
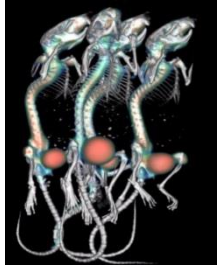
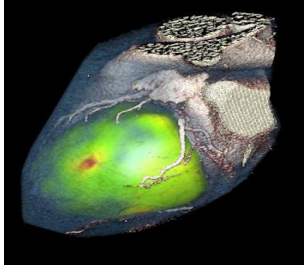
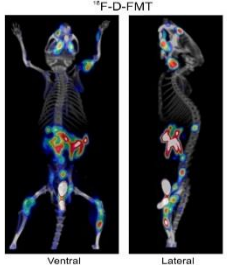

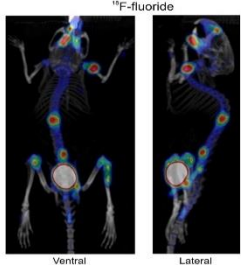

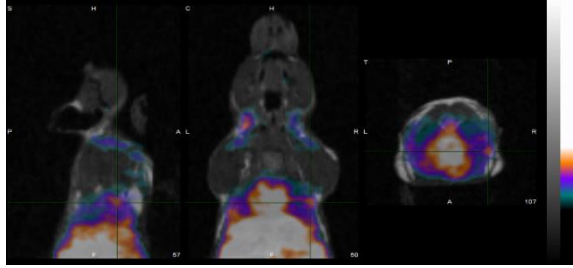

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Preclinical Imaging in Small Laboratory Animals

Instrumentation and Application

Imaging in Oncology & Thera(g)nostics

Sebastian Eigner, M.Sc.

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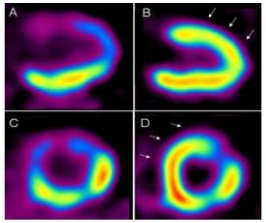
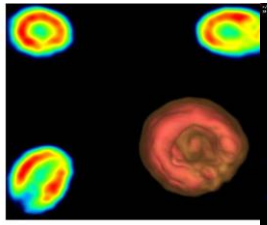
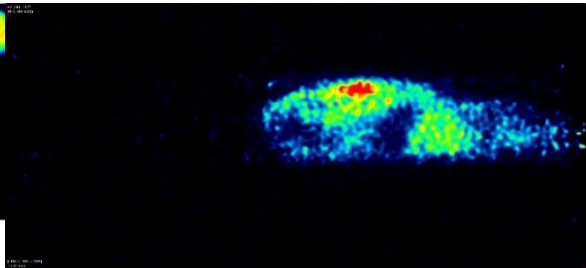
EVROPSKÁ UNIE
EVROPSKÝ FOND PRO REGIONÁLNÍ ROZVOJ
INVESTICE DO VAŠÍ BUDOUCNOSTI

2007-13
OP Výzkum a vývoj pro inovace



^{18}F-FDG – human heart ^{A} ^{18}F-FDG –rat heart ^{B}

Tumor Imaging

Indications

- Diagnosis
  - Identification
  - Staging/ re-staging
- Identification of recurrence or residual disease
- Monitoring therapy response
- Evaluating Prognosis

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Tumor Imaging Agents

common tracers

- Ga-67 citrate (historic)
- Organ imaging, e.g. thyroid, bone
- Thallium-201
- Tc-99m Sestamibi – Breast imaging
- Labeled monoclonal antibodies, fragments
- Peptide receptor imaging In-111 pentetreotide, Ga-68 Octreotide
- Adrenal tumor imaging – I-123 MIBG
- F-18 FDG

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Ga-67 citrate

- Mechanism of uptake – bound to transferrin, uptake in tumor cells by lysosomes and endoplasmic reticulum

- Now nearly obsolete as a tumor imaging agent

→ outperformed by FDG PET

- Probable only remaining indication for Ga-67 citrate in tumor imaging:
  - Differentiating hepatocellular carcinoma from regenerating nodules in patients with cirrhosis

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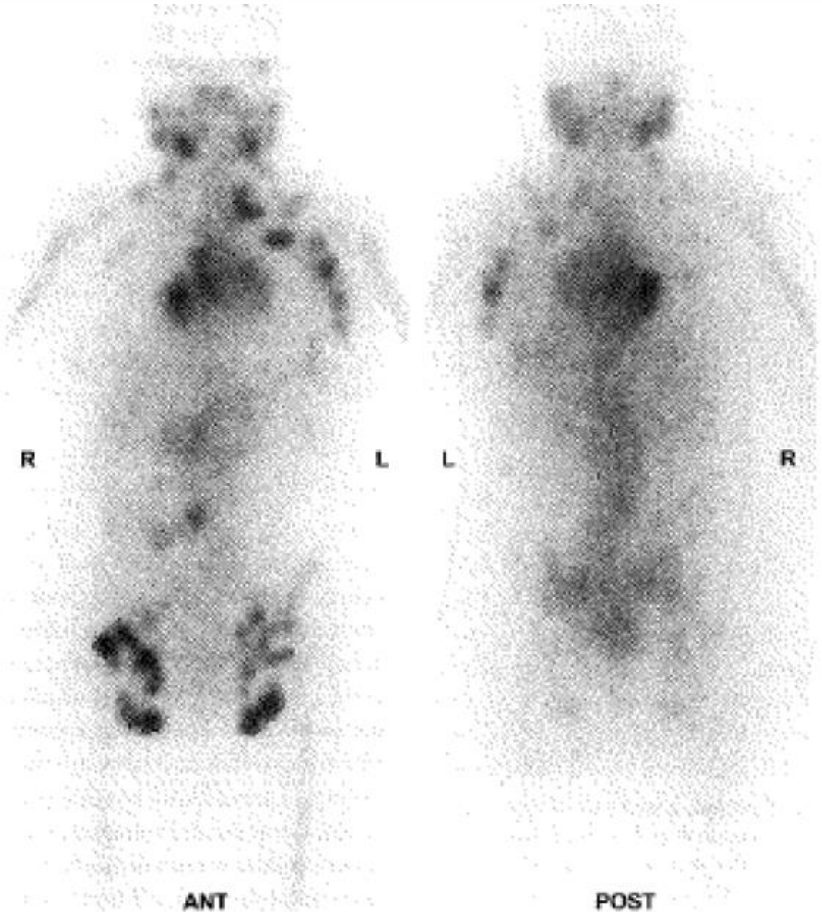
Ga-67 citrate

