

PRECLINICAL AND CLINICAL NUCLEAR MEDICINE

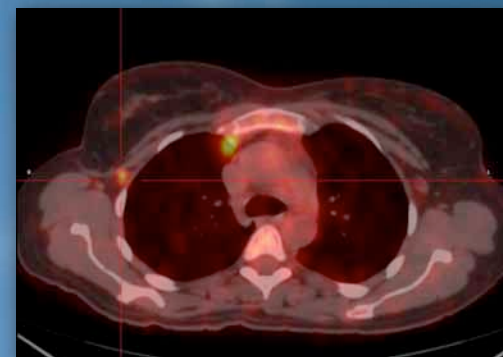
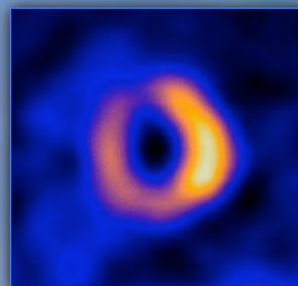
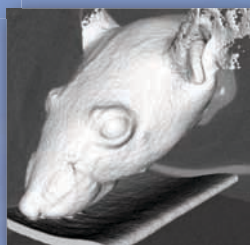
SELECTED TRANSLATIONAL EXAMPLES



Pr André Constantinesco, MD, PhD

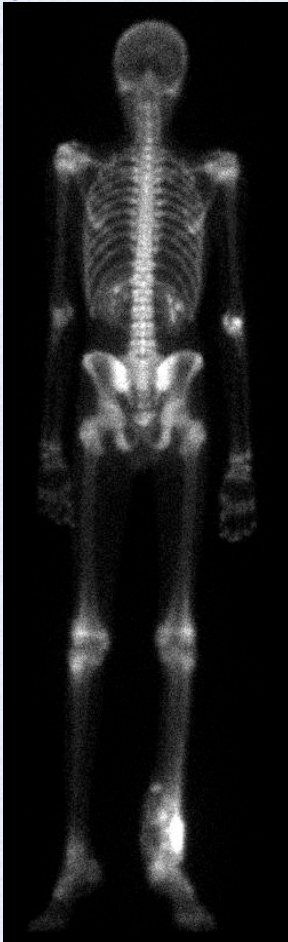
Service de Biophysique et Médecine Nucléaire
Hôpitaux Universitaires de Strasbourg
&
IMFS-CNRS

European Summer University 2009



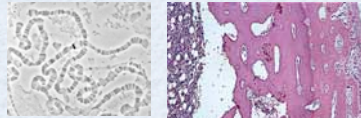
translational medicine: “preclinical & clinical molecular imaging”

clinical imaging
diagnosis & follow-up

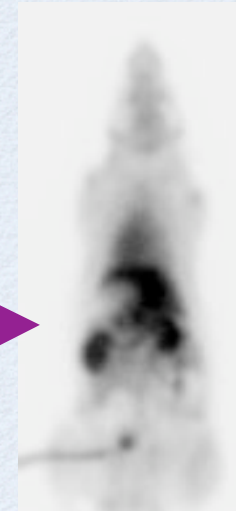


gene

cell



preclinical imaging
(small animal models)

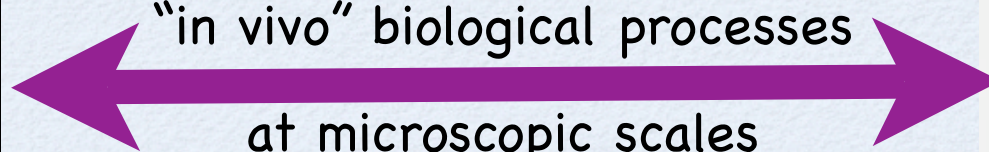


“molecular imaging”

aim at observe and understand

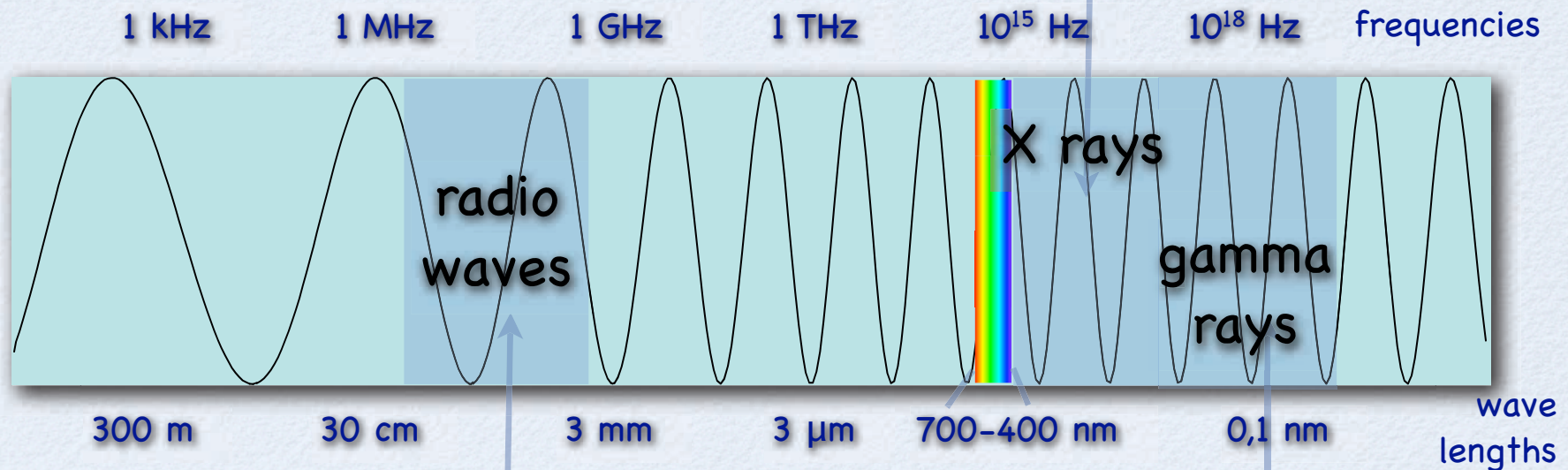
“in vivo” biological processes

at microscopic scales



translational medicine

electromagnetic waves and... Radiology



MRI

**Nuclear
Medicine**

...medical imaging

nuclear medicine and "molecular imaging"

Vector

- small molecule
- virus
- cell
- antibody
- peptide
- nanoparticle
- ...

Disease

- inflammation
- neuro-degenerative
- tumoral
- infectious
- ...

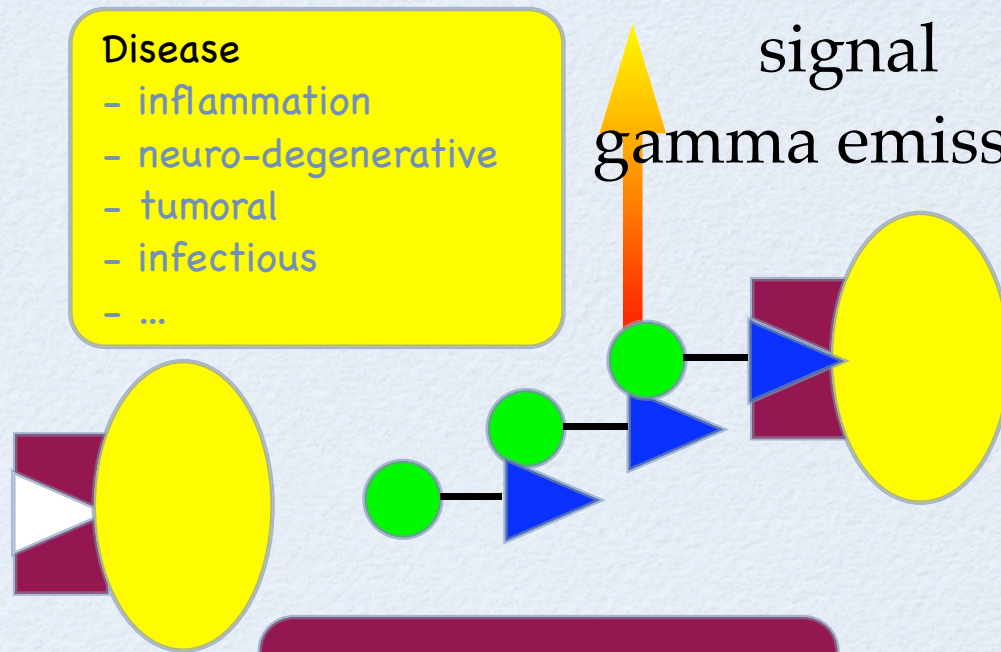
signal
gamma emission

radio-pharmaceutical

contrast agent
- isotope

Target

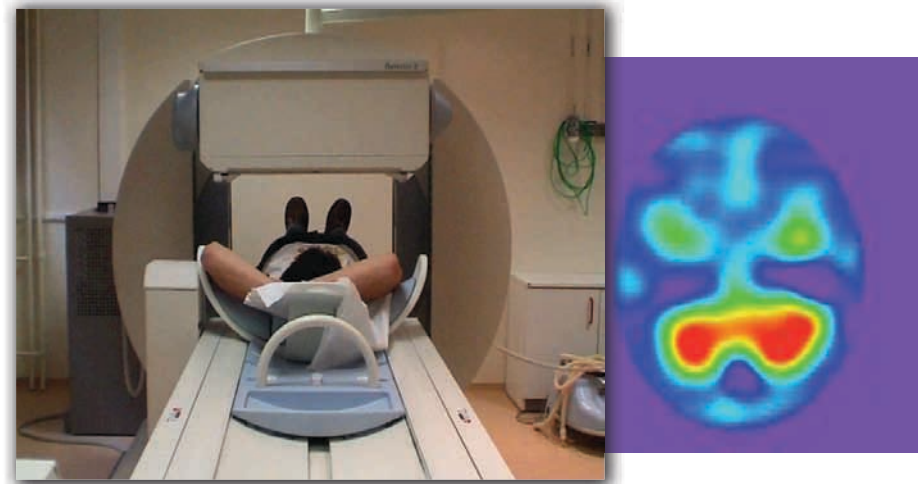
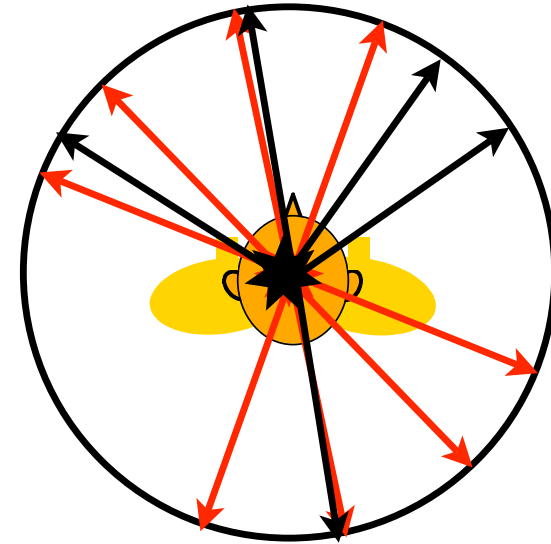
- physiological state
- perfusion
- cell & tissue metabolisms
- receptor
- transporter
- ...

