

nanoScan[®] PC PET/CT

in vivo molecular and preclinical imager

IMAGING FOR SCIENCE



The first sub-half mm³ PET volumetric resolution PET/CT with exceptional image quantification - accuracy over 97 %

Preclinical Line



nanoScan[®] PET/CT Introduction

To unveil fine and accurate details of living organisms, scientists need high resolution, high-sensitivity, time-dependent quantitation. Definition of kinetic constants of biological processes also became a basic scientific aim.

Offering solutions for modern-day science, Molecular Imaging has gone a long way in a relatively short time to become an indispensable tool for virtually any biologist. One of the most established methods in the field, Positron Emission Tomography (PET) remains the cutting edge and it is still the gold standard in Molecular Imaging.

The reasons of this long-lasting premier position are robust quantitation, high time resolution and real three-dimensional results combined with an adequate observational time window. With PET, fast and easy translation of a result from the laboratory bench to its application in the clinic is also imminent.

In the last years almost every PET imaging result is supported by information about anatomical structures of live animals through X-ray Computed Tomography (CT) imaging.

In the recent past Mediso developed innovative technologies that provided new perspectives to small animal imaging. Now, the new **nanoScan[®]** PET/CT system offers user-friendly imaging and a large scope of applications in one simple to use, high resolution, high-end PET/CT system. **nanoScan[®]** PET/CT is equipped with an imaging technology widely considered as the most advanced PET and CT detector construction, data processing and reconstruction chain in the industry.

Main advantages of the system

- Highest PET resolution ever (using the industry's most advanced pixelated modular LYSO detectors)
- State-of-the-art Tera-Tomo™ 3D PET image reconstruction engine
- Extremely fast, parallel workflow of data acquisition, image reconstruction and image quantitation
- Uniquely easy access to the animal from both the front and the back of the PET/CT gantry
- High imaging throughput by large bore size and large field-of-view in both axial and transaxial directions
- No trade-off between resolution and sensitivity: high resolution images are reconstructed from large field-of-view, high-sensitivity data acquisitions
- High resolution and very low dose cone-beam CT imaging
- One-click MultiCell™ animal anesthesia / imaging bed
- Simple to use with reliable detector technology, no need for long calibrations



Pursuit of perfection

Always eager to find an even better solution, Mediso constantly strives to develop the highest level imaging technology possible.

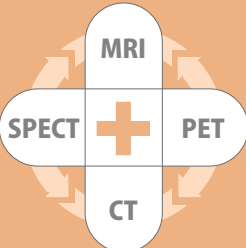
We wish to serve the scientific community with our core value: supreme image quality.

Relying on proven excellence

The gold standard of Molecular Imaging using Mediso's PET/CT technology

Animal imaging studies are performed to provide reliable quantitative results. Moreover, those studies often demand a low limit of detection with high sensitivity. As imaging modality, PET will remain the gold standard of quantitation in biology. This is due to PET's proven measurement accuracy throughout several orders of magnitude and exceptional, unparalleled biological sensitivity inherent in isotopic tracing. PET's leadership in quantitation and sensitivity is established by robust data. **nanoScan**[®] PET/CT ensures reaching the best imaging resolution with the highest sensitivity in the whole body of the animal.

Mediso's unique PET detector technology enables you to detect femtomolar quantities of proteins per milligram of tissue with high resolution and exquisite in vivo image quality.

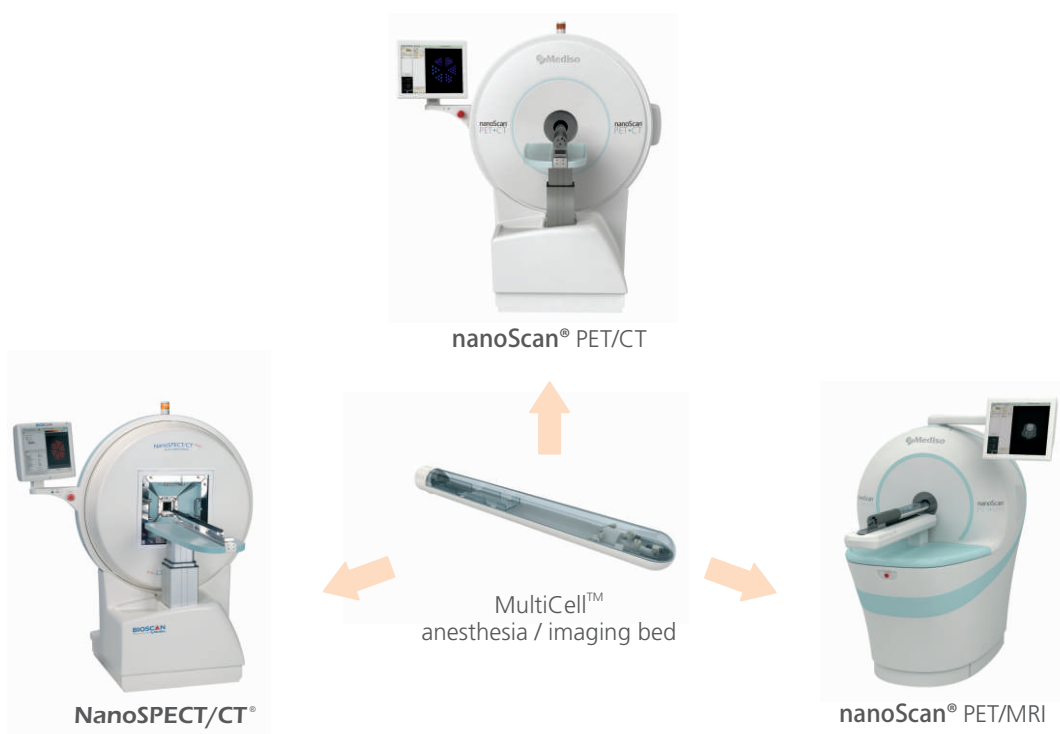


nanoScan[®] - the in vivo multimodality molecular imaging platform

Mediso **nanoScan**[®] family of imaging systems represents the microscopy level of in vivo functional molecular imaging, **nanoScan**[®] is a continuous upgrade path to provide a total solution with four high-power modalities: PET / SPECT / MRI / CT. The common MultiCell[™] animal imaging bed system, common precision gantry mechanics and software tools ensure that as your research grows, all your needs will be served by a Mediso product.

