Parma, 6 giugno 2017

PDTA Lesioni Focali Epatiche
Medicina Nucleare

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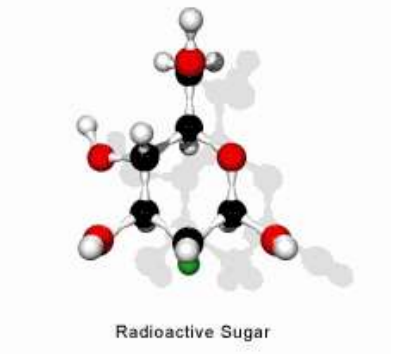
PET-SPECT/CT tracers to study liver lesions

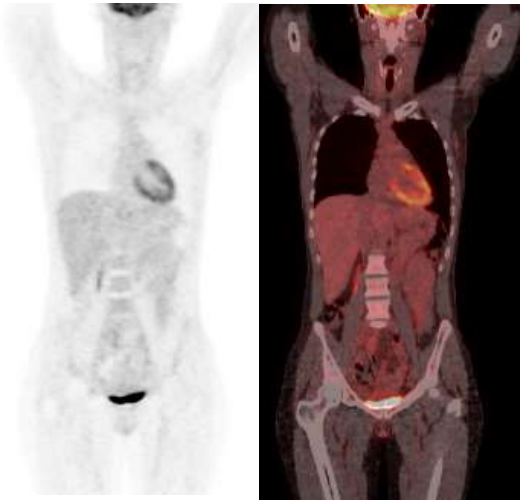
Metabolic activity	[^{18}F]FDG	• Cholangiocarcinoma • Pre-OLT staging of HCC • Liver MTS of colorectal cancer and other tumors • Poorly differentiate NETs G3 (lower SSR expression) • High G2 NETs with Ki67>15-20% (dedifferentiation may indicate the escape phenomenon with worst prognosis)
R status	[^{68}Ga]DOTA-peptide	• Well-differentiated NETs
Membrane synthesis	[^{18}F]choline	• HCC
Specific amine profile	[^{18}F]DOPA [^{123}I]mIBG	• Alternative or problem-solving tool when somatostatin receptor imaging is negative or in assessing response to treatment • Insulinoma • Medullary thyroid carcinoma • Pheochromocytomas and paragangliomas

Metabolic activity: [^{18}F]FDG PET/CT

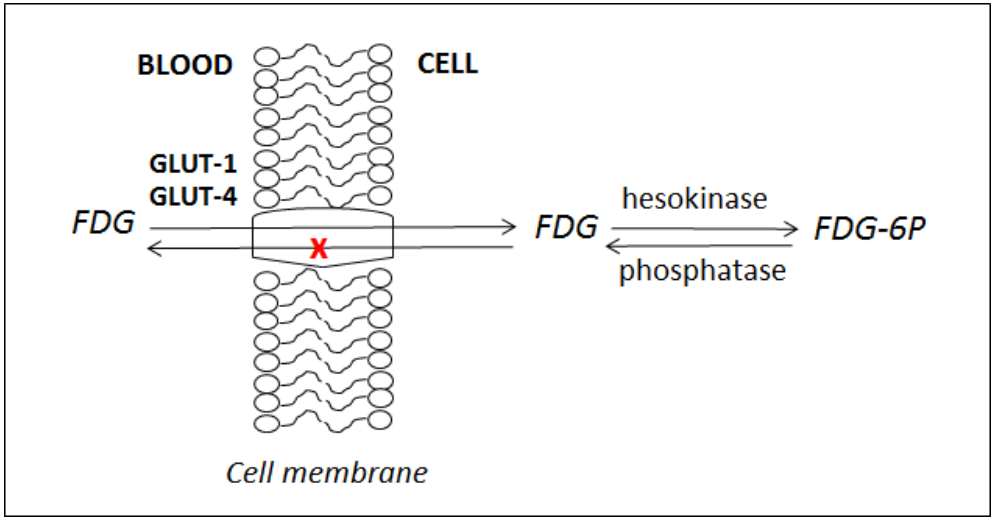
Pathophysiological rationale

- Non-specific tracer targets the glucose pathway of cells
- It enters the cell via glucose transporters
- Its accumulation is an index of increased glucose metabolism, tumor viability and aggressiveness

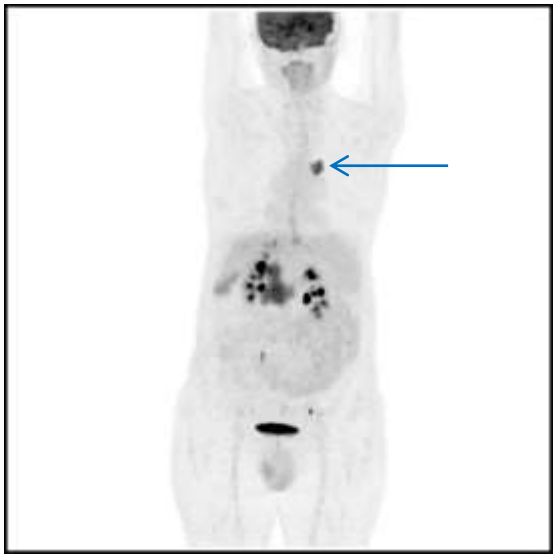


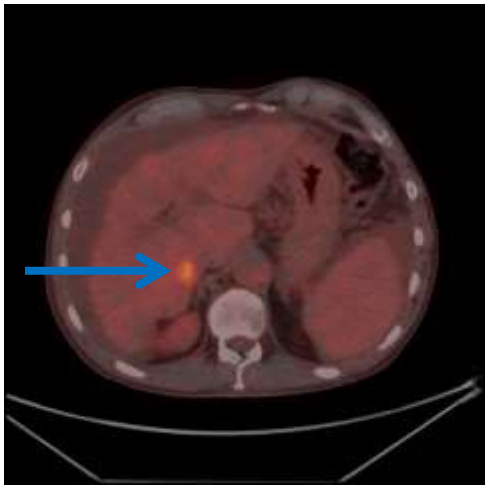


Normal
Uptake time 45-60 min

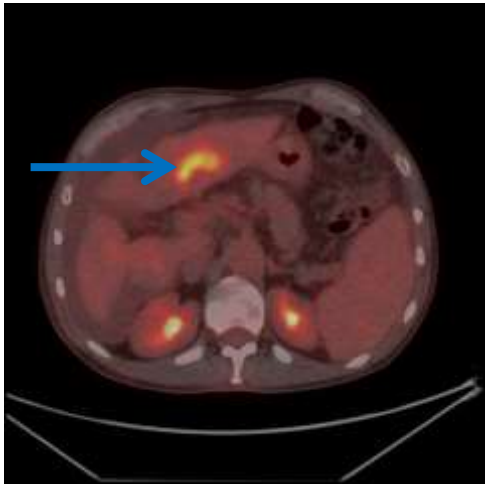


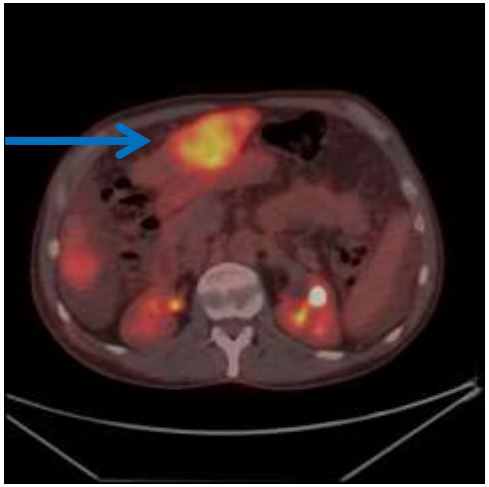
Role of FDG-PET in the assessment of different treatment modalities for HCC pre-OLT

