



## Fluorescence Molecular Tomography (FMT) Imaging Technology & applications

Pre-clinical Imaging Solutions

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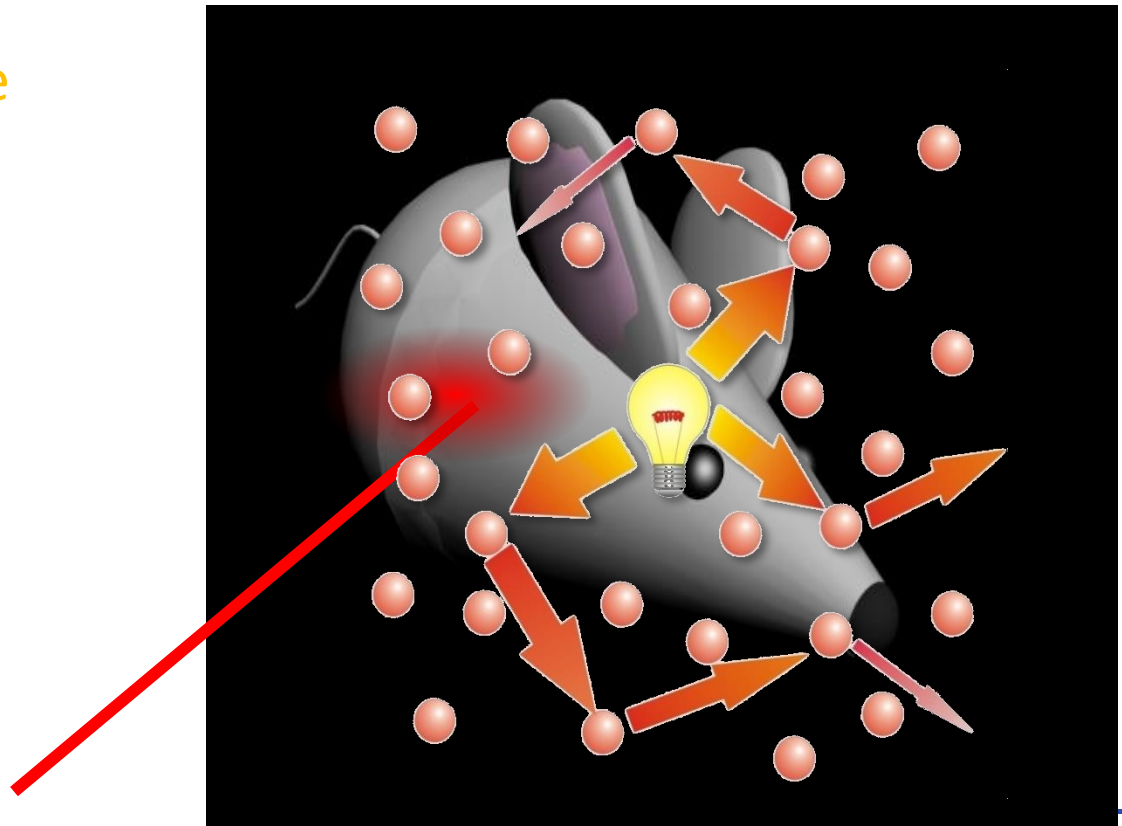
博克科技有限公司 J&H Technology Co., Ltd.

<http://www.jnhotech.com.tw>

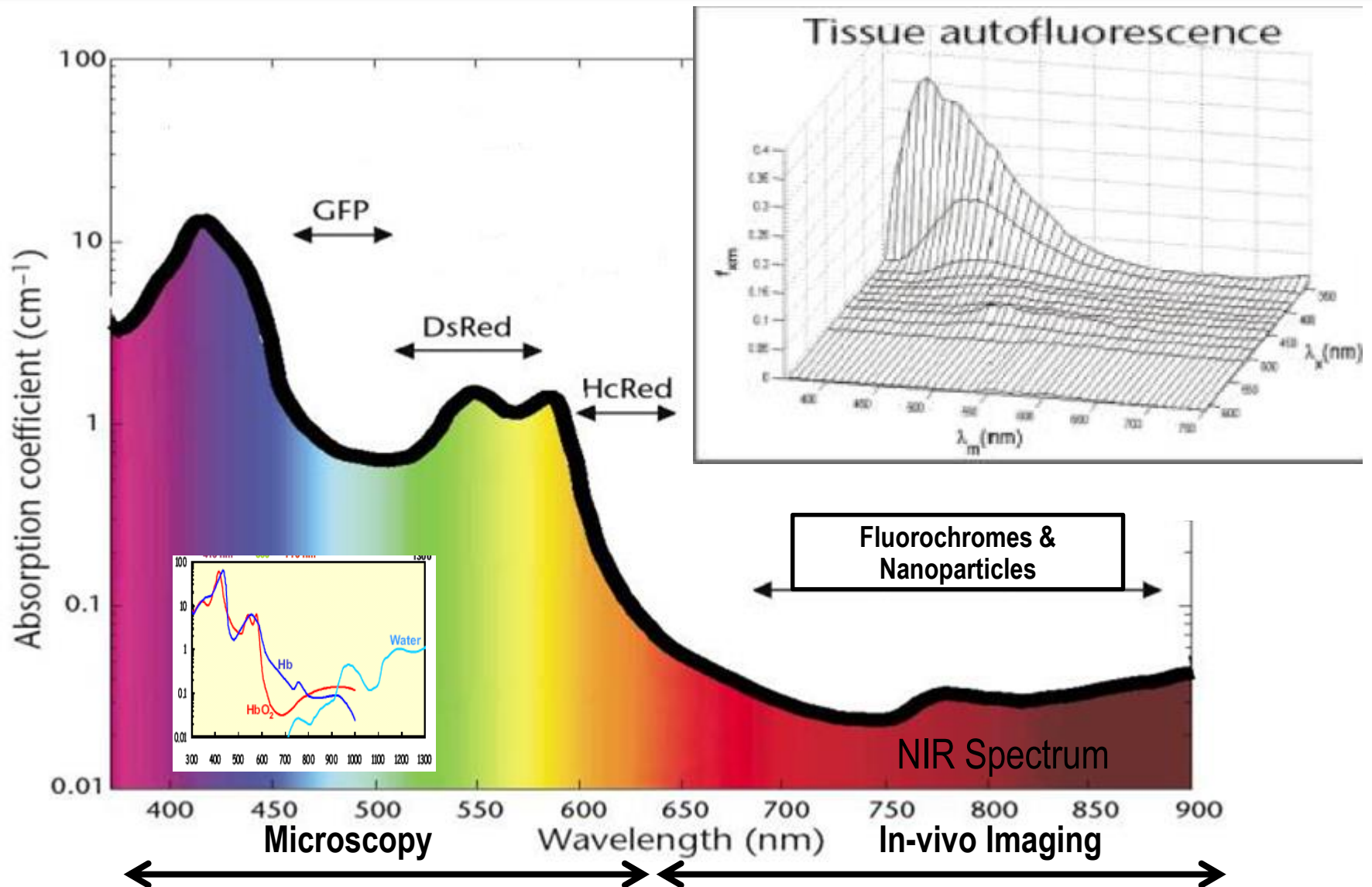
Ovalbumin-induced Asthma Model; Imaged with FMT 2500 + MMPsense 680

Governed by:

- Scattering
- Absorption
- Tissue Autofluorescence
- Deep tissue signal



# Advantages of Imaging in the NIR Spectrum



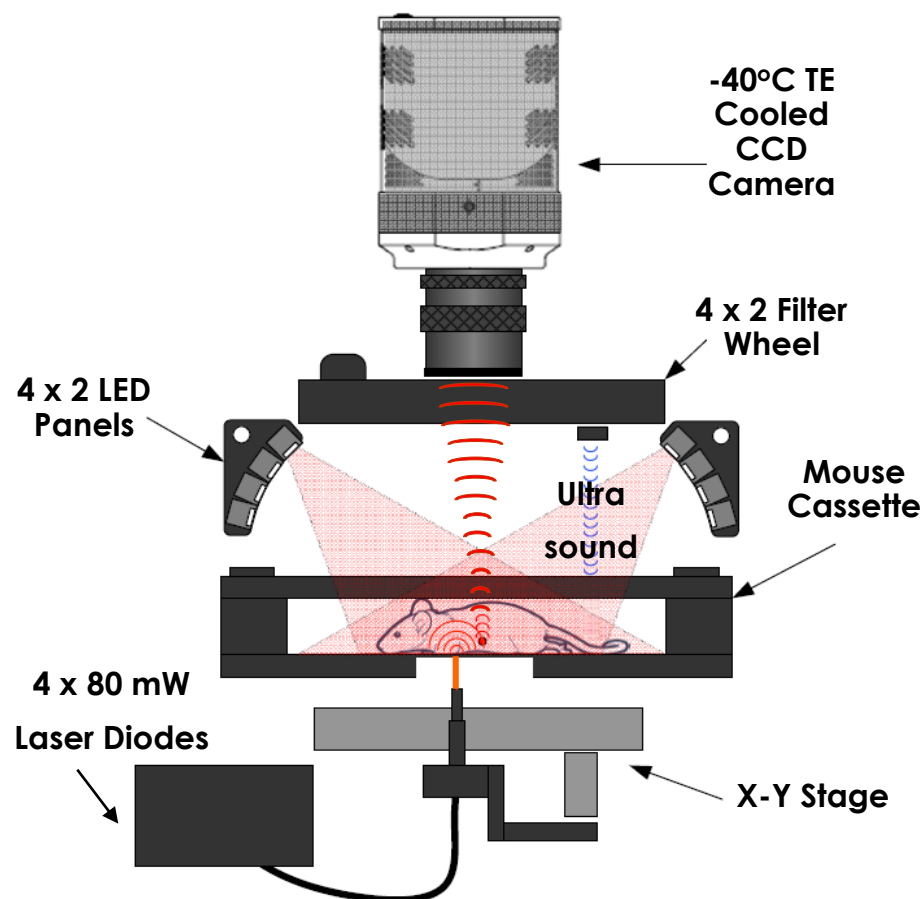
The absorption spectrum for tissue in the visible and near infrared (NIR) regions

- 1,2, or 4 Channel; 635, 680, 750, 790 nm



## Step 1: FMT Data Generation

- Reflectance Fluorescence  
Reference Image Acquired using LEDs
- Transillumination FMT Raster Scan using 80 mW lasers
- Tomographic Data Collected using a 512 x 512 pixel Thermoelectrically Cooled CCD Camera

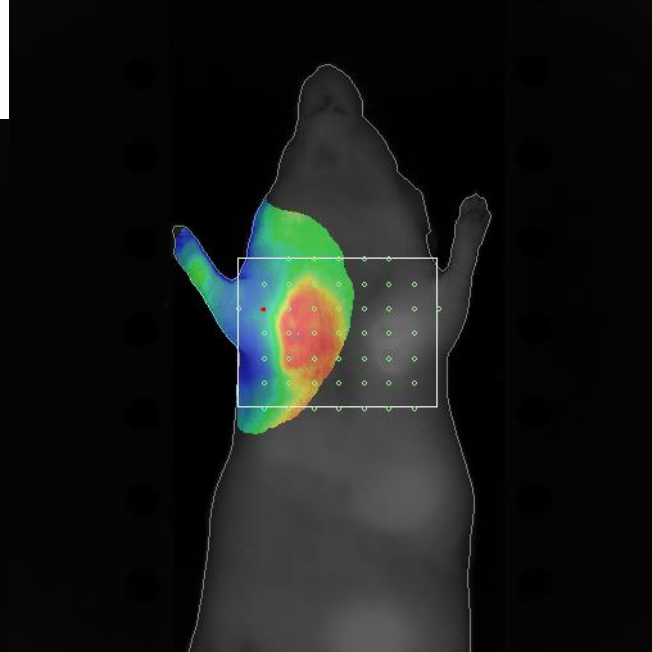
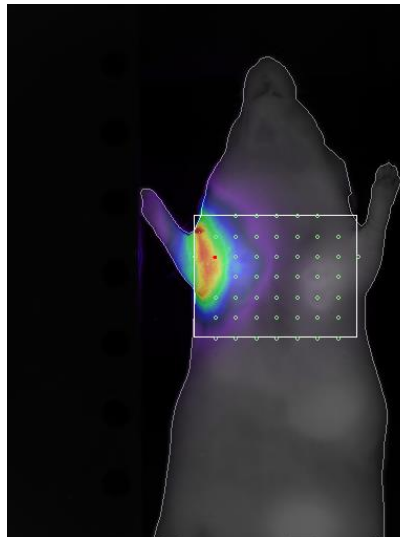


## Step 2: FMT Normalization

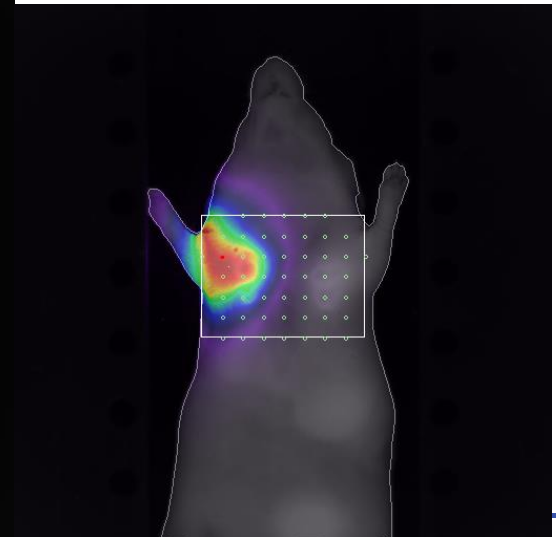
Process all paired Absorption and Fluorescence acquisition data to generate normalized fluorescence measurements

### Normalized Scan

Tissue Attenuation/  
Density Scan

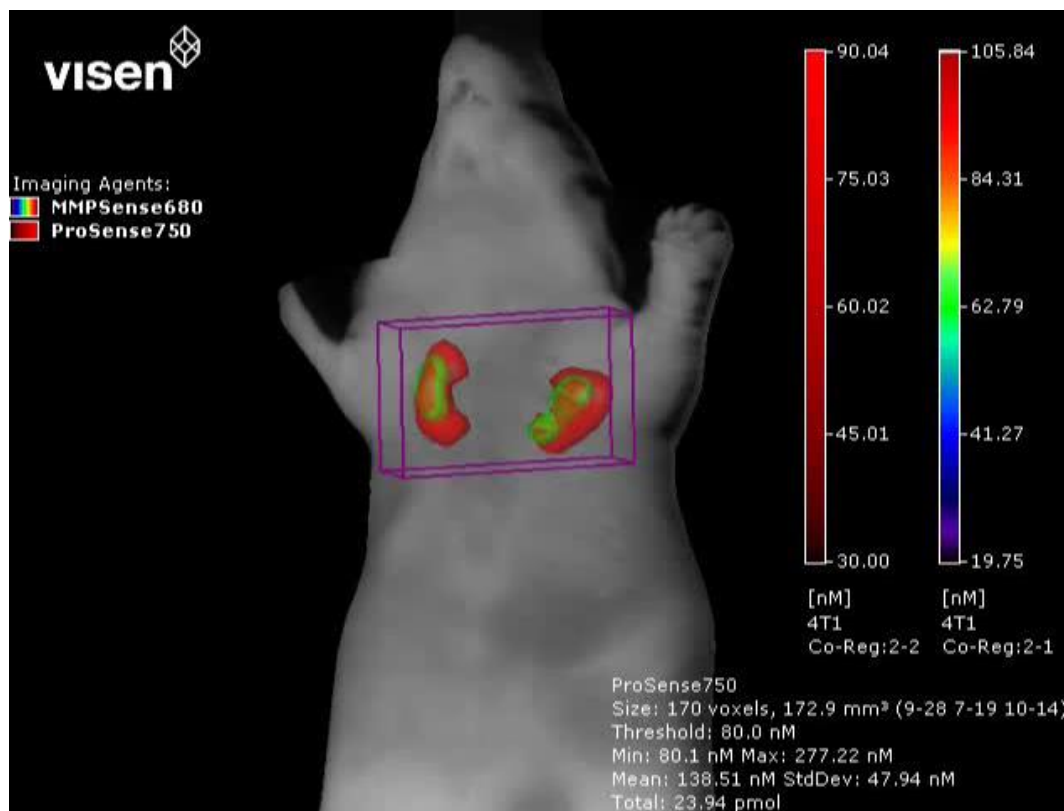


Fluorescent Emission Scan



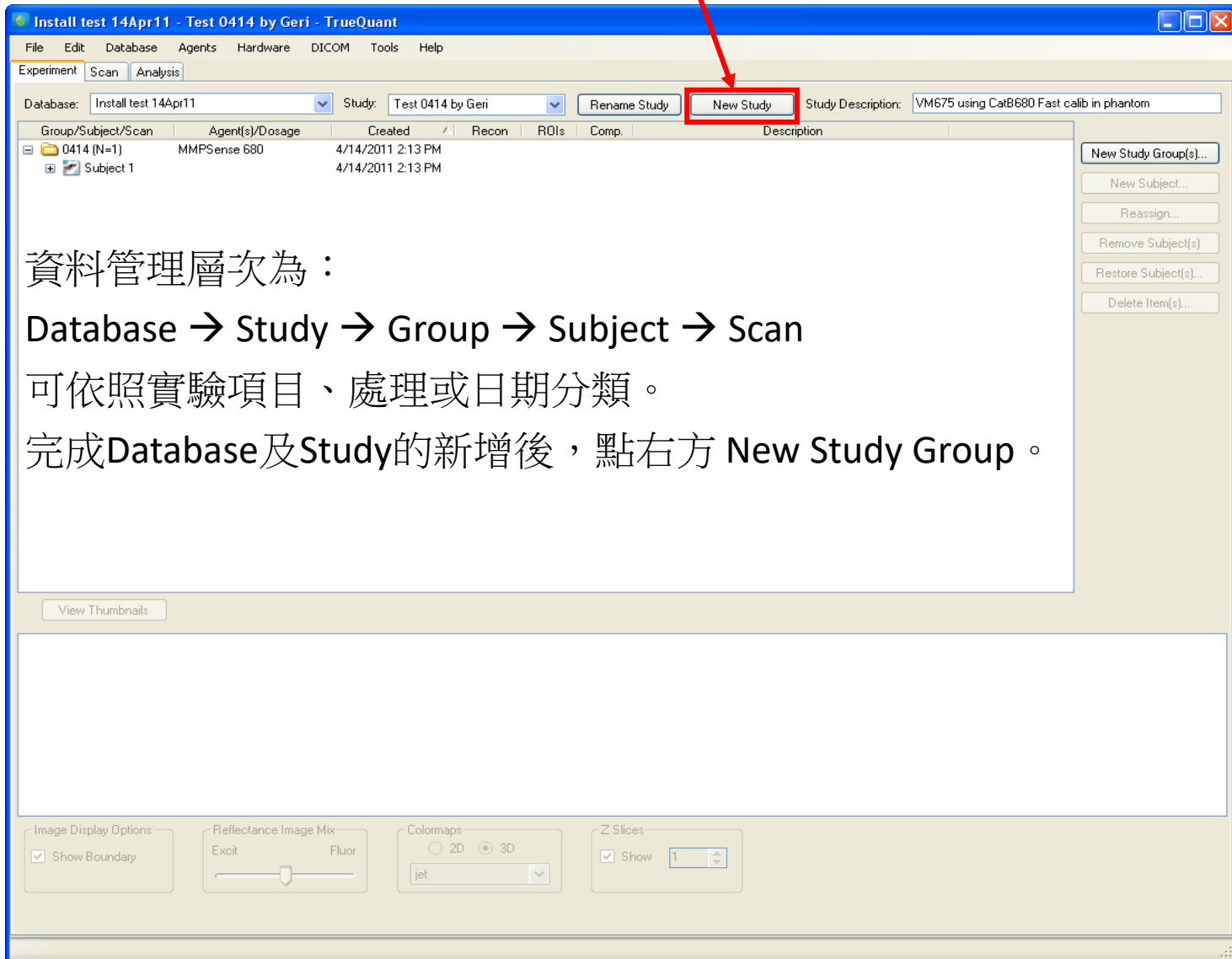
## Step 3: FMT Reconstruction

Fluorescence quantified to the picomole at each point in the subject, including deep tissue targets



# 第一頁：Experiment

點這邊新增



Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Database: Install test 14Apr11 Study: Test 0414 by Geri Rename Study **New Study** Study Description: VM675 using CatB680 Fast calib in phantom

Group/Subject/Scan	Agent(s)/Dosage	Created	Recon	ROIs	Comp.	Description
0414 (N=1)	MMPsense 680	4/14/2011 2:13 PM				
Subject 1		4/14/2011 2:13 PM				

New Study Group(s)...

