

HUMAN HEALTH

ENVIRONMENTAL HEALTH

FLUORESCENCE TOMOGRAPHY FOR DEEPER INSIGHT



FMT Fluorescence Tomography
in vivo Imaging Systems


PerkinElmer[®]
For the Better

DEEPER INSIGHT INTO YOUR TARGETS

Our unique suite of *in vivo* imaging solutions lets you discover more about biological targets, processes and pathways, directly in

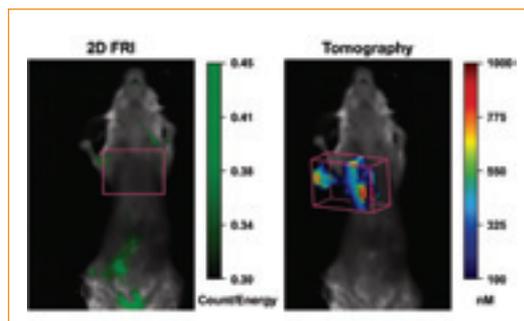
the living animal. Using our proprietary FMT® (Fluorescence Molecular Tomography) technology and fluorescent *in vivo* imaging agents, you can generate non-invasive, deep tissue quantitative data for pre-clinical research applications.

In vivo imaging is easy to learn and incorporate into your workflow. With multiplexed imaging capabilities, you can simultaneously measure, monitor and compare multiple biomarkers or pathways related to a biological question. Whatever answer you're seeking, *in vivo* imaging is the most direct path to gaining deeper insight into relevant biological function and response.

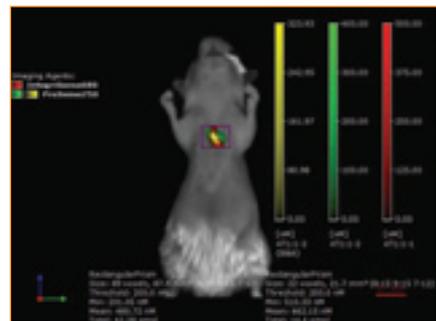
The benefits of PerkinElmer *in vivo* imaging are easy to see

- Easily and efficiently obtain calibrated quantitative data in your animal models of disease
- Measure and monitor multiple biological processes simultaneously
- Obtain functional and biological data to improve study designs and enhance decision making
- Generate 3D, information-rich results
- Complement the molecular functional findings of fluorescence imaging with other anatomical and/or functional modalities like CT, MRI, PET and SPECT
- Deepen understanding of disease mechanisms, disease progression and therapeutic responses
- Manage costs and capture time course data by avoiding sacrifice of animal models

PerkinElmer *in vivo* images represent your biology with translational quantitative data



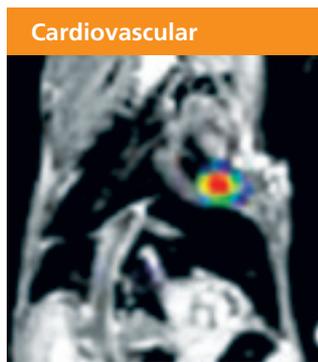
Eosinophil cathepsin activity quantitated with FMT and ProSense® fluorescent imaging agent in an ovalbumin-induced asthma model (right); not visible with planar fluorescence (left) because of the depth of the model.



Regardless of signal depth, FMT imaging systems extract more information from the fluorescence signal than conventional planar or single-view instruments.

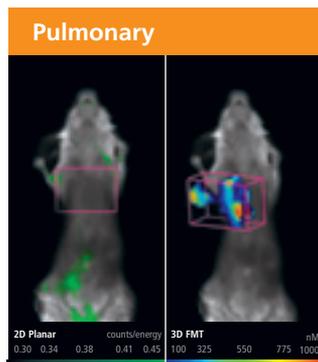
POWERFUL DECISION MAKING FOR ANY APPLICATION

The closer you can get to your target of interest, the better. PerkinElmer's FMT technology provides non-invasive, whole-body, deep-tissue imaging in small animal models and generates 3D, information-rich results. These systems are used for research in oncology, inflammatory, pulmonary, cardiovascular and skeletal diseases. Biological targets and pathways can be monitored and quantitated in real time – giving a deeper understanding of the biology underlying disease mechanisms and therapeutic response.