Lymphoma



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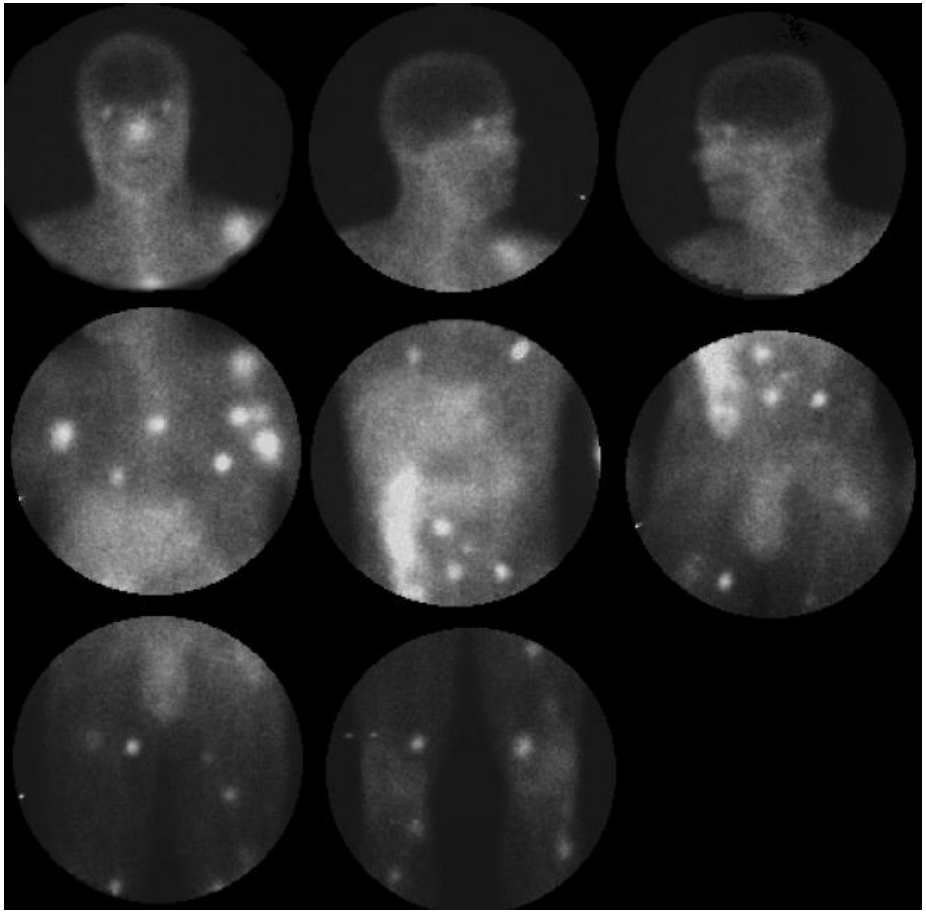
Ga-67 citrate

Lymphoma



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Thyroid Carcinoma

I-131 imaging

- I-131: Oldest radionuclide (RN) in clinical use
- Images are not very pretty, due to the high gamma energy, but the information obtained is extremely useful.
- Having a gamma emission and a beta emission makes this RN uniquely suited to therapy, esp. for thyroid disease.

There is no replacement on the horizon!

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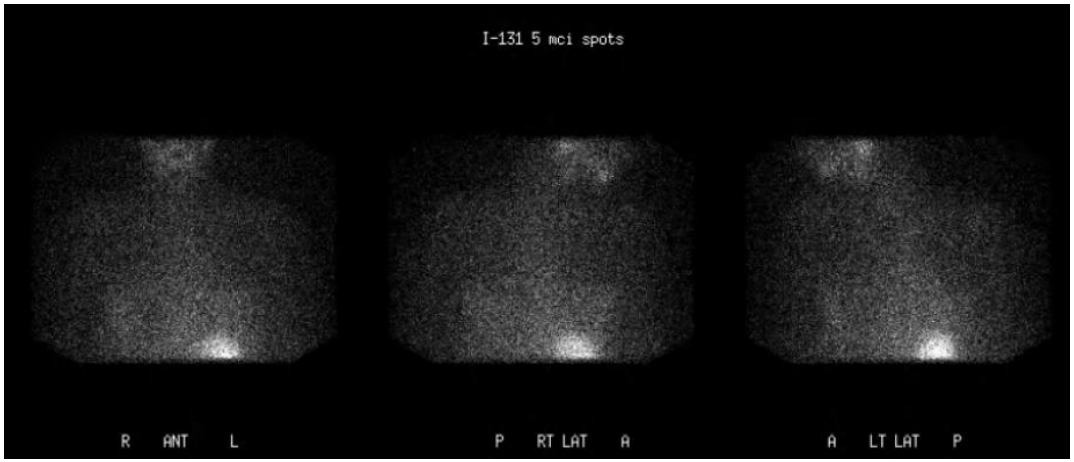
Thyroid Carcinoma

Indications for Imaging with I-131

- Detect active residual disease (papillary or follicular thyroid CA)
- Detect functioning metastases
- Assess results of treatment



Papillary Thyroid Cancer

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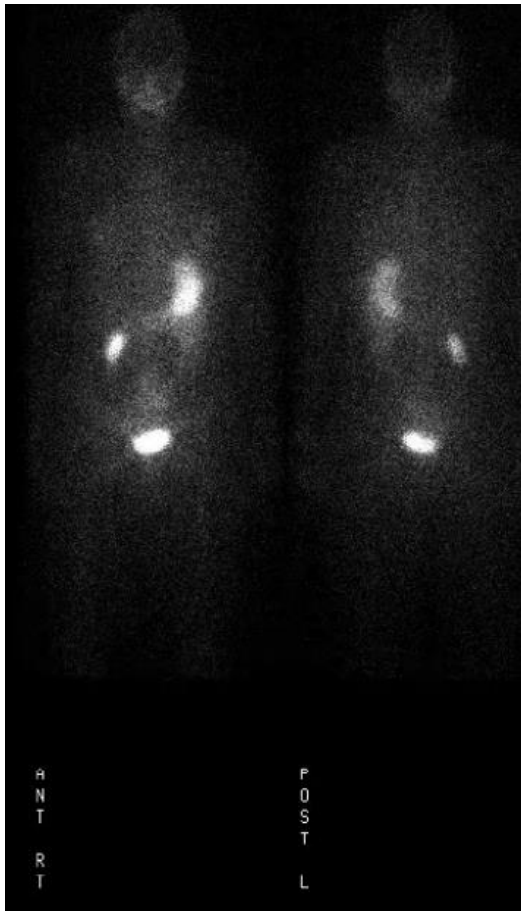
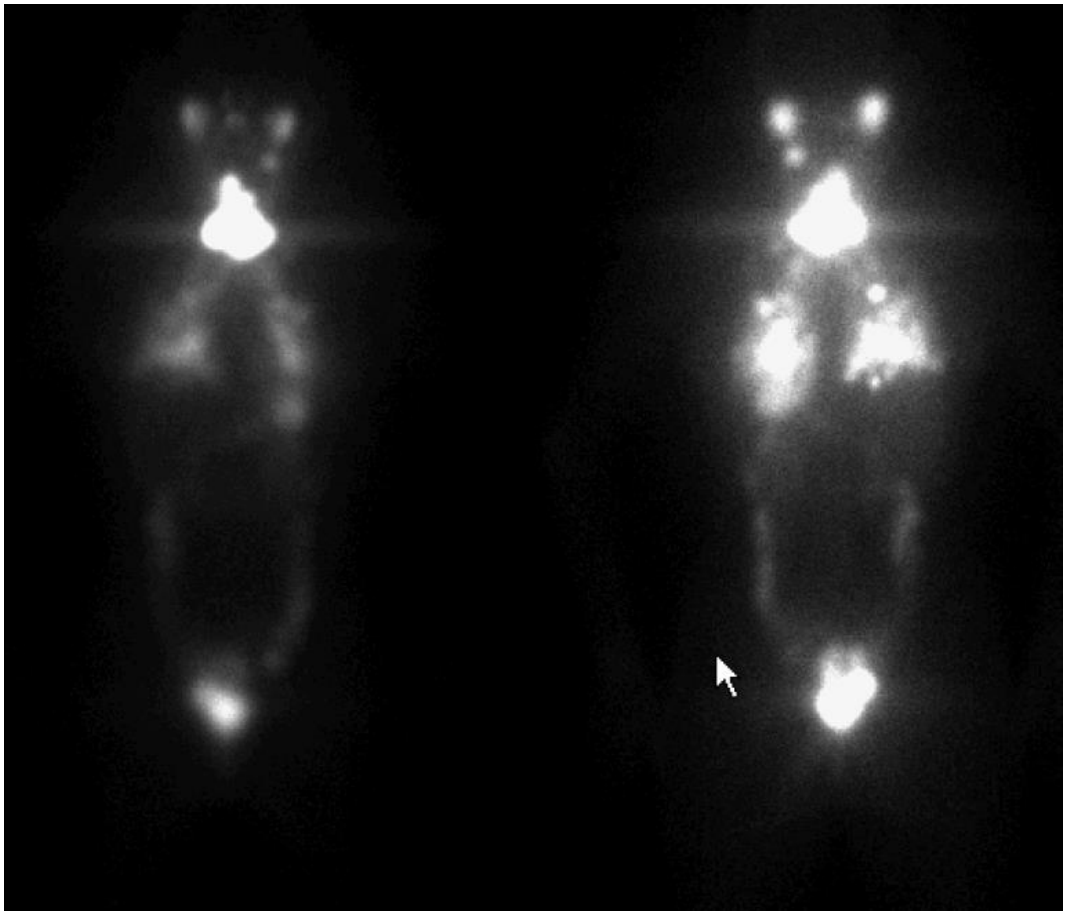
Papillary Thyroid Carcinoma





