


**TEHRAN UNIVERSITY  
OF  
MEDICAL SCIENCES**

**TUMS PRECLINICAL  
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## MICRO-PET AND MICRO-SPECT IMAGING AND APPLICATIONS

Presenter: Mohammad Reza Ay, PhD  
 Professor of Medical Physics and Biomedical Eng.  
 Director of TPCF, Tehran University of Medical Sciences

TPCF Workshop May 28<sup>th</sup>-29<sup>th</sup> 2019, Manila, Philippines

## Forms of Nuclear Imaging

**RADIOACTIVE DECAY**

(EC,  $\gamma$ ), ( $\beta^-$ ,  $\gamma$ ), I.T.

$\beta^+$

one angular view

PROJECTION IMAGING  
collimator needed

PROJECTION IMAGING  
no collimator needed

complete set of angular views 0-180°

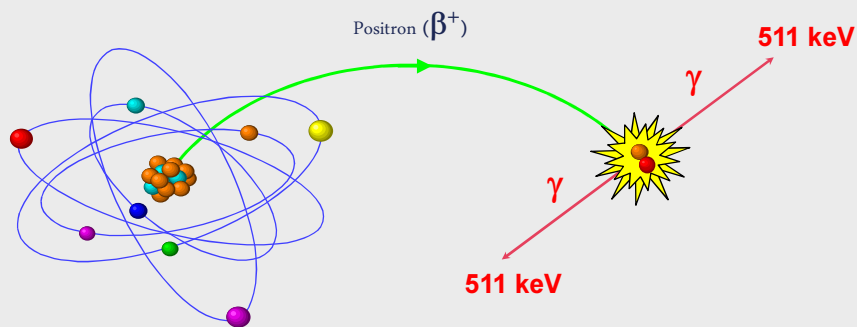
SINGLE PHOTON EMISSION  
COMPUTED TOMOGRAPHY  
(SPECT)

POSITRON EMISSION  
TOMOGRAPHY  
(PET)

Courtesy: Dr. Simon Cherry, UC Davis

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## PET Physics: Positron Decay



*The radioisotope emits a positron. The positron produced interacts with an electron. A reaction transforms the two particles into two photons of 511 keV emitted in exactly opposite directions.*

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## Photon Interactions

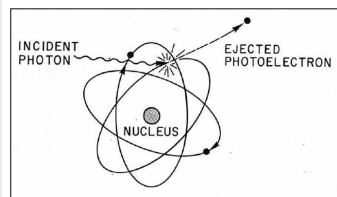


### Physical interactions

#### Photoelectric effect

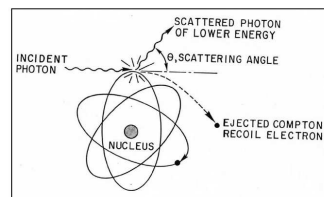
Atom completely absorbs energy of incident photon

Absorbed energy is used to eject an orbital electron from the atom - photoelectron



#### Compton Scattering

Collision between a photon and a loosely bound outer shell orbital electron of an atom




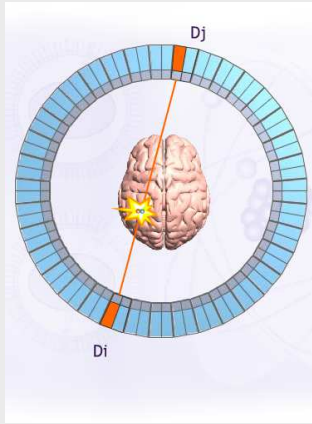
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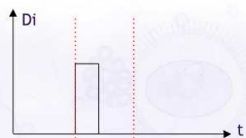
4