Continuous upgrade path for the existing **NanoSPECT/CT**[®] users:

For imaging facilities already using the world market leader NanoSPECT/CT[®] system (that has been also developed and manufactured by Mediso) the **nanoScan**[®] PET/CT and the **nanoScan**[®] PET/MRI are unique opportunities to upgrade onto the next level of multi-modality imaging. With the integrated MultiCell[™] one-click animal bed and physiological monitoring system, the studies will be seamless and referred across all major imaging modalities: SPECT, PET, MRI and CT from the same supplier.



nanoScan[®] PET/CT

PET/CT Acquisition / Gantry Touchscreen User Interface

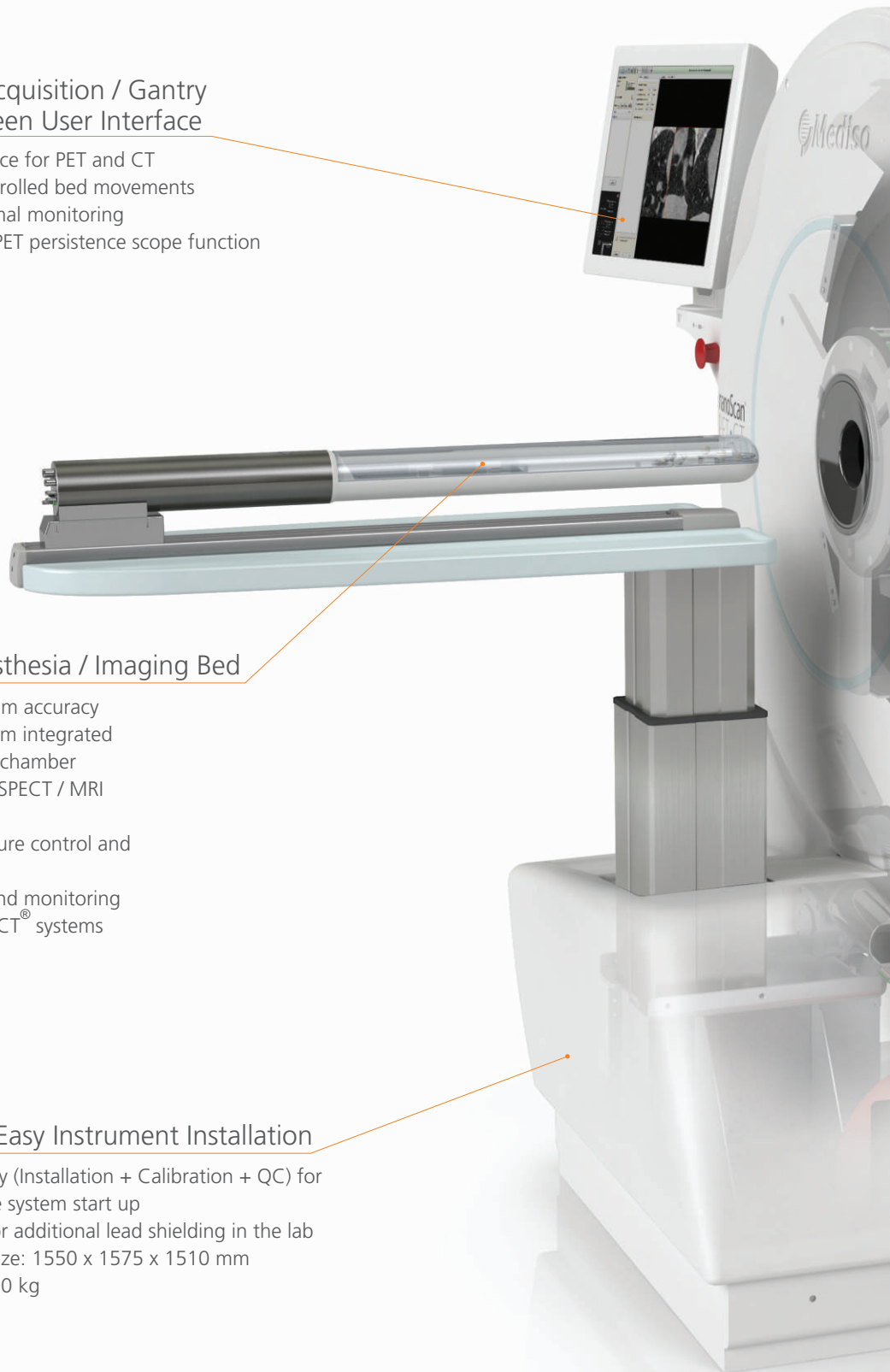
- One interface for PET and CT
- Touch-controlled bed movements
- Online animal monitoring
- On the fly PET persistence scope function

MultiCell[™] Animal Anesthesia / Imaging Bed

- Automated positioning with μm accuracy
- Closed circuit anesthesia system integrated into a pathogen-free imaging chamber
- One-click dockable PET / CT / SPECT / MRI compatible imaging chamber
- Integrated heating / temperature control and monitoring
- Respiratory and ECG gating and monitoring
- Compatible with NanoSPECT/CT[®] systems

Fast and Easy Instrument Installation

- 3 x One day (Installation + Calibration + QC) for fast routine system start up
- No need for additional lead shielding in the lab
- Compact size: 1550 x 1575 x 1510 mm
- Weight: 610 kg



No compromise in image quality



PET Detector Ring

- LYSO crystal full ring geometry
- 1.12 x 1.12 x 13 mm³ pixel size
- 512 ch/module flat panel sensor
- 12 cm transaxial FOV
- 0.3 mm³ spatial resolution by Tera-Tomo™ 3D PET engine

X-Ray CT System

- Wide energy range X-Ray tube
- 7 µm focal spot size
- High DQE at low dose detector
- Variable zoom (35 mm - 120 mm FOV)
- Closed cabinet X-Ray system

High Precision Gantry

- Very precise and robust rotational bearing and drive
- Exceptionally stable gantry with 4 axis movements
- Large bore size with 16 cm opening
- Open tunnel construction: 2-way access to the animals
- Ultra slim front cover (< 30 mm dead space to the PET FOV)