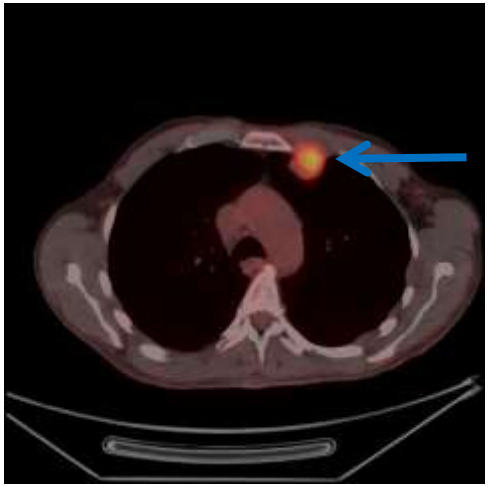


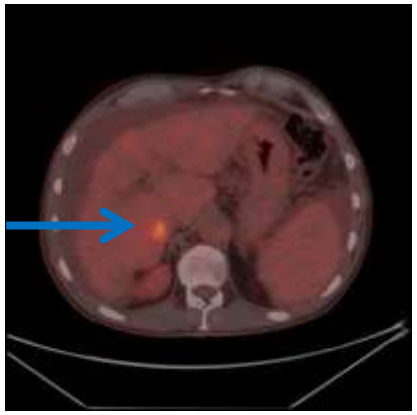


- 2015 HCC S6 lesion → RFA
- 2016 multifocal disease
- 01/2017 CT: pleural lesion

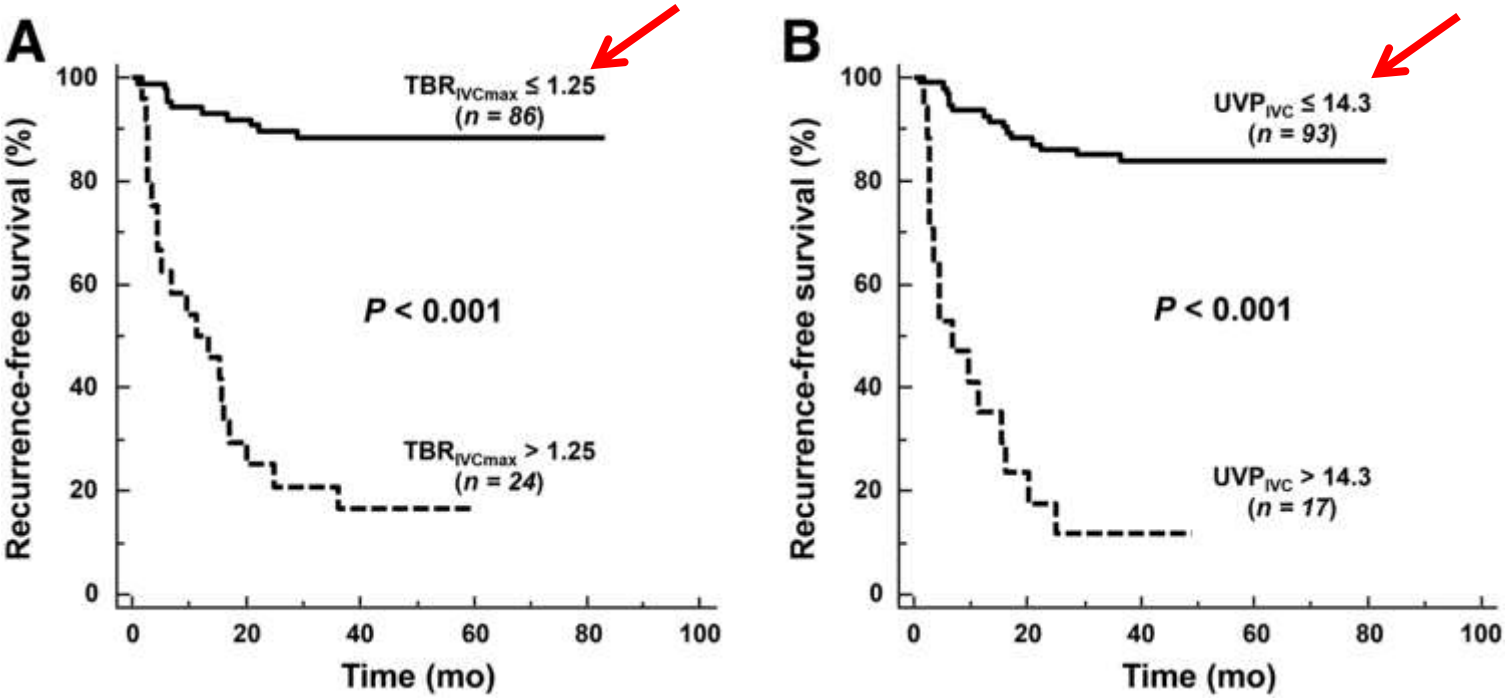








Prediction of Post transplantation Recurrence of Hepatocellular Carcinoma Using Metabolic and Volumetric Indices of 18F-FDG PET/CT.

