Recent Advances in Multi-modality Molecular Imaging of Small Animals

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Outline

- Introduction
- Early developments of molecular imaging (MI) of small animals (SA)
- Development of multi-modality MI of SA
  - Instrumentation
  - Image reconstruction and processing methods
- Recent advances

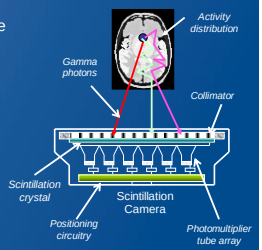
Comparing Biomedical Imaging Techniques

	US	MRI	X-ray CT	SPECT	PET	OPTICAL
Anatomical	Yes	Yes	Yes	No	No	No
Functional	Yes	Yes	No	Yes	Yes	Yes
Resolution	Sub-millimeter	Sub-millimeter	Sub-millimeter	<1 mm (0.6 – 0.3mm)	~1 mm	Sub-micron
Molecular Target	No	Good	No	Excellent	Excellent	Excellent
Molecular targeting sensitivity	No	Poor	No	Good	Excellent	Poor
Translational	Yes	Yes	Yes	Yes	Yes	No

Traditional Nuclear Medicine Imaging Techniques

an important function imaging modality

- labels tracer or biomarkers w/ radioisotope
- administers radio-tracer into patient
- detects photon emissions using position-sensitive detectors
- Provides localization & biodistribution information of radiotracers
  - e.g., perfusion, potassium analog, monoclonal antibody
- Clinical applications
  - e.g., cardiac and kidney functions, cancer detection, neurological disorders



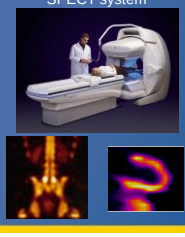
EMISSION COMPUTED TOMOGRAPHY (ECT)

an important function imaging modality

- Nuclear imaging combined with computed tomography *(Image reconstruction from multiple projections)*
- Categories of ECT
  - PET (Positron Emission Tomography)
  - SPECT (Single Photon Emission Computed Tomography)

SINGLE –PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)

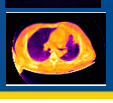
Standard dual-camera SPECT system



SPECT Systems with Transmission data acquisition units

Siemens E.CAM™ Profile

GE Hawkeyes



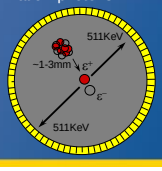
POSITRON EMISSION TOMOGRAPHY (PET)

- Uses positron emitters
  - e.g., F-18, C-11, O-15, N-13
- Requires on-site cyclotron for short-lived isotope
- Requires coincidence detection of 511 keV annihilation photons

RADIONUCLIDES USED IN PET PHARMACEUTICALS

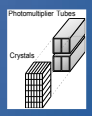
RADIO-NUCLIDES	HALF-LIFE	IMAGING APPLICATIONS
C-11	20 min	metabolism
N-13	10 min	heart perfusion
O-15	2 min	blood flow
F-18	110 min	glucose analogs, neuroreceptor
Rb-82	1.2 min	heart perfusion

Coincidence detection of 2 511 keV annihilation photons



Cyclotron

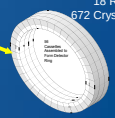
POSITRON EMISSION TOMOGRAPHY (PET)



6 Detector Blocks

Detector Cassette

One Block

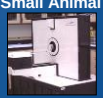
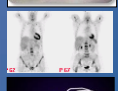
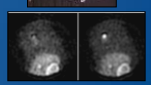
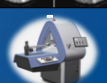


18 Rings
672 Crystals/Ring

GE Advance PET system

- PET systems consists of hundreds of pairs of coincidence detectors to detect the 511 keV annihilation photons
- More expensive systems as compared to SPECT

MOLECULAR IMAGING TECHNIQUES

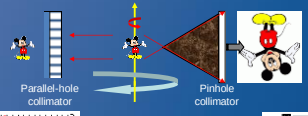
	Human	Small Animal	
PET			Micro PET
~36 cm			~2.5 cm
SPECT			Micro SPECT

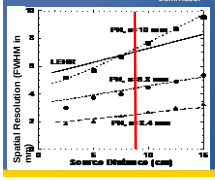
Current resolution: < ~1 cm

Resolution requirement: < ~1 mm

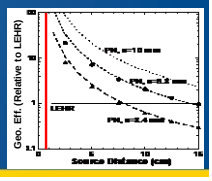
Early Development of Preclinical SPECT and SPECT/CT Instrumentation and Imaging Techniques

PARALLEL-HOLE vs. PINHOLE SPECT





For the same spatial resolution, pinhole collimation provides higher detection efficiency at closer source distances than parallel-hole collimation.



