Nuclear Oncology

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Nuclear Oncology

LEARNING OBJECTIVES…

At the end of the lecture you will be able to answer the following questions:

- What are the tumor imaging and therapeutic radiopharmaceuticals?
- What are the nuclear medicine tumor imaging methods?
- What are the objectives of tumor imaging?
- What are the potential values of nuclear medicine tumor imaging methods?
- What is the role of nuclear medicine in the treatment of tumors?

Tumor Imaging

Tumor Metabolic properties

- Increased vascularization
- Increased capillary permeability
- Newly proliferated capillaries
- Increased blood flow
- Metabolically active cells
- Increased energy demand

Tumor Imaging

Tumor Specific useful properties

- High density of some common receptors
- Expression of several specific receptors
- Expression of some specific tumor antigenes

All these properties could be used for imaging and therapy

Tumor Non-specific Diagnostic radiopharmaceuticals

- **PET or PET-CT**
  - **F-18 FDG – anaerobic metabolism**
- **Planar, SPECT or SPECT-CT**
  - **Diphosphonates** – bone scan
  - **Ga-67 citrate** – similar to FDG – localising agent
  - **Tc99m Nanocolloid** – bone marrow scan
  - **Tc99m MIBI / Thallium 201** – several tumors

Demonstrate tumor sites but are not specific for malignancy

Tumor Specific Diagnostic radiopharmaceuticals

- **PET or PET/CT:**
  - ❖ Gallium -68 –octreotide analogues (Ga-68 DOTA): For neuroendocrine tumors
  - ❖ Fluorine -18-fluorodeoxythymidine(F-18-FLT): For tumor proliferation
  - ❖ Fluorine -18-fluoromisonidazole(F-18-FMISO): For tumor hypoxia
- **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.
  - ❖ Monoclonal antibodies labelled with In-111, I-123/131 or Tc-99m

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

Therapeutic radiopharmaceuticals

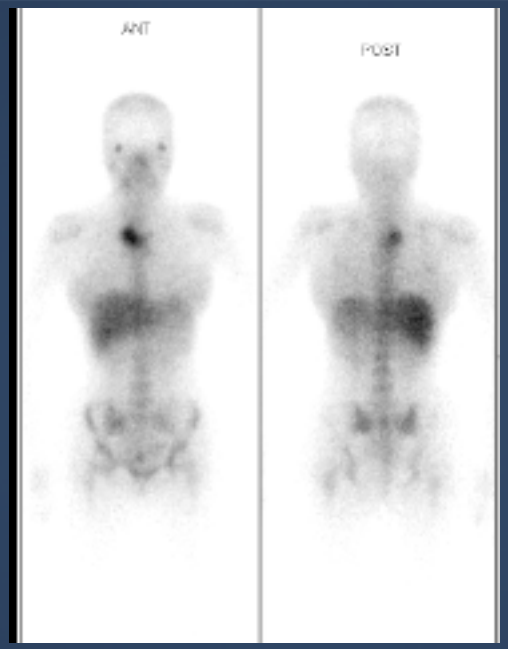
- **Non-specific**
  - ❖ Sr-89, Sm-153, Re-189
  - ❖ Bone pain palliation
- **Specific**
  - ❖ I-131
    - Thyroid cancer, as specific diagnostic if tumor significantly accumulates
  - ❖ Y-90
    - Zevalin – monoclonal antibody for B-cell lymphomas

NM Imaging modalities

Planar Imaging

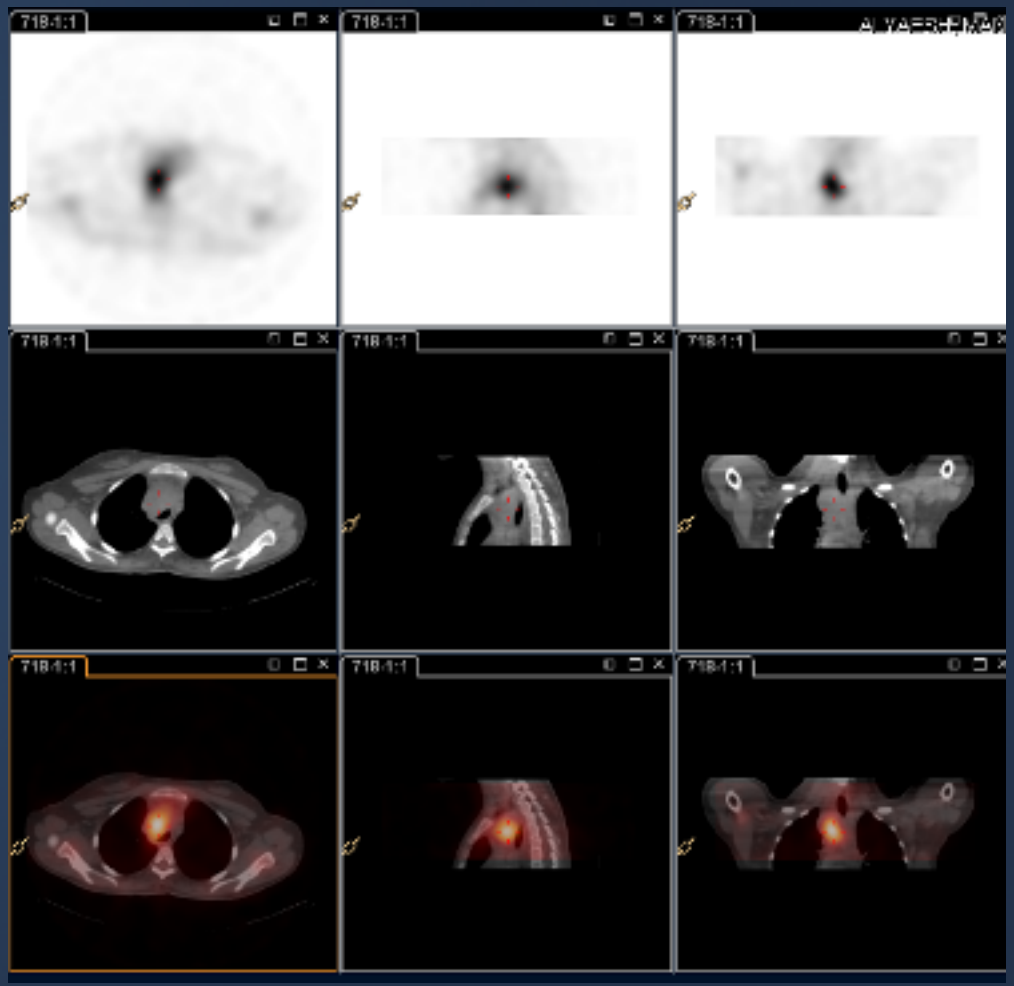
NM Imaging modalities

Single Photon Emission Computed Tomography (SPECT) and SPECT CT



Whole Body Gallium Scan : Planar Image

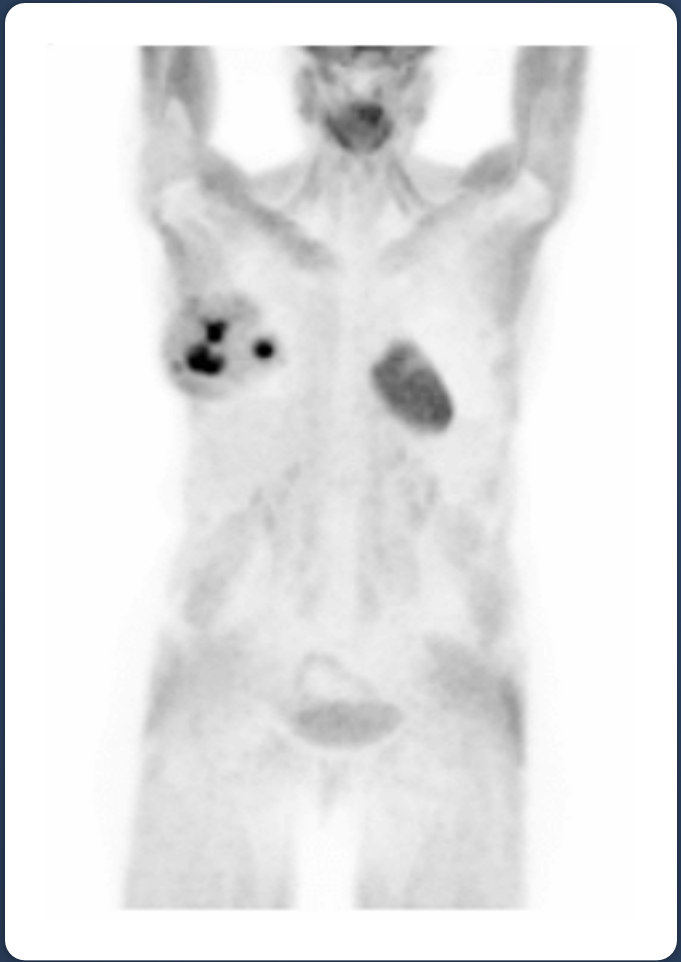
SPECT



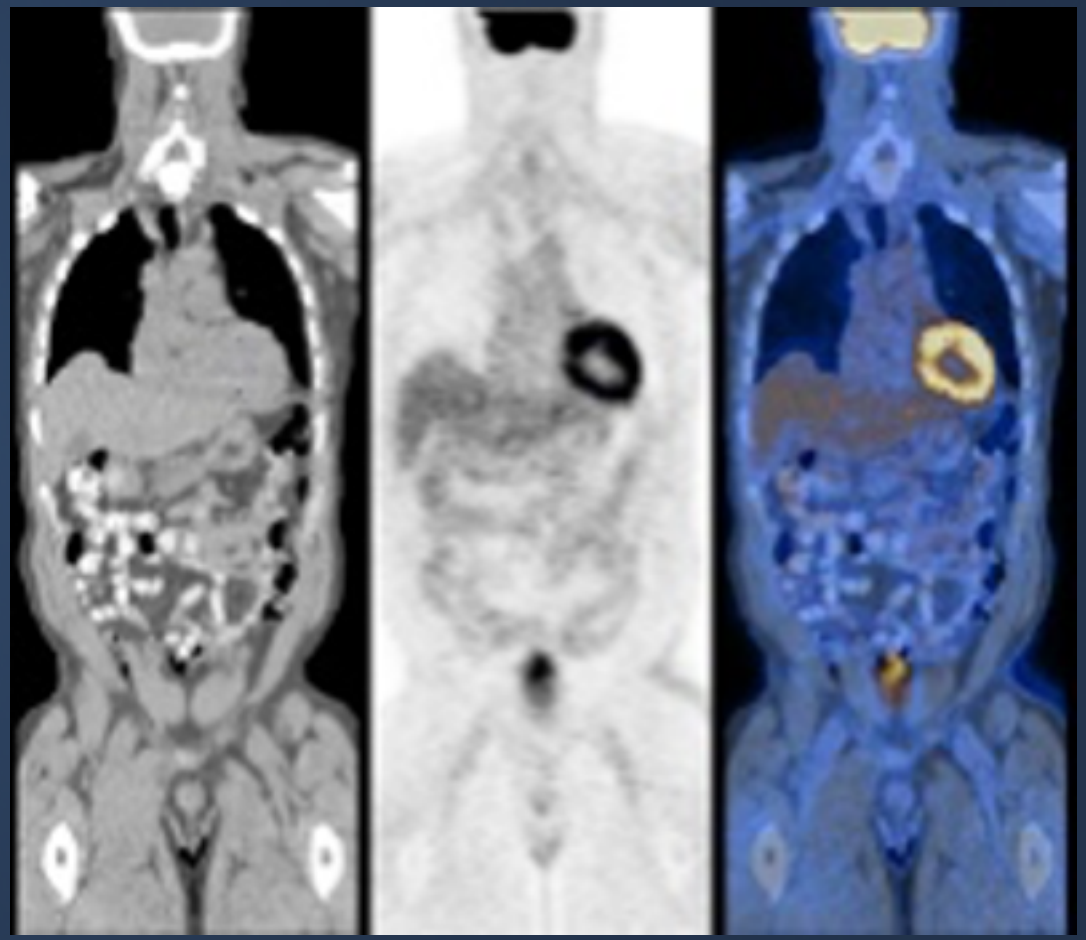
SPECT/C

NM Imaging modalities

Positron Emission Tomography (PET) and PET CT



PET



PET/CT

Role for Nuclear Medicine In Oncology

- **Diagnosis**
  - Specific or non-specific
- **Staging**
  - Important for proper therapy
- **Follow-up**
  - Early detection of recurrence
- **Treatment**
  - Specific or non-specific

Tumor Imaging

Non specific tumor imaging agents:

- **Tc-99m MDP bone scan:** Detection and follow up of bone metastasis
- **Gallium 67 :** Staging ,Restaging & therapy assessment of HD , NHL , Lung cancer
- **Thallium 201 :** Tumor viability & tumor seeking.

{Tc-99 m Agents (MIBI ,TETRO.).}

- **F18 – FDG :** Staging ,Restaging & therapy assessment of HD , NHL , Lung cancer

Specific tumor imaging agents:

- **In–111 (TC99m) Octreotide :** Neuroendocrine tumors
- **I -123 MIBG :** Neuroendocrine tumor
- **I -131 :** Lung mets. thyroid carcinoma

Bone scan

"Procedure"

- **Radiopharmaceuticals**
  Technitium 99m Methylene DiPhosPhonate (Tc-99m MDP)

- **Tissue accumulation depends on**
  - blood flow
  - capillary permeability
  - metabolic activity of osteoblasts and osteoclasts
  - mineral turnover

- **Dose:** 500 to 800 MBq (Megabequerel) / 15- 20 mCi (millicurie)

- **Imaging time:** 2 to 3 hours postinjection – WB + SPECT

  - **Potentials of bone scan:** Positivity many months before an abnormality can be detected on X ray

Bone Scan In Oncology

Indications

I- Metastatic Disease: Lung cancer, prostate, breast, thyroid, and renal tumours

- **Diagnosis.**
- **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 & Ewings sarcoma)**

III- Soft tissue tumors :

- **Primary**
- **Metastases**

Bone Scan In Oncology

Imaging features

a. ***Hot lesions*** : Majority of bone tumors.

b. ***Cold lesions*** : Purely osteolytic tumors (renal cell carcinoma, thyroid cancer, anaplastic tumors),radiation therapy

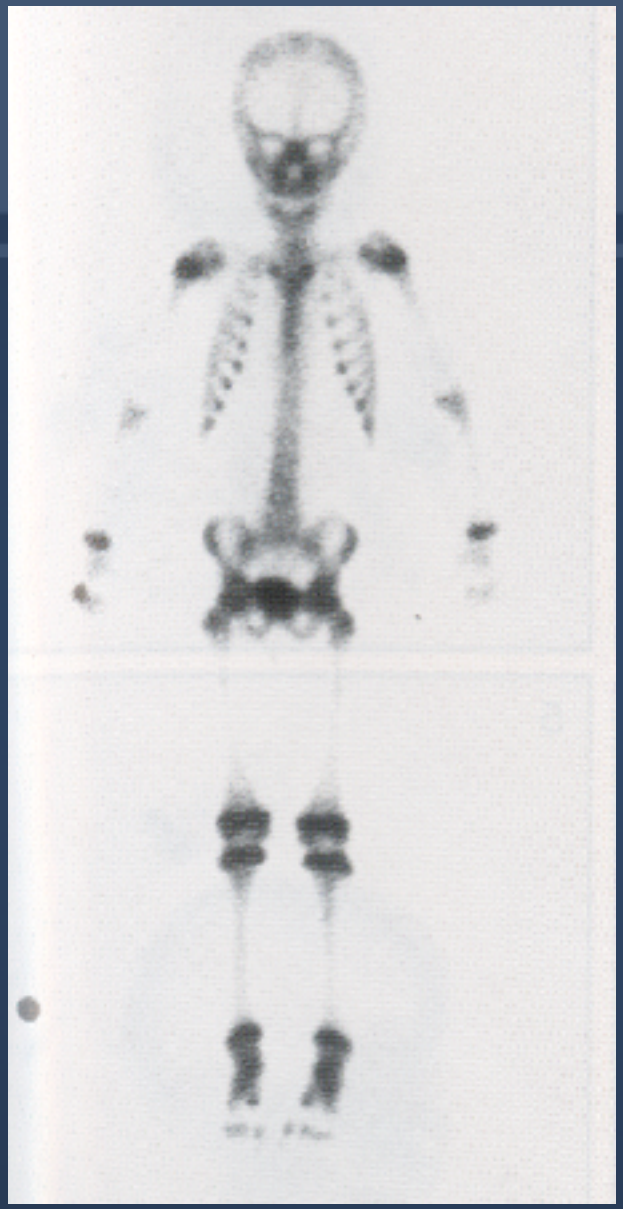
c. ***Superscan*** : Diffuse increased skeletal uptake with no soft tissue or kidney activity (e.g. CA prostate ,breast ,..etc).

d. Normal distribution : Marrow tumors (e.g. lymphomas, leukemia, multiple myeloma).

e. Soft tissue uptake : Soft tissue tumors may concentrate the tracer.

f. Flare phenomenon – increased number of lesions in the case of effective therapy

Normal Whole Body Bone Scan



An 8 year old child

A 25 yrs old adult

Bone Scan : In Metastatic Disease

Access of Nonosseous Tumors To Bone:

- **Direct Extension.**
- **Retrograde venous flow.**
- **Arterial Circulation (after venous or lymphatic access).**

Epithelial Tumors:

- Reach red marrow of axial skeleton via venous and arterial flow.
- **Distribution of red marrow in adult :** calvarium, spine , pelvis , and proximal femurs and humerus
- 90% of metastasis from epithelial tumors are found in red marrow.

Metastatic Foci:

- **Grows in red marrow space.**
- **The surrounding bone remodels through osteoclastic (resorption) and osteoblastic (deposition) activity.**
- **The relative balance between resorption and deposition determine whether the lesion is hot (sclerotic) , cold (lytic) or mixed pattern.**
- **The tracer does not concentrate in the metastatic foci (cancerous tissue) but in the surrounding reactive bone.**

Bone Scan : In Metastatic Disease

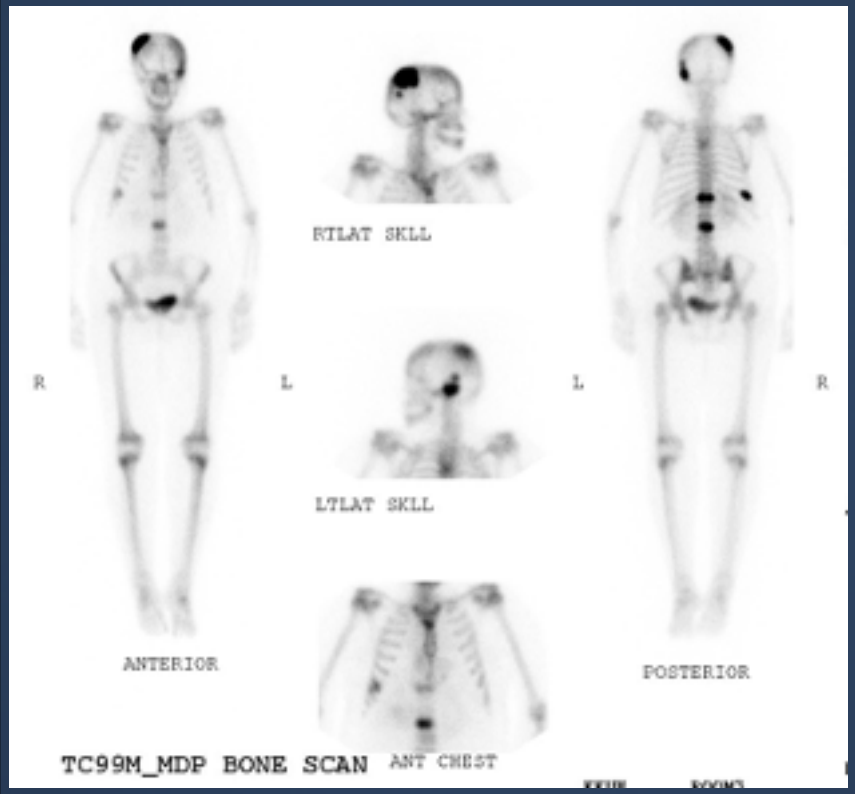
Scan Patterns:

- Solitary lesions.
- Multiple focal lesions.
- Diffuse involvement (Superscan).
- Photon deficient lesions (cold lesions).
- Flare phenomenon.
- Normal (false negative).
- Soft tissue lesions (tracer uptake in tumor).

