microPET
Experiences with Small Animal PET Imaging

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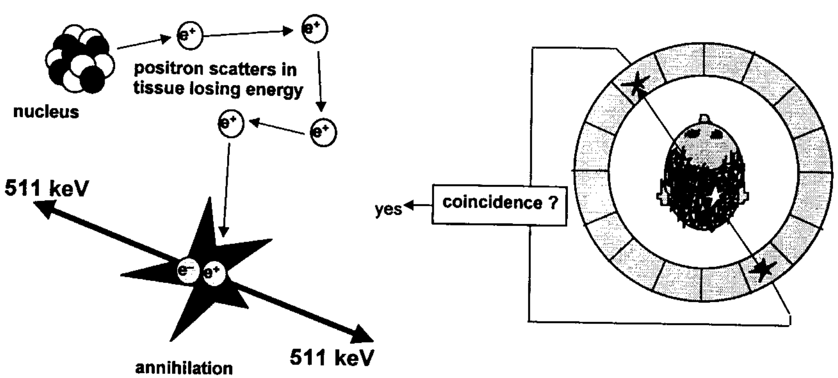
Outline

- PET Basics
- motivation for small animal PET
- design & performance of a small animal PET scanner
- applications for small animal PET

Positron Emission Tomography



Positron-Emitting Radionuclides

Isotope	Halflife	β^+ fraction	Max. Energy	range(mm)	production
C–11	20.4 mins	0.99	0.96 MeV	0.4 mm	cyclotron
N–13	9.96 mins	1.00	1.20 MeV	0.7 mm	cyclotron
O–15	123 secs	1.00	1.74 MeV	1.1 mm	cyclotron
F–18	110 mins	0.97	0.63 MeV	0.3 mm	cyclotron
Cu–62	9.74 mins	0.98	2.93 MeV	2.7 mm	generator
Cu-64	12.7 hours	0.19	0.65 MeV	0.3 mm	cyclotron
Ga–68	68.3 mins	0.88	1.83 MeV	1.2 mm	generator
Br-76	16.1 hours	1.00	1.90 MeV	1.2 mm	cyclotron
Rb–82	78 secs	0.96	3.15 MeV	2.8 mm	generator
I–124	4.18 days	0.22	1.50 MeV	0.9 mm	cyclotron

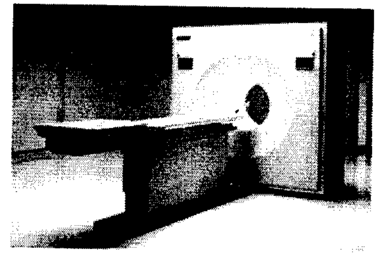
PET-labeled Probes for Biological Imaging

cyclotron
^{11}C, ^{13}N, ^{15}O, ^{18}F

- hemodynamic parameters ($H_2{}^{15}O$, ^{15}O-butanol, ^{11}CO, $^{13}NH_3$.....)
- substrate metabolism(^{18}F-FDG, $^{15}O_2$, ^{11}C-palmitic acid....)
- protein synthesis (^{11}C-leucine, ^{11}C-methionine, ^{11}C-tyrosine)
- enzyme activity (^{11}C-deprenyl, ^{18}F-deoxyuracil...)
- drugs (^{11}C-cocaine, ^{13}N-cisplatin, ^{18}F-fluorouracil...)
- receptor affinity (^{11}C-raclopride, ^{11}C-carfentanil, ^{11}C-scopalamine)
- neurotransmitter biochemistry (^{18}F-fluorodopa, ^{11}C-ephedrine...)
- gene expression (^{18}F-penciclovir, ^{18}F-antisense oligonucleotides...)
- ....

