MED437
King Saud University

RADIOLOGY
437 TEAM

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Editting File

Nuclear medicine in oncology

Sources

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objectives:

- ➔ 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?

Acknowledgment

Here we are!.
Thanks to team 436, and every Radiology team that made this work possible.
Thanks to our valuable members,for the time and effort they put in. They truly showed spirit of teamwork.
Thanks to our Academic leaders, Yazeed and Aseel.
Hopefully we came in handy to our batch and the following ones.
Thank you!...

2nd semester team heros.

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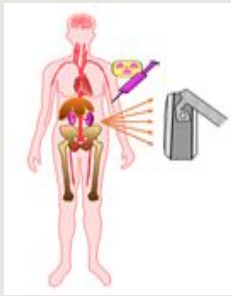
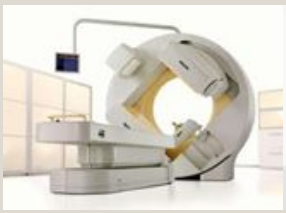
Nuclear Medicine Procedure

Isotopes shows function not structure.
- Patient injected (I.V) most of the time with small amount of radioactive material.
- Radiopharmaceutical localizes in patient according to metabolic properties of that drug.
- Radioactivity decays, emitting gamma rays. The radiation comes out of the patient, nuclear machine doesn't emit radiation.
- Gamma rays that exit the patient are imaged and detected by Gamma camera.



What are the nuclear medicine imaging methods?

	Types	
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.	 

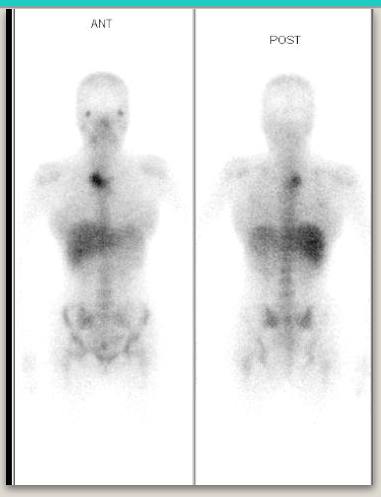
The machine that detects the radiation in nuclear is Gamma camera, there are several types of gamma camera: dual head, triple head, SPECT CT and PET CT.
- PET CT mainly used for oncology patients.
- Nuclear called emission tomography because radiation emitted from the patient unlike x-ray which called transmission: x-ray comes through tube into the patient and give an image according to attenuation from patient tissue.

Planar Imaging

- Planner image means it has 2D.
- Longitudinal and transverse.
- This is a normal bone scan.
- Always compare between right and left.
- Look for asymmetries.

Single Photon Emission Computed Tomography (SPECT) and SPECT CT

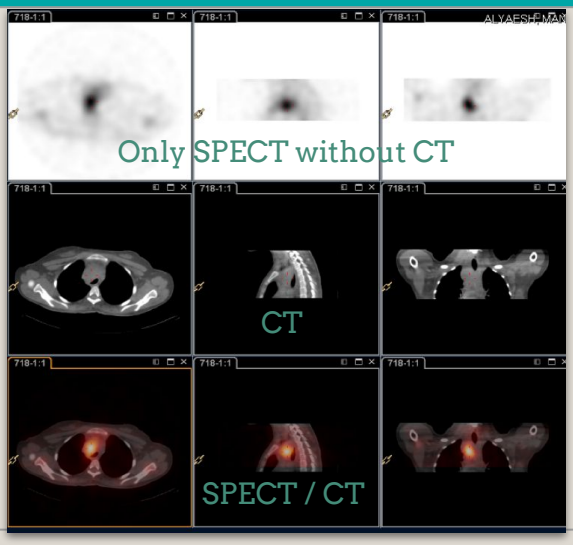
Whole Body Gallium Scan: Planar Image



Gallium scan in a patient with lymphoma showing an increased uptake in the anterior chest wall. You cannot tell the affected site exactly because it is 2D. The SPECT was done and confirmed the site to be intrathoracic in the anterior mediastinum.

SPECT/CT

More effective than planar imaging



- SPECT/CT is 3D and is used to locate the abnormality.
- Transaxial, sagittal and coronal.
- Shows a clear lesion in the mediastinum "behind the sternum".

Positron Emission Tomography (PET) and PET-CT

PET **CT** **PET** **PET+CT**

- The patient was given glucose labeled with a radioactive material which was F18, to see any area with high glucose turnover like muscles.
- Post prandial scan will show heart and brain increase uptake. if pt is fasting then they won't show increased uptake.
- PET is 2D planar (longitudinal and transverse) there is abnormal uptake in Right breast (consistent breast cancer).

Role for Nuclear Medicine in Oncology

1. **Diagnosis:** Specific or non-specific.
2. **Staging:** Important for proper therapy.
3. **Follow-up:** Early detection of recurrence and monitoring the effectiveness of therapy.
4. **Treatment:** Specific or non-specific.

Important agents to note

F-18 (Fluorine 18) is the gold standard radiotracer used for tumor imaging.

- PET isotope, used for pet imaging (positron emitting tomography).
- The most commonly used now is Fluorine 18 with T/2 110, labeled with glucose and injected to the oncology patient to image the tumor.
- The other agents used are Gallium 68 with T/2 68.
- Oxygen-15 and Carbon 11 are for research purposes.

Tumor Imaging

Summary of all the tracers used in nuclear medicine

Specific	Non-Specific
Tumor Imaging Agents	
• In–111 (TC99m) Octreotide: Neuroendocrine tumors (NETs) are neoplasms that arise from cells of the endocrine (hormonal) and nervous systems. • I -123 MIBG (metaiodobenzylguanidine) is a substance that gathers in some tumors, particularly neuroblastoma tumors. When MIBG is combined with radioactive iodine (tracer), it provides a way to identify primary and metastatic (spread) disease. MIBG scans are helpful for locating both bone and soft tissue tumors: Neuroendocrine tumor. • I -131: Lung mets, thyroid carcinoma.	• Tc-99m MDP bone (Tcm-methylene diphosphonate) scan: Detection and follow up of bone metastasis. • Gallium 67: Staging, Restaging & therapy assessment of HD (Hodgkin disease), NHL (Non Hodgkin's lymphoma), Lung cancer. • Thallium 201: Tumor viability & tumor seeking {Tc-99m Agents (MIBI, TETRO)}. • F18 – FDG: Staging, Restaging & therapy assessment of HD, NHL, Lung cancer. skipped by doctor
Therapeutic Radiopharmaceuticals	
1) I-131 – Thyroid cancer Specifically diagnostic & therapeutic for thyroid cancer. 2) Y-90 (Yttrium-90): Zevalin (ibritumomab tiuxetan) Monoclonal antibody for B cell lymphomas.	Sr-89, Sm-153, Re-189 – Bone pain palliation. They don't treat cancer, they only treat the pain it cause. Given to widespread bone metastasis who are not responding to opioids, and alleviate their symptoms.They go to the sites of metastasis regardless of the origin.

Some patient on radiotherapy, once you repeat CT image you see abnormality (e.g. fibrosis). Is it due to radiotherapy or not? you have to assess tumor viability with FDG (fluorodeoxyglucose) or thallium scan, mainly the gold standard for tumor imaging is fluorine 18 PET scan (PET scan FDG is the gold standard to evaluate and monitor therapy for cancer patients "solid tumors").

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 sensetive. 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 tumer's center. You want to know the degree of hypoxia; some centers use oxygen for tumor treatment.

Planar, SPECT or SPECT/CT:

- I-123/131 MIBG for neuroendocrine tumours.
- I-131 for differentiated thyroid carcinomas.
- In-111 or Tc99m octreotide for tumours expressing somatostatin receptors.
  Gallium-68 is more sensitive than Tc99m octreotide.
- Monoclonal antibodies labelled with In111 (Indium-111), I-123/131 or Tc-99m.
  Once we are able to seperate the specific antibody from the tumor cell, we can then label it with a radioactive material, and get an image of the tumor.

Demonstrate tumor sites but are not specific for malignancy.

What does 'non-specific' mean?

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

PET or PET-CT

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

Planar, SPECT or SPECT-CT:

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

Planar Imaging

Increased vascularization.
Increased capillary permeability.
Newly proliferated capillaries.
Increased blood flow.
Increased energy demand We use these properties to indicate the agent.
Increased Metabolically active cells. Most tumors consumes glucose, as they label the Fluorine18 with glucose and inject the patient if there is any tumor anywhere it will capture Fluorine 18 glucose and appear as spots on the scan.

