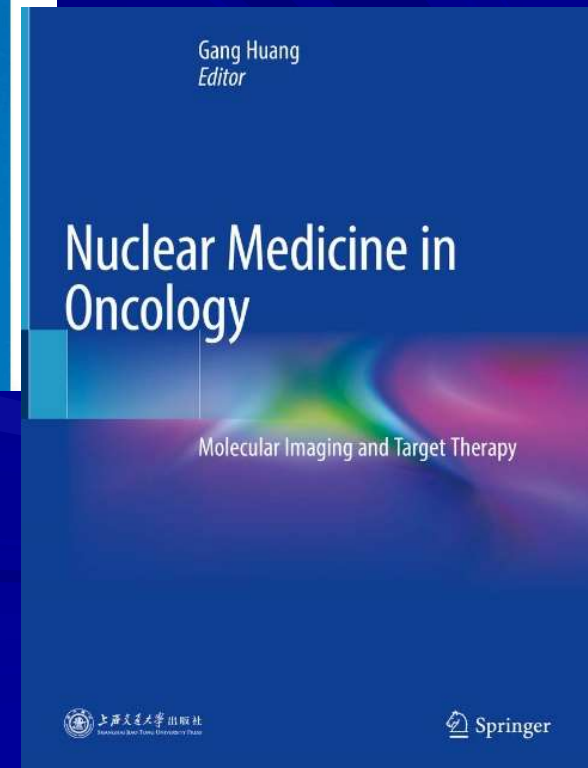
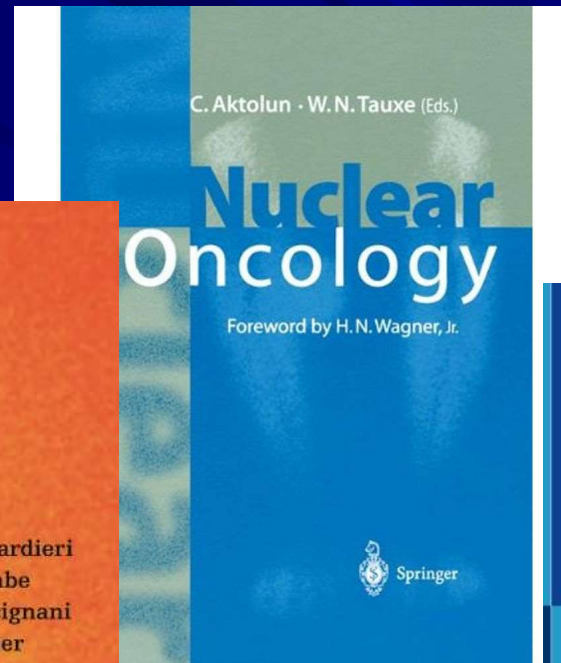
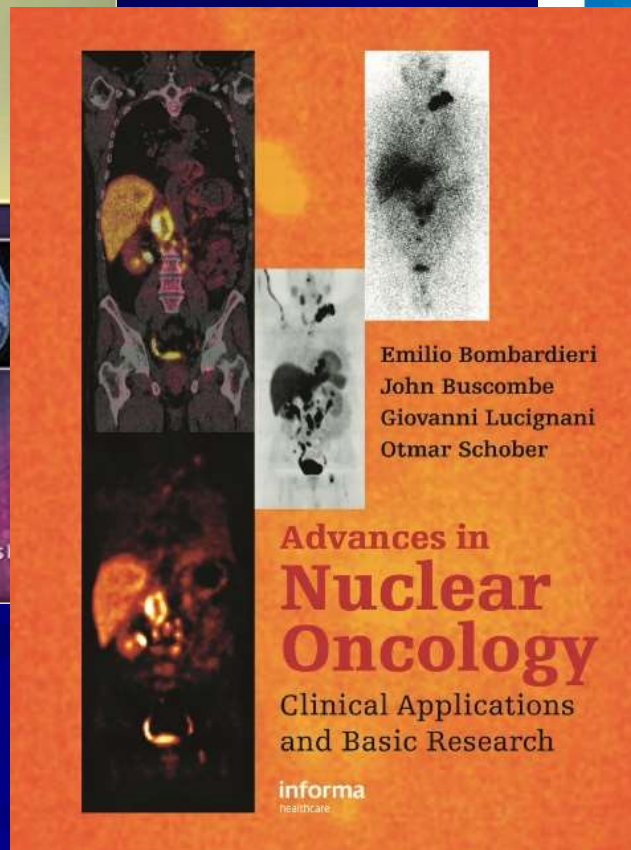
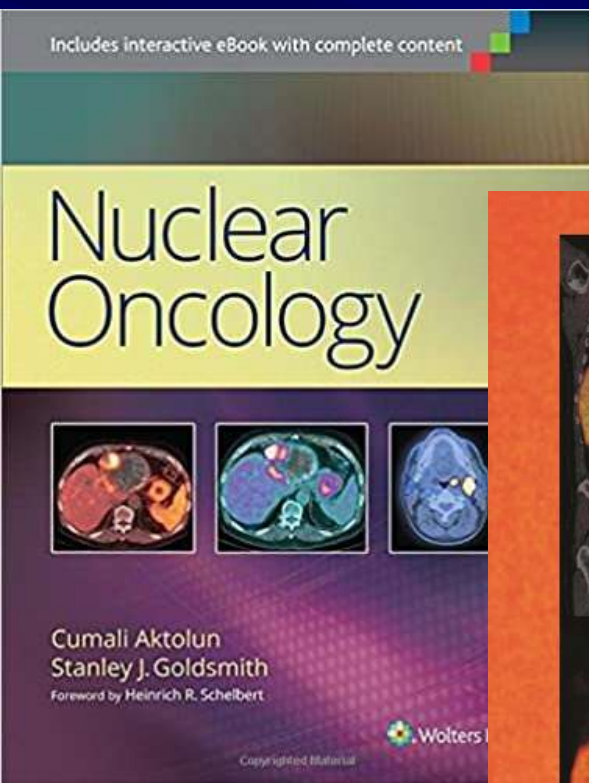


# ONCOLOGY

Nuclear Medicine Scans: Analysis of uptake mechanism and imaging protocols

Malignant tumors are a large group of over 100 diseases that are biologically very different. Malignant transformation is a process in which a healthy cell becomes a cancer cell through a series of alterations and then their uncontrolled proliferation. The transformation process occurs either spontaneously by random mutation, or by gene rearrangement, or by induction by chemical, physical, or viral carcinogens.

# Nuclear oncology, a fast growing field of nuclear medicine



# ONCOLOGY

## Imaging

- "positive uptake"
- non-specific
- specific
- functional imaging



**Y emitting RF (SPECT)**  
**B+ emitting RF (PET)**

## Therapy

**Specific only**



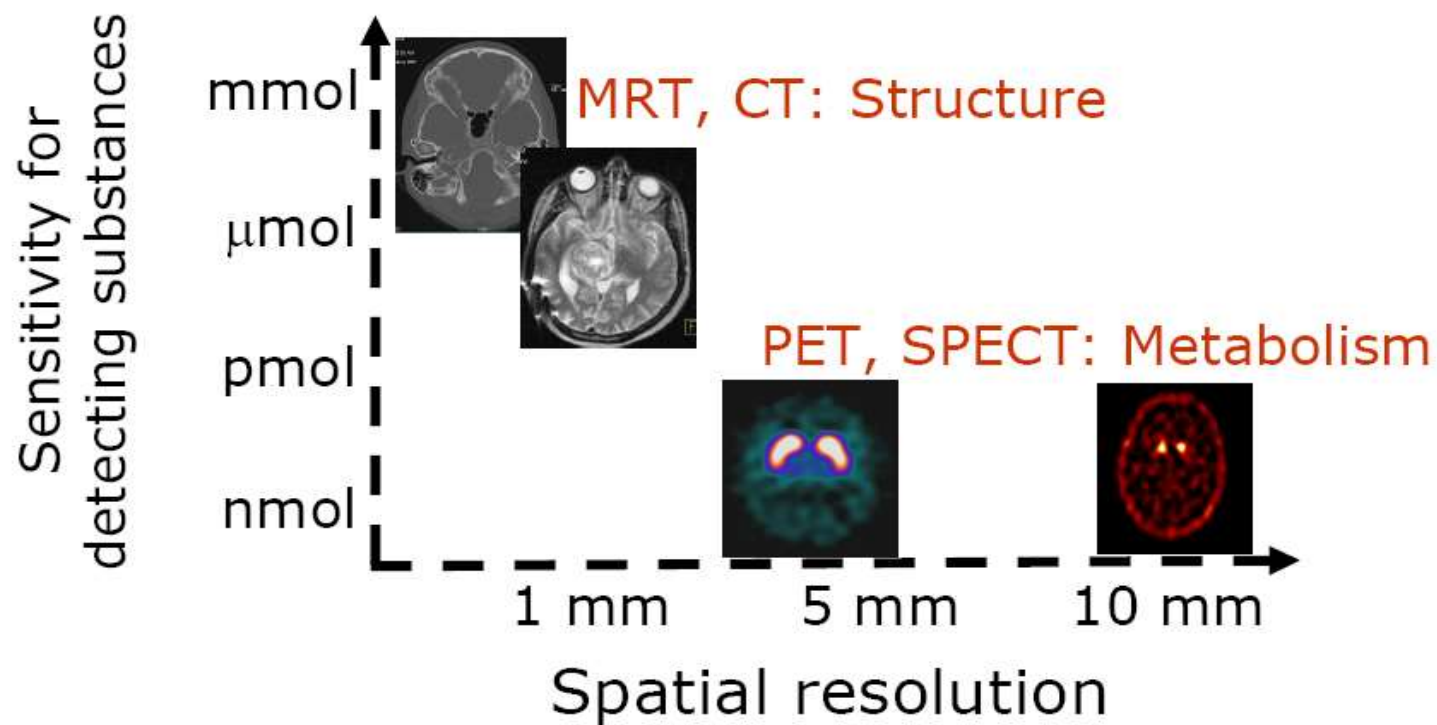
**B+ emitting RF**  
 **$\alpha$  emitting RF**



**The objectives of medical imaging in oncology are:**

- 1. To differentiate benign from malignant lesions**
- 2. To predict the grade of malignancy of cancerous lesions**
- 3. To determine the stage of a malignant disease**
- 4. To evaluate treatment response for:**
  - a) Residual tumor mass after surgery**
  - b) Pre-operative chemotherapy (Immuno Th)**
  - c) Predicting chemotherapeutic response**
- 5. To differentiate post-treatment fibrosis or necrosis from local recurrence**

# Molecular und Morphological Imaging



# What are the nuclear medicine imaging methods?

## Onco PET

PET : 3D

PET -CT : 3D (Function and anatomy).

PET: Positron emission tomography (2 photons)



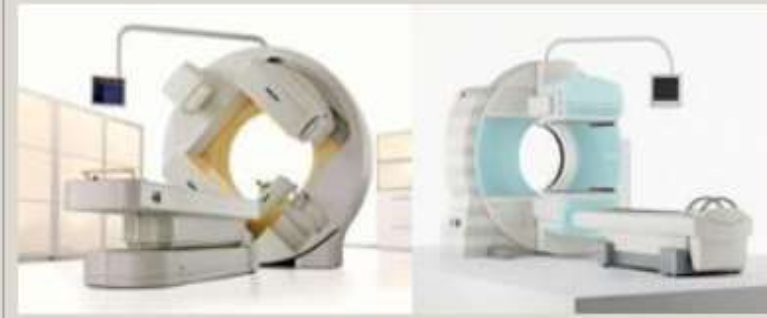
## Conventional tumor imaging

Planar: 2D.

SPECT: 3D.

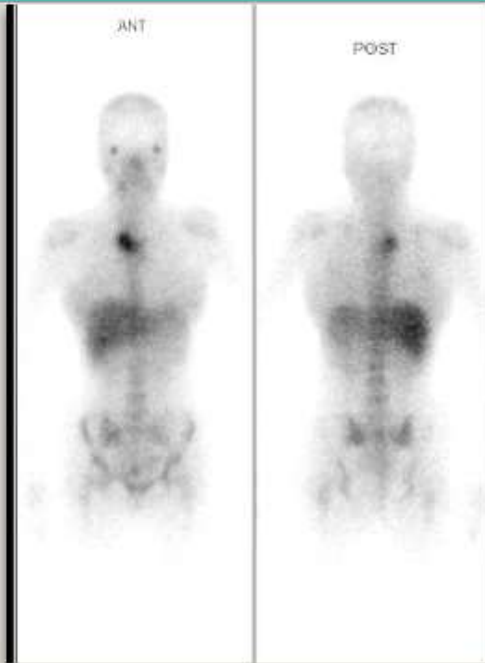
SPECT-CT : 3D (Function and anatomy).

SPECT: Single photon emission computed tomography.



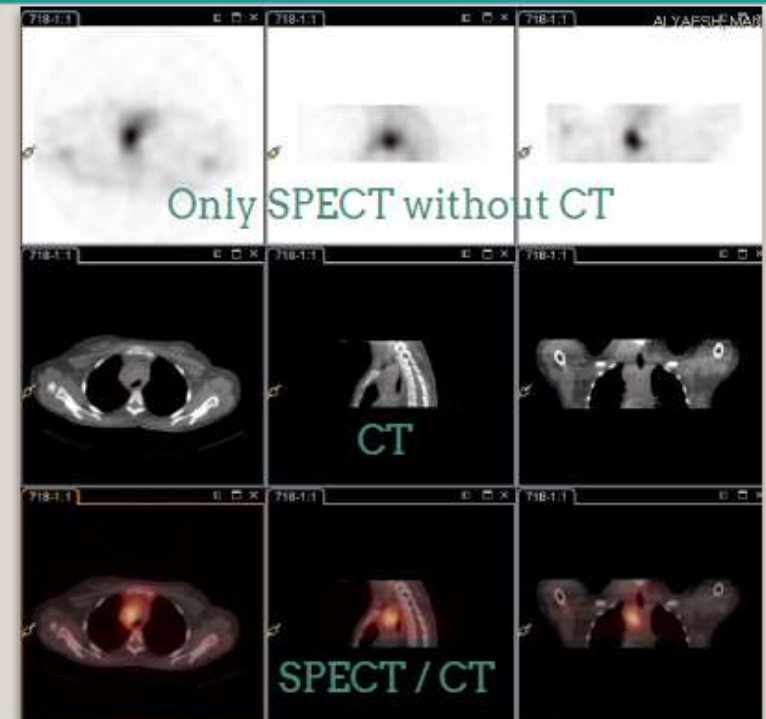
# Single Photon Emission Computed Tomography (SPECT) and SPECT CT

Whole Body **WB** Scan:  
Planar Image



SPECT/CT

More effective than planar imaging



## **TUMOR-SEEKING RF**

- **non-specific - with affinity for tumors and other pathological processes**
- **specific for certain types of tumors.**

### **Mechanism of accumulation in tumor tissue:**

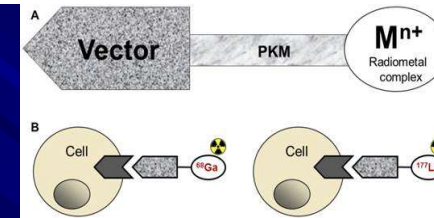
- **extracellular (intracapillary, adsorption)**
- **binding to the cell membrane (receptor, immunoreactive)**
- **intracellular (metabolic).**



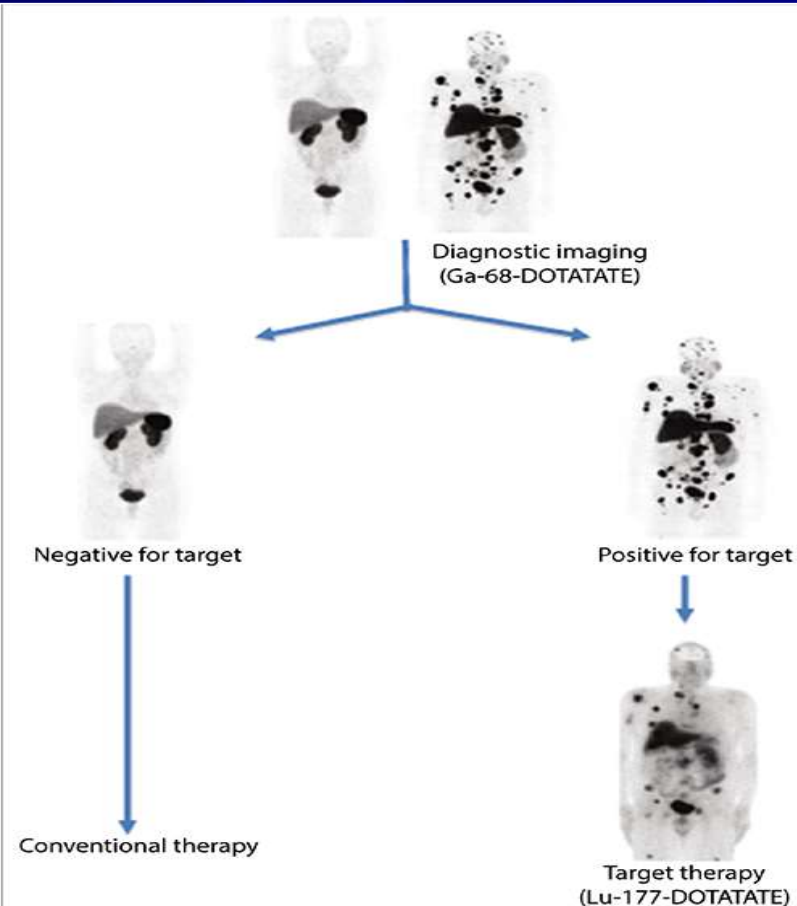
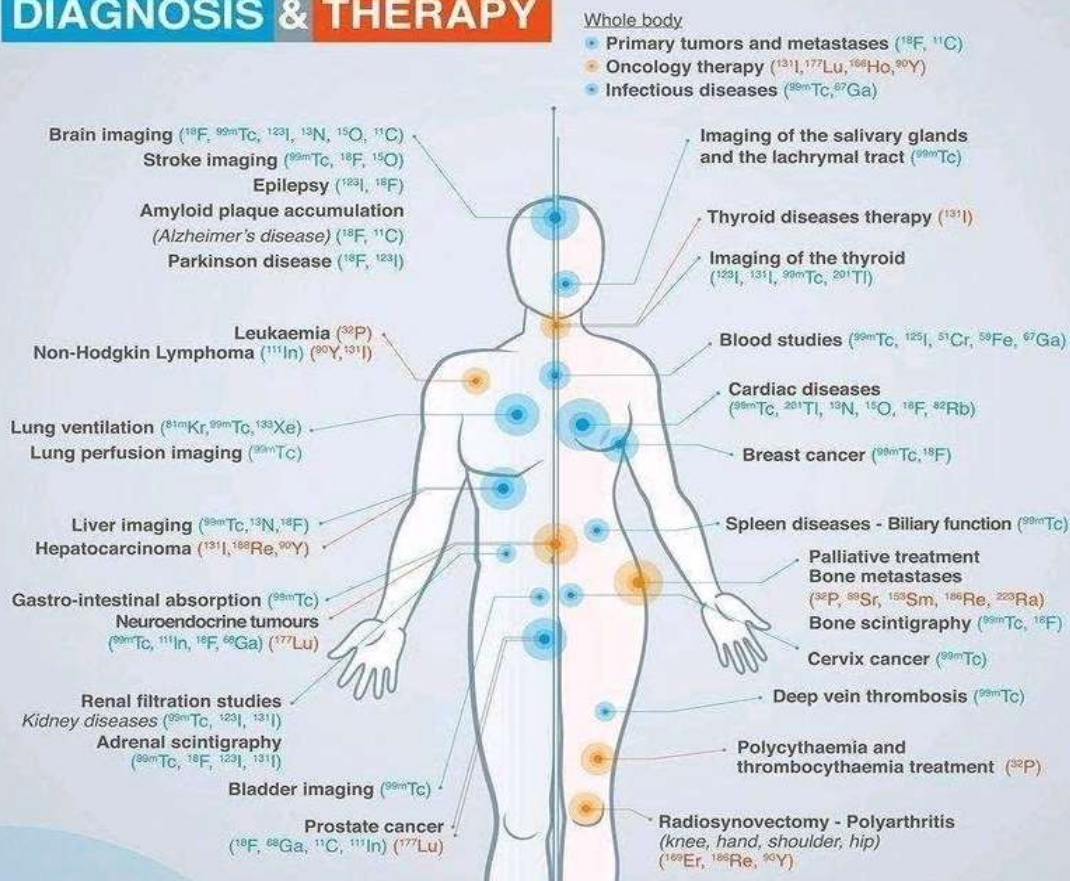
# THERANOSTICS

*"If you can see it, you can kill it"*

Prof. Dr Richard P. Baum



## DIAGNOSIS & THERAPY



## Specific

## Non-Specific

### Diagnostic Radiopharmaceuticals

Binds directly to special tumor antigens or receptors or are accumulated by special metabolic pathway.

#### PET or PET/CT:

- **Gallium 68** – octreotide analogues (mimics natural somatostatin pharmacologically) (**Ga-68 DOTA**): For **neuroendocrine tumors**.  
it's the gold standard and more specific and sensitive. used in KSA
- **Fluorine-18** - fluorodeoxythymidine (F-18- FLT): For tumor **proliferation**.  
The uptake depends on the degree & rate of proliferation.
- **Fluorine-18**-fluoromisonidazole (F-18-FMISO): For tumor **hypoxia**.  
Hypoxia is usually located at the tumor's center. You want to know the degree of hypoxia; some centers use oxygen for tumor treatment.

#### Planar, SPECT or SPECT/CT:

- I-123/131 MIBG for **neuroendocrine tumours**.
- I-131 for **differentiated thyroid carcinomas**.
- In-111 or Tc99m octreotide for tumours expressing somatostatin receptors.  
Gallium-68 is more sensitive than Tc99m octreotide.
- Monoclonal antibodies labelled with In111 (Indium-111), I-123/131 or Tc-99m.

Demonstrate tumor sites but are not specific for malignancy.

#### What does 'non-specific' mean?

They can tell you if there was a tumor, but they cannot tell you what type of a tumor it is.

#### PET or PET-CT

- **Fluorine-18 FDG** – anaerobic metabolism.
- Most commonly used.
- Highly sensitive, but not specific. E.g. if there was an abnormal uptake in the hilar area, we will not be able to know if it was a large lymph node, or a lung tumor.
- Excreted by urine.

#### Planar, SPECT or SPECT-CT:

- **Diphosphonates** – bone scan.
- Most commonly used.
- Can tell if there was any metastasis, but cannot detect its origin.
- **Ga-67 citrate** – similar to FDG – localising agent.
- **Tc99m Nanocolloid** – bone marrow scan.
- **Tc99m MIBI / Thallium 201** – several tumors.



# TUMOR-SEEKING RF

“POSITIVE” UPTAKE - MORE INTENSIVE ACCUMULATIONS OR  
"HOT" SPOTS WHERE THE TUMOR IS LOCATED IN THE BODY

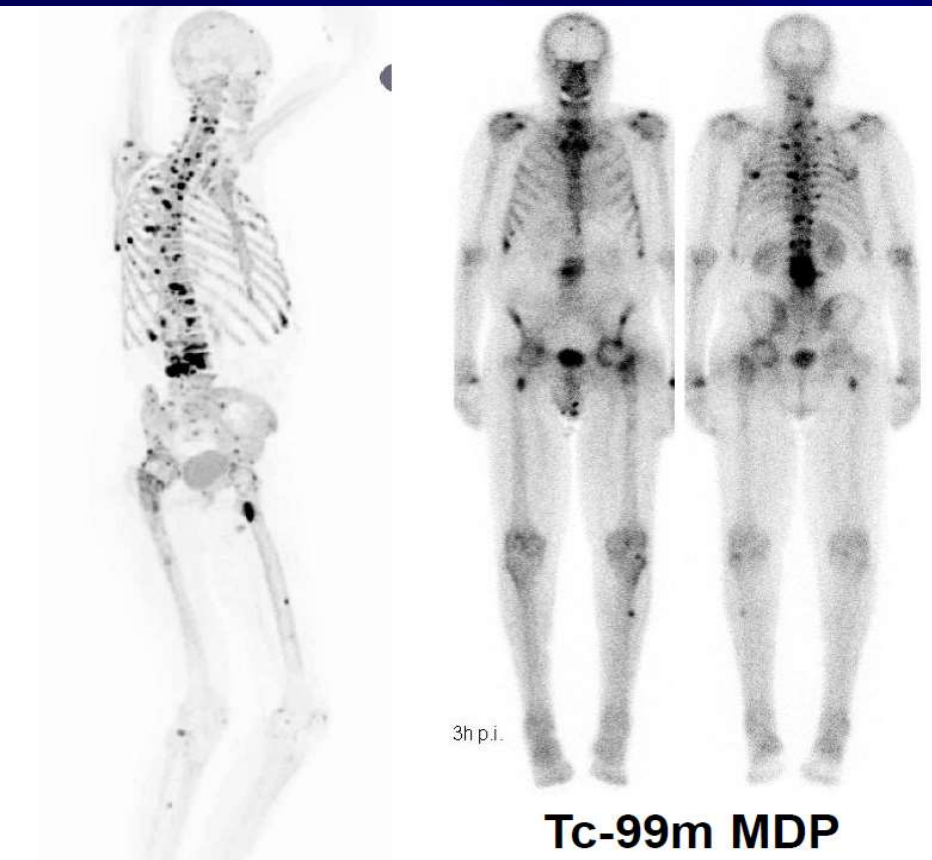
## NON-SPECIFIC TUMOR UPTAKE

- ✓ Increased vascularization.
- ✓ Increased capillary permeability.
- ✓ Newly proliferated capillaries.
- ✓ Increased blood flow.
- ✓ Increased energy demand.
- ✓ Increased metabolically active cells.

# Bone Scan

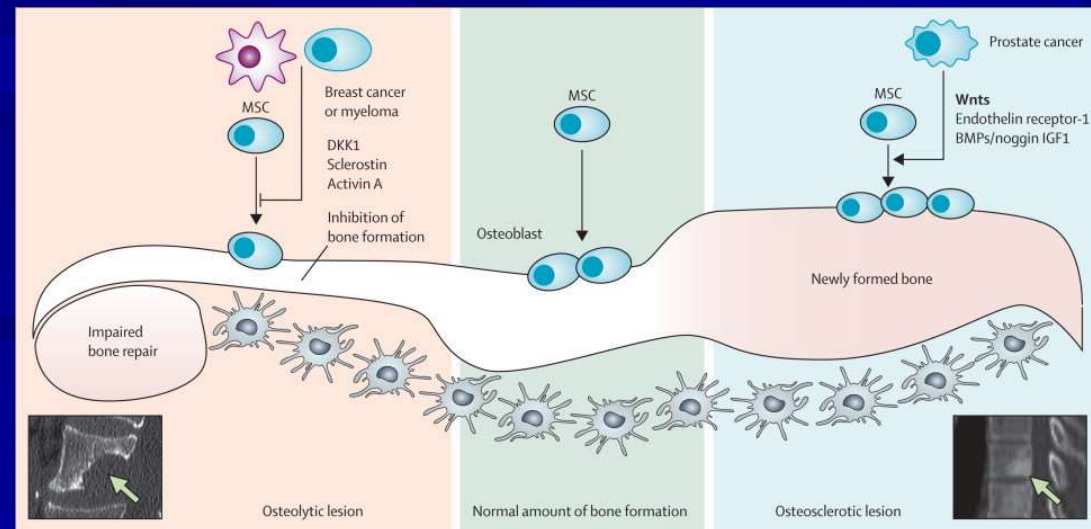
Radiopharmaceuticals: Technetium 99m Methylene DiPhosPhonate (Tc-99m MDP). Bone is composed of Calcium and Phosphate. We label the phosphate with MDP.

**Hot lesions: Focal area with increased uptake.**



The role of bone scan in oncology is:

- 1) detecting metastasis.
- 2) detecting primary tumors.
- 3) evaluate soft tissue tumors of local extent and distant metastasis.



# Bone Scan Indications

## **I. Metastatic Disease: Lung cancer, prostate, breast, thyroid, and renal**

- Initial staging.
- Restaging.
- Asses response to therapy.

