

nanoScan[®] Family

Preclinical PET imaging systems



nanoScan[®] PET/MRI

nanoScan[®] PET/CT

MEDISO Medical Imaging Systems

Tradition in research and development

Mediso Medical Imaging Systems is a global company with headquarters in the European Union in Budapest, Hungary. Mediso is a dynamic manufacturer of nuclear medicine and modern hybrid imaging equipment, which it supplies and supports to healthcare, research institutes and industry worldwide. The company was founded in 1990 and is world leading in R&D and commercialization of cutting edge preclinical and clinical medical imaging systems.

Latest awards

- 2014 - Industrial Innovation Award
- 2012 - Frost & Sullivan 2012 European Preclinical Imaging New Product Innovation Award
- 2011 - Grand Prize of Innovation 2010
- 2008 - Frost & Sullivan 2008 European Medical Imaging Entrepreneurial Company of the Year Award
- 2006 - Grand Prize of Innovation 2006



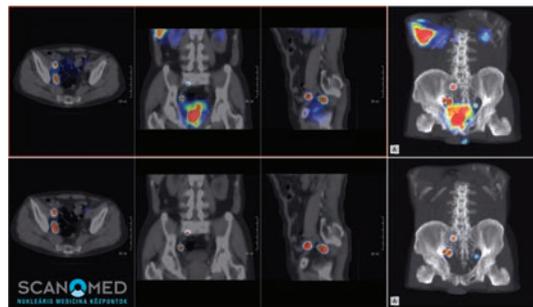
University and clinical diagnostic partners

Mediso have developed special partnership with pre-clinical imaging contract research organizations and leading molecular imaging centers in both preclinical and clinical field around the world.

Partnerships with Karolinska Institutet (Sweden), King's College London (UK), University of Tübingen (Germany), WWU, Münster (Germany), Semmelweis University and CROmed in preclinical imaging field. University of Debrecen Medical School, Hungarian National Institute of Neuroscience and Scanomed in clinical area represents a key drive to Mediso's research and developments.



www.cromedresearch.com



www.scanomed.hu

Customer focused support

Mediso-affiliated subsidiaries and world-wide distributor network with strong factory support ensure direct contact with our customers and quick, professional response to their requests not only in technical but also in application related issues. We at Mediso are proud to serve physicians and researchers at sites with more than 170 preclinical and 1100 clinical installed systems in 90 countries.



Pursuit of perfection in technology to serve perfection in science

Always eager to find an even better solution, Mediso constantly strive to develop the highest level medical imaging technologies possible.

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

nanoScan® PET/MRI & PET/CT

Overview

To unveil fine and accurate details of living organisms, scientists need high resolution, high-sensitivity and time-dependent quantitation. 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 scientist. 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.

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

In the recent past Mediso developed innovative technologies that provided new perspectives to small animal imaging. The new **nanoScan®** PET systems offer user-friendly imaging and a large scope of applications in simple to use, high resolution, high-end imaging systems. **nanoScan®** PET/CT and PET/MRI systems are equipped with an imaging technology widely considered as the most advanced detector design, data processing and reconstruction chain in the industry.



nanoScan® PET/MRI and nanoScan® PET/CT

With the **nanoScan®** Family concept Mediso provides unique and flexible solution for the demands of your imaging facility. Members of the **nanoScan®** Family share the similar easy to use, software platform (**Nucline™** acquisition software) for all modalities, with intuitive workflow and incorporated effortlessly customizable protocols.

For analysis both **InterView™** FUSION and **VivoQuant™** can co-register and analyze multiple images across all modalities.

Under the hood PET/MRI

MRI Magnet

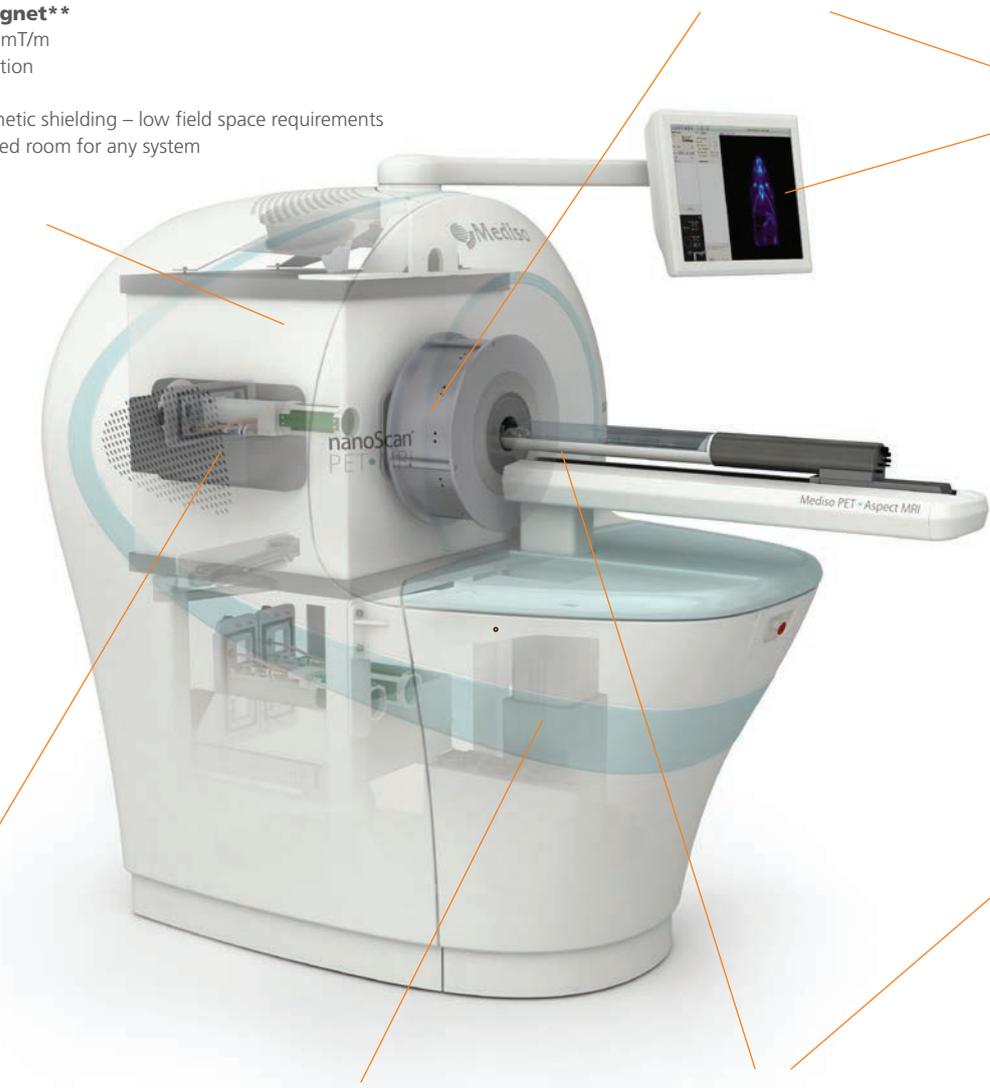
- **3 Tesla cryogen-free***
- Gradient strength: > 450 mT/m
- +/- 0.5 ppm over 50 mm DSV
- Stability: <0.1 ppm/hour
- ≤ 50 μm spatial resolution
- Integrated RF and magnetic shielding – low field space requirements and no need of dedicated room for any system

