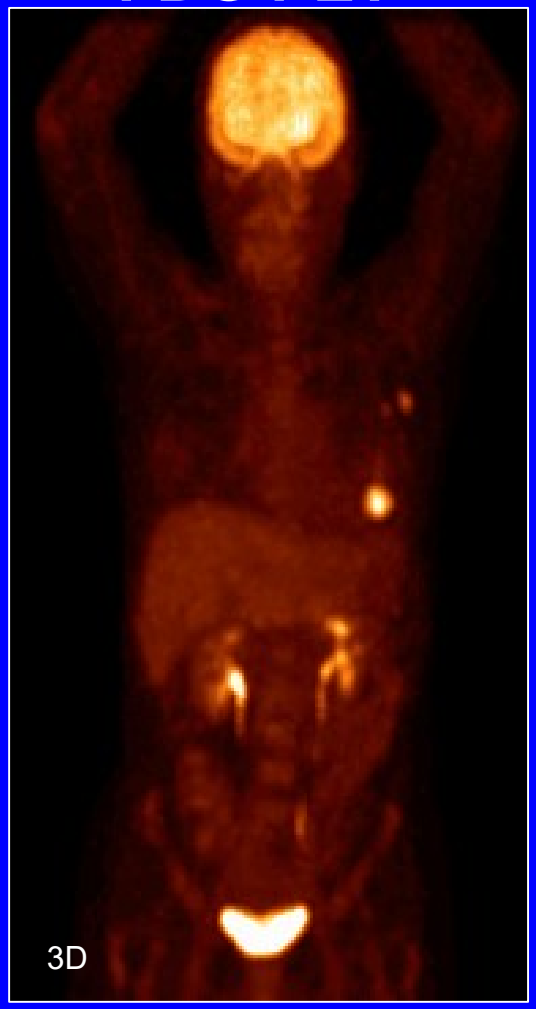
- **<u>Bone mets</u> : Se for bone mets < visceral mets** *(Moon 1998)*
  Se FDG > Se HMDP-Tc lesion based *(Cook 1998, Mahner 2008)*
  (≈ twice more foci for osteoclastic lesions)
  Sp FDG > Sp HMDP-Tc *(Ohta 2001, Yang 2002, Raileanu 2004)*

Different **detection rate** according to the CT image type (*Nakai 2005*):
-for the blastic type, BS =100% vs. FDG PET = 56%
- for the mixed type, BS = 84% vs. FDG PET = 95%
- for the lytic type, BS = 70% vs. FDG PET = 100%
- when no anomaly was visible on CT, BS = 25% vs. FDG PET = 88%.

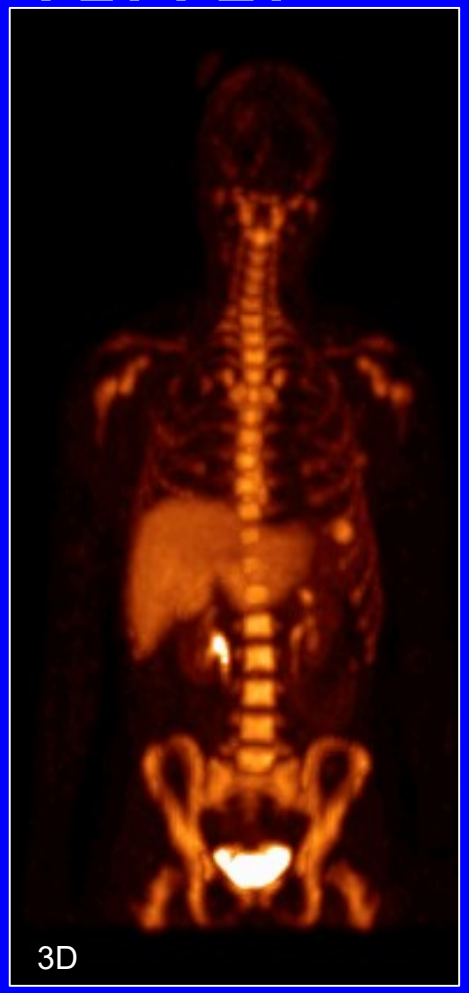
References :

Cook J Clin Oncol 1998: 3375 ; Mahner S. Ann Oncol 2008: 1249 ; Moon DH. J Nucl Med: 431 ; Nakai T. Eur J Nucl Med. 2005: 1253; Ohta M. Nucl Med Commun 2001: 875 ; Raileanu I. Méd Nucl 2004: 297; Yang SN. J Cancer Res Clin Oncol 2002: 325

FDG PET



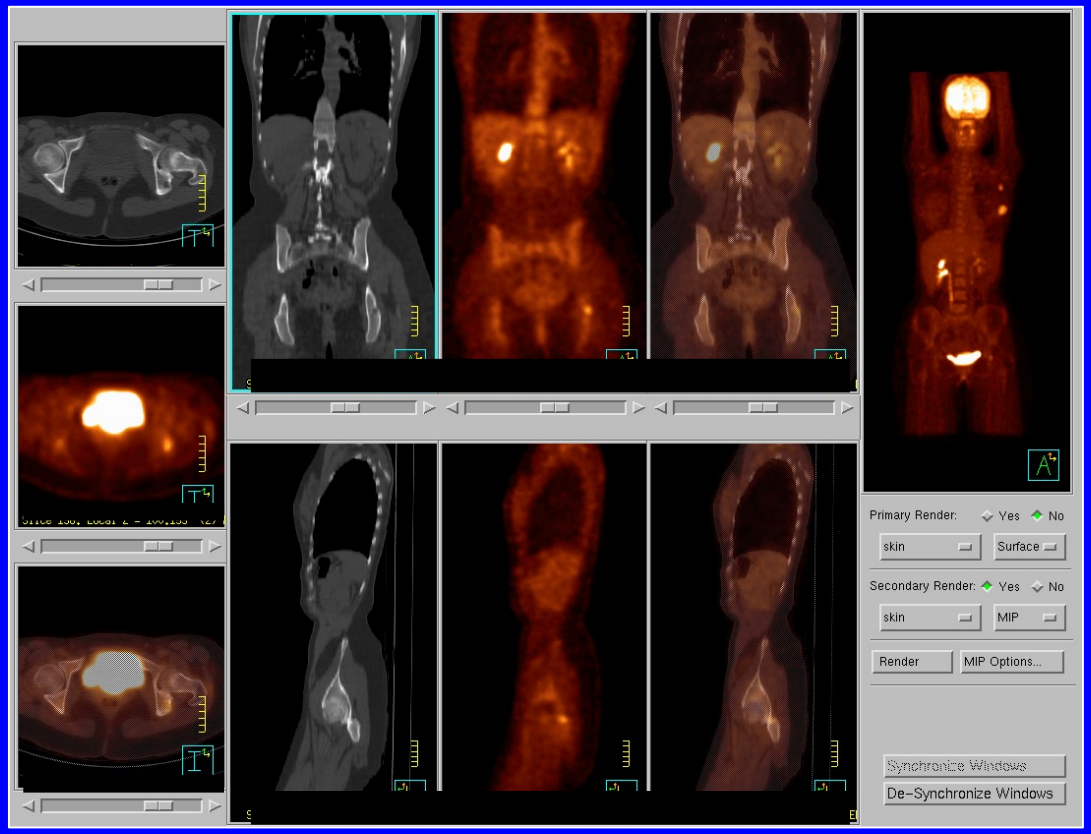
FLT PET



Will FLT improve detection of breast cancer?

Lytic bone metastasis of breast cancer

FDG



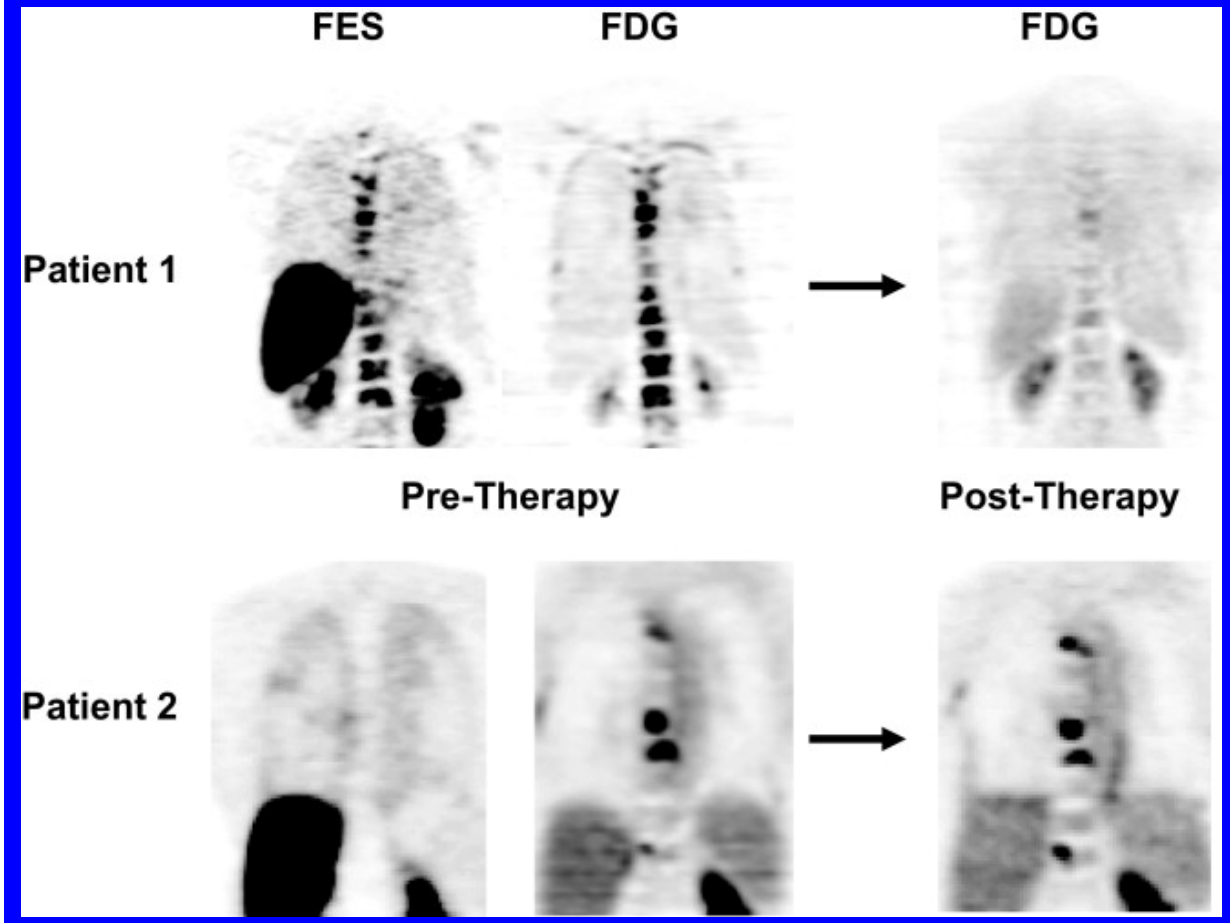
T/NT = 1.60

FLT

T/NT = 0.95

Fluoroestradiol (18F) in breast cancer

Two patients with bone metastases from an ER+ breast cancer



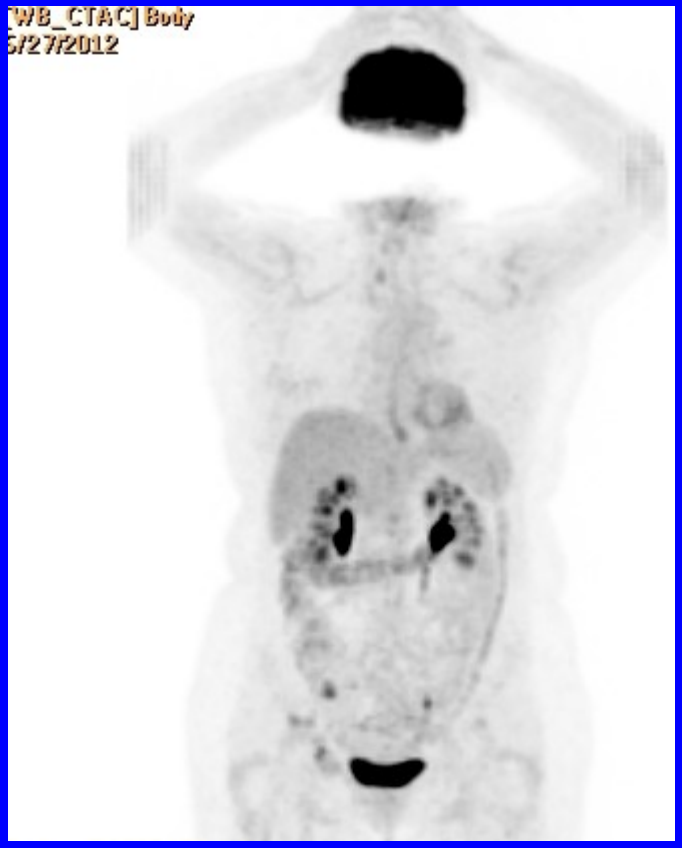
Patient 1: high FES uptake at all sites of active disease, indicating preserved ER expression. This patient subsequently responded to HT.

Patient 2: no FES uptake at active sites of disease seen by FDG-PET, suggesting loss of ER expression, and had no response to hormonal therapy.

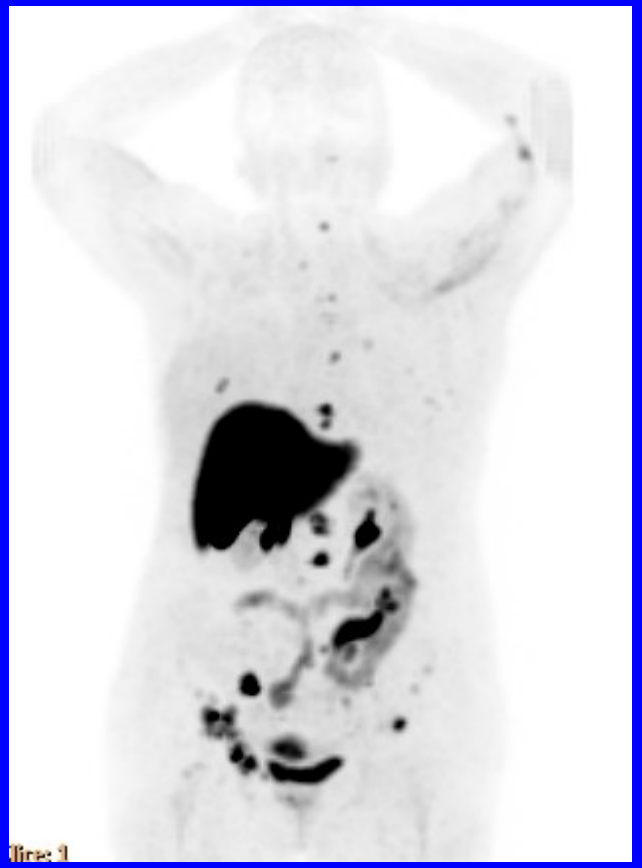
Sundarajan et al. Semin Nucl Med. 2007

Fluoroestradiol (18F) in breast cancer

FDG



FES



Bone mets FES + FDG -

Evaluation of hypoxia in H&N cancers

- Radiotherapy outcome and survival prognosis (radiotherapy or operation) in HNSCC may be predicted by carrying out FMISO PET before treatment. *Kikushi M Ann Nucl Med 2011: 625*

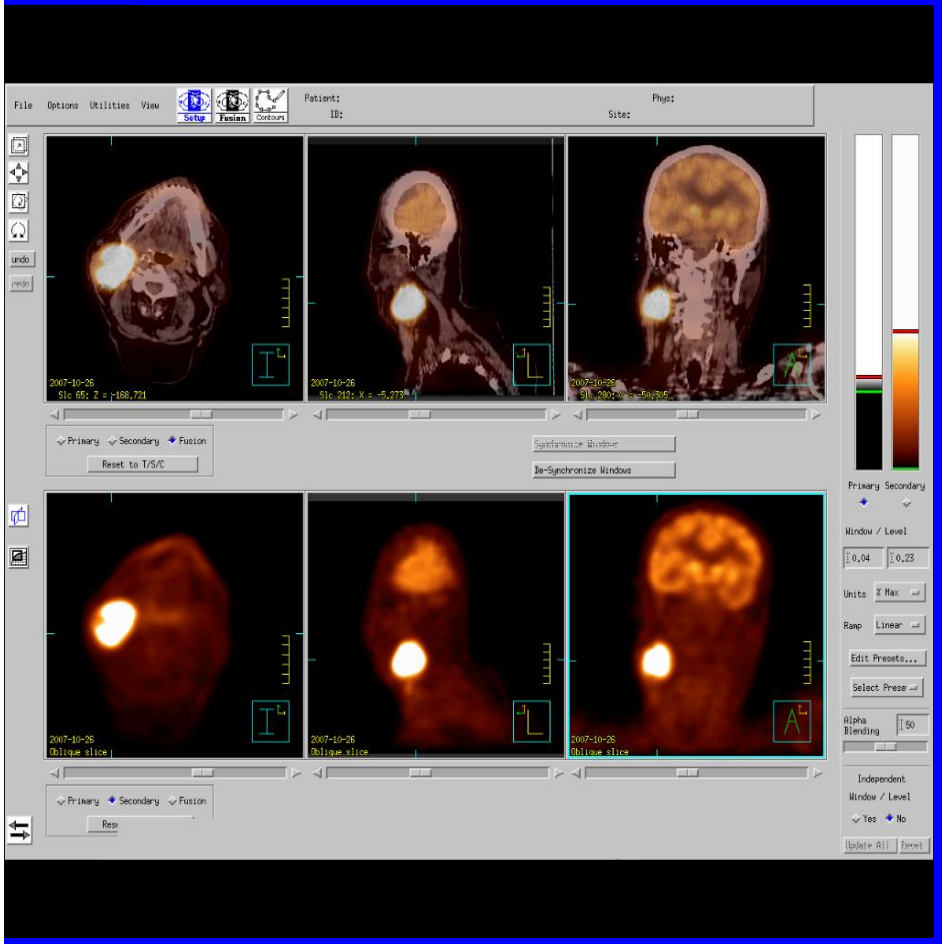
- It was possible to dose escalate the HTV radiation to 78Gy in 6/8 head and neck cancer patients using FMISO PET/CT-guided IMRT *Choi W. Radiother Oncol. 2010: 176.*

- FMISO PET seemed to be a useful noninvasive tool for detecting hypoxia reduction after neoadjuvant chemotherapy (*Yamane T Mol Imaging Biol 2011:227*).