New Subject...

Reassign...

Remove Subject(s)

Restore Subject(s)...

Delete Item(s)...

View Thumbnails

Image Display Options:  Show Boundary

Reflectance Image Mix: Excit Fluor

Colormaps: 2D 3D jet

Z Slices:  Show 1

資料管理層次為：

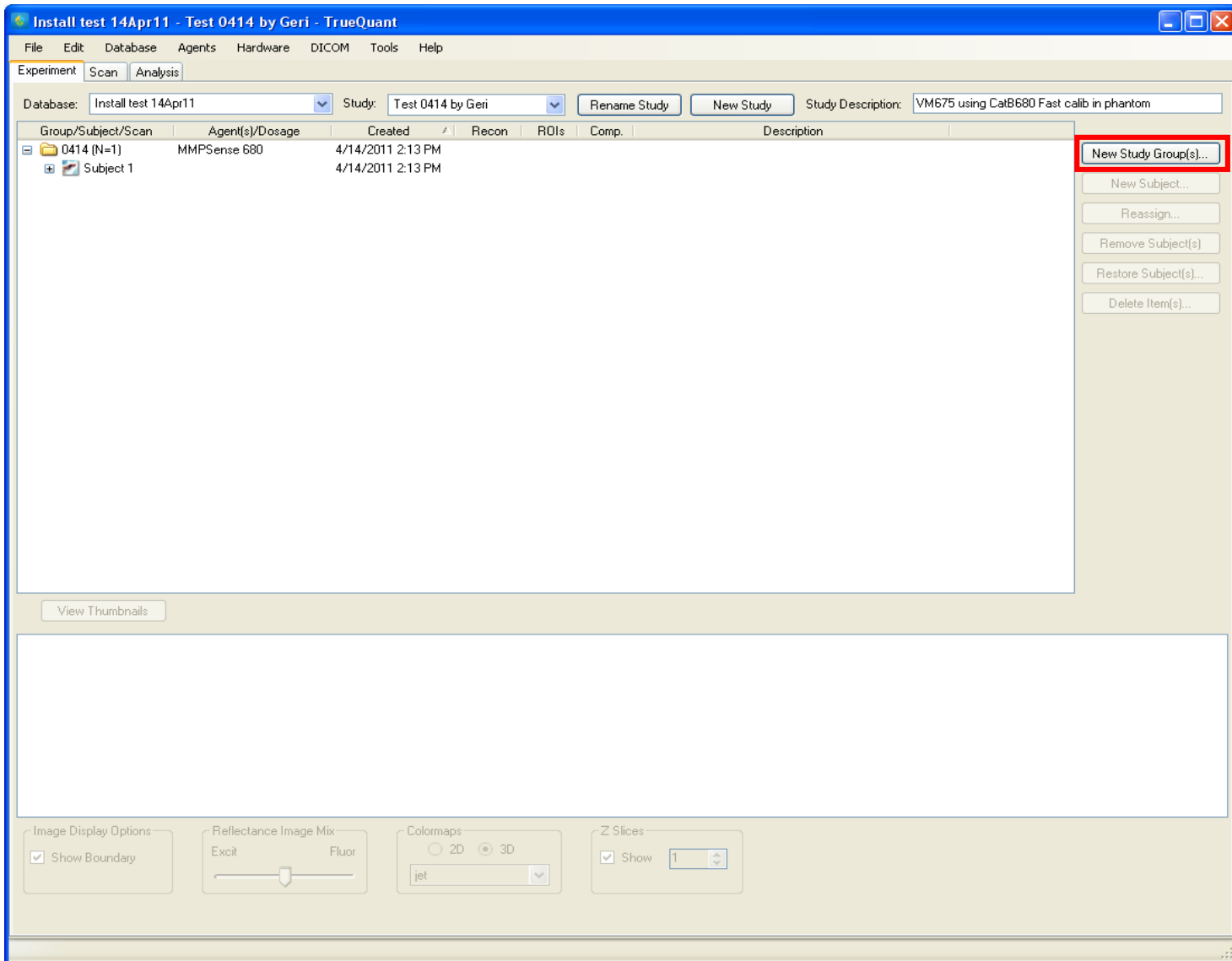
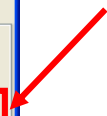
Database → Study → Group → Subject → Scan

可依照實驗項目、處理或日期分類。

完成Database及Study的新增後，點右方 New Study Group。



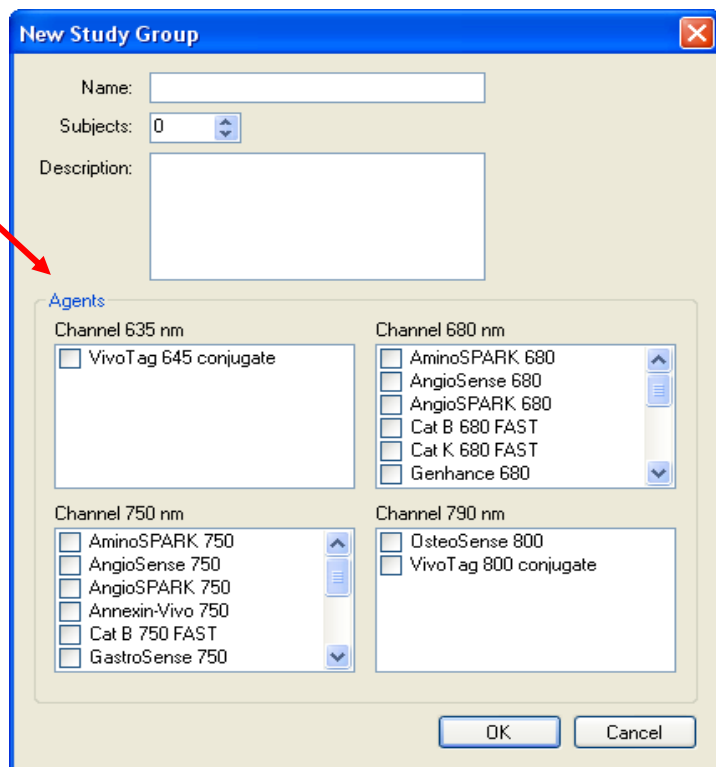
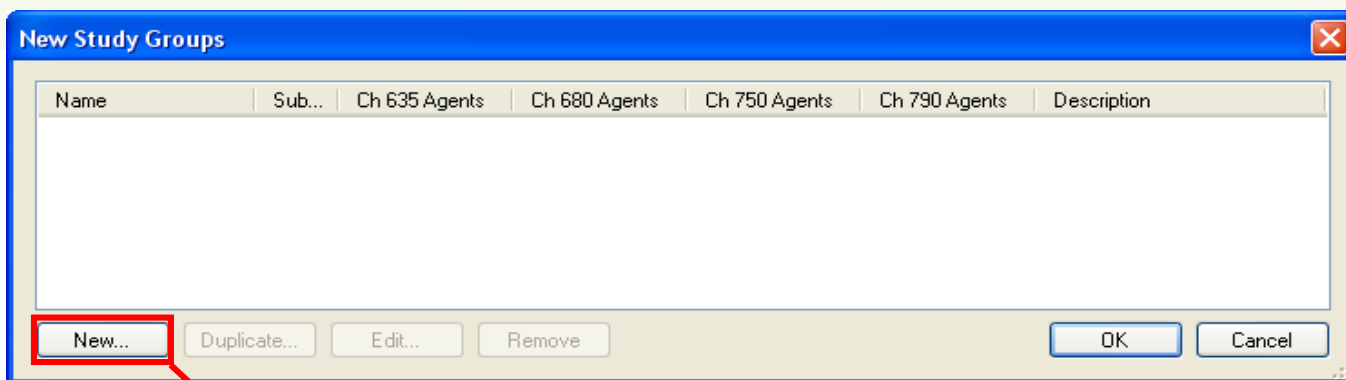
開始掃之前點這



The screenshot shows the TrueQuant software interface. At the top, the title bar reads "Install test 14Apr11 - Test 0414 by Geri - TrueQuant". Below the title bar is a menu bar with "File", "Edit", "Database", "Agents", "Hardware", "DICOM", "Tools", and "Help". The "Experiment" tab is active, showing "Scan" and "Analysis" sub-tabs. The "Database" dropdown is set to "Install test 14Apr11" and the "Study" dropdown is set to "Test 0414 by Geri". There are buttons for "Rename Study" and "New Study". The "Study Description" field contains "VM675 using CatB680 Fast calib in phantom".

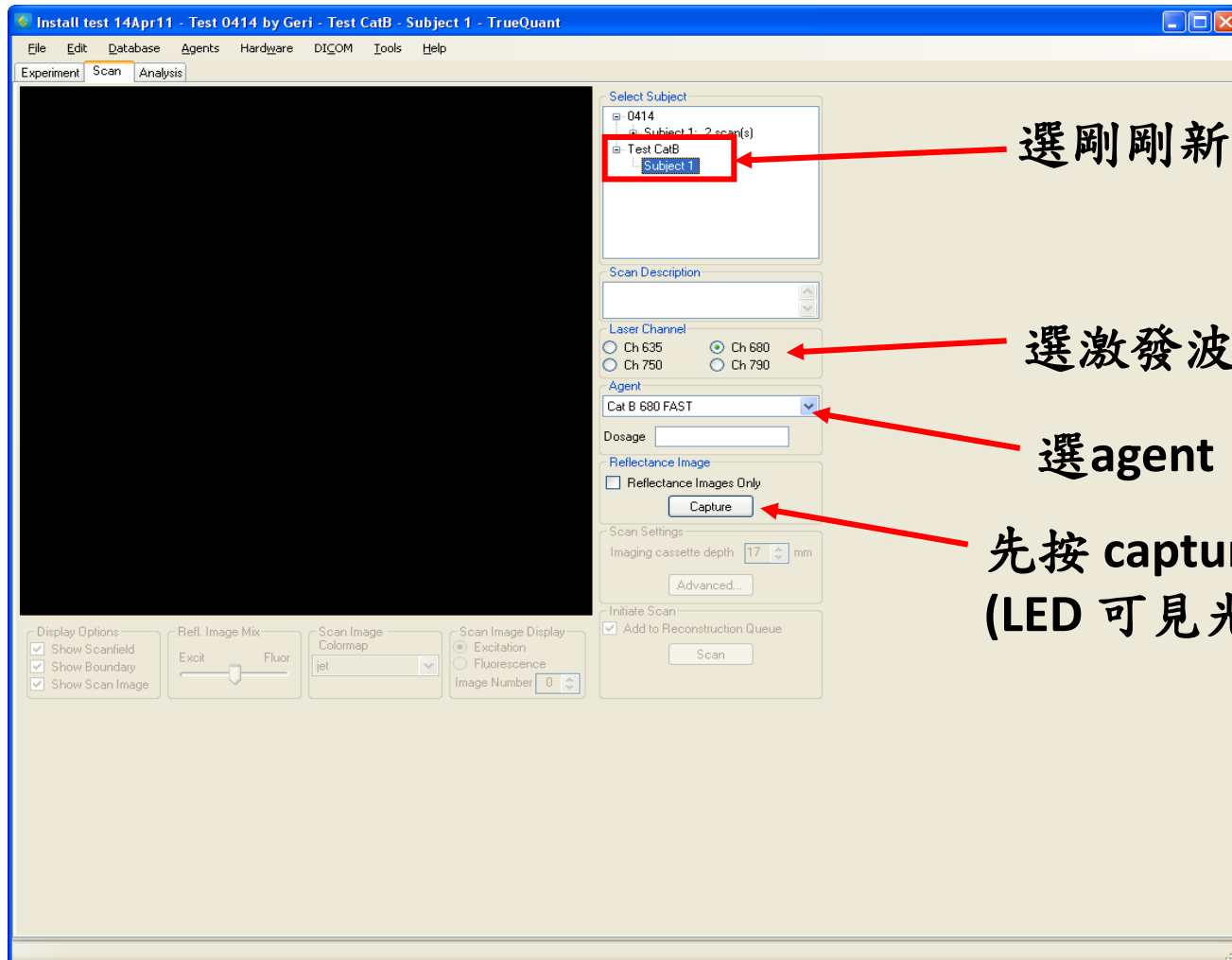
Group/Subject/Scan	Agent(s)/Dosage	Created	Recon	ROIs	Comp.	Description
0414 (N=1)	MMPSense 680	4/14/2011 2:13 PM				
Subject 1		4/14/2011 2:13 PM				

On the right side, there is a vertical toolbar with several buttons: "New Study Group(s)..." (highlighted with a red box), "New Subject...", "Reassign...", "Remove Subject(s)", "Restore Subject(s)...", and "Delete Item(s)...". At the bottom of the interface, there are several control panels: "Image Display Options" with a checked "Show Boundary" checkbox; "Reflectance Image Mix" with a slider between "Excit" and "Fluor"; "Colormaps" with radio buttons for "2D" and "3D" (selected), and a dropdown menu set to "jet"; and "Z Slices" with a checked "Show" checkbox and a numeric spinner set to "1".



選出使用的agent

## 第二頁：Scan



選剛剛新增的study group

選激發波長

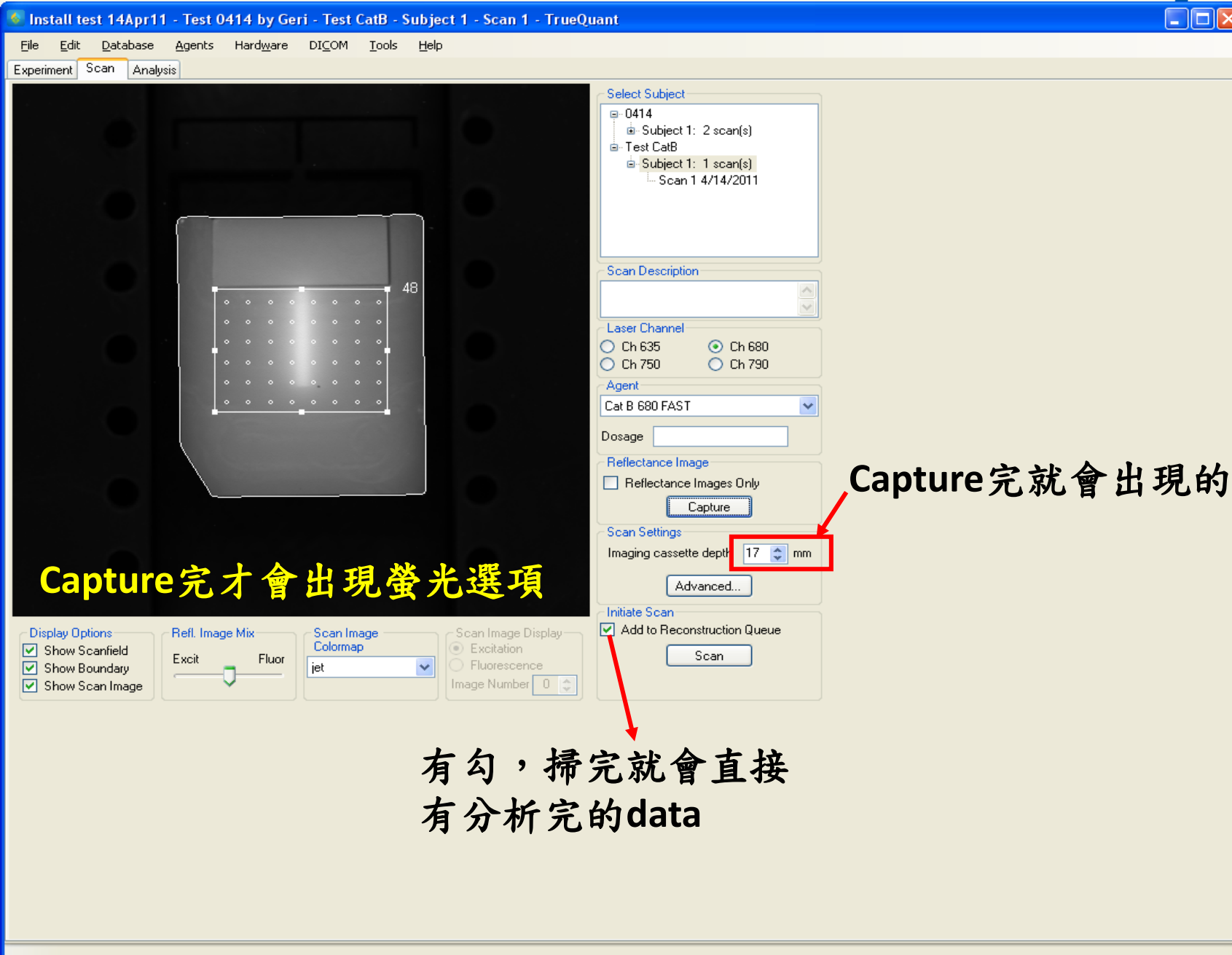
選agent

先按 capture 照一下老鼠位子  
(LED 可見光)

Install test 14Apr11 - Test 0414 by Geri - Test CatB - Subject 1 - Scan 1 - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis



**Capture完才會出現螢光選項**

**Capture完就會出現的**

**有勾，掃完就會直接有分析完的data**

Select Subject

- 0414
  - Subject 1: 2 scan(s)
- Test CatB
  - Subject 1: 1 scan(s)
    - Scan 1 4/14/2011

Scan Description

Laser Channel

Ch 635  Ch 680

Ch 750  Ch 790

Agent

Cat B 680 FAST

Dosage

Reflectance Image

Reflectance Images Only

Capture

Scan Settings

Imaging cassette depth 17 mm

Advanced...