PET Subsystem

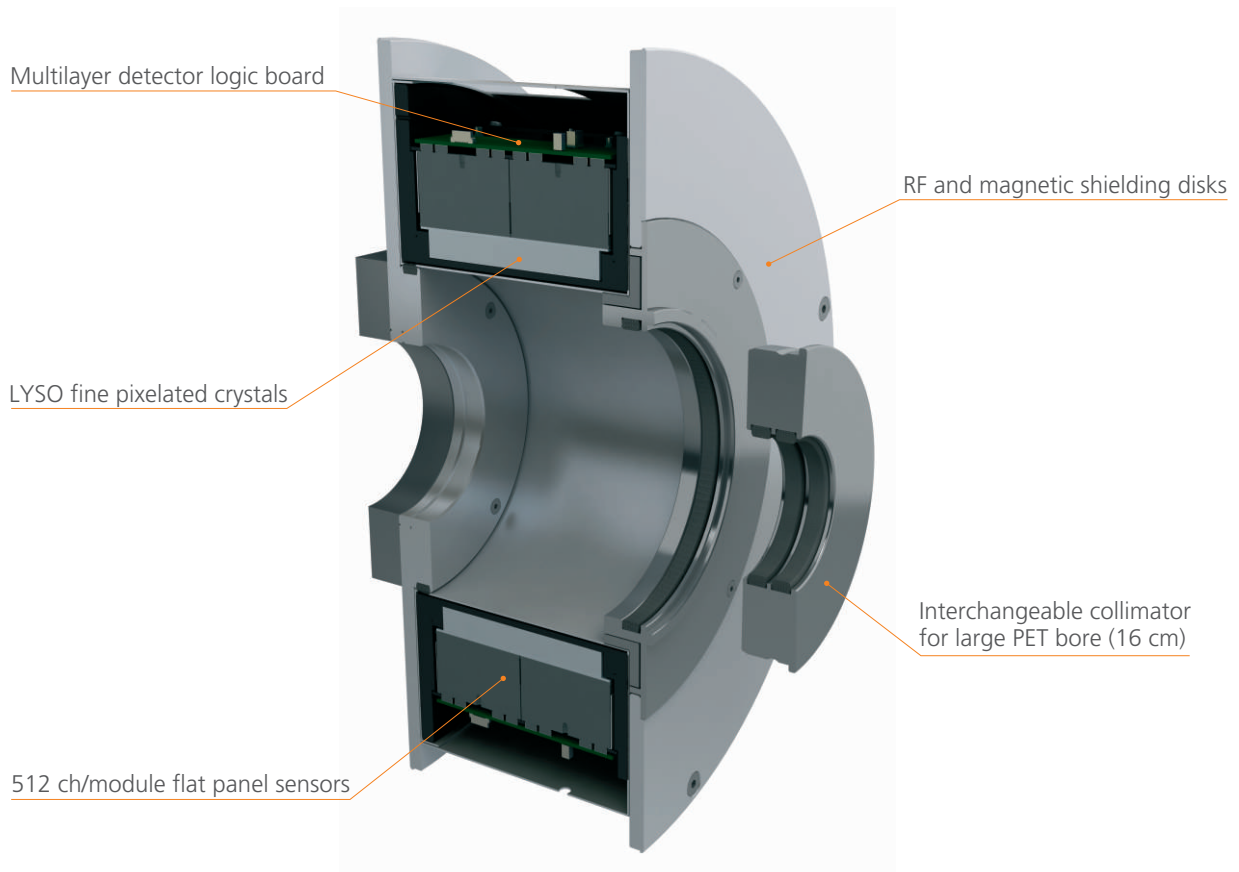
Structure

Mediso's traditions in nuclear detection technology and fine precision mechanics date back almost a century.

Leveraged by our expertise gathered across generations of patented, cutting-edge instrument innovations, the company has designed and built the most advanced PET detector present in the market.

Mediso **nanoScan**[®] PET/CT's LYSO crystal pins are the most tightly packed (92%) and smallest in the industry, minimizing dead detector space. Large-surface modular detector design together with the large detector ring diameter (largest among currently available PET/CT imagers) minimizes parallax error. Mediso's patented proprietary **TeraTomo**[™] 3D PET reconstruction algorithm offers attenuation correction, models the whole system matrix with Monte Carlo simulations and removes parallax error. This achieves a uniform imaging resolution of ≤ 0.8 mm even at 3 cm off the radial center. With a resolution of 0.7 mm at 1 cm off center using the very advanced **TeraTomo**[™] 3D PET algorithm - a value unseen in PET up to now - **nanoScan**[®] PET/CT is the first and only PET imager in the world with sub-half mm³ volumetric resolution (0.3 mm³ volumes are resolved).

The large bore size of the detector allows for a "PET-only" or "CT-only" mode of use in the **nanoScan**[®] PET/CT system. High throughput imaging of larger animals is also possible. Marmoset heads or two rats can be imaged with the standalone PET mode.



0.3 mm³ resolution by Tera-Tomo™ 3D PET engine

Ultra-fast PET data flow and processing

Data collected by the PET detector are sorted and processed using a proprietary, custom-designed circuit and application specific FPGA chip. The data stream is transmitted to the image reconstruction engines, based on a cluster of GPUs. These ultra-high performance systems enable you to simultaneously acquire and reconstruct your PET study data.

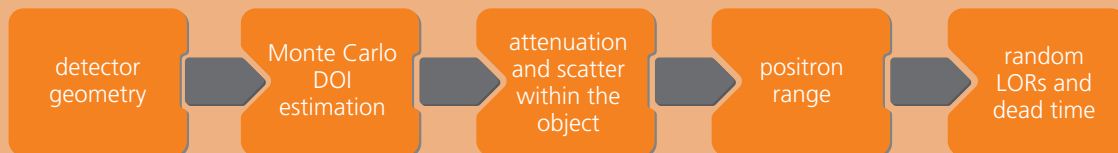
Mediso always uses state-of-the-art computers and acquisition electronics to optimize data processing with the **nanoScan®** PET/CT.

The combination of Mediso high-end PET detector with a very advanced 3D Teraflop Computing for Tomography: **Tera-Tomo™** 3D PET reconstruction engine, also developed by Mediso leads to a PET resolution very near the physical limits.

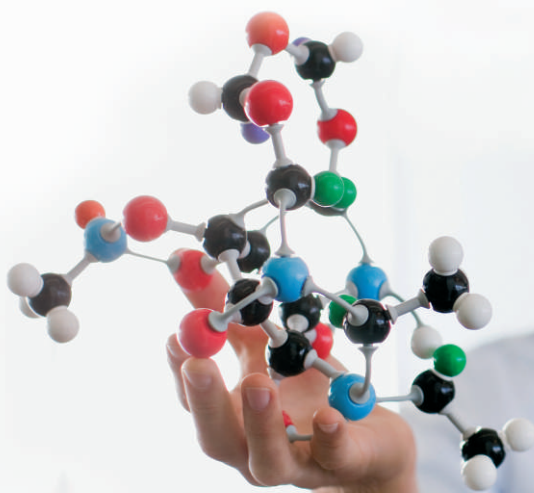
For any tomographic detector, the acquired image is blurred and degraded due to the distortions of the imaging system. This blurring is characterized by the Point Spread Function (PSF) or impulse response of the system. The **Tera-Tomo™** 3D PET reconstruction engine incorporates both projection-space (or data-space) and image-space PSF modeling in order to faithfully recover the original spatial resolution of the imaged objects.

Using corrections for physical factors such as detector geometry, Monte Carlo DOI estimation, object attenuation and scatter, randoms and dead time to even positron range, a quantitative three-dimensional PET reconstruction called **Tera-Tomo™** 3D PET has been developed and applied by Mediso in collaboration with prestigious Hungarian universities.