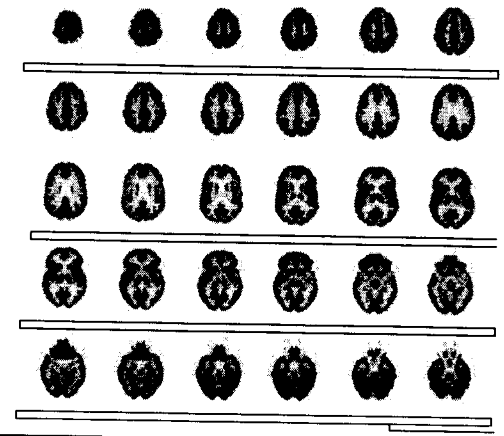
PET can detect and image sub nanomolar levels of these tracers in vivo

Human Whole-Body PET Scanners

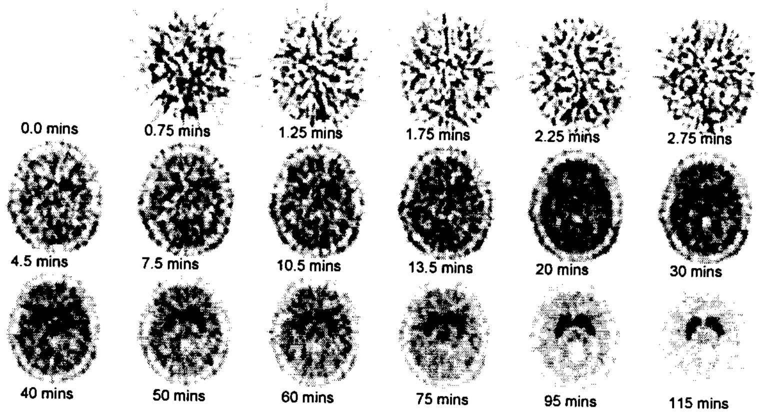


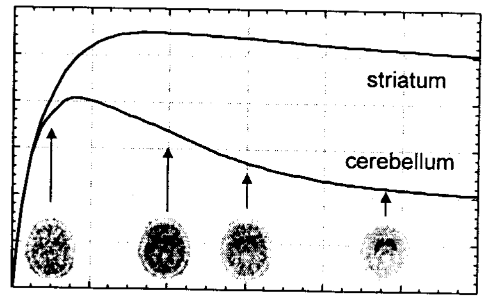
Siemens ECAT EXACT HR+
20,000 scintillator detectors
ring diameter ~ 80 cm
4 mm (64 μL) spatial resolution
(typically 6-12 mm in clinical practice)

^{18}FDG - transaxial sections through brain



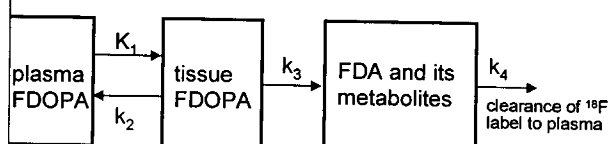
Time Course of ^{18}F-FDOPA in the Brain





Tracer Kinetic Modeling

- Simplified model for FDOPA kinetics in striatum
- Rate constants K_1, k_2, k_3 & k_4 can be estimated using measured PET time activity curves and blood input function.



FDOPA = [^{18}F]fluoroDOPA

Why Small Animal Imaging?

- in vivo ≠ in vitro
- non-destructive - repeat studies in the same animal
- can efficiently survey whole animal
- rapid in vivo screening?
- provides bridge from animal studies to human studies
- better decisions sooner!

In Vivo Small Animal Imaging

Anatomic Physiologic Metabolic Molecular

optical imaging

x-ray CT **PET/SPE CT**

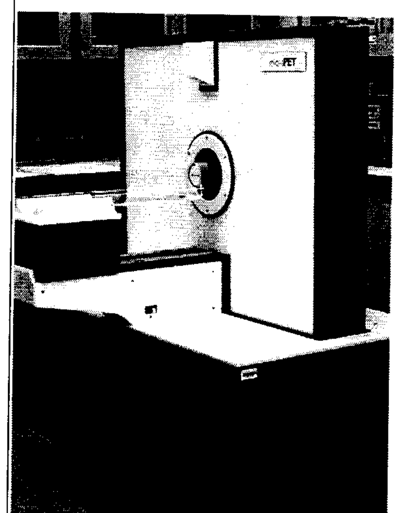
MRI **MR Spectroscopy**

fMRI

ultrasound

Which Imaging Technique?

