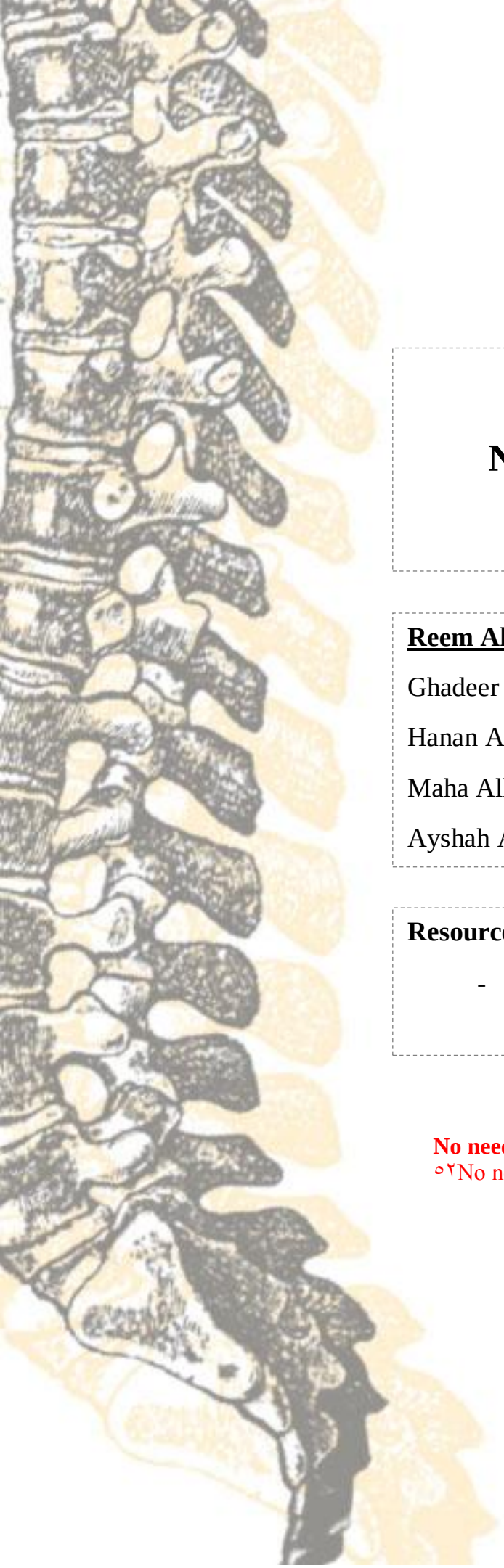


Lecture (2)

Nuclear medicine in oncology

Reem Aljurayyad	**Suliman Alshammari**
Ghadeer Alwuhayd	Khawla Alothman
Hanan Alsalman	Hanan Alrabiah
Maha Alkubaidan	Dalal Alqadi
Ayshah Almahboob	Rawabi Alghamdi

Resources:

- Lecture by dr. Saleh Othman

No need to memorize the doses

٥٢No need to memorize the table in slide

Nuclear Oncology

What is nuclear oncology?

- The use of isotopes in the diagnosis and treatment of tumors
- In nuclear medicine : the radiation comes out of the patient (unlike radiology) and then it is detected by the machine .

What are the nuclear medicine tumor imaging methods?

1. **Conventional tumor imaging:** (they are all found at KKUH)

They are divided to:

1. Specific: can tell you what type of tumor you are looking at.
2. Non-specific: they can't tell you about the type of the tumor.

- **Planar:** like thyroid scan, 2 planes/dimensions = 2D

- **SPECT:** (Single-Photon Emission Computed Tomography)
  - Functional (can not tell the anatomical location of the tracer/isotopes/ materials injected)
  - It's called single, because only one usable photon for each disintegration is emitted.
  - Depends on the blood flow and the turnover of the tissues

- **SPECT- CT:** (functional + anatomical)
  - Here we combined the SPECT with the CT scan
  - **CT:** gives the anatomical information
  - **SPECT**: gives the functional information

2. **Onco PET:** (not started at KKUH yet)
   - **PET:** (positron emitting tomography)
     - Functional (cannot tell the anatomical location of the tracer/isotopes/Materials injected)
     - Depends on glucose metabolism by giving the patient glucose labeled with fluorine 18.

   - **PET-CT: functional + anatomical**

Extra information for your understanding:

1. **Radionuclide imaging:** the radioactive isotopes used in diagnostic imaging emit gamma rays as they decay. Gamma rays are electromagnetic radiation, similar to x-rays, produced by the radioactive decay of the nucleus.

   Radionuclide imaging depends on the fact that certain substances concentrate selectively in different parts of the body. radionuclides can be chemically tagged to these substances.

   The gamma rays emitted by the isotope are detected by a gamma camera

2. **PET (positron emission tomography):**
   PET uses short-lived positron emitting isotopes. 2 gamma rays are produced and can be detected by a specialized gamma camera. The resulting images reflect the distribution of the isotope.

   PET uses isotopes of biologically importance, hence it can be used to study physiological processes such as : blood perfusion of tissues and metabolism of substances such as glucose.

Conventional tumor imaging:

- **Non- specific**:

1. **Gallium 67 citrate (Ga-67)**
2. **Tc-99m Methylendiphosphonate (Tc-99m MDP)**
   - Tc-99m (technetium-99m) is the most commonly used radionuclide.
   - Its half life is: 6hrs !
3. **Thallium Chloride 201 (Tl-201)**
4. **Tc-99m SESTAMIBI**

- **Specific:**

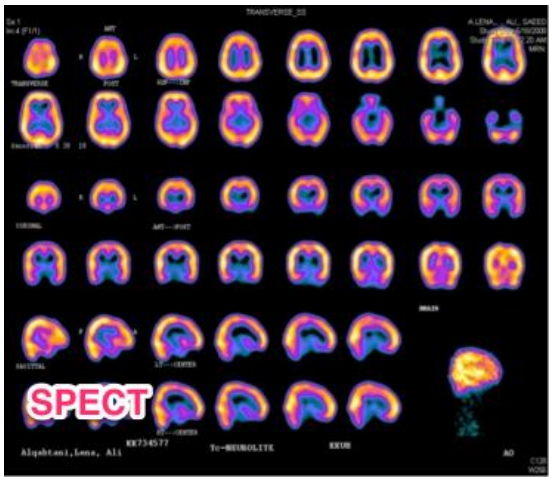
1. **Iodine 131 (I131):** specific for thyroid therapy (b/c iodine is metabolized in the thyroid)
2. **Iodine 123 MIBG(I123 MIBG):**
   - For diagnostic use only
   - Beneficial to diagnose neuroendocrine tumors.
3. **Radiolabelled monochlonal antibodies (MoAB)**
   - For tumors bering antibodies for these agents.
4. **Receptor imaging:** Somatostatin receptors.