Planar Imaging

What does 'specific' mean?
They can tell you if there was a tumor, and specify what type of a tumor it is.
Certain types of tumor cells can have certain radioactively detected receptors on their surfaces, e.g. somatostatin receptors that are commonly expressed in neuroendocrine tumors. We can use a somatostatin analogue (similar looking molecule) like Gallium-68 to fill these receptors for therapeutic purposes. It shall resemble an antibody-antigen reaction.

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

→ All these properties could be used for imaging and therapy.

Bone Scan

most common procedure in nuclear medicine

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.

Procedure

- **Radiopharmaceuticals:**
  Technetium 99m Methylene DiPhosPhonate (Tc-99m MDP).
  Bone is composed of Calcium and Phosphate. We label the phosphate with radioactive material (technetium MDP), inject the patient with it, and scan them after 2-3 hours. It shall show us the whole skeleton.
- **Tissue accumulation depends on:**
- Blood flow.
- Capillary permeability.
- Metabolic activity of osteoblasts and osteoclasts.
- Mineral turnover.
- **Dose:** 500 to 800 MBq (Megabecquerel) / 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.

Indications

I. **Metastatic Disease:** Lung cancer, prostate, breast, thyroid, and renal tumours.
   - Diagnosis with MRI.
   - 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 Imaging features

Important slide!!! question or 2 in exam

A. ***Hot lesions***: Focal area with increased uptake. Majority of bone tumors.
   Majority of hot lesions are bone tumors except trauma and infections. The history will guide you to know is it tumor or fracture.

B. ***Cold lesions***: Purely Osteolytic Tumors (renal cell carcinoma, thyroid cancer, anaplastic tumors), radiation therapy.

C. ***Superscan:*** Widespread bone metastasis with nothing excreted through the kidneys (normally, the radioactive dose will spread as 60% to the bone and 40% excreted with urine). Diffuse increased skeletal uptake with no soft tissue or kidney activity (e.g. CA prostate, breast..etc).

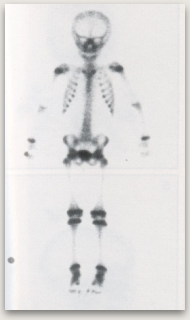
D. ***Normal distribution***: Marrow tumors (e.g. lymphomas, leukemia, multiple myeloma). Normal because the bone marrow is hidden inside the bone.

E. ***Soft tissue uptake***: Soft tissue tumors may concentrate the tracer. The bone scan is made to know whether there was a local extension to the bone, or bone metastasis.

F. ***Flare phenomenon***: increased number of lesions (increased bone uptake) in the case of effective therapy. Indicate good response to chemotherapy. The bone scan appears worsening, or even shows new lesions, during the first several months following chemotherapy, while the patient's clinical condition improves. Click here for more details.

Normal Whole Body Scan

- In the young patient you can see epiphysis growing.
- Remember symmetry between right and left.
- If the tumor within the bone marrow and not touch the bone cortex the bone scan will appear normal.



8 year-old child

25 year-old adult

Bone Scan in Metastatic Disease

Access of Non-osseous Tumors To Bone:

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

Where does the metastasis concentrate? In the red bone marrow. **Where is the red bone marrow located in adults?** In the axial skeleton (skull, spine, ribs, scapula, pelvis). That is why any metastasis below the knee or elbow in the adult is rare. Except for some lung cancers, where it is not uncommon to see metastasis e.g. in the big toe. **Why?** Nobody knows.

Epithelial Tumors: Arise from a variety of glands and surface or lining epithelia.

- 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.

Scan Patterns:

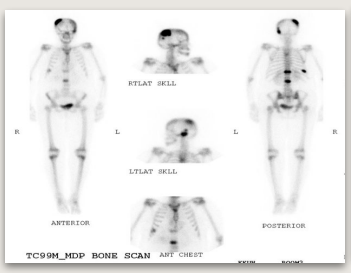
- Solitary lesions.
- Multiple focal lesions.
- Diffuse involvement (Superscan).
- Photon deficient lesions (cold lesions).
  like :Multiple Myeloma/ hypernephroma
- Flare phenomenon.
- Normal (false negative).if tumor limited to bone marrow
- Soft tissue lesions (tracer uptake in tumor). like soft tissue sarcoma

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.

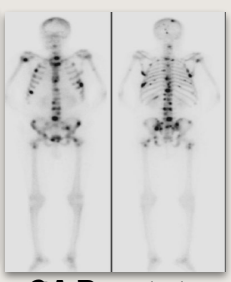
Tumor Staging

Example of multiple bone metastasis, they appear similar in bone scan, so it's sensitive to detect a bone metastasis but cannot tell you the type of tumour.
Metastasis will be confined to red marrow which is located in axial skeleton, proximal femur and humorous.



CA Breast

CA Lung



CA Prostate

Diffuse involvement (Superscan)

Important slide!!! question in exam

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.

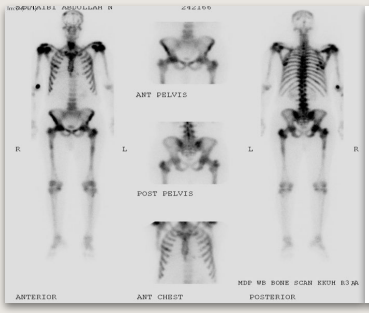
Causes:

A. **Bone metastases:** Prostate, breast, lung, bladder and lymphoma.
B. **Non tumor causes:** hyperparathyroidism, osteomalacia, Paget's disease and fibrous dysplasia.

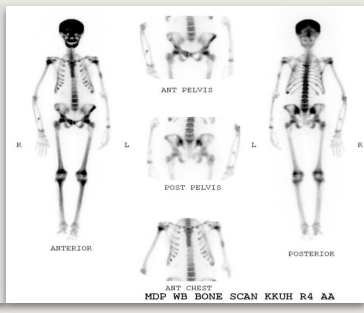
Important clues:

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

Differentiate between benign and metastatic superscan: all the skeleton is affected in benign, while the metastatic affects axial "central" skeleton only.



CA Prostate



HPT

Pure Lytic Lesions

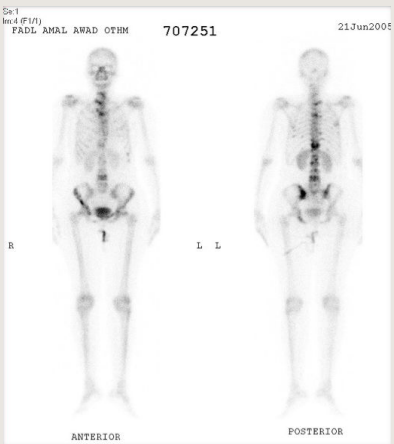
In this patient, the affected vertebrae (posterior) represent a pure lytic metastasis.

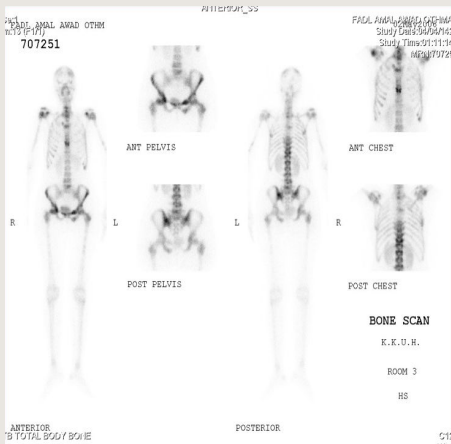
- Metastasis can be: lytic, osteoblastic or mixed.
- Some tumors, e.g. breast cancer, when metastasized to the bone, cause what is called an "osteoblastic reaction". This type is seen as a hot lesion on the bone scan. That is an osteoblastic metastasis.
- Other tumors, e.g. hypernephroma, metastasize to the bone without producing an osteoblastic reaction. They appear as cold lesion on the bone scan. That is a purely lytic metastasis.
- The osteoblastic reaction is the radiographic equivalent of osteoblastic flare and is defined as the appearance of new osteoblastic bone lesions while disease response is observed at other tumor sites.

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.

Look for the baseline study before looking at the image after radiation in order not to mistake these for "lytic lesions". Note the difference between this, and flare phenomena.