MODULAR CAMERA BASED SPECT SYSTEMS

UNC-CH camera based microSPECT system

JHU mini camera based microSPECT system

TJNAF* Modular camera based SPECT system with rotating gantry

* S. Majewski, Ph.D., R. Wojcik, Ph.D.
Thomas Jefferson National Accelerator Facility

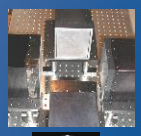
1.2 mm w/ 1.4 pitch pixellated NaI(Tl)
11 cm x 11 cm, 77 x 77 pixels

HAMAMATSU
5" PSPMT(R3292)

SMALL ANIMAL IMAGING SYSTEMS

JOHNS HOPKINS MEDICINE

FASTSPECT II



M3R – Multimodule, multiresolution SPECT

4 modular cameras
Benchtop system

4 multi-pinhole non-identical apertures

FS II acquisition hardware

SemiSPECT

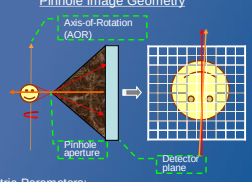
University of Arizona, *PI: Harrison H. Barrett, Ph.D.*

REQUIREMENTS FOR HIGH-RESOLUTION PINHOLE SPECT

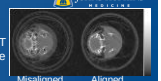
JOHNS HOPKINS MEDICINE

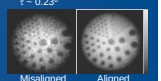
Estimation & Correction of Geometric Misalignments

Pinhole Image Geometry

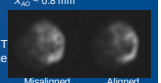


MicroCT Mouse Image





MicroSPECT Mouse Image



Geometric Parameters:

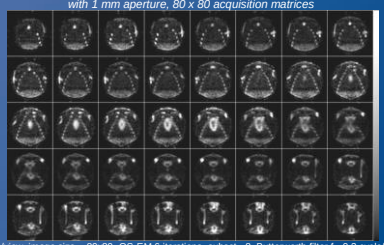
ρ: skew angle of the AOR
τ: tilt angle of AOR
X_{AO}: transversal shift of the AOR
Z_A: distance from the AOR to the detector plane

Z_F: shortest distance from the focal point to the detector plane
X_F Y_F: shifts of the focal point in the world coordinates with respect to the detector

3D PINHOLE IMAGE RECONSTRUCTION METHOD

JOHNS HOPKINS MEDICINE

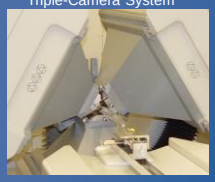
Sample coronal images of a mouse's chest using *the JHU MicroSPECT system*
with 1 mm aperture, 80 x 80 acquisition matrices



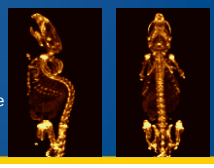
80 sec/view, image size = 80x80, OS-EM 6 iterations, subset =8, Butterworth filter f_c=0.3 cycle/pixel, n=8

Harvard Medical School µSPECT System

Modified Trionix XLT-20
Triple-Camera System



- 2 pinholes per camera x 3 cameras
- single rotation yields complete 3D SPECT volume of whole mouse with sub-mm resolution
- 3 pinhole sizes: 0.8, 1.6, 2.4 mm tungsten inserts
- interchangeable pinhole aperture plates (e.g., for rat imaging)

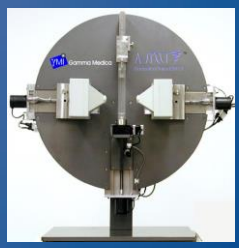


MDP bone SPECT of 25g mouse
710 µCi Tc-99m-MDP in mouse;
30-min. acquisition

S. Moore et al., Harvard Medical School

First Commercial Pre-clinical SPECT System

Gamma Medica, Inc.
~1990

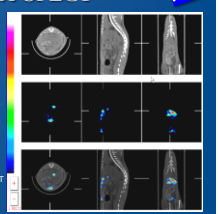


Pre-clinical SPECT/CT System

More Views of X-SPECT™

Gamma Medica, Inc.
~2000

X-ray projection images



Rat with a induced shoulder wound and injected with In-111 labeled stem cells

Pre-clinical SPECT/CT System

More Views of X-SPECT™

Gamma Medica, Inc.
~2000


Door open to change collimator


View from the Back (External)

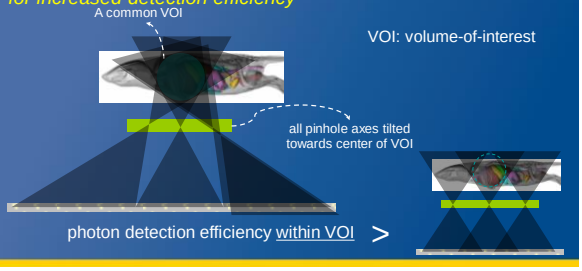

Interchangeable Animal Beds


View from the Front (Internal)


View from the Back (Internal)

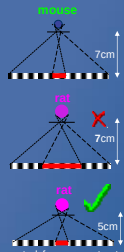
"FOCUSED" MULTI-PINHOLE SPECT

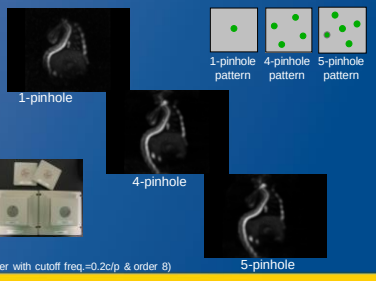
for increased detection efficiency



photon detection efficiency within VOI >

MULTI-PINHOLE COLLIMATOR DESIGN



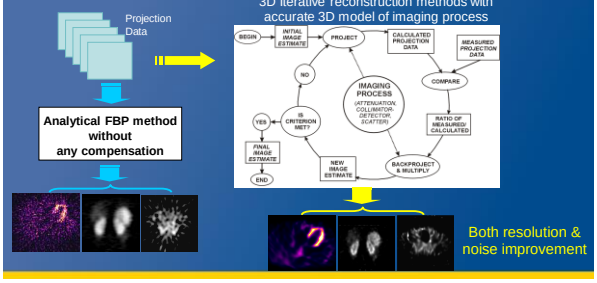


*Generated from reconstructed images
(OS-EM 20 updates w/ Butterworth postfilter with cutoff freq.=0.2c/p & order 8)