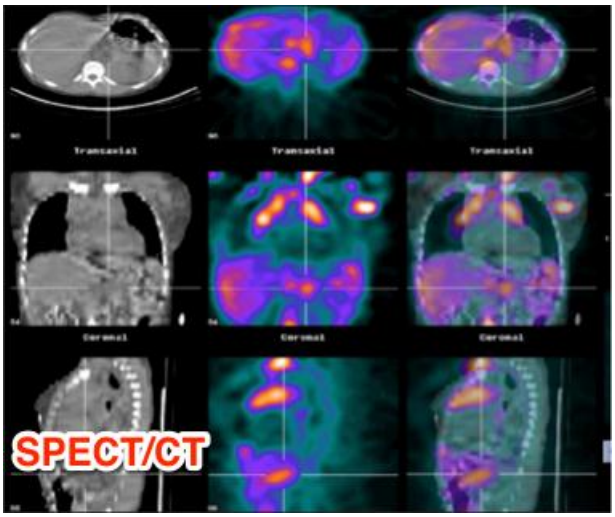
Nuclear medicine procedure :

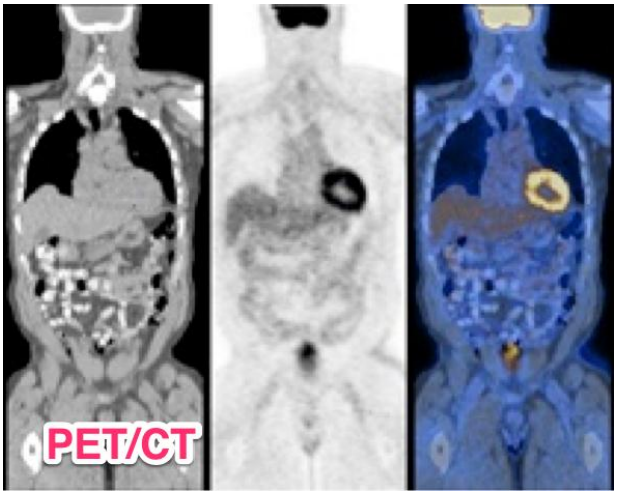
- Patient injected with small amount of radioactive material .
- Radiopharmaceutical localizes in patient according to metabolic properties of that drug.
- Radioactivity decays, emitting gamma rays.
- Gamma rays that exit the patient are imaged.

NM Imaging Systems:

NM Imaging modalities:







This is a patient with right breast

Tumor Imaging: (make sure to memorize the names and numbers)

- **Tc-99m MDP bone scan:** Detection and follow up of bone metastasis
  If you want to look for bone metastasis: order tc- 99m MDP bone scan, which is a complex organic phosphate labeled with TC-99m, that will be taken up by bones and can be used to visualize the skeleton.

- **Gallium 67:** Staging, Restaging & therapy assessment of HD (Hodgkin disease) , NHL , Lung cancer

- **Thallium 201:** Tumor viability & tumor seeking.
  {Tc-99 m Agents (MIBI ,TETRO.).}

- **In–111 (TC99m) Octreotide :** Neuroendocrine tumors
  Examples of neuroendocrine tumors: neuroblastoma, paraganglioma and carcinoid tumors

- **I -123 MIBG :** Neuroendocrine tumor

- **I -131:** Lung metastasis. Thyroid carcinoma

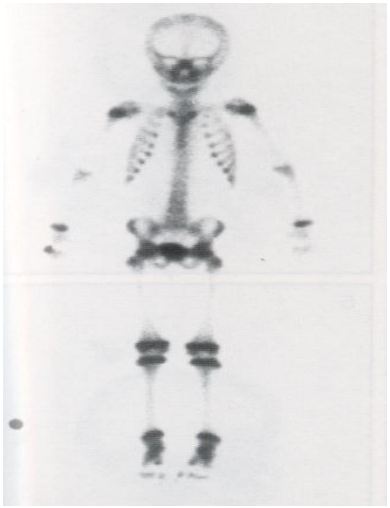
- **F18 – FDG (PET agent):** Staging ,Restaging & therapy assessment of HD , NHL , Lung cancer
  Florin-labeled glucose =Fluoro-2-deoxy-D-glucose **(FDG)**
  F18-FDG: Gold standard for tumor imaging, staging & monitoring of Tx
  It's considered the most common agent used in PET scan
  It's more specific and sensitive than gallium
  It's labeled with glucose, so it's taken by tumor cells and eventually we can localize the tumor

Note: most tumors depend on glucose for their growth!

Bone scan in oncology (procedure):

- Agent: Technitium 99m Methylene DiPhosPhonate (Tc-99m MDP)
- Dose: 20 mCi for adults and minimum 2 mCi
  (250 uCi/Kg) for children.
- Imaging: **Single phase:** 3-4 hrs post iv inj.
  Three phase: Flow, pool & delayed
- Specific Instruction: Well hydration (it's the only preparation for the procedure)

Normal Whole body scan:



An 8 year old child

A 25 year old adult

How to differentiate?
- **Epiphyseal plates** in children are Hot (active), while adults have normal uptake
- **Active epiphyseal** plates in children bone scans (Black shadowing at each pole of the long bones)

Bone Scan In Oncology:

1. Metastatic Disease.
2. Primary Bone Tumors: malignant/benign
3. Soft tissue tumors: primary/metastasis

Imaging features:

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

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

C. **Superscan:** Diffuse increased skeletal uptake with no soft tissue or kidney activity (e.g. CA prostate ,breast ,..etc).
- When you give a tracent, all of it will be uptaken
- It's associated with wide spread metastasis

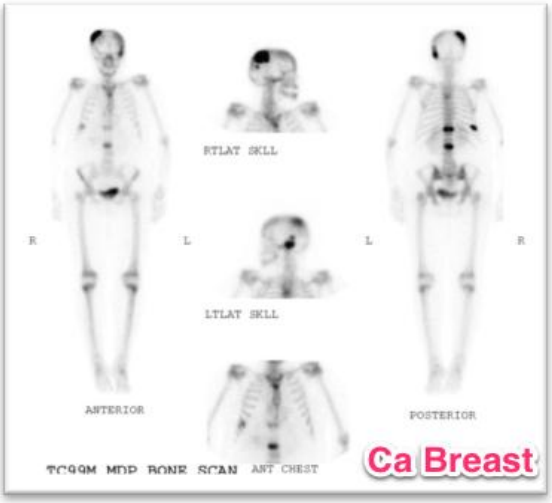
D. **Normal distribution:** Marrow tumors (e.g. lymphomas, leukemia, multiple myeloma).
- we can have a normal distribution of the tracent , but we might have an underlying pathology in the bone marrow, like in cases of bone marrow tumors because the tracer is distributed superficially not deep

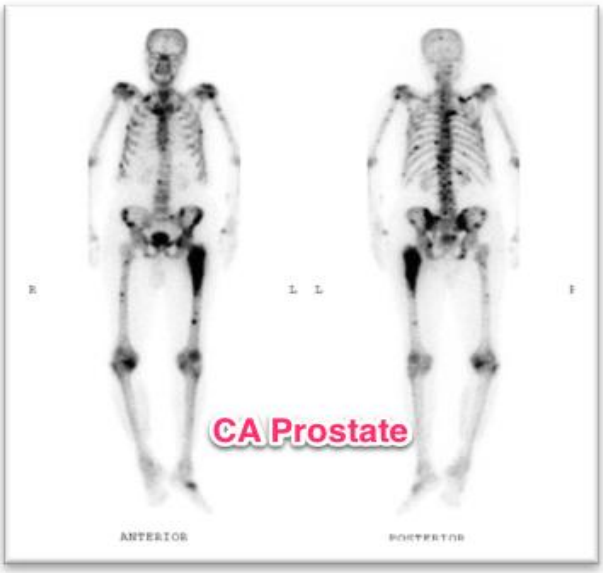
E. **Soft tissue uptake :** Soft tissue tumors may concentrate the tracer

Indications for bone scan:

- **Diagnosis.**
- **Initial staging.**
- **Restaging.**
- **Asses response to therapy.**
- **Therapy planning** for patients with primary bone malignancy (e.g. Osteogenic & Ewings sarcoma)

Examples of tumor staging:



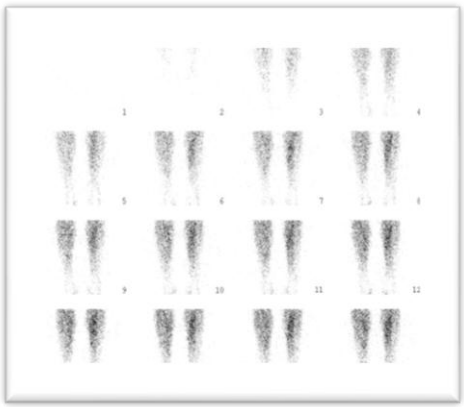


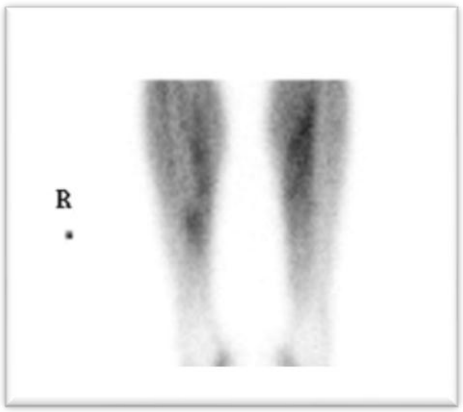
In the image: Wide Spread bone Metastasis.
All the dark spots (hot spots) are metastatic areas to bone

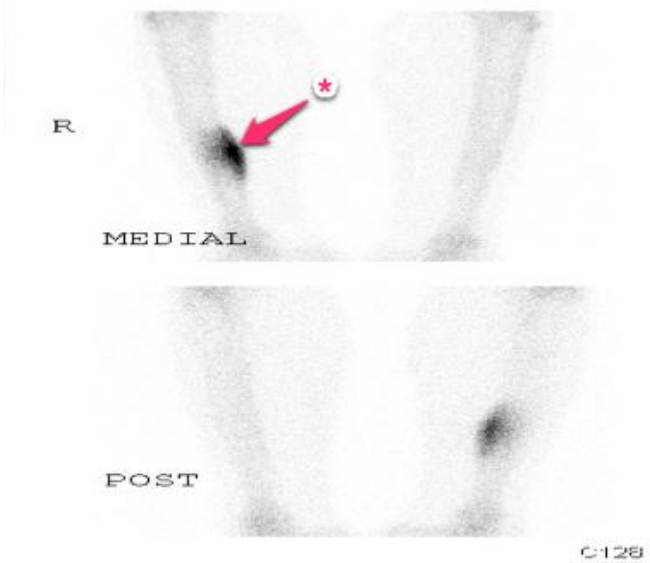
- In the first image: we can see the kidneys of the patient, meaning that the tracer is still being excreted.
- Notice that the kidneys and bladder are not seen in the second picture , indicating superscan lesion with wide spread metastasis
- CA stomach is common with wide spread bone metastasis (skull, spine, scapula, and multiple ribs)

Osteoid Osteoma:

- These images were obtained from a patient complaining of leg pain
- It's a benign tumor which affect children and young adulta

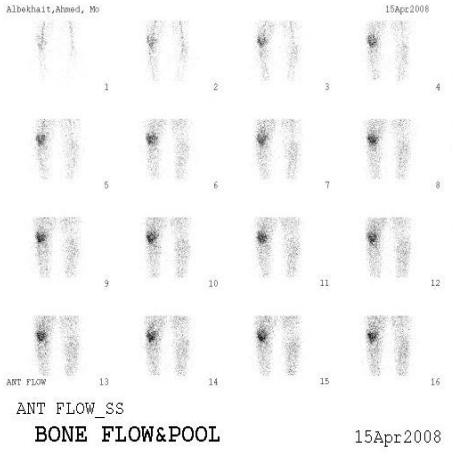


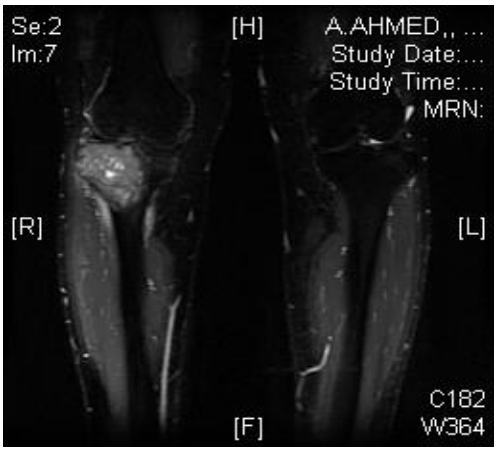


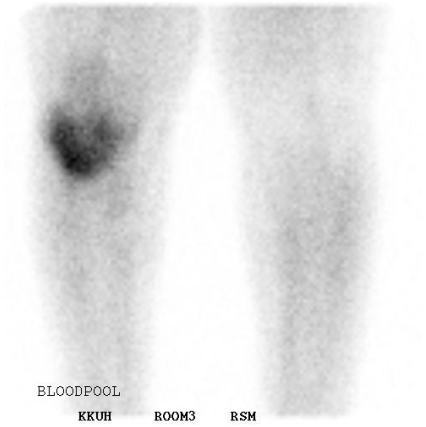


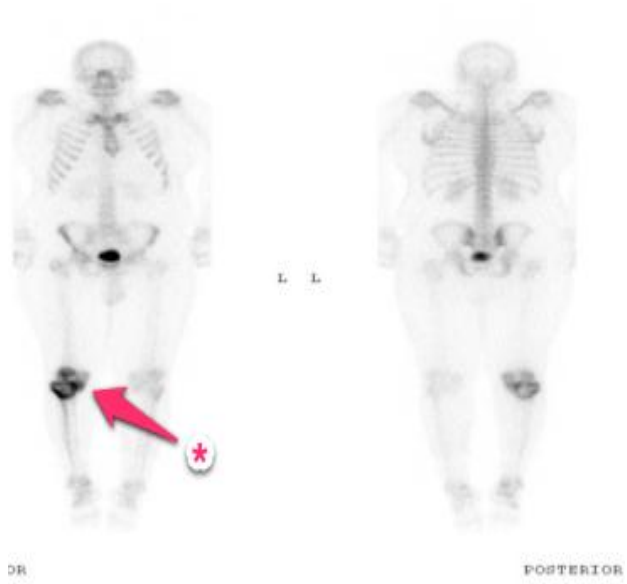
*** Tracer uptake in the right tibia with increased blood flow.**

Giant cell tumor:









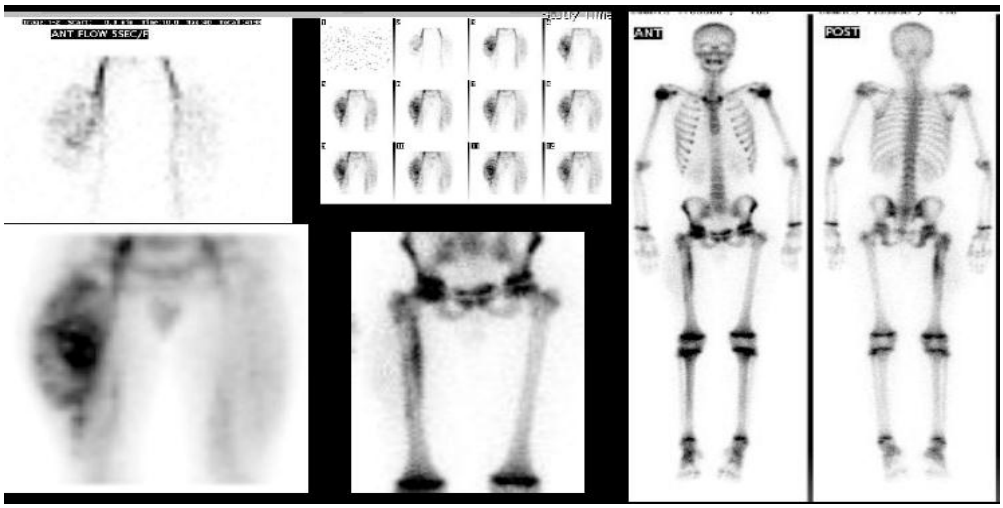
* Right knee metastasis localized in proximal end of tibia

Value of bone scan here is to determine extent of local disease & if there's metastasis or not. 1ry dx of Giant cell tumor is not by bone scan, it's done by conventional radiogram and MRI.