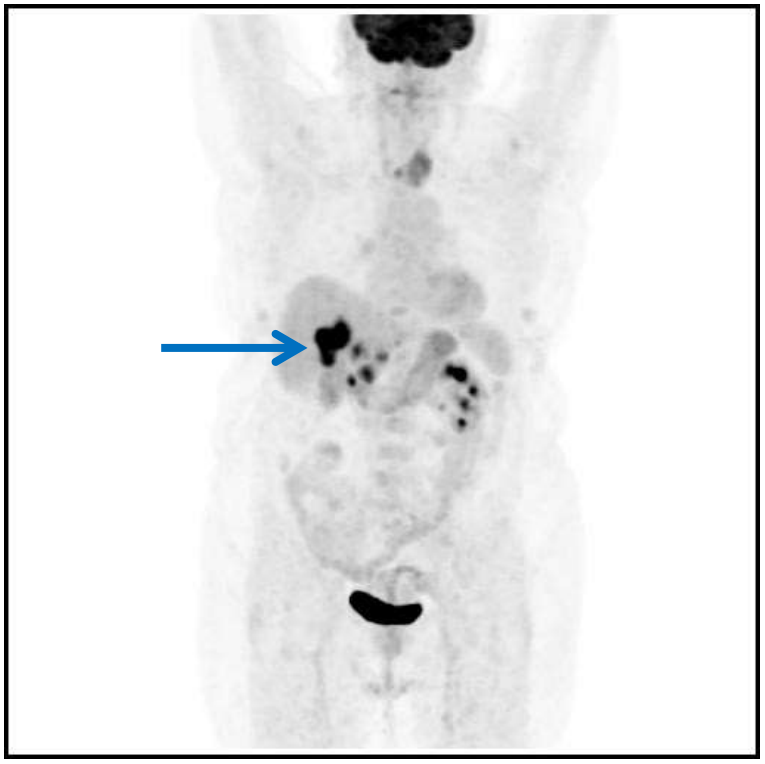


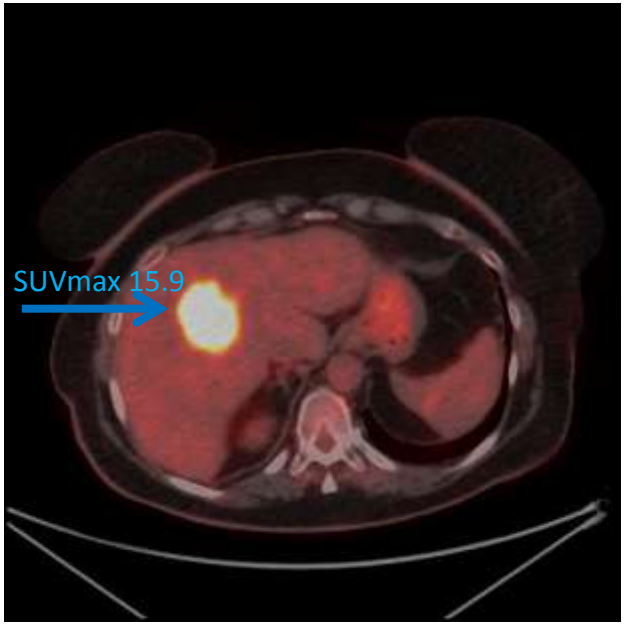
Kaplan–Meier survival analysis with regard to TBR_{IVCmax} and UVP_{IVC}.
(A) Patients with low TBR_{IVCmax} (≤1.25) showed significantly longer recurrence-free survival than those with high TBR_{IVCmax} (>1.25). (B) Patients with low UVP_{IVC} (≤14.3) showed significantly longer recurrence-free survival than those with high UVP_{IVC} (>14.3).

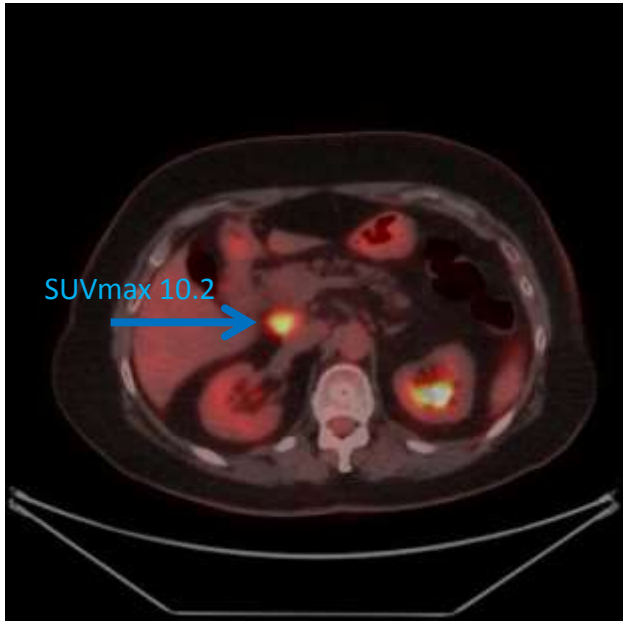
Yong-il Kim J Nucl Med 2016
Hsu CC. Transplantation. 2016

Preoperative FDG-PET/CT in cholangiocarcinoma

- Perihilar intrahepatic cholangiocarcinoma
- Staging
- FDG-PET: T + regional lymph node metastasis

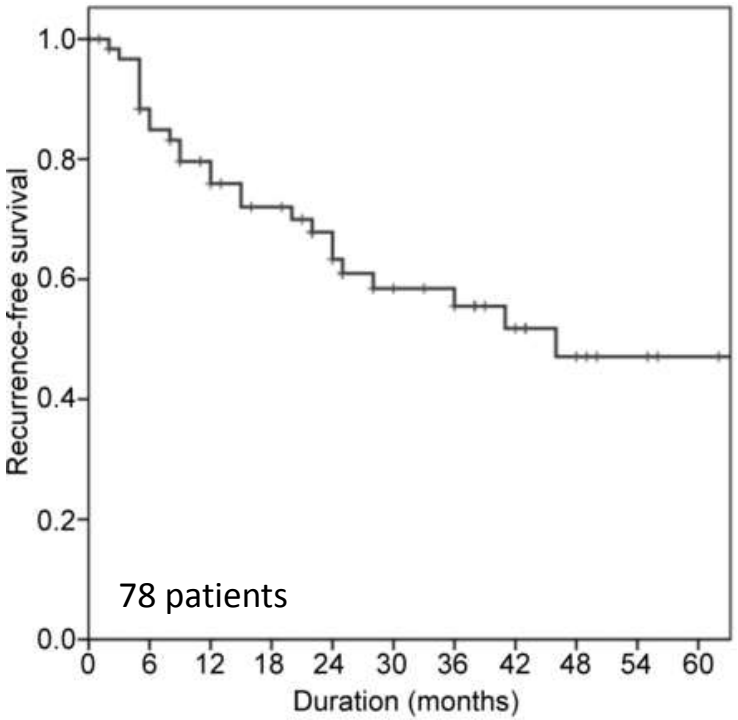


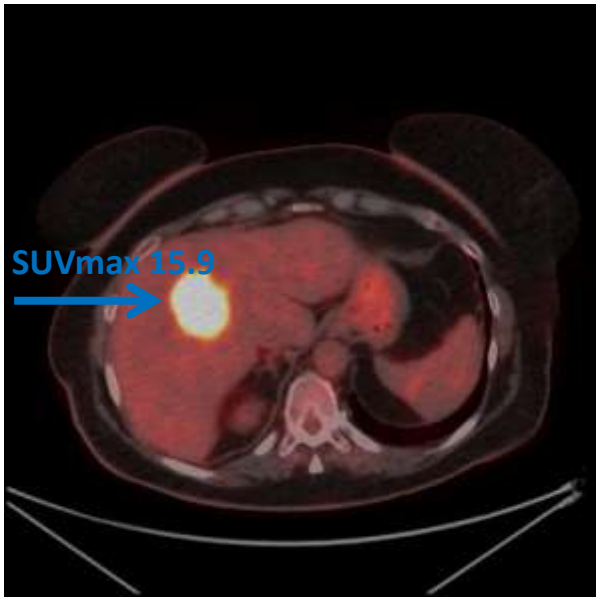




- FDG-PET/CT improve nodal staging and identification of distant metastases,
- Altering clinical management in up to 17–30% of patients recommended for pre-operative staging of both intra- and extra-hepatic cholangiocarcinomas.