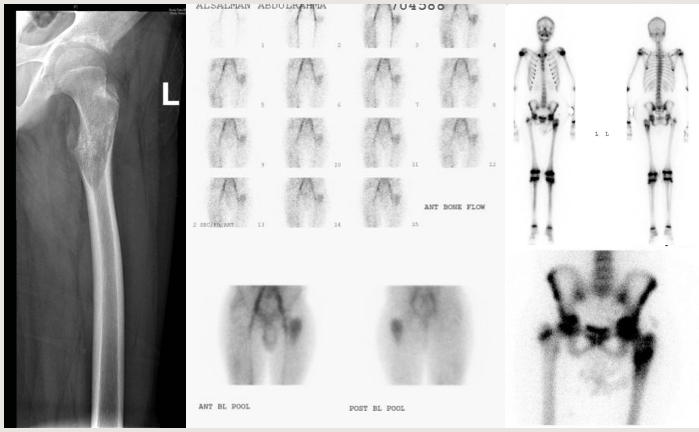




Ewing's Sarcoma

Read more!

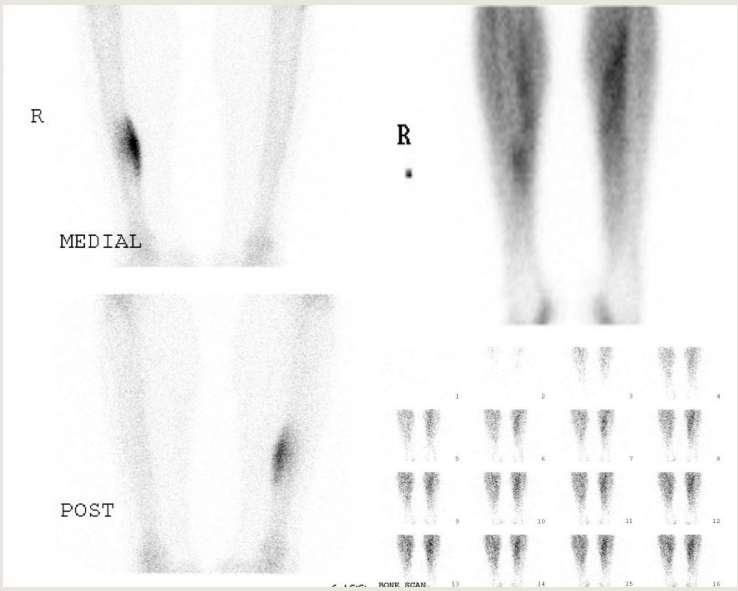
- Usually affects young people, that is why we can see growth plates.
- The primary diagnosis of bone tumor is by radiology. Why they do bone scan? To determine the local extent and to search for distant metastasis.
- In this patient the tumor is confined to proximal left femur but rest of skeleton is clear with no metastasis.



Osteoid Osteoma

Read more!

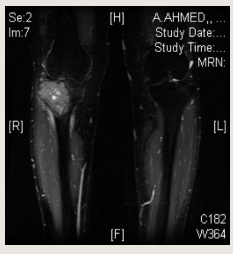
- A benign bone tumor affecting young children.
- Usually, the parent reports their child waking up at night complaining of leg, arm or spine pain that is relieved by aspirin.
- Appears on bone scan as a nidus surrounded by increased uptake.
- The bone scan is very sensitive in osteoid osteoma.
- 3 phases.
- Presentation may mimic osteomyelitis

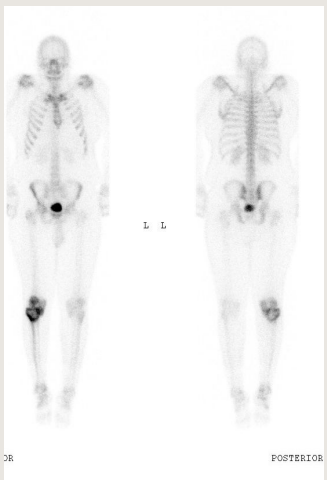


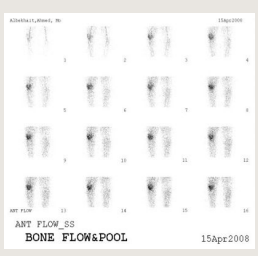
Giant Cell Tumor (Osteoclastoma)

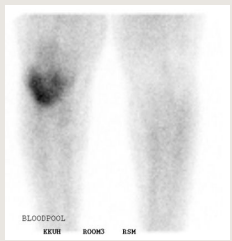
Read more!

- Increased uptake in single proximal right tibia with no distant metastasis.
- The primary diagnosis is by radiology (MRI). Our role is to determine if there was any metastasis.
- 3 phases show increased vascularity, blood pool, and increased hyperemia.



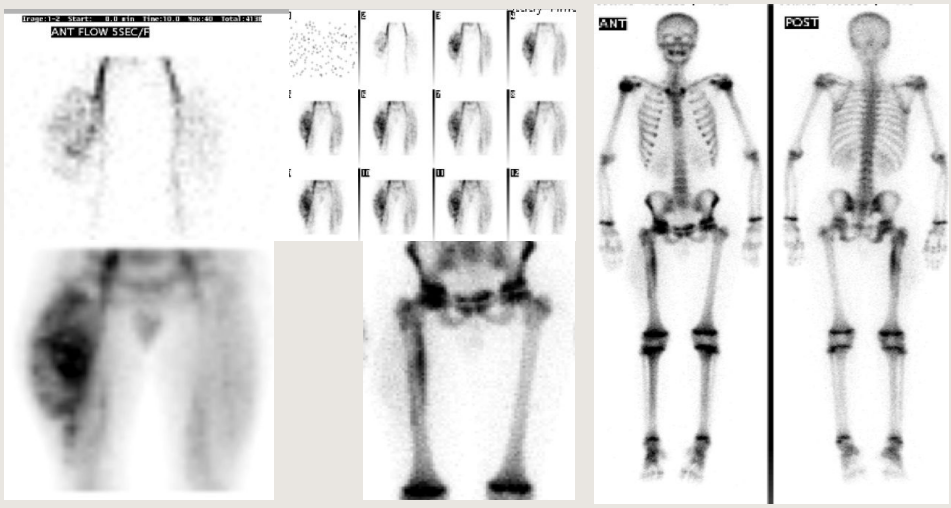






Soft Tissue Sarcoma

- In soft tissue tumors the main point of bone scan is to determine any bone invasion.
- The underlying bone Is not affected.
- No distant metastasis.
- 3 phases bone scan: increased vascularity, hyperemia.
- PET scan for mtastases and staging and therapy.



Gallium 67 Scan. Almost obsolete in KSA

Properties: Introduced in seventies of 20th century for lymphomas, KKUH stopped using it since October 2018. It is outdated, and the gold standard material is Fluorine 18.

- **Mechanisms of accumulation:**
  - Tumour viability.
  - Blood flow.
  - Capillary permeability.
  - Lymphatic drainage.
  - Binds to Transferrin receptors on the tumour cells.

skipped by doctor

- **Non specific for infection-inflammation 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, medium-energy collimator.

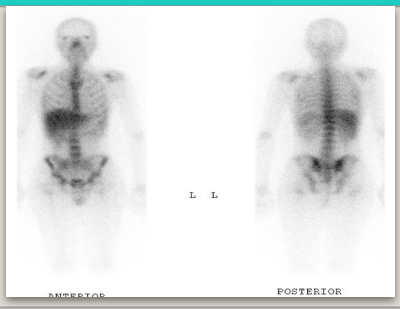
Normal Scan:

- Accumulates in bone marrow and liver.
- Splenic uptake is variable.
- The kidneys are usually visualized, and 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:

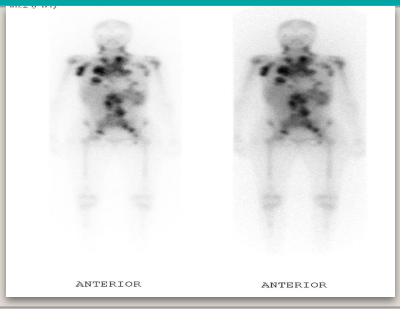
- Lymphoma. - Lung cancer. - Melanoma. - Hepatoma.