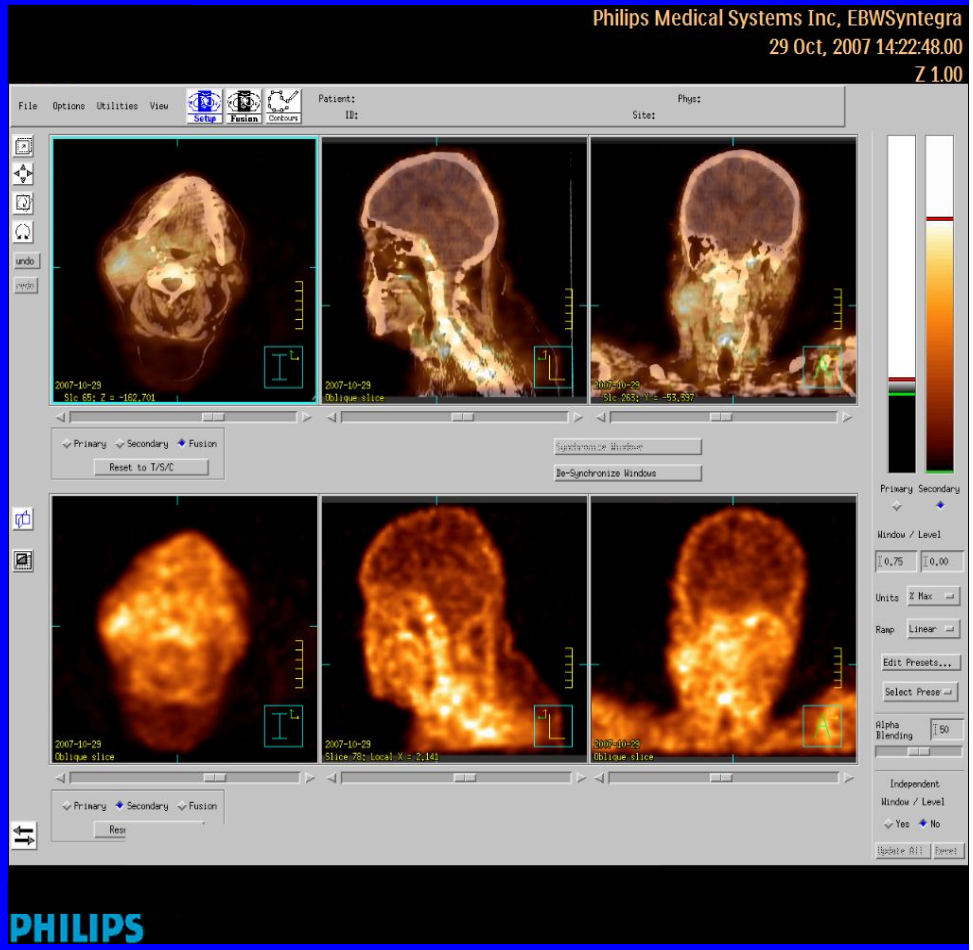
- All locoregional recurrences were within the baseline FDG-avid regions; 3 recurrences mapped outside the hypoxic volume on baseline FMISO PET (*Dirix P JNM 2009: 1020*).

- Variability in spatial uptake can occur between repeat FMISO PET in patients with H&N cancer (*Nehmeh SA, Int J Radiat Oncol Biol Phys. 2008: 235-42).*

FDG & FMISO PET/CT in H&N cancer



FDG



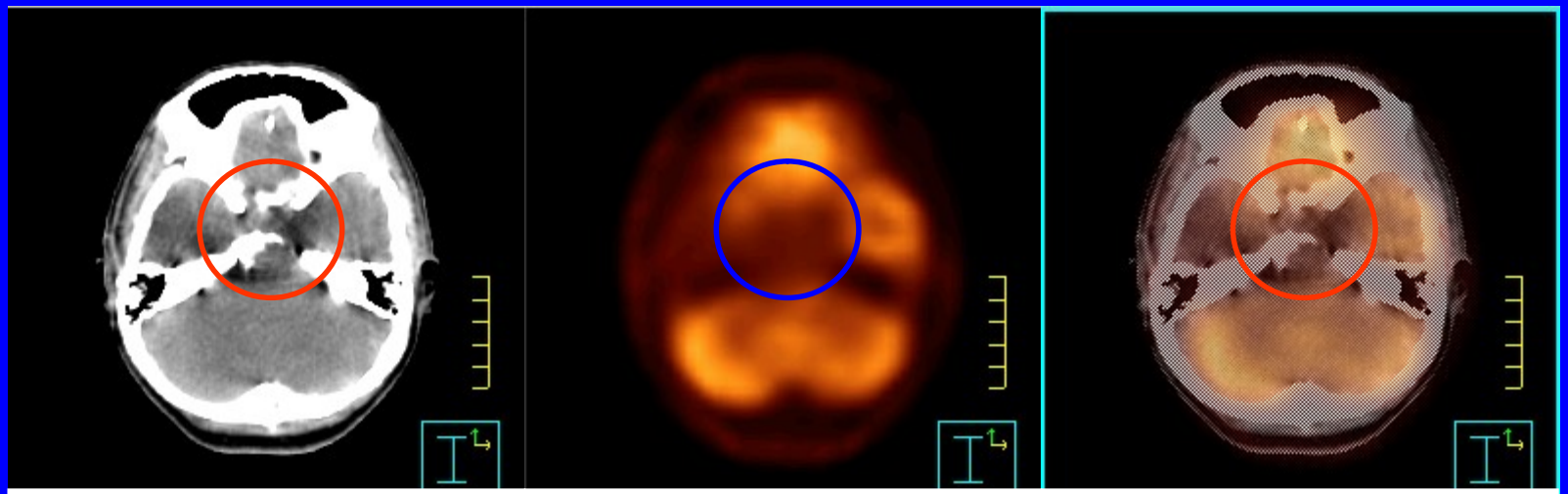
FMISO

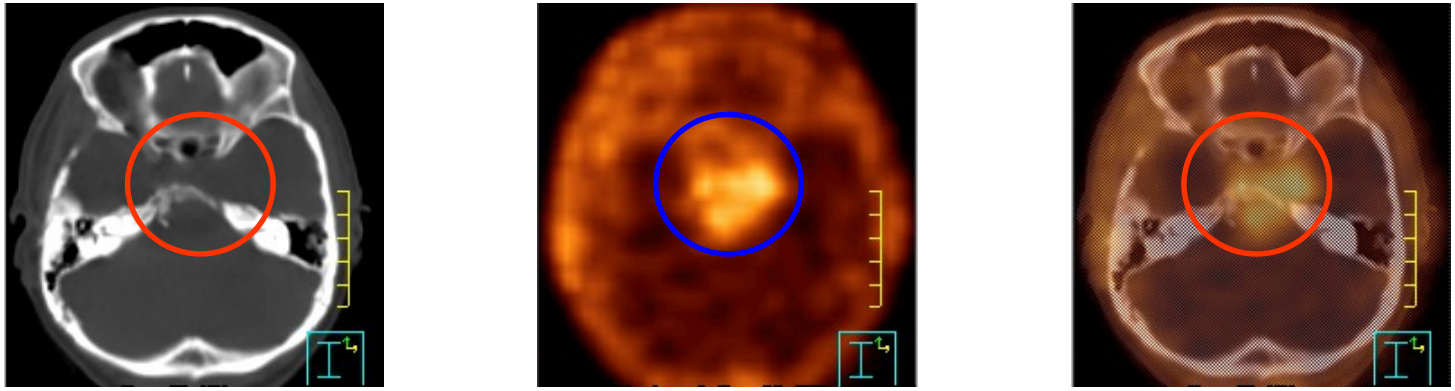
HOPITAL TENON AP-HP

FDG & FMISO in chordoma of the base of the skull

Recurrent chordoma after surgery

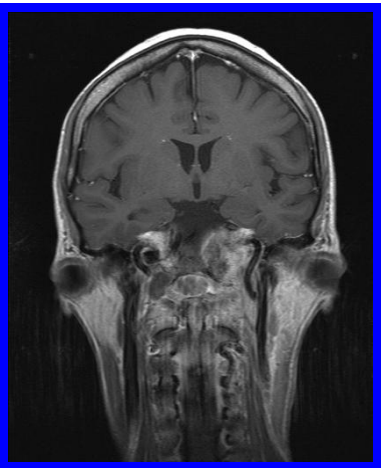
FDG (18F)



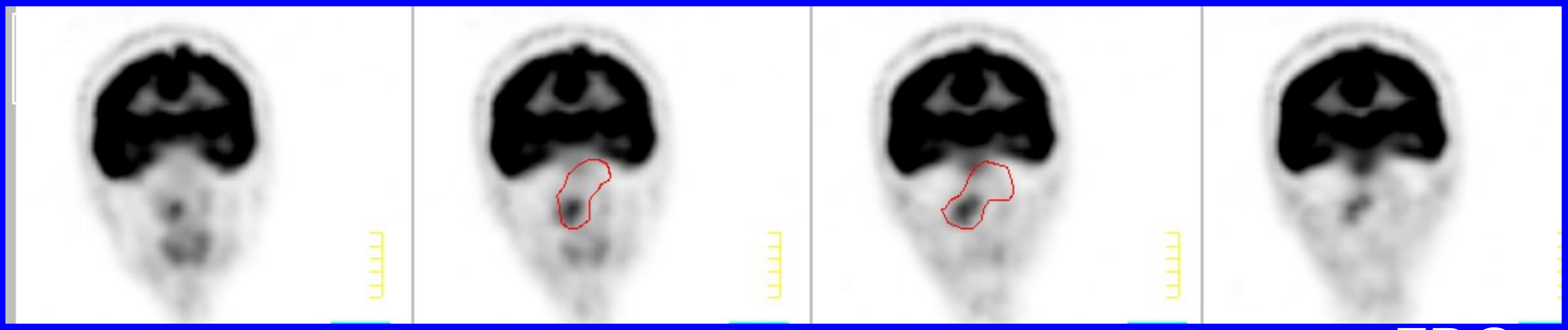


Mammar H Int J Radiat Oncol 2012 Epub

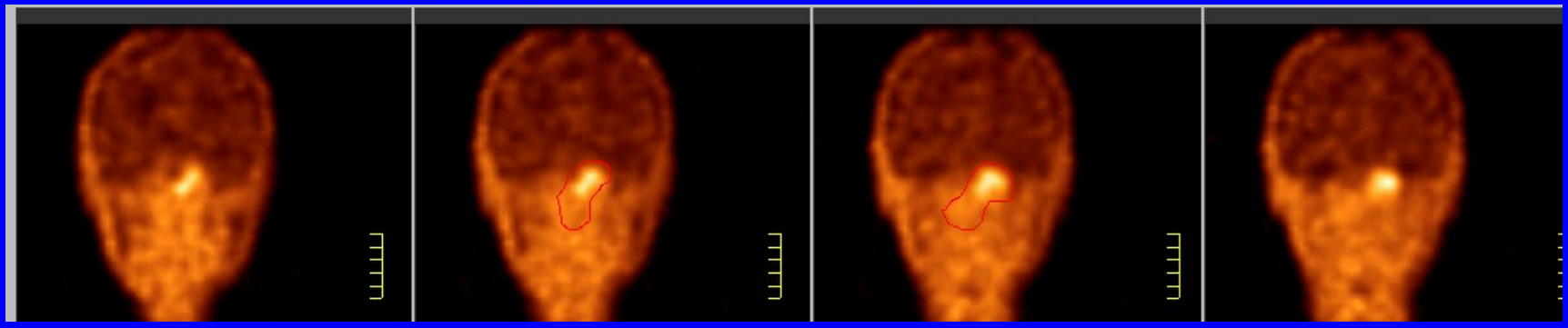
FMISO (18F)



MRI



FDG



FMISO

Partly hypoxic recurrent chordoma

Differentiated thyroid cancer

- PET alternatives:

  - 124I alternative to « diagnostic » 131I

    - with post-treatment 131I as standard of truth, sensitivity of 124I PET was 100% vs. 83% for diagnostic 131I (*Freudenberg Eur Radiol 2004: 2092*).

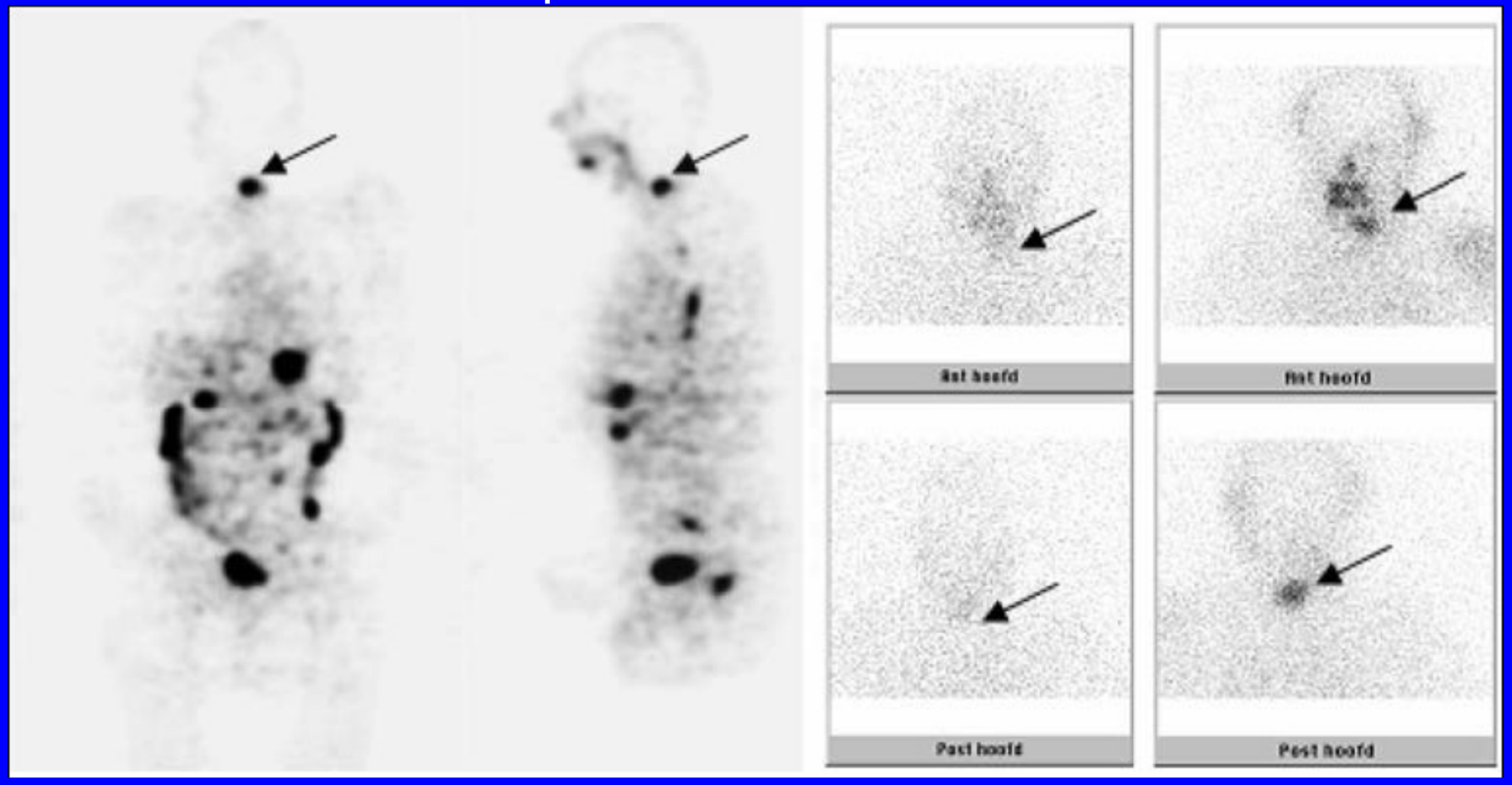
  - FDG alternative to radioiodine

    - before surgery FDG PET has limited sensitivity for the detection of 1ry cancer and lymph nodes (not better than US) (*Choi J Ultrasound Med 2011: 1267*)

    - After surgery c.a.1/3 of lesions take-up FDG or iodine and 1/3 both. FDG is better to detect distant metastases (*Alzahrani AS Eur J endocrinol 2008: 683*)

    - in case of occult recurrence FDG is the only alternative Se=89% Sp=84% (*Dong MJ Nucl Med Commun 2009:639)*

A vertebral metastasis of thyroid cancer visible on the pre-treatment 124I PET but not on « diagnostic » 131I, confirmed on post-treatment 131I