Preoperative SUVmax at 18F-FDG PET-CT Predicts Recurrence of Biliary Tract Cancer

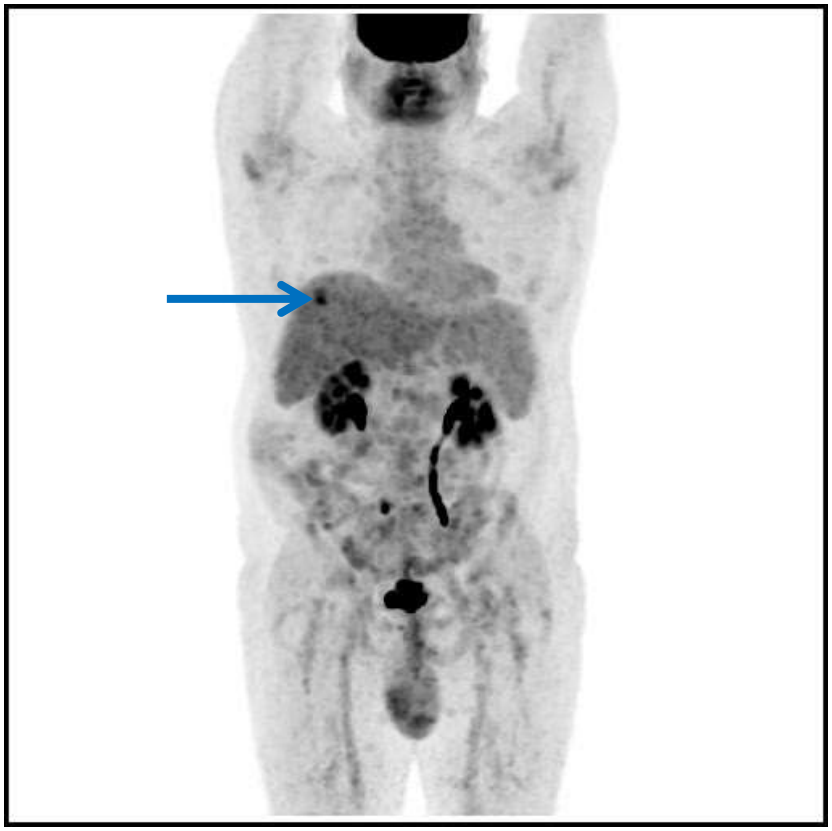




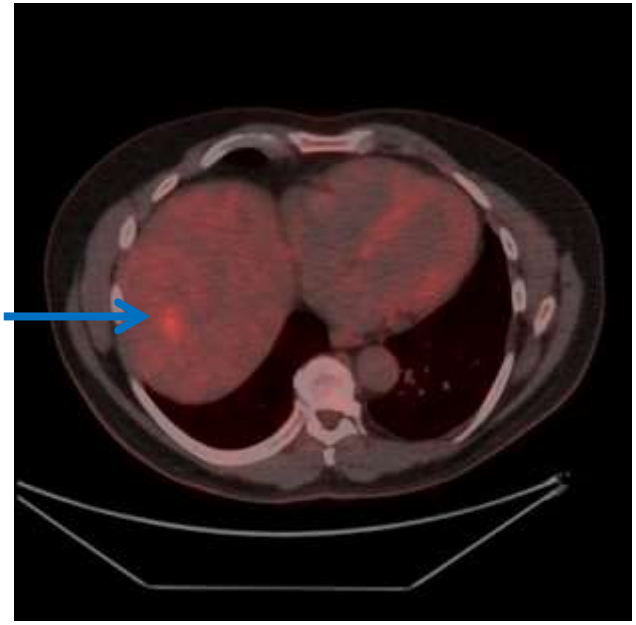
Variable	Category	Hazard ratio (95% confidence interval)	*p*-Value
SUV_{max}	≤5	Reference	0.008
	>5	4.124 (1.459-11.661)	
Lymphatic invasion	Absent	Reference	0.367
	Present	1.710 (0.533-5.489)	
Tumor differentiation	Well/Moderate	Reference	0.972
	Poor	1.269 (0.338-4.760)	
N Stage	0	Reference	0.992
	1	1.006 (0.324-3.118)	

At multivariate analysis high SUVmax (>5.0) independent risk factors for tumor recurrence (p=0.008)

Park M and Lee SM Anticancer Research (2014)



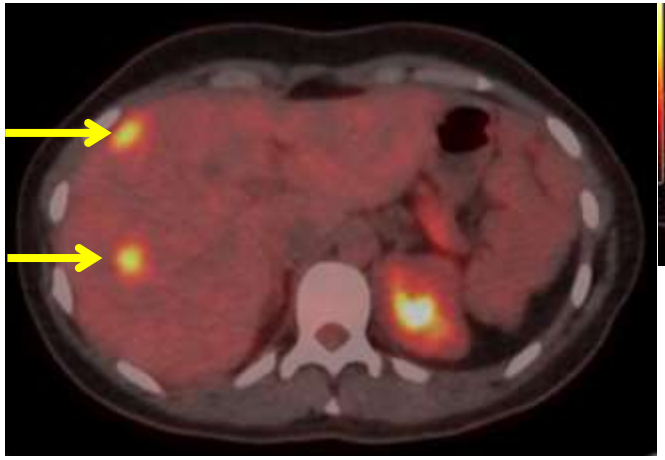
MR

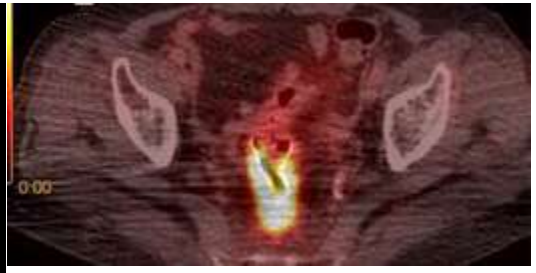


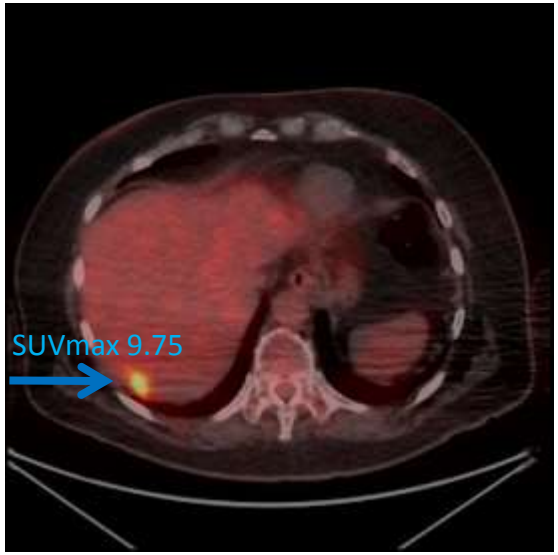
18F-FDG
PET/CT

- Recurrence of cholangiocarcinoma (previous surgery/RFA)
- MR recurrence in the VII-VIIIs
- FDG-PET + SUV 4.3

