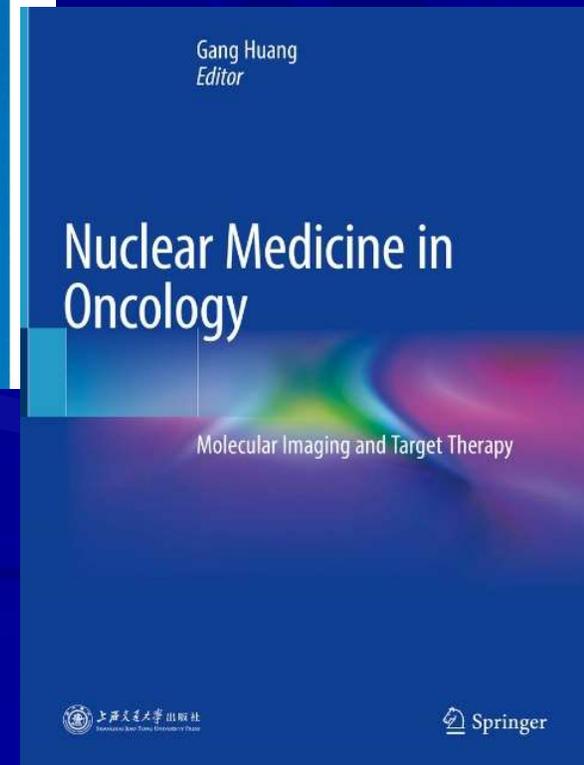
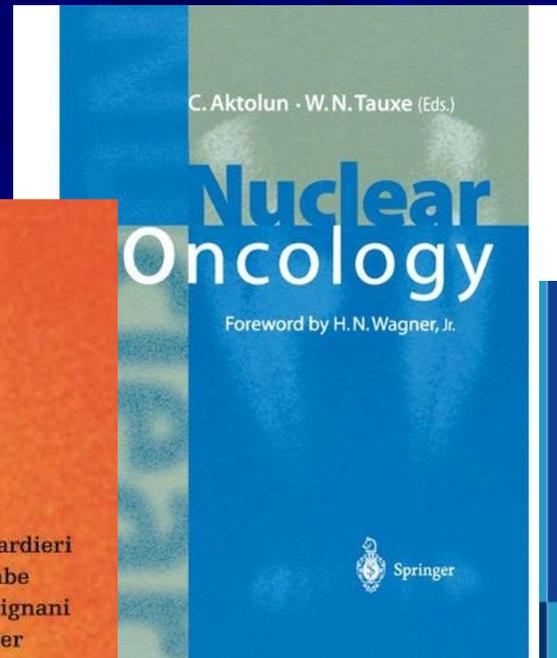
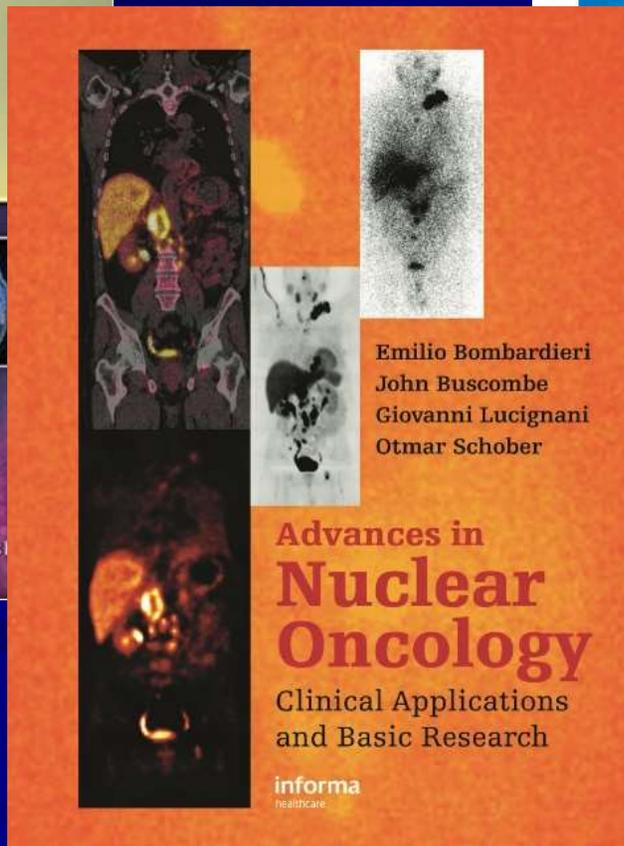
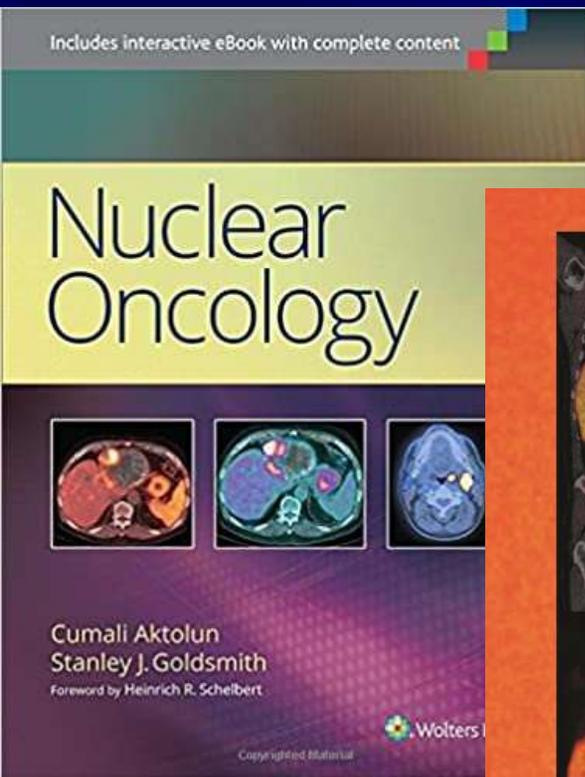


ONCOLOGY 1

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.

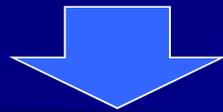
Nuclear oncology, a fast growing field of nuclear medicine



ONCOLOGY

Imaging

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



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

Therapy

Specific only

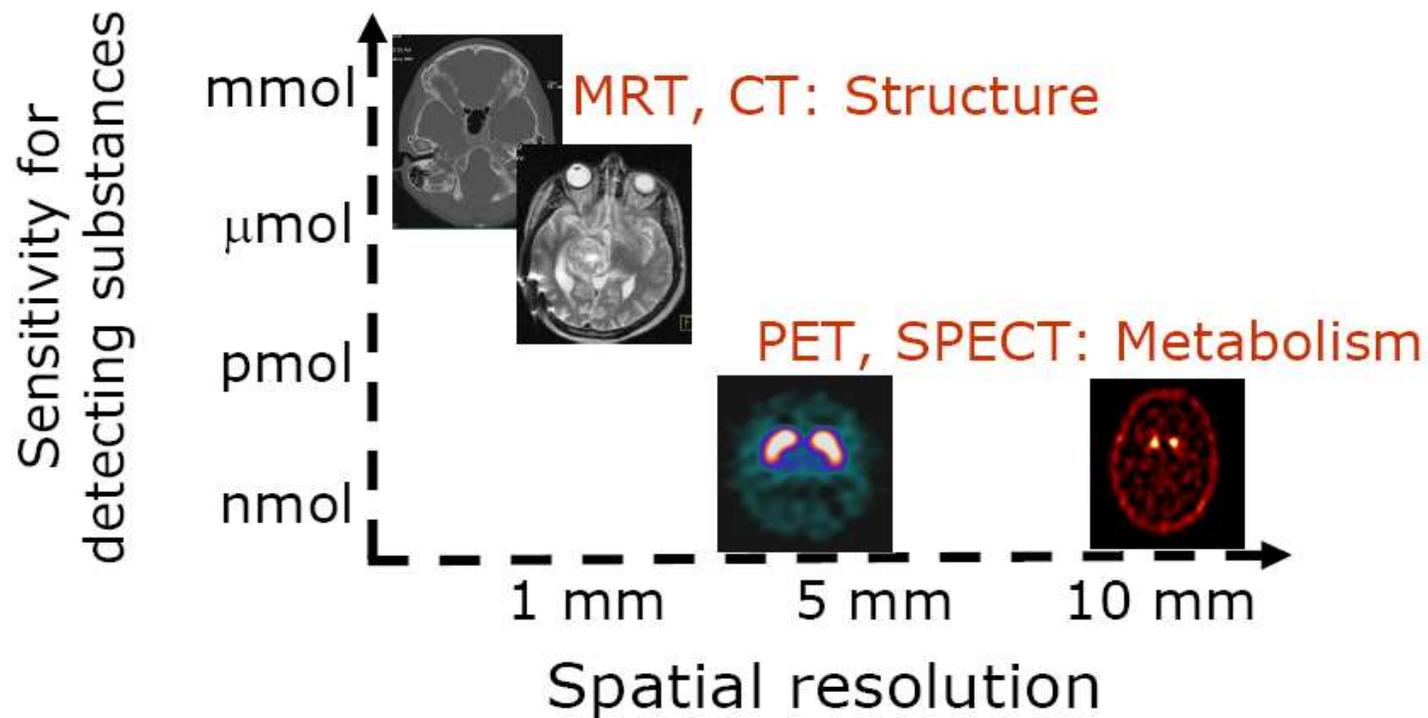


B+ emitting RF
a emitting RF

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)



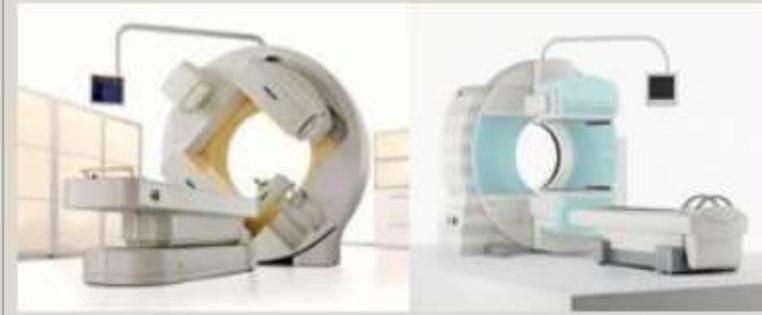
Conventional tumor imaging

Planar: 2D.

SPECT: 3D.

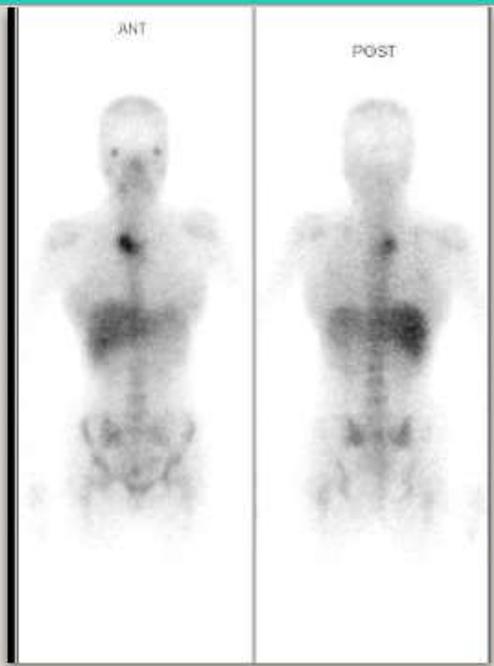
SPECT-CT : 3D (Function and anatomy).

SPECT: Single photon emission computed tomography.