1 Tesla permanent magnet**

- Gradient strength: 450 mT/m
- ≤ 100 μm spatial resolution
- Integrated gradient coil
- Integrated RF and magnetic shielding – low field space requirements and no need of dedicated room for any system

PET Detector

- 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
- Aperture: 16 cm
- 0.3 mm³ spatial resolution by Tera-Tomo™ 3D PET reconstruction engine



RF Coils

- Volume coils for whole body mouse imaging
- Volume coils for whole body rat imaging
- Back door access for easy coil exchange
- Multiple coils available
- Custom coils available upon request

Fast, Easy Instrument Installation

- Compact size
- No need for liquid cryogen
- Negligible magnetic fringe field
- No need for additional RF shielding in the lab

Animal handling

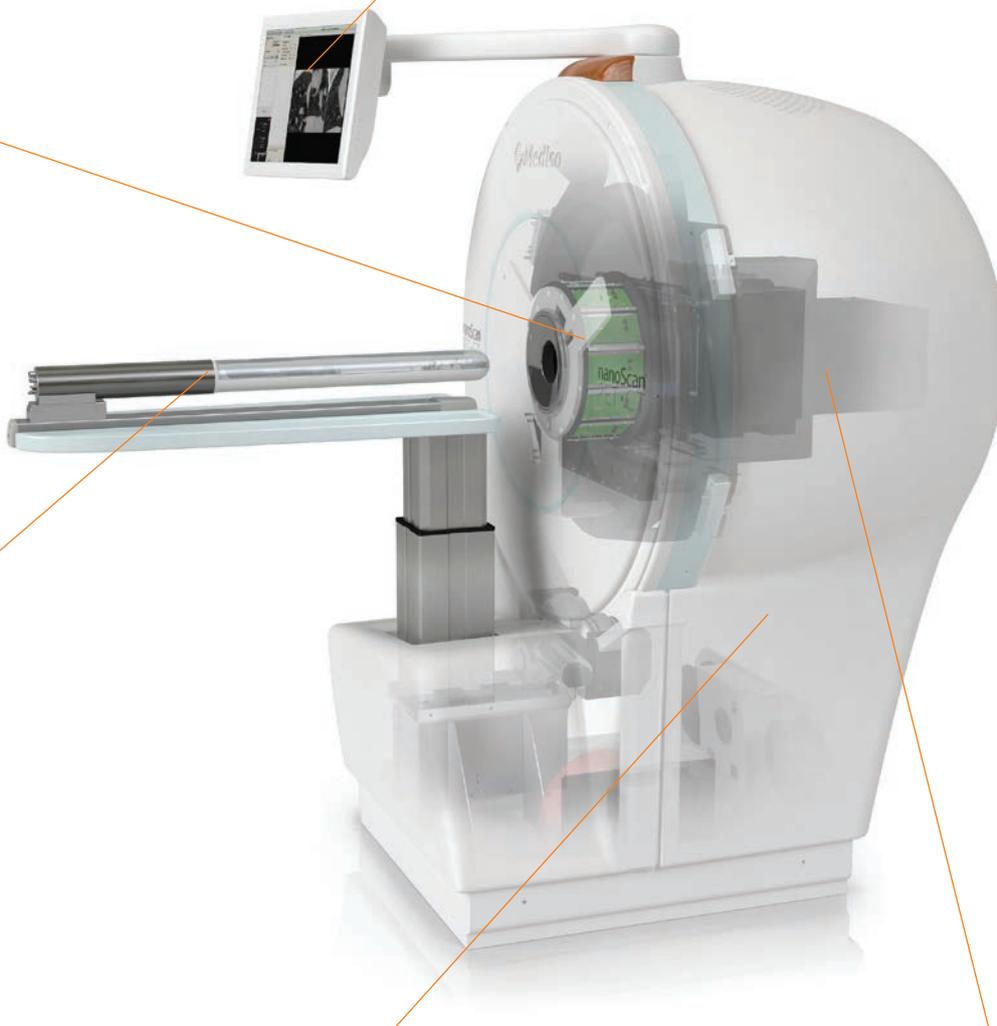
- Direct access possibility to the animal during scan
- Zero dead space: easy manipulation of the animal (injection, blood sampling, etc.)
- Automated bed positioning
- Automatic imaging chamber recognition
- Integrated heating and gas anaesthesia possibility
- Physiology monitoring
- ECG/respiratory gating

*Developed in collaboration by RS2D
**Manufactured by Aspect Imaging

Under the hood PET/CT

Touchscreen interface

- Shared interface for PET and CT
- Bed movement control through touchscreen interface or from the acquisition workstation
- Online animal vital function monitoring
- PET persistence scope function



High Precision Gantry

- Precise and robust rotational bearing and drive
- Exceptionally stable gantry with 3 axis movements
- Large bore size up to 160 mm
- Touchscreen interface
- Vibration free rubber pads

X-Ray CT System

- 80 W X-ray tube power
- up to 1 mA tube current
- <10 mGy exposure CT dose
- 2-12 cm variable TFOV
- up to x 7,6 zoom
- $\leq 10 \mu\text{m}$ isotropic voxel size

nanoScan[®] PET subsystems

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 the detection of femtomolar quantities of proteins per milligram of tissue with high resolution and exquisite image quality in vivo.



Modell	PET 122S	PET 82S	Benefit
Single Axial FOV	10 cm	10 cm	Enabling whole-body mouse scan in one FOV
Number of rings*	2	2	
Transaxial FOV	12 cm	8 cm	122S: Enabling marmoset, guinea pig and rabbit studies
Gantry opening	16 cm	11 cm	
LYSO Crystal size	1.12x1.12x13 mm	1.51x1.51x10 mm	122S: Super-fine crystal needles resulting in excellent resolution
Total number of crystals	36 504	13 456	
Spatial Resolution with 3D OSEM	0.7 mm	0.9 mm	Highest resolution on the market providing best available image quality
Spatial Resolution with FBP	1.25 mm	1.4 mm	
Sensitivity	8%	7%	High sensitivity for fast and high quality imaging
NEC for mouse	850 kcps	460 kcps	High count rate supporting high activity studies with various isotopes (¹¹ C, ¹⁵ O)
NEC for rat	230 kcps	130 kcps	
Temporal resolution	1.2 ns	1.0 ns	For efficient corrections supporting high quantitation accuracy and good resolution
Energy resolution	19%	14%	
Combination with CT	Yes	Yes	High resolution and low dose CT imaging
Combination with MRI 1T	Yes	Yes	Improved soft tissue contrast, cost-effective MRI
Combination with MRI 3T	Yes	No	Translational field, excellent image quality