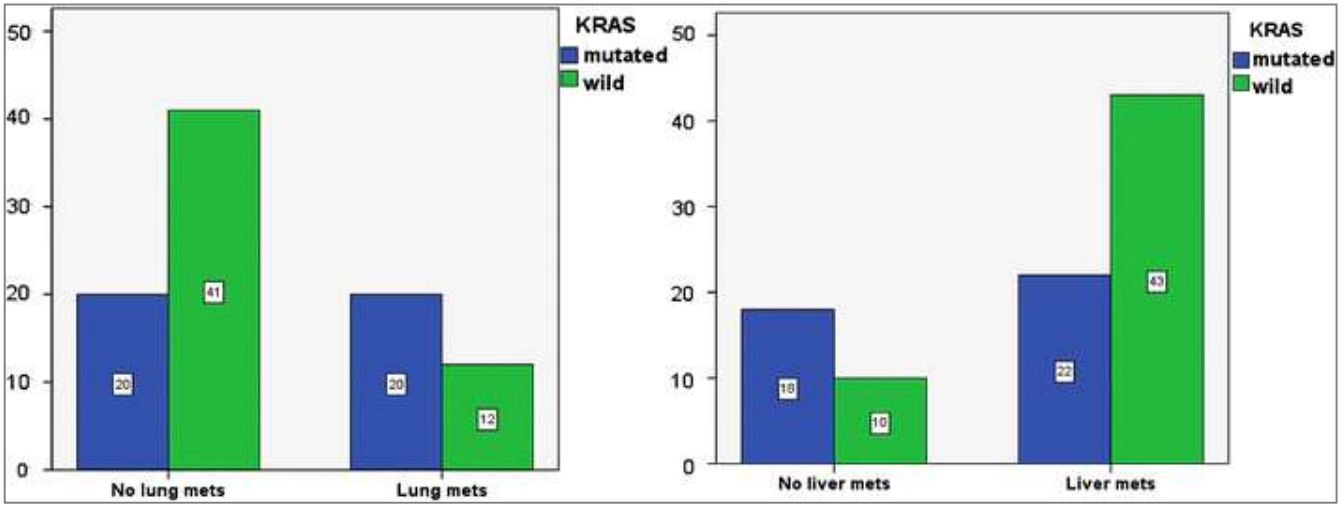
Correlation between KRAS mutation and ^{18}F-FDG uptake in colorectal cancer





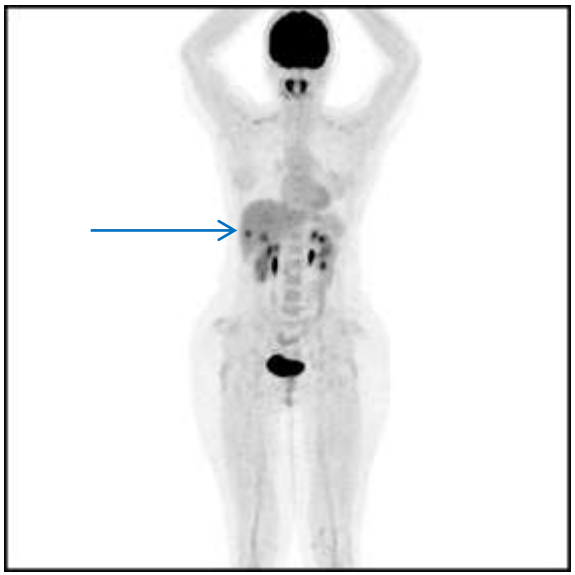


- Patients harboring mutant KRAS tended to metastasis to lung rather than liver.
- *Wild-type KRAS tended to metastasis to the liver than to lung.*
- Patients with KRAS mutation has higher ^{18}F-FDG uptake



Abdom Radiol (2017)

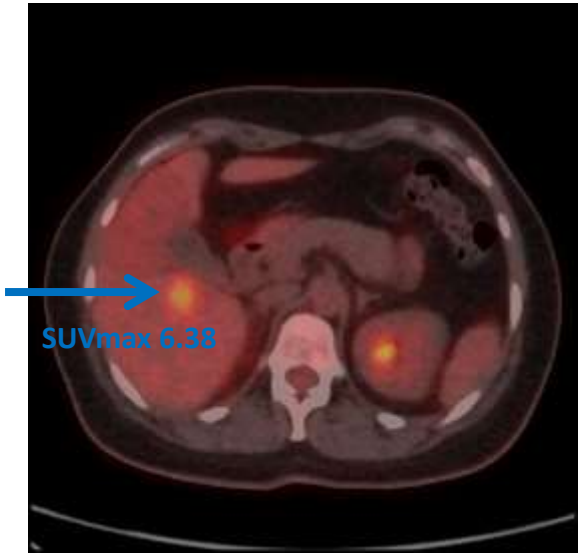
FDG-PET/CT for systemic staging of patients with newly diagnosed breast cancer



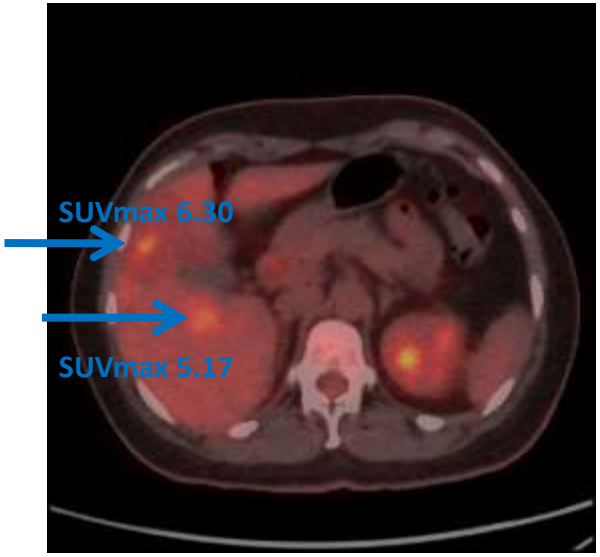
- Breast IDC , progression during fulvestrant
- Liver MTS

High accuracy of PET/CT in stage IIB or higher stage whatever the BC cancer phenotypes (TNBC, HER2+ and ER+/HER2-), whatever the tumour grade and whatever the patient's age.

