


**TEHRAN UNIVERSITY
OF
MEDICAL SCIENCES**

**TUMS PRECLINICAL
CORE FACILITY (TPCF)**





INTRODUCTION OF TEHRAN UNIVERSITY OF MEDICAL SCIENCES (TUMS) PRE- CLINICAL CORE FACILITY (TPCF)

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

TPCF Workshop
May 28th-29th 2019, Manila, Philippines

Why Preclinical Imaging

“Researchers are not mouse doctors”

↓

**Fundamental
Understanding
of Biology/
Biochemistry**

- transfer in-vitro to in-vivo
- verify models

Massoud T.F., Gambhir S.S.;
Molecular Imaging in living subjects:
seeing fundamental
biological processes in a new light; Genes
Dev, 17, 545-580, 2003

↓

**Design and
Evaluation of new
Biomarkers (drugs)
(diagnosis/therapy)**

- dynamics and kinetics
- efficacy (candidate selection)
- dosing

Rudin M., Weissleder R.;
Molecular Imaging in drug discovery
and development
Nat. Rev. Drug Discov., 2, 123-131, 2003

↓

**Test Bed for new Imaging
Technologies and
Techniques**

- small size prototypes
- low capital investment
- POC (proof of concept)

Gleich B., Weizenecker J.;
Tomographic Imaging using the
nonlinear response of
magnetic particles
Nat., 435(30), 1214-1217, 2005

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Why Preclinical Imaging?



• Rats & mice = models of many human diseases

⇒ Opportunity to study progression of disease and response to treatment

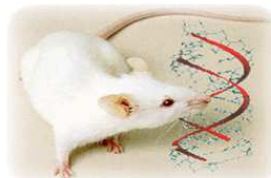
- ✓ under controlled conditions
- ✓ non-invasive
- ✓ repeatedly
- ✓ in the same animal

⇒ Genomics / Proteomics

- Gene expression \leftrightarrow Phenotype
- Evaluation of gene therapy

⇒ Preclinical bridge \leftrightarrow Phase I Trials

- PK/PD, ADME(T), dosage
- Study of specificity, site & mechanisms of action of new agents
 - fast sifting of new molecules (< time)
 - quick decision for promising agents (< cost)






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The PCI Resolution Problem



	→	Human	175 cm 75 kg
	→	Rat	20 cm 300 g
	→	Mouse	5 cm 30 g

The volume of a mouse is 2500 times smaller than that of a human.


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Detectability vs. Sensitivity

Higher Sensitivity
Poorer Resolution



Simulated image increase PSF by 45% increase sensitivity by 20%

Lower Sensitivity
Higher Resolution



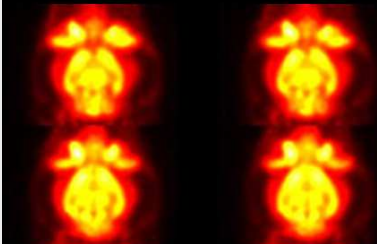
Infrared portrait of the Small Magellanic Cloud, taken by NASA's Spitzer Space Telescope - nasa.gov

Would NASA settle for this tradeoff?

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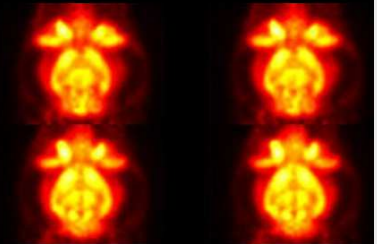
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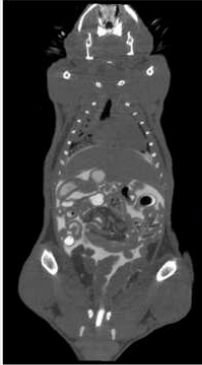
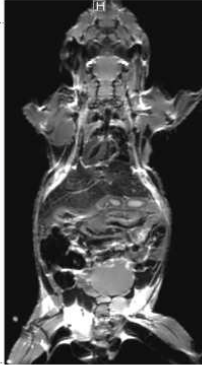
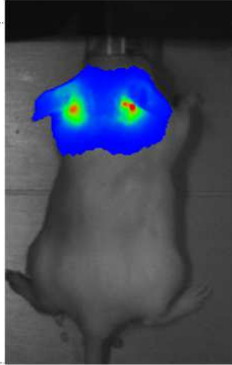
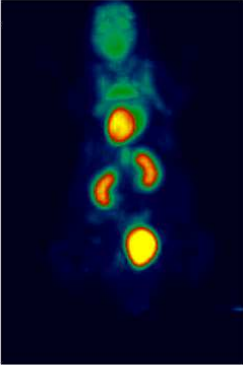