Initiate Scan

Add to Reconstruction Queue

Scan

Display Options

Show Scanfield

Show Boundary

Show Scan Image

Ref. Image Mix

Excit Fluor

Scan Image Colormap

jet

Scan Image Display

Excitation

Fluorescence

Image Number 0

Install test 14Apr11 - Test 0414 by Geri - Test CatB - Subject 1 - Scan 1 - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

用滑鼠在框框上拉動，框出真正要scan的範圍，上面的點就是等一下scan掃的點

48

Select Subject

- 0414
  - Subject 1: 2 scan(s)
- Test CatB
  - Subject 1: 1 scan(s)
    - Scan 1 4/14/2011

Scan Description

Laser Channel

Ch 635  Ch 680  
 Ch 750  Ch 790

Agent

Cat B 680 FAST

Dosage

Reflectance Image

Reflectance Images Only

Capture

Scan Settings

Imaging cassette depth 17 mm

Advanced...

Initiate Scan

Add to Reconstruction Queue

Scan

Advanced Settings

Source Density

Coarse (5 mm)  
 Medium (3 mm)  
 Fine (2 mm)  
 Manual

X 3 mm Y 3 mm

Illumination [counts/pixel]

Minimum 5000 Maximum 50000

Defaults OK Cancel

Display Options

Show Scanfield  
 Show Boundary  
 Show Scan Image

Ref. Image Mix

Excit Fluor

Scan Image Colormap

jet

Scan Image Display

Excitation  
 Fluorescence

Image Number 0

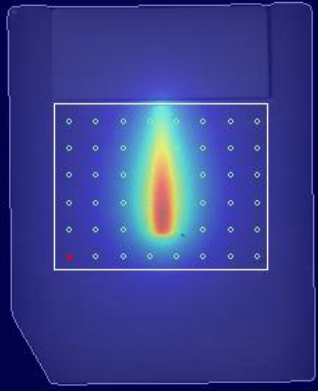
可以設定各種掃瞄的密度，看target大小而決定要設成怎樣的間隔比較好

直接再按 Scan就開始

Install test 14Apr11 - Test 0414 by Geri - Test CatB - Subject 1 - Scan 1 - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis



Select Subject

- 0414
  - Subject 1: 2 scan(s)
  - Test CatB
    - Subject 1: 1 scan(s)
      - Scan 1 4/14/2011

Scan Description

Laser Channel

Ch 635  Ch 680  
 Ch 750  Ch 790

Agent

Cat B 680 FAST

Dosage

Reflectance Image

Reflectance Images Only

Capture

Scan Settings

Imaging cassette depth 17 mm

Advanced...

Initiate Scan

Add to Reconstruction Queue

Scan

Display Options

Show Scanfield  
 Show Boundary  
 Show Scan Image

Ref. Image Mix

Excit Fluor

Scan Image Colormap

jet

Scan Image Display

Excitation  
 Fluorescence

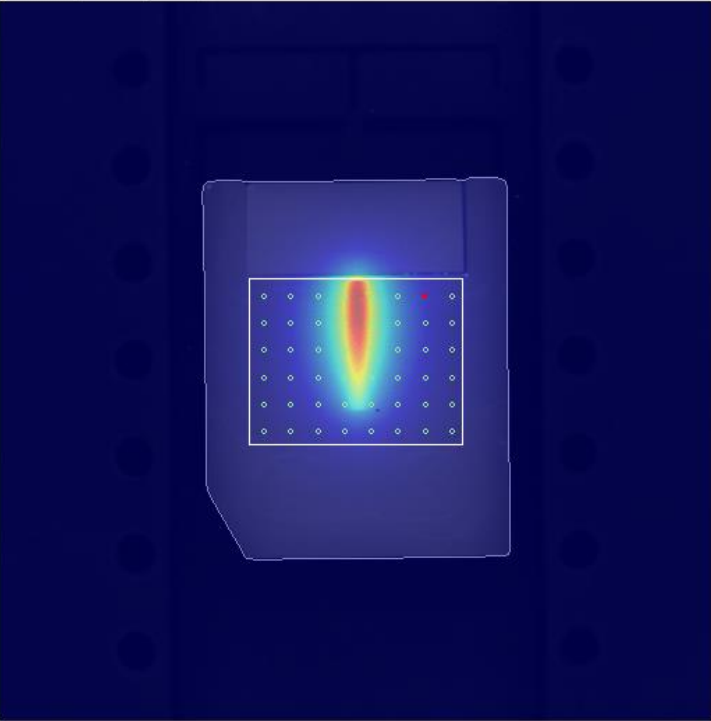
Image Number 48

正在 normalization....  
準備產生 data

Install test 14Apr11 - Test 0414 by Geri - Test CatB - Subject 1 - Scan 1 (viewing archived scan) - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis



Select Subject

- 0414
  - Test CatB
    - Subject 1: 1 scan(s)
      - Scan 1 4/14/2011

Scan Description

Laser Channel

Ch 635  Ch 680  
 Ch 750  Ch 790

Agent

Cat B 680 FAST

Dosage

Reflectance Image

Reflectance Images Only

Capture

Scan Settings

Imaging cassette depth 17 mm

Advanced...

Initiate Scan

Add to Reconstruction Queue

Scan

Display Options

Show Scanfield  
 Show Boundary  
 Show Scan Image

Ref. Image Mix

Excit Fluor

Scan Image Colormap

jet

Scan Image Display

Excitation  
 Fluorescence

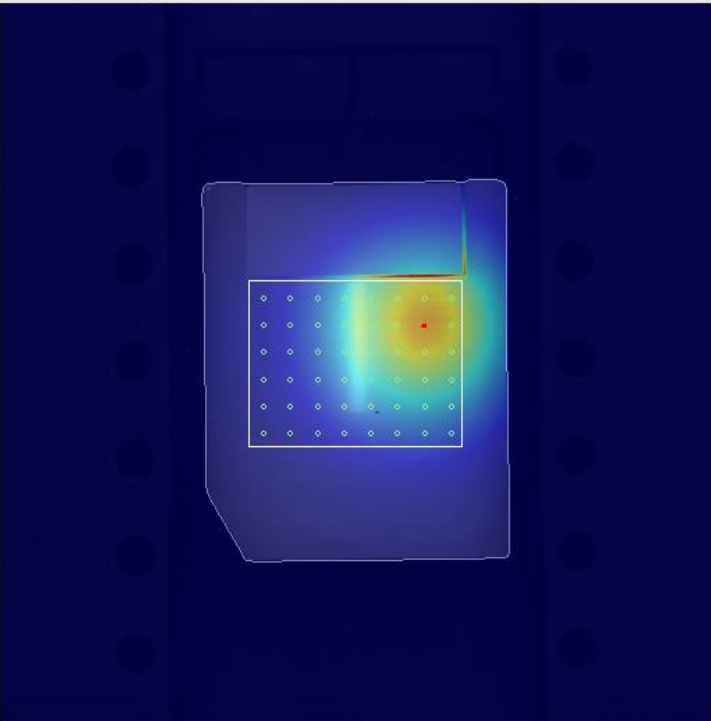
Image Number 17

全部都掃完之後(真的沒花多少時間)，這邊可點影像回顧，選excitation(即第一次的absorption)或fluorescence(第二次的emission)，選影像編號就是不同位子的影像會出現～

Install test 14Apr11 - Test 0414 by Geri - Test CatB - Subject 1 - Scan 1 (viewing archived scan) - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis



Select Subject

- 0414
  - Test CatB
    - Subject 1: 1 scan(s)
      - Scan 1 4/14/2011

Scan Description

Laser Channel

Ch 635  Ch 680  
 Ch 750  Ch 790

Agent

Cat B 680 FAST

Dosage

Reflectance Image

Reflectance Images Only

Capture

Scan Settings

Imaging cassette depth 17 mm

Advanced...

Initiate Scan

Add to Reconstruction Queue

Scan

Display Options

Show Scanfield  
 Show Boundary  
 Show Scan Image

Ref. Image Mix

Excit Fluor

Scan Image Colormap

jet

Scan Image Display

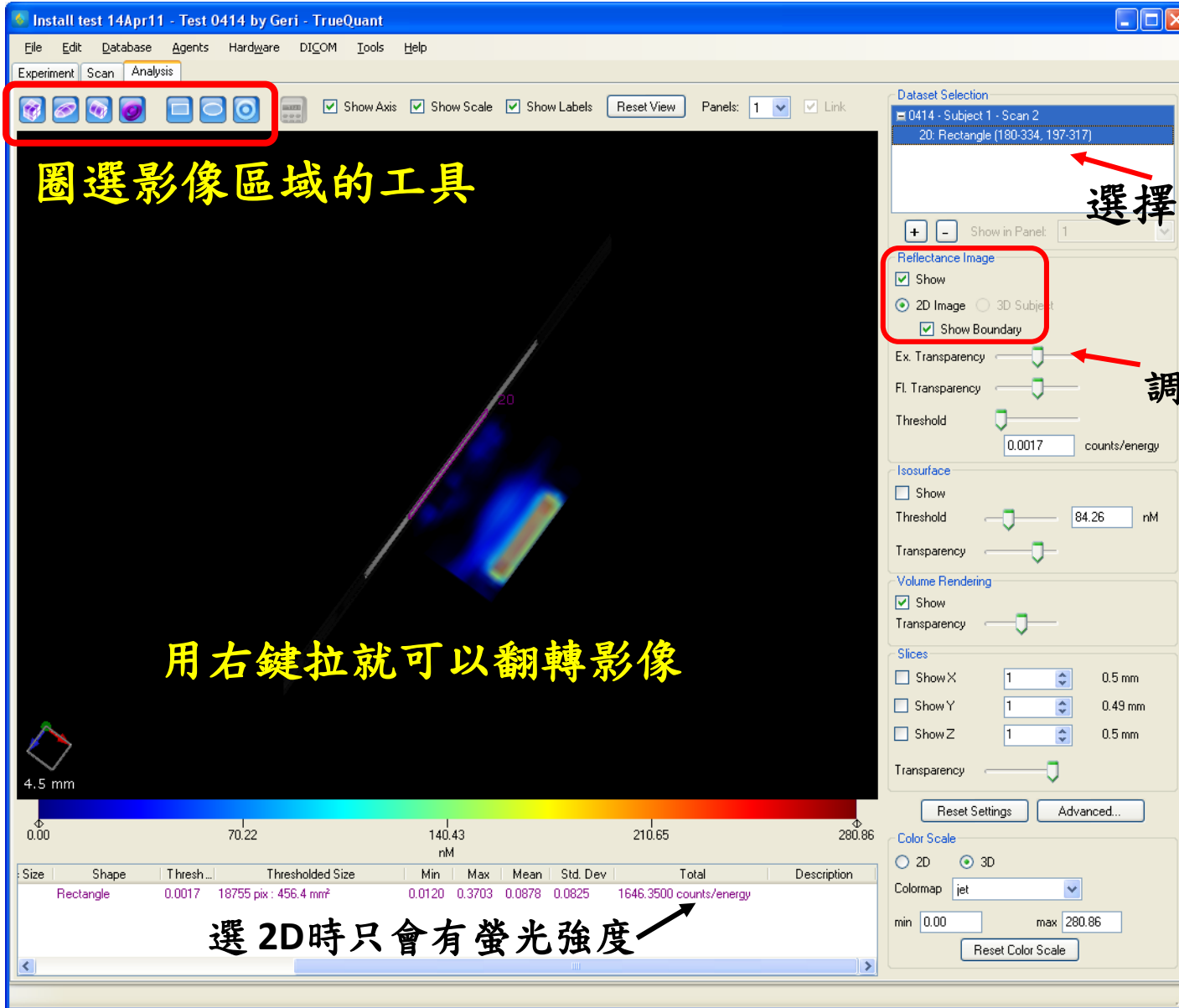
Excitation  
 Fluorescence

Image Number 10

跟live時一樣.....excitation(即第一次的absorption)影像是擴散的



# 第三頁：Analysis



Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Show Axis Show Scale Show Labels Reset View Panels: 1 Link

**圈選影像區域的工具**

Dataset Selection

- 0414 - Subject 1 - Scan 2
  - 20. Rectangle (180-334, 197-317)

選擇要看哪次的結果

Reflectance Image

- Show
- 2D Image** (Selected)
- 3D Subject
- Show Boundary

調到最低時就等於關

Ex. Transparency

Fl. Transparency

Threshold: 0.0017 counts/energy

Isosurface

- Show
- Threshold: 84.26 nM
- Transparency

Volume Rendering

- Show
- Transparency

Slices

- Show X: 1 0.5 mm
- Show Y: 1 0.49 mm
- Show Z: 1 0.5 mm
- Transparency

Reset Settings Advanced...

Color Scale

- 2D (Selected)
- 3D
- Colormap: jet
- min: 0.00 max: 280.86
- Reset Color Scale

用右鍵拉就可以翻轉影像

選 2D 時只會有螢光強度

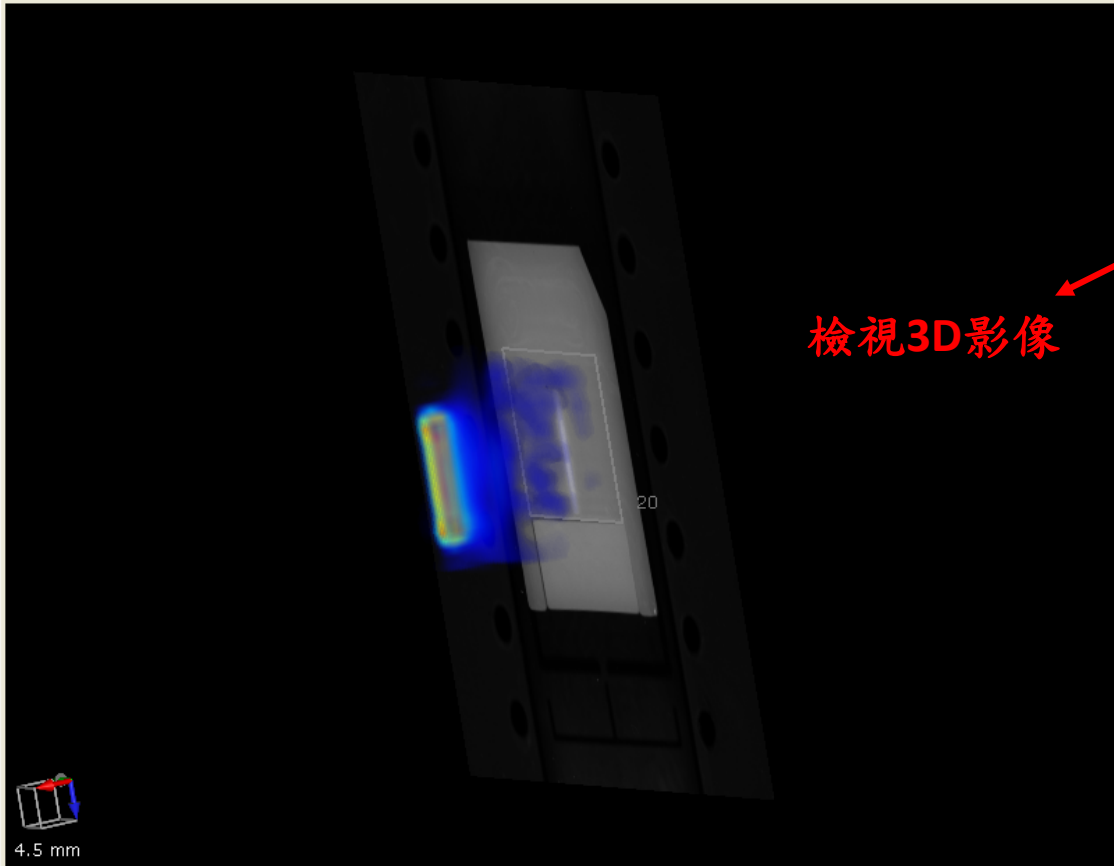
Size	Shape	Thresh...	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
Rectangle		0.0017	18755 pix : 456.4 mm <sup>2</sup>	0.0120	0.3703	0.0878	0.0825	1646.3500 counts/energy	

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Show Axis  Show Scale  Show Labels  Panels: 1  Link



Dataset Selection

- 0414 - Subject 1 - Scan 2
  - 20: Rectangle (180-334, 197-317)
- Test CatB - Subject 1 - Scan 1

Show in Panel: 1

Reflectance Image

Show  
 2D Image  3D Subject  
 Show Boundary

Ex. Transparency

Fl. Transparency

Threshold  counts/energy

Isosurface

Show  
 Threshold  nM  
 Transparency

Volume Rendering

Show  
 Transparency

Slices

Show X 1 0.5 mm  
 Show Y 1 0.49 mm  
 Show Z 1 0.5 mm  
 Transparency

Color Scale

2D  3D  
 Colormap jet  
 min 0.00 max 274.95

4.5 mm

0.00 70.22 140.43 210.65 280.86 nM

Size	Shape	Thresh...	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
	Rectangle	0.0017	18755 pix : 456.4 mm <sup>2</sup>	0.0120	0.3703	0.0878	0.0825	1646.3500 counts/energy	

檢視3D影像

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Show Axis Show Scale Show Labels Reset View Panels: 1 Link

Dataset Selection

0414 - Subject 1 - Scan 2  
20: Rectangle (180:334, 197:317)

+

Show in Panel: 1

Reset Face Image

Show

2D Image  3D Subject

Show Boundary

Ex. Transparency

Fl. Transparency

Threshold 0.0017 counts/energy

Isosurface

Show

Threshold 84.26 nM

Transparency

Volume Rendering

Show

Transparency

Slices

Show X 1 0.5 mm

Show Y 1 0.49 mm

Show Z 1 0.5 mm

Transparency

Reset Settings Advanced...