Normal Gallium Scan



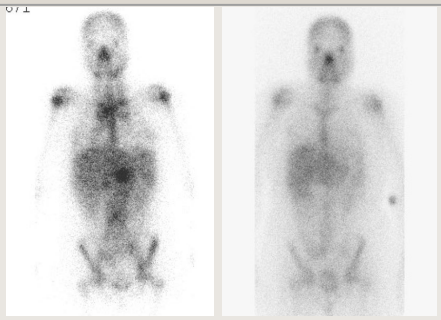
GA attaches to Ferritin. Wherever the concentration of Ferritin is high, it shall appear on the scan (Liver, Bone marrow, spleen). Image shows normal (baseline) Liver and bone marrow because Ga is iron analogue.

Gallium Scan in Lymphoma



- Staging.
- Follow up and monitoring of therapy.
- Detection of tumor recurrence.
- Differentiate post therapy changes: tissue necrosis and fibrosis from local recurrence.
- Image shows an abnormality as focal areas above and below the diaphragm, spleen, and liver. Stage 4.

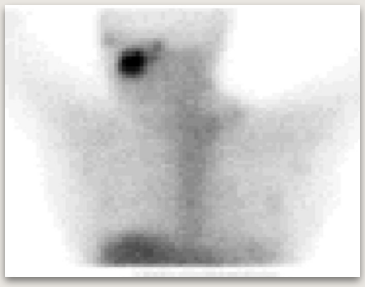
Prediction of response to therapy:



Comparison: Baseline and after 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.
Hot spots in the chest and abdomen after 1 course of chemotherapy, indicating a good response.

Prediction of Outcome:

Residual gallium uptake after treatment is a poor prognostic sign, indicates viable tumor and treatment should be modified. Usually, we use a more aggressive dose in these cases.



Ga-67 SPECT/CT: Staging HD

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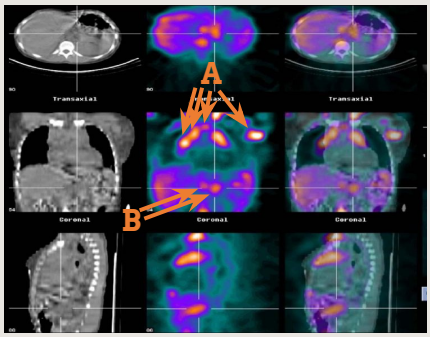
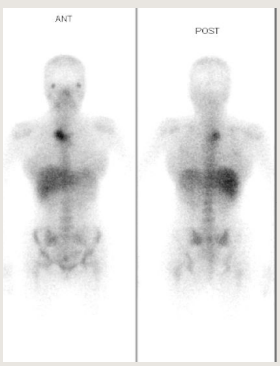


Abnormal Ga (Gallium) uptake **(A)** in supraclavicular, axillary, paratracheal, parahilarand para-aortic lymph nodes and in the spleen, at lesion sites corresponding to those observed on CT. The para-aortic lymph node uptake **(B)** combined with CT findings allowed the diagnosis of subdiaphragmatic disease and excluding bowel activity.

Gallium Scan NHL: Planar vs SPECT CT

skipped by doctor



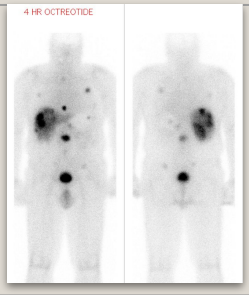
This patient shows an abnormal uptake in anterior mediastinum.

Neuroendocrine Tumors

- In-111 octreoscan.
- I123 MIBG Scan.

All neurogenic tumors are close to the spine, **why?** In the embryo, the sympathetic chain extends from the base of the tongue to the urinary bladder, around the spine. That is why the tumors present in the paraspinal area (eutopic or ectopic).

Somatostatin Receptor Imaging / Indium-111 Octreoscan

Normal Study		Abnormal Study (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.			
	You can see the spleen and liver, excreted through the kidneys, and slightly through the gallbladder. Otherwise, you should not see anything.		Abnormality shows the primary tumor and metastasis above and below the diaphragm.

I-123 MIBG Scan

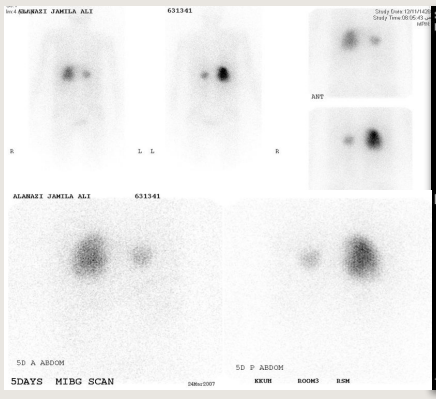
- **MIBG:** Meta Iodo Benzyl Guanidine.
- Is a noradrenaline analog.
- Localizes in adrenergic tissues: catecholamines producing tumors and their metastases.
- Patient preparation: stop drugs interfering with MIBG uptake. Lugol's solution to protect thyroid gland.

Indications:

1) Pheochromocytoma. 2) Paraganglioma. 3) Insulinoma.
4) Neuroblastoma. 5) Medullary thyroid carcinoma. 6) Carcinoid tumors.

MIBG in Pheochromocytoma (Bilateral Disease)

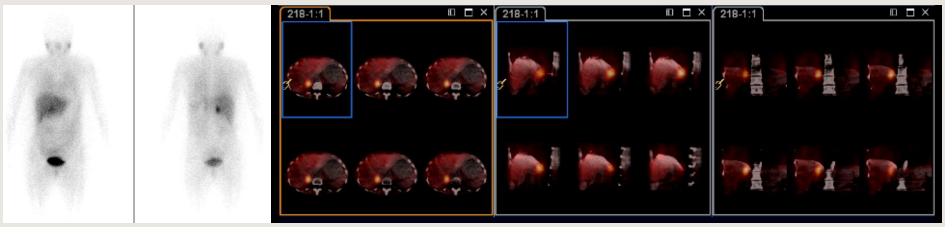
A patient with secondary hypertension, and bilateral adrenal masses.
The bilateral abnormal uptake represent bilateral Pheochromocytoma.



Pheochromocytoma: Planar vs SPECT CT

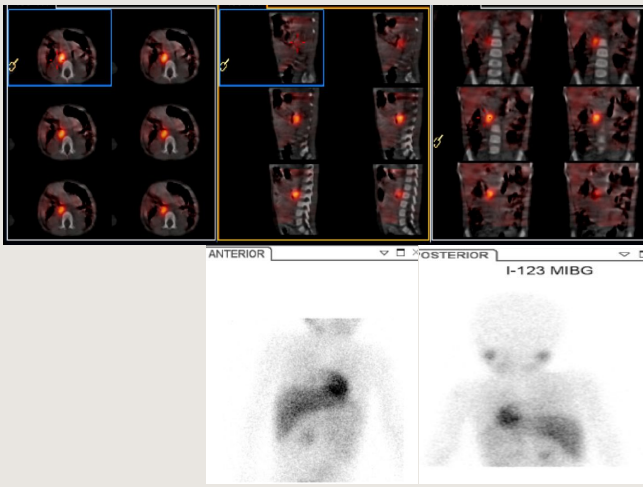
SPECT-CT shows a focal area of increased uptake and a paraspinal lesion on the right side along the sympathetic chain just superior to the kidney. This represent a single, eutopic PCC.

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



Neuroblastoma: Planar vs SPECT CT

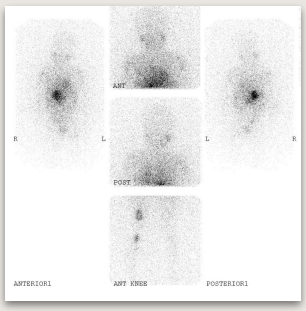
- A common tumor in children under the age of five.
- They usually present complaining of abdominal masses.
- The role of MIBG scan is to detect the primary tumor and distant metastases.
- Planner image shows a focal area of abnormal uptake in the abdomen.
- SPECT CT shows its exact localization.



I-131 MIBG Total body scan

1ry (primary) neuroblastoma / Bone metastases

Usually used for therapy, not for diagnosis.



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

skipped by doctor "go back to thyroid lecture if you want more."

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

Patient Preparation:

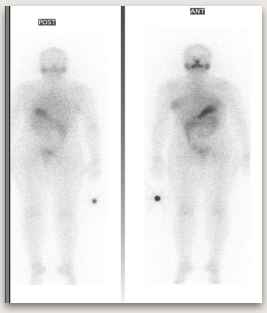
- Stimulation of potentially functioning thyroid tissue:
  - A. Inject recombinant human thyrotropin on 2 consecutive days and administer the iodine on the third day.
  - B. Withdraw thyroid replacement hormones:
    1. Thyroxine (T-4) for at least 4 weeks.
    2. Triiodothyronine (T-3) for at least 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 → for Dx.
B. I-131 as sodium iodide : 2-10 mCi → higher dose for therapy 100-200 mCi.