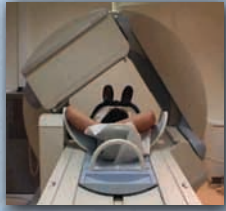


clinical nuclear imaging

radio-pharmaceutical 

- **Positron Emission Tomography (PET)**
- **Single Photon Emission Tomography (SPECT)**





examples of **SPECT** radiopharmaceuticals

- Phosphonates- **^{99m}Tc** (Bone Metabolism)
- Dimercaptosuccinic Acid- **^{99m}Tc** (Renal Tubule)
- Mebrofenin - **^{99m}Tc** (Hepato-Biliary Function)
- Thallium 201** (Myocardium, Muscle, Tumors)
- Red Blood Cells - **^{99m}Tc** (Blood Pool)
- White Blood Cells - **^{111}In** (Sepsis)
- Iodine 123** (Thyroid)
- Ethyl Cysteinate Dimer - **^{99m}Tc** (Brain Perfusion)
- Krypton 81m** (Pulmonary Ventilation)
- Albumin - **^{99m}Tc** (Pulmonary Perfusion)
- Beta CIT- **^{123}I** (Dopamin Transporter)
- ...

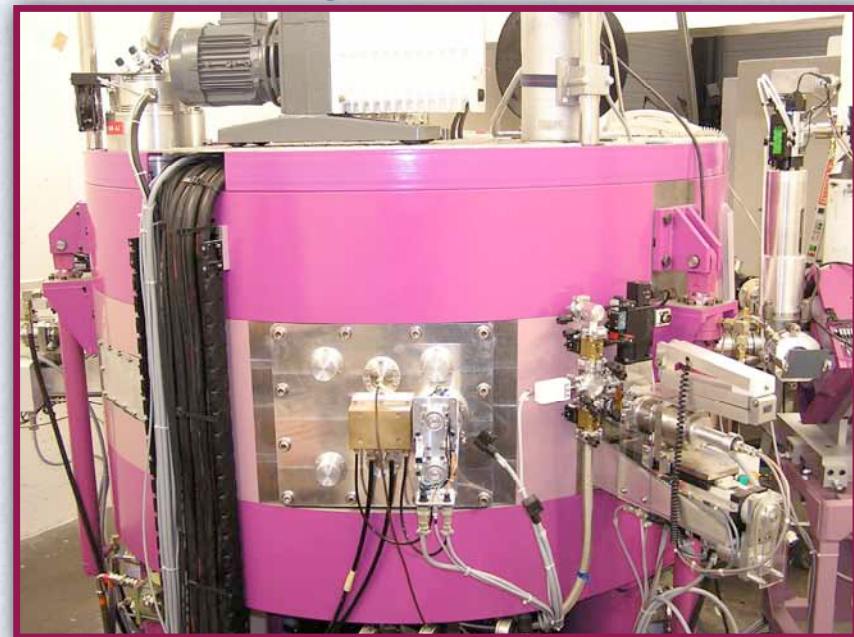




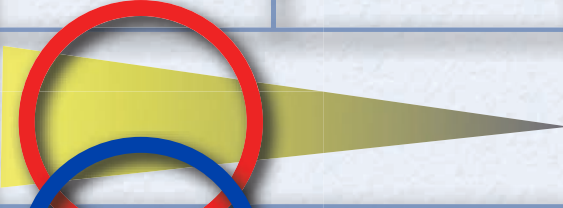

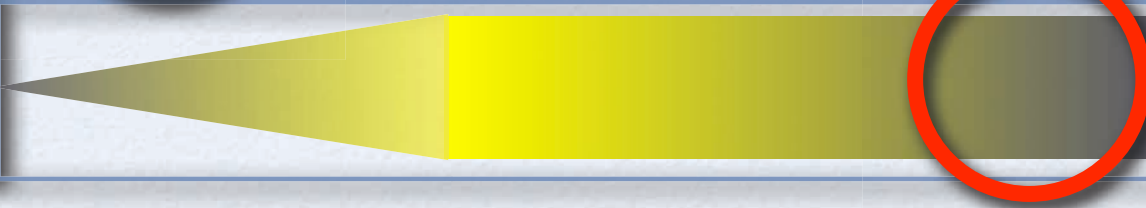
examples of PET radio-pharmaceuticals

- Deoxyglucose -¹⁸F (Glucose metabolism)
- Fluoro-thymidine -¹⁸F (Cell proliferation)
- Dopamine -¹⁸F (Receptors)
- Met-¹¹C (Protein synthesis)
- Choline-¹¹C (Cell membranes)
- Dotatoc -⁶⁸Ga (Somatostatin receptors)
- ...

cyclotron

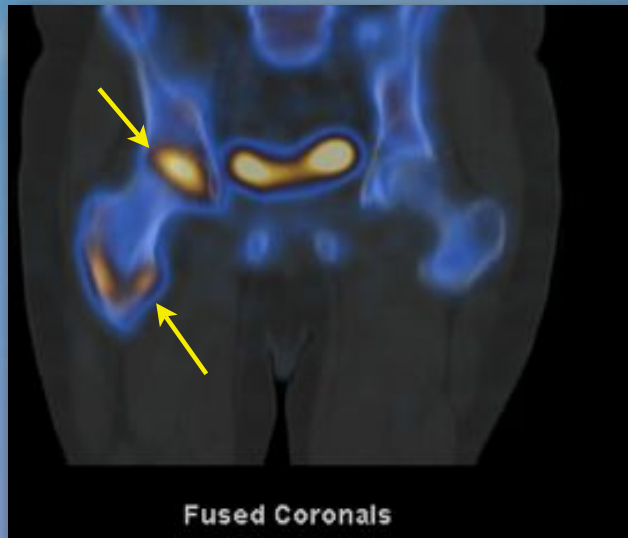


resolution(s) & sensitivities(s)

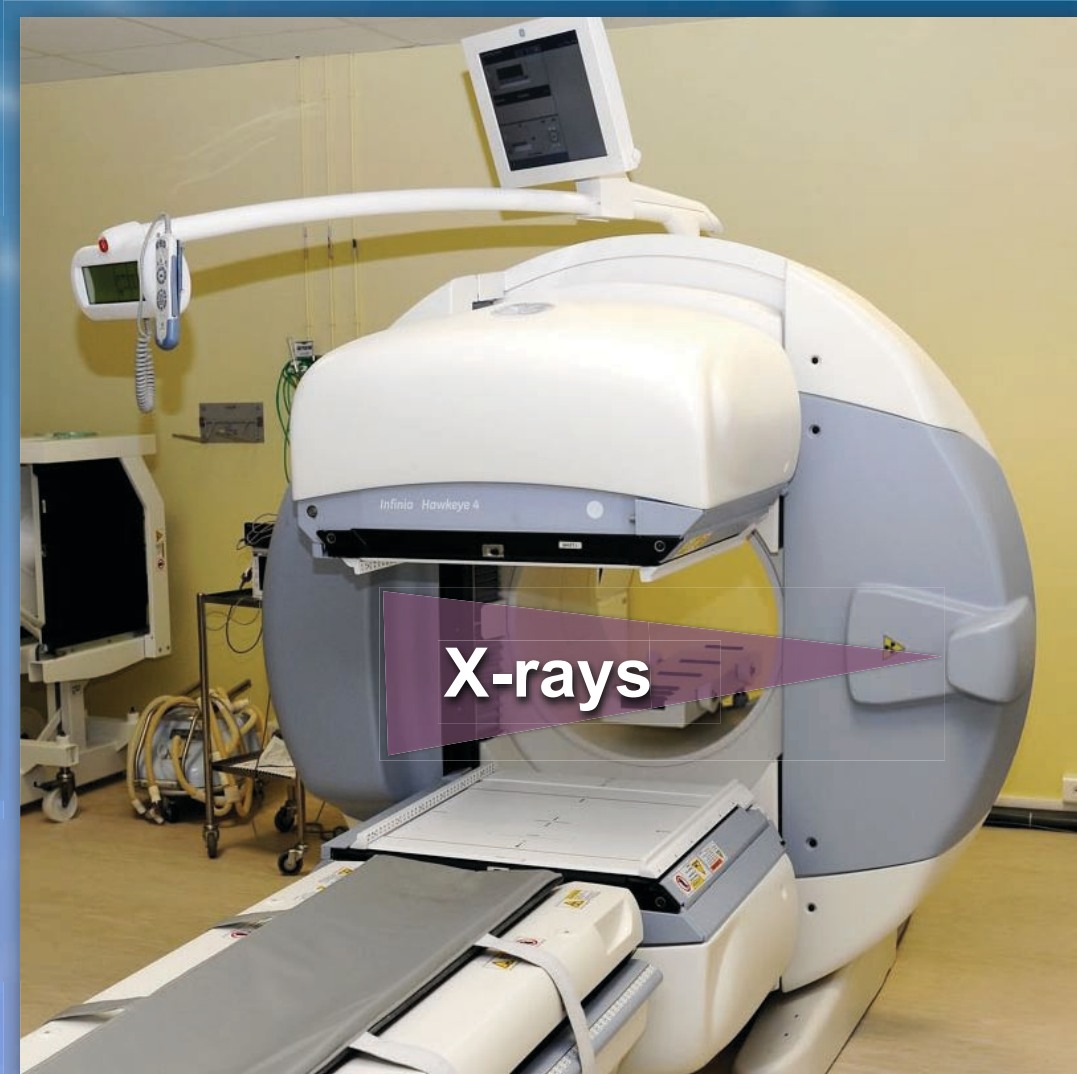
| RESOLUTION | Anatomical | Physiological | Metabolical | Molecular | SENSITIVITY |
|-------------|---|---------------|-------------|-----------|-------------|
| CT |  | | | | milli molar |
| MRI |  | | | | micro molar |
| PET & SPECT |  | | | | pico molar |

hybrid scanners: **SPECT-CT, PET-CT, PET/SPECT-MRI**
"multimodality imaging"