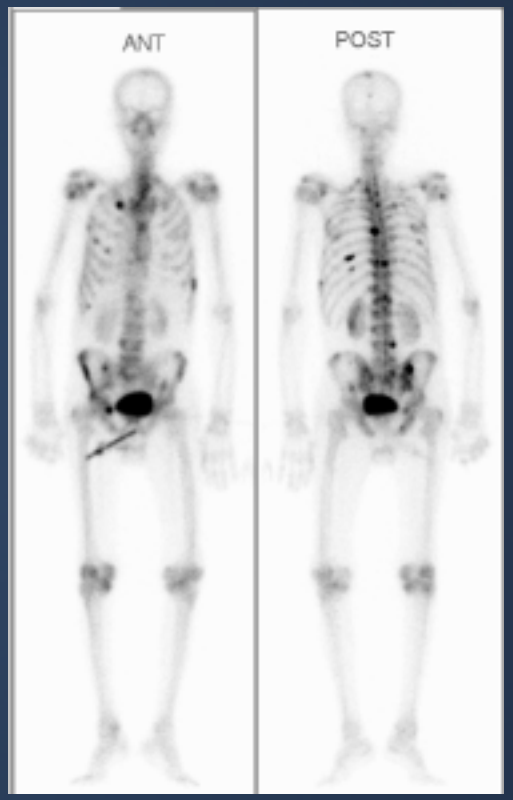
Sensitivity:

- In early stage superior to x-ray.
- In advanced stage both have high sensitivity.
- The accuracy of bone scan not known because of the lack of reference standard.
- The sensitivity is agreed to be 90% or more.

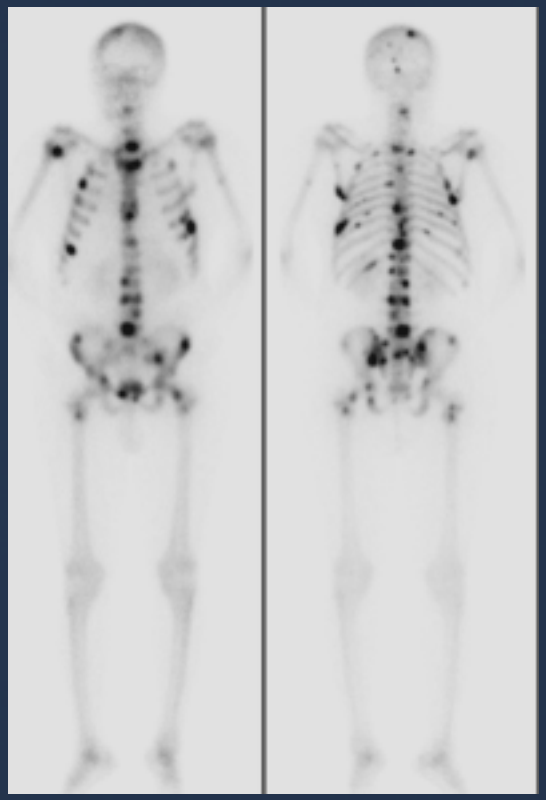
TUMOR STAGING



Ca Breast



CA LUNG



CA STOMACH

Bone Scan In Metastatic Disease

Diffuse involvement (Superscan)

Definition : Bone scan with diffuse symmetrical increased uptake and almost absence of soft tissue activity, lack of kidney activity and bone uptake seen in blood pool images.

Causes :

a. Bone metastases : Prostate, breast, lung, bladder and lymphoma.

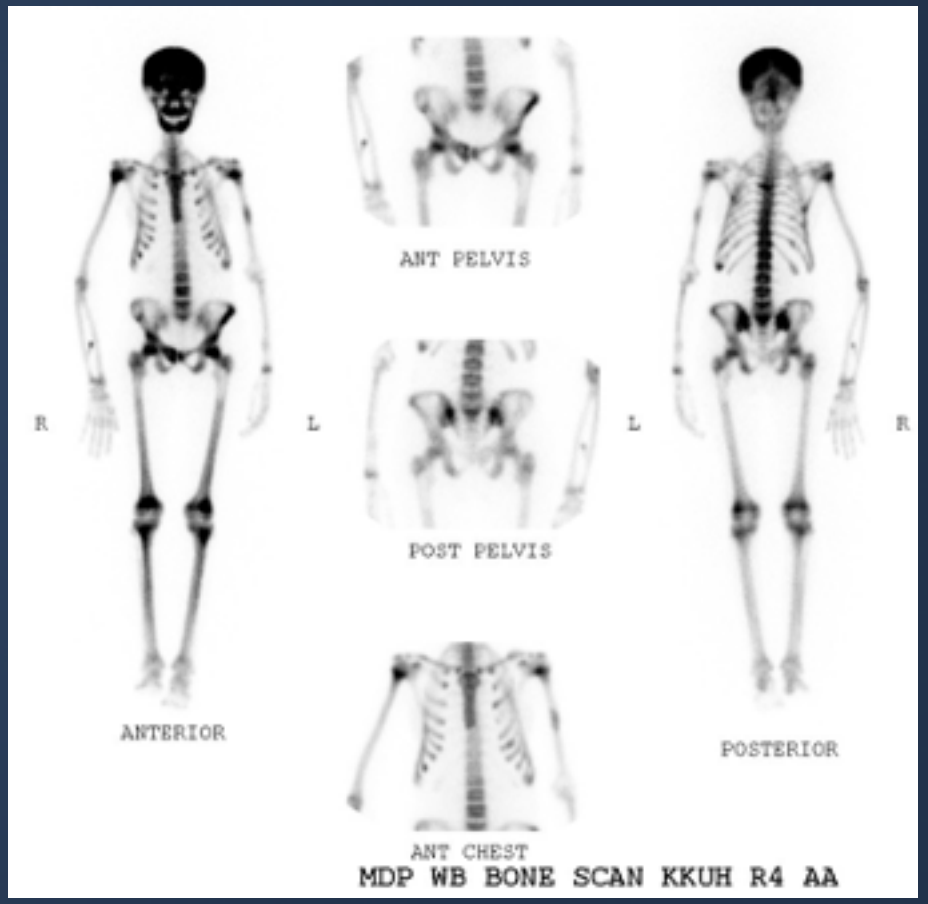
b. Non tumor causes: HPT, osteomalacia, Pagets disease and fibrous dysplasia

Important clues :

In metabolic bone disease the calvarium and long bones are involved unlike in bone metastases.

Superscan

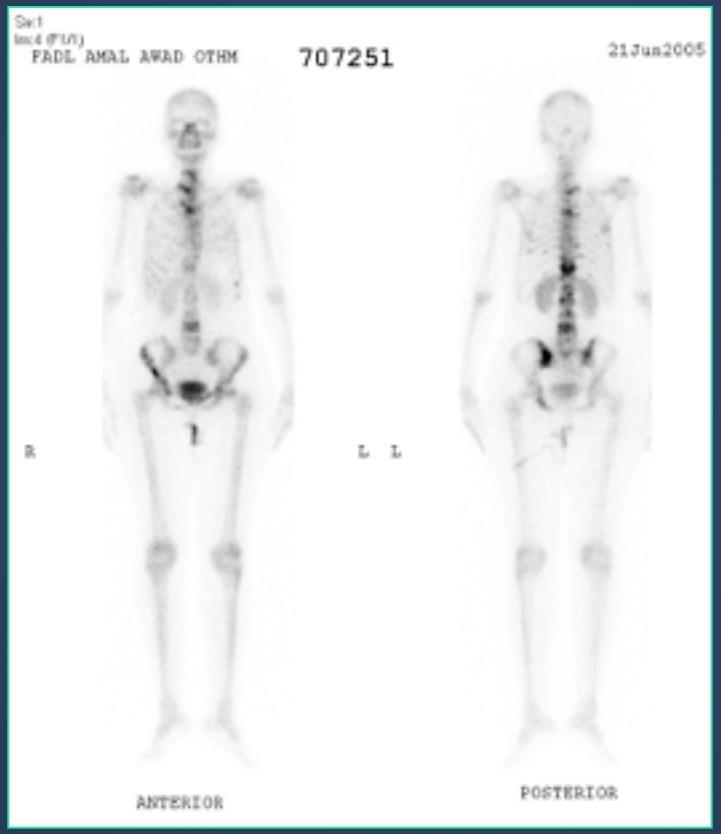
CA Prostate

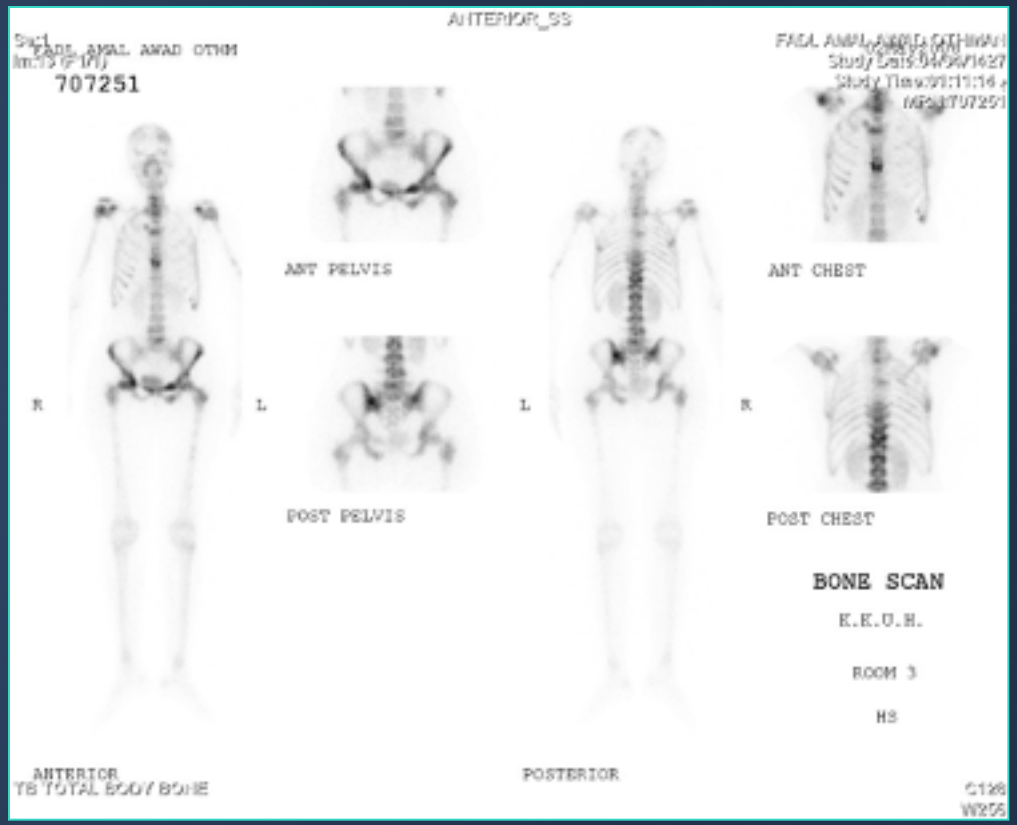


HPT

Pure Lytic Lesions

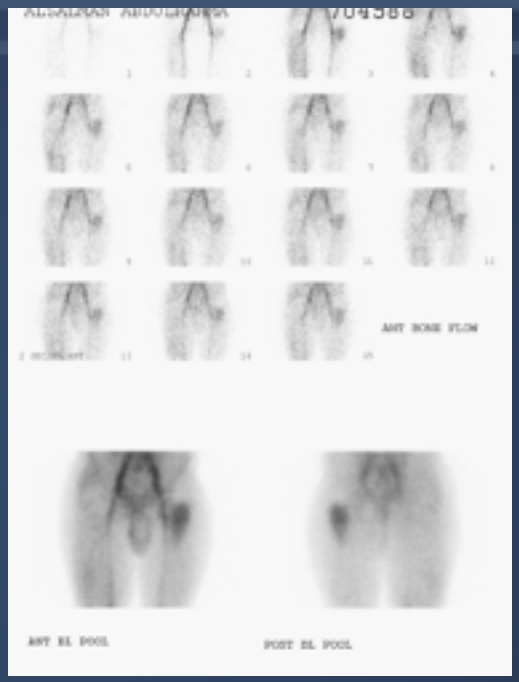
Bone Scan : Radiation Effects





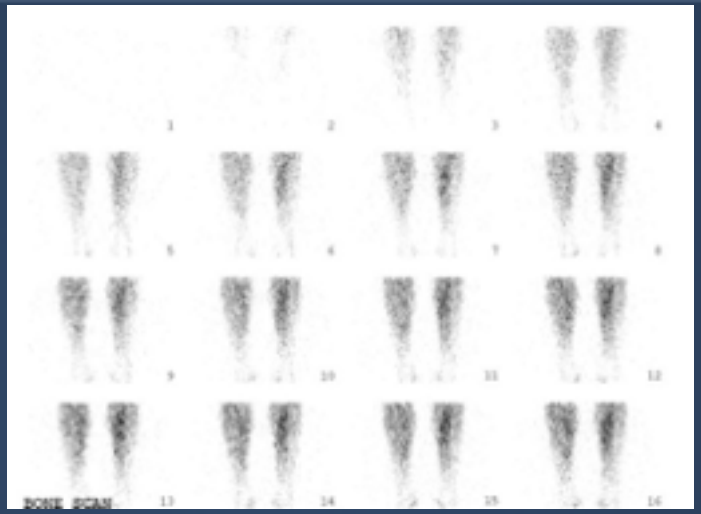
- **Hours following radiation** : **Increased uptake** due to increased blood flow and vascular permeability.
- **3-6 months post radiation : Decreased uptake** due to microvascular injury. Dose related (>2000 rads).
- **Following Radiotherapy** : Spontaneous ribs fracture may occur.