Extra notes for more understanding:

- Giant-cell tumor of the bone (GCTOB) is a relatively uncommon tumor of the bone.
- It is characterized by the presence of multinucleated giant cells (osteoclast-like cells).
- Malignancy in giant cell tumor is not common.
- On x-ray, giant-cell tumors (GCTs) are lytic/lucent lesions that have an epiphyseal location and grow to the articular surface of the involved bone

Soft tissue sarcoma:



Rhabdomyosarcoma (Soft Tissue Sarcoma) is a cancerous (malignant) tumor of the muscles that are attached to the bones. It can occur in many places in the body. The most common sites are the structures of the head and neck, the urogenital tract…etc.

Gallium 67 Citrate (Ga-67):

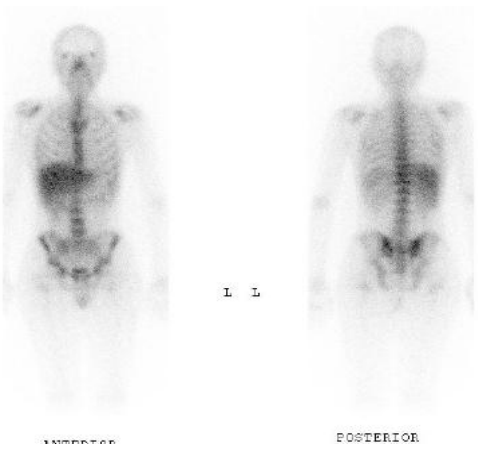
- Non specific for infection-inflamation and tumors
- Mechanism: Binds to transferrin
- Excretion: Kidneys and large bowel
- Dose: 5-10 mCi
- Imaging: 24-72 hours postinjection
- Tumors: Lymphoma, bronchogenic carcinoma, malignant melanoma, hepatoma

Gallium 67 Citrate (Ga-67) In Lymphoma:

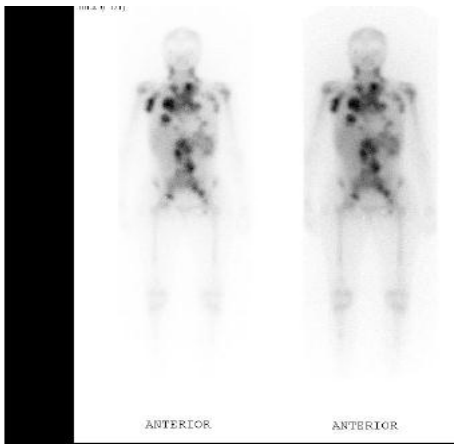
- Staging
- Follow up and monitoring of therapy
- Detection of tumor recurrence
- Differentiate post therapy changes : tissue necrosis and fibrosis from local recurrence.

Note: Lymphomas are best diagnosed with PET/CT, but if we don't have the modality like in KKUH, we use other nuclear medicine modalities like: Gallium.

Gallium Scan in Lymphomas:



Normal Gallium Scan



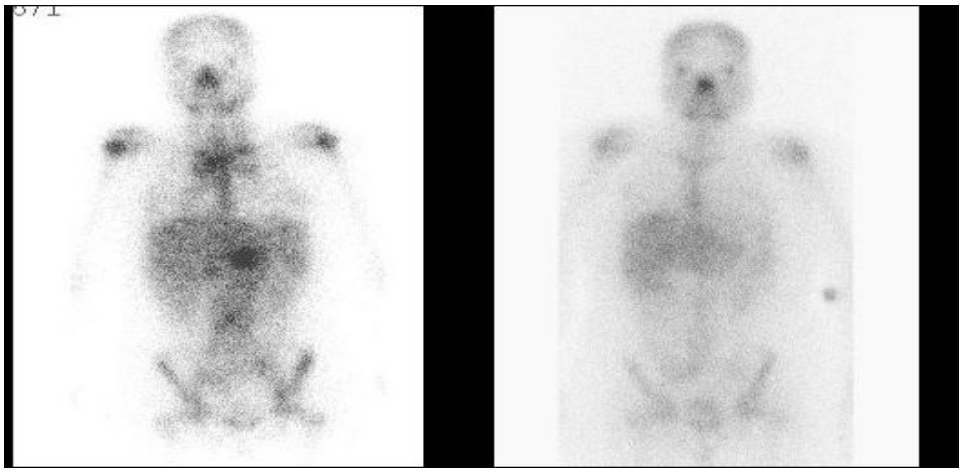
Ga-67 Scan is useful in initial evaluation and monitoring response to treatment in HD and NHL.

In the normal: as the Ga binds to transferrin it will be more up-taken by the liver and bone marrow because transferrin is concentrated in them

In the second image:

- Multiple focal areas m where there is increase uptake in the cervical area, mediastinum, hilium, axilla and abdomen
- Normally lymph nodes shouldn't be seen because they are small.
- The lymphoma is extending above and below the diaphragm so it's considered stage 4 disease.

Monitoring the response to therapy using gallium:

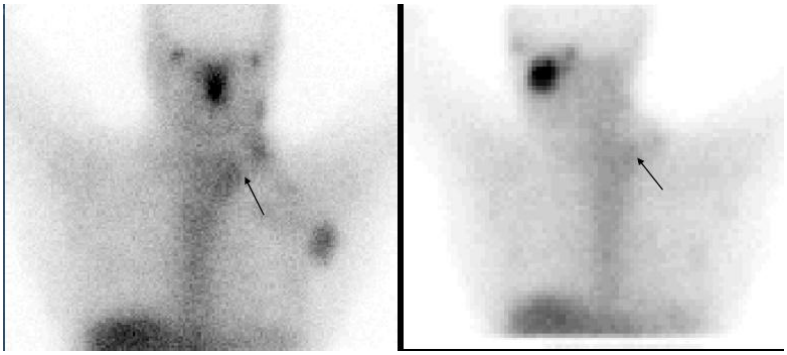


Normalization of a positive pre-therapy scan: A negative scan after one cycle or at mid cycle is associated with a high likelihood of complete response.

In the first image: Prior to therapy: there is increased uptake in the mediastinum and epigastric lymph nodes.

In the second image: After 2 weeks of chemotherapy: all previous up taking areas are disappeared indicating excellent response to chemotherapy and complete cure.