*Both models are available in single-ring configuration upon request

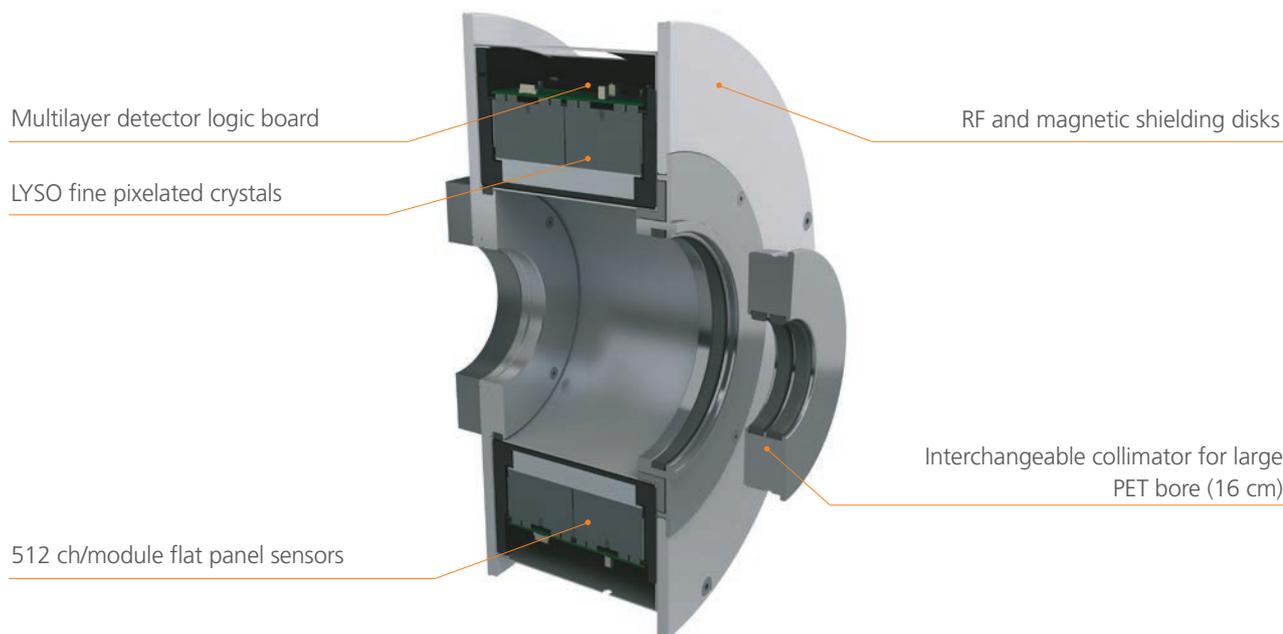
PET Subsystem

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'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 **Tera-Tomo**™ 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 **Tera-Tomo**™ 3D PET algorithm - a value unseen in PET up to now - **nanoScan**® PET is the first and only PET imager in the world with sub-half mm³ volumetric resolution (0.3 mm³ volumes are resolved).



Main advantages of the system

- **More than 50 installed PET-based cameras worldwide:**
 - ensuring reliable systems with matured technology
 - supported by proven and experienced service and application network
- 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
- One-click **MultiCell**™ animal anesthesia / imaging bed
- Simple to use with reliable detector technology, no need for long calibrations



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.

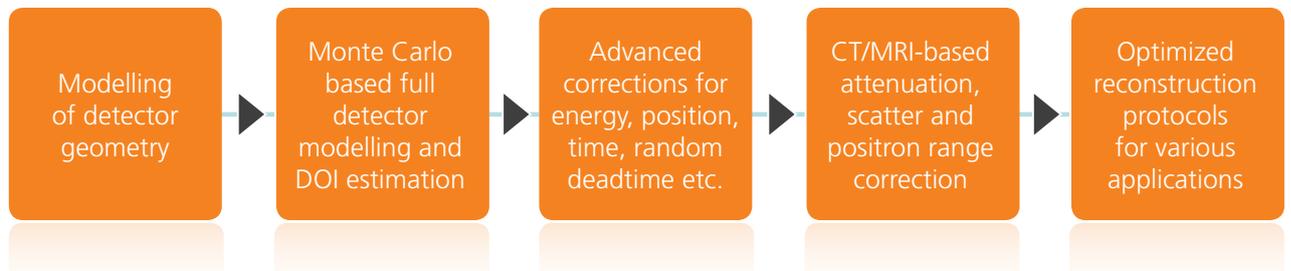
Mediso always uses state-of-the-art computers and acquisition electronics to optimize data processing with the **nanoScan®** PET/CT.

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.

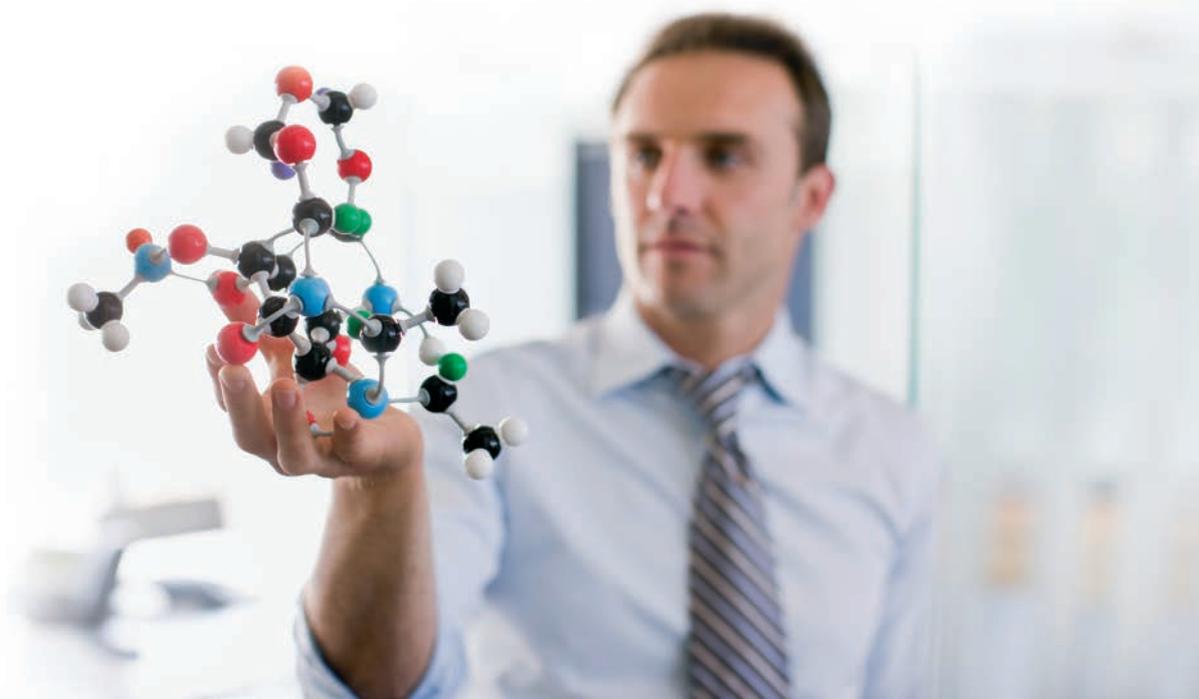
The **Tera-Tomo™** 3D PET reconstruction engine incorporates both projection-space (or data-space) and image-space PSF modeling in order to faithfully recover the original spatial resolution of the imaged objects.

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 with on the fly system matrix generation



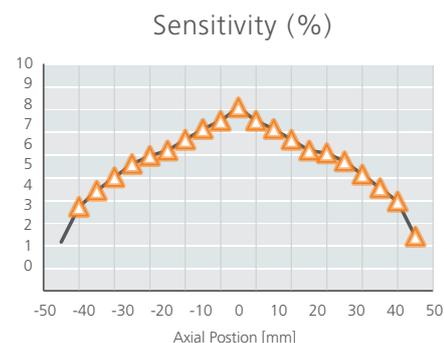
High-speed transfer and teraflops computing speed provides you with ultra-fast reconstructions for enhanced PET study throughput.