clinical SPECT-CT camera



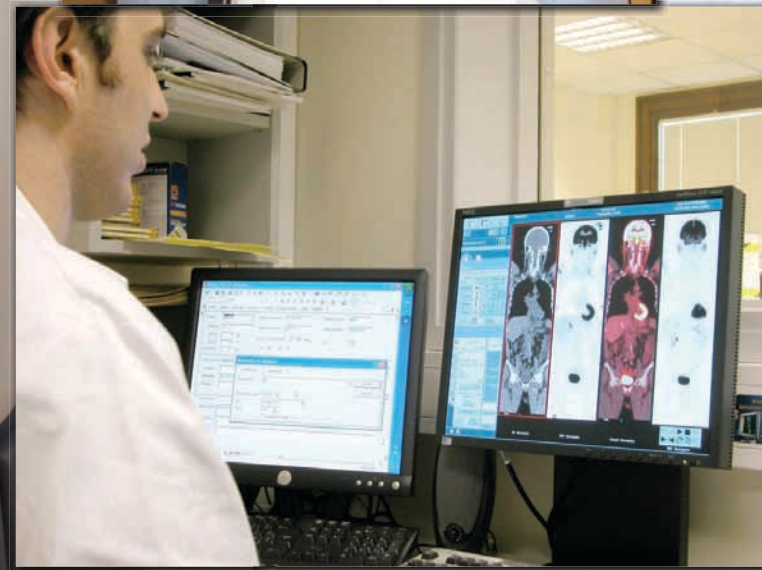
side by side CT and
SPECT cameras



clinical PET-CT camera

side by side CT and PET cameras

PET: molecular imaging
CT: anatomical imaging

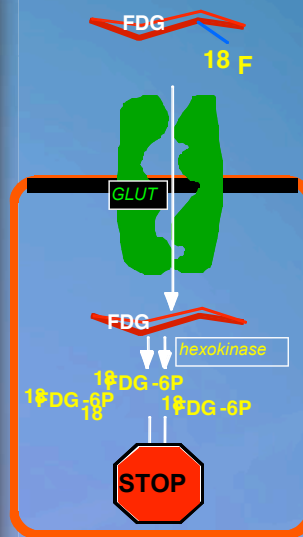


metabolism of ^{18}F -D_éoxyG_lucose (FDG) in oncology using PET scanner

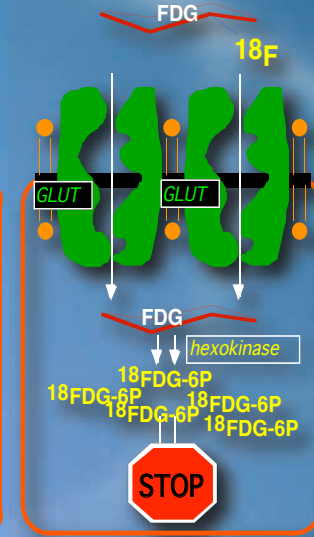
- ↑ GLUT1 cell proliferation
- ↑ hexokinase reflecting cell viability