## Coincidence Detection



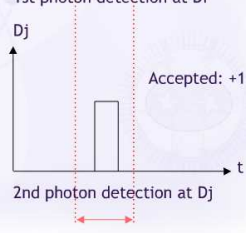


Di



1st photon detection at Di

Dj




2nd photon detection at Dj

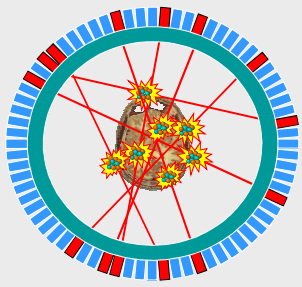
Accepted: +1


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## PET Data Acquisition





Detector ring



➔


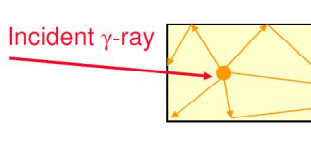
The response lines joining the detector pairs having recorded coincidence events are used for clinical data reconstruction

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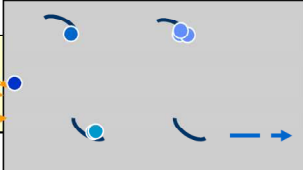
### PET gamma-ray detector principle

Scintillator




Scintillator converts gamma rays into light



PMT

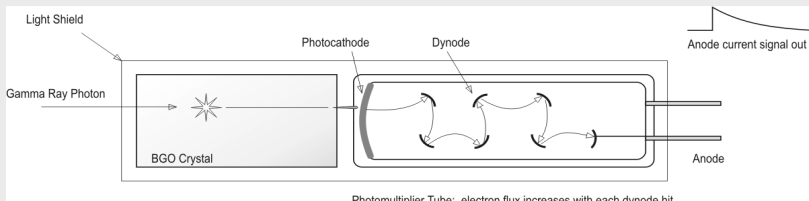


Light detector converts light into electronic signal



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Photomultiplier Tube: electron flux increases with each dynode hit.

### Tubes? Why are we using tubes?

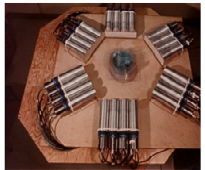
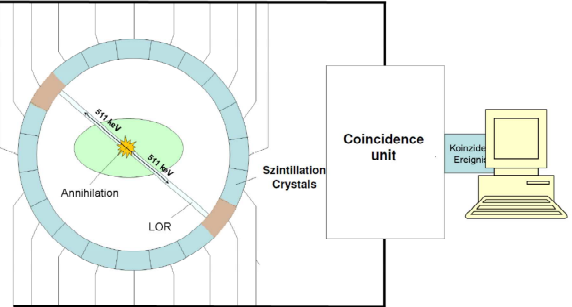
- High Gain (>1,000,000)
- Low-noise signal
- Fast timing response
- Small timing variance

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### Operation of a PET Scanner

- Coincidence detection defines line along which positron emission occurred (LOR)
- No need for collimators (tungsten/ lead) – electronic collimation
- Coincidence unit needs time window in the nanosecond range

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### Commercial Small Animal PET Scanners








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## Pre-Clinical PET Applications



**Oncology**

- Tumor biology
- Metastasis
- Therapeutic effect

**CNS**

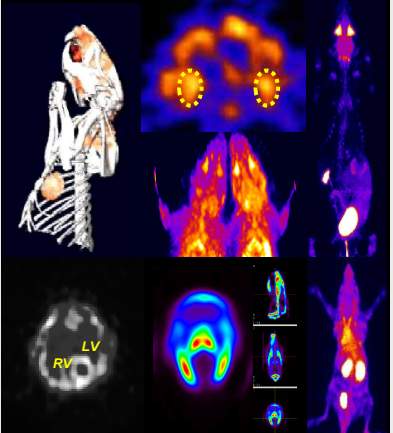
- Receptor density
- Occupancy studies

**Disease biology**

- Metabolic function
- Gene expression
- Cell trafficking

**Cardiovascular disease**


- Vascular disease & development
- Injury/repair



Policlinico S.Orsola, University of Bologna  
Martin Pomper, Johns Hopkins


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## PET :Versatile applications



High sensitivity for superior organ-specific imaging  
High resolution and uniformity for whole body imaging