Why would YOU accept this tradeoff?

Images courtesy of Olivier Clerck-Lamalice, Prof. Roger Lecorche, Prof. Martin Lévesque (Université de Sherbrooke, Sherbrooke, Canada) and Lionel Carroon, MD (Hôpital Ste-Justine, Montreal, Canada)

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Dedicated Small Animal Imaging Modalities

Morphology
Morphology (Function)
Function
Function

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Modern Imaging Technologies and their Limitations

	Anatomy	Physiology	Metabolism	Molecular
Micro CT	▶			
Ultrasound	▶			
MRI	▶			
SPECT	▶			
Micro PET	▶			
Optical	▶			
Autoradiography Histology	INVASIVE			


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TUMS Core Facility




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Made in Iran (TUMS Companies)



- Micro SPECT
- Micro PET
- Optical Tomography
- Optical Planar
- Micro CT
- Micro Ultrasound
- Imaging Analysis Software



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Quality Management System and AEOI Certificate




ISO 9001

CERTIFICATE of REGISTRATION

BRSM
ISO 9001

Certificate Number: QMS0324040617
TUMS Preclinical Core Facility
 No. 41, Haly St., Between Vasa and Quds St., Tehran, IRAN

Assessment of the management system demonstrates evidence that the organization adheres to legal and regulatory obligations and contractual agreements by addressing Quality Management System ISO 9001 for the purpose to protect communities and consumers. This certification-instrument is not transferable and remains the property of the International Registration Body BRSM.

Scope of activities: Providing Knowledge Based Preclinical Imaging, Signaling, Stimulating And Laboratory Services

Date of Effectiveness: 03 June 2017
 Date of Renewal: 03 June 2020

H. A. Layhi
 BRSM
 BRSM, Europe Office

03 June 2017
 Date




سازمان آموزش عالی تهرآن
 دانشگاه علامه طباطبائی
 واحد تحقیقات

گواهی ثبت سیستم مدیریت کیفیت
 استاندارد ایزو ۹۰۰۱

شماره گواهی: QMS0324040617
 نام سازمان: مرکز تخصصی تجهیزات پزشکی
 آدرس: تهران، خیابان هالی، بین خیابان وصال و خیابان قدس، پلاک ۴۱
 تاریخ اعتبار: ۰۳/۰۶/۱۳۹۶
 تاریخ تمدد: ۰۳/۰۶/۱۴۰۰

این گواهی بر مبنای ارزیابی سیستم مدیریت کیفیت سازمان صادر شده و نشان دهنده آن است که سازمان با الزامات استاندارد ایزو ۹۰۰۱ در زمینه خدمات ارائه دهنده خدمات تخصصی تجهیزات پزشکی مطابقت دارد. این گواهی به صورت دائمی صادر می‌گردد و قابل انتقال به سایر سازمان‌ها نیست.