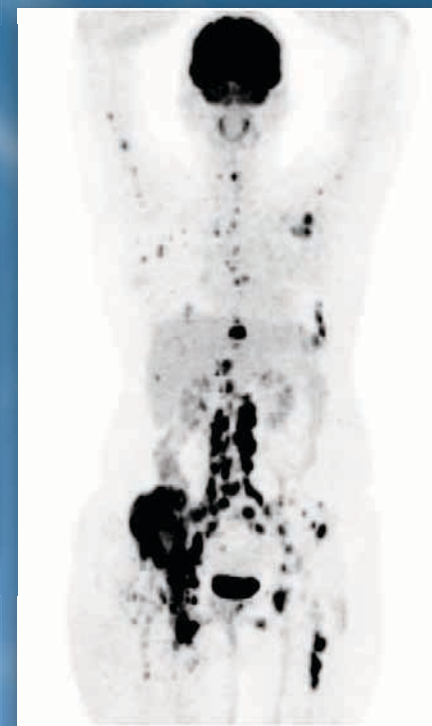
normal biodistribution of ^{18}F FDG



normal cell

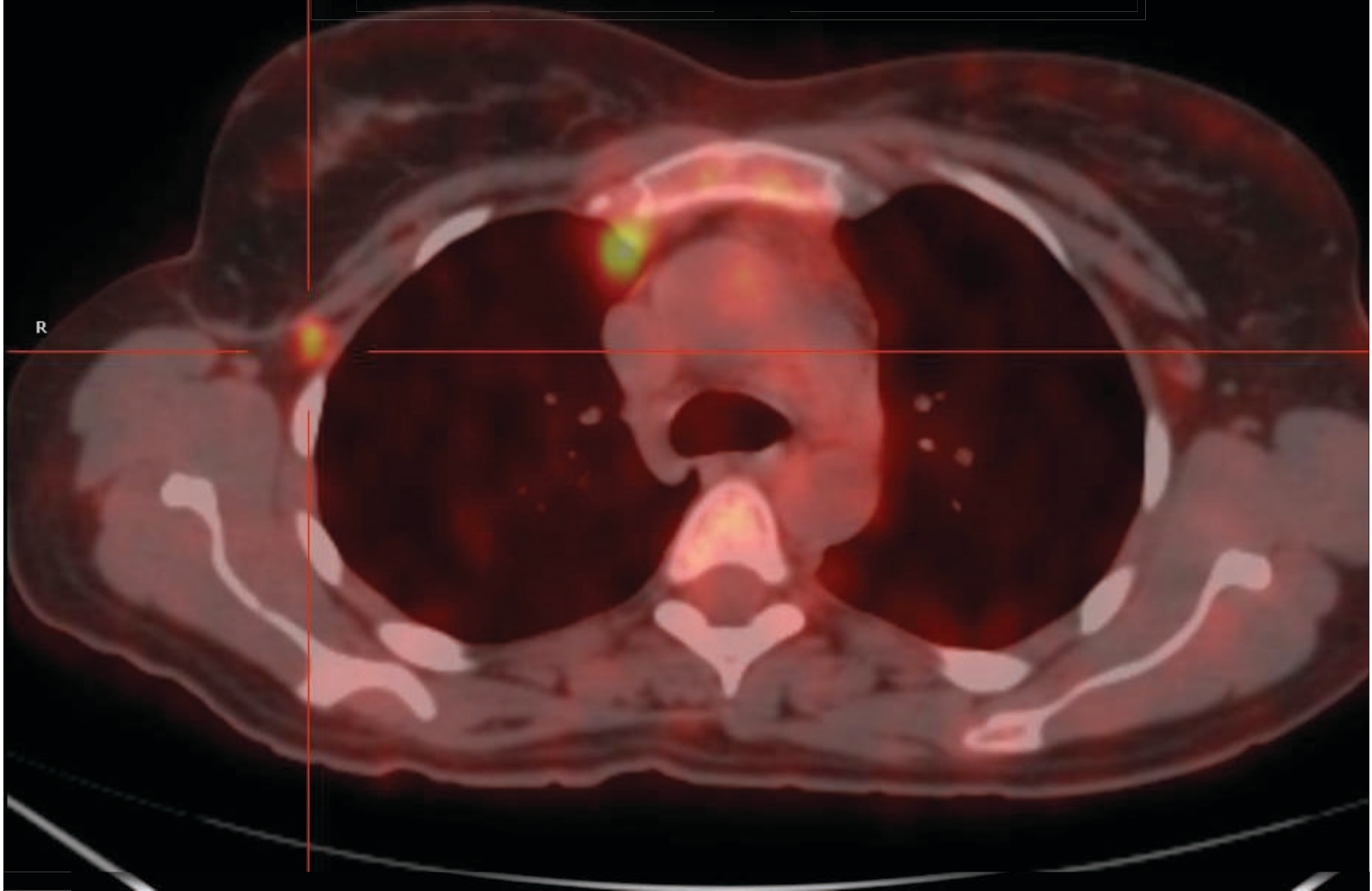


tumor cell

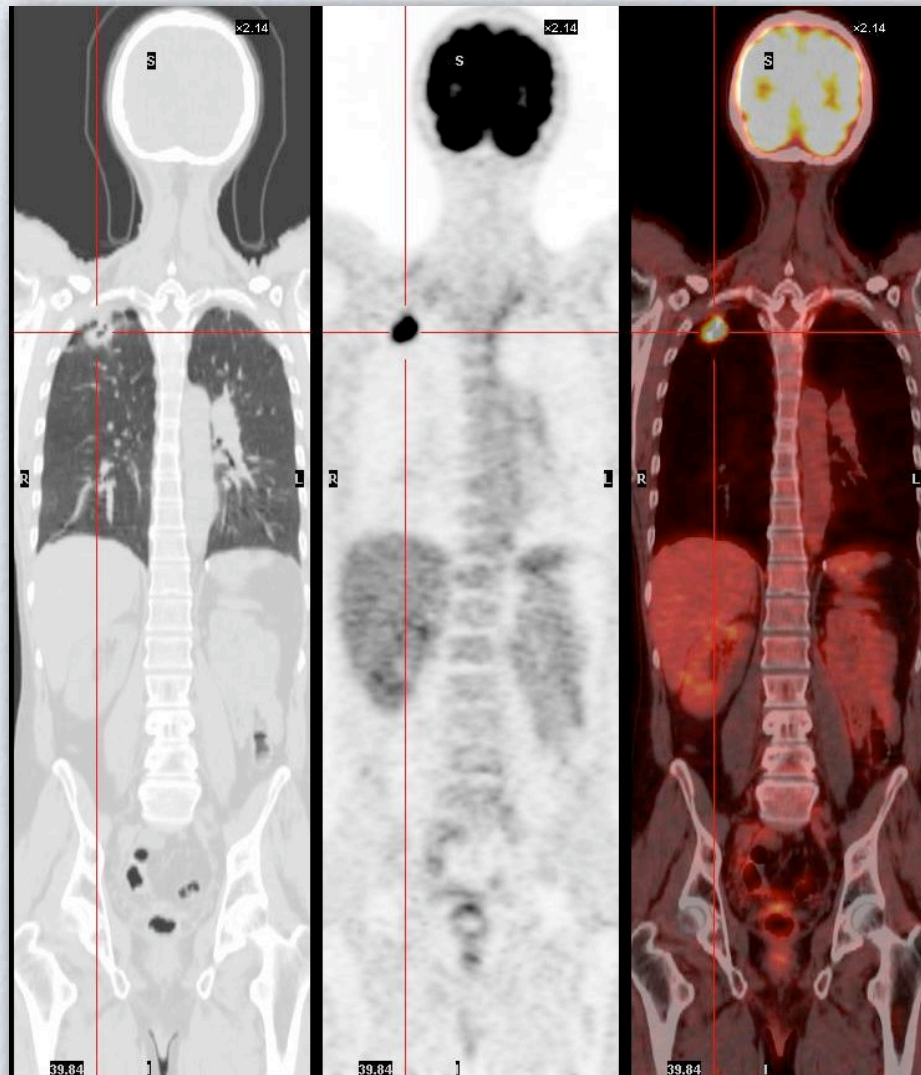


metastatic breast cancer

^{18}F FDG PET-CT image fusion



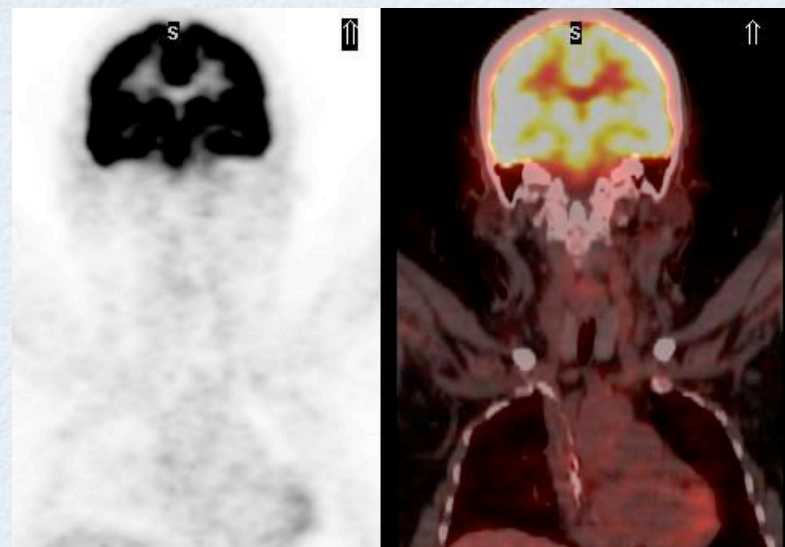
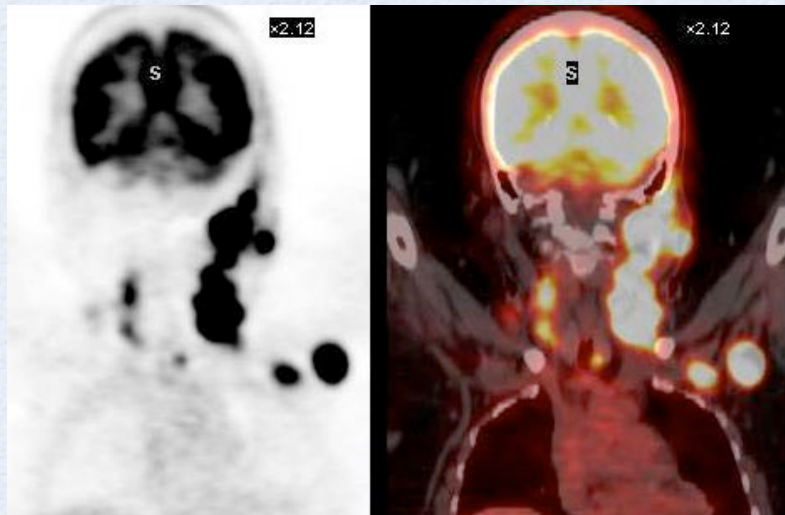
oncology: pulmonary nodule



"PET-CT"
 ^{18}F FDG

oncology: follow-up and control of chemotherapy

"PET-CT"
 ^{18}F FDG



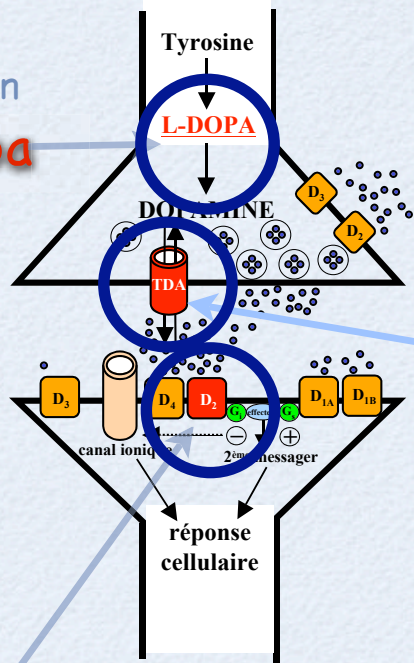
before
chemotherapy



after
chemotherapy

neurology: PET & SPECT imaging of dopamine metabolism

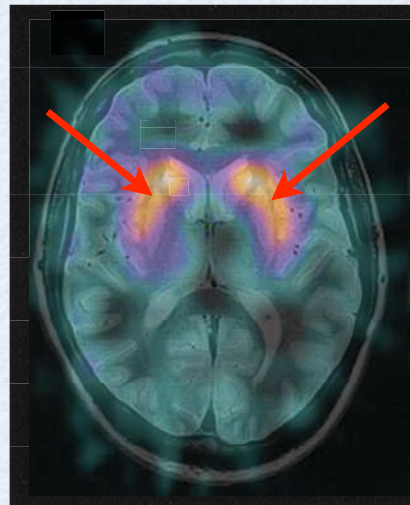
tracer of dopamine production
 ^{18}F -Dopa



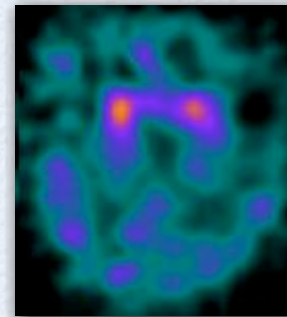
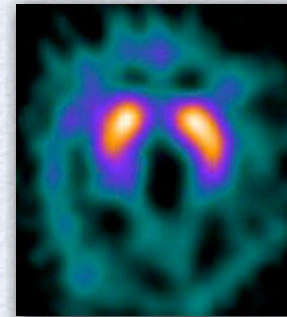
tracer of presynaptic transporter of dopamine
 ^{123}I FPCIT

tracer of post synaptic receptor of dopamine
 ^{123}I -IBZM

**SYNAPSE
DOPAMINERGIQUE**



normal

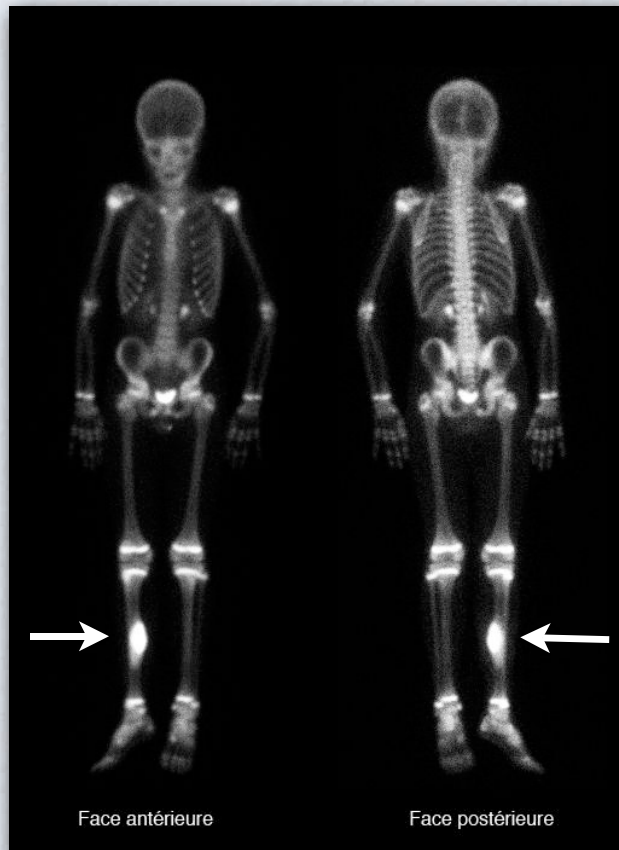


Parkinson disease



clinical multimodality imaging **MRI, SPECT, PET-CT** & tumor metabolism

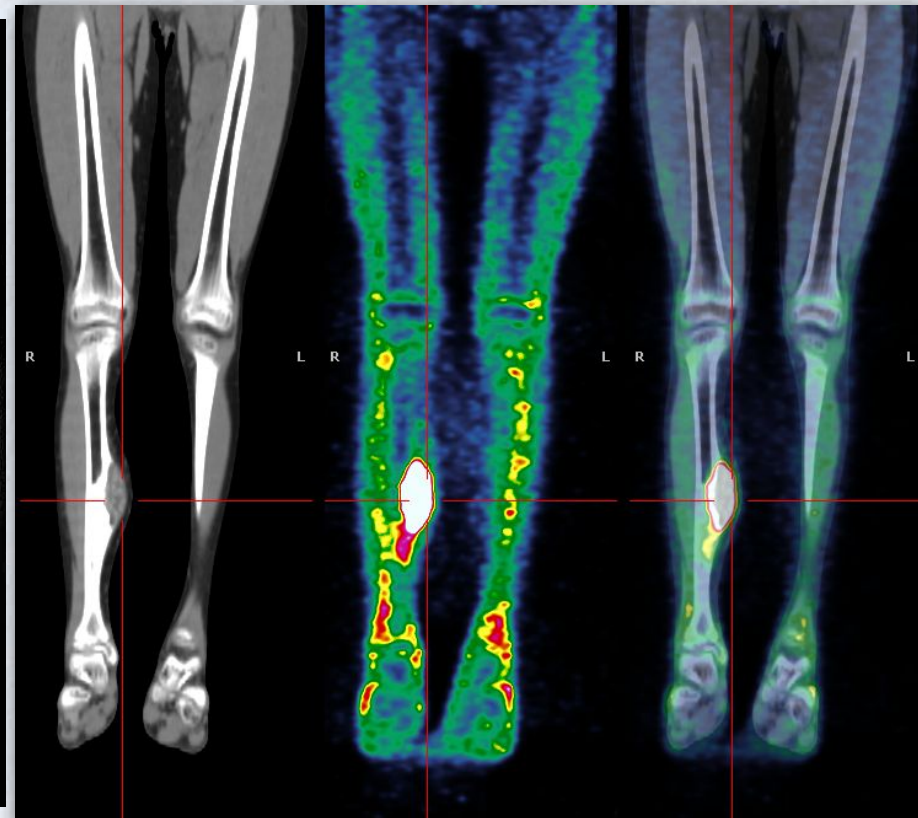
child (9 years old), staging of right tibial osteosarcoma