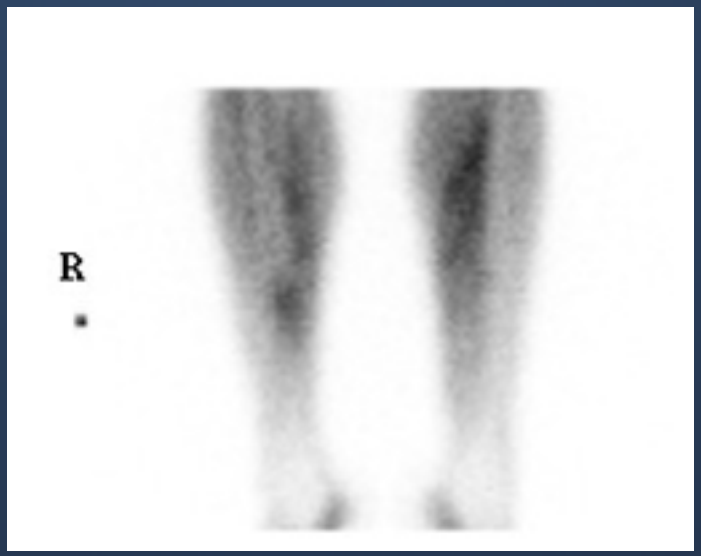
Ewing's Sarcoma

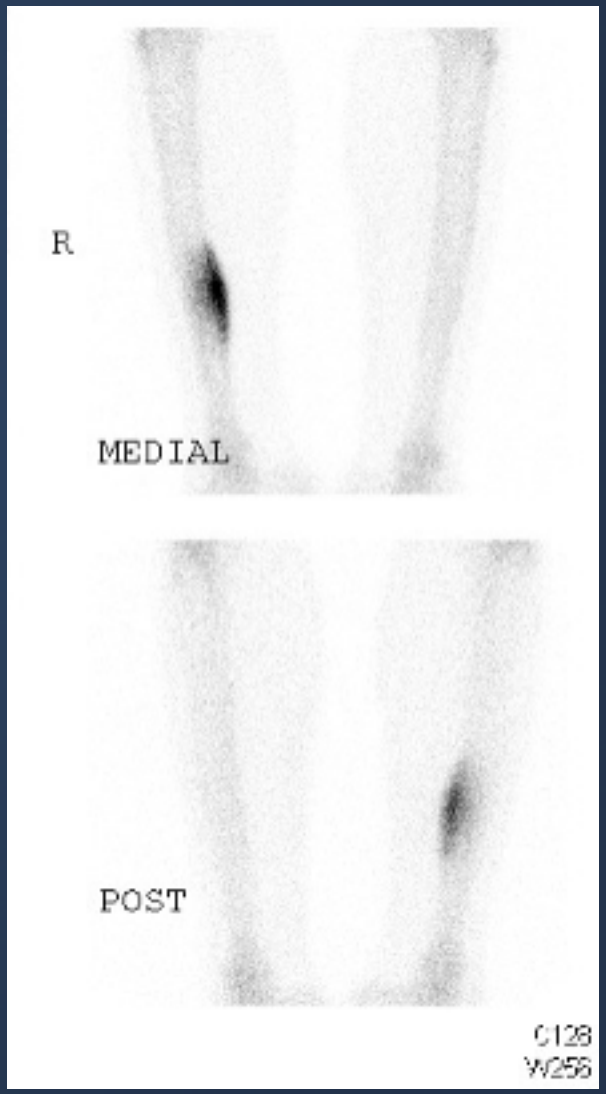


Bone Scan In Bone Tumors

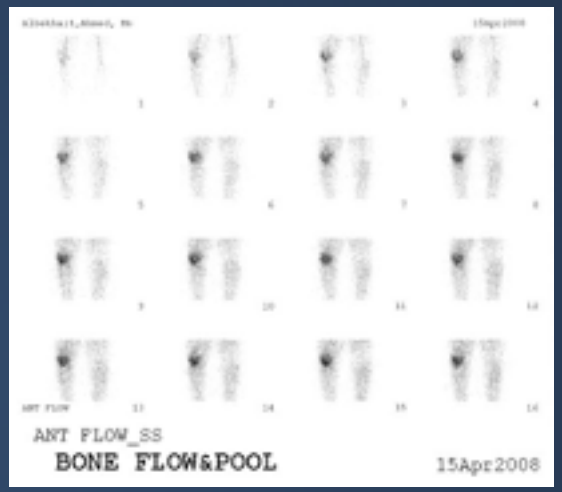
Osteoid Osteoma

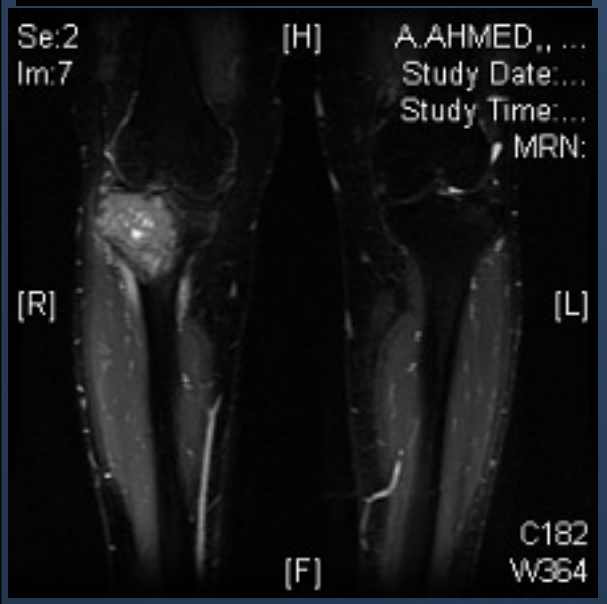


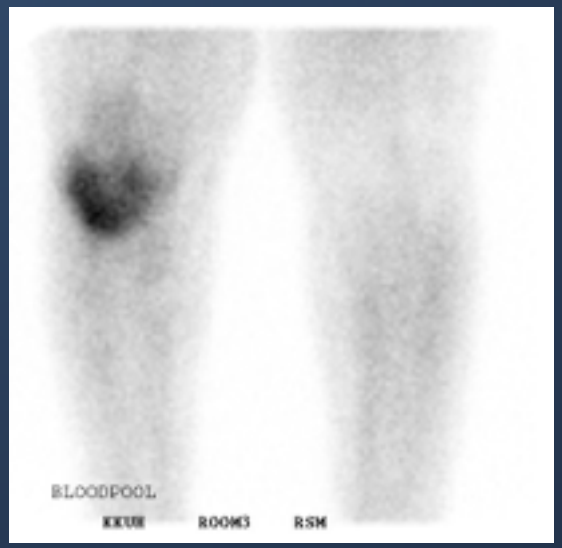




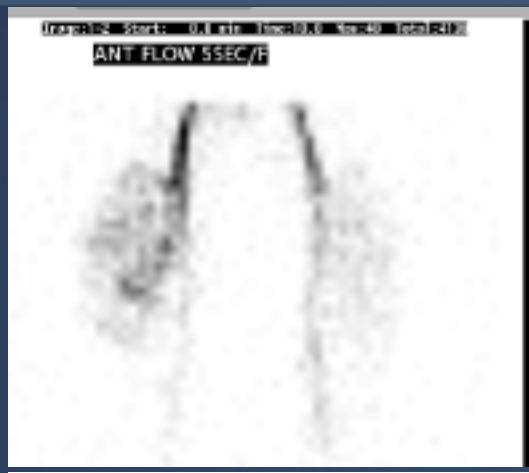
Giant Cell Tumor

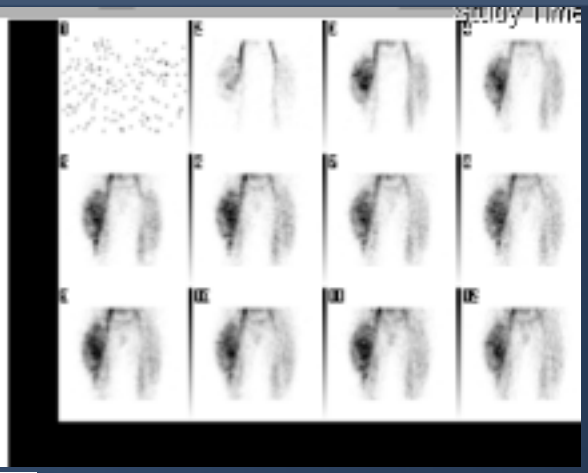


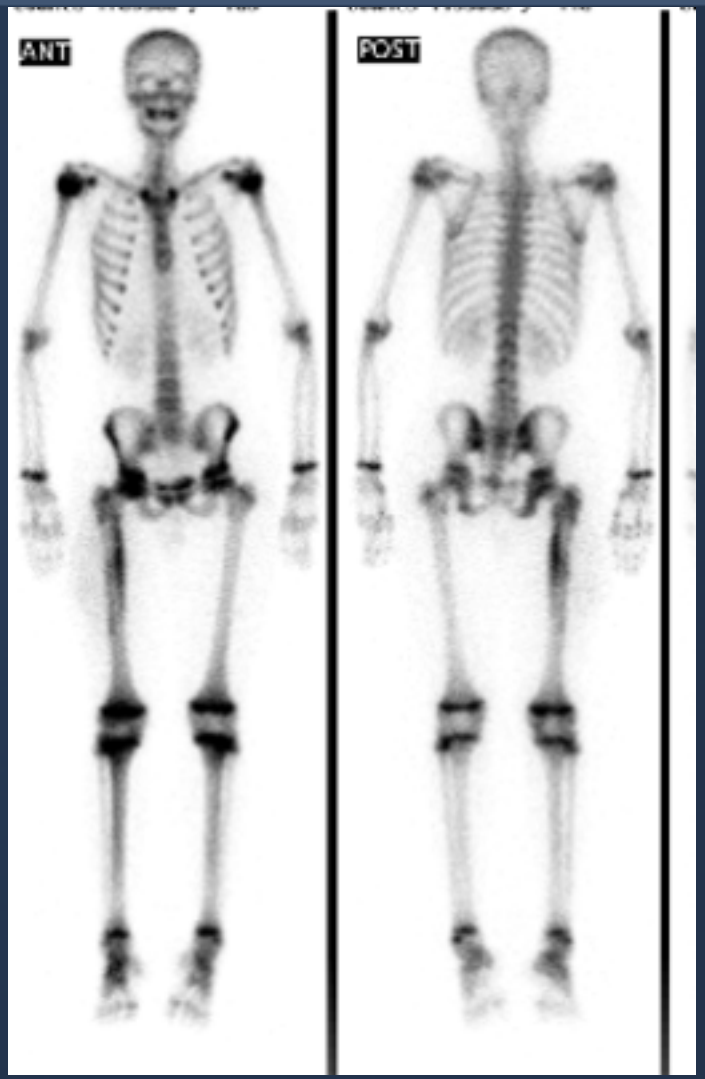




Soft Tissue Sarcoma







Gallium 67 (Ga-67) scan

Properties: Introduced in seventies of 20th century for lymphomas

- Mechanisms of accumulation
  - Tumour viability
  - Blood flow
  - Capillary permeability
  - Lymphatic drainage
  - Binds to Transferrin receptors on the tumour cells
- Non specific for infection-inflamation and tumors
- Excretion: Kidneys and large bowel

Imaging Protocol:

- **Patient preparation :** Laxatives for bowel preparation post injection, nothing else

- **Several weeks post tumor therapy (FN)**

  Radiation therapy and chemotherapy can alter the normal pattern of gallium distribution

- **180 MBq (4-5 mCi) is usually administered**

  Imaging follows after 48 – 72 hours

  WB + SPECT/SPECT CT, midium-energy collimator

Normal Ga-67 scan

Normal scan

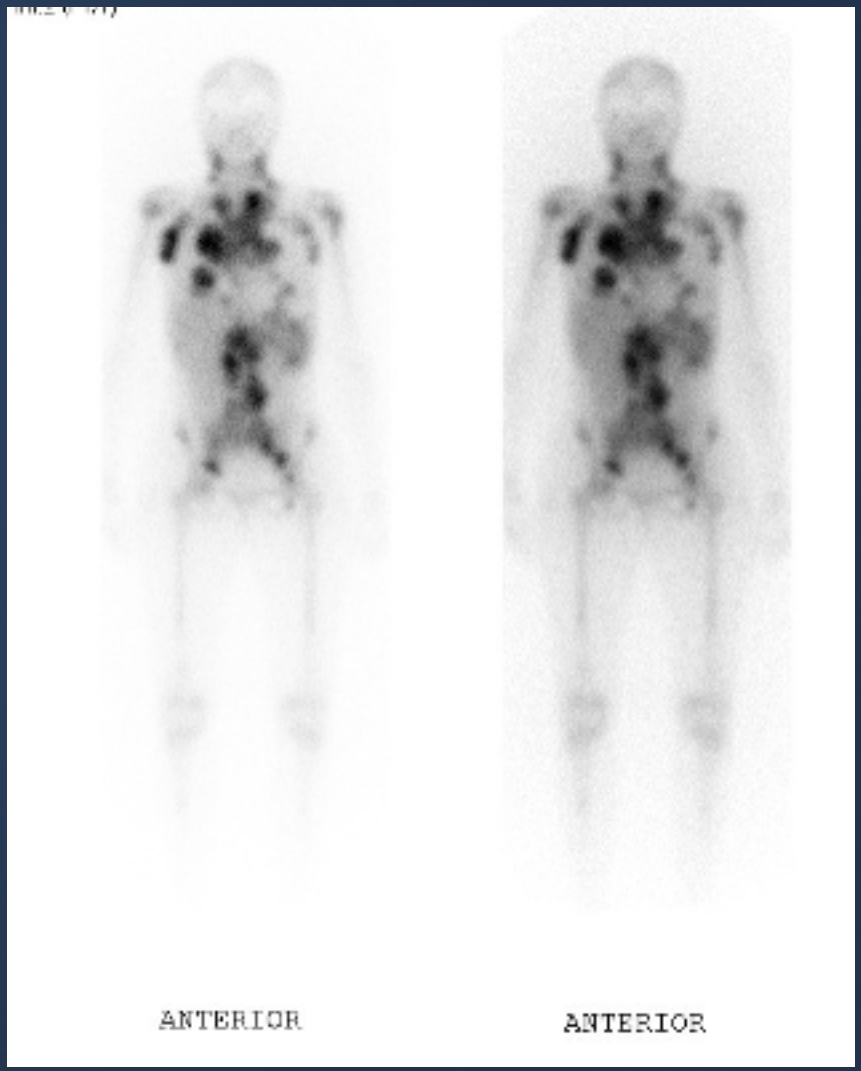
- Accumulates in bone marrow and liver.
- Splenic uptake is variable.
- The kidneys are usually visualized and also lacrimal, salivary, nasopharyngeal and genital activity is often present.
- Female breasts can be visualized, but accumulation is physiologically symmetrical
- Radioactivity is commonly seen in the colon

Clinical indications

- **Lymphoma**
- **Melanoma**
- **Lung cancer**
- **Hepatoma**

Gallium Scan in Lymphomas

- Staging
- Follow up and monitoring of therapy
- Detection of tumor recurrence
- Differentiate postherapy changes : tissue necrosis and fibrosis from local recurrence.



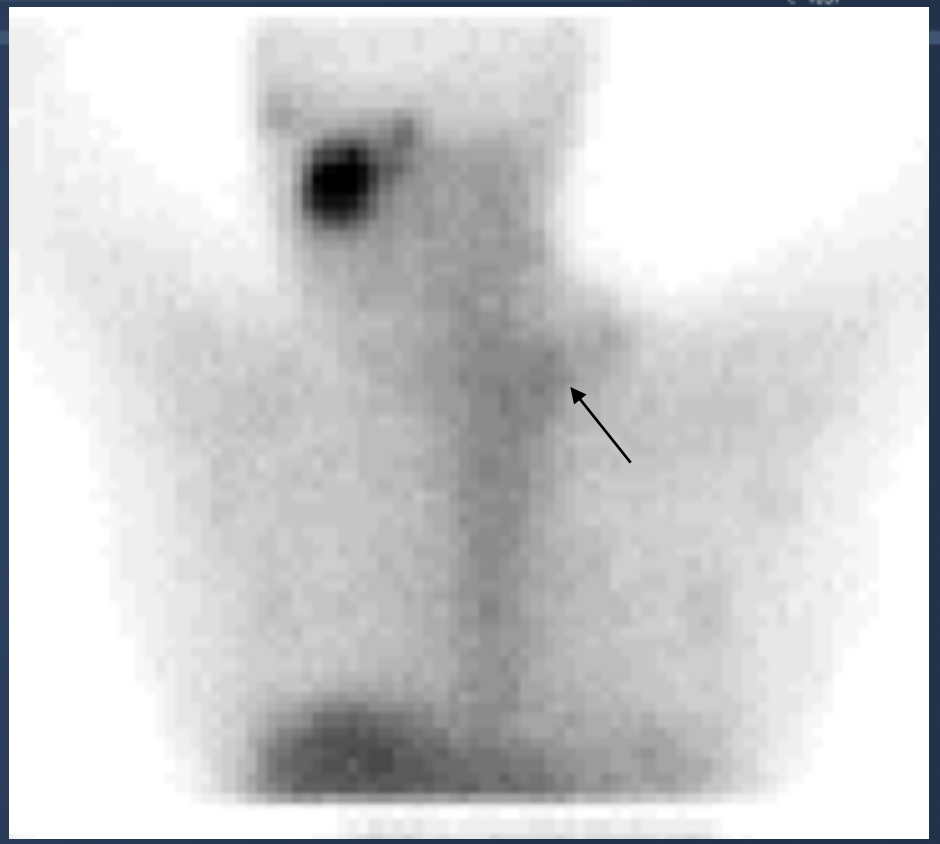
Ga-67 Scan In Lymphoma

Prediction of response to therapy

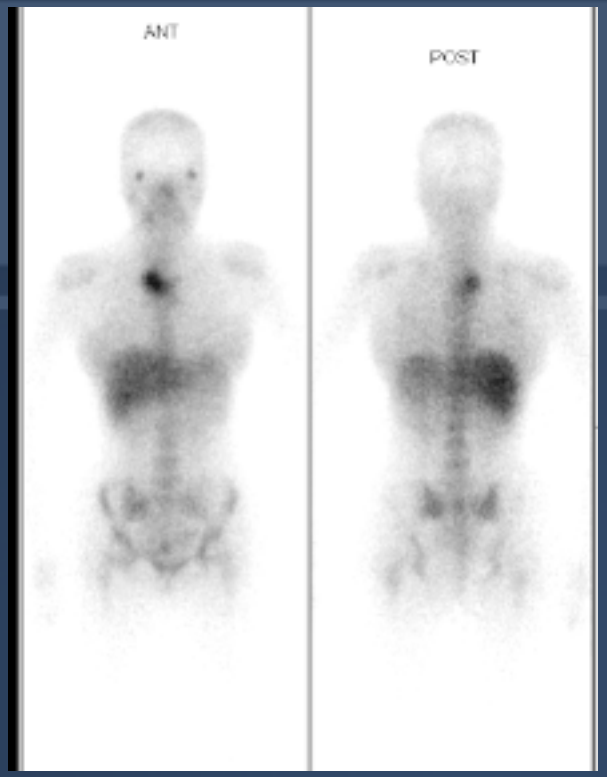
Normalization of a positive pre-therapy scan : A negative scan after one cycle or at mid cycle is associated with a high likelihood of complete response .

Ga-67 Scan In Lymphoma

Prediction of outcome



Residual gallium uptake after treatment is a poor prognostic sign, indicates viable tumor and treatment should be modified.



Gallium Scan NHL

Planar Vs SPECT CT

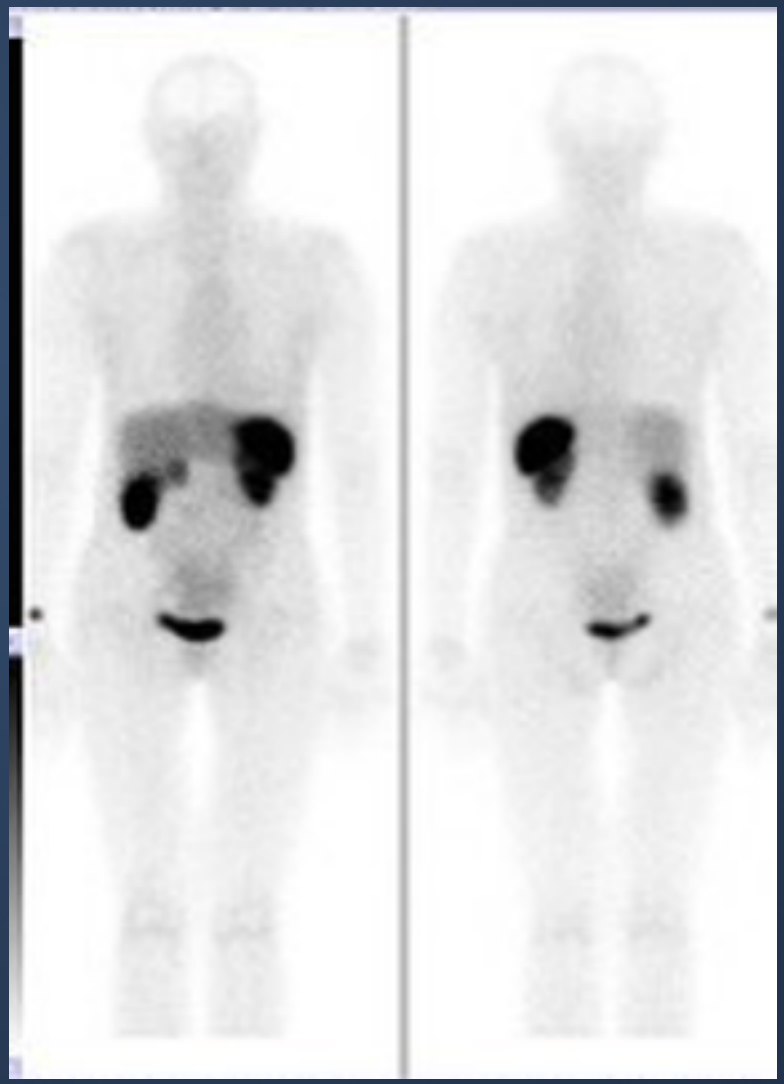
Neuroendocrine Tumors

- In-111 octreoscan.
- I123 MIBG Scan.

Somatostatin Receptor Imaging

Indium-111 Octreoscan

NORMAL STUDY



In - 111 octreoscan

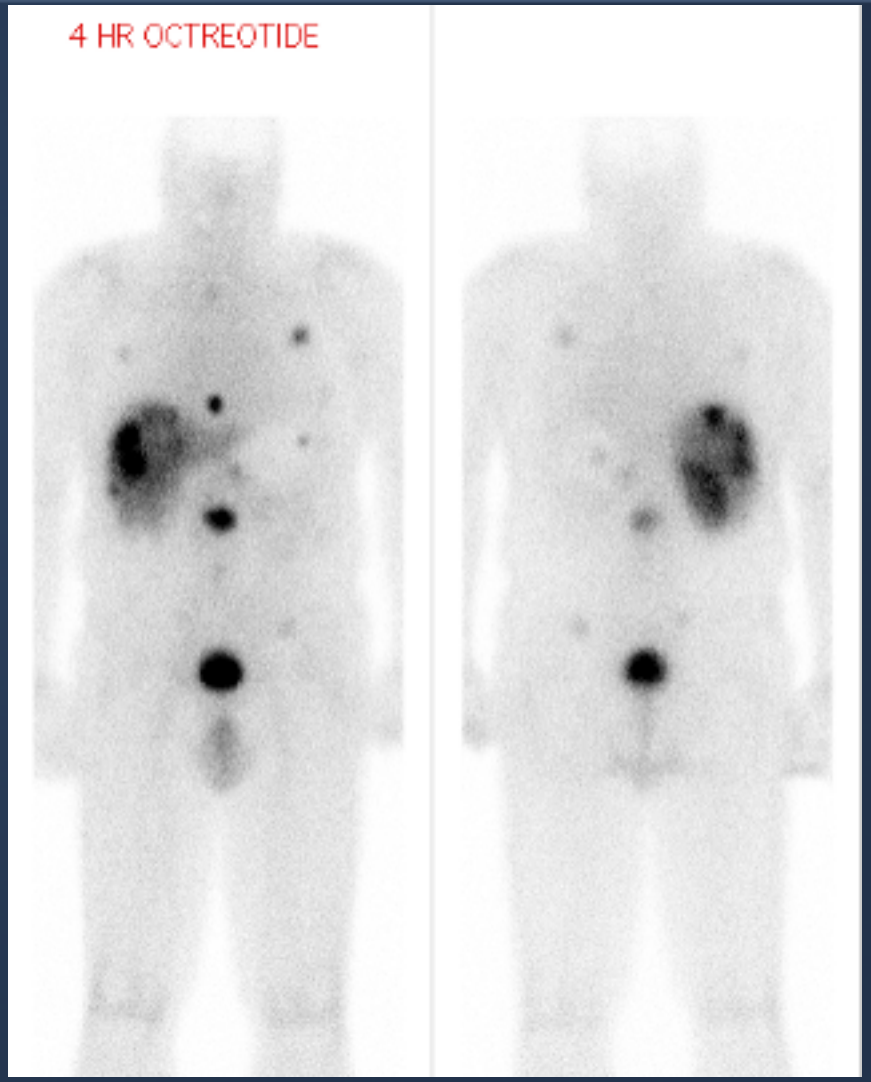
Insulinoma

Clinical History

The patient is a 66-ys male with insulinoma, now being evaluated for evidence of recurrent and/or metastatic disease.

Findings :

Multiple lung, mediastinum , liver and abdominal metastases.