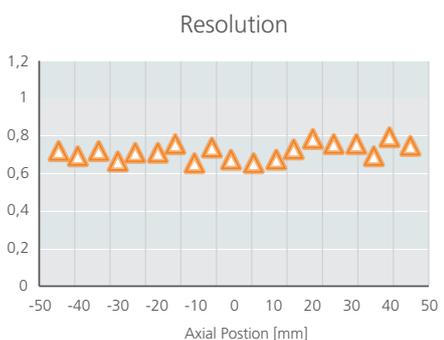
PET Subsystem

High sensitivity with high resolution

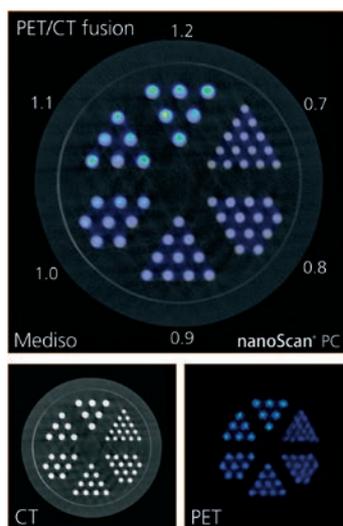
Mediso offers several different PET-subsystem models (see page 6 for details) all providing high sensitivity and resolution resulting in excellent image quality and reliable quantitation accuracy. Please note that all results below are referring to the nanoScan PET 122S model.



Absolute sensitivity profile of 122S PET subsystem



Resolution by Tera-Tomo™ 3D PET Reconstruction with Full detector modelling



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

NEMA Image Quality Phantom Evaluation*

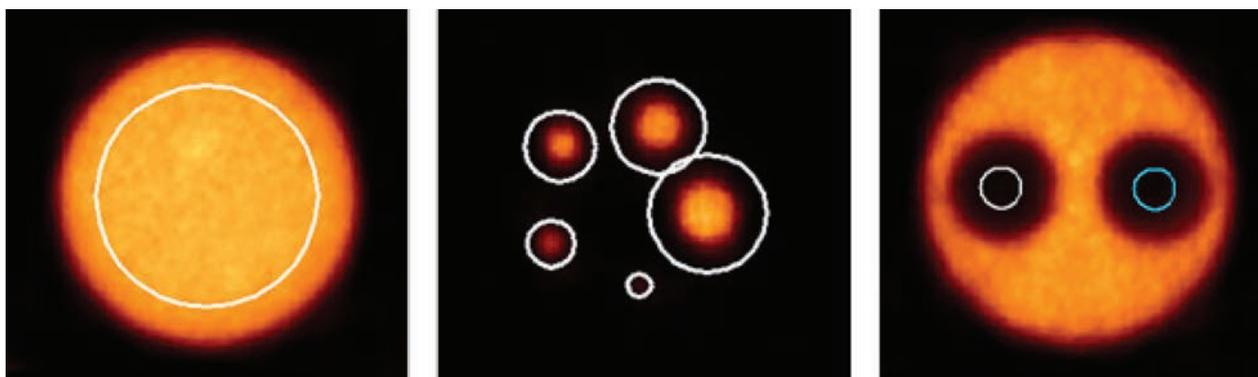


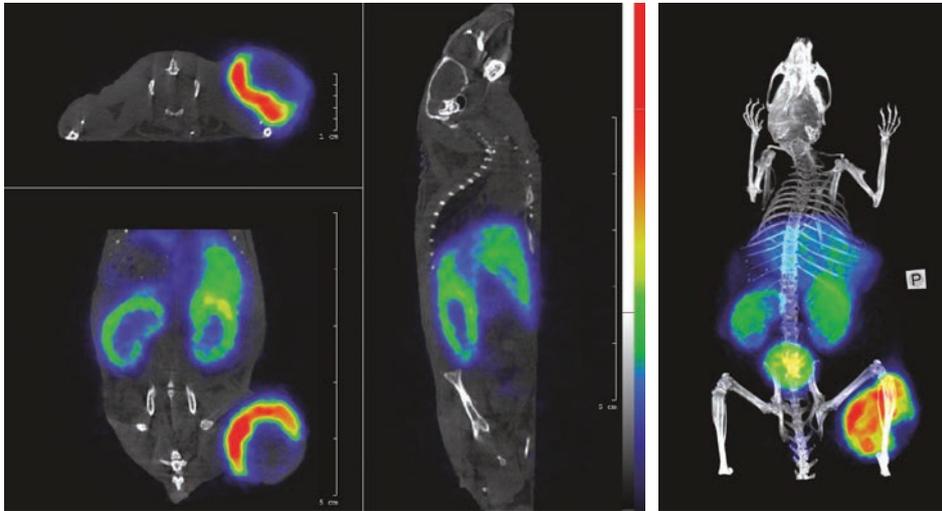
Image quality phantom evaluation reconstructed with Tera-Tomo™ 3D PET Reconstruction with Full detector modelling

Uniformity	4%	Spill over ratio Air/Water		0.04 ±0.004	0.05 ±0.004
Recovery Coefficient values	5 mm	4 mm	3 mm	2 mm	1 mm
	0.98	0.98	0.97	0.87	0.37

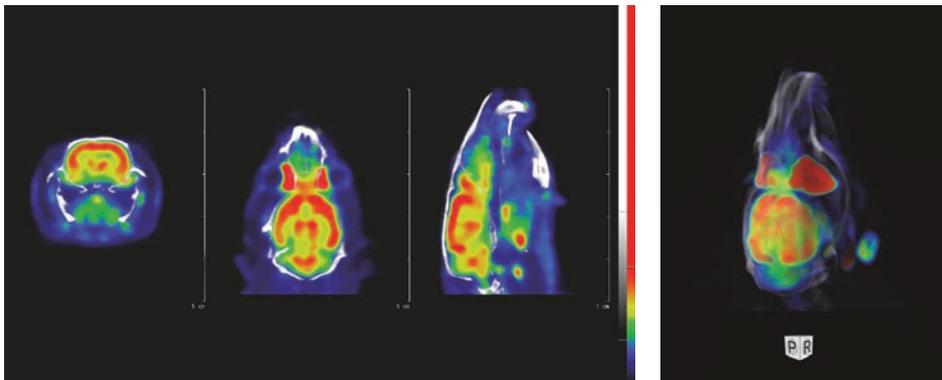
NEMA Image quality phantom results with Tera-Tomo™ 3D PET Reconstruction with Full detector modelling

* Nagy et al, Journal of Nuclear Medicine 2013; 54; 1-8

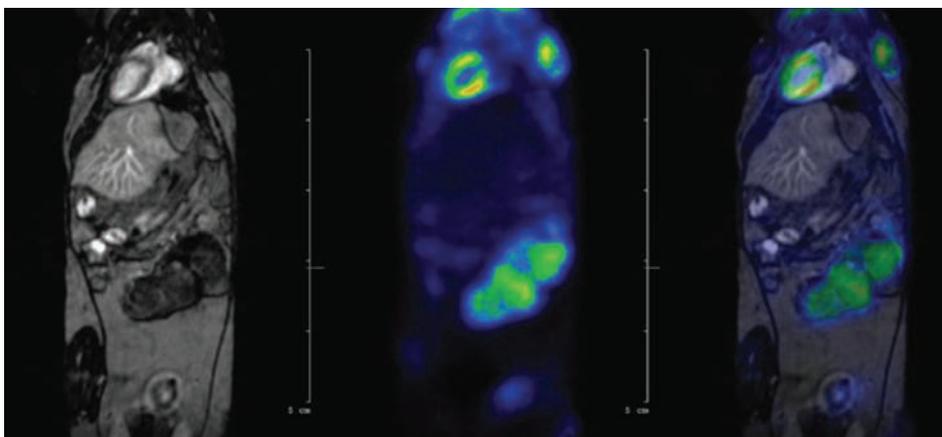
Exclusive PET Imaging Performance



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. 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.