Groheux, D. Eur J Nucl Med Mol Imaging (2017)



Baseline

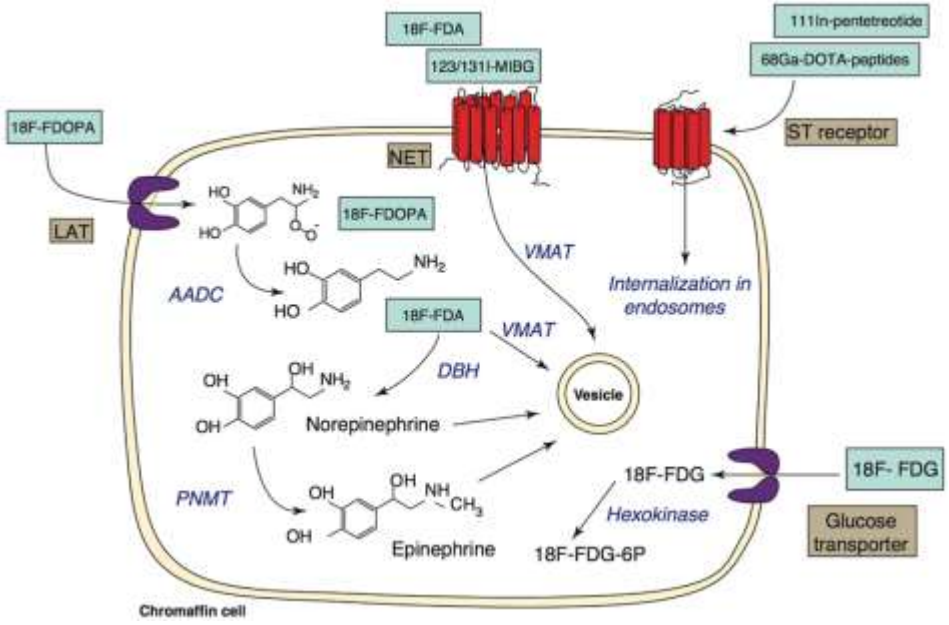


Follow-up

PET AND SPECT TO STUDY NETs

Different tracers to determine:

- Receptors status
- Specific amine profile
- Metabolic activity
- Receptors ligands behaviour



Receptor imaging:

- [^{111}In]DTPA-octreotide (Octreoscan)
- [^{68}Ga]DOTA-peptide

Metabolic Imaging:

- [^{123}I/^{131}I]*m*IBG
- [^{18}F]DOPA
- [^{18}F]FDG

Somatostatin receptor (SSR) status: [^{68}Ga]DOTA-peptide

- [^{68}Ga]: ***positron emitter*** (emission β+ ; 1.9 Mev); **T1/2: 67.6 min**
- DOTA : (*1,4,7,10-TetraazaCycloDodecan-1,4,7,10 Tetraacetic Acid*)
- *peptide (NOC/TOC/TATE):* ***somatostatin analogue***

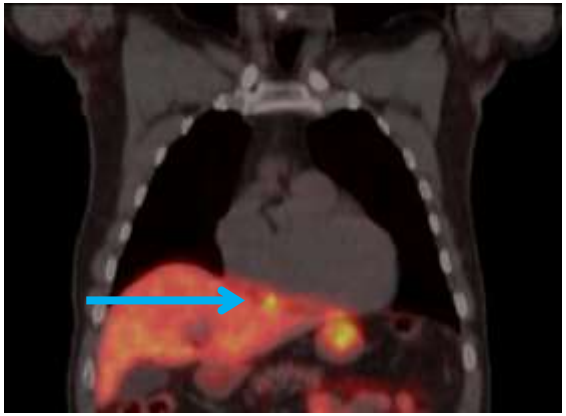
- NOC binds SSTR 2-3-5
- TOC binds SSTR 2-5
- TATE binds SSTR 2

^{68}Ga

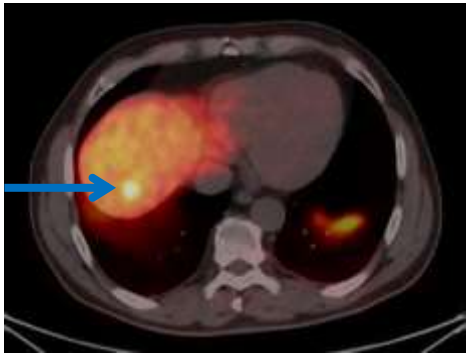
Radionuclide	Half-life	Positron decay (%)	Emax (keV)	Production
^{11}C	20.3 min	100	961	Cyclotron
^{13}N	9.97 min	100	1190	Cyclotron
^{15}O	2.1 min	100	1732	Cyclotron
^{18}F	110 min	97	634	Cyclotron
^{64}Cu	12.8 h	19	656	Cyclotron
^{68}Ga	67.6 min	89	1899	Generator
^{82}Rb	76 s	95	3150	Generator
^{124}I	4.17 d	23	2100	Cyclotron

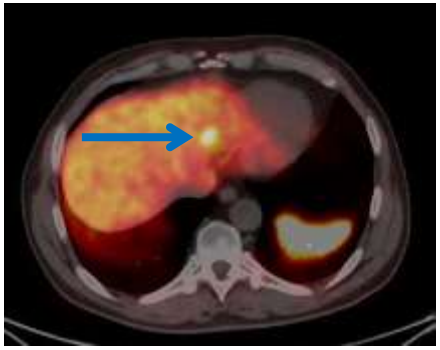
[^{68}Ga]DOTA-TOC/NOC - Staging

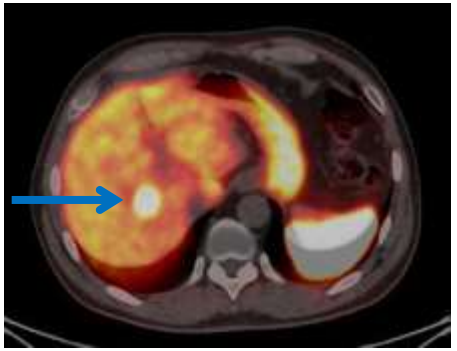
- ✓ Localize primary tumours and detect sites of metastatic disease (staging): to provide information for therapeutic planning.
- ✓ Particularly, NETs with a Ki67 index <20% (WHO G1 and G2) have an overexpression of membrane bound somatostatin receptors (SSTRs), which can be targeted with radiolabeled analogs