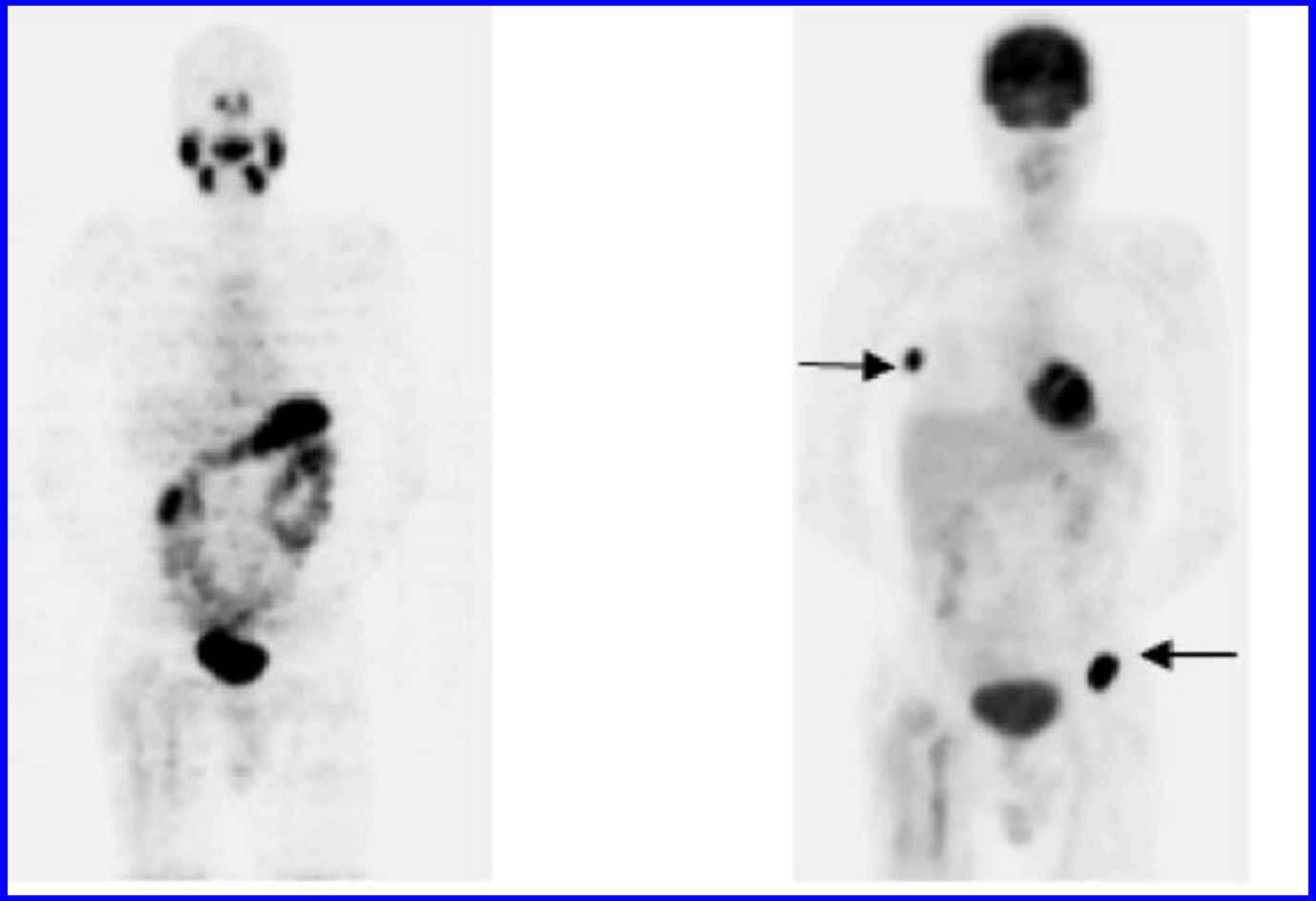


Pre-treatment 124I

Diagnostic 131I Post-treatment 131I

Pham et al. EJNM 2008: 958

Differentiated thyroid cancer « Flip-Flop » 124I & FDG

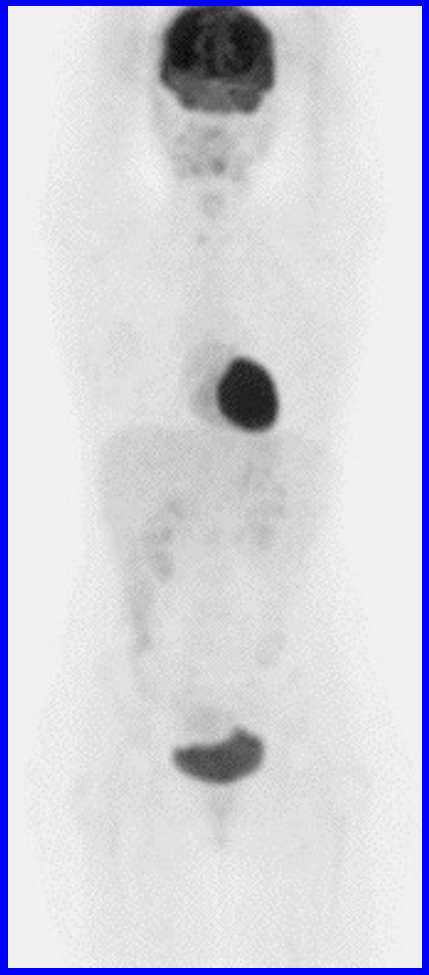


Pham et al. EJNM 2008: 958

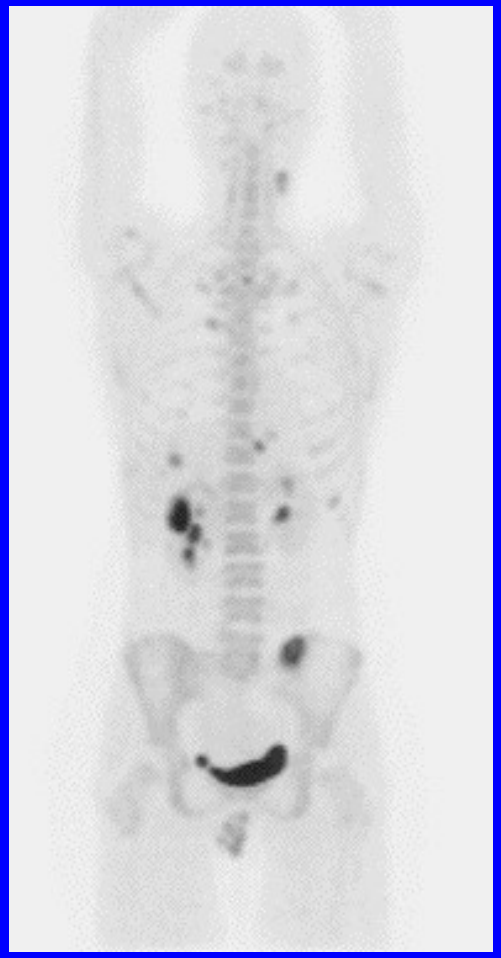
Medullary thyroid cancer (MTC)

- EMA FDOPA : Recurrent MTC with rising serum calcitonin levels
- Since the study of *Hogerle S* on 11 patients (*Eur J Nucl Med 2001: 64*) , FDOPA has shown better diagnostic performance than FDG.
- This has been confirmed by several authors, lastely *Treglia G (Eur J Nucl Med 2012: 569)*
  72 lesions in 13 patients, PET/CT detection rate:
  - FDOPA = 85%
  - FDG = 28%
  - somatostatin analogue (68Ga) = 20%

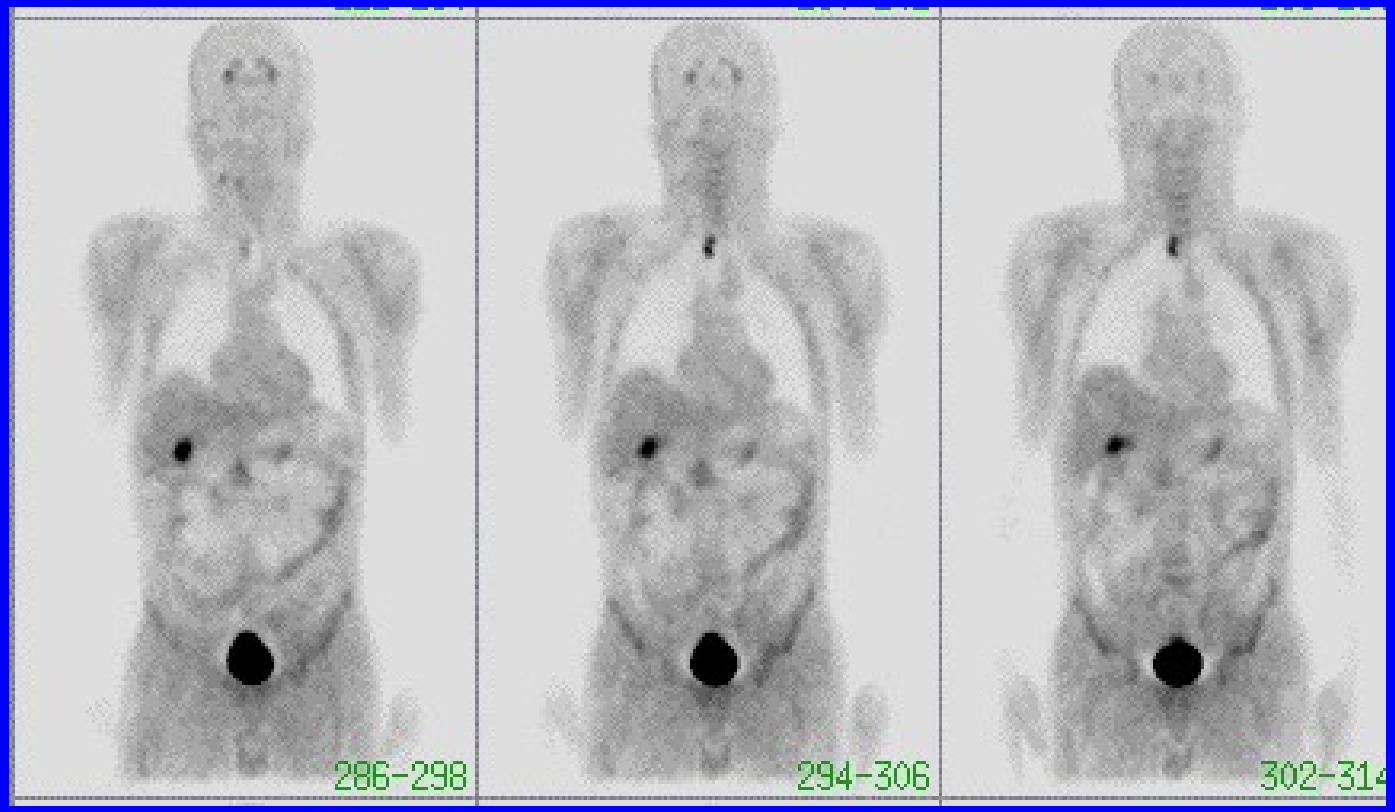
Restaging : **Medullary thyroid cancer** (MTC) with known secondary bone lesions. Patient referred for FDG and FDOPA PET/CT to characterise hepatic lesions



False negative FDG PET

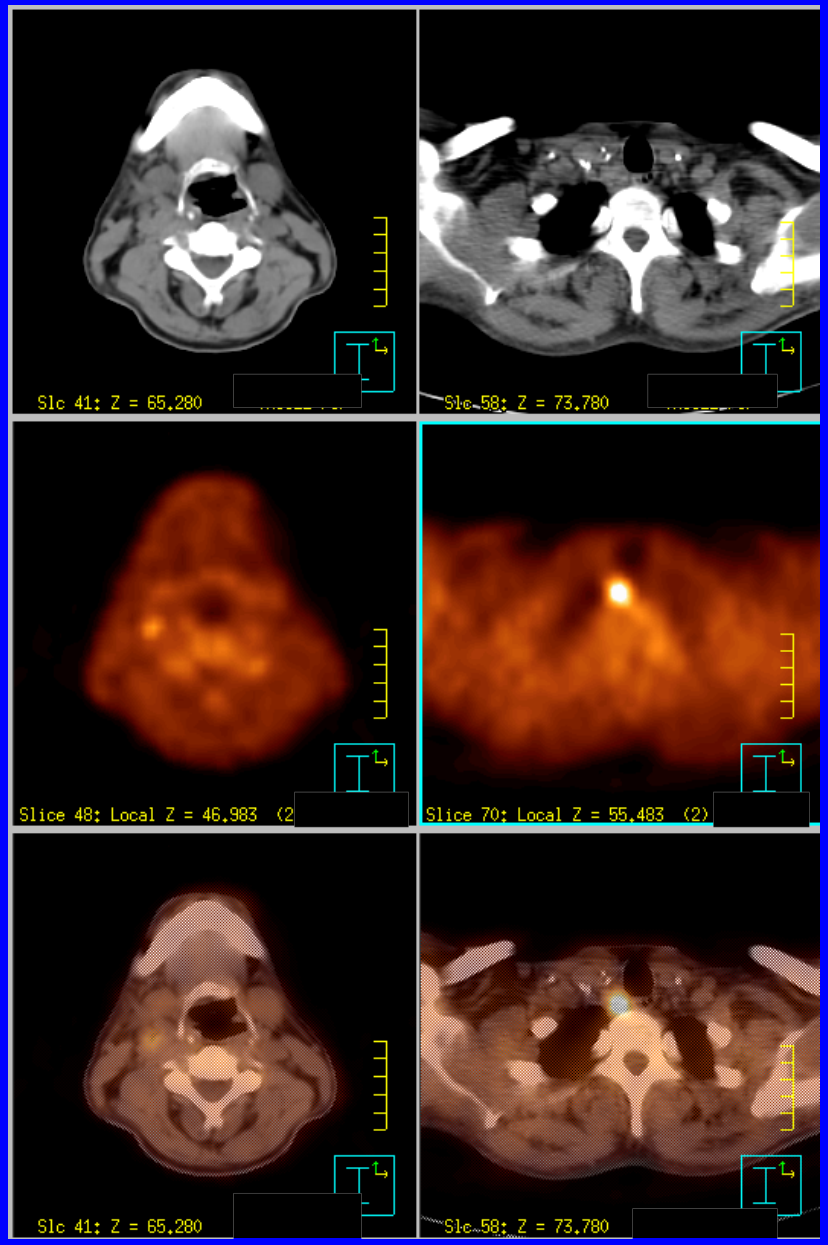


True positive FDOPA PET

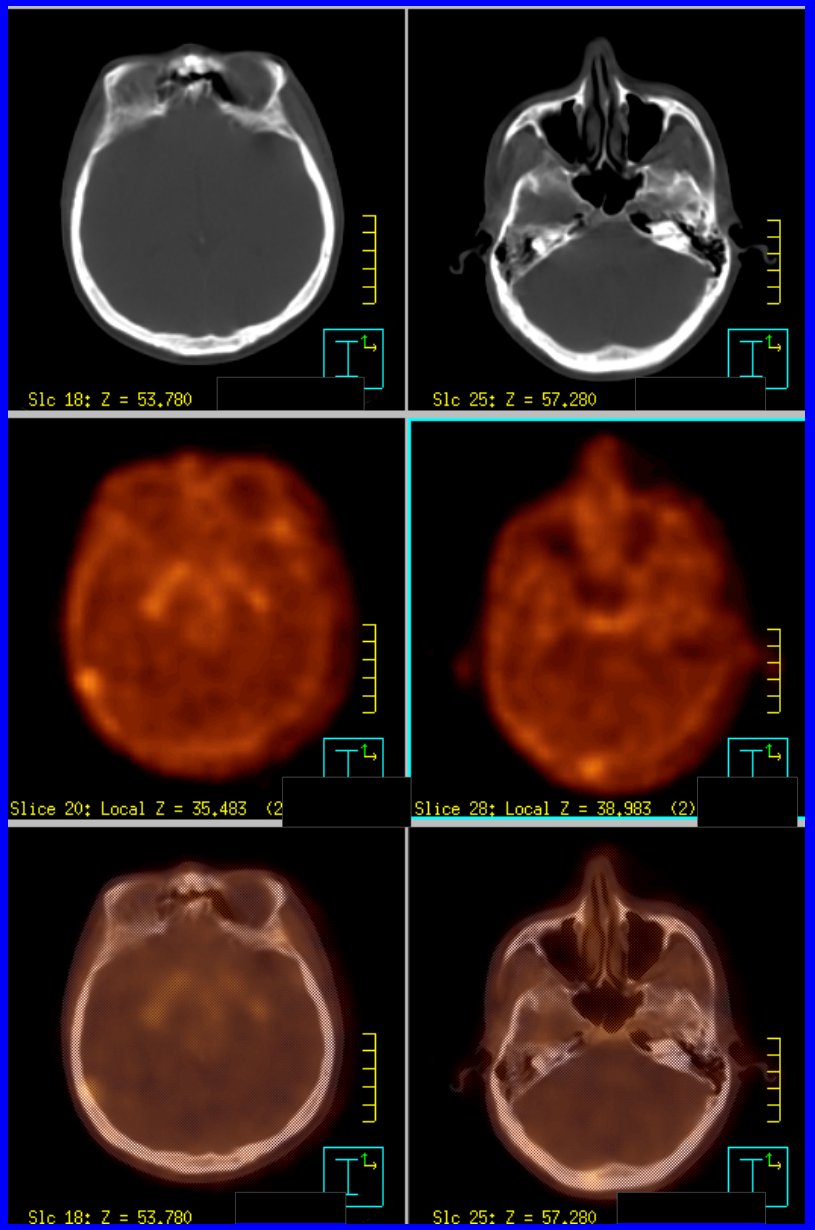


Occult recurrence : MTC operated 5 years before. Unexplained continuous raise in calcitonin serum levels (900 pg/mL at FDOPA PET).

continued

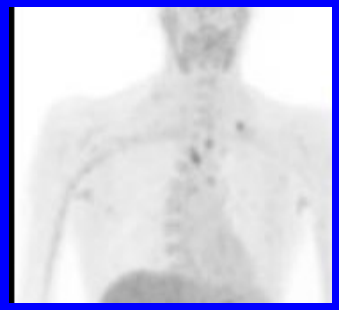


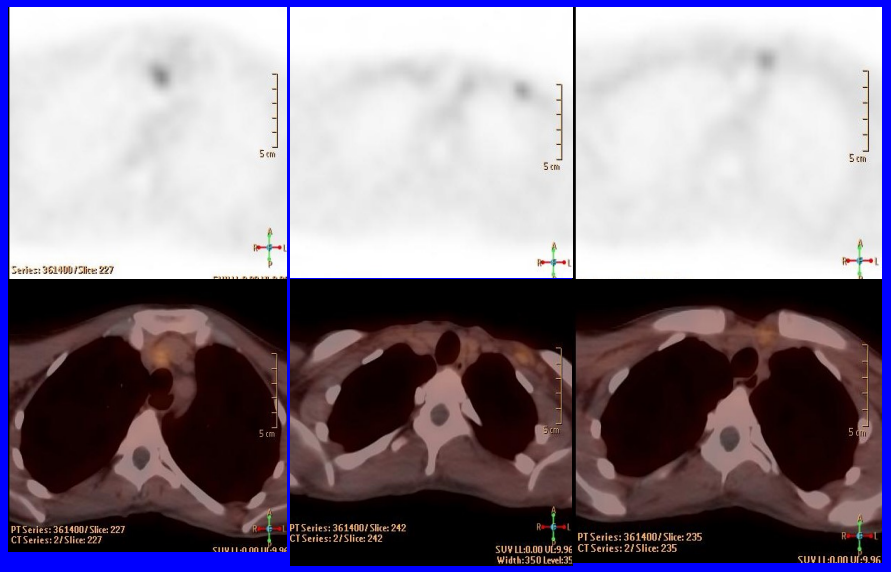
Lymph node recurrence



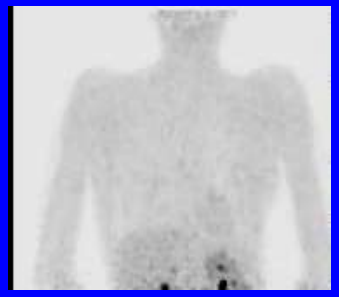
Bone metastases which were proven

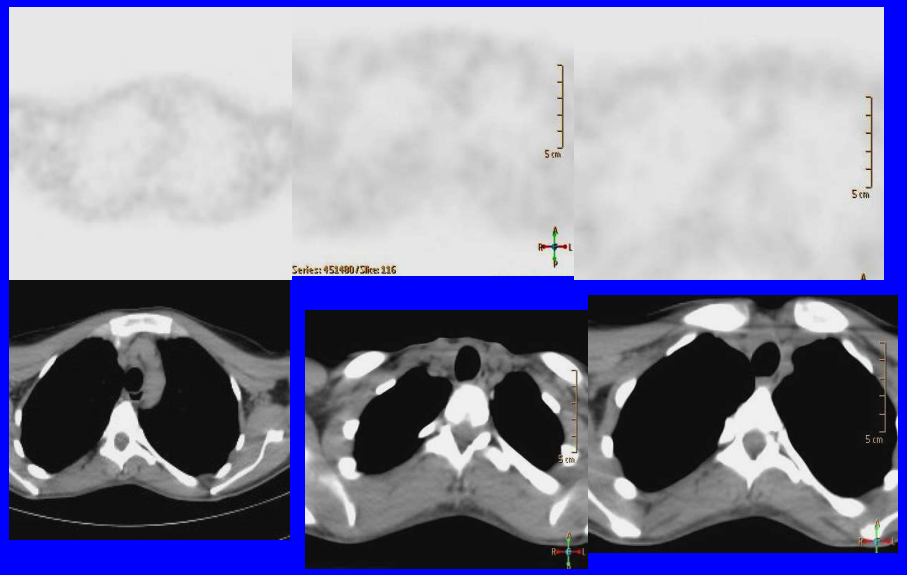
MTC: best detection on early FDOPA PET images





Early FDOPA PET/CT imaging: 3 foci corresponding to mediastinal lymph node metastases (SUV_{max}: 3.9 to 4.7)