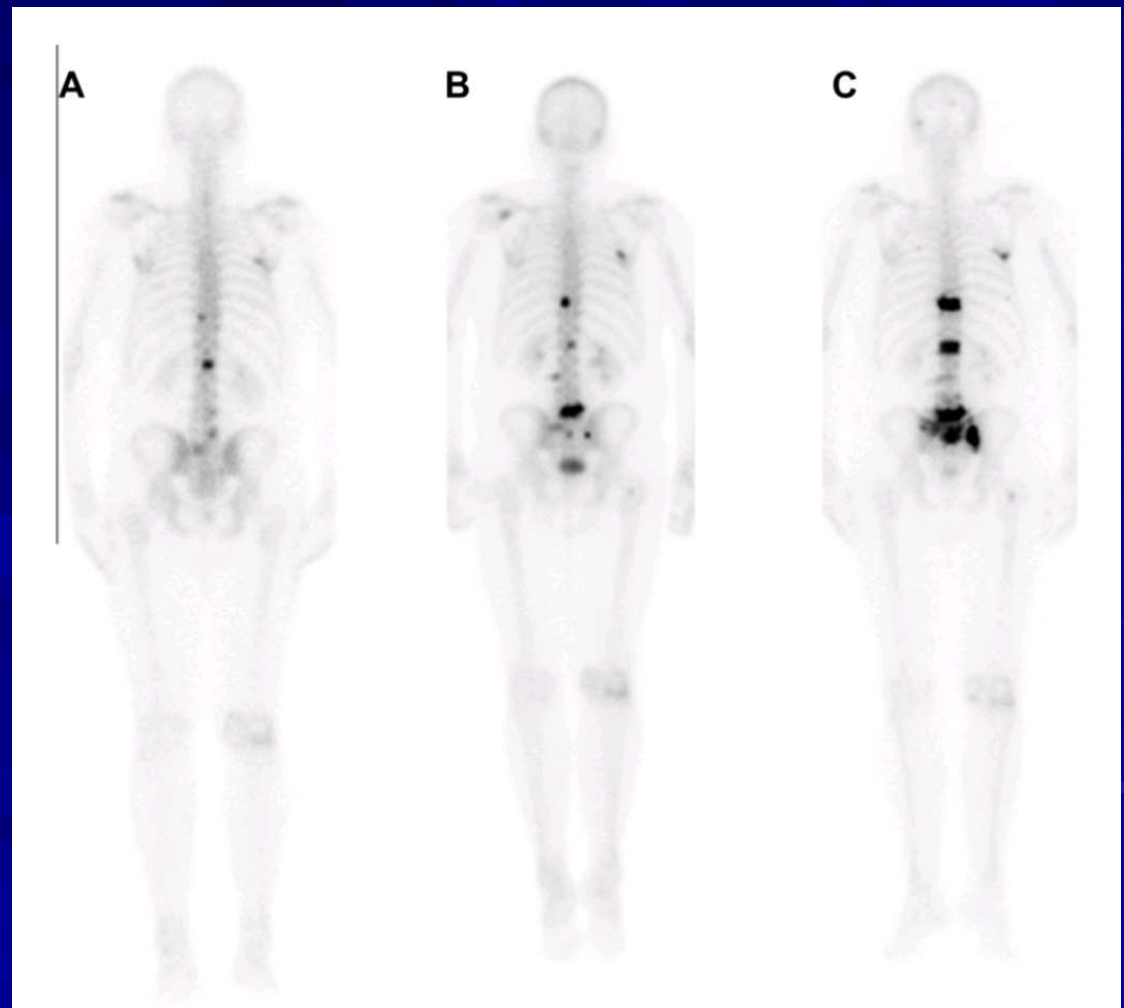
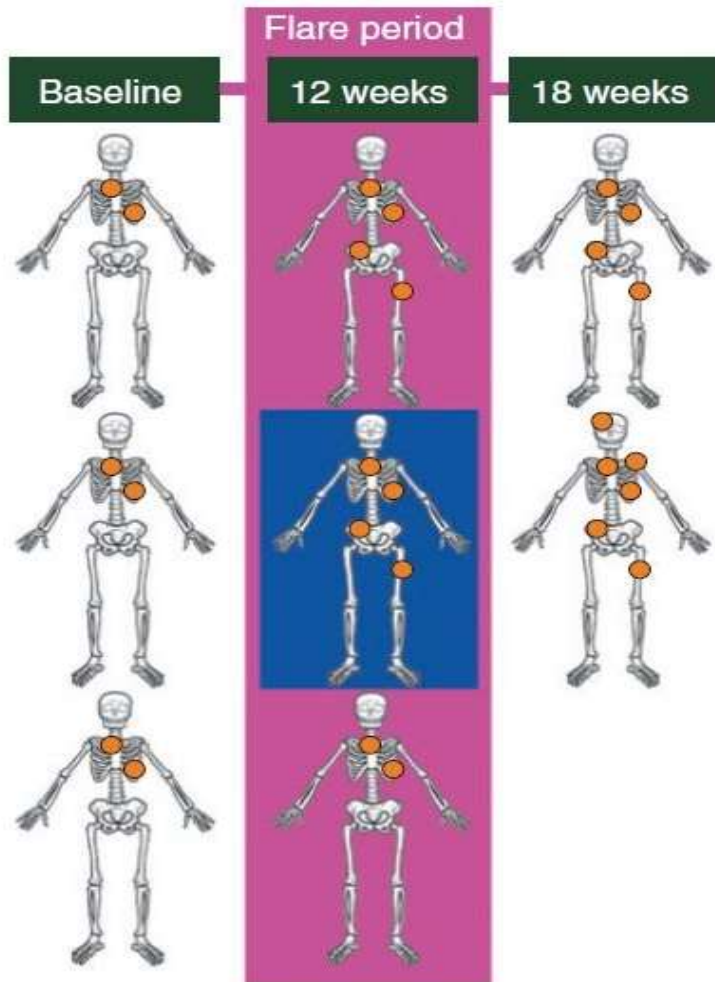
## **II. Primary Bone Tumors:**

- Malignant or Benign.
- Therapy planning for patients with primary bone malignancy (e.g. Osteogenic & Ewing's sarcoma).

## **III. Soft tissue tumors:**

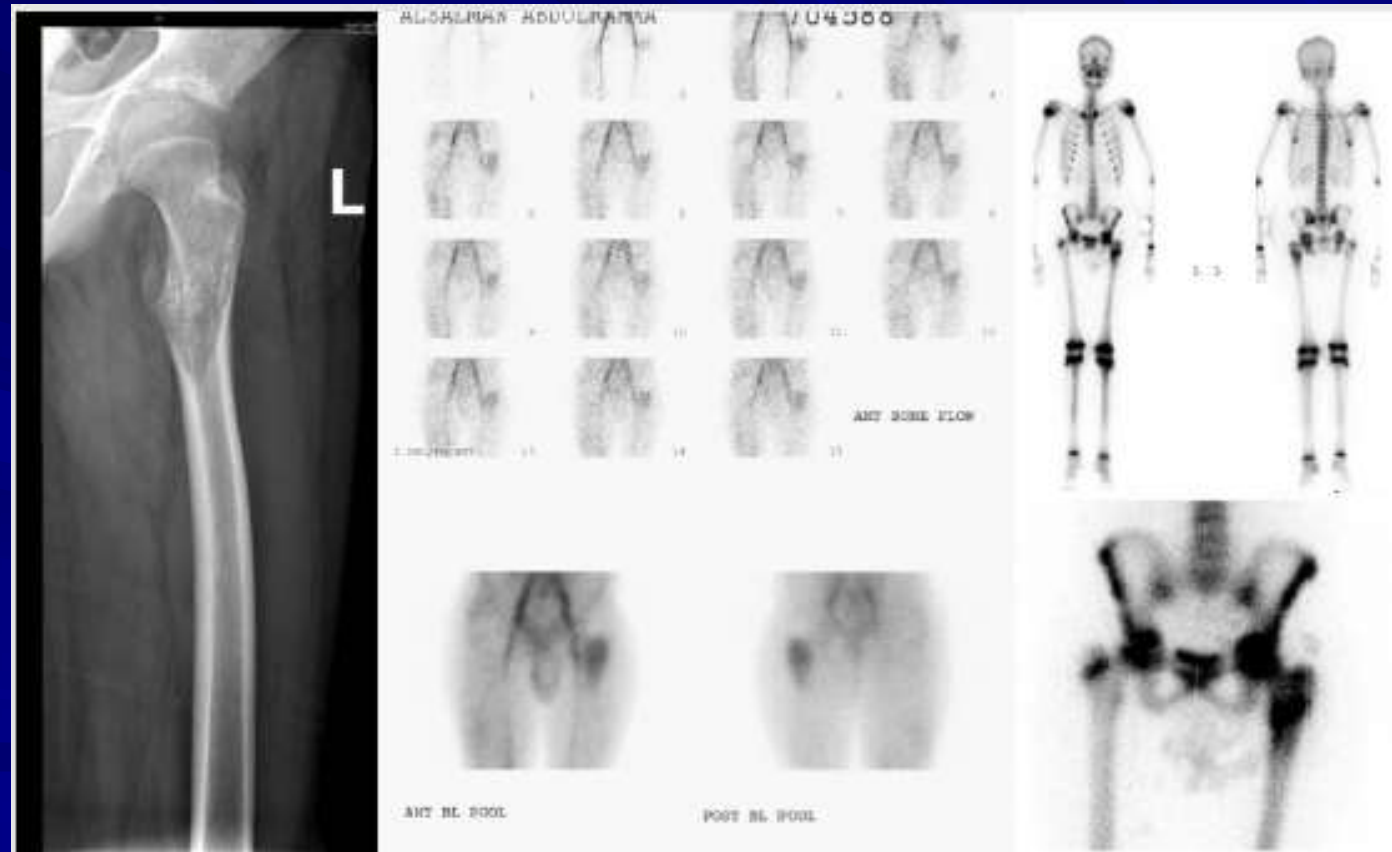
- Primary
- Metastases.

# Bone Scan Tumor Staging



# Ewing's Sarcoma

Usually affects young people, that is why we can see growth plates. The primary diagnosis of bone tumor is To determine the local extent and to search for distant metastasis.

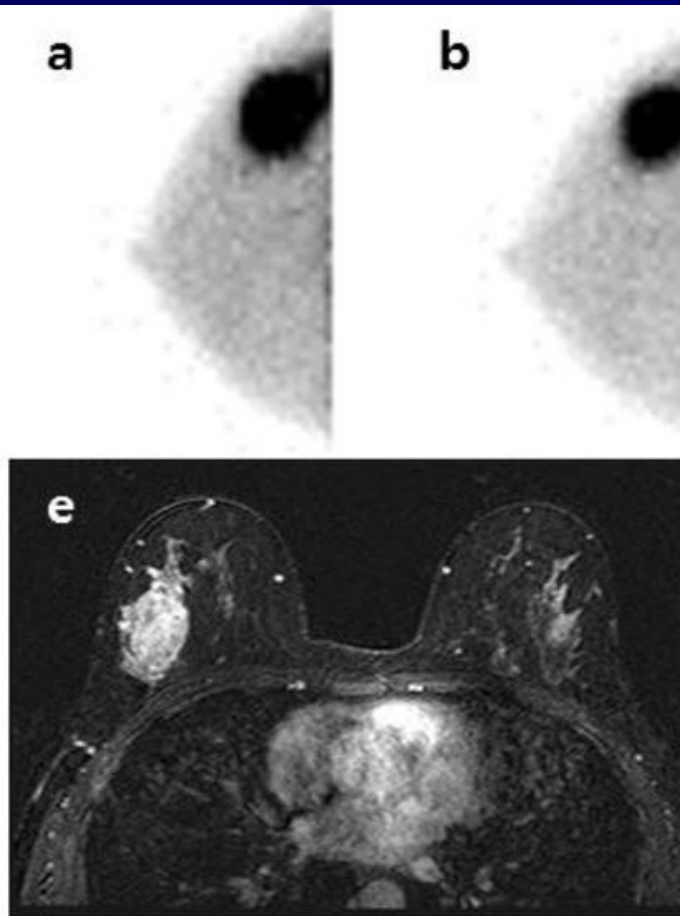


- In this patient the tumor is confined to proximal left femur but rest of skeleton is clear with no metastasis.

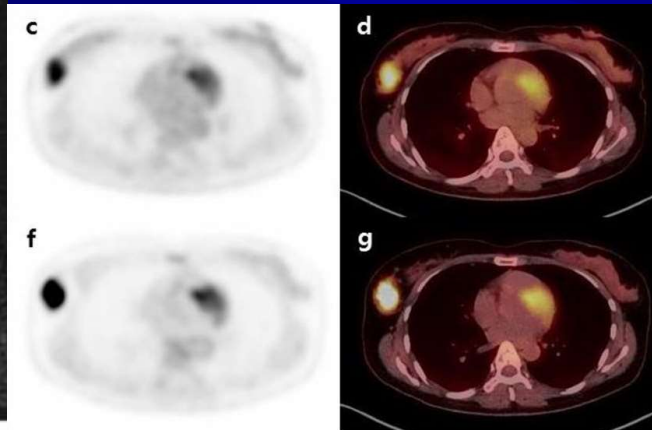


## $^{99m}\text{Tc}$ -MIBI (methoxyisobutyl isonitrile)

CA mamme



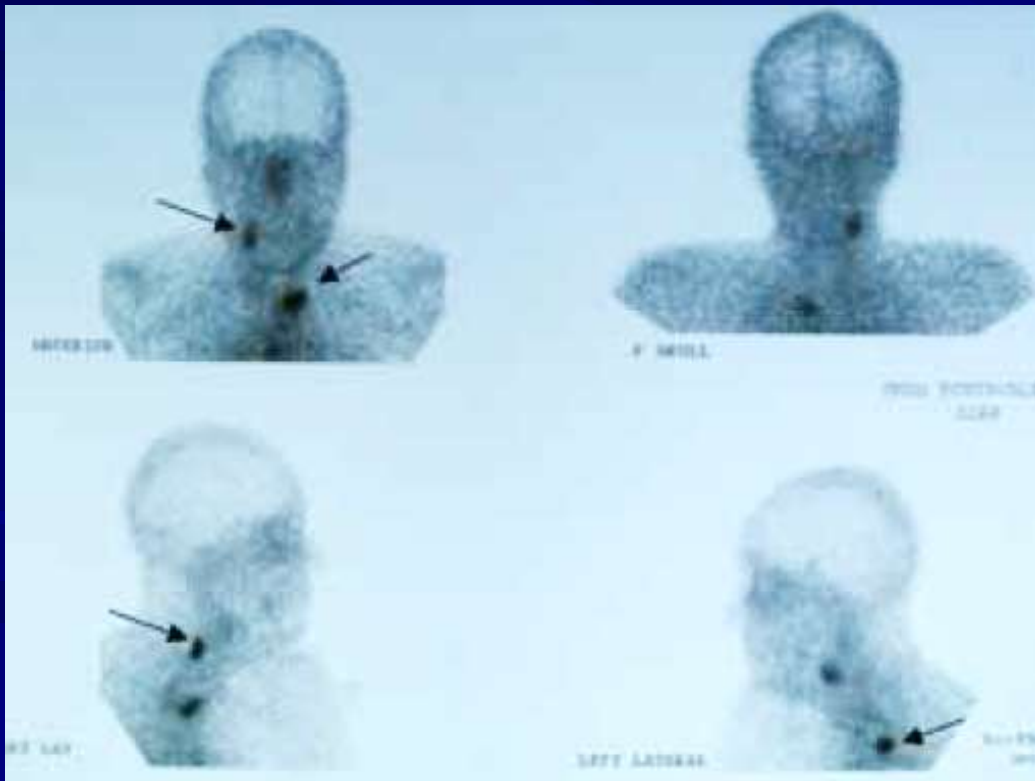
$^{99m}\text{Tc}$ -MIBI scan in different types of malignancy including breast and lung cancer, lymphoma and sarcoma. Mechanisms of cell resistance, mainly involving alterations of apoptosis, may affect uptake in tumors.



	Scintimammography %	X-rays mammography %
Sensitivity	85	89
Specificity	66	14
Positive Predictive value	70	49
Negative Predictive value	83	57

## **$^{99m}\text{Tc}(\text{V})\text{-DMSA}$**

Pentavalent dimercaptosuccinic acid  
detection of primary and metastatic  
medullary thyroid cancer and various soft  
tissue tumors like lung, brain and prostate



## **Medullary Thyroid Cancer**

Thyroid cancers are classified as  
papillary, follicular (including Hürthle  
cell), medullary, and anaplastic.  
(MTC) constitutes about 3-10% of all  
thyroid cancers

$^{99m}\text{Tc}(\text{V})\text{-DMSA}$  (50%-80%)

$^{111}\text{In}$ -pentetreotide (Octreoscan)

$^{99m}\text{Tc}$ -Depreotide (Neospect)

$^{99m}\text{Tc}$ -EDDA/HYNIC-TOC (Tektrotyd)

$^{18}\text{F}$ -DOPA

$^{68}\text{Ga}$ -DOTATOC/TATE 72%

$^{131}\text{I}$ -MIBG (30%)

74% and 87%



# TUMOR-SEEKING RF

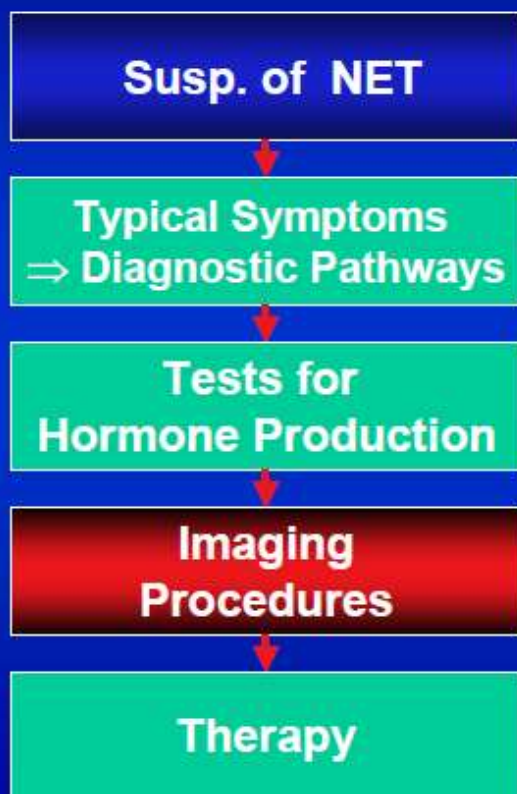
“POSITIVE” UPTAKE - MORE INTENSIVE ACCUMULATIONS OR  
"HOT" SPOTS WHERE THE TUMOR IS LOCATED IN THE BODY

## SPECIFIC TUMOR UPTAKE

1. High density of some common receptors .
2. Expression of several specific receptors.
3. Expression of some specific tumor antigens.

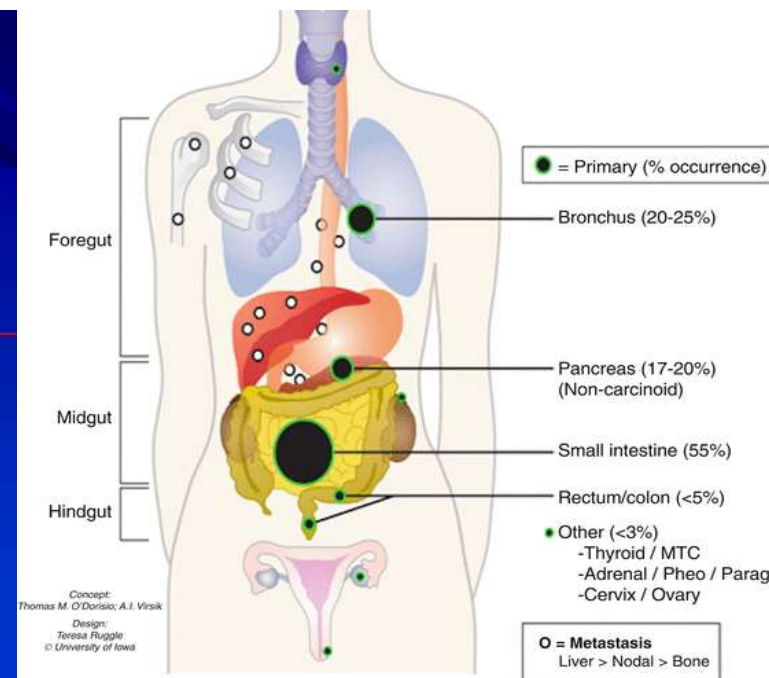
# Somatostatin Receptor Imaging

## Neuroendocrine Tumors (NET) – Diagnosis –



### Diagnostic Methods:


- (Endo-) Sonography
- Endoscopy
- MRI (CT Scan)
- Somatostatin Receptor PET/CT or Scintigraphy (SRS)



### *in vitro* receptor status

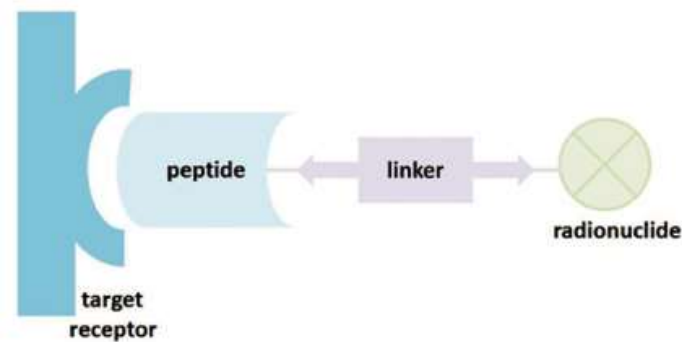
• Gastrinoma, Glucagonoma	100 %
• Insulinoma	72 %
• Paraganglioma	92 %
• MTC	38 %
• Carcinoid	88 %
• SCLC	57 %
• Pheochromocytoma	73 %

# Dg management

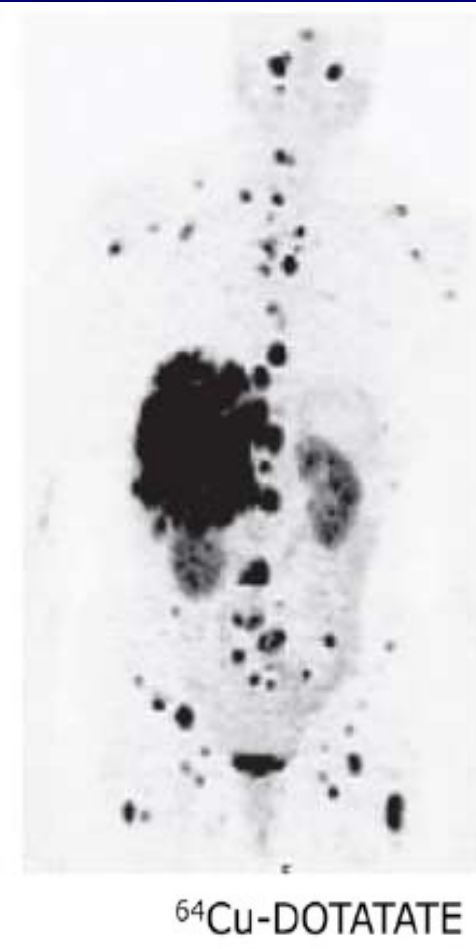
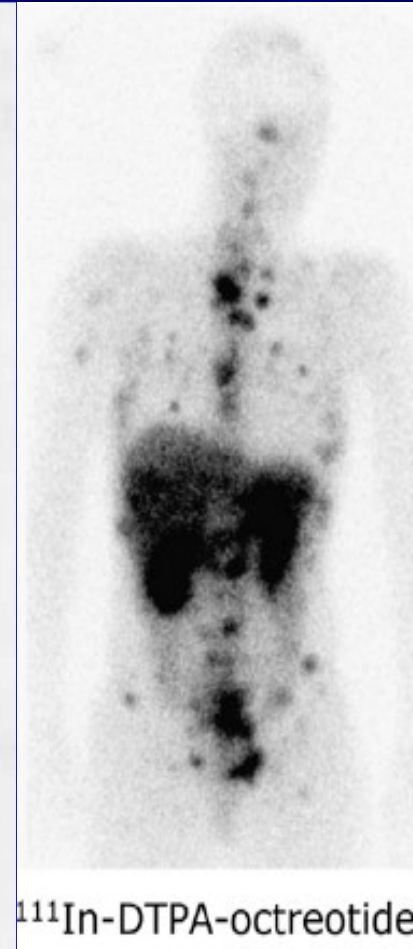
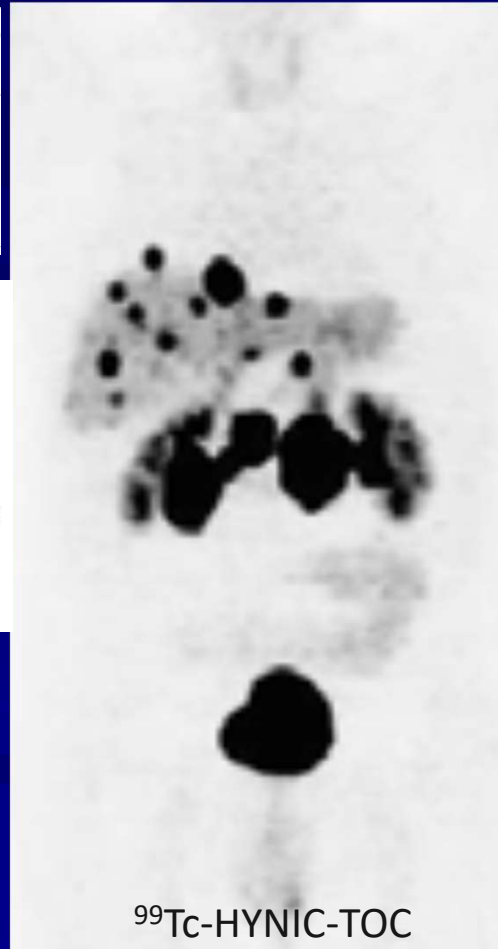
	Well-differentiated		Poorly differentiated
Grade (ENETS)	Low (G1)	Intermediate (G2)	High (G3)
Ki-67 index (%)	≤2	3-20	>20
Anatomic imaging	more rapid growth on serial imaging		
Functional imaging			
Prognosis	Indolent (slowly growing)		Aggressive
Treatment options	Surgery for localised +/- resectable metastatic disease		
	Observation Somatostatin analogues Radionuclide therapy		Chemotherapy
	Everolimus, sunitinib, α-interferon Liver metastases: radiofrequency ablation, hepatic embolisation, TACE, SIR-Spheres		

# SSTR imaging

Tumor	SST1 (%)	SST2 (%)	SST3 (%)	SST4 (%)	SST5 (%)
Gastrinoma	79 <sup>a</sup>	93	36	61	93
Insulinoma	76	81	38	58	57
Non-functioning pancreatic tumor	58	88	42	48	50
Carcinoid tumor of the gut	76	80	43	68	77

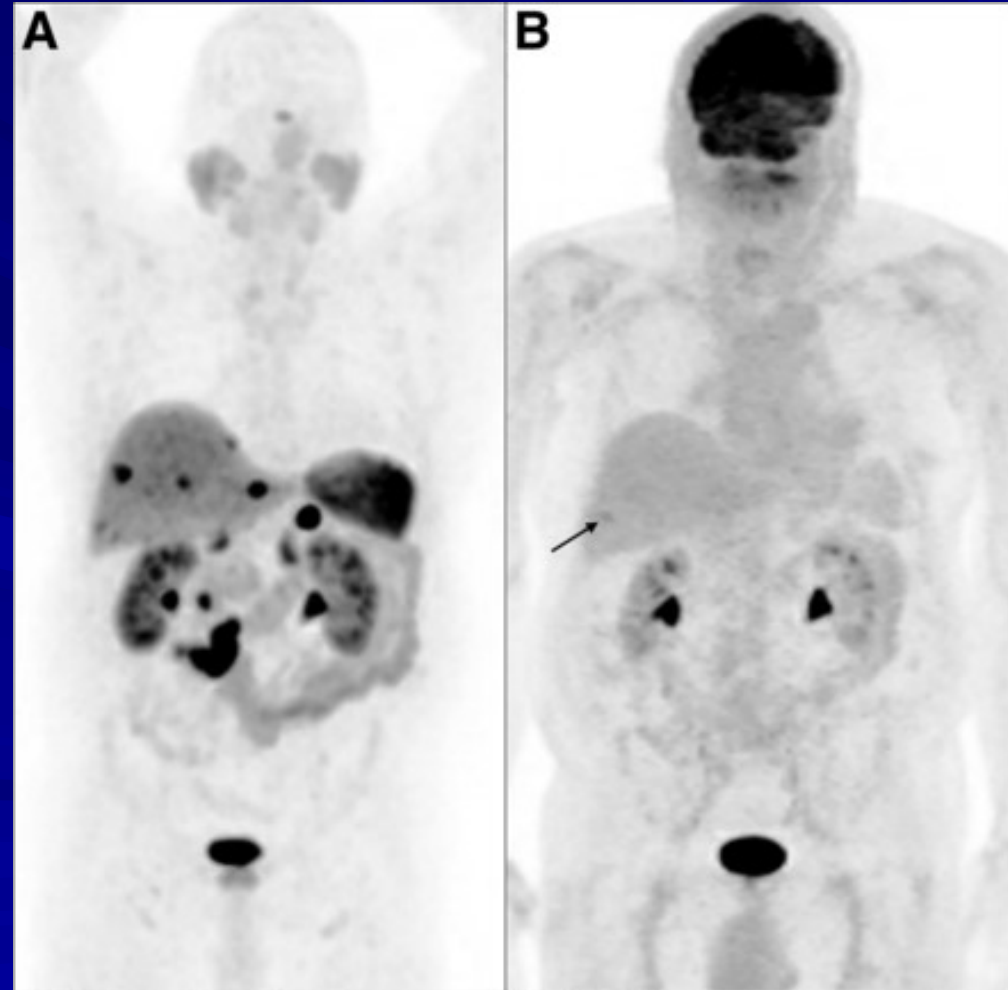


**<sup>111</sup>In-DTPA-octreotide  
(Octreoscan®)**  
**<sup>99m</sup>Tc-HYNIC-TOC  
(Tektrotyd®)**



# SSTR imaging

NET grade 1 (Ki-67 < 2%) NEN from small-bowel primary. (A)  $^{68}\text{Ga}$ -DOTATATE PET shows prominent uptake in primary tumor, lymphadenopathy, and liver metastases. (B)  $^{18}\text{F}$ -FDG PET shows no abnormal uptake (arrow points out incidentally noted fractured rib).