Imaging user Gamma camera: Whole body scan.

Thyroid Cancer I-123 WB Scan

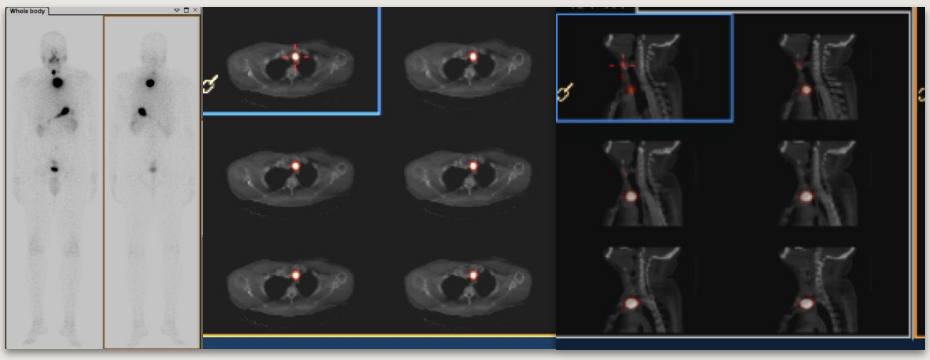


Negative I-123 WB Scan

I-123 WB Scan: Post-operative Thyroid remnants. How do we get rid of them? If small, I-131.
If large, like this image, surgery.

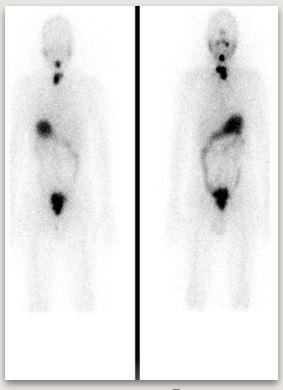
I-123 WB Scan (Post operative Thyroid remnants) Planar vs SPECT CT

Had thyroid remnants in the thyroid bed, the surgery was not complete.
Give them I-131(very specific for thyroid) to treat him, if there are large remnants do surgery again.

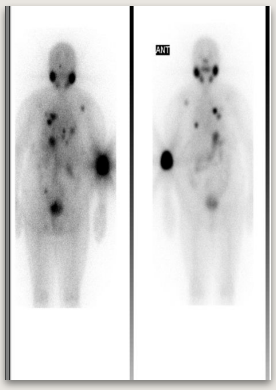


Thyroid Metastasis Study (I-123 or I-131 as Sodium Iodide)

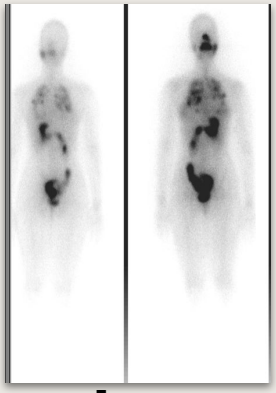
Tumors from thyroid are of 2 types: differentiated and undifferentiated. The differentiated are follicular (hematological spread so it go to all places of the body), or papillary (local spread via lymph node). This patient is having wide spread follicular. In the middle pic the black in his hand is due to injection site.



Local Recurrence

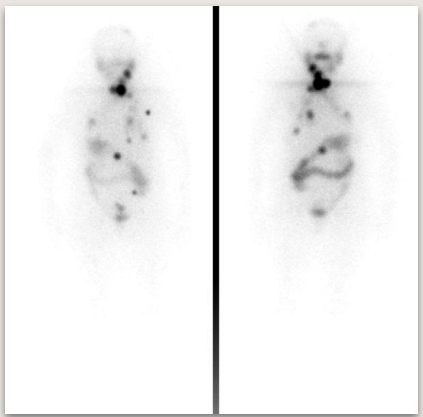


Bone Metastases
on ribs



Lung Metastases

Thyroid Cancer (I-131 Pre & Post therapy)



December 04
Wide spread metástasis local bone lung.

March 06
Recovery

Nuclear Medicine Procedure

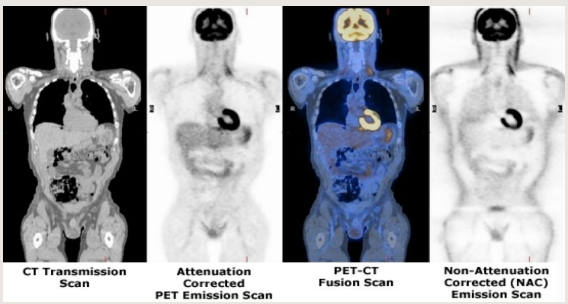
Positron Emitting Isotopes Memorize the T/2! it's easy

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

Planar Imaging

Now PET CT is gold standard for staging and monitoring oncology patient "butter and bread of our department"

- 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. We fuse the attenuation corrected with the non attenuation corrected an with the CT, which gives us the PET CT.
- Note the skin. Only the non attenuation corrected can show it. You can miss melanoma if you did not fuse them.



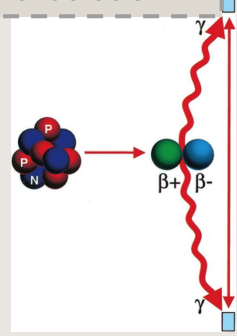
PET CT = PET + CT = Function + From

- he most commonly used agent is Fluorine 18 with t/2 under 110 min & Gallium 68 t/2 68 min.
- Normal distribution of FDG happens in the brain, where the main source of energy is glucose.
- بالنسبة للقلب. نخلي المريض. يصوم عشان. نجوّع. الورم (Tumor). ويأخذ. الجلوكوز. لما. نعطيه، بينما. الأنسجة الطبيعية. بتعتمد على الدهون
- - We add CT to PET for localizing and attenuation correction to get the exact margin of tumor.

How is it performed?

There are two types of radiation: **1) Electromagnetic radiation** (photons) like in x-ray and gamma-ray. **2) particle radiation like** Beta and Alpha.

We have two types of Beta: **Beta minus, and beta plus**. We use Beta plus radiation (like in F-18). Beta plus fuse with the Beta minus electrons inside the patient's body. This reaction forms two photons of gamma rays going in opposite directions (as seen in the picture) and PET imaging detects this radiation.



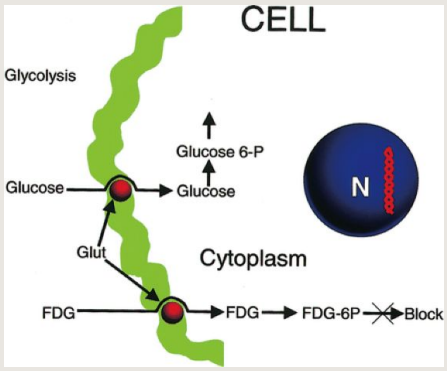
- **Positron emitters (e.g. F18)** labelled with biologically active natural compounds such as oxygen, carbon or glucose are given intravenously and reacting in the body identically to their non-radioactive counterparts.
- **Positrons** are emitted from F18 and react with tissue electrons → Annihilation 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.

skipped by doctor

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

Don't memorize it, just understand it :)

- FDG is a glucose analogue (similar to it) used to assess glucose metabolism.
- The only difference between them is kidney excretion.
- FDG transported from intravascular space to the cells by the same mechanism as the glucose.
- In the cell, a substance called "hexoKinase" acts on both FDG and glucose to form:
  - FDG-6-phosphatase (FDG-6-PO4-).
  - Glucose-6-phosphatase.
- FDG-6-PO4- can't progress further into glucose metabolism and remains trapped intracellularly in proportion to glycolytic rate of the cell.



In tumors, there is high rate of glycolysis (High compounds concentration) compared to normal cells as well as higher level of hexoKinase. **FDG is labeled with F18.*

FDG: Normal distribution

- **Brain**: High uptake (brain's main energy source is glucose).
- **Heart**: Should **NOT** be seen in the fasting image.
- **Liver**: less uptake.
- **Kidneys**: unlike glucose, FDG is excreted in urine.
- **GI**: Mild clearance, faintly seen.
- **Muscles**: Low, increase with exercise.