I123 MIBG Scan

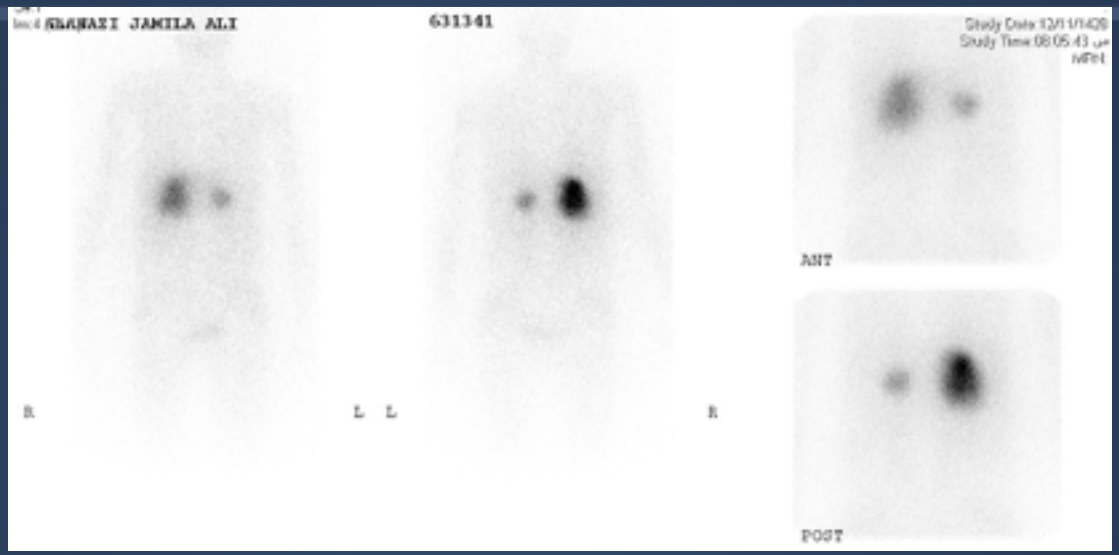
- MIBG : Meta Iodo Benzyl Guanidine
- Is a nor adrenaline analog
- Localizes in adrenergic tissues: catecholamines producing tumors and their metastases.
- Patient preparation: stop drugs interfering with MIBG uptake. Lugols solution to protect thyroid gland

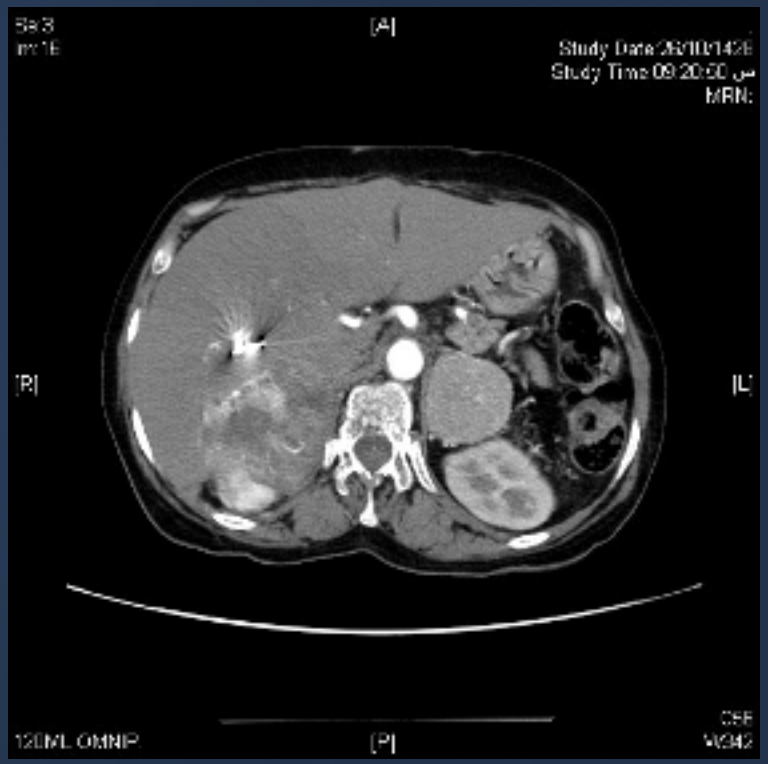
I123 MIBG Scan
Indications

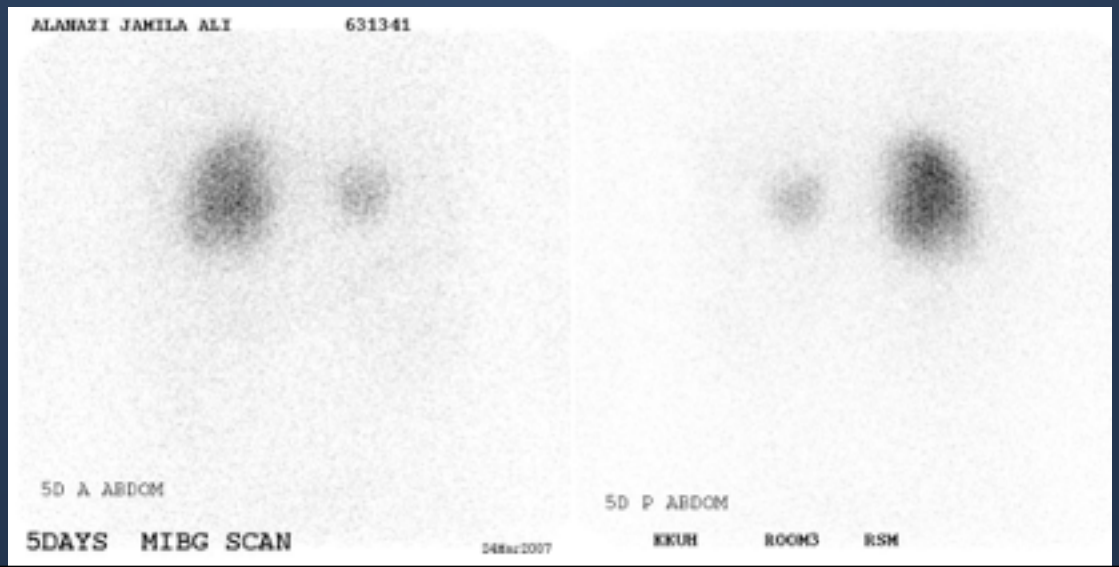
- Pheochromocytoma
- Paraganglioma
- Insulinoma
- Neuroblastoma
- Medullary thyroid carcinoma
- Carcinoid tumors

MIBG In Pheochromocytoma

Bilateral Disease



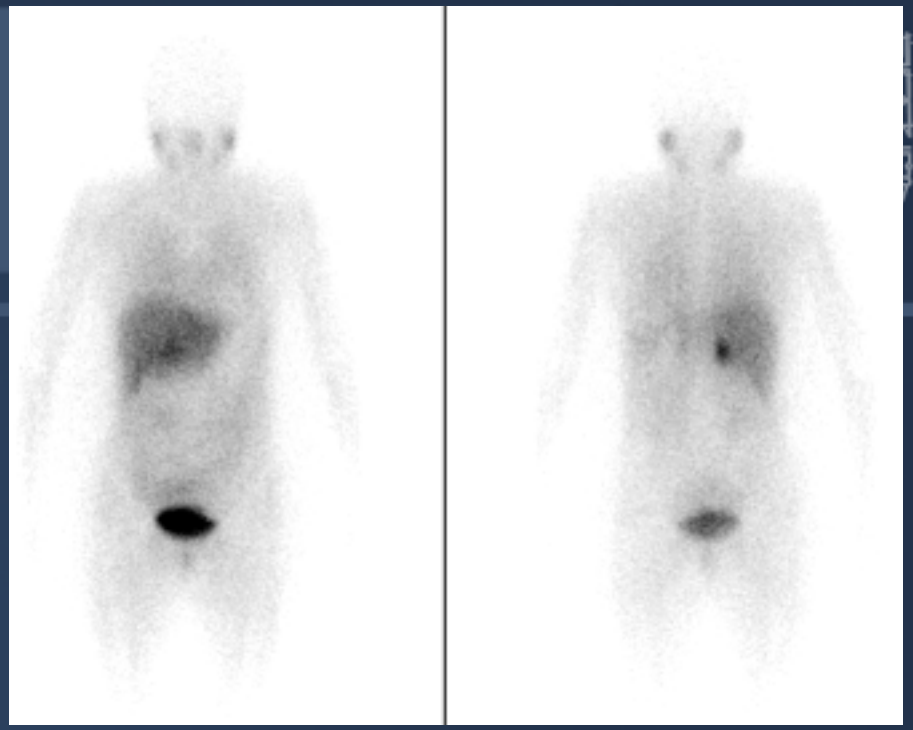


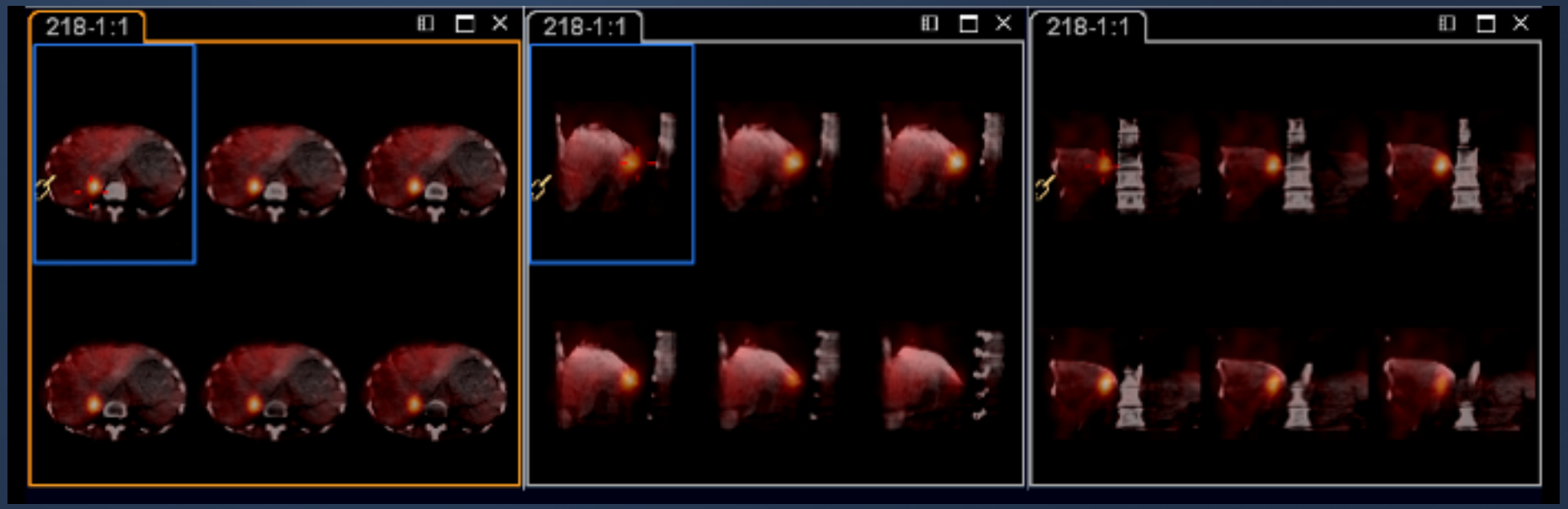


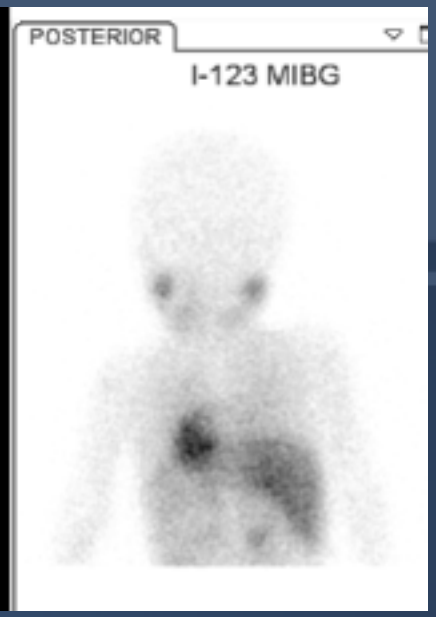
Pheochromocytoma

Planar Vs SPECT CT

A 41 years old female patient is with 2ndary hypertension. Right adrenal mass. ?Pheochromocytoma.

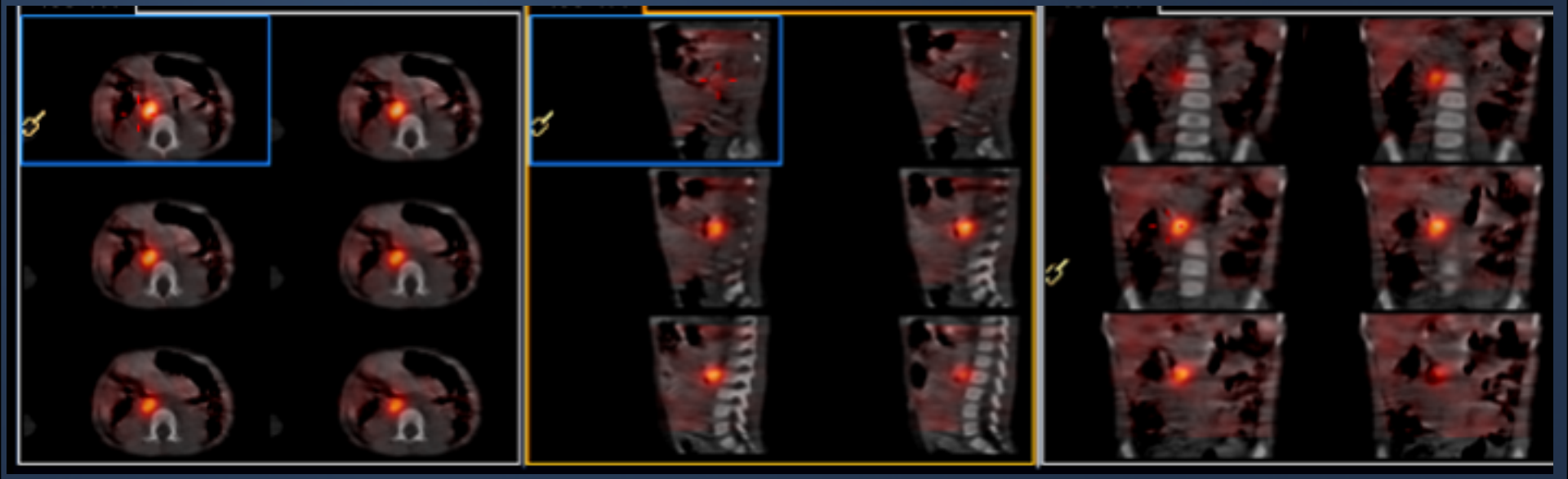






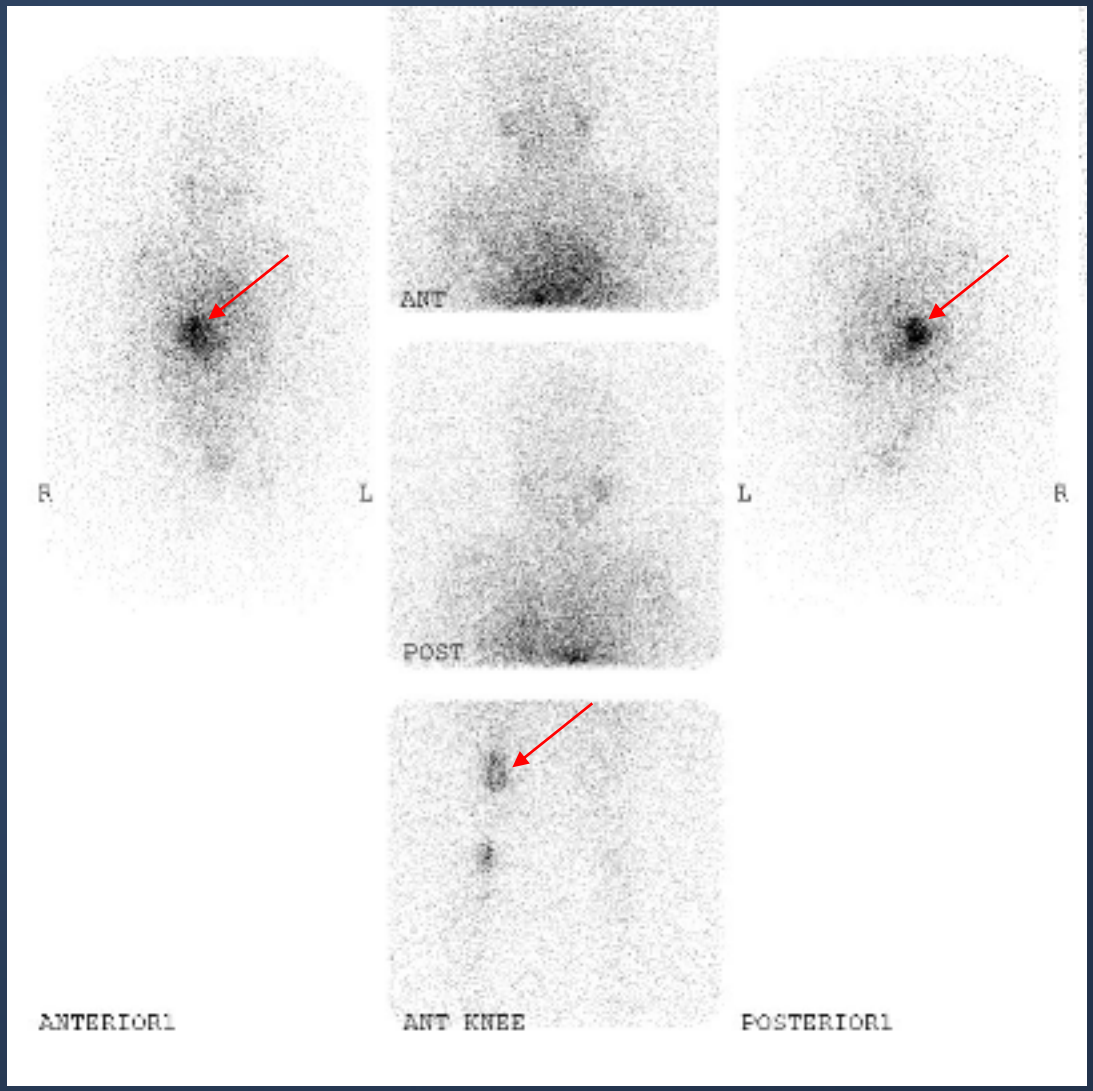
Neuroblasoma

Planar Vs SPECT CT



I131 MIBG Total body scan

1ry neuroblastoma /bone mets



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

Patient Preparation

- Stimulation of potentially functioning thyroid tissue:

A. Inject recombinant human thyrotropin on 2 consecutive days and administer the iodine on the third day .

B. Withdraw thyroid replacement hormones :

1. Thyroxine (T-4) for at least 4 weeks.
2. Triiodothyronine (T-3) for at least 10 days.

- The patient must not have had i.v iodinated contrast material (IVP, CT with contrast, myelogram, angiogram) for at least 3 weeks .

- The patient should be NPO for at least 4 hours prior to radiopharmaceutical administration and for at least 1 hour afterwards .