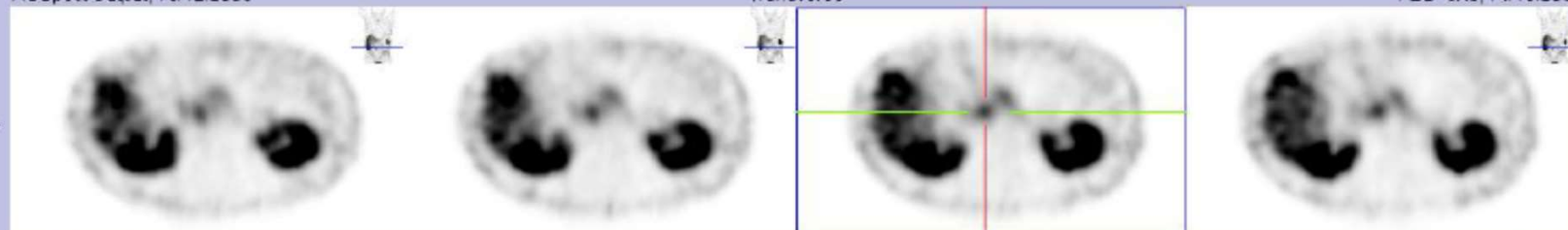


WBSpect Output, 10/12/2008

Transverse

ABD 8X8, 14/10/2008

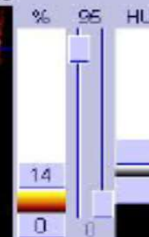
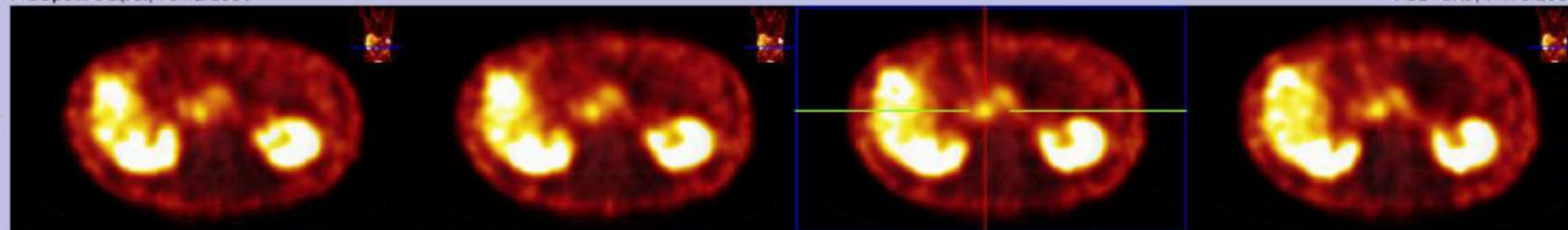
A



WBSpect Output, 10/12/2008

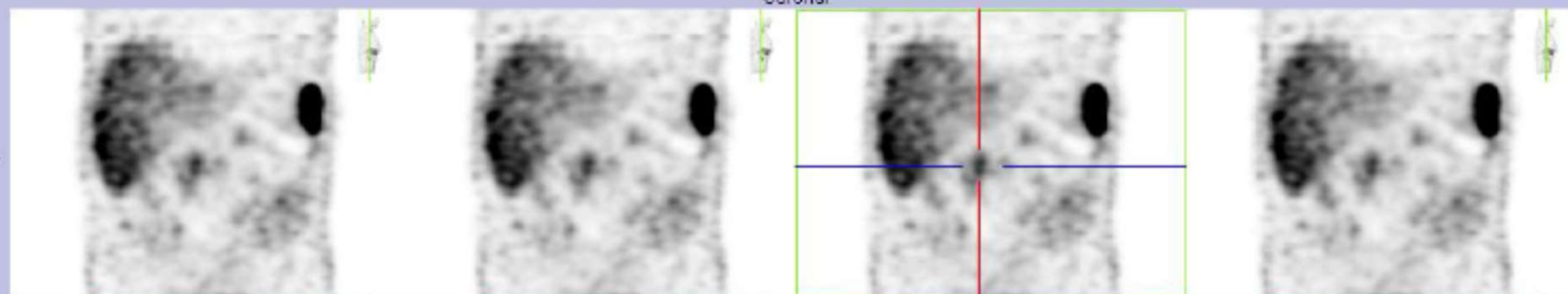
ABD 8X8, 14/10/2008

C

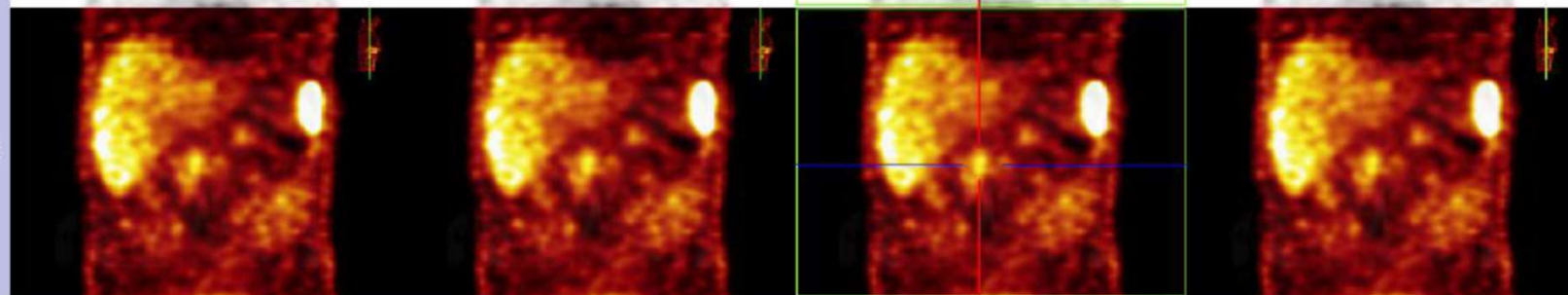


Coronal

A



C

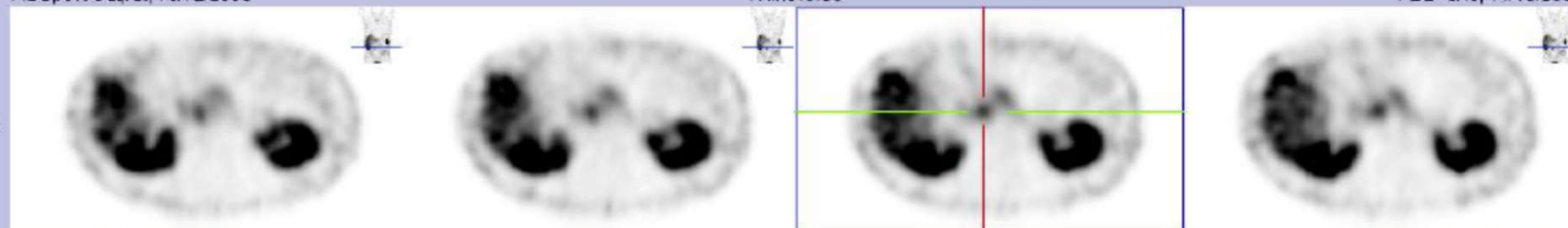


WBSpect Output, 10/12/2008

Transverse

ABD 8X8, 14/10/2008

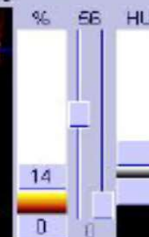
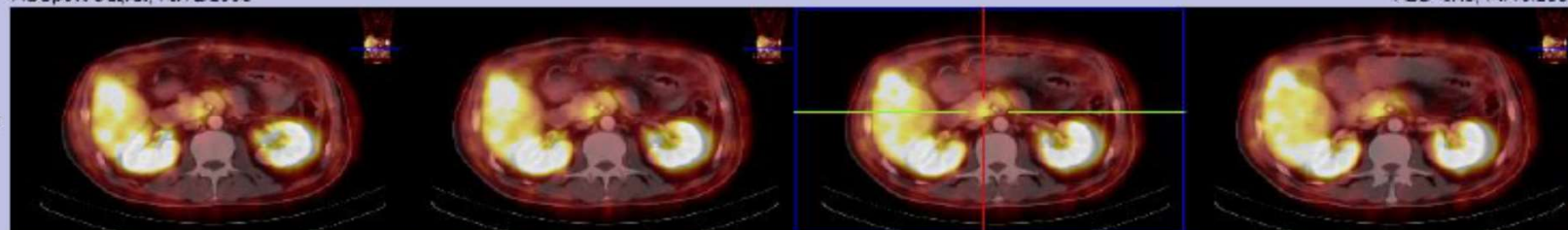
A



WBSpect Output, 10/12/2008

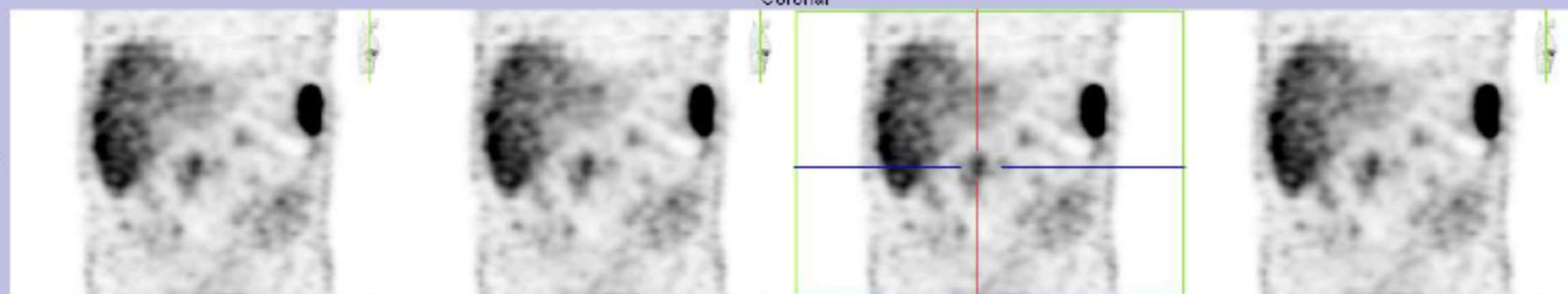
ABD 8X8, 14/10/2008

C

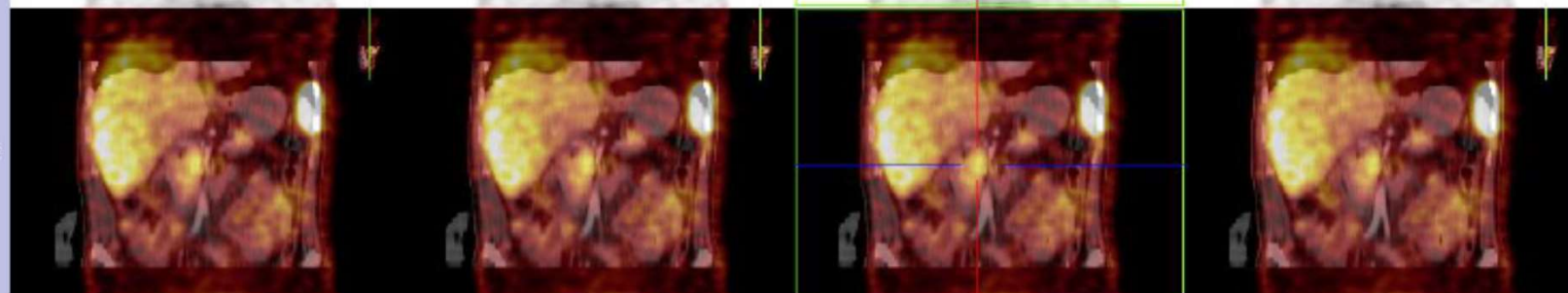


Coronal

A



C

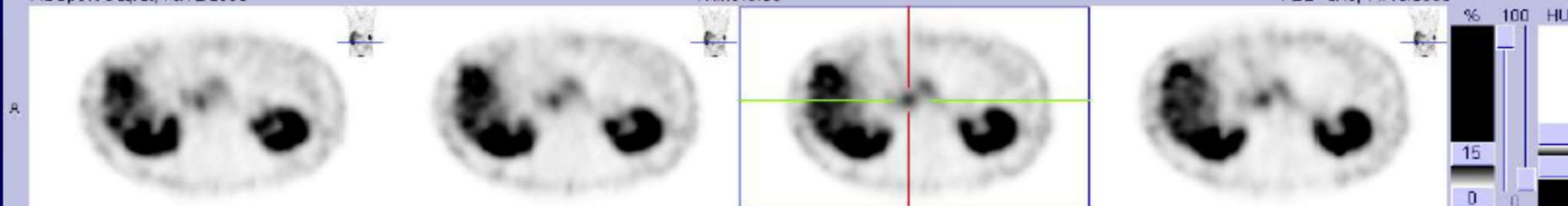




WBSpect Output, 10/12/2008

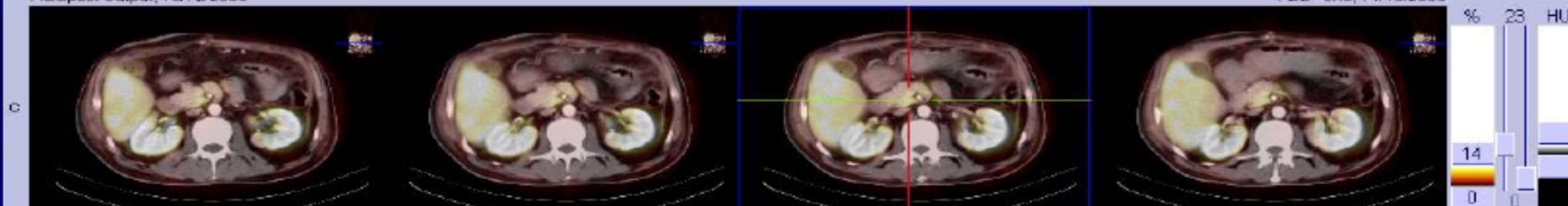
Transverse

ABD 8x8, 14/10/2008

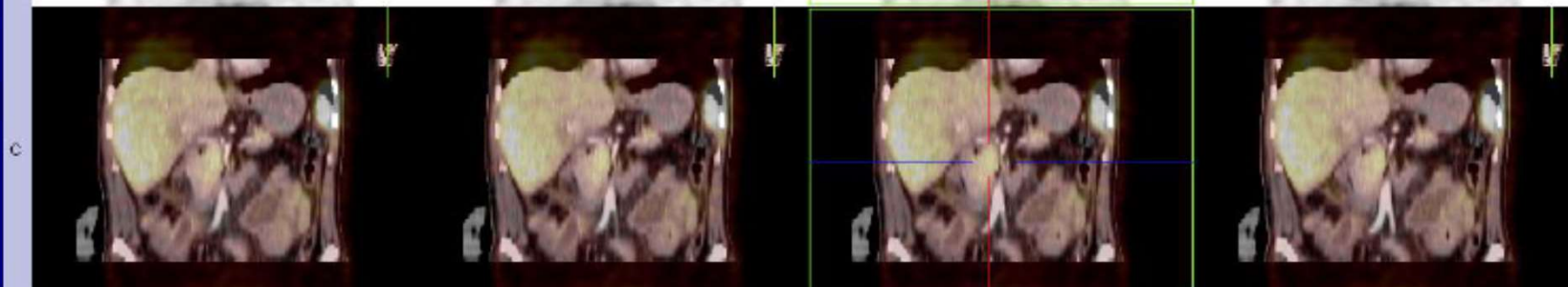
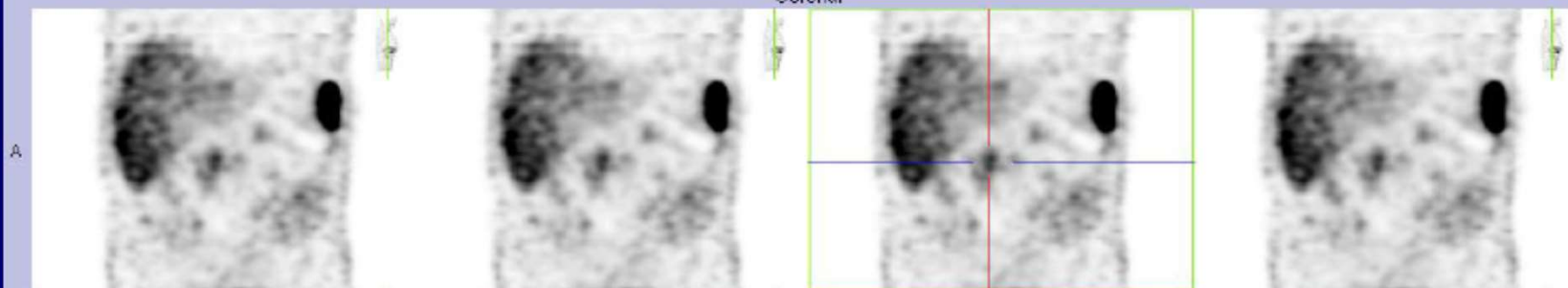


WBSpect Output, 10/12/2008

ABD 8x8, 14/10/2008

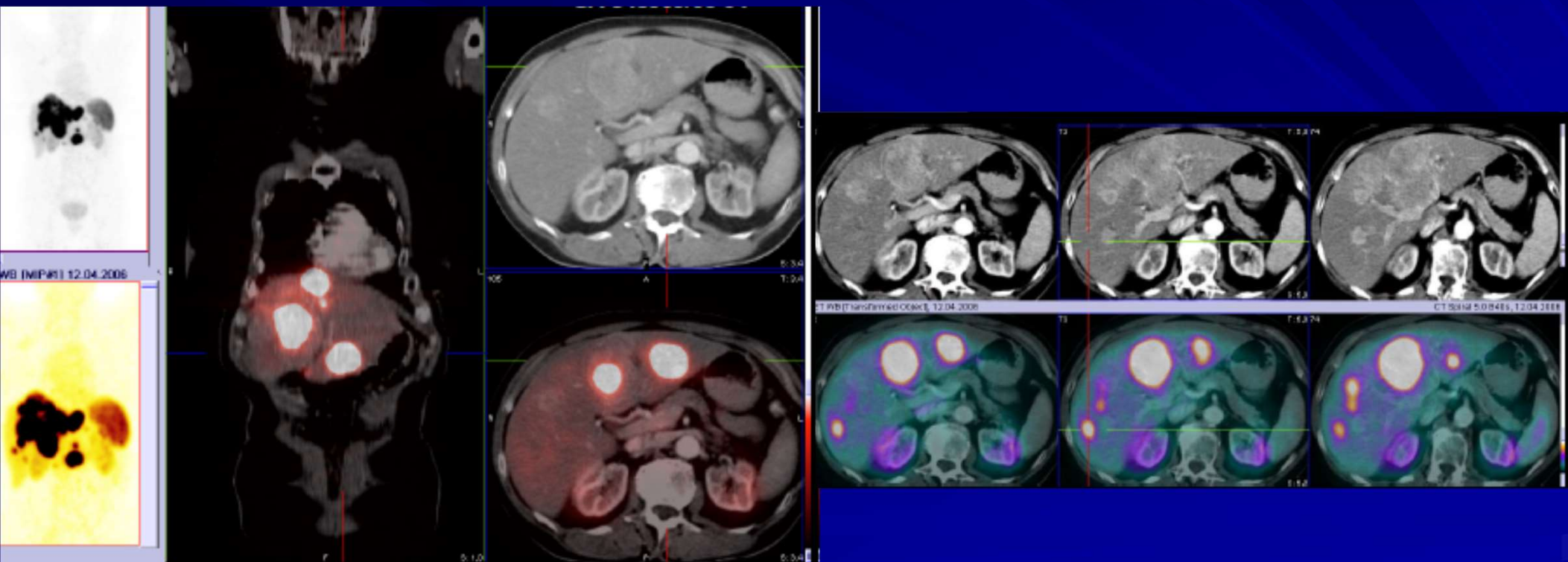


Coronal



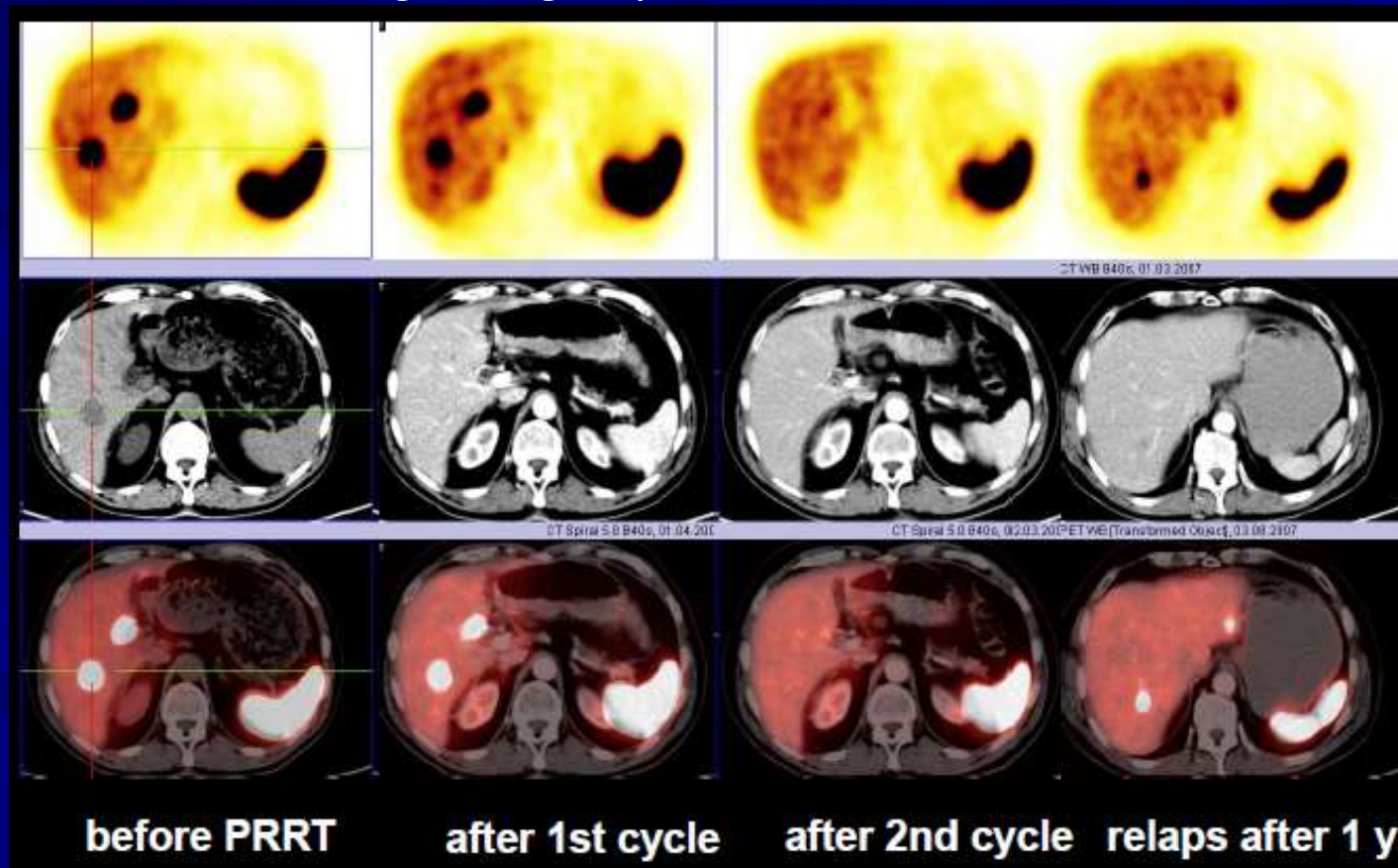
# SSTR Staging

e.g. before PRRT, evaluation of receptor status, detection of unknown primary tumors (CUP syndrome)



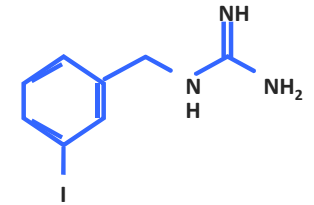
## Re-staging, Follow-up

e.g. in patients with rising tumor markers (chromogranin, serotonin, calcitonin, glucagon) for detection of recurrence

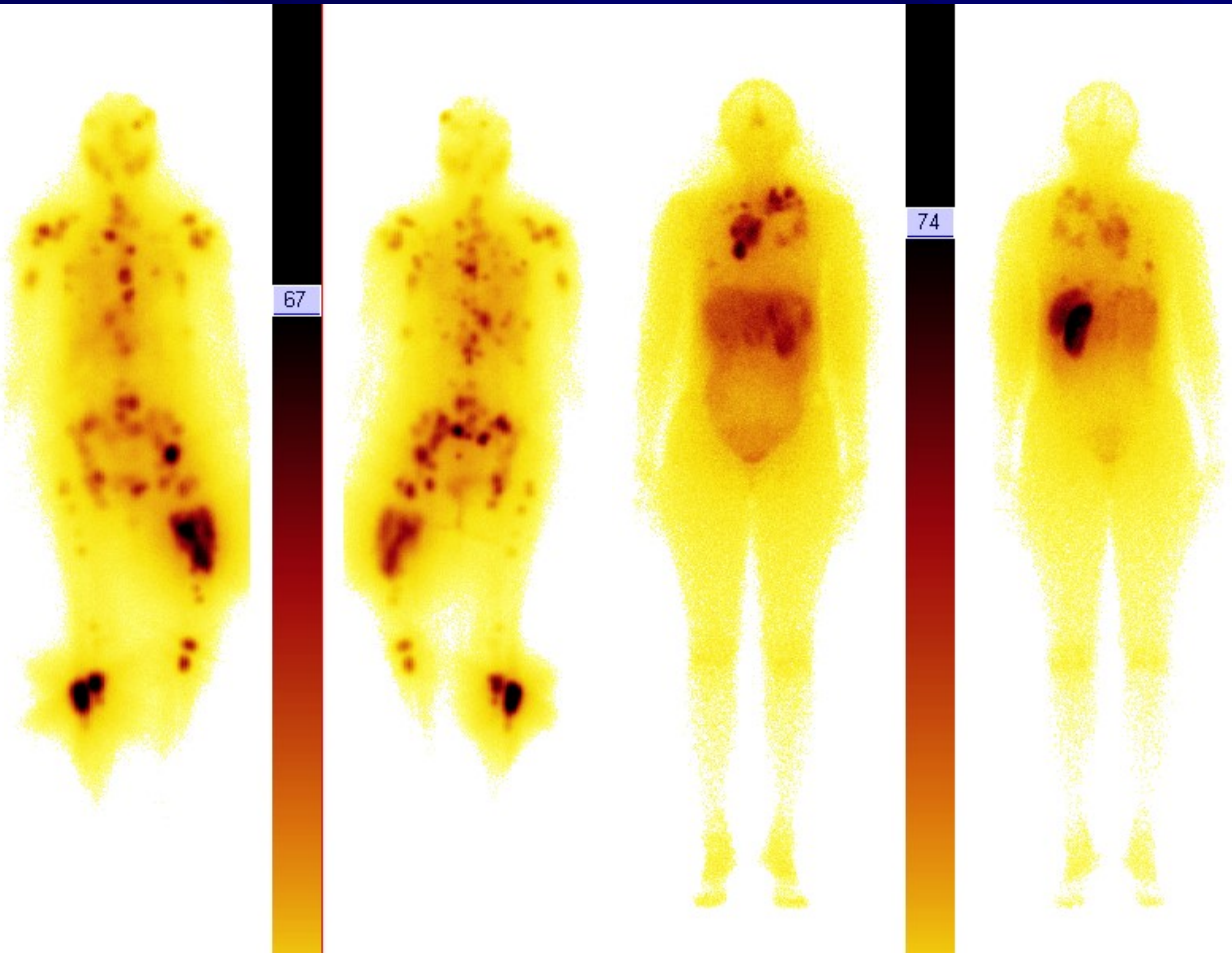




## <sup>31</sup>I-MIBG Meta Iodo Benzyl Guanidine.



Meta-iodobenzylguanidine  
(MIBG)

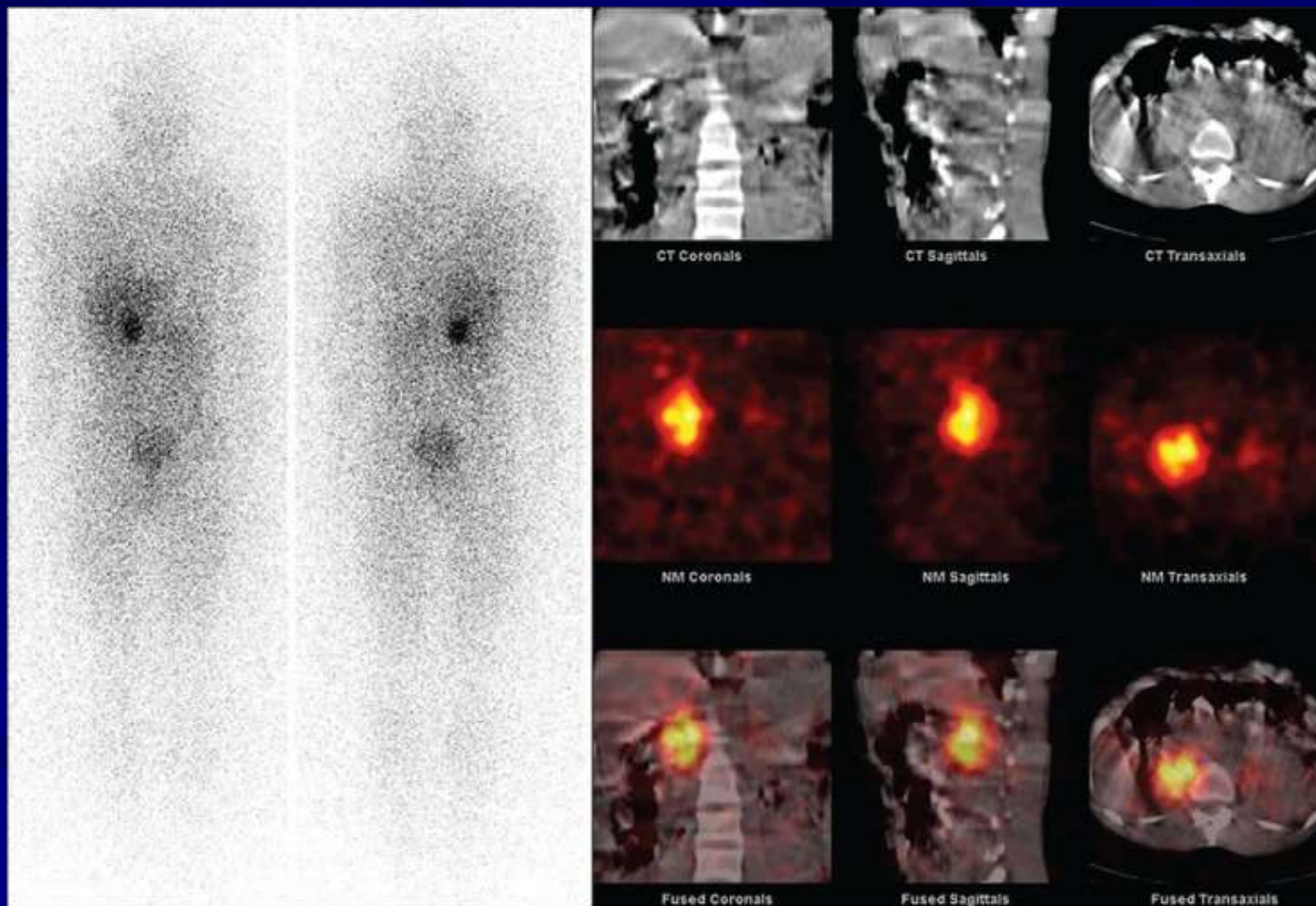


Is a noradrenaline analog.  
Localizes in adrenergic tissues:  
catecholamines producing tumors  
and their metastases.

