TEHRAN UNIVERSITY OF MEDICAL SCIENCES

TUMS PRECLINICAL CORE FACILITY (TPCF)

MICRO-CT

PHYSICAL PRINCIPLES & APPLICATIONS

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Introduction

Computed Tomography,

- To see what a sample looks like both inside and out
- X-rays is used to visualize differences in the density within a sample
- A detailed 3D image or a model is produced
- The x-rays do not damage or alter the sample/patient material

Introduction

Micro-Computed Tomography,

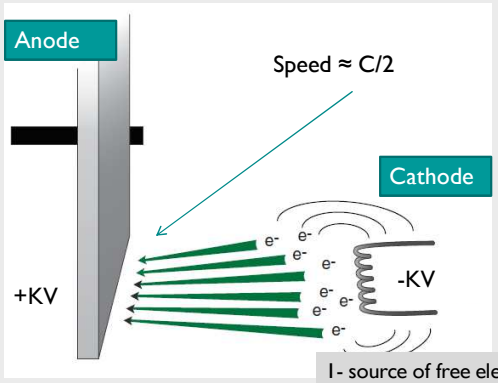
- Micro-CT is the same as a hospital CT
- Micro-CT can achieve much higher resolution on small samples
- Same as hospital CT, it is constructed by:
  - An x-ray source
  - A x-ray detector
  - A rotating mechanism
  - A reconstruction software to make tomographic image

Introduction

Table 1 Essential parameters of CT-scanners

	In-vitro micro-CT	In-vivo micro-CT	C-arm CT	Clinical CT
Spatial resolution	1…200 μm	50…200 μm	200…400 μm	250…1000 μm
FOM diameter	1…200 mm	30…100 mm	100…250 mm	500…700 mm
Tube voltage	10…160 kV	10…160 kV	50…125 kV	80…140 kV
Tube current	0.04…2 mA	0.04…2 mA	10…800 mA	10…600 mA
Tube power	1…30 W	1…30 W	20…80 kW	20…100 kW
Scan time	<1 h	10 s…10 min	5…20 s	0.3…20 s
mAs_{eff}	5…200 mAs	5…200 mAs	10…750 mAs	10…750 mAs
Detector	1024^2…4096^2	1024^2…4096^2	1024^2…2048^2	≈1000 × 64
Dose	≤1500 mGy	50…500 mGy	1…70 mGy	1…70 mGy
Acquisition rate	≤20 MB/s	≤20 MB/s	≤60 MB/s	≤600 MB/s

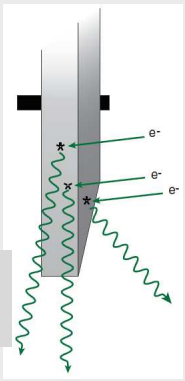
How is x-ray Produced



1- source of free electrons: thermionic emission from heated filament (~2000° C)

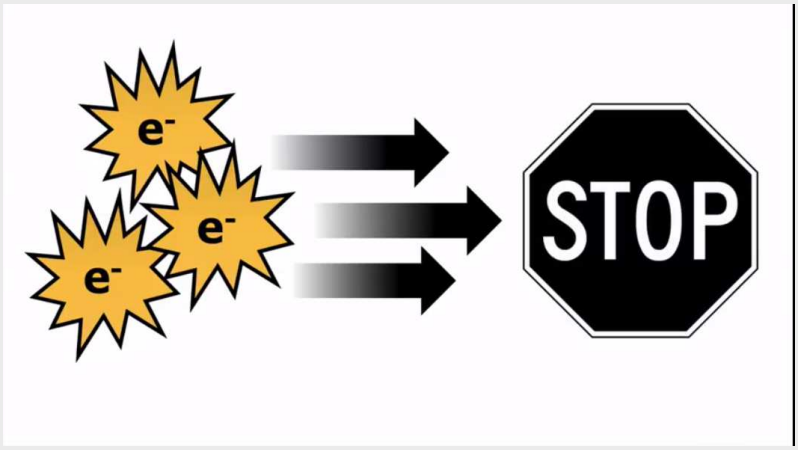
2-Accelerating the electrons to extreme speeds by applying extremely high-voltage

3-Suddenly decelerating the electrons.