- what do you want to measure?
- spatial resolution (μm or mm?)
- temporal resolution (ms or mins?)
- sensitivity (mM or nM?)
- field of view (striatum or whole animal?)
- what's available



microPET

- 30 detector modules
- 1920 detector elements
- ring diameter: 172 mm
- axial field of view: 18 mm

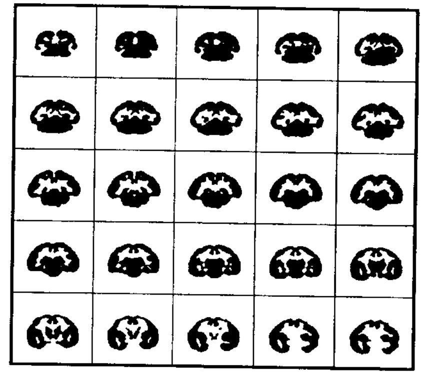
- spatial resolution: 1.8 mm (6 μL)
- sensitivity: 200 cps/μCi (CFOV)

Small Animal PET Scanner Development

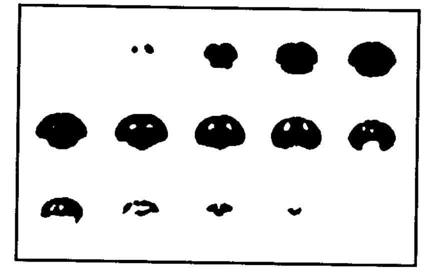
- microPET (UCLA/Concorde Microsystems)
- HIDAC (Oxford Positron Systems)
- SHR-7700 (Hamamatsu, Japan)
- Sherbrooke Animal PET (Sherbrooke, Canada)
- RATPET (MRC Hammersmith)
- TierPET (Jülich, Germany)
- YAP-PET (Ferrara, Italy)
- MAD-PET (Munich, Germany)
- ANI-PET (Montreal, Canada)

microPET images

baby monkey brain phantom (25 cc)