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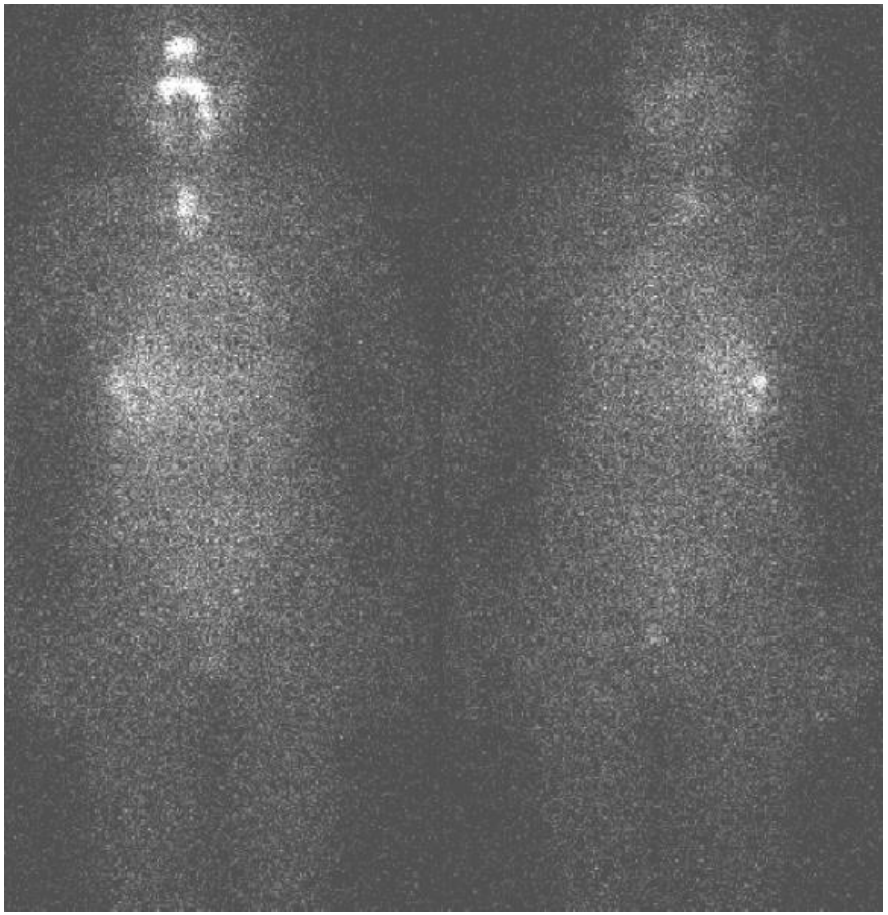
Metastatic Thyroid Carcinoma



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Bone Scintigraphy

Tracing bone metastasis

- GOLD-standard: ^{99m}Tc-methylene diphosphonate (^{99m}Tc-MDP) bone scintigraphy
- ^{18}F-Fluoride PET has been reported to be more sensitive for detection of metastases than ^{99m}Tc-MDP
- Many studies comparing detection of bone metastasis by ^{99m}Tc-MDP planar bone scintigraphy (BS), SPECT, ^{18}F-Fluoride PET, and ^{18}F-Fluoride PET/CT

SPECT and PET are better suitable than planar BS – difference in price and availability of tracer!

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Bone Metastasis

Prostate cancer

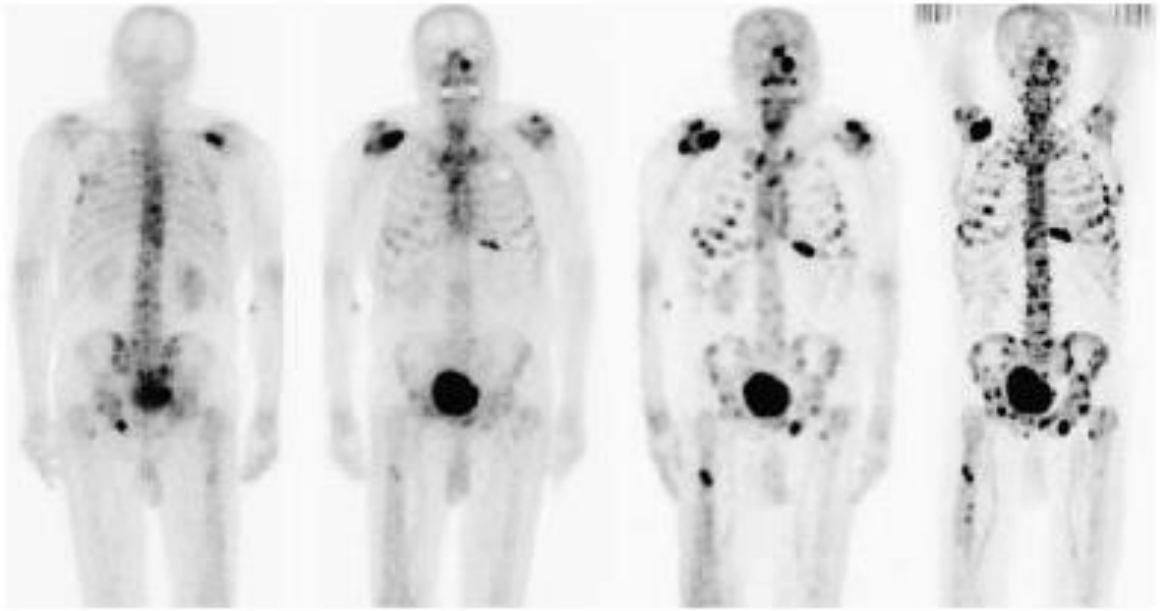

FIGURE 1. An 82-y-old patient with numerous bone metastases. From left to right: posterior and anterior planar BS, multi-FOV SPECT, and ^{18}F-Fluoride PET images. More lesions are detected on SPECT compared with planar images and on ^{18}F-Fluoride PET compared with SPECT images.