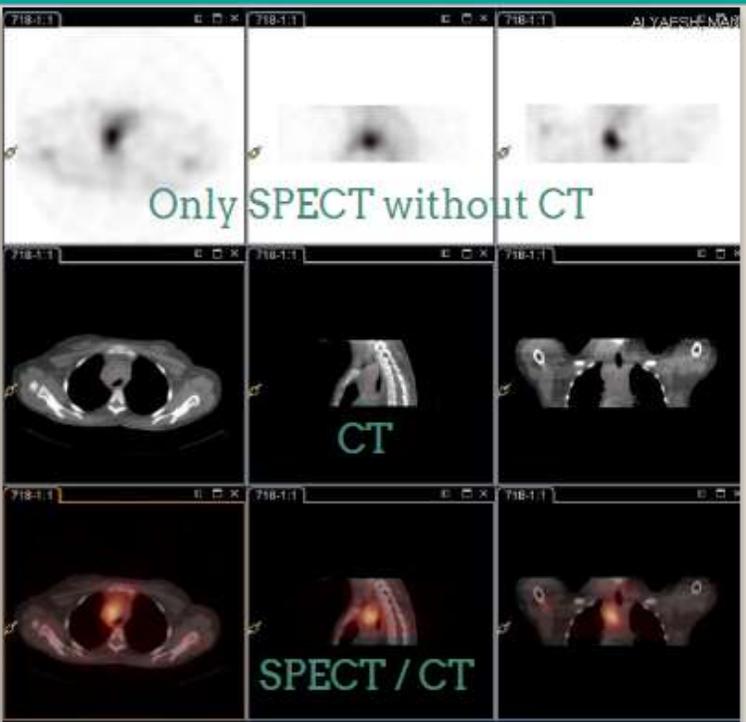
Single Photon Emission Computed Tomography (SPECT) and SPECT CT

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.**

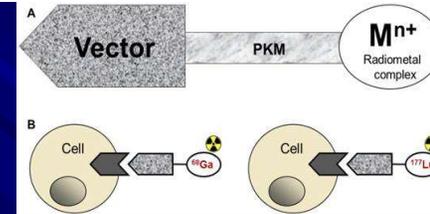
Mechanism of accumulation in tumor tissue:

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

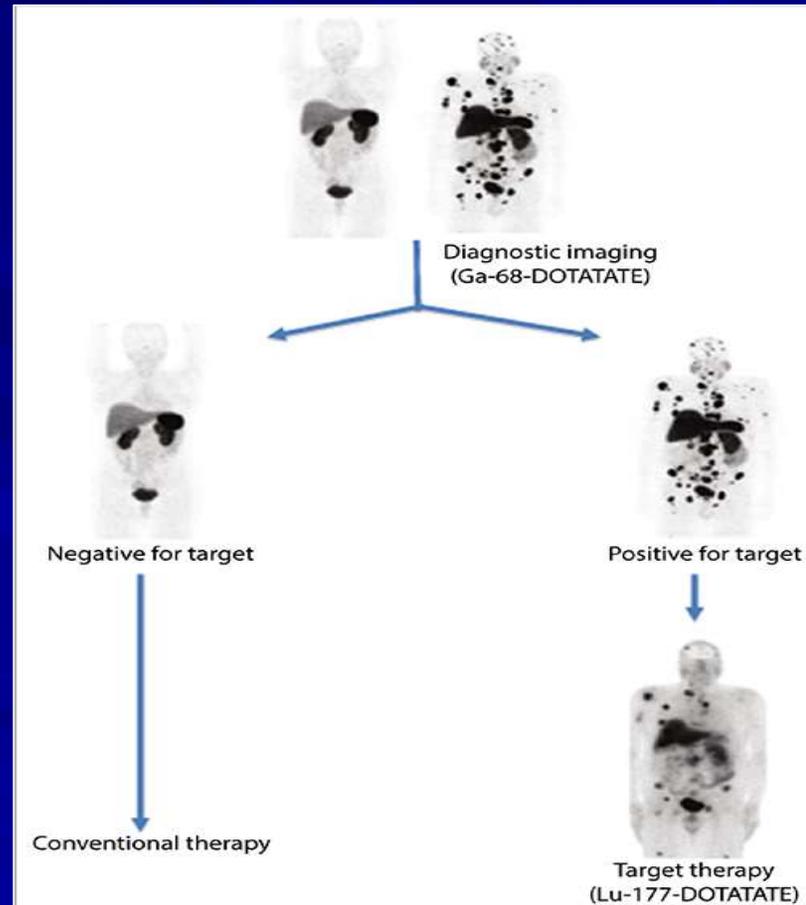
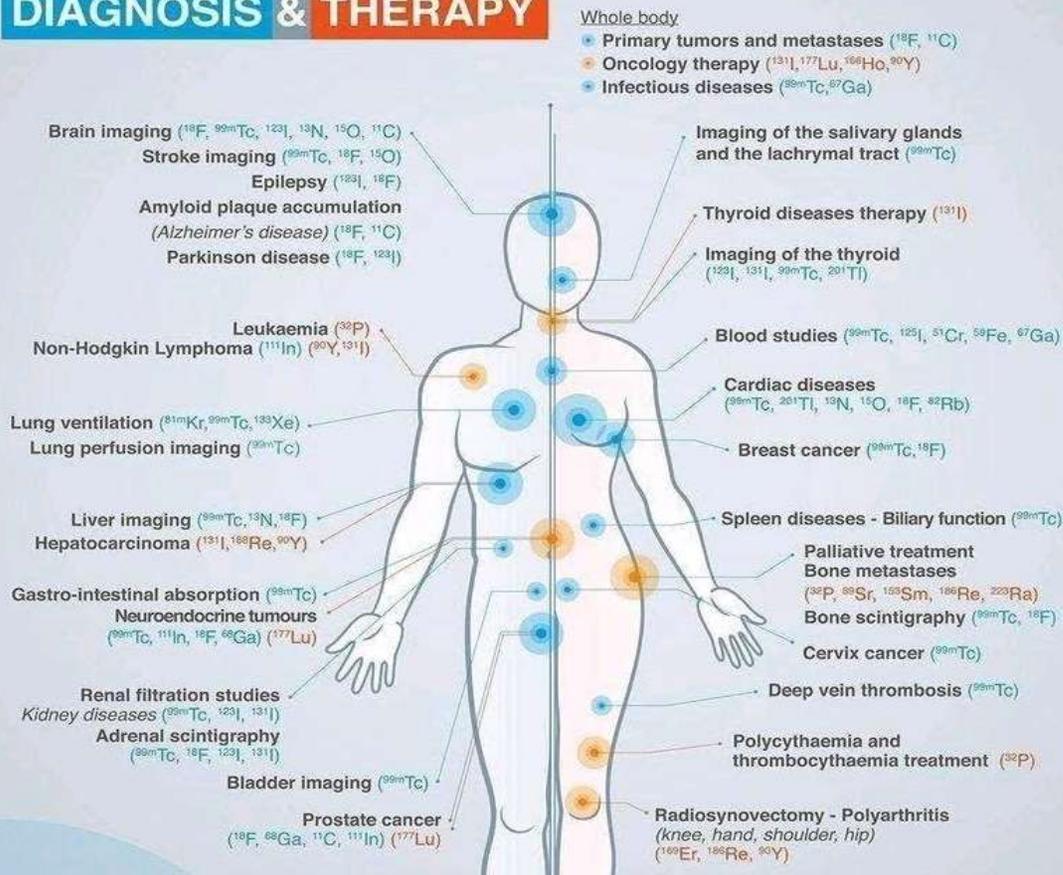
THERANOSTICS

"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 Tc-99m octreotide for tumours expressing somatostatin receptors.
Gallium-68 is more sensitive than Tc-99m octreotide.
- Monoclonal antibodies labelled with In-111 (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.
- **Tc-99m Nanocolloid** – bone marrow scan.
- **Tc-99m 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

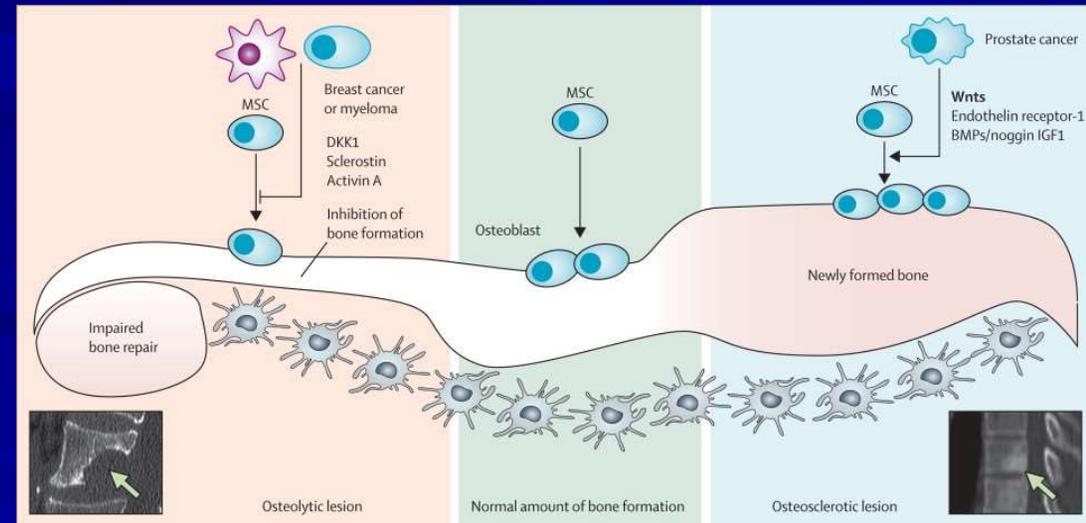
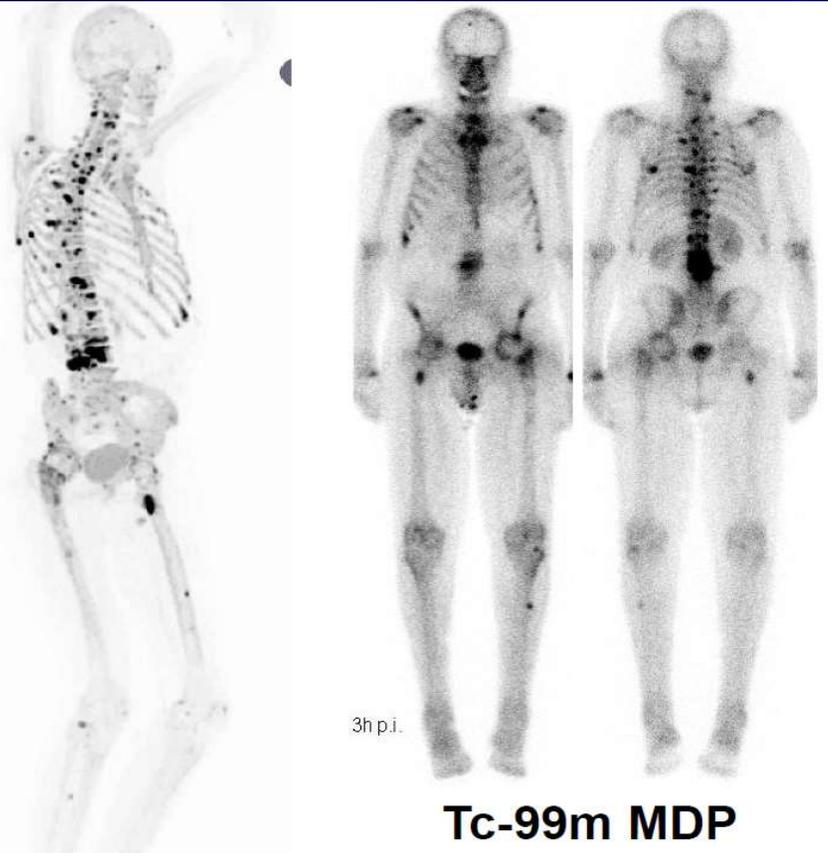
- ✓ Increased vascularization.
- ✓ Increased capillary permeability.
- ✓ Newly proliferated capillaries.
- ✓ Increased blood flow.
- ✓ Increased energy demand.
- ✓ Increased metabolically active cells.

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.