Tracer , Dose, & Technique of Administration

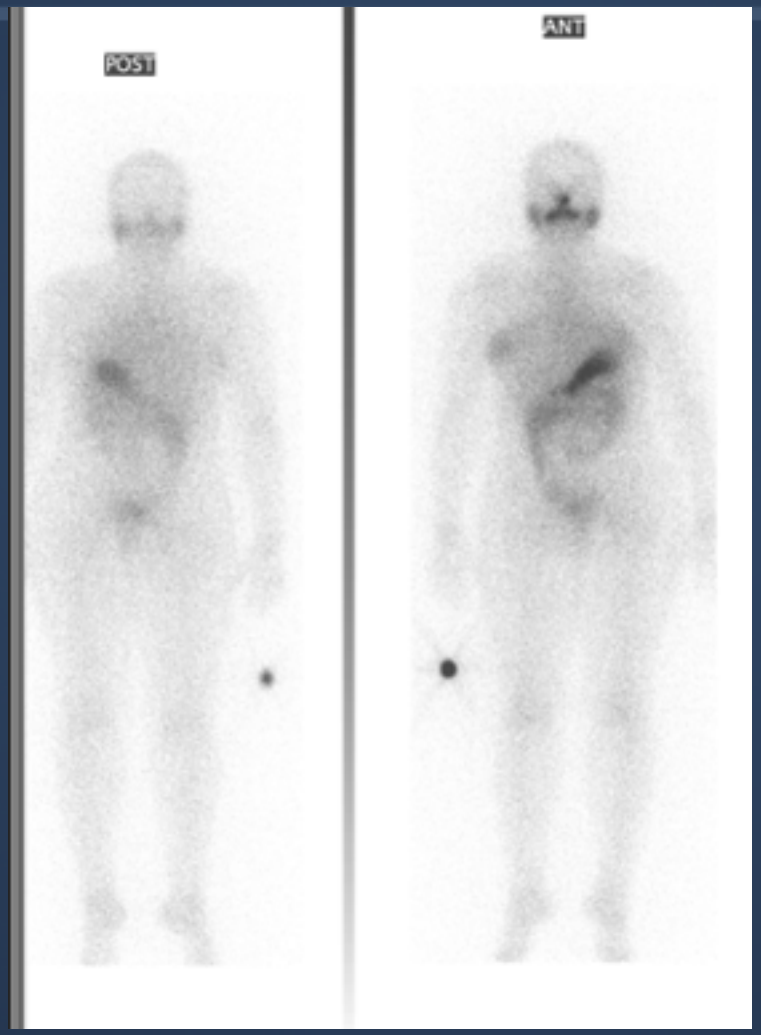
- Radiopharmaceutical: Oral administration

a. I-123 as sodium iodide : 2 mCi
b. I-131 as sodium iodide : 2-10 mCi

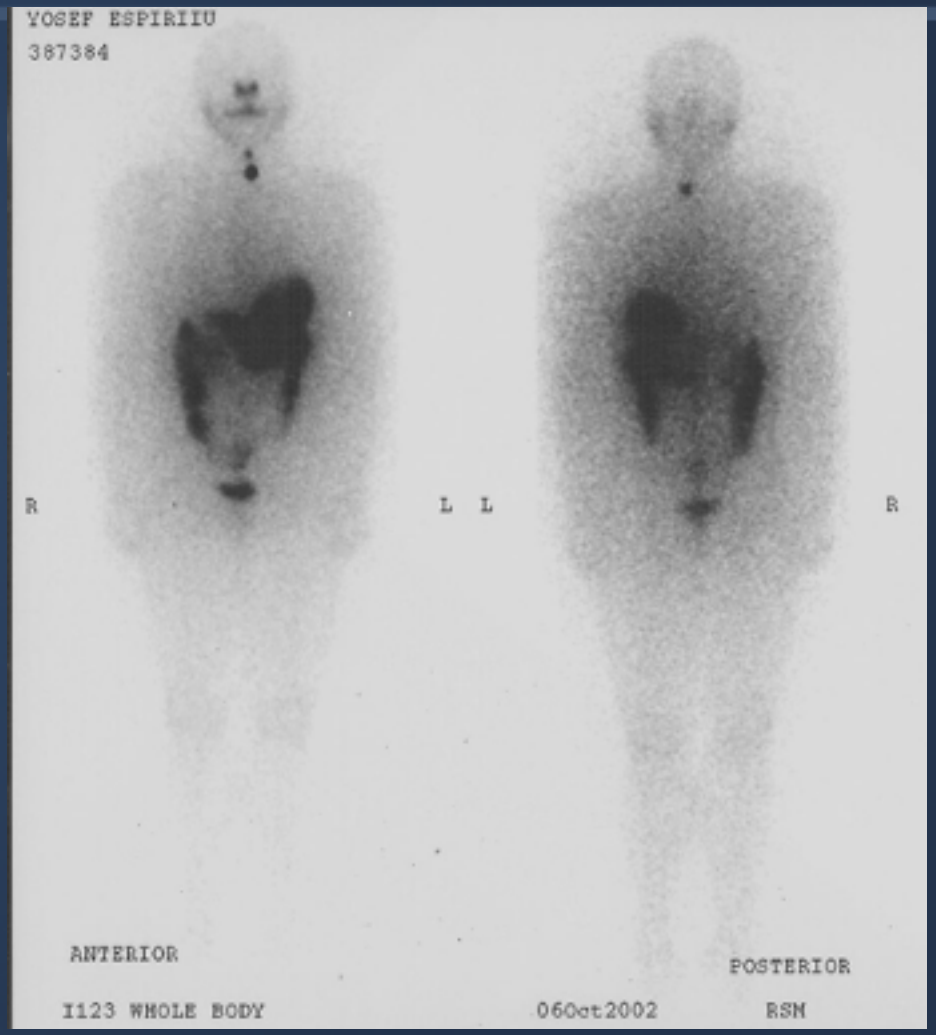
Imaging using Gamma camera : Whole body scan

Thyroid Cancer

I-123 WB Scan



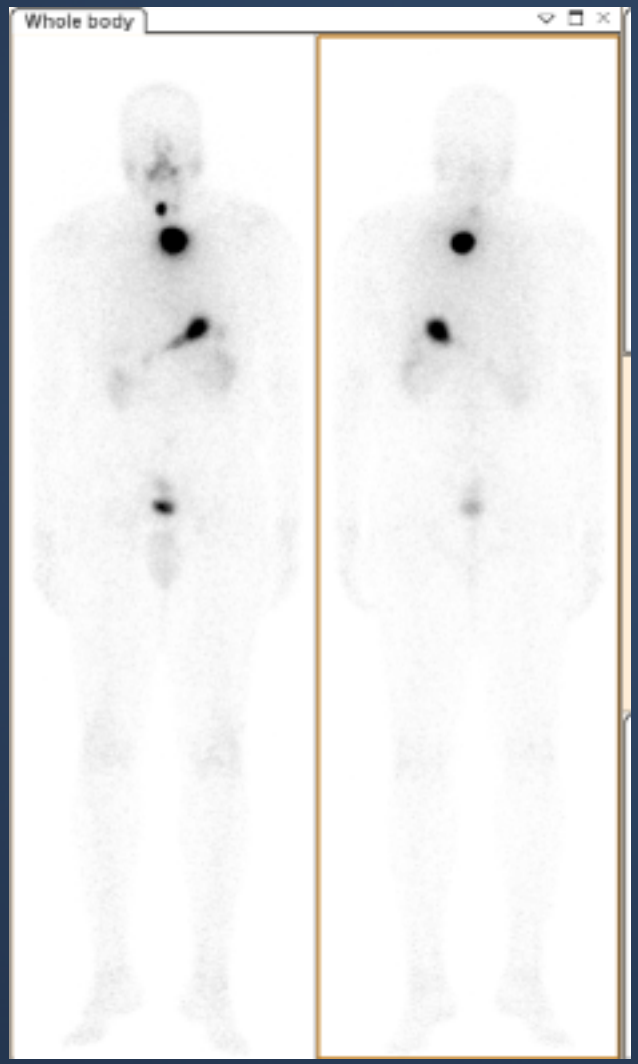
Negative I-123 WB Scan



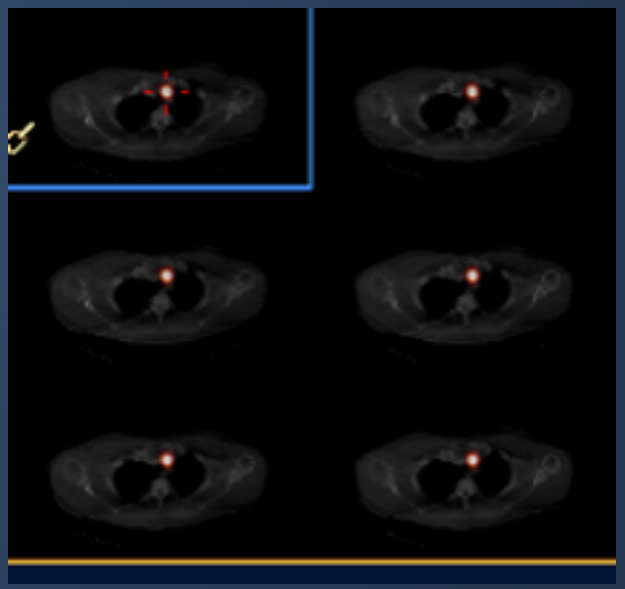
I-123 WB Scan : Post operative Thyroid remnants

I-123 WB Scan

Post operative Thyroid remnants

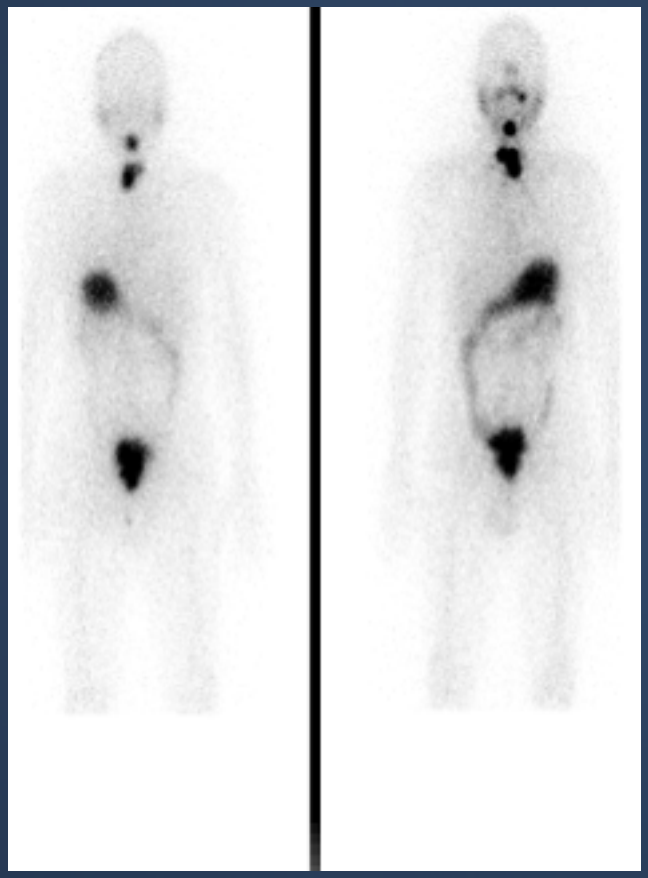


Planar Vs SPECT CT

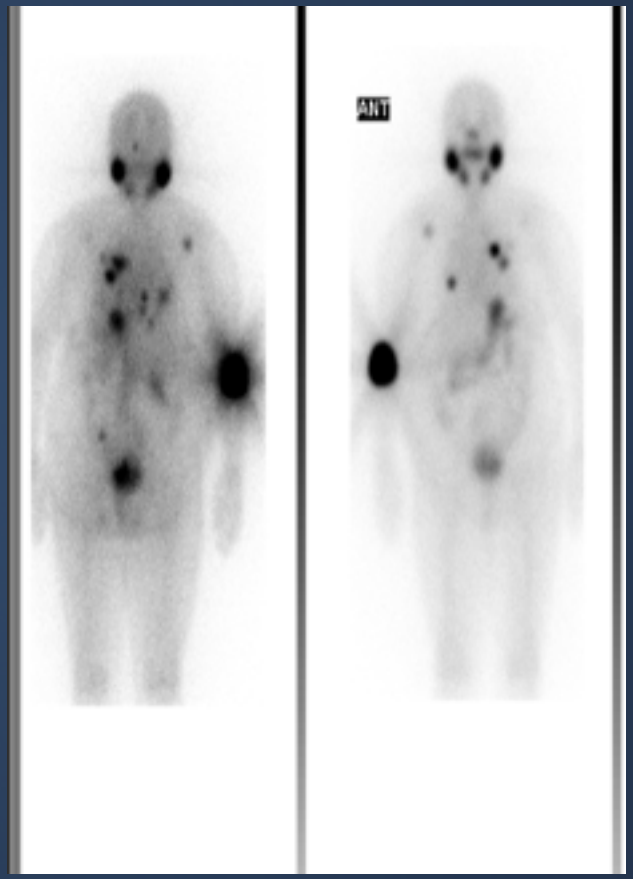


THYROID METASTASES STUDY

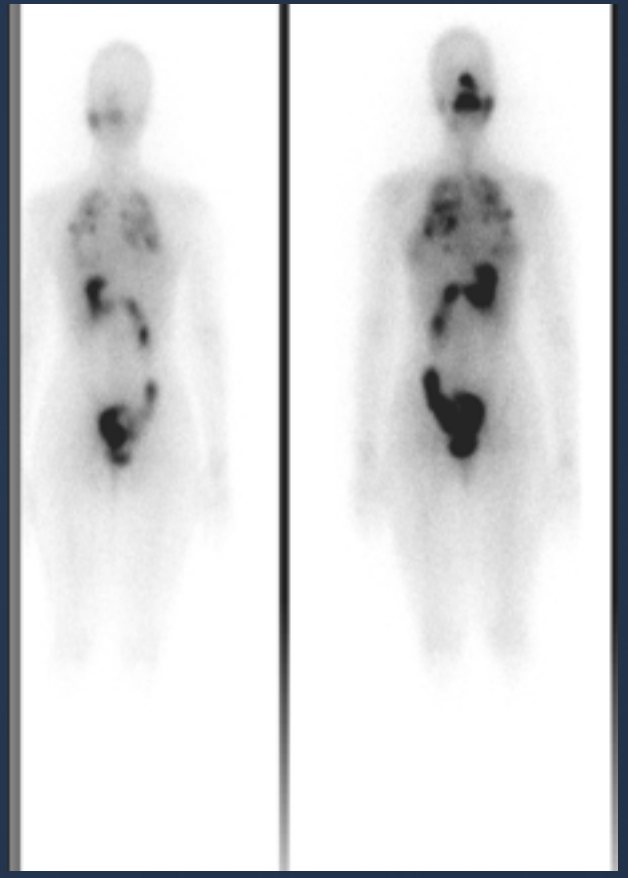
(I-123 or I-131 as Sodium Iodide)



Local Recurrence



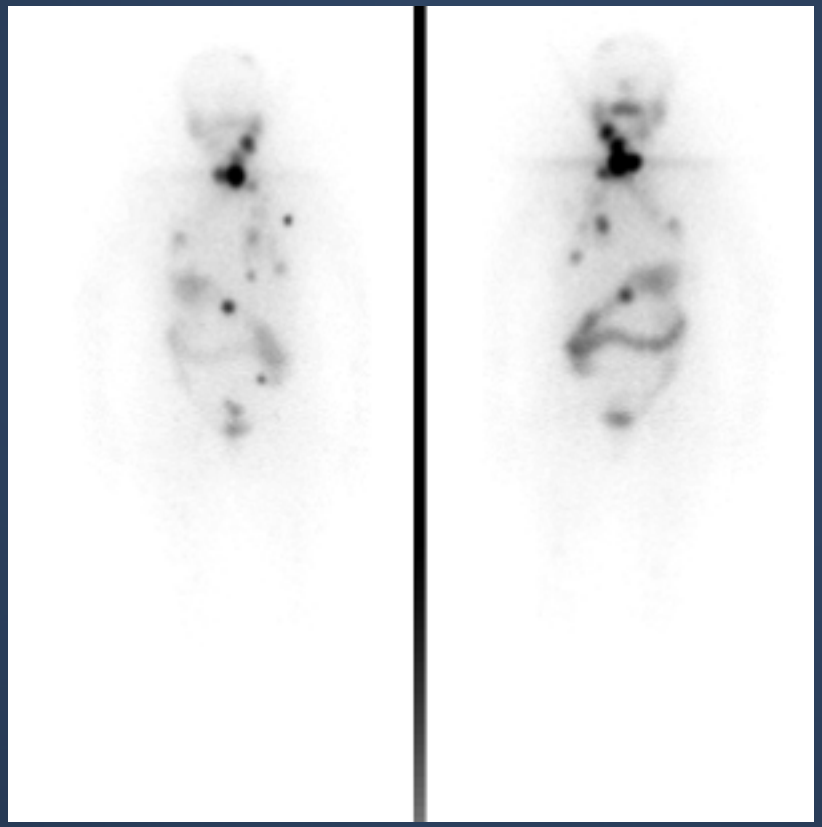
Bone Metastases

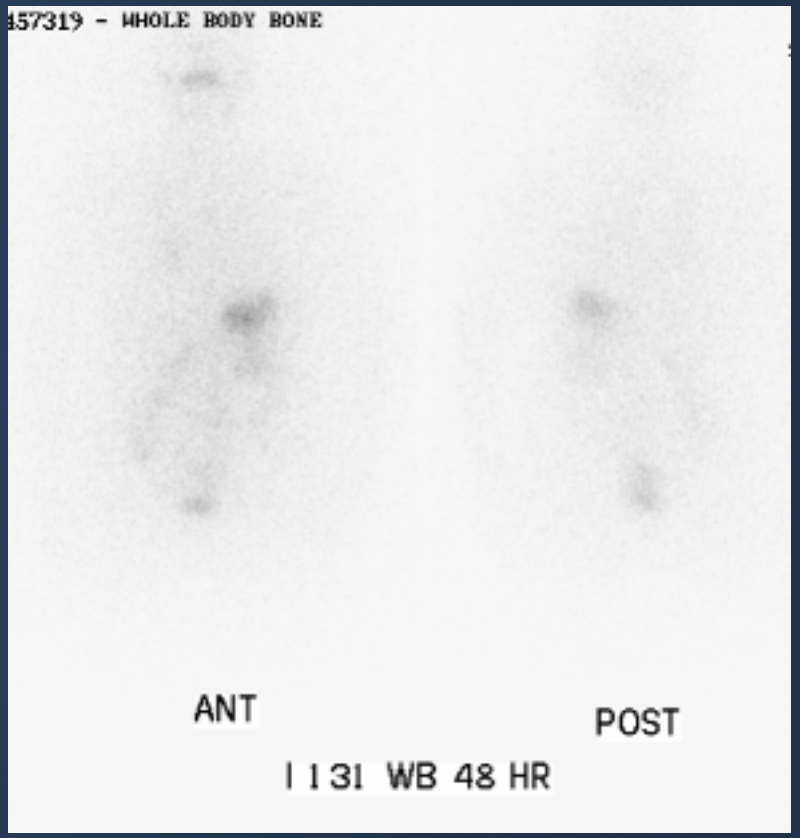


Lung Metastases

Thyroid Cancer

I-131 Pre & Post therapy





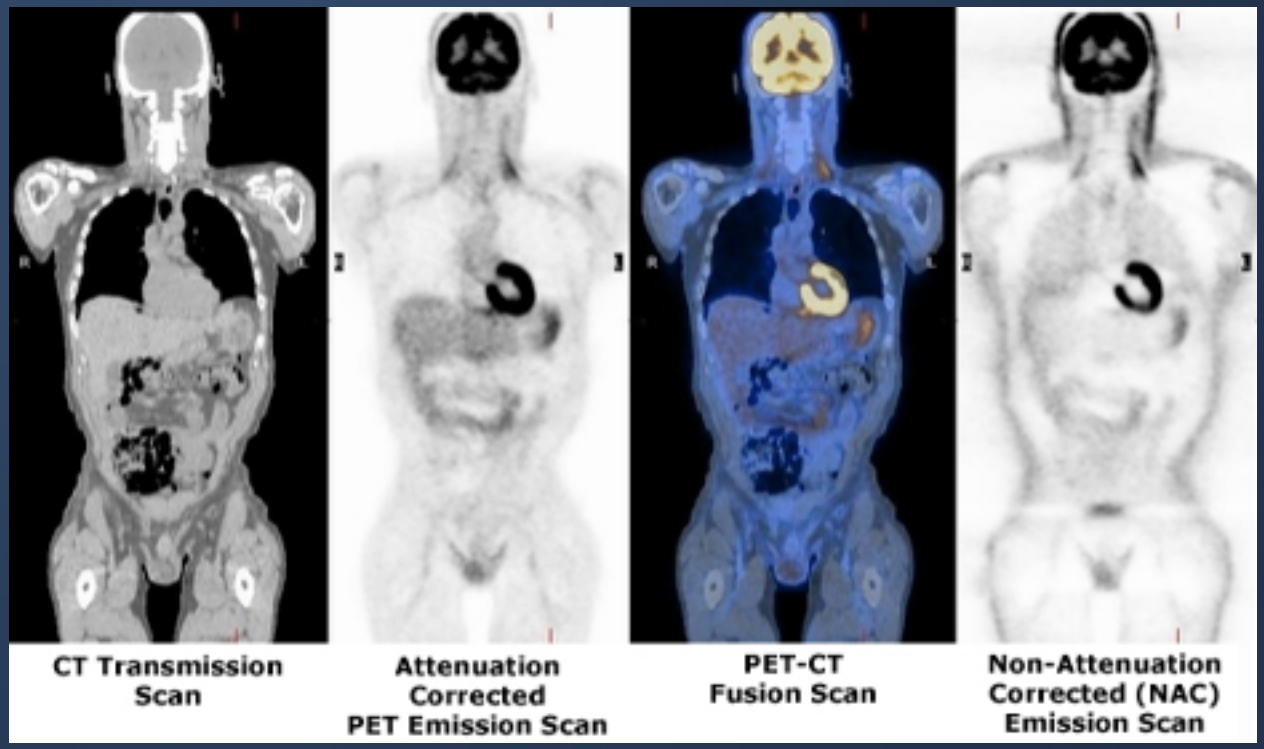
Dec04

March06

Onco PET (PET and PET CT)

What is PET - CT ……?