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Bone Metastasis

Prostate cancer

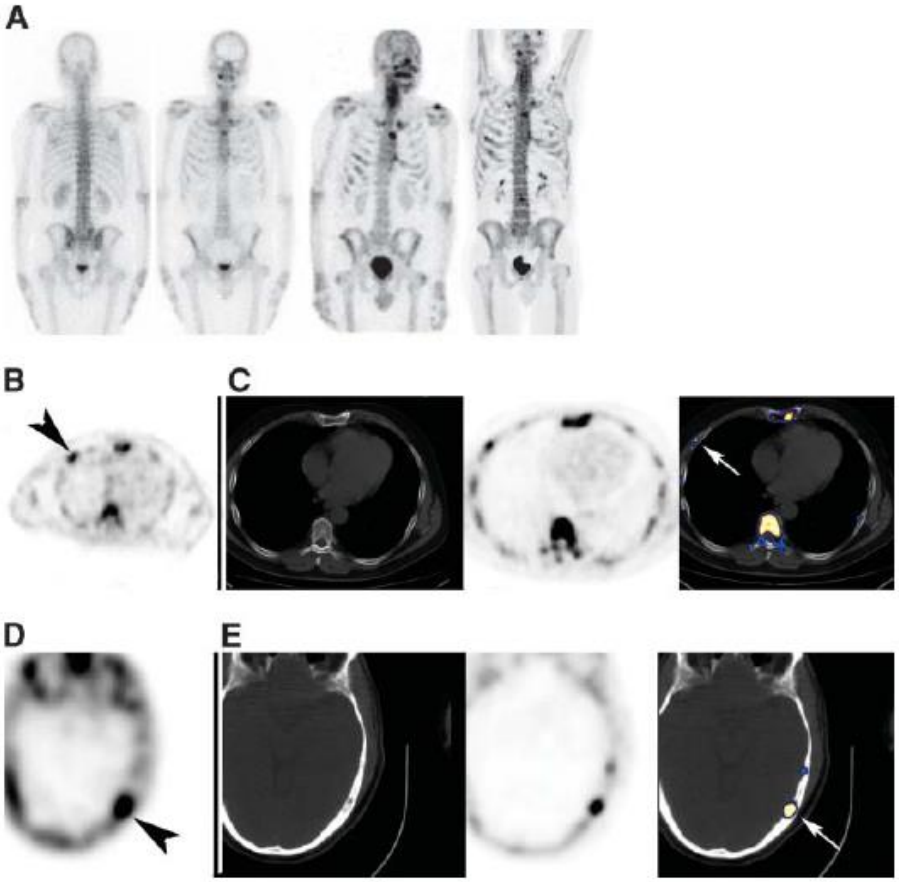

FIGURE 2. Early metastatic spread missed on planar BS in 57-year-old patient with prostate cancer at diagnosis. (A) From left to right: posterior and anterior planar BS, multi-FOV SPECT, and ^{18}F-Fluoride PET images. Planar BS was interpreted as negative for bone metastases. (B and C) Osteoblastic rib metastasis on SPECT (B) and on ^{18}F-Fluoride PET/CT (C). From left to right: SPECT (metastasis marked by arrowhead), CT, ^{18}F-Fluoride PET, and fused ^{18}F-Fluoride PET/CT (metastasis marked by arrow). (D and E) Osteoblastic metastasis in skull on SPECT (D) and on ^{18}F-Fluoride PET/CT (E). From left to right: SPECT (metastasis marked by arrowhead), CT, ^{18}F-Fluoride PET, and fused ^{18}F-Fluoride PET/CT (metastasis marked by arrow).

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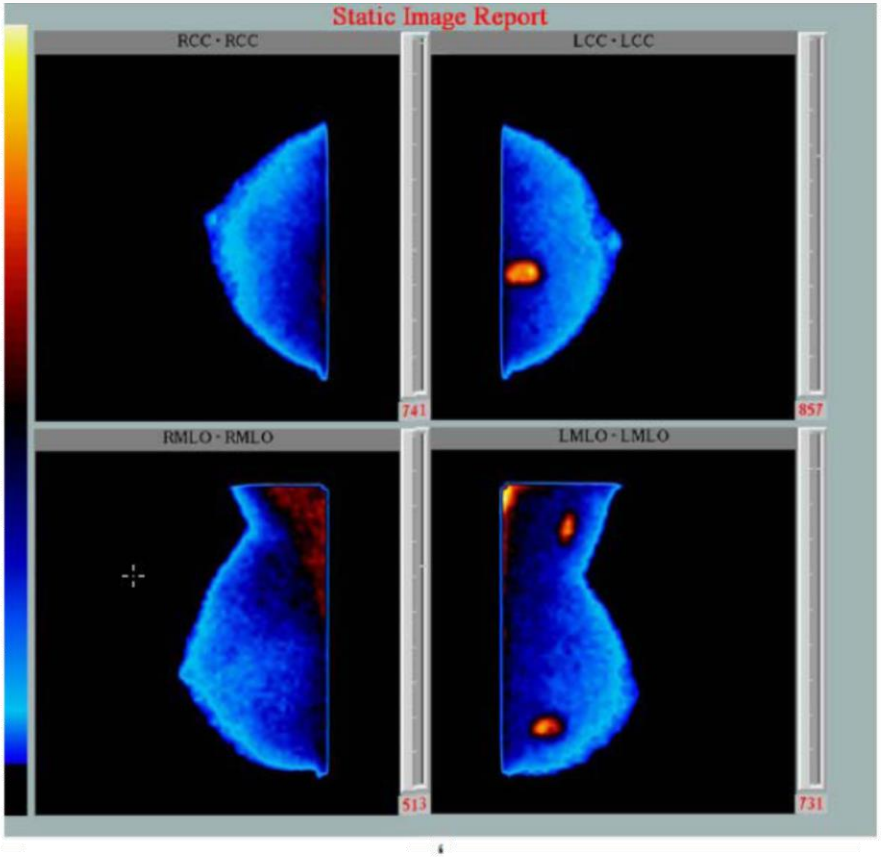
Mama Carcinoma

^{99m}Tc-Sestamibi



BSGI Case Study: Left infiltrating ductal carcinoma & axillary metastasis.