FDG in Oncology

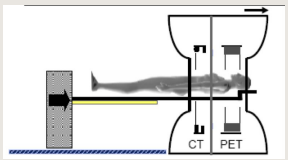
skipped by doctor

- 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:

- Locating unknown primaries.
- Differentiation of tumor from normal tissue.
- Preoperative 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

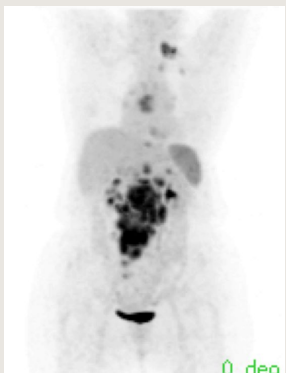


- Fasting: 4 – 6 hours.
- Dose: Inject 10 mCi F18 FDG.
- Wait (uptake phase): 45 -60 min then scan.
- Scanning time: 30 min to complete PET CT study.
- SUV: Standard uptake value (N: 0.5-2.5 and Tumors > 3.0)

FDG PET

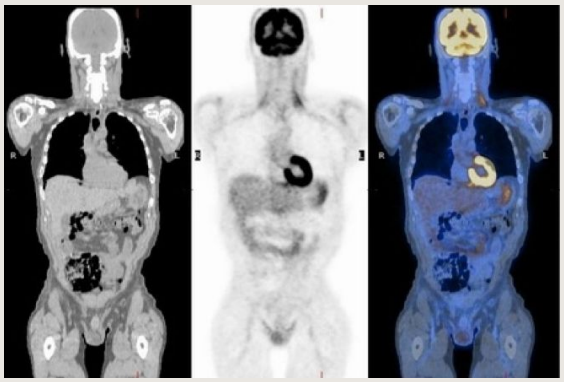
Normal

Abnormal image showing dark spots as multiple increased uptake (increase in glucose metabolism) below and above diaphragm with organ involvement, hence, this is a stage 4 lymphoma.

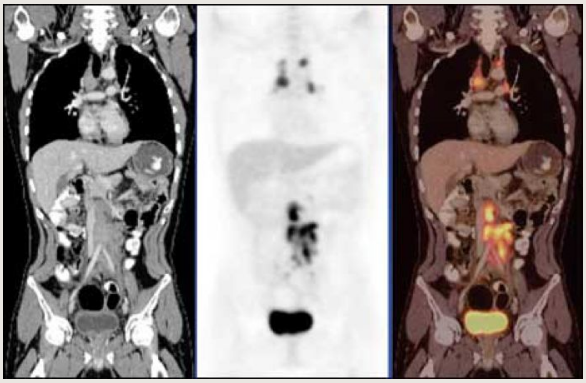


Staging of NHL

FDG PET-CT



Normal
We perform a CT and PET and combine them together.

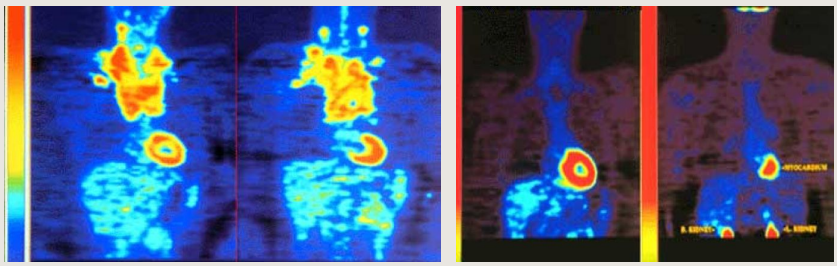


Staging of Lymphoma
Planner image did not show the exact localization, hence, PET-CT was performed and showed a stage 3 lymphoma.

Assessment of therapy response FDG PET in HD

Not in lecture slides

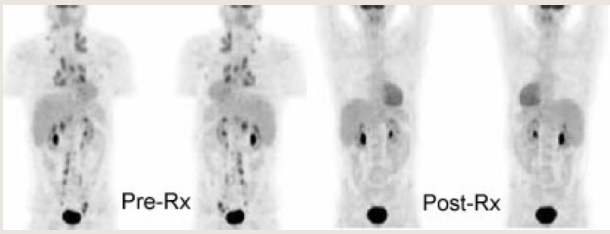
A 22 years old male patient with Hodgkin's lymphoma with cervical, supraclavicular and mediastinal lymph node involvement. Six months after chemotherapy, CT scan showed bilateral hilar abnormalities. **FDG-PET scan did not show any abnormal metabolic activity in described CT changes.**



Baseline **Post Therapy**

FDG in Non-Hodgkin's lymphoma: Response to therapy

Pre-Rx, the patient had involvement above and below the diaphragm. Post-Rx, the CT showed a focus in the left supraclavicular area. However, it did not appear on the PET-CT, which means that it is an area of fibrosis (happens due to therapy) that is not metabolically active. So the patient has good response to chemotherapy, and shall continue with the same Rx. So note that the anatomical imaging (CT) alone cannot evaluate the viability and metabolic state of the tumor.s

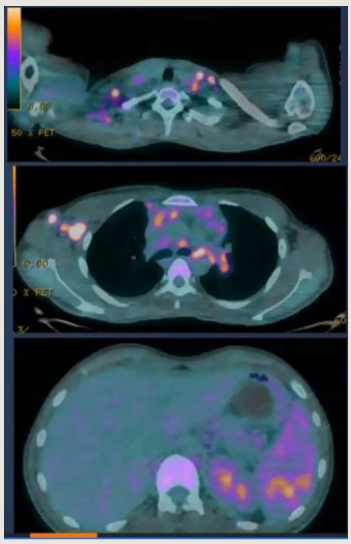


PET CT in Lymphoma

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

New Cases 437 slides

FDG PET-CT. Non hodgkin lymphoma: stage IV



There's organ involvement . spleen ,supraclavicular lymph nodes and bilateral hilar

FDG PET-CT: Hodgkin lymphoma

Post 6 cycles of chemotherapy for assessment

Baseline

Interim

Final

Intreim means: repeat scan after first dose of therapy.

- PET-CT also used for therapy monitoring .
- Baseline picture: shows stage IV HL. and organ involvement.
- Interim : post 1 cycle of therapy show good response to Tx. and fewer lymphnodes.
- Final:Complete response after finishing therapy cycles.

New Cases 437 slides

FDG PET-CT. hodgkin lymphoma

Post 6 cycles of chemotherapy for assessment
"partial metabolic response". (Deauville score5)

Baseline

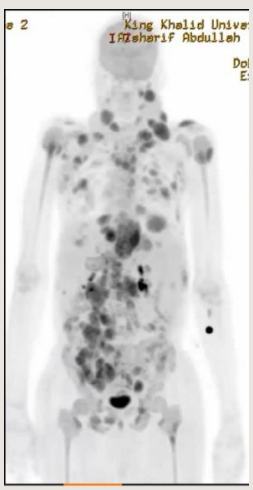
Interim

Final

- This case has an extensive diseases.
- Interim: there's still a significant diseases.
- Final: there's some some supraclavicular lymph nodes.
- Overall this is a partial response therapy, add another chemotherapeutic agent.

FDG PET-CT: marginal zone lymphoma

progressive disease (Deauville score5)

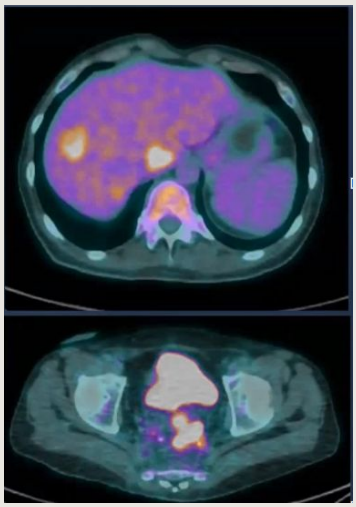


- left picture is baseline.
- Right picture is final.
- final picture shows: the treatment was not effective at all. not only that, but further progression.
- in this case we need to stop Tx and decide the effective Tx.
- So, PT-CT also tell us whether the Tx is effective or not.

New Cases 437 slides

FDG PET-CT. rectal cncer with liver metastases

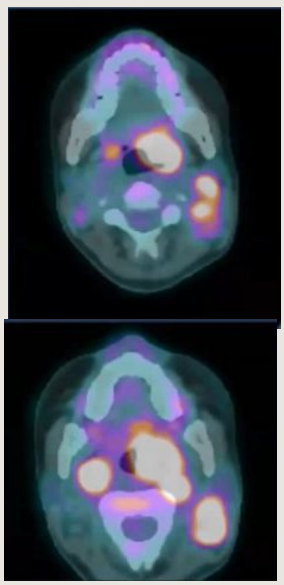




- first pic to the left: Planner PET show liver metastases.
- last pic on the right: PET-CT pelvic view. shows the rectal mass and liver metastases.