Color Scale

2D  3D

Colormap jet

min 0.00 max 280.86

Reset Color Scale

Load dataset

Name	Created	Recon	Description
0414 (N=1)	4/14/2011 2.1...		
Test CatB (N=1)	4/14/2011 2.3...		with done calibration file
Subject 1	4/14/2011 2.3...		
Scan 1	4/14/2011 2.3...	Preview	

Study Group: Test CatB  
Subject #: 1  
Agent: Cat B 680 FAST  
Dosage:  
Description:

Load Cancel

4.5 mm

0.00 70.22 140.43 210.65 280.86

Size	Shape	T thresh...	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
Rectangle		0.0017	18755 pix : 456.4 mm <sup>2</sup>	0.0120	0.3703	0.0878	0.0825	1646.3500 counts/energy	

可以再開別的 dataset 看分析結果

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Rectangle

Show Axis 
  Show Scale 
  Show Labels 
 Reset View 
 Panels: 1 
  Link

Dataset Selection

- 0414 - Subject 1 - Scan 2
  - 20: Rectangle (180-334, 197-317)
- Test CatB - Subject 1 - Scan 1
  - 21: Rectangle (180-334, 197-317)

Show in Panel: 1

Reflectance Image

Show 
  2D Image 
  3D Subject

Show Boundary

Ex. Transparency

Fl. Transparency

Threshold  0.0017 counts/energy

Isosurface

Show

Threshold  82.48 nM

Transparency

Volume Rendering

Show

Transparency

Slices

Show X 1 0.5 mm  
 Show Y 1 0.49 mm  
 Show Z 1 0.5 mm

Transparency

Reset Settings Advanced...

Color Scale

2D 
  3D

Colormap jet

min 0.00 max 274.95

Reset Color Scale

4.5 mm

0.00 70.22 140.43 nM 210.65 280.86

Size	Shape	Thresh...	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
	Rectangle	0.0017	18755 pix : 456.4 mm <sup>2</sup>	0.0120	0.3703	0.0878	0.0825	1646.3500 counts/energy	
	Rectangle	0.0017	18755 pix : 456.4 mm <sup>2</sup>	0.0122	0.3654	0.0864	0.0812	1620.3700 counts/energy	

點工具之後，畫面中會出現剛剛圈的scan區域，此時可再修改範圍和圈選形狀

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Rectangular Prism

右邊跟下方表格就有各個圈選範圍的定量結果

3D 時會出現絕對定量單位 pmol

The screenshot shows the TrueQuant software interface. The main window displays a 3D visualization of a rectangular prism with a blue volume inside. A color scale at the bottom ranges from 0.00 to 280.86 nM. The right-hand panel contains various settings for the selected dataset, including 'Reflexance Image' (set to 3D Subject), 'Isosurface' (set to 82.48 nM), and 'Volume Rendering'. The bottom table provides quantitative data for different shapes, with the 'Total' column showing values in pmol.

Shape	Threshold	Thresholded Size	Min	Max	Mean	Std. Dev	Total
urface	82.48	12579 vox : 12375.0 mm³	0.00	81.92	3.77	9.90	46.70 pmol
oid	82.48	144 vox : 141.7 mm³	83.15	271.94	155.21	58.19	21.99 pmol
angularPrism	82.48	171 vox : 168.2 mm³	83.15	274.95	155.26	56.27	26.12 pmol

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

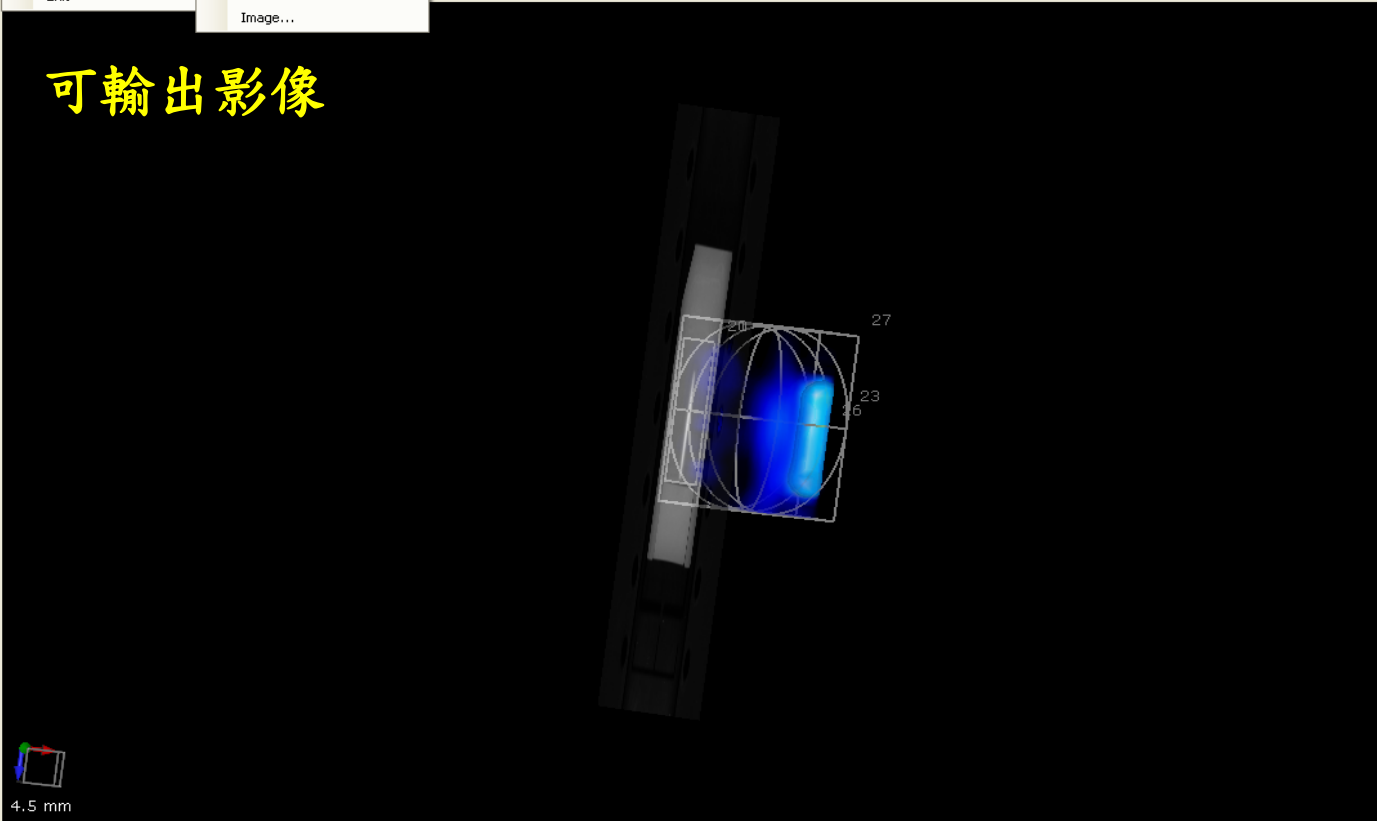
File Edit Database Agents Hardware DICOM Tools Help

Import... Export Exit

Scans & Analyses... Study Design... Image...

Axis  Show Scale  Show Labels  Panels: 1  Link

# 可輸出影像



4.5 mm

0.00 70.22 140.43 nM 210.65 280.86

**Dataset Selection**

- 24: IsoSurface (1-30, 1-25, 1-17)
- 25: IsoSurface (1-30, 1-25, 1-17)
- 26: Ellipsoid (1-30, 1-25, 1-17)
- 27: RectangularPrism (1-30, 1-25, 1-17)
- 28: IsoContour (180-334, 197-317)

Show in Panel: 1

**Reflectance Image**

Show

2D Image  3D Subject

Show Boundary

Ex. Transparency

Fl. Transparency

Threshold  counts/energy

**Isosurface**

Show

Threshold  nM

Transparency

**Volume Rendering**

Show

Transparency

**Slices**

Show X  0.5 mm

Show Y  0.49 mm

Show Z  0.5 mm

Transparency

**Color Scale**

2D  3D

Colormap

min  max

X	Y	Z	Geometric Size	Shape	Threshold	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
1-30...	1-25...	1-17...	N/A	IsoSurface	82.48	12579 vox : 12375.0 mm <sup>3</sup>	0.00	81.92	3.77	9.90	46.70 pmol	
1-30...	1-25...	1-17...	6567.6 mm <sup>3</sup>	Ellipsoid	82.48	144 vox : 141.7 mm <sup>3</sup>	83.15	271.94	155.21	58.19	21.99 pmol	
1-30...	1-25...	1-17...	12543.2 mm <sup>3</sup>	RectangularPrism	82.48	171 vox : 168.2 mm <sup>3</sup>	83.15	274.95	155.26	56.27	26.12 pmol	
180-...	197-...	N/A	N/A	IsoContour	0.0017	0 pix : 0.0 mm <sup>2</sup>	0.0000	0.0000	0.0000	0.0000	0.0000 counts/energy	

Install test 14Apr11 - Test 0414 by Geri - TrueQuant

File Edit Database Agents Hardware DICOM Tools Help

Experiment Scan Analysis

Analysis Settings Load... Save... new Panels: 1 Link

4.5 mm

0.00 70.22 140.43 210.65 280.86 nM

20 27 23 26

Dataset Selection

- 24: IsoSurface (1-30, 1-25, 1-17)
- 25: IsoSurface (1-30, 1-25, 1-17)
- 26: Ellipsoid (1-30, 1-25, 1-17)
- 27: RectangularPrism (1-30, 1-25, 1-17)
- 28: IsoContour (180-334, 197-317)

Reflectance Image

- Show
- 2D Image 3D Subject
- Show Boundary
- Ex. Transparency
- Fl. Transparency
- Threshold: 0.0017 counts/energy

Isosurface

- Show
- Threshold: 82.48 nM
- Transparency

Volume Rendering

- Show
- Transparency

Slices

- Show X: 1 0.5 mm
- Show Y: 1 0.49 mm
- Show Z: 1 0.5 mm
- Transparency

Reset Settings Advanced...

Color Scale

- 2D 3D
- Colormap: jet
- min: 0.00 max: 274.95
- Reset Color Scale

X	Y	Z	Geometric Size	Shape	Threshold	Thresholded Size	Min	Max	Mean	Std. Dev	Total	Description
1-30...	1-25...	1-17...	N/A	IsoSurface	82.48	12579 vox : 12375.0 mm <sup>3</sup>	0.00	81.92	3.77	9.90	46.70 pmol	
1-30...	1-25...	1-17...	6567.6 mm <sup>3</sup>	Ellipsoid	82.48	144 vox : 141.7 mm <sup>3</sup>	83.15	271.94	155.21	58.19	21.99 pmol	
1-30...	1-25...	1-17...	12543.2 mm <sup>3</sup>	RectangularPrism	82.48	171 vox : 168.2 mm <sup>3</sup>	83.15	274.95	155.26	56.27	26.12 pmol	
180-...	197-...	N/A	N/A	IsoContour	0.0017	0 pix : 0.0 mm <sup>3</sup>	0.0000	0.0000	0.0000	0.0000	0.0000 counts/energy	

分析方式也可以存，  
下次要用就 load



## PerkinElmer Pre-clinical *In Vivo* Imaging Agents

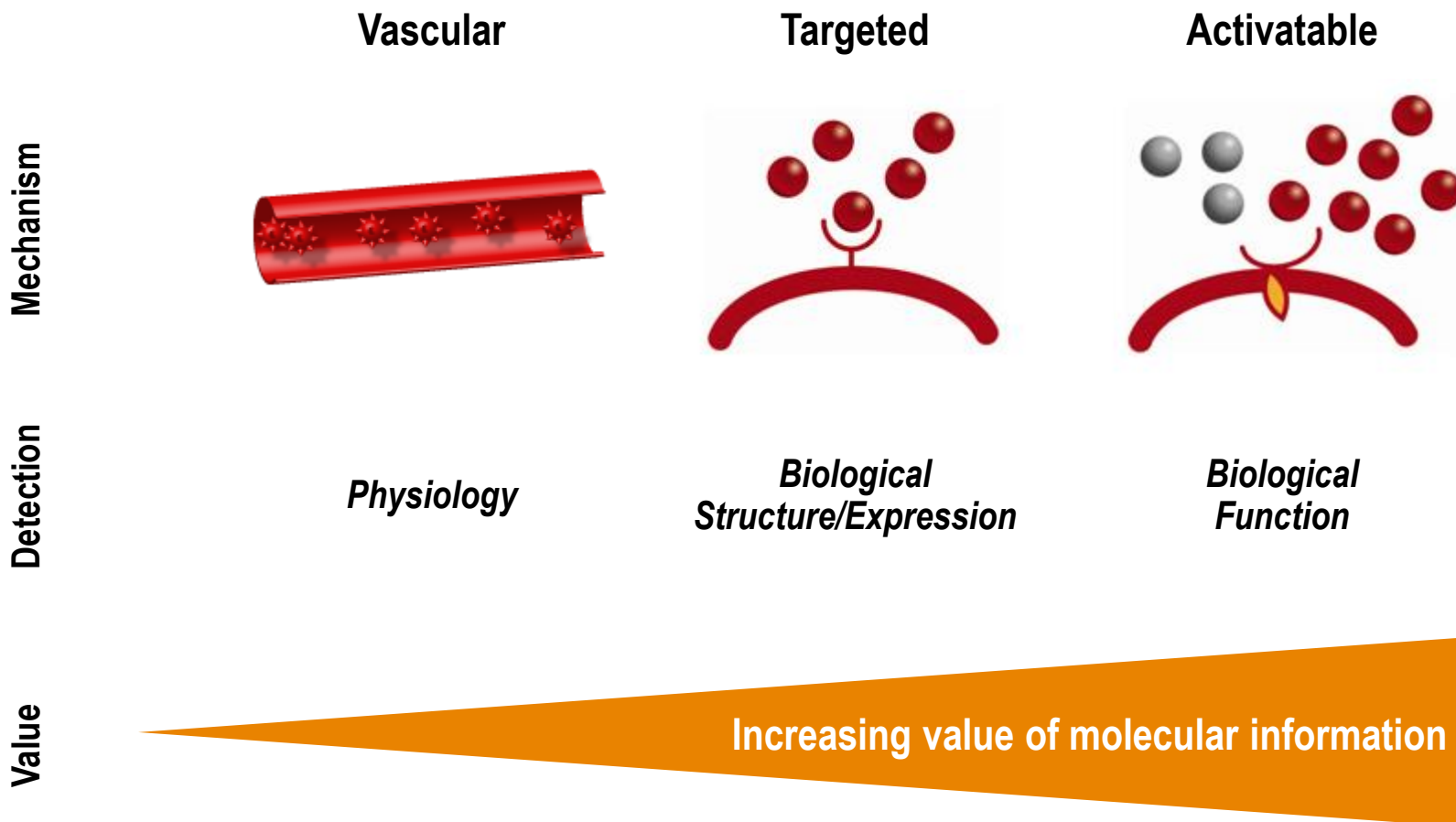
February 20, 2019



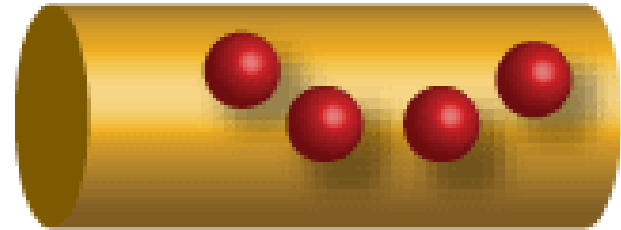
# Agent Platforms: Robust Readouts *In Vivo*



## Agent Categories



- A range of highly fluorescent Physiologic Agents
- Remain stable and localized in the anatomy for various periods of time
- Always fluorescent, circulate with blood or move through GI tract
  - Designed for in vivo use
  - Limited in vitro applications



<p><b>AngioSense</b></p>	<p>Agent that remains localized in vasculature for 0-4 h; accumulates in tumours and arthritic joints at 24 h.</p>	<ul style="list-style-type: none"> <li>● Angiogenesis ● Arthritis</li> <li>● Cardiovascular ● Infectious</li> <li>● Inflammation ● Oncology</li> <li>● Pulmonary ● Neurological</li> <li>● Vascular</li> </ul>
<p>AngioSPARK</p>	<p>Pegylated fluorescent nanoparticles (5 doses); remains localized in vasculature.</p>	<ul style="list-style-type: none"> <li>● Arthritis ● Atherosclerosis</li> <li>● Hypertension ● Inflammation</li> <li>● Oncology ● Neurological</li> <li>● Vascular</li> </ul>
<p>Genhance</p>	<p>Small molecule fluorescence agent. Use as a control or in vascular permeability imaging.</p>	<ul style="list-style-type: none"> <li>● Vascular</li> </ul>
<p>Superhance</p>	<p>Small molecule agent. Binds to albumin in blood for extended (30 m-1 h) vascular imaging.</p>	<ul style="list-style-type: none"> <li>● Angiogenesis ● Arthritis</li> <li>● Inflammation ● Neurological</li> </ul>
<p>GastroSense</p>	<p>Agent to monitor gastric emptying and the impact of various drugs on gastric motility.</p>	<ul style="list-style-type: none"> <li>● Gastric Emptying</li> <li>● Anatomical reference marker for the gastrointestinal tract</li> </ul>