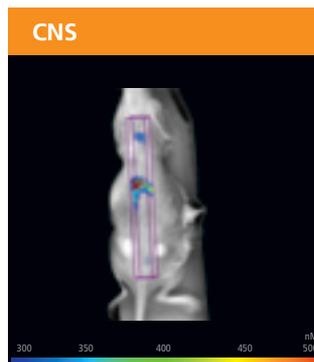
Cardiovascular

Co-registered FMT-MRI imaging data of proteolytic activities validating splenic deployment of monocytes to the heart following myocardial infarction.*



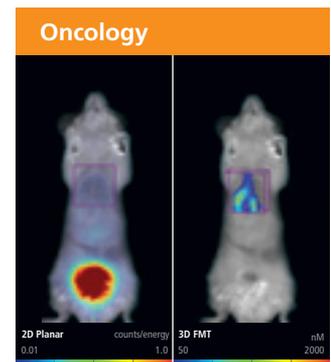
Pulmonary

Eosinophil cathepsin activity quantitated with FMT and ProSense fluorescent imaging agent in an ovalbumin-induced asthma model (right); not visible with planar fluorescence (left).



CNS

FMT tomographic imaging in brain for EAE disease severity. Quantitation of AngioSense® fluorescent imaging agent.



Oncology

FMT quantitative imaging of breast cancer metastasis to the lung, using ProSense fluorescent imaging agent (right); not visible with planar fluorescence (left).

*Image courtesy of Swirski et al, Science, 31 July 2009, Vol 325, p 612



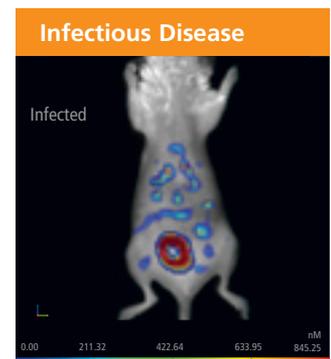
Bone and Skeletal Disease

FMT quantitative imaging of arthritis using ProSense fluorescent imaging agent to quantitate arthritic inflammation *in vivo*, in CAIA mice.



Inflammation

FMT quantitation of acute edema and cellular inflammatory response. Quantitation of AngioSense fluorescent imaging agent.



Infectious Disease

FMT quantitative imaging of schistosomiasis using ProSense fluorescent imaging agent showing infection of liver and lower gastrointestinal tract.

PerkinElmer *in vivo* imaging technologies and targeted fluorescent agents provide effective and quantifiable measurement of disease progression and therapeutic response *in vivo*.

CHOOSE THE SYSTEM THAT FITS YOUR RESEARCH

The FMT imaging system is the leading platform for tomographically quantitating a broad range of *in vivo* imaging biomarkers, disease pathways and therapeutic response levels *in vivo*.

Whether you're part of a research facility focusing on a single application or a core imaging facility serving multiple departments, you will find the FMT easy to learn and fast to implement. FMT will efficiently provide quantitative, insightful data in your disease areas. FMT is available in three platforms, the FMT 1000 (1-Channel), the FMT 2000 (2-Channels), and the FMT 4000 (4-Channels) Fluorescence Tomography *in vivo* Imaging Systems.

Configured to fit your laboratory

For individual labs or single-application facilities, the FMT 1000 comes with one channel for fluorescence tomography, and the ability to add additional channels in the future. All systems include 3D software, two imaging cassettes, and a high-powered workstation for data analysis.

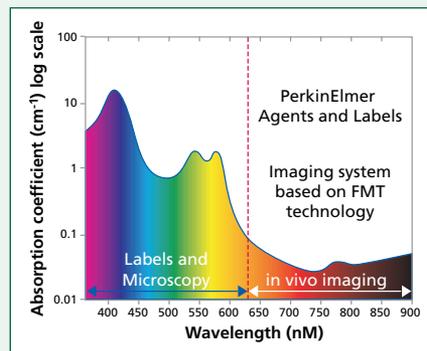
For laboratories with a broader range of applications, the FMT 2000 offers two channels and the FMT 4000 offers four channels that enable a broader spectral fluorescence range for multiplexing of fluorescent agents and dyes.