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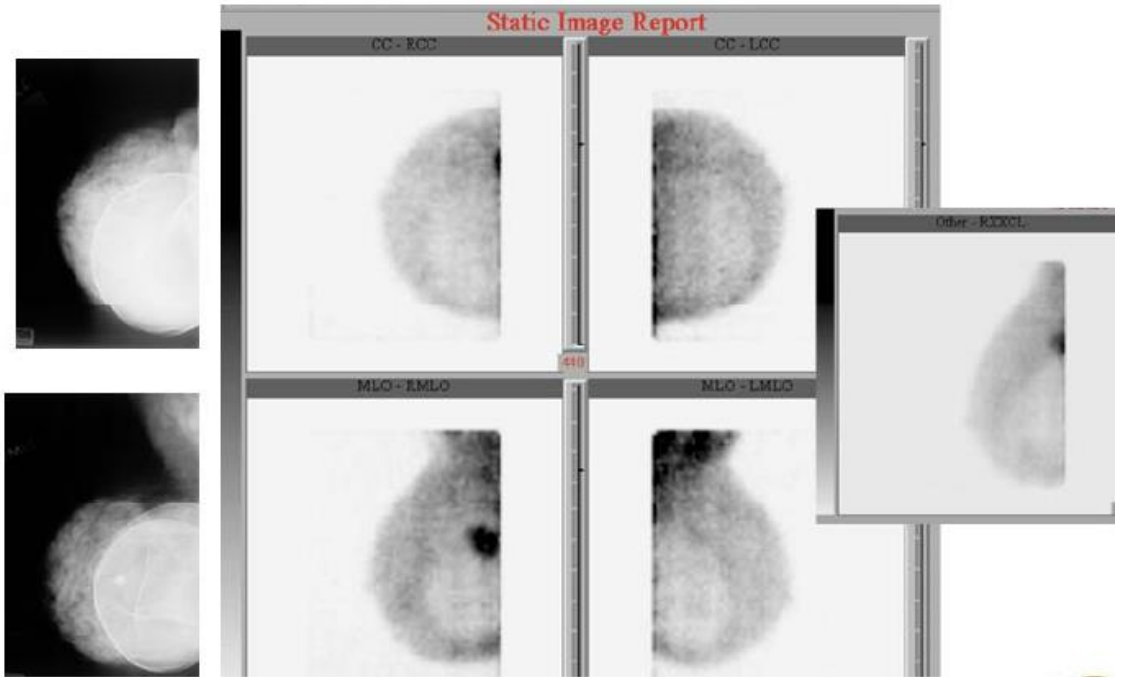
Mama Carcinoma

^{99m}Tc-Sestamibi

Clinical Summary: Patient with bilateral breast implants and a palpable mass. Mammographically negative, BSGI subsequently pursued. Additional XCCL view obtained to include more of the mass in the CC plane. Pathology: Infiltrating ductal carcinoma, 2.7 x 2.3 x 2.0 cm mass. Patient spared prophylactic contralateral implant removal because of normal exam on left.



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Peptide Receptor Imaging

Somatostatin receptor

- In-111 pentetreotide (Octreotide, Octreoscan)
- Ga-68 DOTATOC
- Neuroendocrine tumors – derived from APUD (Amine Precursor Uptake and Decarboxylation) system cells
- Examples: carcinoid, pituitary adenoma, pancreatic islet cell tumor, small cell lung cancer, pheochromocytoma, neuroblastoma

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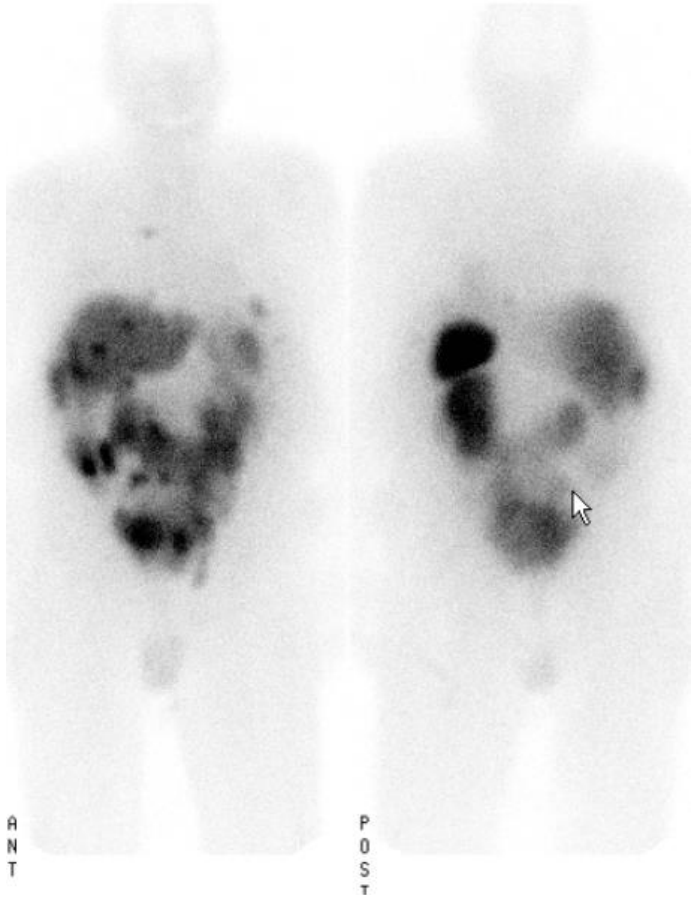
In-111 Pentetreotide (Octreoscan)

Merkel Cell Tumor



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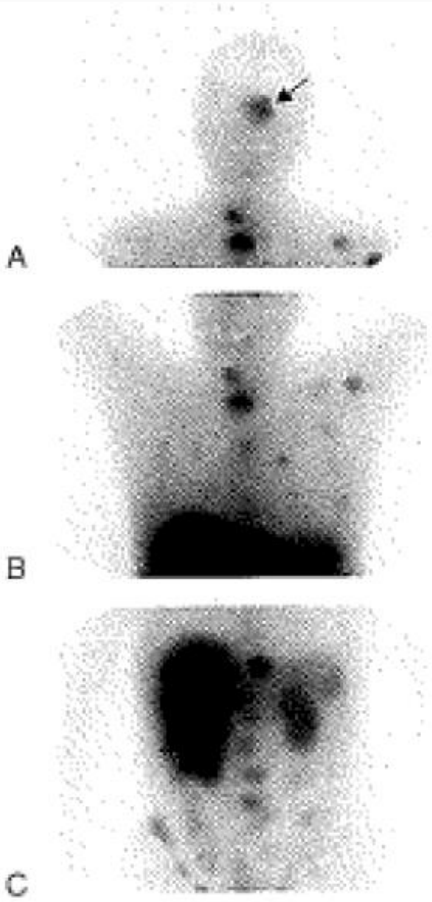
In-111 Pentetreotide (Octreoscan)