Image Degrading Factors

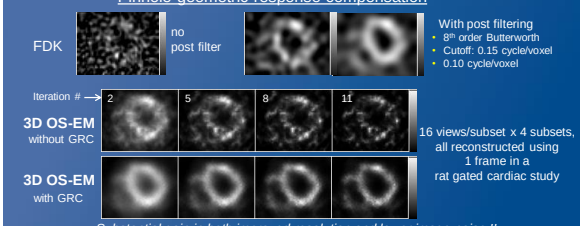
- Photon attenuation, scatter cause reconstruction artifacts and inaccurate quantitation
  - Smaller effect due to the smaller size of the imaged object
  - Affect quantitative accuracy of reconstruction
- Pinhole collimator-detector response (CDR) cause resolution loss
  - CDR = GRF ⊗ DRF
    - GRF: Pinhole geometric response function
    - DRF: Detector intrinsic resolution
    - CDR is the convolution of GRF and DRF

QUANTITATIVE SPECT RECONSRUCTION METHODS



Quantitative SPECT Reconstruction

Pinhole geometric response compensation



Substantial gain in both improved resolution and lower image noise !!
The improved image quality can be traded for reduce radation dose or imaging time.

Early Development of Preclinical PET Instrumentation and Imaging Techniques

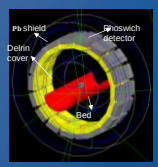
A TYPICAL SMALL ANIMAL PET SCANNER

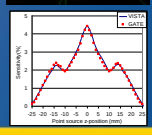
A small animal PET scanner is modeled based on GATE, validated on the basis of:

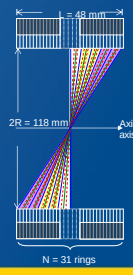
- *Sensitivity*
- *Spatial resolution*
- *Scatter fraction*
- *Count rate performance*

Count profile of point source (axial direction)

- *^{18}F Point source*
- *Energy window : 250-700 keV*
- *dmax (max ring difference)= 30*







EVOLUTION OF SMALL ANIMAL PET SYSTEMS

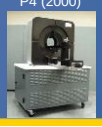
microPET I (1996)

microPET II (2002)

NIH Atlas (2000)

Explorer-Vista (2004)

P4 (2000)



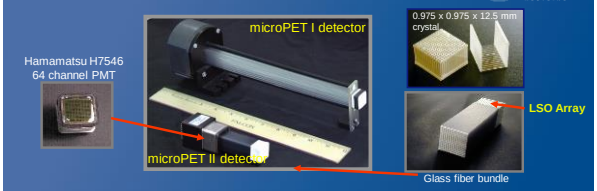
R4 (2000)

Focus 220 (2003)

Focus 120 (2004)

Courtesy of Y.C. Tai, Ph.D., Washington University

BASIC DESIGN OF microPET DETECTORS



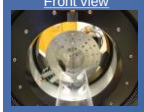
	microPET I	microPET II
Scintillator	lutetium oxyorthosilicate (LSO)	lutetium oxyorthosilicate (LSO)
Crystal size	2 x 2 x 10 mm^3	0.97 x 0.97 x 12.5 mm^3
Photodetector	Phillips XP-1722	Hamamatsu H7546-M64
Optical fiber coupling	individual fibers	fiber bundle

Courtesy of Y.C. Tai, Ph.D., Washington University

A Prototype Insert for microPET-F220

(to Achieve Sub-millimeter Mouse Imaging)

Front view



Back view

microPET F-220

LSO crystals:*1.6 x 1.6 x 10 mm^3*

Micro-Insert

LSO crystals

0.86 x 1.72 x 3.75 mm^3

Sample Images

A 23.2 g mouse imaged 4 h post-injection of 1.0 mCi of ^{18}F.

F-220 without micro-insert

Scan time: 9 min

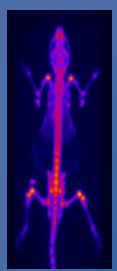
With micro-insert

Scan time: 120 min

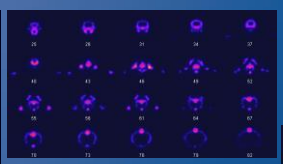
(equivalent to 9 min acquisition if using a half-ring micro-insert system with 9 detectors)

Y-C Tai et al presented at SNM 2006

^{18}F microPET Bone Scan of a mouse

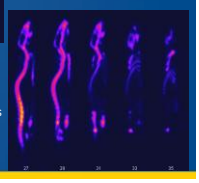


MIP rendered image



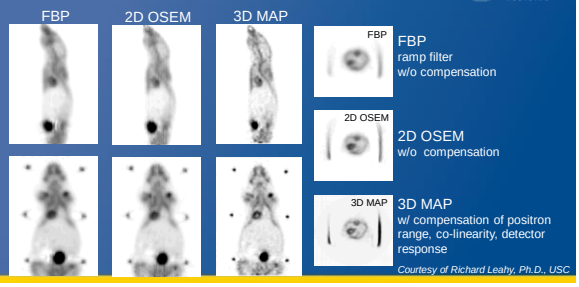
Transaxial images

Saggital images



Source: ArcusGE Explorer-Vista MicroPET System

MAP Reconstruction with Physics Modeling



Current Status and Major Advances in Pre-clinical SPECT and SPECT/CT Instrumentation