FMT Fluorescence Tomography *in vivo* Imaging System



Quantitative Data In 3D

The PerkinElmer FMT system preserves a linear relationship between activity *in vivo* and detector signal when imaging deep (non-surface) targets and biologies by reconstructing three-dimensional (3D) maps of fluorophores inside living animals. PerkinElmer's proprietary FMT technology and biocompatible fluorescence agents are specially designed for use in the near-infrared spectral region, ensuring maximum light penetration and highest sensitivity.



Working within the near-infrared spectral region (600-900 nm), light absorption by physiologically abundant molecules is reduced to a minimum.

AMPLIFY YOUR RESULTS WITH FUNCTIONAL AGENTS

PerkinElmer's comprehensive suite of fluorescent agents and labels is designed to deliver biological specificity, with wavelengths spanning the Red and NIR spectrum for better performance in *in vivo* research. While developed and optimized for use with systems based on FMT technology, our agents are compatible with a variety of *in vivo* and *in vitro* imaging systems. Visit www.perkinelmer.com/invivoimaging or write agentinfo@perkinelmer.com for a complete list of fluorescent agents.

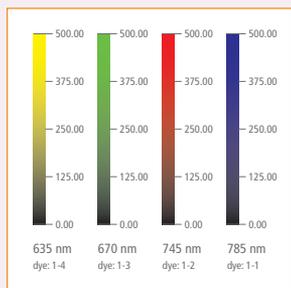
Choose the Agent That's Right for Your Application

- **Activatable agents** alter their fluorescence profiles *in vivo* to provide molecular and functional information in real time. Optically silent upon injection, they are activated *in vivo* with specific protease biomarkers of disease.
- **Targeted agents** bind to specific biomarkers for highly specific targeting of key biologies.
- **Vascular agents** enable the monitoring of blood vessels and observation of phenomena such as blood leakage in tumors or inflamed regions and angiogenesis.



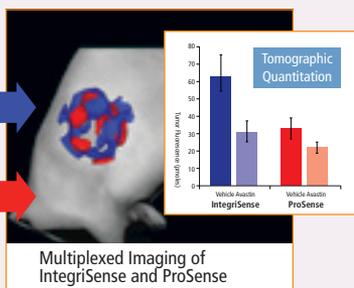
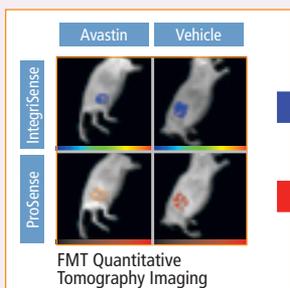
Combine Agents to Monitor Multiple Molecular Processes

With PerkinElmer's complete line of *in vivo* imaging instruments, multiple agents can be imaged and quantitated simultaneously for multiplexing analysis to evaluate a number of biomarkers or pathways relating to a biological question. With the FMT 4000, up to four different agents can be imaged in the four separate channels, allowing for a four-dimensional analysis of a particular application.



With the FMT 4000, four agents can be imaged simultaneously to allow for the quantitation of four separate biomarkers relating to a particular application. This image (left) illustrates this capability with agents imaged in the 635 nm, 670 nm, 745 nm and 785 nm channels.*

*Image courtesy of Waterman, P and Nahrendorf, M, MGH/Harvard.



In this sequence, **IntegriSense™** and **ProSense** are imaged simultaneously to evaluate the effect of Avastin® on a tumor. Representative isosurface renderings of a mouse treated with Avastin and a mouse treated with vehicle are shown. Note the differential localization of **IntegriSense** (blue), highlighting integrin presence, and **ProSense** (red), quantitating cathepsin activity within the same tumor. In addition, treatment with Avastin showed quantitative changes in integrin imaging with as little as one week of treatment.

FROM ANIMAL TO ANALYSIS IN THREE EASY STEPS

PerkinElmer's powerful FMT imaging helps to advance the investigation, understanding and quantitation of underlying biological mechanisms and therapeutic responses. Whatever your applications – inflammatory, cardiovascular, skeletal, pulmonary, oncology – quantitative data is only three steps away.