Tera-Tomo™ 3D PET reconstruction engine principle with on the fly system matrix generation



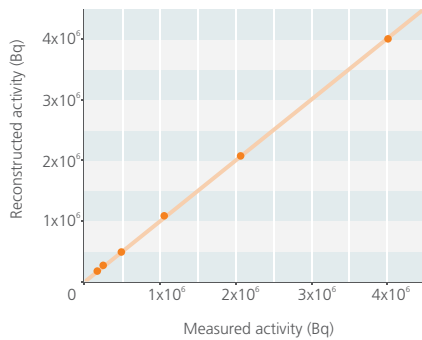
High-speed transfer and teraflops computing speed provides you with ultra-fast reconstructions for enhanced PET study throughput.



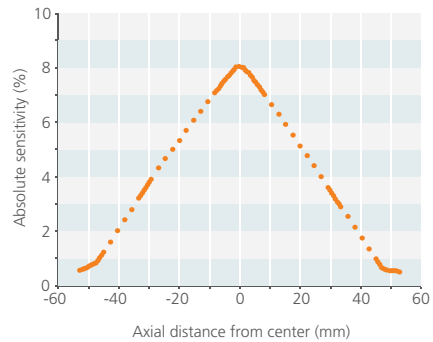
PET Subsystem

Quantitative reconstruction with high sensitivity

This is available to every **nanoScan**® PET/CT user. Receptor binding potential or high precision SUV studies are robustly performed on the **nanoScan**® PET/CT.



Activity concentration linearity for quantification
Quantification error: < 3%

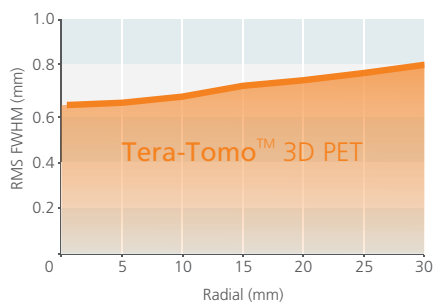


Absolute sensitivity according to NEMA NU 4-2008: > 8.0%
Maximum sensitivity: > 9.0% (150-750 keV window)

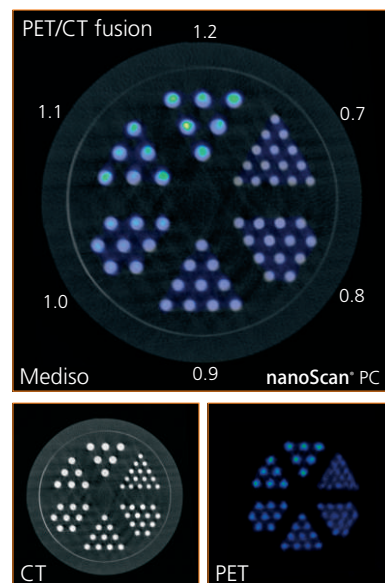
Representation of quantitative accuracy of the **nanoScan**® PET/CT's PET component over 2 orders of magnitude. The radioactivity measured in the syringes is well repeated by the reconstructed values.

700 µm resolution by Tera-Tomo™ 3D PET engine

Below are the measured full width at half maximum resolution values of the PET subsystem in all 3 dimensions in the FOV, (x=horizontal, y=vertical, z=axial, averaged with the RMS method) using Tera-Tomo™ 3D PET. Even your routine PET scans will bring you to the yet unseen resolution of 0.7 mm.

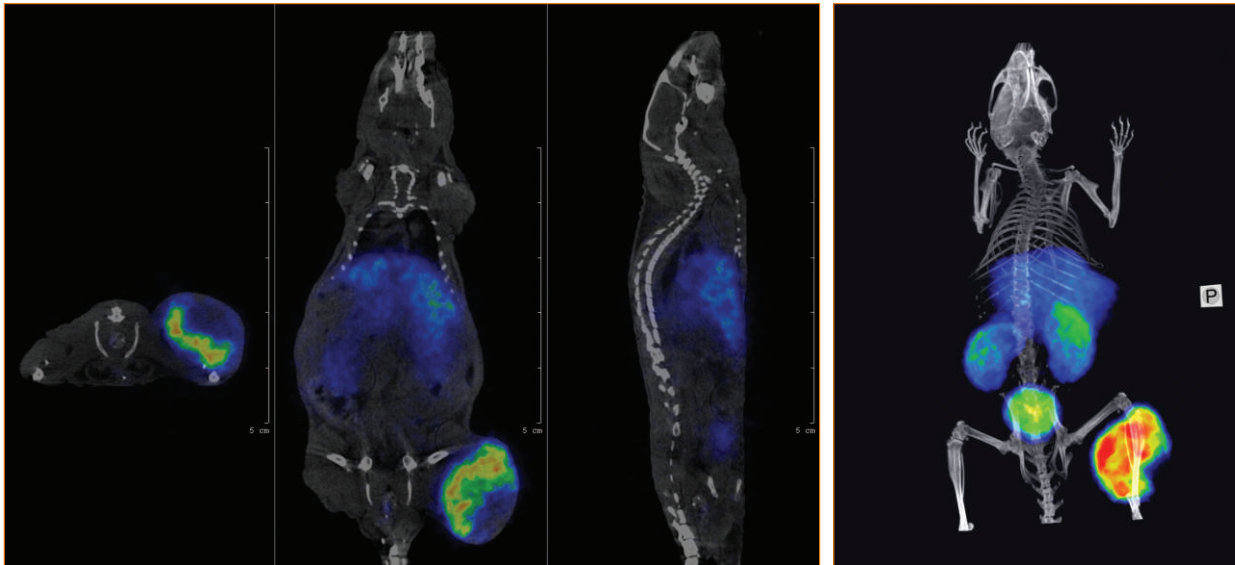


Point source 3D reconstructed spatial resolution with Tera-Tomo™ 3D PET reconstruction engine