The NanoSPECT Advantage: MMP-SPECT™

Siemens SPECT/CT system

JOHNS HOPKINS MEDICINE

Inveon SPECT
System Features

SIEMENS

- Available as a trimodality system with integrated PET-SPECT-CT or an integrated SPECT-CT with dockable PET
- Self-shielded system enables CT scans up to 80 kVp @ 40 Watts

- SPECT & CT are coplanar, mounted on the same rotating gantry plate
- The gantry rotates 360° around the subject
- SPECT & CT components are mounted to computer-controlled linear motion stages, providing automatic variable magnification & zoom
- User selects detector radius of rotation for desired field of view + resolution combination
- Bed motion during scan permits helical scan orbit to extend the axial FOV and improve image quality

Helical scanning

Siemens Healthcare Molecular Imaging

Siemens SPECT/CT system

JOHNS HOPKINS MEDICINE

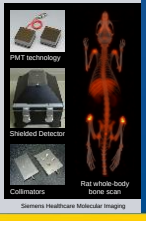
Inveon SPECT
Data Acquisition

SIEMENS

Detector:
- Reliable PMT technology
- Pixelated NaI(Tl) scintillator for improved spatial resolution, 1 cm thick for improved efficiency over broad energy range
- Fully shielded lead housing

Collimators:
- Single & multi-pinhole collimators for mouse and rat imaging with pinhole diameters ranging from 0.5 – 3 mm
- Parallel-hole collimators for planar imaging
- Patented collimator design permits quick change without opening the gantry or requiring any tools
- Can acquire scans with matched or mixed collimator sets

Acquisition & Post-Processing:
- All data captured in true list-mode format
- Energy discrimination applied during post-processing permits "unlimited" energy windows
- Supports gating with up to 2 inputs (e.g., respiratory + cardiac)
- Reconstruction algorithms include OSEM-3D and MAP-3D



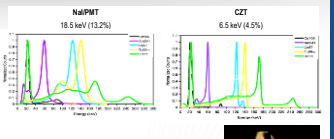
Siemens Healthcare Molecular Imaging

Solid-State CZT Detector

JOHNS HOPKINS MEDICINE

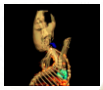
CZT gives better energy resolution than NaI/PMT

TriFoil Imaging



Accelerates Research By Probing Multiple Biological Pathways - Simultaneously

Scan summary
- ^{99m}Tc MDP (orange)
- ^{201}Tl (green)
- ^{123}I (blue)



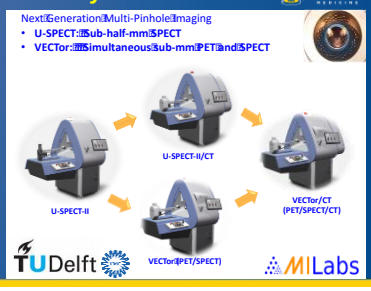
Courtesy of Timothy Doyle, Ph.D., Stanford University, USA

excellence through innovation

Pre-clinical SPECT System with CZT Detector

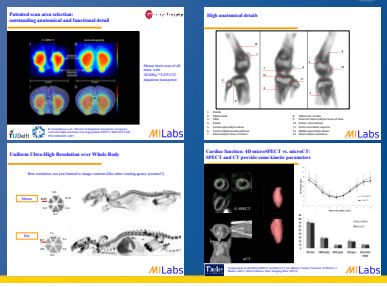
Commercial SPECT/CT Systesms

MILabs
The Netherlands



MILabs Multi-Pinhole Stationary SPECT System

MILabs Multi-Pinhole Stationary SPECT System

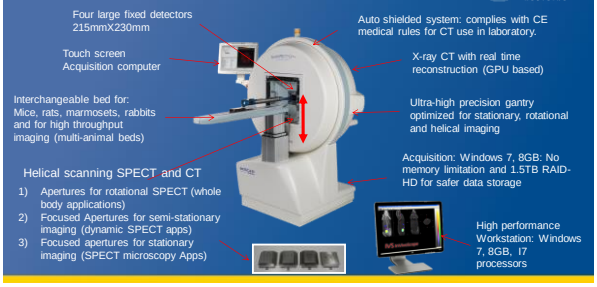


X-SPECT® Subsystem

Current Status and Major Advances in Preclinical PET and PET/CT Instrumentation

Current Status and Major Advances in Multi-Modality Pre-Clinical Imaging Instrumentation and Imaging Techniques

NanoSPECT/CT-Plus: System Overview



Helical scanning SPECT and CT

1) Apertures for rotational SPECT (whole body applications)
2) Focused Apertures for semi-stationary imaging (dynamic SPECT apps)
3) Focused apertures for stationary imaging (SPECT microscopy Apps)

Bruker Albira PET/SPECT/CT

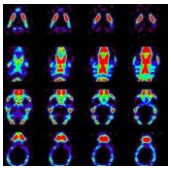
- 2 gamma cameras in each system
  - CsI(Na) single crystals
  - 64 anode PSPMT
  - Dedicated SPECT electronics
- Choice of two configurations: S102 or S108
  - Increased sensitivity
  - Larger FOV
  - Broader energy range
- Single and multi-pinhole collimators included, no tools needed for exchange
- High-energy and high-resolution collimators available*
- Fully automated and variable FOV selection to balance sensitivity and resolution