Prediction of outcomes using gallium:



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

Extra information for more understanding:

- Poor response (no response) to therapy because the increased uptake in the cervical region persisted even after the chemotherapy.
- In this case the oncologist will change the regimen of chemotherapy

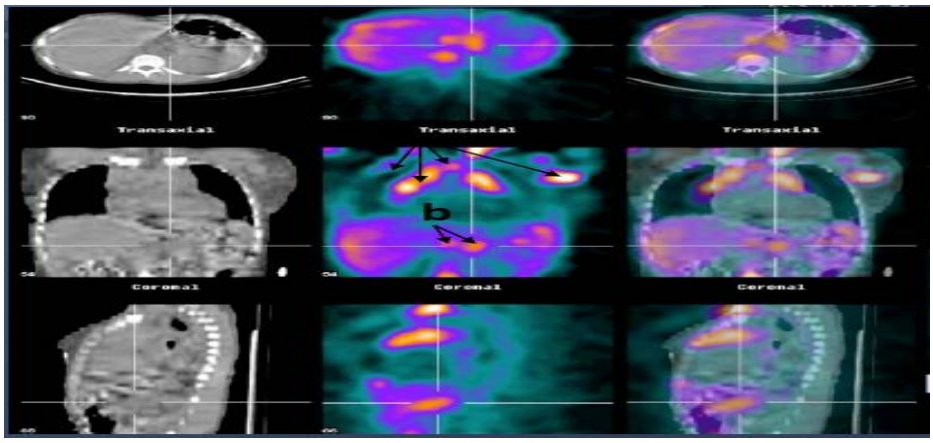
When we want to assess the response to the chemotherapy, we either says:

1-**Complete response:** where the uptake disappear

2-**No response:** when there is uptake of Ga even if it is a little uptake

We do not say "partial uptake" only response or no response. And in this case oncologist will give more aggressive chemotherapy

Ga-67 SPECT/CT: Staging HD



Abnormal Ga uptake (a) in supraclavicular, axillary, Paratracheal , parahilar and para-aortic lymph nodes and in the spleen, at lesion sites corresponding to those observed on CT.

The para-aortic lymph node uptake (b) combined with CT findings allowed the diagnosis of sub diaphragmatic disease and excluding bowel activity.

- First CT scan is done, then SPECT . After that the computer will fuse both images in order to tell you which group of lymph nodes is affected.
- CT is used to improve the localizaMon of uptake that seen in nuclear scan

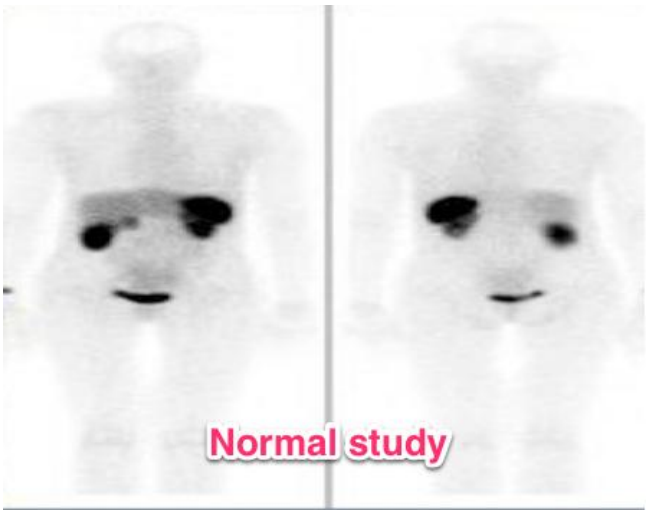
Neuroendocrine tumors:

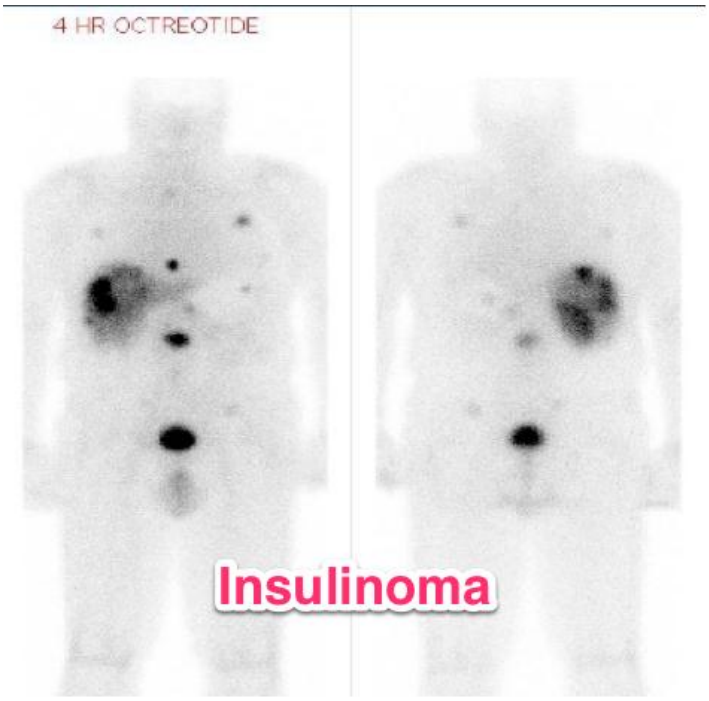
These tumors can be diagnosed by the following modalities:

- **In-111 octreoscan**: Somatostatin receptor imaging, absorbed by somatostatin receptors found in sympathetic chain tumors: gastrinoma + inulinoma ..etc

- **I123 MIBG Scan**: works in the same way but does not need somatostatin receptors to be absorbed by sympathetic chain tumors. You can see the liver, kidneys, spleen and gall bladder

❖ Somatostatin Receptor Imaging (Indium-111 Octreoscan):





Clinical History

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

Findings:

Multiple lung, mediastinum, liver and abdominal metastases

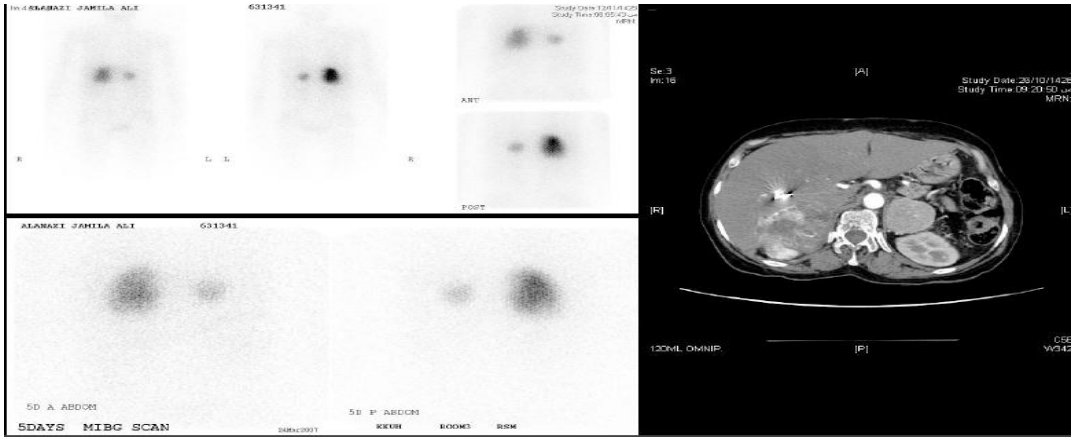
❖ I123 MIBG Scan:

- 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

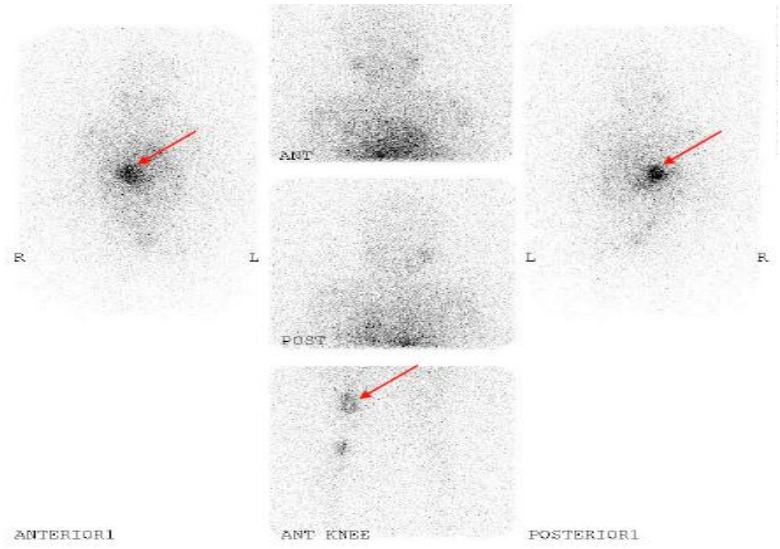
MIBG in pheocromocytoma: Bilateral disease



I131 MIBG Total body scan:

1ry neuroblastoma /bone mets

This is a 1ry neuroblastoma with distant metastasis to the bone in the right femur and tibia.