Metastatic Carcinoid with Meningioma



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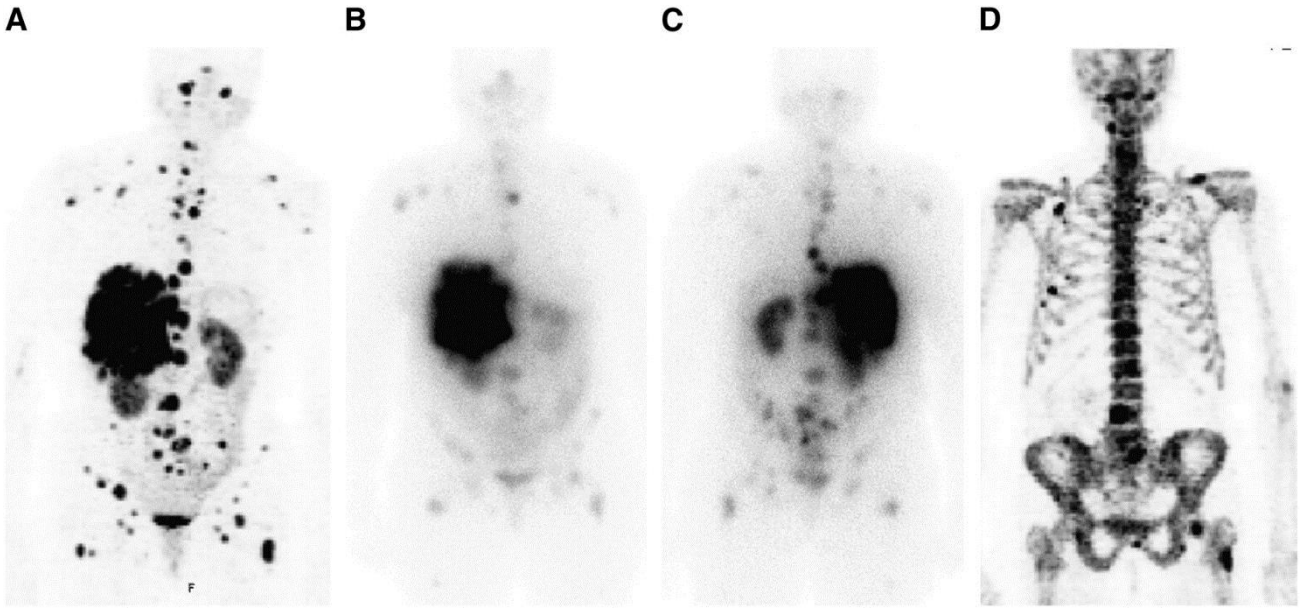
Ga-68 DOTATOC

Neuroendocrine Tumors



A 56-y-old woman with multiple liver and lymph node metastases was referred for restaging after surgery and chemotherapy. CT presented these tumor lesions; however, it was negative for bone lesions. Beside the visceral metastases, some additional osteoblastic and osteolytic bone metastases were clearly depicted with ^{68}Ga-DOTA-TOC (A). Only some of these bone metastases were delineated by conventional scintigraphy (B, anterior view; C, posterior view). Osteoblastic bone lesions were confirmed by ^{18}F-Na-fluoride PET (D). Retrospective CT analysis after image fusion revealed some of these bone metastases.
Michael Gabriel et al. J Nucl Med 2007;48:508-518

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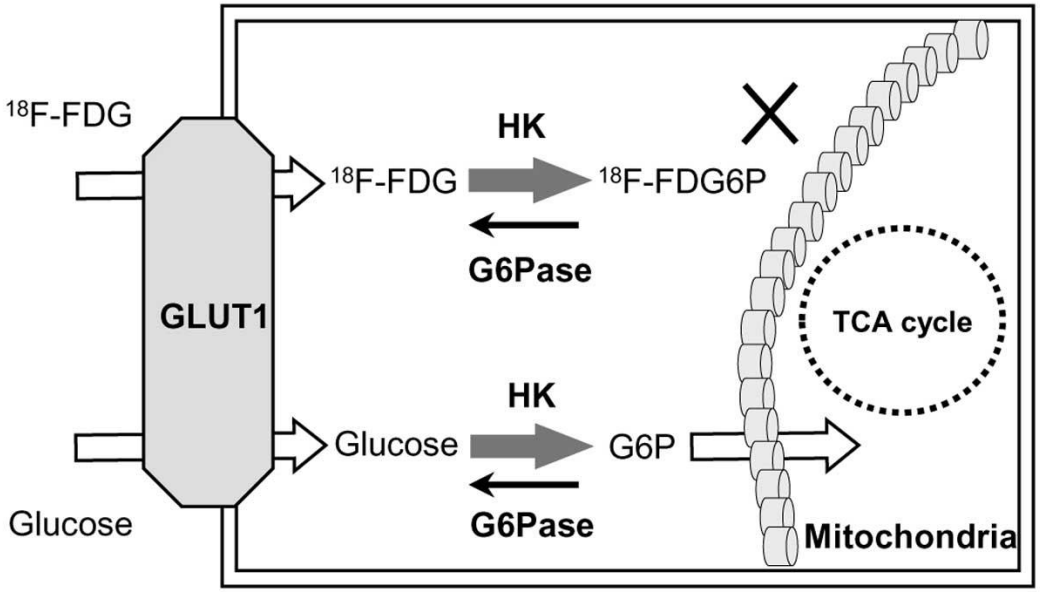
F-18 FDG

Most commonly used PET tracer for many tumors for staging/re-staging, monitoring response to therapy, detecting recurrent or residual disease (Head and neck, lung, lymphoma, melanoma, esophageal, colorectal, breast, cervical CA, ….)



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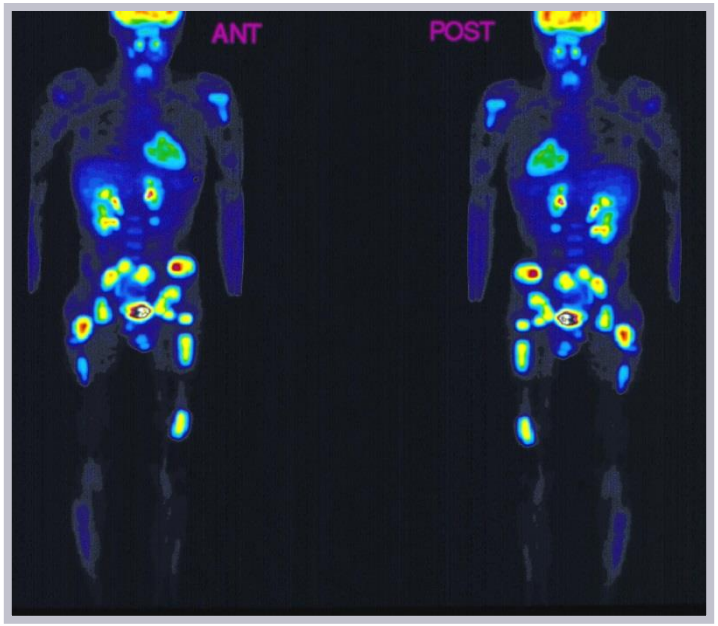