FDG PET-CT: Nasophargeal cancer with LN metastasis

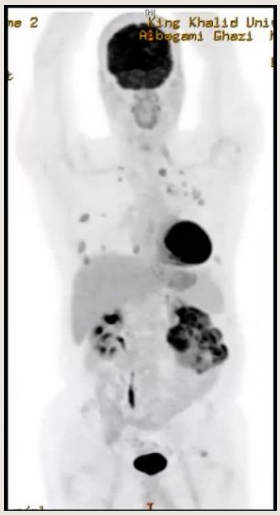


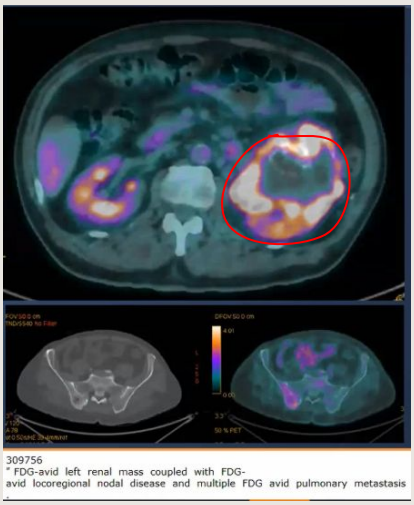


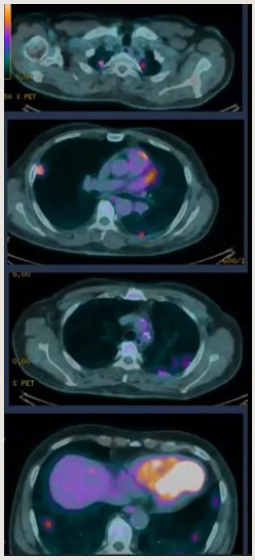
- PET-CT on the right show lymph node involvement with no metastasis

New Cases 437 slides

FDG PET-CT. Renal cell carcinoma with bone/lung metastases

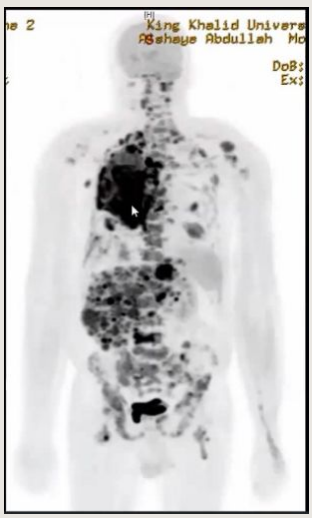


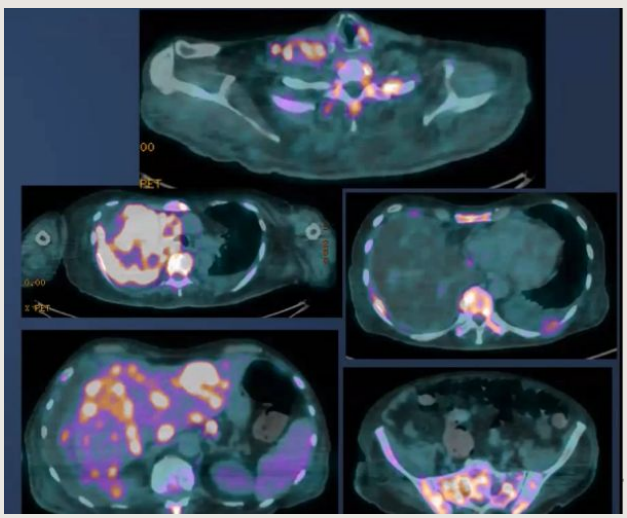




- First picture to the left: bone metastases on the left hip.
- Second picture: PET-Ct abdomen shows the primary left renal mass in red circle.
- Third picture: show long and chest lymph node involvement.

FDG PET-CT: metastatic lung cancer





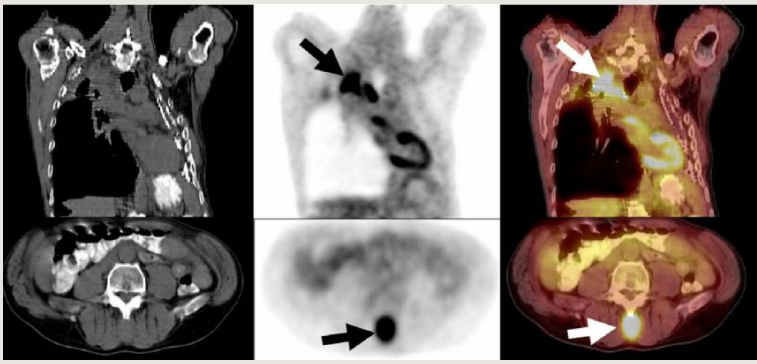
- Planner image: show right lung cancer with metastases everywhere.
- PECT-CT: bilateral lung involvement, multiple bone metastases, liver metastases and avid lymph node lesions.
- This is stage 4 lung cancer.

PET CT Lung Cancer

FDG PET CT in Solitary Pulmonary Nodule (SPN):
Sensitivity : 82 – 100 %
Specificity : 67 – 100 %

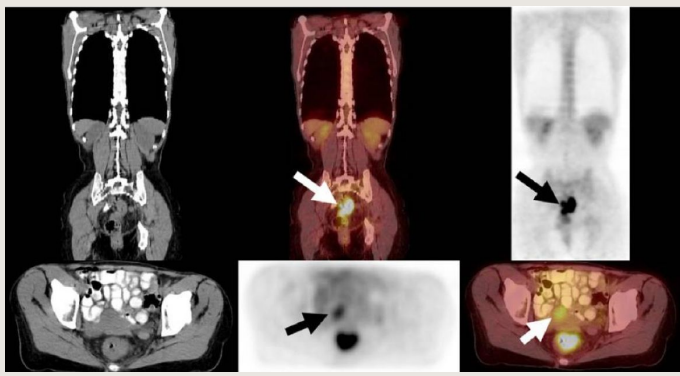
FDG avid soft tissue mass associated with a destructive L5 spinous process consistent with metastatic deposit (arrow).

Note the metastasis to the spine. Any patient with lung cancer is a candidate for PET-CT.



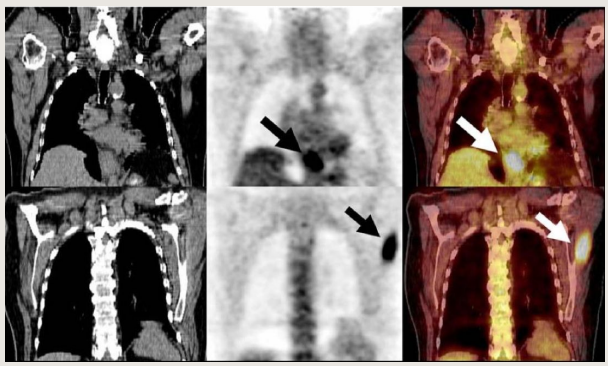
CA Rectum: Staging

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. Patient with rectal cancer and bone metastasis.

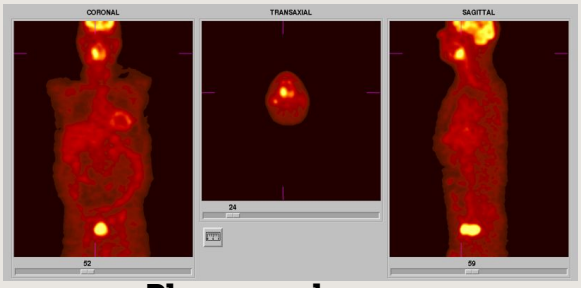


CA Esophagus: Staging

Patient with esophageal cancer and scapular metastasis.
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.