Flexibility

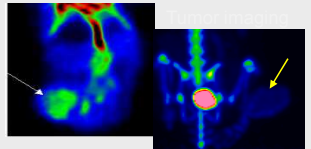


Greater sensitivity

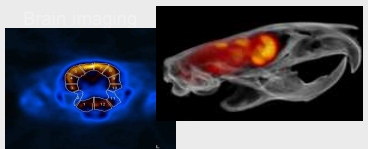
Higher resolution

Resolution uniformity

Tumor imaging

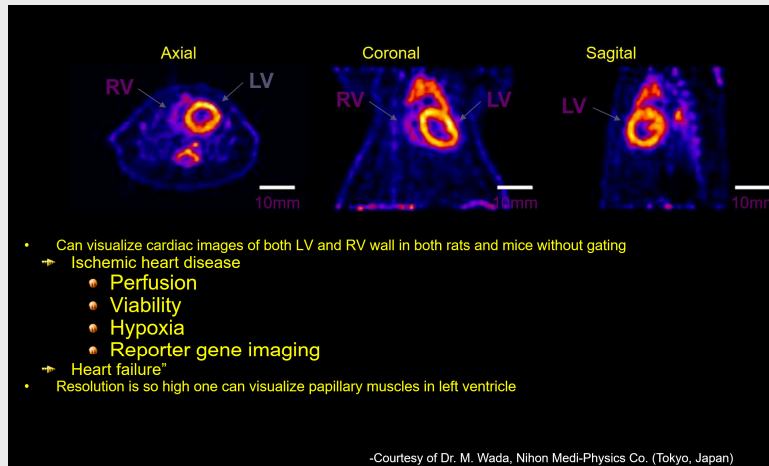


Brain imaging



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## Cardiology – Viability Model



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## Influence of Reconstruction Algorithms

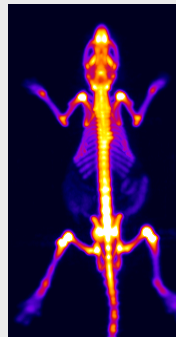


F18-Fluoride Whole Body Mouse - Bone

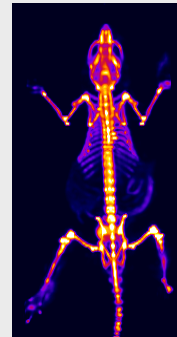
**Protocol:**

- 30 gm mouse
- 100  $\mu$ Ci F18 Fluoride
- 45 min uptake
- 3 bed positions
- 20 min / bed position
- 4 slice overlap
- 3D OSEM (20 min/bed position)

**FBP Reconstruction**



**3D-OSEM Reconstruction**



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## Detector Design Challenges in PET

APD

High spatial resolution

PMT

High sensitivity

What is the most important?

It depends on the kind of experiment?

Recover details  
(e.g. bone scan)

Small lesion  
detection

Short scan (dynamic & gating)

Fine organ tissue  
activity uptake

Broad organ  
tissue activity  
uptake

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## SiPM Based Animal PET Scanner

We are developing the fast PET electronic and also software. The concept is based on using SiPM.




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## Animal PET Detector Concept



PNP preclinical solutions are removing the limits on driving medical research from the laboratory to the clinic. Xtrim provides the high performance and versatility available to address your preclinical imaging research needs. From basic science and disease progression, to drug discovery and development, Xtrim offers an unrivaled solution for optimizing your research outcomes.



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## Xtrim Animal PET Scanner



### PET detector

- LYSO crystal full ring geometry
- Up to 100mm transaxial FOV
- Bore opening: 120mm
- Spatial resolution without resolution recovery: 1.7mm

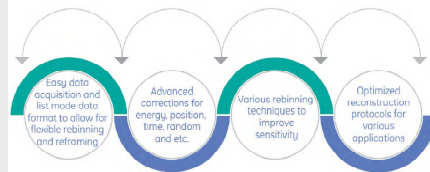
### Touch screen interface

- Bed movement control monitoring
- Count rate performance monitoring
- Basic acquisition control/monitoring
- Stop command