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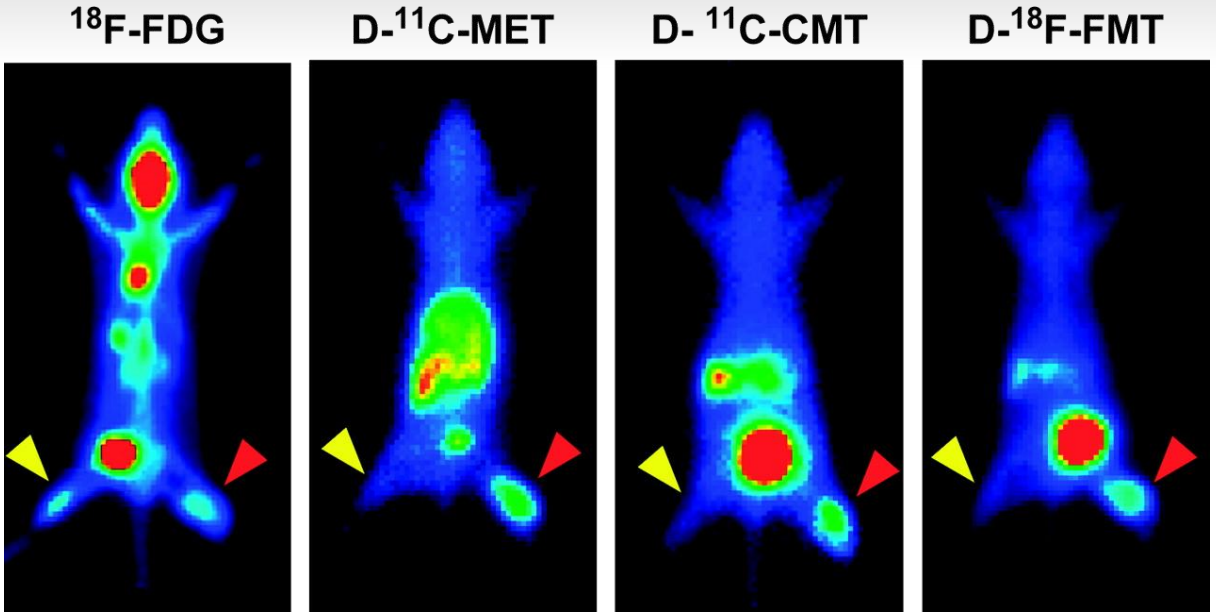
F-18 FDG



Effects of inflammation on uptake of ^{18}F-FDG and D-isomers of ^{11}C-MET,^{11}C-CMT, and ^{18}F-FMT in HeLa-bearing mice. HeLa cells were inoculated in right hind legs 2 wk before tracer injection (red arrowheads), and turpentine (0.05 mL) was administered subcutaneously in left hind legs 3 d before tracer injection (yellow arrowheads). Mice were imaged with PPIS for 60 min after injection of ^{18}F-FDG, D-^{11}C-MET, D-^{11}C-CMT, and D-^{18}F-FMT, and the accumulated images from 41 to 60 min after injection were created.

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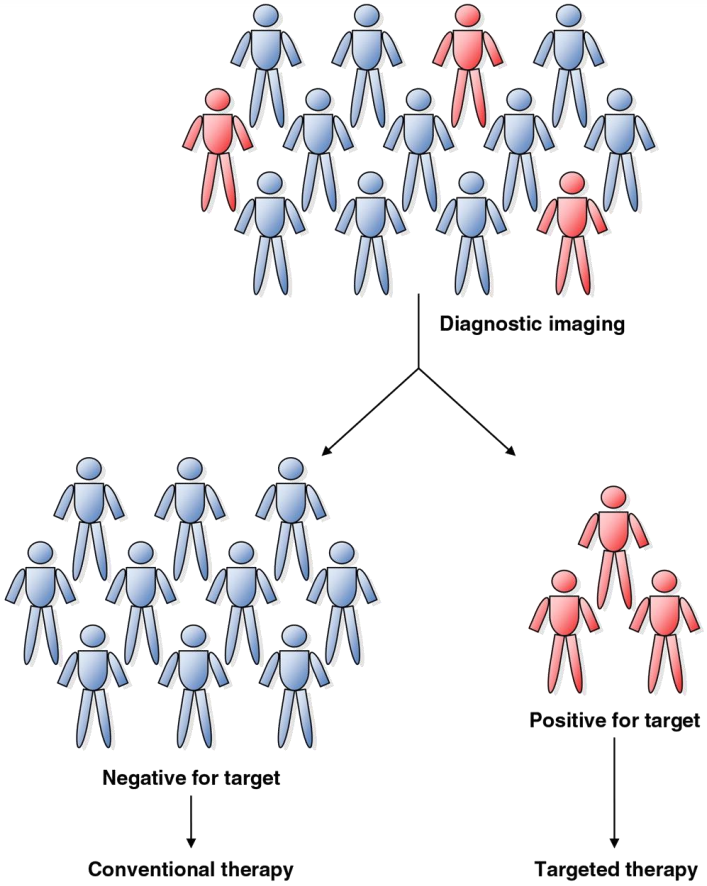
Thera(g)nostics

Therapy meets Diagnostics

Combination of two words:

- Therapeutic + Diagnostic
- Sometimes interchangably refered to as Theragnostics
- Use of radionuclide-labeled agents that specifically permit us to diagnose disease in individuals and then use identical or closely related agents to treat these diseases



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Thera(g)nostics

Therapy meets Diagnostics

- Theranostics involves the administration of a diagnostic agent:
- To determine localization in the site or disease state under study as a surrogate for a potential therapeutic agent with similar chemical properties;
- To examine its biodistribution as predictive of off-target(adverse) effects of the potential therapeutic agent;
- As an aid in determining the optimal therapeutic dosage or activity to be administered, based on the anticipated tumoricidal doses measured in the tumor site;
- To monitor the response to this treatment
- Theranostics is a term that has been used in the context of molecular targeting vectors (eg, peptides)
- labeled either with diagnostic or with therapeutic radionuclides for the diagnosis and therapy of a particular disease, targeted specifically by the vector at its molecular level