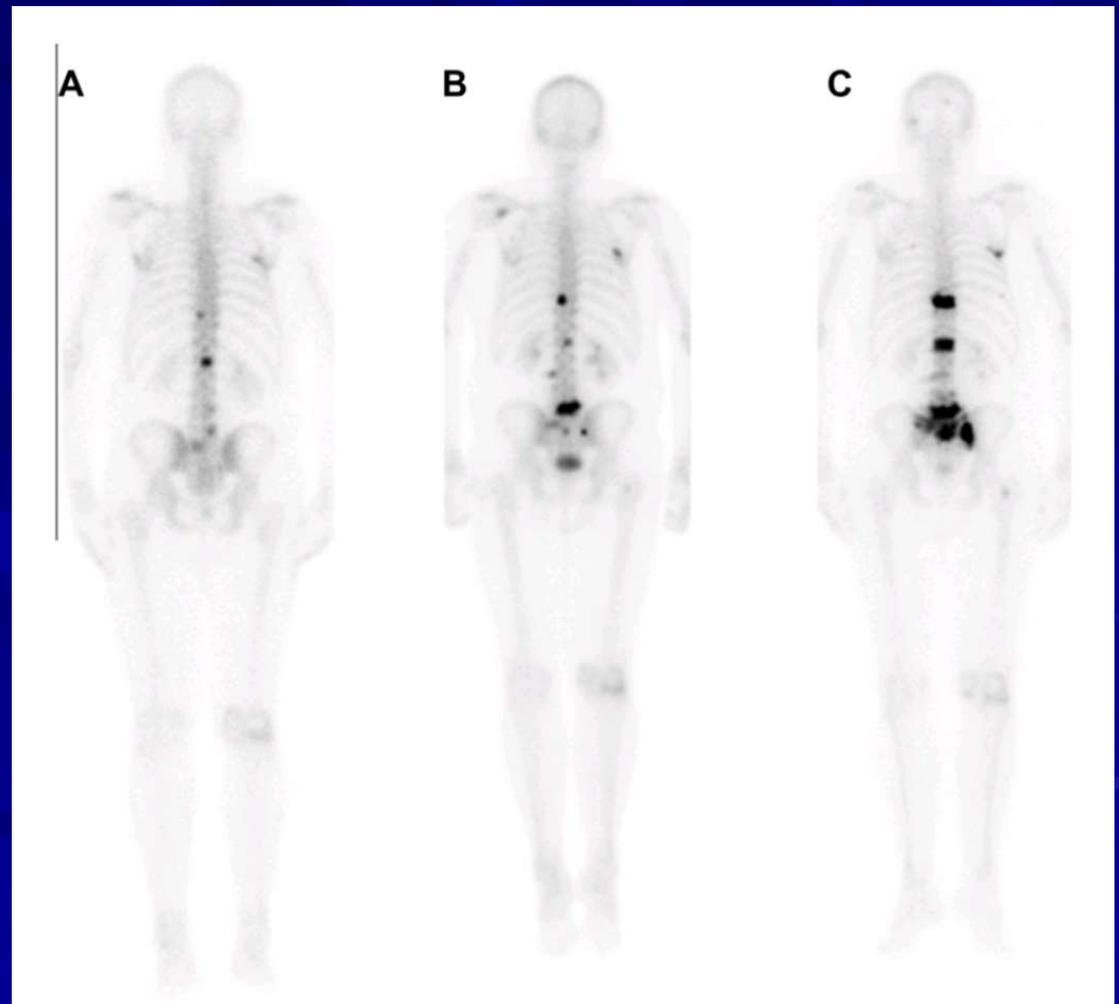
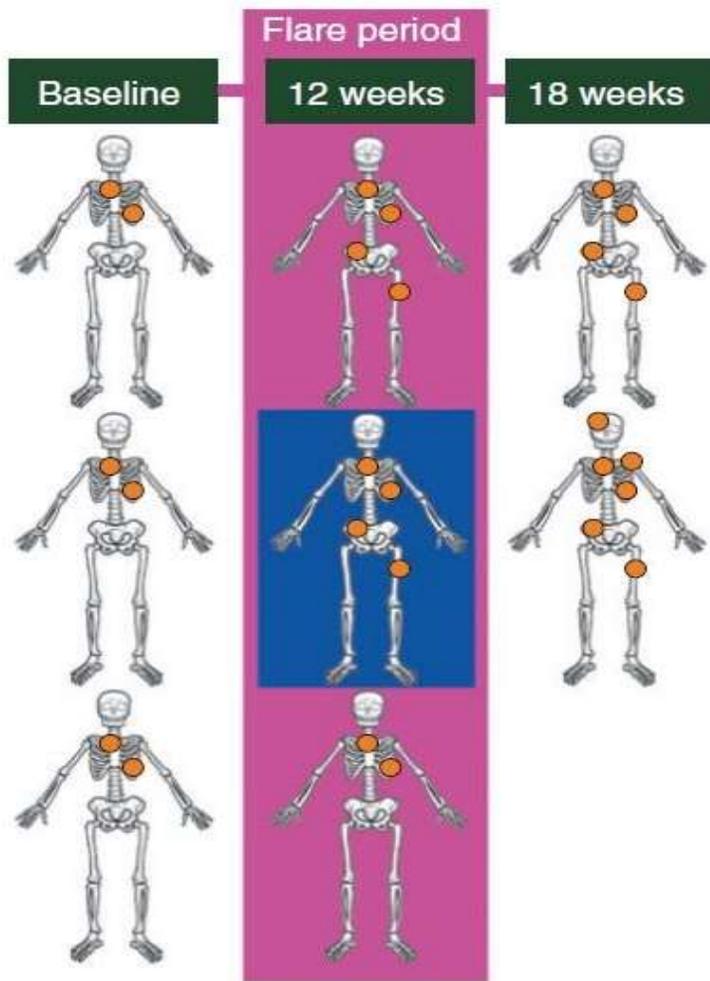
II. Primary Bone Tumors:

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

III. Soft tissue tumors:

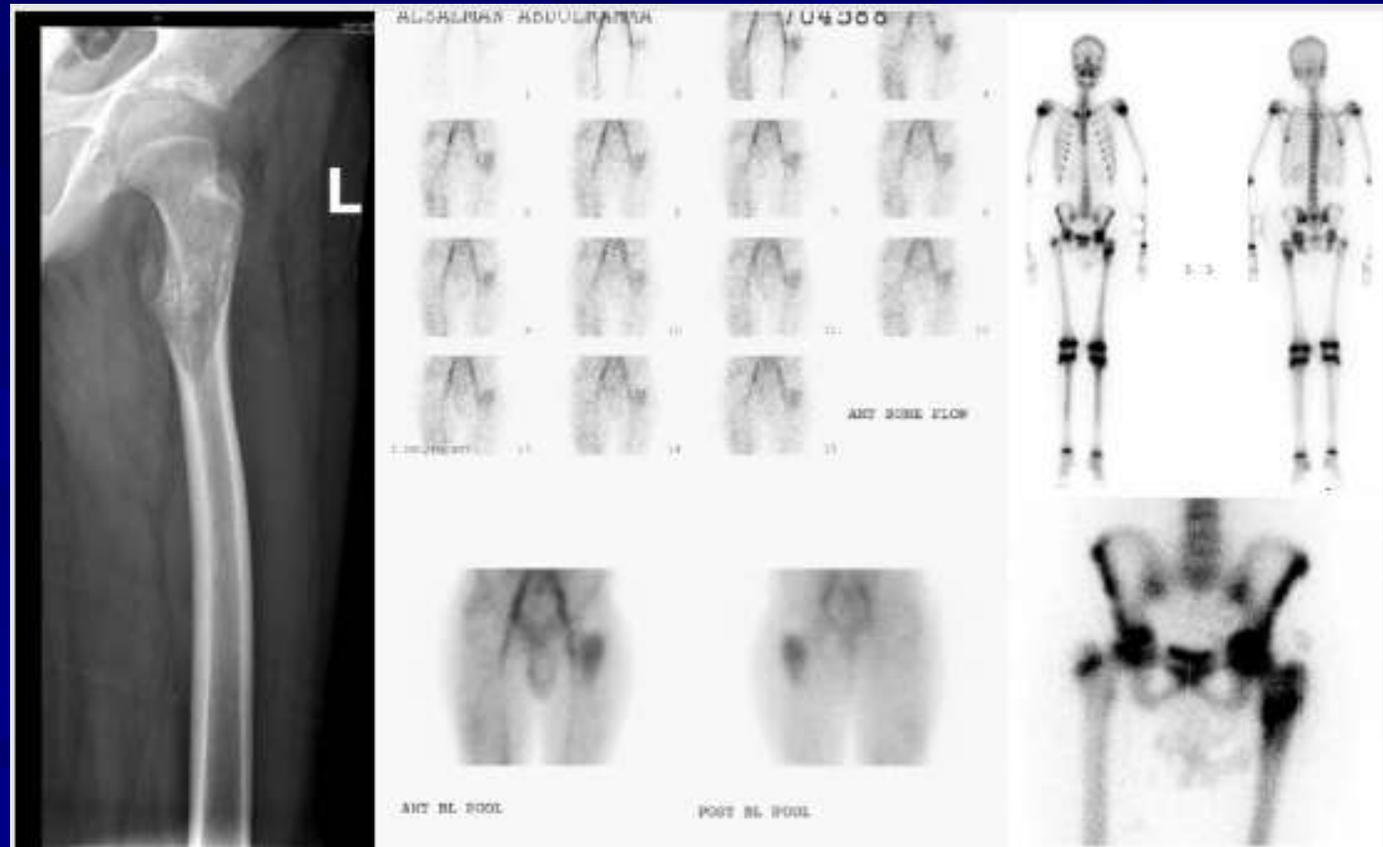
- Primary
- Metastases.

Bone Scan Tumor Staging



Ewing's Sarcoma

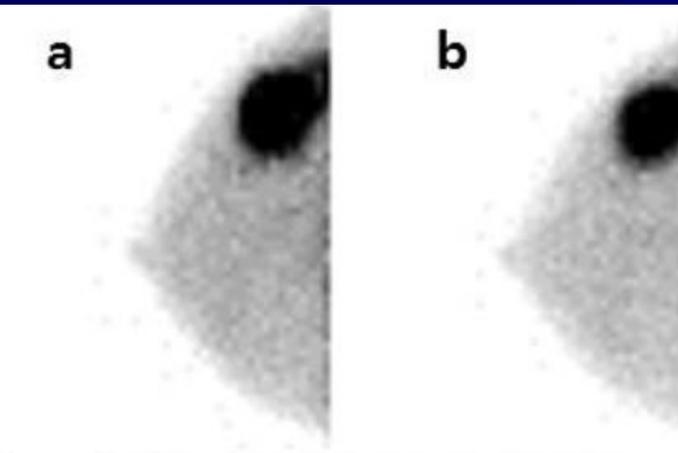
Usually affects young people, that is why we can see growth plates. The primary diagnosis of bone tumor is To determine the local extent and to search for distant metastasis.



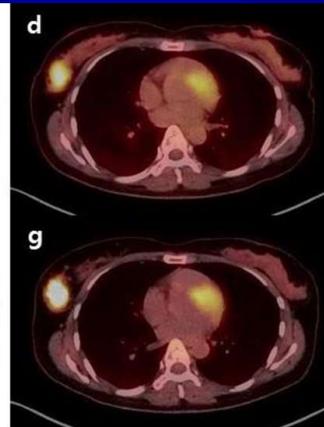
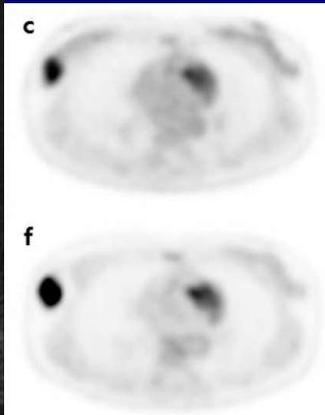
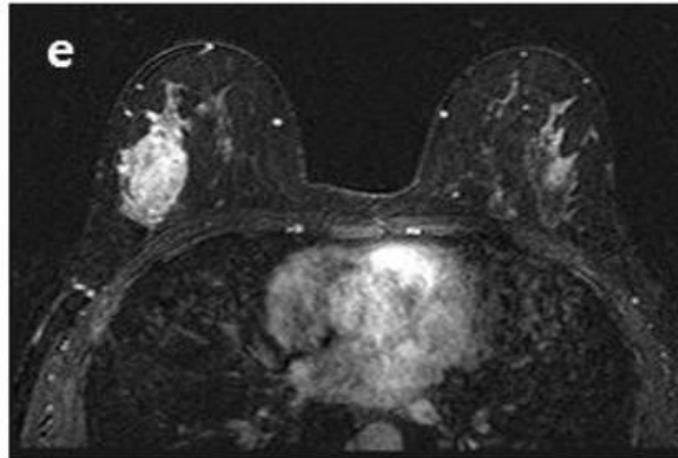
- In this patient the tumor is confined to proximal left femur but rest of skeleton is clear with no metastasis.

^{99m}Tc -MIBI (methoxyisobutyl isonitrile)

CA mamme



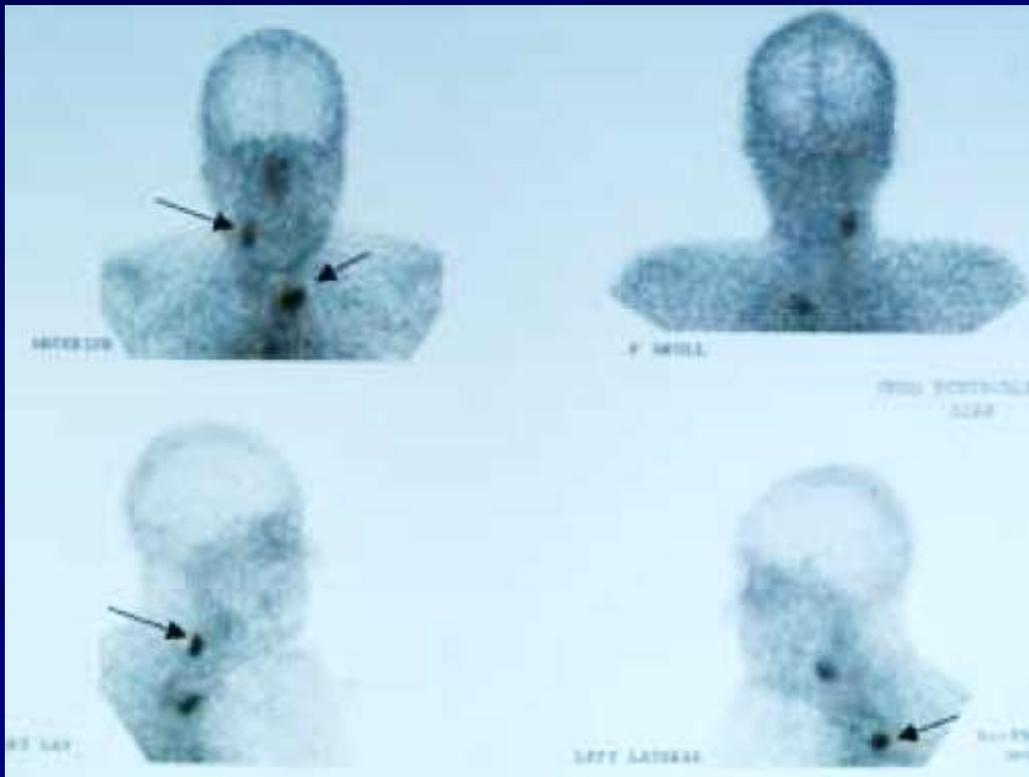
^{99m}Tc -MIBI scan in different types of malignancy including breast and lung cancer, lymphoma and sarcoma. Mechanisms of cell resistance, mainly involving alterations of apoptosis, may affect uptake in tumors.