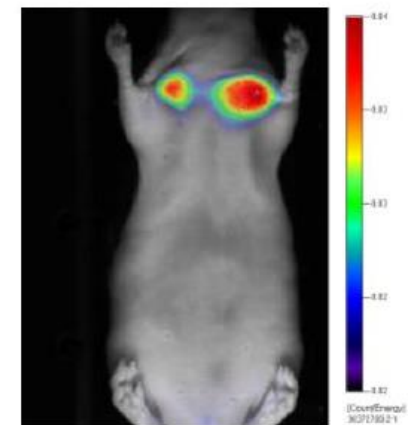
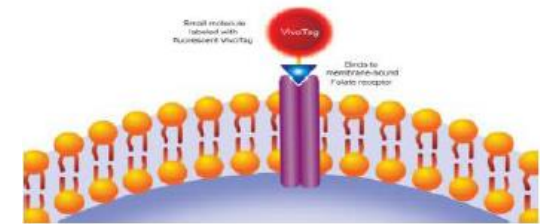
➤ Optimized agents that actively target and bind to specific biomarkers

- Designed for *in vivo* use
- *Emerging In vitro applications*



*Target specific biomarkers*

Agent	Binds to...
BombesinRSense	Bombesin receptors
HER2Sense	Her2/Neu Receptor
FolateRSense	Folate Receptor
TlectinSense	Vascular endothelial cell
OsteoSense	hydroxyapatite
IntegriSense	integrin $\alpha\beta3$
BacteriSense	Negatively charged phospholipids in Bacterial membrane
Annexin Vivo	Phosphatidylserine during early apoptosis
HypoxiSense	Carbonic Anhydrase IX in hypoxic tissue and cells
COX-2 Probe	Cyclooxygenase-2 (COX-2)
2-DG	Glucose uptake Imaging
Transferrin-Vivo	Transferrin receptors (TfRs)

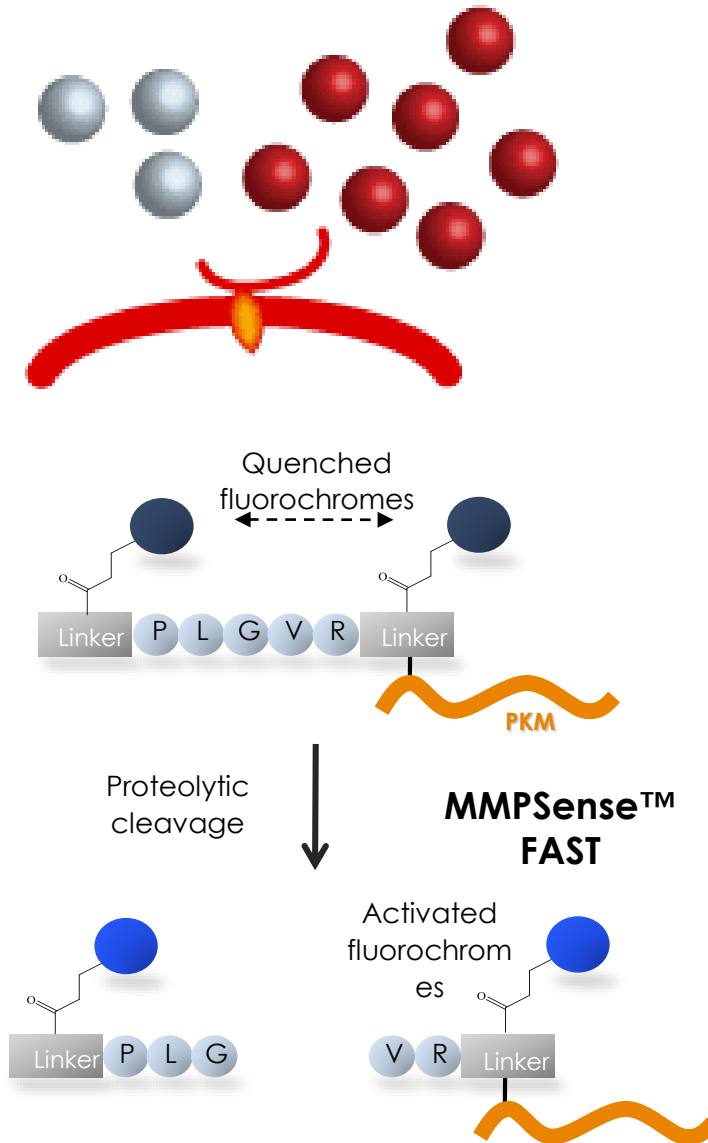


HER2/Neu+ tumor targeting by  
HER2Sense 645

agent	application
IntegriSense	<ul style="list-style-type: none"><li>● Angiogenesis</li><li>● Atherosclerosis</li><li>● Oncology</li><li>● Neurological</li></ul>
Annexin-Vivo	<ul style="list-style-type: none"><li>● Apoptosis</li><li>● Atherosclerosis</li><li>● Inflammation</li><li>● Oncology</li><li>● Neurological</li></ul>
OsteoSense	<ul style="list-style-type: none"><li>● Arthritis</li><li>● Atherosclerosis</li><li>● Bone Turnover</li><li>● Skeletal</li><li>● Oncology</li></ul>
HypoxiSense	<ul style="list-style-type: none"><li>● Oncology</li></ul>
FolateR-Sense	<ul style="list-style-type: none"><li>● cancer and inflammation</li></ul>
BacteriSense	<ul style="list-style-type: none"><li>● infection</li></ul>
Transferrin-Vivo	<ul style="list-style-type: none"><li>● Oncology</li><li>● Inflammation</li></ul>

## ▶ Activatable Agents

- Protein type
- “Quenched” in their native state
- Activated by a select panel of disease-associated proteases
  - Designed for *in vivo* use
  - *Emerging In vitro applications*



Monitor protease activity associated with disease state



<b>ProSense</b>	<b>Activated by cathepsin B, L, S and plasmin</b>
ProSense Control	Non-activatable analog of ProSense for use as a negative control
ProSense FAST	FAST version of ProSense, with faster kinetics and a broader imaging window.
Cat B FAST	Cathepsin B selective FAST activatable agent
Cat K FAST	Cathepsin K selective FAST activatable agent
MMPsense	Activated by MMP (matrix metalloproteinases, including MMP-2, -3, -9 and -13)
MMPsense FAST	MMP FAST activatable agent
Neutrophil Elastase FAST	Activated by elastase produced by neutrophil cells using FAST
ReninSense FAST	A renin-angiotensin FAST activatable agent

*Monitor protease activity associated with disease state*

**ProSense** ● Arthritis ● Oncology

ProSense Control Negative control in ● Arthritis ● Oncology

ProSense FAST ● Oncology ● Inflammation

Cat B FAST ● Cardiovascular disease ● Oncology ● Inflammation ● Certain neurological diseases

Cat K FAST ● Oncology applications involving metastasis to the bone ● Broad range of bone applications including osteoporosis and bone changes following arthritis

MMPSense ● Oncology

MMPSense FAST ● Oncology ● Inflammation ● Pulmonary ● Cardiovascular disease

Neutrophil Elastase FAST ● Acute lung Injury Models ● Acute respiratory distress syndrome ● Emphysema ● Cystic Fibrosis ● COPD ● Wound Healing ● Rheumatoid Arthritis ● Ischemia-reperfusion

ReninSense FAST ● Cardiovascular disease ● Certain models of impaired renal function ● Chronic hyperthyroidism ● Hypertension ● Some neurological diseases

*Monitor protease activity associated with disease state*

PerkinElmer offers four categories of fluorescent *in vivo* imaging agents:

## LABELS and NANOPARTICLES

**VivoTag™ 680XL Protein Labeling Kit** : designed for preparing fluorescently labeled antibodies, proteins or peptides for small animal in vivo imaging applications.

**VivoTrack 680** : cell labeling agent that intercalates into the plasma membrane of primary cells and cell lines.

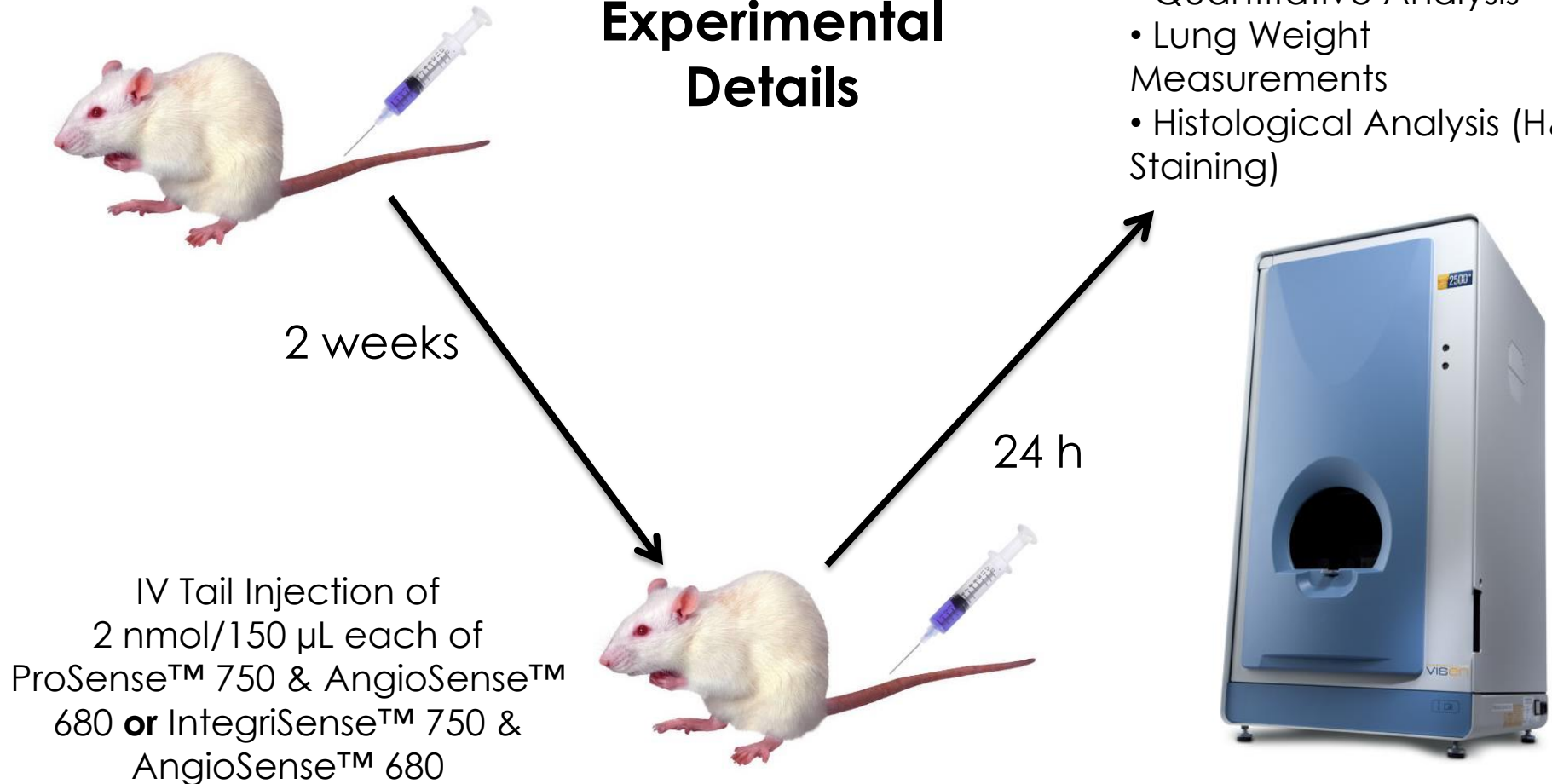
# How to perform the experiment?

- 4T1 Mouse Breast Adenocarcinoma Cells
- IV Tail Injection of  $0.5 - 5 \times 10^5$  Cells
- BALB/c Mice

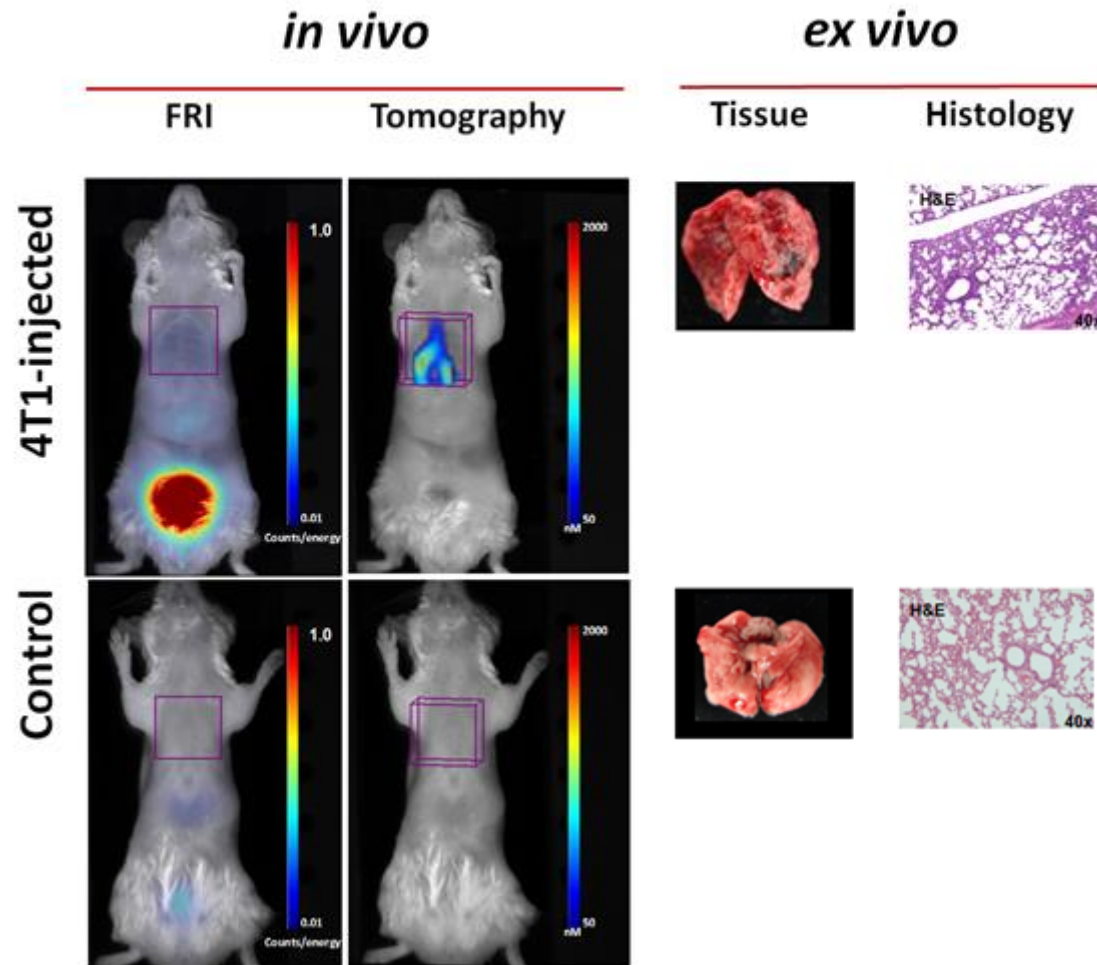
## Experimental Details

### Assessments:

- FMT Imaging *in vivo*
- Quantitative Analysis
- Lung Weight Measurements
- Histological Analysis (H&E Staining)



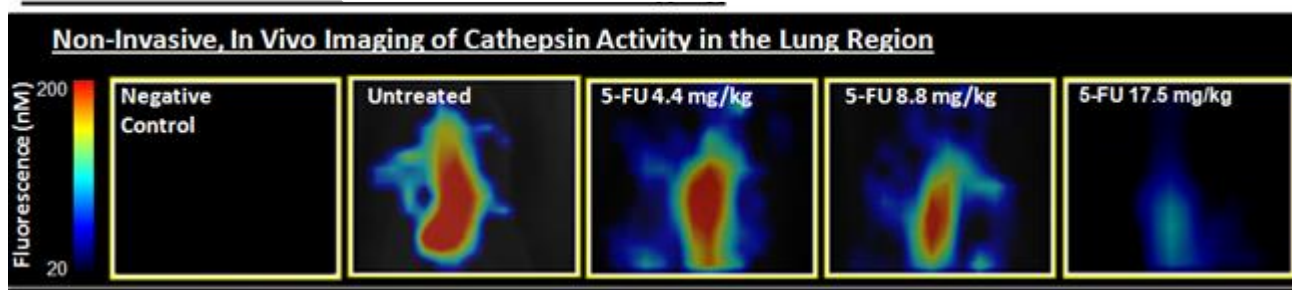
## FMT Imaging of Tumor Cathepsin Activity



- ❖ FMT and ProSense detect tumor-associated protease activity non-invasively in living animals
- ❖ FMT results correlated well with Lung Weight measurements

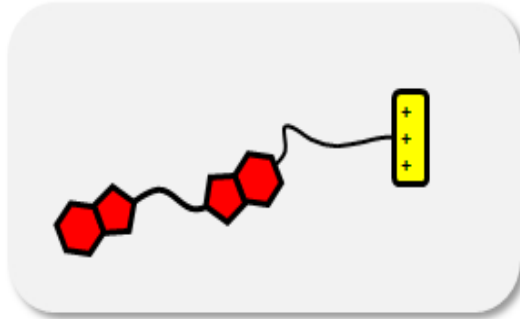
## Quantification of 5-Fluorouracil/2'-deoxyinosine (5-FU/2DI) with ProSense<sup>®</sup> 750

### Whole animal FMT

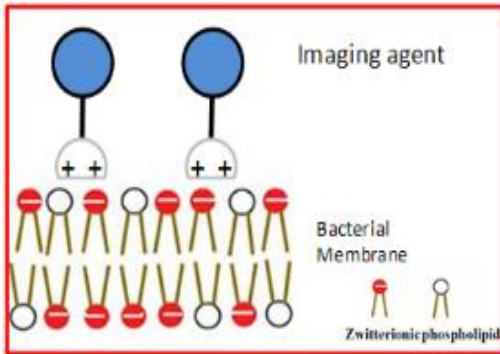


- ❖ FMT and ProSense successfully monitors prophylactic treatment in deep tissue compartments non-invasively
- ❖ Total fluorescence showed the greatest sensitivity in drug efficacy