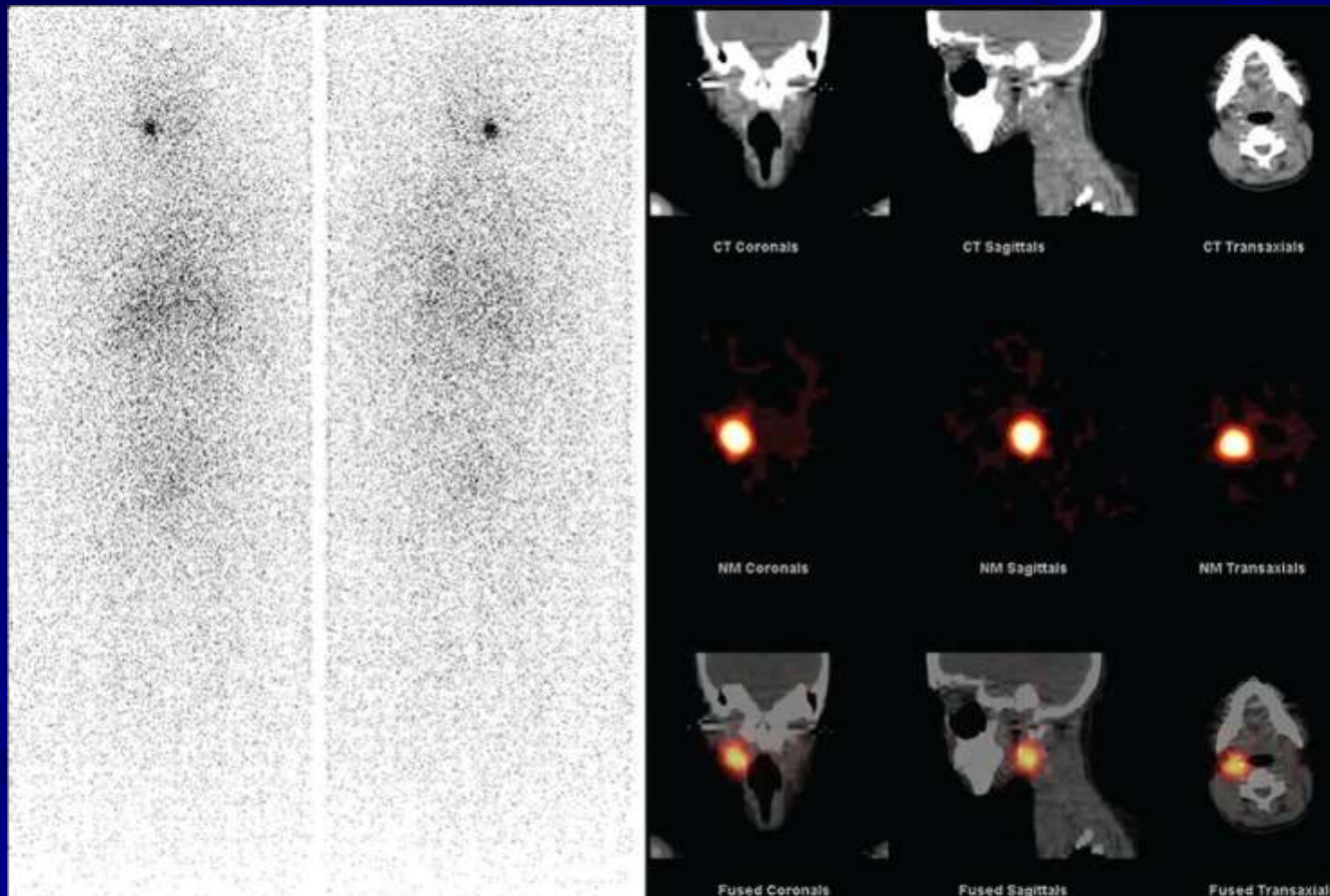
### Indications:

- ❖ Pheochromocytoma.
- ❖ Paraganglioma.
- ❖ Insulinoma.
- ❖ Neuroblastoma.
- ❖ Medullary thyroid carcinoma.
- ❖ Carcinoid tumors

## $^{131}\text{I}$ -mIBG Pheochromocytoma gl. suprarenalis dex.



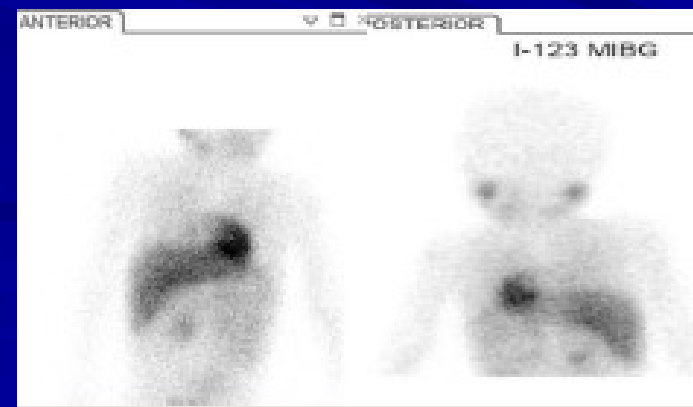
## $^{131}\text{I}$ -mIBG - Paraganglioma carotid body dex.



## **$^{31}\text{I}$ -MIBG** Meta Iodo Benzyl Guanidine.

### Neuroblastoma:

- A common tumor in children under the age of five.
- They usually present complaining of abdominal masses.
- The role of MIBG scan is to detect the primary tumor and distant metastases.
- Planner image shows a focal area of abnormal uptake in the abdomen.
- SPECT CT shows its exact localization.

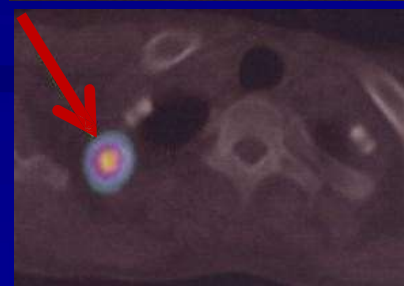
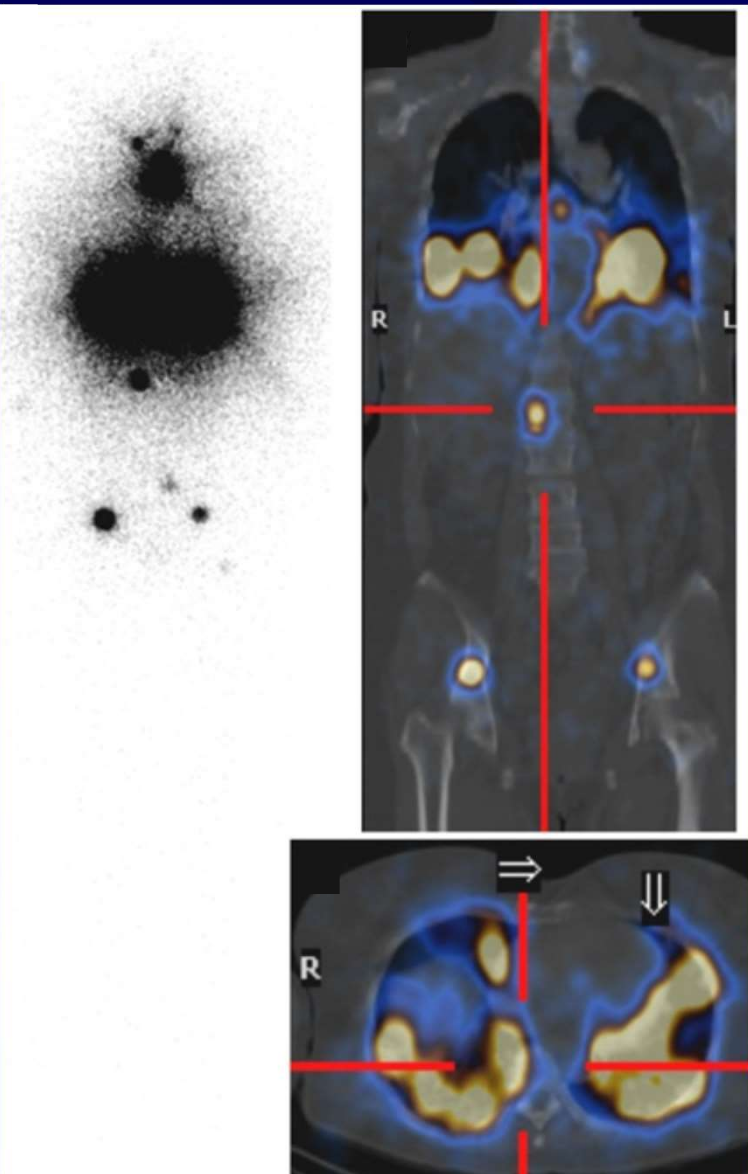




## Thyroid Metastases Study (I-123 or I-131 as Sodium Iodide)

### Indications:

Detection and localization of persistent or recurrent local or distant functioning thyroid cancer.

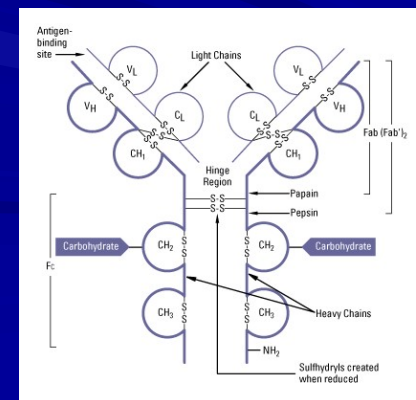
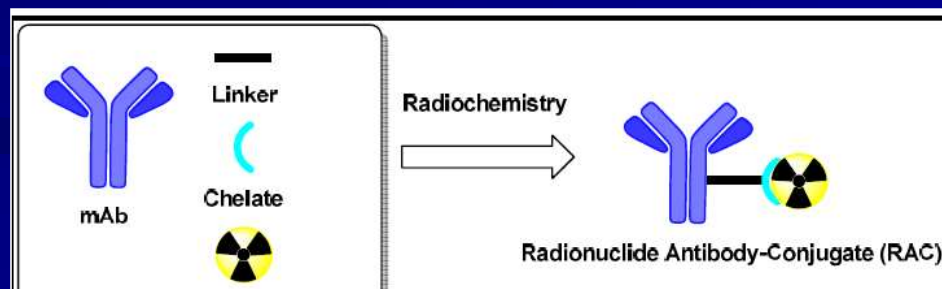


# TUMOR-SEEKING RF

“POSITIVE” UPTAKE - MORE INTENSIVE ACCUMULATIONS OR  
"HOT" SPOTS WHERE THE TUMOR IS LOCATED IN THE BODY

## Ag-Ab SPECIFIC TUMOR UPTAKE

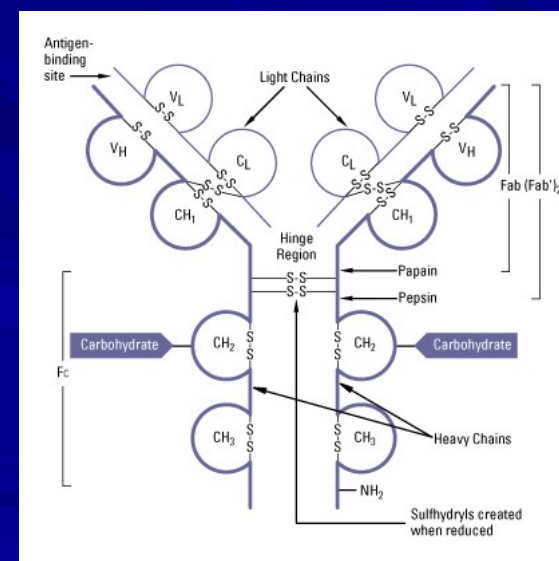
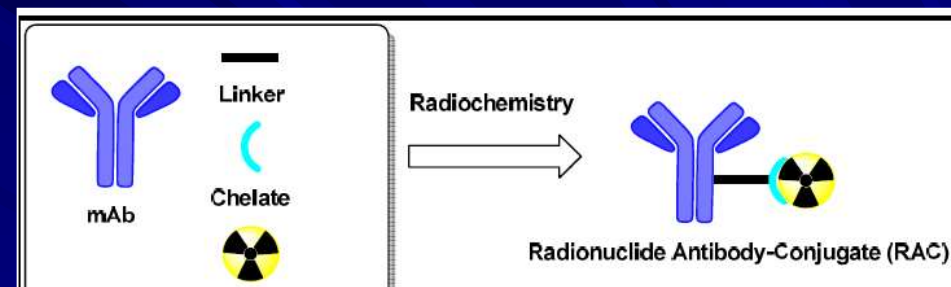
Radioimmunosintigraphy is presented as a new imaging modality in nuclear medicine, using specific antigen-antibody interactions. Monoclonal antibodies to tumor-associated antigens facilitate the characterization of molecular differences between tumors and normal cells. Labelled with gamma-emitting radioisotopes like I-131, I-123, In-111, and Tc99M, these antibodies can be used for in-vivo imaging



# ТУМОРОТРОПНИ РАДИОФАРМАЦИ

Специфична акумулација у тумору  
(имунска специфичност Ag-Ab)

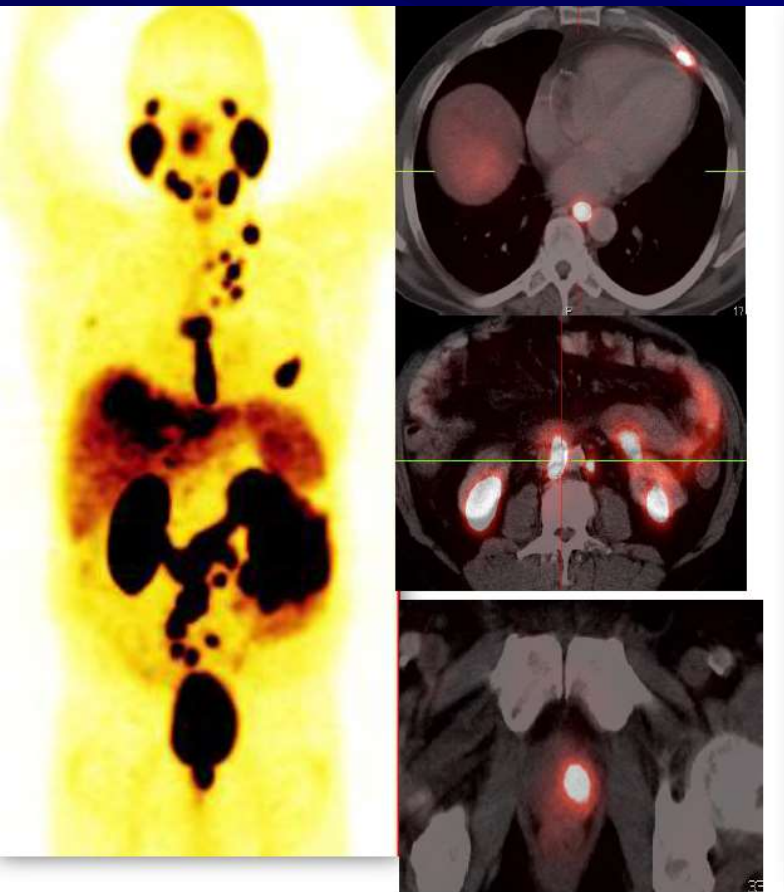
<b><math>^{111}\text{In}</math>-ANTI CEA</b>	<b>КОЛОРЕКТАЛНИ СА, МТС</b>
<b><math>^{111}\text{In}</math>-B 72-3</b>	<b>КОЛОРЕКТАЛНИ СА, СА ОВАРИЈУМА</b>
<b><math>^{99\text{m}}\text{Tc}</math>-MOV 18</b>	<b>СА ОВАРИЈУМА</b>
<b><math>^{111}\text{In}</math>-OVTL 3</b>	<b>СА ОВАРИЈУМА</b>
<b><math>^{111}\text{In}</math>-OC 125</b>	<b>СА ОВАРИЈУМА</b>
<b><math>^{99\text{m}}\text{Tc}</math>-225 .28S</b>	<b>ММ</b>
<b><math>^{99\text{m}}\text{Tc}</math>-NR-LU 10</b>	<b>СА ПЛУЋА</b>
<b><math>^{111}\text{In}</math>-ANTI MIOZIN</b>	<b>РАБДОМИОСАРКОМ</b>
<b><math>^{131}\text{I}</math>-ANTI CEA+ANTI DTPA</b>	<b>МТС</b>
<b><math>^{111}\text{In}</math>-CYT 356</b>	<b>СА ПРОСТАТЕ</b>
<b><math>^{99\text{m}}\text{Tc}</math>-CYT 351</b>	<b>СА ПРОСТАТЕ</b>
<b><math>^{131}\text{I}</math>-ANTI CEA+ANTI CA 19-9</b>	<b>СА КОЛОНА</b>



# PROSTATE CANCER

anti-PSMA At

$^{111}\text{In}$  capromab pendetide (Prostascint)



National  
Comprehensive  
Cancer  
Network®

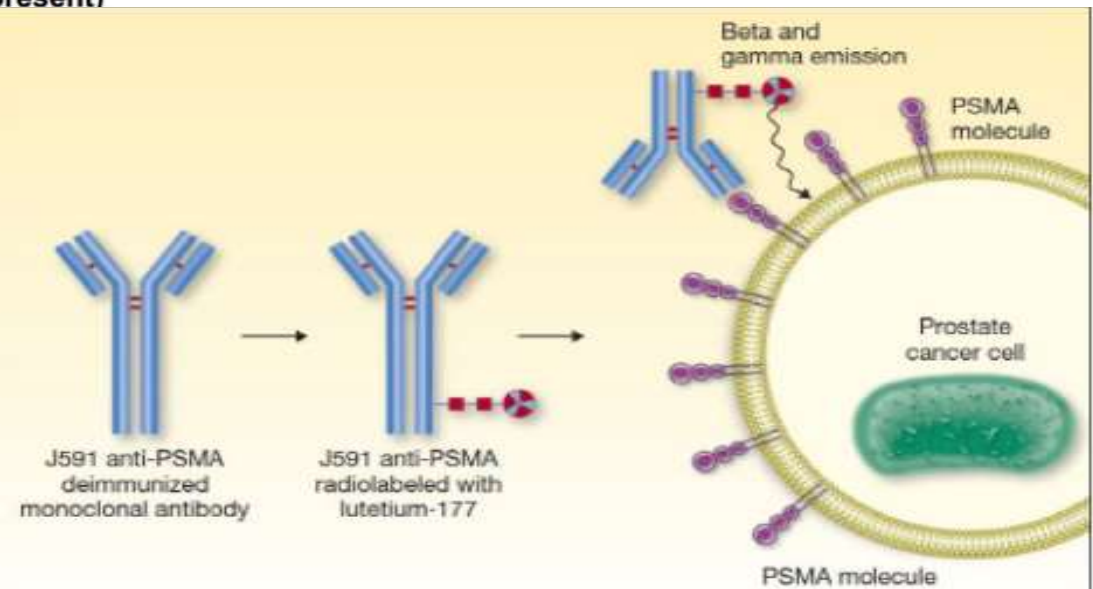
## NCCN Guidelines Version 4.2022 Prostate Cancer

Prior docetaxel and prior novel hormone therapy<sup>iii,ooo</sup>

• Useful in certain circumstances

▶ Lutetium Lu 177 vipivotide tetraxetan (Lu-177-PSMA-617) for PSMA-positive metastases (category 1)<sup>sss</sup>

(The following systemic therapies are category 2B if visceral metastases are present)



© 2013 American Association for Cancer Research



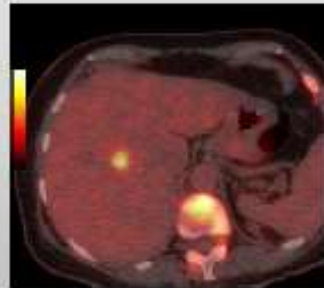
# BREAST CANCER

## ■ HER2/neu receptor (human epidermal growth factor 2)

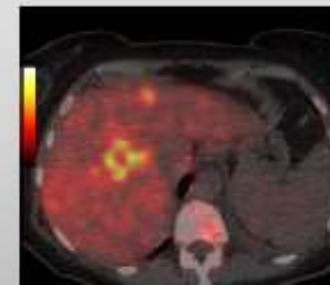
$^{89}\text{Zr}$ -labeled mAbs in (pre-)clinical trials:



FDG  
1 h p.i.



Zr89-trastuzumab  
4 days p.i.



G. Gebhart & P. Flamen  
Jules Bordet Institute, Brussels



# FUNCTIONAL *IN VIVO* DIAGNOSTIC

Radioguided  
surgery



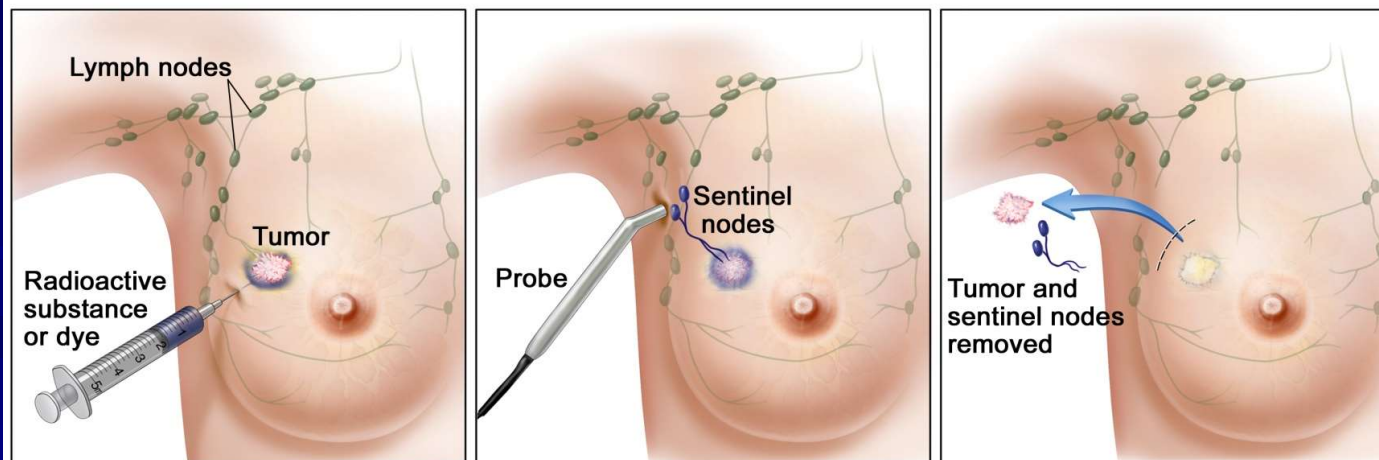
# LYMPHOSCINTIGRAPHY

preoperative and/or intraoperative detection of metastatic involvement of one or more so-called sentinel lymph nodes (English: sentinel - guardian), that is, lymph nodes that, depending on the localization of the examined malignant tumor, are first affected by lymphatic drainage from the tumor tissue.

colloids with specific characteristics labeled with  $^{99m}\text{Tc}$  is applied to the tumor or its surroundings. Preoperative lymphoscintigraphy aims to facilitate the surgeon's planning and execution of the following surgical intervention, i.e. accelerate the intraoperative detection of sentinel nodes.

During the surgical intervention itself, the suspicious sentinel lymph node is first identified, thanks to the previous application of radiocolloid and registration of radioactivity in the zone of the operative field using a scintillation detector.

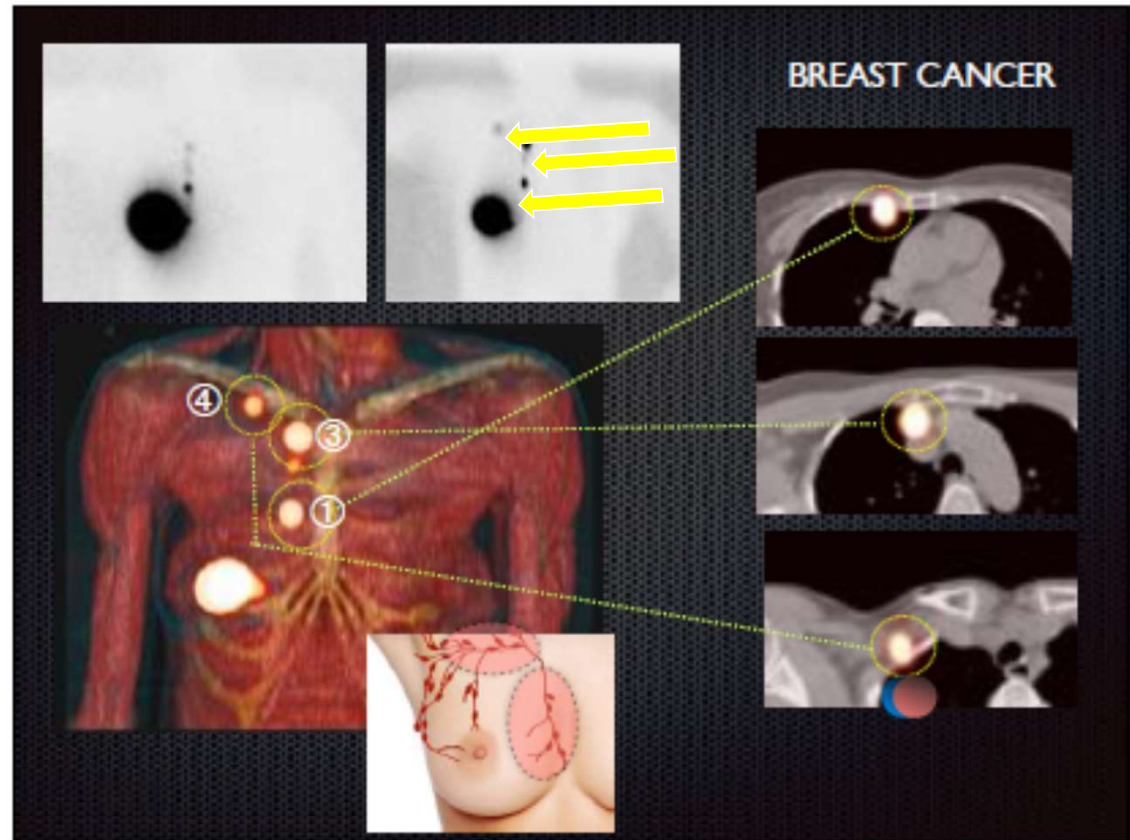
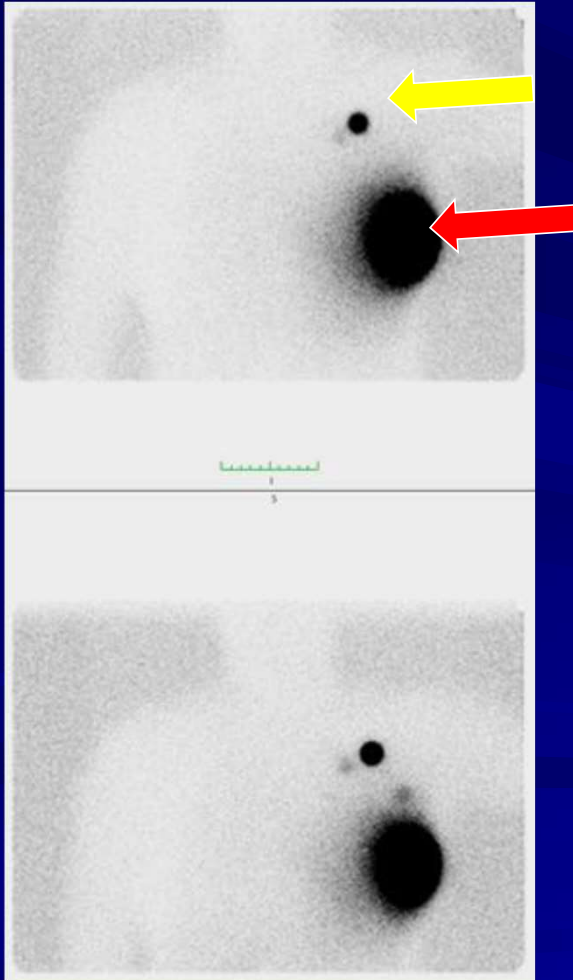
- Extirpation and ex tempore histological diagnosis are performed. If, however, it is established that the sentinel lymph node(s) is not affected by metastasis, the surgical intervention that follows is significantly smaller, and the prognosis of the malignant disease is very good and vice versa.
- Both nuclear medicine methods (or only intraoperative) are most often applied in breast cancer and malignant melanoma surgery.