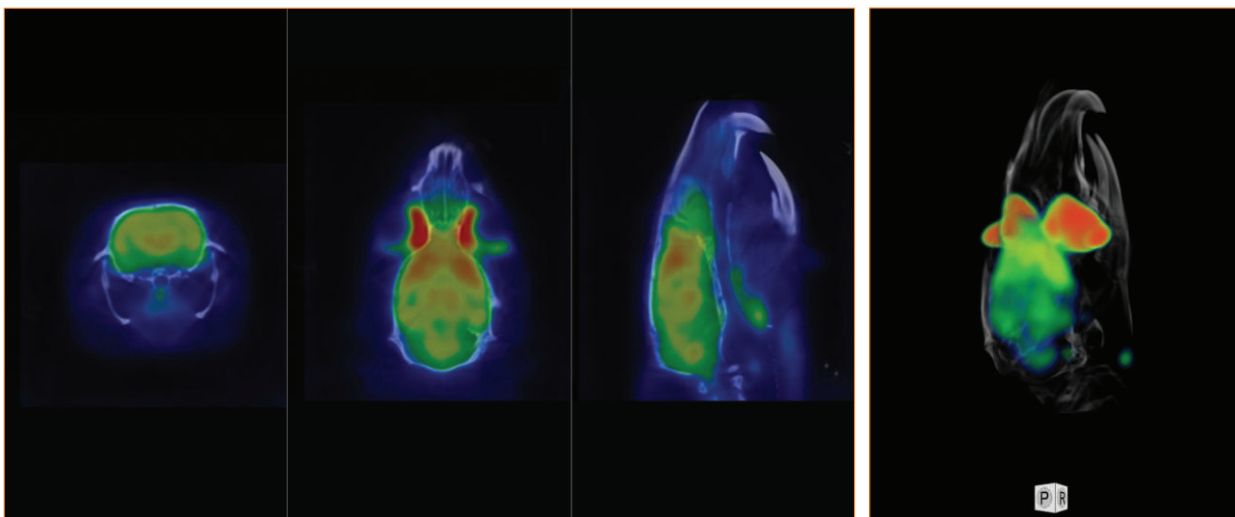


Imaging performance with Tera-Tomo™ 3D PET Reconstruction Engine using 10 MBq ¹⁸F-FDG and 30 min image acquisition in an ultra micro-Derenzo phantom
Size of the rods: 0.7 mm – 1.2 mm

Exclusive PET Imaging Performance



Three plane sections of a Nude mouse bearing FaDu xenograft tumor. 34 MBq of ^{64}Cu -labelled antibody fragment injected i.v., imaging 24 h post injection for 20 min. Note the accumulation in kidney cortex and the tumor uptake inhomogeneities. MIP image of the same Nude mouse.



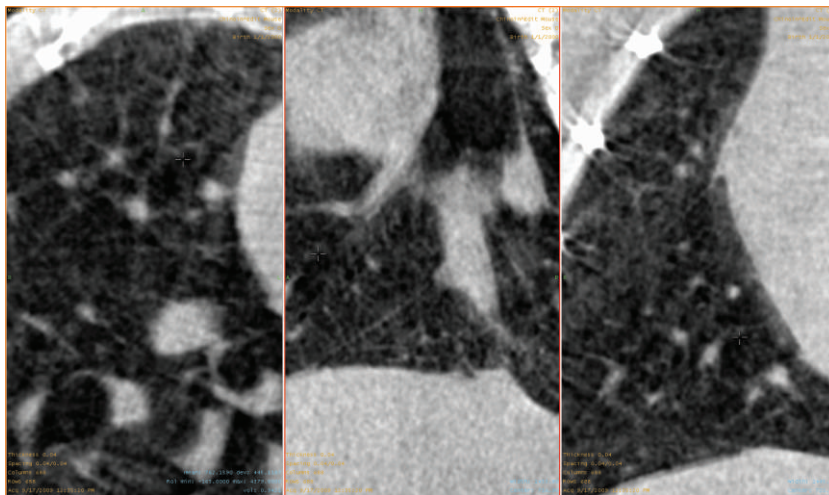
^{18}F -fluoro-deoxy-glucose uptake in rat brain, PET/CT MIP image. 30 MBq of ^{18}F -FDG injected into awake rat and imaged 50 min p.i. for 20 min.

CT Subsystem

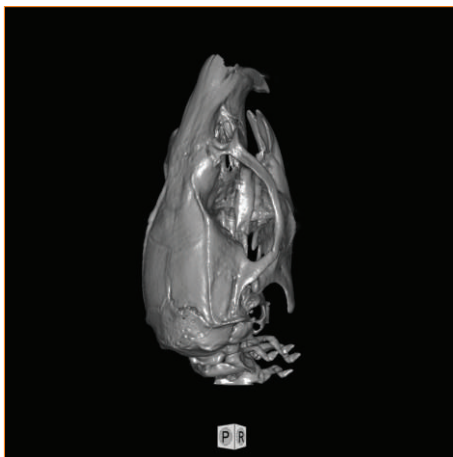
Fine structures revealed in high quality at low dose

Mediso designed a low-dose, fast but high quality zoomable cone-beam X-ray CT to complement **nanoScan**[®]'s exceptional PET qualities. Indeed the X-ray CT alone is a whole-body imaging system on its own right. Offering a very large detector surface and large bore, the CT of **nanoScan**[®] PET/CT can image the largest variety of animal species in industry.

CT image quality depends on pixel number, focal point size and image zoom. To prevent trade-offs in these fields, **nanoScan**[®] PET/CT features the industry's largest surface, largest pixel number and smallest focal point CT where the user can choose the zoom by setting it from 1.4 to 5.0. The results are a superb soft tissue contrast, low dose to the animal, and breath-taking details. With the highest resolution mode 9.6 micron isotropic voxels are defined whereas in overview mode large detector surface means image stitching is avoided. Mediso InterView[™] FUSION software effectively complements the CT by providing advanced Volume-of-Interest statistical tools of Hounsfield Units. Full radiation shielding of the closed X-ray cabinet type approved in more than 16 countries complement the CT system. The open back-door of the CT part ensures animal access but can also be used as a traditional closed CT.



X-ray CT of a mouse lung lobe. Three plane sections (from left to right: transaxial, horizontal and saggital plane) of the lung lobe are presented. Acinar walls and lung vessels are visible. Image courtesy of CROmed Ltd. Budapest



CT images of a rat skull and a mouse whole body. Imaging time 3.4 min for the rat, 6 min for the mouse study.

Image courtesy of CROmed Ltd. Budapest

MultiCell™ Animal Anesthesia / Imaging Bed

Continuous digital temperature control: by closed circuit airflow integrated into the wall of the chamber – avoiding the side effect of the open airflow (dehydration of the eyes, contamination by pathogens etc.)