### Animal handling

- Capsule structure of the bed
- Semi-automated bed positioning
- Easy bed attach/detach
- Animal body temperature control
- Anesthesia and oxygen gas flow ports
- Easy changeable Rat and Mice bed



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## Scanner Specifications

Characteristics	
Single bed axial FOV	5cm
Number of detector rings	24
Transaxial FOV	100mm
Bore opening	110mm
LYSO crystal size	2mmx2mmx10mm
Crystal pixel pitch	2.1mm
Total number of crystals	5760
Spatial Resolution	1.7mm @ center
Energy Resolution	17%

Room Requirements	
Minimum room size	10m <sup>2</sup>
Single phase operation	220V
Size [WxDxH]	120cmx140cmx180cm
Weight	250kg
Standard air condition	20-25° C

IEC 61010-1:2013  
IEC 61326-1:2005

Animal Imaging Example

Rat bone scan using Na<sup>22</sup>-18. The vertebra and ribs was resolved

Mice Heart scan using FDG

NEMA Image Quality Phantom

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## SPECT Principal

### Forms of Nuclear Imaging

SPECT

**RADIOACTIVE DECAY**  
(EC,  $\gamma$ ), ( $\beta^-$ ,  $\gamma$ ), I.T.

one angular view

PROJECTION IMAGING  
collimator needed

complete set of angular views 0-180°

SINGLE PHOTON EMISSION  
COMPUTED TOMOGRAPHY  
(SPECT)

$\beta^+$

PROJECTION IMAGING  
no collimator needed

POSITRON EMISSION  
TOMOGRAPHY  
(PET)

Courtesy: Dr. Simon Cherry, UC Davis

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**SPECT Principal**

**Projection Imaging with  $\gamma$ -Emmiting Radionuclides**

Mouse injected with radiotracer

Position-sensitive scintillation detector

Projection image

Courtesy: Dr. Simon Cherry, UC Davis

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**SPECT Principal**

**Parallel-Hole Collimation**

Mouse injected with radiotracer

Position-sensitive scintillation detector with collimator (Slit collimator)

Projection image

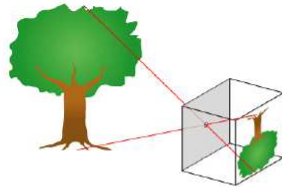
Courtesy: Dr. Simon Cherry, UC Davis

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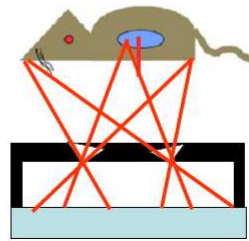
## SPECT Principal



### Pinhole Collimation



- Like with very first cameras: use pinhole to obtain projection
- Magnification possible due to distance variation
- Multi-pinhole for higher sensitivity



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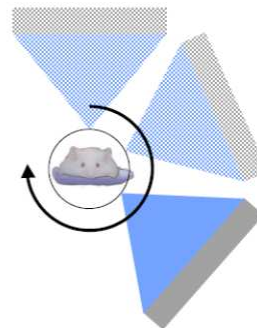
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## SPECT Principal



### Data Acquisition of a SPECT system

- Rotate imaging system to collect projection views around the object
- Use reconstruction algorithms to determine 3-D distribution of radiotracer
- Multiple pinholes often used to improve sensitivity



Courtesy: Dr. Simon Cherry, UC Davis

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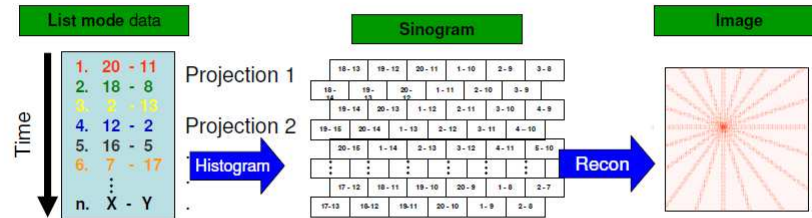
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## SiPM Based Animal PET Scanner



### Workflow of Static SPECT Acquisitions



#### Considerations:

- Dynamic framing is in theory determined by the time for one revolution
- Different Pinhole configurations allow for choice of different sensitivity and image resolution
- More pinholes, lower resolution → higher sensitivity

## High Resolution SPECT



**HiReSPECT** is a Dual Head Small Animal SPECT (Single Photon Emission Computed Tomography) imaging system that provides in vivo high resolution three-dimensional (3D) images of physiological functions in small laboratory animals.