- PET : Positron Emission Tomography.
- CT : Computerized Tomography.
- PET-CT is the fusion of functional and anatomic information acquired almost simultaneously from which we are able to visualize form and function.



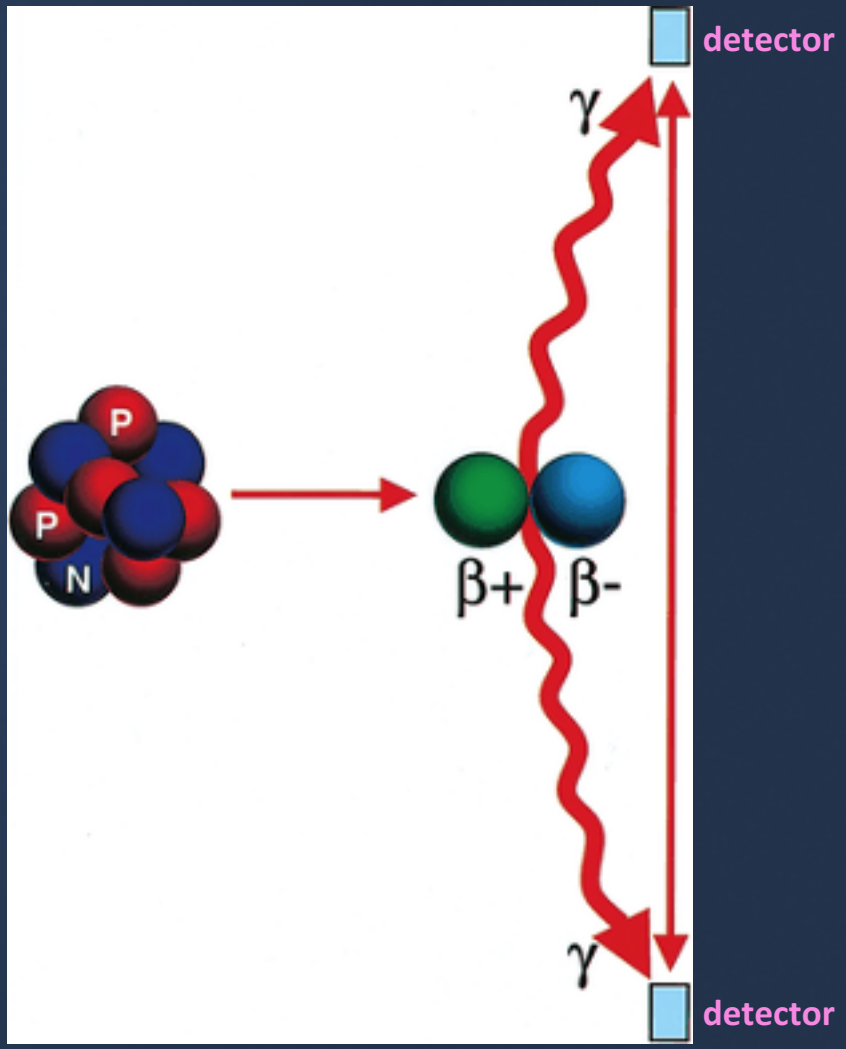
PET CT = PET + CT = Function + Form

PET : How it is performed…?

Positron emitters (e.g. F18) labelled with biologically active natural compounds such as oxygen, carbon or glucose give intravenously and reacting in the body identically to their non-radioactive counterparts.

Positrons are emitted from F18 and react with tissue electrons.....Anhillation occurs...

Two photons 511 kev each in opposite direction are emitted and detected by PET SCANNERgiving an image of the normal and abnormal distribution of tracer in the body.



Positron Emitting Isotopes

I. Cyclotron produced isotopes:

Isotope	T/2
Oxygen-15	2 min
Nitrogen-13	10 min
Carbon-11	20 min
Fluorine-18	110 min

II. Generator produced isotopes:

Parent	T/2	daughter	T/2
Strontium-82	25 days	Rubidium-82	75 seconds
Zin-62	9.3 hrs	Copper-62	10 min.
Germanium-68	288 days	Gallium-68	68 min

FDG : Fluoro-2-deoxy-D-Glucose

Uptake Mechanism

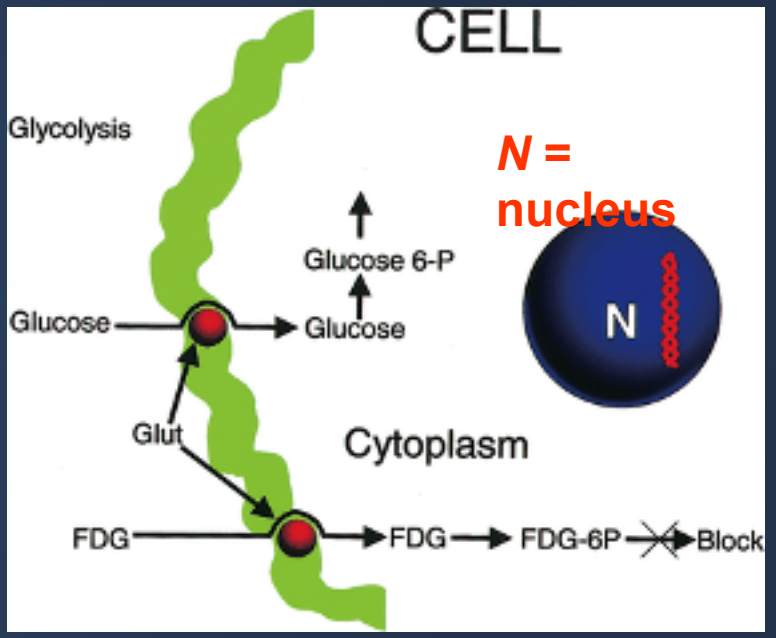
FDG is a glucose analogue used to asses glucose metabolism.

FDG transported from intravascular space to the cells by the same mechanism as the glucose.

In the cell, hexoKinase acts on both FDG and glucose to form:

- **FDG-6-phosphatase (FDG-6-PO4-)**
- **Glucose-6-phosphatase.**

FDG-6-PO4- cannot progress further into glucose metabolism and remains trapped intracellularly in proportion to glycolitic rate of the cell.



In tumors, there is high rate of glycolysis compared to normal cells as well as higher level of hexoKinase.
FDG is labeled with F18

FDG : Normal distribution

Brain & heart --- High uptake

Liver --- Less uptake

Kidneys --- Unlike glucose, FDG is excreted with urine

GI --- Mild clearance, faintly seen

Muscles --- Low, increase with exercise

FDG in Oncology

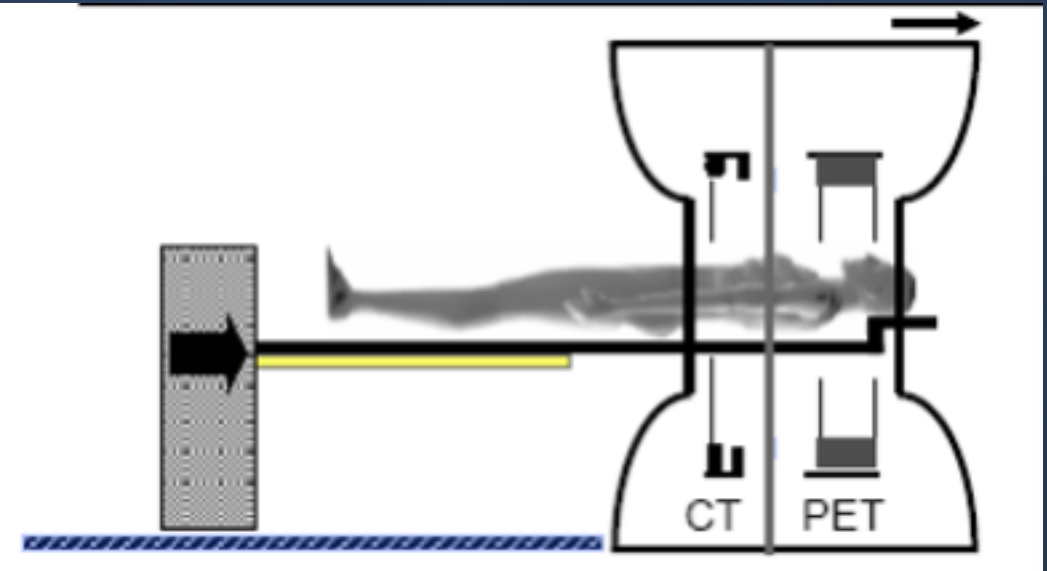
- Tumors do not have a blood tumor barrier
- FDG transport into tumors occurs at a *higher* rate than in the surrounding normal tissues.
- FDG is de-phosphorylated and can then leave the cell.
- The de-phosphorylation occurs at a *slower* rate in tumors.

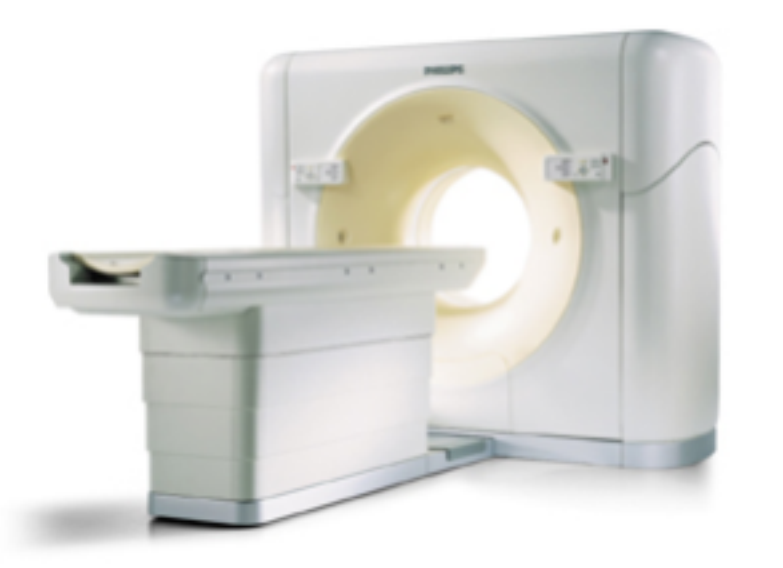
- **Applications of FDG**
  - Locating unknown primaries
  - Differentiation of tumor from normal tissue
  - Pre-operative staging of disease (lung, breast, colorectal, melanoma, H&N, pancreas)
  - Recurrence vs necrosis
  - Recurrence vs post-operative changes (limitations with FDG)
  - Monitoring response to therapy

PET CT

F18 FDG IMAGING PROTOCOL

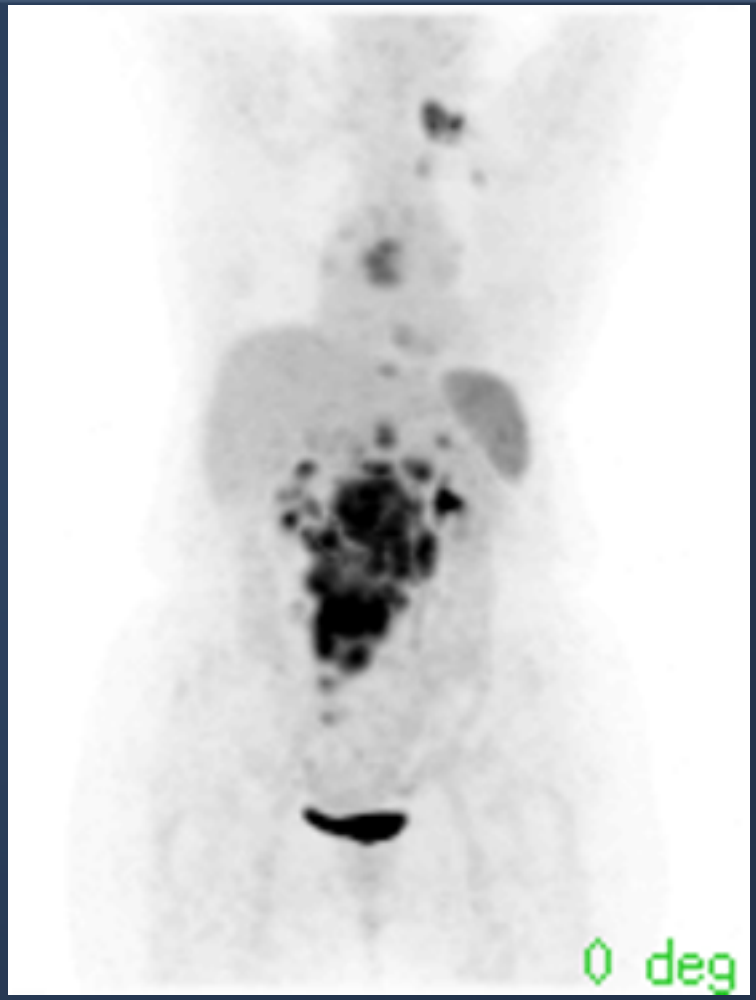
- **Fasting :** 4 – 6 hours
- **Dose :** Inject 10 mCi F18 FDG
- **Wait (uptake phase):** 45 -60 min then scan
- **Scanning time :** 30 min to complete PET CT study
- **SUV :** Standard uptake value (N:0.5-2.5 and Tumors > 3.0)





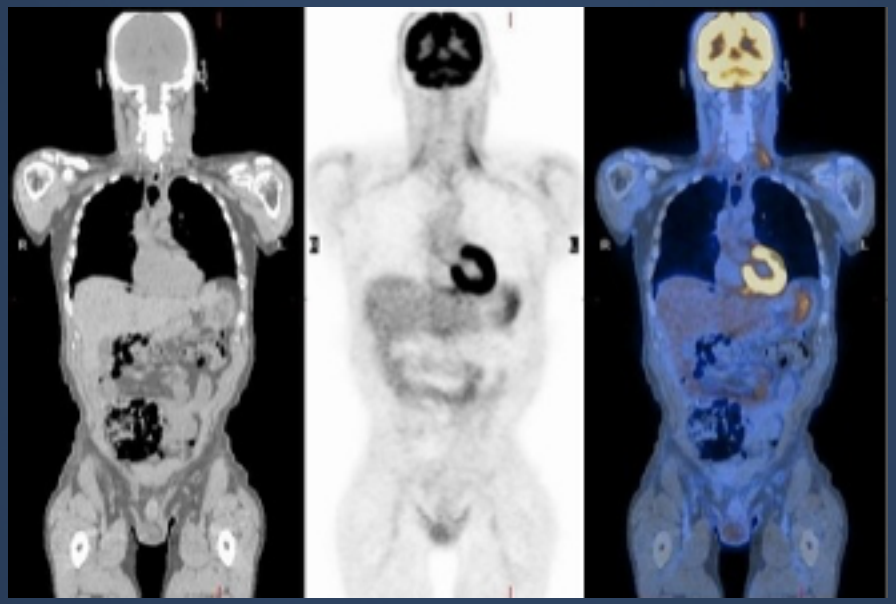
FDG PET

FDG PET : Normal



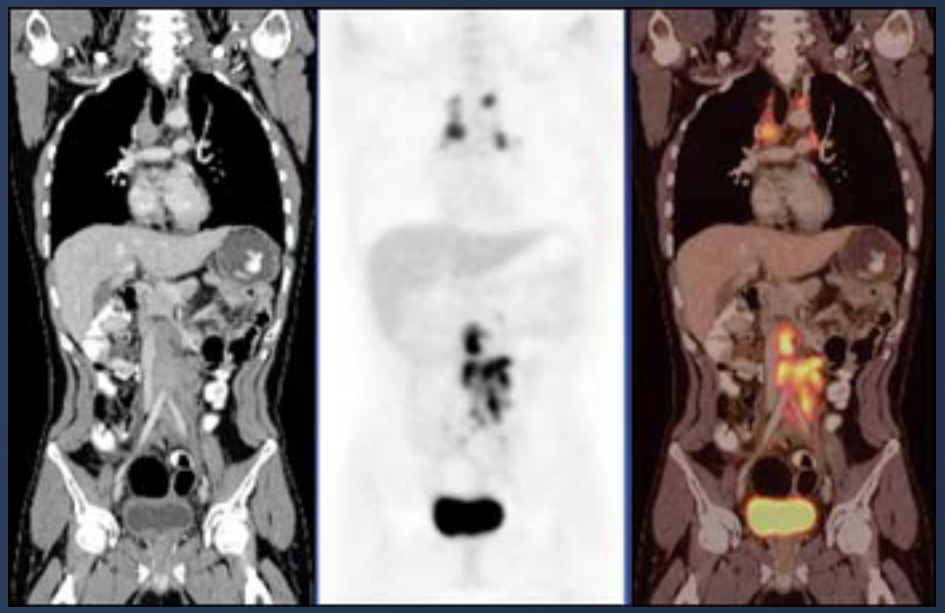
FDG PET : Staging of NHL

FDG PET-CT



FDG PET-CT

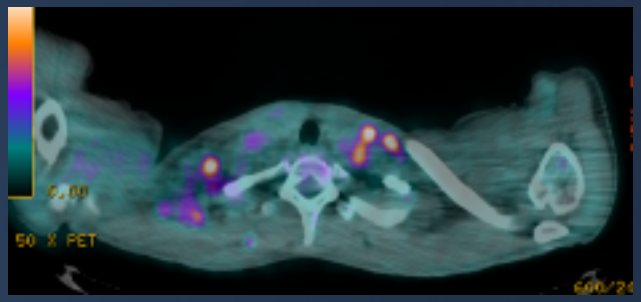
Normal

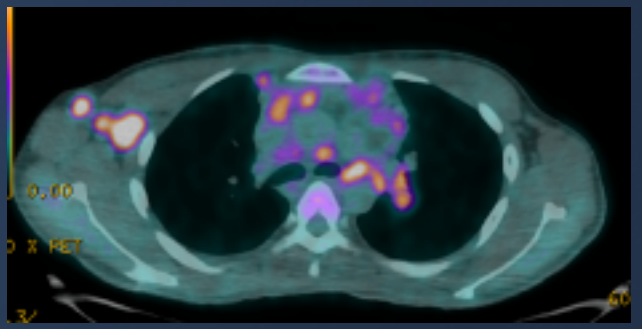


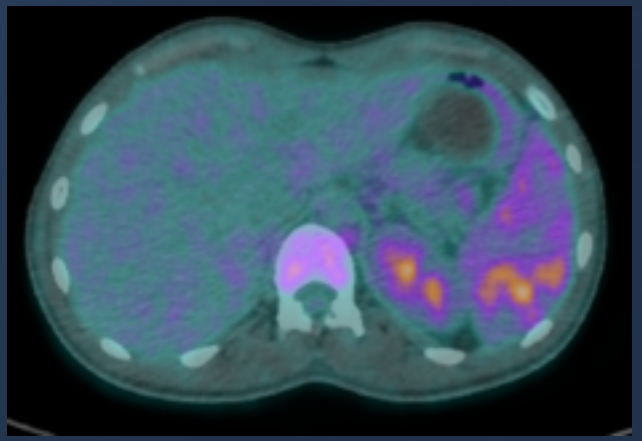
FDG PET-CT

Staging Of Lymphoma

FDG PETCT
NHL : Stage IV







FDG PETCT : Hodgkin's lymphoma

Post 6 cycles of chemotherapy for assessment.

Baseline
24.10.2018

Interim
1.1.2019

Final
19.5.2019

FDG PETCT: Hodgkin's lymphoma.

Post 6 cycles of chemotherapy for assessment.

"Partial metabolic response
(Deauville Score 5).