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Micro-PET Scanner






Preclinical PET Imaging System

PET Detector

- LYSO crystal full ring geometry
- Up to 120 mm transaxial FOV
- Bore opening: 120 mm
- Up to 1.5 mm spatial resolution

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
- ECG gating (optional)



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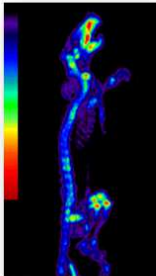

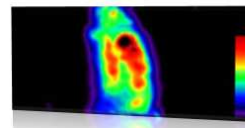
Software Package

XtrimVision is the software with a user-friendly GUI developed exclusively for Xtrim covering all needs of calibration correction, data acquisition, rebinning, and image reconstruction. NaF PET image of Rat using Xtrim PET Scanner. Imaging with NaF is the initial method of choice to detect skeletal metastases in cancer.


Characteristics	
Single-bed axial POV	5 cm
Number of detector rings	24
Transaxial FOV	100 mm
Bore opening	120 mm
LYSO crystal size	2 mm × 2 mm × 10 mm
Total number of crystals	5,760
Spatial resolution	1.8 mm without resolution recovery
Energy resolution	17%

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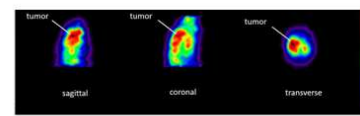
Micro-PET Scanner

Rat Bone Scan
Radio tracer: ^{18}F -NaF



Rat Brain
Radio tracer: FDG




sagittal coronal transverse

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PET : Versatile applications

High sensitivity for superior organ-specific imaging

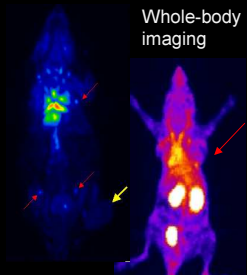


High resolution and uniformity for whole body imaging


Greater sensitivity

Higher resolution

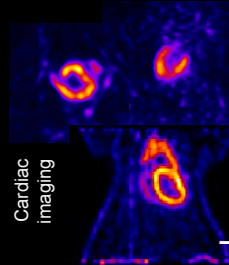
Whole-body imaging



Flexibility

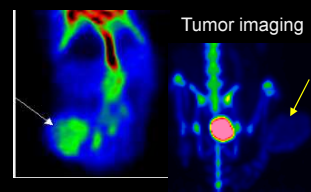


Cardiac imaging




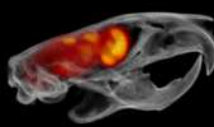
Resolution uniformity

Tumor imaging



Brain imaging





Micro-SPECT Scanner



HiReSPECT

High Resolution Animal SPECT Imaging System

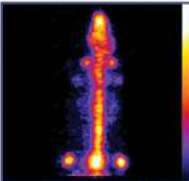
HiReSPECT provides the highest performance and versatility available to address your preclinical imaging research needs from academic and translational research, to drug discovery and development.

The 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.



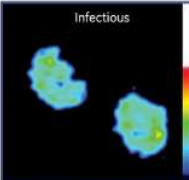
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Images acquired by HiReSPECT at TPCF

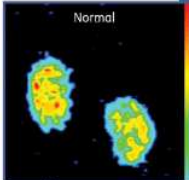


Mice Bone Scan

- Model: Healthy
- Radio Isotope: ^{99m}Tc-MDP



Infectious



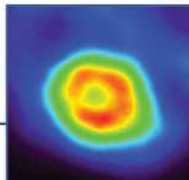
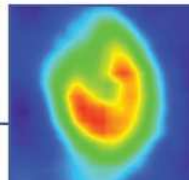
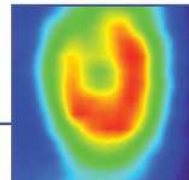
Normal