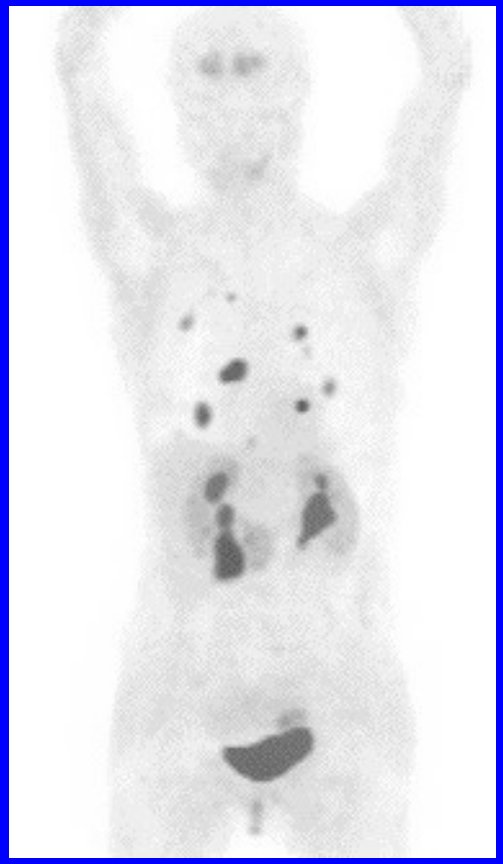
Delayed FDOPA PET/CT imaging: complete disappearance of the foci

Phaeochromocytoma & paraganglioma

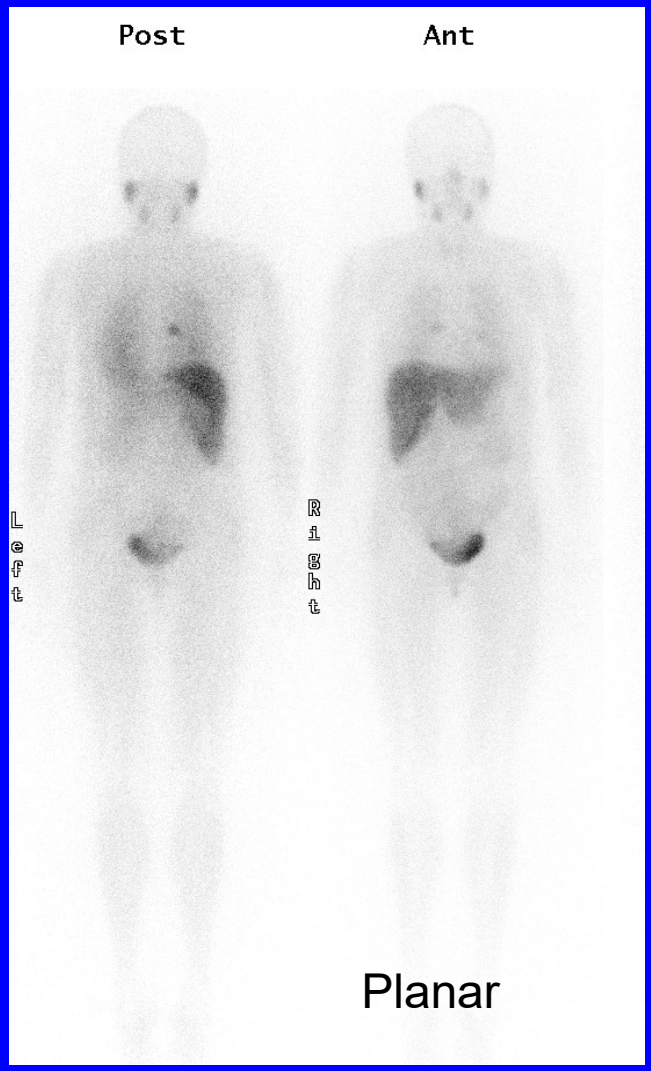
- Several EU countries FDOPA : - Diagnosis and localisation of glomus tumours in patients with a gene mutation of the succinate dehydrogenase D variant
  - Localisation of pheochromocytoma and paraganglioma
  - Staging phaeochromocytoma and paraganglioma
  - Detection of recurrence of phaeochromocytoma and paraganglioma

- FDG is sensitive in aggressive forms.
- Main PET alternatives are FDOPA for both indications and/or DOTATOC (68Ga) in case of paraganglioma

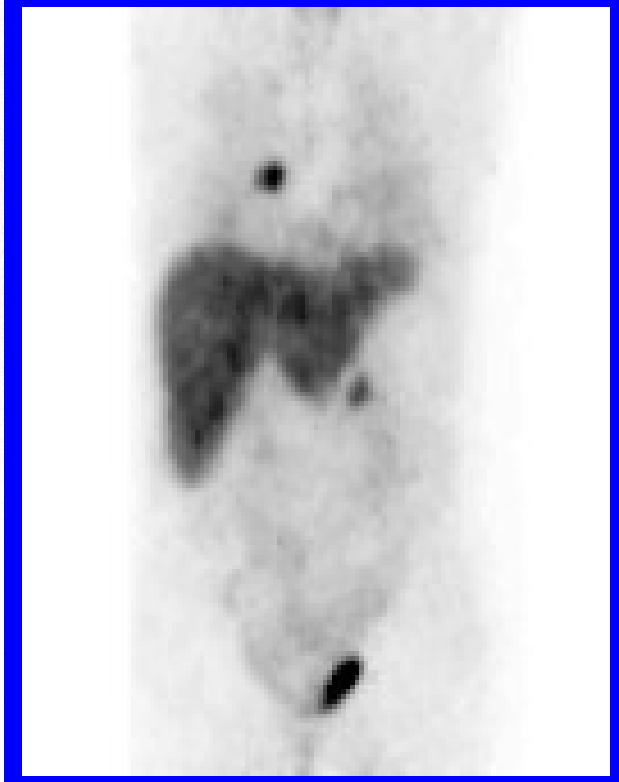
Malignant **phaeochromocytoma** of the left adrenal, operated 7 years before. Unexplained rising metanephrine levels.
MIBG showed 1 focus in the right lung while FDOPA PET showed multiple foci



FDOPA (18F) PET



Planar



SPECT

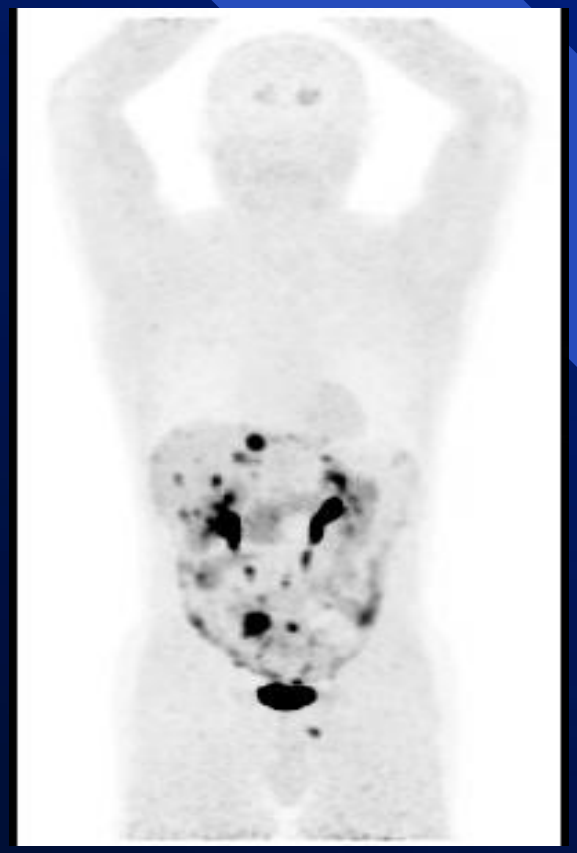
mIBG (I123)

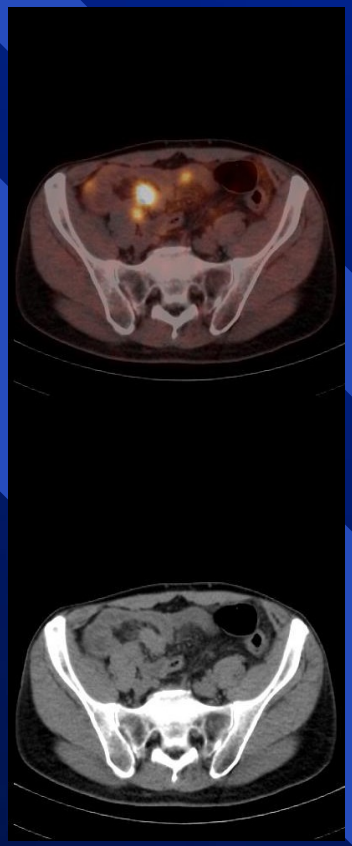
Gastroenteropancreatic neuroendocrine tumours

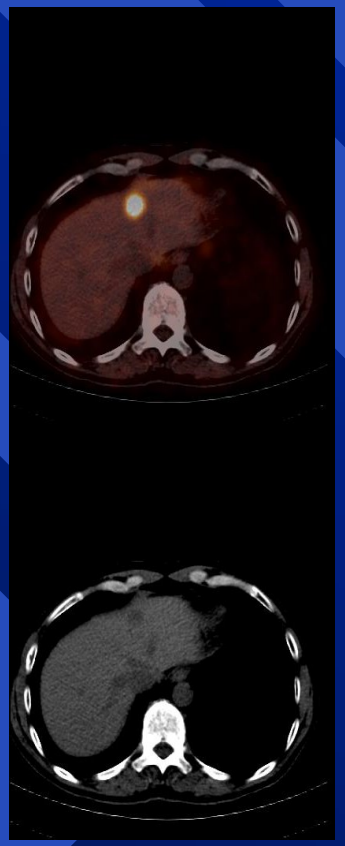
- Several EU countries FDOPA :
  - carcinoid tumours of the gut : staging, recurrence
  - other GEP NET if pentetreotide SPECT is non contributive.

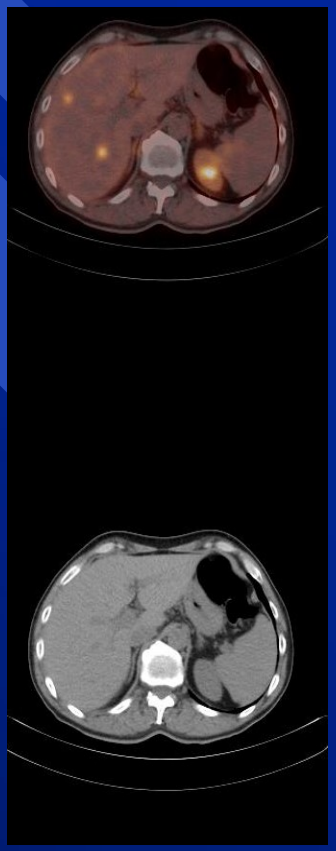
- ESMO (all GEP-NET) : PET scanning with specific tracers, such as [11C]5-HTP, [18F]DOPA or [68Ga]DOTA-octreotate can further optimize the staging of the disease. However, FDG PET is only of value in poorly differentiated GEP-NET tumours.

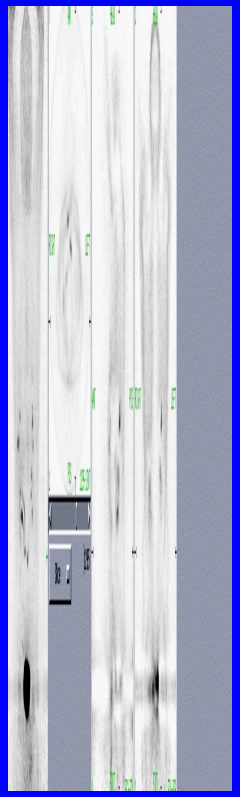
•Carcinoid syndrome and liver lesions. Radiology did not find the tumour which was discovered on FDOPA PET/CT, that also showed adenopathy, liver metastatses and peritoneal carcinomatosis



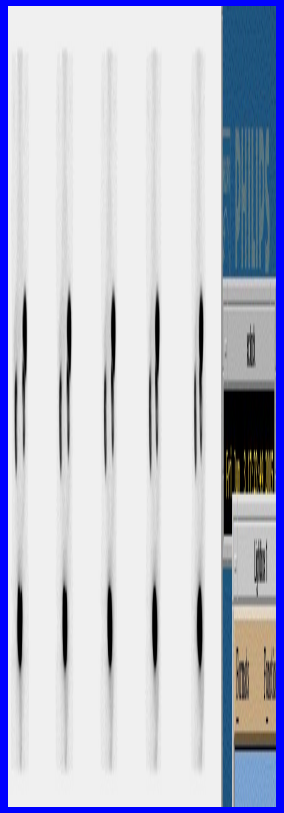








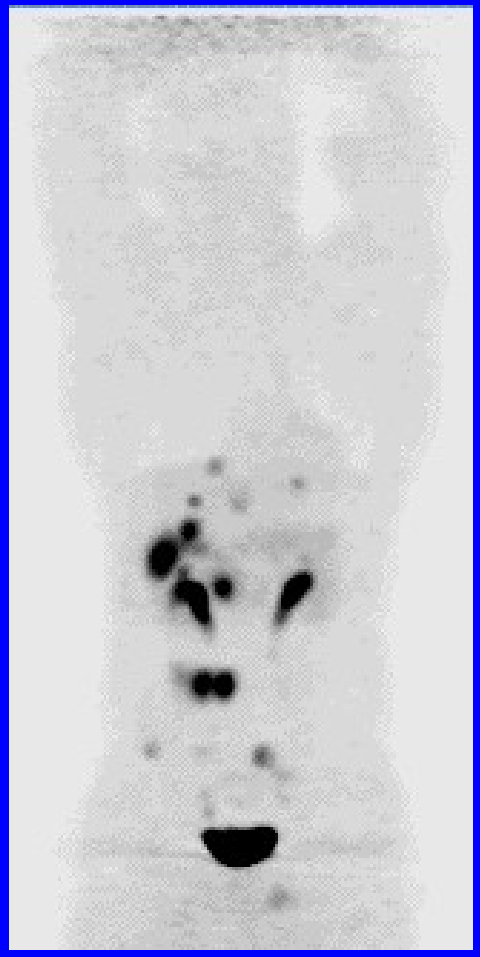
FDOPA PET
True positive



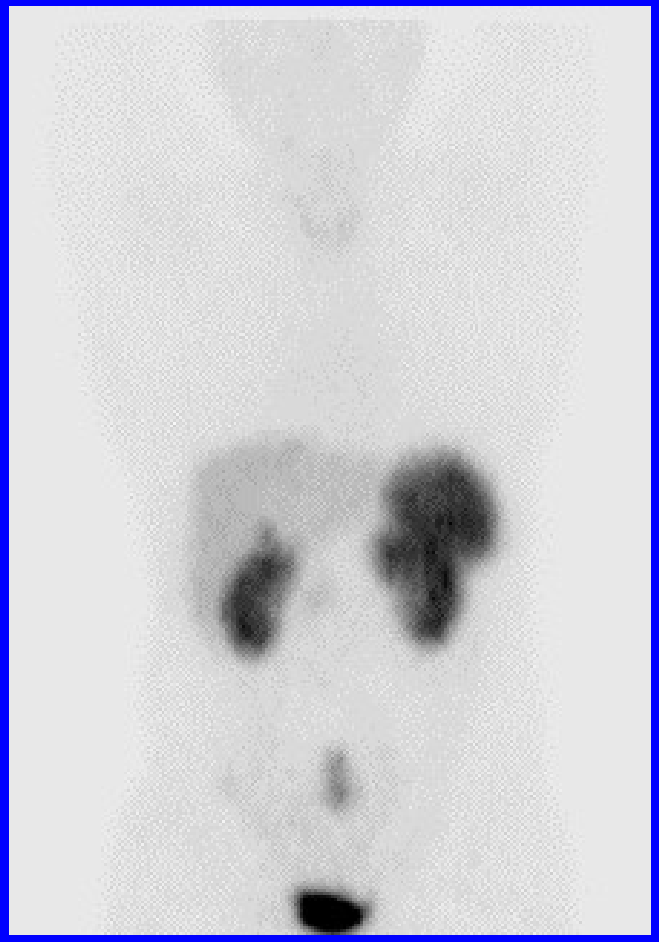
Pentetreotide SPECT false negative
(19 days before FDOPA)

TNE of the midgut
Suspicion of recurrence due to high 5HIAA blood levels

Impact: chemoembolisation



FDOPA PET

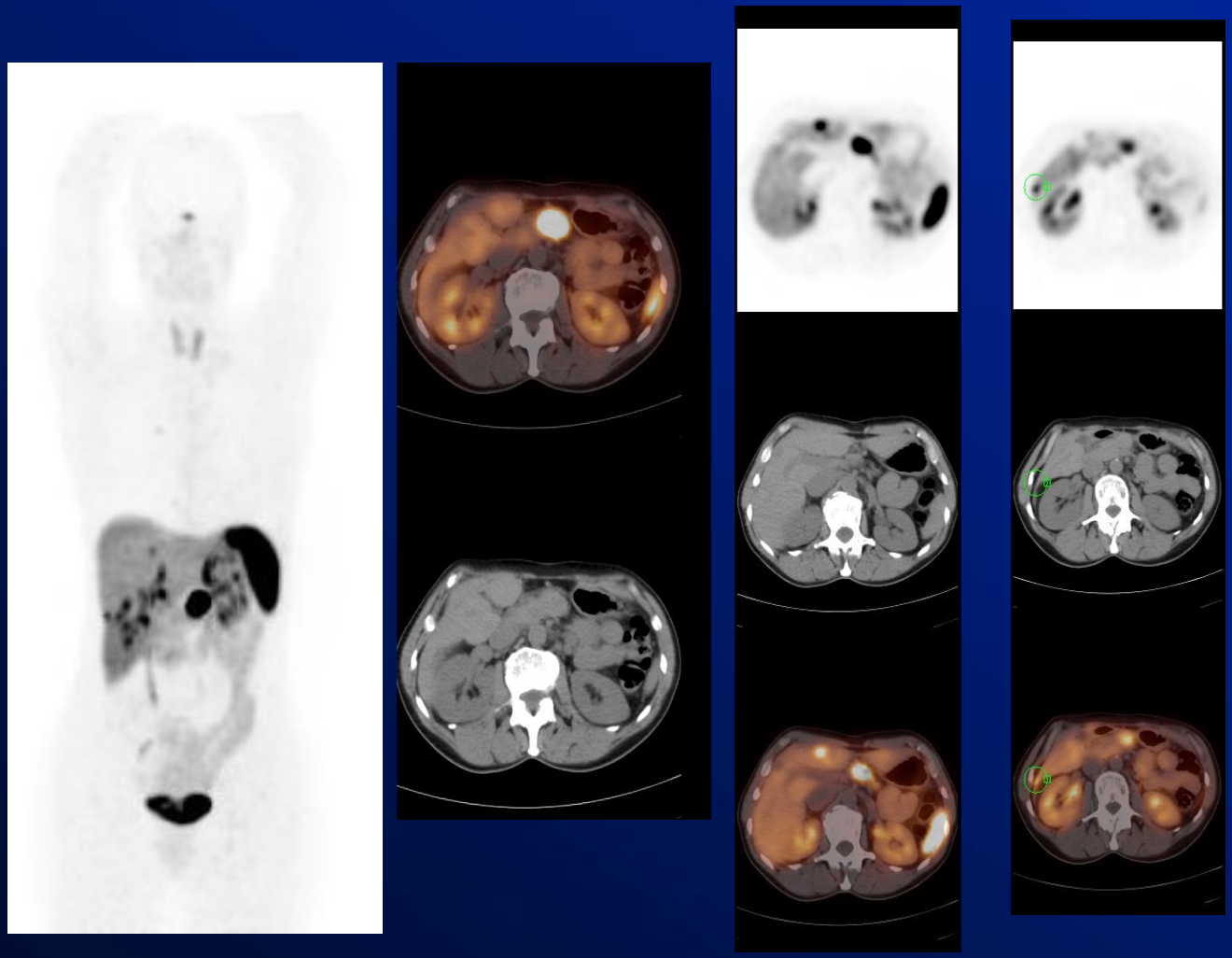


Pentetreotide SPECT

Evaluation of treatment of a carcinoid peritoneal carcinomatosis by chemotherapy and interferon