Tumor imaging with ^{18}F -FDG in LM6 1y old mouse
 PET: 15 MBq, 30 min post inj.
 MRI: GRE SP 3D, scan time 12 min
 Image courtesy: Charité, Berlin

MRI subsystem 3T cryogen-free or 1T permanent

High imaging performance

3T MRI* – Excellent resolution with high sensitivity on translational 3T field strength

Mediso accepts no compromises in the imaging performance of the **nanoScan**® PET/MRI 3T system. Due to the tailor-made shielding developed as an integral part of the specially designed and shimmed cryogen-free magnet with low fringe field, and avoiding any non-established techniques the unique high performance of the PET subsystem is intact.

The **nanoScan**®MRI 3T system delivers images with excellent resolution together with high sensitivity. Thanks to its clinical magnetic field of 3T, the system enables translational in-vivo imaging of small animal and benefits from the same main clinical applications.

1T MRI** – High soft tissue contrast, cost-effective solution

The compact, high-performance magnet system is optimized to perform fast (seconds to minutes) routine studies with high resolution soft tissue contrast.

Easy-to-use workflow

The ease of use of the MRI subsystems matched with their powerful imaging capabilities, making it simple to correlate functional PET data with anatomical morphology.

Cost effective operation

The compact cryogen-free design of the systems guarantees low running costs with a small footprint. The negligible fringe field allows for safe operation with no need for additional magnetic shielding in the room.



Angiography - MIP of Mn-based contrast media
Images courtesy of CROMed, Budapest

Available RF coils:

Coils for 3T systems:

- ID 42 mm for whole body mouse
- ID 72 mm for whole body rat
- Surface coils (optional)
- Coils for various isotopes (optional)

Coils for 1T systems

- ID 35 mm for whole body mouse
- ID 60 mm for whole body rat

Optional coils for both systems

- Dedicated coils for mouse brain
- Dedicated coils for rat brain

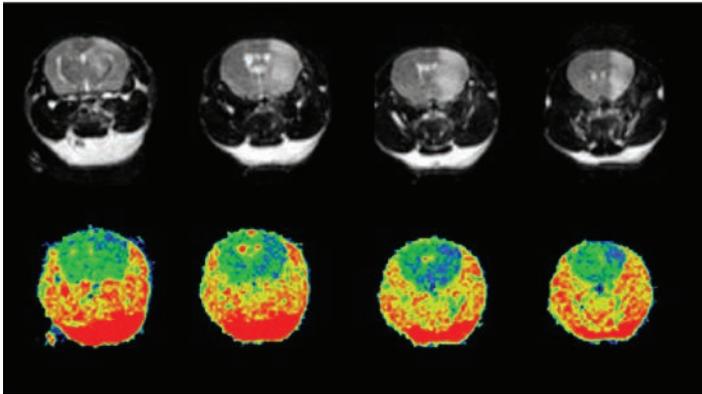
Several 2D and 3D pulse sequences

- 3D Localiser
- Quick sagittal Localiser for ultrafast anatomical reference
- Spin Echo (SE) 2D and 3D
- Fast Spin Echo (FSE) 2D and 3D
- Gradient echo 3D (GRE)
- Inversion Recovery – Spin and Gradient Echo (IR-SE, IR-GRE)
- Angiography with contrast agent
- Fat-water imaging (Dixon-method)
- Perfusion imaging
- T1, T2 and T2*-mapping
- Several multi-Field of view sequences with up to 240 mm extended axial FOV
- Echo Planar Imaging (EPI)
- Fat-suppression with IR FSE (STIR)
- Dynamic Contrast Enhancement (DCE);
- Apparent Diffusion Coefficient (ADC) map creation by Diffusion Weighted Imaging (DWI);
- fMRI¹
- Cardiac imaging¹
- Magnetic Resonance Spectroscopy (MRS)¹
- Easy-to-use environment available for sequence development

¹ Only with the 3T system

* In collaboration with RS2D

** Manufactured by Aspect Imaging



Stroke model – Diffusion-weighted Imaging

Extension of induced perfusion defect, visualized by T2 weighted FSE sequence and by Apparent Diffusion Coefficient map obtained from DWI sequence
 Images courtesy of CROMed, Budapest

CT subsystem

To complement the nanoScan® PET's exceptional qualities Mediso designed unique combination of low dose, high resolution and high speed CT with real time reconstruction to further improve the throughput of the system.

The large bore size of the CT allows even larger rodents to be examined such as rabbits or small monkeys.

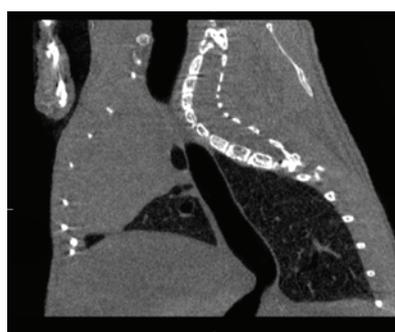
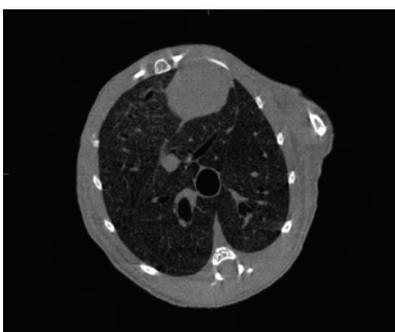


Advantages of the CT subsystems

Available in different configurations to further tailor the system to the researchers needs. For detailed information please contact your local sales representative.

- Large bore size
- Variable zoom (up to x 7.6 magnification)
- Real time CT reconstruction
- Low animal dose
- Fast speed (whole body mouse less than 36 sec)
- Large bore transaxial field of view (up to 12 cm)

High Resolution Reconstruction of Mouse Head 20 μ m voxel size 70 kV 750 mA 720 projections, 3.5 minute scanning time



Mouse Lung CT imaging 50 μ m voxel size 50 kV 750 mA 720 projections/FOV, 4.4 minute scanning time

Animal handling – MultiCell™

Integrated vital function monitoring is included in the base system which consist of respiratory, cardiac and temperature feedback during preparation and acquisition.