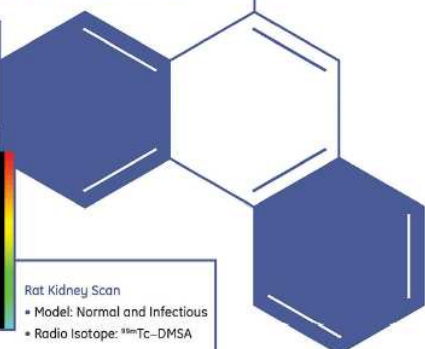
Rat Kidney Scan

- Model: Normal and Infectious
- Radio Isotope: ^{99m}Tc-DMSA

Mice Heart Scan

- Model: Healthy
- Radio Isotope: ^{99m}Tc-MIBI



TUI

Typical SPECT imaging applications



- Cardiac and cerebral blood flow, cardiac tissue viability and apoptosis;
- Uptake and retention of dopamine receptor & transporter
- markers: Schizophrenia, ADHD, Parkinson, obesity, addiction, depression
- Amyloid plaques (e.g., Alzheimer, diabetes,...)
- Gene expression, angiogenesis, apoptosis and metabolism in tumours
- Infection imaging
- Cell trafficking and homing
- Image based therapy



Planar Gamma Camera



SERGEOSIGHT

SERGEOSIGHT installed in TPCF is a portable mini camera developed for pre-surgical lymphoscintigraphy thyroid scan and intra-operative localizing sentinel lymph nodes. Lymphoscintigraphy and sentinel lymph node biopsy is an area of increasing utility in determining which lymph node basins serve the diseased tissue. The presence or absence of regional lymph node involvement often determines the staging and treatment of many malignant tumors. In some clear words, it can play the role of a ((Surgeons sight)) in an operation room



Specifications

- **Number of pixels:** 36 × 36
- **Pixels size:** 1.2 mm × 1.2 mm
- **PSPMT:** H8500
- **Field of View:** 42mm × 42mm
- **Spatial Resolution:** <2.6 mm FWHM @ Collimator Surface
- **Energy Range:** 60 – 300 keV
- **Weight:** 1.2 kg

Micro-CT Scanner



in-vivo Micro CT

This high technology device is capable of displaying non-living micro objects at the micrometer resolution of two-dimensional (Thin Slices) or three-dimensional images, while displaying the anatomy of small animals.

The advanced software of this device can display images in different ways and present them in standard image formats. The power of three-dimensional reconstruction of data in different rendering methods significantly increases the analytical strength of the researcher.

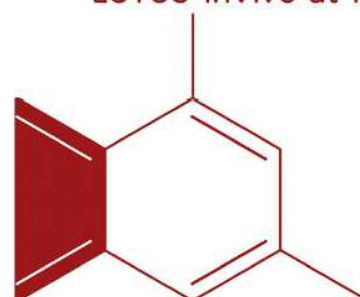


Micro-CT Small Animals (Lotus-In Vivo)

- Imaging mode
 - Micro-Radiology and Micro-Fluoroscopy
- Micro Focus X-ray tube
 - Focal Spot Size: Less than 5µm
 - 8W power
- High Resolution X-Ray Detector
 - resolution: from 10µm to 35µm
- Maximum diameter of the scanned object: 80mm
- Maximum length of scanned object: 200mm
- Reconstruction Filters: 16 levels, Ultra-Smooth to Ultra-Sharp
- Radiation Safety: Less than 1µSv at a distance of 5 cm from anywhere on the surface of the device


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Images acquired by LOTUS-inVivo at TPCF




Micro-CT Imaging Applications


- Osseous structures
- Vascular structures
- Cardiothoracic imaging
- Imaging of abdominal organs
- Gastrointestinal tract
- Cerebral structures
- Dental Research
 - Analysis of root canal morphology
 - Evaluation of root canal preparation
 - Craniofacial skeletal development and structure
 - Tissue engineering
 - Mineral concentrations of teeth
 - Implant and peri-implant bone