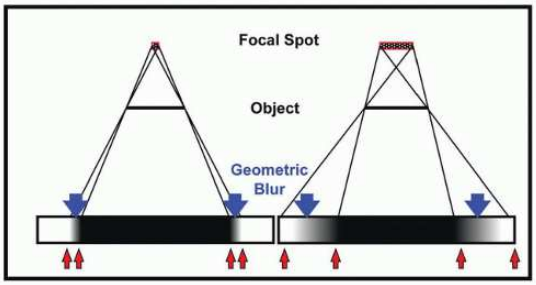
x-rays
(0.5% to 1% of Kinetic energy)

How is x-ray Produced



X-ray Tube in Micro-CT

- Micro-Focus x-ray tubes are used in Micro-CT
- Micro-Focus means: the size of spot generating x-ray is micron-sized
- it should be Micro-Focus, because:
  - Minimum value of blurring
  - Maximum value of resolutio



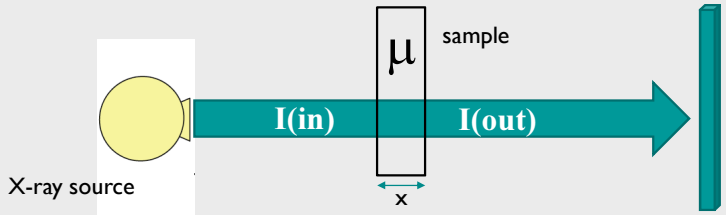
X-ray Tube in Micro-CT

- As the focal spot is very small, the current generated is small
- So, the x-ray photon flux is so small
- And, the scanning time in Micro-CT is long
- Compare to Hospital CT

Sample attenuates x-ray

Lambert–Beer's Law:

Radiation intensity decreases exponentially while running through object along the incident direction.



$$I_{out} = I_{in} . e^{-\mu x}$$

Linear Attenuation Coefficient

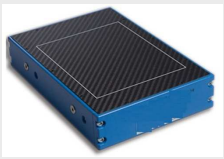
Sample attenuates x-ray

- Attenuation is the reduction of the intensity of an x-ray beam as it traverses matter.
- The reduction may be caused By absorption or By scattering of photons from the beam
- Absorption can be affected by different factors such as x-ray beam energy and atomic number/density of the absorber.
- Traversed photons are detected and converted into a useful image by an image receptor.

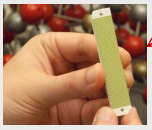
Images are formed when different structures in the body absorb different amounts of radiation from the beam

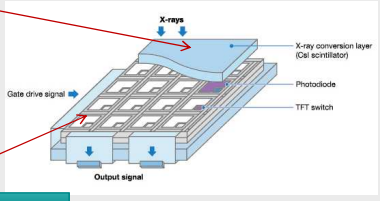
Micro-CT x-ray detectors

- Micro-CT detectors are made up of a scintillator
- scintillator crystals convert x-rays to visible light
- Generated light is then read by a photodiode array.



Ability to convert x-ray energy to light





Ability to convert light energy to signal

MICRO-CT DESIGN AND GEOMETRY

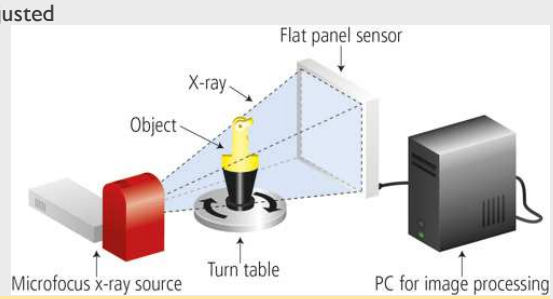
Micro-CT Design and Geometry

- Rotating object Micro-CT
  - tube-detector is stationary
  - Object rotates
- Rotating gantry
  - tube-detector rotates
  - object is stationary

Micro-CT Design and Geometry

Rotating object Micro-CT,

- For in-vitro & industry imaging
- robust and cost-efficient
- high spatial resolution
- magnification can be easily adjusted



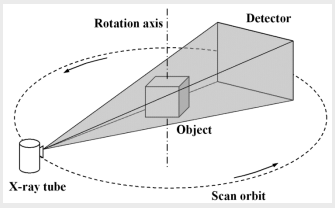
Micro-CT Design and Geometry

Lotus-NDT (rotating object Micro-CT)