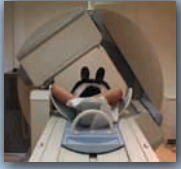
$^{99m}\text{Tc-MDP}$ Bone Scan



MRI



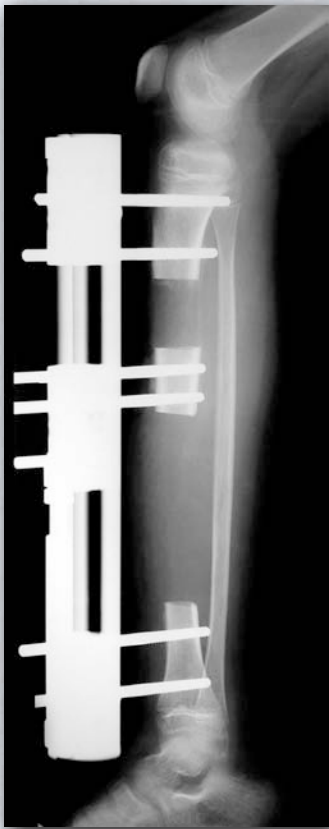
^{18}F FDG (PET-CT)



clinical multimodality imaging **MRI, SPECT,** **PET-CT** & tumor metabolism

child (9 years old), treatment of right tibial osteosarcoma

surgery following
chemotherapy



final surgery step



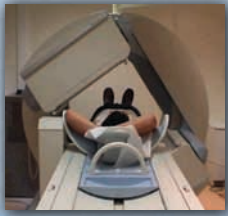
efficacy of pre-operative
chemotherapy is assessed by
imaging and biopsies



before chemotherapy

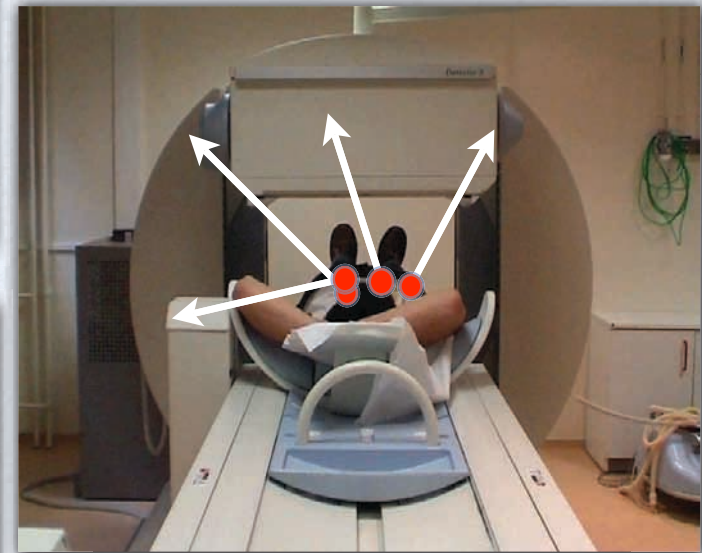
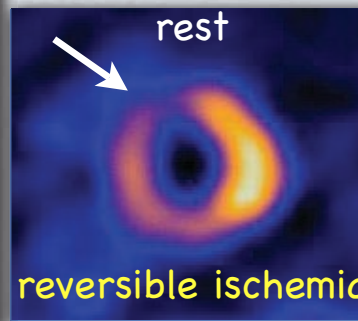
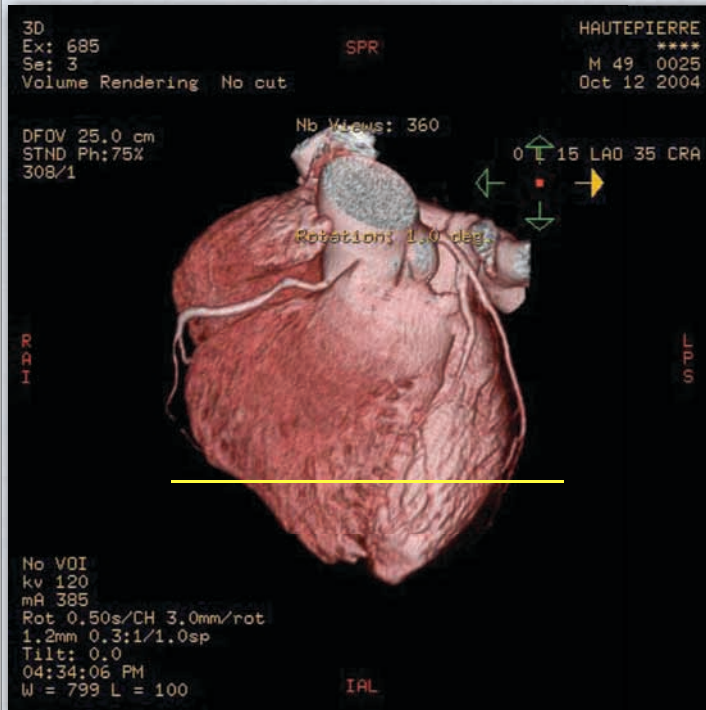


after chemotherapy



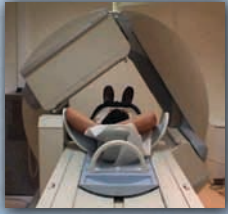
cardiology: coronary artery disease & myocardial perfusion

mid ventricular Left Ventricle slice

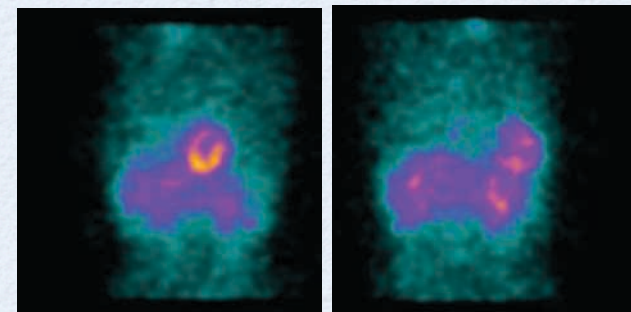
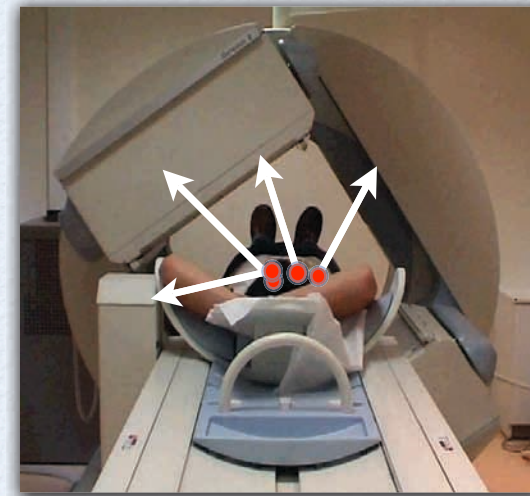
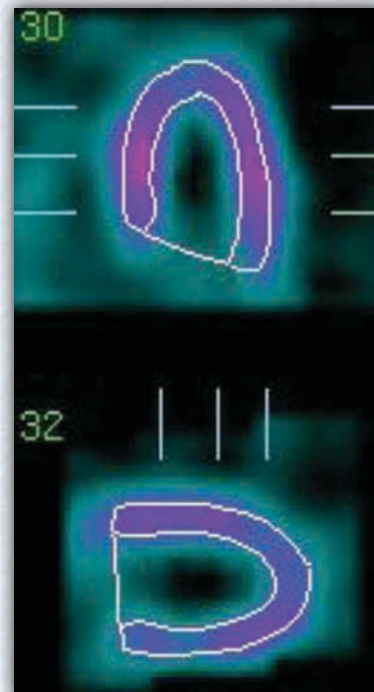
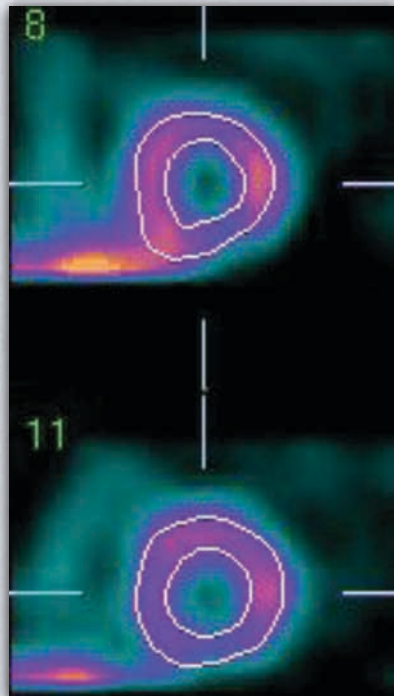