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

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

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

^{111}In -pentetreotide (Octreoscan)

^{99m}Tc -Depreotide (Neospect)

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

^{18}F -DOPA

^{68}Ga -DOTATOC/TATE 72%

^{131}I -MIBG (30%)

74% and 87%

TUMOR-SEEKING RF

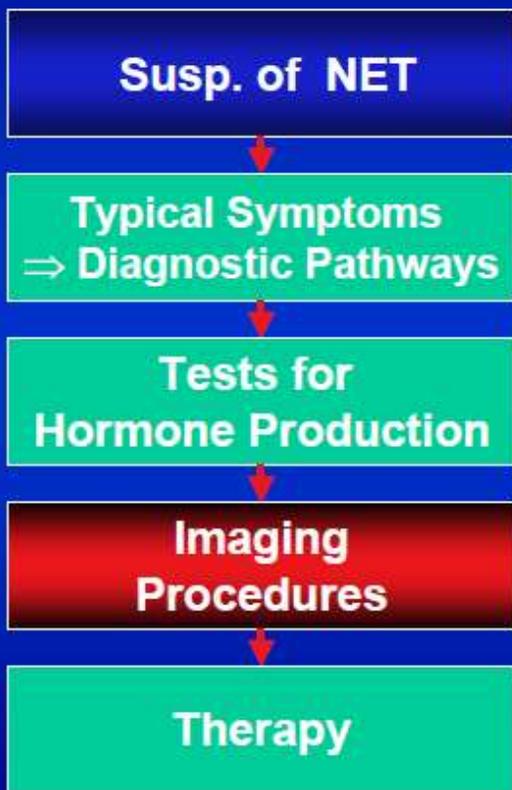
“POSITIVE” UPTAKE - MORE INTENSIVE ACCUMULATIONS OR
"HOT" SPOTS WHERE THE TUMOR IS LOCATED IN THE BODY

SPECIFIC TUMOR UPTAKE

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

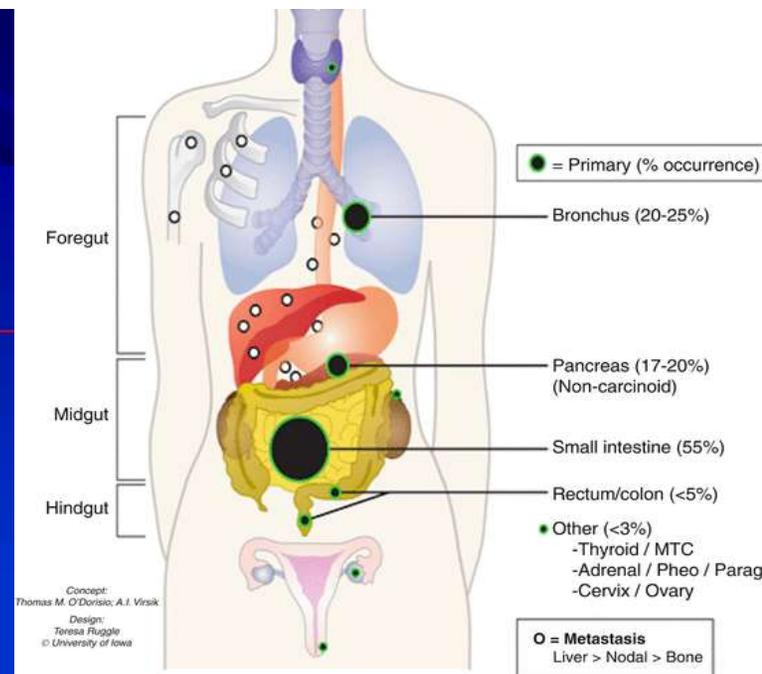
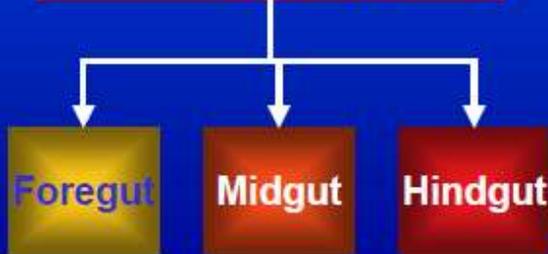
Somatostatin Receptor Imaging

Neuroendocrine Tumors (NET) – Diagnosis –



Diagnostic Methods:

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



in vitro receptor status

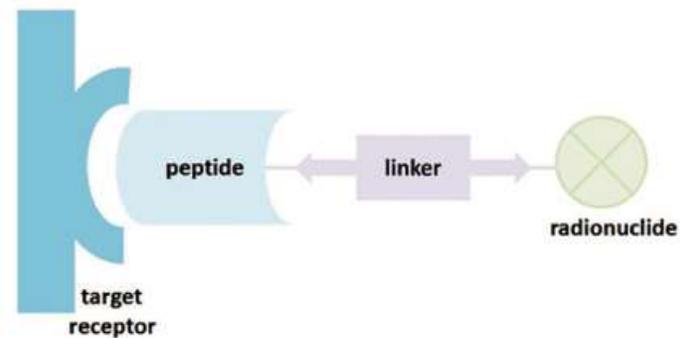
| | |
|---------------------------|-------|
| • Gastrinoma, Glucagonoma | 100 % |
| • Insulinoma | 72 % |
| • Paraganglioma | 92 % |
| • MTC | 38 % |
| • Carcinoid | 88 % |
| • SCLC | 57 % |
| • Pheochromocytoma | 73 % |

Dg management

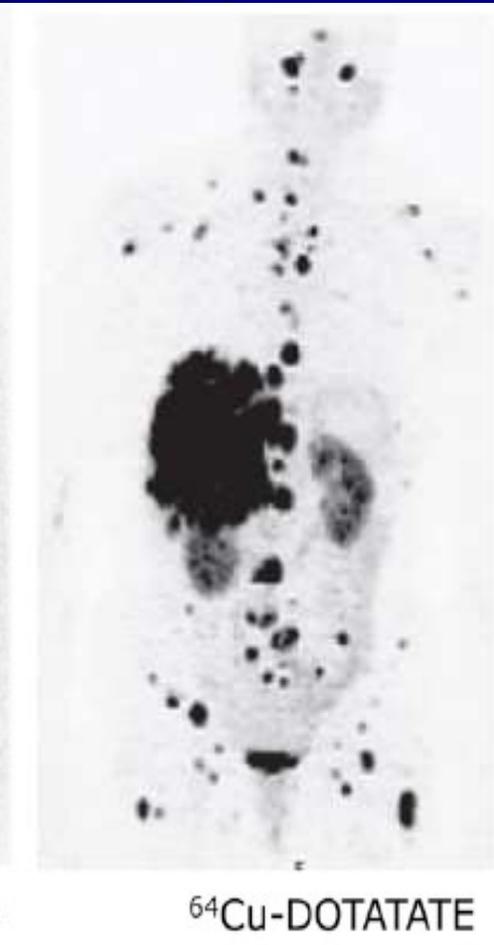
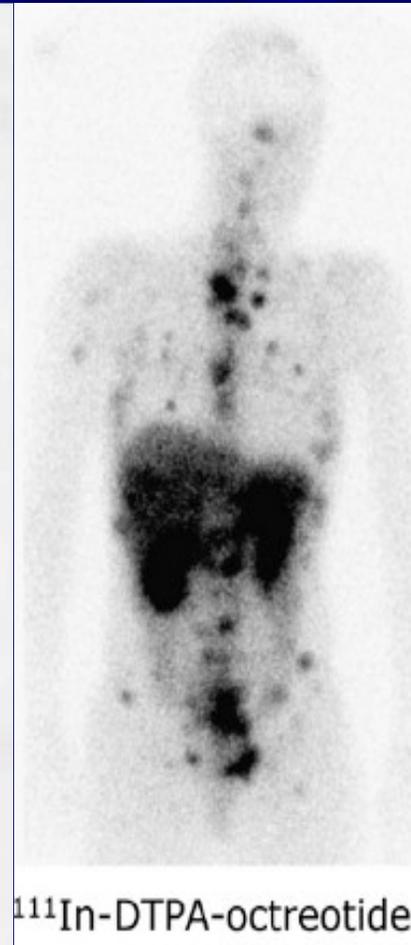
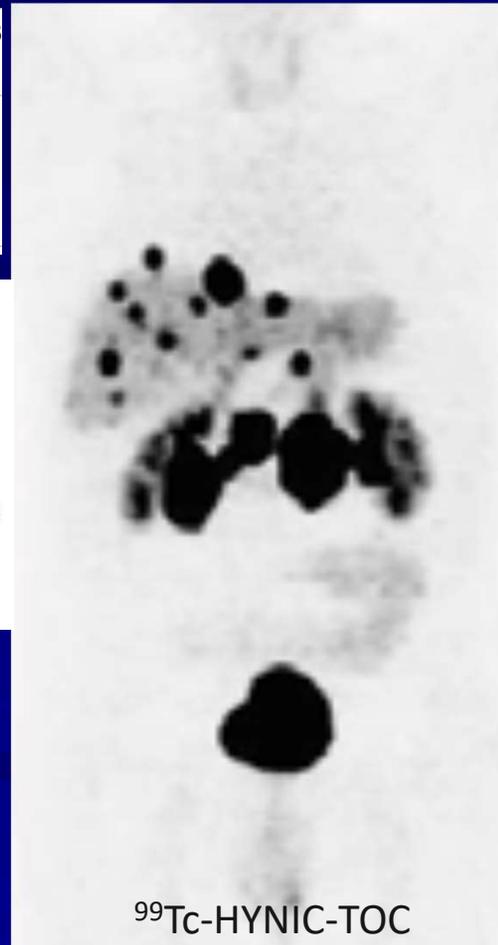
| | Well-differentiated | | Poorly differentiated |
|--------------------|---|-------------------|-----------------------|
| Grade (ENETS) | Low (G1) | Intermediate (G2) | High (G3) |
| Ki-67 index (%) | ≤2 | 3-20 | >20 |
| Anatomic imaging | more rapid growth on serial imaging | | |
| Functional imaging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

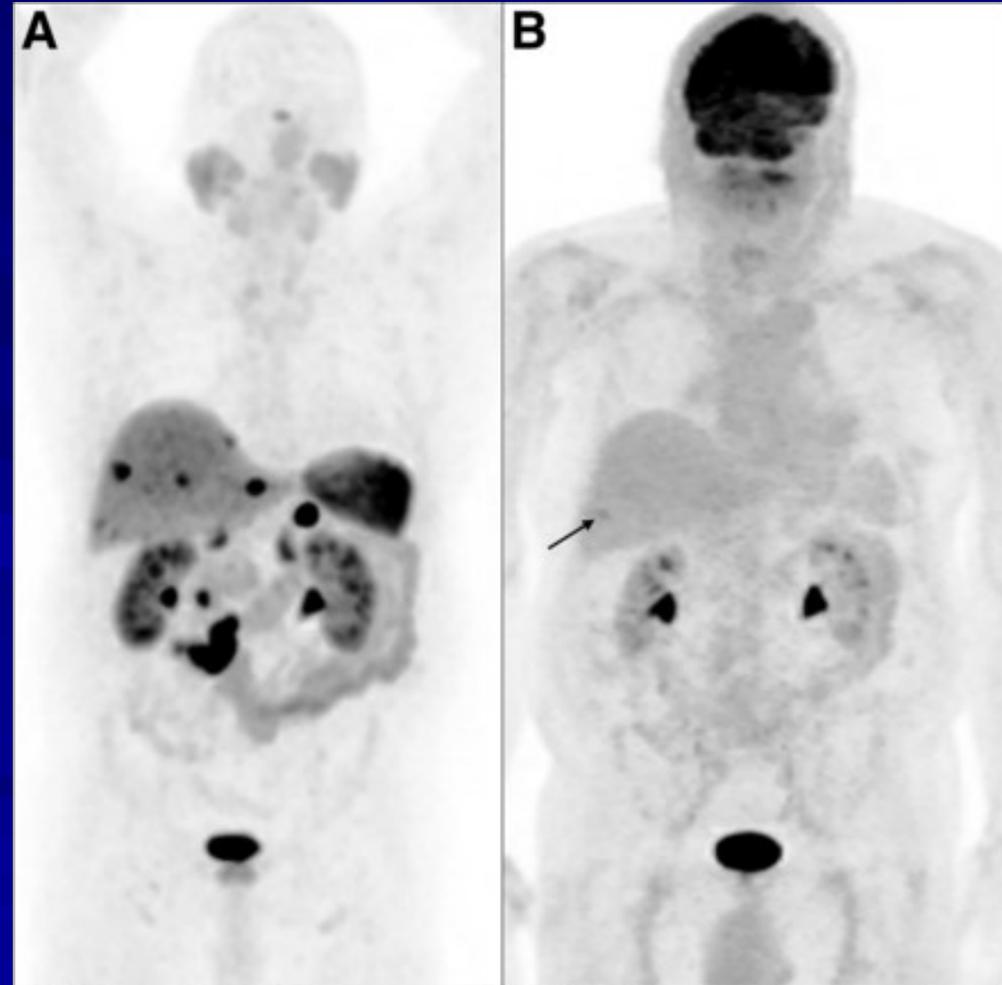


¹¹¹In-DTPA-octreotide
(Octreoscan[®])
^{99m}Tc-HYNIC-TOC
(Tektrotyd[®])