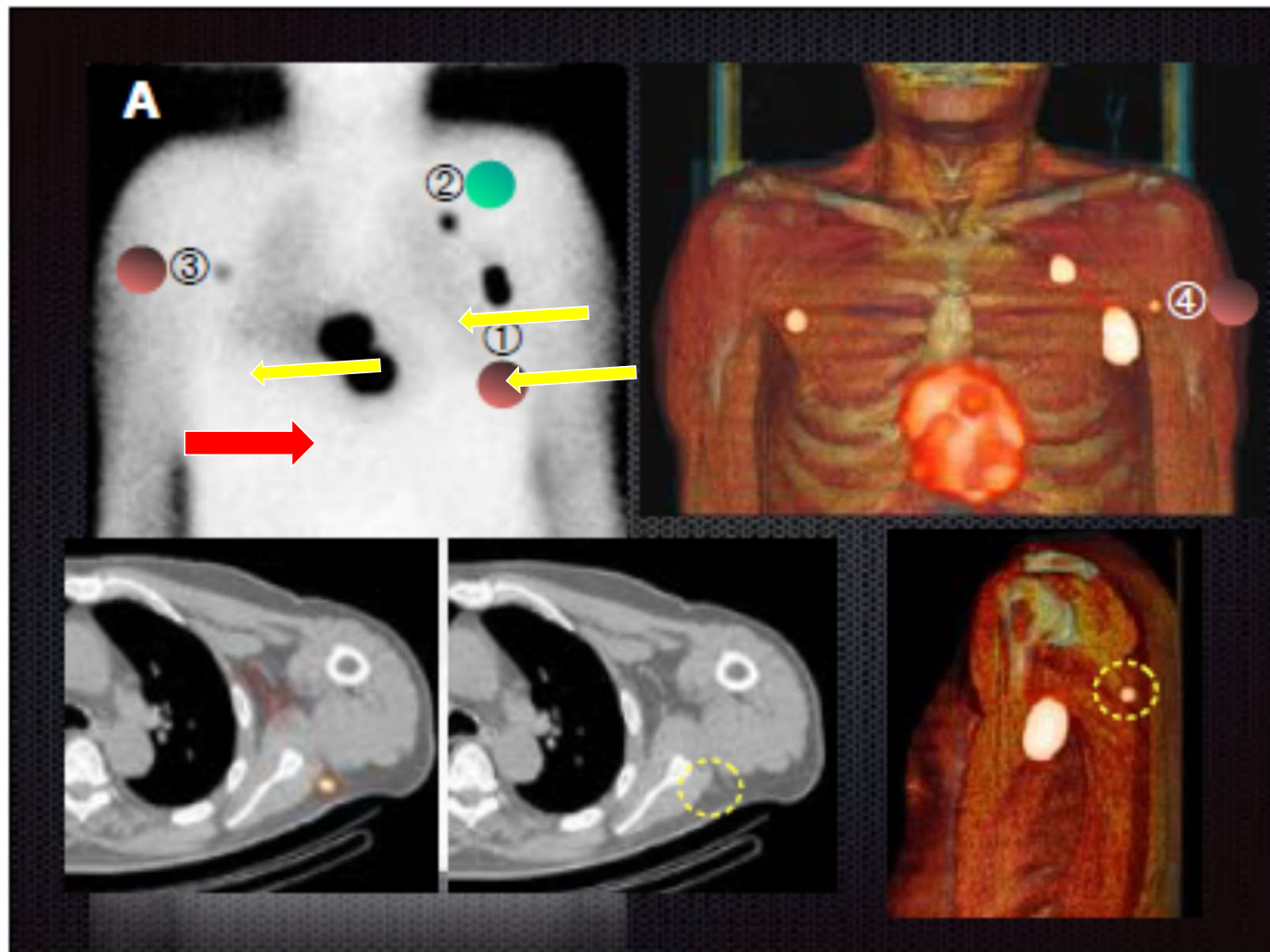
© 2010 Terese Winslow  
U.S. Govt. has certain rights



**Sentinel lymph node (yellow) after application of  $^{99m}\text{Tc}$  nanocolloid (red)**







# ONCOLOGY

## Imaging

- "positive uptake"
- non-specific
- specific
- functional imaging



**Y emitting RF (SPECT)**

**B+ emitting RF (PET)**

## Therapy

**Specific only**



**B+ emitting RF**  
**α emitting RF**

# What are the nuclear medicine imaging methods?

## Onco PET

PET: 3D  
PET-CT: 3D (Function and anatomy).  
PET: Positron emission tomography (2 photons)

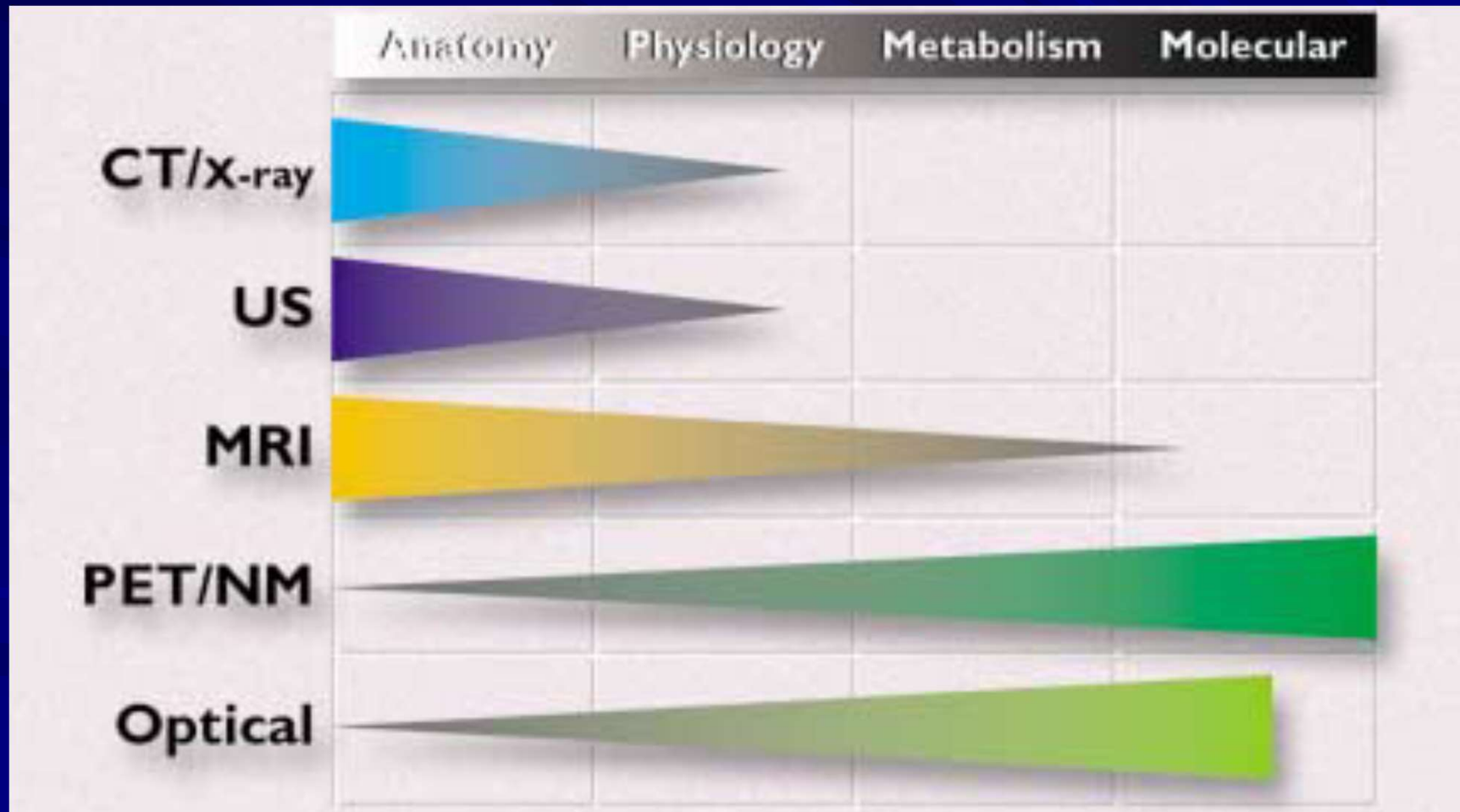


## Conventional tumor imaging

Planar: 2D.  
SPECT: 3D.  
SPECT-CT: 3D (Function and anatomy).  
SPECT: Single photon emission computed tomography.



## IMAGING clinical practice & research

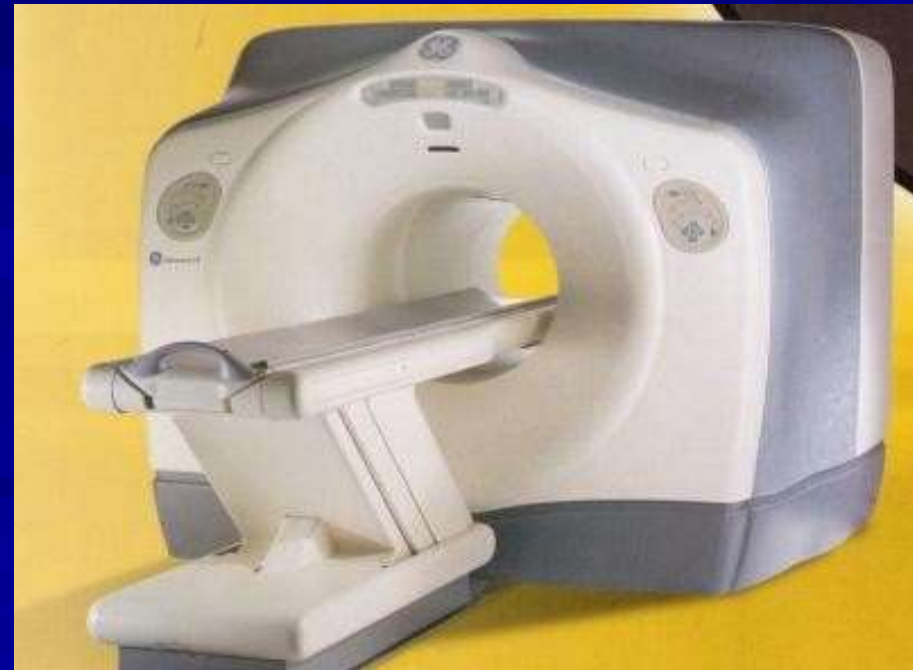
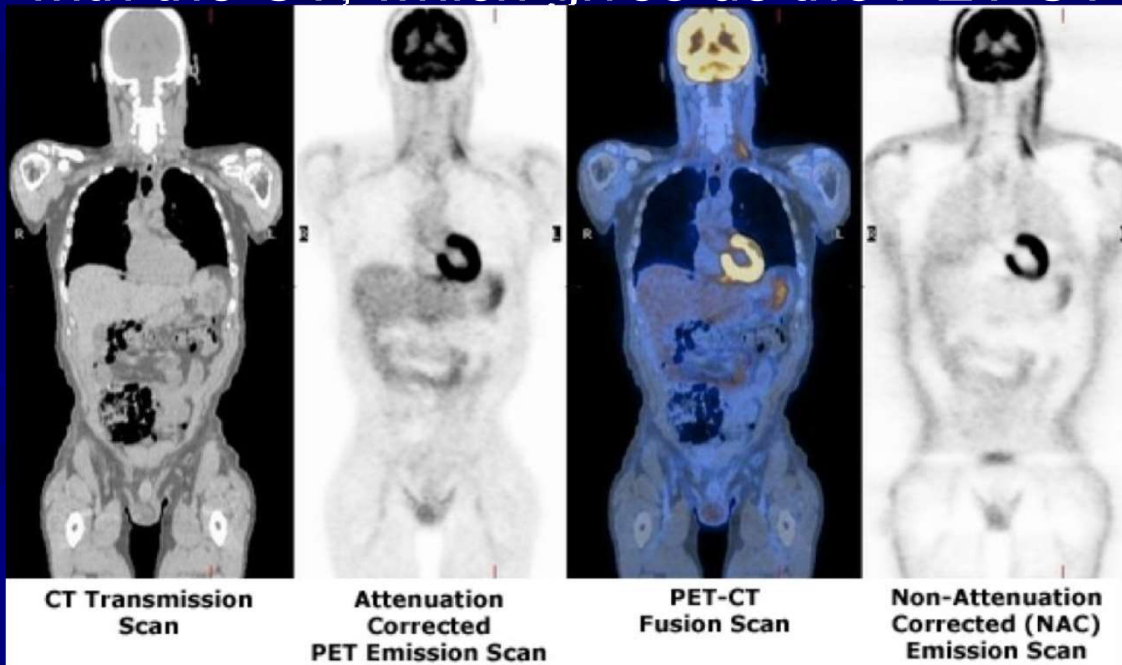




# Positron Emission Tomography

PET+CT=PET-CT

the fusion of functional and anatomic information acquired almost simultaneously from which we are able to visualize form and function. an with the CT, which gives us the PET CT



## Specific

## Non-Specific

### Diagnostic Radiopharmaceuticals

Binds directly to special tumor antigens or receptors or are accumulated by special metabolic pathway.

#### PET or PET/CT:

- **Gallium 68** – octreotide analogues (mimics natural somatostatin pharmacologically) (**Ga-68 DOTA**): For **neuroendocrine tumors**.  
it's the gold standard and more specific and sensitive. used in KSA
- **Fluorine-18** - fluorodeoxythymidine (F-18- FLT): For tumor **proliferation**.  
The uptake depends on the degree & rate of proliferation.
- **Fluorine-18**-fluoromisonidazole (F-18-FMISO): For tumor **hypoxia**.  
Hypoxia is usually located at the tumor's center. You want to know the degree of hypoxia; some centers use oxygen for tumor treatment.

#### Planar, SPECT or SPECT/CT:

- I-123/131 MIBG for **neuroendocrine tumours**.
- I-131 for **differentiated thyroid carcinomas**.
- In-111 or Tc99m octreotide for tumours expressing somatostatin receptors.  
Gallium-68 is more sensitive than Tc99m octreotide.
- Monoclonal antibodies labelled with In111 (Indium-111), I-123/131 or Tc-99m.

Demonstrate tumor sites but are not specific for malignancy.

#### What does 'non-specific' mean?

They can tell you if there was a tumor, but they cannot tell you what type of a tumor it is.

#### PET or PET-CT

- **Fluorine-18 FDG** – anaerobic metabolism.
- Most commonly used.
- Highly sensitive, but not specific. E.g. if there was an abnormal uptake in the hilar area, we will not be able to know if it was a large lymph node, or a lung tumor.
- Excreted by urine.

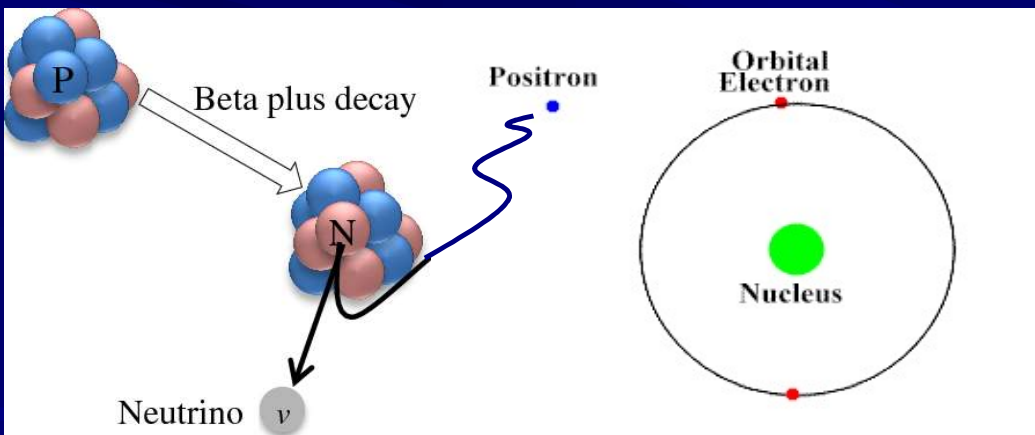
#### Planar, SPECT or SPECT-CT:

- **Diphosphonates** – bone scan.
- Most commonly used.
- Can tell if there was any metastasis, but cannot detect its origin.
- **Ga-67 citrate** – similar to FDG – localising agent.
- **Tc99m Nanocolloid** – bone marrow scan.
- **Tc99m MIBI / Thallium 201** – several tumors.

# Radiopharmaceuticals - Positron Emitting Isotopes

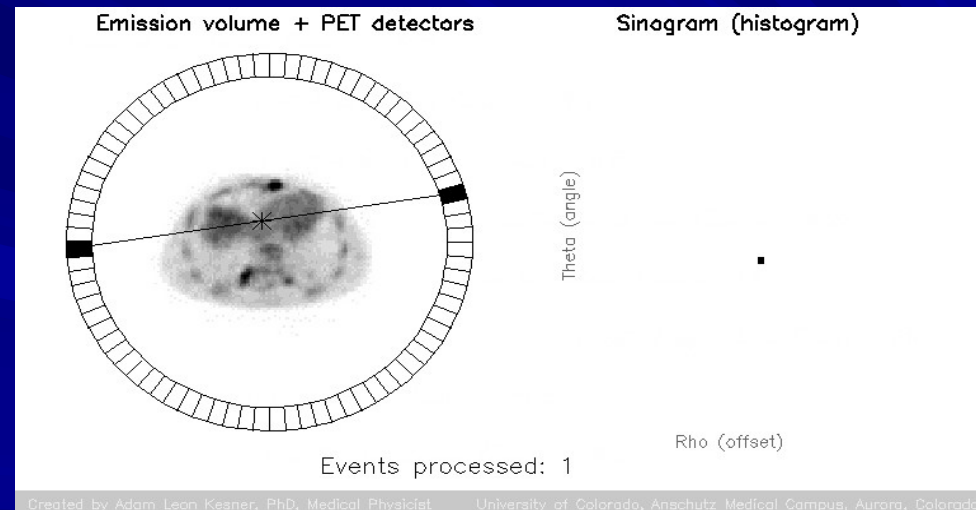
## $\beta^+$ Decay

Neutron-deficient isotopes can decay by emitting positrons



- Positron travels ~1mm
  - Decelerates
- Annihilates with  $e^-$
- Gamma photons

## Positron Emission Tomography (PET)



Scanner is just a photon counter!  
Counts gamma-ray pairs vs. single gammas



## Positron Emitting Isotopes

Cyclotron produced isotopes		Generator produces isotopes			
Isotope	T/2	Isotope	T/2	Daughter	T/2
Oxygen-15	2 min	Strontium-82	25 days	Rubidium-82	75 sec
Nitrogen-13	10 min	Zinc-62	9.3 hrs	Copper-62	10 min
Carbon-11	20 min	Germanium-68	288 days	Gallium-68	68 min
Fluorine-18	110 min				

Organic 4



## **Radiopharmaceuticals - Positron Emitting Isotopes**

### **Uptake mechanism**

- **Glucose metabolism**  
**F-18-fluorodeoxyglucose (FDG)**
- **Amino acid metabolism**  
**C-11-methionine, F-18-tyrosine**
- **Nucleic acids metabolism**  
**F-18-thymidine**
- **Blood flow**  
**N-13-ammonia, O-18-water**
- **Receptor uptake**  
**F-18-estradiol, somatostatine**

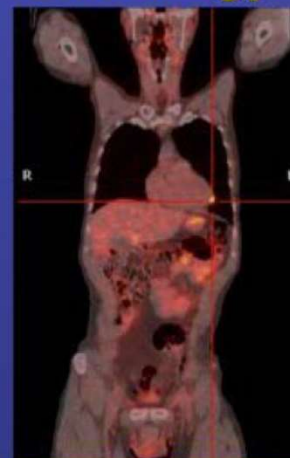
## Clinical Research - Oncology



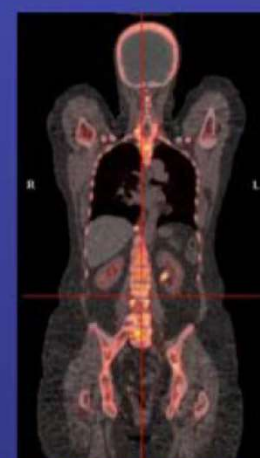
**Malignant tumors**  
<sup>18</sup>F Fluorodeoxyglucose



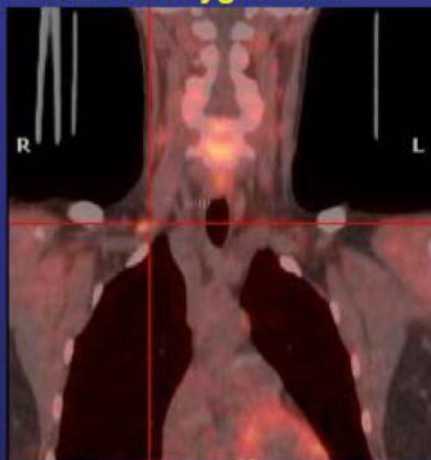
**Neuroendocrine tumors**  
<sup>68</sup>Ga DOTA-TOC



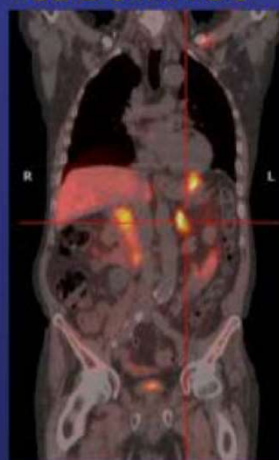
**Neuroendocrine tumors**  
<sup>11</sup>C 5-Hydroxytryptophan



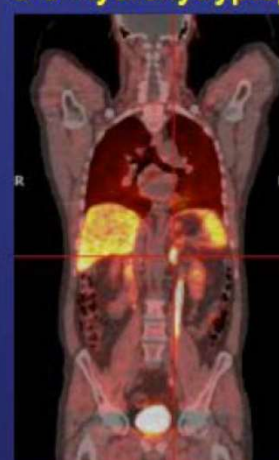
**Bone metastases**  
<sup>18</sup>F-Fluoride



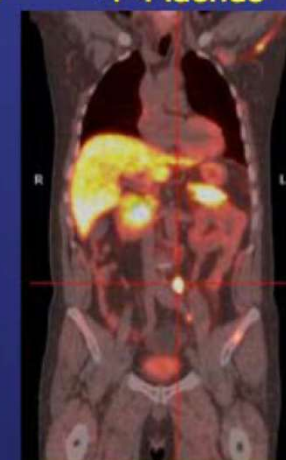
**Parathyroid cancer**  
<sup>11</sup>C Methionin



**Adrenocortical tumors**  
<sup>11</sup>C Metomidate



**Pheochromocytomas**  
<sup>11</sup>C Hydroxyephedrine



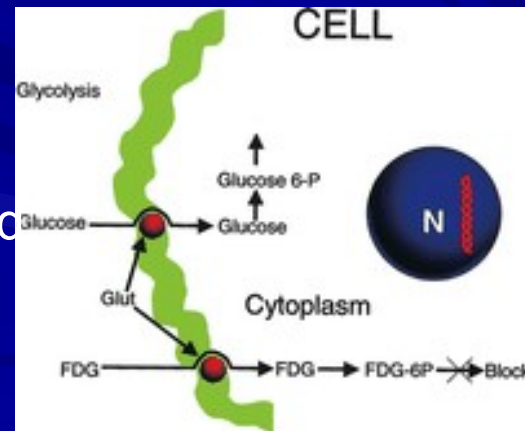
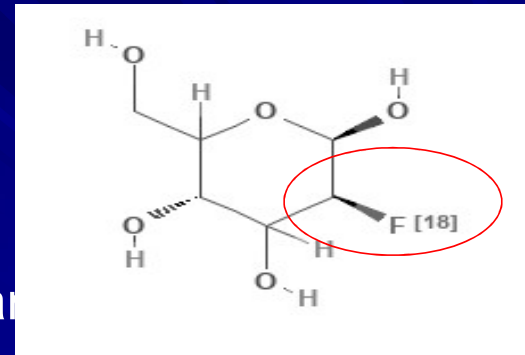
**Prostate cancer**  
<sup>11</sup>C Acetate

## FDG: Fluoro-2-deoxy-D-Glucose Uptake Mechanism

FDG is a glucose analogue (similar to it) used to assess glucose metabolism.

- The only difference between them is kidney excretion.
- FDG transported from intravascular space to the cells by the same mechanism as the glucose.
- In the cell, a substance called “hexoKinase” acts on both FDG and glucose to form:
  - FDG-6-phosphatase (FDG-6-PO<sub>4</sub><sup>-</sup>).
  - Glucose-6-phosphatase.
- FDG-6-PO<sub>4</sub><sup>-</sup> can't progress further into glucose metabolism and remains trapped intracellularly in proportion to glycolytic rate of the cell.

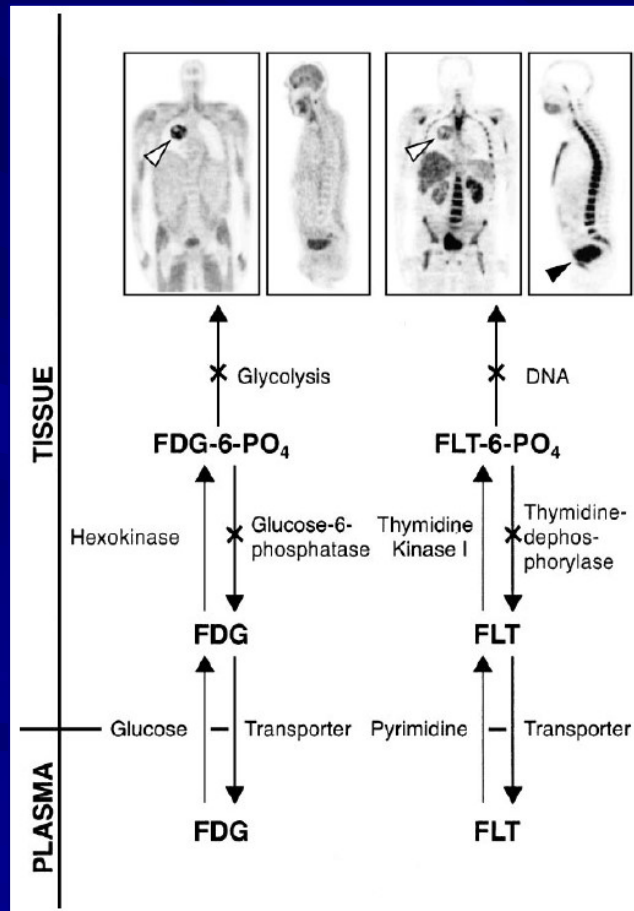
\*In tumors, there is high rate of glycolysis (High compounds concentration) compared to normal cells and higher level of hexoKinase.



# RADIOPHARMACEUTICALS

## - Cellular functional Specificity -

**Fluorodeoxyglucose (FDG)** is phosphorylated to FDG-6-PO<sub>4</sub> by hexokinase. Since the activity of glucose-6-phosphatase is negligible, FDG-6-phosphate is essentially trapped in tumor cells.

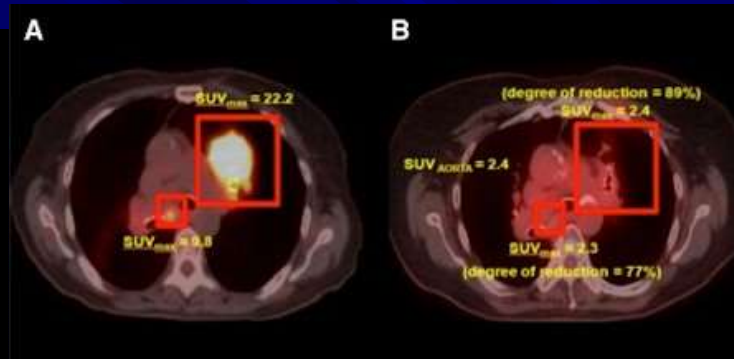
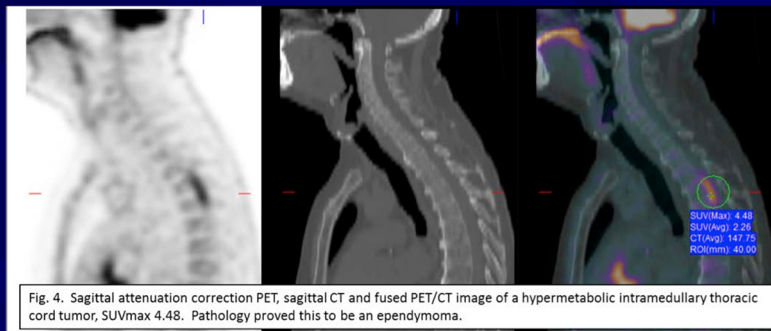


**Fluorothymidine (FLT)** is phosphorylated by thymidine kinase to FLT-6-PO<sub>4</sub> and accumulates in tumor cells.

It is described as a marker of cell proliferation.