THYROID METASTASES STUDY: (IMP)
(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.

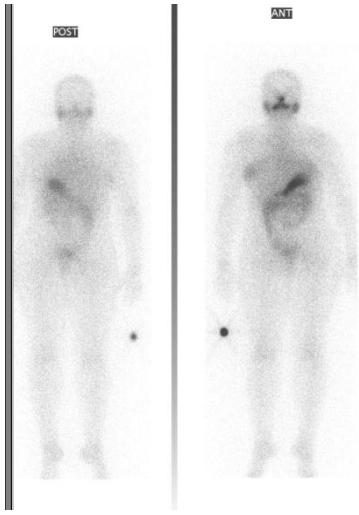
Tracer, Dose, & Technique of Administration

- Radiopharmaceutical: Oral administration
  a) **I-123 as sodium iodide : 2 mCi**
  b) **I-131 as sodium iodide : 2-10 mCi**

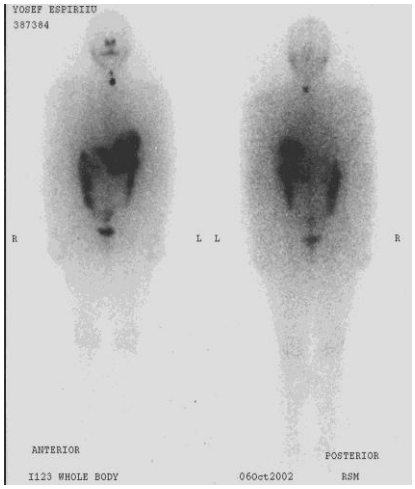
- I-131 can be used as a treatment if given in high doses

Imaging using Gamma camera: Whole body scan

Thyroid cancer: I-123 WB scan



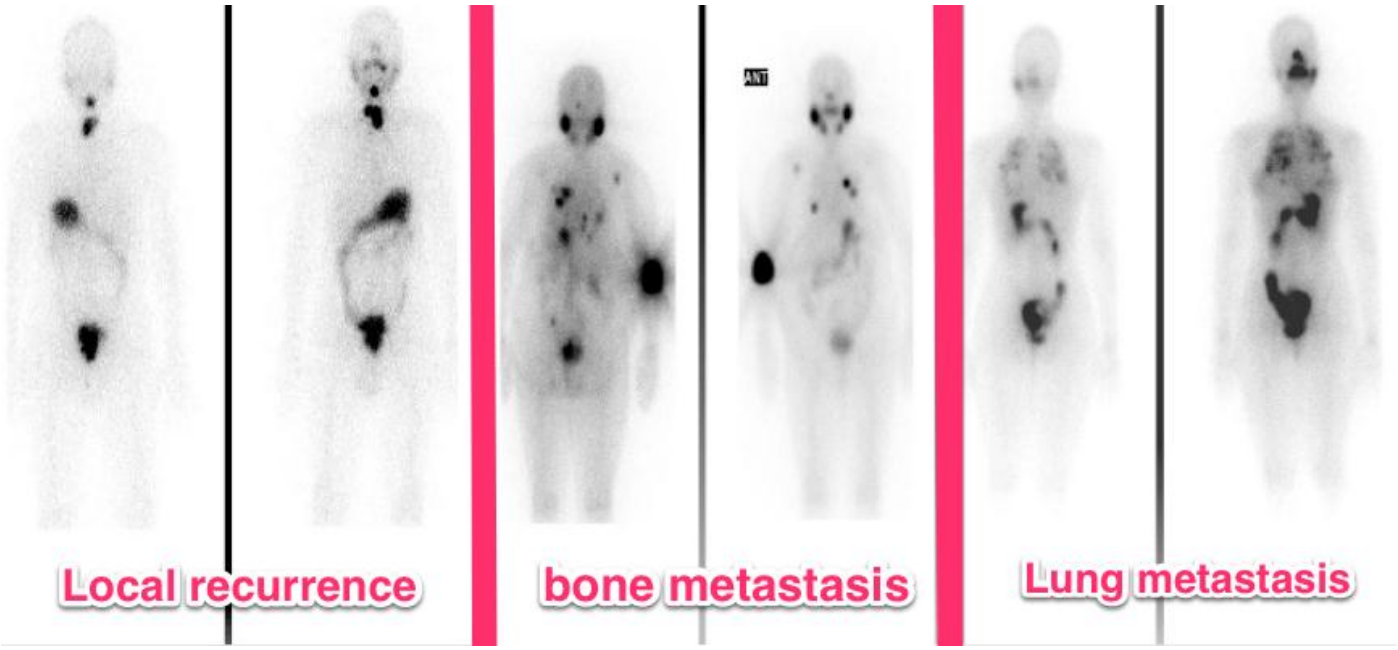
Negative I- 123 body scan:
post surgery
showing stomach and colon activity and there are no thyroid remnants



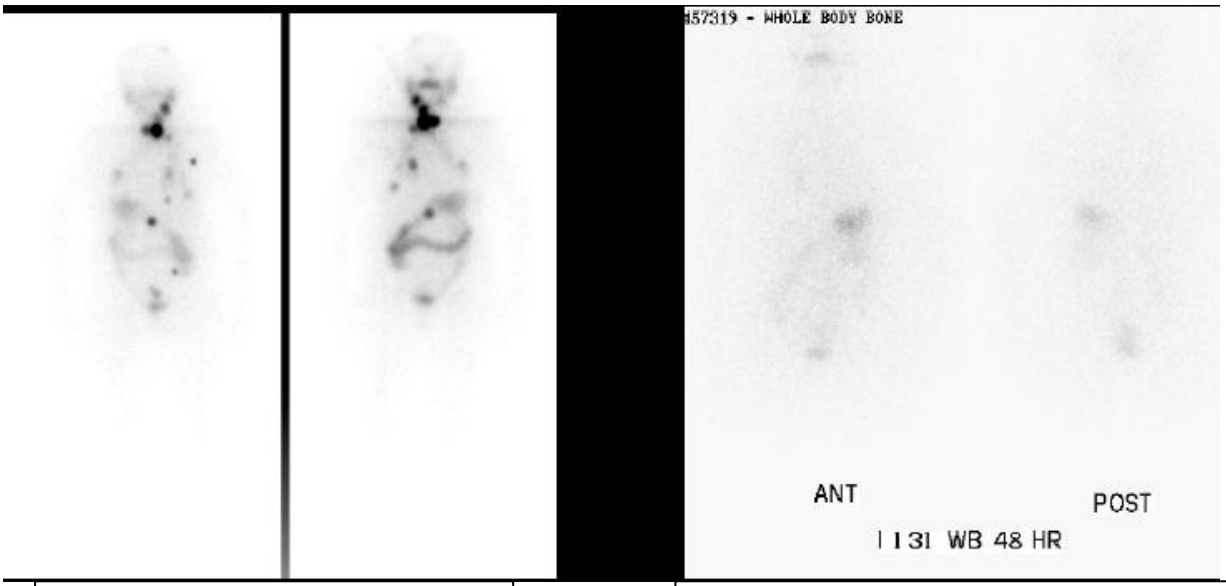
Post- surgery scan for thyroid cancer showing remnant of the thyroid . These remnants are treated by radioactive iodine 131. This I 131 will go to these remnant and destroy them without damaging the surrounding tissues.