SSTR imaging

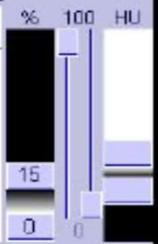
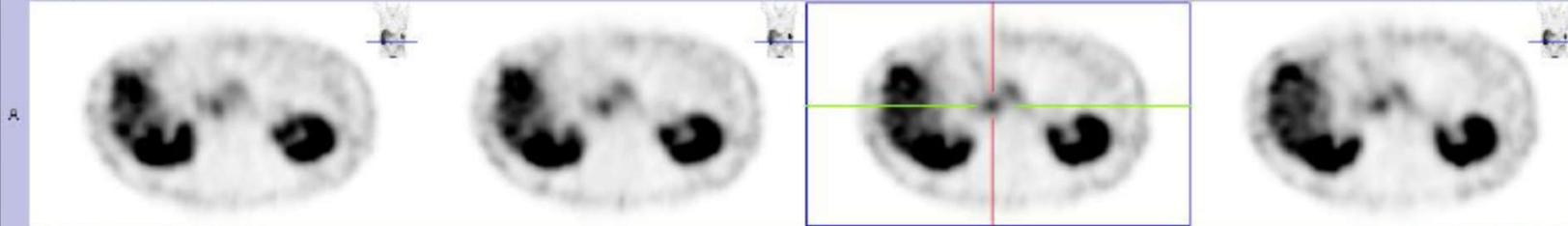
NET grade 1 (Ki-67 < 2%) NEN from small-bowel primary. (A) ^{68}Ga -DOTATATE PET shows prominent uptake in primary tumor, lymphadenopathy, and liver metastases. (B) ^{18}F -FDG PET shows no abnormal uptake (arrow points out incidentally noted fractured rib).



WBSpect Output, 10/12/2008

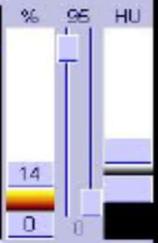
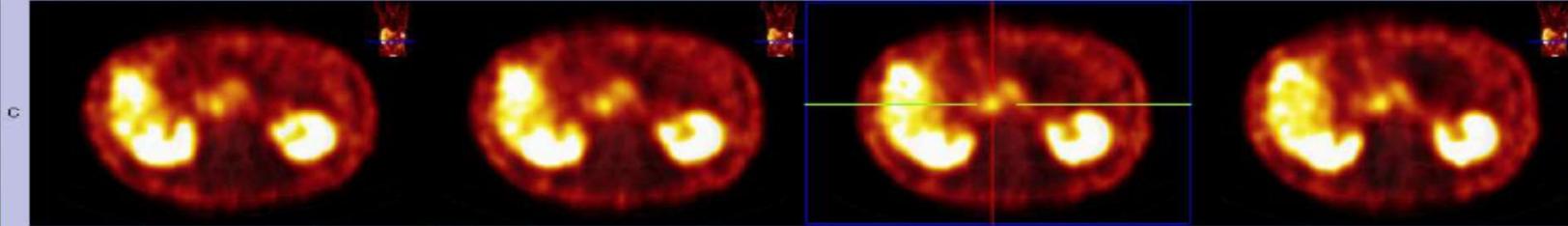
Transverse

ABD 8x8, 14/10/2008

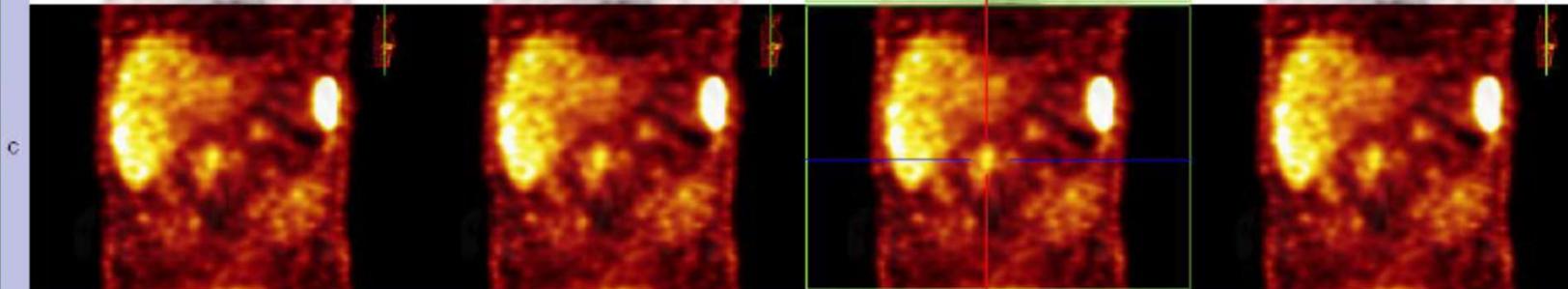
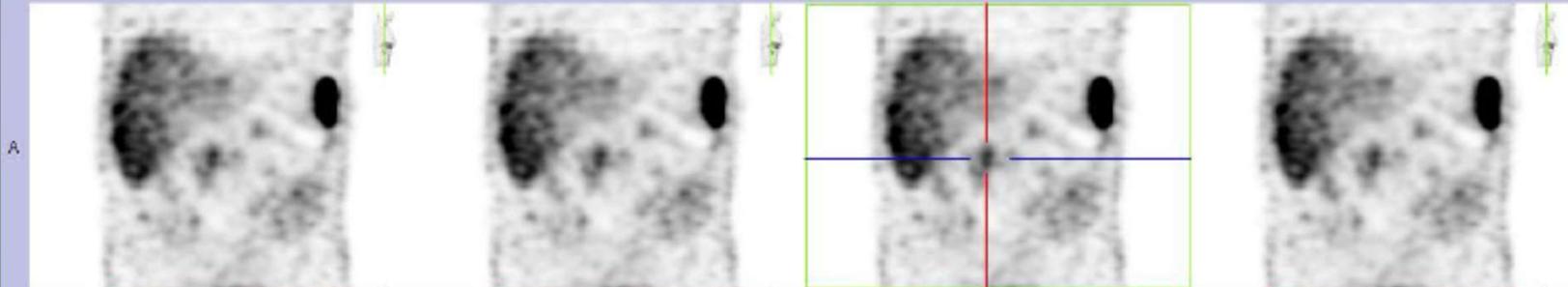


WBSpect Output, 10/12/2008

ABD 8x8, 14/10/2008



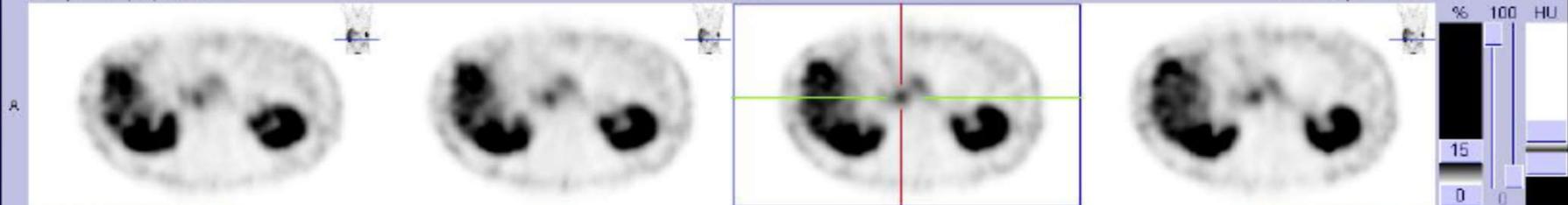
Coronal



WBSpect Outbut, 10/12/2008

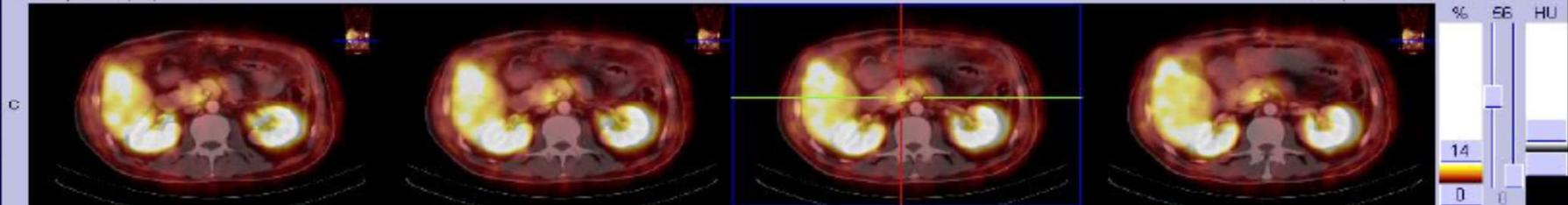
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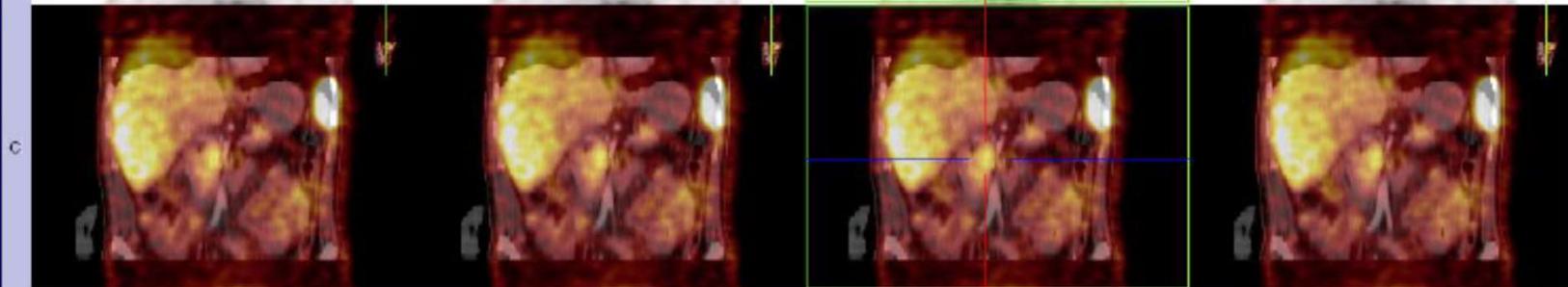
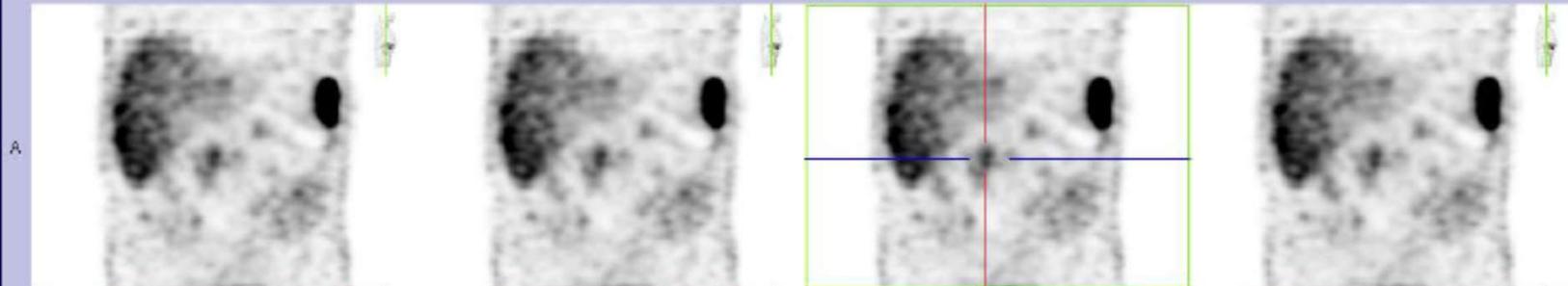


WBSpect Outbut, 10/12/2008

ABD 8X8, 14/10/2008



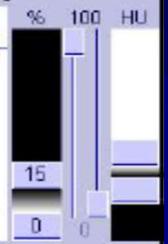
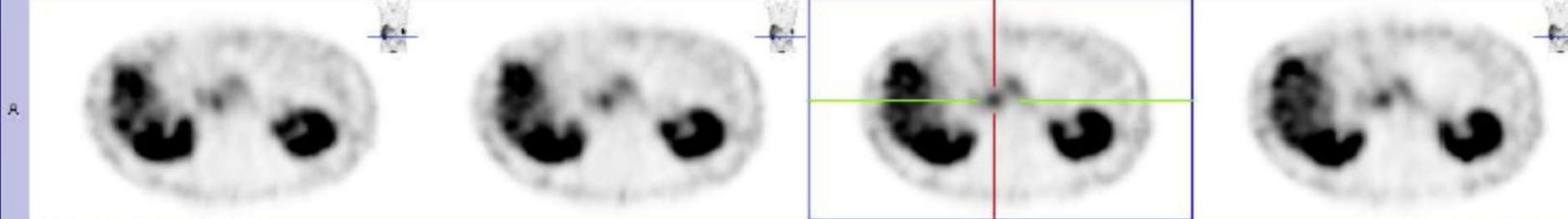
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WBSpect Output, 10/12/2008