Bruker Albira SPECT/CT System

Albira SPECT

Rapid Acquisition and High Resolution

- Sensitivity of up to 1000 cps/MBq
- High spatial resolution of up to 0.5 mm with HR collimator*
- Broad energy range: 30-400 keV for a variety of SPECT isotopes
- Single pin hole, multi pin hole, high energy and high resolution collimators available *
- Main energy resolution of 14 % at 140 keV
- Reconstruction times below 5 min
- Scatter correction and PSF based reconstruction for improved image quality*

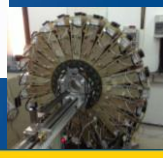


*WIP, specification subject to change, available 2014

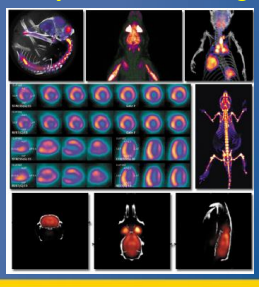
State-of-the-Art Commercial PET/CT System

- PET subsystem
  - 1.45x1.45x15mm^3 pixellated dual-layer LYSO and GSO cyrstal
  - Inner bore size of 16cm
  - Axial FOV of 9.7cm
  - transaxial FOV of 12cm
  - energy resolution of 25%
  - timing resolution of 1.3 ns
  - detection efficiency of 8%
  - resolution 1.3mm & <1mm w/ 3D reccon
- CT subsystem
  - Flat panel detector 14.5x11.5cm^2 in size
  - 35-90kVp, 1mA
  - 33micro focal spot size
  - Resolution ~20micron

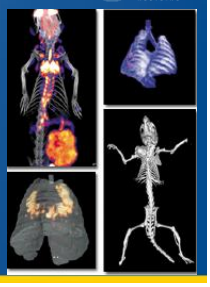
Co-planar PET/CT system



Sample PET/CT Images



Sedecal 4R PET/CT system



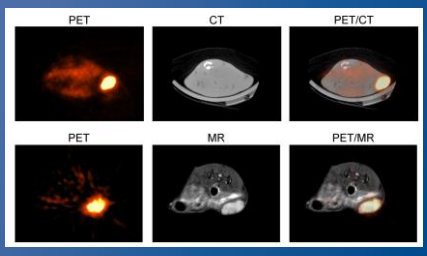
Rationale of
Simultaneous PET/MR and SPECT/MR

RATIONALE FOR PET/MRI AND SPECT/MRI

	PET	SPECT	CT	MR
Information	Functional	Functional	Anatomical	Anatomical/Functional
Anatomical Detail	Poor	Poor	Good	Excellent
Soft tissue differentiation	- - -	- - -	Poor	Excellent
Ionizing Radiation	Yes (Internal)	Yes (Internal)	Yes (External)	No radiation
Sensitivity	pico molar	nano molar	- - -	Poor
Spatial Resolution (Clinical)	3 – 8 mm	8 – 15 mm	1 mm	1 mm
Spatial Resolution (Pre-clinical)	1 - 1.5 mm	0.5 – 1.5 mm	0.05 – 0.2 mm	0.02 – 0.2 mm

PET/MRI and SPECT/MRI can potentially provide
- improved multi-modality information
- no additional ionizing radiation
- excellent soft tissue differentiation

COMPARING PET/CT and PET/MRI



Courtesy of Bernd Pichler, Ph.D., University of Türingen, Germany

PET/MR & SPECT/MR IMAGING METHODS

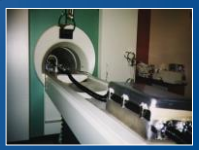
- Sequential PET/MR imaging
  - Separate PET and MRI
    - Advantages:
      - *Existing systems (lower start-up cost)*
    - Disadvantages:
      - *Difficult study set-up*
      - *Long data acquisition time*
      - *Possible misalignment of small structures in PET/MR images*
  - Coplanar PET and MRI system
    - Advantages:
      - *Easier study set-up*
      - *Better registration of SPECT/MR images*
    - Disadvantages:
      - *Higher special system cost*
      - *Long data acquisition time*
      - *Possible misalignment of small structures in PET/MR images*
- Simultaneous PET/MR imaging
  - Advantages:
    - *Easy study set-up,*
    - *Shorter imaging imaging & faster throughput*
    - *Perfectly registered PET/MR images*
    - *Allow simultaneous dynamic PET/MR studies*
  - Disadvantages:
    - *Higher special system cost*

Major Advances in Preclinical PET/MR Instrumentation

First Simultaneous Pre-clinical PET/MRI

Readout by light fiber & PMTs

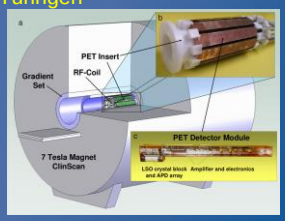
56 mm ring diameter
72 2x2x25 mm LSO scintillators



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

Shao Y, Cherry SR, Farahani K, et al. *Phys Med Biol* 42: 1965-1970; 1997

Pre-clinical PET/MRI System at U of Türingen



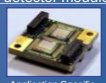
PET Scanner Parameters	
Crystal size	1.6 x 1.6 x 4.5 mm³
Crystal material	LSO
Number of detector blocks	10
#r of crystals per block / ring / total	144 / 120 / 1440
FOV axial / transaxial	19 mm / 38 mm
Coincidence timing resolution	8 ns
Resolution	< 2 mm