^{201}Tl -SPECT

tracer uptake (^{201}Tl) by myocardium is proportional to coronary blood flow

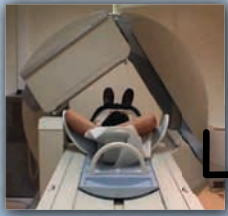


cardiology: coronary artery disease
& Left Ventricle mechanical function



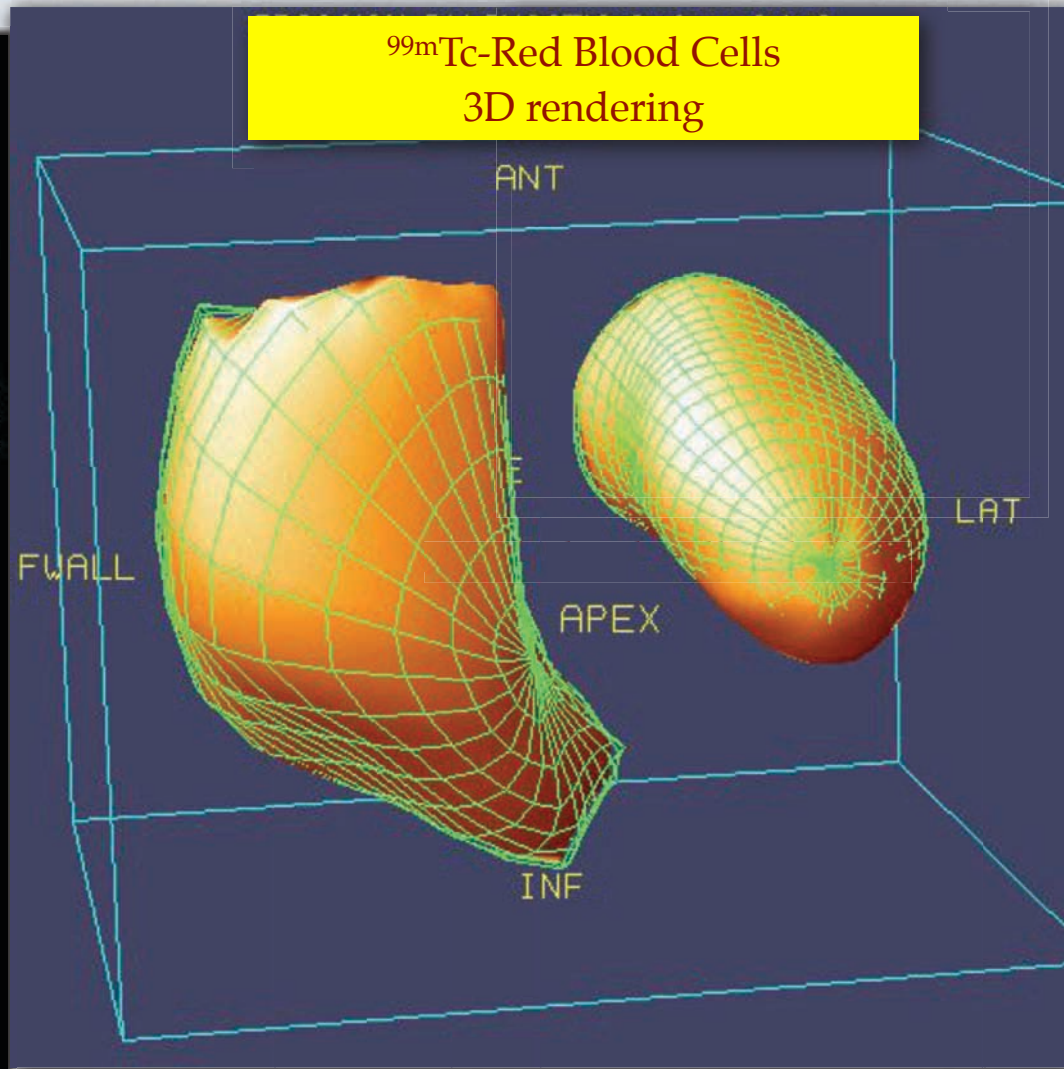
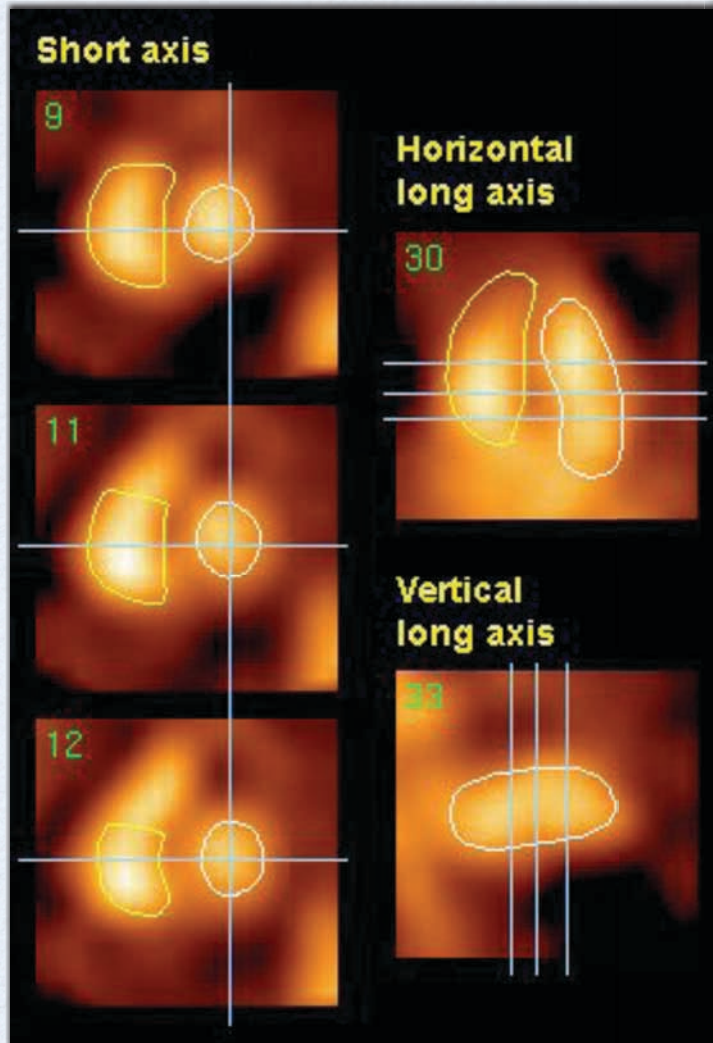
ECG gating

^{201}Tl : perfusion tracer



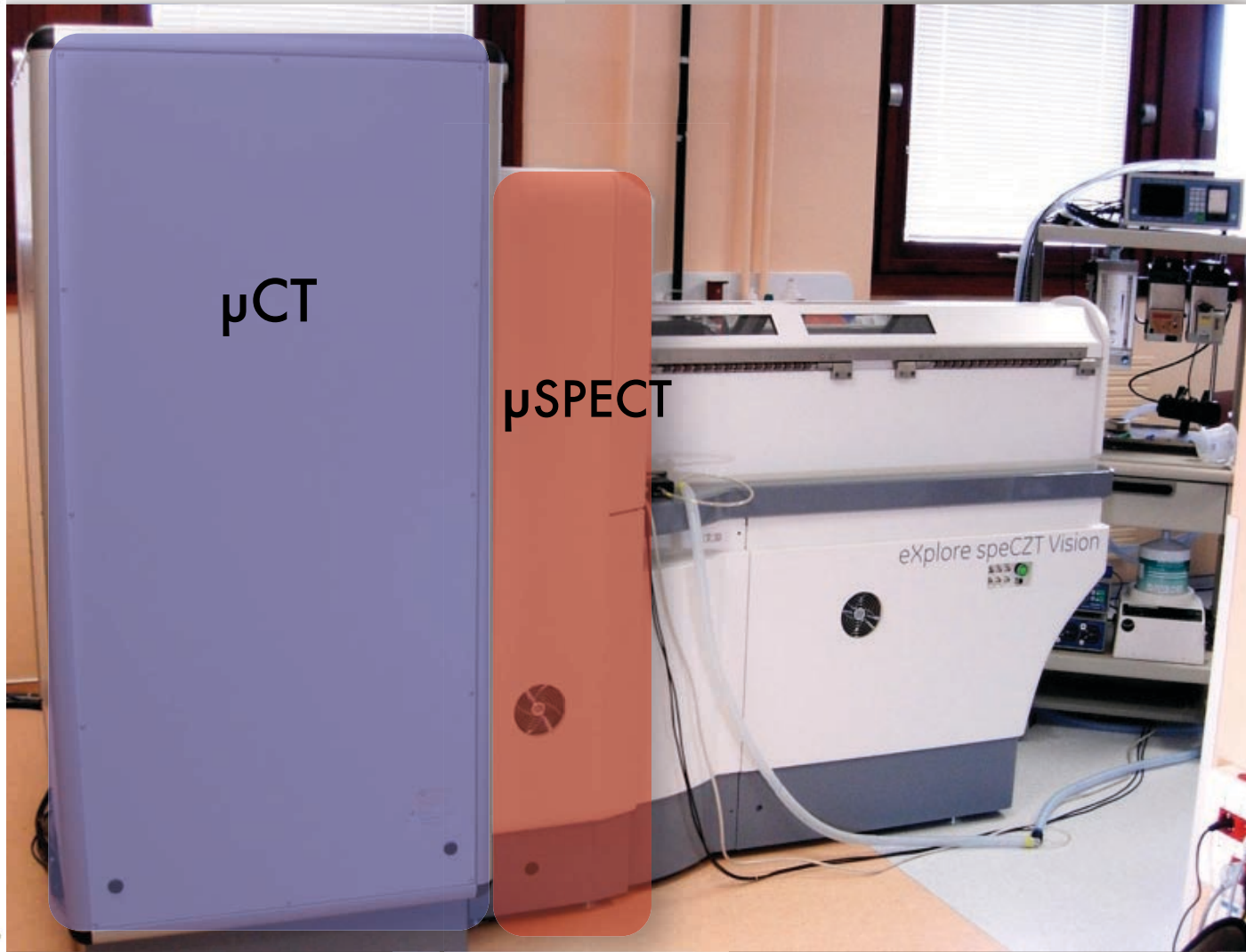
cardiology: coronary artery disease:

Left & Right Ventricles mechanical functions



● **PRECLINICAL multimodality micro SPECT-CT**

eXplore speCZT vision 120



3D preclinical SPECT/CT mouse imaging

SPECT



^{99m}Tc -MDP, 150 MBq IV

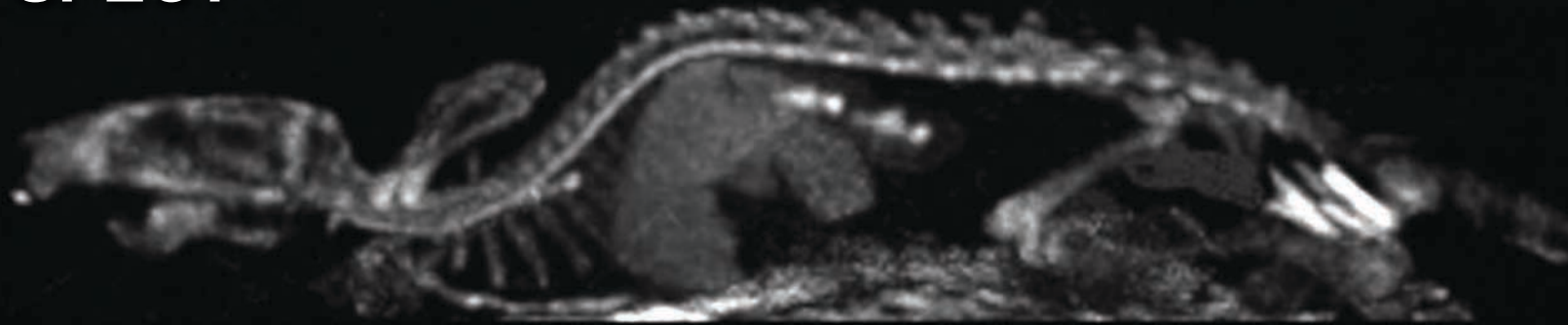
CT



MIP images

3D preclinical SPECT/CT mouse imaging

SPECT



^{99m}Tc -MDP, 150 MBq IV

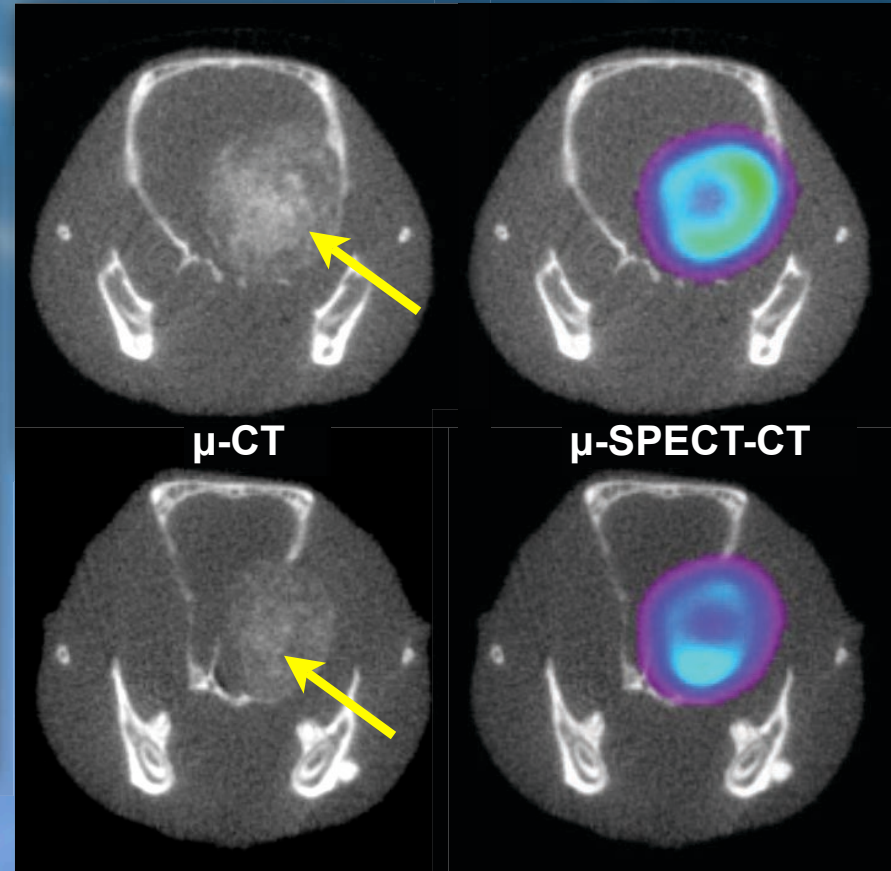
CT



MIP images



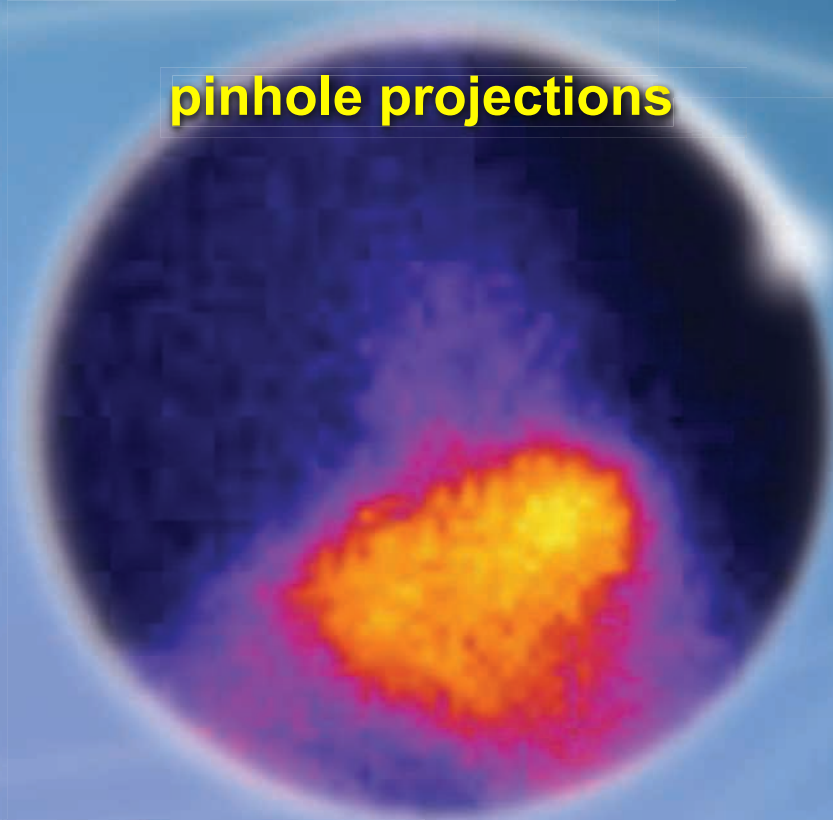
preclinical μ -SPECT-CT in transgenic **APC \times TWIST** mice: model of osteosarcoma bone tumor



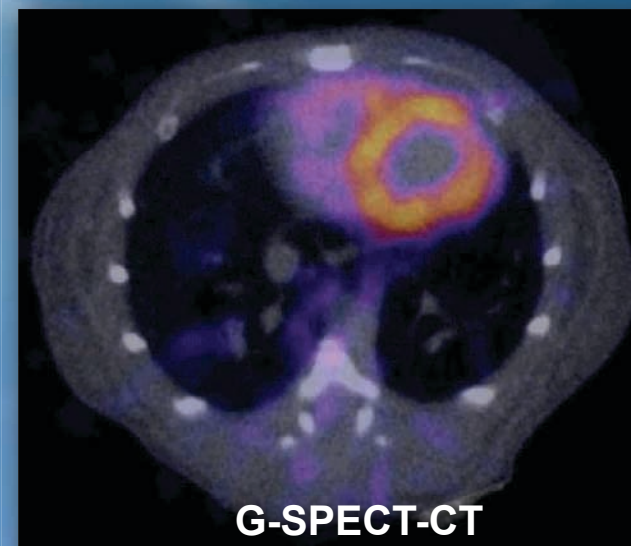
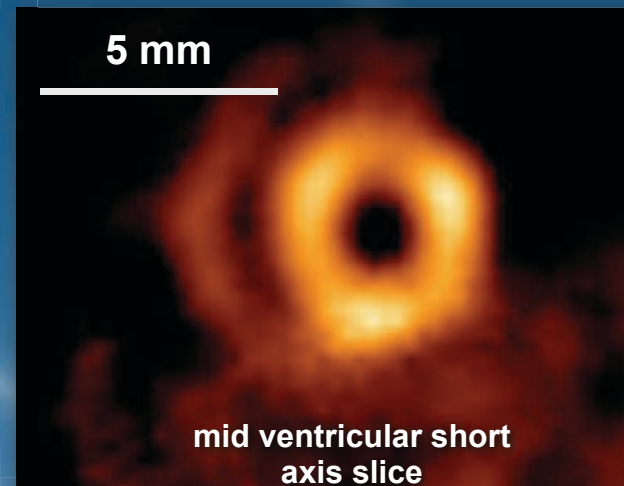
histology **directed** by preclinical imaging confirmed
chondroblastic osteosarcomas subtypes in most cases