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 head positioning:

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:

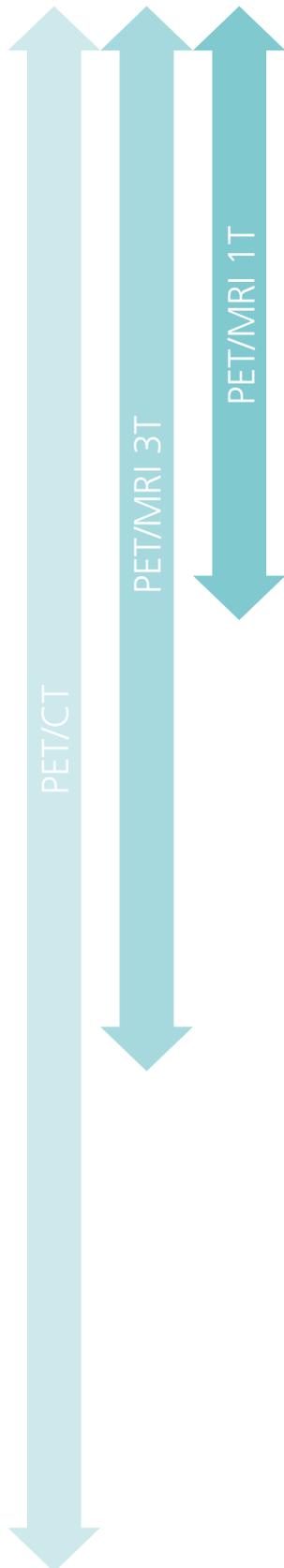
for easy and fast connection of mouse/rat imaging cells to any of the **nanoScan®** scanners or to the dual bed docking station

Automatic bed identification:

Click the imaging chamber to the system and it will be recognized automatically



Available MultiCell™ imaging chambers



Imaging chamber for Mouse - medium

Inner space: 29 x 290 mm
Outer dimensions: 33 x 460 mm
Up to 35 g



Imaging chamber for Rat - medium

Inner space: 52 x 400 mm
Outer dimensions: 56 x 540 mm
Up to 450 g



Imaging chamber for two Mice

Inner space: 2 x 26 x 260 mm
Outer dimensions: 56 x 470 mm
Up to 2 x 28 g



Imaging chamber for Mouse - large

Inner space: 36 x 290 mm
Outer dimensions: 40 x 460 mm
Up to 80 g



Imaging chamber for Rat - large

Inner space: 65 x 440 mm
Outer dimensions: 70 x 540 mm
Up to 600 g



Imaging chamber for Rat - XL

Inner space: 70 x 440 mm
Outer dimensions: 75 x 580 mm
Up to 800 g



Imaging chamber for Rat - XXL

Inner space: 102 x 510 mm
Outer dimensions: 110 x 650 mm
Up to 1.5 kg



Imaging chamber for Rabbit

Inner space: 150 x 600 mm
Outer dimensions: 160 x 760 mm
Up to 6.5 kg



Optional animal handling accessories

PrepaCell™ Preparation station



- Two docking possibilities
- Closed, temperature controlled system (up-tight container) with transparent removable cover
- Vital monitoring functions
- Embedded anaesthetic 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 head positioning: for ultra-precise and reproducible stereotactic animal positioning
- Fully compatible with all **nanoScan®** Family systems

Mediso Gating Package (Respiratory/ECG)

Respiratory and ECG cycles are monitored in real-time to synchronize image acquisition eliminating image blur caused by respiratory and/or cardiac motion.

ECG trigger module:

- Trigger detection: threshold
- Exclusion of abnormal cardiac cycles based on histogram of R-R interval
- Number of time bins (phases) within a cardiac cycle: up to 16

Respiratory trigger module

- Trigger detection: threshold
- Exclusion of abnormal cardiac cycles based on histogram

Additional gating signals:

- 2 independent TTL input channel for external triggering

MultiCell™ adapter for third party imaging systems

Customized adapter is available for third party imaging systems including high field MRI (up to 11T)

Operating hardware



Room requirements

All nanoScan® PET-based systems

- Minimum room size: 10 m²
- Single phase operation 115 / 230 V
- No additional RF shielding required
- No additional magnetic shielding required – self shielded systems

Additional system specific requirements

nanoScan® PET/CT

- Size (W x D x H): 1136 x 2177 x 1550 mm
- Weight: 830 kg

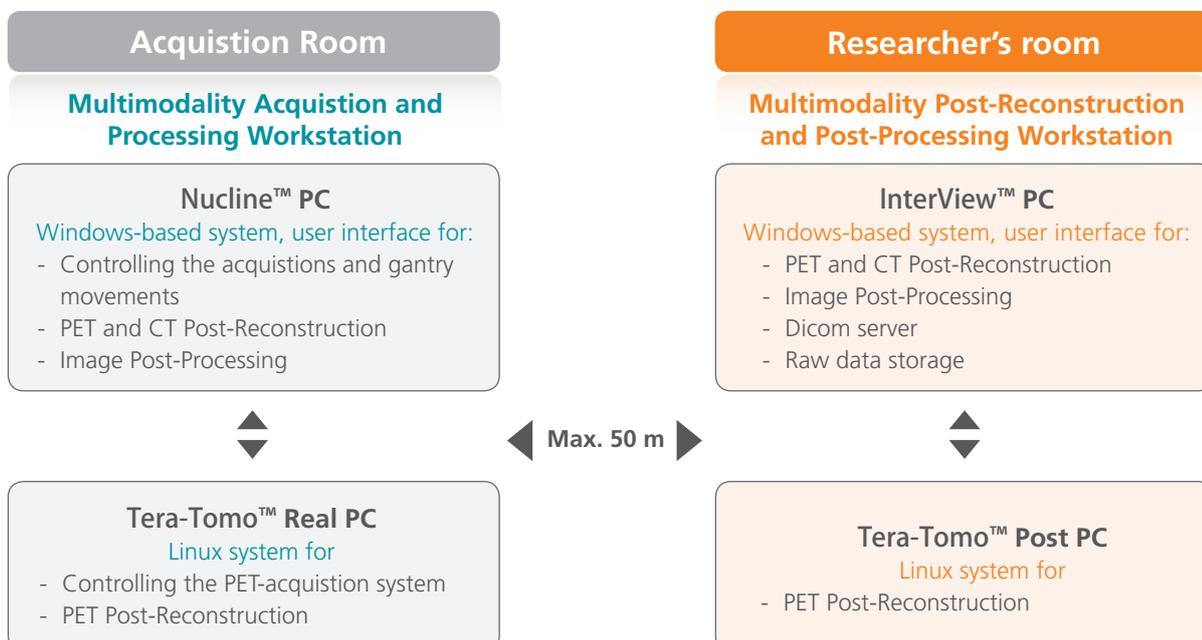
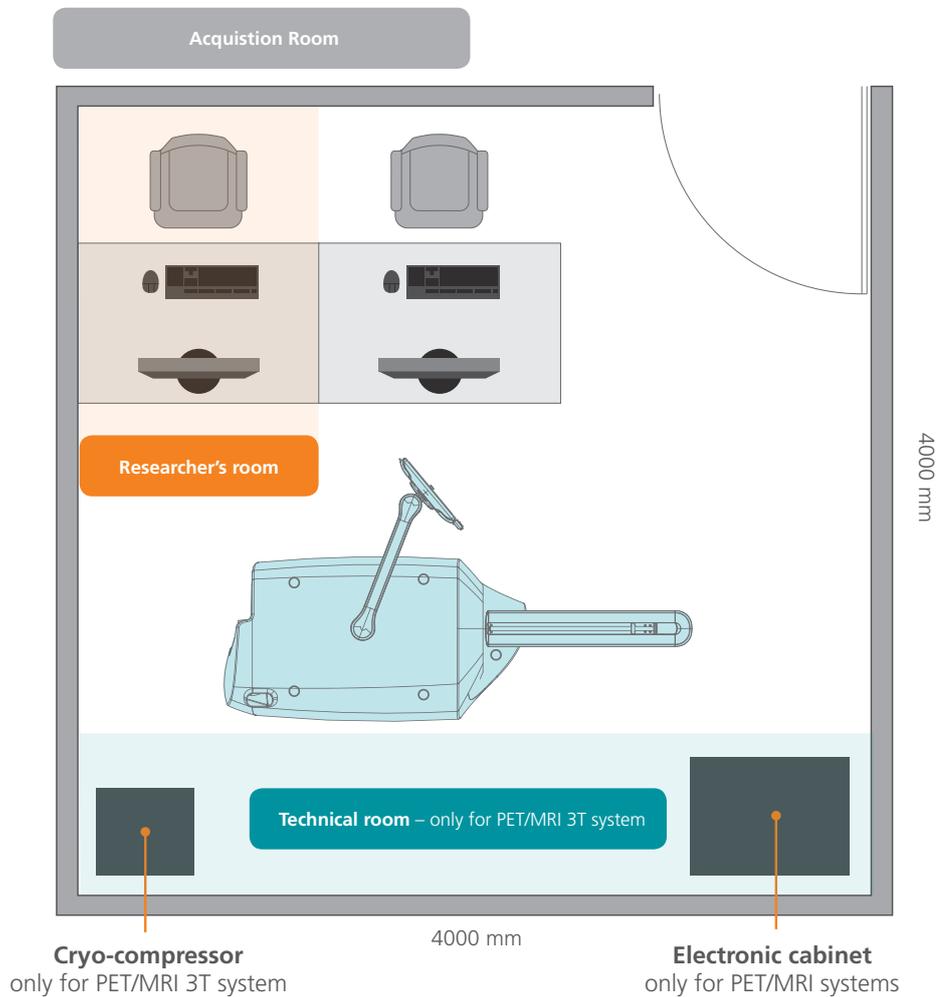
nanoScan PET/MRI 1T