Courtesy of Bernd Pichler, Ph.D., University of Türingen, Germany

2nd-GENERATION MR-COMPATIBLE SPECT INSERT

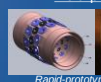
MR Compatible CZT detector module

- *CZT detector modules: 2.5 cm x 2.5 cm x 5 mm*
- *16 x 16 1.6 mm pixels*



Application Specific Inegrated Circuit (ASIC)

Multi-pinhole Collimator



Rapid-prototyping model of 36-pinhole collimator

Pinhole aperture size: 0.5 mm

System configuration

A detector ring consists of 19 CZT detectors w/ outer diameter of 20 cm

5 detector rings of 2.54x2.54cm² CZT detectors

5 detector rings w/ MPH collimator & pinhole projections

Quadrature Birdcage RF Coil Design

128 MHz transmit/receive quadrature birdcage RF coil for mouse MR imaging

Transmit/receive quadrature birdcage RF coil with RF shield

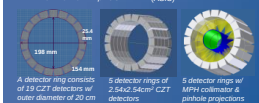
Sample MR image of a mouse Kidney.

2nd-GENERATION MR-COMPATIBLE SPECT INSERT

System configuration and multi-pinhole collimator

- *CZT detector modules: 2.5 cm x 2.5 cm x 5 mm*
- *16 x 16 1.6 mm pixels*

Application Specific Inegrated Circuit (ASIC)



A detector ring consists of 19 CZT detectors w/ outer diameter of 20 cm

5 detector rings of 2.54x2.54cm² CZT detectors

5 detector rings w/ MPH collimator & pinhole projections

18-Pinhole Collimator

36-Pinhole Collimator

2 collimator sleeve designs w/ 3 rows of 6 pinhole inserts & cavity to hold non-magnetic & high-Z collimator material

Rapid-prototyping model of 36-pinhole collimator

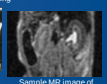
Pinhole aperture size: 0.5 mm

Quadrature Birdcage RF Coil Design

128 MHz transmit/receive quadrature birdcage RF coil for mouse MR imaging

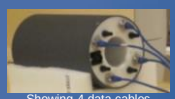
RF shielding

Transmit/receive quadrature birdcage RF coil with RF shield



Sample MR image of a mouse Kidney.

2nd-GENERATION MR-COMPATIBLE SPECT INSERT



Showing 4 data cables from the backside

With additional 4 air cooling hoses

Inside a Philips Achieva 3T clinical MRI system

With cover off showing 5 rings of 19 CZT modules at the bottom and electronic on top

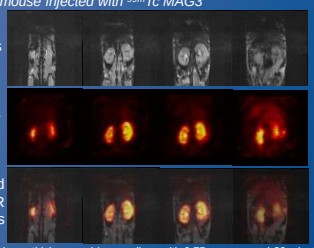
Simultaneously Acquired SPECT/MR Images

From a simultaneously acquired dynamic SPECT/MR study of the kidney of a mouse injected with ^{99m}Tc MAG3

MR Images

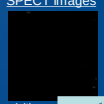
SPECT Images

Fused SPECT/MR Images



8 sec dynamic MR images

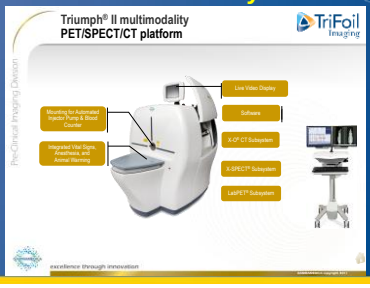
1 sec dynamic SPECT images



Four 1 mm thick coronal image slices with 0.75 mm gap and 30 minutes acquisition

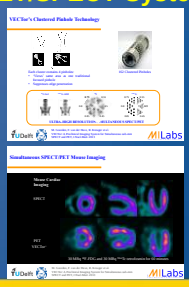
Recent Advances in Multi-Modality Preclinical Molecular Imaging Instrumentation and Imaging Techniques

Commercial PET/SPECT/CT System



Commercial PET/SPECT System

MILabs
The Netherlands



Commerical Multi-Modality Pre-clinical Imaging Systems

Mediso Medical Imaging Systems, Hungary

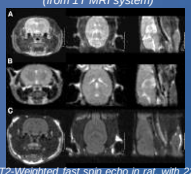
Co-planar
SPECT/CT system

Co-planar
SPECT/MRI system

1T MRI with
permanent magnet

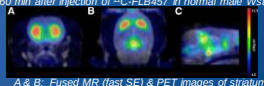
Sample PET/MR Images

Sample MR images
(from 1T MRI system)



A: T2-Weighted fast spin echo in rat, with 22:24 min scan time
B: T2-Weighted fast spin echo in mouse, with 20:00 min scan time
C: Spoiled gradient echo in rat, with 14:13 min scan time

Sample fused PET/MR images
(5-60 min after injection of ^{11}C-FLB457 in normal male Wstar rat)



A & B: Fused MR (fast SE) & PET images of striatum
C: Fused MR (fast SE) & PET images of hypophysis

Fused T1w SE 2D MR + ^{18}F-FDG images

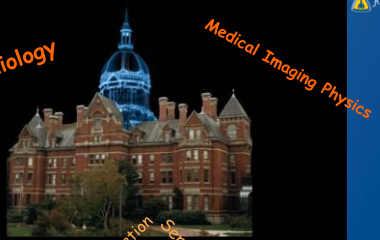
Fused T2w FSE 2D MR + ^{18}F-FDG images

** Nagy K, et al., Performance evaluation of the small-animal nanoScan PET/MRI system, JNM 2013.*

CONCLUSIONS

- SPECT is a major molecular imaging technique
- With the application of pinhole and multi-pinhole (MPH) collimators, small animal SPECT provides high spatial resolution and high detection efficiency as compared with conventional parallel-hole collimators
- Advances in instrumentation, accurate calibration techniques and quantitative image reconstruction methods have offered significant improvement in SPECT image quality in recent years
- The improvements can be traded for reduced radation dose and/or imaging time

Thank you for your attention



JOHNS HOPKINS MEDICINE

JOHNS HOPKINS MEDICINE

Learning objectives:

1. To learn about the two major multi-modality molecular imaging techniques of small animals.
2. To learn about the spatial resolution achievable by the molecular imaging systems for small animal today.
3. To learn about the new multi-modality imaging instrumentation and techniques that are being developed.