Baseline
31.3.2019

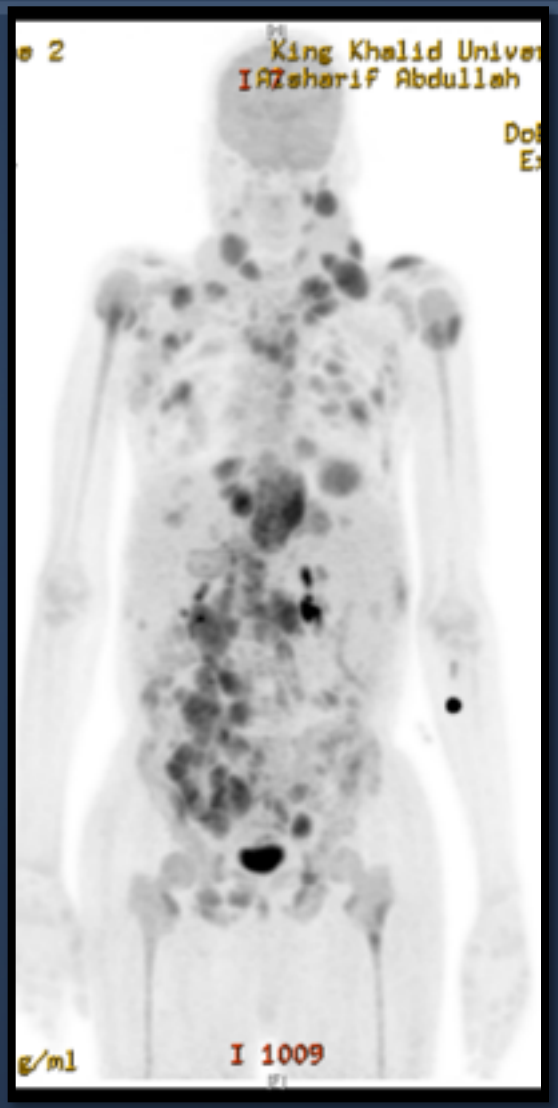
Interim
9.6.2019

Final
4.8.2019

FDG PETCT: Marginal zone lymphoma

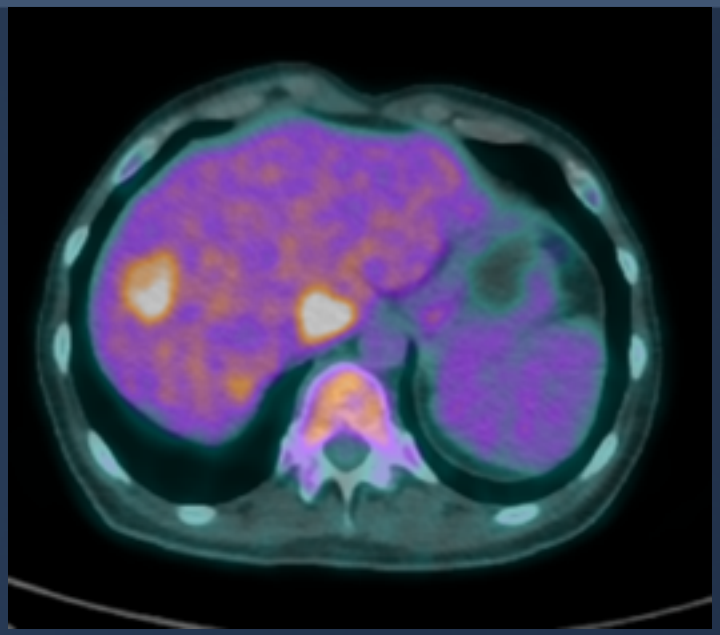
Progressive disease (Deauville Score 5)

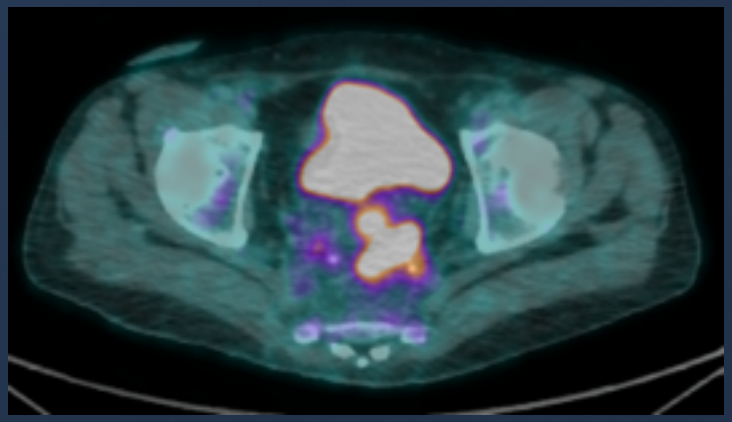
Baseline
19.2.2019



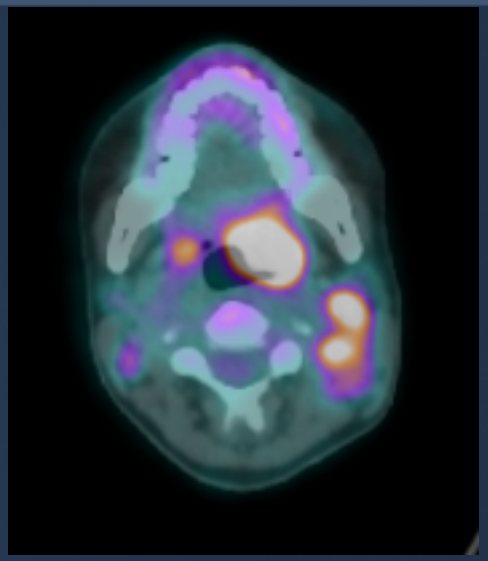
Interim
17.7.2019

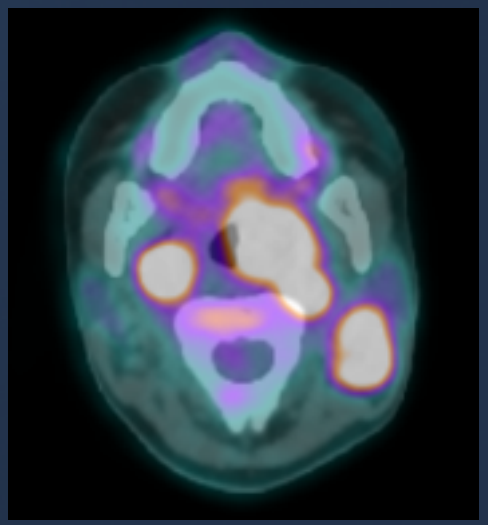
FDG PETCT
Rectal cancer with liver metastases



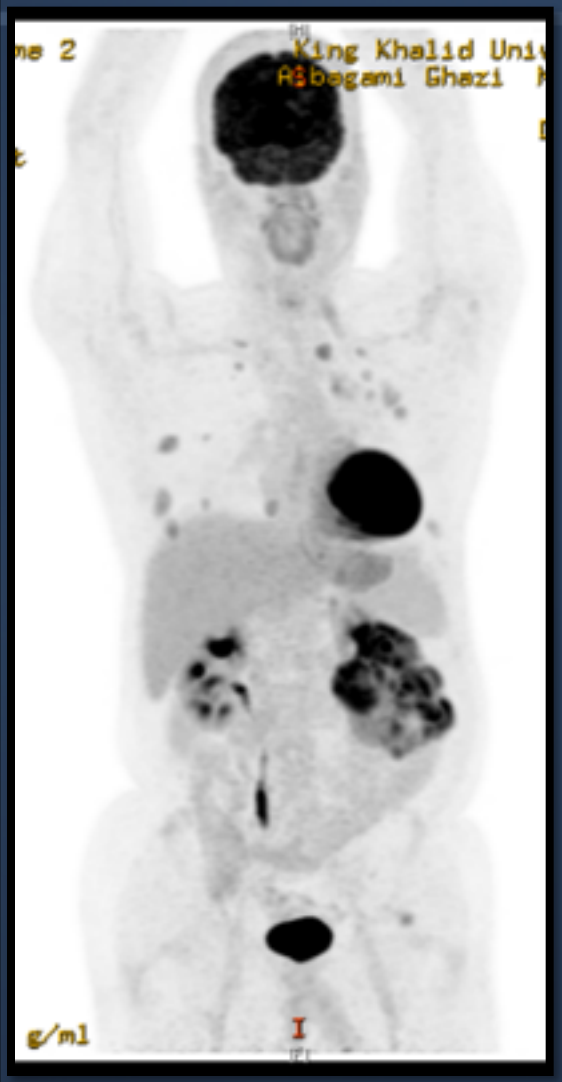


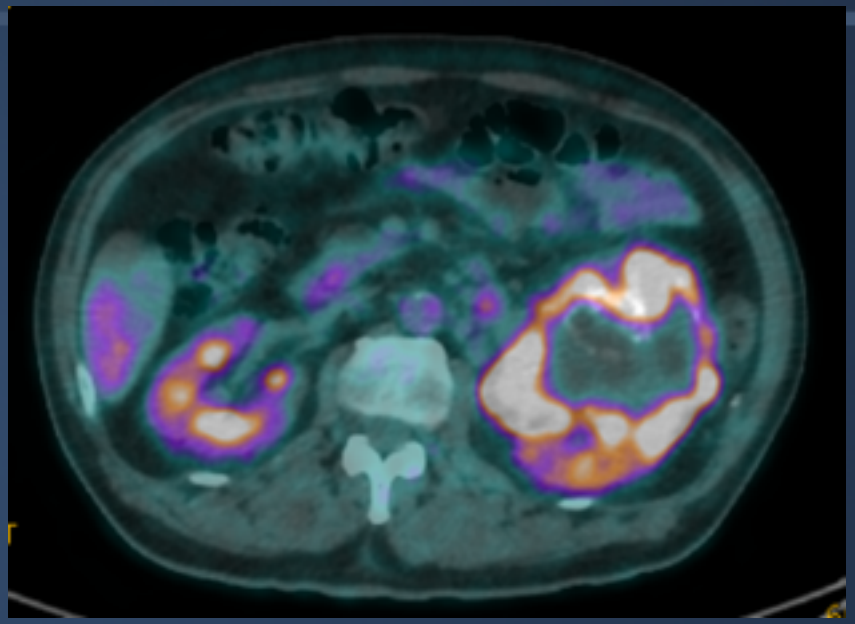
FDG PET CT : Nasopharyngeal cancer with LN metastasis

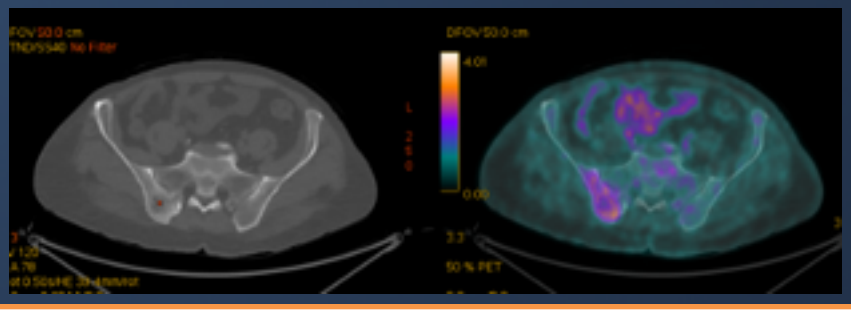




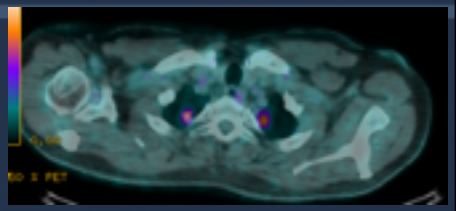
FDG PET CT : RCC with bone and lung metastases

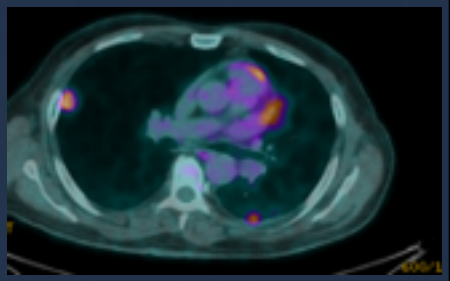


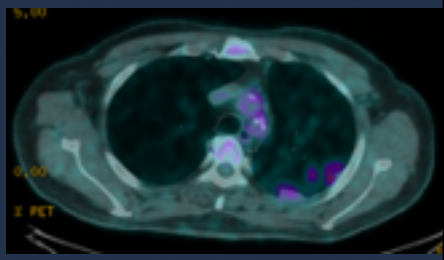


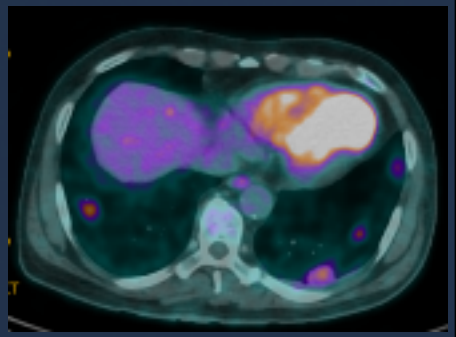


309756
" FDG-avid left renal mass coupled with FDG-avid locoregional nodal disease and multiple FDG avid pulmonary metastasis.
"Solitary sclerotic area of hypermetabolism at the right iliac bone, worrisome for bone metastasis.