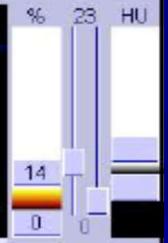
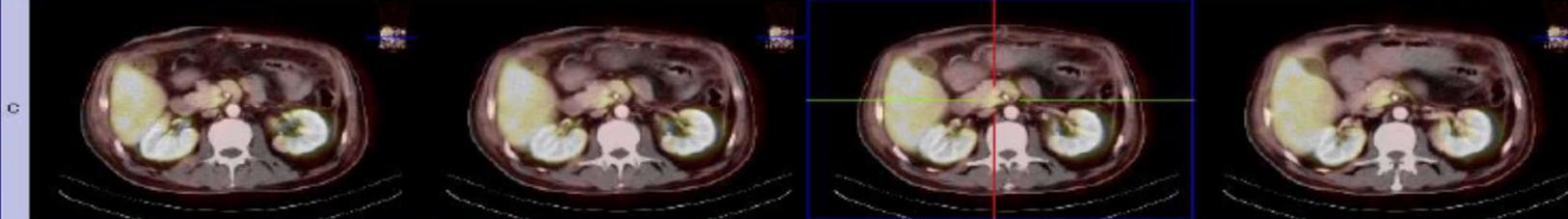
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ABD 8x8, 14/10/2008

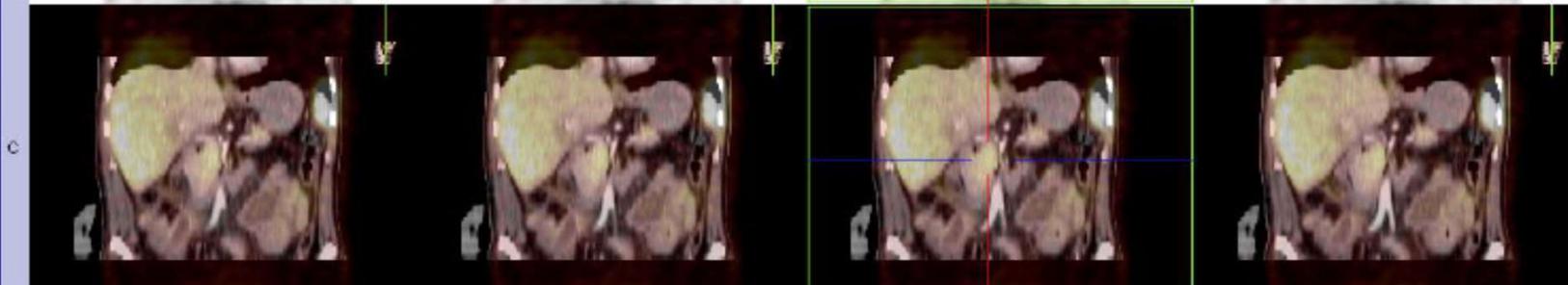
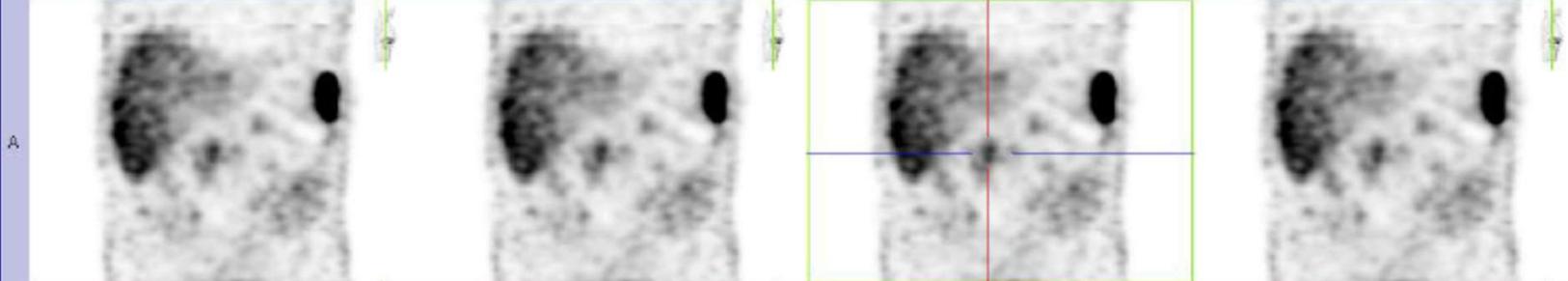


