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Preclinical Imaging in Small Laboratory Animals
Instrumentation and Application

Imaging in Oncology & Thera(g)nostics

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Tumor Imaging
Indications

- Diagnosis
  - Identification
  - Staging/re-staging
- Identification of recurrence or residual disease
- Monitoring therapy response
- Evaluating Prognosis
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
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
Ga-67 citrate
Lymphoma
Ga-67 citrate
Lymphoma
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!
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
Papillary Thyroid Carcinoma
Metastatic Thyroid Carcinoma
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!
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.
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).
Mama Carcinoma

$^{99m}$Tc-Sestamibi

BSGI Case Study: Left infiltrating ductal carcinoma & axillary metastasis.
**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.
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
In-111 Pentetreotide (Octreoscan)
Merkel Cell Tumor
In-111 Pentetretotide (Octreoscan)
Metastatic Carcinoid with Meningioma
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.

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, ….)
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, ….)
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.
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
Thera(g)nostics
Therapy meets Diagnostics

• Thera(nostics) 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
• Thera(nostics) is a term that has been used in the context of molecular targeting vectors (e.g., 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
Theranostics
Personalized Medicine

Initial staging/diagnostic molecular imaging → Targeted therapy → Restaging

Positive: retreatment?  

No therapy

Negative: follow up

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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
Theranostics in NETs

$^{68}$Ga-DOTATOC

$^{177}$Lu-DOTATOC
THANK YOU FOR YOUR ATTENTION