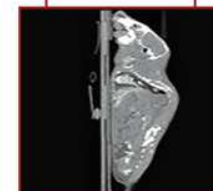
Human Dental Void Fraction




Coronal




Human Dental Micro Fraction



Sagittal



Axial



Rat Whole Body Scan

Pre-clinical CT Applications



Musculoskeletal

- Bone Metastasis
- Arthritis
- Osteoporosis
- Remodeling

Vascular

- Disease progression
- Therapeutic effect

Oncology

- Angiogenesis
- Metastases – liver, lung, bone

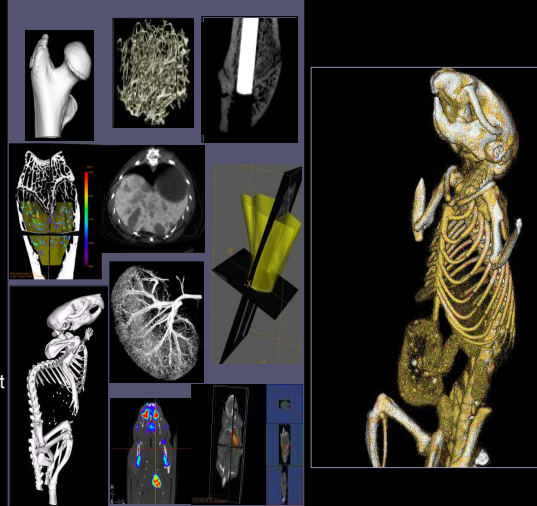
Phenotyping

Cardiovascular disease

- Stenosis
- Vascular disease & development
- Injury/repair
- Vessel geometry

Respiratory disease

- Lung Tumor
- Airway structures
- Lung vasculature



Courtesy of:
 Dr. David Holdsworth, Roberts Research Institute, London, ON, Canada
 Dr. Dianna Cody, MD Anderson Cancer Center, Houston, TX
 Dr. Jamey Weichert, University of Wisconsin, Madison, WI

Optical Imaging System



FluoVision® Preclinical System


FluoVision is a range of systems for in vivo fluorescence imaging. It provides real time images and videos of fluorescent signals in living animals, for non-invasive imaging, surgery or dissection (intraoperative imaging), for small and large animals.




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FluoVision Specifications:	
Camera and Lens	16MP CCD camera
Detector Type	8x8
Pixel Size (W x H; μm)	8.4x9.8
Read noise (e-)	<1 to 18 @ 13.5 MHz
FOV (cm)	Max 12x12
Lens	f/1.1-f/16, 30 mm lens
Quantum efficiency	>85% from 500-650 nm >40% from 650-850 nm
Frame Rate	15 fps at 1024x1024 pixels
LED Excitation Wavelength (nm)	390, 460, 485, 630
Emission Filter	450/40, 500/40,
Wavelength/Bandwidth (nm)	540/10, 560/10, 700/40, 800/40
System Size (WxDxH; cm)	80 x 70 x 90
Resolution (mm)	<0.5
Weight (kg)	6

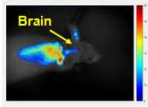
Optical Imaging System



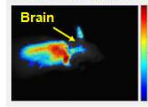
Before



After 30 minutes




After 60 minutes




**Mice brain drug delivery for Alzheimer disease
Fluorescent agent: FITC**

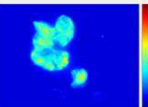
In Vivo Imaging




Light Imaging



Ex Vivo Imaging



**Sepsis Mice
Fluorescent agent: GFP labeled USSC Cell Tracking**



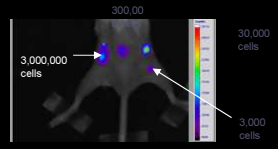
**FluoVision®
Preclinical System**

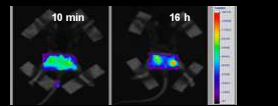
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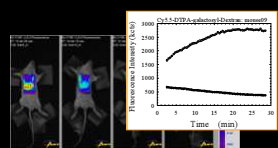
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Fluorescence Optical Applications