Persistence of multiples lesions

Initial staging of a grade 1 TNE of the pancreas discovered during follow-up of a breast cancer. In foregut TNE, PET of the somatostatin receptors is more effective than FDOPA



DOTATOC (68Ga) PET/CT

Intense uptake by the pancreatic tumur and discovery of hepatic spread, which was confirmed

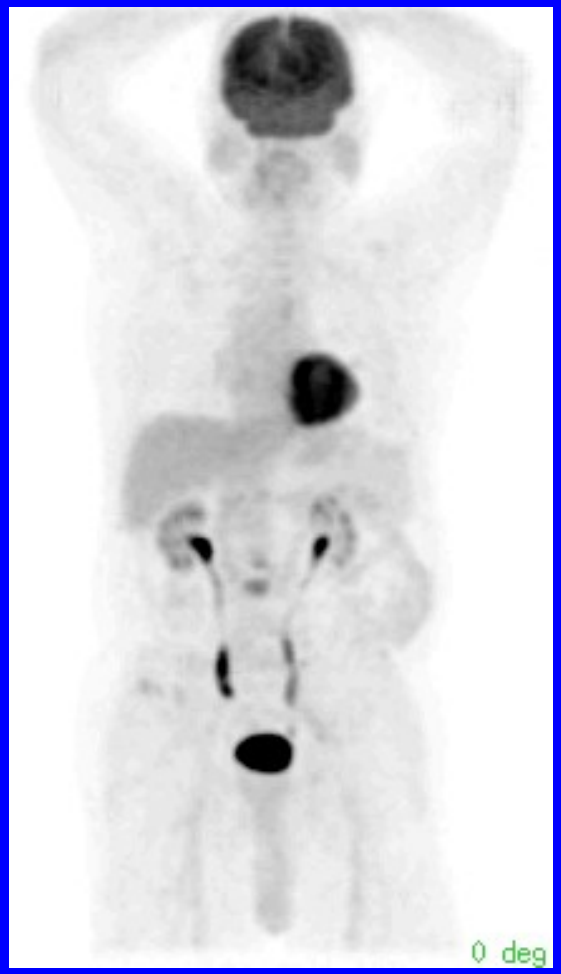
Cancers with a low FDG PET sensitivity

Prostate cancer

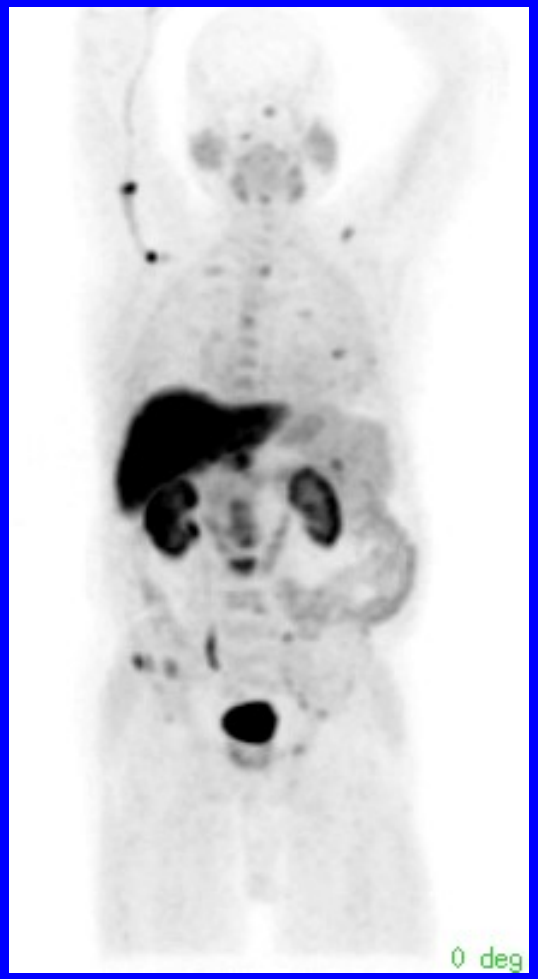
- FDG could be used in rare cases with a vey aggressive form

- PET alternatives to FDG:
  - For all cancer sites (including bone metastases): acetate (11C), choline (11C), FCH, and recently PSMA (68Ga)
  - For bone metastases only: F Na

Initial staging of advanced prostate cancer (Gleason 8)

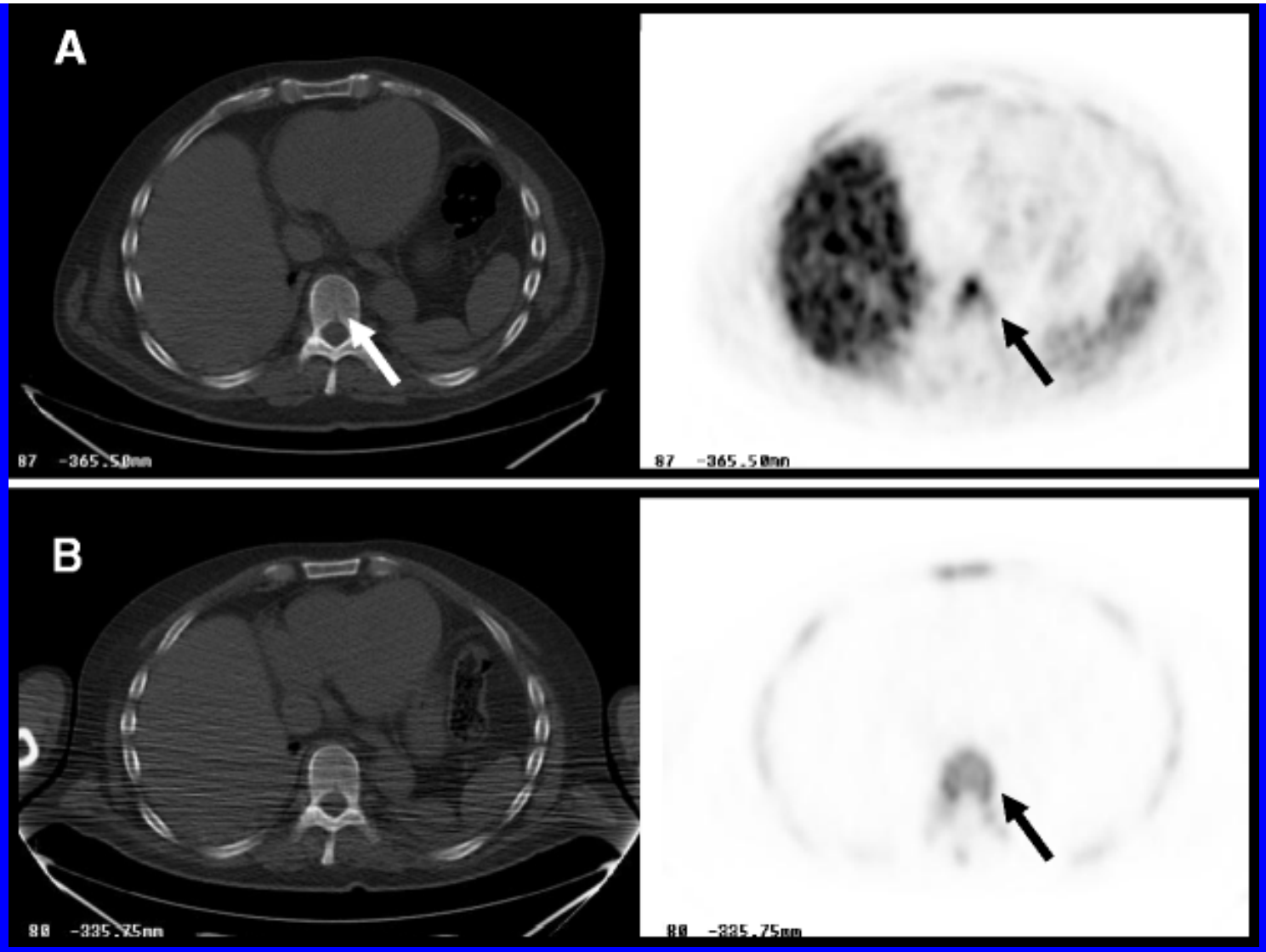


FDG



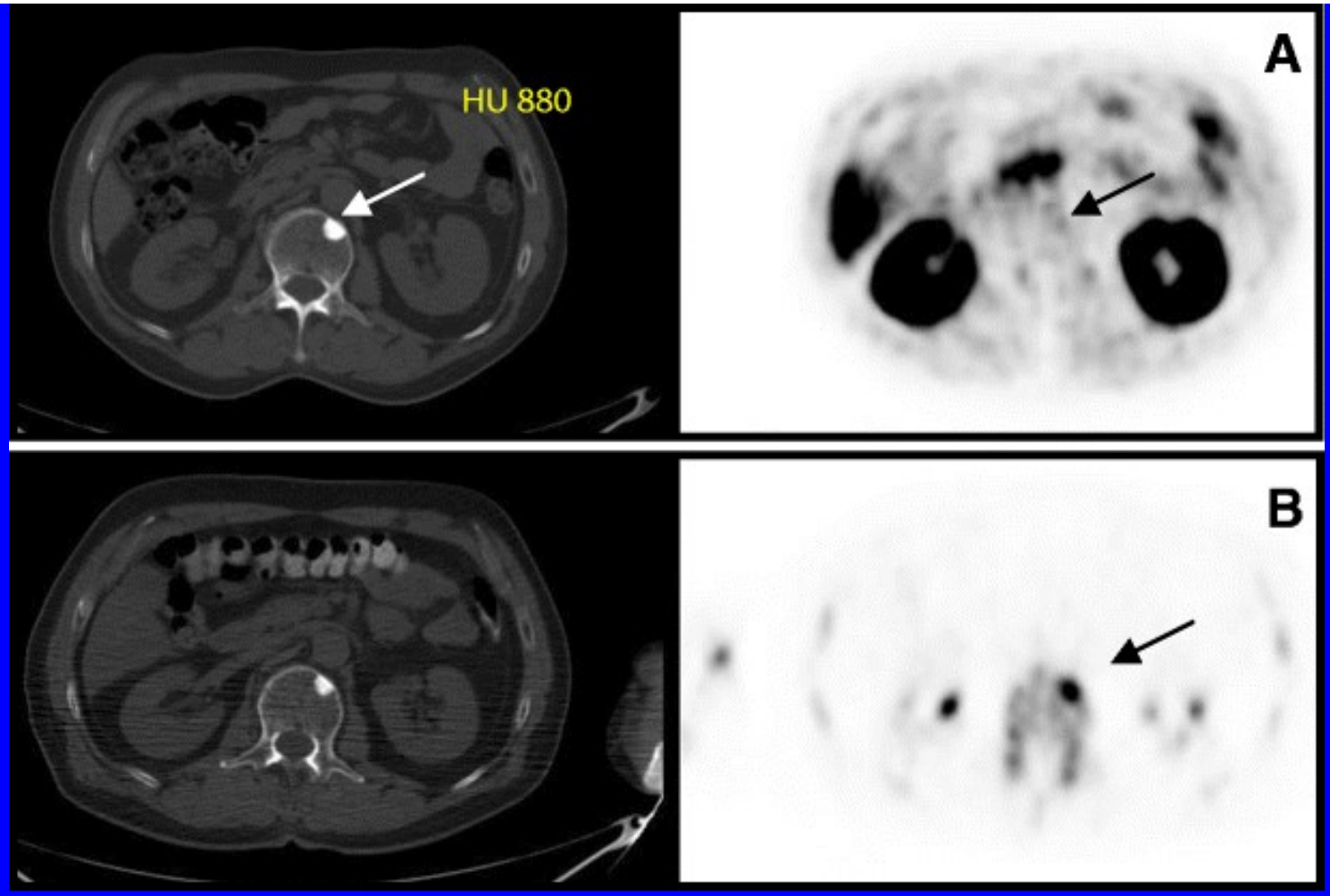
FCH

(same patient)



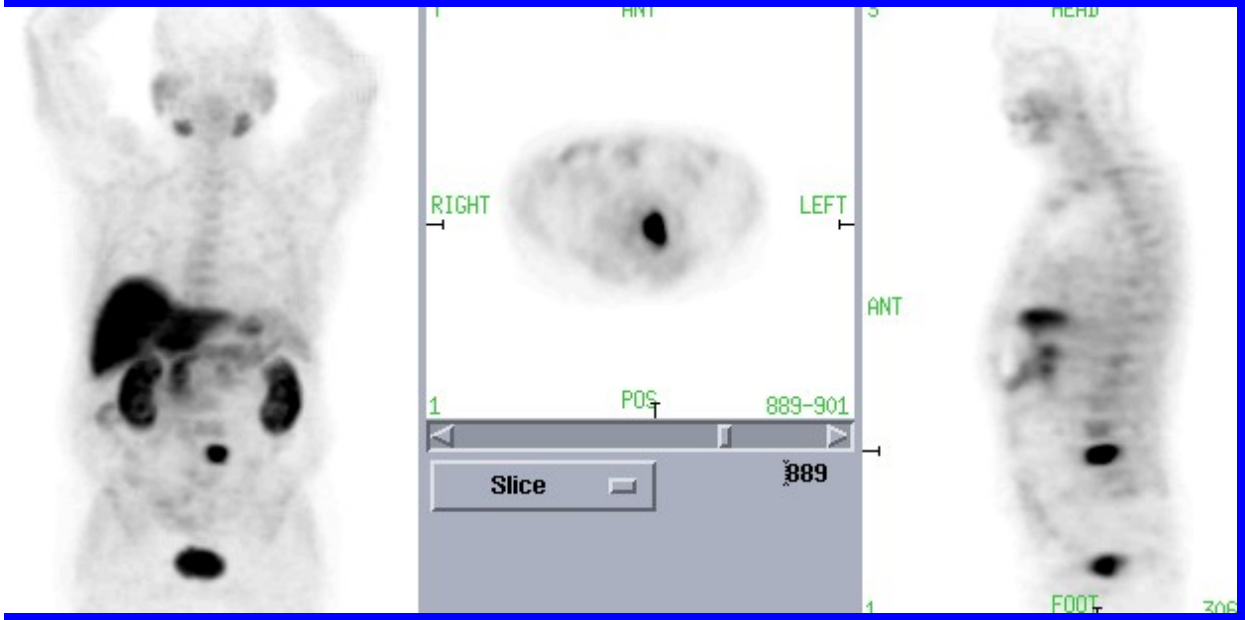
FCH positive (**a**) and F Na negative (**b**) bone marrow metastases (*black arrow*) of the thoracic spine without morphological CT changes (*white arrow*). Lesion was finally confirmed by follow-up; no hormone therapy.

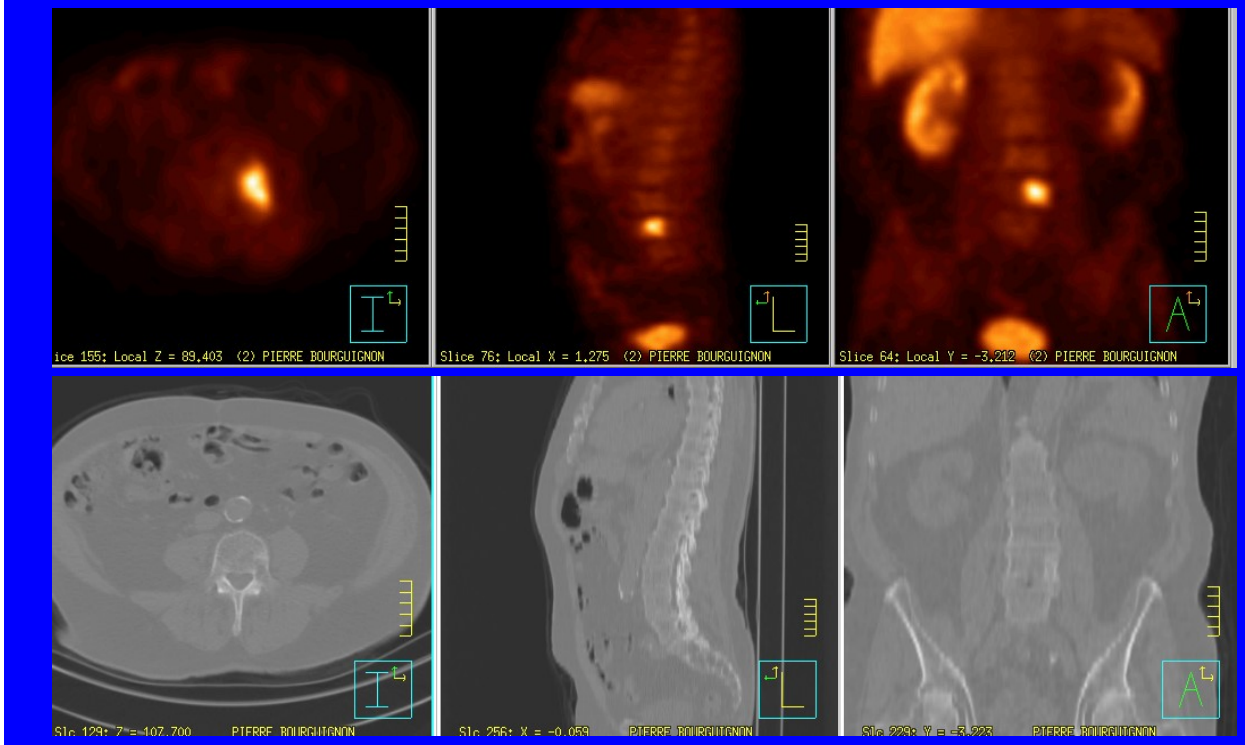
Beheshti M. Eur J Nucl Med Mol Imaging 2008:1766



FCH negative (**a**) and F Na PET/CT positive (**b**) lesion (*arrow*) in a malignant sclerotic lesion (HU 880) of the lumbar spine (L1). Lesion was finally confirmed by follow-up; patient was under hormone therapy.