Micro-CT Design and Geometry

Rotating gantry Micro-CT,

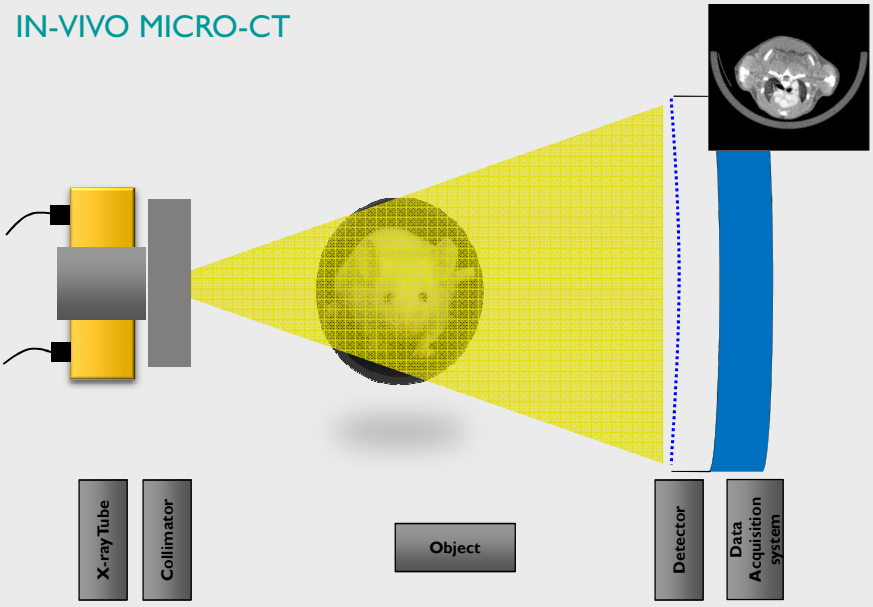
- Mostly for in-vivo imaging
- Easy animal handling
- Resemble the clinical CT scanners that also have a patient bed



Micro-CT Design and Geometry

Lotus-inVivo (rotating gantry Micro-CT)

IN-VIVO MICRO-CT



Data Processing

Three steps:

1- Raw data pre-processing: to facilitate the reconstruction in next step
- ❑ Corrections
- ❑ Reformatting

2-Image reconstruction: scan data(attenuation reading) converted into image. Each pixel in this image represent μ values

3-CT Value transformation: the μ values converted to CT Numbers as follow:

Material	μ (73 KeV)	~CT #
Water	0.19 cm^{-1}	0
Bone	0.38 cm^{-1}	1000
Air	0.0004 cm^{-1}	-1000

$$\text{CT-Value} = \frac{\mu - \mu_{water}}{\mu_{water}} 1000$$

MICRO-CT PRECLINICAL APPLICATIONS

Micro-CT Preclinical Applications:

1. **Anatomical Imaging:**
   - Bone Micro-Structure Evaluation
   - Lung Imaging
   - Skeletal Evaluation
   - Vasculature
   - Cardiac

Micro-CT Preclinical Applications:

2. **Functional Imaging:**
   - Tumor Detection
   - Perfusion (Cardiac, Tumor,…)
   - Inflammatory Bowl Disease
   - Evaluation of bone metabolism

Micro-CT Preclinical Applications:

3. **Molecular Imaging:**
   - Targeted Contrast Agent
   - Drug Delivery
   - Nano-Medicine
   - Hybrid Imaging:
     - Micro-SPECT/Micro-CT
     - Micro-PET/Micro-CT
     - Micro-CT/BIO-luminance

Micro-CT Preclinical Applications:

The micro-CT data are more informative and quantitative compared with 2D histological examination:

- in vitro Examination of three-dimensional bone architecture
- 3D measurements of trabecular bone morphology parameters such as:
- Trabecular thickness, spacing, density and connectivity.
- Evaluation of osteoarthritis,
- Evaluation of bone metabolism

Micro-CT Preclinical Applications:

Using micro-CT to investigate the mice pulmonary structure and function

- Evaluation of lung in Mice
- Obtaining physiologic information for normal, acute or chronic diseased mice
- In vivo respiratory-gated micro-CT imaging in small-animal oncology models
- assessment of emphysema in mice

Micro-CT Preclinical Applications:

To study the structure of the vasculature structure filled with contrast agent

- produce 3D images of vasculature structure at a spatial resolution typically less than 30 micro-meter
- Quantitatively investigation of three-dimensional connectivity

Micro-CT Preclinical Applications:

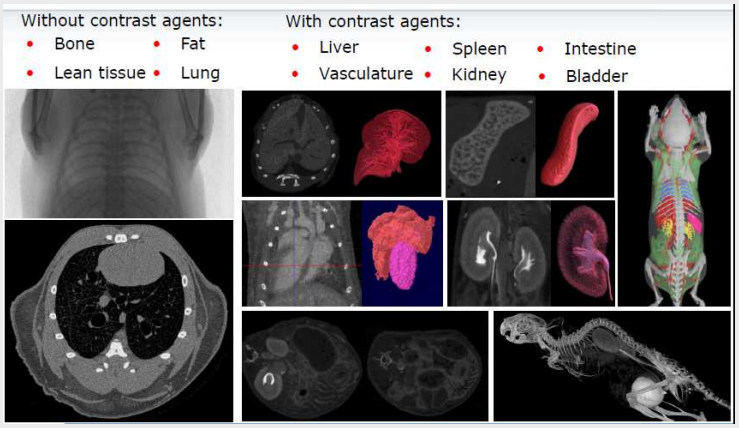
- imaging tumor angiogenesis
- Dynamic micro-CT has also been applied to the direct measure of perfusion in tumors following the injection of extracellular contrast agent

Multi-modality imaging

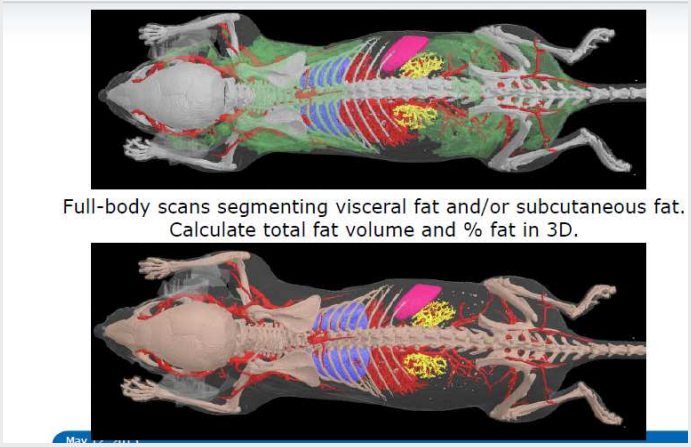
The multi-modality imaging which combines micro-CT with other imaging techniques such as micro-PET and micro-SPECT

- micro-PET/micro-CT suitable for small animal imaging
- provide metabolic information of the tissue, while having the information provided by the micro-CT to delineate the anatomical structure
- Investigation of anatomical-functional relationship
- **Or,** Micro-CT/Micro-SPECT
- micro-CT provides the linear attenuation map of the scanned small animal. The correction might be evident when low-energy radionuclides are used

Micro-CT Preclinical Applications:



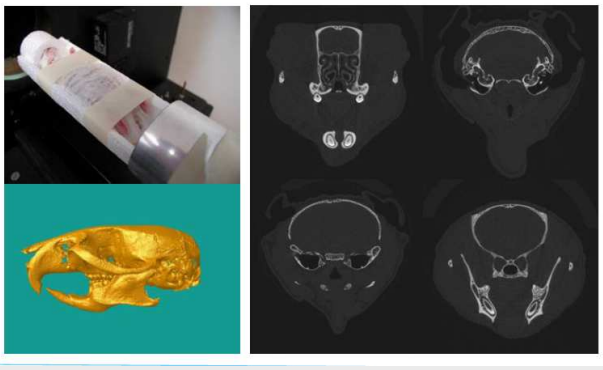
Micro-CT Preclinical Applications:



Full-body scans segmenting visceral fat and/or subcutaneous fat.
Calculate total fat volume and % fat in 3D.

Micro-CT Preclinical Applications:

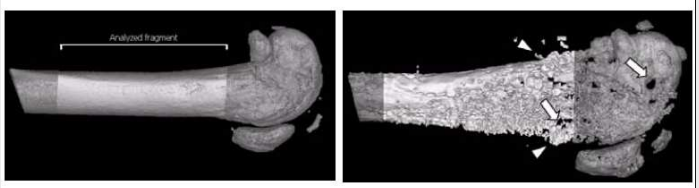
In vivo micro-CT: the head



Micro-CT Preclinical Applications:

Imaging and quantitative analysis of tumor damage to mouse bone

Cultured tumour cells were injected into femur of mice.
Visualization of hindlimbs using the in vivo micro-CT Skyscan 1076