## HiReSPECT Platform




### Detector Architecture

The HiReSPECT pre-clinical system detector design includes the latest technology for detection of gamma radiation with high accuracy including pixelated scintillator crystal with the FOV of 50x100 mm and position sensitive H8500 PMT.





High Resolution Animal SPECT Imaging System  
**HiReSPECT**



### Integrated Front End Electronic

HiReSPECT's versatile data acquisition electronics provides optimal SPECT performance on a platform designed as a true molecular imaging system. Networked computers embedded in the gantry coordinate SPECT data acquisition, and an innovative new nuclear pulse processing and event handling architecture for high resolution, high count rate gamma ray processing




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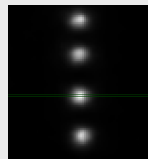
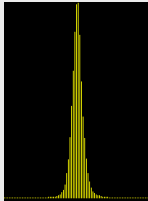
## HiReSPECT Image Reconstruction


### Image Reconstruction

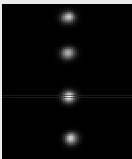
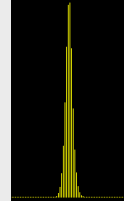
The HiReSPECT system uses a newly developed accelerated iterative reconstruction algorithm with adjustable percentage of resolution recovery using accurate modeling of collimator detector response.





**Resolution Recovery**



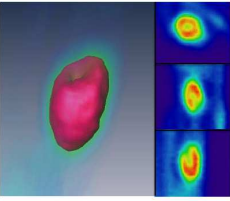



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## Some Typical SPECT Images

### CARDIAC SPECT

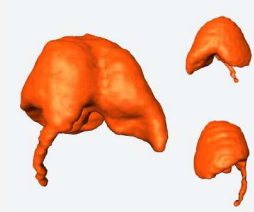


Rat Study

Persian Gulf Nuclear Medicine Research Center

This document is a report on Rat-Cardiac SPECT scan using HR/SPECT animal SPECT imaging system.  
November 10, 2013

### Liver imaging

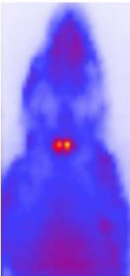


Mice Study

Atomic Energy Organization of Iran

This document is a report on Mice-Liver SPECT scan using HR/SPECT animal SPECT imaging system.  
December 15, 2013

### THYROID SPECT SCAN





Rat Study

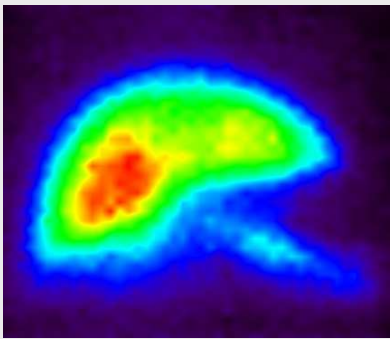
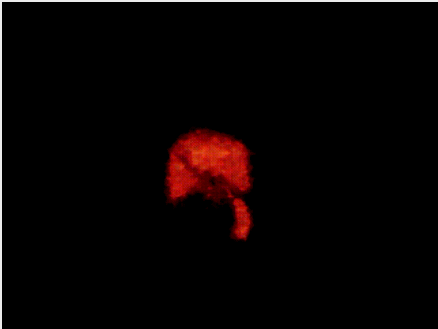
**REPORT**  
This document contains the results of Rat-Thyroid SPECT scan using HR/SPECT animal SPECT imaging system.