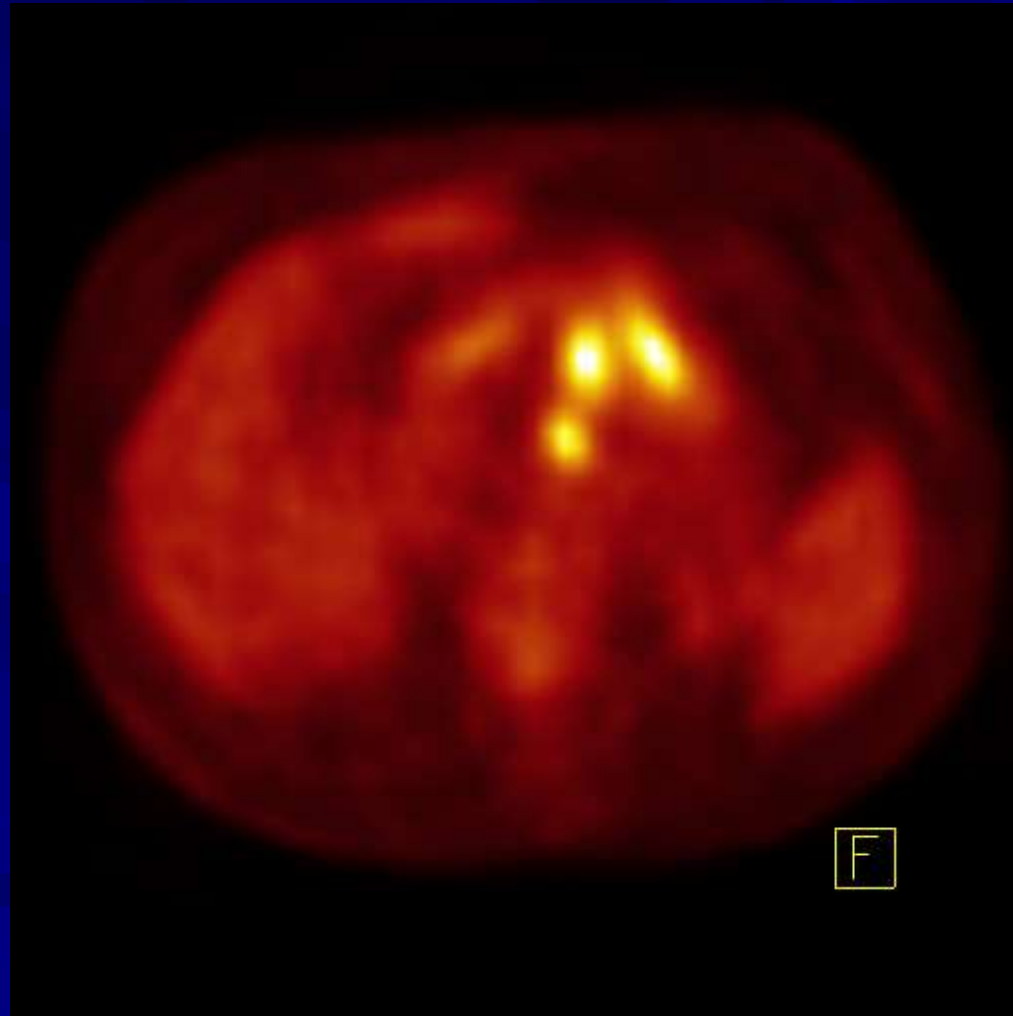
# Quantification in PET



## Standardized Uptake Values (SUV)

$$SUV = \frac{Act_{voi}(kBq/ml)}{Act_{administered}(MBq)/BW(kg)}$$

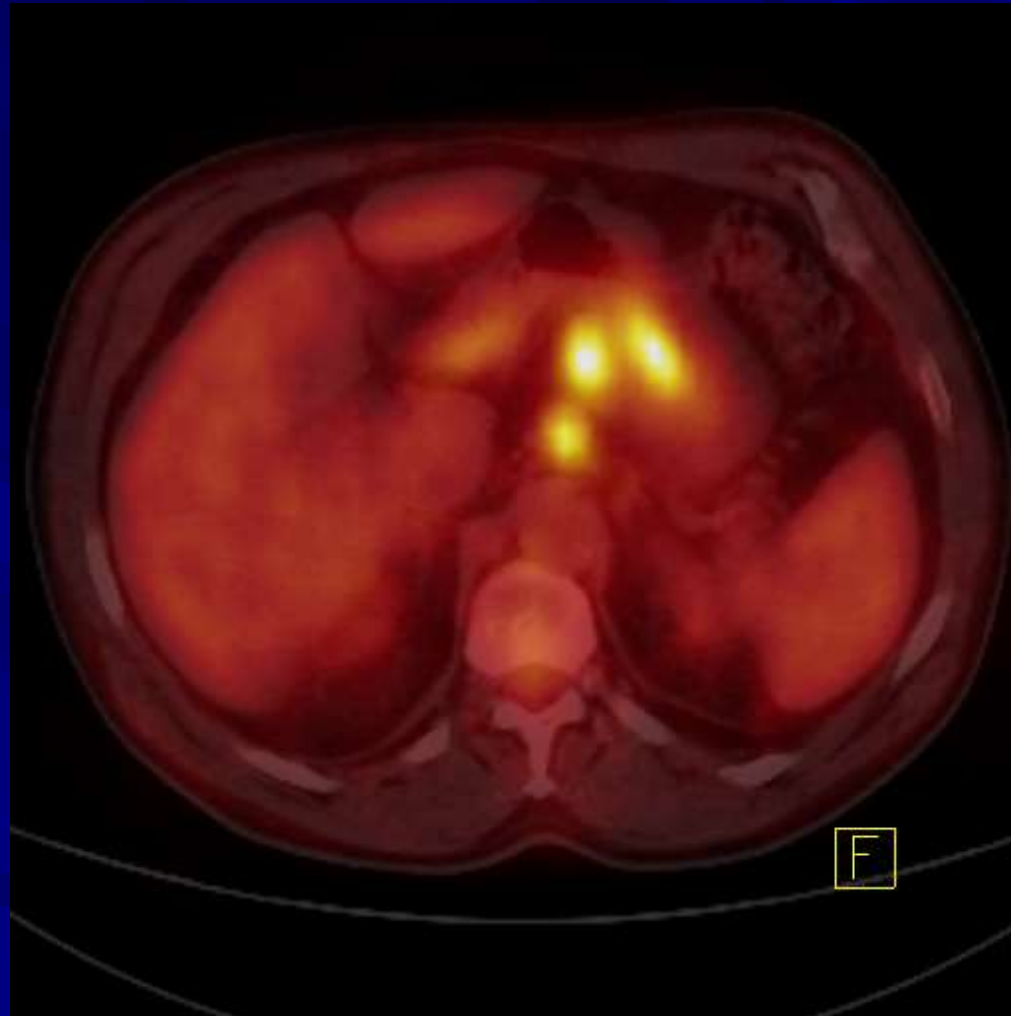
Quantification provides the link between the concentrations of radioactivity measured in tissue and the underlying physiologic processes occurring in the organ. It relates the rate at which radioactivity levels in the body change over time to quantitative parameters such as absolute rate glucose metabolism, regional blood flow, or concentrations of receptors or other binding sites



PET: 100 %

CT: 0 %

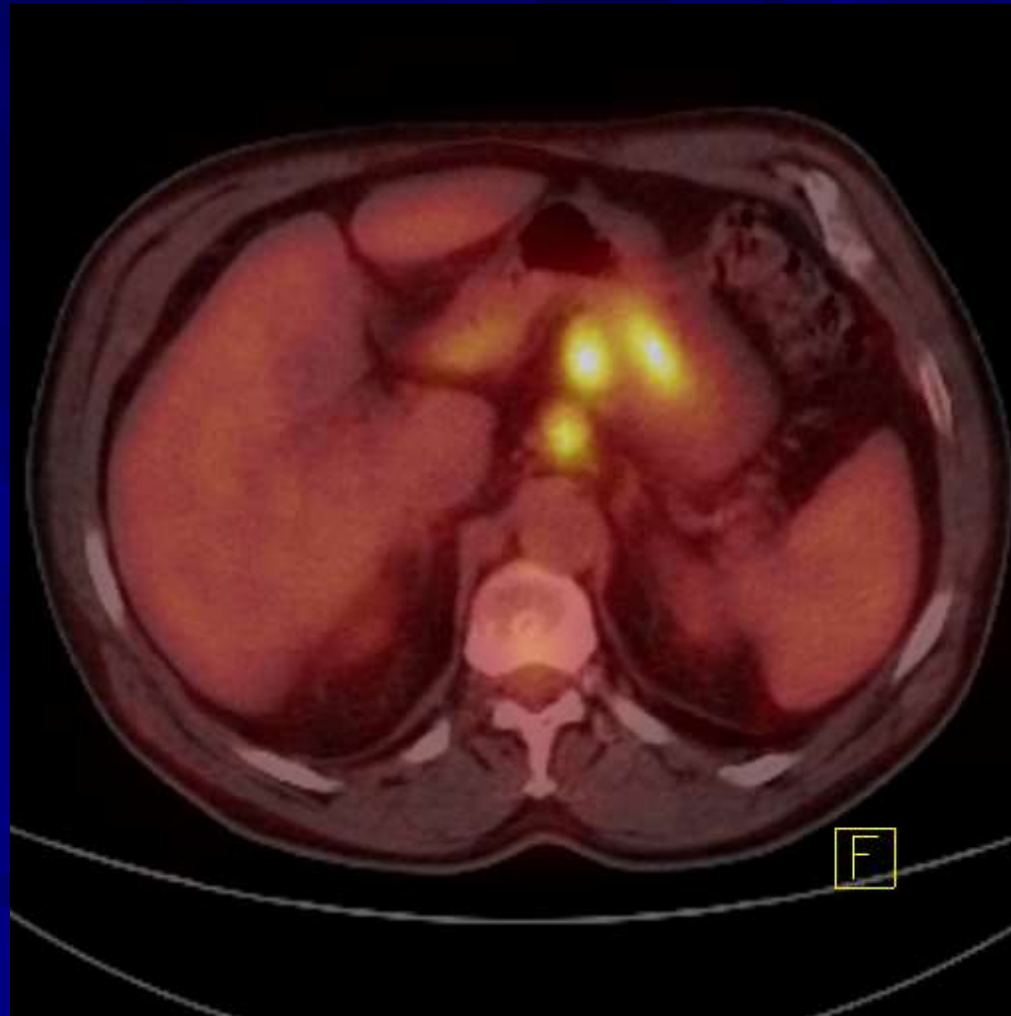
***Stomach cancer***



PET: 80 %

CT: 20 %

***Stomach cancer***

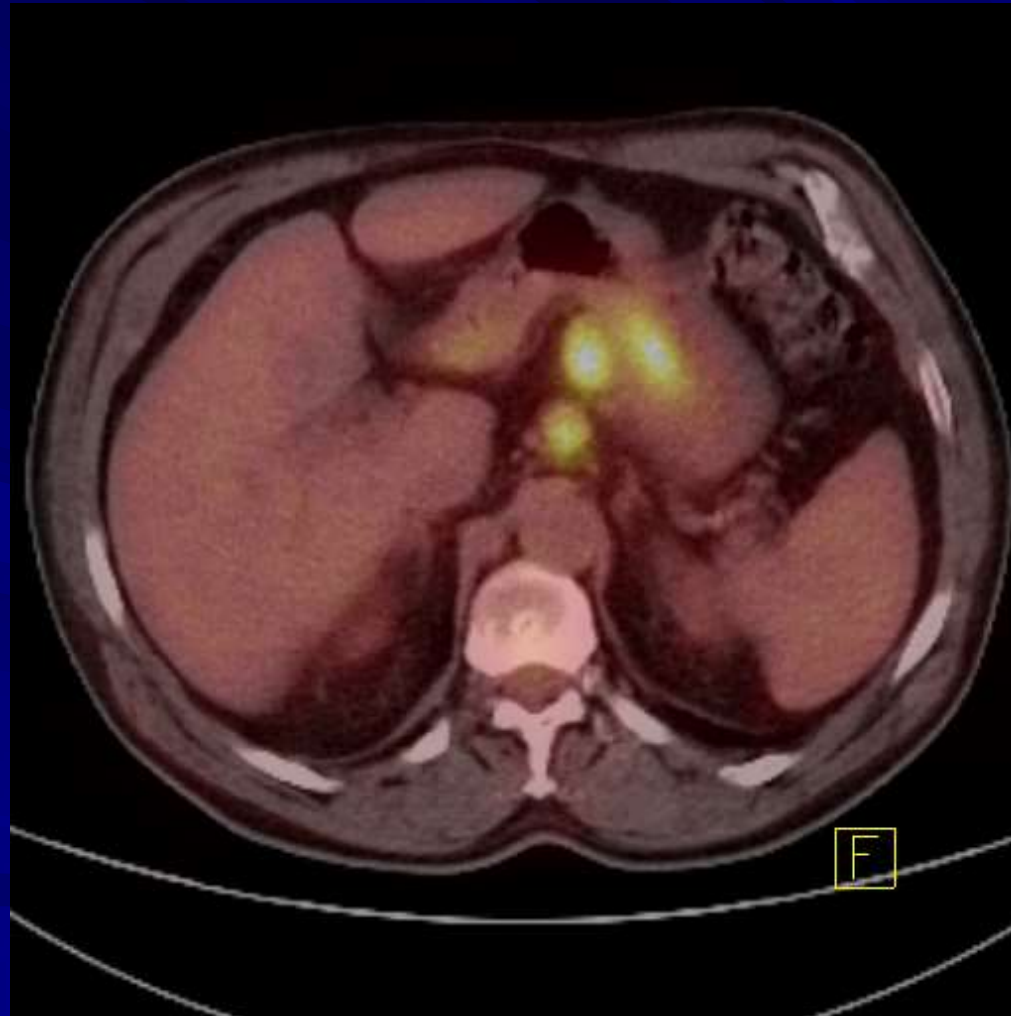


PET: 60 %

CT: 40 %

***Stomach cancer***

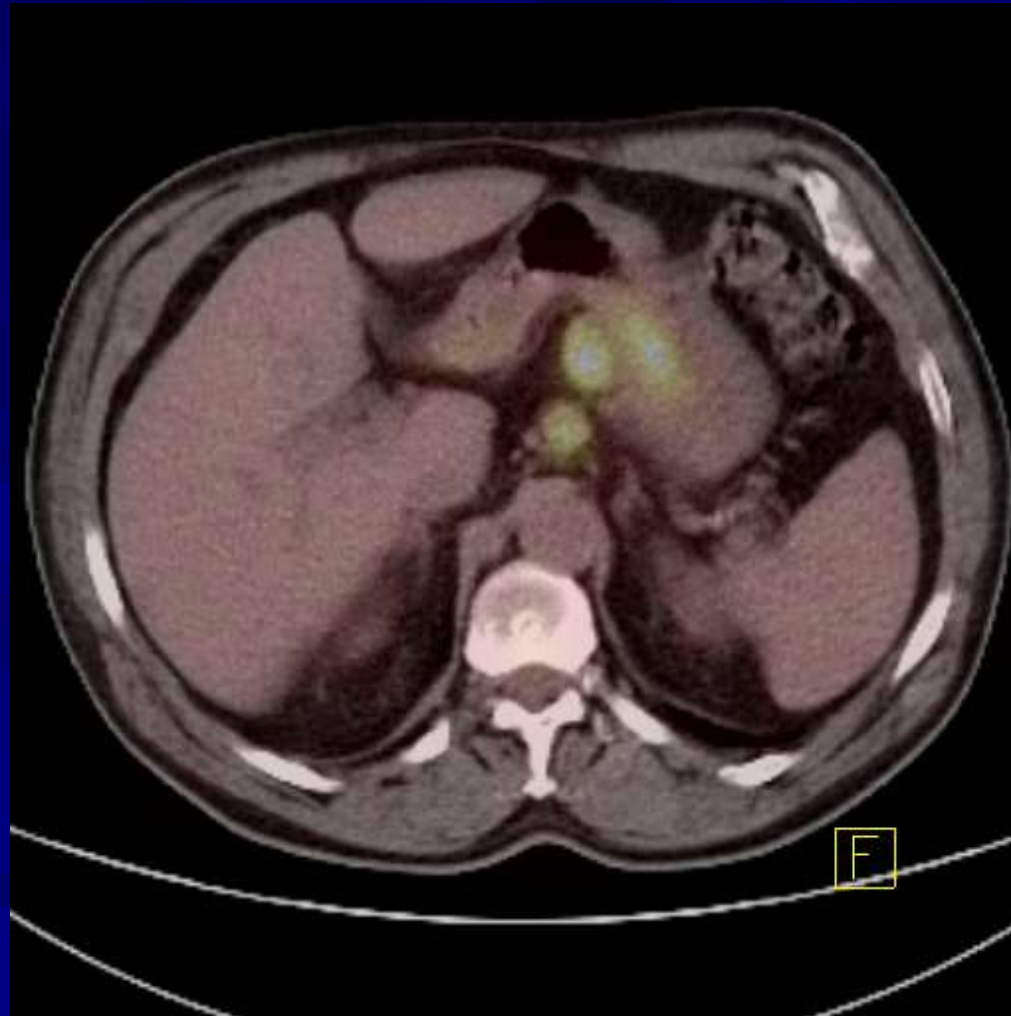




PET: 40 %

CT: 60 %

***Stomach cancer***



PET: 20 %

CT: 80 %

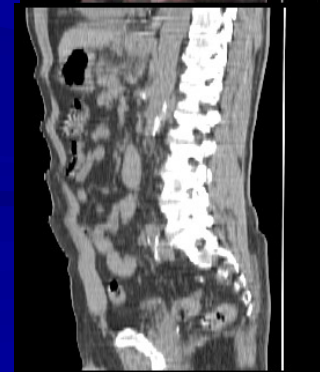
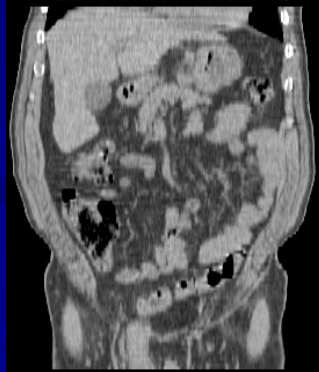
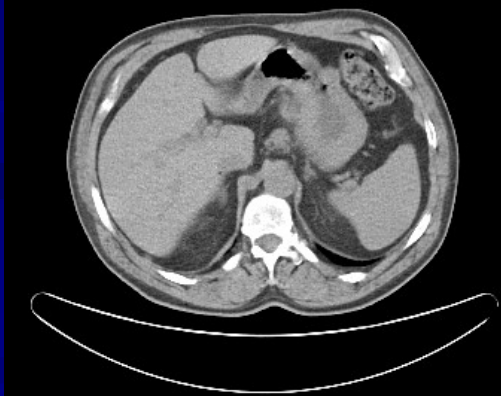
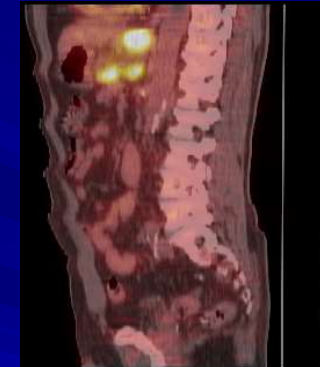
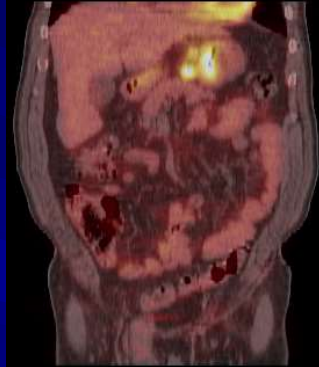
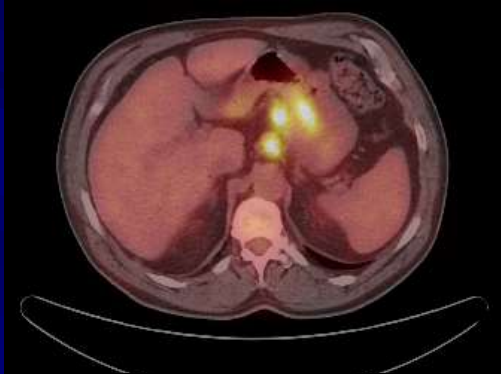
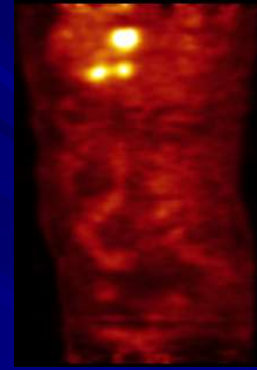
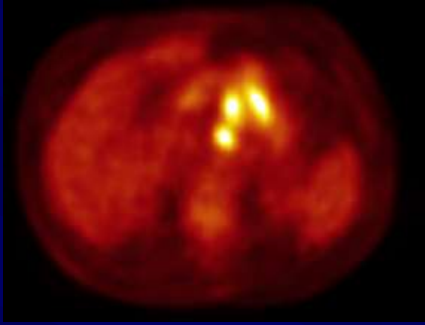
***Stomach cancer***



PET: 0 %

CT: 100 %

***Stomach cancer***





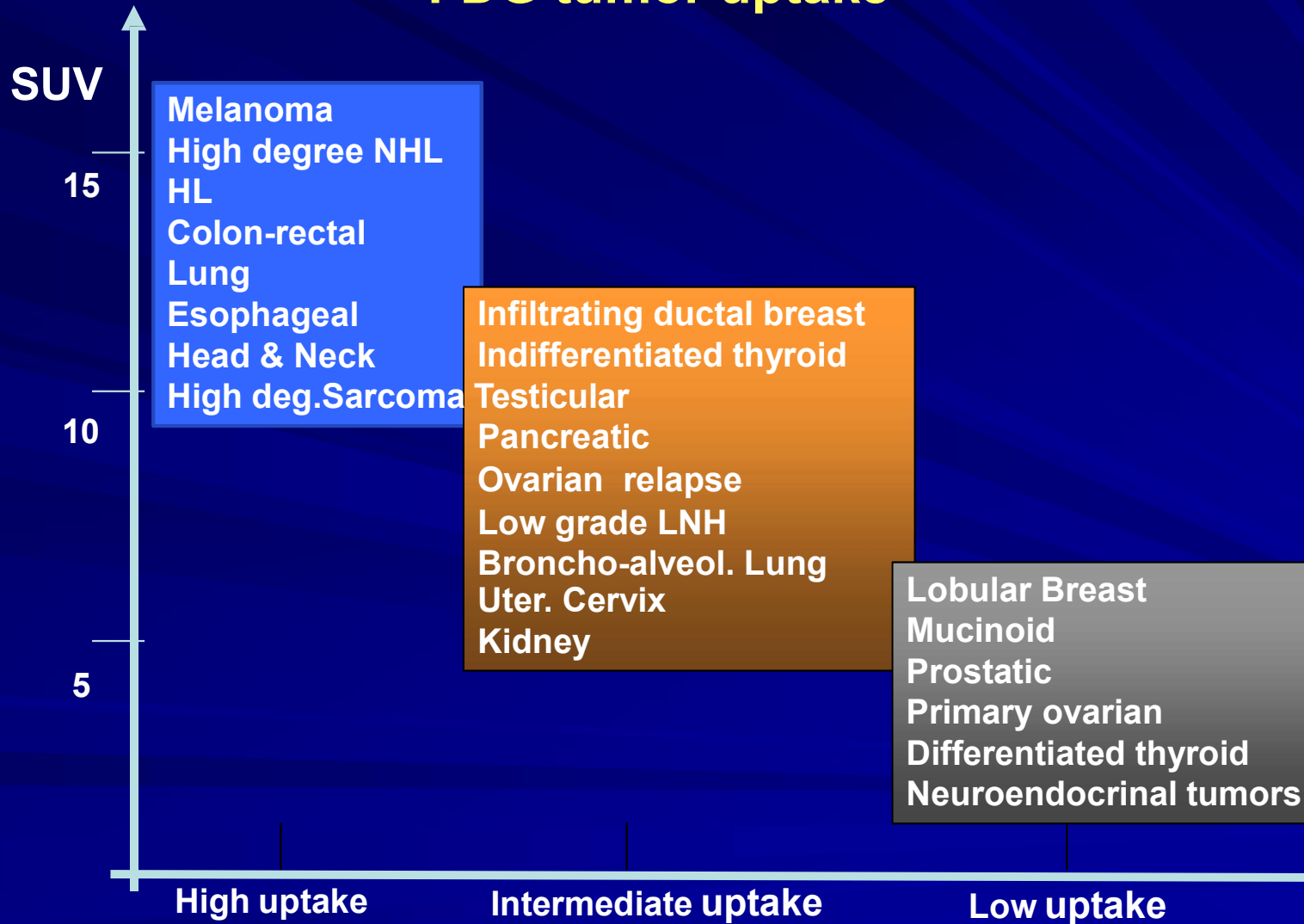
# $^{18}\text{F}$ -FDG PET/CT in Oncology

# FDG PET in ONCOLOGY

## UTILITY in CLINICS

1. Identification and localisation of disease foci  
unknown primary (paraneoplastic syndromes)
2. Diagnosis and “grading” of malignant disease  
staging and restaging TNM
3. Evaluation and monitoring of response to therapy
4. Identification of recurrent disease in comparison with “raising”  
tumour markers and anatomic/structural changes (CT and MR)
5. RadioTherapy guidance and “management”
6. Guide for biopsy

## FDG tumor uptake



## Identification and localisation of disease foci

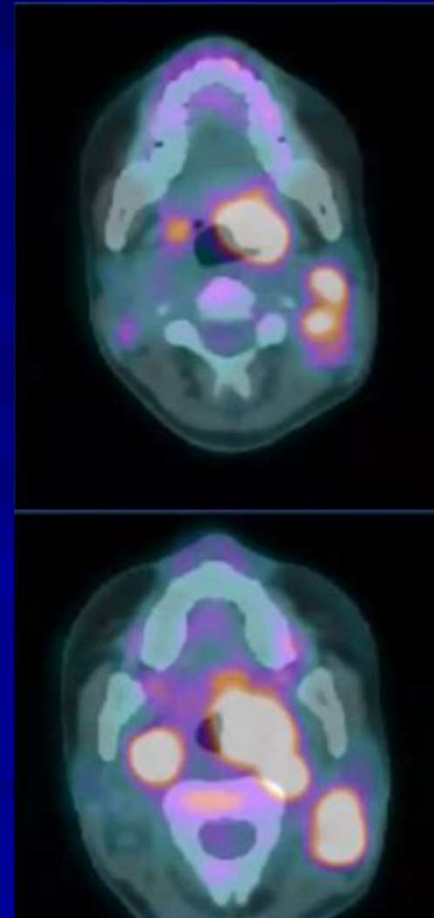
$^{18}\text{F}$ -FDG-PET can reveal the primary location of the tumor in 1/3 of patients with cancer of unknown location

Statistic	CT	PET	CT and PET Side-by-side Evaluation	Intrinsically Fused PET/CT
Sensitivity (%)	19 (8/42)*	28 (11/39)*	31 (13/42)*	35 (15/42)*
Positive predictive value (%)	73 (8/11)	65 (11/17)	81 (13/16)	83 (15/18)
Sensitivity (%)	19 (8/42)*	28 (11/39)*	31 (13/42)*	35 (15/42)*
Positive predictive value (%)	73 (8/11)	65 (11/17)	81 (13/16)	83 (15/18)

*Gutzeit A et al Radiology. 2005 Jan;234(1):227-34.*

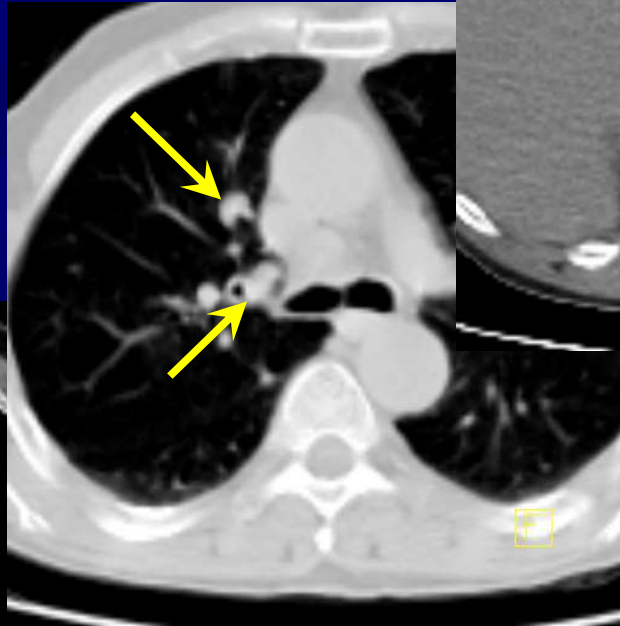
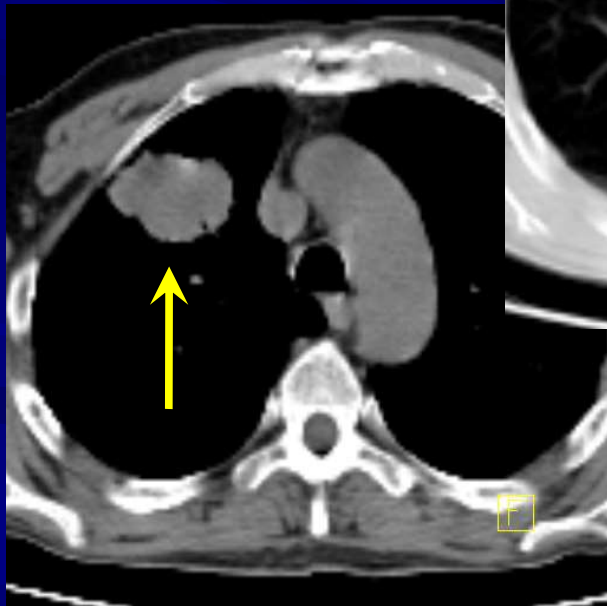


## Nasopharyngeal cancer with LN metastasis



## “Staging” TNM

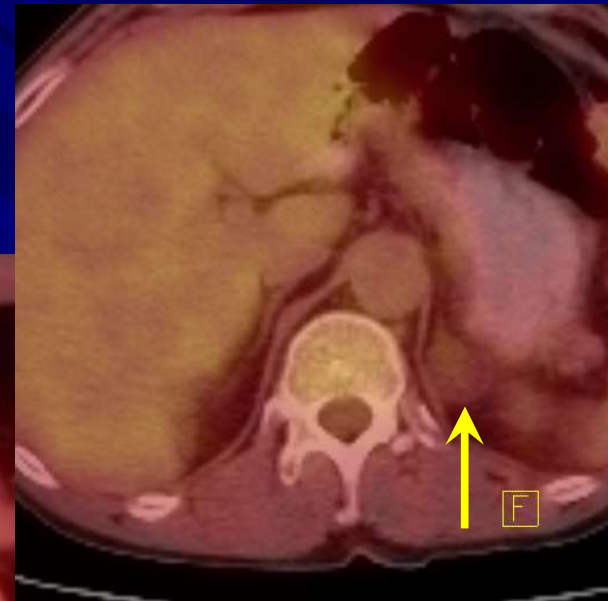
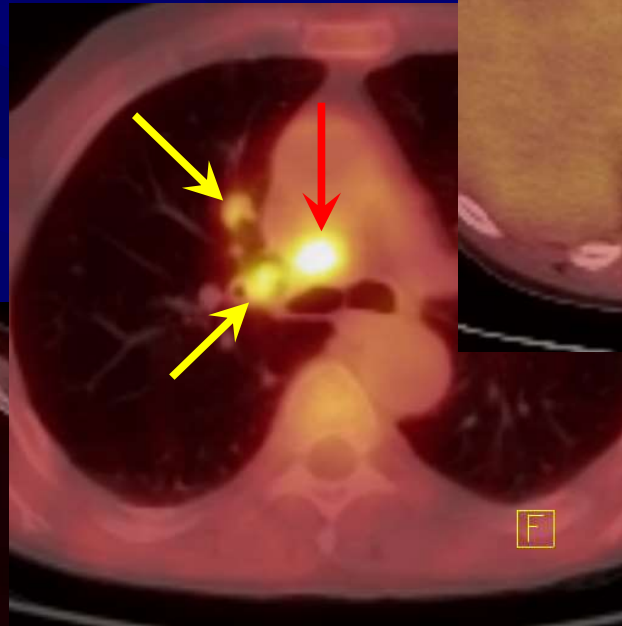
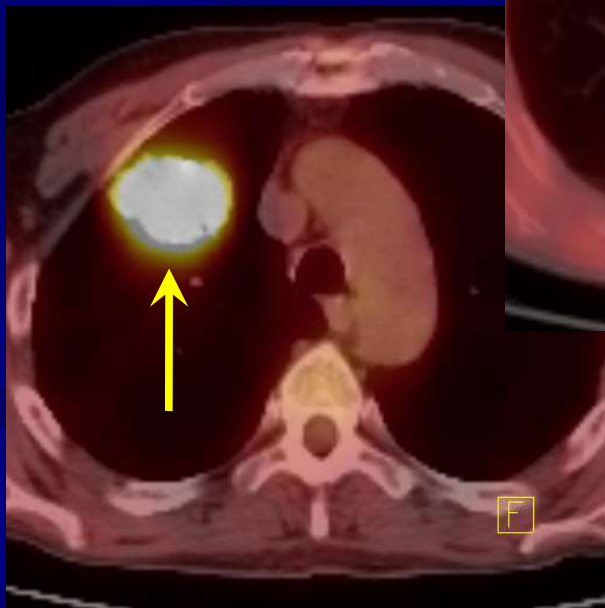
NSCLC CT: T2 N1 M1 ~ stg. IVa ?