Step 1: Administration of Agent and Animal Placement

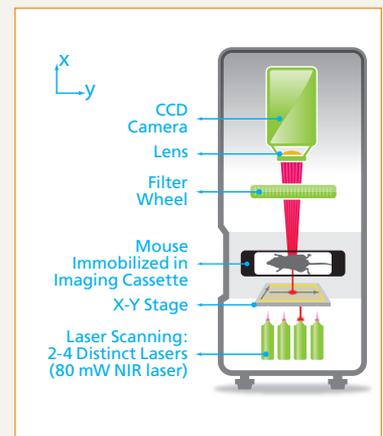
- The agent is injected into the mouse.
- The mouse is anesthetized and comfortably placed in the portable Animal Imaging Cassette.



The imaging sessions are rapid (2-3 minutes per animal), animal handling is simple and the mouse remains stable and immobilized for consistent, repetitive imaging results.

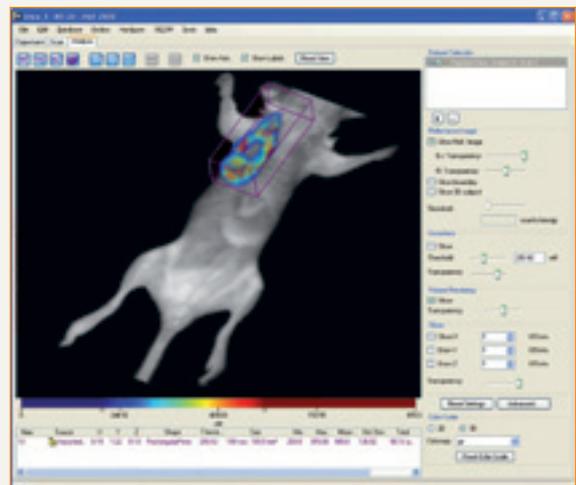
Step 2: FMT Data Generation

- Transillumination: FMT transillumination of animal using dynamically powered lasers.



Step 3: FMT Reconstruction

- Fluorescence quantitated at each point in the subject including deep tissue targets.
- Fluorescence concentration measurements calculated throughout the user-selected regions of interest (ROI).
- Data provided in universal formats for analysis (including DICOM), database building and decision making.
- Easily create animated movies including dynamic presentation of quantitation data for presentation.



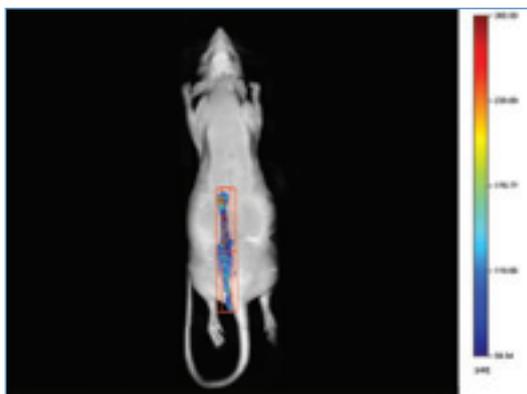
MULTISPECIES IMAGING MODULE FOR FMT

The new Multispecies Imaging Module (MSIM) for the PerkinElmer Fluorescence Molecular Tomography (FMT)

system opens up the possibility of studying disease models in larger animals. The module is now available for 3D non-invasive quantitative imaging of adult rats in the FMT 1000, FMT 2000, and FMT 4000.

- Better Data: the biology of interest in larger animal models is easier to see and quantify; important rat models of disease can now be imaged by optical tomography.

- Innovation: 3-dimensional fluorescent imaging for adult rats (up to 450 grams).
- More Relevance: perform biodistribution studies in rats that are non-invasive, quantitative and within a physiologically relevant context.
- Safety: the heating and anesthesia systems are designed to keep the specimen comfortable and sedated throughout the scan.
- Flexibility: hardware and software components of the new module have been designed to make it easy to switch from imaging mice to rats and back again.



Imaging normal bone turnover in the Lumbar vertebrae of the Zucker rat using **OsteoSense**[®] 750 (NEV100S3). Even in larger sized rats, it is possible to see differences in bone turnover along the vertebrae



The Multispecies Imaging Module contains the imaging cassette for large animals (left), and an adapter (right) for the standard small animal imaging cassette (center).