Control - no injection

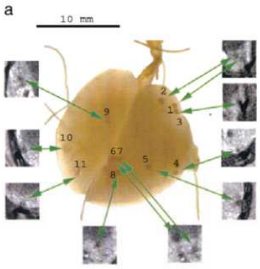
Tumour injected – severe effect

Micro-CT Preclinical Applications:

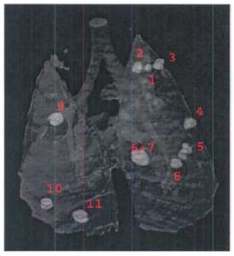
In-vivo detection of lung tumors

Urethane induced lung tumors in A/J mice

in-vivo detection of lung tumors using the SkyScan 1076 correlate with macroscopic and histopathological evaluation



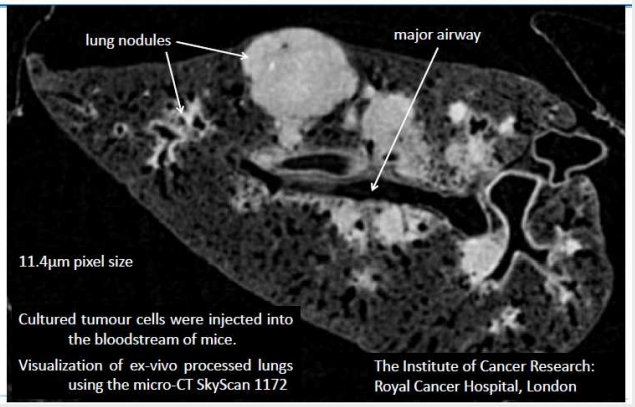
In vivo detectability:
tumor diameter = 200 to 300 µm



De Clerck et.al. 2004, Neoplasia, 6, 374-379

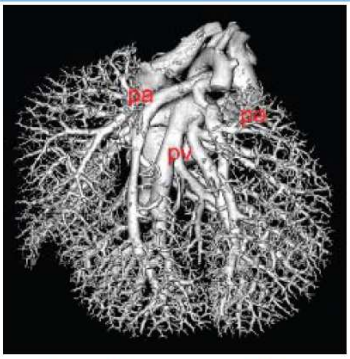
Micro-CT Preclinical Applications:

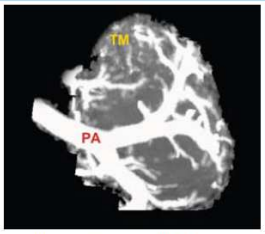
Ex-vivo detection of lung tumors



Micro-CT Preclinical Applications:

In vivo injection of Microfil showing mouse lung vasculature





Lung tumour with surrounding blood vessels

TM = tumour mass
PA = pulomonary arteries
PV = pulmonary veins

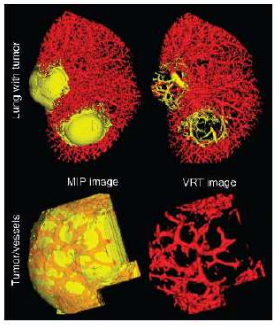
Savai R. et.al. 2005, Am J Pathol, 167, 937-946
Savai R. et.al. 2009, Neoplasia, 11, 48-56

Micro-CT Preclinical Applications:

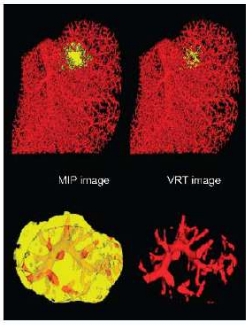
Quantification of lung tumour vasculture destruction

Mouse lung tumour (yellow) and lung vasculature (red)

no treatment



Anti-VEGF treatment



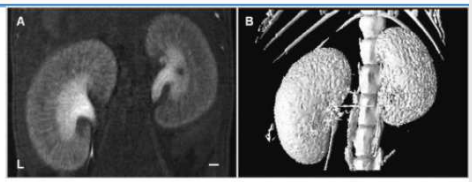
Savai R. et.al. 2009, Neoplasia, 11, 48-56

Micro-CT Preclinical Applications:

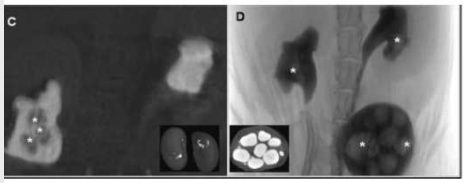
Mouse kidney phenotyping

In vivo scanning using SkyScan 1076

129/Sv male injected with Vivipaque1



kidney size asymmetry



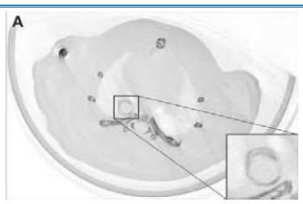
kidney stones bladder stones

Almadjub M. et.al., contrast media mol Imaging 2008, vol 3, 120-126

Micro-CT Preclinical Applications:

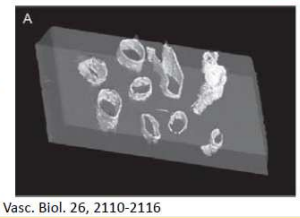
In-vivo detection of aortic calcification

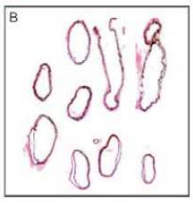
In-vivo micro-CT SkyScan 1076



histological confirmation (Von Kossa staining)

3D model of the calcified parts of aortic tissue embedded in paraffin.

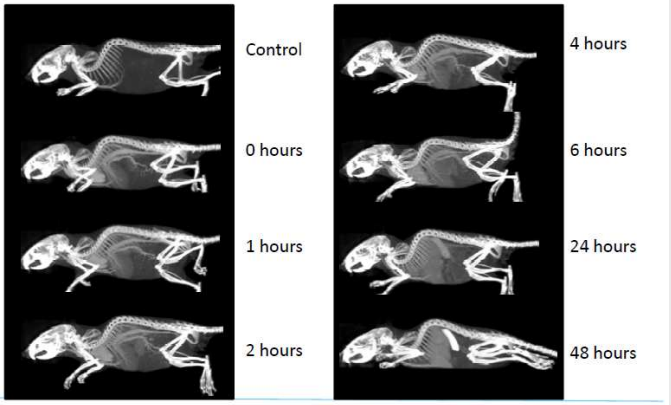




Persy V. et.al. 2006, Thromb. Vasc. Biol. 26, 2110-2116

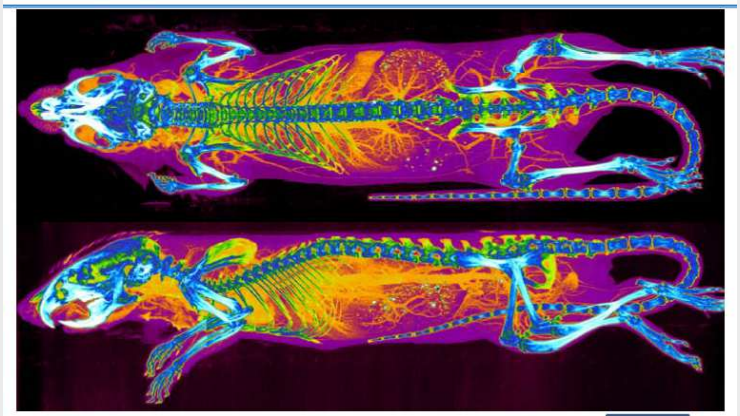
Micro-CT Preclinical Applications:

Gold nano-particles as contrast agent



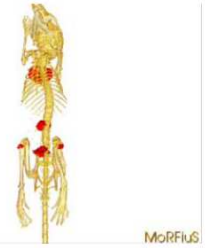
Micro-CT Preclinical Applications:

In-vivo: the iodinated contrast agent eXIA160



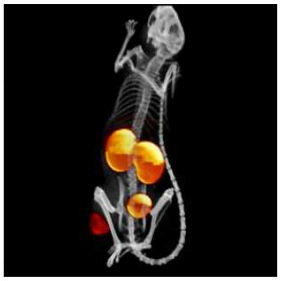
Micro-CT Preclinical Applications:

Multimodality



fluourescence
+
micro-CT

University of Leiden

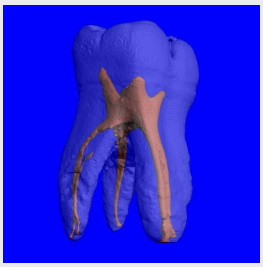


SPECT
+
micro-CT

Brussels University

Micro-CT Preclinical Applications:

- Human teeth



Thanks for Your Attention