N.B. Iodine 131 is used to remove the remnants

THYROID METASTASES STUDY
(I-123 or I-131 as Sodium Iodide)



Thyroid metastatic study: **(pre and post therapy with I-131)**



A patient with multiple; local and distant metastasis

Same patient was treated by I 131 and the scan was repeated on 2006 and there was complete cleaning of the body without metastasis

Onco PET (PET and PET CT):

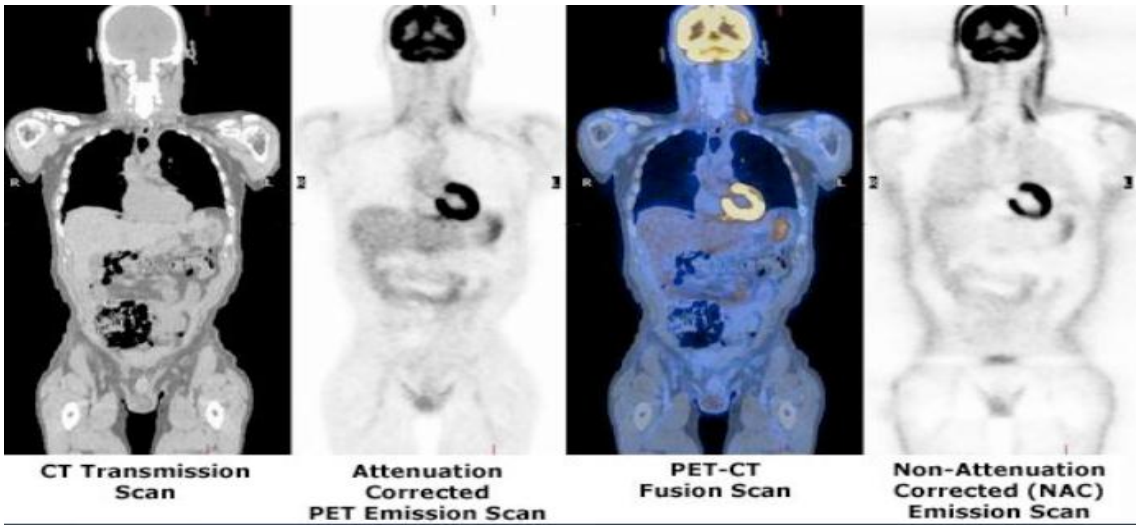
What is PET – CT?

- **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.

How it is performed?

Positron emitters (e.g. F18) labelled with biologically active natural compounds such as oxygen, carbon or glucose given 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 SCANNER giving an image of the normal and abnormal distribution of tracer in the body.

PET CT:



Normal CT scan (brain and heart will appear in the image because their main source of energy is glucose and it will be concentrated in them), hence their viability in F18 (glucose based) PET scan

Positron Emitting Isotopes:

Cyclotron produced isotopes:

Isotope	T/2
Oxygen-15	2 min
Nitrogen-13	10 min
Carbon-11	20 min
Fluorine-18	**110 min(main isotope)**

FDG PET CT : Procedure:

- **Fasting**: 4 – 6 hours
- **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 in Oncology:

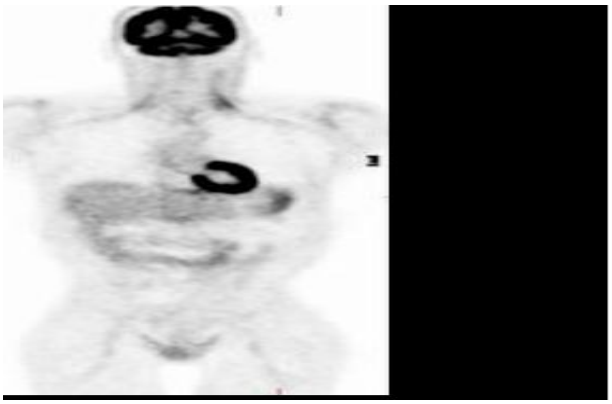
- Tumors do not have a blood tumor barrier(so any tracer we give will reach to the tumor, unlike normal tissues which have blood barrier)
- FDG transport into tumors occurs at a *higher* rate than in the surrounding normal tissues.
- FDG is de-phosphorylated and can then leave the cell.
- The de-phosphorylation 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

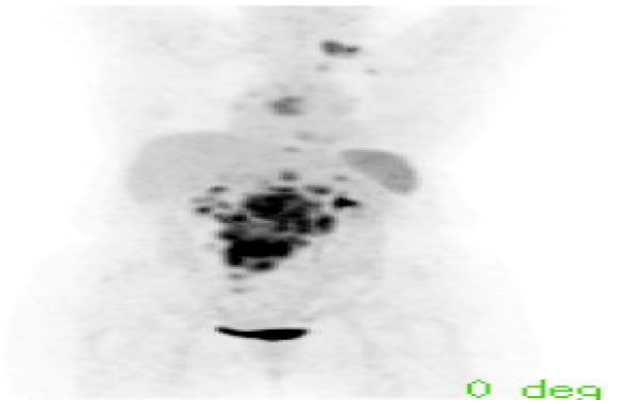
- Notice that: the scan can tell whether the tumor is viable m where there is increase in the uptake glucose labeled material or not .

FDG PET:



Normal FDG PET

The brain appears black because it depends highly on glucose, so there is increase uptake.

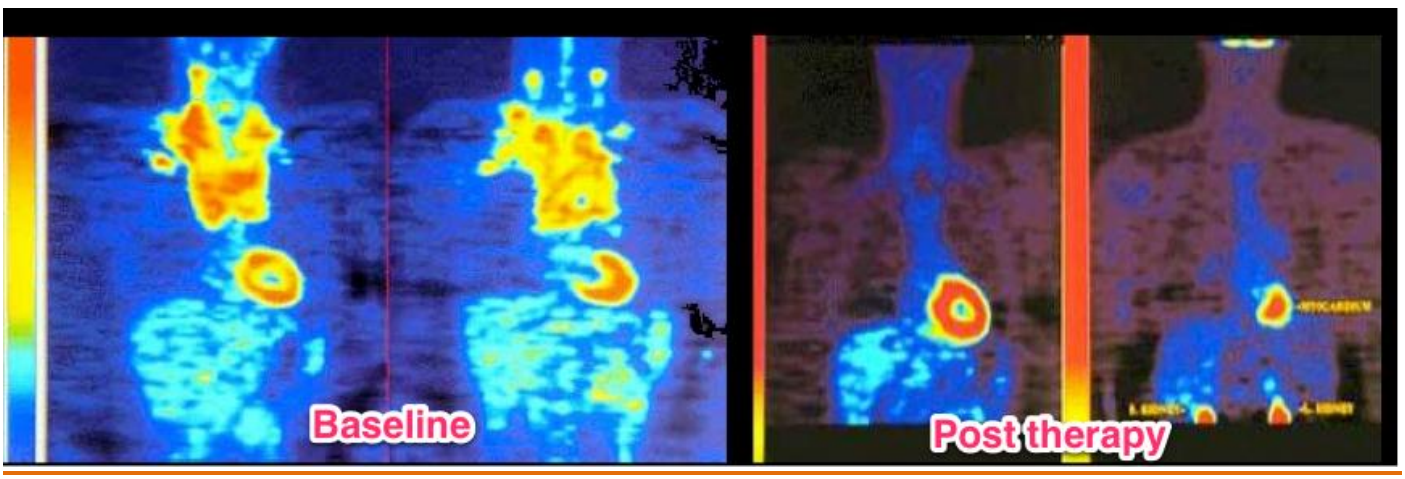


Patient is having NHL

There are multiple lesions above and below the diaphragm.