Embedded anesthetic gas connection: for any isoflurane system through dockable connection to the mouse /rat nose cone via closed circuit tubes integrated into the wall of the chamber

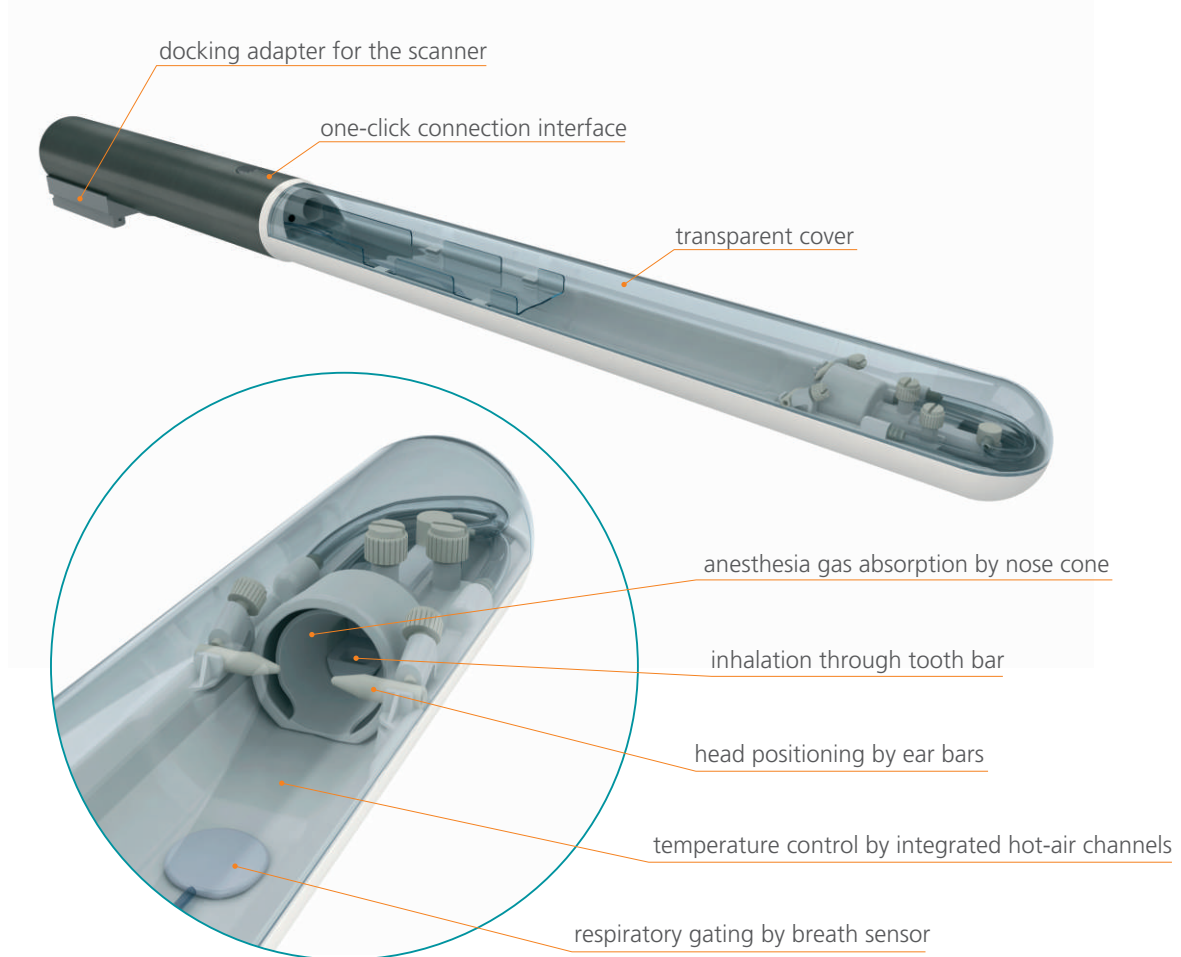
Integrated animal head mounting: for precise and reproducible animal positioning

4D/5D imaging accessories: dockable connections for ECG and respiratory gating

Pathogen-free construction: for immuno-compromised animals

One-click connection imaging cells: for easy and fast connection of mouse /rat imaging cells to the PET/CT, PET/MRI and SPECT/CT scanners or dual bed docking station

PrepaCell™ Preparation Station: for complete preparation of the animal before the scan (“click and scan”)



MultiCell™ Imaging bed

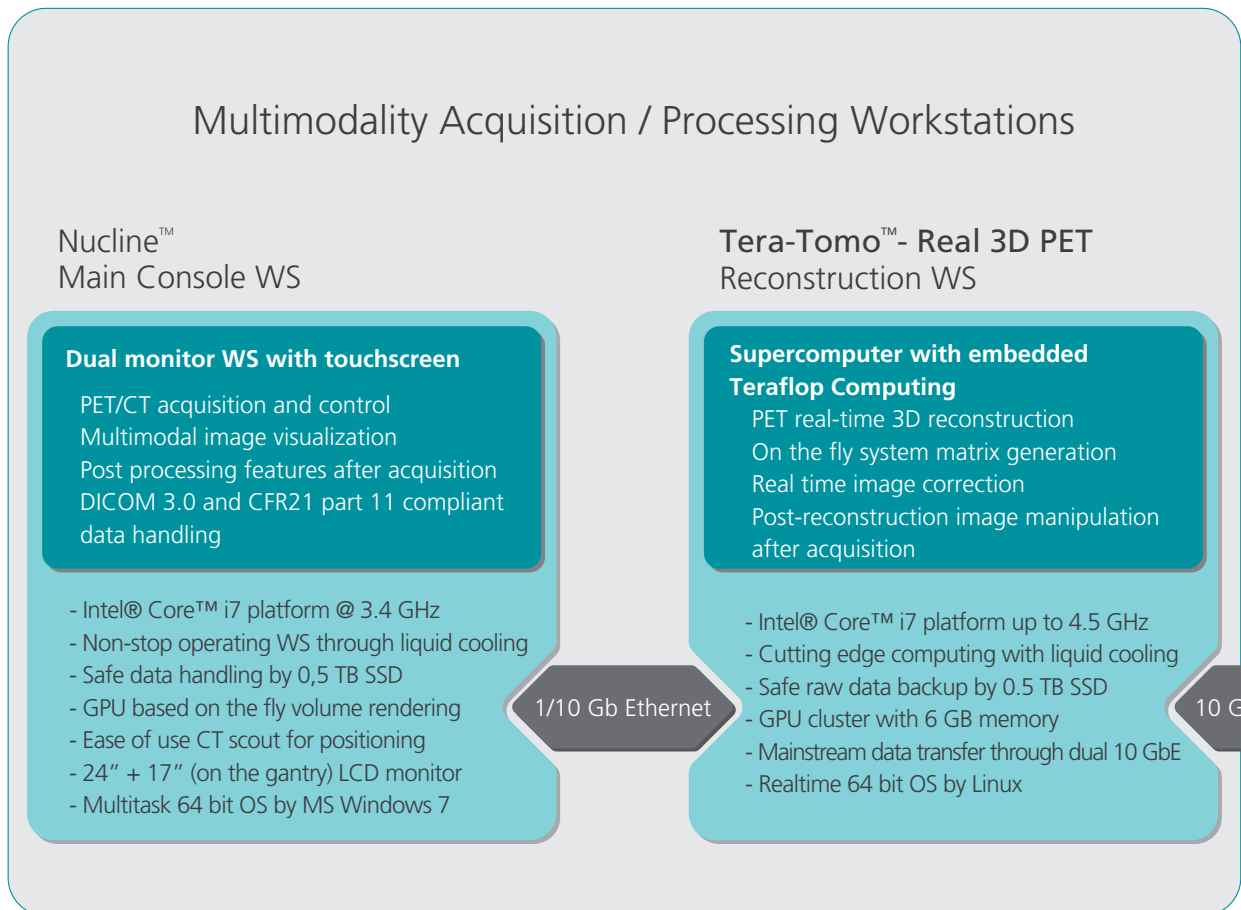
- Multimodality imaging for PET+CT+SPECT+MRI modalities
- Multipurpose applications 4D-, 5D imaging by one-click connection
- Multiple mouse scanning in one scan (optional)
- Multifunctioning preparation station for the imaging cells

Shared Components

Acquisition and real-time reconstruction shall be a routine – quick and comfortable

- Faster and safer acquisition and data management via state-of-the-art, high-stability and high capacity solid state disks
- The ergonomic design of the common PET/CT user interface and the touch-screen based bed movements make the acquisition control comfortable and fast.