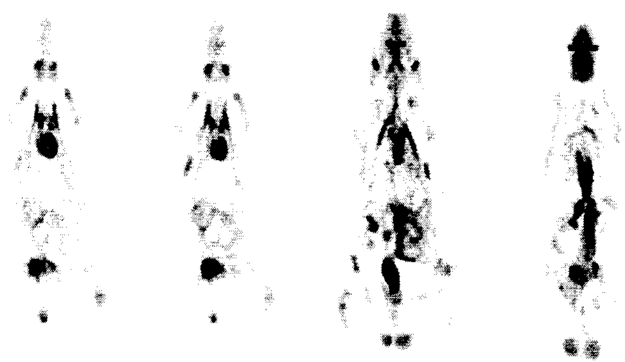


microPET



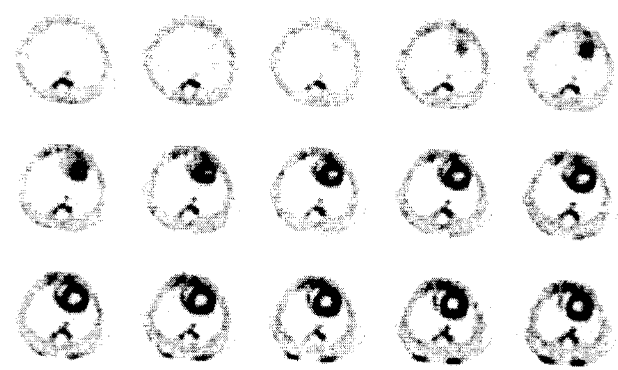
Siemens EXACT HR+

^{18}F-FDG Whole Body Rat Study

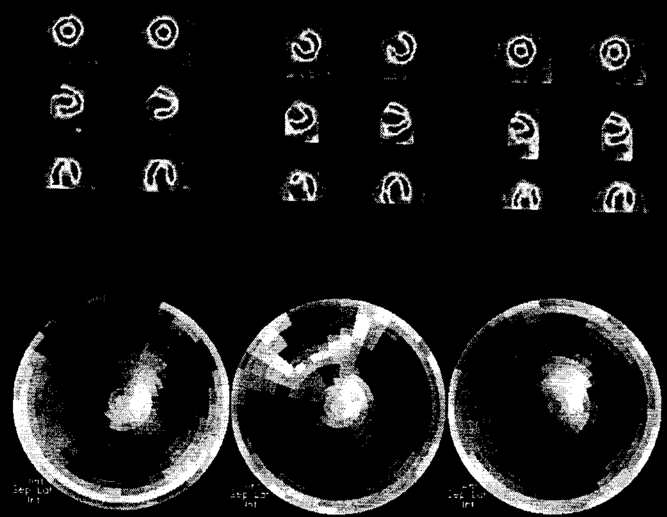


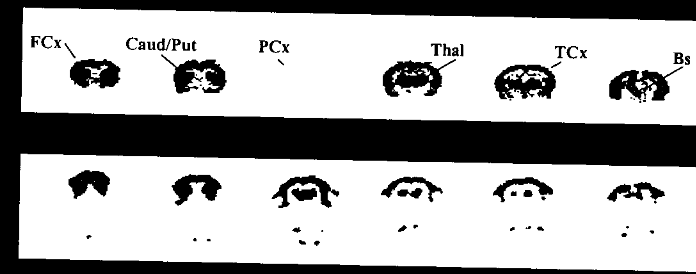
microPET

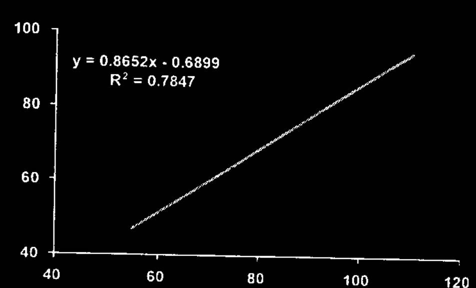
^{18}F-FDG Rat Heart

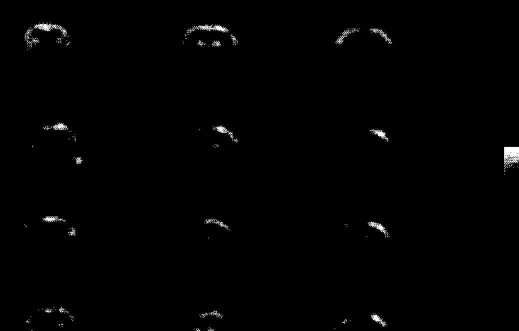


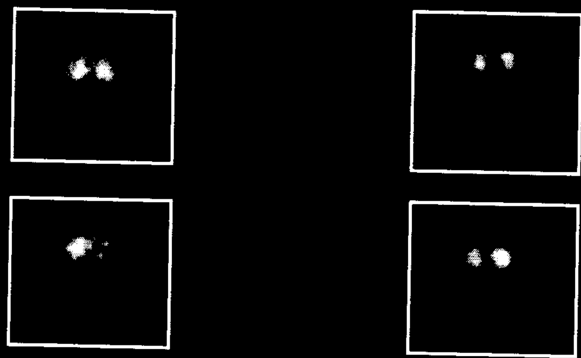
microPET




FCx
Caud/Put
PCx
Thal
TCx
Bs

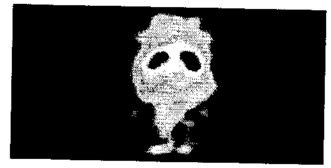

y = 0.8652x - 0.6899
R² = 0.7847
100
80
60
40
40
60
80
100
120





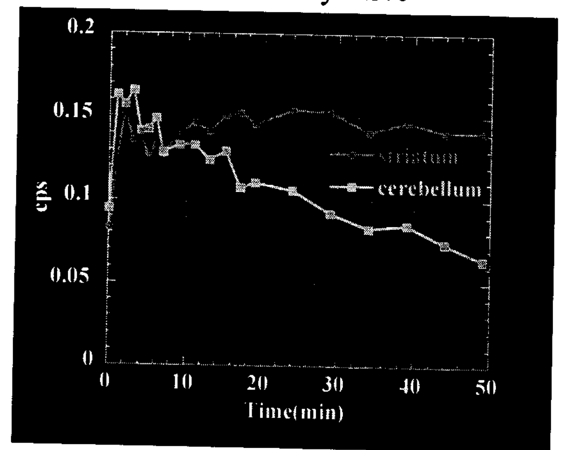
Mouse Brain: ^{11}C-WIN 35,428

30g mouse
transverse brain section



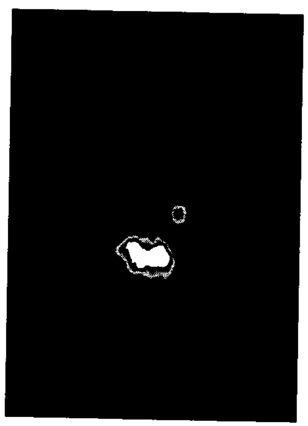
180μCi of ^{11}C-WIN 35,428
(0.018μg)

Time Activity curve



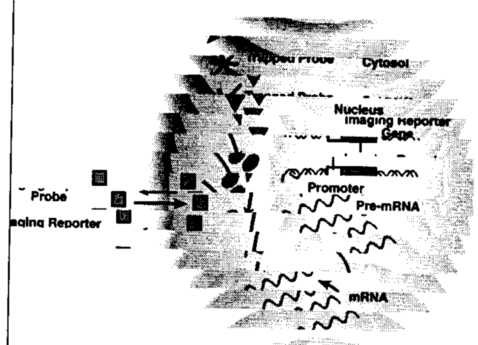
MicroPET Tumor Imaging ^{64}Cu-DOTA anti-CEA Minibody