## **NSCLC**

**CT: T2 N1 M1 ~ stg. IVa ?**

**PET/CT: T2 N2 M0 ~ stg. IIIa**



## Evaluation and monitoring of response to therapy

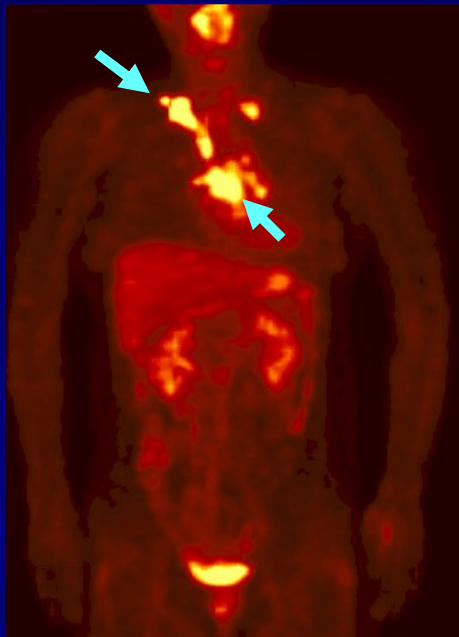
- ❖ 2 to 3 weeks after chemotherapy
- ❖ 6 to 12 weeks after radiotherapy (due to the stunning effect on malignant cells: transiently reduced metabolism and proliferation, false negative finding, or radiation pneumonitis, false positive finding)
- ❖ 2-6 months after surgery



# Chemotherapy

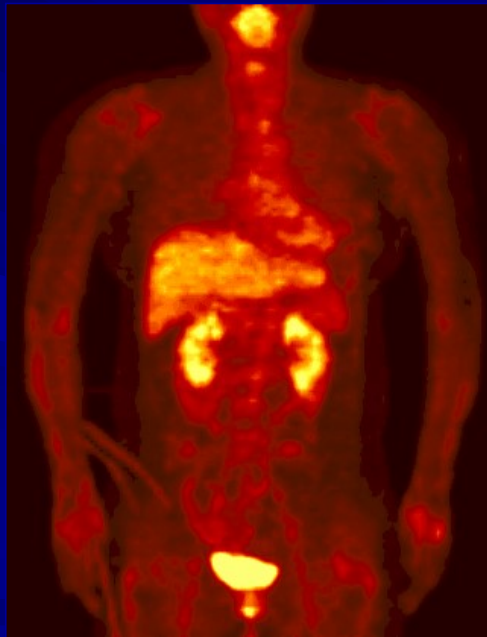
Before

('01.7.25.)



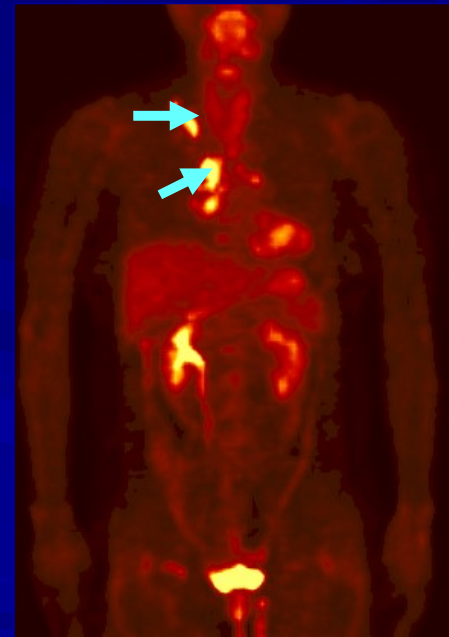
After

('01.12.14.)



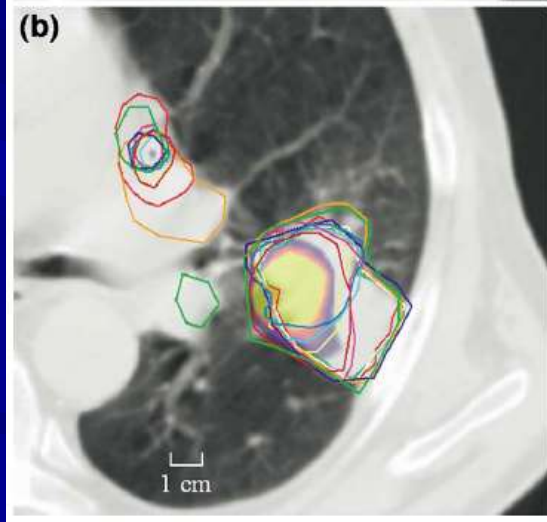
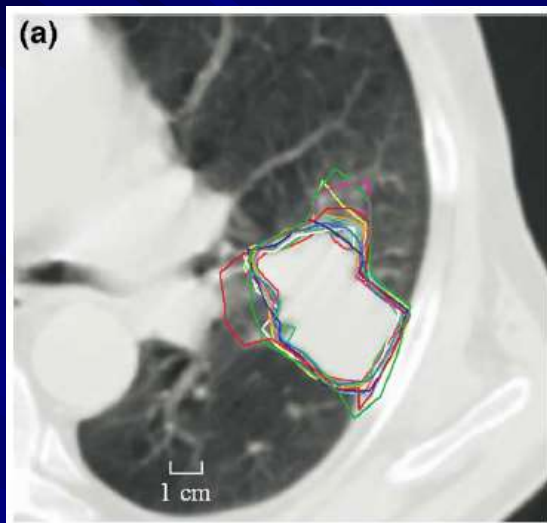
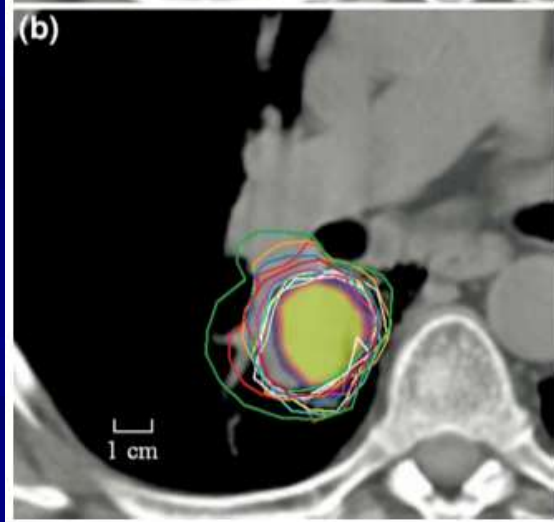
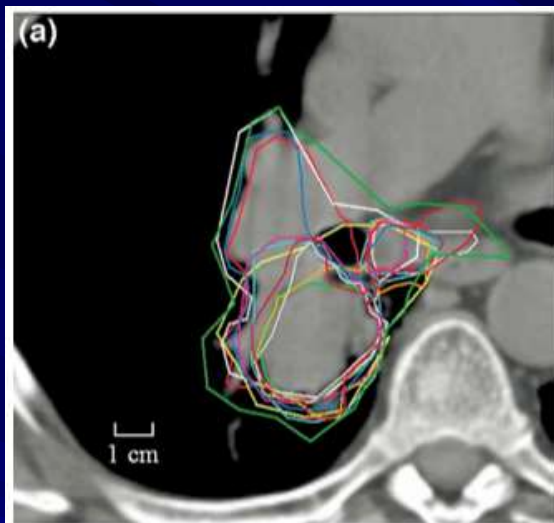
Relapse

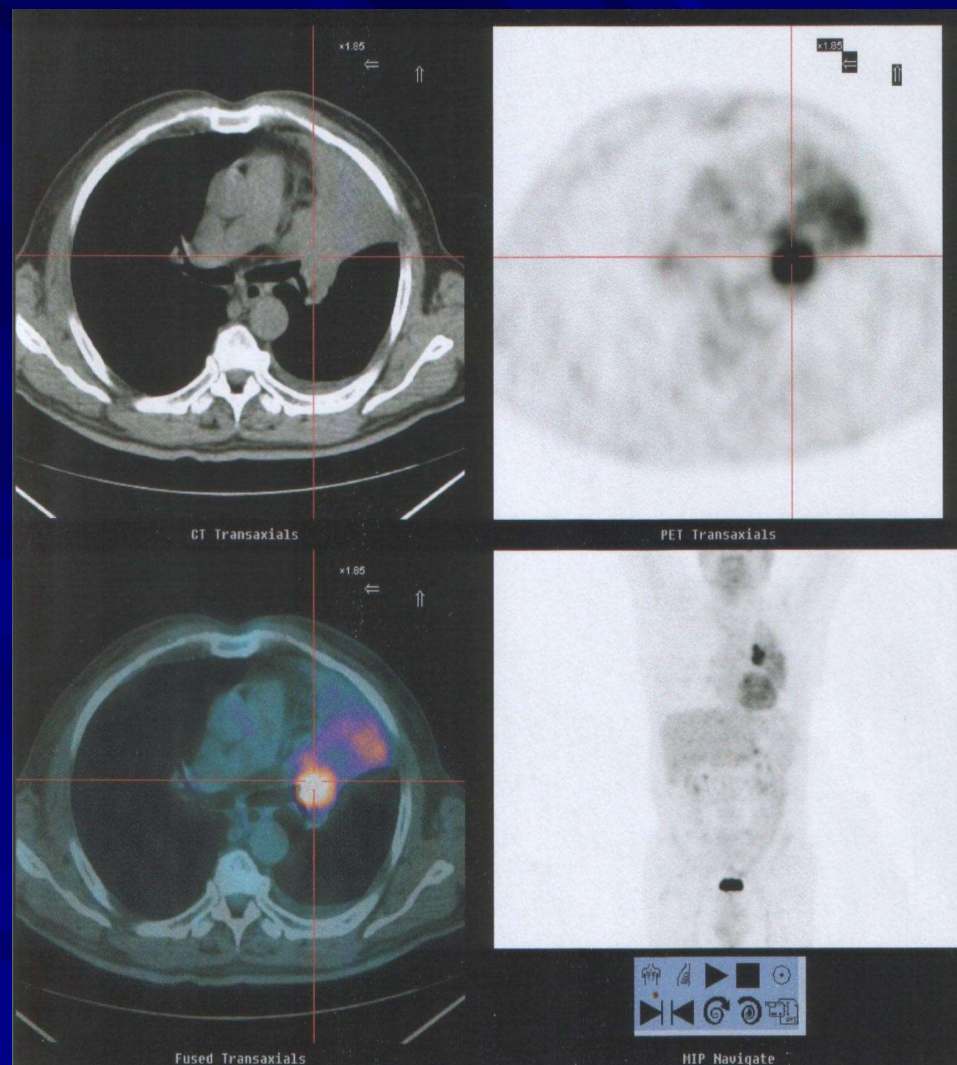
('02.4.16.)



## RadioTherapy guidance and management

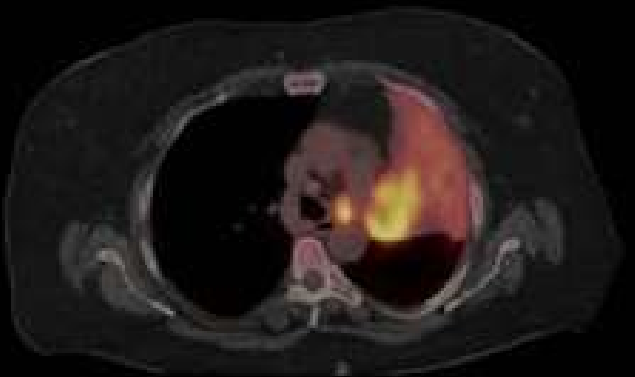
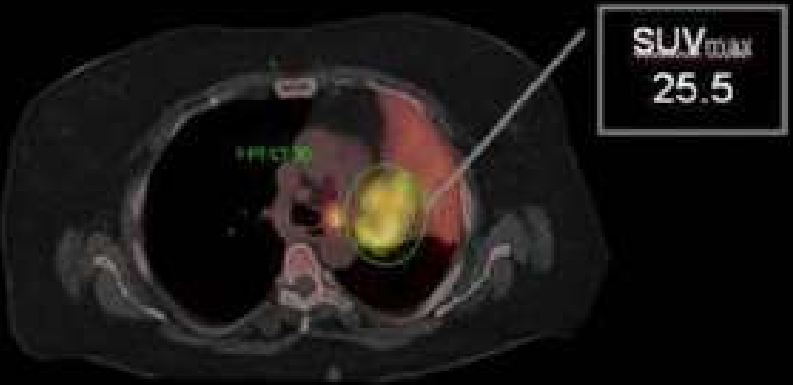
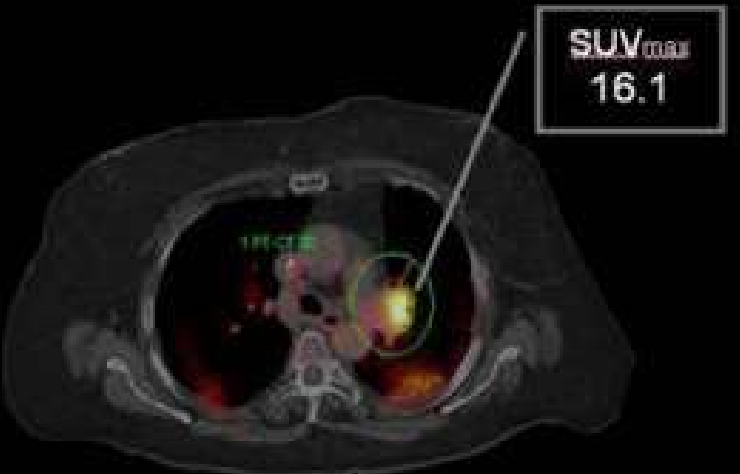
- More precise planning of the beam field depending on the metabolic and biological activity in the malignant tumor itself
- Fusion functional-morphological imaging using PET/CT significantly improves the accuracy of planning the air field:
- In NSCLC, the removal of atelectasis and infection zones from the air field, and the shift and increase of the dose to the area of lymph nodes that accumulate FDG.





NSCLC. atelectasis





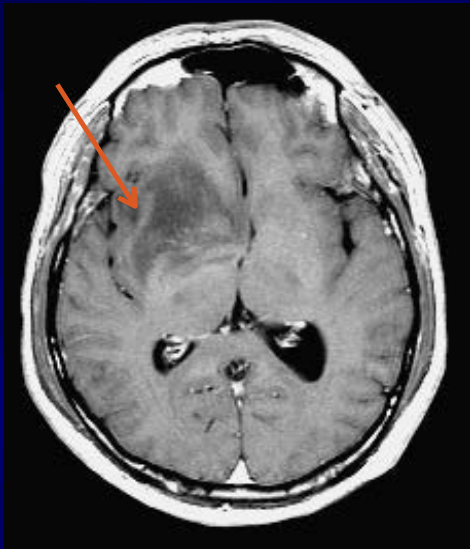
Post-therapy

Pre-therapy

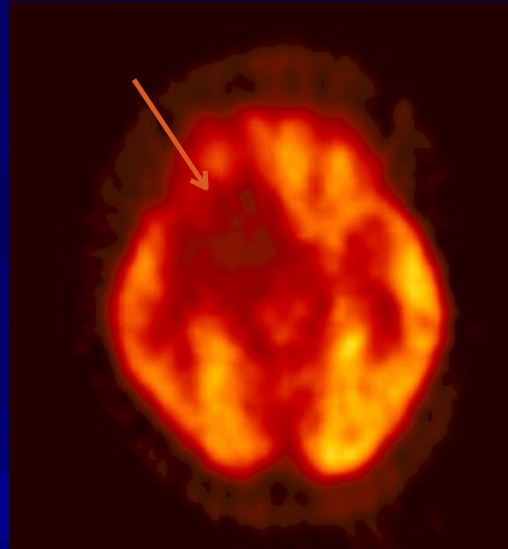
## Indications of PET CT

Breast Cancer*	Staging*, restaging*, and monitoring response to therapy*
Colorectal Cancer	Diagnosis*, staging* and restaging*
Esophageal Cancer	Diagnosis*, staging* and restaging*
Head & Neck Cancers (excluding CNS and thyroid)	Diagnosis*, staging* and restaging*
Lung Cancer (Non-Small Cell)	Diagnosis*, staging* and restaging*
Lymphoma	Diagnosis*, staging* and restaging*
Melanoma (Excludes evaluation of regional nodes)	Diagnosis*, staging* and restaging*
Solitary Pulmonary Nodule	Characterization of indeterminate single pulmonary nodule
Thyroid Cancer*	Restaging
Cervical Cancer*	Staging as an adjunct to conventional imaging

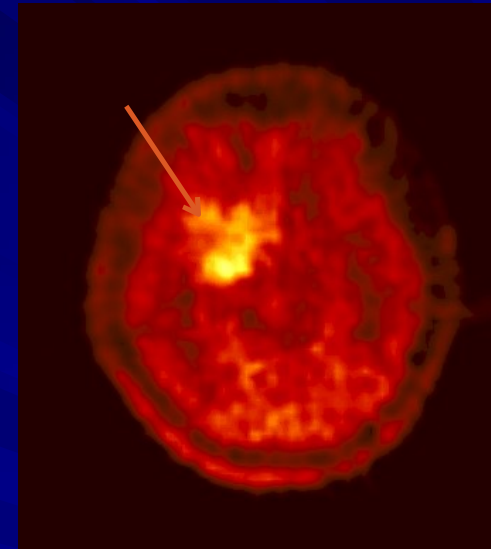
## Brain tumors



**MRI**



**$^{18}\text{F}$ -FDG**

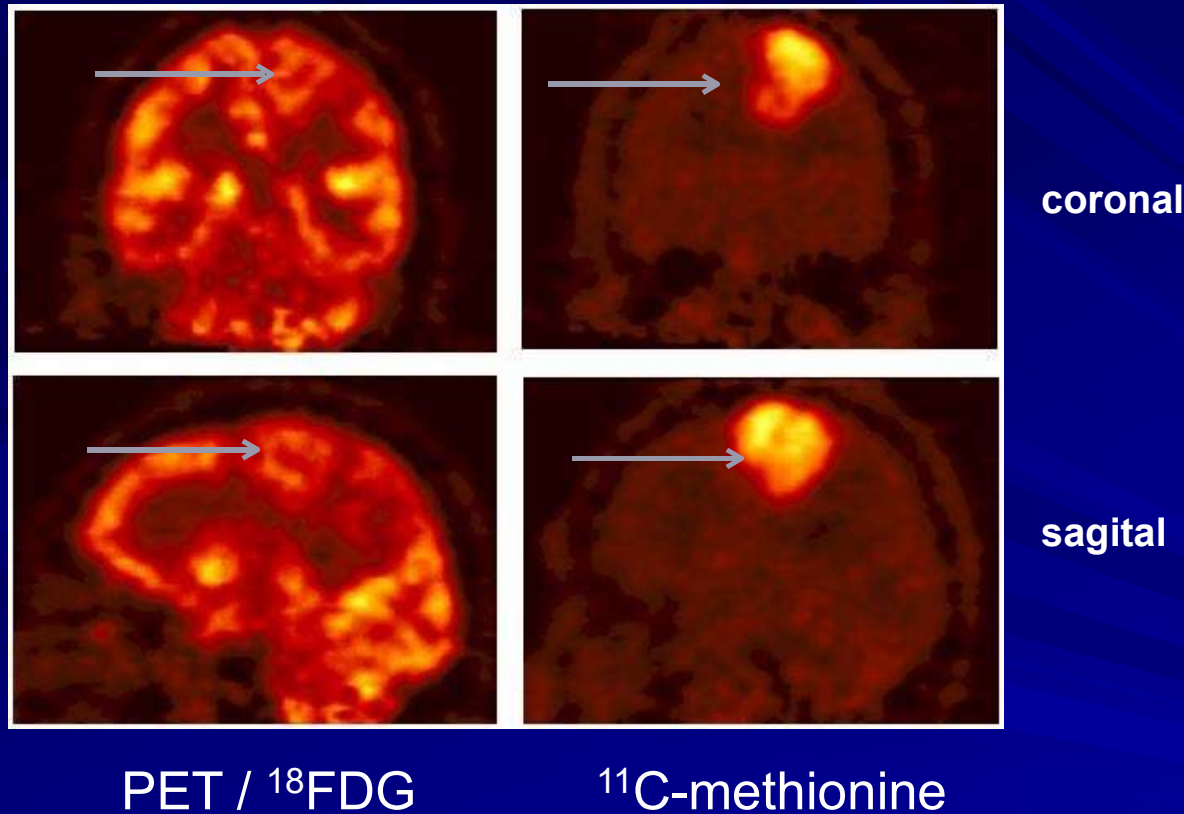


**$^{11}\text{C}$ -metionine**

Astrocitoma

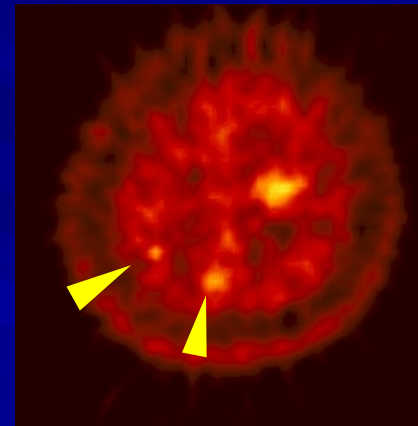
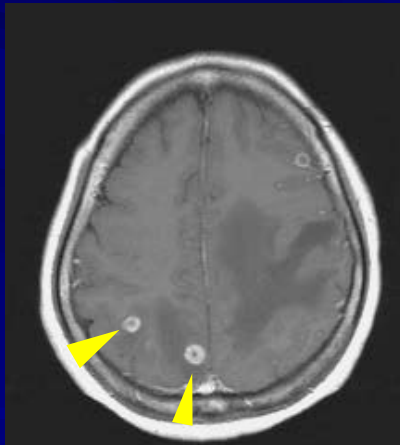
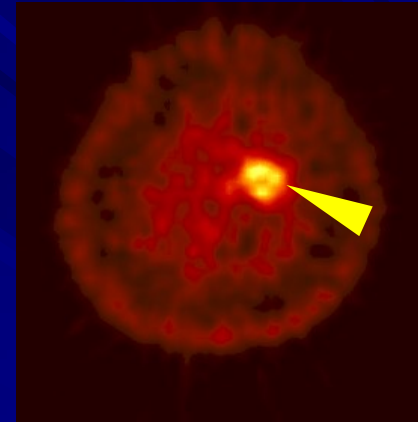
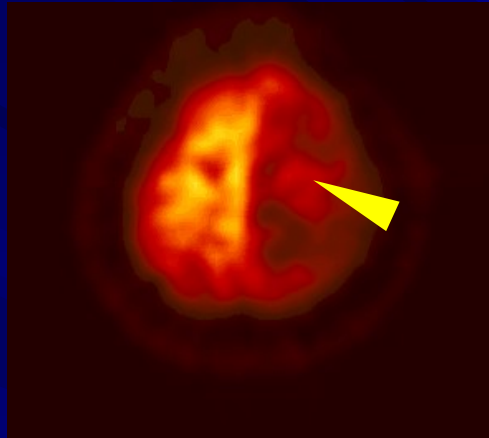
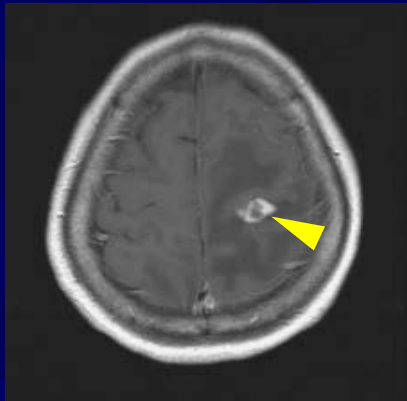
$^{18}\text{F}$ -FDG negative uptake

$^{11}\text{C}$ -метионин positive uptake



accumulation of FDG in the tumor (left, arrows) does not differ from physiological methionine (right) accumulates in the tumor much more intensively than in the surrounding brain tissue (anaplastic oligodendroglioma).

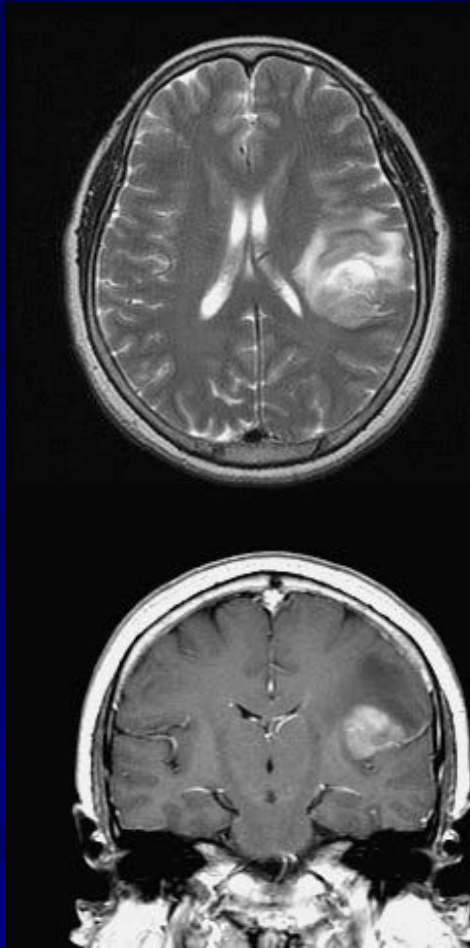




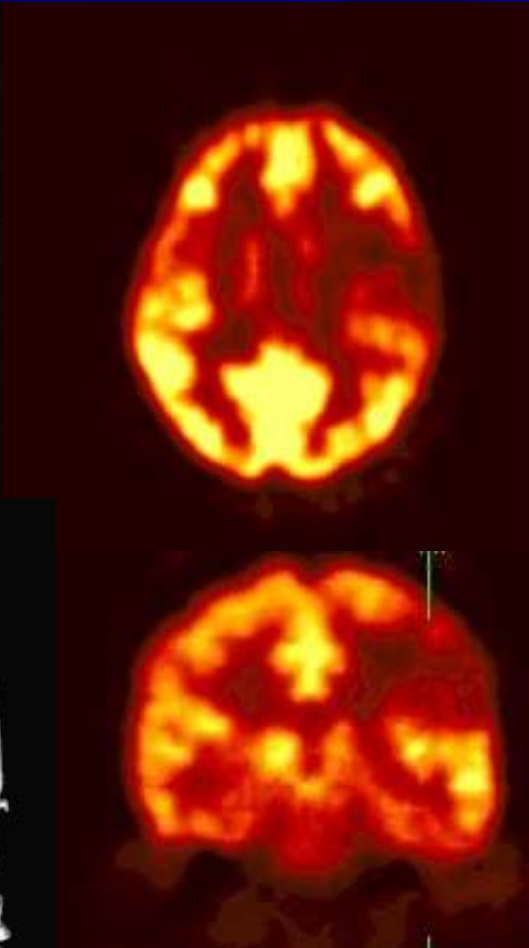
$^{11}\text{C}$ -methionine

Brain metastases (non small cell lung carcinoma)