Beheshti M. Eur J Nucl Med Mol Imaging 2008:1766



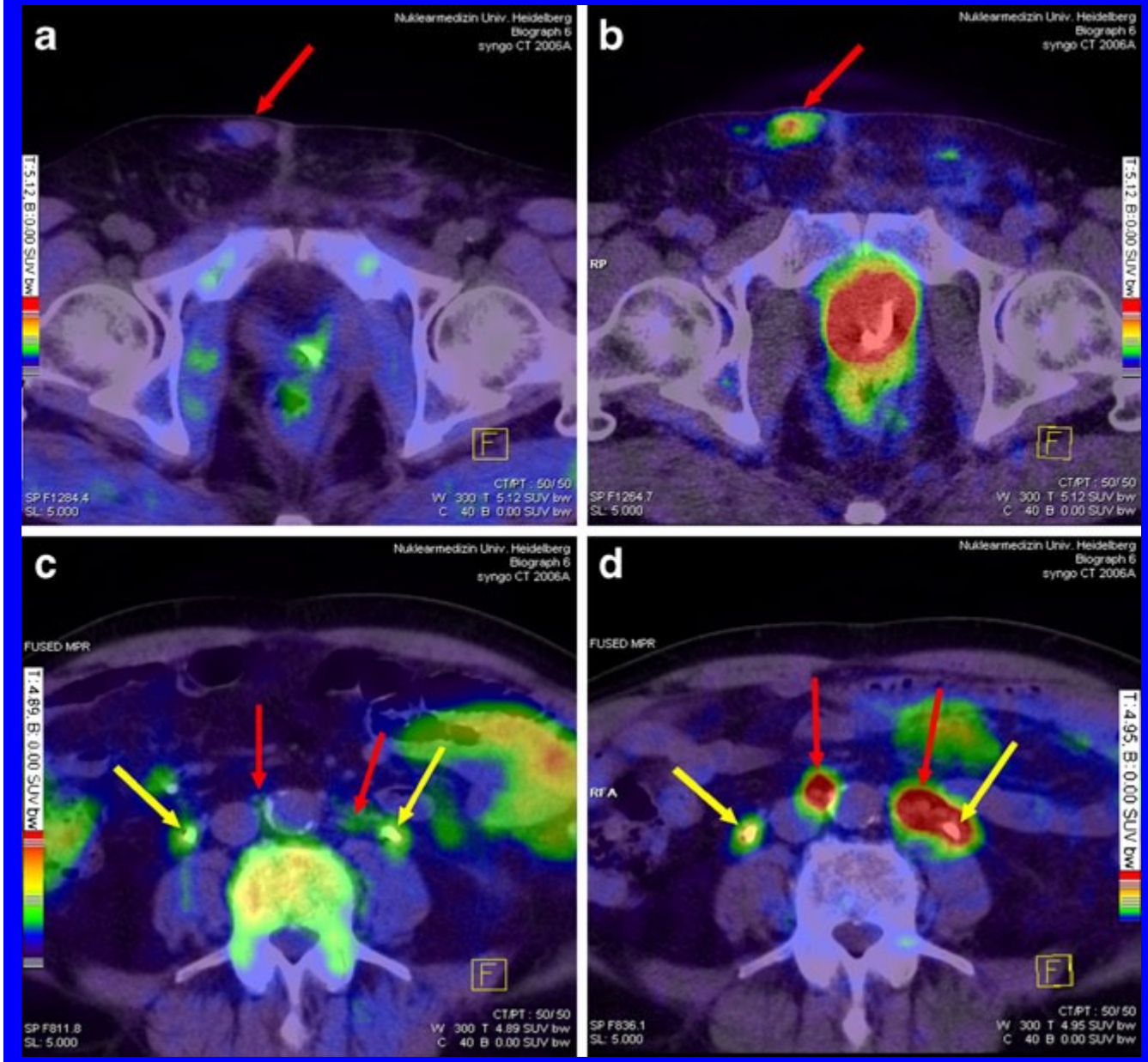


Prostate cancer recurrence

- Prostatectomy 1998
- PSA = 9 ng/mL
- Zoladex

HOPITAL TENON AP-HP

PSMA ligand (68Ga)



FCH (18F)

PSMA-11 (68Ga)

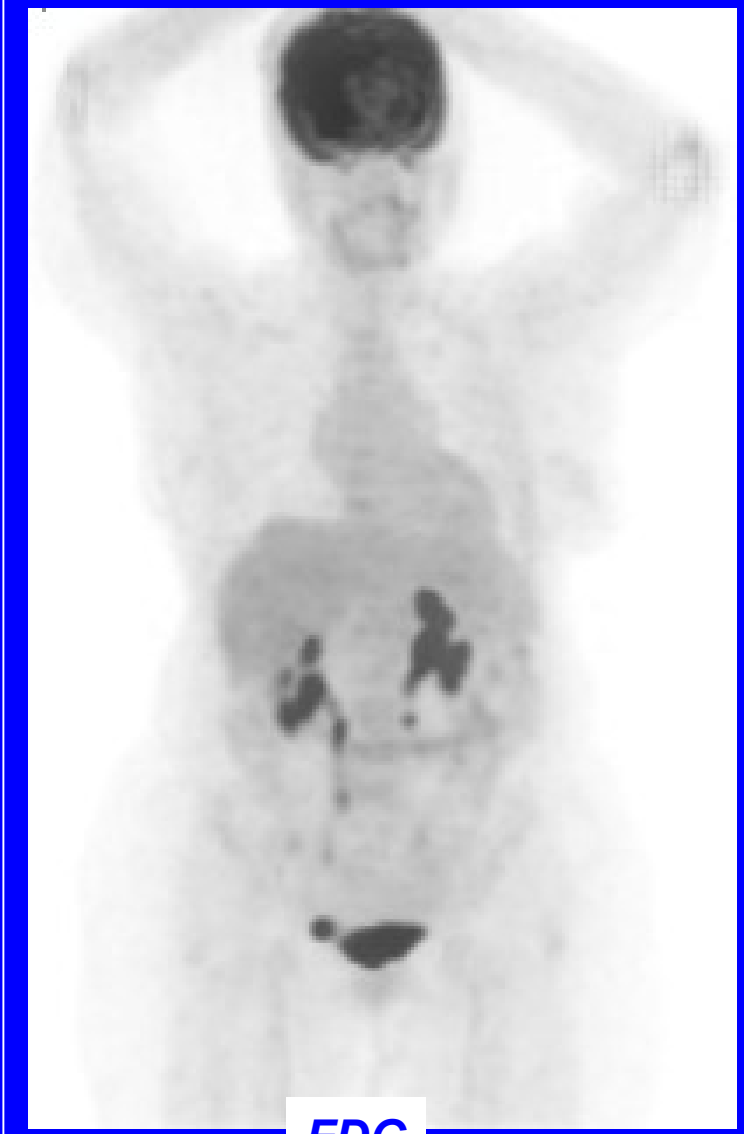
Afshar-Oromieh EJNMI 2014:11.

37 patients suspected of recurrence.
56 detected lesions in 26 patients with FCH vs. 78 lesions in 32 patients with PSMA-11 (68Ga)

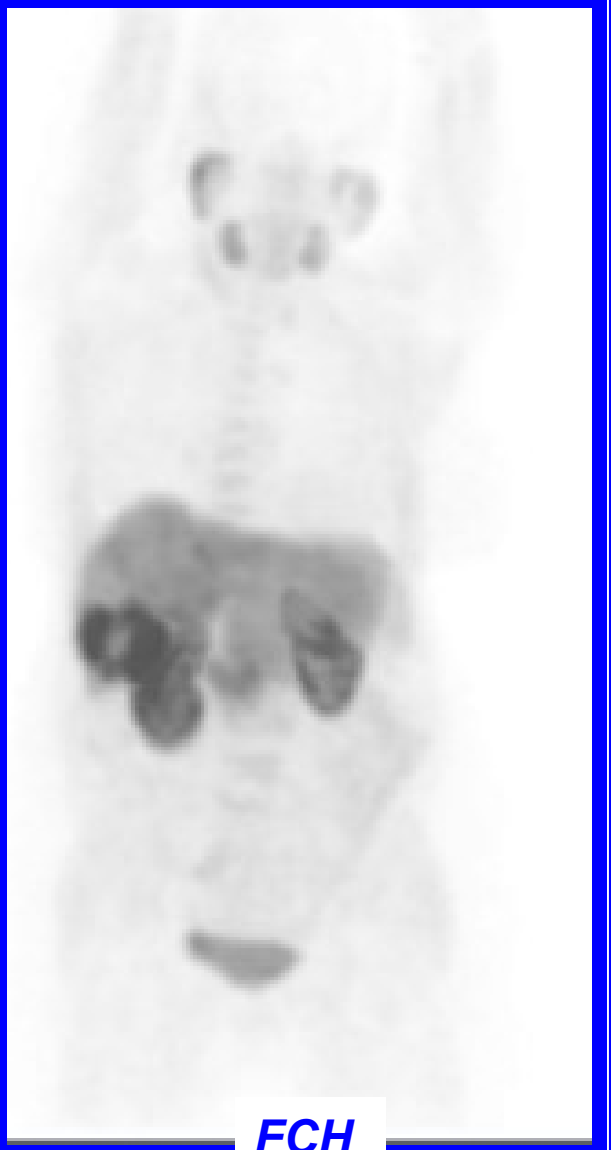
Lesions in the abdominal wall and lymph nodes

Hepatocellular carcinoma

- In several EU countries
- FCH : Localisation of lesions of proven well-differentiated hepatocellular carcinoma
- Alternatives: choline (11C) or acetate (11C)
- FDG and FCH : characterisation of liver nodes and/or staging of proven or very likely hepatocellular carcinoma, when FDG PET is non conclusive or when surgery or grafting is scheduled



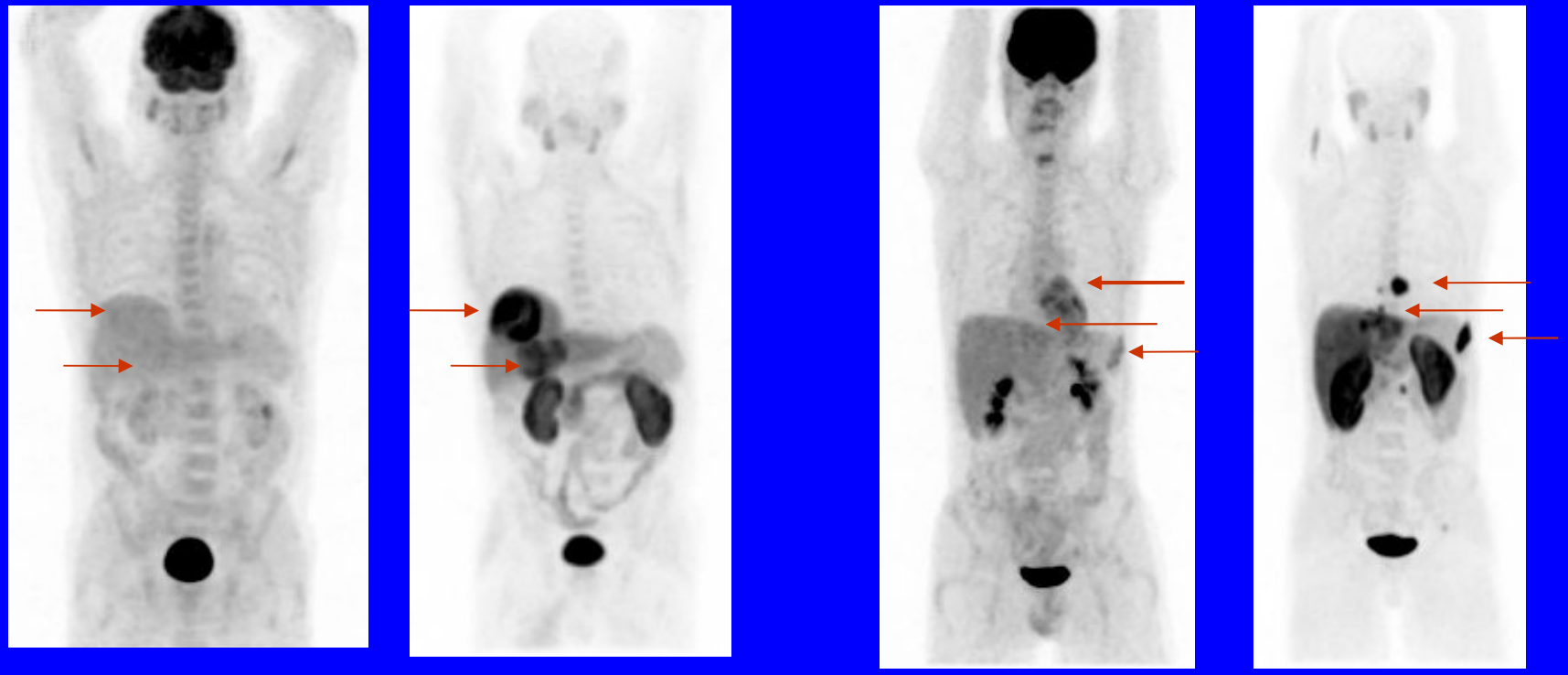
FDG



FCH

Hepatocellular carcinoma

FCH was more sensitive than FDG to detect primary or metastastatic hepatocellular carcinoma (similar results have been reported with acetate (11C))



FDG FCH

Primary HCC

FDG FCH

Primary + metastatic HCC

Cancers of organs with a high physiologic uptake or accumulation of FDG in the non-pathologic tissue

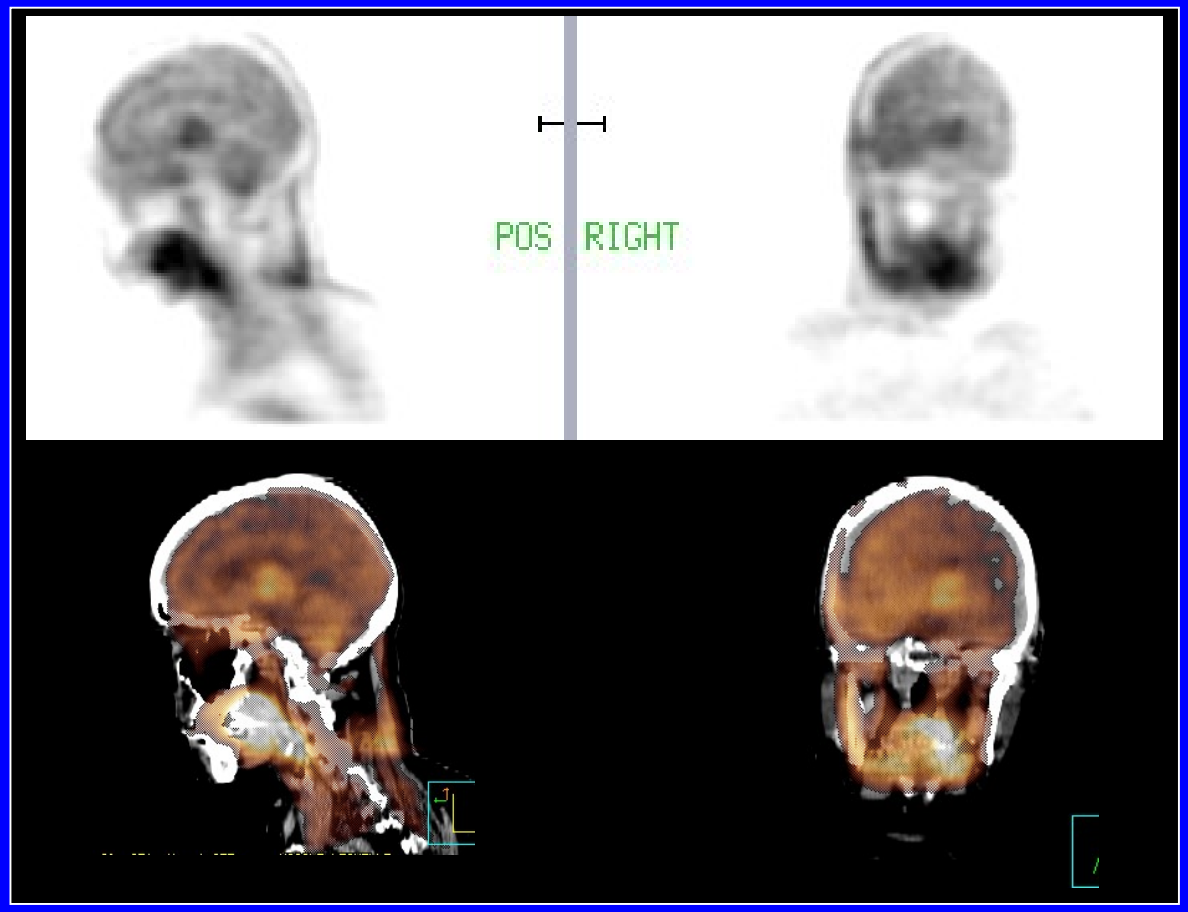
Brain tumours

- EMA FDG : Detection of recurrent glioma with high grade of malignancy (III or IV)
- Several EU countries FDOPA : Detection of recurrence of primary brain tumours

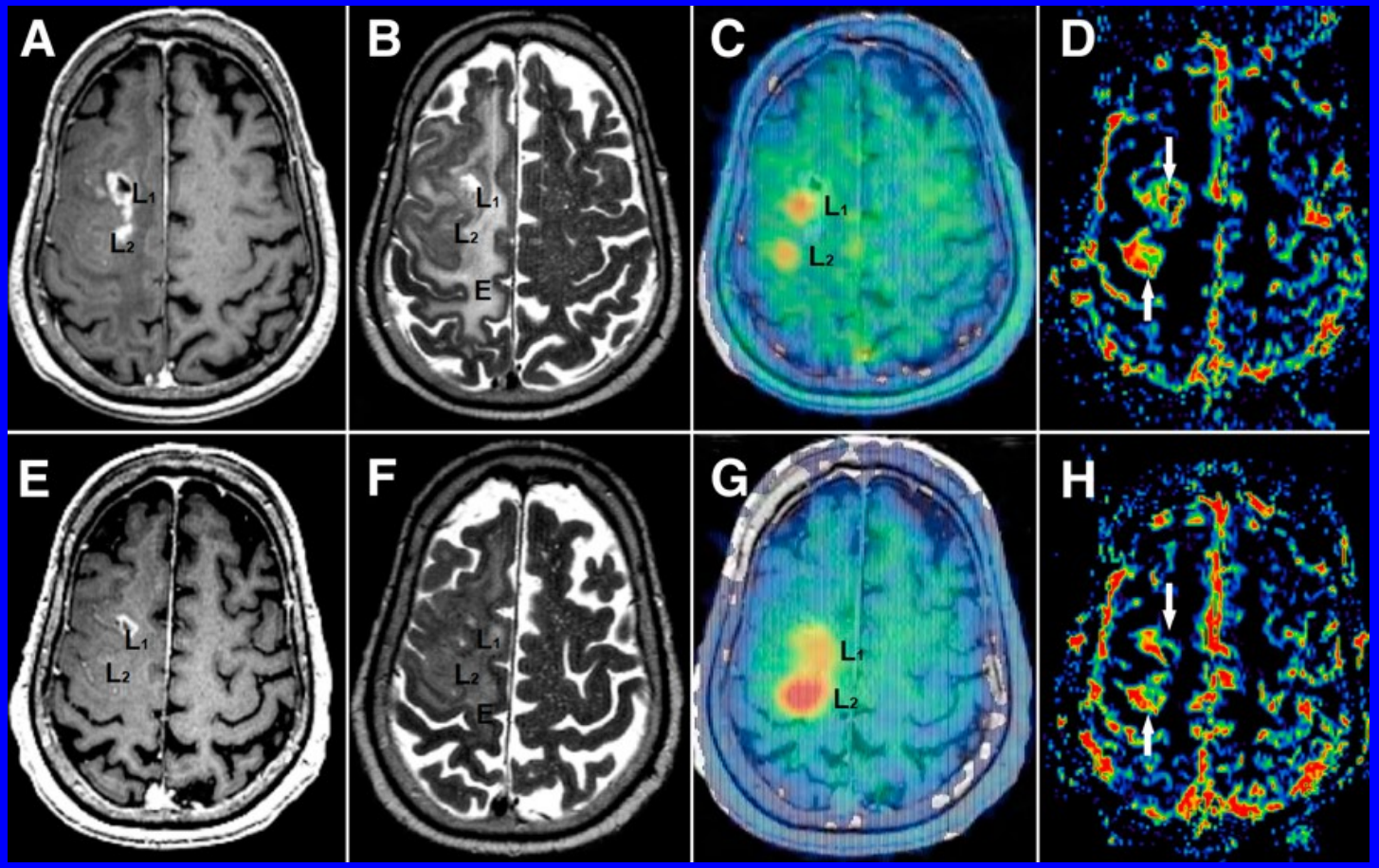
- ESMO : In cases of doubtful differential diagnosis between glioma recurrence and treatment-induced changes (especially after multimodal therapy), PET with an amino acid tracer (e.g. methionine, FET) may be helpful.