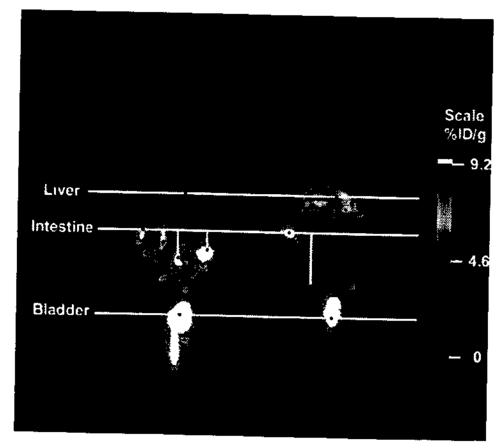
- Athymic mouse with LS174T (CEA+) and C6 (CEA-) xenografts
- Injected with 70 μCi ^{64}Cu-anti-CEA minibody (engineered antibody fragment, scFv-C_{H3})
- Scanned 12 hr post injection



Data courtesy of Anna Wu (UCLA and City of Hope)

Imaging Gene Expression by PET





PET in Drug Development

- direct radiolabeling of drug
  - biodistribution and pharmacokinetics
- binding/competition studies
  - dosing and pharmacodynamics
- indirect markers
  - pharmacodynamic effect on secondary marker (e.g. metabolism or blood flow)

Positron Emission Tomography

Advantages:

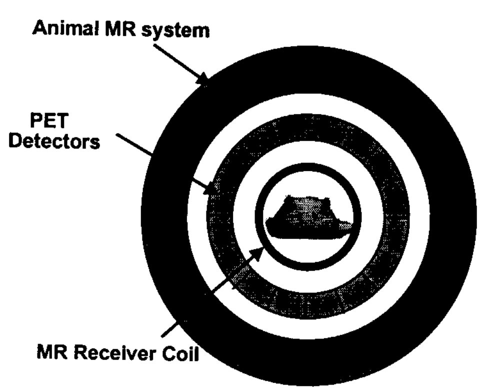
vast range of biological processes can be measured quantitatively
sensitivity can be in nM to pM range
whole animal biodistribution and kinetics