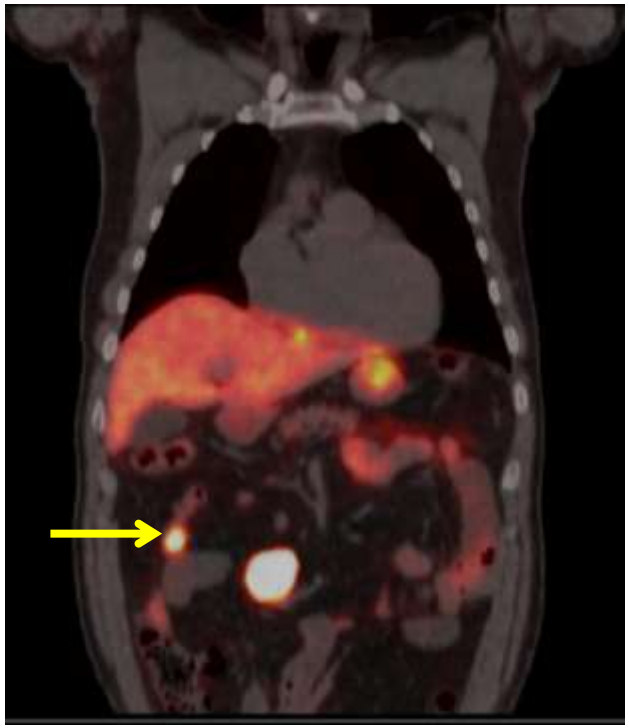
GEP staging before debulking surgery

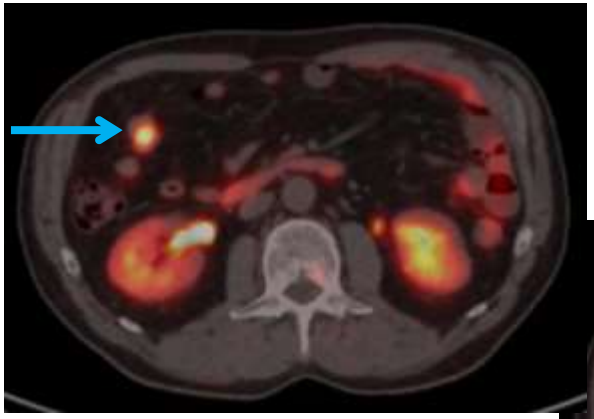


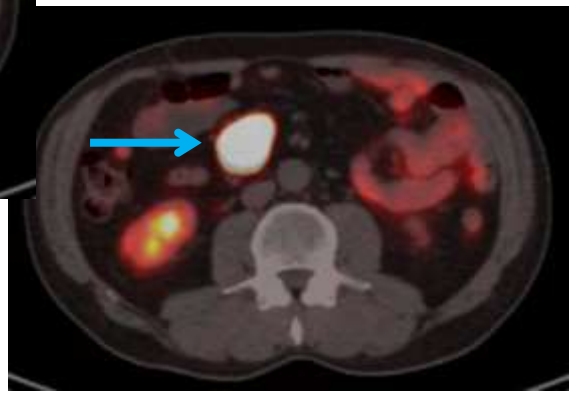


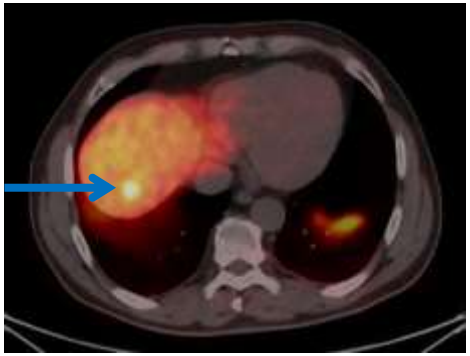


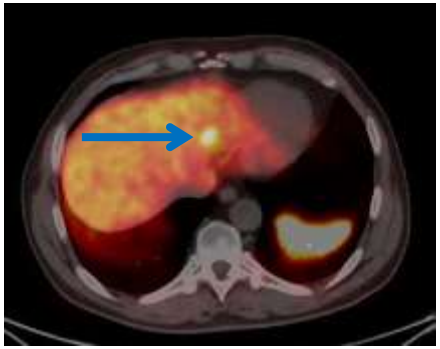
GEP Staging before debulking surgery

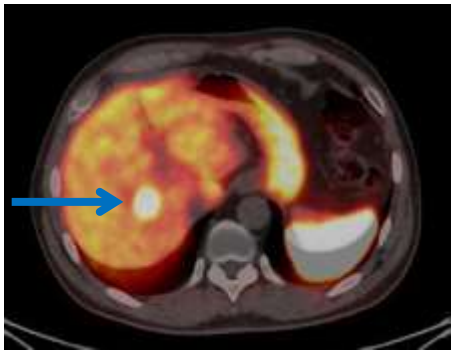








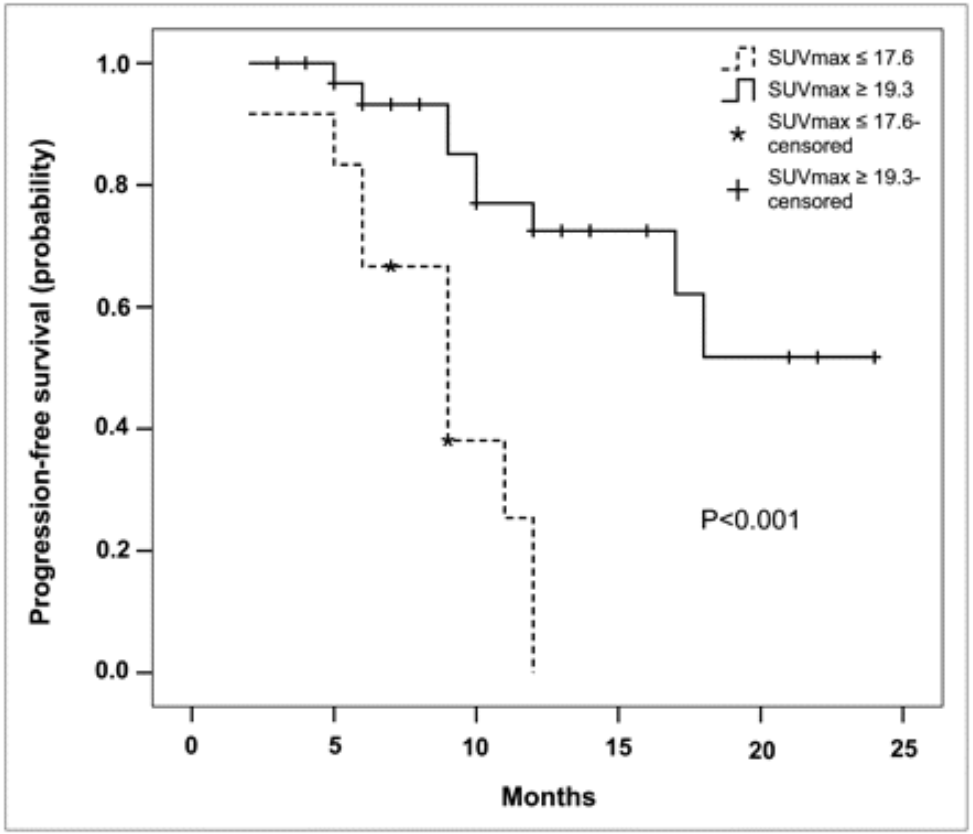




[^{68}Ga]DOTA-TOC/NOC - Risk stratification of NET

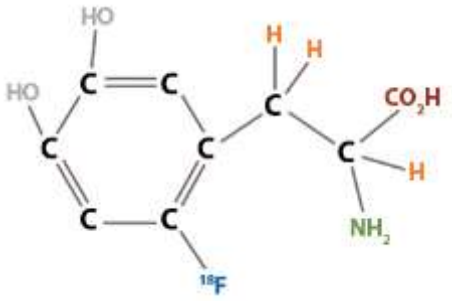
Quantitative assessment of SST receptor status

- SUVmax, measured at 68Ga-DOTA-TOC/NOC PET, correlated with the clinical and pathologic features of NETs.
- SUVmax was significantly higher in patients with pancreatic endocrine tumors and in those with well-differentiated carcinoma.