Residual mass on MRI

The residual mass takes-up FET, indicating tumour viability



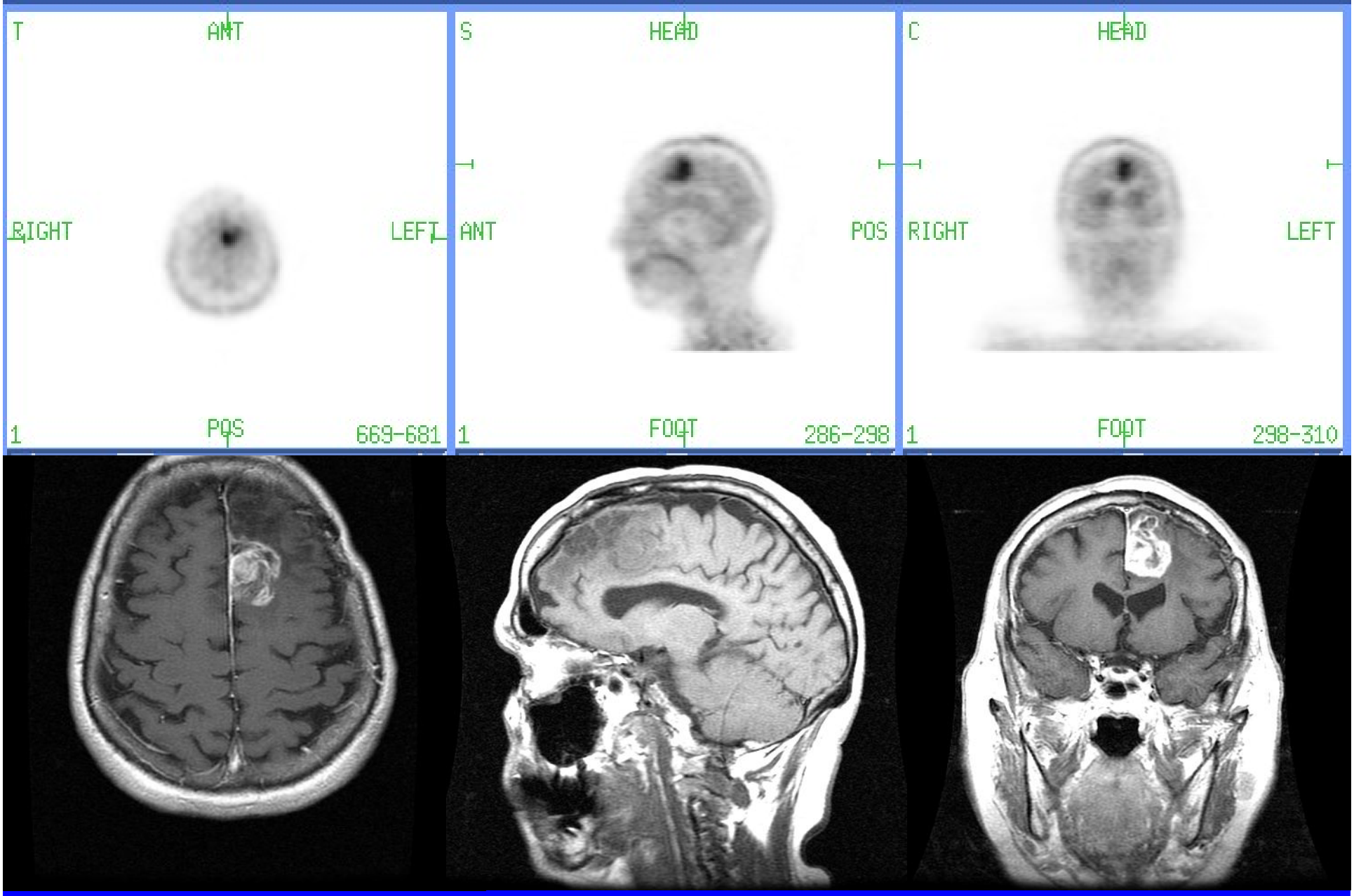
Antiangiogenic treatment and FET



MRI T1, T2, FET PET and perfusion MRI before (A-D) and 12 weeks after treatment (E-H) with bevacizumab (Avastin) and irinotecan. Partial response of L1 focus, progression of L2.

Hutterer J Nucl Med 2011:856

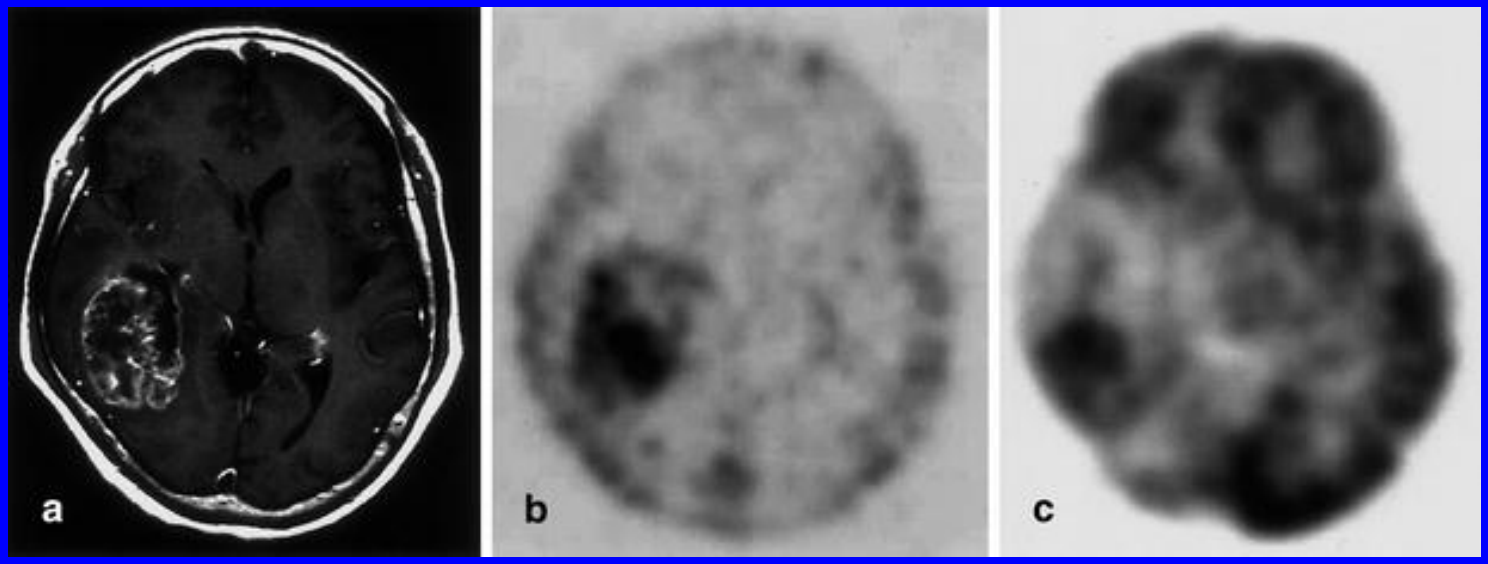
FDOPA (18F) and glioma follow-up



Glioblastoma. Post surgery follow-up.

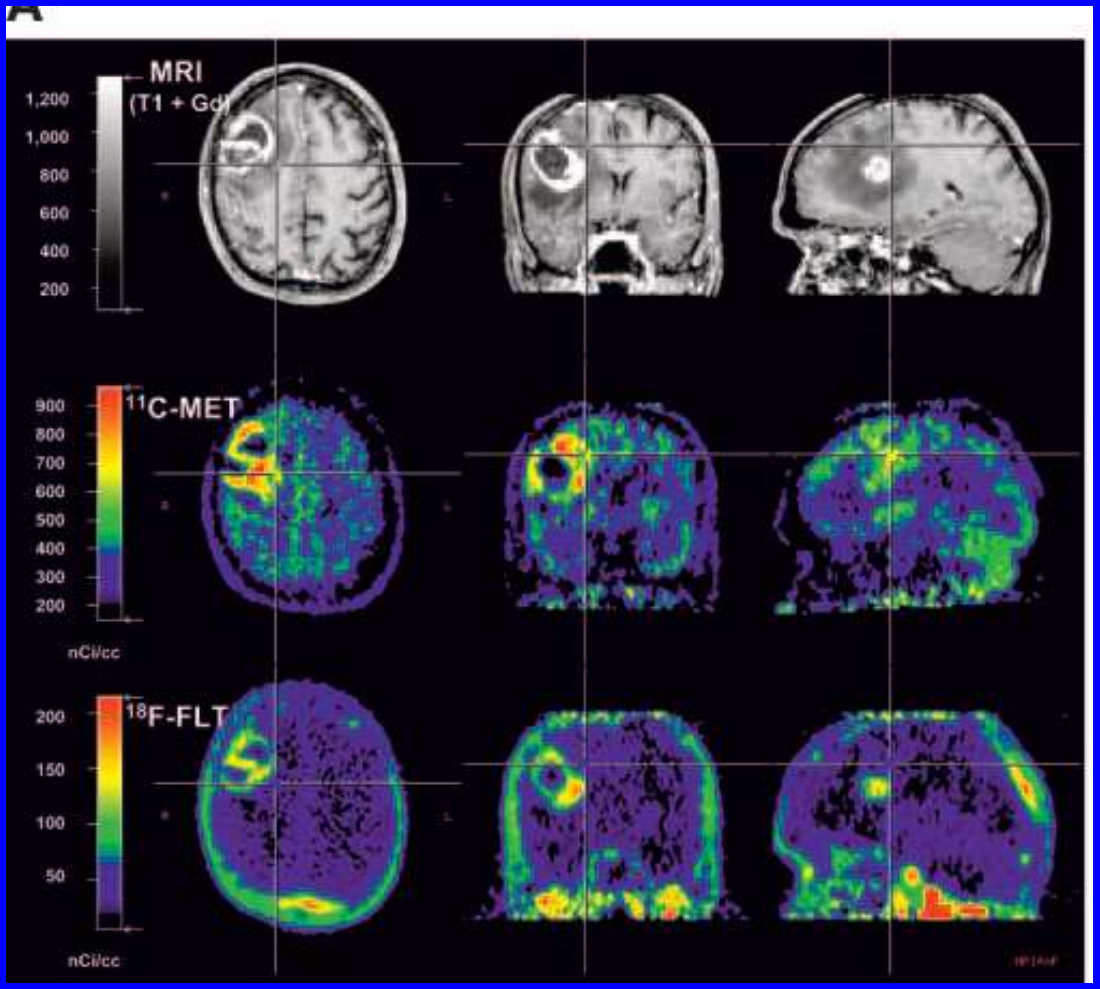
Choline (11C) and brain tumours

- The uptake is depending on the tumour grade (high >> low)
- Could complement MRI for tumour grading
  - Ohtani, Eur J Nucl Med 2001



Temporal glioblastoma choline-(11C) : T/NT (5min) = 9
FDG : T/NT (50min) = 2

FLT : 64-y-old man with newly diagnosed glioblastoma



Jacobs J Nucl Med 2005:1948

FLT has been proposed in brain tumours, for detection of viable tumour and response to therapy.

Detection is limited to high grade tumours (*Jacobs JNM 2005*), correlated to Ki 67.

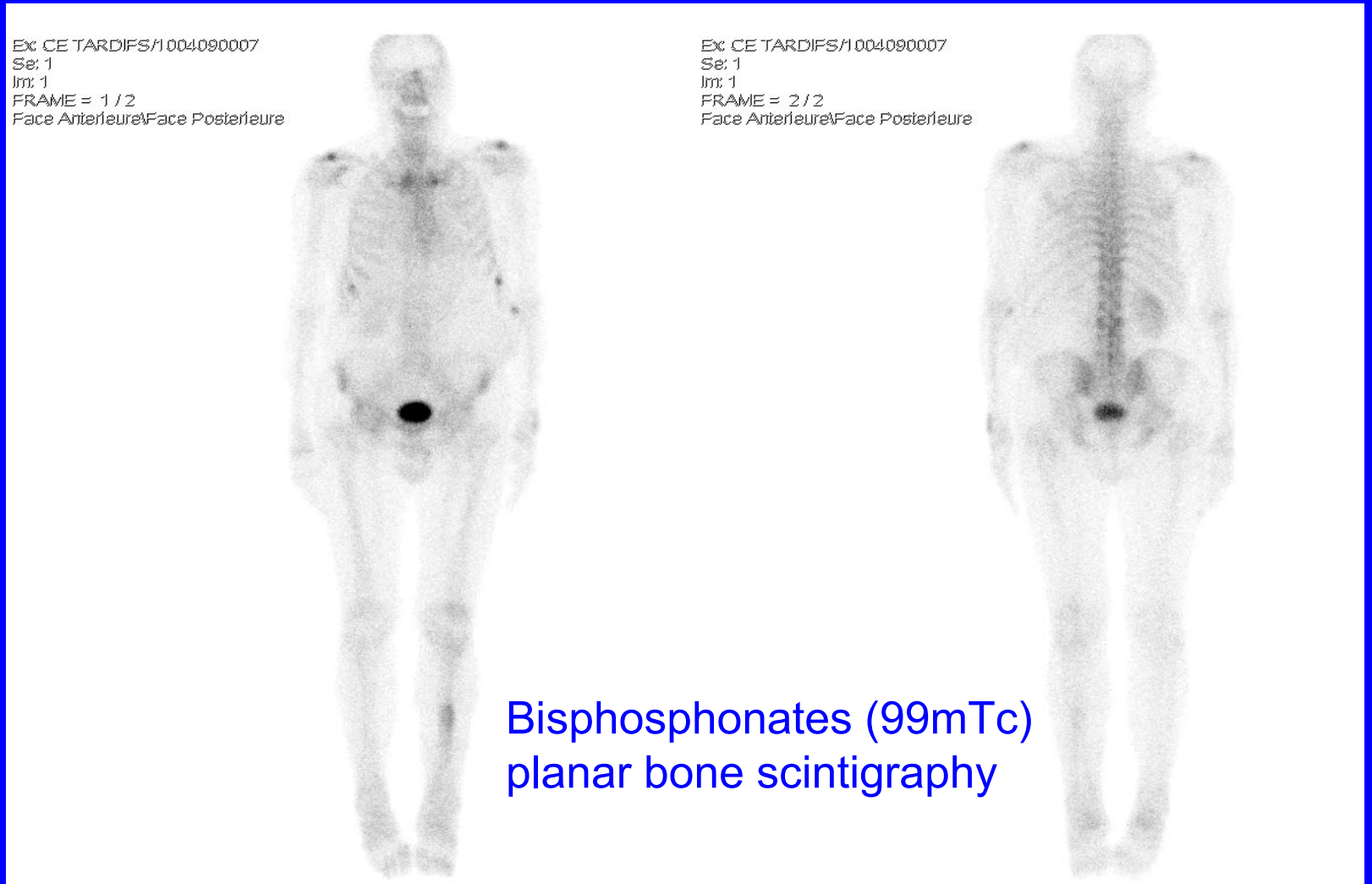
Images acquisition from 5 min, SUV is less than that of FDG but tumour/background is superior (*Chen JNM 2005: 945*).

Prediction of efficacy of gioblastoma by bevacizumab and irinotecan is only possible at completion (*Schipers JNM 2010: 720*).

Renal cell carcinoma

- FDG sensitivity is generally low in renal cell carcinoma and often in its metastatic deposits.
- Detection of bone metastases may benefit from F Na

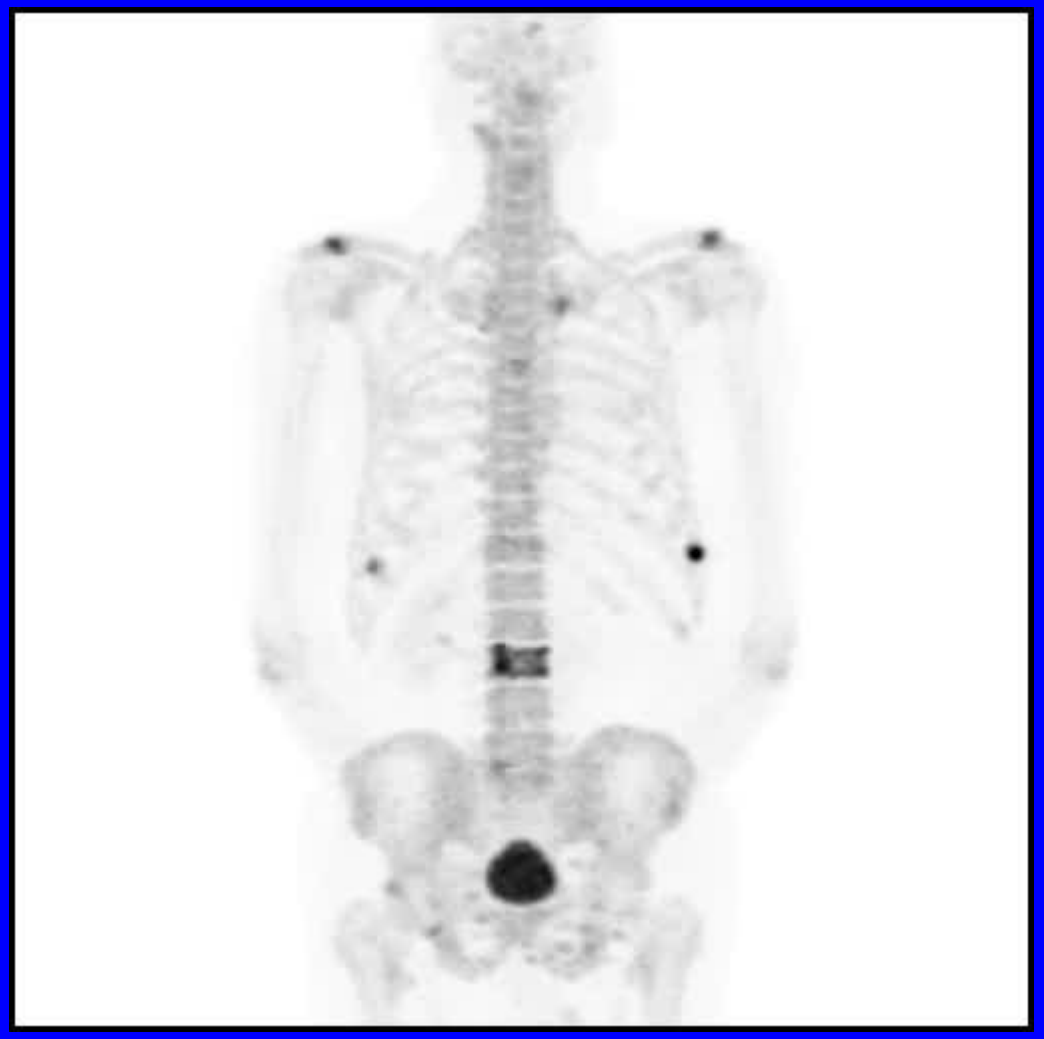
The interest of the higher resolution of PET in the detection of partially or totally osteolytic bone lesions