Disadvantages:

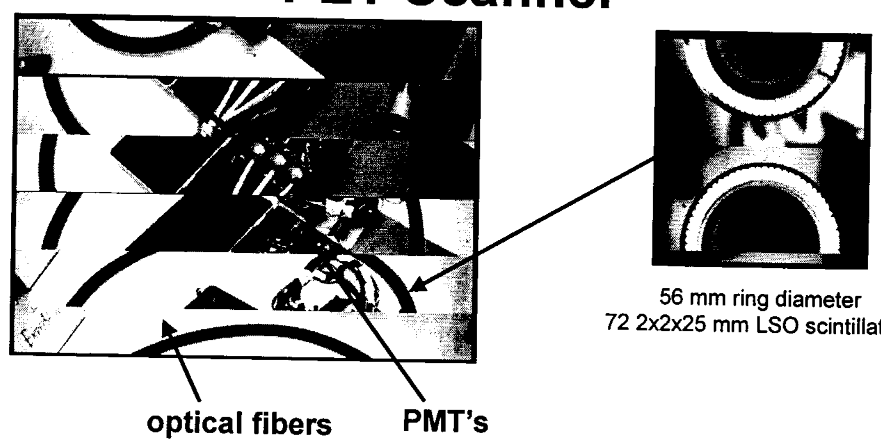
relatively coarse spatial (~mm) and temporal (~mins) sampling
synthesis of radiolabeled compounds can be a bottleneck
little or no anatomical information

MR Compatible PET System

Concept

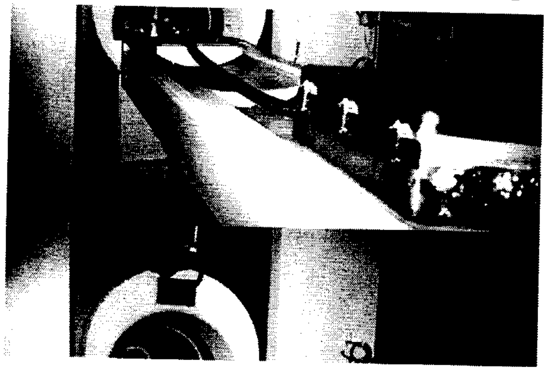


Prototype MR Compatible PET Scanner



56 mm ring diameter
72 2x2x25 mm LSO scintillators

Experimental Setup



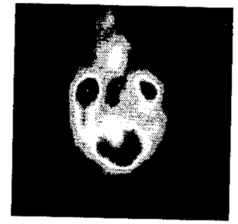
Prototype MR compatible PET scanner

inside 1.5T clinical MR

Simultaneous In Vivo Imaging

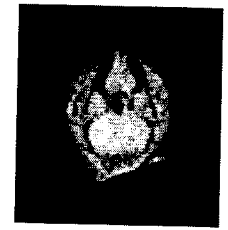
200 g Rat - ^{18}F-FDG Brain Study

PET



1.3 mCi ^{18}F-FDG
imaging time 30 mins
slice thickness ~ 2mm

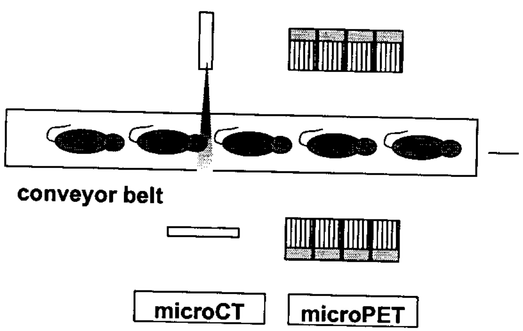
MRI



TE=12 msec, TR=280 msec
continuous 75 secs
acquisitions during PET study
slice thickness 4 mm

Rapid In Vivo Drug and Genetic Screening with PET and CT

- combined anatomical & molecular imaging
- for use with ^{18}F-labeled ligands or secondary markers such as ^{18}F- FDG
- throughput of >20 mice per hour
- sophisticated bioinformatics to assist in analysis



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