WBSpect Output, 10/12/2008

ABD 8x8, 14/10/2008

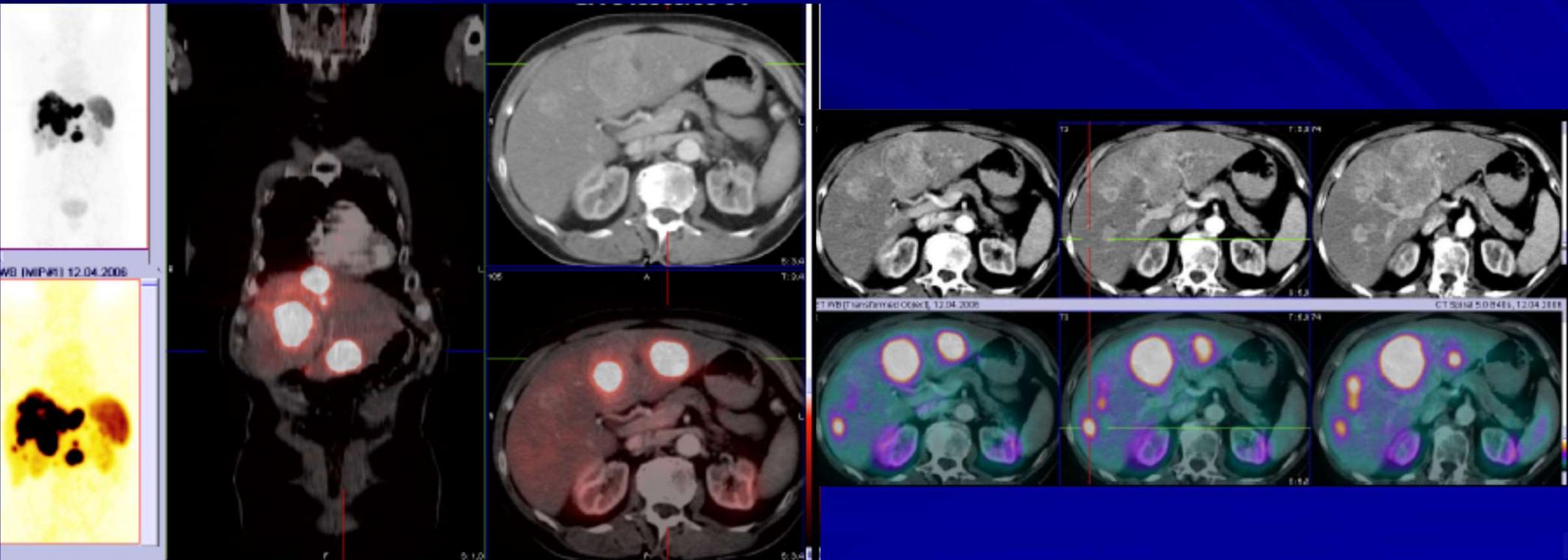


Coronal



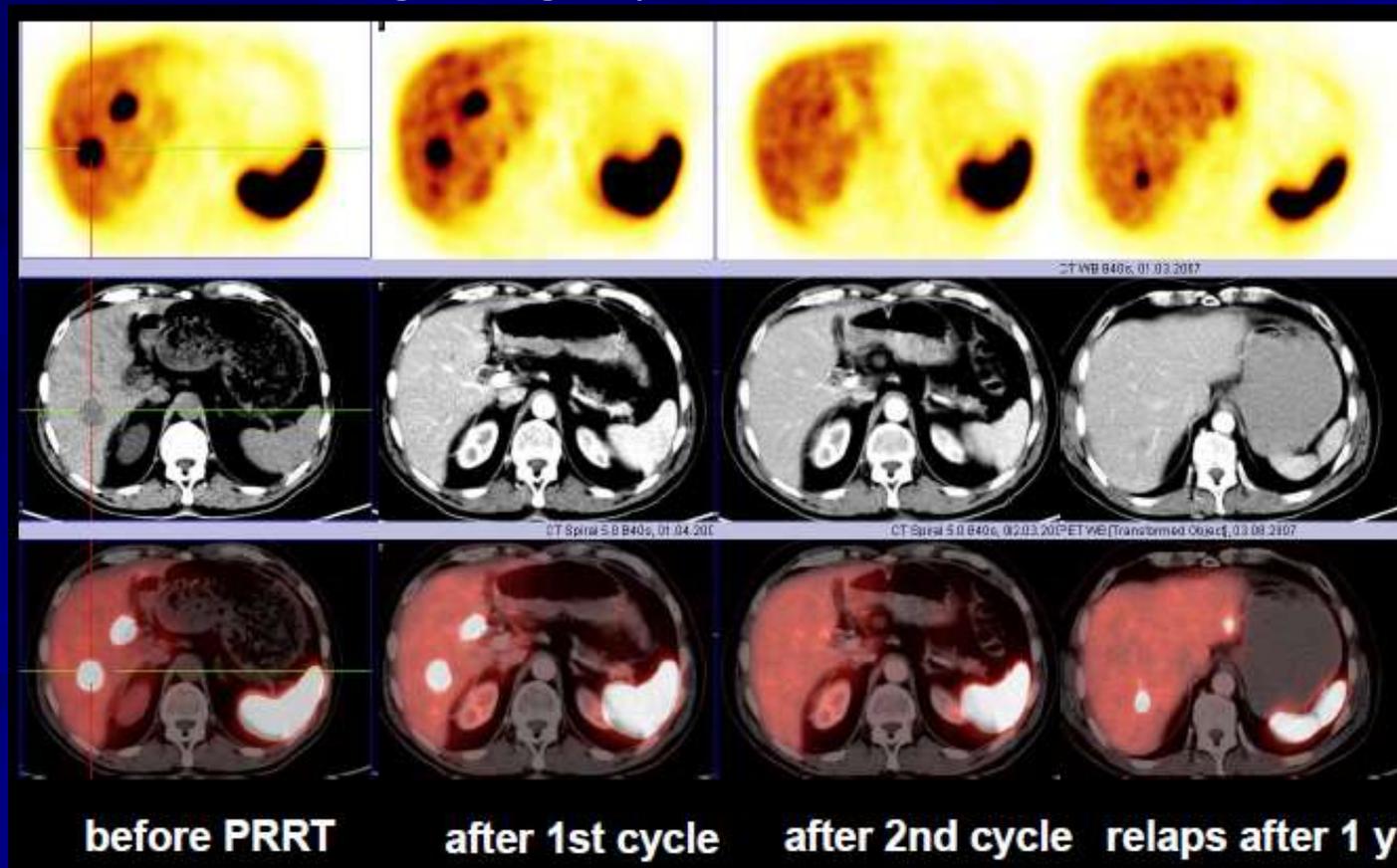
SSTR Staging

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

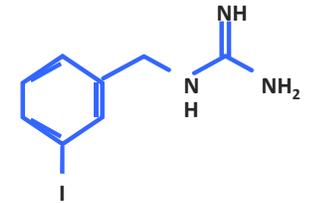


Re-staging, Follow-up

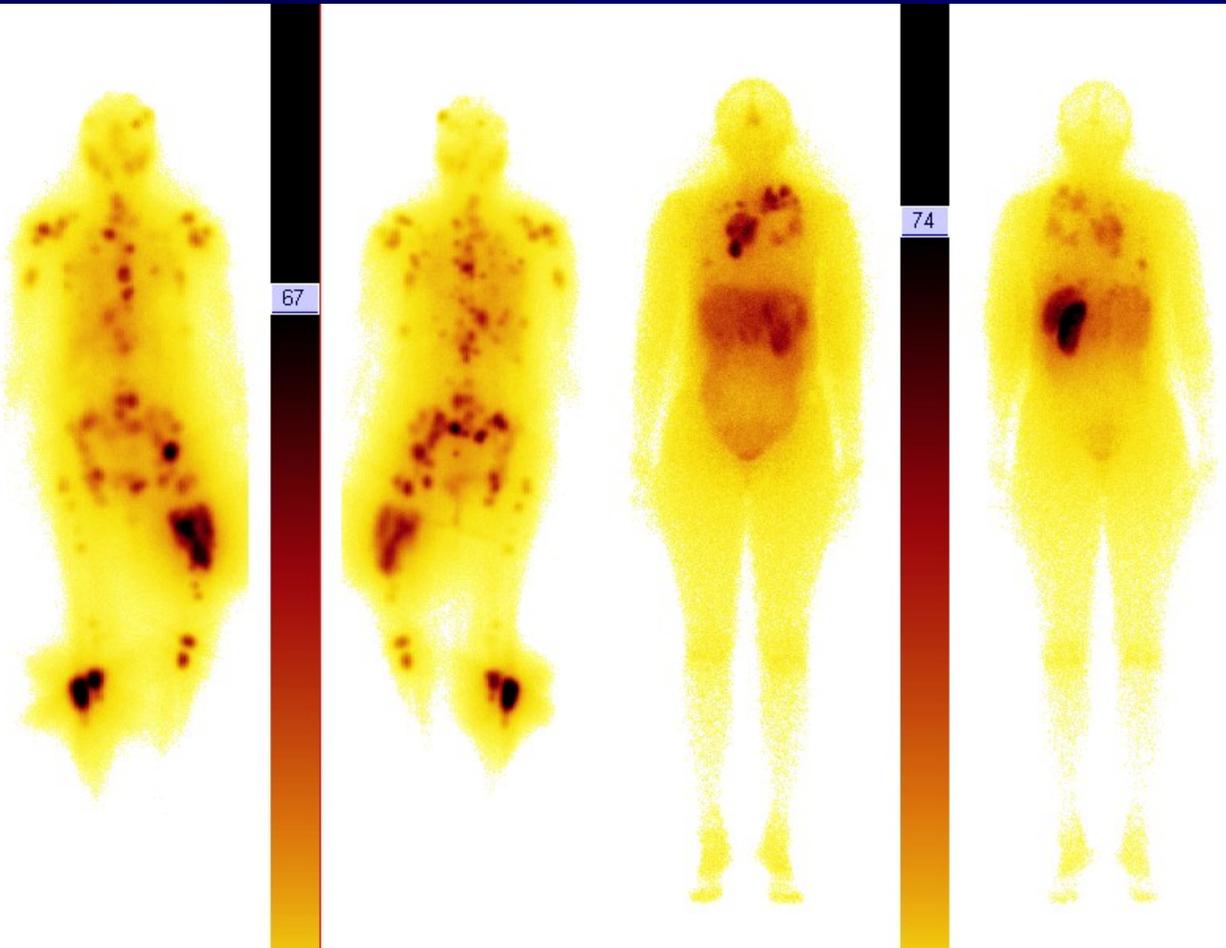
e.g. in patients with rising tumor markers (chromogranin, serotonin, calcitonin, glucagon) for detection of recurrence



³¹I-MIBG Meta Iodo Benzyl Guanidine.



Meta-iodobenzylguanidine
(MIBG)

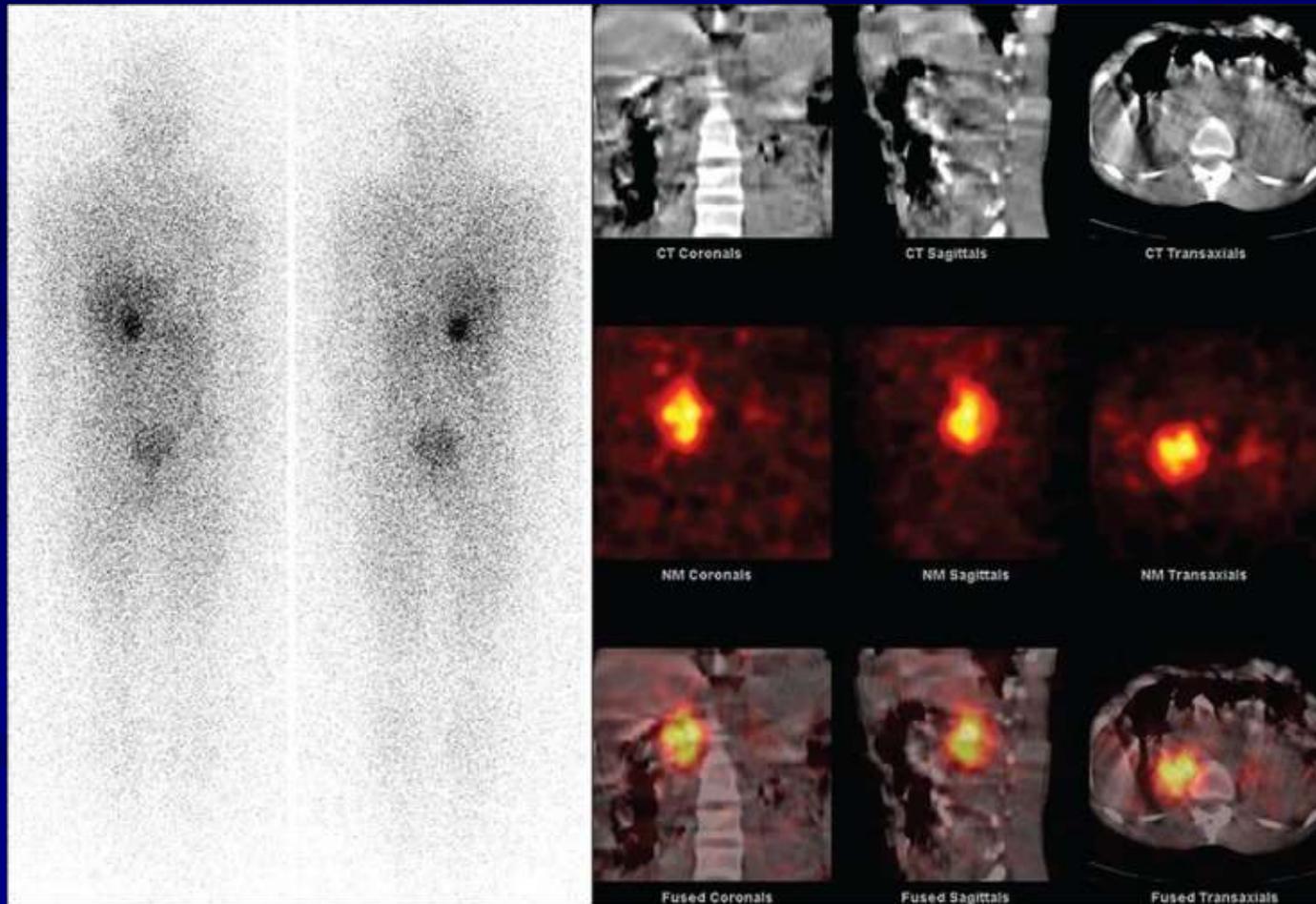


Is a noradrenaline analog.
Localizes in adrenergic tissues:
catecholamines producing tumors
and their metastases.

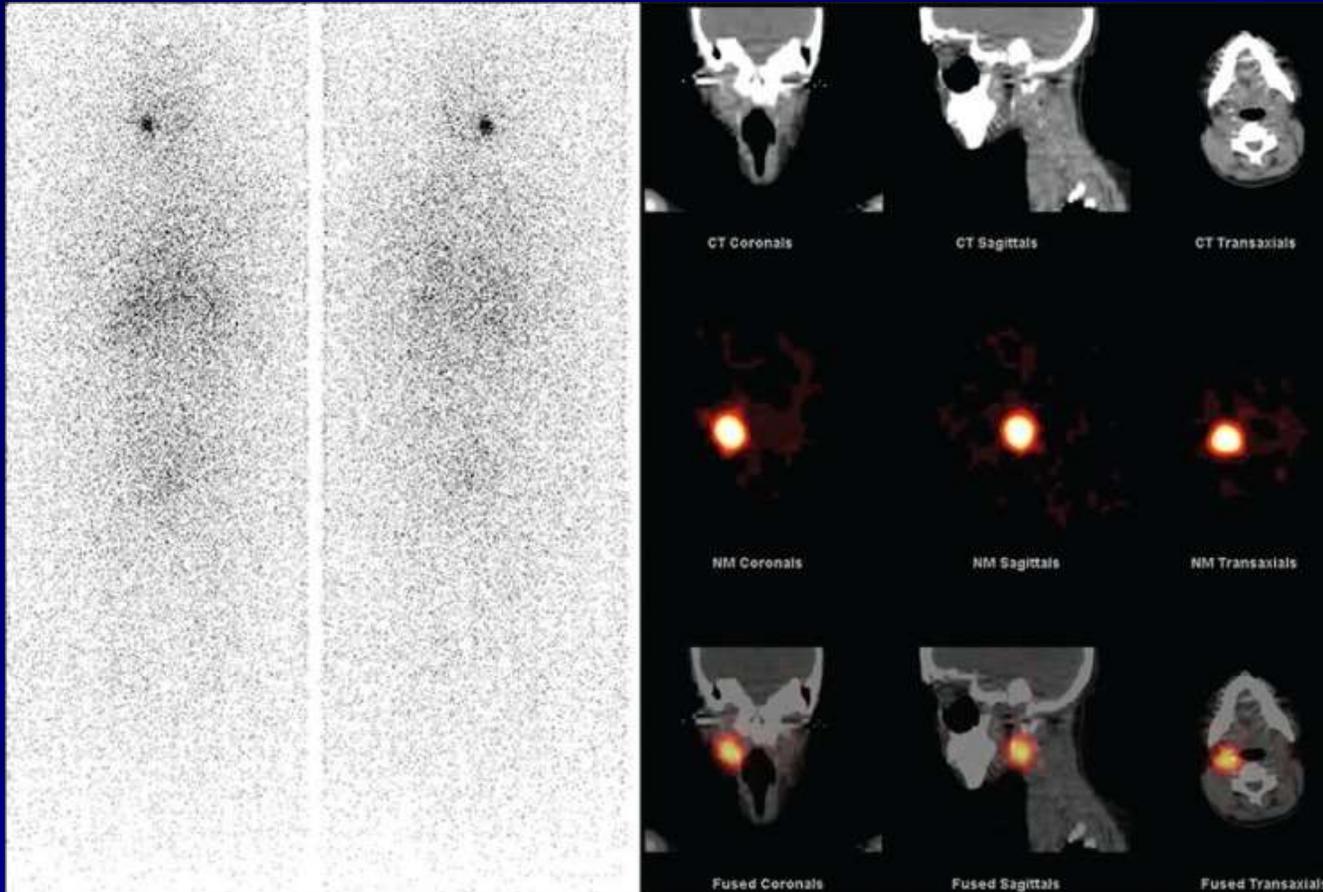
Indications:

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

^{131}I -mIBG Pheochromocytoma gl. suprarenalis dex.



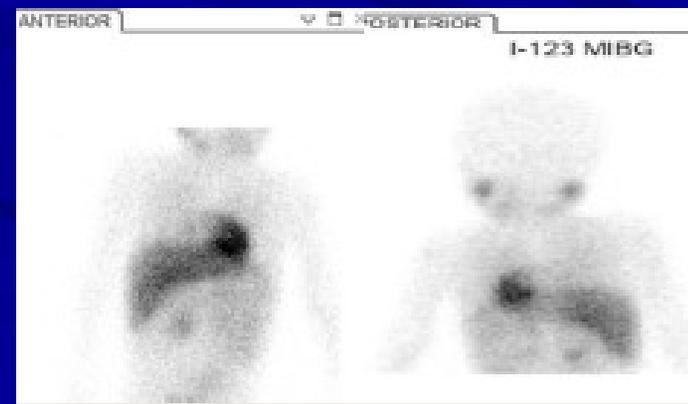
^{131}I -mIBG - Paraganglioma carotid body dex.



³¹I-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.

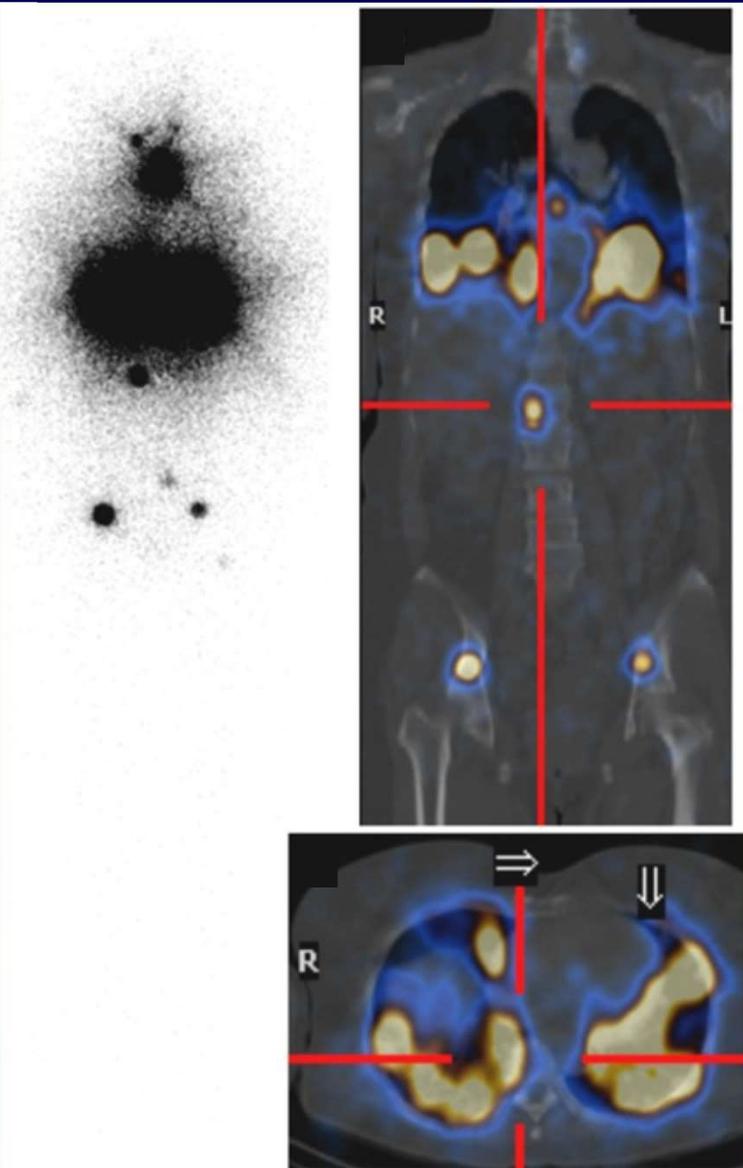


Thyroid Metastases Study

(I-123 or I-131 as Sodium Iodide)