## Detecting thigh infection of *Pseudomonas* Xen5



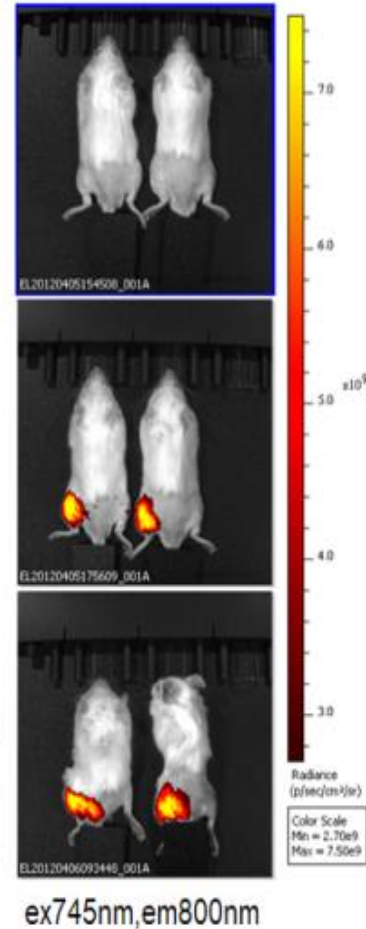
T=0



T=1

T=20

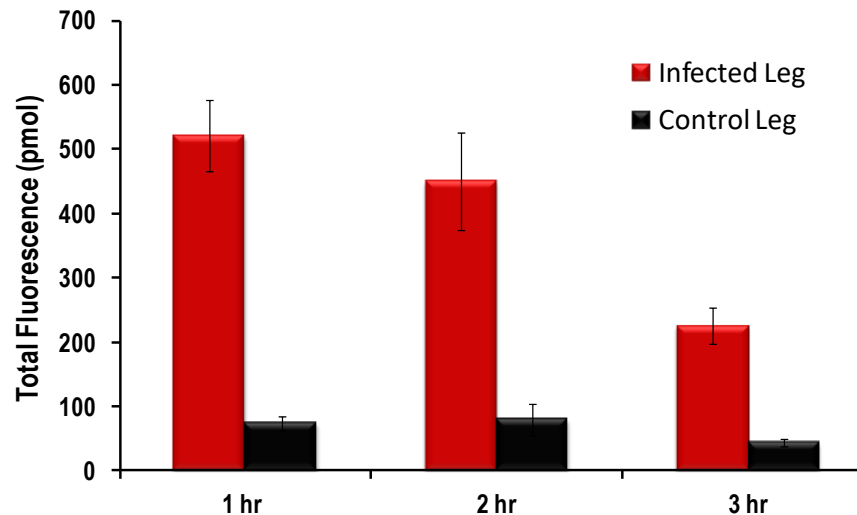
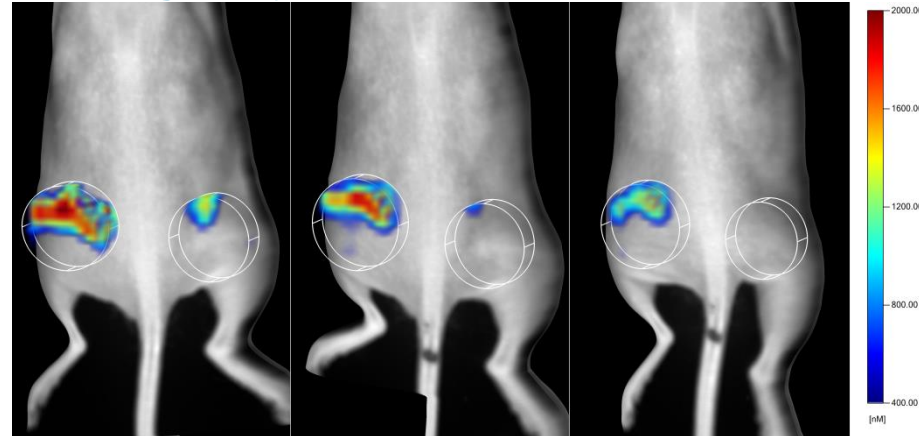
## RediJect Bacterial Detection Probe 750



# In vivo imaging of *S. epidermidis* infections

- SKH-1 E female mice, aged 6-8 weeks, were injected IM with  $10^8$  CFUs of *S. Epidermidis* in the flank region.
- 24 hours after bacteria injection, mice were injected with 5 nmoles of VM3235
- 1, 2, & 3 hours following agent injection, mice were imaged on the 3D fluorescence Imaging with emphasis on the flank area

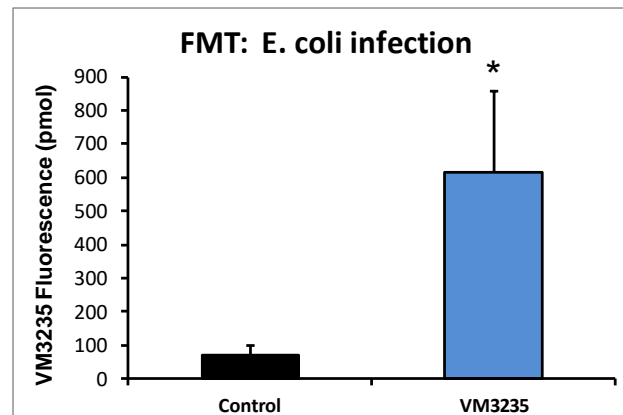
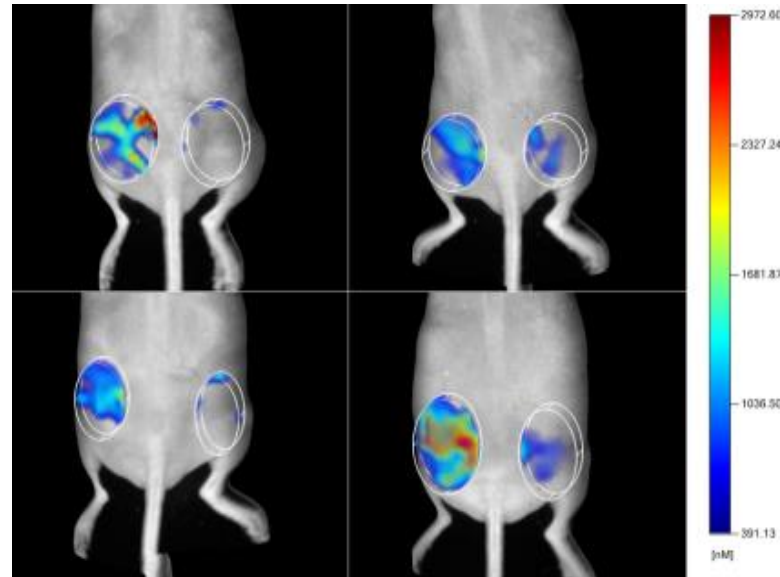
## Tomography





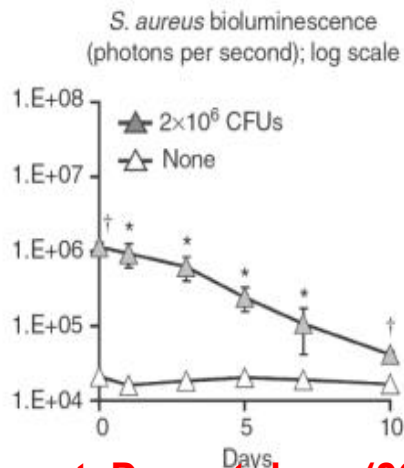
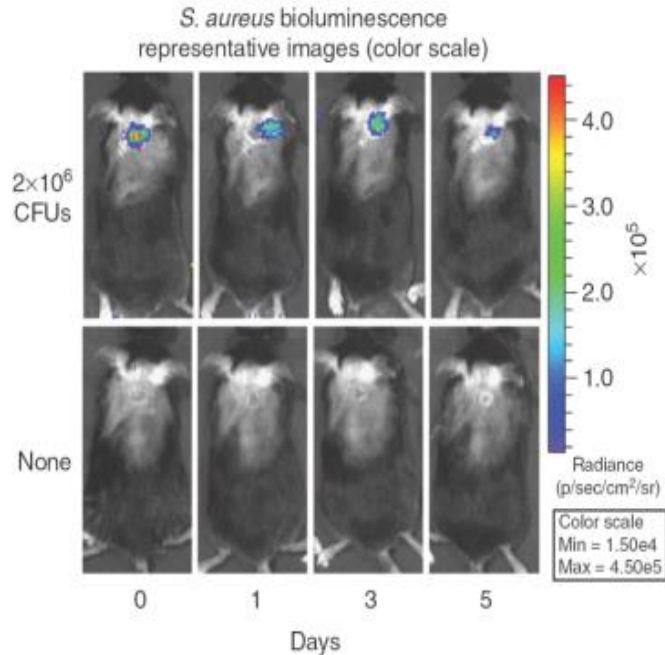
# In Vivo Imaging of *E. Coli* Infection

- 18 SKH-1 E female mice, aged 6-8 weeks, were injected IM with  $1 \times 10^8$  CFUs of *E. coli* in the flank region.
- 24 hours after bacteria injection, mice were injected with 5 nmoles of VM3235
- 1 hour following agent injection, mice were imaged on the FMT2500 with emphasis on the flank area

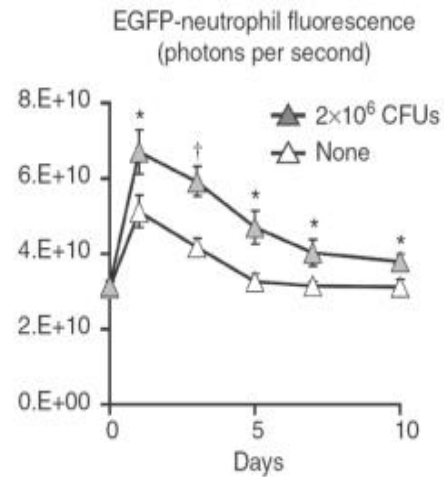
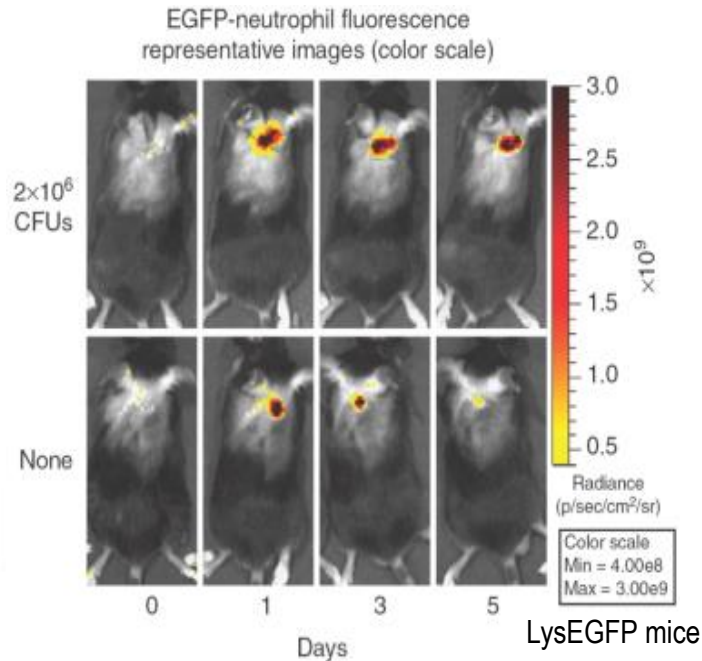


# Infection-induced inflammation neutrophil infiltration as measured by in vivo fluorescence imaging

## RediJect Bacterial Detection Probe 750

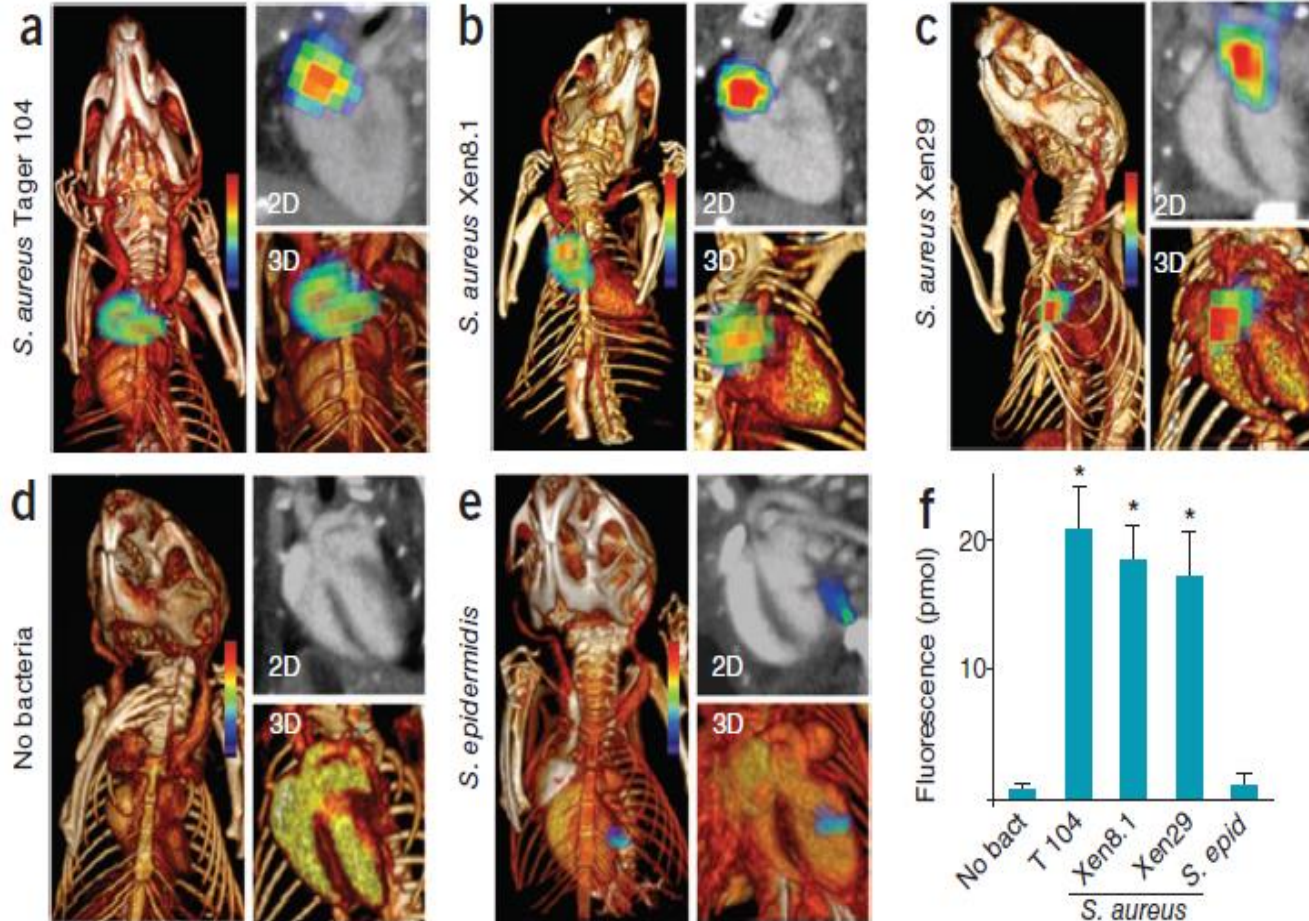


## Neutrophil elastase-680



# In vivo detection of *Staphylococcus aureus*

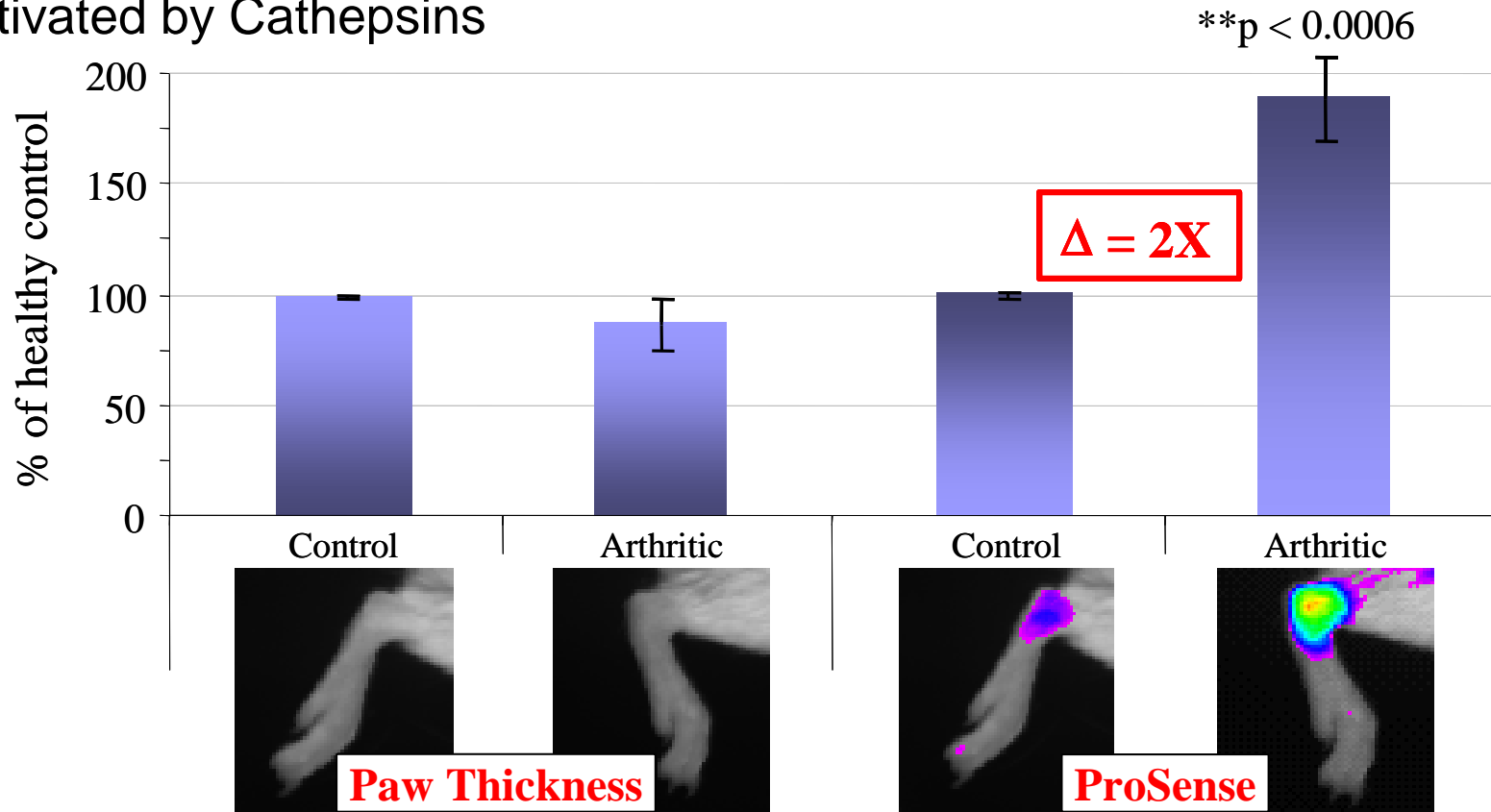
AF680-ProT (prothrombin derivatives) bound staphylocoagulase