Area	Activity	Requirements
Oncology	<ul style="list-style-type: none"> • Tumor detection • Tumor size • Tumor localization • Angiogenesis 	<ul style="list-style-type: none"> ✓ Sensitivity ✓ Quantitation ✓ Tomography ✓ Deep tissue
Disease biology	<ul style="list-style-type: none"> • Disease progression • Gene expression • Protein-protein interaction • Receptor studies • Antibody labeling 	<ul style="list-style-type: none"> ✓ Sensitivity ✓ Quantitation ✓ Multiplexing
	<ul style="list-style-type: none"> • Kinetics • Gastric Emptying • Organ screening 	<ul style="list-style-type: none"> ✓ Sensitivity ✓ Quantitation ✓ Dynamic imaging







Analysis Workstation



SANIVIS™

This SaniVis system has been designed and developed to show simultaneous images in different imaging systems from small animals – pets - such as MRI, CT, Optical Imaging, 3D Sono, PET, SPECT and other imaging systems. Based on the goals which are set, this software has following specifications:



SaniVis System Specifications

- Saving information of each subject in the database
- Automatic saving of the last changes made in the database
- Immediate view of images and studying the necessary characteristics
- Controls and corrections of anatomical positions of the image
- Immediate control of the imaged scopes by using 3D models
- The possibility of reading the file of animal specimen crated via PACS, flash memory, CD or DVD
- Sophisticated GPU-based 3D volumetric module
- Capability of adding the module of image compatibility
- The capability of adding an advanced segmentation module

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Project Acceptance Process

To register a project in the TPCF, the following steps are necessary to take:

1 Registration Request

There are two options to register either online or in-person. Online registration is possible by accessing the TPCF site, creating an account, filling out a project registration form, and submitting the application. For in-person registration, the project registration form should be completed in-person.

2 Validation and Verification

Upon receiving a project request, the registration team will review and contact the requester within few working days. Then, the researcher will be contacted by the TPCF scientific officers.

3 Project Description

If the project is approved, a project description form must be filled out and handed in-person. Then, the registry administrator will inform the researcher about the project cost and an invoice would be issued.

4 Project Order

After the invoice has been paid, the researcher can schedule an appointment for the experiments. After filling out a project order form in-person, the project shall be started.

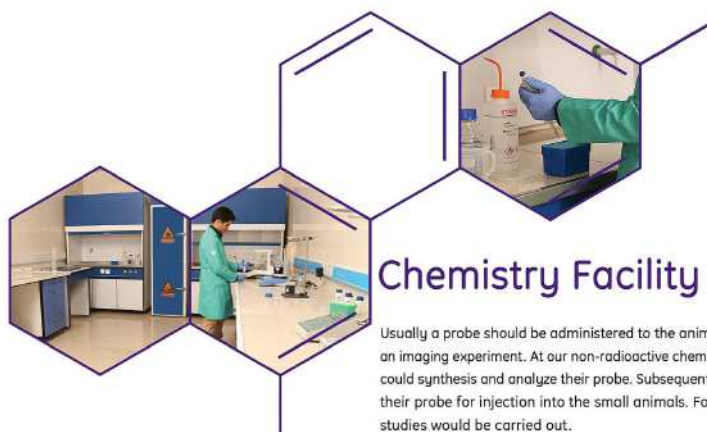
5 Data Delivery

To deliver the data, a separate data delivery request form must be filled out and outstanding debt for the cost of all provided services must be fully paid.

The Registry Administrator is available to assist the requester throughout the registration process.

TUMS Preclinical

Chemistry Facility



Chemistry Facility

Usually a probe should be administered to the animal before conducting an imaging experiment. At our non-radioactive chemistry facility, scientists could synthesis and analyze their probe. Subsequently they could prepare their probe for injection into the small animals. Following this, imaging studies would be carried out.

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Radiochemistry Facility



Radiochemistry Facility

All procedures for radionuclides preparation that are needed for imaging by PET, SPECT and Gamma Camera devices are performed in this facility. These include determining the type of radioactive component and the activity level that should be injected in accordance with the protocol of the study.

The main services of this laboratory are as follows:

- Performing a qualitative control on radiopharmaceuticals, including the diagnostic and therapeutic radiopharmaceuticals for research purposes.
- Consulting the feasibility study on the implementation of research projects in the field of production of radiopharmaceuticals.