MULTIPLE BENEFITS IN MULTIMODALITY IMAGING

Because one modality does not answer all biological questions, FMT imaging

in vivo is designed to easily integrate its molecular tomographic data with other functional and anatomical modalities. You can easily combine imaging approaches and fuse data sets from both FMT and a second modality including MRI, CT, SPECT or PET. This resulting integration of quantitated FMT biomarker readouts with precise anatomic context provides users the unprecedented ability to measure and monitor disease pathways and therapeutic efficacy *in vivo*.

- Combine molecular/functional and anatomical data (FMT + CT/MRI/SPECT/PET)
- Leverage core facility instrumentation and investments to gather more robust biological insights
- Combine different benefits/attributes of different modalities
- Gather multivariant, multiplexed insights
- Utilize your expensive murine subjects repeatedly for data collection over time

Step 1: Administration of the Agent

The agent is injected into the mouse and may take 4-6 hours to reach full effect.



Step 2: Anesthetize Animal in Imaging Cassette

Animals are anesthetized and secured in the Animal Cassette for imaging. Fiducial markers on the side of the cassette allow for co-registration using FMT and a secondary modality.



Step 3: Select a Multimodality Adaptor

PerkinElmer has four models of its Multimodality Adaptor available for imaging with CT, MRI, SPECT and PET.



Siemens Inveon® CT/PET/SPECT Multimodality Adaptor



Bruker MRI Multimodality Adaptor



Gamma Medica CT Multimodality Adaptor



GE CT Multimodality Adaptor

Step 4: Place Cassette

The Animal Cassette is then placed inside the Multimodality Adaptor. The animal remains immobilized for easy multimodality imaging.

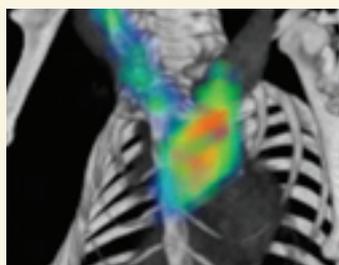


Step 5: Place Adaptor

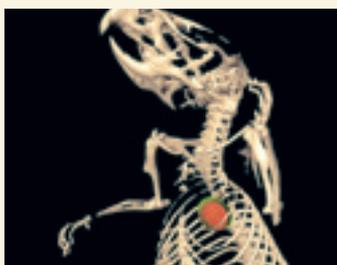
The Multimodality Adaptor is placed in the second modality and the animal is imaged. The fiducial markers allow for easy alignment of images between the two modalities.



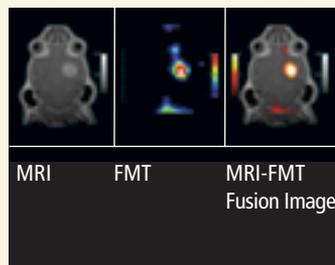
Step 6: Generation of Fused Multimodality Images and Data Sets



Multimodality FMT – CT imaging of atherosclerotic plaque. Quantitation of **ProSense** in ApoE $-/-$ mice.



Multimodality FMT – CT imaging of lung carcinoma in adult mouse. Quantitation of **AngioSense** (green) for tumor vascularity and **ProSense** (red) for cathepsin activity.



Combined MRI and FMT in mouse brain in a study of glioma response to chemotherapy. Fluorescent signal penetrates the skull to enable quantitative data capture.

FMT Imaging Systems are Available in Three Platforms:

- FMT 1000 (1-Channel – Choose between 670 nm or 745 nm)
- FMT 2000 (2-Channel – Comes with 670 nm and 745 nm)
- FMT 4000 (4-Channel – Comes with 635 nm, 670 nm, 745 nm, and 790 nm)

Channels

Four pre-configured NIR channels for reflectance imaging and optical tomography:

Channel No.	Excitation λ [nm]	Fluorescence λ [nm]
1	635	650-670
2	670	690-740
3	745	770-800
4	790	805+

Scan time: 2-5 minutes/animal (depending on region of interest)

Reconstruction time: 0.5-6 minutes/animal (depending on region of interest)

System dimensions:

Volume: 46 x 48 x 89 cm (18 x 19 x 35 in)
Weight: 89 kg (195 lbs)

Light Sources

4 distinct laser diodes provided at 635 nm, 670 nm, 750 nm and 785 nm (*lasers included depend on system platform, see page 1*)

Laser output power: 80 mW for each wavelength

The entire laser spectral energy is condensed within < 3 nm FWHM to ensure sufficient spectral power density for deep tissue penetration and subsequent quantification.