Indications:

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

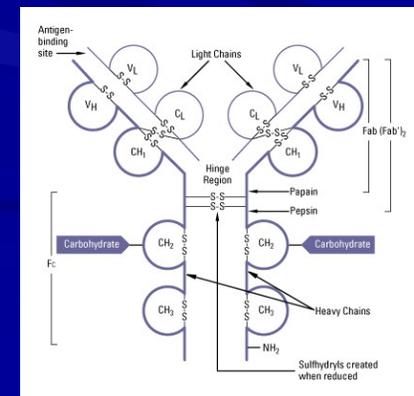
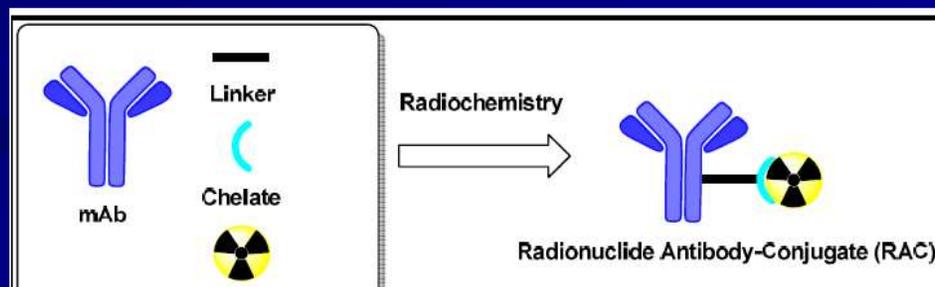


TUMOR-SEEKING RF

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

Ag-Ab SPECIFIC TUMOR UPTAKE

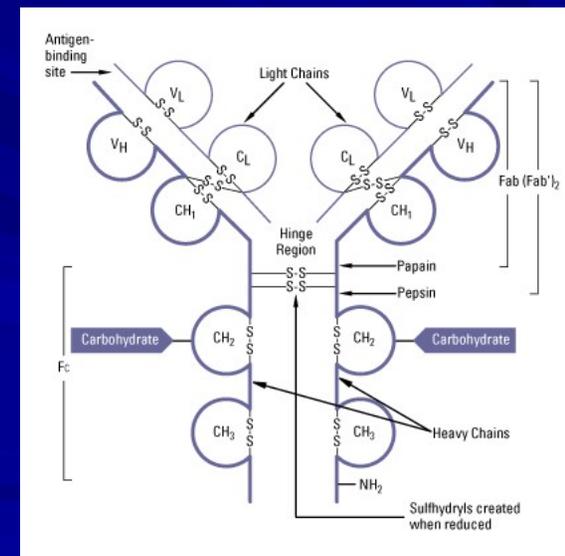
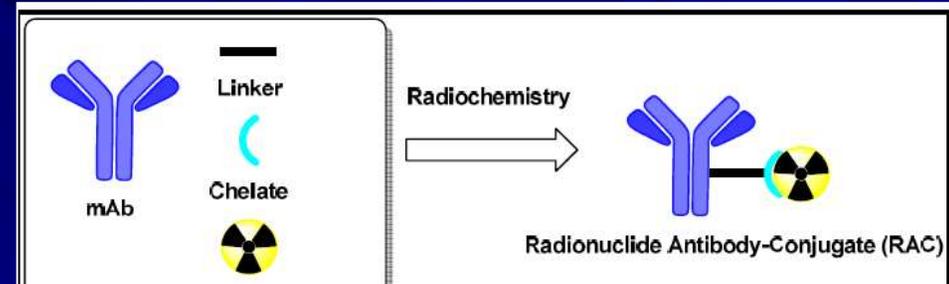
Radioimmunosintigraphy is presented as a new imaging modality in nuclear medicine, using specific antigen-antibody interactions. Monoclonal antibodies to tumor-associated antigens facilitate the characterization of molecular differences between tumors and normal cells. Labelled with gamma-emitting radioisotopes 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)

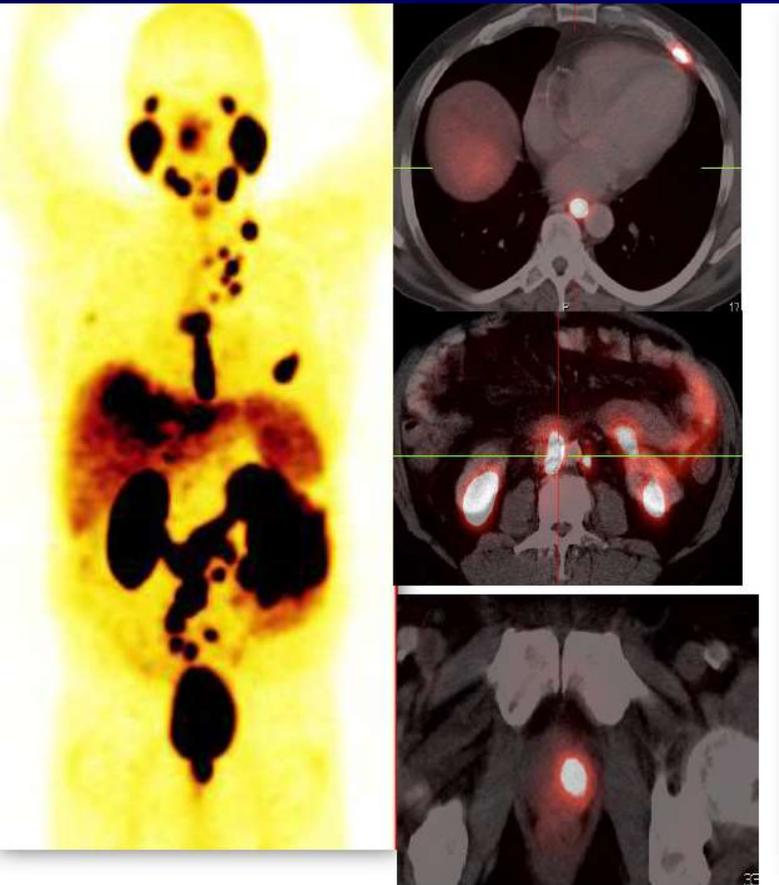
| | |
|---|-------------------------------|
| ^{111}In -ANTI CEA | КОЛОРЕКТАЛНИ СА, МТС |
| ^{111}In -B 72-3 | КОЛОРЕКТАЛНИ СА, СА ОВАРИЈУМА |
| $^{99\text{m}}\text{Tc}$ -MOV 18 | СА ОВАРИЈУМА |
| ^{111}In -OVTL 3 | СА ОВАРИЈУМА |
| ^{111}In -OC 125 | СА ОВАРИЈУМА |
| $^{99\text{m}}\text{Tc}$ -225 .28S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



PROSTATE CANCER

anti-PSMA At

^{111}In capromab pendetide (Prostascint)



National
Comprehensive
Cancer
Network®

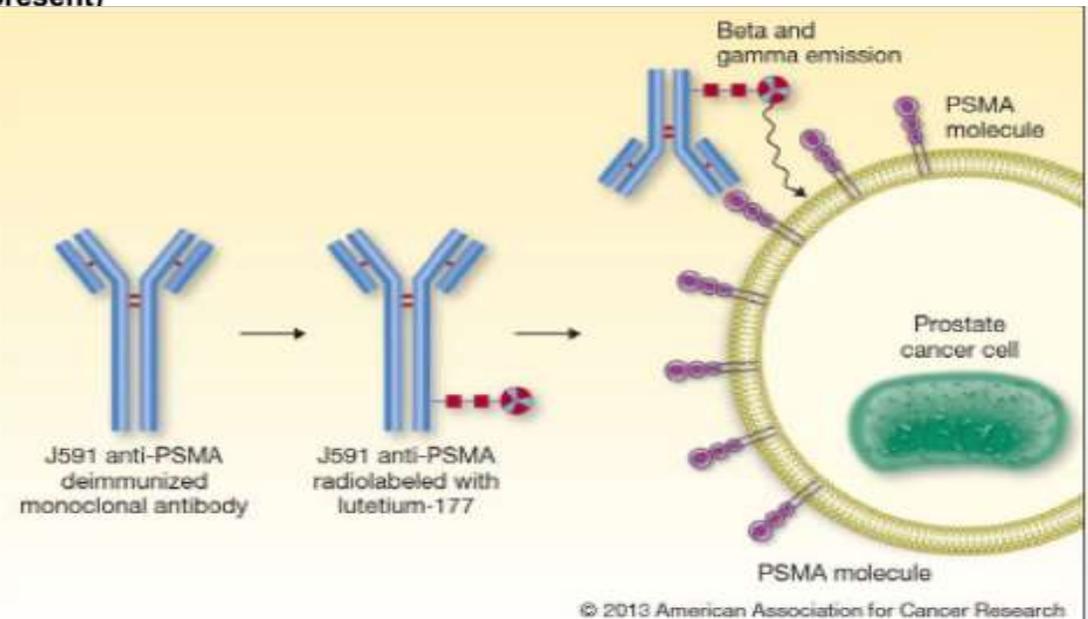
NCCN Guidelines Version 4.2022 Prostate Cancer

Prior docetaxel and prior novel hormone therapy^{iii,ooo}

• Useful in certain circumstances

▶ Lutetium Lu 177 vipivotide tetraxetan (Lu-177-PSMA-617) for PSMA-positive metastases (category 1)^{sss}

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



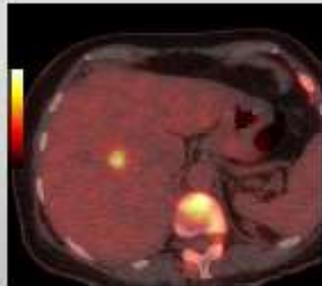
BREAST CANCER

- HER2/neu receptor (human epidermal growth factor 2)

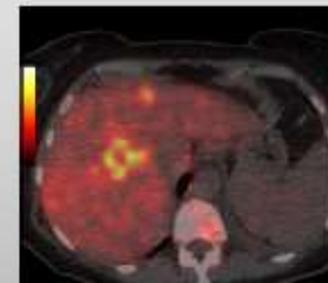
⁸⁹Zr-labeled mAbs in (pre-)clinical trials:



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



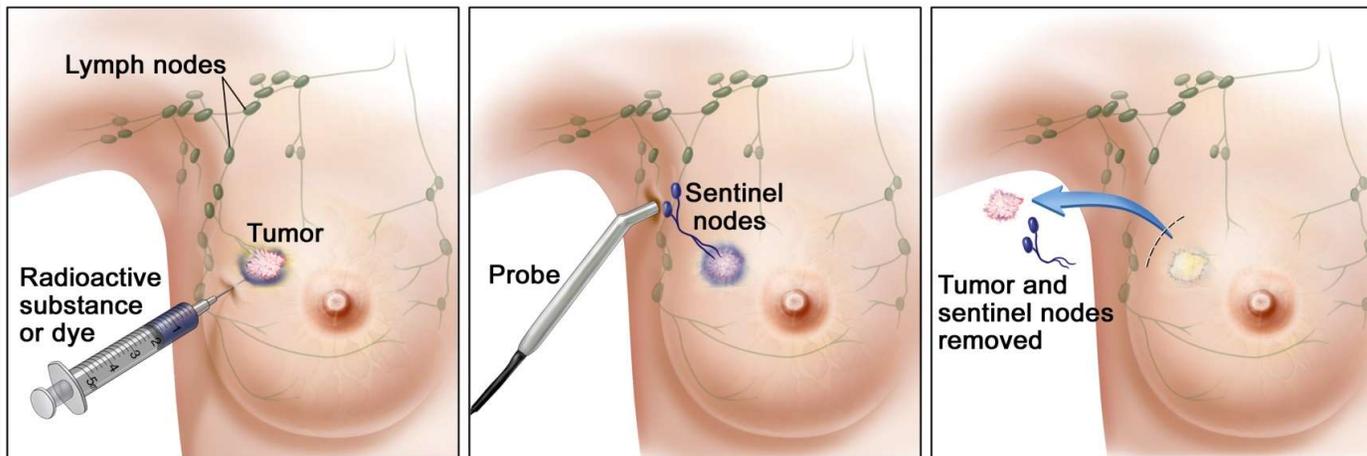
LYMPHOSCINTIGRAPHY

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}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.



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