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Histology Facility



Histology Facility

The tissue laboratory has been considered in conjunction with other laboratories to investigate biological interventions on tissues of different animal organs after imaging. The necessary equipment for testing different tissues in this laboratory is available.

The major services of this laboratory are:

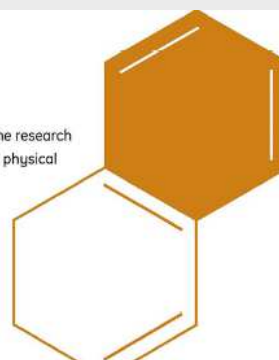
- Creating slides with the required thickness from the organ of the body to study histological tests
- Coloring various parts of the tissue treated with monoclonal antibodies

Molecular Biology Facility



Molecular Biology Facility

Today, molecular imaging has been expanded rapidly and plays a fundamental role in the research and applied sciences. The molecular imaging is the interface between the biological and physical sciences and provides a new look to biomedical research to observe the characteristics and monitor the biological processes in cells, tissues and organisms by means of the sensitive and precise imaging modalities and also by using contrasting mechanisms. Therefore, it is predictable that the future of imaging would be molecular imaging. At TPCF, molecular imaging could be provided considering the substance synthesized by the researcher with modalities such as CT, Optical imaging, PET, SPECT, and MRI. Scientists could also perform molecular biology tests on proteins, DNA and RNA before and after their imaging study at TPCF's molecular biology facility.



Cell Culture Facility






Cell Culture Facility

Understanding the amazing world of cells requires studying their morphological, behavioral, molecular, developmental and interaction processes. Before conducting *in vivo* studies, it is necessary to examine the cell through *in vitro* methods.

The major services of this laboratory are as follows:

- Isolation and culture of normal and cancerous cells
- Maintaining cells for long periods
- Measuring the cell survival and drug interventions
- Labeling cells for different imaging modalities

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Surgery Facility






Small Animal Surgery Facility

Micro-surgery and related procedures are performed in this facility. This facility is vital as there could be a limited time interval between injection of the desired drugs and imaging study. The researchers can conduct surgical procedures on animals with the instruments provided by themselves, or by the TPCF. They can also utilize this facility if they want to perform biodistribution studies.


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Animal Holding Facility




Small Animal Holding Facility

Animal holding area of TPCF has been organized to supply the researchers with an areawhere they can hold their animals throughout the experiment. It is possible to hold small animal Such as mouse, rat and rabbit in the facility for limited time. Maintenance of animal models and injections of different drugs for imaging is also provided in this facility.



Animal Section Services

- Providing Scientific consultancy in animal models
- Brain and nervous system models
- Cardiovascular disease models
- Gastrointestinal models
- Skin disease models
- Cancer models

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TPCF Symposium






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Training Activities




ALL IN ONE WORKSHOP

JOIN US FOR A HALF-DAY TO UNDERSTAND WHAT IS INVIVO IMAGING AND ITS IMPORTANCE

CONTENTS:
 SPECT IMAGING
 PET IMAGING
 ULTRASOUND
 OPTICAL IMAGING
 MRI
 CT
 ANIMAL HANDLING

VENUE: LOWER GROUND FLOOR, TUMS PRECLINICAL CORE FACILITY, ITALIA STREET, TEHRAN

FOR BOOKING: WWW.TPCF.IR

Journal Club: Preclinical Imaging

Venue: TUMS Preclinical Core Facility

Date: Last Wed of Every Month
Time: 2-3pm

Students and Faculty are welcome!!!

Who could present?
MD/DDS/MPharm/BS/MSc/PhD/Post-Docs

Volunteering to present?
- Papers should have a preclinical imaging component.
- Can be on any discipline

FOR MORE INFORMATION VISIT: WWW.TPCF.IR
TPCF ON SOCIAL MEDIA: @TUMS_PRECLINICAL_CF

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Thanks for Your Attention






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