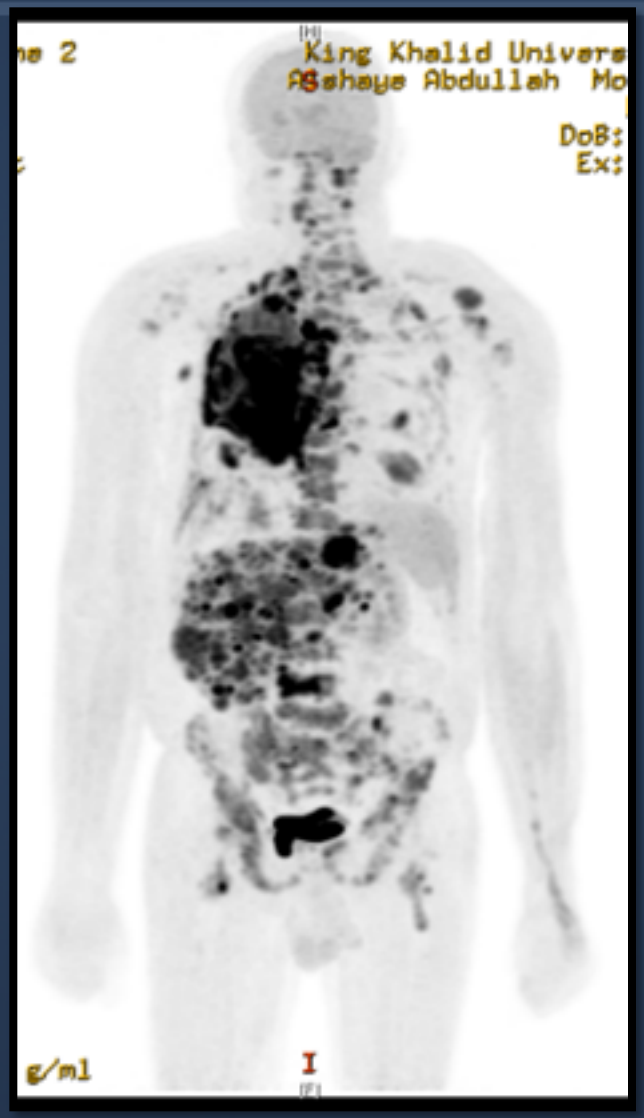


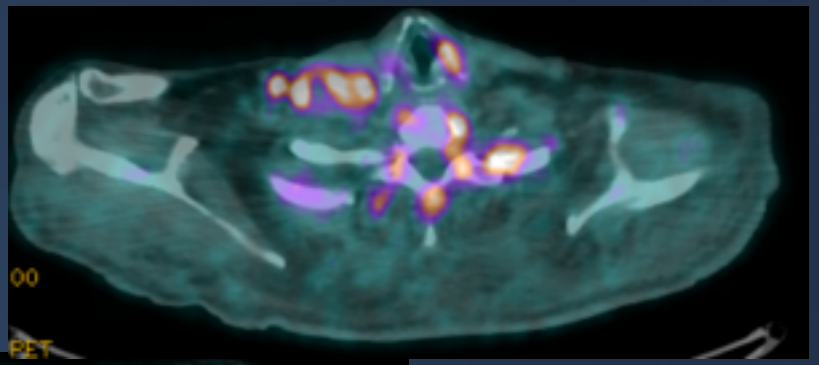


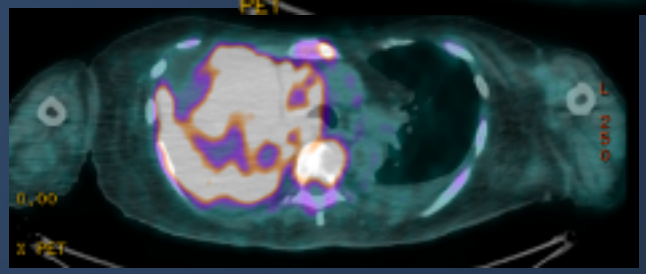


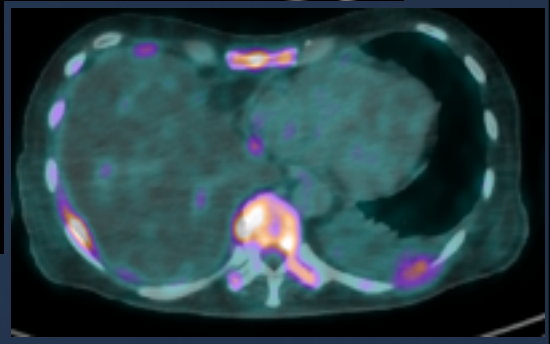


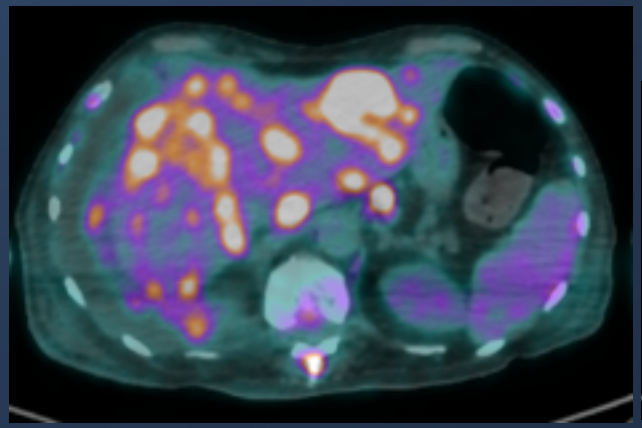
FDG PET CT : Metastatic Lung Cancer

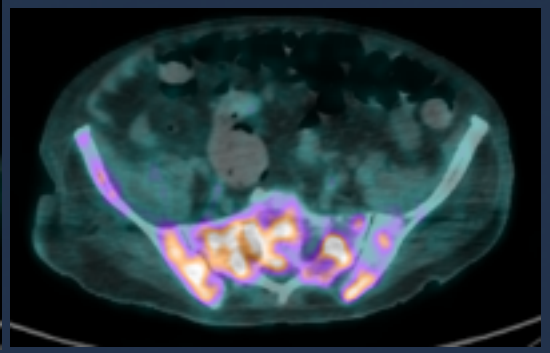




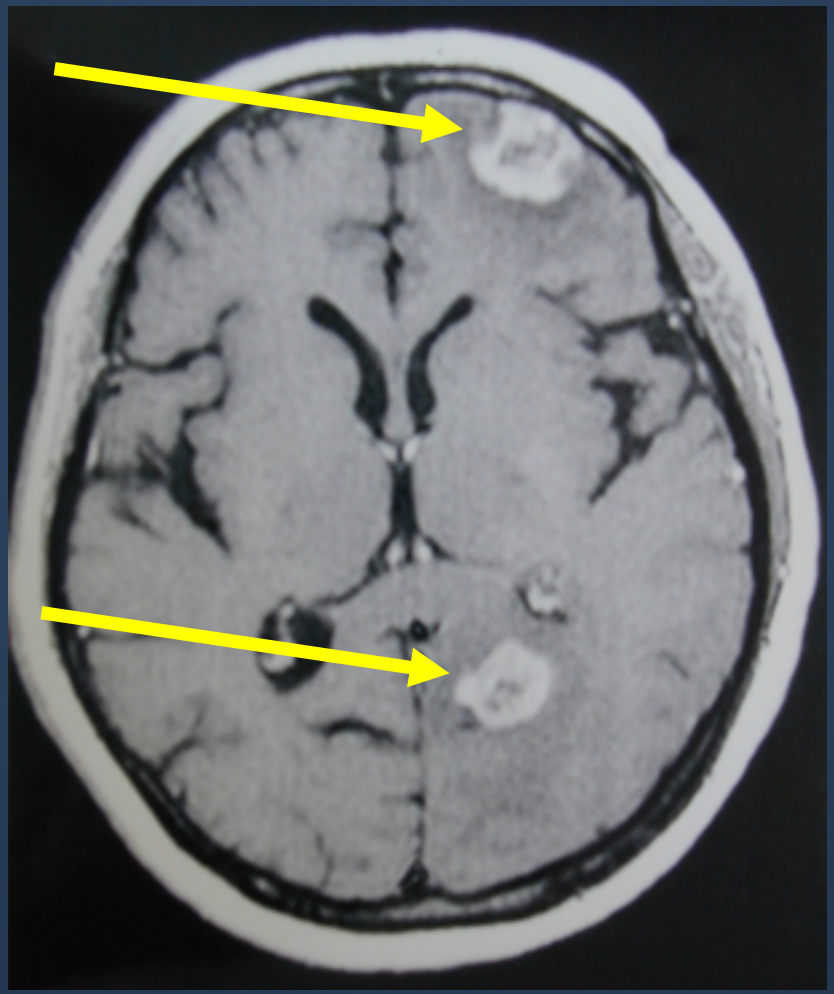


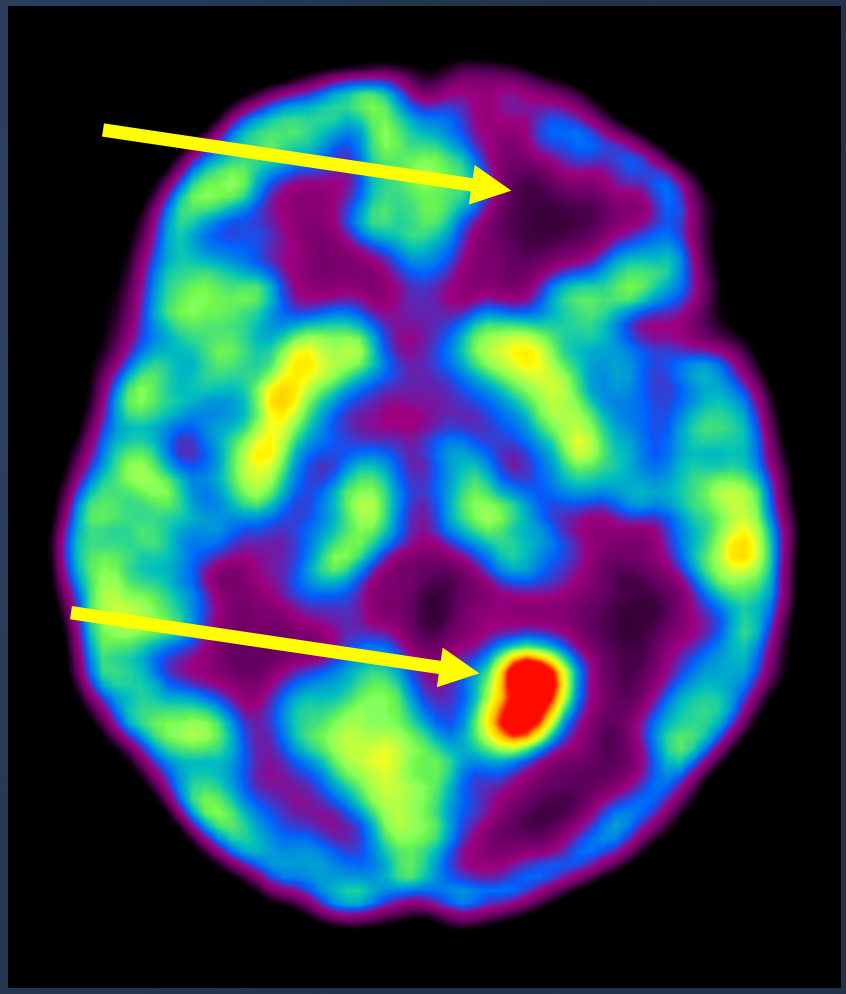






FDG PET – brain tumor





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

Somatostatin receptor PET tracers
Ga-68 DOTANOC

Radiopharmaceutical: **DOTANOC , DOTATOC or DOTATATE is labeled with Ga-68**

Dose: **3-5 mCi given intravenously.**

PET Imaging time: **45-60 min postinjection**

Clinical value: higher lesion detection rate than is achieved with (18)F-fluorodihydroxyphenyl-l-alanine PET, 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, etc.),
2. Sympathoadrenal system tumours (phaeochromocytoma, paraganglioma, neuroblastoma, ganglioneuroma)
3. Medullary thyroid carcinoma
4. Pituitary adenoma
5. Medulloblastoma
6. Merkel cell carcinoma
7. Small-cell lung cancer (mainly primary tumours)
8. Meningioma

Normal Distribution
68Ga-DOTA peptide PET/CT

Normal tracer uptake is seen in the pituitary, salivary glands, thyroid, liver, spleen, adrenals, pancreas, kidneys, ureters, and bladder

Ga-68 DOTANOC PET

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

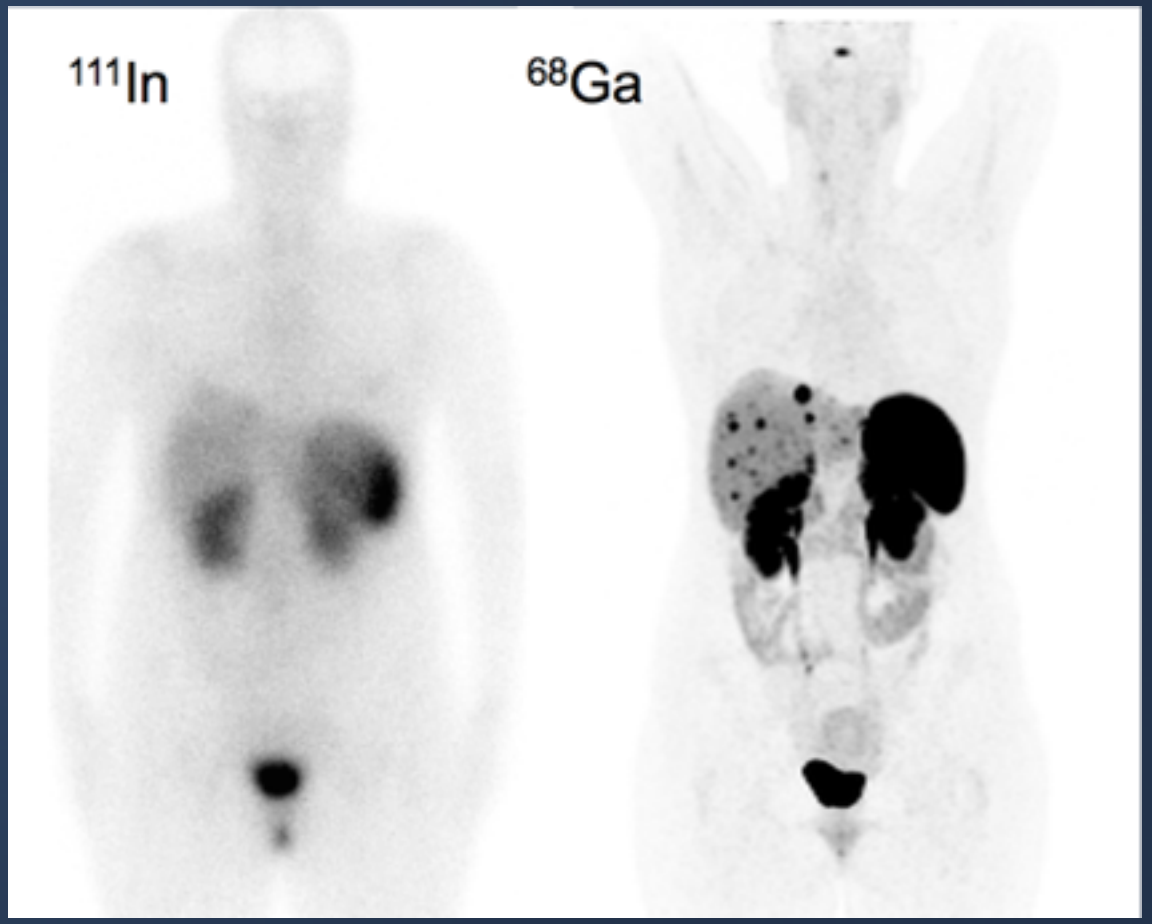
NET with extensive metastatic lesions throughout the body

Ga-68 DOTANOC PET superior to In- 111 Octreoscan

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

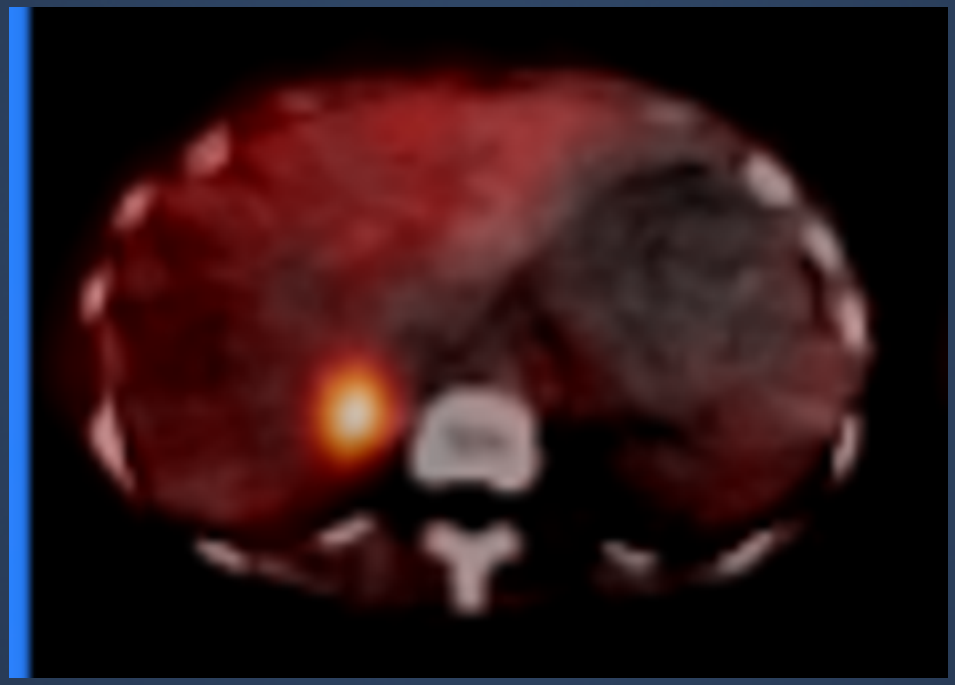
^{68}Ga DOTA-NOC Findings:
Multiple metastatic lesions in the liver. (The pituitary also expresses somatostatin receptors and is visualized in the ^{68}Ga PET image, along with normal uptake in the spleen, kidneys, and bladder.)

Indication of ^{68}Ga DOTA-NOC: The ^{68}Ga PET scan was performed because the patient's symptoms were inconsistent with the ^{111}In-Octreoscan findings.

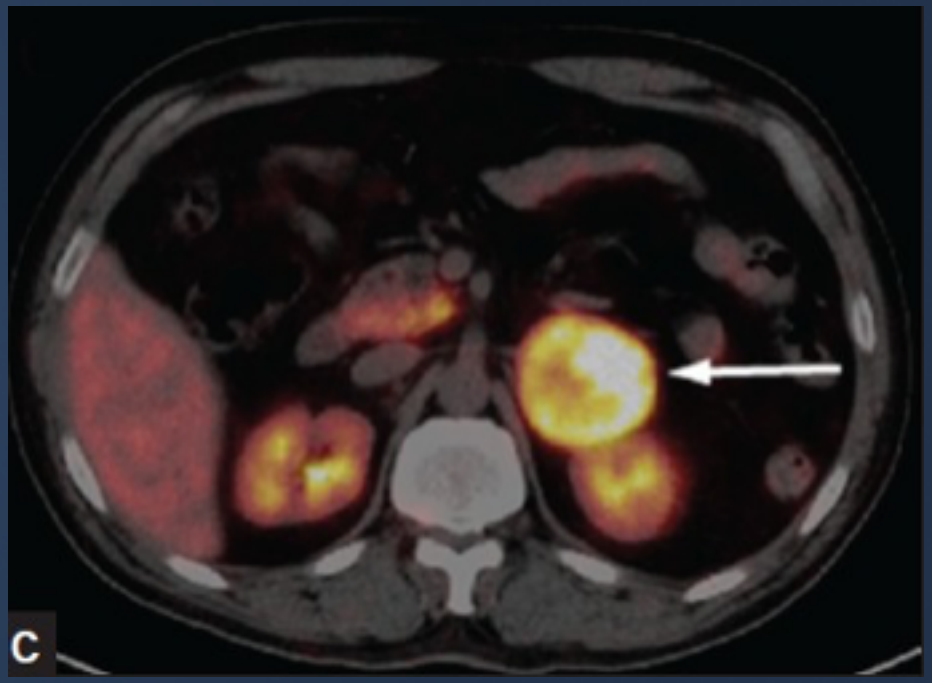


Pheochromocytoma

Ga68 DOTANOC superior to MIBG



SPECT CT - I123 MIBG



PET CT Ga68 DOTANOC

Radionuclide Therapy
Properties of the Ideal Therapeutic Radiopharmaceutical

1. Pure beta minus emitter

2. Medium/high energy (>1 meV).

3. Effective half-life = moderately long, e.g., days.

4. High target:nontarget ratio

5. Minimal radiation dose to patient and Nuclear Medicine personnel

6. Patient Safety

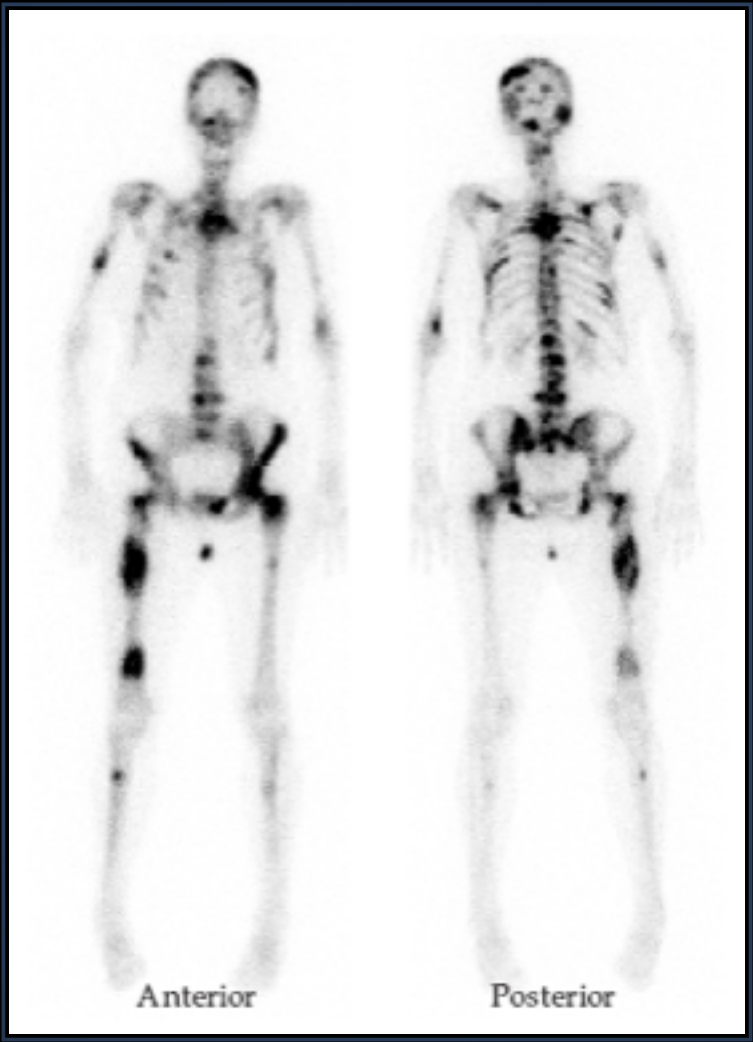
7. Inexpensive, readily available radiopharmaceutical.

8. Simple preparation and quality control if manufactured in house.

Radionuclide Therapy

Agent	Indication	Dose
I131 :	Thyroid cancer	100-200 mci
131 MIBG :	Neuroblastoma	100-300 mCi
Strontium-89 :	Bone metastasis	40-60uCi/kg
Sm-153-EDTMP:	Bone metastasis	1.0 mCi per kg
Phosphorus- 32 :	Polycythaemia	2.3 mCi/m2
Y-90-Ibritumomab Tiuxetan [Zevalin®]:	B-Cell NHL	0.3 mCi/kg
> Platelet count > 150,000 cells/mL: 0.4 mCi/kg		
> Platelet count 100,000-150,000 cells/mL: (1,184 MBq)		The dose should never exceed 32 mCi

Strontium-89 Therapy for Palliation of Bony Metastases



History :
A 65 Ys ,M, with CA prostate and widespread bone metastases and severe bony pain.

Admitted for palliative Strontium-89 therapy.

Procedure :

- Bone metastases was confirmed by bone scan.
- The patient was given 40 mCi of Strontium-89 I.V.according to body weight of the patient.
- The patient experienced one day of exacerpated pain which was controlled by opiates but the following day showed gradual pain relieve.

Teaching Points

NM tumor imaging

- Functional
- Sensitive
- Whole body evaluation
- Specific : Some tumors
- Targeted therapy

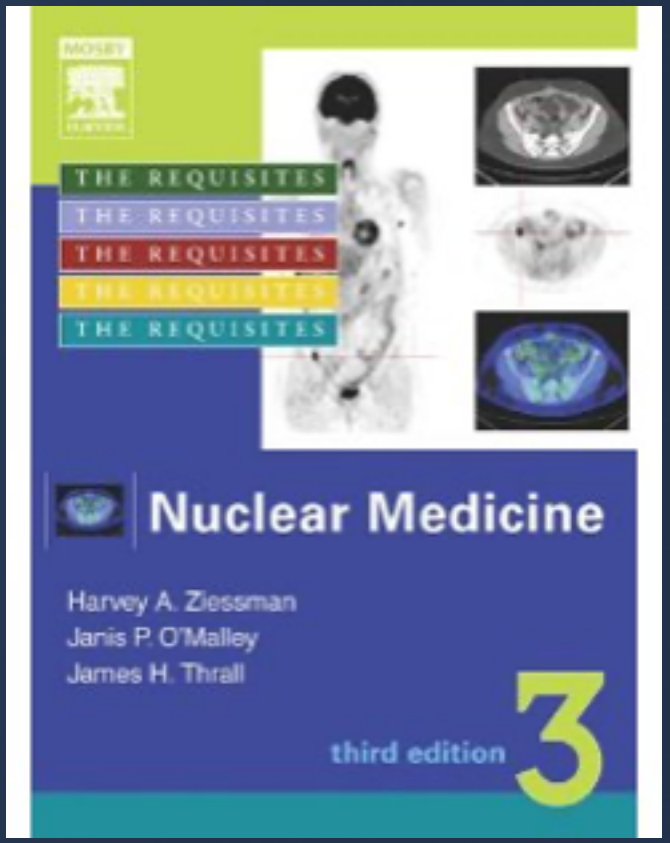
Objectives of NM tumor imaging

- Diagnosis
- Staging
- Guiding biopsy
- Follow up and therapy monitoring
- Detection of recurrence.

Reference book and the relevant page numbers..

- **Nuclear Medicine: The Requisites, Third Edition (Requisites in Radiology) [Hardcover]**

  Harvey A. Ziessman MD, Janis P. O'Malley MD, James H. Thrall MD



Relevant Pages :

Oncology : 264-274 , 279 -283 ,302 -345 , 119-133 , 109 -112 ,296 -299