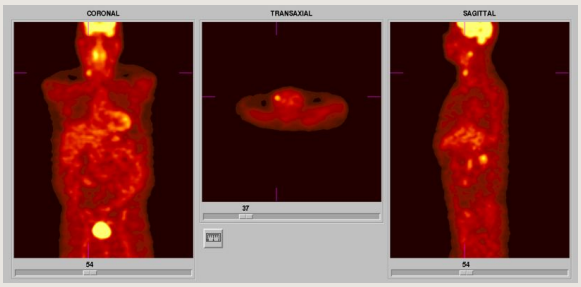


FDG PET: Tumor of unknown origin



Pharyngeal cancer

The only way to confirm the diagnosis through a biopsy (it could be lymphoma)

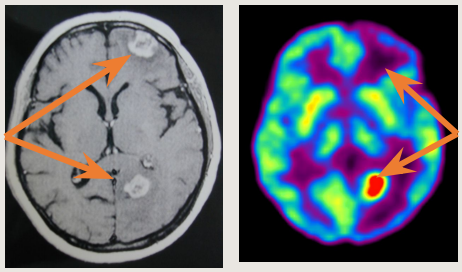


Metastatic involvement of neck lymph nodes

FDG PET: Brain tumor post therapy

A patient with lung cancer and brain metastasis.
CT showed two focal areas of high density in the frontal and occipital lobes. Which one of them is a viable tumor and which is fibrotic? The one in the occipital area appears metabolically active on PET (viable tumor), while the one in the frontal lobe is just fibrosis.

Two foci on CT, only one viable tumor



Indications of PET CT For your knowledge

Breast, SPN, Thyroid and cervical were in pink. The rest were green. We don't know why + We don't know the meaning of the stars but we copied Dr's slides anyway.

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

Ga-68 DOTANOC

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 post-injection.
Clinical value:
Somatostatin has 5 receptors, in which the SPECT agent can bind with 1 receptor, while Ga-68 DOTA binds with 3 receptors. Therefore, Ga-68 is more sensitive. Higher lesion detection rate than what 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 (pheochromocytoma, 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

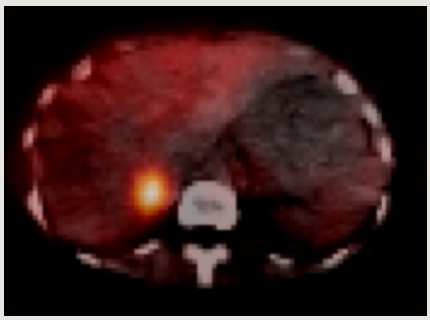
Normal tracer uptake is seen in the pituitary, salivary glands, thyroid, liver, spleen, adrenals, pancreas, kidneys, ureters, and bladder. Any uptake outside these areas is considered abnormal.

Ga-68 DOTANOC PET

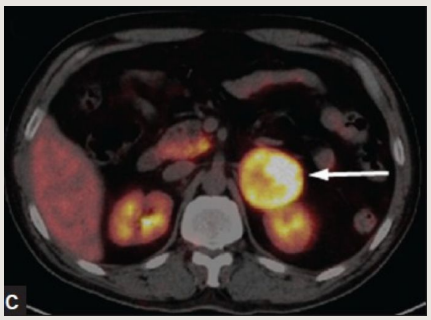
NET with multiple metastatic disease confined to the liver and abdominal cavity limited below diaphragm.

NET with extensive metastatic lesions throughout the body to Lung liver and lymph nodes above and below diaphragm.

Pheochromocytoma: Ga-68 DOTANOC superior to MIBG



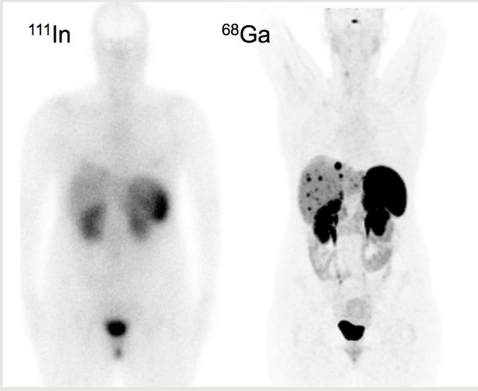
SPECT CT - I-123 MIBG



PET CT Ga68 DOTANOC

In oncology the G-68 is superior to other agents in neuroendocrine tumors.

Ga-68 DOTANOC PET superior to In- 111 Octreoscan



Carcinoid tumor: Positive 68Ga-DOTA-NOC and Negative 111In-Octreoscan.
^{68}Ga DOTA-NOC Findings: Multiple metastatic lesions in the liver. (The pituitary also expresses somatostatin receptors and is visualized in the 68Ga PET image, along with normal uptake in the spleen, kidneys, and bladder)
Indication of ^{68}Ga DOTA-NOC: The 68Ga PET scan was performed because the patient's symptoms were inconsistent with the 111In-Octreoscan findings.
Gallium-**68** is PET agent, the other gallium is **67** (SPECT agent), so they are different.
Two images of the same patient. Ga-68 is much more sensitive than In-111 in detecting neuroendocrine tumors.

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:non target 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.

The most important for therapy is **beta emitter**, not gamma radiation, because it travels for meters (outside the body and to the room) but beta stays confined to the tissue with travelling few millimeters only.

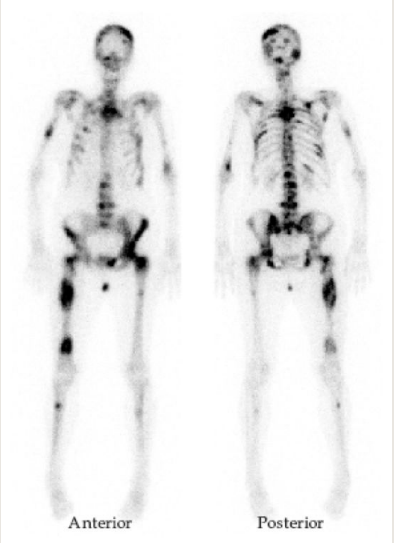
Radionuclide Therapy		
Agent	**Indication**	**Dose** (don't memorize it)
I-131	Thyroid cancer	100-200 mCi
131 MIBG	Neuroblastoma	100-300 mCi
Strontium-89	Bone metastasis	40-60 uCi/k
Sm-153-EDTMP	Bone metastasis	1.0 mCi per Kg
Phosphorus-32	Polycythemia	2.3 mCi/m2
Y-90-Ibritumomab Tiuxetan [Zevalin®]	B-cell NHL	> Platelet count > 150,000 cells/mL: **0.4 mCi/kg** > Platelet count 100,000- 150,000 cells/mL : **0.3 mCi/kg** The dose should never exceed 32 mCi (1,184 MBq)

Strontium-89 Therapy for Palliation of Bony Metastases

History:
- A 65 Year-old, Male, 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 exacerbated pain which was controlled by opiates but the following day showed gradual pain relieve.

Not responding to morphine or any other analgesics so he is a candidate of Strontium-89. A few days after therapy, the pain is expected to increase, then, it will decrease and stay effective for about a year.



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.

radionuclides:

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 tumorimaging agents:

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

Radionuclide therapy:

Properties of the Ideal Therapeutic Radiopharmaceutical

- Pure beta minus emitter.
- Effective half-life
- High target:non target ratio.
- Minimal radiation dose
- Inexpensive

Agent	Indication
I-131	Thyroid cancer
131 MIBG	Neuroblastoma
Strontium-89	Bone metastasis
Sm-153-EDTMP	Bone metastasis
Phosphorus-32	Polycythemia
Y-90-Ibritumomab Tiuxetan [Zevalin®]	B-cell NHL

QUESTIONS

1. Which ONE of the following tumors can give the "superscan" appearance on bone scan?

A. Multiple myeloma
B. Leukemia
C. Prostatic cancer
D. Renal cell carcinoma

2. A patient has breast cancer, the best modality to exclude any bony metastasis is:

A. Radionuclide scan
B. MRI
C. CT scan.
D. X-ray

3. Which one of the following isotope has a 110 min half life ?

A. Oxygen-15
B. Nitrogen-13
C. Carbon-11
D. Fluorine-18

4. Ga 68 is use to diagnose which one of the following ?

A. Tumor proliferation
B. Tumor hypoxia
C. Neuroendocrine tumor
D. None of the above

5. Which one of the following radiopharmaceutical is use as therapy in case of B cell lymphoma ?

A. I 131
B. Y90
C. Sr 98
D. F 95

6. Which one of radioactive is commonly use in PET ?

A. Fluorine 18
B. Ga 68
C. Carbon 11
D. Nitrogen-13

Answers: 1. C 2. A 3. D 4. C 5. B 6. A

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RadiologyRadiology437@gmail.com

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References

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We did it !