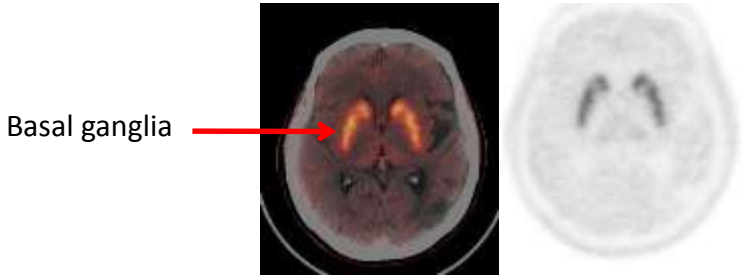


Campana D. Et al. J Nucl Med 2010

Specific amine profile: [^{18}F]DOPA PET/CT



- DOPA decarboxylase activity
- Functional state of dopamine innervations *in vivo*



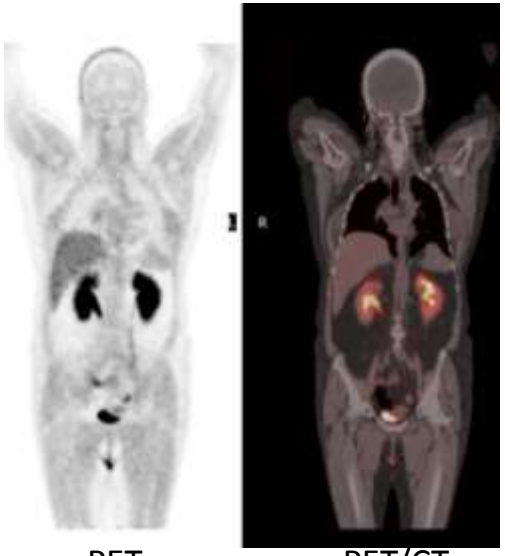
Normal
Uptake time 60 min

Pathophysiological rationale

Several types of NETs are able to take up, decarboxylate and store amino acids, such as DOPA, and their biogenic amines

Indications

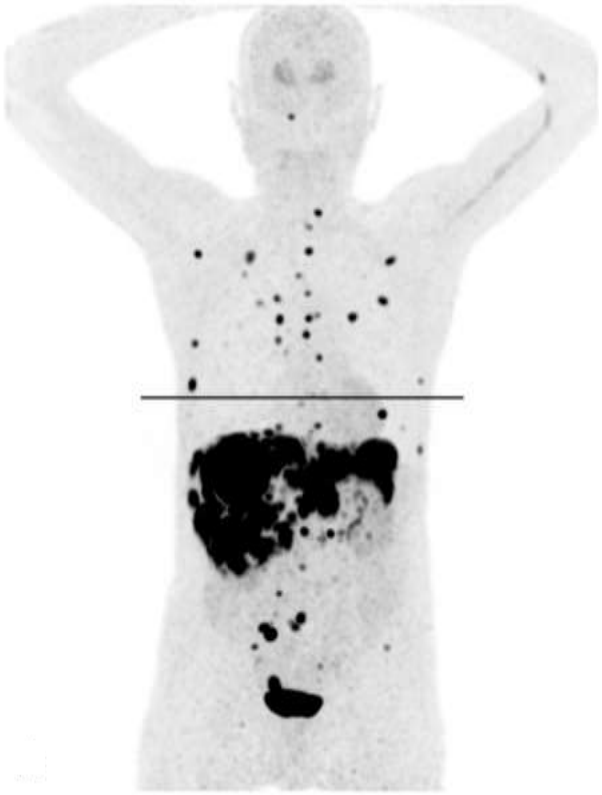
- Diagnosis of insulinoma and beta-cell hyperplasia in adult patients
- Diagnosis of focal congenital hyperinsulinism in infants
- Medullary thyroid carcinoma
- Pheochromocytomas and paragangliomas



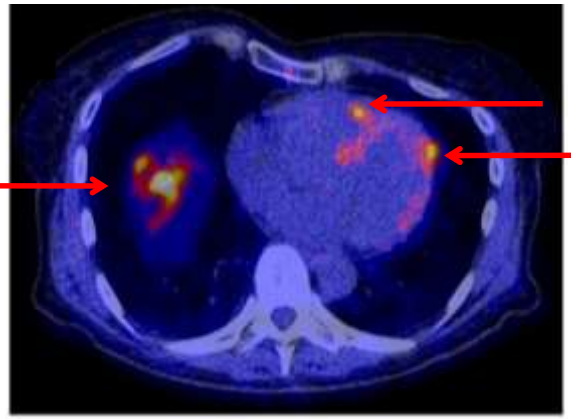
PET PET/CT

Serotonin producing NET

[^{18}F]DOPA PET/CT



MIP



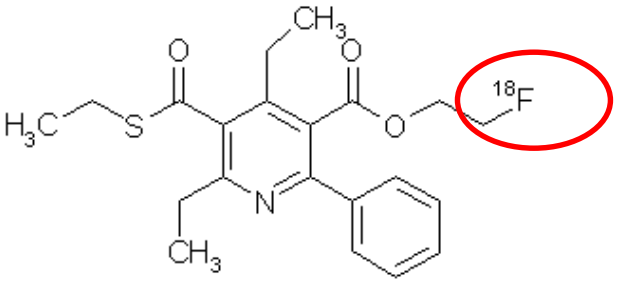
Fused (PET/CT)

Cell membrane metabolism: 18F-choline PET/CT

- Essential component of phospholipids and cell membrane metabolism
- Choline is incorporated into cell membrane phospholipids through phosphorylcholine synthesis

  RoivainenA et al 2000
- Choline is phosphorylated by choline kinase & trapped in the cell
- Malignant tumours increased cell membrane metabolism, increased choline use and increased CK expression (enzyme which phosphorylates choline)

  Ackerstaffet al, Can Res 2001

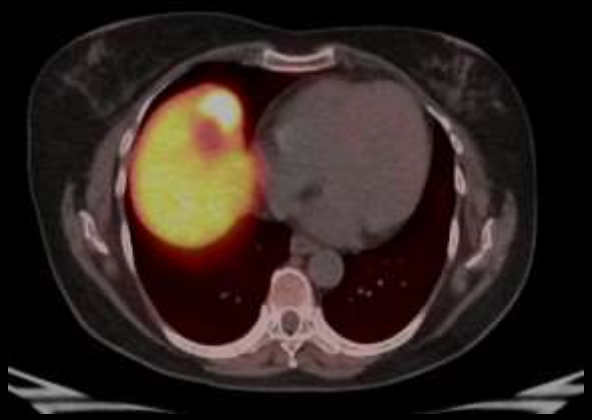


Treatment monitoring of HCC treated with EBRT

Baseline

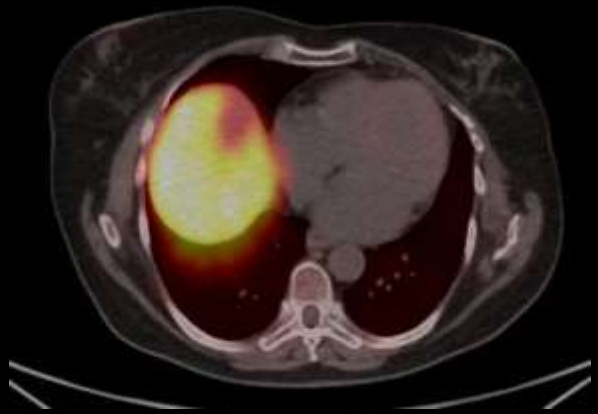
^{18}F-FDG PET/CT

post RFA



^{18}F-choline PET/CT

post EBRT



^{18}F-choline PET/CT