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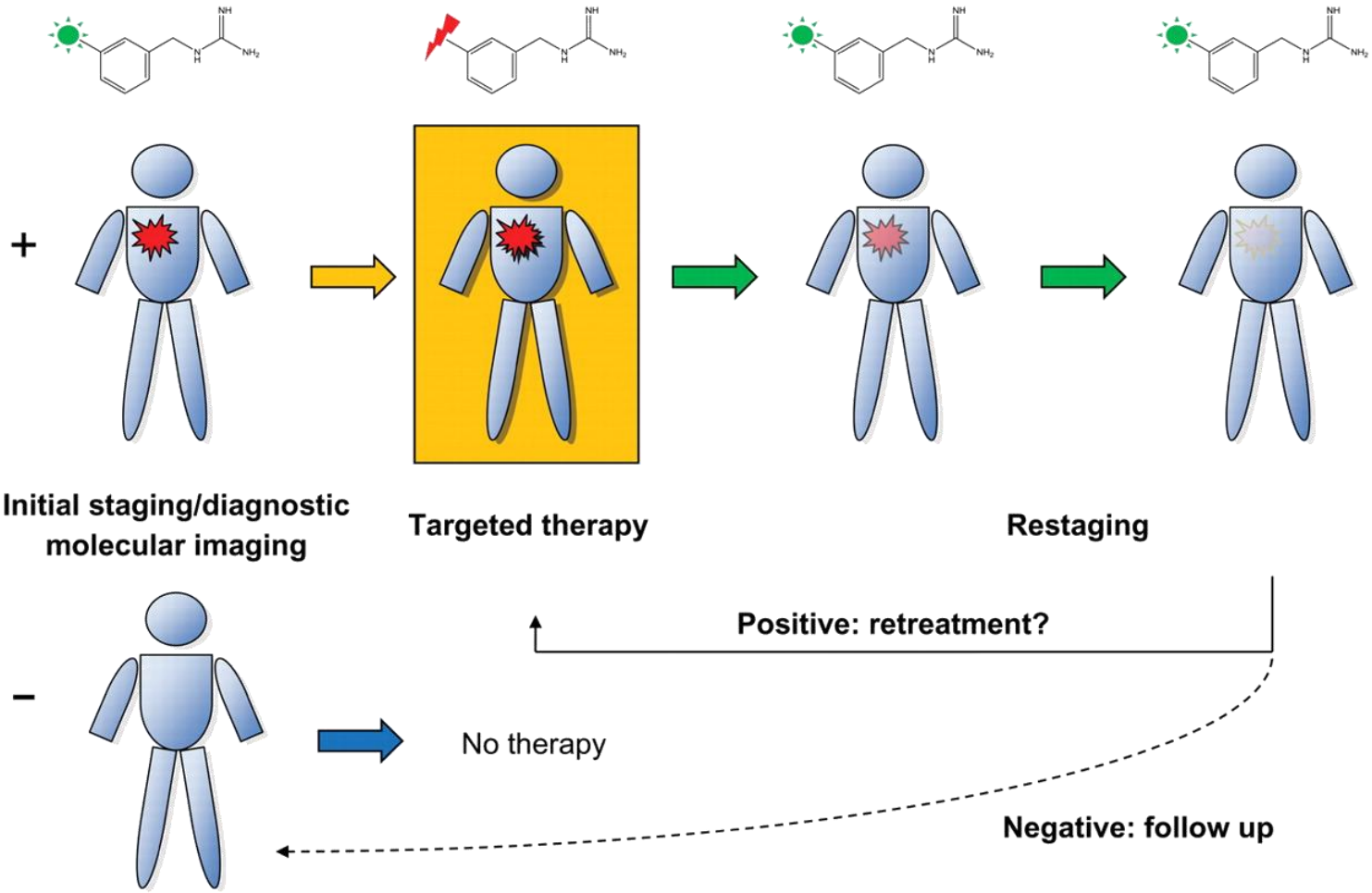
Theranostics

Personalized Medicine



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Theranostics in NETs

- ^{68}Ga labeled somatostatin analogs(derivatives of octreotide, lanreotide) for diagnosis
- ^{177}Lu and ^{90}Y labeled to identical/similar analog for PRRNT
- Advantages of peptide-based targeting:
- Better pharmacokinetics
- Minimal/no antigenicity

OR

Use of therapeutic radionuclide to image biodistribution during therapy

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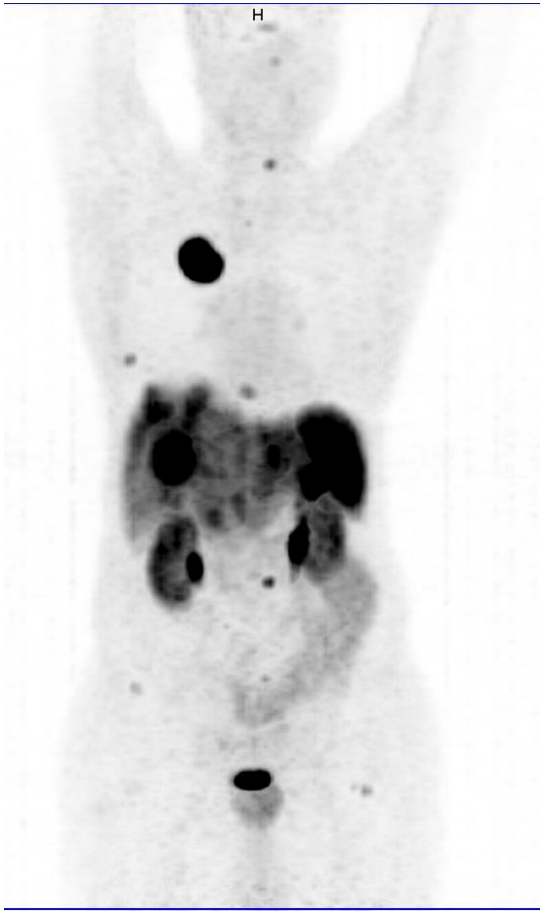
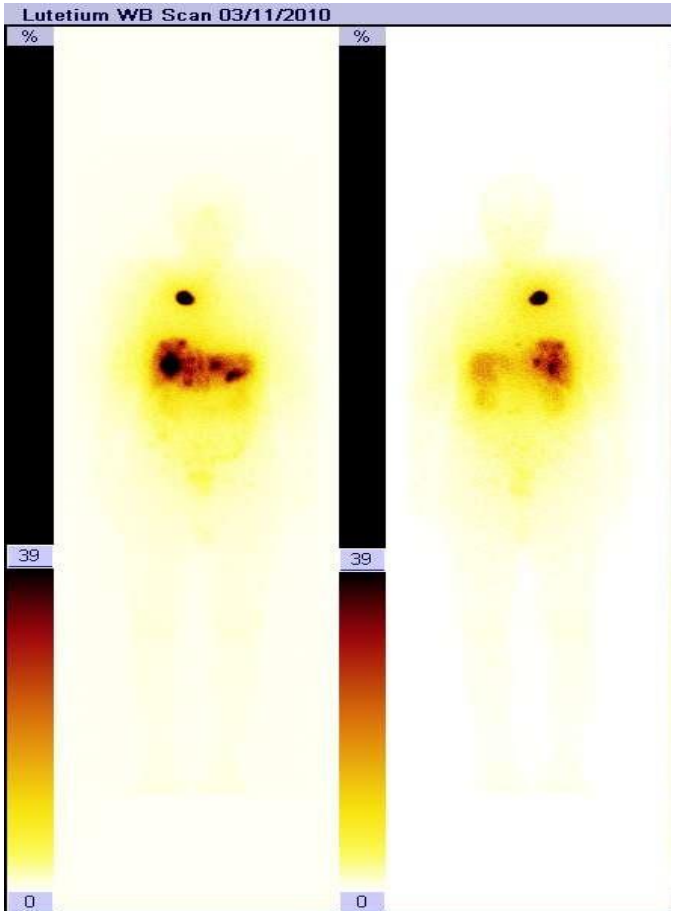
Theranostics in NETs



^{68}Ga-DOTATOC



^{177}Lu-DOTATOC

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Thank you for your Attention

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