- Size (W x D x H): 1909 x 956 x 1448 mm
- Weight: 1170 kg
- No cryogen or water cooling required
- Standard air conditioning is sufficient

nanoScan® PET/MRI 3T

- Size (W x D x H): 2229 x 830 x 1470 mm
- Weight: 500 kg
- Minimum 5m² technical room required with
 - Three-phase power supply (7 kW)
 - Water access for the cryo-compressor water cooling is recommended

Room layout

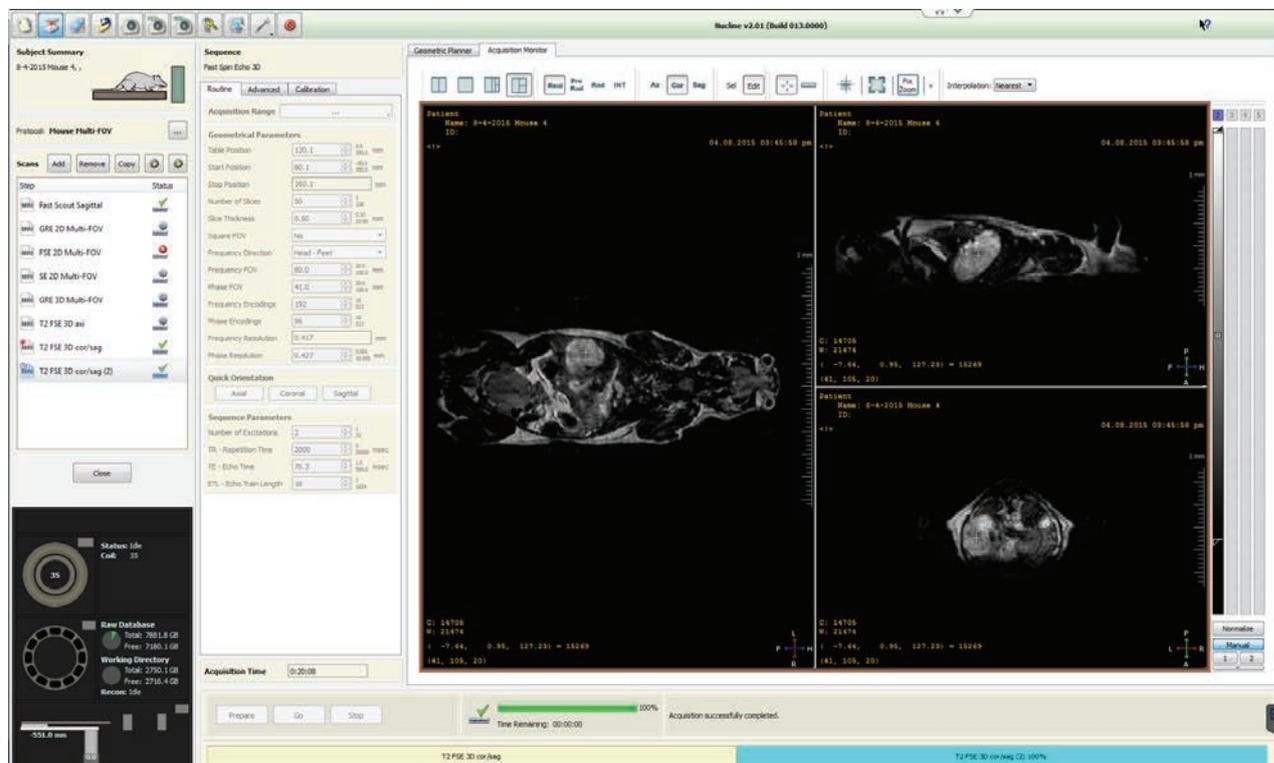


Software solutions

Nucline™ all modality acquisition software

Nucline™ is an easy to use and intuitive interface for high throughput workflow across all the nanoScan® Family systems - there is no need to learn different software solutions. In a 21CFR Part 11 compliant data management environment predefined and customizable acquisition protocols makes the experiments daily routine.

The integrated gantry with common coordinates gives the opportunity to seamlessly co-register images and allowing for accurate image quantification. Furthermore list mode data collection provides wide range of flexibility in data analysis according to the requirements of the experiment.