Uses a dedicated high-fidelity laser source for each wavelength of operation.

Detector

Low noise TE-cooled back-illuminated high quantum efficiency CCD camera with air assist

Additional Optical Specifications

Camera sensor	Back illuminated 16-bit dynamic range CCD
CCD size	12.3 x 12.3 mm
Imaging pixels	512 x 512
Quantum efficiency	90% at 700 nm; 75% at 775 nm
Pixel size	24 x 24 microns
Field of view	8 x 8 cm
Min. image pixel resolution	156 microns
Dark current @ -70 °C	0.002 e-/p/sec
Excitation filter positions	4
Emission filter positions	4
Excitation filters	4
Emission filters	4
Transilluminating stage	yes
Heated chamber	yes
Diffuse tomography software	yes
Gas anesthesia	yes
Workbench	N/A
CCD operating temp.	-55 °C
Power requirements	115/230 VAC 4/2 A 50/60 Hz
Chamber temp.	37 °C
Signal-to-noise	>38 dB

Parts Description

Portable animal imaging cassette:

- Easy animal preparation for both 3D tomographic and 2D reflectance imaging. Elegant approach to maintain and secure animals in stable position during imaging
- Facilitates rapid and easy co-registration between MR, CT, SPECT and PET imaging modalities and FMT data sets
- Internal docking station provides automatic dispensing of gas anesthesia (isoflurane) and physiological temperature control

Four channel LED front illuminators for reflectance imaging

View Field

Planar view: 8 x 8 cm (3.1 x 3.1 in)

- Tomographic view field: user definable up to 6 x 5 cm (2.0 x 2.0 in)
- Physiological temperature control
- Automatic dispensing of gas anesthesia

Multiplexing

The FMT 2000 and FMT 4000 can quantify multiple NIR imaging agents at superficial and deep targets to the pmol in true 3D.

Workstation Computer for Scanning and Reconstruction

- Windows® 7 PC with NTFS file system
- Dual Six Core Processor X5650 2.66 GHz or faster
- 24 GB of 1333 MHz DDR3 RAM
- Video card 1 GB nVIDIA® Quadro® FX3800 or better
- 2 TB SATA 7200 RPM hard drive or better
- Standard Ethernet NIC, DVD burner/reader
- USB 2.0 ports, 2 RS232 ports
- Dell® UltraSharp™ 2007 FP 20" flat panel monitor or equivalent
- TrueQuant™ software for system control, data acquisition, tomographic reconstruction, 3D image analysis and display, including DICOM compatibility (Seats per system: 1 host PC license and 4 satellite PC licenses)
- Provides Microsoft® SQL Server® for data archiving and manipulation

Resolution

Multiple source/detector projections, powerful algorithms, and robust optics enable FMT to measure and report fluorochrome concentration deep within the animal with sub millimeter spatial resolution.

Power Requirements

115/230 VAC 4/2 A 50/60 Hz



PerkinElmer's powerful suite of FMT IVIS[®], Maestro[™], and Quantum FX systems plus our industry-leading range of *in vivo* imaging agents and biologics are the foundation of our continuing commitment to advance the field of *in vivo* imaging technology. Let us help you design an imaging solution tailored to your needs. We welcome your questions at invivoimaging@perkinelmer.com.

Turn questions into breakthroughs

At PerkinElmer, we share your commitment to answering challenging biological questions. Our broad portfolio of instruments, reagents, software and services empowers you to do more. You'll have the multidirectional solutions you need to locate, detect and quantitate target activity in a wider context. No matter where your research stands, PerkinElmer can help you move it forward with the data and analysis that lead to insight – and breakthrough answers.

Contact us at 800 762-4000 (U.S.), 00 800 33 29 0000 (Europe) or 800 820 5046 (China). Or contact us by e-mail at fmtinfo@perkinelmer.com.

Learn more at www.perkinelmer.com/invivoimaging

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