A simple question:

1. What are the two major multi-modality molecular imaging techniques of small animals and what are their highest achievable spatial resolution.

JOHNS HOPKINS MEDICINE

Multi-modality molecular imaging instrumentation and techniques have been major developments in small animal imaging that has contributed significantly to biomedical research during the past decade. The initial development was an extension of clinical PET/CT and SPECT/CT from human to small animals and combine the unique functional information obtained from PET and SPECT with anatomical information provided by the CT in registered multi-modality images. The requirements to image a mouse whose size is an order of magnitude smaller than that of a human have spurred advances in new radiation detector technologies, novel imaging system designs and special image reconstruction and processing techniques. Examples are new detector materials and designs with high intrinsic resolution, multi-pinhole (MPH) collimator design for much improved resolution and detection efficiency compared to the conventional collimator designs in SPECT, 3D high-resolution and artifact-free MPH and sparse-view image reconstruction techniques, and iterative image reconstruction methods with system response modeling for resolution recovery and image noise reduction for much improved image quality. The spatial resolution of PET and SPECT has improved from ~6-12 mm to ~1 mm a few years ago to sub-millimeter today. A recent commercial small animal SPECT system has achieved a resolution of ~0.25 mm which surpasses tsolution is limited by the positron range. More recently, multimodality SA PET/MRI and SPECT/MRI systems have been developed in research laboratories. Also, multi-modality SA imaging systems that include other imaging modalities such as optical and ultrasound are being actively pursued. In this presentation, we will provide a review of the development, recent advances and future outlook of multi-modality molecular imaging of small animals.

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CURRENT COMMERCIALLY AVAILABLE SMALL ANIMAL SPECT SYSTEMS

- All are part of multi-modality small animal imaging systems, including SPECT/CT and SPECT/PET/CT
- An exciting wide selection of detector modules, system configurations, multi-pinhole collimator designs, data acquisition, image reconstruction and analysis methods
- They all provide much improved SPECT image quality with increasing high detection efficiency and sub-millimeter resolution

Current Status and Major Advances in Preclinical Simultaneous PET/MR and SPECT/MR Instrumentation Imaging Techniques

CO-PLANAR SPECT/CT SYSTEM

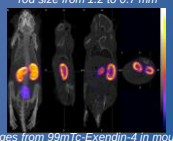
- SPECT subsystem
  - Quad-camera each 28x28cm^2 in size
  - Small angle system rotation needed
  - 27cm bore diameter
  - Resolution <~0.5mm demonstrated & ~0.35mm expected
- CT subsystem
  - Flat panel detector14.5x11.5cm^2 in size
  - 35-90kVp, 1mA
  - 33micro focal spot size
  - Resolution <30micron

Co-planar SPECT/CT system

Sample Images

Sample SPECT images

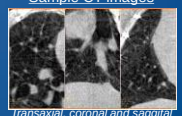
Images of a hot-rod phantom with rod size from 1.2 to 0.7 mm



Images from 99mTc-Exendin-4 in mouse

**courtesy of Prof. Wang, Peking University, Beijing, China*

Sample CT images



Transaxial, coronal and saggital CT images of a mouse's lung lobe

CT images of a rat skull (left) and whole body moise (right)

**courtesy of CROmed Ltd., Hungary*

PROPOSED SYSTEMS FROM VENDOR #2

MILabs, The Netherlands

SPECT system

Sedecal, Spain

Co-planar

VENDOR AND EQUIPMENT SELECTION

- Original proposed vendor of the multi-modality imaging system was under Chapter 11 bankruptcy protection proceedings
- Invited 4 other vendors to present their products in February and March 2013
- Narrowed selection to 2 vendors for in-depth evaluation
- Final decision will be made soon

CO-PLANAR PET/MRI SYSTEM FROM VENDOR #1

- PET subsystem
  - 1.12x1.12x13mm^3 pixellated LYSO crystal with H9500 PSPMTs
  - Inner bore size of 16cm
  - Axial FOV of 9.4cm
  - transaxial FOV of 12cm
  - energy resolution of 19%
  - timing resolution of 1.3 ns
  - detection efficiency of 8.4%
  - resolution 1.2mm & 0.7mm w/ 3D reccon
- MR subsystem
  - 1T maintenance-free permanent magnet
  - 450mT/m gradient strength
  - 2500T/m/s slew rate
  - ~100micron resolution