Persian Gulf Nuclear Medicine Research Center  
November 12, 2013

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## Images from our Studies in TPCF





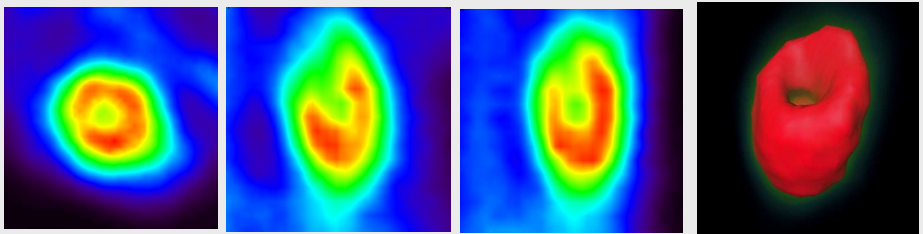



- SPECT scan of rat's liver with  $^{99m}\text{Tc}$ -PHYTATE

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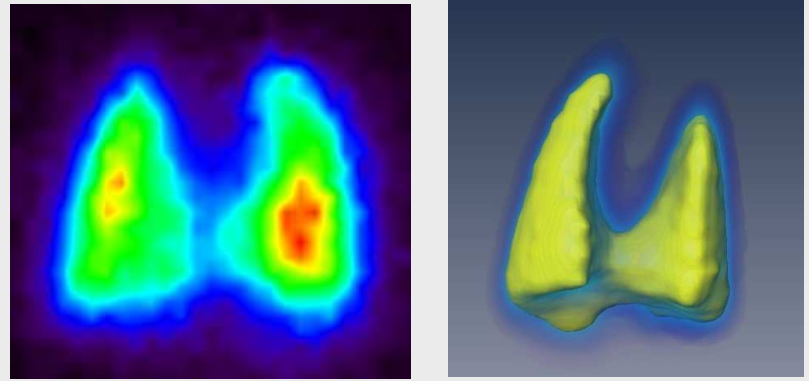
Images from our Studies in TPCF 



- Cardiac SPECT scan of rat with  $^{99m}\text{Tc}$ -MIBI

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Images from our Studies in TPCF 



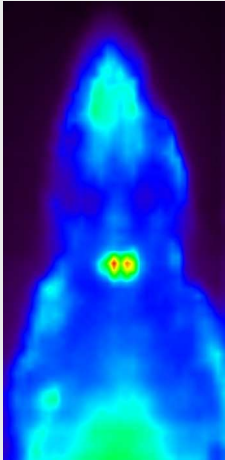
- SPECT scan of rat's lung with  $^{99m}\text{Tc}$ -MAA

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Images from our Studies in TPCF


- SPECT scan of rat's thyroid with  $^{99m}\text{Tc}$



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Images from our Studies in TPCF

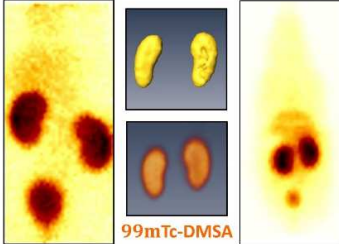
- SPECT scan of kidney with  $^{99m}\text{Tc}$ -DMSA



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



## Typical Quantitative Report

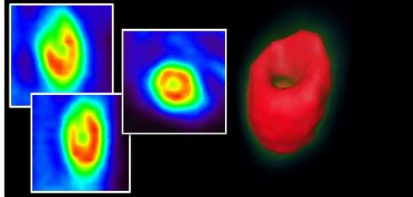


**99mTc-DMSA**

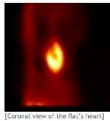
**Renal Scan**  
Renal scintigraphy was performed 1 h after intravenous injection of 99mTc-DMSA. The images show the results of our recent projects on renal scintigraphy in rat.

**HiReSPECT; Small-animal SPECT**  
Radionuclide scan imaging was conducted using HiReSPECT, a small-animal SPECT.




**Cardiac SPECT**  
The images show the transverse, coronal and sagittal views as well as the 3D reconstructed images of the Rat's heart radionuclide scan.