**cardiac μ -SPECT in mice:
normal perfusion**

pinhole projections

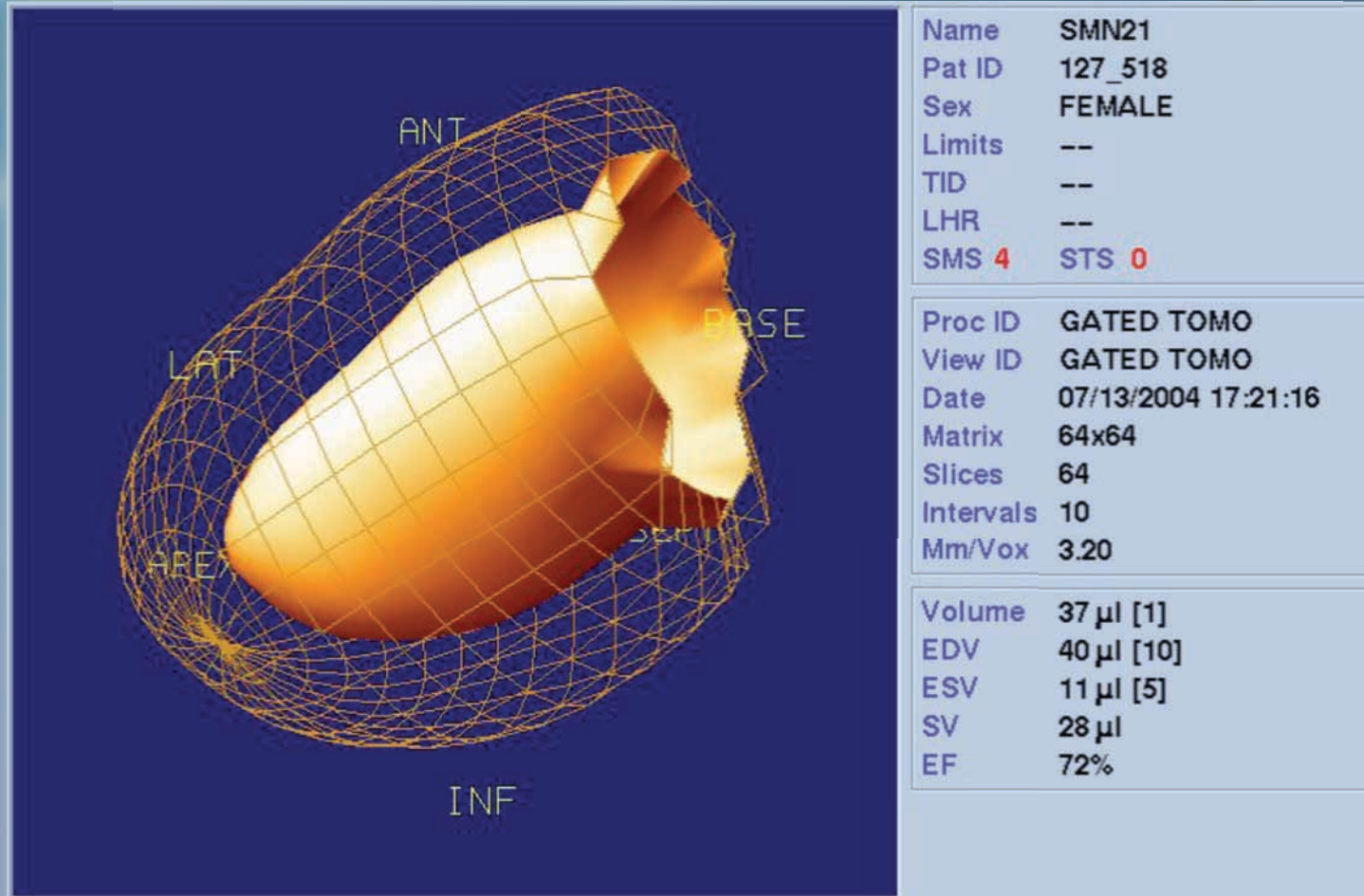


CD1 mouse, 27g
300 MBq ^{99m}Tc -tetrofosmin
0.2 mL IV



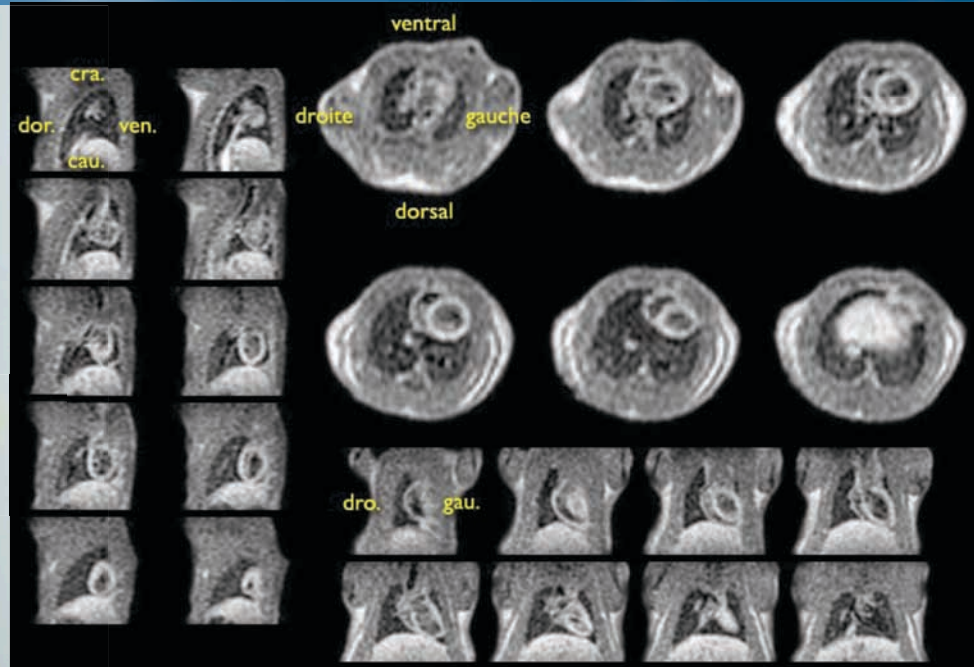
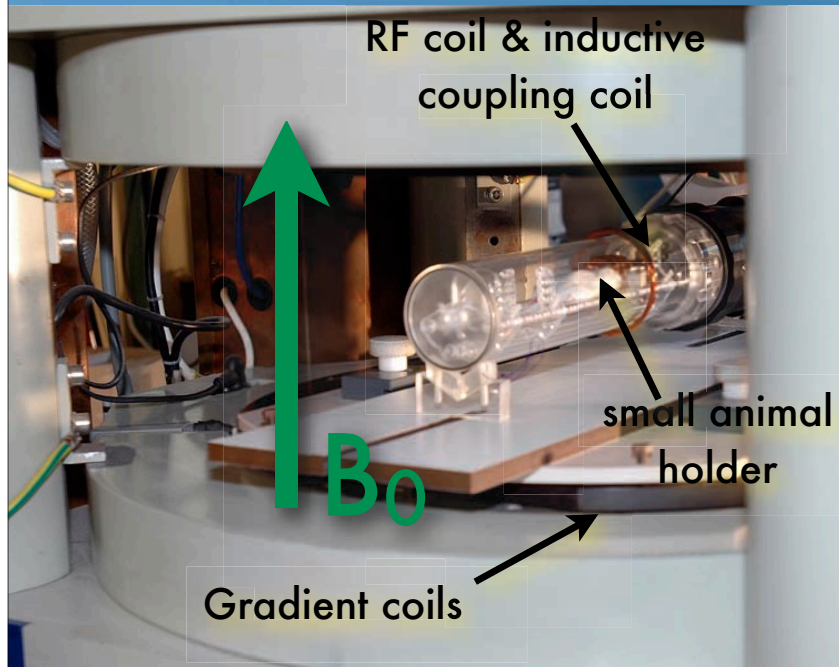
- C.Goetz et al. *CR Biol* 2008;331:637-647
- A. Constantinesco et al. *J Nucl Med* 2005, 46; 1005-1011

perfusion **Gated-SPECT** & 3D left ventricle volume rendering



L.Monassier, A. Constantinesco. in "Standards of Mouse Models Phenotyping" De Angelis, Chambon & Brown Eds. Wiley 2006: pp177-199

preclinical **MRI** & **SPECT** imaging

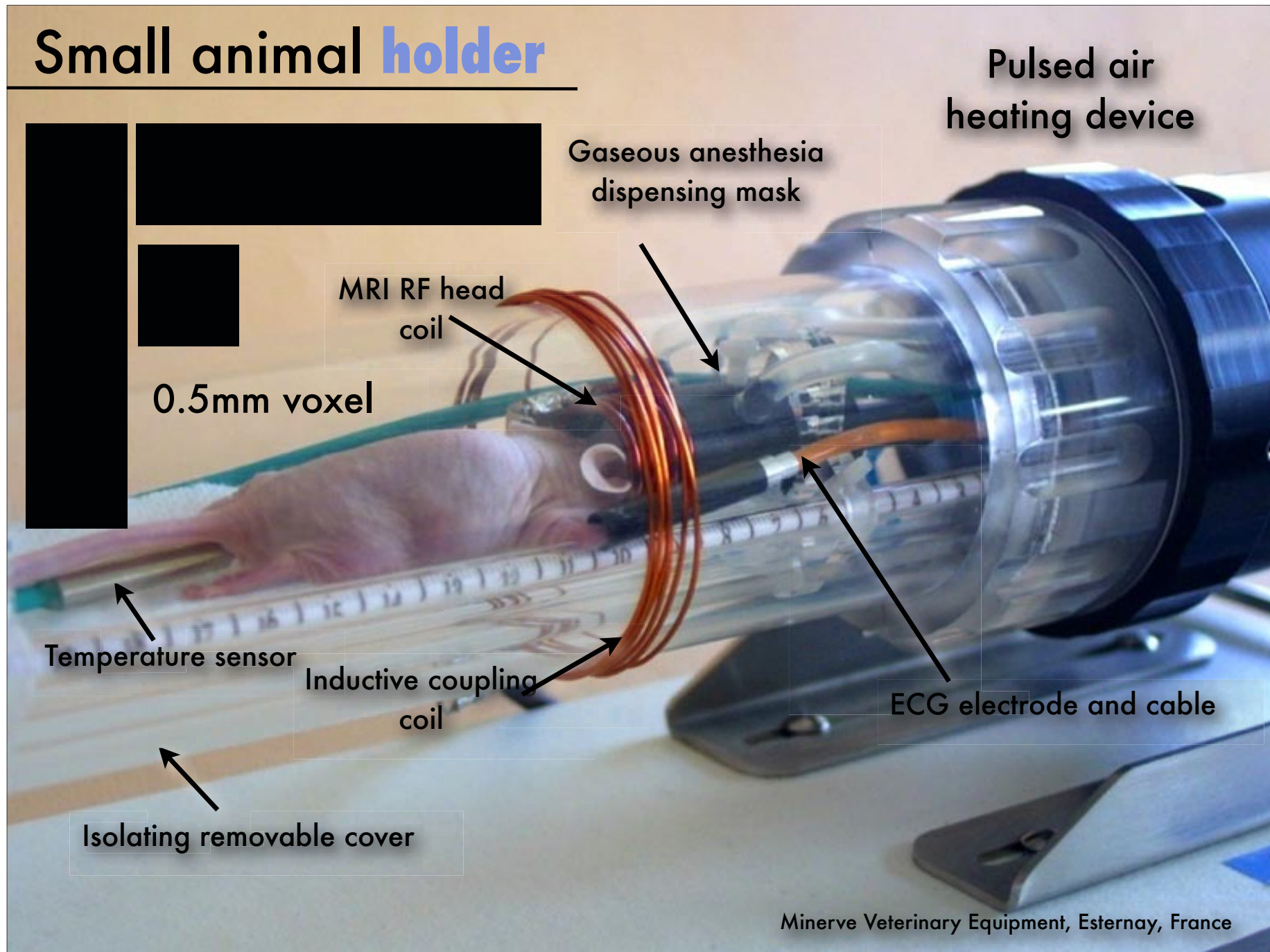


0.1 Tesla MRI

T1 weighted cine-MRI of rat heart

- E.Breton et al. *Nucl Inst Methods A* 2007;49:88-93
- C.Goetz et al. *J Nucl Med* 2008;49:88-93
- P.Choquet et al. *PMB* 2009 in press

Small animal holder



Pulsed air heating device

Gaseous anesthesia dispensing mask

MRI RF head coil

0.5mm voxel

Temperature sensor

Inductive coupling coil

ECG electrode and cable

Isolating removable cover

○ ● ● **SPECT MRI** imaging device



Acquisition
consoles



SPECT
device



MRI device



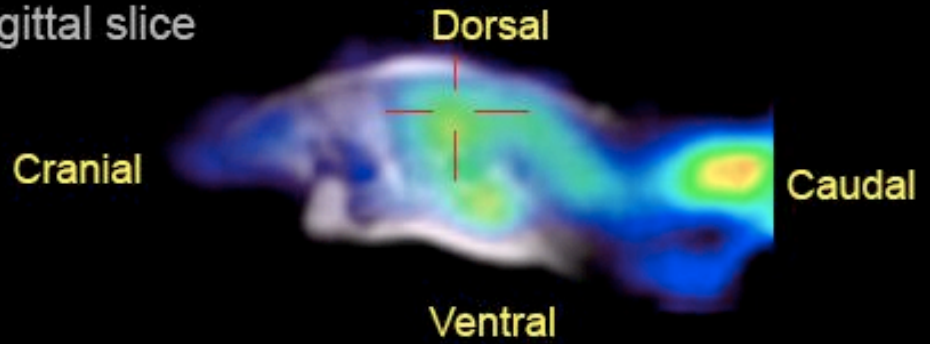
Small animal
monitoring &
anesthesia

Sagittal slices

color: brain perfusion ^{99m}Tc -HMPAO

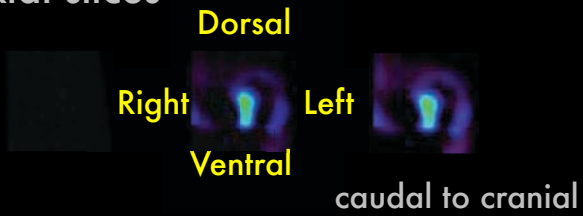
Dorsal
Cranial
Ventral
Caudal

Sagittal slice

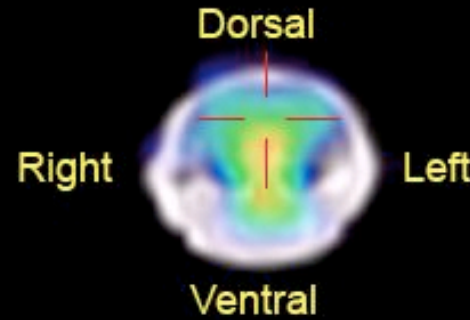


left to right

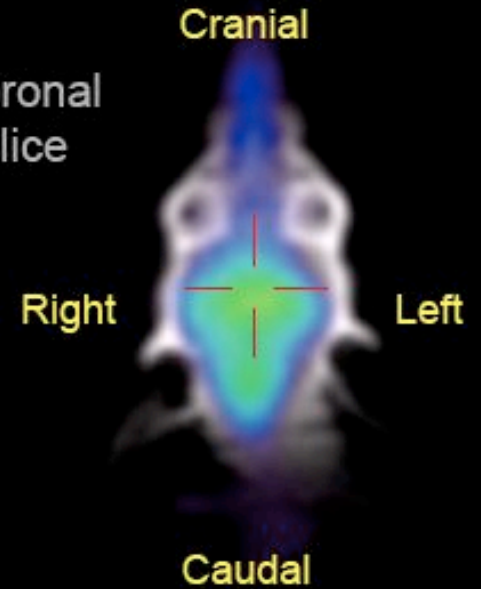
Axial slices



Axial slice



Coronal slice



Coronal slices

Cranial
Right
Left
Caudal
ventral to dorsal