Peter Panizzi et al., nature medicine 2011

# CAIA Model : ProSense & Early Disease (Day 4)

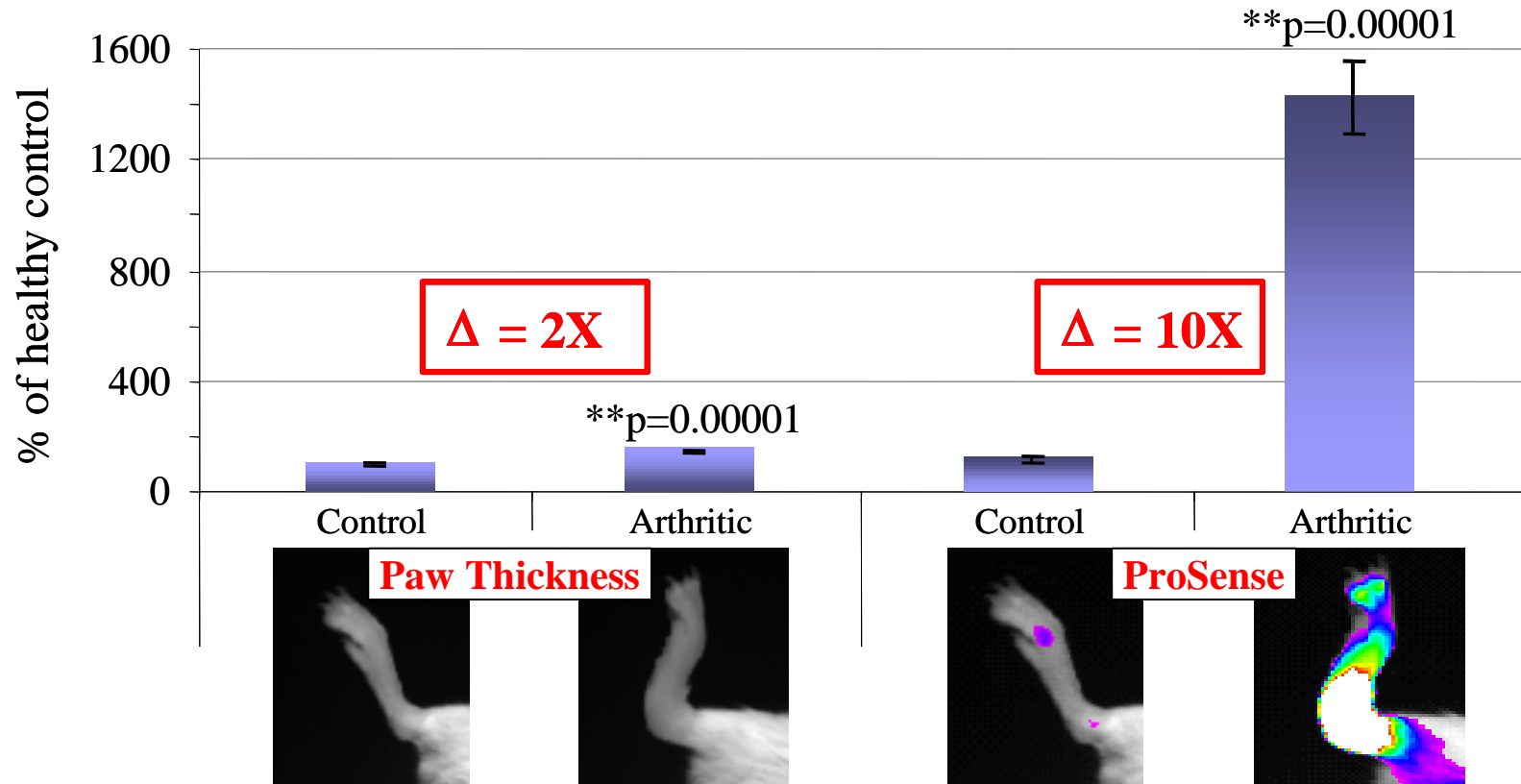
- ❖ Arthritis is not clinically detectable
- ❖ 24 hrs after ProSense probe injection
- ❖ Activated by Cathepsins



imaging with ProSense can detect disease at earlier time points, prior to detection by paw thickness

# CAIA Model : ProSense & Late Disease (Day 8)

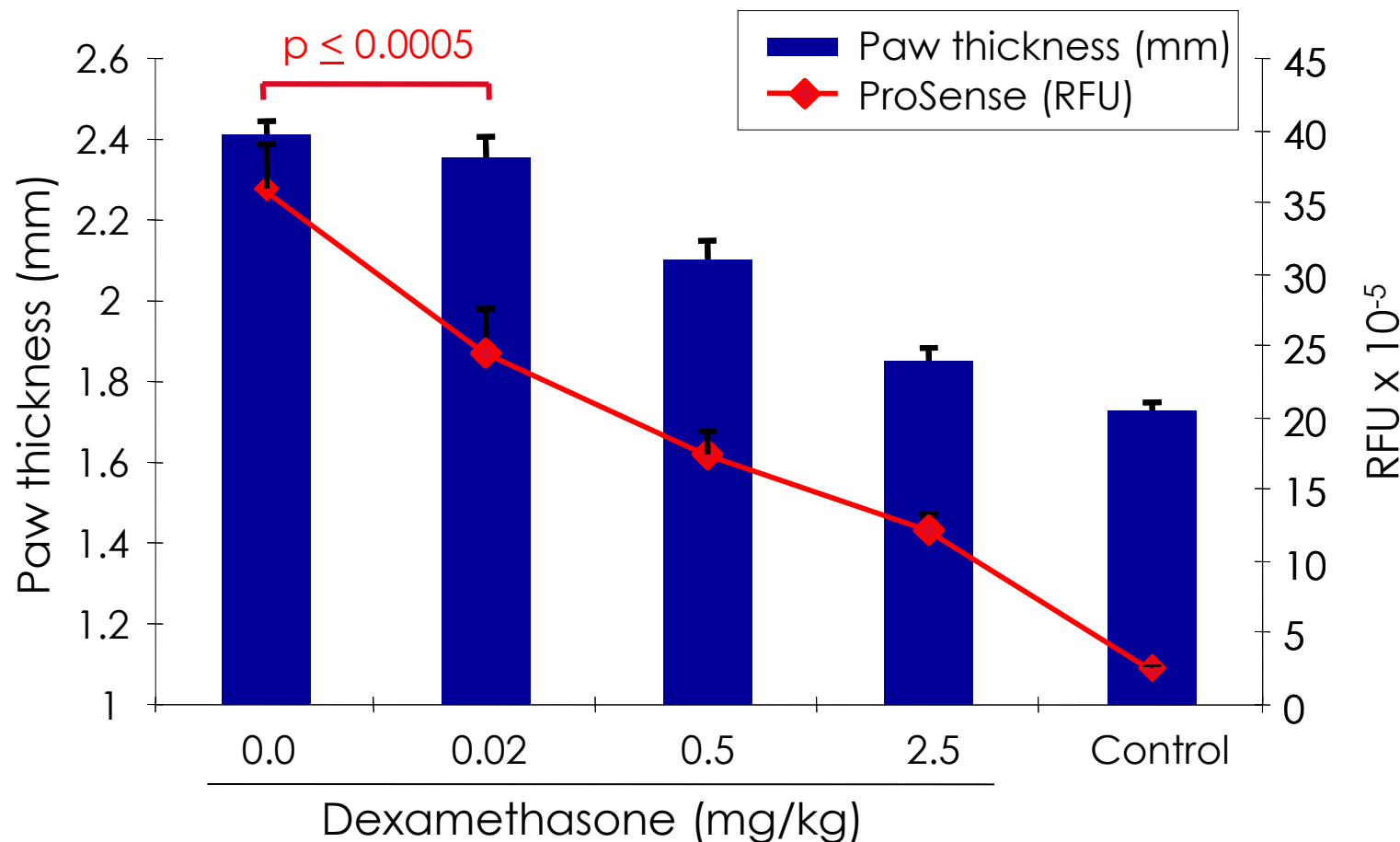
- ❖ Arthritis is clinically detectable and at its peak
- ❖ 24 hrs after ProSense probe injection



imaging with ProSense provides a 10-fold signal over control animals at the peak of the disease

# Anti-inflammatory Treatment of CAIA

## ❖ Dexamethasone: Days 5 & 6 following Collagen Ab Injection

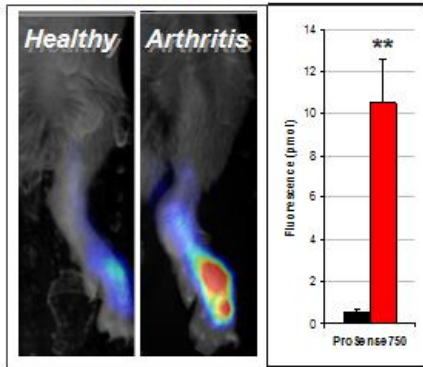


ProSense correlates well with classical measures but is significant at lower doses

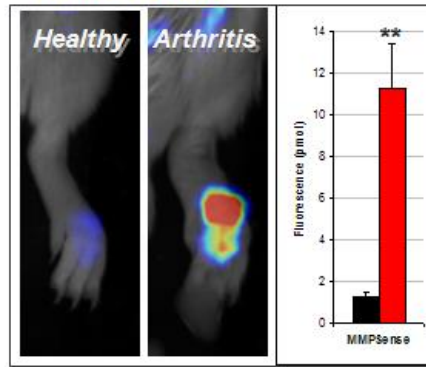
## Multiplex FMT Imaging

### Inflammation Protease Activity

#### ProSense

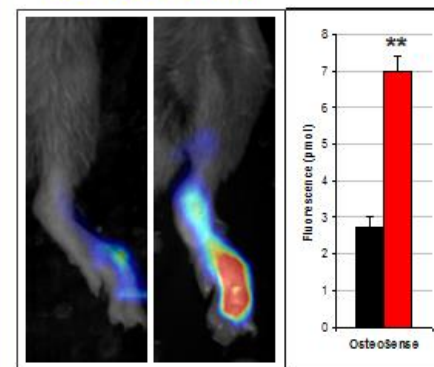


#### MMPsense

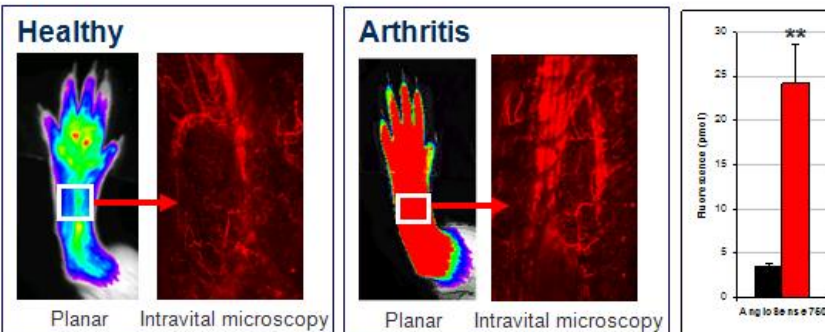


### Bone Changes

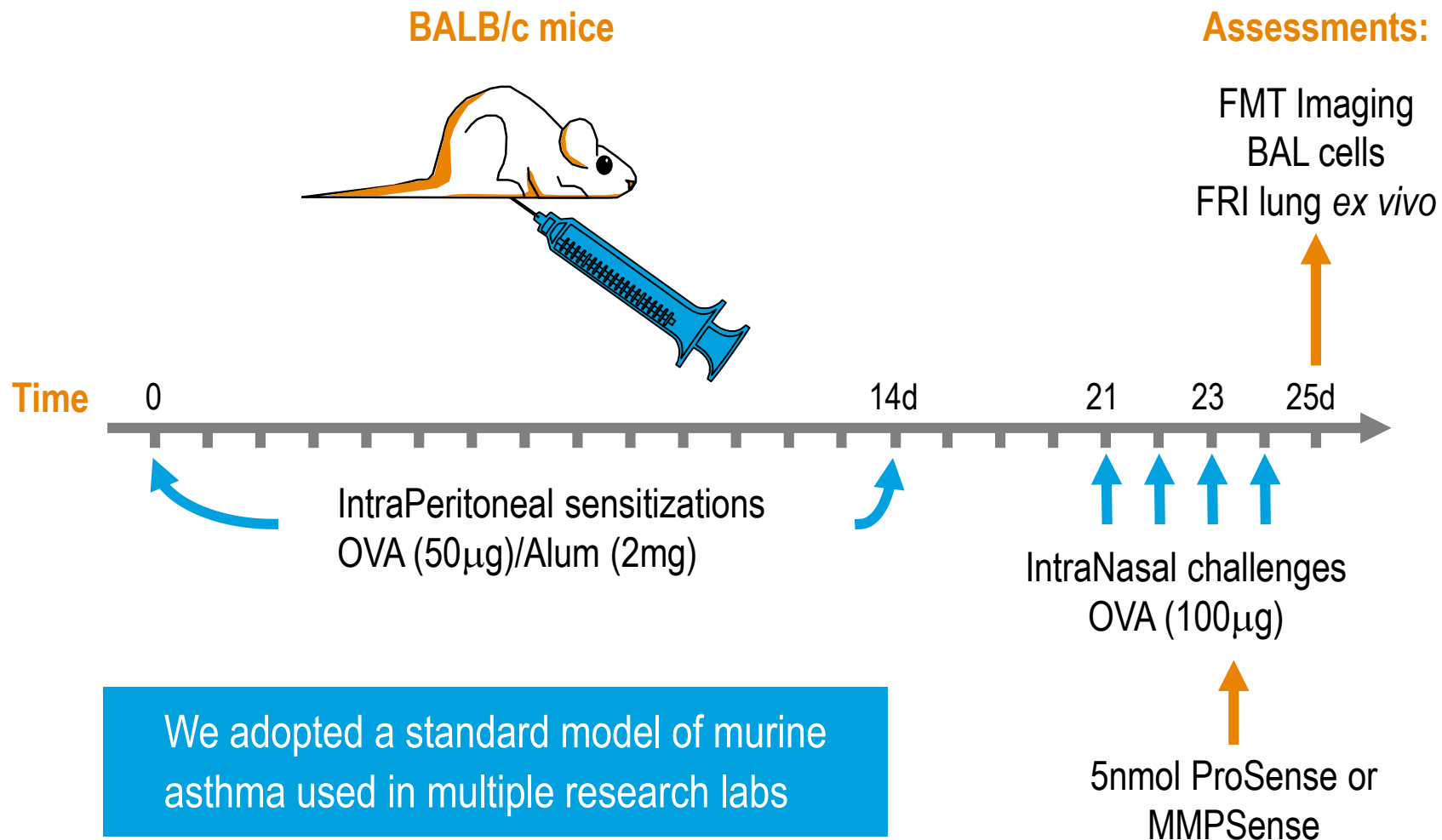
#### OsteoSense



### Vascular Leak



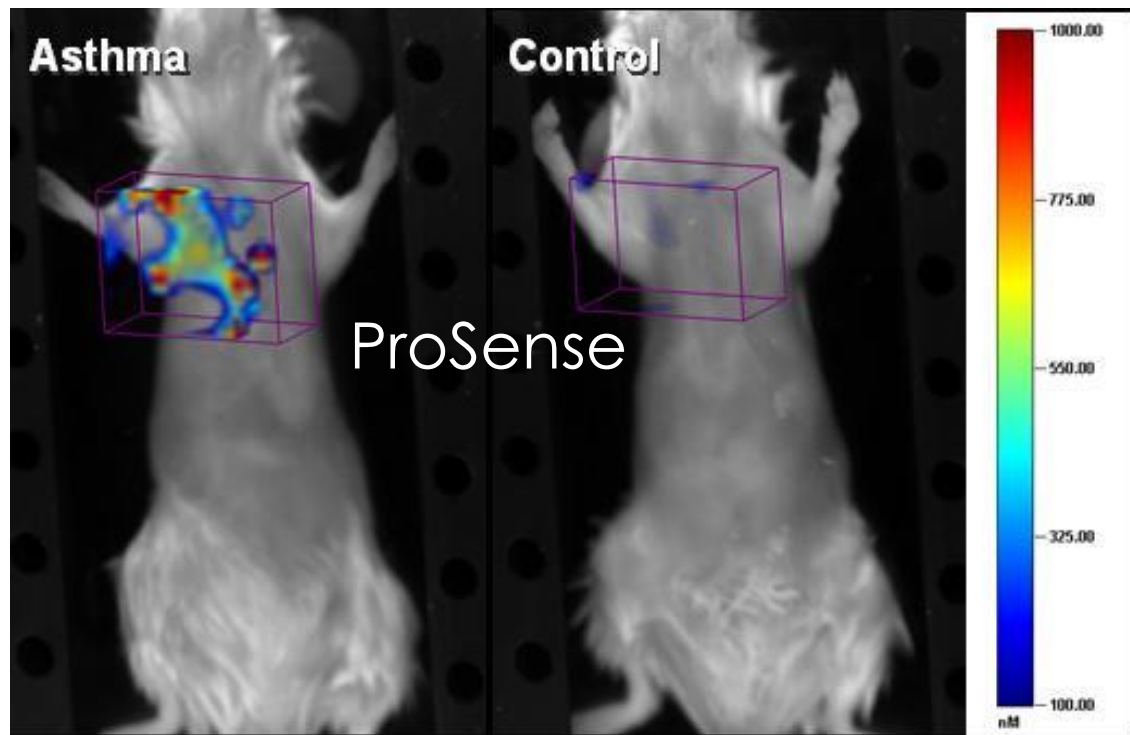
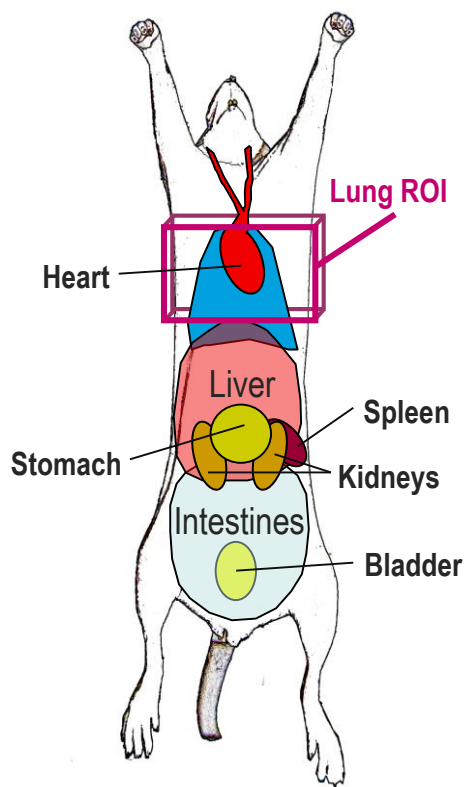
# Ovalbumin (OVA)-induced Asthma