Control / Equipment Room



Enhanced Routine and Research Workflow

Fast routine / ultra precision research tool

Workflow management is designed to enhance throughput.

- High performance visualization and computational tools supported by ultra-large capacity (12 TB) on-line archiving system
- Parallel work of two scientists is supported: while reconstruction is running on the Reconstruction WS the additional post-processing workstation enables to analyze and quantify images from another study.

Researcher`s Room

Multimodality Post-processing / Archiving Workstations

InterView™ FUSION Multimodality Processing WS

12 TB raw/processed data archiving

Post processing and comprehensive evaluations
Quantification and kinetic modeling
Advanced multimodality 3D/4D visualization
Auto-registration of PET & CT images
Automatic CT segmentations

- Intel® Core™ i7 platform @ 3.4 GHz
- 12 TB fault tolerant RAID5 archiving
- GPU engine with CUDA™ based algorithms
- Full functionality DICOM server services
- 24 " LCD monitor
- Mainstream data transfer through dual 10 GbE
- Multitask 64 bit OS by MS Windows 7

max. 100 m

10 Gb Ethernet

Tera-Tomo™ - Post 3D PET Reconstruction WS

Best image quality for research

Advanced PET post reconstruction
Detector and physical effect modeling
On the fly image correction by GPU engine
3D/2D reconstructions (real-time /adaptive)
CT-based PET correction

- Intel® Core™ i7 platform up to 4.5 GHz
- Cutting edge computing with liquid cooling
- RAID 0.5 TB SSD for safe and fast data handling
- GPU cluster with up to 9 GB memory
- Mainstream data transfer through 10 GbE
- Real-time 64 bit OS by Linux

Management

Post-processing by *InterView*[™] FUSION

InterView[™] FUSION multi-modal application developed by Mediso is an essential part of **nanoScan**[®] PET/CT system. The application provides a wide range of functionalities to evaluate preclinical PET/CT data. 2D single, orthogonal and tiled, as well as 3D MIP and Volume Rendering viewers represent fast and flexible visualization techniques built on GPU acceleration. Viewers provide dual, triple and quadruple fusion to accurately compare and enhance multi-modal single and follow-up studies. Dynamic PET images together with CT can be fused, and PET images can be studied over time. Multiple Time Activity Curves (TAC) of dynamic PET studies over time can be visualized and evaluated.

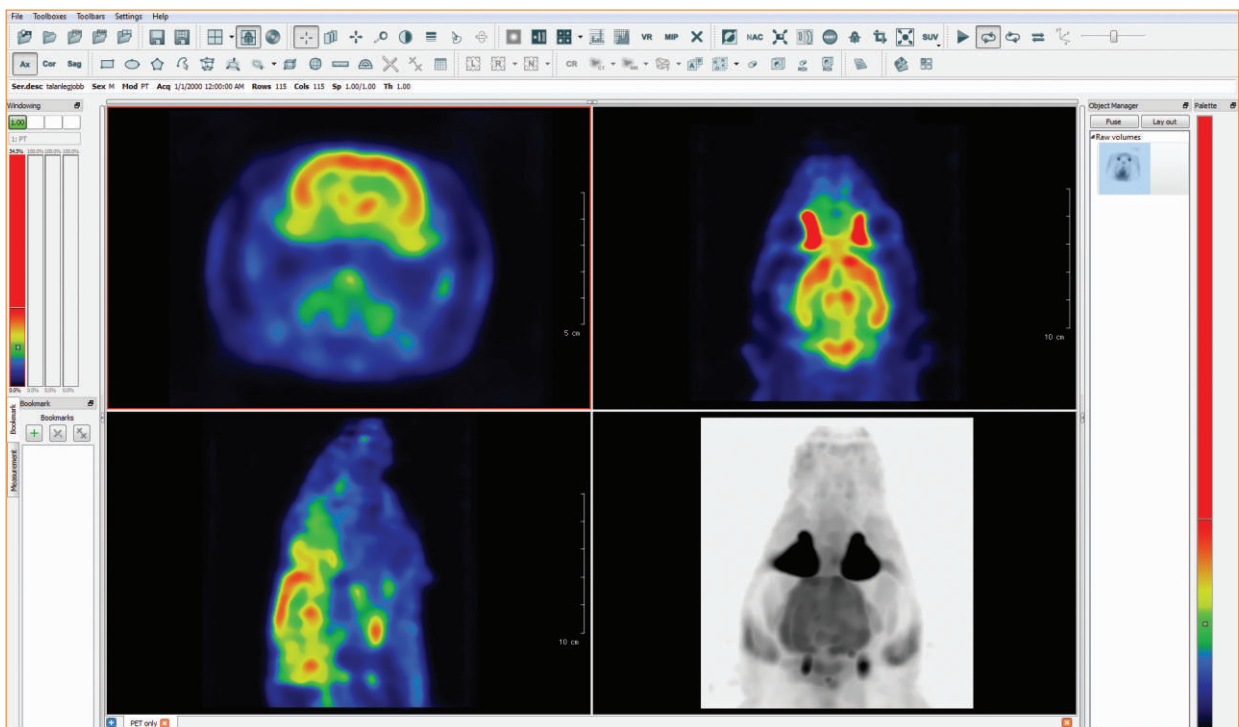
Calculations and statistical evaluations for PET are available on voxel and ROI or VOI level. A wide range of ROI and VOI tools are available for evaluation (e.g. freehand, polygon, ellipse, rectangle, sphere, box and isocount).

CT based body-air-bone-lung segmentation methods are provided for effective PET attenuation correction.

An in-built state of the art automated rigid, affine and non-linear image registration framework provides a quick and accurate way to superimpose different studies for comparison.