Post-processing by *InterView™* FUSION software

InterView™ FUSION is a multi-modal application, developed by Mediso, is an essential part of system. The application provides a wide range of functionalities to evaluate PET, SPECT, CT and MRI preclinical data. 2D single, orthogonal and tiled, as well as 3D MIP and Volume Rendering viewers represents 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

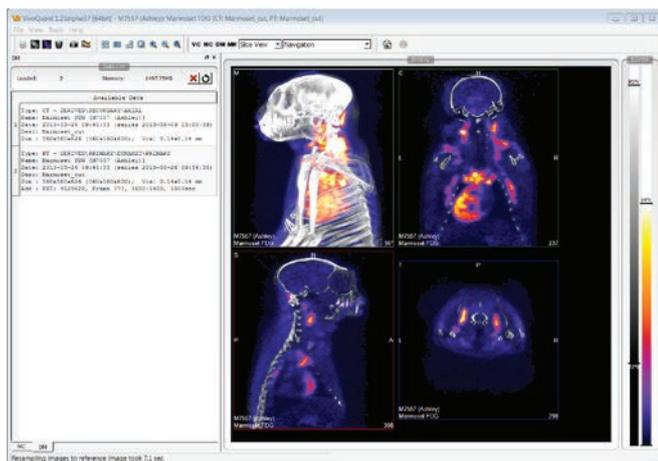
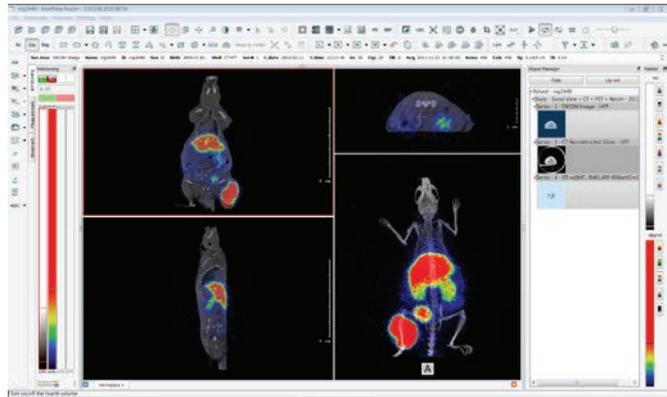
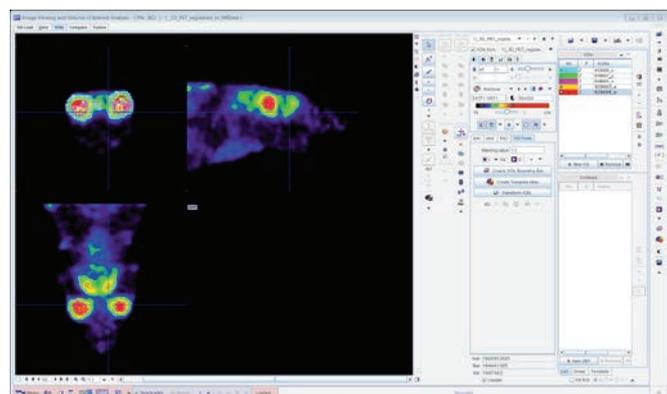


Image processing and quantification by *VivoQuant™* software

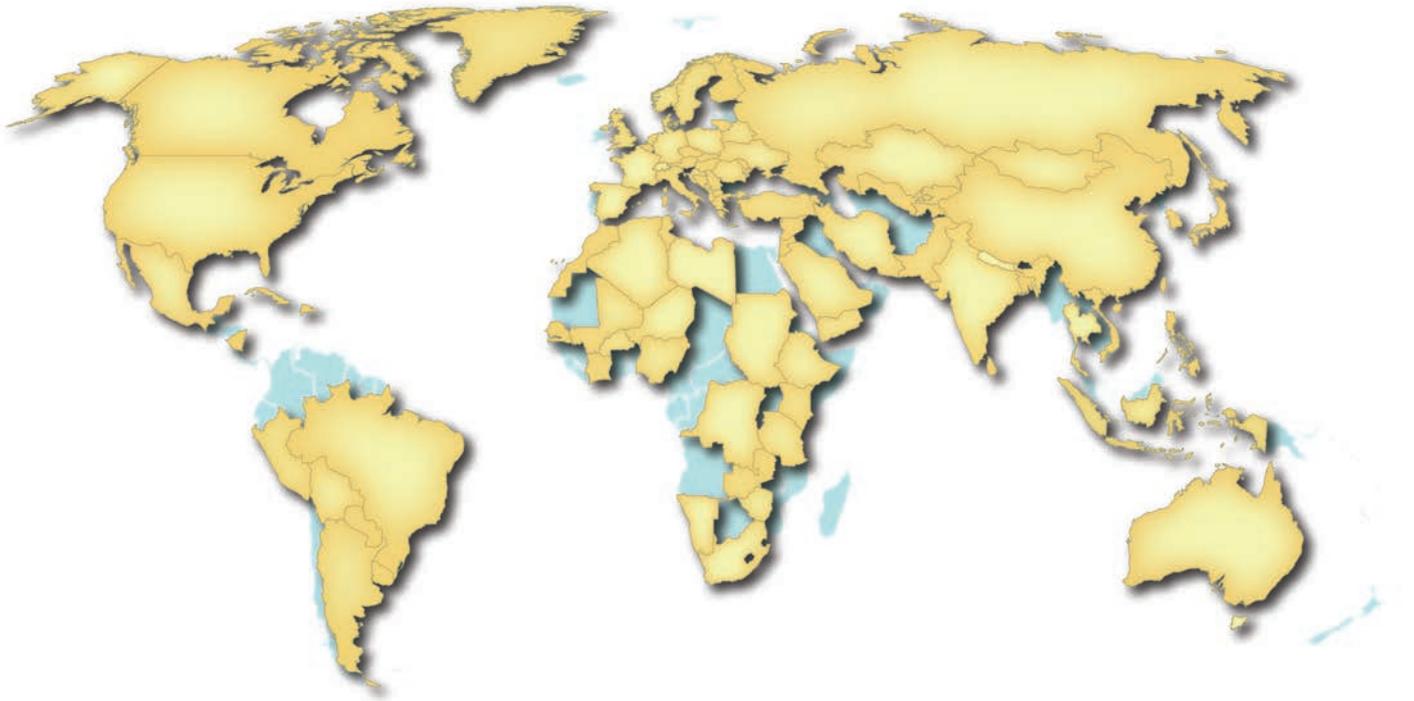
VivoQuant™ is an image viewing, processing and analysis software suite from inviCRO, LLC. *VivoQuant™* supports data from both nuclear medicine and magnetic resonance imaging systems and supports advanced co-registration, viewing, processing and quantification of data with plug-in modules dedicated to neurology and oncology applications address the challenging bottlenecks imaging laboratories face in day-to-day operations.

Image analysis and kinetic modeling by *PMOD*

Pharmacokinetic analysis is an essential task of SPECT imaging. Translational research and neuroscience rely more and more on non-invasive, in-vivo measurements of pharmacokinetic parameters. *PMOD* modeling tool gives an easy and intuitive access to the wealth of developed methods to any *nanoScan®* user. Blood and time-activity data of tissue regions can easily be imported into the modeling tool. More than 40 model configurations are available to be fitted to the data. All results can readily be exported for statistical analysis.



More than 1100+ clinical and 170+ preclinical Mediso manufactured single and multimodality imaging systems were distributed in 90 countries of the world.



Conformance Statement

Quality management system operated by Mediso Medical Imaging Systems complies with Council Directive 93/42/EEC Annex II.

Product design, development, production and services comply with EN ISO 13485 and EN ISO 14971.

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

The supplied software complies with DICOM standard.

The technical information provided here is not a detailed specification.

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

Trademarks:

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Core™ i7 is trademark of Intel.

Windows® is registered trademark of Microsoft.

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