Bisphosphonates (99mTc)
planar bone scintigraphy

A patient complaining from bone pain with a past history of renal cancer

Same patient. F Na PET/CT
MIP image (anterior view).
Consequence: upstaging to multiple bone metastases status



Bladder cancer

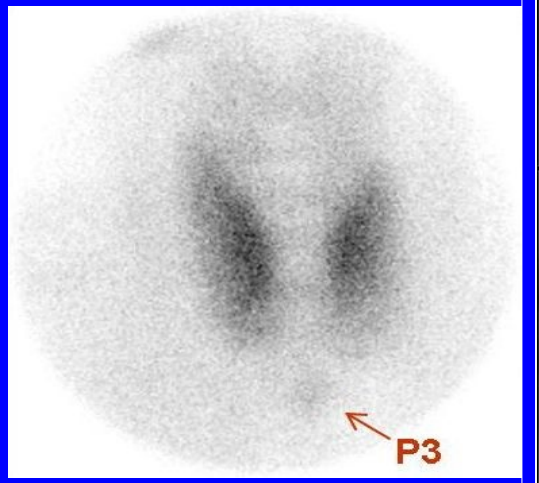
- FDG has a urinary excretion, which impedes the detection of the 1ry tumour.
- However FDG can be useful to detect distant metastases
- Choline (11C) has been proposed for initial staging with better detection of 1ry tumour and lymph node mets than CT (*Picchio M JNM 2006: 938*)

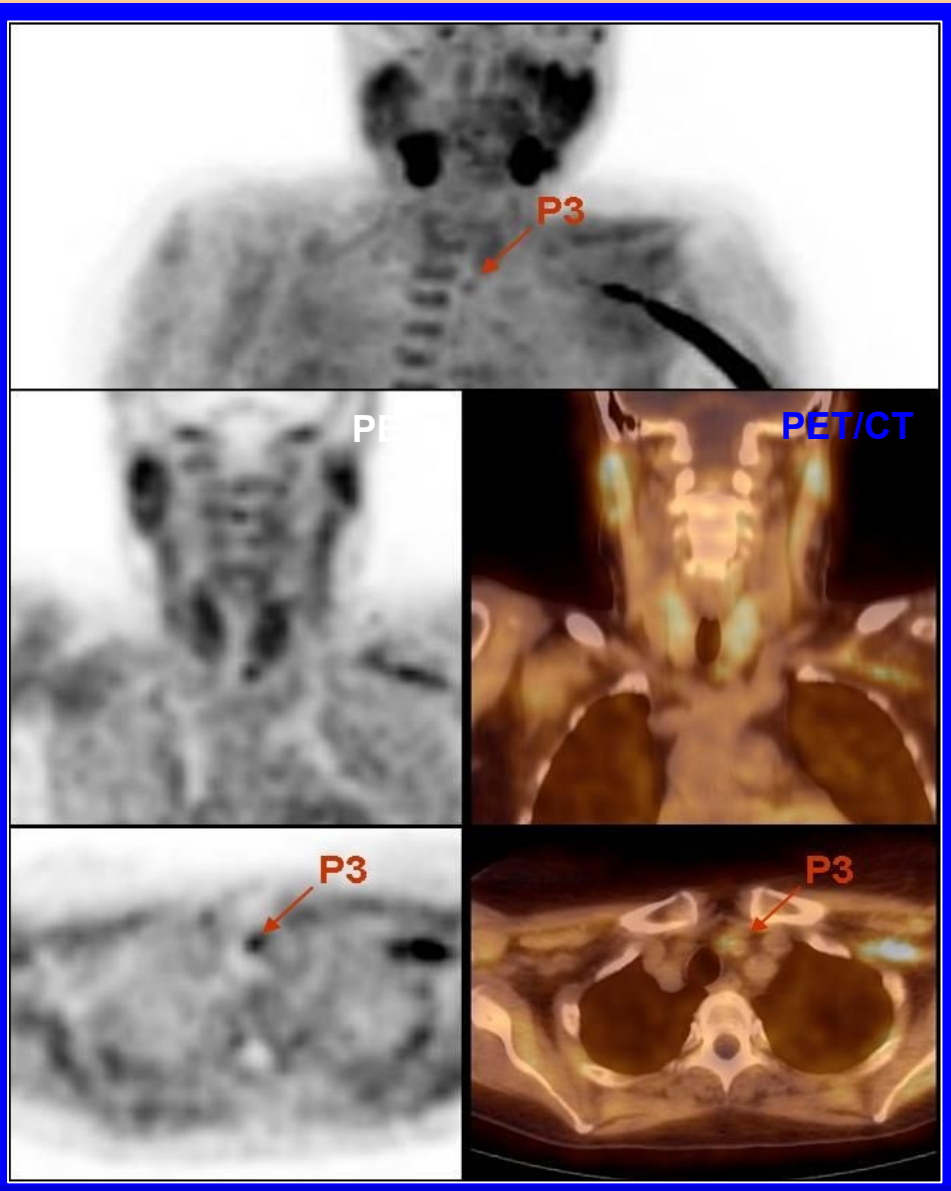
NON-ONCOLOGIC APPLICATIONS

FCH in primary hyperparathyroidism (HPT)

^{123}I

^{99m}Tc-sestaMIBI

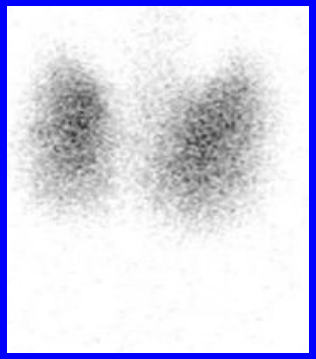




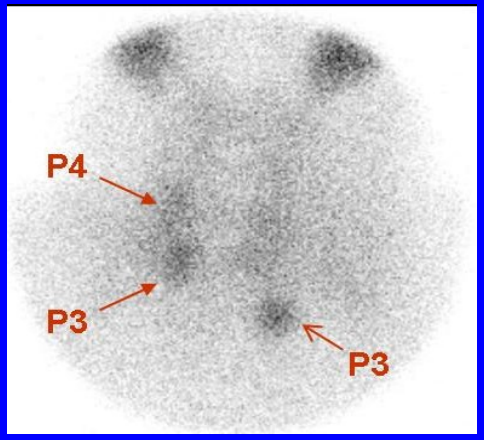
Post-surgical histology: a 0.3 g adenoma of P3. PTH serum levels decreased from 70 pg/mL preoperatively to 4 pg/mL on the day following surgery

FCH in secondary HPT in a dialysed patient

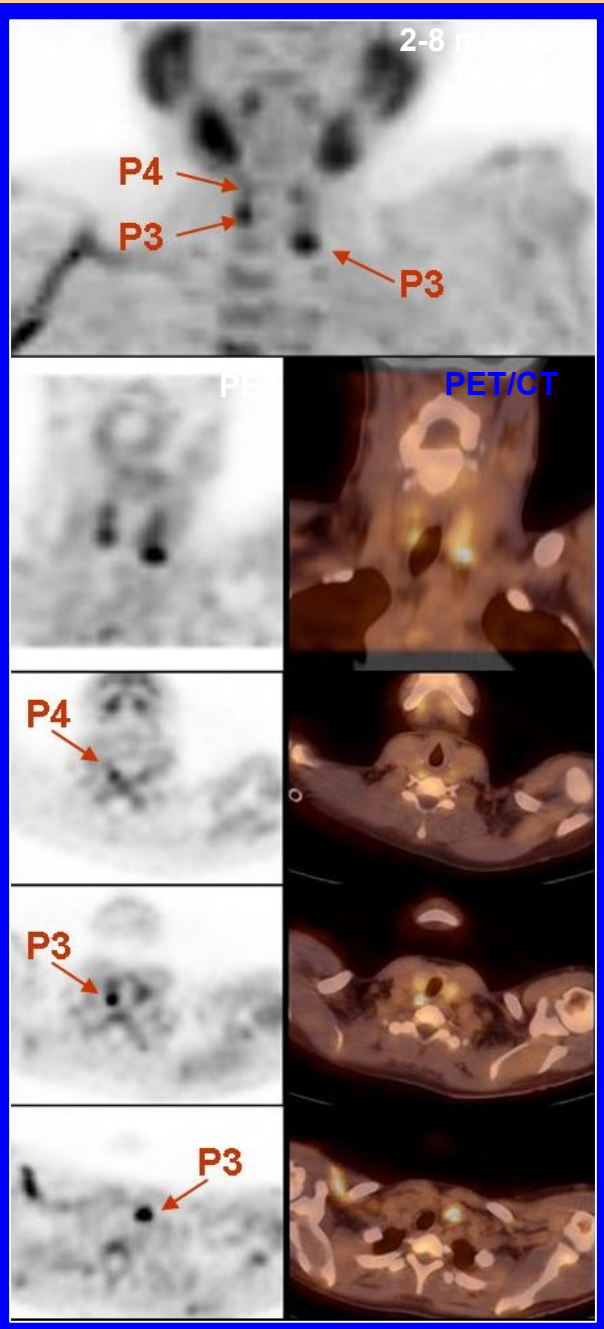
^{123}I

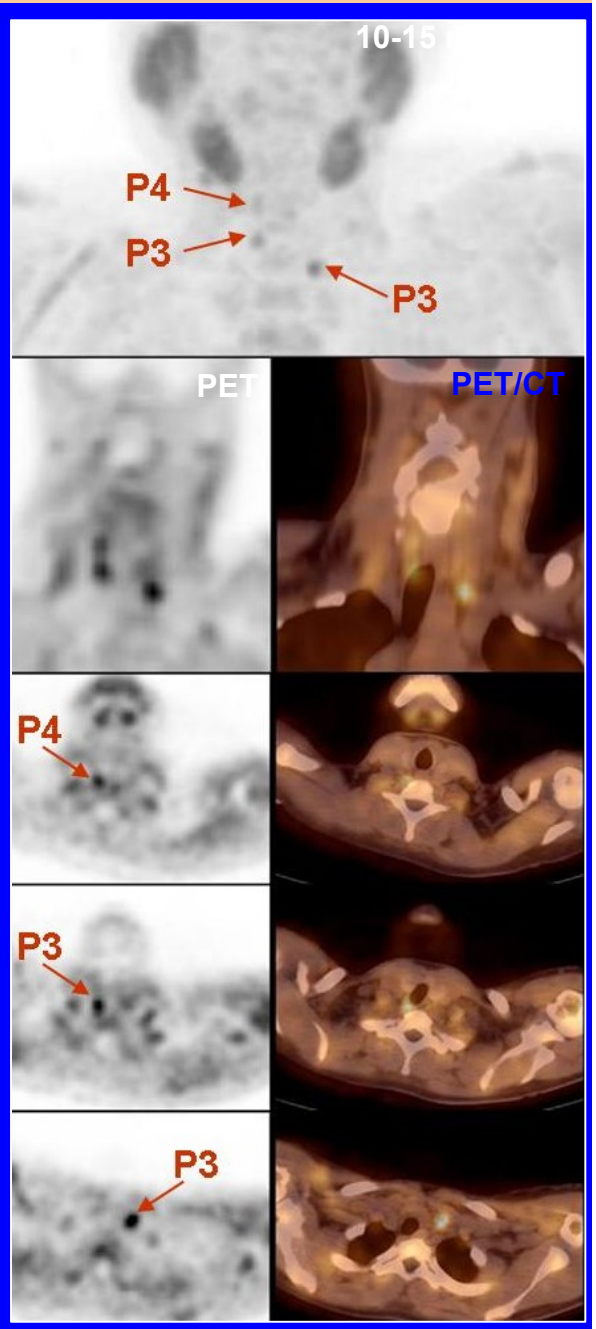


^{99m}Tc-sestaMIBI

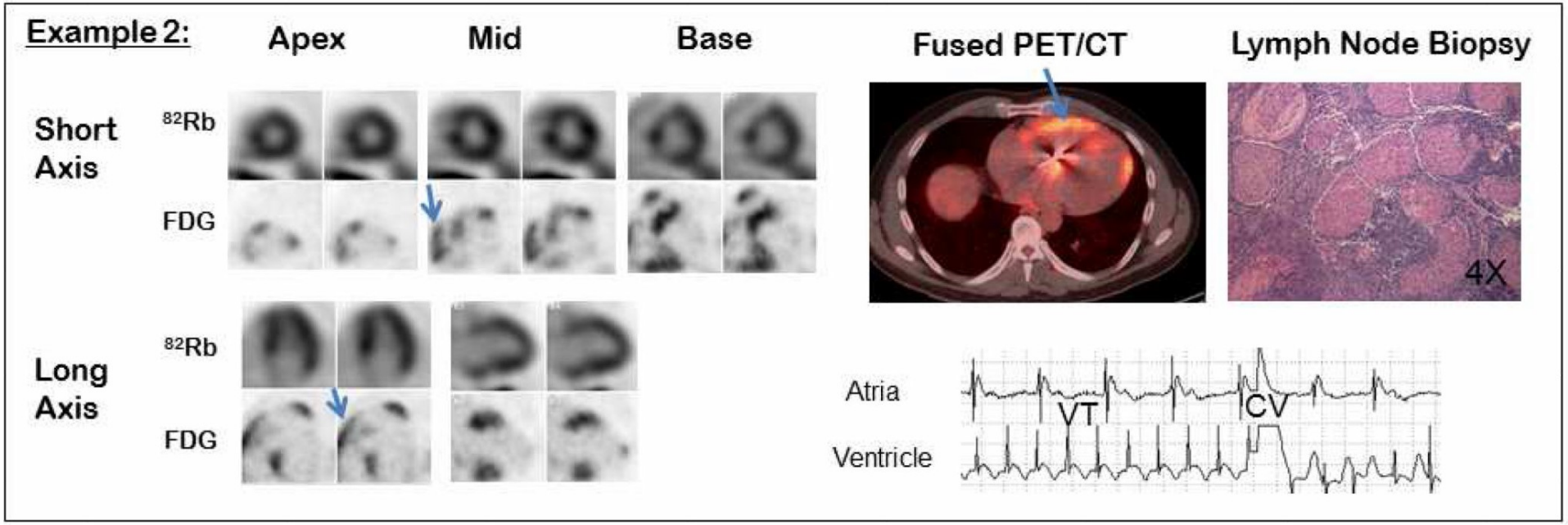


Post-surgical histology: three 0.1 g hyperplastic PGL corresponding to these foci. PTH serum levels decreased from 1946 pg/mL preoperatively to 146 pg/mL on the day following surgery.





Evaluation of cardiac sarcoidosis 82Rb and FDG PET/CT

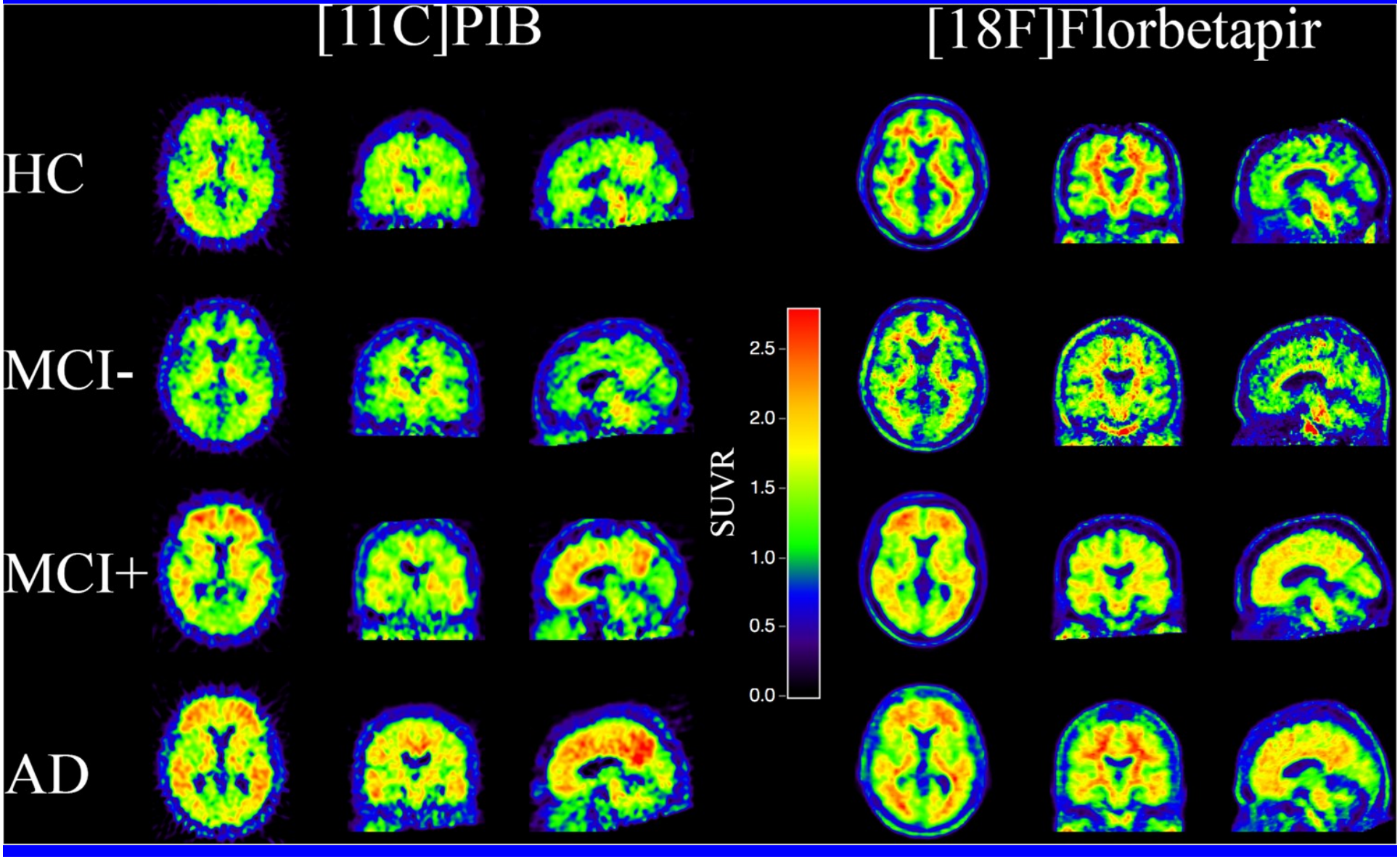


Perfusion defect associated with focal FDG uptake along the basal anterior- and inferiorseptum as well as multiple focal areas of FDG uptake throughout the right ventricle

Blankstein J Am Coll Cardiol. 2014 : 329

PET imaging of amyloid

HC : controls, MCI : mild cognitive impairment, AD : Alzheimer disease. *Chiotis EJMMI 2015 : 492*



In conclusion,

- We reviewed the PET radiopharmaceuticals which are registered in EU and those which have been already documented and may be registered soon, as potential complementary/alternative tools when FDG PET sensitivity is inconstant or limited.
- This list does not pretend to be complete.
- The message to clinicians is that clinical PET is NOT limited to FDG.