Co-planar
PET/CT system

MILabs PET/SPECT systesm

CONVENTIONAL 2D FILTERED BACKPROJECTION (FBP) IMAGE RECONSTRUCTION METHOD

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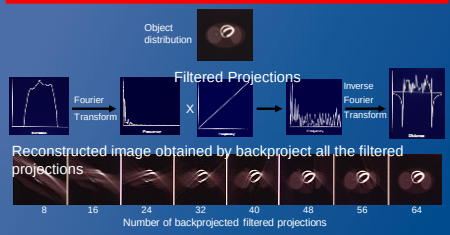
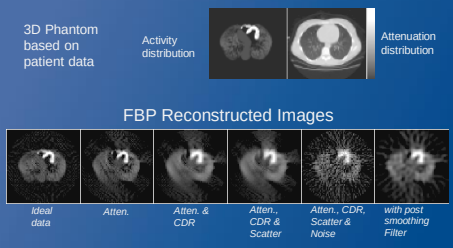


FBP image reconstruction methods provide accurate SPECT images 'if and only if' the projection data are 'ideal' and noise-free

EFFECTS OF DEGRADING FACTORS

JOHNS HOPKINS MEDICINE

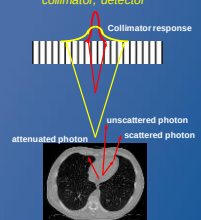


Degrading effects included in projection data

IMAGE DEGRADING FACTORS IN SPECT

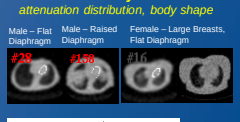
JOHNS HOPKINS MEDICINE

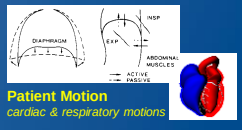
Instrumentation
collimator, detector



Physical factors
attenuation, scatter

Patient Anatomy
attenuation distribution, body shape

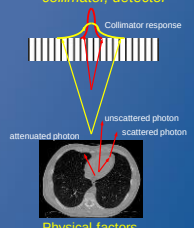




Patient Motion
cardiac & respiratory motions

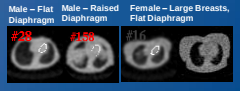
IMAGE DEGRADING FACTORS

Instrumentation
collimator, detector



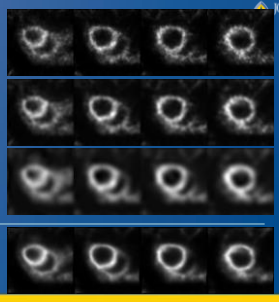
Physical factors
attenuation, scatter

Patient Anatomy
attenuation distribution, body shape



Patient Motion
respiratory motion, upward creep

80 minutes Acquisition



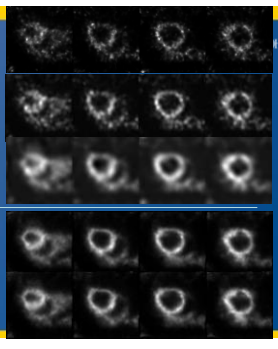
Respiratory-Summed
8 cardiac Gates

Respiratory-Summed
8 cardiac Gates
Butterworth filtered
(order = 4, cutoff = 0.2 cycle/pix)

Respiratory-Summed
8 cardiac Gates
Butterworth filtered
(order = 4, cutoff = 0.1 cycle/pix)

Dual Respiratory & Cardiac
Motion Compensation
8 Cardiac Gates
(NO Post-filtering)

20 minutes Acquisition



Original
Respiratory-Summed
8 cardiac Gates

Respiratory-Summed
8 cardiac Gates
Butterworth filtered
(order = 4, cutoff = 0.2 cycle/pix)

Respiratory-Summed
8 cardiac Gates
Butterworth filtered
(order = 4, cutoff = 0.1 cycle/pix)

Dual Respiratory & Cardiac
Motion Compensation
8 Cardiac Gates
(NO Post-filtering)

Dual Respiratory & Cardiac
Motion Compensation, 8
Cardiac Gates

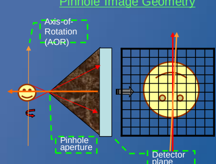
CURRENT COMMERCIALLY AVAILABLE SMALL ANIMAL SPECT SYSTEMS

- All are part of multi-modality small animal imaging systems, including SPECT/CT and SPECT/PET/CT
- An exciting wide selection of detector modules, system configurations, multi-pinhole collimator designs, data acquisition, image reconstruction and analysis methods
- They all provide much improved SPECT image quality with increasing high detection efficiency and sub-millimeter resolution

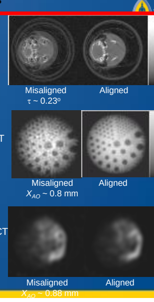
REQUIREMENTS FOR HIGH-RESOLUTION PINHOLE SPECT

Estimation & Correction of Geometric Misalignments

Pinhole Image Geometry

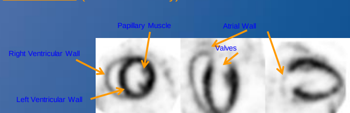


Geometric Parameters:
ρ: skew angle of the AOR
τ: tilt angle of AOR
X_{AO}: transversal shift of the AOR
Z_A: distance from the AOR to the detector plane
Z_F: shortest distance from the focal point to the detector plane
X_F, Y_F: shifts of the focal point in the world coordinates with respect to the detector



Outstanding anatomical, molecular and functional details in a single scan

Mouse Heart (Perfusion Study)



^{99m}Tc-Tetrofosmin in gated mouse SPECT

4D in vivo Molecular Microscopy of the Mouse Heart
N. Befera MD, C. Badea Ph.D. & G. Johnson Ph.D.
Center for In Vivo Microscopy, Duke University