**Scan details:**  
Four hours after injection of the radionuclide, the animal anesthetized using a combination of Ketamine and Xylazine. SPECT imaging performed with 60 projections in 360 degrees. After the image reconstruction, the images processed with Amira image analysis software.

**Radionuclide: [Tc99m-MIBI]**

**HiReSPECT; Small-animal SPECT**  
Radionuclide scan imaging was conducted using HiReSPECT, a small-animal SPECT. The imaging system consisted of two gamma cameras. The image spatial resolutions and the planar spatial resolution of the system at the head surface is 1.2-1.6 mm and 1.7 mm, respectively.



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## Typical Quantitative Report






**Thyroid Scan**  
Thyroid scintigraphy in rats and mice with 99mTc was attempted to examine whether this modality might be used to describe the possibilities of its application in examining experimentally produced thyroid diseases.

- Thyroid images with 99mTc were obtained 15 minutes after injection.
- The radionuclide scan displayed salivary gland images, demonstrated sufficiently clear images in size and shape.
- The results showed that thyroid scintigraphy in small animals is applicable in examining experimentally produced thyroid diseases.

**Radionuclide: 99mTc**  
Rat's Thyroid Scan

**HiReSPECT; Small-animal SPECT**  
Radionuclide scan imaging was conducted using HiReSPECT, a small-animal SPECT.

- The imaging system consisted of two gamma cameras.
- The image spatial resolution and the planar spatial resolution of the system at the head surface is 1.2-1.6 mm and 1.7 mm, respectively.





**99mTc-PHYTATE**

**Liver/Spleen Scan**  
The animal was anesthetized using a combination of Ketamine and Xylazine, and injected with 99mTc-phytate. Planar and SPECT images performed using the HiReSPECT imaging system.

**HiReSPECT; Small-animal SPECT**  
Radionuclide scan imaging was conducted using HiReSPECT, a small-animal SPECT.

- The imaging system consisted of two gamma cameras.
- The image spatial resolutions and the planar spatial resolution of the system at the head surface is 1.2-1.6 mm and 1.7 mm, respectively.

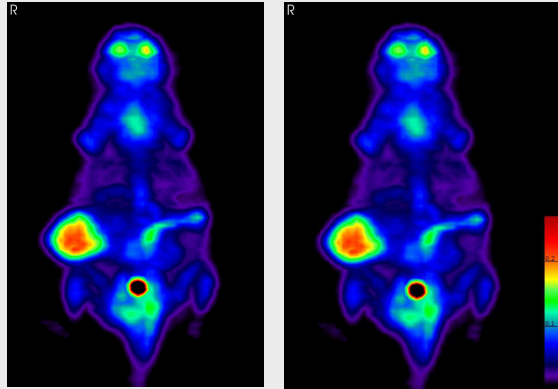


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## Images from our Studies in TPCF



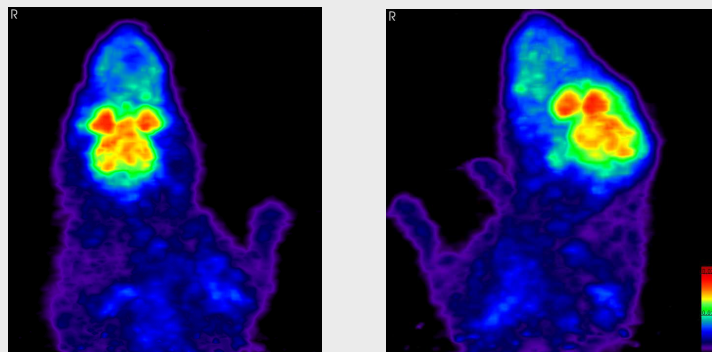
- PET scan of a C57 mice with melanoma tumor using  $^{18}\text{F}$ FDG. The image shows the size of the tumor and radionuclide uptake.

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## Images from our Studies in TPCF



- PET scan of rat with Glioblastoma (GBM) tumor using  $^{18}\text{F}$ FDG.