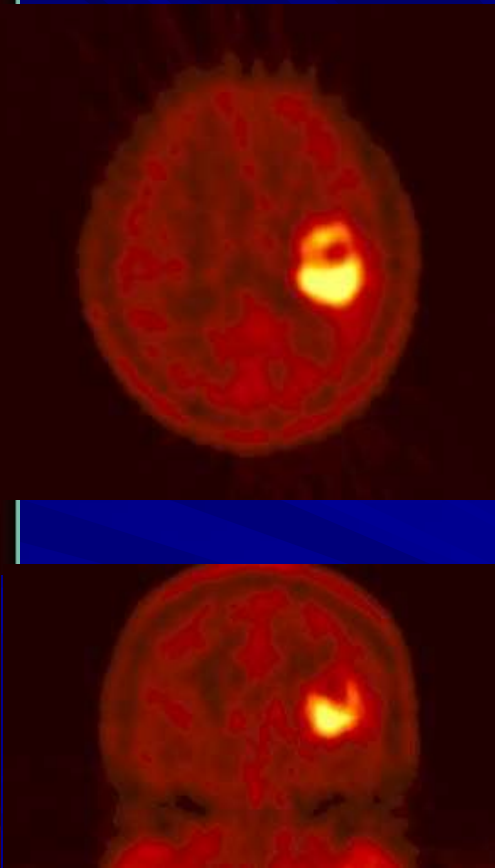
## Glioblastoma multiforme



**MRI**



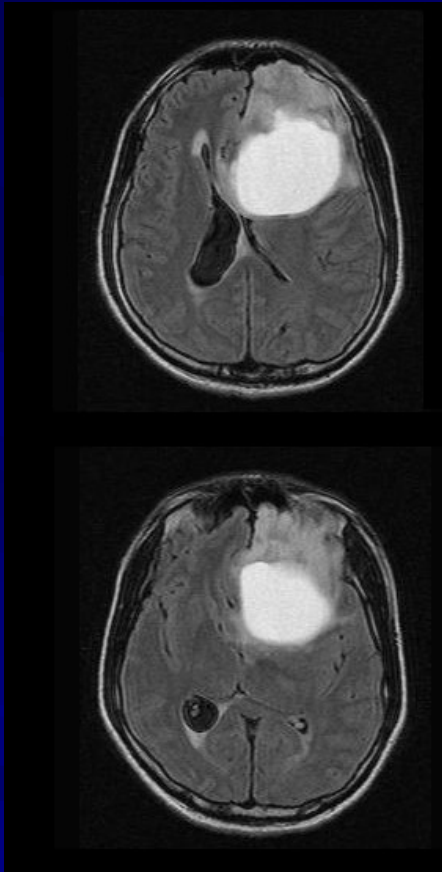
**$^{18}\text{F}$ -FDG**



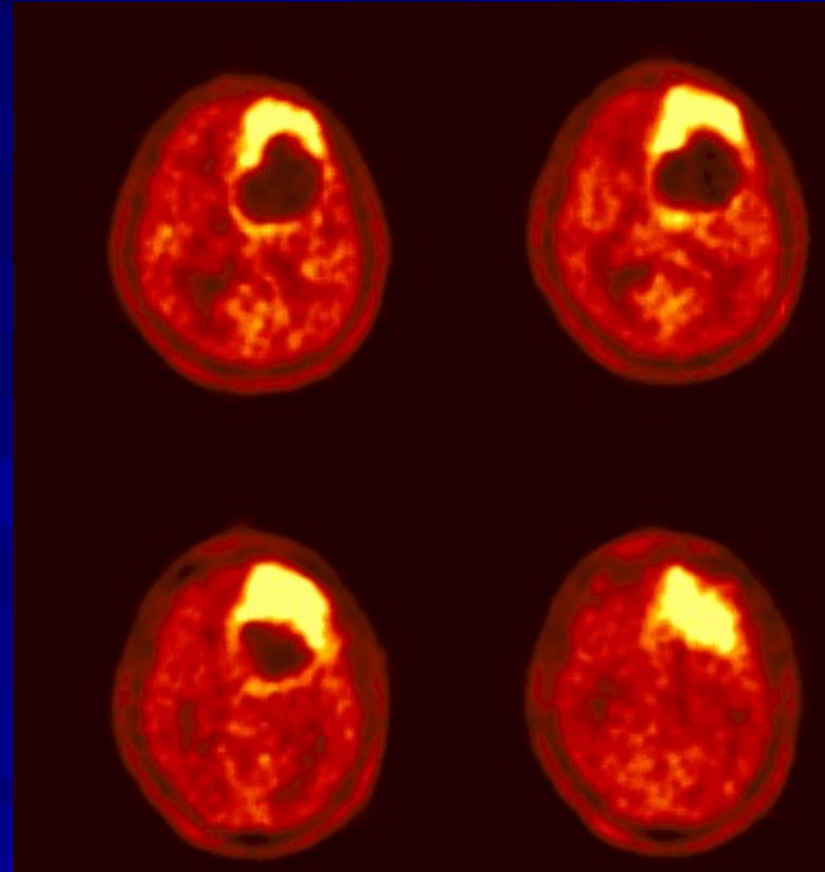
**$^{11}\text{C}$ -methionine**

## праћење ефекта радиотерапије

MRI

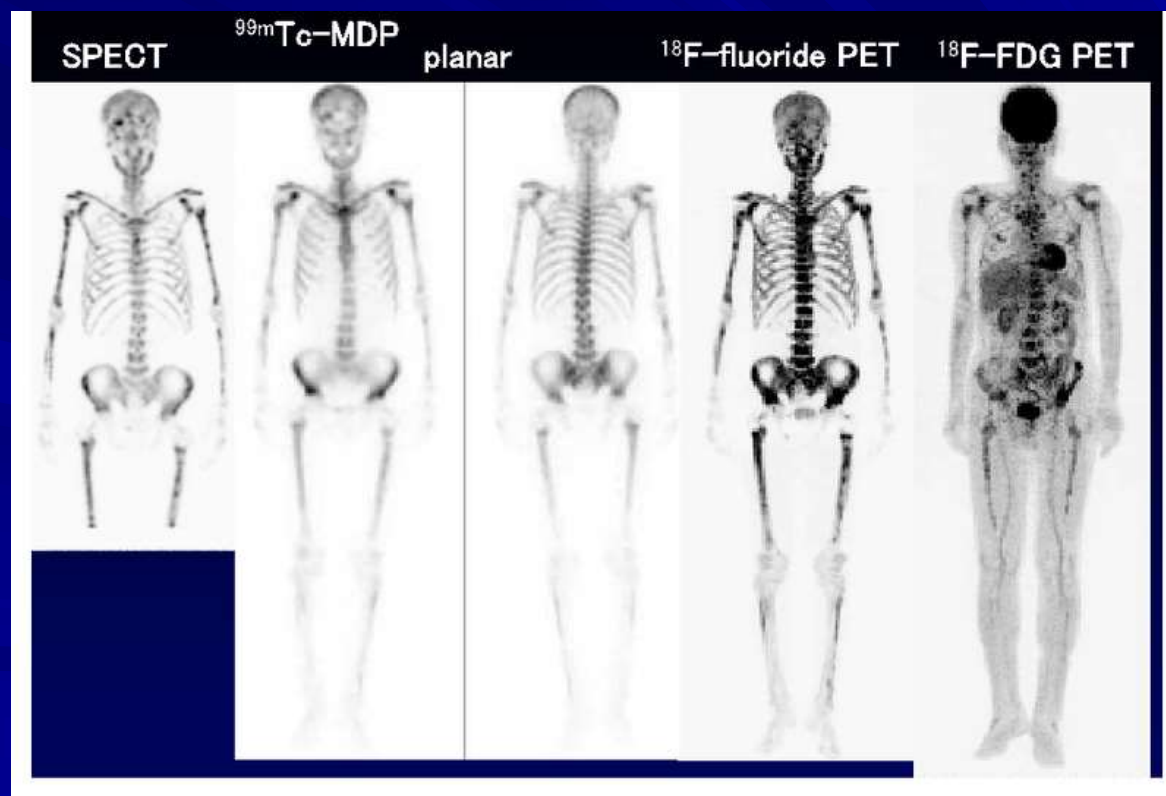
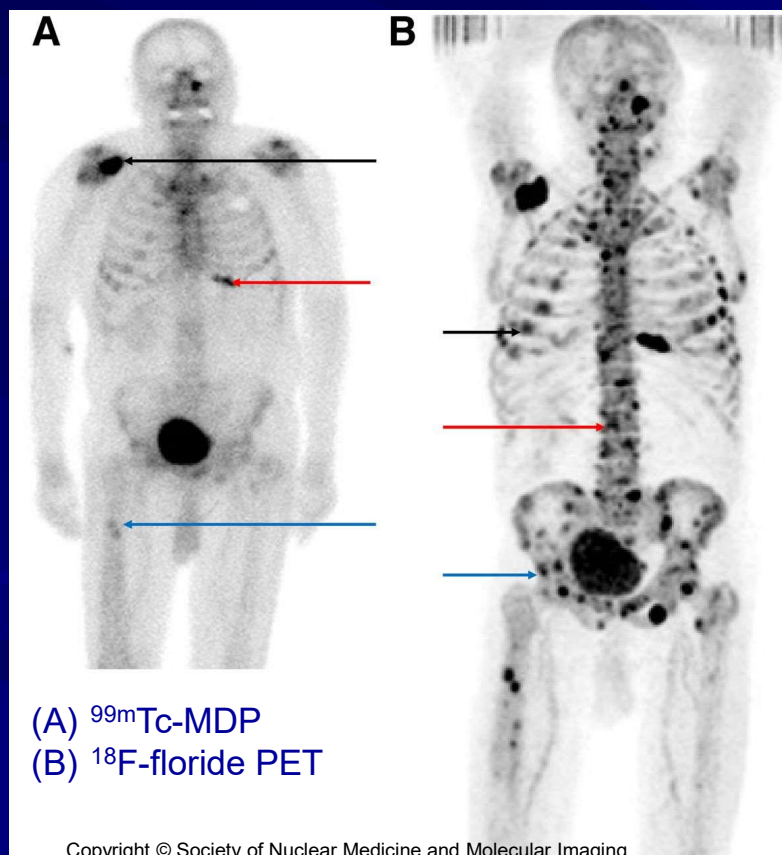


$^{11}\text{C}$ -methionin



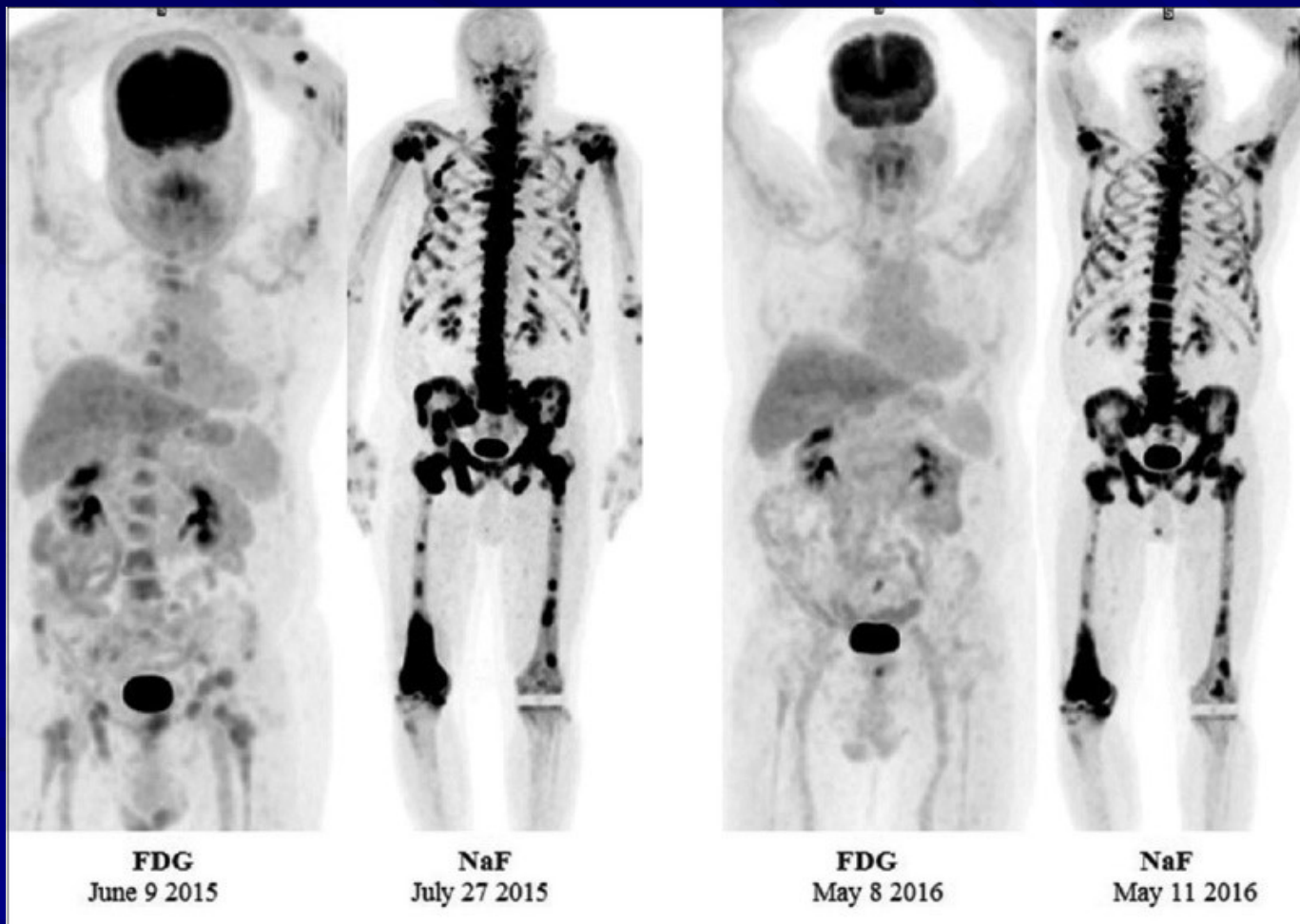
Тумор високог степена малигнитета са зоном некрозе у којој изостаје накопљање РФ

## Bone metastases $^{18}\text{F}$ -Na Fluoride





## Bone metastases $^{18}\text{F}$ -Na Fluoride



## Somatostatin receptor PET tracers: Ga-68

Somatostatin has 5 receptors. Ga-68 is more sensitive.

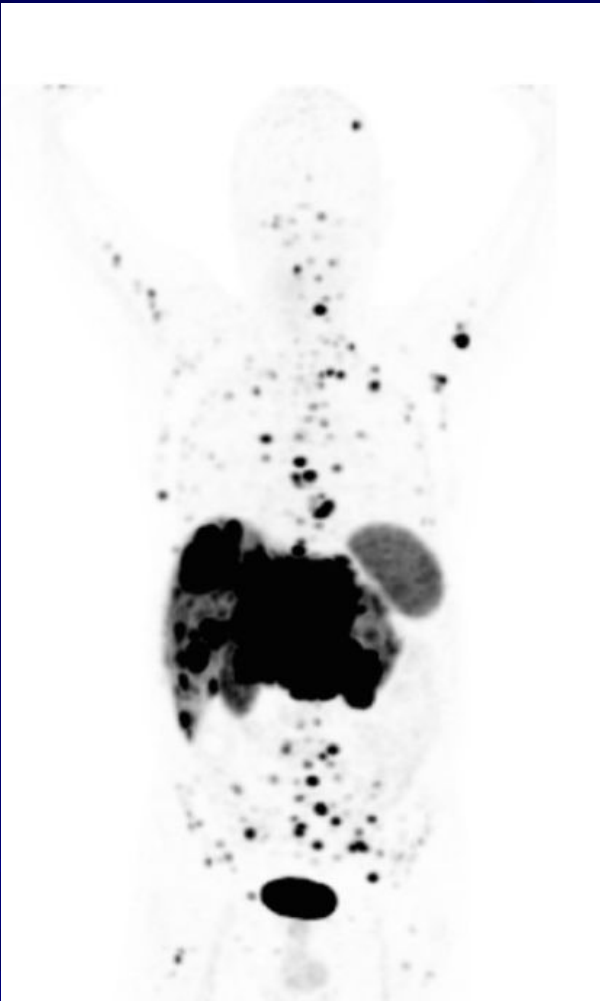
Higher lesion detection rate than what is achieved SSTR PET, than somatostatin receptor SPECT, CT, or MR imaging.

Sensitivity: 70-100% (depends on density of somatostatin receptors in the tumor).

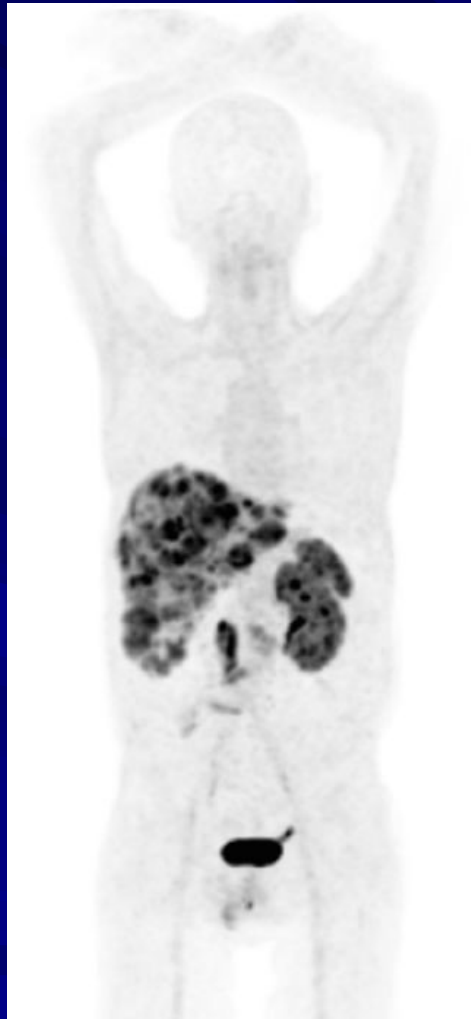
**Indications:** Tumours with high expression of receptors of somatostatin.

1. Gastroenteropancreatic tumours (e.g. carcinoids, gastrinoma, insulinoma, glucagonoma, VIPoma,
2. Sympathoadrenal system tumours (pheochromocytoma, paraganglioma, neuroblastoma, ganglioneuroma).
3. Medullary thyroid carcinoma.
4. Pituitary adenoma.
5. Medulloblastoma.
6. Merkel cell carcinoma.
7. Small-cell lung cancer

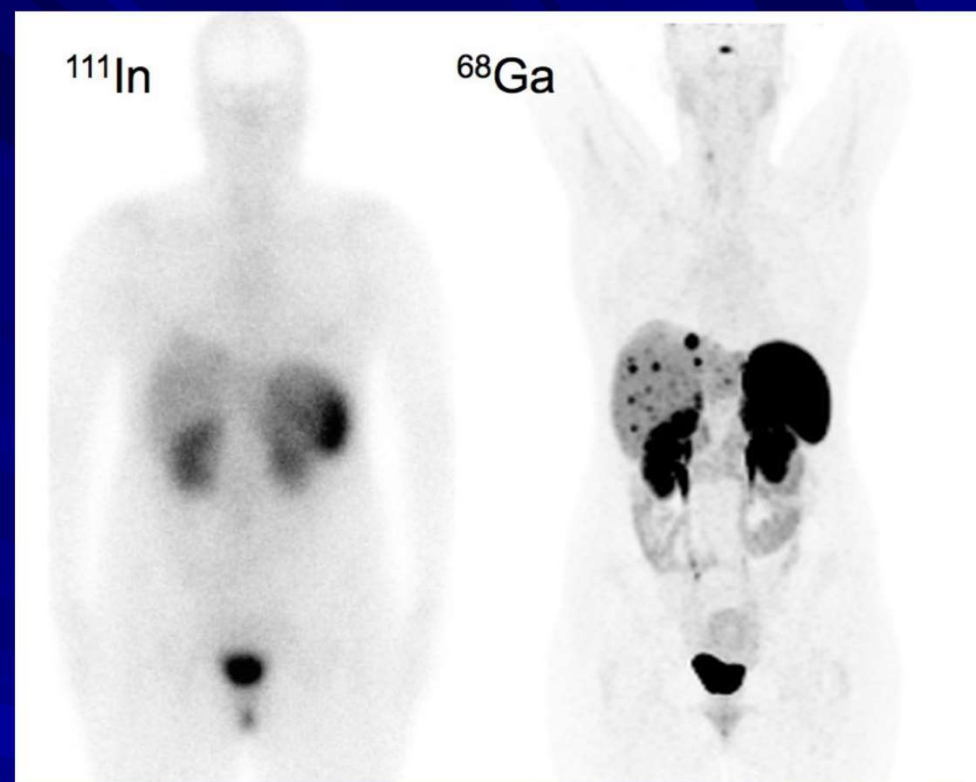
	Well-differentiated		Poorly differentiated
Grade (ENETS)	Low (G1)	Intermediate (G2)	High (G3)
Ki-67 index (%)	≤2	3-20	>20
Anatomic imaging	more rapid growth on serial imaging		
Functional imaging	<div> <div>Octreoscan SPECT or SSTR PET +ve</div> <div>FDG PET +ve</div> </div>		



NET with extensive metastatic lesions throughout the body



NET with multiple metastatic disease confined to the liver and abdominal cavity




**Carcinoid tumor:** Positive  $^{68}\text{Ga}$ -DOTA-NOC and Negative  $^{111}\text{In}$ -Octreoscan.

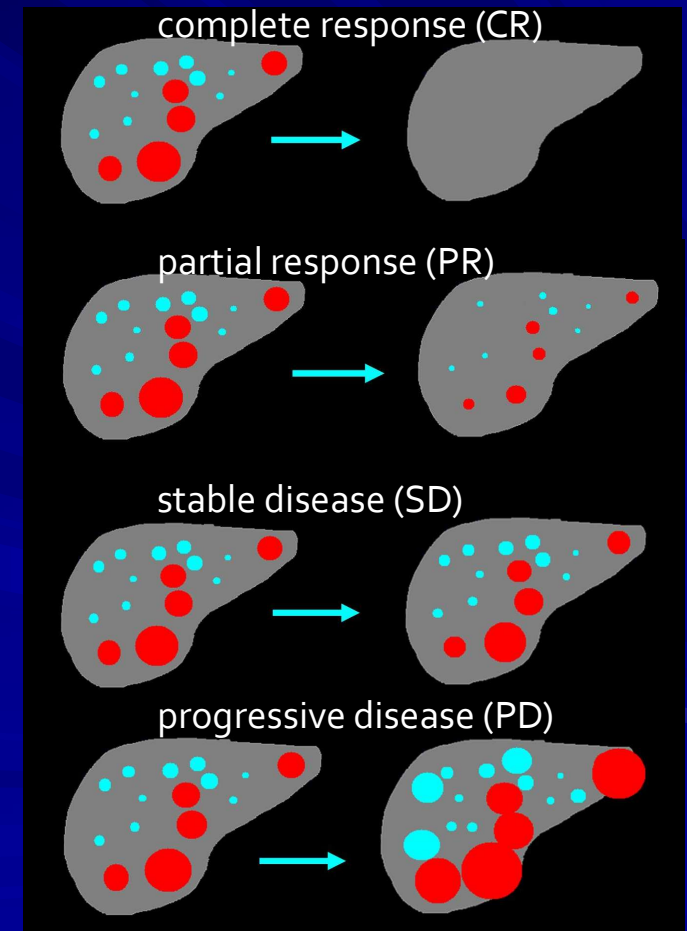
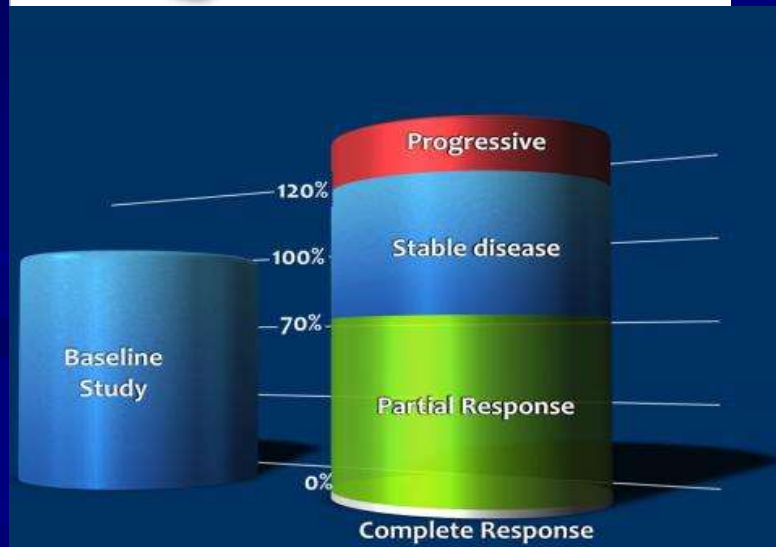
**Ga DOTA-NOC Findings:** Multiple metastatic lesions in the liver.

# Evaluation and monitoring of response to therapy

RECIST (Response Evaluation Criteria in Solid Tumours) v.1.1 - MDCT

SLD-sum of length diameter

Criteria for target lesions	
Tumours	Malignant lymph nodes
CT scan: long axis $\geq$ 10mm Chest X-ray: long axis $\geq$ 20mm	Short axis diameter $\geq$ 15mm
	

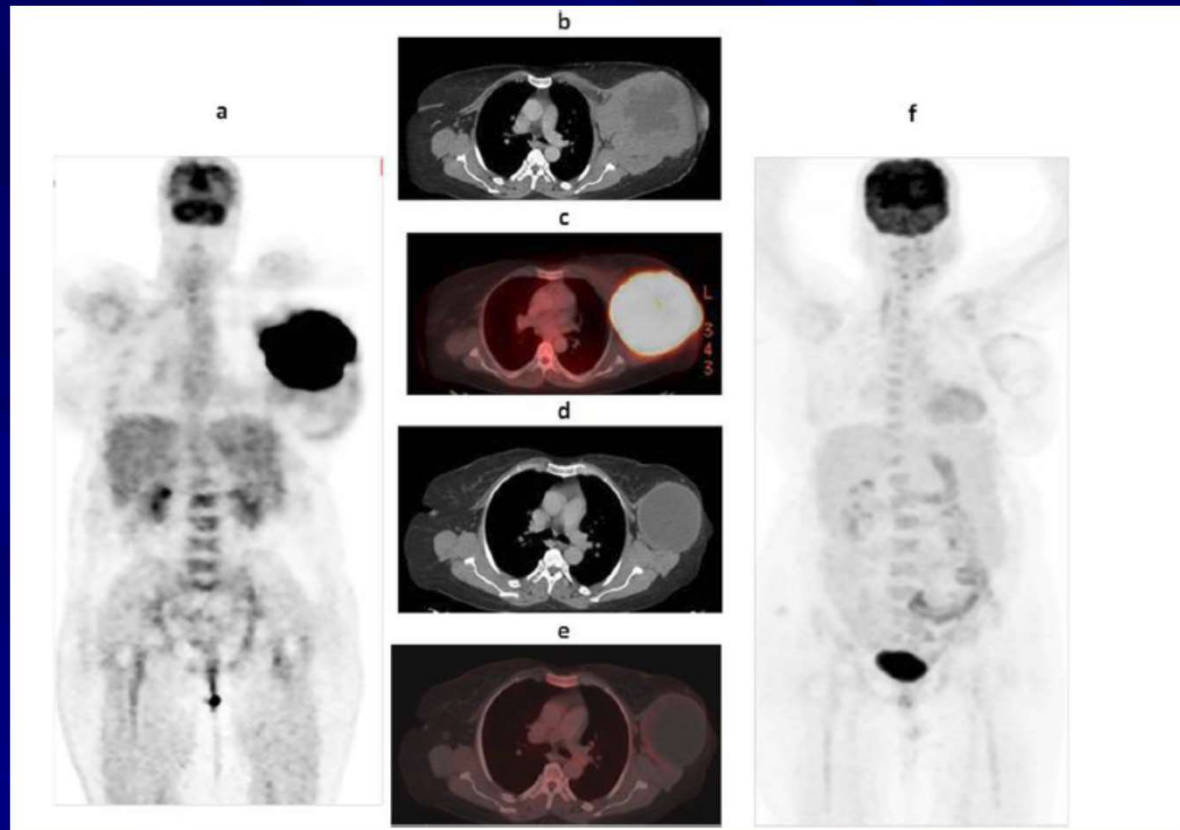


## Evaluation and monitoring of response to therapy

CRITERIA	RECIST 1.1	PERCIST
<b>Complete response (CR)</b>	Disappearance of all lesions No new lesions	Disappearance of all metabolically active lesions
<b>Partial response (PR)</b>	30 % decrease in the sum of diameters of the target lesion	30% and a 0.8-unit decline in SUL peak between the most intense lesion before treatment and the most intense lesion after treatment, although not necessarily the same lesion
<b>Progression disease (PD)</b>	20% increase in the sum of diameters of the target lesions	30% and 0.8-unit increase in SUL peak or new lesions or 75% increase in total lesion glycolysis
<b>Stable Disease (SD)</b>	Neither PR or PD	Neither PR or PD



## NHL (large B cell type).

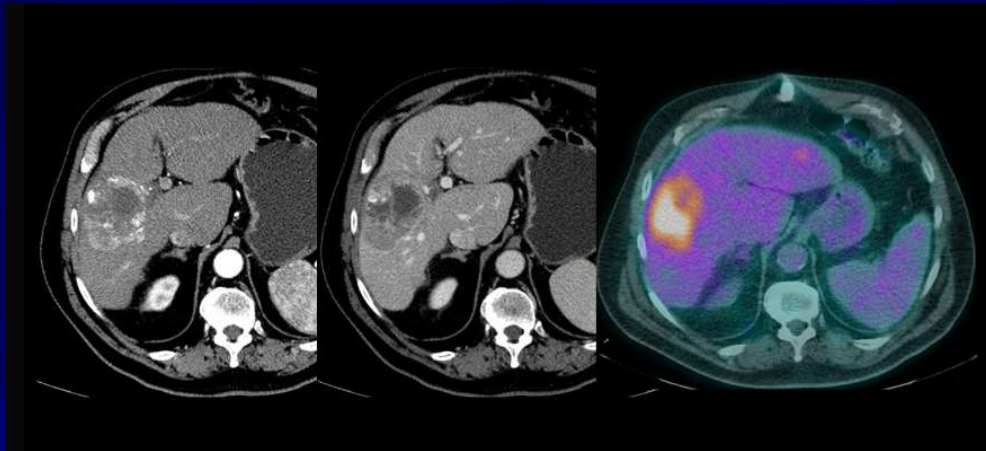


A) Left axila 16 x 16 x 15 cm , SUV-19

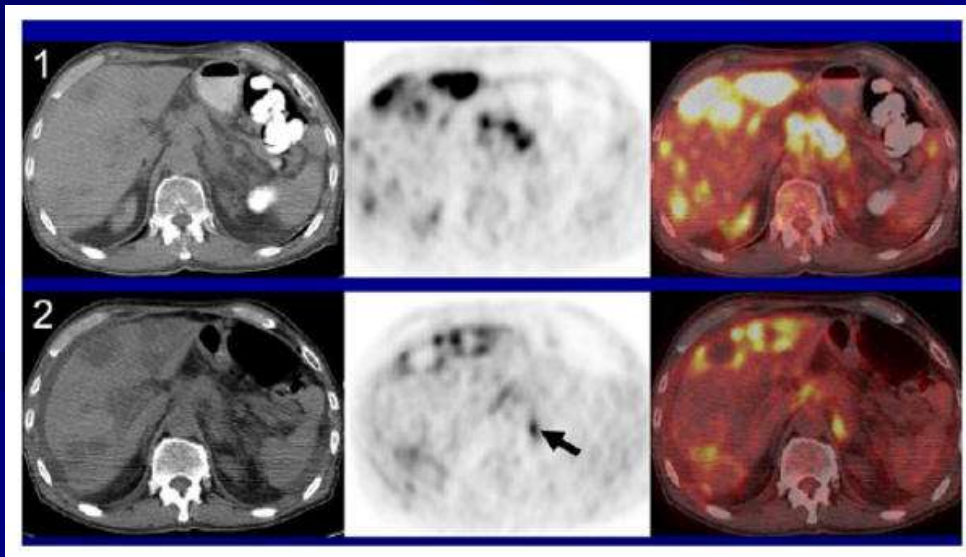
F) Post-therapy– negative uptake 10 x 9,5 x 9,3 cm

PR-RECIST

CR-PERCIST



HCC post -therapy  
RECIST-SD  
PERCIST-PR



Pancreatic cancer post-therapy  
RECIST-PR  
PERCIST-PD

# CONCLUSION

Integrated PET/CT provides:

- More precise staging than all the other imaging techniques
- Allows better selection of patients for new modalities of treatment
- Helps in re-staging after induction therapy
- It is cost-effective
- Precise delineation - EBRT Planning
- Helps in follow up evaluation by differentiating Residual or recurrent tumor from Post-treatment scarring

But....

# CONCLUSION

## $^{18}\text{F}$ -FDG-PET/CT

- False positive results (High metabolic activity in):
  - Inflammation, infection
  - Granulomatous diseases (Sarcoidosis...)
  - Benign tumors
  - Brown fat... Artifacts....

# Instead of CONCLUSION

## $^{18}\text{F}$ -FDG-PET/CT

- False negative results:
  - Small lesions < 8-10mm (limited spatial resolution of PET)
  - Necrotic tissue
  - Bronchoalveolar carcinoma, carcinoid....
  - Hyperglycemia, hyperinsulinemia, corticosteroid therapy