Use of FDG PET in the assessment of the therapy response :

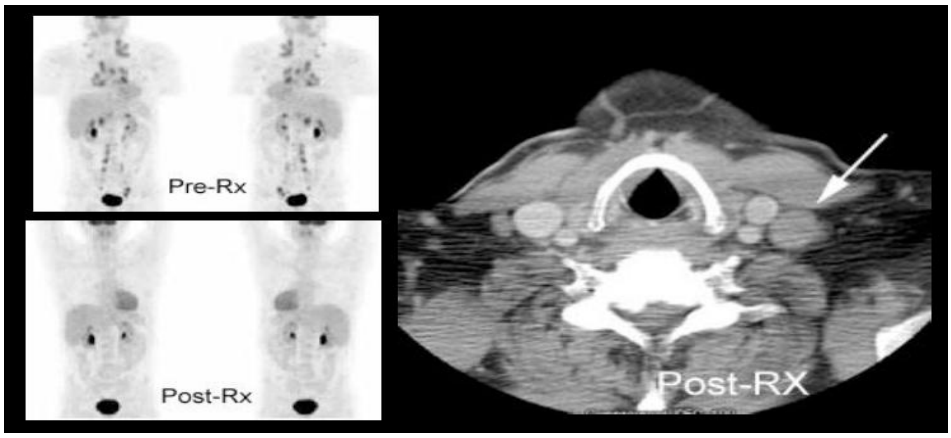
FDG PET in Hodgkin disease:



A 22 years old male patient with Hodgkin's lymphoma. Six months after chemotherapy, CT scan showed bilateral hilar abnormalities.

FDG-PET scan did not show any activity in described CT changes(excellent response to the management. There was an excellent clearance of mediastinal lymph nodes after therapy)

FDG in non-Hodgkin lymphoma:



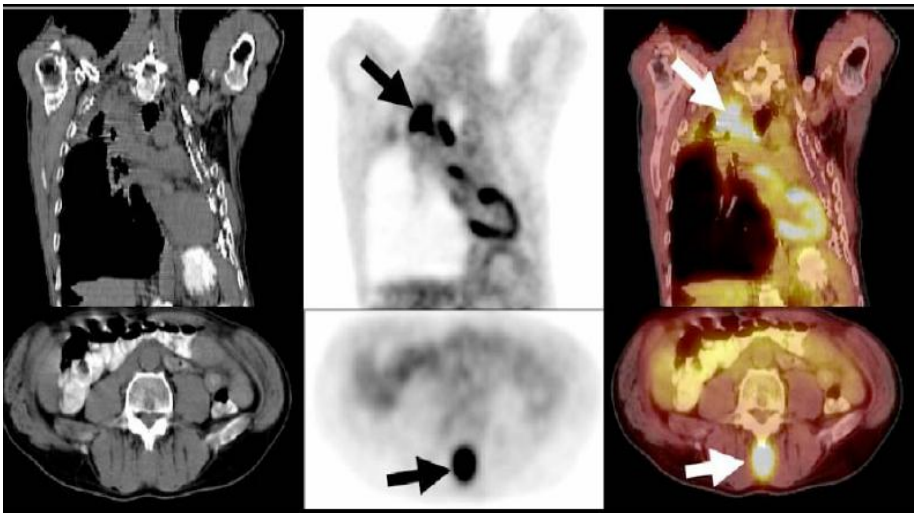
Stage 4 NHL, which showed excellent response to the treatment in the 2nd image .

PET CT in lymphoma:

	Sensitivity (%)	Specificity (%)
CT	61	89
FDG-PET	78	98
FDG-PET and CT	91	99
FDG-PET/CT	96	99

PET CT: Lung cancer

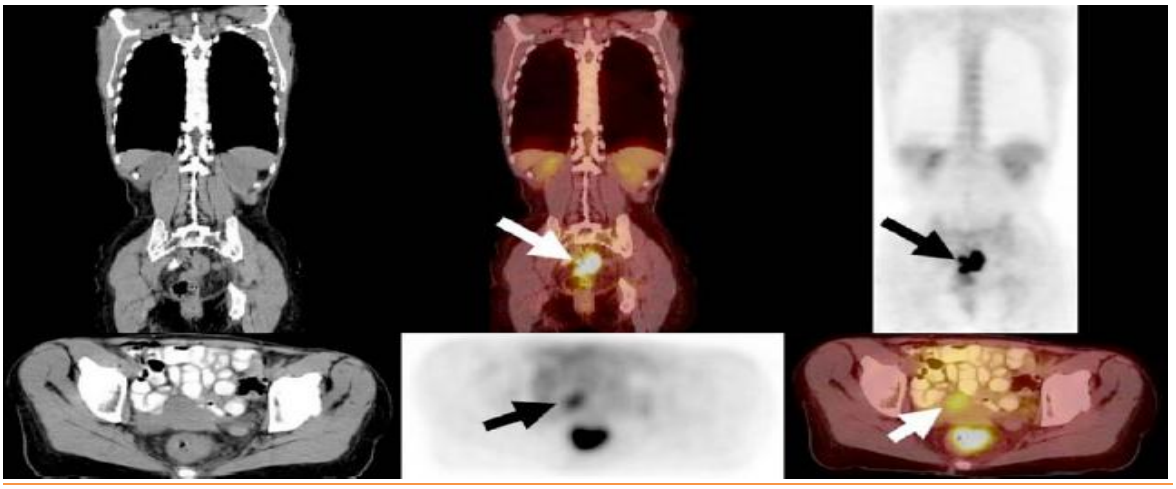
FDG avid soft tissue mass associated with a destructive L5 spinous process consistent with metastatic deposit (arrow).



FDG PET CT IN Solitary Pulmonary Nodule (SPN):

- **Sensitivity :** 82 – 100 %
- **Specificity :** 67 – 100 %

CA Rectum: (PET CT)



A 57-year-old woman presented with pain and constipation and colonoscopy revealed an obstructing rectal mass. A staging FDG-PET/CT demonstrated intense FDG avidity in a circumscribed mass-like thickening of the proximal rectum (arrows in top row images) and a focus of mild metabolic activity anterior to the rectum (bottom row arrow) which was not avid as the rectal malignancy. This was located within the uterus as seen on CT images (bottom row), and was subsequently shown to be a uterine fibroid on other imaging studies.

CA of esophegous :

Based on FDG-PET/CT results the clinical management of this patient was changed from surgical resection of the primary tumor to combined chemo-radiation therapy**.**

There is no metastasis

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.

AGENT	INDICATION	DOSE
- I131 - 131 MIBG - Strontium-89 - Sm-153 EDTMP - Phosphorus- 32 - Y-90-Ibritumomab Tiuxetan [Zevalin®]	- **Thyroid cancer** - **Neuroblastoma** - **Bone metastasis** - Bone mets - Polycythemia - B-cell NHL	- 100-200 mci - 100-300 mCi - 40-60uCi/kg - mCi per kg - 2.3mCi/m2 - The dose should never exceed 32 - mCi (1,184 MBq).