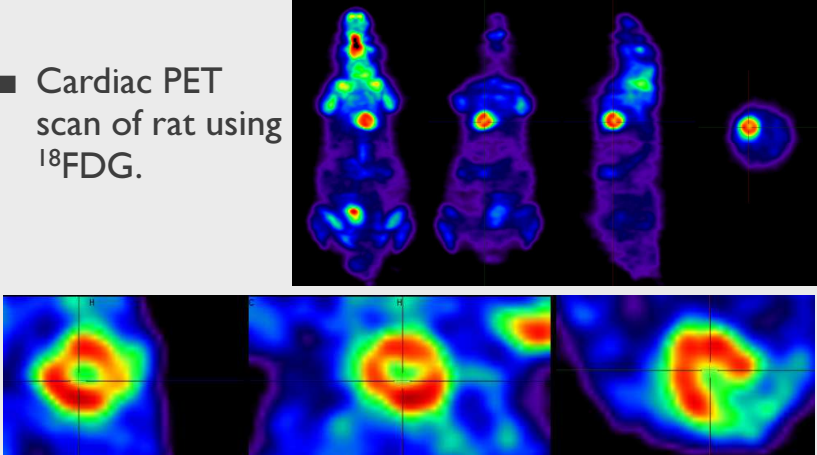
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Images from our Studies in TPCF

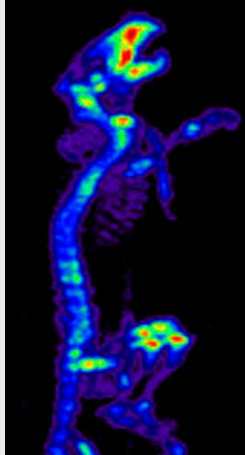
- Cardiac PET scan of rat using  $^{18}\text{F}$ FDG.



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Images from our Studies in TPCF

- Bone scan



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**Quantitative Analysis Report**

Doc. No.:  
Project No.: P97-067  
Date: 1397.10.26

**Materials and Methods:**

*Small-Animal PET Imaging and Image Analysis:*

The small-animal PET scans were obtained with a micro-PET scanner (Xrim PET). Mice were each injected via the tail vein with about 100 µCi of the <sup>18</sup>F-DG under general anesthesia. For each small-animal PET scan, 3-dimensional regions of interest (ROIs) were manually drawn over the abdomen area on whole-body coronal images. The ROI's were converted to the activity uptake ratio as: 100 \* (ROI counts) / (total body counts - ROI counts).

**Results:**

*Small-Animal PET Imaging*

Table 1 - The amount of the radiotracer uptake ratio of the selected ROIs for each mouse. The uptake ratio calculated as 100\*(ROI counts) / (Total body counts - ROI counts).

Radiotracer Uptake Ratio (%)					
11.9.1397			18.9.1397		
Normal	Tumor	N1	N2	T1	T2
22.31	60.09	14.65	16.82	30.13	30.6

Figure 1 - Representative small-animal PET images for each mouse 1 hour after injection of FDG. The Red arrow indicates the higher amount of radiotracer uptake (Tumor). The yellow dash line shows the selected region of interest (ROI).

## Quantitative Analysis Report

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## Organizing a Research Collaboration

```

graph TD
    A[Idea for a Scientific Project] --> B[First Meeting]
    B --> C[NO]
    B --> D[Scientifically interesting?<br/>Realistic scientific goal?<br/>Manpower?]
    D --> E[YES]
    D --> F[NO]
    E --> G[Animal Use & Care]
    G --> H[Pilot Study]
    H --> I[Discuss First Results]
    I --> J[2nd Pilot]
    I --> K[Stop Study]
    I --> L[Full Project]
    L --> M[Financing, Grant Proposal (PI, co-PI)<br/>Manpower, Commitment, Effort<br/>Animal Use & Care<br/>Publications]
    
```

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Thanks for Your Attention



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TPCF

www.TPCF.ir  
tpcf.tums.ac.ir

info@TPCF.ir  
tpcf@tums.ac.ir