# Imaging Ovalbumin (OVA)-induced Asthma

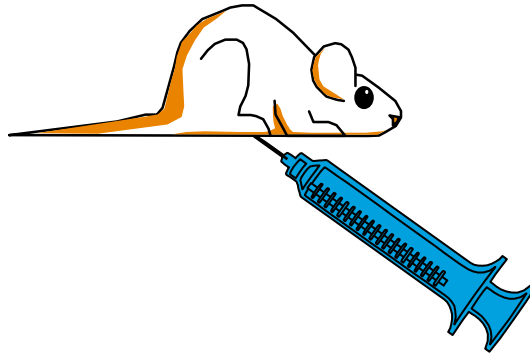
## *In vivo* FMT Tomographic Imaging



Asthma lung signal using ProSense is considerably higher and involves a larger volume than in control mice

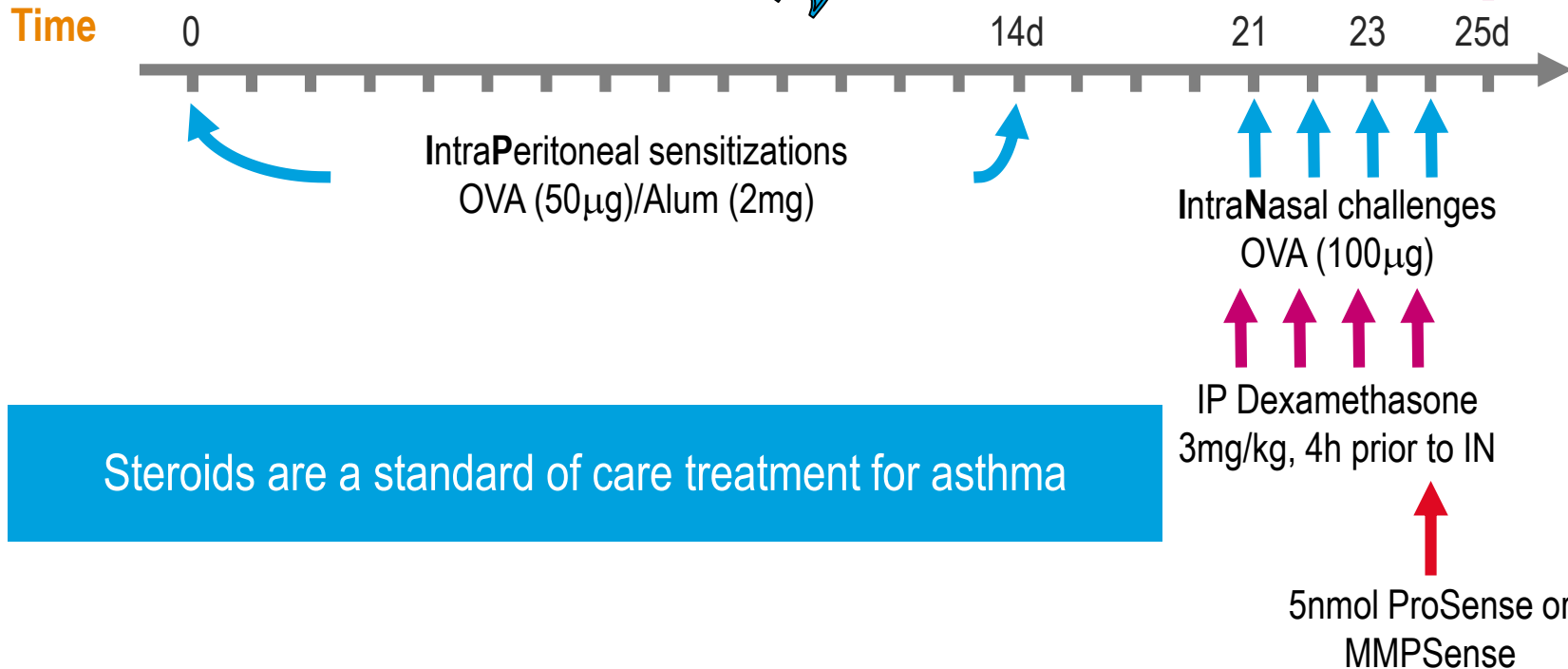
# Steroid inhibition of OVA-induced Asthma

BALB/c mice



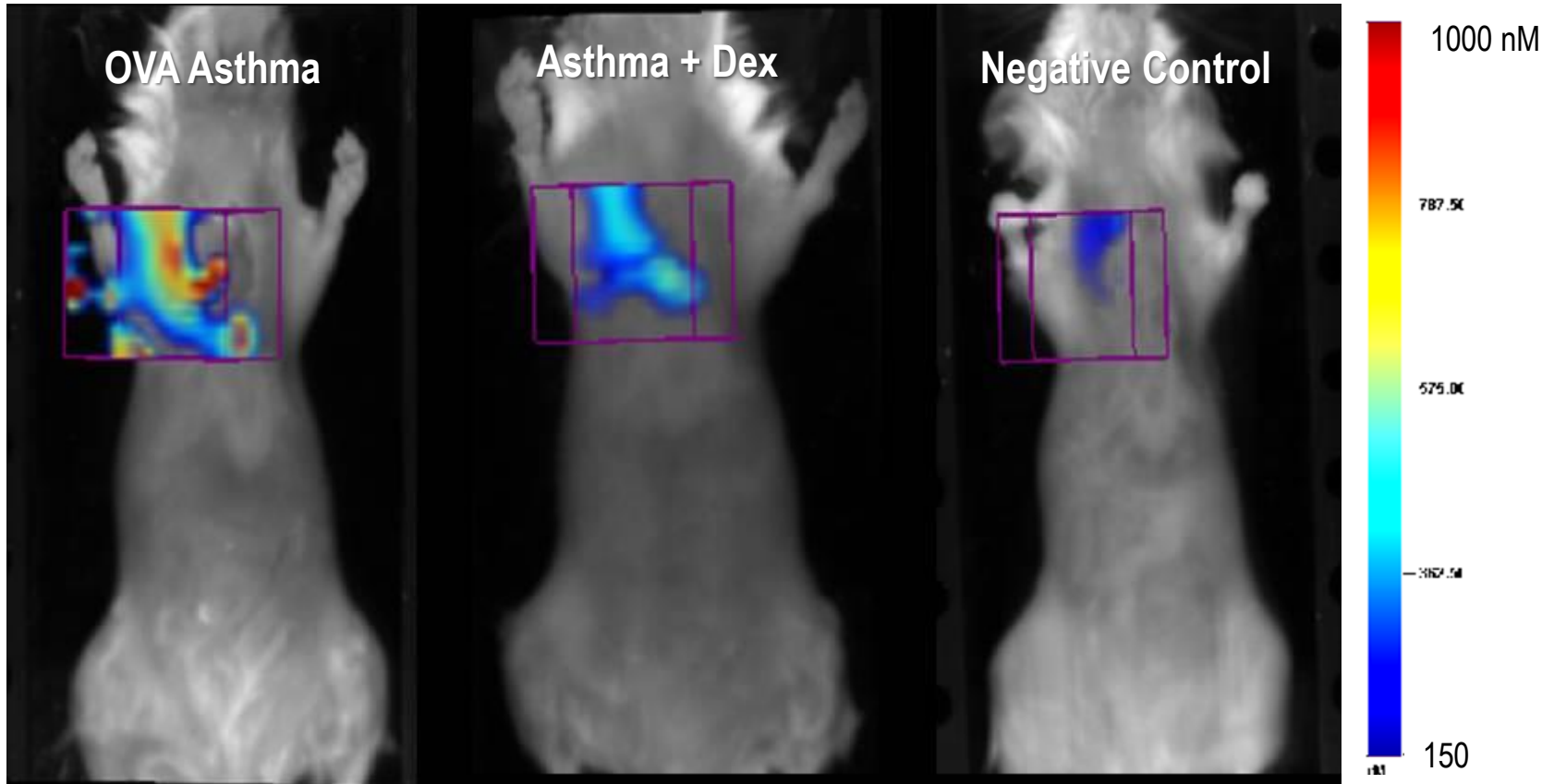
Assessments:

FMT Imaging  
BAL cells  
FRI lung ex vivo



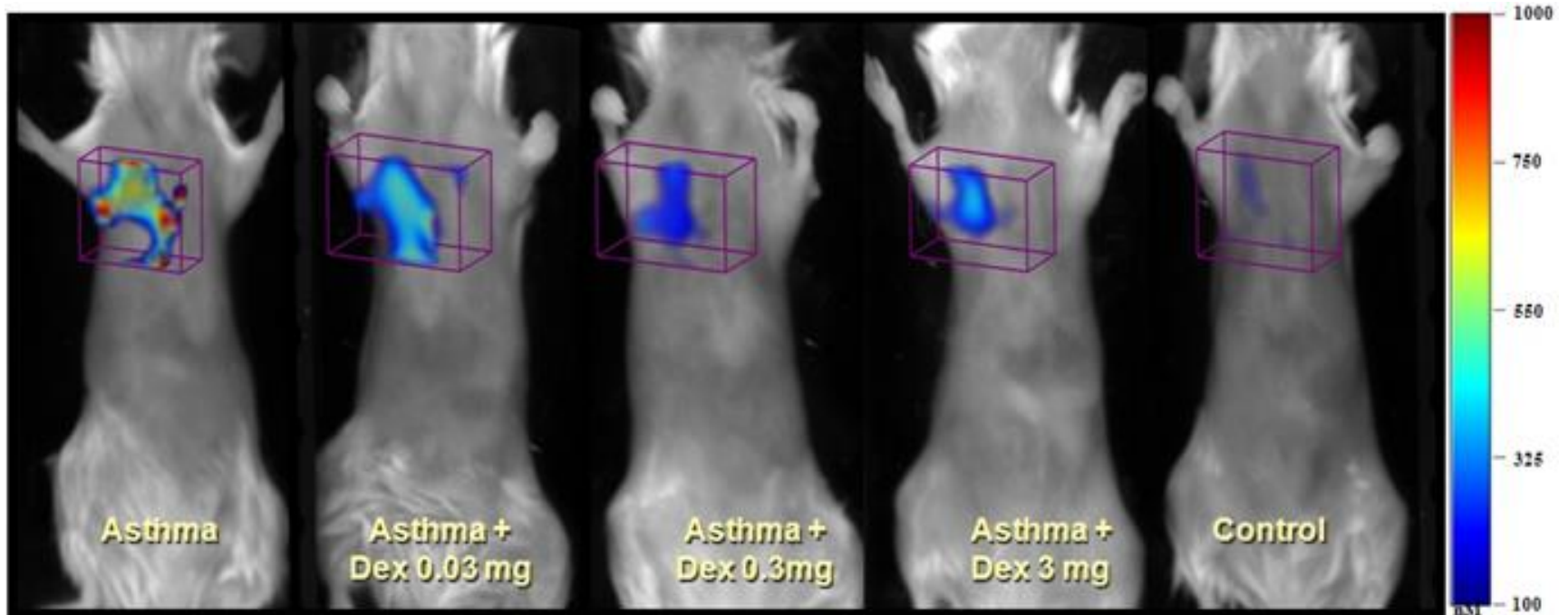
Steroids are a standard of care treatment for asthma

# Dexamethasone Therapeutic Activity in Asthma

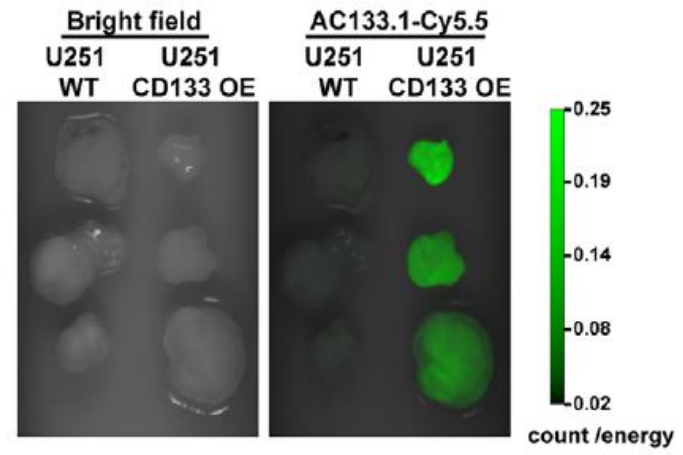
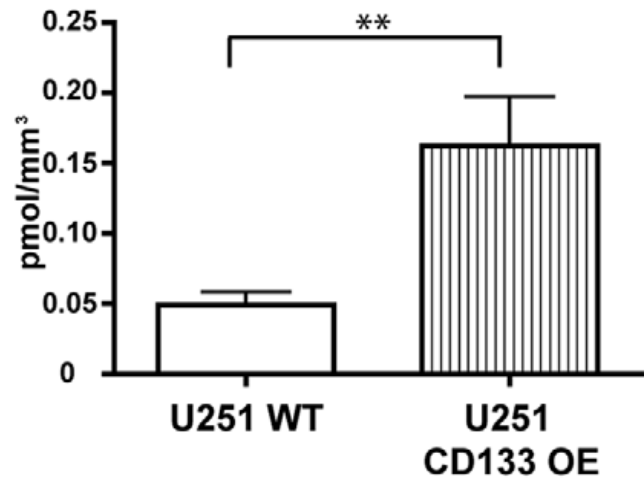
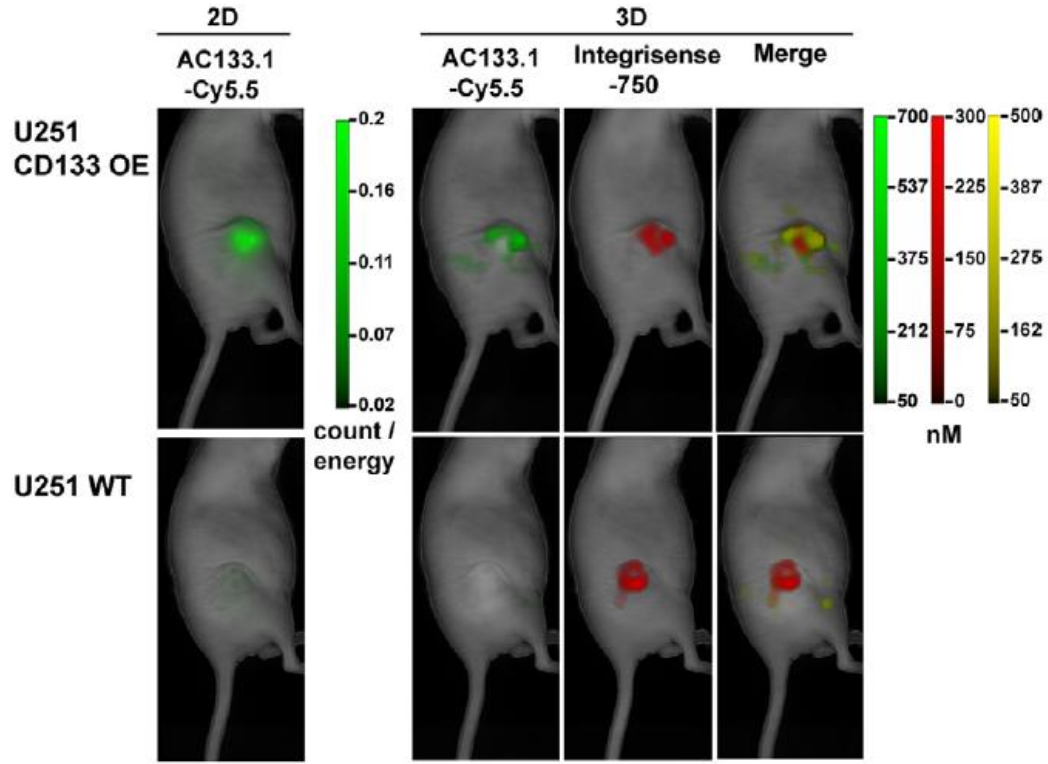


Tomographic images readily show clear differences in asthmatic, treated, and control mice

# Dexamethasone Dose Response in Asthma



A



In vivo imaging of U251 xenografts in mice injected with Cy5.5-labeled AC133.1 antibody. (A) U251 s.c. xenograft mice [U251 wild-type cells (lower panel) and CD133-overexpressing U251 cells (upper panel)] were injected with 75 mg AC133.1-Cy5.5 and 2 nmol of IntegriSense 750. 7 days later, the mice were imaged using the VisEn FMT-1500 Fluorescence Molecular Tomography system.

Citation: Tsurumi C, Esser N, Firat E, Gaedicke S, Follo M, et al. (2010) Non-Invasive In Vivo Imaging of Tumor-Associated CD133/Prominin. PLoS ONE 5(12):e15605. doi:10.1371/journal.pone.0015605



# Thank you!

For More Information:  
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