Advanced segmentation methods for different modalities, tissues and organs are available for feature extraction (e.g. lung, vessel, bone, CT body-air-bone-lung, PET lesion detection)

Arithmetic operations help differentiating follow-up studies on voxel level by several methods (e.g. sum, difference, absolute difference, average, minimum, maximum, multiply).



Visualization of ¹⁸F-fluoro-deoxy-glucose uptake in rat brain. After the intravenous injection of 30 MBq of ¹⁸F-FDG rats were kept awake for 50 min. The static PET image was collected during 20 min in isoflurane anesthesia. Cortical gyri, thalamus, cerebellum and brain stem uptake is visualized. Note the FDG uptake in brown fat tissue over the scapular region. Image courtesy of Karolinska Institute.

To enable researchers with all necessary image visualization, analysis and quantification tools, Mediso offers a uniquely complete and flexible software package for the **nanoScan**[®] PET/CT system. Beside Mediso's InterView[™] FUSION both **invicRO**'s VivoQuant providing advanced 3D segmentation, data sharing and atlas tools and **PMOD**'s industry standard pharmacokinetic analysis and post-processing modules are supported.

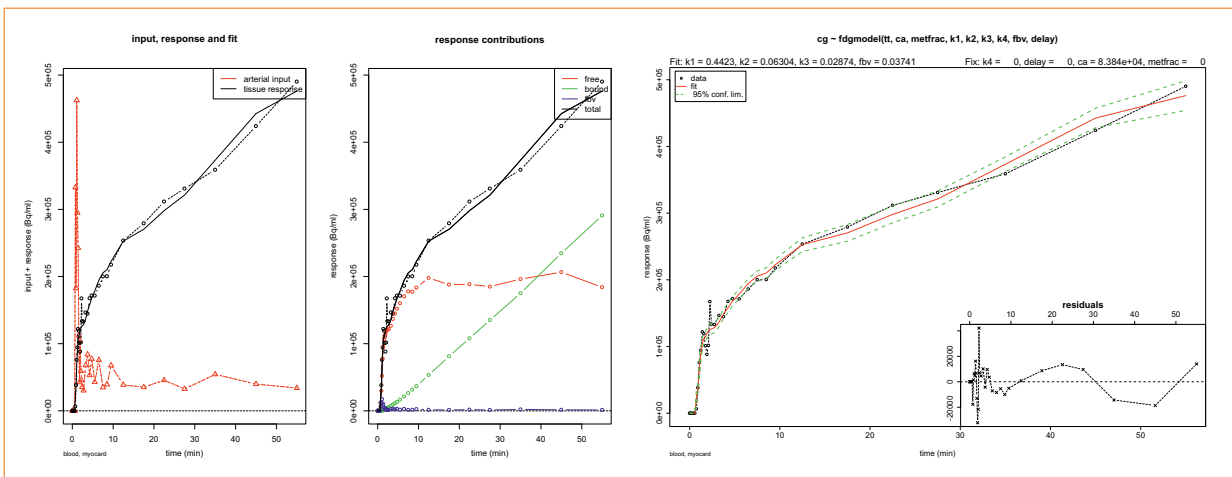
Applications



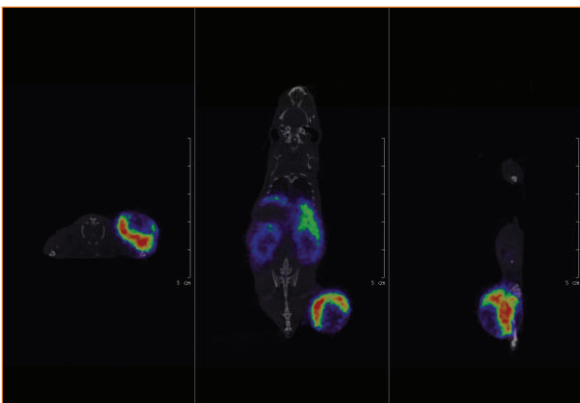
Dr. Ralf Bergmann
 Institut für Radiopharmazie
 Radiopharmazeutische Biologie
 Helmholtz-Zentrum Dresden-Rossendorf



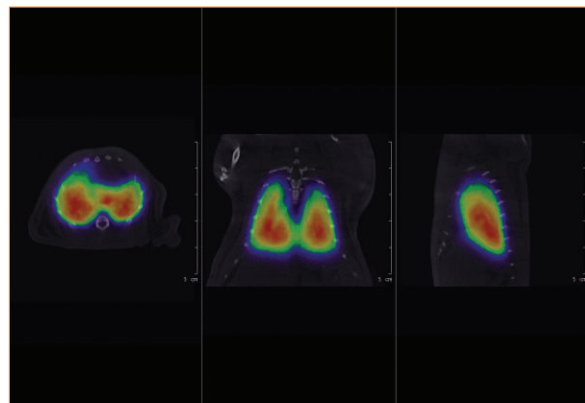
„I am very satisfied with the results obtained on our Mediso nanoScan® PET/CT system. A very good sensitivity and stunning PET/CT resolution are combined with easy animal access. Our high throughput radiopharmaceutical development tasks and tumour biology work are well supported by the nanoScan®. It is a flexible and user-friendly PET/CT system with no compromise on image quality and functionality.“



Time-activity curves of heart myocardial [¹⁸F]FDG uptake.
 Data and diagrams courtesy of Helmholtz-Zentrum Dresden Rossendorf, Germany



[⁶⁴Cu]Cu-NOTA-AntiEGFR-Fab whole-body imaging of a NMRI Nu/Nu mouse with FaDu tumor xenograft 48 hours post i.v. injection of 34 MBq labeled Fab. Imaging duration 30 min, imaged actual activity cca. 3 MBq. Three plane sections. Besides heterogeneous uptake in the tumor, kidney cortex and liver is visible, too.
 Image courtesy of Helmholtz-Zentrum Dresden Rossendorf, Germany



[⁶⁸Ga]Ga-NOTA-microspheres PET/CT study on the lungs of a Wistar rat. 40 MBq of i.v. injected activity imaged for 20 min.
 Image courtesy of Helmholtz-Zentrum Dresden Rossendorf, Germany

Conformance Statement

Product design, development, production and services comply with ISO 9001:2001 and with ISO 13485:2004.

The **nanoScan**[®] multimodality molecular imaging system conforms to EC Directive 93/42/EEC; Annex II, Article 3 Full Quality Assurance System Medical Devices Design and safety testing has been performed in accordance with IEC 60601-1 and IEC 60601-1-2 EMC standards.

Safety labels are attached to appropriate places on equipment and appear in all operation manuals.

The supplied software conforms to DICOM and CFR 21 part 11 standard.

The technical information provided here is not a detailed specification.

For exact details and up to date information please contact your local distributor or Mediso Medical Imaging Systems.

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This product was partially established by the support of the National Development Agency of Hungary using funds of the Research and Technology Fund (code: TeraTomo).



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